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
Daily supplements of vitamin D and calcium (800 IU/day, D3, and 1 gram of elemental calcium) were compared with hip protectors (worn daily) and no treatment (scenario 1). The study also compared daily supplements of vitamin D and calcium in combination with hip protectors (worn daily) with no treatment (scenario 2). The author reported that the dosages corresponded to those used in clinical trials currently taking place in the UK.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised men and women in the UK who were over 70 years of age. Hypothetical cohorts of 1,000 male or female patients were analysed separately in the model. Four different cohorts were analysed. These corresponded to men and women who had never incurred a fracture and were, therefore, at average age- and gender-specific risk of fracture (i.e. the general population), and men and women at high risk of fracture because they had incurred a prior fracture (i.e. high-risk population).

Setting
The setting was primary, secondary and residential care in the UK. The economic study was conducted at the University of York, UK.

Dates to which data relate
The effectiveness data were derived from studies dating from 1990 to 2003. The price year was 2000.

Source of effectiveness data
The evidence for the final outcomes was derived from a review of published data, supplemented by the author’s assumptions based on the literature.

Modelling
A Markov model was developed to follow up, over a lifetime, a hypothetical cohort of males and females at high risk and general risk of fracture.

Outcomes assessed in the review
The outcomes assessed were:
the age- and gender-specific hip, vertebral, Colles’ and general fracture rates in the UK;
the excess mortality due to hip fractures;
the effectiveness of vitamin D and calcium, and of hip protectors;
the proportion of patients that fully comply with nutritional supplements; and
health state utilities.

**Study designs and other criteria for inclusion in the review**
Age- and gender-specific fracture rates were obtained from published population surveys in the UK. Data on the proportion of patients complying with nutritional supplements were derived from unblinded ongoing clinical trials.

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

**Criteria used to ensure the validity of primary studies**
UK-specific data were preferred when possible, as the rates of fracture have been shown to vary considerably geographically. Where possible, the author compared data on fracture rates from the studies used with other published results in order to assess the validity of the data.

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

**Number of primary studies included**
Approximately 13 primary studies were included in the review.

**Methods of combining primary studies**
Not relevant.

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

**Results of the review**
The annual incidence of hip fracture rates ranged from 0.002 to 0.012 for men and from 0.003 to 0.025 for women, depending on age.

The annual incidence of vertebral fracture rates ranged from 0.002 to 0.013 for women, depending on age.

The annual incidence of Colles’ fractures ranged from 0.001 to 0.003 for men and from 0.005 to 0.006 for women, depending on age.

The all-age average annual fracture rate at all sites, excluding hip, vertebral and Colles’, was 0.006.

The relative risk of a hip, vertebral, Colles’ or other fracture given a previous fracture were 2 (hip), 2 (vertebral), 1.9 (Colles) and 1.9 (other), respectively.
The relative risk of hip fracture was 0.73 with vitamin D plus calcium and 0.25 for hip pads.

The proportion of patients fully complying with nutritional supplements was set at 85%. Compliance was set at 35% for hip protectors.

The baseline utility values for non-fracture patients were 0.747 for age 70 to 74, 0.731 for age 75 to 79, 0.699 for age 80 to 84, and 0.676 for 85 and older.

A multiplier of 0.797 was used to account for the proportionate effect of a fracture on the health state utility in the first year.

Methods used to derive estimates of effectiveness
The author supplemented the data derived from the literature with assumptions based on the literature.

Estimates of effectiveness and key assumptions
In the absence of data on vertebral age-specific fracture rates for males, it was assumed that the vertebral fracture rates for males were half those of females.

For the combination of vitamin D, calcium and hip protectors, the relative risk of hip fracture was assumed to be that of hip protectors alone for patients compliant with them, as this was the most effective treatment.

For non-compliant hip protector patients, the relative risk of hip fracture was assumed to be that of vitamin D and calcium supplement for those compliant with them.

In the absence of empirical data on the effect of hip fractures on health state utilities after the first year, the model assumed that fractures had the same relative degree of impact in subsequent years.

