Cost-effectiveness strategies to treat osteoporosis in elderly women

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
A strategy of screening all women aged 65 years or older for osteoporosis, and treatment for those who tested positive, was evaluated. The treatments considered were:

- no treatment;
- daily oral raloxifene, 60 mg;
- daily nasal calcitonin, 200 U;
- daily oral bisphosphonates (5 mg risedronate or 10 mg alendronate); and
- daily injectable recombinant parathyroid hormone (PTH), 20 microg.

Calcium supplements with vitamin D (total 1,500 mg/day and 600 IU vitamin D) were administrated to each treatment group. With the exception of an 18-month administration of PTH, the duration of treatment for each agent was 5 years.

Type of intervention
Screening and treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised all women aged 65 years or older in the county where the study was performed (20,129 women). The population was divided into the following age intervals: 65 to 69 (4,976 women), 70 to 74 (5,057 women), 75 to 79 (4,359 women), 80 to 84 (2,965 women) and 85 to 100 (2,772 women).

Setting
The setting was the community. The economic study was performed in Kanawha County (WV), USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1991 and 2003. No dates for resource use were reported. The costs came from studies and local sources dating from 1997 to 2004. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a review of published studies supported by authors' assumptions.
Modelling
A decision tree model was developed to analyse the cost-effectiveness of the five strategies considered in this study. The model had 1-year cycles over a 5-year period (2000 - 2005). The model was adjusted for annual compliance rates, as well as expected mortality and excess mortality incurred by certain fractures. In addition to the hip and spine fractures, non-hip and non-vertebral fractures were also included in the model (ankle, non-ankle tibial-fibular, patella, distal femur, pelvic, wrist, non-wrist radial-ulnar, distal humeral shaft, and proximal humeral).

Outcomes assessed in the review
The outcomes estimated were the age-group prevalence of osteoporosis, the fracture incidence rates, the fracture reduction efficacy of each treatment, and the compliance rates.

Study designs and other criteria for inclusion in the review
Randomised controlled trials (RCTs) were used to assess the fracture reduction efficacy of each therapy. The age-group prevalence of osteoporosis was based on the results of 204 consecutive central dual X-ray densitometer (DXA) examinations. The percentages obtained from these 204 studies were applied to the whole population. Other study designs were not reported.

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
The validity of the primary studies does not appear to have been assessed.

Number of primary studies included
Twenty-one 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 prevalence of osteoporosis was 15% in women aged 65 to 69 years, 20% in women aged 70 to 74, 20.4% in women aged 75 to 79, 25.8% in women aged 80 to 84, and 62.5% in women aged 85 or older.

The cumulative 5-year hip fracture incidence rate ranged from 59.9 (age group 65 to 69) to 345.5 (age group 85 and older).

The cumulative 5-year non-hip, non-vertebral fracture incidence rate ranged from 385.2 (age group 80 to 84) to 549.1 (age group 70 to 74).

The cumulative 5-year vertebral fracture rate ranged from 53.8 (age group 65 to 69) to 130.9 (age group 80 to 84).
The vertebral fracture reduction efficacy was 0.34 with calcitonin, 0.36 with raloxifene, 0.50 with bisphosphonates and 0.65 with PTH.

The hip fracture reduction efficacy was 0 with calcitonin and with raloxifene, and 0.50 with bisphosphonates.

The non-hip, non-vertebral fracture reduction efficacy was 0 with calcitonin and with raloxifene, 0.51 with bisphosphonates and 0.35 with PTH.

The annual compliance over a 5-year period was 0.676 with calcitonin (compliance rates for year 1 to 5: 0.80, 0.73, 0.68, 0.61, 0.56).

For years 1 to 3, the compliance rate with raloxifene was 0.80 for year 1, 0.71 for year 2 and 0.62 for year 3.

For years 1 to 3, the compliance rate with bisphosphonates was 0.80 for year 1, 0.60 for year 2 and 0.40 for year 3.

Methods used to derive estimates of effectiveness
The authors supplemented the data derived from the literature with some assumptions.

Estimates of effectiveness and key assumptions
It was assumed that the hip fracture reduction efficacy with PTH equated that of other peripheral fractures (i.e. 0.35).

Although PTH displayed a compliance rate of 79 to 83% in a randomised trial, the authors reduced this to 50% based on patients who would be medically ineligible for treatment. Since published compliance rates were not available for the 5-year span in the raloxifene and bisphosphonates strategies, the data for the last 2 years were estimated on the basis of the last 3 years. The estimated figures were 0.53 and 0.44 for raloxifene and 0.35 and 0.30 for bisphosphonates. Therefore, annual compliance over a 5-year period was 0.62 with raloxifene and 0.49 with bisphosphonates.

It was assumed that the fracture reduction efficacy of each agent continued throughout a 5-year period based on clinical trials of different durations (i.e. the raloxifene trial ended at 3 years, while PTH was administrated over an 18-month period).

Measure of benefits used in the economic analysis
The summary measures of health benefit used were the number of fractures prevented and the quality-adjusted life-years (QALYs) gained. These were estimated through the decision model, using data found in the literature. The health benefits were not discounted.

Direct costs
A discount rate of 3.5% was applied since the costs were incurred during 5 years. The direct costs included were those related to the screening process and the treatment of osteoporosis (DXA examinations, physician visits, comprehensive metabolic profiles, venous Doppler and prothrombin time studies, drugs and costs of fracture). The cost of fractures included physician visits, X-rays, materials, analgesic agents, physical therapy and hospitalisation. The unit costs and the quantities of resource used were presented separately for some items only. Some costs, such as the costs of fracture, were reported as macro categories. The costs were obtained from published data and several local sources, such as Medicare reimbursement rates; local pharmacy prices were used to calculate drug expenses. The price year was 2000.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included.
Currency
US dollars ($).

