Cost-effectiveness of bone densitometry followed by treatment of osteoporosis in older men

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 study evaluated the use of bone densitometry followed by 5 years of oral bisphosphonate therapy in elderly white men for the treatment of osteoporosis.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-utility analysis.

Study population
The hypothetical population comprised a cohort of elderly white men found to have densitommetrical osteoporosis (femoral neck T score <= -2.5). Two sub-groups were evaluated, those with and those without prior clinical fracture since age 50 years.

Setting
The settings for the study were outpatient, inpatient and institutional care. The economic study was carried out in Minnesota, USA.

Dates to which data relate
The effectiveness evidence was derived from the period 1993 to 2006. The cost data referred to 1997 to 2007. The price year was 2004.

Source of effectiveness data
The parameters associated with the intervention included:

the background mortality and mortality for the first year after hip fracture;
the age-adjusted probability and risk functions of each type of fracture;
the odds ratio of a radiographic vertebral fracture;
the incidence rate of radiographic vertebral fracture;
a gradual linear loss of fracture reduction benefit with alendronate;
the prevalence of osteoporosis at the femoral neck;
the proportions of those with and without prior clinical fracture who had osteoporosis at each age; and
medication adherence.

Modelling
A computer simulation state transition Markov model was constructed to follow the course of events. The model considered multiple clinical fractures. The health states were well reported and a number of modelling assumptions were fully justified. Individuals were at risk of transition to a different state once every 3 months and were followed up until death or age 105 years. For the base-case analyses, the model was run for sub-sets of elderly men with or without a prior clinical fracture at five different starting ages (65, 70, 75, 80 and 85 years) using Monte Carlo simulations. For each simulation, 50,000 men were put through each of the two strategies of the model, one at a time.

Sources searched to identify primary studies
Data were taken from:

- 2003 US vital statistics and national health survey (NHANES);
- several US and foreign observational studies;
- published and unpublished data from a large observational study, Osteoporotic Fractures in Men (MrOS) study (Cummings et al. 2006, Blank et al. 2005 and Orwoll et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details);
- a meta-analysis of published prospective, randomised clinical trials of alendronate in men (Sawka et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details); and
- a meta-analysis of hip fracture (Johnell et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details).

Methods used to judge relevance and validity, and for extracting data
The process used to identify the data was not reported. No inclusion criteria were specified for any of the parameters. The method used to select the estimates was neither reported nor discussed.

Measure of benefits used in the economic analysis
The authors used quality-adjusted life-years (QALY) as a measure of benefit. The utility data were derived from population-based surveys for the no-fracture state for elderly men (QALY value of 0.7). Fracture disutility was modelled as a lower value of a QALY compared with the no-fracture state. The disutilities for the first year following fractures were derived from Swedish prospective studies of elderly men and women (Borgstrom et al. 2006 and Kanis et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details). Secondary analyses were performed, assuming a QALY value of 1.0, to compare estimated life-years saved with the densitometry and treatment (DT) strategy versus NI. The benefits were discounted at an annual rate of 3%.

Direct costs
The cost categories included in the model were:

- the cost of oral bisphosphonates and annual physician visits;
- the cost of a bone density test and one additional test after 2 years' drug therapy;
- the costs of acute hip, clinical vertebral, distal forearm and other fractures;
- the long-term care cost for the first year after hip fracture and the cost per day of long-term care; and
permanent long-term care.

Adverse effects of bisphosphonate were excluded as it was assumed they would generate only trivial direct medical costs. The cost sources included the average US wholesale price for alendronate and the mean Medicare reimbursement rate for bone density tests. The price year was 2004. The resources and the unit costs were not reported separately. The costs were discounted at an annual rate of 3%.

**Statistical analysis of costs**
The data were treated deterministically.

**Indirect Costs**
Lost productivity from fractures was estimated in years. The indirect costs were calculated using the mean yearly earnings for employed white men in the USA for 2004 (stratified according to age) and adjusted by age-specific workforce participation rates. The costs were discounted at an annual rate of 3%.

**Currency**
US dollars ($).

**Sensitivity analysis**
Parameter uncertainty was investigated by means of one-way, two-way and probabilistic sensitivity analysis. Univariate sensitivity analyses were performed. The parameters varied included discount rates, fracture rates, costs, disutility, medication adherence and yearly oral bisphosphonate cost. Two-way sensitivity analyses, assuming reduced nonvertebral fracture efficacy, were performed using different yearly oral bisphosphonate costs. Probabilistic sensitivity analyses were performed using log-normal distributions of fracture direct costs and normal distributions of fracture rates and permanent long-term care costs following hip fracture. Cost-effectiveness acceptability curves were generated from these analyses. Additional analyses of the densitometry and follow-up treatment strategy compared with NI were also performed. These assumed treatment femoral neck T-score thresholds of -2.0 or lower and -3.0 or lower.

