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Systematic Review/Meta-analysis

The Impact of Dietary Changes and Dietary Supplements on Lipid Profile

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ABSTRACT

With a growing number of dietary interventions that claim to improve lipid profile, it is important to ensure that these claims are evidence based. The objective of this study was to make recommendations for dietary regimens by analyzing their effectiveness and the level of evidence. We searched MEDLINE as well as the Cochrane Database of Systematic Reviews for nutritional studies. Meta-analyses and randomized controlled trials published in English and including data on the effect on blood lipid levels were used. Randomized controlled trials were included if they were at least 4 weeks in duration and had a minimum of 50 participants. We identified 22 different dietary interventions and reviewed 136 studies published between January 1990 and December 2009 that met our inclusion criteria. Our literature review showed that to improve lipid profile, the following regimens can be recommended fully: Mediterranean and Portfolio diets; low-fat diet; diet high in soy protein, fibre, or phytosterols; whole grain foods, and omega-3 fatty acid supplementation. The consumption of nuts, a diet high in carbohydrates and protein, green tea, and red wine, as well as the supplementation with policosanol and red yeast rice extract, can be considered for improvement of the lipid profile, while the supplements of guggulipid, garlic, chromium, vitamin C, magnesium-pyridoxal-phosphate-glutamate, tocotrienols, and absorbitol cannot be recommended.

RÉSUMÉ

En raison du nombre croissant d'interventions diététiques qui prétendent améliorer le profil lipidique, il est important de s'assurer que ces affirmations soient basées sur des données probantes. L'objectif de cette étude était de faire des recommandations sur les régimes alimentaires en analysant leur efficacité et le niveau de preuve. Nous avons cherché des études nutritionnelles aussi bien dans MEDLINE que dans les revues systématiques de la base de données Cochrane. Des métaanalyses et des essais cliniques aléatoires publiés en anglais et incluant des données des effets sur les niveaux lipidiques sanguins étaient utilisés. Les essais cliniques aléatoires étaient inclus s'ils étaient d'au moins quatre semaines et s'ils comportaient un minimum de 50 participants. Nous avons trouvé 22 interventions diététiques différentes et revu 136 études publiées entre janvier 1990 et décembre 2009 qui ont répondu à nos critères d'inclusion. Notre revue de la littérature a montré que pour améliorer le profil lipidique, les régimes suivants peuvent tous être recommandés : les diètes méditerranéenne et Portfolio; le régime hypolipidique; le régime riche en protéines de soya, les fibres et les phytostérols; les aliments à grains entiers et la supplémentation en acides gras oméga-3. La consommation de noix, un régime riche en glucides et en protéines, le thé vert et le vin rouge, de même que la supplémentation en policosanol et l'extrait de levure de riz rouge peuvent être considérés dans l'amélioration du profil lipidique, tandis que les suppléments de guggulipides, d'ail, de chrome, de vitamine C, de glutamate de pyridoxal-5'-phosphate de magnésium, de tocotriénols et d'absorbitol ne peuvent pas être recommandés.

Dyslipidemia is one of the major risk factors for cardiovascular disease, the leading cause of death in North America. The overall prevalence of dyslipidemia between the ages of 45 and 84 years is more than 50%.[1] According to the Canadian cholesterol guidelines, lifestyle changes remain the cornerstone for the treatment of dyslipidemia and prevention of cardiovascular disease in adults. The dietary recommendations for dyslipidemia include reducing saturated fats and refined sugars; increasing fruits, vegetables, and fibres; and increasing consumption of omega-3 and omega-6 polyunsaturated fats in the diet.[2] Despite clinical evidence of benefits from lipid-lowering medications, more than 50% of individuals with dyslipidemia are

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Table 1. Numbers of randomized controlled trials and meta-analyses of dietary interventions

Dietary interventions (total n = 22)	Randomized controlled trials		Meta-analyses n	Total
	Double blinding	n		
Dietary changes (n = 12)				
Soy protein	Yes	15	3	18
High-fibre diet	Yes*	11	3	14
Phytosterols (plant sterols and stanols)	Yes	7	2†	8†
Whole grain foods	Yes	2	1	3
Nuts	No	2‡	0	2‡
Green tea	Yes	1	0	1
Red wine	No	1	0	1
Low-fat diet	No¶	12	6	18
Mediterranean diet	No¶	8‡	0	8‡
Portfolio diet	No	3	0	3
High-carbohydrate diet	No	2§	0	2§
High-protein diet	No	2§	0	2§
Dietary supplements (n = 10)				
Omega-3 fatty acids	Yes	22	1	23
Garlic (*Allium sativum*)	Yes	8	4	12
Policosanol	Yes	9	1†	10†
Red yeast rice extract	Yes	4‖	1	5
Guggul	Yes	2	0	2
Vitamin C	Yes	2	0	2
Chromium	Yes	1	0	1
MPPG	Yes	1	0	1
Tocotrienols	Yes	1	0	1
Absorbitol	Yes	1	0	1
Duplicated study†		2	1	1
Total		115	21	136

MPPG, magnesium-pyridoxal-5′-phosphate-glutamate.
* Except 1 large multicentre randomized controlled trial (RCT).
† Duplicated study occurred in both phytosterols and policosanol.
‡ Duplicated study occurred in both nuts and Mediterranean diet.
§ Duplicated study occurred in both high-carbohydrate diet and high-protein diet.
¶ Except 1 double-blinded RCT.
‖ Except 1 large multicentre RCT and 1 RCT for patients with statin intolerance.

not treated phamacologically.[1,3] The incidence of side effects of lipid-lowering medications is estimated to be 5% to 10%.[4] Furthermore, 2% of patients with dyslipidemia are intolerant of any type of medication.[5] Thus, dietary changes and dietary supplements become a potentially safe and cost-effective alternative. In addition, increasing numbers of individuals want to improve their lipid profile by integrating the dietary interventions with pharmacologic treatment.[6,7] It is, therefore, important to objectively review the level of evidence, efficacy, and safety of these dietary interventions.

