Cost of non-persistence with oral bisphosphonates in post-menopausal osteoporosis treatment in France
Cotte FE, De Pouvourville G

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
The study examined the cost-effectiveness of osteoporosis treatment with oral bisphosphonates focusing on the issue of poor persistence in post-menopausal women. The authors concluded that improving persistence with oral bisphosphonate was likely to improve health benefits and reduce costs compared to current levels of treatment adherence and interventions aimed at enhancing compliance should be implemented. The study used a conventional cost-effectiveness framework and reported key data sources and assumptions. The authors’ conclusions appear robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study examined the cost-effectiveness of osteoporosis treatment with oral bisphosphonates focusing on the issue of poor persistence in post-menopausal women.

Interventions
Three scenarios were considered: no treatment, treatment under current (poor) persistence and treatment under ideal persistence. Use of alendronate was assumed in the base case.

Location/setting
France/primary care.

Methods
Analytical approach:
The analysis was based on a published Markov model with a 10-year time horizon. The perspective was that of the public health care system.

Effectiveness data:
Relevant sources of clinical inputs were identified using a selective approach. In particular, country-specific population level databases were used to model the features of patients in France diagnosed with post-menopausal osteoporosis. Efficacy of treatment was based on data from clinical trials reported in Health Technology Assessment guidance for health economic models in osteoporosis. Data on real-world persistence were taken from a longitudinal database of more than 1,200 general practitioners (GPs) in France. Mortality data were estimated from the European Prospective Osteoporosis Study (vertebral) and from Swedish data (hip). Fracture events (hip, vertebrae and wrist) were key inputs of the model.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The summary benefit measures were fracture rate and death rate after a fracture.

Cost data:
The economic analysis included the cost of bisphosphonate treatment (based on the generic price of alendronate set by
the public payer) and costs of vertebral fractures calculated using diagnosis-related groups and official French sources. Costs were in Euros (€) and were discounted at an annual rate of 5%. The price year was 2010. The Student t-test was used to test for the statistical significance of cost differences.

Analysis of uncertainty:
A Monte Carlo simulation was performed to investigate the robustness of model outcomes using 30,000 microsimulations. A sensitivity analysis calculated costs without discounting. The branded price of risedronate was considered in an alternative scenario.

**Results**
No treatment: total clinical fractures 20,401, fracture rate 67.1% and death rate after fracture of 6.1%. Total cost was €3,402.

Real-world persistence treatment: total clinical fractures 16,711, fracture rate of 60% and death rate after fracture of 4.9%. Total cost was €3,110.

Ideal persistence treatment: total clinical fractures 12,378, fracture rate of 49.1% and death rate after fracture of 3.4%. Total cost was €2,833.

The scenario of real-world persistence treatment dominated (more beneficial and less expensive than) no treatment and the ideal persistence treatment strategy dominated real-world persistence treatment.

Undiscounted costs did not alter the ranking of the strategies.

When the branded price was considered, the cost per fractured woman saved was €309 and premature death avoided was €2,251 with ideal persistence compared to real-world persistence treatment.

It was estimated that a 10% increase in persistence would save €58 per patient. Extrapolated to the French population a situation of ideal persistence would lead to savings of €30.5 million per year.

**Authors’ conclusions**
The authors concluded that improving persistence with oral bisphosphonates was likely to improve health benefits and reduce costs. Interventions aimed at enhancing compliance should be implemented.

**CRD commentary**
Interventions:
The rationale for the selection of the comparators was clear. The strategies studied appeared to be appropriate and generalisable to other settings.

Effectiveness/benefits:
The authors did not mention a review of the literature and it appeared that a selective approach was used to identify relevant sources of data. Real-world persistence was based on a large database of GPs in France that should be representative of the authors’ setting. Other French databases were used to estimate country-specific epidemiological parameters. Treatment effect was taken from a meta-analysis of clinical trials that should have ensured high internal validity. Other well-known international studies were used for mortality data. The main benefit measure, namely fractures avoided, was disease-specific and might not be comparable with the benefits of other health care interventions. Premature deaths avoided represented a more generalisable measure. The impact of the disease on health-related quality of life (which may be a relevant measure health for this patient population) was not considered.

Costs:
The cost categories and sources used in the analysis appeared to be representative of the public payer (as stated by the authors). A clear description of cost items and some unit costs were reported, but most data were presented as macro-categories. This reflected the use of diagnosis-related groups that were selected and justified. Costs varied in the sensitivity analysis. Other details such as price year and discount rate were provided. A scenario analysis showed that use of a more expensive bisphosphonate might change the dominance of an ideal persistence situation but was likely to
remain cost-effective given standard thresholds.

Analysis and results:
The study results were reported extensively. An incremental analysis was used to combine the costs and benefits of the alternative strategies using incremental cost-effectiveness ratios among the three strategies studied. The authors pointed out that the 10-year horizon was deemed appropriate to capture the economic and clinical impact of treatment on patients' health. Key information on the decision model was reported. The issue of uncertainty relied on a micro-simulation and the impact of variations in two selected inputs was tested using a deterministic approach. An extensive discussion on possible methods to increase persistence in these patients and comparisons with other disease areas were made. The issue of transferability of the study results was not addressed explicitly but similar findings might occur in other developed countries.

Concluding remarks:
The study used a conventional cost-effectiveness framework and reported key data sources and assumptions. The authors' conclusions appear robust.

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