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RESEARCH

Original Research

The Comparative Efficacy of Plant Sterols and Stanols on Serum Lipids: A Systematic Review and Meta-Analysis

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ABSTRACT

Background Plant sterols and stanols are plant steroids with a similar chemical structure and cellular function to human cholesterol, and are recommended as dietary modifiers of serum lipids. Plant sterols have a higher degree of absorption than plant stanols, suggesting differential efficacy between the two.

Design A meta-analysis of randomized controlled trials was performed to summarize direct comparisons between the effect of plant sterols vs plant stanols on serum lipid levels in healthy patients and patients with hypercholesterolemia.

Methods A systematic literature search of MEDLINE, EMBASE, Cochrane CENTRAL, and the Natural Medicines Comprehensive Database was conducted from January 1950 through January 2009. Trials were included in the analysis if they were randomized controlled trials evaluating the effect of plant sterols vs plant stanols in healthy patients or patients with hypercholesterolemia who reported efficacy data on total, low-density lipoprotein, and high-density lipoprotein cholesterols or triglycerides. The weighted mean difference (WMD) of the change from baseline (in mg/dL) with 95% confidence interval was calculated as the difference between the means in the plant sterol and plant stanol groups using a random-effects model.

Results Fourteen studies (n=531 patients) met the inclusion criteria. Upon meta-analysis, the results showed that there is no statistically or clinically significant difference between plant sterols and plant stanols in their abilities to modify total cholesterol (WMD −1.11 mg/dL [−0.0286 mmol/L], 95% confidence interval [CI] −4.12 to 1.90, P=0.47), low-density lipoprotein cholesterol (WMD −0.35 mg/dL [−0.0091 mmol/L], 95% CI −2.98 to 2.28, P=0.79), high-density lipoprotein cholesterol (WMD −0.28 mg/dL [−0.00073 mmol/L], 95% CI −1.18 to 0.62, P=0.54), or triglycerides (WMD −1.80 mg/dL [−0.0203 mmol/L], 95% CI −6.80 to 3.21, P=0.48).

Conclusions Plant sterols and plant stanols do not have statistically or clinically relevant differing effects on total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, or triglyceride levels. The selection of plant sterols vs plant stanols should then be based on potential differences in safety parameters and further study is required to elucidate such differences.

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Increased risk of developing coronary heart disease (CHD) is associated with elevated serum lipid levels, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, along with low levels of high-density lipoprotein (HDL) cholesterol (1). Because dietary modification is the first step toward improving serum lipid levels, the National Cholesterol Education Program Adult Treatment Panel III guidelines recommend increasing intake of plant sterols or stanols (2 g/day) to help achieve cholesterol treatment goals (1).

Plant sterols (including beta-sitasterol, campesterol, and stigmasterol) have similar structure and cellular function to cholesterol, and are present in vegetable oils, nuts, and seeds (2). Plant stanols (beta-sitastanol and campestanol) are saturated derivatives of sterols (3). Both decrease intestinal absorption of ingested cholesterol by displacing cholesterol from intestinal micelles, thereby reducing transluminal migration (2). A previous meta-analysis found that ingesting either plant sterols or stanols were able to reduce LDL cholesterol by as much as 11.3% when the data were pooled together (3).

Previous systematic reviews have grouped plant sterols and plant stanols together without regard to potential differences in comparative efficacy (3,4). Plant sterols have a higher bioavailability than plant stanols (5,6), which may suggest differences in the degree of cholesterol displacement in the intestinal micelles. Randomized controlled trials directly comparing plant sterols to plant stanols have yielded conflicting results (7-20). Therefore, a systematic review was conducted to evaluate the com-

parative efficacy of plant sterols vs plant stanols on serum lipid parameters.

