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.

Health technology
The use of an alendronate-based therapy to prevent the risk of hip fracture in women with osteoporosis. The therapy consisted of 10 mg/day alendronate, 500 mg/day calcium and 250 IU vitamin D3.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised menopausal women suffering from established osteoporosis, who had had a vertebral fracture.

Setting
The setting was primary care. The economic study was carried out in Spain.

Dates to which data relate
The effectiveness and resource use data were gathered from studies published in 1996. The price year was 1998.

Source of effectiveness data
The effectiveness data were gathered from published studies.

Modelling
A decision analytic model (decision tree) was used to the estimate costs and the benefits of alendronate over placebo in a cohort of 1,000 women with established osteoporosis. The time horizon of the model was 3 years.

Outcomes assessed in the review
The outcomes assessed from the literature were:

the percentage of patients not presenting with a hip fracture during the study period (i.e. success rate); and

the incidence of severe lesions of the oesophagus (oesophagitis or ulcers of the oesophagus) from October 1995 to March 1996 in the USA.
Study designs and other criteria for inclusion in the review
The evidence concerning the success rate was derived from a blind, randomised, clinical trial comparing alendronate and placebo. The design of the second study was not described.

Sources searched to identify primary studies
MEDLINE was searched from 1990 to 1998 using the following keywords: "osteoporosis", "hip fracture", "treatment", "prevention", menopause", and "randomised study".

Criteria used to ensure the validity of primary studies
The studies to be included in the review had to be blind, randomised, clinical trials comparing alendronate and placebo.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
The effectiveness evidence was obtained from two primary studies.

Methods of combining primary studies
The primary studies were not combined.

Investigation of differences between primary studies
Not stated.

Results of the review
The success rate was 98.9% in the alendronate group and 97.8% in the placebo group.

The number of patients reporting more than one episode of adverse effects in the oesophagus was 199 (the sample size of the primary study was unclear).

Measure of benefits used in the economic analysis
The benefit measure used in the economic analysis was the proportion of patients free from hip fracture and severe adverse events at the end of the 3-year period (success rate). This was derived from the decision model. The authors stated that no discount rate was used.

Direct costs
A 2% discount rate was used for the future costs since the time horizon of the study was 3 years. The unit costs and the quantities of resources were not reported separately. The items included in the analysis were the costs of drug therapies, severe adverse effects requiring hospitalisation, and surgical intervention for hip fracture. The costs of moderate side-effects and laboratory tests for assessing previous hip fractures were excluded, because they appeared to be similar between the treatment groups. It was assumed that the costs were linear over time. The cost/resource boundary adopted was that of the service provider. The costs were estimated using actual data obtained from the DRG classification of hospital charges at the Complejo Hospitalario Mostoles-Alcorcon. The quantities of the resources were gathered from studies published in 1996. The price year was 1998.
Statistical analysis of costs
No statistical analysis of the costs was carried out.

Indirect Costs
No indirect costs were included.

Currency
Spanish pesetas (Pta).

Sensitivity analysis
One-way sensitivity analyses were conducted due to uncertainty around some estimates, relating to the cost and efficacy of alendronate and the incidence of adverse effects.

Estimated benefits used in the economic analysis
The estimated benefits were not reported.

Cost results
The three-year drug costs were Pta 279,121 for alendronate, Pta 7,570 for calcium, and Pta 509 for vitamin D3.

The costs for treating adverse effects (surgical intervention) were Pta 668,616.

From the decision tree, the total costs were Pta 294,574 for alendronate and Pta 22,789 for placebo.

Synthesis of costs and benefits
Average and incremental (alendronate over placebo) cost-effectiveness analyses were conducted. The average cost per patient free from hip fracture and severe adverse events after 3 years was Pta 297,879 for alendronate and Pta 23,301 for placebo. The incremental cost of alendronate over placebo, per successfully treated patient, was Pta 25,621,491. The cost-effectiveness ratios were not sensitive to variations in the efficacy of alendronate and the incidence of severe side-effects. For the cost-effectiveness ratio of alendronate to be equal to that of placebo, the cost of alendronate should not be greater than Pta 210 per box.

Authors' conclusions
The alendronate-based intervention was not cost-effective in preventing hip fracture in postmenopausal women with osteoporosis and previous vertebral fracture, due to the high cost of the drug, which did not justify the expected benefits.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator was clear. Placebo was selected since the objective of the study was to assess the active value of alendronate. The authors stated that several drug therapies for the prevention of hip fracture were available on the market, but that none had been assessed in a randomised clinical trial. You should assess whether the intervention in the study represents a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis was based on a review of the literature. The search criteria and the methods used to validate the primary studies were clearly reported. The authors only focused on primary studies providing effectiveness evidence from blind, randomised clinical trials. Observational and retrospective studies were not included in the review.
This process led to the selection of only two primary studies, which were not combined.

**Validity of estimate of measure of benefit**
The benefit measures used in the economic analysis were derived from the decision tree, but the expected benefits were not reported. It would have been useful had the authors adopted a benefit measure reflecting the patients’ preferences for the different health states resulting from the interventions. However, the authors noted that it was unlikely that the use of a different benefit measure would cause a dramatic change in the study's results.

**Validity of estimate of costs**
The analysis of the costs was carried out from the perspective of the third-party payer. Therefore, only the direct costs related to the interventions were included in the study. As with the benefit measure, it is doubtful whether the inclusion of the indirect and intangible costs would change the authors’ conclusions. The authors also noted that the long-term effects of alendronate were unclear and, therefore, if more adverse effects were likely to occur, the estimated costs could be even greater. The costs and the quantities were treated deterministically and no statistical analyses were conducted.

**Other issues**
The issue of generalisability of the study to other settings was implicitly addressed by performing a few sensitivity analyses on key variables. The conclusions of the study should not be extended to populations different from that considered in the analysis. The authors made some comparisons of their findings with those from other studies.

**Implications of the study**
It would be interesting to assess the long-term effects of alendronate. Also, to carry out randomised clinical trials comparing different drug therapies for the prevention of hip fracture.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
10592546

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Aged; Alendronate /adverse effects /economics /therapeutic use; Cost-Benefit Analysis; Decision Support Techniques; Female; Hip Fractures /economics /prevention & control /surgery; Humans; Middle Aged; Osteoporosis, Postmenopausal /complications /drug therapy /economics; Placebos; Sensitivity and Specificity

**AccessionNumber**