Measure of benefits used in the economic analysis
The measure of benefits used was the quality-adjusted life-years (QALYs). Health state values for the general population were obtained using EQ-5D. To obtain the health state utility after the occurrence of a hip fracture, values for the general population were adjusted using a multiplier based on the proportionate effect of a fracture on the health state utility. This multiplier was obtained from an empirical study conducted in the UK using the time trade-off method.

Direct costs
The direct costs included in the analysis were those of the UK NHS. These included the average utilisation costs to the NHS, preventive treatment costs and fracture treatment costs. Specific costs were obtained from the Department of Health web pages. The costs of supplements were obtained from the UK drug prescription index. The cost of different fractures was obtained from a single study on the cost of treating fractures in the UK population. Discounting was relevant as the costs were incurred during the lifetime of the patient. Hence, the costs were appropriately discounted at a rate of 6% per annum. The study reported the average costs. The resource quantities and the unit costs were not reported separately. The costs were reflated to the 2000 price year using the Retail Price Index when necessary.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($). UK pounds (£) were converted to $. The exchange rate was 1 = $1.4.

**Sensitivity analysis**
A probabilistic sensitivity analysis was undertaken. This analysed uncertainty so that simultaneous variations in input parameters within the model could be taken into consideration. Each input parameter was assigned an appropriate statistical distribution and 95% confidence intervals, representing a range of plausible variables obtained from the literature. Log normal distributions were used for the cost and effectiveness inputs. Beta distributions were used for compliance, excess mortality from hip fractures, fracture rates and health state utilities. A Monte Carlo simulation was then run to obtain 10,000 iterations of the model.

**Estimated benefits used in the economic analysis**
In the female general population, the QALYs gained were 7.19 with no treatment, 7.21 with vitamin D plus calcium, 7.22 with hip protectors, and 7.23 with a combination of vitamin D, calcium and hip protectors.

In the male general population, the QALYs gained were 6.37 with no treatment, 6.38 with vitamin D plus calcium, 6.38 with hip protectors, and 6.39 with a combination of vitamin D, calcium and hip protectors.

In the female high-risk population, the QALYs gained were 7.10 with no treatment, 7.14 with vitamin D plus calcium, 7.15 with hip protectors, and 7.17 with a combination of vitamin D, calcium and hip protectors.

In the male high-risk population, the QALYs gained were 6.34 with no treatment, 6.35 with vitamin D plus calcium, 6.36 with hip protectors, and 6.37 with a combination of vitamin D, calcium and hip protectors.

**Cost results**
In the female general population, the average cost per patient was $48,647 with no treatment, $49,252 with vitamin D plus calcium, $48,946 with hip protectors, and $49,647 with a combination of vitamin D, calcium and hip protectors.

In the male general population, the average cost per patient was $41,814 with no treatment, $42,477 with vitamin D plus calcium, $42,233 with hip protectors, and $42,934 with a combination of vitamin D, calcium and hip protectors.

In the female high-risk population, the average cost per patient was $50,018 with no treatment, $50,339 with vitamin D plus calcium, $50,009 with hip protectors, and $50,516 with a combination of vitamin D, calcium and hip protectors.

In the male high-risk population, the average cost per patient was $42,390 with no treatment, $42,937 with vitamin D plus calcium, $42,689 with hip protectors, and $43,309 with a combination of vitamin D, calcium and hip protectors.

**Synthesis of costs and benefits**
The costs and benefits were combined by calculating a cost-utility ratio (i.e. the additional cost required per QALY gained).

The incremental cost-utility ratio of hip pads compared with no treatment was $11,722 for females ($47,426 for males) in the general population and $17,017 for males in the high-risk population. Hip pads were cost-saving in the female high-risk population. For no treatment versus hip pads combined with vitamin D and calcium, the incremental cost-utility ratio was $25,123 for females ($80,998 for males) in the general population and $6,527 for females ($33,565 for males) in the high-risk population. Vitamin D plus calcium alone was dominated in all four sub-groups, that is, it was less effective and more costly than the next more-effective intervention.