METHODS

A systematic literature search of MEDLINE (from 1950), EMBASE (from 1990), Cochrane CENTRAL (indexed January 2009), and the Natural Medicines Comprehensive Database was conducted through January 2009. A search strategy was performed using the Medical Subject Headings and text keywords: sterol, stanol, sitosterol, sitostanol, beta-sitosterol, beta-sitostanol, phytosterol, phytostanol, stanol ester, sterol ester in combination with lipids, cholesterol, hypercholesterolemia, hypercholesterolemic, hyperlipidemia, hyperlipidemic, low-density lipoproteins, high-density lipoproteins, LDL cholesterol, HDL cholesterol, and triglycerides. For the MEDLINE search, the Cochrane Collaboration's Highly Sensitive Search Strategy sensitivity-maximizing version was used (21). The McMaster University Health Information Research Unit search strategy was used for the EMBASE search (22). No language restrictions were imposed. In addition, a manual search of references from primary or review articles was performed to identify additional relevant trials.

Trials were included in the analysis if they were randomized controlled trials comparing plant sterols and plant stanols in healthy or hypercholesterolemic patients and reported efficacy data (suitable for calculation of change from baseline) on at least one of the following lipid endpoints: total cholesterol, LDL cholesterol, HDL cholesterol, or triglyceride levels. Both parallel and crossover trials were eligible for inclusion. To be included, crossover studies needed to have at least a 2-week washout period or, if the washout was shorter or absent, needed to measure lipid levels at least 3 weeks after switching therapies. This allows for the effect of the previous therapy to dissipate, the effects of the newer therapy to manifest, and patients to reach new steady-state lipid levels (23). Trials evaluating multiple treatment arms were included by evaluating each pairwise comparison separately, but with the repeated groups' sample size divided evenly among the comparisons. Three investigators (D.M.S., S.S.M., C.I.C.) reviewed potentially relevant articles independently and abstracted necessary data with differences resolved through discussion. When applicable, efforts were made to contact investigators for clarification or additional data.

Statistical Analyses

The mean change in lipid parameters from baseline was treated as a continuous variable and the weighted mean difference (WMD) was calculated as the difference between the mean in the plant sterol and plant stanol groups. If mean change from baseline with some measure of deviation was not reported, the unadjusted difference from baseline to final measure and corresponding standard deviation was calculated using methods suggested by Follman and colleagues (24). Sensitivity analyses were also conducted to assess whether inclusion of studies with double-blinding, parallel design, diet modification, or enrolling patients with hypercholesterolemia would affect the results. A DerSimonian and Laird random-effects model was used to calculate the WMD and 95% confidence intervals (CIs) (25). Statistical heterogeneity was evaluated using the I^2 statistic (which assesses the degree of inconsistency across studies and ranges from 0% to 100%, with the higher percentage representing a higher likelihood of the existence of heterogeneity and a value >25% suggesting important heterogeneity is present) (26). Publication bias was assessed by visual inspection of funnel plots and Egger's weighted regression statistic P values, where values <0.05 indicate presence of publication bias. For analyses in which significant publication bias was detected, Trim-and-Fill analyses were conducted whereby theoretical studies are statistically imputed or removed (12). Statistics were performed using StatsDirect (version 2.7.8, 2008, StatsDirect Ltd, Cheshire, UK) and MIX for Meta-Analysis (version 1.7, 2008, Leon Bax, Sagamihara, Kanagawa, Japan). A P value of <0.05 was considered statistically significant.

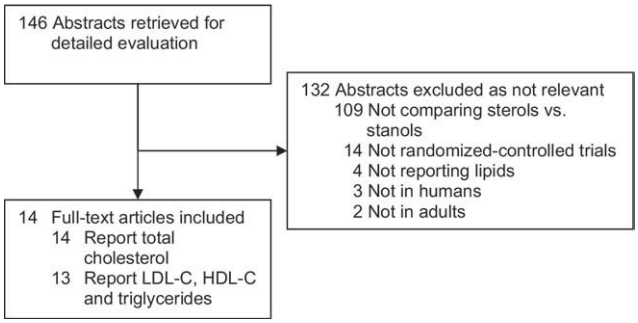

Figure 1. Flow diagram of identification, inclusion, and exclusion of studies comparing the effect of plant sterols vs plant stanols on serum lipid parameters. HDL-C=high-density lipoprotein cholesterol. LDL-C=low-density lipoprotein cholesterol.

