Soy isoflavone intake inhibits bone resorption and stimulates bone formation in menopausal women: meta-analysis of randomized controlled trials
Ma D F, Qin, L Q, Wang P Y, Katoh R

CRD summary
This review assessed the use of soy isoflavones on bone resorption and formation in peri- or postmenopausal women. The authors concluded that isoflavones inhibited bone resorption and stimulate bone formation. The review methodology was generally sound, but the conclusion was based upon a small number of subjects, which may limit its reliability.

Authors' objectives
To assess the effects of isoflavone intake on bone resorption and bone formation in women.

Searching
MEDLINE/PubMed, EMBASE, the Cochrane Controlled Trials Register and the Science Citation Index were searched from January 1966 to April 2006. Search terms were reported. References of identified articles and reviews were checked and experts were contacted.

Study selection
Randomised controlled trials (RCTs) with a parallel design which assessed soy products or soy isoflavones for at least four weeks in female participants were eligible for inclusion. The primary review outcomes were urinary deoxypyridinoline (Dpyr) as a marker of bone resorption and serum bone-specific alkaline phosphatase (BAP) as a marker of bone formation.

Included studies used either soy protein containing mainly isoflavones or isoflavone tablets. Isoflavone intake ranged from 37.3 to 118 mg/day and treatment duration from four to 48 weeks. Studies enrolled either Caucasian or Asian women who were not undergoing other osteoporosis therapy, and the majority enrolled post-menopausal women, with mean ages ranging from 51 to 62.4 years. All studies restricted common soy foods in the diet of subjects.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Two reviewers independently assessed the studies for validity using the Jadad scale. Disagreements were resolved through discussion.

Data extraction
Two reviewers independently extracted the data using a pre-specified form. Mean differences from post-randomisation baseline and post-treatment values with 95% confidence intervals (CIs) were calculated.

Methods of synthesis
Weighted mean differences (WMDs) with 95% CIs were calculated using a random-effects model. Statistical heterogeneity was assessed using $\chi^2$ tests. Sensitivity analyses were used to assess the impact of outliers. Subgroup analyses were used to investigate the effects of intervention type and dose, and participant ethnicity and menopausal status. Publication bias was assessed through a funnel plot and the failsafe N was calculated.

Results of the review
Nine RCTs ($n = 432$) were included in the review. The studies were generally considered to be good quality with Jadad scores of between 3 and 5 (out of 5 points). Sample sizes ranged from 23 to 78 subjects.

Isoflavones significantly decreased urinary Dpyr (WMD -2.08 nmol/nmol, 95% CI: -3.82, -0.34, nine RCTs). Results of
subgroup analyses indicated that the effect was only significant in studies using isoflavone tablets and not in those using isolated soy protein. In subgroup analyses significant reductions were found for studies evaluating isoflavone doses of 90 mg/day or lower (seven studies), but not for doses higher than 90 mg/day (two studies), for studies lasting less than 12 weeks (six studies), but not for longer term studies (three studies), for Asian women (three studies) but not for western women (seven studies) and for postmenopausal women (seven studies), but not for pre-menopausal women (two studies).

Isoflavones significantly increased serum BAP (WMD 1.48 microgram/l, 95% CI: 0.22, 2.75).

There was no strong evidence of publication bias and the failsafe N was calculated to exceed 30.

Authors’ conclusions
Isoflavone intervention significantly inhibits bone resorption and stimulates bone formation. These favourable effects occur even if doses less than 90mg/day are used or if the duration of treatment is less than 12 weeks.

CRD commentary
The review question and the inclusion criteria were clear and specific. The authors searched a number of relevant databases and other sources, and used appropriate tools to assess publication bias. However, the inference the authors drew from the funnel plot did not appear appropriate, as the presence of publication bias was indicated. The authors reported using methods designed to reduce reviewer bias and error for the extraction of the data and the assessment of validity, but not for the selection of studies. The assessment of validity used appropriate criteria. The decision to adopt a meta-analytic synthesis appeared appropriate, as was the a priori specification of sub-group analyses. However, the number of studies included was small, and the studies themselves were of small size. Therefore, the results of the sub-group analyses should be regarded only as hypothesis-generating, rather than as evidence for a conclusion. Despite these caveats the primary conclusion was based on the evidence of the review, but its reliability may be limited by the small number of participants.

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Bibliographic details

Other publications of related interest
Practice: the authors did not state any implications for practice.
Research: the authors stated that further RCTs were required to determine the effective amount and duration of isoflavone intake for the reduction of bone resorption and stimulation of bone formation in women who are peri- or postmenopausal.

Indexing Status
Subject indexing assigned by NLM

MeSH
Amino Acids /urine; Bone Resorption /prevention & control; Female; Humans; Isoflavones /administration & dosage /pharmacology; Menopause; Middle Aged; Osteogenesis /drug effects /physiology; Osteoporosis, Postmenopausal /prevention & control; Randomized Controlled Trials as Topic; Soybeans /chemistry; Treatment Outcome

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.