Results of the economic evaluation of the FIRST study: a multinational prospective economic evaluation


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
Pharmaceutical: Epoprostenol (Flolan), a potent vasodilator for the treatment of severe congestive heart failure.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Male and female patients with severe congestive heart failure.

Setting
Hospital. The economic study was performed in USA, Canada and twelve European countries.

Dates to which data relate
Effectiveness and resources data related to the period 1992-1993. 1994 prices were used.

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

Link between effectiveness and cost data
Costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
471 patients were enrolled in the study of whom 239 (51%) received epoprostenol/usual care and 232 (49%) received usual care alone. The two groups were similar except for the proportion of patients receiving assistance in daily living from someone other than a friend or home health aide.

Study design
This was a multinational randomised controlled trial. The enrolment into the trial was on a rolling admission basis, hence the patients’ follow-up time ranged from a few weeks to 18 months. In total, data for 1,932 patient months were collected.
Analysis of effectiveness
The analysis was based on intention to treat. The primary outcome in the effectiveness analysis was mortality (survival time).

Effectiveness results
Actual survival time (observed time the patient was enrolled in the study) was an average of 4.3 months (95% CI: 3.9 -4.7) for epoprostenol/usual care and 4.7 months (95% CI: 4.2 - 5.2) for usual care alone. This difference was not significant. Potential survival time (amount of time between the date of randomisation and the date at which the study was halted) was 6.2 months for epoprostenol/usual care and 6.3 months for usual care alone.

Clinical conclusions
Use of epoprostenol is associated with an increase in mortality.

Modelling
Modelling was performed to project (beyond the trial period) the costs and outcomes that would have been observed had all patients been randomised and followed for 12 months.

Measure of benefits used in the economic analysis
The benefit measure was quality-adjusted life months (QALMs). Quality of life expectancy was estimated based on responses to the EuroQol instrument. The product of the patient's survival time and their EuroQol scores generated quality-adjusted life months. Multiple regression analyses were used to allow for the assessment of differences in outcomes attributable to epoprostenol/usual care or usual care alone by controlling for other patient characteristics and also to project survival time (and costs) that would have been observed had all patients been followed for 12 months. A non-parametric bootstrap technique was used to estimate the 95% confidence intervals (CI) around the QALMs (and expected costs) and differences were assumed to be statistically significant if the 95% CI around the differences in QALMs (and mean costs) excluded zero.

Direct costs
Quantities and costs were analysed separately. Only health service costs were considered: inpatient hospital days, inpatient procedures, inpatient/outpatient physician visits, inpatient/outpatient nursing visits, outpatient laboratory evaluations, and non-acute care resources (e.g., nursing home, hospice or spa). Costs for inpatient services were derived from a cost accounting system in a single university hospital in the United States and costs for physician services were derived from the 1994 Medicare Fee Schedule. The use of epoprostenol and the resources required for the epoprostenol infusion system were recorded, but were not assigned costs and were omitted from the analysis because there was no market price for epoprostenol therapy at the time of writing. Costs of concomitant medications were also excluded.

Statistical analysis of costs
95% confidence intervals (CI) were generated around the projection of expected costs and QALMs had all patients been followed for 12 months using the nonparametric bootstrap procedure. Due to the potentially skewed nature of costs, an additional analysis to test for differences was performed on the log of total costs.

Indirect Costs
Not stated.

Currency
US dollars ($).
Sensitivity analysis
A sensitivity analysis was not performed.

Estimated benefits used in the economic analysis
Epoprostenol/usual care patients experienced 2.2 months (95% CI: 1.9 - 2.5) and usual care alone patients experienced 2.3 quality adjusted months of survival (95% CI: 2.0 - 2.6). Quality-adjusted survival times at 12 months were 3.7 (95% CI: 3.08 - 4.23) months for patients receiving epoprostenol/usual care, and 4.35 (95% CI: 3.8 - 4.9) months for patients receiving usual care alone.

Cost results
The costs for patients receiving epoprostenol/usual care were $16,819 (95% CI: $13,453 - $20,187) and for patients receiving usual care alone $11,797 (95% CI: $9,184 - $14,412). At 12 months, costs for patients receiving epoprostenol/usual care was $27,747 (95% CI: $21,806 - $34,228) which were $5,271 (95% CI: $4,793 - $5,322) greater than for patients receiving usual care alone.

Synthesis of costs and benefits
The costs and benefits were not combined. Usual care was the dominant strategy.

Authors’ conclusions
The authors concluded that the use of epoprostenol requires more resources and is less effective in terms of quality-adjusted survival than usual care. They believe that the evaluation was successful in quantifying resource utilisation and quality of life in patients with severe congestive heart failure and in explaining the variation among patients receiving epoprostenol therapy/best usual care versus best usual care alone.

CRD COMMENTARY - Selection of comparators
The comparator chosen was best usual care, which is acceptable. However it would have been helpful to specify what 'usual care' consists of in this context.

Validity of estimate of measure of benefit
The study was based on a randomised controlled trial. Due to the rolling admission basis and early conclusion of the trial, the authors acknowledged that the period of follow-up was inconsistent (ranged from a few weeks to 18 months). This resulted in a mean follow-up time which at less than 5 months, was relatively short for a survival trial. Hence the authors attempted to project the costs and outcomes that would have been observed had all patients been followed for 12 months.

Validity of estimate of costs
Adequate details were given of the sources of estimates, resource use and prices and price date. Costing resources in different countries is a potentially difficult and expensive exercise. Unit costs were taken from a single study centre and applied to all resources in all centres participating in the trial. These costs are unlikely to reflect the true average unit costs nor the variation in unit costs among the study centres.

Other issues
The clinical study was terminated prematurely due to the disappointing outcome of increase in mortality for patients receiving epoprostenol/usual care. However, the authors were able to demonstrate some of the problems encountered when analysing economic data collected alongside (multinational) randomised controlled trials, as well as providing useful information for clinicians caring for heart failure patients. As recognised by the authors, the cost data may not be generalisable to other settings or countries.
Implications of the study
Had the clinical results been positive, this economic evaluation would have been helpful to policy makers in terms of reimbursement decisions about epoprostenol therapy. If the study had resulted in increased mortality, but with decreased costs of care for epoprostenol patients, policy makers would have faced the unusual case of assessing the incremental costs and benefits of usual care as an addition to epoprostenol therapy.

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