RESULTS

Study Characteristics

A total of 14 randomized controlled trials (n= 531 patients) met all inclusion criteria (7-20). All 14 trials reported usable data for total cholesterol, whereas 13 trials (7-19) reported useable data for LDL cholesterol, HDL cholesterol, and triglycerides (Figure 1). Eleven trials (7,9-11,13-17,19,20) enrolled patients with hypercholesterolemia, whereas three trials (8,12,18) enrolled patients with either normal lipid levels or mild hypercholesterolemia. Patients were randomized to be treated with either plant sterol or plant stanol (dosing range 0.6 to 2.5 g/day) in various dosage forms (margarine, seed or canola oils, or yogurt) for a period of 3 to 16 weeks (Table 1). All but one trial (15) was double-blinded. Four were parallel trials (7,12,19,20) and 10 were crossover trials (8-11,13-18). Only three trials (14,16,17) required patients to undergo concurrent dietary modification. Manufacturers of plant sterol or plant stanol products funded eight out of 14 trials.

Quantitative Data Synthesis

Upon meta-analysis, the use of plant sterol compared to plant stanol did not significantly lower total (WMD −1.11

Table 1. Characteristics of randomized controlled trials comparing the effect of plant sterols vs plant stanols on serum lipid parameters, including total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride (TG) levels

Author(s), (reference), year, (n)	Study design	Population	Follow-up (wk)	Baseline lipid level (mg/dL)[a]	Follow-up lipid level (mg/dL)[a]	Sterol dosing	Stanol dosing	Concurrent diet[b]
De Jong and colleagues (7), 2008 (n=30)	Double-blinded, parallel	Hypercholesterolemia	16	TC[c]: 223; 216 LDL-C[c]: 138; 133 HDL-C[c]: 50; 61 TG[c]: 155; 115	TC[c]: 213; 202 LDL-C[c]: 129; 118 HDL-C[c]: 51; 62 TG[c]: 143; 112	2.5 g/d in margarine (ester form)	2.5 g/d in margarine (ester form)	Usual diet
Kratz and colleagues (8), 2007 (n=17)	Double-blinded, crossover	Normal or heterozygous sitosterolemia	6	TC: 208 LDL-C: 107 HDL-C: 69 TG: 120	TC[c]: 191; 184 LDL-C[c]: 94; 89 HDL-C[c]: 69; 66 TG[c]: 116; 116	2 g/d in margarine	2 g/d in margarine	Usual diet
Hallikainen and colleagues (9), 2006 (n=39)	Double-blinded, crossover	Mild hypercholesterolemia	10	TC: 215 LDL-C: 132 HDL-C: 64 TG: 95	TC[c]: 202; 206 LDL-C[c]: 117; 121 HDL-C[c]: 60; 62 TG[c]: 117; 107	2 g/d in low erucic acid rapeseed oil-based spread	2.07 g/d in low erucic acid rapeseed oil-based spread	Usual diet
Noakes and colleagues (10), 2005 (n=40)	Double-blinded, crossover	Mild hypercholesterolemia	Average of first 3 weeks reported	TC: 252 LDL-C: 173 HDL-C: 55 TG: NR[f]	TC[c]: 243; 245 LDL-C[c]: 163; 165 HDL-C[c]: 57; 58 TG[c]: 116; 114	1.8 g/d in low-fat yogurt (ester form)	1.7 g/d in low-fat yogurt (ester form)	Usual diet
Ketomaki and colleagues (11), 2004 (n=5)	Double-blinded, crossover	Familial hypercholesterolemia	4	TC: 261 LDL-C: 186 HDL-C: 50 TG: 125	TC[c]: 233; 240 LDL-C[c]: 157; 160 HDL-C[c]: 53; 53 TG[c]: 119; 128	2 g/d in rapeseed oil spread	2 g/d in rapeseed oil spread	Usual diet
O'Neill and colleagues (12), 2004 (n=134)	Double-blinded, parallel	Normal or familial hypercholesterolemia	8	TC[d]: 224; 224/236 LDL-C[d]: 147; 148/146 HDL-C[d]: 51; 53/50 TG[d]: 127; 127/142	TC[d]: 215; 207/215 LDL-C[d]: 142; 129/138 HDL-C[d]: 51; 48/52 TG[d]: 115; 120/116	1.6 g/d in flora pro-active margarine	Low dose: 1.6 g/d in Benecol[g] light margarine; High dose: 1.6 g/d in Benecol light margarine and 1g/d in cereal bar	Usual diet
Noakes and colleagues (13), 2002 (n=46)	Double-blinded, crossover	Mild hypercholesterolemia	3	TC: 245 LDL-C: 170 HDL-C: 45 TG: 151	TC[c]: 231; 228 LDL-C[c]: 155; 152 HDL-C[c]: 47; 47 TG[c]: 148; 144	2.3 g/d in margarine with 31%-36% fat (ester form)	2.5 g/d in margarine with 31%-36% fat (ester form)	Usual diet
Vanstone and colleagues (14), 2002 (n=15)	Double-blinded, crossover	Familial hypercholesterolemia	3	TC: 252 LDL-C: 167 HDL-C: 36 TG: 224	TC[c]: 216; 217 LDL-C[c]: 140; 140 HDL-C[c]: 43; 44 TG[c]: 163; 167	1.8 g/d in butter (unesterfied form)	1.8 g/d in butter (unesterfied form)	Individually adjusted study diet

