Effect of adherence on lifetime fractures in osteoporotic women treated with daily and weekly bisphosphonates
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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.

CRD summary
This study evaluated the effect of optimal adherence to regimens of bisphosphonates for the prevention of fractures in osteoporotic women who were aged 50 years or older. The authors concluded that improving adherence with bisphosphonates could have important clinical benefits for patients, but increased the total medical costs. The results were adequately reported, but there were a few limitations to the methods and the authors’ conclusions should be considered with caution.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to evaluate the effect of optimal adherence to daily or weekly bisphosphonates in the prevention of fractures in osteoporotic women who were aged 50 years or older.

Interventions
Optimal adherence was compared with the usual adherence to daily or weekly bisphosphonates. Usual adherence was the actual level of adherence with daily or weekly bisphosphonate therapy in the United States at the time of the study; this included a distribution people who had different compliance levels and different times to discontinuation. Optimal adherence was defined as 90% compliance or more, with no discontinuation.

Location/setting
USA/primary care.

Methods
Analytical approach:
A decision model, using first- and second-order Monte Carlo simulations, was constructed to combine the data from published studies. A lifetime horizon was used and the authors did not report the study perspective.

Effectiveness data:
The effectiveness data for usual adherence was from a published study (Huybrechts, et al. 2006, see 'Other Publications of Related Interest' below for bibliographic details). The authors used these data and their assumptions to estimate the effectiveness of optimal adherence. The risks associated with fractures were from a published study. The main clinical effectiveness estimate was the number of fractures prevented.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit was the number of fractures prevented.

Cost data:
The cost categories were drugs and fracture events. The costs of gastrointestinal adverse events were added in a sensitivity analysis. Fracture costs were site-specific US estimates. Drug costs were their wholesale acquisition costs,
based on an equal market share between branded, generic daily, and generic weekly bisphosphonates. Adverse event costs were adapted from a previous cost-effectiveness study. All costs were expressed in US dollars ($), for 2008, and discounted at a rate of 3% per year.

Analysis of uncertainty:
In addition to the second-order Monte Carlo simulations used in the decision model, a series of one-way sensitivity analyses were conducted. The results of these analyses were presented in tables.

Results
With optimal adherence, compared with usual adherence, there were 258 fractures prevented per 1,000 women with osteoporosis who were treated for a lifetime. The expected total cost of medication and fractures per patient over a lifetime was $16,600 with usual adherence and $18,300 with optimal adherence; optimal costing $1,700 more than usual adherence.

The results remained robust in the sensitivity analysis when age, bisphosphonate, and bone density T-score threshold estimates were varied; fracture rates did increase with increasing age. With a 10-year limit to time on therapy added to the model, the fracture rate increased for both adherence groups and the benefits of increased adherence were reduced. The costs of optimal adherence compared with usual adherence increased when the adverse event costs were included.

Authors’ conclusions
The authors concluded that improving adherence with bisphosphonates could have important clinical benefits for patients in reduced fractures, but it increased the total medical costs.

CRD commentary
Interventions:
The interventions were described, but more information on the authors’ assumptions for optimal adherence would have been useful. The interventions appear to have been appropriate comparators and the population was described. Some of the data and assumptions might not be generalisable to settings outside the USA.

Effectiveness/benefits:
The authors derived the effectiveness data from several published studies, but it was unclear if a systematic review was undertaken and so unclear if all the best available evidence was used. Many of the relationships in the simulation were assumed by the authors and no validation of these assumptions was reported, making their quality unclear. The measure of benefit appears to have been appropriate, but discounting was not reported.

Costs:
The perspective was not reported and so it was unclear if all the relevant costs were identified. The sources of the included costs appear to have been of good quality. The costs were appropriately discounted and adjusted for inflation.

Analysis and results:
The costs and outcomes were synthesised appropriately, using a decision model, and the details and a diagram of this model were provided. The impact of uncertainty in the model's results was tested. The results were sufficiently reported, except for the incremental cost-effectiveness data, which were not reported and would have enabled the results of this study to be compared more easily with those of other studies. The authors reported some limitations to their study.

Concluding remarks:
The results were adequately reported, but there were a few limitations to the methods and the authors’ conclusions should be considered with caution.

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