The effects of phytosterols/stanols on blood lipid profiles: a systematic review with meta-analysis

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CRD summary
This review concluded that dietary phytosterols/stanols could significantly reduce blood serum levels of low density lipoprotein cholesterol in individuals with non-familial hypercholesterolaemia. Given the differences between the trials and the risk that relevant trials may have been missed, the authors' conclusions may not be reliable.

Authors' objectives
To assess the lipid-lowering effects of dietary phytosterols/stanols in individuals with non-familial hypercholesterolaemia.

Searching
MEDLINE, EMBASE, IPA (International Pharmaceutical Abstracts), CBMdisc (Chinese Biological Medicine database), VIP and CNKI (China National Knowledge Infrastructure) were searched between 1980 and 2007 for published studies in any language. Search terms were reported. Reference lists of retrieved articles and reviews were searched for additional studies.

Study selection
Parallel randomised controlled trials (RCTs) that investigated the effects of phytosterols/stanols on blood lipid levels in adults (16 years or older) without familial hypercholesterolaemia, severe hepatic or renal disorders, and diabetes mellitus, were eligible for inclusion. Trials had to measure levels of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and/or triacylglycerol. Other relevant outcomes included levels of apolipoprotein B, apolipoprotein A-1, total cholesterol/high-density lipoprotein cholesterol and low-density lipoprotein cholesterol/high-density lipoprotein cholesterol.

Interventions included in the review assessed products such as spreads, bread, cream, beverages and yoghurts which contained between 0.45g and 3.2g (mean dose of 2.08g/day for three weeks to one year) of plant sterols, plant stanols or plant stanol esters. The included trials were performed under free-living conditions and included participants with normal, borderline or hyper-cholesterol levels. Participants (with or without dyslipidaemia) ranged in age from 20 to 70 years. Trials varied in duration from three weeks to one year.

The authors did not state how any reviewers performed the selection.

Assessment of study quality
Two reviewers independently assessed the methodological quality of the trials using a modified Jadad scale (sequence generation, allocation concealment, blinding, withdrawals and drop-outs). Each trial was awarded a score up to a maximum of 5 points. Only studies scoring 4 or 5 points were included in the review.

Data extraction
Two reviewers independently extracted mean values and standard deviations for each outcome using a standardised form. If not available, standard deviations were estimated using the methods of Follman et al. Total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triacylglycerol were expressed in millimoles per litre (mmol/L); apolipoprotein B and apolipoprotein A-1 were expressed in grams per litre (g/L). Data expressed as mg/L were converted to mmol/L using conversion factors. For total cholesterol, and low-density lipoprotein cholesterol, values were multiplied by 0.0258 and for high-density lipoprotein cholesterol values were divided by 88.2.

Methods of synthesis
Outcomes were pooled and weighted mean differences (WMDs) with 95% confidence intervals (CIs) calculated using a fixed-effect method, or if significant heterogeneity was identified (p≤0.05 or I²>50%), a random-effects model. Statistical heterogeneity was assessed using the χ² and I² tests. Subgroup analyses were conducted to determine the
effects of varying baseline blood lipid levels: normal (total cholesterol less than 200mg/dL), borderline (total cholesterol between 200 and 239mg/dL) or hyper (total cholesterol above 240mg/dL) and intervention regimens.

Results of the review
Twenty RCTs (n=1,273 participants) were included in the meta-analysis. Two studies were awarded a Jadad score of 5 points and the remaining trials scored 4 points. One additional trial (n unknown) was included in the review, but had a Jadad score less than 4, so was not included in the meta-analysis.

Changes in serum lipid concentrations: Significant reductions in total cholesterol (WMD 0.36mmol/L, 95% CI -0.46 to -0.26), low-density lipoprotein cholesterol (WMD 0.35mmol/L, 95% CI -0.47 to -0.22), total triacylglycerols (WMD 0.1 mmol/L, 95% CI -0.16 to -0.03) and apolipoprotein B (WMD 0.0912g/L, 95% CI -0.106 to -0.076) were reported for phytosterol/stanol interventions in comparison with control groups (n=1,273 participants). Significant statistical heterogeneity was evident for all of the analyses, with the exception of the apolipoprotein B analysis (which used a fixed-effect analysis). No significant differences between intervention and control groups were reported for high-density lipoprotein cholesterol.

Subgroup analysis:
Subgroup analyses showed no statistically significant differences between phytosterol/stanol interventions and control groups for participants with normal baseline serum lipid levels with respect to any of the outcomes. No evidence of significant statistical heterogeneity was reported.

For participants with borderline serum lipid levels, significant differences in favour of phytosterol/stanol interventions in comparison with control groups were reported for total cholesterol, low-density lipoprotein cholesterol and triacylglycerols; but no significant differences were reported for high-density lipoprotein cholesterol. However, many of the subgroup analyses for borderline serum lipid level patients were associated with significant levels of statistical heterogeneity.

For hyper serum lipid level patients, significant differences in favour of phytosterol/stanol interventions were reported for all of the outcomes, except for triacylglycerols. However, many of the subgroup analyses for hyper serum lipid level patients were associated with significant levels of statistical heterogeneity.

Subgroup analyses for intervention dosage 2g/day or above found significant differences in favour of phytosterols/stanol interventions in comparison with control groups for total cholesterol, triacylglycerols, and low-density lipoprotein cholesterol; dosages less than 2g/day found significant differences for total cholesterol and low-density lipoprotein cholesterol.

Authors' conclusions
Dietary phytosterols/stanols could significantly reduce blood low-density lipoprotein cholesterol levels.

CRD commentary
This review answered a clearly defined research question. A number of resources were search for relevant trials and no language limitations were applied. However, only published studies written in English were included, so there was some risk of publication and possibly language bias. Some efforts were made to reduce the risk of reviewer error and bias, with two reviewers independently assessing the quality of the included trials and extracting the trial data. However, it was unclear whether similar precautions were taken when selecting trials for inclusion.

Trial quality was assessed using appropriate criteria and only those trials considered to be of high methodological quality were included in the review, suggesting that the data were reliable. Appropriate methods were used to synthesise the data and assess the level of heterogeneity. Many of the analyses showed significant levels of heterogeneity. Some attempts were made to assess the effects of varying baseline lipid levels and intervention dosages, but the findings may not be reliable, given the significant levels of heterogeneity. Control groups were not reported. There was also evidence of clinical variation, particularly with regard to the type of interventions used.

Given the differences between the trials and the risk that relevant trials may have been missed, the findings of the review may not be reliable.
Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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