At a ceiling ratio of $20,000 per QALY for women at general risk, the probability that vitamin D plus calcium with hip pads was cost-effective was 51%, compared with 49% for no treatment. At $30,000 per QALY, the probabilities were 63% (combined treatment) and 37% (no treatment), respectively.
Authors' conclusions
Current information on interventions to prevent fractures in the elderly in the UK suggested that, at a ceiling ratio of $20,000 per quality-adj usted life-year (QALY), hip protectors were cost-effective in the general female population and high-risk male population, and were cost-saving in the high-risk female population.

CRD COMMENTARY - Selection of comparators
The study compared different prevention treatments (including no treatment). No treatment was chosen as the comparator, to provide a benchmark to which the other interventions could be compared. You should decide if these prevention treatments are widely used interventions in your own setting.

Validity of estimate of measure of effectiveness
The author reported that a systematic and extensive review of the literature had been undertaken. However, the author failed to report either the number of sources searched or whether grey literature was searched, in order to find all relevant research and minimise biases. As this study had a UK setting, UK-specific data were preferred where possible, which was appropriate. Whenever possible, the author also compared the data used in the model with that of other published studies to assess its validity. The results from multiple studies were not combined to derive the outcome data. When data were unavailable from the literature, the author supplemented the data in the model by making several assumptions, generally backed by the literature. An appropriate probabilistic sensitivity analysis was conducted to account for uncertainty in the model parameters.

Validity of estimate of measure of benefit
The estimation of benefits was modelled using a Markov model. The author appropriately assessed the internal validity of this model by using debugging techniques, which involved extreme sensitivity analyses, and by checking that the fracture rates reported by the model were consistent with the primary data input. Checking that the model's results were consistent with information contained in other relevant primary research studies allowed the author to assess the external validity of the model.

Validity of estimate of costs
All the categories of cost relevant to the NHS perspective adopted were included in the analysis. For each category of cost, all the relevant costs appear to have been included in the analysis. The costs and the quantities were not reported separately, which will limit the generalisability of the author's results. The costs were derived from published sources. A sensitivity analysis of the costs was performed within the probabilistic sensitivity analysis. The author performed appropriate currency conversions and reported the exchange rate between the two currencies (US$ and UK). Since all the costs were incurred during the lifetime of the patient, discounting was necessary and was appropriately performed.

Other issues
The author made appropriate comparisons of their results with those from two other studies that modelled the cost-effectiveness of vitamin D and calcium supplements in the UK. Although the comparators and several other elements differed from those in the model in this paper, the studies found vitamin D alone to be potentially more cost-effective than vitamin D plus calcium. The issue of generalisability to other settings was partly addressed by the sensitivity analysis, although the author warned readers that the results of the model might not be applicable to non-UK settings. The author does not appear to have presented the results selectively and the conclusions reflected the scope of the analysis.

The author reported a number of further limitations to the study. First, it was assumed that patients did not suffer any loss of quality of life with fractures other than hip fractures. Second, although the model accounted for the finding that the high-risk population had a higher average risk of fracture than the general population, the occurrence of a subsequent fracture was assumed to be independent of prior fractures. Third, quality of life data, although age specific, were not gender specific, so the model had to use averages. Finally, the effectiveness of hip protectors was obtained from a Cochrane systematic review and two recent trials of hip protectors in elderly populations have been published.
since that review was undertaken. One of these trials showed a 40% reduction in hip fractures, while the other showed no effect for the intervention.

Implications of the study
According to the author, the study highlighted the important role of treatments involving hip protectors, with or without daily supplements of vitamin D and calcium, in the prevention of fractures in men and women over 70 years of age, in the UK. The study also had several implications for research policy. According to the author, the uncertainty surrounding several of the input parameters used in the model made them good candidates for further research.

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Eli Lilly funded the literature review of economic models of fracture prevention.

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Other publications of related interest


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