Cost-effectiveness of vertebral fracture assessment to detect prevalent vertebral deformity and select postmenopausal women with a femoral neck T-score > -2.5 for alendronate therapy: a modeling study

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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.

Health technology
The use of vertebral fracture assessment (VFA) with spine imaging on a dual-energy densitometer to detect prevalent vertebral deformity in osteopenic postmenopausal women, and to select them for alendronate therapy, was studied. The strategies compared were:

- no initial drug therapy;
- 5 years of initial alendronate therapy; or
- VFA followed by radiologic confirmation and 5 years of alendronate therapy in those with one or more vertebral deformities confirmed on radiography (VFA strategy).

Type of intervention
Screening and treatment.

Economic study type
Cost-utility analysis.

Study population
The hypothetical population comprised a cohort of postmenopausal women aged at least 60 years, without osteoporosis and with varying levels of BMD (T-score from -1.5 to -2.4).

Setting
The setting was primary and secondary care. The economic study was carried out in Minnesota, USA.

Dates to which data relate
The studies used for the effectiveness evidence were from the 1991 to 2005. The cost data were derived from sources published between 2000 and 2004. The price year was not reported.

Source of effectiveness data
The evidence was based on a review or synthesis of published studies and estimates based on authors’ assumptions.

Modelling
A computer simulation state transition Markov model was used to estimate the cost and utility of strategies during a lifetime horizon. Eight health states were used in the model. These were no fracture, post-distal forearm fracture, post-
clinical vertebral fracture, post-incident radiographic vertebral fracture, post-hip fracture, post-other fractures, post-hip and vertebral fracture, and death.

**Outcomes assessed in the review**
In the model, the following parameters were incorporated for each BMD and age strata:

- the probability of vertebral deformity on spinal imaging;
- the true- and false-positive rates and specificity of VFA; and
- the probabilities of fractures.

The relative risk of vertebral and nonvertebral fractures for women with deformities was also included, as were relative mortality for hip fracture, relative benefit of alendronate and age-specific mortality.

**Study designs and other criteria for inclusion in the review**
Epidemiological, population-based and observational studies, meta-analyses and other published literature were included in the review.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

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

**Number of primary studies included**
Fifty-five studies were included in the review.

**Methods of combining primary studies**
A narrative method was used to combine the primary studies.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The paper clearly reported the clinical data entered into the model. However, since there was too much detail to report in full here, only the more important effectiveness data are reported below.

The relative benefit of alendronate was 1.0 for non-spine fractures and 0.5 for vertebral fractures, except in those with T-score -1.5 and no vertebral deformity where it was 0.8.

The sensitivity of VFA for postmenopausal women with one or more prevalent vertebral deformities was assumed to be 77% and the specificity 89%.
Methods used to derive estimates of effectiveness
Some clinical data were based on authors' assumptions.

Estimates of effectiveness and key assumptions
The following assumptions were made.

The age-specific prevalence of vertebral deformity in this setting accurately reflected the true prevalence among the US population of Caucasian postmenopausal women. The authors assumed that 70% of these deformities were clinically unapparent, and an odds ratio of 1.5 for prevalent radiographic vertebral deformity for each standard deviation decrease in femoral neck BMD.

When alendronate was discontinued after a 5-year treatment period, there was a gradual loss of fracture-reduction benefit over 5 years. Medication adherence was 100%. Because the excess mortality associated with vertebral fracture or deformity may be attributable to pre-existing mortality, it was assumed that no excess mortality would be directly attributable to vertebral fractures or to other non-hip fractures.

Measure of benefits used in the economic analysis
The measure of benefit used was the quality-adjusted life-years (QALYs). The utility data were derived from published studies using the EQ-5D questionnaire. Values for hip, distal forearm, clinical vertebral and other fractures relative to the age-matched population were derived from direct prospective estimates from a published study (Kanis et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details). Those for post-vertebral and hip fracture state were taken from another published study (Tosteson et al. 2001, see 'Other Publications of Related Interest' below for bibliographic details). Discounting was performed at a rate of 3%.

Direct costs
The direct medical costs included were for VFA, bone densitometry and spine radiography, alendronate, acute fractures, long-term care during the first and subsequent years after a hip fracture, and yearly physician visits. All the costs were based on published literature. The average wholesale price was used for alendronate, while the US Medicare reimbursement schedule was used for VFA and follow-up services. The price year was not reported but most costs were from 2001. Discounting was performed at a rate of 3%. Estimations of the quantities and the total costs were derived using modelling. The resource quantities and the costs were not reported separately. The authors adequately referenced most of the costs included in the model.