(continued on page 722)

Table 1. Characteristics of randomized controlled trials comparing the effect of plant sterols vs plant stanols on serum lipid parameters, including total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride (TG) levels (continued)

Author(s), (reference), year, (n)	Study design	Population	Follow-up (wk)	Baseline lipid level (mg/dL)[a]	Follow-up lipid level (mg/dL)[a]	Sterol dosing	Stanol dosing	Concurrent diet[b]
Nestel and colleagues (15), 2001 (n=22)	Single-blinded, crossover	Hypercholesterolemia	4	TC: NR LDL-C: NR HDL-C: NR TG: NR	TC[c]: 250; 244 LDL-C[c]: 161; 170 HDL-C[c]: 60; 61 TG[c]: 126; 118	2.4 g/d in cereal, bread, and canola oil-based margarine (ester form)	2.4 g/d in cereal, bread, and canola oil-based margarine (unesterified form)	Usual diet
Hallikainen and colleagues (16), 2000 (n=34)	Double-blinded, crossover	Mild to moderate hypercholesterolemia	4	TC: 242 LDL-C: 171 HDL-C: 62 TG: 98	TC[c]: 220; 215 LDL-C[c]: 146; 142 HDL-C[c]: 60; 59 TG[c]: 91; 97	1.98 g/d in rapeseed oil based margarine	1.92 g/d in rapeseed oil based margarine	NCEP Step I Diet
Jones and colleagues (17), 2000 (n=15)	Double-blinded, crossover	Hypercholesterolemia	3	TC[c]: 247; 247 LDL-C[c]: 166; 168 HDL-C[c]: 38; 36 TG[c]: 223; 212	TC[c]: 214; 223 LDL-C[c]: 143; 154 HDL-C[c]: 36; 36 TG[c]: 158; 164	1.84 g/d in margarine (esterified form)	1.84 g/d in margarine (esterified form)	Study diet—prepared fixed intake North American solid food diet
Westrate and Meijer (18), 1998 (n=95)	Double-blinded, crossover	Normal or mild hypercholesterolemia	3.5	TC[c]: 184; 186 LDL-C[c]: 113; 115 HDL-C[c]: 48; 48 TG[c]: 97; 102	TC[c]: 185; 188 LDL-C[c]: 116; 115 HDL-c 49; 49 TG[c]: 97; 101	3.25 g/d in margarine fortified with ester from soybean	2.75 g/d in margarine fortified with sitostanol-ester from Benecol	Usual diet
Miettinen and Vanhanen (19), 1994 (n=23)	Double-blinded, parallel	Hypercholesterolemia	9	TC[e]: 245; 228/214 LDL-C[e]: 158; 144/132 HDL-C[e]: 58; 61/62 TG[e]: 145; 115/97	TC[e]: 247; 230/216 LDL-C[e]: 160; 145/132 HDL-C[e]: 59; 61/65 TG[e]: 144; 114/96	0.7 g/d in rapeseed oil mayonnaise	0.7 g/d in rapeseed oil mayonnaise (unesterified); 0.8 g/d in rapeseed oil mayonnaise (esterified)	NR
Vanhanen and Miettinen (20), 1992 (n=16)	Double-blinded, parallel	Hypercholesterolemia	9	TC[c]: 232; 219 LDL-C: NR HDL-C: NR TG: NR	TC[c]: 223; 218 LDL-C[c]: NR HDL-C[c]: NR TG[a]: NR	0.625 g/d in rapeseed oil (sitosterol)	0.630 g/d in rapeseed oil (sitostanol)	NR

