Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures
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Authors' objectives
To determine the ability of bone mineral density (BMD) measurements in women to predict later fractures.

Searching
MEDLINE, EMBASE and SweMed were searched using the keywords 'bone and bones', 'bone density', 'bone mineral content' and 'densitometry', combined with the different techniques and equipment. Reference lists of selected papers, references from colleagues, and relevant, known grey literature were also searched. All searches were restricted to articles published in the English language from 1985 to 1994 (1990 to 1994 for case-control studies).

Study selection
Study designs of evaluations included in the review
Prospective cohort studies with a baseline measurement of bone density and subsequent follow-up for fracture, and case-control studies of hip fractures (where measurement of bone density occurred within 14 days of fracture) age matched to controls were eligible for inclusion in the review.

Specific interventions included in the review
To be eligible for inclusion in the review studies must have measured BMD by absorptiometry (single or dual energy, photon or x ray), quantitative computed tomography, quantitative magnetic resonance imaging, or ultrasound scanning. Studies using roentgenograms or metacarpal measurements were excluded.

Studies included in the review took the BMD measurement at a number of sites: proximal radius, distal radius, proximal femur, femoral neck, lumbar spine, spine, calcaneus, middle radius and forearm.

Reference standard test against which the new test was compared
Included studies were required to have follow-up for fractures; fractures must have occurred after the BMD measurement was taken.

Participants included in the review
Only studies of adult women were included. Patients must not have received treatments for bone or hormonal related disorders. Patients may have had previous fractures at the start of the study.

Outcomes assessed in the review
No inclusion criteria were specified with respect to outcome measures.

Included studies measured the following types of fracture: forearm; humerus; wrist; proximal femur; hip; fragility; vertebral; all non-spine; all.

The primary outcome measure calculated in the review (for prospective cohort studies) was the relative risk (RR) of fracture associated with a decrease in bone density of one standard deviation (SD), adjusted for age. Sensitivity, specificity, positive predictive value, and population attributable risk for lifetime incidence of hip fracture were also calculated. For case-control studies the odds ratios (ORs) of fracture for one SD decrease in BMD were calculated.

How were decisions on the relevance of primary studies made?
Articles were reviewed independently by three people, (an expert in osteoperosis, an epidemiologist or biostatistician, and a public health worker,) and any disagreements were resolved through discussion.
Assessment of study quality
A quality score developed for this analysis was used to assess each study. This considered potential bias from patient selection, number and types of patient lost to follow-up, and the method used to identify fractures. Each study was given a quality score, with a maximum score of 25. The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The risks in included papers were small and relative risks and odds ratios were considered equivalent. Pooled risk ratio (RR) and 95% confidence interval was calculated in a meta-analysis using a fixed-effect model based upon the Mantel-Haenszel method, (a detailed description was given in the paper). All study data were transformed to have the individual, rather than the fracture, as the unit of analysis. The studies were weighted by sample size, or alternatively, by the quality scores. Sensitivity, specificity, positive predictive value, and the population attributable risk fraction for three different lifetime incidences of hip fracture were also calculated.

How were differences between studies investigated?
Tests of homogeneity were performed at a level of P=0.05. Estimates were divided by type of fracture (forearm, hip, vertebral, and all fractures) and by measurement site (proximal radius, distal radius, hip, lumbar spine, calcaneus, and all sites).

Results of the review
Eleven study populations were identified from 25 articles describing prospective cohort studies, (total of 29,952 participants); 8 case-control studies were also identified, but not included in the meta-analysis.

Measurement at the spine had a predictive ability for a decrease of 1SD in bone density for spine fractures, with a RR of 2.3 (95% confidence interval, CI: 1.9, 2.8). Measurement at the hip was better for predicting hip fractures, with a RR of 2.6 (95% CI: 2.0, 3.5). All other measurements had similar predictive ability, RR of 1.5 (95% CI: 1.4, 1.6). Homogeneity was rejected for measurements at the proximal and distal radius, and hip for all types of fracture.

The average total scores for quality ranged from 11.7 to 19.3 out of a possible total of 25. Weighting for quality scores gave similar results.

The sensitivity, specificity, positive predictive value, and population attributable risk for a cut-off point in bone density of 1 SD below the age adjusted mean were calculated for 3 different lifetime incidences of hip fracture, i.e. 3, 15 and 30% (the RR of hip fracture was assumed to be 2.6). The sensitivity and population attributable risk decreased as incidence increased, and the positive predictive value was much larger for higher incidence (9, 36 and 58% for an incidence of 3, 15 and 30%, respectively).

For case-control studies, the average odds ratio for a difference of one SD in BMD was 2.7, 2.8, 2.1, and 1.8 for BMD measurements at the femoral neck, trochanter, Ward's triangle, and lumbar spine respectively. These results also suggest that measurements of BMD at the hip are superior to measurements at the spine for predicting hip fractures.

Authors' conclusions
Measurements of bone mineral density can predict fracture risk but cannot identify individuals who will have a fracture. We do not recommend a programme of screening menopausal women for osteoporosis by measuring bone density.
CRD commentary
This is a thorough review. The research question is clearly identified and defined in terms of intervention, comparator, population and study design; though the rationale for including a restricted number of case-control studies for comparison is unclear. The literature search was adequate, however, language and date restrictions may have lead to incomplete retrieval of the available published literature. No assessment of publication bias was reported. The review methods were, in general, rigorous and well reported. However, it is unclear whether the quality assessment was undertaken for both the case-control and cohort studies. Details of included primary studies were reported clearly in tabular form. The methods of analysis used were, in the main, appropriate and well conducted; given the results of homogeneity testing the application of a fixed-effect model may be questionable.

Broadly, the authors' conclusions concerning the limited value of BMD for predicting fracture risk follow from the results of the review as reported. However, the authors' assertion that measurement at the spine had a better predictive ability for vertebral fractures is not clear from the table of results presented.

Implications of the review for practice and research
Research: The authors made no specific recommendations for future research.

Practice: The authors stated that although bone mineral density measurements can predict fracture risk, they cannot identify individuals who will have a fracture, and a screening programme for osteoporosis cannot be recommended.

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