Universal bone densitometry screening combined with alendronate therapy for those diagnosed with osteoporosis is highly cost-effective for elderly women

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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 study examined universal bone densitometry in women aged 65 years and older combined with alendronate treatment for 5 years for those diagnosed with osteoporosis (femoral neck T-score \( \geq -2.5 \)).

Type of intervention
Screening and treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised women aged 65 years and older. Both women living independently and those residing in nursing homes were considered.

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

Dates to which data relate
The effectiveness data and some resource use data were derived from studies published between 1982 and 2005. Other resources used and costs came from studies published in 2002. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A Markov model with a lifetime horizon and 6-month cycles was used to assess the costs and benefits of screening followed by alendronate treatment in comparison with no intervention. Four different starting ages (65, 75, 85 and 95 years) were assessed using Monte Carlo simulation with 40,000 trials each. The health states of the model were:

- no fracture,
- post distal forearm fracture,
- post clinical vertebral fracture (clinically evident at onset),
- radiographic vertebral fracture (not recognised clinically at onset),
post hip fracture,

post other fractures (of the proximal forearm, humerus, scapula, clavicle, sternum, ribs, pelvis, distal femur, patella, tibia, or proximal fibula),

post hip and vertebral fracture, and

dehth.

An increased risk of subsequent fractures at sites different from those of the incident fracture was not modelled. Similarly, an increased risk of a subsequent other fracture after an incident other fracture was not modelled.

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

the probabilities of fractures,

the effectiveness of drug therapy,

mortality, and

the quality-adjusted life-years (QALYs) associated with specific health states.

**Study designs and other criteria for inclusion in the review**
The primary studies appear to have been identified selectively rather than through a systematic review of the literature. Some information on the design of the studies was reported. The relative risk of fractures on drug therapy (versus no therapy) was based on a large meta-analysis. Most of the data on the baseline risk of fractures came from a comprehensive population-based age-specific study for women from the Rochester Epidemiology Project. The 1999 National Nursing Home Survey was used to derive the proportions of women residing in nursing homes. The utility weights used to calculate QALYs were derived from age-stratified population surveys using the EQ-5D.

**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**
Twenty-one primary studies provided clinical evidence.

**Methods of combining primary studies**
A narrative approach appears to have been used to combine the primary estimates.

**Investigation of differences between primary studies**
Not reported.
Results of the review
Most results were age dependent and were not reported.

The incidence rate of radiographic (but clinically unapparent) vertebral fracture was set to be 1.86 times that of clinical vertebral fracture.

The mean femoral neck T-score for those with T-scores of -2.5 or less was -2.94 for those aged 65 years, -2.99 for those aged 75, -3.10 for those aged 85, and -3.17 for those aged 95.

Bone density decreased by 0.00554 g/cm² per year.

The relative risks of fractures were estimated for each change of T-score of 1. The relative risk was 2.6 for hip fractures, 1.8 for vertebral fractures, 1.4 for distal forearm fractures, and 1.6 for other fractures.

The relative risk of subsequent fracture was 4.0 for a subsequent vertebral fracture after an incident vertebral, 1.7 for a subsequent hip fracture after an incident hip fracture, and 2.1 for a subsequent distal forearm fracture after an incident distal forearm fracture.

Hip fracture rates in older people in nursing homes were four times higher than in older people living independently. The proportions of 85- and 95-year-old women residing in a nursing home were 13% and 21%, respectively.

Other fracture rates in nursing home residents were assumed to be 1.7 times those of older people living independently.

The relative risk of all fractures was 0.5 while on alendronate versus no drug therapy for those aged 65 or 75 years. Relative risks of 0.6 for nonvertebral fractures and 0.5 for vertebral fractures while on alendronate were estimated for those aged 85 or 95 years.

The mortality associated with acute hip fracture was estimated to be 1.375 times the base rate. No excess mortality was directly attributable to vertebral fractures or to other nonhip fractures.

The following estimates of QALYs were considered:
no-fracture state, 0.7 in both the first and subsequent years;
post distal forearm fracture, 0.684 in the first year and 0.699 in subsequent years;
post other fracture, 0.627 in the first year and 0.677 in subsequent years;
post hip fracture, 0.554 in the first year and 0.569 in subsequent years;
post clinical vertebral fracture, 0.438 in the first year and 0.636 in subsequent years;
post radiographic vertebral fracture, 0.574 in the first year and 0.639 in subsequent years; and
post hip and clinical vertebral fracture, 0.342 in the first year and 0.500 in subsequent years.

Measure of benefits used in the economic analysis
The summary benefit measure used was the QALYs associated with screening and treatment in comparison with no intervention. The QALYs were estimated by combining survival data and utility weights, which were derived from the literature. An annual discount rate of 3% was applied to benefits occurring in the future.

Direct costs
The perspective adopted in the study was that of society, but indirect costs were not relevant given that the patients were older than 65 years. The cost analysis included upfront costs of screening (including bone densitometry, a physician
visit, and nursing time for women living in a nursing home), alendronate, treatment of fractures, and long-term care after hip fracture. The unit costs were not presented separately from the quantities of resources used for all items, as most costs were reported as macro-categories. The costs were derived from published studies, average wholesale prices, and Medicare reimbursement rates. Much of the resource use data were obtained from the same sources as those used to derive the costs. The authors also made some assumptions. Discounting was relevant given that a lifetime horizon was used in the analysis and an annual rate of 3% was applied. The price year was 2001.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were carried out on several model inputs including adherence rate (assumed to have been 100% in the base-case), discount rates, fracture rates, fracture costs, the disutility from fractures, and the costs of screening. Secondary analyses were conducted for 85- and 95-year-olds (considering older people living independently and nursing home residents separately) and assuming reduced fracture benefit from alendronate. A probabilistic sensitivity analysis was also performed by assigning probabilistic distributions to all model inputs, with 400 simulations and 2,000 trials per simulation. The types of distribution associated with the model parameters were reported.

