Cost-effectiveness of a fixed dose combination of alendronate and cholecalciferol in the treatment and prevention of osteoporosis in the United Kingdom and The Netherlands


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 evaluate the cost-effectiveness of treatments for osteoporosis in the UK and the Netherlands. The authors concluded that the alendronate vitamin D3 combination was cost-effective in women aged 70 years or older with osteoporosis, and in women aged 60 years or older with a history of vertebral fracture. The methodology was appropriate and the methods used and the results were appropriately reported. The authors’ conclusions appear to be appropriate given the scope of the study.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to evaluate the cost-effectiveness of a fixed dose combination of alendronate 70mg and cholecalciferol 2800 IU compared with alendronate with dietary vitamin D supplements, ibandronate, and no treatment, for osteoporosis in the UK and the Netherlands.

Interventions
The four interventions were a fixed dose combination of alendronate 70mg and cholecalciferol 2800 IU (alendronate/vitamin D3), alendronate with dietary vitamin D supplements, for patients with a history of vertebral fractures one monthly ibandronate 150mg, and no treatment.

Location/setting
UK and Netherlands/primary care.

Methods
Analytical approach:
A Markov health-state transition model was used to estimate the costs and outcomes associated with each intervention. The authors reported that the model was a replicate of one developed by Kanis and colleagues and adapted by Stevenson and colleagues (Kanis, et al. 2002, Stevenson, et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). The time horizon of the study was ten years. The authors reported that the perspective was that of the health care payer.

Effectiveness data:
The effectiveness data for the model were based on the publications by Kanis and Stevenson and their colleagues (Kanis, et al. 2002, Stevenson, et al. 2006). However, the model was adapted to the situation in the Netherlands using available Dutch data, mainly for mortality. For other clinical parameters such as disease rates and fracture risks, due to a lack of appropriate data, UK information was assumed to be valid in the Netherlands. The main clinical effectiveness parameter was the relative risk of entering a transition state, which included hip fracture, vertebral fracture, wrist fracture, and humerus fracture.

Monetary benefit and utility valuations:
The gender and age-specific utility values were obtained using the EuroQol-5D from a representative sample of the UK general population. The authors assumed that these values were applicable for women with osteoporosis without a history of fractures. The effect of subsequent events on quality of life was assessed using quality of life multipliers,
which were derived from the literature.

Measure of benefit:
The measure of benefit was the number of quality-adjusted life-years (QALYs) gained.

Cost data:
The direct costs were those of medications and treatment of events including hip fracture, hip fracture resulting in nursing home confinement, death, and vertebral, wrist and proximal humerus fractures. For the UK, these costs were taken from those reported by Kanis (Kanis, et al. 2002), whereas for the Netherlands they were derived from a Dutch cost-of-illness study. Drug costs were derived from the British National Formulary for the UK and from pharmacy purchase prices for the Netherlands. All costs were reported in 2004 prices. The costs for the UK were reported as UK pounds sterling (£), and for the Netherlands they were reported as Euros (EUR). As costs could be incurred over 10 years, discounting was applied using an annual rate of 3.5% for the UK and 4% for the Netherlands.

Analysis of uncertainty:
The uncertainty in the model was evaluated using probabilistic sensitivity analyses, where probability distributions are given with each parameter. Following a series of Monte Carlo simulations, the results of the probabilistic sensitivity analyses were presented using cost-effectiveness acceptability curves. Furthermore, an additional scenario analysis was completed by varying the adherence to vitamin D3.

Results
For women in the UK with no history of vertebral fractures, compared with no treatment, treatment with alendronate vitamin D3 combination resulted in additional costs ranging from £775 for women aged 80 years, to £1,570 for women aged 50 years, and an increase in QALYs ranging from 0.0046 QALYs for women aged 50 years, to 0.1316 for those aged over 80. The cost per QALY gained ranged from £5,887 women aged 80 years to £340,981 for those aged 50 years. The results of the probabilistic sensitivity analysis showed that, for women aged 80 years, the probability that treatment with alendronate vitamin D3 combination was cost-effective at thresholds of £20,000 to £30,000 per QALY gained was over 90%. For these same women, alendronate vitamin D3 combination was found to be cost-saving when compared with alendronate plus dietary supplements of vitamin D, with no loss in quality of life.