[a]To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.026. To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.6. Cholesterol of 200 mg/dL=5.2 mmol/L. To convert mg/dL triglyceride to mmol/L, multiply mg/dL by 0.011. To convert mmol/L triglyceride to mg/dL, multiply mmol/L by 88.6. Triglyceride of 159 mg/dL=1.80 mmol/L.

[b]Diets applied in both groups: National Cholesterol Education Program (NCEP) Step 1 diet: total fat <30% of total energy, saturated fat <10% of total energy, <300 mg/d dietary cholesterol.

[c]Presented as sterol value; stanol value.

[d]Presented as sterol value; low dose/high dose stanol values.

[e]Presented as sterol value; unesterified/esterified stanol values.

[f]NR=not reported.

[g]McNeil Nutritionals, Fort Washington, PA.

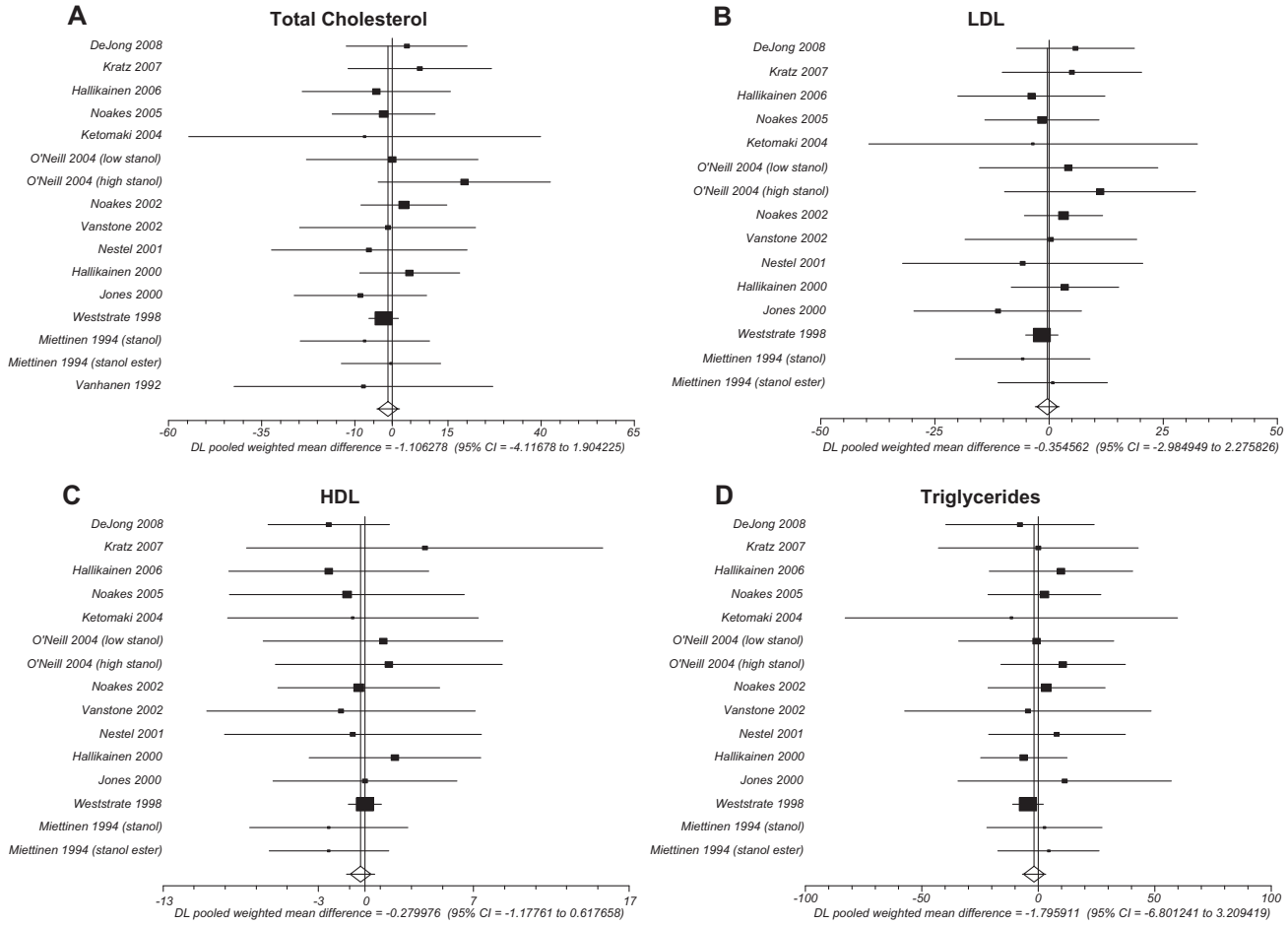

Figure 2. Forest plots depicting the effect of plant sterols vs stanols on total cholesterol (A), low-density lipoprotein cholesterol (B), high-density lipoprotein cholesterol (C), and triglycerides (D). The squares represent individual studies, and the size of the square represents the weight given to each study in the meta-analysis. Error bars represent 95% confidence intervals (CIs). The diamonds represent the pooled results. The solid vertical line extending upward from zero is the null value. DL=DerSimonian and Laird's random-effects model. HDL-C=high-density lipoprotein cholesterol. LDL-C=low-density lipoprotein cholesterol. *Negative values for total cholesterol, LDL-C, and triglycerides and positive values for HDL-C favor plant sterols.

