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Title **A Systematic Review and Economic Evaluation of Alendronate, Etidronate, Risedronate, Raloxifene, and Teriparatide for the Prevention and Treatment of Postmenopausal Osteoporosis**

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Aim

To evaluate the use of alendronate, etidronate, risedronate, raloxifene, or teriparatide to reduce the risk of osteoporotic fracture in postmenopausal women.

Conclusions and results

Ninety randomized controlled trials (RCTs) met the inclusion criteria. They related to 5 interventions (alendronate, etidronate, risedronate, raloxifene, and teriparatide) and 5 comparators (calcium, calcium plus vitamin D, calcitriol, hormone replacement therapy, and exercise), and placebo or no treatment. All 5 interventions reduce the risk of vertebral fracture in women with severe osteoporosis with adequate calcium intakes. However, none of these drugs has been demonstrated, by direct comparison, to be significantly more effective than either each other or the other active interventions reviewed in this report. The intervention costs of treating all osteoporotic women for 5 years were 900 to 1500 million British pounds (GBP) for alendronate, etidronate, risedronate, and raloxifene. The cost per QALY ratios fell dramatically with age. (See the full report for a detailed description of the cost per QALY of the interventions.)

Recommendations

Of the 5 interventions, only alendronate and risedronate show significant reductions in hip fracture using RCT data from postmenopausal women with low bone mineral density (BMD). In postmenopausal women unselected for low BMD, only raloxifene appeared to reduce the risk of vertebral fracture. None of the 5 interventions reduced the risk of nonvertebral fracture. All of the proposed interventions provided gains in QALYs compared to no treatment in women with sufficient calcium and vitamin D intakes. Estimated costs varied widely by intervention and differed markedly by age, with some interventions saving costs at higher age ranges in patients with a prior fracture.

Methods

Studies that met the review's entry criteria were eligible for inclusion in the meta-analyses, provided they reported fracture incidence. Meta-analysis used the random effects model. A model was constructed to estimate the cost effectiveness of osteoporosis interventions. The model calculated the number of fractures that occurred and provided the costs associated with osteoporotic fractures and QALY. Breast cancer was also modeled, as some interventions have been shown to affect the risk of this condition.

Further research/reviews required

A stronger evidence base is needed on the efficacy of fracture prevention in the very elderly. The results calculated for women aged 80 years assumed the applicability of results from RCTs (where a minority of patients were of this age). If this were not true, then the results would be markedly different. To assess accurately the true potential of raloxifene, reanalysis should be conducted using a dedicated breast cancer model. Results for women at the threshold of osteoporosis, and with a prior fracture that ignore these benefits, produced a high cost per QALY ratio (>GBP 70 000), which fell significantly (<GBP 40 000) when including the effect on breast cancer. The latter results cannot be guaranteed, owing to simplifying assumptions on the etiology, costs, and QALYs of breast cancer. The cost effectiveness of teriparatide depends on the assumed efficacy on hip fracture. Since the decrease is nonsignificant, a further trial is recommended to reduce the uncertainty in this parameter.

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