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 compared the cost-effectiveness of three prostacyclins (iloprost, epoprostenol and treprostinil) for patients with pulmonary arterial hypertension (elevated blood pressure in the pulmonary artery) in New York Heart Association functional class III (moderate heart failure symptoms). The authors concluded that iloprost was less costly with a good efficacy profile. The study was well conducted and the results were clearly reported. The authors' conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study compared the cost-effectiveness of prostacyclins (iloprost, epoprostenol and treprostinil) for patients with pulmonary arterial hypertension in New York Heart Association functional class III.

Interventions
The three prostacyclin treatments compared were intravenous epoprostenol, inhaled iloprost and subcutaneous treprostinil. Patients on iloprost and treprostinil in New York Heart Association class III (moderate heart failure symptoms) could continue the treatment or, if worsening to class IV (severe symptoms), switch to epoprostenol.

Location/setting
Spain/secondary care.

Methods
Analytical approach:
The analysis was based on a Markov model with 12 week cycles and a three year time horizon. The authors stated that the perspective of Spanish National Health System was adopted.

Effectiveness data:
A search of PubMed and MEDLINE was performed to identify clinical trials for the treatment of pulmonary arterial hypertension. The transition probabilities between health states were based on data collected from three pivotal trials that compared each prostacyclin to placebo. The probabilities of transition to death came from a meta-analysis.

Monetary benefit and utility valuations:
The utility values for each of the four health states in the model according to functional class came from a published study that used the Short Form health survey (SF-36).

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years gained were the summary benefit measures. Future benefits were discounted at an annual rate of 3%.

Cost data:
The direct medical costs included those associated with disease management and medication including pharmacological, preparation and administration costs. Unit costs came from the Spanish Drug Catalogue and a Spanish database (e-Salud). The resource use assumptions came from a panel of four experts with clinical expertise in pulmonary arterial hypertension management (two pneumologists, one cardiologist, and one hospital pharmacist). All costs were in Euros.
(EUR) and were discounted at an annual rate of 3%. The price year was 2009.

Analysis of uncertainty:
A probabilistic sensitivity analysis was performed by assigning distributions to sets of model inputs. One-way sensitivity analyses were carried out on the key model inputs, including time horizon, drug costs, utility valuations, treatment in functional class I and II, drug doses, and discount rate.

Results
For iloprost, the expected three-year costs were EUR 132,840, the QALYs were 1.737 and the life-years gained were 2.695.

For treprostinil, the expected three-year costs were EUR 359,869, the QALYs were 1.728, and the life-years gained were 2.690.

For epoprostenol, the expected three-year costs were EUR 429,775, the QALYs were 1.780, and the life-years gained were 2.729.

The incremental analysis showed that treprostinil was more costly and less effective than iloprost. The incremental costs-effectiveness ratio with epoprostenol over iloprost was EUR 6,847,284 per QALY and EUR 8,825,982 per life-year gained.

The probabilistic analysis showed that, at thresholds of EUR 30,000 per QALY gained, iloprost was the preferred strategy in 85% of cases over epoprostenol. Iloprost was dominant compared with treprostinil in 45% of the cases.

Authors' conclusions
The authors concluded that iloprost was less costly with a good efficacy profile for patients in Spain with pulmonary arterial hypertension, New York Heart Association functional class III.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the available medications for patients with pulmonary arterial hypertension were considered.

Effectiveness/benefits:
The clinical data were from pivotal trials of medications versus placebo. Limited information on these sources was provided, but they appear to have been appropriately selected as a search of two databases was conducted. The authors stated that no head-to-head trials (which should have had high internal validity) were available. The use of QALYs was appropriate for patients pulmonary arterial hypertension, as this could have a big impact on quality of life. The utility valuations were collected from published study. The derivation of the utility values was adequately described and came from a published study.

Costs:
The categories of costs were consistent with the economic viewpoint; the cost analysis was satisfactorily carried out. Appropriate costs were used and reflected the Spanish setting. Details of the unit costs were reported for all items, which enhanced the transparency of the analysis. The price year was explicitly stated, which would allow reflation exercises. Alternative cost assumptions were assessed in the sensitivity analyses.

Analysis and results:
The authors conducted an appropriate incremental analysis to combine the costs and benefits of the treatment alternatives; the full results were reported. Uncertainty was satisfactorily investigated using deterministic and probabilistic analyses. The findings were well illustrated and clearly reported for both methods. The authors acknowledged some limitations of their analysis that mostly related to the lack of good long-term data and the need for assumptions.

Concluding remarks:
The study was well conducted and the results were clearly reported. The authors’ conclusions appear to be valid.

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