mg/dL [−0.0286 mmol/L], 95% CI −4.12 to 1.90, P=0.47), low-density lipoprotein cholesterol (WMD −0.35 mg/dL [−0.0091 mmol/L], 95% CI −2.98 to 2.28, P=0.79), high-density lipoprotein cholesterol (WMD −0.28 mg/dL [−0.00073 mmol/L], 95% CI −1.18 to 0.62, P=0.54), or triglycerides (WMD −1.80 mg/dL [0.0203 mmol/L], 95% CI −6.80 to 3.21, P=0.48) (see Figure 2) (negative values for total cholesterol, LDL cholesterol, and triglycerides and positive values for HDL cholesterol favor plant sterols). No statistical heterogeneity was observed in any of the lipid endpoint analyses (I^2=0% for all).

Review of funnel plots (not shown) and the Egger's weighted regression statistic P values suggested a low potential for publication bias for the total cholesterol, LDL cholesterol, and HDL choleseterol analyses (P>0.44 for all). Although an asymmetrical funnel plot and an Egger's P=0.03 suggested a higher likelihood of publication bias in the triglyceride analysis, results of the Trim and Fill analysis again suggested no significant difference between plant sterols and stanols (WMD −3.51 mg/dL [−0.09 mmol/L), 95% CI −8.19 to 1.16) (see Figure 3).

Subgroup and sensitivity analyses are presented in Table 2. No noteworthy changes in the meta-analysis' conclusions were seen in any of these analyses.