Sensitivity analysis
Two-way sensitivity analyses were performed only on those drugs which had been proven to reduce fractures in both vertebral and non-vertebral areas. The compliance rate and efficacy of fracture reduction in the non-vertebral sites were varied using the least and most conservative values.

Estimated benefits used in the economic analysis
The total number of fractures prevented by treatment was 47 with raloxifene, 55 with calcitonin, 245 with PTH and 281 with bisphosphonates.

The QALYs gained with each strategy were 0.0282 with no treatment, 0.0339 with raloxifene, 0.0348 with calcitonin, 0.0574 with PTH and 0.0637 with bisphosphonates.

The incremental QALYs gained with raloxifene compared with no treatment were 0.0057. The incremental QALYs gained with calcitonin compared with raloxifene were 0.0009. The incremental QALYs gained with PTH compared with calcitonin were 0.0226. The incremental QALYs gained with bisphosphonates compared with PTH were 0.0063.

Cost results
The total treatment costs were not reported.

Synthesis of costs and benefits
The costs and the benefits were combined by calculating incremental cost-effectiveness and cost-utility ratios. A value up to $100,000 per QALY gained was considered an acceptable cost-effective outcome.

The incremental saving per fracture prevented was $23 with raloxifene, $27 with calcitonin, $650 with PTH and $718 with bisphosphonates.

The total discounted (undiscounted) costs per QALY (i.e. average costs) were $3,041 ($3,368) with no treatment, $5,676 ($6,255) with raloxifene, $5,761 ($6,356) with calcitonin, $6,833 ($7,315) with PTH and $4,200 ($4,623) with bisphosphonates.

The authors did not report the incremental costs per QALY gained, but reported the difference in average costs between strategies.

The authors reported that raloxifene, calcitonin and PTH strategies were dominated since the bisphosphonate strategy was more effective and less costly, and that there were cost-savings with bisphosphonates. In effect, conducting a relevant incremental cost-effectiveness analysis showed that raloxifene, calcitonin and PTH strategies were dominated based on their incremental cost-effectiveness ratios (ICERs), which were higher than the ICER of bisphosphonates (i.e. extended dominance for bisphosphonates). In addition, the bisphosphonate strategy was not a cost-saving option in comparison with no intervention; it was more effective and cost more than no intervention (its ICER was $5,120).

The sensitivity analyses showed that changes in cost per QALY were more sensitive to the efficacy of non-vertebral fracture reduction than compliance. Further, even with the lowest compliance and efficacy of fracture reduction with the bisphosphonate strategy, almost all values fell below the $100,000 per QALY threshold. In the PTH strategy, over 50% of the values fell between the $100,000 and $150,000 per QALY thresholds and an additional 40% were between the $150,000 and $200,000 per QALY thresholds.

Authors' conclusions
Using a cost-effectiveness threshold of $100,000 or less per quality-adjusted life-year (QALY) gained, the universal screening of women aged 65 years or older for osteoporosis, and subsequent treatment with bisphosphonates, was a cost-effective preventive intervention. This economic advantage was maintained in sub-sets of women who had a lower relative risk of future fracture.

CRD COMMENTARY - Selection of comparators
The authors did not explicitly justify their selection of the comparators. Nevertheless, it appears that most of the relevant treatments available for osteoporosis were taken into account, and only doses approved by the Food and Drug Administration (FDA) were used in the model. You should decide whether these are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The estimates of effectiveness were based on data derived from several published studies. However, no systematic review of the literature was undertaken and the differences between the primary studies were not taken into account in the analysis. The internal validity of the effectiveness estimations would have been higher had 'face to face' studies been available. Moreover, the authors acknowledged that several assumptions were used in the decision model. The impact of these assumptions was partly addressed in the sensitivity analyses, but they may still have had an influence on the overall conclusion of the analysis. Finally, the authors stated that the model was adjusted for expected as well as excess mortality incurred by certain fractures, but no mortality rates were reported in the article.

Validity of estimate of measure of benefit
The benefit measures used in the analysis were appropriate. The use of QALYs permits comparisons with the results of other studies. However, the health benefits were not discounted even though it would have been appropriate to do so since the time horizon of the model was 5 years.

Validity of estimate of costs
The analysis of the costs appears to have been performed from the perspective of the health care provider since the costs included were consistent with this viewpoint. The indirect costs were not included. The unit costs and the quantities of resource used were presented separately for some items only, thus limiting the possibility of replicating the study in other settings. The costs were derived from published sources. No sensitivity analyses were performed. The costs were appropriately discounted and the price year was reported, which will aid any future inflation exercises.

Other issues
The authors compared their results with those from other studies. The findings of this study contrast, in part, those of other economic evaluations. The authors stated that the differences might be explained by the fact that, in this study, compliance rates and non-hip, non-vertebral fracture rates were taken into account. The issue of generalisability was not explicitly addressed, but some sensitivity analyses were performed. The authors acknowledged several limitations to the study. The most important of these seems to have been that it was assumed that the fracture reduction efficacy of each agent continued throughout a 5-year period, based on clinical trials of shorter durations.

Implications of the study
The study results supported the recommendations from the United States Services Task Force and the National Osteoporosis Foundation for the screening of osteoporosis in all women aged 65 and older. The authors suggested that cost-analysis studies of osteoporosis should be structured on fracture reduction by FDA-approved drug doses and reasonable compliance rates, and should also include non-vertebral sites.

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