**Estimated benefits used in the economic analysis**
The lifetime outcomes were:

for age 65 years with no prior fracture, 8.317 QALYs for the DT strategy and 8.291 QALYs for the NI strategy;
for age 65 years with prior clinical fracture, 8.083 QALYs for DT and 8.036 QALYs for NI;
for age 70 years with no prior fracture, 6.884 QALYs for DT and 6.853 QALYs for NI;
for age 70 years with prior fracture, 6.747 QALYs for DT and 6.696 QALYs for NI;
for age 75 years with no prior fracture, 5.592 QALYs for DT and 5.558 QALYs for NI; and
for age 75 years with prior fracture, 5.461 QALYs for DT and 5.402 QALYs for NI.

Results were also presented to age 80 and 85 years.

**Cost results**
The lifetime costs were:

for age 65 years with no prior fracture, $24,093 for the DT strategy and $20,713 for the NI strategy;
Synthesis of costs and benefits
For age 65 years, the costs per QALY gained for the DT strategy compared with the NI strategy were $129,665 in the group with no prior clinical fracture and $47,537 in the group with prior clinical fracture. For age 70 years, the values were $92,769 and $35,037 respectively. For age 75 years, the values were $66,071 and $23,260 respectively.

The costs per QALY gained decreased with age and were substantially lower for men with a self-reported history of clinical fracture since age 50 years for the DT strategy compared with NI. The results were sensitive to the assumed yearly cost of oral bisphosphonate therapy.

Authors' conclusions
Universal bone densitometry followed by oral bisphosphonate therapy may be cost-effective for men aged 65 years or older with a prior clinical fracture and for men aged 80 years or older without a prior fracture, assuming a societal willingness-to-pay per quality-adjusted life-year (QALY) gained of $50,000. This densitometry and treatment (DT) strategy might also be cost-effective for white men aged 70 years or older without a prior clinical fracture, if the cost of oral bisphosphonate therapy is less than $500 per year or if the societal willingness-to-pay is $100,000 per QALY gained.

CRD COMMENTARY - Selection of comparators
A justification (and an acknowledgement of a limitation) was given for the comparator used, mainly that there were no studies for nonvertebral fracture reduction efficacy of oral bisphosphonates among elderly men. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors combined data from existing models with data from several published studies of varying designs, unpublished data and assumptions. No systematic search for data was reported, which could represent an important limitation. However, the parameters for the model were derived from published studies, mainly a large observational study (Cummings et al. 2006, Blank et al. 2005 and Orwoll et al. 2005) and two meta-analyses, one of published prospective, randomised clinical trials of alendronate in men (Sawka et al. 2005) and the other of hip fracture (Johnell et al. 2005).

Validity of estimate of measure of benefit
The estimation of health benefits (QALYs) was modelled using a Markov model. The no-fracture state for elderly men was taken from a population-based survey. The disutilities for the first year following incident hip, distal forearm, clinical vertebral fractures and other fractures were derived from two Swedish prospective studies of elderly men and women (Borgstrom et al. 2006 and Kanis et al. 2004).

Validity of estimate of costs
The relevant cost categories and their associated costs appear to have been taken into consideration. The authors stated that they performed the study from a societal perspective, so they included productivity costs appropriately. The price year and the sources of resource use and unit costs were adequately reported. The costs were discounted at an annual rate of 3%, which would appear appropriate in this instance. Sensitivity analyses of the costs were conducted to assess the robustness of the estimates used.
Other issues
The authors compared their findings with those from other studies and the results were generally in agreement. The results of the study do not appear to have been presented selectively. The authors acknowledged some limitations to their study. Specifically, their results apply only to treatment for 5 years, are not applicable to treatment decisions based on bone mineral density measured at skeletal sites other than the femoral neck, and are applicable only to white men residing in the USA. In addition, the estimates of fracture disutility and fracture costs were based on foreign studies in which a minority of the participants were men, although these studies did not indicate a significant difference in these parameters between the sexes. Also, there were no precise estimates of the nonvertebral fracture reduction efficacy of oral bisphosphonates among elderly men. Finally, these analyses were applicable only to those with average risks based on age and prior fracture status and did not incorporate additional fracture risk factors, such as long-term systemic glucocorticoid use.

Implications of the study
Since alendronate will lose patent protection in the United States in 2008, the cost of oral bisphosphonate therapy in the near future might be much less than the current average US wholesale price. However, additional clinical trials yielding accurate estimates of nonvertebral fracture reduction with bisphosphonate therapy are needed to allow completion of more precise modelling studies of the cost effectiveness of oral bisphosphonate therapy.

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Other publications of related interest
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Subject indexing assigned by NLM

MeSH
Absorptiometry, Photon /economics; Aged; Aged, 80 and over; Alendronate /economics /therapeutic use; Bone Density Conservation Agents /economics /therapeutic use; Cost-Benefit Analysis; Fractures, Bone /epidemiology /etiology /prevention & control; Humans; Male; Markov Chains; Models, Economic; Osteoporosis /diagnosis /drug therapy /epidemiology; Quality-Adjusted Life Years

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