Methods

Study search

The search was restricted to studies published in English-language journals, conducted in adults, and reported to affect blood lipid levels. We first used the terms "lipid," "dietary," and "RCT" or "meta analyses" in MEDLINE to identify studies published between January 1990 and December 2009. The first search produced a total of 1787 article abstracts, from which 22 dietary interventions (Table 1) and 109 studies that met the inclusion criteria were identified. According to the individual dietary interventions, a second search for review papers from MEDLINE published from January 2000 through December 2009 was conducted with the terms "review" and "lipid" in addition to the type of dietary intervention. It produced a total of 293 review article abstracts, from which 39 review articles that met the inclusion criteria were identified. Using the terms "dietary supplement" or "dietary intervention," we also searched review articles from the Cochrane Database of Systematic Reviews, which produced a total of 68 review article abstracts, from which we identified 5 review articles meeting the search criteria. There were 41 and 26 studies that met the inclusion criteria and were retrieved from searching the bibliographies of MEDLINE and Cochrane Database review articles, respectively, from which an additional 22 and 5 studies were included, respectively. In all, 136 studies were reviewed.

The flow diagram for the study search is shown in Figure 1, and the details of the search strategy are shown in Online Appendix S1 and Table 1.

Because of the large number of articles, we selected only review articles published in MEDLINE between January 2000 and December 2009 and nonreview articles published between January 1990 and December 2009.

Study selection

Studies included were placebo-controlled RCTs and meta-analyses. The majority of the RCTs were double blind and placebo controlled (RCTs-DB), large, and/or multicentre. Only a few placebo-controlled RCTs lacked double blinding. The inclusion criteria for RCTs were number of participants $\geq$ 50, 4 weeks, and data on blood lipid levels. The studies included in the meta-analysis were placebo-controlled RCTs with duration of intervention $\geq$ 3 weeks. The vast majority of

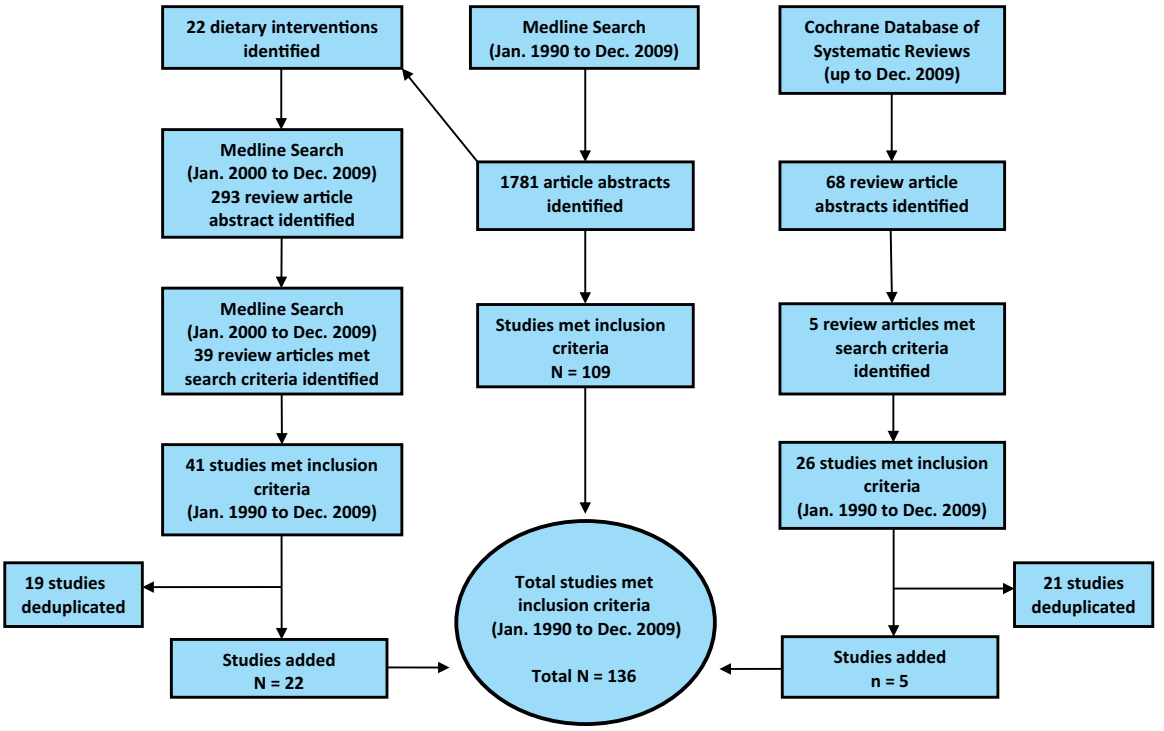

Figure 1. Flow diagram for study search. We first searched MEDLINE to identify studies between January 1990 and December 2009 that were reported to have an effect on blood lipid levels. The first search produced a total of 1787 article abstracts, from which 22 dietary interventions and 109 studies that met inclusion criteria were identified. According to the individual dietary intervention, a second search for review papers from MEDLINE published from January 2000 to December 2009 was conducted. It produced a total of 293 review article abstracts, from which 39 review articles meeting our search criteria were identified. We also searched for review articles published up to December 2009 in the Cochrane Database of Systematic Reviews (CDSR). The CDSR search produced a total of 68 review article abstracts, from which 5 review articles meeting search criteria were identified. There were 41 and 26 studies that met the inclusion criteria and were retrieved from searching the bibliographies of MEDLINE and CDSR review articles, respectively, from which an additional 22 and 5, respectively, were included after duplicates were removed. Therefore, a total of 136 studies were fully reviewed.

subjects were healthy adults or patients with hyperlipidemia, coronary artery disease (CAD), and/or CAD risk factors such as diabetes mellitus. The dropout rate for participants was restricted to ≤ 10%. Two of us independently reviewed and selected these publications from the article abstracts that met our inclusion criteria. If it was unclear whether an article was appropriate for inclusion, the full-text version was reviewed. Full-text articles that met the inclusion criteria were retrieved. The numbers of RCTs and meta-analyses for each individual dietary intervention are shown in Table 1.

