Phytosterols/stanols lower cholesterol concentrations in familial hypercholesterolemic subjects: a systematic review with meta-analysis

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CRD summary
This review concluded that phytosterols/stanols may offer an effective adjunct to the cholesterol lowering treatment strategy of familial hypercholesterolaemia patients. Despite some limitations in the reporting of review methods, these conclusions reflect the data presented and are likely to be reliable.

Authors’ objectives
To assess the efficacy of phytosterols/stanols in lowering total cholesterol and low-density lipoprotein cholesterol concentrations in patients with familial hypercholesterolaemia.

Searching
Bibliographic databases (such as Science Direct, MEDLINE, Health Source and Academic Search Premier) were searched from 1976 to August 2004; the trial register of Current Controlled Trials was also searched. Search terms were reported. Bibliographies of original and review articles were screened for additional studies. No language restrictions were applied, but all identified studies were in English.

Study selection
Randomized controlled trials (RCTs) that investigated the effects of phytosterols/stanols on total cholesterol and low-density lipoprotein cholesterol concentrations, in children or adults with familial hypercholesterolaemia, were eligible for inclusion.

All the included trials were conducted in heterozygous subjects, aged between 2 and 69 years. Trials were conducted under normal living conditions; plant sterols or plant stanols were used, delivered as fat spreads (dose range 1.6 to 2.8g sterols/stanols per day) or in granulate form (12 or 24g/day). Trial duration ranged from four weeks to three months.

The authors did not state how many reviewers assessed studies for inclusion.

Assessment of study quality
Two reviewers independently assessed the methodological quality of included trials, based on nine criteria: allocation concealment; blinding; method of randomization; controlled; eligibility criteria pre-specified; baseline equivalence of study groups; handling of carry over between treatments; compliance; and justification of sample size. Studies were given an overall score of 1 if all criteria were met, 2 if they were controlled studies and up to two criteria were not met, and 3 if they were non-controlled studies and three or more criteria were not met.

Studies with a quality score of 3 (lowest quality) were excluded from the review.

Data extraction
Data were extracted on the difference in total cholesterol and low-density lipoprotein cholesterol (mmol/L) between treatment and control groups, and weighted mean differences (WMDs) with 95% confidence intervals (CIs) were reported for each trial.

Two reviewers extracted data independently.

Methods of synthesis
A random-effects model was used to generate pooled estimates of weighted mean difference, treatment versus control, in total cholesterol and low-density lipoprotein cholesterol, with 95% confidence intervals.
Between trial heterogeneity was assessed by visual inspection of the forest plots and using the $I^2$ statistic.

**Results of the review**

Six trials (182 participants) met the inclusion criteria for the review. Of these, two trials that used very high dosages administered in granulate form were excluded from the meta-analyses. The authors stated that these trials were excluded because their results showed that high intakes of phytosterols/stanols may lower carotenoid concentrations without additional cholesterol-lowering effects. Three of the four studies (155 participants) included in the meta-analyses met all the quality criteria.

Fat spreads enriched with $2.3\pm0.5$g phytosterols/stanols per day significantly reduced total cholesterol (WMD -0.65 mmol/L, 95% CI -0.88 to -0.42) compared with control treatment. Low-density lipoprotein cholesterol was similarly reduced with treatment (WMD -0.64mmol/L, 95% CI -0.86 to -0.43). There was no evidence of heterogeneity for any of these analyses ($I^2=0$).

No adverse effects were reported.

**Authors' conclusions**

Phytosterols/stanols may offer an effective adjunct to the cholesterol lowering treatment strategy of familial hypercholesterolaemia patients.

**CRD commentary**

The review presented a clear research question and defined inclusion criteria. A number of sources were searched for relevant articles without language restrictions, although it was unclear whether any publication status restrictions were applied; no assessment of publication bias was reported. The data extraction and quality assessment procedures included measures to minimise error and/or bias, but it was unclear whether similar measures were applied to study selection.

Methodological quality assessment was reported as an overall score and used to exclude some trials from the review; details of the quality assessment of individual trials were not reported, but three of the four trials included in the analyses met all criteria. Appropriate analytical methods were used.

The authors' conclusions reflect the data presented and are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that phytosterols/stanols may offer an acceptable and effective hypocholesterolaemic treatment in children, where adherence to lipid lowering drugs and diet may be insufficient. They also stated that children and adults including plant sterol-enriched food products in their hypocholesterolaemic diets should be advised to also include sufficient amounts of fruits and vegetables, especially carotenoid-rich vegetables or fruits, in their diet.

**Research:** The authors did not specify any recommendations for future research.

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