CRD summary
This well-conducted and clearly reported review addressed the diagnostic performance of quantitative ultrasound for identifying patients with osteoporosis. The authors’ conclusions, that based on currently available data quantitative ultrasound cannot reliably rule-in or rule-out osteoporosis, follow from the data presented. The exclusion of non-English language studies might have resulted in the loss of relevant data.

Authors’ objectives
To determine the diagnostic performance of calcaneal quantitative ultrasound, compared with X-ray absorptiometry, for identifying patients who meet the World Health Organization criteria for osteoporosis.

Searching
MEDLINE (1966 to October 2005), EMBASE (1993 to May 2004), the Cochrane Controlled Trials Register and Cochrane Database of Systematic Reviews (1952 to March 2004), and the Science Citation Index (1945 to April 2004) were searched for relevant articles in the English language; the search strategies were reported. Reference lists of eligible studies and reviews were also screened.

Study selection
Study designs of evaluations included in the review
Only studies that performed quantitative ultrasound and DXA in all patients, and had at least 10 participants with and 10 without DXA-defined osteoporosis, were eligible for inclusion.

Specific interventions included in the review
Studies of calcaneal quantitative ultrasound were eligible for inclusion. Performance using a range of diagnostic thresholds (T-scores of 0 to -2.5) was reported in the review. All of the included studies that assessed the quantitative ultrasound index parameter used the same device (the Hologic Sahara quantitative ultrasound device).

Reference standard test against which the new test was compared
The included studies were required to use dual-energy X-ray absorptiometry (DXA) at the hip and spine as the reference standard. The diagnosis of osteoporosis was defined by a T-score of -2.5 or less on DXA, at either site.

Participants included in the review
Studies of adult populations were eligible for inclusion. The majority of included studies (23 out of 25) were conducted in all female populations and many exclusively enrolled postmenopausal women. The age range of the participants, across all included studies, was 22 to 90 years. The prevalence of osteoporosis ranged from 7.1 to 59%.

Outcomes assessed in the review
The included studies were required to report at least one pair of sensitivity and specificity values.

How were decisions on the relevance of primary studies made?
Two authors independently reviewed articles for inclusion.

Assessment of study quality
The methodological quality of the included studies was assessed using the following criteria: sample size (30 or more participants with and without DXA-defined osteoporosis); percentage of participants completing the study (more than 90); patient selection (random or consecutive); time between ultrasound and DXA (less than 1 month); independent interpretation of ultrasound and DXA results.
Two authors independently assessed study validity. Any discrepancies were resolved by repeated review and discussion.

**Data extraction**
Two authors independently extracted information on study design, participant characteristics and results. Any discrepancies were resolved by repeated review and discussion.

**Methods of synthesis**
How were the studies combined?
Summary receiver operating characteristic (ROC) curves, with upper and lower confidence intervals (CIs), were calculated for each of the ultrasound parameters using the method of Moses and Littenburg. The area under the curve (AUC), along with 95% CI, was calculated as an overall estimate of accuracy for each parameter.

Post-test probabilities of DXA-defined osteoporosis were calculated for pre-test probabilities from 0 to 1 using Bayes theorem, and sensitivity and specificity estimates were derived from regression analyses. The results were tested for robustness to the removal of individual studies.

How were differences between studies investigated?
Weighted least-squares regression was used to assess how sensitivity and specificity changed with diagnostic threshold for studies that evaluated the quantitative ultrasound index parameter. The results of subgroup analyses for women and postmenopausal women were reported; however, these did not appear to have been specified a priori.

**Results of the review**
Twenty-five studies (n=6,676) were included in the review. The studies evaluated a number of parameters: broadband ultrasound attenuation (11 studies, n=2,519), speed of sound (4 studies, n=989), velocity of sound (4 studies, n=770), quantitative ultrasound index (11 studies, n=3,054) and stiffness parameter (4 studies, n=1,729).

Study quality (for studies that evaluated the quantitative ultrasound index parameter).
All of the included studies enrolled participants prospectively and 3 studies selected patients either consecutively or by random sampling. All studies had 30 or more participants with and without DXA-defined osteoporosis, and had completion rates greater than 90%. Most studies did not report the time elapsed between ultrasound and DXA, and no study reported that the ultrasound and DXA results were assessed independently.

Diagnostic accuracy.
The AUC was 0.76 (95% CI: 0.72, 0.79) for the quantitative ultrasound index parameter (11 studies), 0.77 (95% CI: 0.73, 0.81) for broadband ultrasound attenuation (11 studies), 0.74 (95% CI: 0.71, 0.77) for speed of sound and velocity of sound (4 studies), and 0.79 (95% CI: 0.71, 0.86) for stiffness (4 studies).

Subgroup analyses for the quantitative ultrasound index parameter gave an AUC of 0.76 (95% CI: 0.70, 0.82) for studies of women only, and an AUC of 0.75 (95% CI: 0.66, 0.82) for studies of postmenopausal women only.

Pre- and post-test probabilities of DXA-defined osteoporosis were tabulated by age group (50 to 59 years, 60 to 69 years, 70 to 79 years, and 80 years or older), and for three ultrasound T-score thresholds. For example: at a pre-test probability of 22% (65-year-old white woman at average risk), the post-test probability was 34% (95% CI: 26, 41) after a positive test and 10% (95% CI: 5, 12) after a negative test, using a T-score threshold of -1.

**Authors’ conclusions**
The available literature suggests that calcaneal quantitative ultrasound, at commonly used diagnostic thresholds, does not definitively confirm or rule-out DXA-defined osteoporosis. Additional research is needed before this test can be recommended as a screen for osteoporosis.
CRD commentary

The review addressed a clearly stated research question, which was defined by appropriate inclusion criteria. An adequate search of the published literature was described. However, no attempt to identify unpublished studies was reported and the restriction to studies in English might have resulted in the loss of relevant data. Appropriate measures to reduce the introduction of error and/or bias during the review process were reported, and the quality of the included studies was assessed (quality assessment reported in full in the online version of the article).

Since the data were reported for a number of clinically relevant index test thresholds, the construction of summary ROC curves was an appropriate method of synthesis. The results of the review were clearly reported, in tabular and graphical form, and are expanded in the online version of the article. The authors’ conclusions follow from the data presented, with the caveat that relevant studies might have been omitted.

Implications of the review for practice and research

Practice: The authors stated that calcaneal quantitative ultrasound results, at commonly used screening thresholds, appear insufficient to rule-out or rule-in DXA-defined osteoporosis. In the absence of data on the therapeutic efficacy of fracture risk reduction in persons selected by quantitative ultrasound, additional information is needed before this technique can be recommended as part of a screening programme.

Research: The authors stated that additional research is needed to assess treatment efficacy in persons selected by quantitative ultrasound, as well as the cost-effectiveness of such screening strategies.

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