Meta-analysis of the effects of soy protein containing isoflavones on the lipid profile  
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CRD summary  
This review looked at the effect on blood cholesterol of soy protein containing isoflavones. Total cholesterol, low-density lipoprotein cholesterol and triacylglycerol levels were all reduced, while high-density lipoprotein cholesterol levels were increased. There are some problems with the review that could affect the reliability of its findings.

Authors' objectives  
To identify and quantify the effects of soy protein containing isoflavones on serum lipid profiles.

Searching  
PubMed was searched from 1995 to June 2002; the search terms were not reported. The reference lists of relevant articles were checked. Only studies published in the English language were eligible for inclusion.

Study selection  
Study designs of evaluations included in the review  
Only randomised controlled trials (RCTs), parallel or crossover, were eligible for inclusion.

Specific interventions included in the review  
Studies that assessed the effects of soy protein containing isoflavones, or isoflavone extracts, were eligible for inclusion. The amount of soy isoflavones had to be specified. Studies that assessed whole soy protein were excluded. Some of the included studies used isolated soy protein containing isoflavones, some used tablets containing extracted isoflavones, and some used textured soy food. Isoflavone dosages, where given, ranged from 3 to 185 mg/day. Most control groups received casein or whey, but some had isoflavone-depleted soy protein, animal protein or placebo. Some participants were also on 'modified' diets or the National Cholesterol Education Program (NCEP) Step I or Step II diets. The length of treatment ranged from 3 to 26 weeks.

Participants included in the review  
No inclusion criteria were given for the participants. Both men and women participated in the included studies. Some studies included postmenopausal women. Some participants were hypercholesterolaemic while others had normal cholesterol levels. The total cholesterol ranged from 3.87 to 7.68 mmol/L.

Outcomes assessed in the review  
Studies where the outcome of interest was serum lipid levels, expressed as changes in concentrations from baseline to end of study, were included. Changes in levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and triacylglycerol were given. Where studies assessed outcomes at more than one time point, only the results for the longest time period were used.

How were decisions on the relevance of primary studies made?  
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality  
The authors did not state that they assessed validity.

Data extraction  
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The mean changes in lipid levels for each group in each study were given. The net mean difference in
changes in lipid levels between baseline and follow-up (treatment versus control group) were calculated.

**Methods of synthesis**

**How were the studies combined?**

The net mean differences in lipid levels were pooled using both random-effects and fixed-effect models. The random-effects results were presented where heterogeneity was significant, otherwise fixed-effect results were given. A funnel plot was used to assess publication bias.

**How were differences between studies investigated?**

The authors say they tested for heterogeneity, but did not give details. In addition, they performed pre-specified subgroup analyses according to gender, lipid levels (normal versus high), menopausal state, concomitant diet and concentrations, or forms, of isoflavones used. A regression analysis was used to investigate dose responses and initial lipid levels.

**Results of the review**

Twenty-three RCTs (1,381 participants) were included. Since some studies had more than two arms, 34 comparisons were included.

Soy protein containing isoflavones decreased total cholesterol; the mean difference was -0.22 mmol/L (95% confidence interval, CI: -0.29, -0.16). LDL was also lowered (mean difference -0.21 mmol/L, 95% CI: -0.30, -0.13), as were triacylglycerol levels (mean difference -0.109 mmol/L, 95% CI: -0.16, -0.05).

HDL levels were increased with soy proteins; the mean difference was 0.04 mmol/L (95% CI: 0.00, 0.07).

**Subgroup analysis.**

Total cholesterol was reduced more in men than in women: mean changes of -0.26 and -0.16 mmol/L, respectively. Those with hypercholesterolaemia had greater reductions than those with normal cholesterol levels: changes of -0.25 and -0.17 mmol/L, respectively. In the regression analysis, the amount of soy protein containing isoflavones was independently associated with the change in total cholesterol. When the results were analysed according to quartiles, based on initial lipid levels, there was no significant differences in the responses to treatment.

The authors stated that funnel plots for the outcome total cholesterol indicated no significant publication bias.

Full details of other results were presented.

**Authors' conclusions**

Soy protein containing isoflavones significantly reduced total cholesterol, LDL cholesterol and triacylglycerol, and significantly increased HDL cholesterol. The changes were related to level and duration of intake, and the gender and initial serum lipid levels of the participants.

**CRD commentary**

The aims of this review were clearly stated. The database search was limited to PubMed and only articles published in English were included. It is therefore possible that other relevant studies were missed, and this could affect the results of the review. The methods of the review (study selection, data extraction) were not described; bias can be introduced at these stages of a review. There was no mention of any quality assessment. There is some confusion in the tables and text about the numbers of included participants. Although the authors considered heterogeneity, in some analyses they pooled studies where the forest plots indicated that studies should not have been pooled because heterogeneity was too great. Some studies included more than two treatment arms and the authors used the same control groups more than once within the pooled analysis; this might have distorted the results. In addition, when a large number of subgroup analyses are performed it is always possible that some chance effects are identified. The authors' conclusions should be interpreted in the light of these comments.
Implications of the review for practice and research

The authors did not state any implications for practice or further research.

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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.