DISCUSSION

Meta-analysis of 14 randomized controlled trials evaluating the effect of plant sterols vs plant stanols at doses of 0.6 to 2.5 g/day in healthy patients and patients with hypercholesterolemia showed no significantly different effects between the two on total cholesterol, LDL cholesterol, HDL cholesterol, or triglyceride levels. The subgroup and sensitivity analyses revealed no difference in lipid effects when using plant sterols or plant stanols regardless of the trial design (parallel or crossover), type

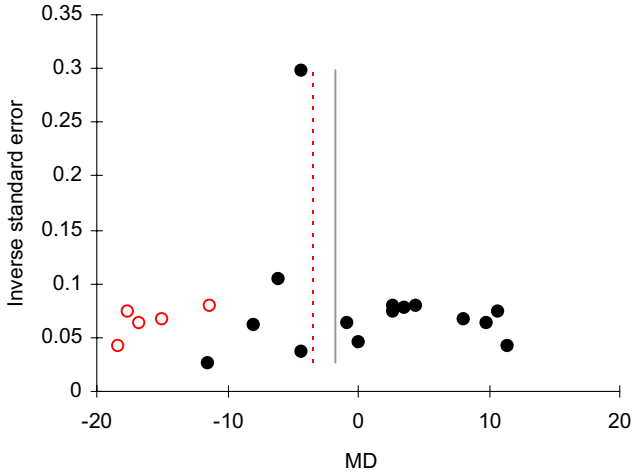

Figure 3. Trim-and-Fill Funnel plot of trials comparing the effect of plant sterols vs plant stanols on serum lipid parameters. The solid circles represent actual identified studies and open circles represent imputed studies from a trim-and-fill analysis. The vertical lines represent the effect of plant sterols or stanols on triglycerides observed before (solid line) and after (dotted line) allowing for publication bias. Studies favoring plant sterols fall to the left and plant stanols to the right of the pooled effect line(s). MD=mean difference.

of patient population (healthy or hypercholesterolemic), or dietary status (concurrent diet modification or usual diet).

Although not evaluated in this meta-analysis, several well-controlled trials suggest that the consumption of plant sterols results in increased serum plant steroid concentrations in human subjects, whereas the use of plant stanols does not (16,18,27,28). Fransen and colleagues (29) found that serum sitosterol and campesterol concentration (cholesterol standardized) increased by 22% and 103%, respectively, with long-term plant sterol consumption and decreased by 18% and 11% with plant stanol consumption. In patients with phytosterolemia (a rare, autosomal inherited defect in intestinal cholesterol transport proteins causing a hyperabsorption of plant steroids, mostly in the absence of hypercholesterolemia), elevated serum concentrations of plant sterols have been implicated as a risk factor for premature athersclerosis and CHD (30-32). Whether elevated plant sterol concentrations are risk factors for CHD in patients without phytosterolemia is still debatable. Assmann and colleagues (33) conducted a nested case-control study to explore this question further and found that among men with a 10-year absolute CHD risk of 20% or higher, elevated sitosterol concentrations were associated with an additional threefold increase in the incidence of coronary events ($P=0.032$). Based upon the theoretically increased CHD risk in both patients with and without phytosterolemia due to elevated serum plant sterol concentrations (5), and the comparable efficacy on lipid parameters, plant stanols may be preferred. Ingestion of plant stanols may increase serum stanol concentrations by nearly 200%, but the relationship between serum stanols and CHD risk is unknown (31). Further study is required to make definitive judgments on CHD risk effects between the plant sterols and plant stanols. Currently, both plant sterol and stanol products are available and show similar efficacy on lipid lowering. Future studies regarding the comparative safety of plant sterols and stanols may shift consumer preferences and, thereby, influence manufacturing practices.