Results

Dietary changes

We identified 12 types of dietary changes reported to have effect on serum lipid profiles (Table 1). Their effects on serum lipid profiles are summarized in Tables 2 through 7.

Soy protein and isoflavones. Isoflavones comprise a class of organic compounds related to the isoflavonoids. It has been shown that isoflavones may interact with estradiol to enhance endothelial function.[8] Whether daily consumption of soy protein with isoflavones can result in positive vascular effects in healthy postmenopausal women is still controversial.[9,10] Soybeans are the most common source of isoflavones in food. A large number of RCTs-DB,[11-20] as well as 3 meta-analyses,[21-23] have reported that daily consumption of either 30 to 50 g soy protein powder, which contains about 100 to 200 mg isoflavones, or 50 to 100 mg isolated soy isoflavones, in addition to a usual diet, lowered total cholesterol (TC) by 2% to 10% and low-density lipoprotein cholesterol (LDL-C) by 3% to 11%.[11-23] However, there was no significant effect on either high-density lipoprotein cholesterol (HDL-C)[11,12,14,16,17,19,20,23-30] or triglycerides (TGs)[12-14,16-20,24-30] in the majority of the studies. The effect of soy protein and isoflavones on serum lipid profile in clinical trials is summarized in Table 2.

High–soluble-fibre diet. There are 2 major groups of dietary fibre, insoluble structural fibre and soluble natural gel-forming fibre, such as oats, psyllium, pectin, and guar gum. For example, 60 g of uncooked oatmeal and 1 tablespoon psyllium seeds contains 6 g and 5 g of soluble fibre, respectively. Three meta-analyses,[31-33] 1 large multicentre RCT,[34] as well as a number of RCTs-DB[35-44] have shown that a diet containing 5 to 15 g soluble fibre resulted in reductions of TC and LDL-C by 2% to 12% and 5% to 20%, respectively.[31-33,35-44] There was no significant difference in the lipid-lowering effects between dosages of soluble fibre ranging from 5 to 15 g.[36,39,41] The majority of these studies did not show any beneficial

Table 2. The effect of soy protein and isoflavones on serum lipid profile in clinical trials

	Participants					Intervention & daily dose		Result (Δ%)			
Author (year)	N	Sex	Characteristics	Design	Duration	Soy protein (g)	Isoflavones (mg)	TC	LDL-C	TG	HDL-C
Taku (2007)[23]	430	M/F	Hyperlipidemia	Meta	4-12 wk	29.0-133.0	0	−5.7	−5.0	NS	+3.0
						29.0-133.0	1.6-318.0	−1.8	−3.0	NS	NS
Reynolds (2006)[22]	1756	M/F	Hyperlipidemia	Meta	3-52 wk	20.0-106.0	2.0-192.0	−2.5	−2.8	−4.8	+1.5
Anderson (1995)[21]	564	M/F	Hyperlipidemia	Meta	4-12 wk	17.0-140.0	NA	−9.3	−12.9	−10.5	+2.4
Welty (2007)[20]	60	F	Healthy-PM	RCT-DB	8 wk	25.0	101.0	NS	−11.0	NS	NS
Hall (2006)[25]	117	F	Healthy-PM	RCT-DB	8 wk	0	50.0	NS	NS	NS	NS
Hermansen (2005)[26]	100	M/F	Hyperlipidemia	RCT-DB	24 wk	30.0	100.0	NS	NS	NS	NS
Ma (2005)[30]	159	M/F	Hyperlipidemia	RCT-DB	5 wk	31.5	120.0	NS	NS	NS	NS
Hoie (2005)[15]	121	M/F	Hyperlipidemia	RCT-DB	8 wk	25.0	101.0	−3.4	−5.4	NS	NS
Puska (2004)[17]	143	F	Hyperlipidemia-PM	RCT-DB	8 wk	41.4	100.0	−5.2	−7.6	NS	NS
Nestel (2004)[16]	80	M/F	Healthy	RCT-DB	12 wk	0	40.0	NS	−9.5	NS	NS
Kreijkamp-Kaspers (2004)[29]	202	F	Healthy-PM	RCT-DB	1 y	25.6	99.0	NS	NS	NS	NS
Dalais (2003)[13]	106	F	Healthy-PM	RCT-DB	3 mo	40.0	118.0	NS	−5.9	−20.0	NS
Teede (2001)[18]	213	M/F	Healthy	RCT-DB	3 mo	40.0	118.0	NS	NS	−16.0	NS
Gardner (2001)[122]	94	F	Hyperlipidemia-PM	RCT-DB	12 wk	42.0	0	−1.5	−9.5	NS	NS
						42.0	80.0	−6.2	−12.5	NS	NS
Crouse (1999)[12]	156	M/F	Healthy	RCT-DB	9 wk	25.0	62.0	−4.0	−6.0	NS	NS
Washburn (1999)[19]	51	F	Healthy-PM	RCT-DB	6 wk	20.0	NA	−6.0	−7.0	NS	NS
Baum (1998)[11]	61	F	Hyperlipidemia-PM	RCT-DB	6 mo	40.0	56.0	NS	−5.9	NS	+8.4
						40.0	90.0	NS	−5.3	NS	+7.0
Hodgson (1998)[27]	59	M/F	Healthy	RCT-DB	8 wk	0	55.0	NS	NS	NS	NS

F, women; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, men; Meta, meta-analysis; M/F, men and women; NA, not available; NS, not significant; PM, postmenopausal; RCT-DB, double blinded randomized control trial; TC, total cholesterol; TGs, triglicerides.