Estimated benefits used in the economic analysis
At a starting age of 65 years, the estimated QALYs were 9.050 with screening and treatment and 8.895 with no intervention.

The corresponding values were 6.299 and 6.150 at a starting age of 75 years, 3.919 and 3.820 at a starting age of 85 years, and 2.210 and 2.419 at a starting age of 95 years.

Cost results
At a starting age of 65 years, the lifetime costs per patient were $43,850 with screening and treatment and $37,635 with no intervention.

The corresponding values were $29,708 and $28,865 at a starting age of 75 years, $19,973 and $20,001 at a starting age of 85 years, and $11,908 and $12,825 at a starting age of 95 years.

Synthesis of costs and benefits
Incremental cost-utility ratios were calculated to combine the costs and benefits of the alternative strategies. Ratios were not calculated when one strategy dominated the other, meaning that the former was both more effective and less expensive.

The incremental analysis revealed that screening and treatment became more and more effective with increasing age. For example, the incremental cost per QALY gained with screening and treatment over no intervention was $40,097 at a starting age of 65 years and $5,657 at a starting age of 75 years, while it was dominant for older women.

The univariate sensitivity analysis showed that screening combined with treatment remained a cost-effective strategy in
the majority of cases (the incremental cost per QALY gained was always below the threshold of $50,000), with some exceptions for women aged 65 years. For this group of patients, the incremental cost per QALY was above the threshold of $50,000 (but below the threshold of $100,000) with substantially lower fracture disutility or fracture rates, a 6% discount rate, higher screening costs, and 50% or 75% adherence.

The probabilistic sensitivity analysis suggested that, in the group of 85-year-old women, there was a 99% probability that the cost per QALY gained from the screening combined with a treatment strategy was less than $50,000. The probability that the intervention was cost-saving was 47.8%. For the cohort of 95-year-old women, the probability that the intervention was cost-saving was 77.2%.

Results similar to those observed in the base-case were reported for the secondary analyses.

Authors' conclusions
Universal screening with bone densitometry for Caucasian women aged 65 years and older, combined with alendronate therapy for those found to have osteoporosis using bone density criteria, was cost-effective from the perspective of society in the USA. It was noted that universal bone densitometry became more cost-effective with increasing age, largely because the prevalence of those with a femoral neck T-score of -2.5 or less increases substantially with age. The analysis suggested that medication non-adherence affected the cost-effectiveness of the intervention.

CRD COMMENTARY - Selection of comparators
The rationale for the selection of the comparators was clear. The authors compared a combined strategy (screening and treatment) with no intervention, which should reflect the current standard of care in the authors' setting. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were estimated from published studies. It was not stated whether a systematic review of the literature was undertaken to identify the primary studies, which appear to have been included selectively. Limited information on the design and other characteristics of the primary studies was reported. Data on mortality were derived from life tables, which represent a typical source of information for all-cause mortality. The issue of heterogeneity among studies was not addressed, but data variability was investigated in the sensitivity analysis. The relative risk of fracture while on drug therapy was derived from a large meta-analysis; this should ensure high internal validity. Other data were obtained from large cohorts of women. Some data were varied in the univariate and probabilistic analysis to enhance the external validity of the study.

Validity of estimate of measure of benefit
The use of QALYs as the summary benefit measure was appropriate as they capture the effect of the interventions on quality of life and survival, which represent two relevant dimensions of health for women with osteoporosis. Discounting was applied to life expectancy, as guidelines for economic evaluation suggest. The impact of using alternative discount rates was investigated in the sensitivity analysis.

Validity of estimate of costs
The authors stated that the analysis of costs was carried out from a societal perspective. The indirect costs (i.e. productivity losses) were not included, which might have been appropriate given the non-working age of most women included in the study. However, the costs associated with non-medical services such as informal care were not included, even though their impact on the total costs could have been substantial. The source of the data was provided for each category of costs and the same sources were also used for much of the resource use data. In effect, the unit costs were not presented separately from the quantities of resources used, which limits the possibility of replicating the cost analysis in other settings. Statistical analyses of the costs were performed in the sensitivity analysis and the impact of altering cost estimates was also investigated. The price year was reported, which means that reflation exercises in other time periods should be possible.
Other issues
The authors did not make extensive comparisons of their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. However, the extensive use of sensitivity analyses enhances the external validity of the analysis. The authors pointed out that the study did not refer to bedridden, nonambulatory individuals who have a lower risk of falls and fracture than ambulatory older people. Some strengths and limitations of the study were highlighted. For example, the current study was the first to investigate the cost-effectiveness of pharmacological therapy in the oldest of older people under several assumptions. Further, the study explicitly considered nursing home residents. Drawbacks of the analysis were as follows: drug treatment for women with osteopenia was not modelled; fracture risk equations might not be accurate; the prevalence of osteoporosis could vary depending on the context in which women live.

Implications of the study
The study results support screening for and subsequent treatment of osteoporosis in older people, including nursing home residents.

Source of funding

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