There are some limitations with this meta-analysis that should be considered when evaluating the clinical relevance of the results. First, the duration of follow-up in more than half of the trials included in the meta-analysis was short (4 weeks or less), leaving doubt as to the long-term comparative efficacy of plant sterols vs stanols. Whereas the durations of trials may be sufficient to assess initial changes in serum lipid levels, they are inadequate to determine the effect on the terminal outcome of CHD risk. Lipid-modifying effects of plant sterols or stanols are intended to reduce CHD risk, but with the potential for chronic elevations of serum plant sterols to increase CHD risk, this area requires further follow-up to determine the balance of harm to benefit. Although most trials in this meta-analysis evaluated doses of plant sterols or stanols of approximately 2 g/day (consistent with National Cholesterol Education Program Adult Treat-

Table 2. Results of meta-analysis of randomized controlled trials evaluating plant sterols vs stanols on serum lipid parameters[a]

Study detail	Total cholesterol (mg/dL)[b]	Low-density lipoprotein cholesterol (mg/dL)[b]	High-density lipoprotein cholesterol (mg/dL)[b]	Triglycerides (mg/dL)[c]
	← *mean difference (95% confidence interval)* →			
All studies	−1.11 (−4.12-1.90)	−0.35 (−2.98-2.28)	−0.28 (−1.18-0.62)	−1.80 (−6.80-3.21)
Fixed effect	−1.11 (−4.12-1.90)	−0.35 (−2.98-2.28)	−0.28 (−1.18-0.62)	−1.80 (−6.80-3.21)
Excluding studies not double-blinded	−1.04 (−4.07-1.99)	−0.30 (−2.94-2.34)	−0.27 (−1.18-0.63)	−2.09 (−7.17-2.99)
Excluding crossover studies	1.28 (−6.57-9.13)	2.42 (−4.45-9.29)	−1.70 (−4.05-0.66)	2.70 (−9.53-14.94)
Excluding studies with healthy patients	−0.82 (−5.82-4.17)	0.23 (−4.02-4.48)	−1.26 (−2.99-0.48)	1.24 (−7.35-9.83)
Studies with diet modification	−0.31 (−10.07-9.44)	−0.53 (−9.27-8.22)	0.57 (−3.08-4.23)	−3.79 (−20.17-12.60)
Studies without diet modification	−1.90 (−4.35-1.98)	−0.34 (−3.10-2.42)	−0.33 (−1.26-0.59)	−1.59 (−6.85-3.67)

[a]A DerSimonian and Laird random-effects model was used in calculating the weighted mean difference and its 95% confidence interval. Negative values for total cholesterol, low-density lipoprotein cholesterol, and triglycerides and positive values for high-density lipoprotein cholesterol favor sterols.
[b]To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.026. To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.6. Cholesterol of 200 mg/dL=5.2 mmol/L.
[c]To convert mg/dL triglyceride to mmol/L, multiply mg/dL by 0.011. To convert mmol/L triglyceride to mg/dL, multiply mmol/L by 88.6. Triglyceride of 159 mg/dL=1.80 mmol/L.

ment Panel III recommendations [1]), two of the included trials (19,20) evaluated doses <1 g/day. The effects of plant sterols and stanols on serum lipid levels have previously been established as dose-dependent (34), so the inclusion of lower-dose trials may potentially skew results. However, the low doses were common to both the plant sterol and stanol groups, so alterations in results would be unlikely. Serum stanol and sterol levels would likely be useful safety monitoring parameters, but they were not evaluated due to inconsistent and sparse reporting within the randomized controlled trials. With any meta-analysis, the potential for publication bias must be evaluated. For total cholesterol, LDL cholesterol, and HDL cholesterol analyses, nonsignificant Egger's statistic *P* values suggest that the presence of publication bias was unlikely. Also, although publication bias was detected in the triglycerides analysis, Trim-and-Fill analysis did not significantly alter results.

CONCLUSIONS

Based on the current literature it appears that plant sterols and stanols have similar effects on total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride levels. Further study is required to determine the long-term efficacy of plant sterols and plant stanols, on not only lipid parameters but on CHD risk. In addition, long-term safety must also be established. At this time, effects on lipid parameters appear similar, so the decision of which to use should be based on safety considerations, which may be determined upon further research.

STATEMENT OF POTENTIAL CONFLICT OF INTEREST: No potential conflict of interest was reported by the authors.

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