Table 3. The effect of soluble fibre on serum lipid profile in clinical trials

Author (year)	Participants			Design	Duration	Intervention	Daily dose (g)	Result (Δ%)			
	N	Sex	Characteristics					TC	LDL-C	TG	HDL-C
Anderson (2000)[31]	656	M/F	Hyperlipidemia	Meta	8-24 wk	Psyllium	10.2*	−4.0	−7.2	NS	NS
Brown (1999)[32]	2990	M/F	Hyperlipidemia DM-type 1	Meta	46 d*	Soluble fibre (oat, psyllium, or pectin)	9.5*	−7.0	−12.0	NS	NS
Olson (1997)[33]	404	M/F	Hyperlipidemia	Meta	35 d*	Psyllium	9.4*	−5.0	−9.0	NS	NS
Estruch (2009)[34]	772	M/F	CAD RF	RCT-LMC	3 mo	Soluble fibre	5.9	−4.5	−5.0	NS	NS
Salas-Salvado (2008)[41]	200	M/F	Overweight	RCT-DB	16 wk	Plantago ovate husk	6.0/9.0	NS	−7.0/−11.1	NS	NS
Zunft (2003)[44]	58	M/F	Hyperlipidemia	RCT-DB	6 wk	Carob fibre	15.0	−7.5	−10.5	−11.3	NS
Jenkins (2002)[142]	68	M/F	Hyperlipidemia	RCT-DB	1 mo	Soluble fibre (β-glucan or psyllium)	8.0	−2.1	NS	−5.2	NS
Tai (1999)[43]	83	M/F	Hyperlipidemia	RCT-DB	3 mo	Minolest (guar gum and psyllium)	16.5	−3.2	−5.4	NS	NS
Davidson (1998)[35]	286	M/F	Hyperlipidemia	RCT-DB	6 mo	Psyllium	10.2	−3.0	−5.3	NS	NS
MacMahon (1998)[39]	340	M/F	Hyperlipidemia	RCT-DB	12 wk	Soluble fibre (ispaghula husk)	7.0/10.5	−7.7/−8.9	−8.7/−9.7	NS	NS
Rodriguez-Moran (1998)[40]	125	M/F	DM-type 2	RCT-DB	6 wk	Psyllium	15.0	−11.7	−20.0	−50.0	+26.3
Jensen (1997)[38]	51	M/F	Hyperlipidemia	RCT-DB	6 mo	Mixed fibre (psyllium, pectin, guar gum)	15.0	−6.4	−10.5	NS	NS
Sprecher (1993)[42]	118	M/F	Hyperlipidemia	RCT-DB	16 wk	Psyllium	10.2	−5.8	−7.2	NS	NS
Haskell (1992)[36]	62	M/F	Hyperlipidemia	RCT-DB	4-12 wk	Mixed fibre (psyllium, pectin, and guar gum)	5.0/15.0	−8.3/−9.5	−5.6/−120.4	NS	NS

CAD, coronary artery disease; DM, diabetes mellitus; F, women; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, men; Meta, meta-analysis; M/F, men and women; NA, not available; NS, not significant; PM, postmenopausal; RCT-DB, double blinded randomized control trial; RCT-LMC, large-scale and multicentre randomized control trial; RF, risk factors; TC, total cholesterol; TGs, triglicerides.

*Mean value.

Table 4. Effect of phytosterols, oatmeal, nuts, green tea extract, and red wine on serum lipid profile in clinical trials

Author (year)	Participants			Design	Duration	Intervention	Daily dose (g unless otherwise indicated)	Result (Δ%)			
	N	Sex	Characteristics					TC	LDL-C	TG	HDL-C
Phytosterols											
Demonty (2009)[52]	6805	M/F	Healthy	Meta	1-20 mo	Phytosterols	2.15*	NA	−8.8	NA	NA
Chen (2005)[53]	1662	M/F	Hyperlipidemia	Meta	8 wk-2 y	Phytosterols	2.0-9.0	−7.7	−11.0	NS	NS
Earnest (2007)[46]	54	M/F	Hyperlipidemia	RCT-DB	12 wk	Phytosterols	2.6	−3.5	−5.0	NS	NS
Korpela (2006)[47]	164	M/F	Hyperlipidemia	RCT-DB	6 wk	Phytosterols	2.0	−6.5	−10.4	NS	NS
Maki (2003)[49]	112	M/F	Hyperlipidemia	RCT-DB	6 wk	Phytosterols	1.8	−2.3	−3.7	NS	NS
Tikkanen (2001)[50]	78	M/F	Hyperlipidemia	RCT-DB	15 wk	Phytosterols	1.25-5.0	−8.0	−13.0	NS	NS
Christiansen (2001)[45]	55	M/F	Hyperlipidemia	RCT-DB	6 mo	Phytosterols	1.25-3.0	−7.5	−11.6	NS	NS
Maki (2001)[48]	184	M/F	Hyperlipidemia	RCT-DB	5 wk	Phytosterols	1.1	−5.2	−7.6	NS	NS
						Phytosterols	2.2	−6.6	−8.1	−10.4	NS
Weststrate (1998)	100	M/F	Hyperlipidemia	RCT-DB	14 wk	Phytosterols	1.5-3.3	−(8.0-13.0)	−(8.0-13.0)	NS	NS
Oatmeal											
Kelly (2007)[54]	496	M/F	CAD	Meta	4-8 wk	Oat meal	30.0–80.0	−4.0	−4.5	NS	NS
Onning (1999)[56]	66	M	Hyperlipidemia	RCT-DB	5 wk	Oat milk	0.75 litres	−6.0	−6.0	NS	NS
Keenan (1991)[55]	145	M/F	Hyperlipidemia	RCT-DB	6 wk	Oat bran	56.0	−2.2	−3.9	NS	NS
Nuts											
Wien (2003)[57]	65	M/F	Overweight	RCT	24 wk	Almonds	84.0	NS	−7.0	NS	−6.0
Zambon (2000)[58]	55	M/F	Hyperlipidemia	RCT	6 wk	Walnuts	41.0–56.0	−4.1	−5.9	−5.8	NS
Green tea extract											
Hsu (2008)[59]	100	F	Overweight	RCT-DB	3 mo	Green tea extract	1.2	−2.3	−10.0	−6.0	+3.8
Red wine											
Hansen (2005)[60]	69	M/F	Healthy	RCT	4 wk	Red wine	M: 300 mL F: 200 mL	NS	NS	NS	+13.0

