Cost-effectiveness model of using zoledronic acid once a year versus current treatment strategies in postmenopausal osteoporosis

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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
The objective was to compare the cost-effectiveness of a single infusion of zoledronic acid against current treatment strategies for postmenopausal osteoporosis in France. The authors concluded that zoledronic acid was cost-effective regardless of fracture type. The methods of the study were satisfactory, but neither the methods nor the results were fully presented, which means that the conclusions should be considered with caution.

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

Study objective
The objective was to assess the cost-effectiveness of a single infusion of zoledronic acid compared with the usual treatment for postmenopausal osteoporosis in France.

Interventions
A single annual infusion of zoledronic acid was compared with the usual treatment, which was 74% of patients receiving bisphosphonates, 16% receiving raloxifene, 9% receiving strontium ranelate, and the remaining 1% receiving teriparatide.

Location/setting
France/secondary care.

Methods
Analytical approach:
Twelve models were constructed to simulate the impact of treatment on vertebral fractures, non-vertebral fractures, and hip fractures. The time horizon of the analysis was three years and the authors reported that all costs were estimated from the public payer perspective.

Effectiveness data:
The evidence on effectiveness and adherence was derived from published studies and, for adherence, it was validated using expert opinion. Two effectiveness assumptions were assessed. The first was specific effectiveness, where the overall difference in effectiveness was driven by differences in both effectiveness and adherence. The second was standard effectiveness, where the overall difference in effectiveness was driven solely by differences in adherence. The absolute risks of the three fracture types with each treatment were derived from pivotal clinical studies.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The measures of benefit were avoided vertebral fractures, non-vertebral fractures, and hip fractures.

Cost data:
The direct costs were those of prescriptions, medical visits, laboratory tests, and management of different bone fractures. The costs of bone fractures were derived from published French studies. All other costs were derived from
approved French product monographs. They were reported in 2007 prices and the currency was the Euro (EUR).

Analysis of uncertainty:
A probabilistic sensitivity analysis was undertaken by applying probability distributions to each model parameter and then selecting random values for 500 Monte Carlo simulations. This produced standard deviations and probabilities.

Results
Using standard effectiveness estimates (conservative assumptions):

**Vertebral fractures:** Patients receiving zoledronic acid had a fracture rate of 12% and mean average costs of EUR 1,306. Those receiving usual treatments, had a fracture rate of 14.2% (p<0.001 compared with zoledronic acid) and mean average costs of EUR 1,437. The cost per vertebral fracture avoided was EUR 1,497 for zoledronic acid and EUR 1,685 for usual treatment.

**Non-vertebral fractures:** Patients receiving zoledronic acid had a fracture rate of 10.6% and mean average costs of EUR 1,195. Those receiving usual treatments, had a fracture rate of 11.3% (p<0.001 compared with zoledronic acid) and mean average costs of EUR 1,245. The cost per non-vertebral fracture avoided was EUR 1,337 for zoledronic acid and EUR 1,404 for usual treatment.

**Hip fractures:** Patients receiving zoledronic acid had a fracture rate of 2.8% and mean average costs of EUR 1,181. Those receiving current treatments, had a fracture rate of 4.6% (p<0.001 compared with zoledronic acid) and mean average costs of EUR 1,261. The cost per hip fracture avoided was EUR 1,216 for zoledronic acid and EUR 1,323 for usual treatment.

For all types of fracture, zoledronic acid had lower average cost-effectiveness ratios (costs per fracture avoided) than current treatments (p<0.01).

Using specific effectiveness estimates, the differences in average cost-effectiveness ratios between zoledronic acid and usual treatment remained statistically significant (p<0.01).

Authors’ conclusions
The authors concluded that zoledronic acid was cost-effective regardless of the fracture type.

CRD commentary

**Interventions:**
The interventions were reported clearly and in detail.

**Effectiveness/benefits:**
The authors did not provide any details of the methods of a literature review to identify the relevant studies and it is not clear if all the relevant evidence was included. The outcome measure (fractures avoided) was disease specific, hampering comparisons with outcomes of other interventions in other disease areas. There was a general lack of information on the identification and selection of the effectiveness data.

**Costs:**
The perspective was explicitly reported and all the relevant major cost categories and costs, for this third-party payer perspective, appear to have been included. The authors adequately reported the sources from which these costs were derived. The price year, time horizon, and currency were all adequately reported. Discounting was relevant as the costs were incurred over a three-year period, but no discounting was reported.

**Analysis and results:**
All the identified evidence on costs and outcomes was synthesised using a series of models and adequate details of these models were reported, including a diagram. The authors combined the costs and outcomes in average cost-effectiveness ratios, but, in all the scenarios assessed, zoledronic was dominant over the usual treatments as it was more effective and cheaper. This means that the combination of costs and benefits was not necessary in the base case. The authors reported...
that the model uncertainty was assessed using probabilistic sensitivity analysis, but these analyses were not presented in full. For example, no cost-effectiveness acceptability curves were presented for the probability of zoledronic acid being cost-effective at a particular threshold. They reported the limitations of their study and the main one was that the costs and outcomes were only assessed for a three-year period due to lack of evidence.

Concluding remarks:
The methods of the study were satisfactory, but neither the methods nor the results were fully presented, which means that the conclusions should be considered with caution.

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