Statistical analysis of costs
No statistical analysis of the quantities or costs was reported.

Indirect Costs
The indirect costs of fractures included were taken from a published study (Meerding et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details). Discounting was performed at a rate of 3%. Estimations of the quantities and the total costs were derived using modelling. The resource quantities and the costs were not reported separately.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were carried out on most parameters. Such analyses also evaluated the effect of medication non-adherence. Secondary analyses were carried out in which the authors adjusted the relative risks of...
incident fractures attributable to deformities on VFA. Another secondary analysis was performed in which it was assumed that there was no additional alendronate treatment following incident fracture, or a 10-year offset of fracture reduction benefit after alendronate discontinuation. Finally, probabilistic sensitivity analyses, using two-stage Monte Carlo simulations, were performed for 80-year-old women with T-scores of -1.5 and -2.0. The ranges for the sensitivity analyses were reported, but how they were selected was not.

**Estimated benefits used in the economic analysis**
For the treat all strategy, the QALYs gained were:

- **-1.5 T-score group**: 13.3533 for women aged 60 years, 9.8106 for women aged 70 and 6.4508 for women aged 80;
- **-2.0 T-score group**: 13.1249 for women aged 60 years, 9.5778 for women aged 70 and 6.2291 for women aged 80;
- **-2.4 T-score group**: 13.1267 for women aged 60 years, 9.4529 for women aged 70 and 6.1915 for women aged 80.

For the no initial treatment strategy, the QALYs gained were:

- **-1.5 T-score group**: 13.3333 for women aged 60 years, 9.7911 for women aged 70 and 6.4371 for women aged 80;
- **-2.0 T-score group**: 13.0873 for women aged 60 years, 9.5424 for women aged 70 and 6.2051 for women aged 80;
- **-2.4 T-score group**: 13.0798 for women aged 60 years, 9.4116 for women aged 70 and 6.1636 for women aged 80.

For the VFA strategy, the QALYs gained were:

- **-1.5 T-score group**: 13.3408 for women aged 60 years, 9.8024 for women aged 70 and 6.4462 for women aged 80;
- **-2.0 T-score group**: 13.0985 for women aged 60 years, 9.5573 for women aged 70 and 6.2177 for women aged 80;
- **-2.4 T-score group**: 13.0886 for women aged 60 years, 9.4237 for women aged 70 and 6.1739 for women aged 80.

**Cost results**
For the treat all strategy, the lifetime costs were:

- **-1.5 T-score group**: $15,445 for women aged 60 years, $12,692 for women aged 70 and $9,888 for women aged 80;
- **-2.0 T-score group**: $19,499 for women aged 60 years, $15,664 for women aged 70 and $11,886 for women aged 80;
- **-2.4 T-score group**: $24,913 for women aged 60 years, $19,470 for women aged 70 and $14,683 for women aged 80.

For the no initial treatment strategy, the lifetime costs were:

- **-1.5 T-score group**: $11,388 for women aged 60 years, $8,814 for women aged 70 and $6,425 for women aged
in the -2.0 T-score group, $15,582 for women aged 60 years, $11,950 for women aged 70 and $8,587 for women aged 80;

in the -2.4 T-score group, $21,062 for women aged 60 years, $15,827 for women aged 70 and $11,485 for women aged 80.

For the VFA strategy, the lifetime costs were:

in the -1.5 T-score group, $11,711 for women aged 60 years, $9,303 for women aged 70 and $7,128 for women aged 80;

in the -2.0 T-score group, $15,852 for women aged 60 years, $12,397 for women aged 70 and $9,289 for women aged 80;

in the -2.4 T-score group, $21,228 for women aged 60 years, $16,076 for women aged 70 and $11,852 for women aged 80.

Synthesis of costs and benefits
To combine the results, incremental cost-effectiveness ratios (ICERs) were calculated.

For those with one or more vertebral deformities on VFA confirmed on radiography, the costs per QALY gained ranged from $18,864 for a 60-year-old woman and a T-score of -2.4 to $77,189 for an 80-year-old woman and a T-score of -1.5, compared with no drug therapy.

For those without prevalent vertebral deformity at baseline, the costs per QALY gained were all well in excess of $100,000, except for a 60-year-old with a T-score of -2.4 ($96,659).

Sensitivity analyses showed these results to be modestly sensitive to changes in fracture rates, fracture disutility, discount rates, and relative risks of fracture attributable to prevalent vertebral deformity.