CAD, coronary artery disease; F, women; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, men; Meta, meta-analysis; M/F, men and women; NA, not available; NS, not significant; RCT, randomized control trial (not double blinded); RCT-DB, double blinded randomized control trial; TC, total cholesterol; TGs, triglicerides.

*Mean value.

Table 5. Effect of low fat diet on serum lipid profile in clinical trials

Author (year)	Participants N	Sex	Characteristics	Design	Duration	Intervention	Result (Δ%) TC	LDL-C	TG	HDL-C
Tang (1998)[63]	4768	M/F	Healthy	Meta	6 mo	AHA Step II diet*	−5.0	NS	NS	NS
Yu-Poth (1999)[64]	9276	M/F	Hyperlipidemia	Meta	6 wk-4 y	AHA Step I diet†	−10.0	−12.0	−8.0	NS
						AHA Step II diet	−13.0	−16.0	−8.0	−7.0
Howell (1998)[62]	8143	M/F	CAD RF	Meta	NA	AHA Step I diet	−5.0	−5.0	NA	NA
			CAD			AHA Step II diet	−7.7	−7.7	NA	NA
Garg (1998)[143]	133	M/F	DM-type 2 hyperlipidemia	Meta	2-6 wk	High-MUFA diet‡	−3.0	NS	−19.0	+4.0
Gardner (2005)[68]	120	M/F	Hyperlipidemia	RCT	4 wk	AHA Step I diet	−4.1	−4.6	+5.5	NS
Aquilani (1999)[66]	126	M/F	CAD	RCT	6 mo	Very low-fat diet (fat ≤ 20%)	−13.0	−18.0	−11.0	+29.0
						AHA Step II diet	−5.0	−6.0	−9.0	−4.0
Ginsberg (1998)[69]	103	M/F	Healthy	RCT-X§	8 wk	AHA Step I diet	−5.0	−7.0	NS	−7.0
						AHA Step II diet	−9.0	−11.0	NS	−11.0
Knopp (1997)[73]	444	M	Hyperlipidemia	RCT	1 y	Diet with fat 30%	−3.8	−6.3	NS	NS
						Diet with fat 26%	−10.4	−14.1	NS	NS
						Diet with fat 22%	−7.2	−9.6	+21.7	−3.4
						Diet with fat 18%	−9.0	−13.8	+31.8	−4.4
Walden (1997)[77]	409	M/F	Hyperlipidemia	RCT	6 mo	AHA Step II diet	−7.0	−8.0	NS	−6.4%
McCarron (1997)[74]	560	M/F	Hyperlipidemia DM-type 2	RCT-MC¶	10 wk	AHA Step I diet	−4.9	−4.3	−7.4	−2.4
						AHA Step II diet	−5.9	−15.0	−5.0	−3.4
Davidson (1996)[67]	89	M/F	Hyperlipidemia	RCT	8 wk	AHA Step I diet	−8.0	−10.0	NS	NS
Sarkkinen (1994)[76]	160	M/F	Hyperlipidemia	RCT	6 mo	AHA Step I diet§	−7.2	−7.7	NS	NS
						Monoene-enriched diet‖	−6.9	−6.6	NS	NS
						Low-fat diet§	NS	NS	NA	NA
Insull (1994)[72]	61	M/F	Healthy	RCT-DB	5 wk	Low-fat diet (fat 22–26%)	−11.0	−13.0	NS	−10.0
Hunninghake (1993)[71]	111	M/F	Hyperlipidemia	RCT	36 wk	AHA Step II diet	−5.0	−5.0	NS	−6.0
Anderson (1993)[65]	163	M/F	Hyperlipidemia	RCT	1 y	AHA Step I diet	−10.0	−14.0	NS	NS
Hellenius (1993)[70]	157	M	CAD RF	RCT	6 mo	AHA Step I diet	NS	−7.0	NS	NS

AHA, American Heart Association; CAD, coronary artery disease; DM, diabetes mellitus; F, women; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, men; Meta, meta-analysis; M/F, men and women; MUFA, cis-monounsaturated fatty acid (see footnote‡ below); NA, not available; NS, not significant; PM, postmenopausal; RCT, randomized control trial; RCT-DB, double blinded RCT; RCT-MC, multicentre RCT; RCT-X, RCT-crossover; RF, risk factors; TC, total cholesterol; TGs, triglicerides.

*Step II diet: total fat no more than 30% of total calories, saturated fat < 7% of total calories, and cholesterol < 200 mg/day; ratio of polyunsaturated to saturated fatty acid > 1.4:1.