For women in the UK with history of vertebral fractures, the results were similar to those for women with no history. For women with a history, alendronate vitamin D3 combination, compared with ibandronate, generated additional costs of £128 for women aged 50 years, but cost savings for older age groups. The QALYs gained ranged from 0.0067 for women aged 50 years to 0.1181 for those aged 80 years, with the additional cost per QALY being £19,095 for women aged 50 years and the intervention being dominant (i.e. more effective and less costly) for older age groups.

In the Netherlands, for women with no history of vertebral fractures, compared with no treatment, treatment with alendronate vitamin D3 combination resulted in additional costs ranging from EUR 1,480 for women aged 80 years to EUR 2,447 for women aged 50 years, and an increase in QALYs ranging from 0.0043 QALYs for women aged 50 years to 0.1314 for those aged over 80. The cost per QALY gained ranged from EUR 11,258 for women aged 80 years, to EUR 563,825 for those aged 50 years. The results of the probabilistic sensitivity analysis showed that for women aged 80 years the probability that treatment with alendronate vitamin D3 combination was cost-effective at thresholds of EUR 20,000 per QALY gained was 85%. As in the UK, the combination was found to be dominant over alendronate plus dietary supplements of vitamin D.

In the Netherlands, for women with history of vertebral fractures, the results were similar to those for women with no history. For women with a history, alendronate vitamin D3 combination, compared with ibandronate, generated additional costs of EUR 242 for women aged 50 years, but cost savings for older age groups. The QALYs gained ranged from 0.0064 for women aged 50 years to 0.1164 for those aged 80 years, with the additional cost per QALY being EUR 37,806 for women aged 50 years and the intervention being dominant for older age groups.

Authors' conclusions
The authors concluded that the alendronate vitamin D3 combination was cost-effective in women aged 70 years or older with osteoporosis, and in women aged 60 years or older with a history of vertebral fractures, in the UK and the
Interventions:
All the interventions were well described by the authors. A justification was given for using ibandronate as the comparator, namely that it has been shown to be effective in reducing the incidence of spinal fractures. In addition, no treatment was also used as a comparator because ibandronate had not been assessed in previous models, and there was a lack of data for women with no history of vertebral fractures. The reader should consider whether there are other relevant comparators that should have been included in this analysis.

Effectiveness/benefits:
The effectiveness data were derived mainly from two previous models published in 2002 and 2005. As these models used a UK setting, the authors added information for the Netherlands using Dutch data. However, due to lack of appropriate data for many clinical parameters, the authors assumed that the UK data was applicable to the Dutch setting. The quality of life for women with osteoporosis was assumed to be the same as that of the UK general population (after controlling for age). However, the authors did not justify this assumption and provided no evidence from published studies.

Costs:
The perspective was clearly reported as that of the health care system. The authors reported the main costs incurred as those needed to treat and cure a series of bone fractures, but did not report the cost categories included for each of these. As a result it is not possible to determine whether all the categories of cost relevant to the perspective were included. Despite this, the authors appropriately reported their sources both for the UK and the Netherlands, and the costs for each health state in the model. In addition the authors adequately reported the time horizon, discount rate and price year.

Analysis and results:
Overall, the analysis was well reported and the model structure was described in detail, although a diagram was not presented. The model was based on a modified published model. The authors appropriately referred readers to both these original articles. Additionally, the results were fully and clearly presented. The authors performed exhaustive sensitivity analyses including a probabilistic sensitivity analysis. The authors also acknowledged the main limitations of their analyses.

Concluding remarks:
The methodology of the study was appropriate, with the methods used and the results reported appropriately. The conclusions reached by the authors appear to be appropriate given the scope of the study.

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