Authors' conclusions
For postmenopausal women aged 60 to 80 years with a femoral neck T-score between -2.0 and -2.4, the strategy of vertebral fracture assessment (VFA) with follow-up confirmatory radiography, and alendronate therapy for those with one or more prevalent vertebral fracture, is cost-effective in comparison with no drug therapy over a broad range of assumed societal willingness-to-pay per quality-adjusted life-year (QALY) gained. The VFA strategy is also cost-effective in comparison with no drug therapy in women aged 60 or 70 years with a T-score of -1.5. These conclusions were robust to reasonable changes in fracture rates, fracture disutility, discount rates, relative risk of fracture attributable to vertebral deformity, and assumed fracture reduction benefit following alendronate discontinuation.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. The authors considered the no initial treatment strategy as the comparator since it is the current practice in their setting for osteopenic postmenopausal women, based on World Health Organization criteria (T-score > -2.5). The other comparator was initial drug treatment for 5 years. In relation to the drug selected, the authors stated that their results were also applicable to other oral bisphosphonates and raloxifene, which have similar cost and efficacy to alendronate in terms of reducing incident vertebral fractures in osteopenic women with prevalent vertebral deformity. You should decide if these represents widely used drugs and technologies in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state whether they performed a systematic review of the literature. They appear to have used data
from the available studies selectively. The authors derived estimates of effectiveness from published literature and made assumptions, but they did not provide any justification for their choice of assumptions. The estimates were investigated using sensitivity analyses, but the authors provided no justification for the ranges selected.

**Validity of estimate of measure of benefit**
The authors used QALYs as the measure of benefits, based on published literature. The methods used in the literature were reported and the preferences were based on a comparable population. Sensitivity analyses on fracture disutility were conducted, but the authors provided no justification for the ranges selected.

**Validity of estimate of costs**
The authors reported that the study had been conducted from a societal perspective. Productivity costs were appropriately included. The costs and the quantities were not reported separately, which would make it difficult to rework the analysis for other settings. The authors used medical charges for the study based on a reimbursement schedule as a substitute for costs. The unit costs were taken from published sources. Sensitivity analyses of the medical costs were conducted to assess the robustness of the estimates used. Discounting was appropriately carried out as the model had a lifetime horizon. The price year was not reported and this will hinder any future reflation exercises.

**Other issues**
The authors compared their findings with those from other studies, finding them generally to be concordant. They also addressed the issue of the limited generalisability of the results to other settings. The authors’ conclusions reflected the scope of the analysis, but it should be noted that they addressed the cost-effectiveness of spinal imaging in postmenopausal Caucasian women with a femoral neck T-score of between -1.5 and -2.4. They did not model the use of this technology in those with T-scores better than -1.5 because there are little data on how effective anti-resorptive drugs are in this population.

The authors acknowledged some limitations of their study. For example, they did not account for the fact that the fracture risks associated with prevalent vertebral deformity vary with the number and severity of those deformities. Also, the relative risks of incident fracture attributable to prevalent vertebral deformity were estimated on the basis of full quantitative morphometric methods on X-ray, which were digitised to improve accuracy, instead of semi-quantitative methods of radiographic fracture ascertainment, which are more practical to use in routine clinical practice.

**Implications of the study**
When reviewing current medical practice criteria, health care providers and third-party payers should take the fact that a new technology using a dual-energy X-ray densitometer to detect vertebral deformity is available, and that it provides spine images with a resolution close to that of radiographs, into consideration. Also, prevalent vertebral deformity is one of the most powerful independent predictors and usually clinically unapparent. Further, it should be considered that at least half of all fractures among postmenopausal women occur in those who do not have osteoporosis as defined by the World Health Organisation criterion (T-score > -2.5). An additional advantage for medical practice is the fact that spine images could be conveniently obtained at the same time as bone densitometry, which is still the main method for determining fracture risk among postmenopausal women.

**Source of funding**
None stated.

**Bibliographic details**
PubMedID
16785071

DOI
10.1016/j.jocd.2005.11.004

Other publications of related interest
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Indexing Status
Subject indexing assigned by NLM

MeSH
Absorptiometry, Photon /economics; Aged; Aged, 80 and over; Alendronate /therapeutic use; Bone Density; Bone Density Conservation Agents /therapeutic use; Bone Diseases, Metabolic /epidemiology; Comorbidity; Cost-Benefit Analysis; Female; Femur Neck /physiopathology; Humans; Markov Chains; Middle Aged; Monte Carlo Method; Osteoporosis, Postmenopausal /drug therapy; Quality-Adjusted Life Years; Spinal Fractures /economics /epidemiology /radiography; United States

AccessionNumber
22006001296

Date bibliographic record published
31/03/2007

Date abstract record published
31/03/2007