†Step I diet: total fat no more than 30% of total calories, saturated fat no more than 10% of total calories, and cholesterol < 300 mg/day.

‡High cis-monounsaturated fatty acid (MUFA) diet: MUFA provides 22% to 32% of energy.

§RCT-X.

¶RCT-MC.

‖Energy percentage from fat (saturated:monounsaturated:polyunsaturated fatty acids) for AHA Step I diet, monoene-enriched diet, and low-fat diet are 32 (10:8:8), 34 (11:11:5), and 30 (12:8:3), respectively.

effect on TGs and HDL-C levels.[31-36,38,39,41-43] The effect of soluble fibre on serum lipid profile in clinical trials is summarized in Table 3.

Phytosterols (plant sterols and stanols). Phytosterols (plant sterols and stanols) occur naturally in small quantities in vegetable oils. The compounds inhibit intestinal cholesterol absorption, thereby significantly lowering TC and LDL-C. Several RCTs-DB studies[45-51] and 2 recent meta-analyses[52,53] have shown that a daily intake of 1 to 3 g phytosterols in addition to a usual diet reduced TC and LDL-C levels by 2% to 13% and by 4% to 13%, respectively. The effect of phytosterols on TG and HDL-C did not achieve significance in the majority of the studies.[45-47,49-52] These data are summarized in Table 4.

Oatmeal. Oatmeal is rich in dietary fibre, phytosterols, and other important micronutrients. A meta-analysis[54] as well as 2 RCTs-DB[55,56] have shown that uncooked oatmeal (average daily intake of 60 g) lowered LDL-C by 2% to 6% and TC by 4% to 6% compared with its control group diet. However, there were no significant effects on HDL-C and TG levels.[54-56] The effect of oatmeal on serum lipid profile in clinical trials is shown in Table 4.

Nuts. Two placebo-controlled RCTs that met our inclusion criteria have shown that a daily intake of either 80 g almonds or 50 g walnuts, replacing approximately 30% of the energy obtained from monounsaturated fat, reduced LDL-C by 5%. However, the effects on TC, TG, and HDL-C levels were inconsistent.[57,58] The data are shown in Table 4.

Green tea extract. One recent RCT-DB that met our inclusion criteria demonstrated that daily use of 1200 mg green tea extract for 3 months reduced TC, LDL-C, and TG levels by 2.3%, 10%, and 6%, respectively, with a 3.8% increase in HDL-C.[59] The effect of green tea extract on serum lipid levels in the clinical trial is shown in Table 4.

Table 6. Effect of high-carbohydrate diet and high-protein diet on serum lipid profile in clinical trials

Author (year)	Participants N	Sex	Characteristics	Design	Duration	Intervention	Result (Δ%) TC	LDL-C	TG	HDL-C
High-carbohydrate diet										
Retzlaff (1995)[75]	3	M/F	Hyperlipidemia	RCT	2 y	Carbohydrate intake < 45%	NA	NA	NS	NA
	7					Carbohydrate intake 45% to 51.9%	NA	NA	NS	NA
	2					Carbohydrate intake 52% to 59.9%	NA	NA	NS	NA
						Carbohydrate intake ≥ 60%	NA	NA	+31.0	NA
High-protein diet										
Swain (2008)[79]	1	M/F	Prehypertension hypertension	RCT	19 wk	Carbohydrate diet*	NA	−8.9	NS	−2.8
	6					Protein diet†	NA	−11.0	−16.2	−5.2
	4					Unsaturated fat diet‡	NA	−10.1	−9.2	NS
Farnsworth (2003)[78]	5	M/F	Overweight	RCT	16 wk	High-protein diet§	−9.5	NS	−23.0	+8.7
	7					Standard-protein diet¶	−5.6	NS	−10.0	+6.4

F, women; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, men; M/F, men and women; NA, not available; NS, not significant; RCT, randomized control trial; TC, total cholesterol; TGs, triglicerides.

* Carbohydrate diet: carbohydrate 58%, protein 15%, and fat 27% (saturated fat 6%, unsaturated 21%) of total energy.

† Protein diet: carbohydrate 48%, protein 25%, and fat 27% (saturated fat 6%, unsaturated 21%) of total energy.

‡ Unsaturated fat diet: carbohydrate 58%, protein 15%, and fat 37% (saturated fat 6%, unsaturated 31% by using olive oil, canola oil and olive oil spread) of total energy.

§ High-protein diet: 27% of energy as protein, 44% as carbohydrate, and 29% as fat.

¶ Standard-protein diet: 16% of energy as protein, 57% as carbohydrate, and 27% as fat.

Red wine. Only 1 recent RCT showed that moderate red wine consumption (300 mL for men and 200 mL for women daily) resulted in a 13% increase in HDL-C.[60] However, there were no significant reductions in TC, LDL-C, or TG levels. The effect of drinking red wine on serum lipid levels in the clinical trial is shown in Table 4.

Low-fat, high-carbohydrate and high-protein diets. American Heart Association (AHA) dietary guidelines recommend adapting its Step I diet as the starting point for patients who have high cholesterol levels and its Step II diet for people already at the Step I goals or for patients with a cholesterol level ≥ 6.19 mmol/L or who had a heart attack.[61] Three meta-analyses concluded that the AHA Step I diet and Step II diet effectively reduced TC and LDL-C by 5% to 10% after 6 weeks to 4 years.[62-64] A large number of RCTs have shown that a diet with from 18% to 30% of total energy intake as fat significantly reduced TC and LDL by 5% to 15%.[65-77] Beneficial effects of low fat intake on TGs[63,67-73,75,77] and HDL-C[63,64,67-73,75,77] were not supported by most studies. A fat intake of less than 18% of total energy did not produce any further benefit.[70] Several studies have shown that a high-protein diet (25% of total energy from protein) and a high-carbohydrate diet (50% to 60% of total energy from carbohydrate) lowered TC, LDL-C, and TGs by 5% to 10%.[78,79] However, an extremely high-carbohydrate diet (> 60% of total energy) increased TG levels.[75] The effects of a low-fat diet are summarized in Table 5. The data for high-carbohydrate and high-protein diets are shown in Table 6.

