Soy isoflavones and bone mineral density in perimenopausal and postmenopausal Western women: a systematic review and meta-analysis of randomized controlled trials

Ricci E, Cipriani S, Chiaffarino F, Malvezzi M, Parazzini F

CRD summary
The review’s conclusions suggested that isoflavone mixtures are not effective in decreasing bone loss in perimenopausal and postmenopausal Western women. Limitations relating to searches, the statistical analyses, and the reporting of study quality means the authors’ conclusions should be interpreted with caution.

Authors’ objectives
To evaluate the effectiveness of phytoestrogens on bone mineral density in menopausal Western women.

Searching
MEDLINE and EMBASE were searched from 1990 to February 2010 for studies published in English; search terms were reported. Reference lists of selected articles and reviews were examined.

Study selection
Parallel-group randomised controlled trials (RCTs) of soy products (containing soy isoflavone) taken for at least three months by Western perimenopausal or postmenopausal women and that reported bone mineral density as an index of bone mass were eligible for inclusion. Comparator groups could not take phytoestrogens. Studies with main outcome measures that were markers of bone turnover were excluded.

All studies except one were of postmenopausal women. Isoflavone doses (administered in various ways) ranged from 52 to 120mg/day of aglycone equivalents. All trials were placebo controlled. Most trials were conducted in USA.

Treatment duration ranged from 24 weeks to three years.

Two reviewers independently selected studies. Disagreements were resolved by a third reviewer.

Assessment of study quality
Study quality was evaluated independently by two reviewers who assessed selection bias, performance bias and attrition bias.

Data extraction
Data were extracted in order to calculate mean differences (MD) with 95% confidence intervals (CI). Authors were contacted for missing data when necessary.

Two reviewers independently extracted data.

Methods of synthesis
Studies that reported pre- and post-treatment (or change from baseline) lumbar spine bone mineral density as an outcome were eligible for meta-analysis using a fixed-effect model (or random effects when significant heterogeneity was found). Heterogeneity was assessed with $\chi^2$. Five pre-specified subgroup analyses were reported. A funnel plot was used to detect publication bias. A narrative synthesis was also performed.

Results of the review
Seventeen RCTs were included (2,042 completers, range 16 to 362). The authors reported that all 12 trials (n=1,433) included in the meta-analyses were properly randomised and double-blinded with biases unlikely to occur. They also reported that attrition bias appeared to be an issue with a high proportion of participants who stopped treatment (and placebo). No further details relating to study quality were reported.

Seven of the 17 RCTs found bone-sparing effects with isoflavones, but meta-analysis indicated lumbar spine bone mineral density was not significantly different from placebo (MD 9.86mg/cm², 95% CI -2.64 to 22.36 mg/cm²; 12
RCTs, p<0.00001 for heterogeneity). When the one study that used isolated genistein was excluded from the analysis there was no significant heterogeneity.

Subgroup analyses that examined dose and treatment duration resulted in no significant differences between groups. Pooled results from studies that looked at femoral neck or whole body mineral density yielded results with no significant differences. There appeared to be no indication of publication bias.

**Authors' conclusions**
Results suggested that isoflavone mixtures were not effective in decreasing bone loss in perimenopausal and postmenopausal Western women.

**CRD commentary**
The review addressed a clear question supported by appropriate eligibility criteria. A fairly basic search was conducted only for studies published in English, so it was possible that relevant studies were missed. Independent duplicate procedures were used to minimise risks of reviewer error and bias throughout the review processes. Although attrition bias was reported as being an issue, neither actual rates were not provided. Individual result details for other quality assessment criteria were not provided. The authors acknowledged that double counting of control groups in trials of different doses was a potential limitation.

The authors' conclusions appear to be a fair reflection of the data presented, although uncertainties remain regarding attrition rates (and the absence of an intention-to-treat analysis), the effect of double-counting in the meta-analyses and the possibility that studies were missed during searches. The conclusions should, therefore, be interpreted with caution. It should also be noted that the conclusion relating to perimenopausal women was informed by only one trial.

**Implications of the review for practice and research**
The authors did not state any implications for practice.

**Research**
The authors stated that the effect of isolated isoflavones and the role of equol status were still open to evaluation. They also stated a need for more research into genistein.

**Funding**
Part funded by Fondazione IRCCS Policlinico, Italy.

**Bibliographic details**

**PubMedID**
20673147

**DOI**
10.1089/jwh.2010.2021

**Original Paper URL**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Bone Density /drug effects; Female; Genistein /pharmacology; Humans; Isoflavones /pharmacology; Perimenopause /physiology; Postmenopause /physiology; Soybean Proteins /pharmacology

**AccessionNumber**
12010006955

Date bibliographic record published
10/11/2010

Date abstract record published
01/05/2012

Record Status
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.