Mediterranean diet. The Mediterranean diet (Med-diet) is characterized by relatively high intake of total fat (25% to 35% of total calories); moderate to high intake of fish; low consumption of red meat; moderate alcohol intake; small amounts of dairy products; and high consumption of nonrefined grains, legumes, nuts, fruits, and vegetables. One large multicentre RCT, the PREDIMED study (PREvención con DIeta MEDiterránea),[80] and a number of other RCTs have shown that the Med-diet not only reduced TC and LDL-C by 5% to 15%[58,80-84] but also increased HDL-C by 3% to 15%.[80-83,85] Therefore, the Med-diet has been suggested as a better option for managing dyslipidemia than the AHA's Step I and Step II diets. Moreover, the Med-diet has been consistently shown to reduce cardiovascular mortality.[86,87] The effect of the Med-diet on serum lipid profile in clinical trials is summarized in Table 7.

Portfolio diet. The Portfolio diet is a dietary portfolio that combines various cholesterol-lowering foods in one diet. It is more effective than single dietary change, even if the effect is only additive.[68,88,89] It reduces TC and LDL-C levels by approximately 10% to 15%. The effect of the Portfolio diet on serum lipid levels is shown in Table 7.

Dietary supplements. Ten types of dietary supplements affecting serum lipid levels have been identified for the purpose of this review (Table 1). Their effects are summarized in Tables 8 through 10.

Omega-3 fatty acids. Nutritionally important omega-3 fatty acids include α-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid. One meta-analysis concluded that dietary omega-3 polyunsaturated fatty acids reduced overall mortality in patients with CAD, although the effect on serum lipid levels was not consistent.[90] Two large-scale RCTs, the JELIS (Japan EPA [eicosapentaenoic acid] Lipid Intervention Study) trial and the GISSI-Prevenzione trial (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico), have shown that 1 to 2 g per day of omega-3 fatty acids lowered TG levels by 3% to 9%. In addition, the total mortality was reduced by 20% to 30%. However, there was no significant change on TC, LDL-C, or HDL-C levels.[91,92] The JELIS trial further demonstrated that omega-3s and high fish consumption had an addi-

Table 7. Effect of Mediterranean diet and Portfolio diet on serum lipid profile in clinical trials

Author (year)	Participants			Design	Duration	Intervention	Control diet	Result (Δ%)			
	N	Sex	Characteristics					TC	LDL-C	TG	HDL-C
Mediterranean diet (Med-diet)											
Papadaki (2008)[85]	72	M/F	Healthy	RCT	9 mo	Med-diet*	Low fat diet	NS	NS	NS	+19.0
Estruch (2006)[80]	772	M/F	CAD RF	RCT-LMC	3 mo	Med-diet + VOO†	Low fat diet	−1.6	−3.5	−1.7	+5.7
						Med-diet + VOO + nuts 30 g/d	Low fat diet	−2.1	−2.3	−5.1	+1.9
Michalsen (2006)[144]	101	M/F	CAD	RCT	6 mo	Med-diet + statin	Low fat + statin	NS	NS	NS	NS
Vincent-Baudry (2005)[84]	212	M/F	CAD RF	RCT	3 mo	Med-diet	Low fat	−6.0	−11.3	−12.5	NS
Esposito (2004)[81]	180	M/F	Metabolic Syndrome	RCT	2 y	Med -diet	Regular diet	−5.8	NA	−8.9	+12
Jula (2002)[82]	120	M	Hyperlipidemia	RCT-DB	12 wk	Modified Med-diet†	Regular diet	−7.6	−10.8	NS	−4.9
Perez-Jimenez (2001)[83]	59	M/F	Healthy	RCT-X	4 wk	Med-diet	High-fat diet	−12.4	−16.4	NS	+8.0
Zambon (2000)[58]	55	M/F	Hyperlipidemia	RCT	6 wk	Med-diet	As control diet	−4.9	−5.5	−1.9	NS
						Med-diet with walnuts§		−8.9	−11.2	−7.7	NS
Portfolio diet											
Jenkins (2006)[88]	66	M/F	Hyperlipidemia	RCT	1 y	Portfolio diet§	Regular diet	−10.3	−12.8	−3.2	+13.5
Lukaczer (2006)[89]	59	F	Hyperlipidemia-PM	RCT	12 wk	Soy protein 30 g + phytosterols 4 g	Regular diet	−15.8	−14.8	−44.8	+5.6
Gardner (2005)[68]	120	M/F	Hyperlipidemia	RCT	4 wk	AHA Step I plus diet¶	AHA Step I diet	−7.9	−9.3	+7.7	NS

AHA, American Heart Association; CAD, coronary artery disease; F, women; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, men; M/F, men and women; NA, not available; NS, not significant; PM, postmenopausal; RCT, randomized control trial; RCT-DB, double blinded RCT; RCT-LMC, large-scale and multicentre randomized control trial; RCT-MC, multicentre RCT; RCT-X, RCT-crossover; RF, risk factors; TC, total cholesterol; TGs, triglicerides; VOO, virgin olive oil.

*Med-diet: Total fat (25% to 35% of total calories), mainly derived from olive oil rich in monounsaturated fatty acid (≥ 17% of total calories) and less from saturated fat (≤ 8% of total calories); moderate to high intake of fish (at least twice a week) such as salmon high in omega-3 fatty acids and poultry; low consumption of red meat (≤ 15% of total calories); moderate alcohol intake (300 mL and 200 mL red wine daily for men and women, respectively); small amounts of dairy products; and high consumption of nonrefined grains, legumes, nuts, fruits, and vegetables.

†Modified Med-diet: no more than 10% energy from saturated and *trans*unsaturated fatty acids; cholesterol intake no more than 250 mg/d; omega-3 fatty acid intake of plant origin (α-linolenic acid) and marine origin of at least 4 g/d and the ratio of omega-6 to omega-3 polyunsaturated fatty acids less than 4; and increased intakes of fruits, vegetables, and soluble fibre.

‡Walnuts: 41.0-56.0 g, about 35% of total energy.

§Portfolio diet: diets low in total fat (30% of total energy) and saturated fatty acids (6% of total energy), high in plant sterols (1.0 g/1000 kcal), soy protein (22.5 g/1000 kcal), viscous fibres (10 g/1000 kcal), and almonds (23 g/1000 kcal).

¶AHA Step I plus diet: AHA Step I plus 16 g soy protein, 1.4 cloves of garlic, and 5 g soluble fibre (more vegetables, legumes, and whole grains).

Table 8. Effect of omega-3 fatty acids on serum lipid profile in clinical trials

Author (year)	Participants			Design	Duration	Intervention	Daily dose (g)	Results (Δ%)			
	N	Sex	Characteristics					TC	LDL-C	TG	HDL-C
Bucher (2002)[90]	15,806	M/F	CAD	Meta	≥6 mo	EPA	0.3-6.0	NS	NS	NS	NA
						DHA	0.7-3.72				
						ALA	2.0				
Bowden (2009)[145]	87	M/F	ESRD	RCT-DB	6 mo	Fish oil capsule*	1.0	−8.9	−2.2	−12.6	+40.0
Kaul (2008)[104]	86	M/F	Healthy	RCT-DB	12 wk	Fish oil capsule	2.0	NS	NS	NS	NS
Svensson (2008)[99]	206	M/F	ESRD	RCT-DB	3 mo	PUFA	1.7	NS	NS	−4.8	NS
Saito (2008) [97]	14,981	M/F	Hyperlipidemia	RCT- LS	4.6 y	EPA	1.8	NS	NS	−8.6	NS
Yokoyama (2007)[92]	18,645	M/F	CAD & CAD RF	RCT- LS	4.6 y	EPA	1.8	NS	NS	−9.0	NS
Davidson (2007)[93]	254	M/F	Hypertriglyceridemia	RCT-DB	0.8 wk	Fish oil capsule	4.0	−3.5	NS	−23.2	+4.3
Harper (2006)[103]	56	M/F	CAD RF	RCT-DB	26 wk	ALA	3.0	+7.0	NS	NS	NS
Maki (2005)[146]	57	M/F	Low HDL-C	RCT-DB	6 wk	DHA	1.52	NS	NS	NS	NS
Dodin (2005)[147]	199	F	Healthy-PM	RCT-DB	1 y	Flaxseed	40.0	NS	NS	NS	NS
Lovegrove (2004)[95]	84	M/F	Healthy	RCT-DB	12 wk	Fish oil capsule	4.0	NS	NS	−9.0	+4.0
Woodman (2002)[101]	59	M/F	DM-type 2	RCT-DB	6 wk	EPA	4.0	NS	NS	−19.0	NS
						DHA	4.0	NS	NS	−15.0	NS
Bemelmans (2002)[102]	282	M/F	CAD RF	RCT-DB	2 y	ALA	6.3	NS	NS	+16.7	+3.9
Noone (2002)[96]	51	M/F	Healthy	RCT-DB	8 wk	50:50 CLA	3.0	NA	NS	−29.4	NS
						80:20 CLA	3.0	NA	NS	−24.9	NS
Riserus (2002)[148]	60	M/F	Overweight	RCT-DB	8 wk	CLA mixture	3.4	NS	NS	NS	−2.0
GISSI-Prevenzione (1999)[91]	11,324	M/F	Post MI	RCT-LS	3.5 y	Fish oil capsule	1.0	NS	NS	−3.4	NS
Von Schacky (1999)[105]	223	M/F	CAD	RCT-DB	2 y	Fish oil capsule	3.0–6.0	NS	+3.7	NS	NS
Johansen (1999)[149]	500	M/F	Post PTCA	RCT-DB	6 mo	Fish oil capsule	5.1	NS	NS	NS	NS
Singh (1997)[98]	360	M/F	Suspected acute MI	RCT-DB	1 y	EPA	1.08	−4.7	NA	−9.6	+9.9
Toft (1995)[100]	78	M/F	Hyperteion	RCT-DB	16 wk	Fish oil capsule	4.0	NS	NS	−23.5	+9.2
Leaf (1994)[106]	470	M/F	Post PTCA	RCT-DB	6 mo	Fish oil capsule	10.0	−8.6	NS	−41.0	NS
Bairati (1992)[150]	205	M/F	Post PTCA	RCT-DB	6 mo	Fish oil capsule	15.0	NS	NS	NS	NS

ALA, alpha-linolenic acid; CAD, coronary artery disease; CLA, conjugated linoleic acid, a cis-9,trans11-trans10,cis-12 isomeric blend (50:50) or a cis-9,trans11-trans10,cis-12 isomeric blend (80:20); DHA, docosahexanoic acid; DM, diabetes melitis; EPA, eicosapentaenoic acid; ESRD, end stage renal disease; F, women; GISSI Prevenzione, Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, men; Meta, meta-analysis; M/F, men and women; MI, myocardial infarction; NA, not available; NS, not significant; PM, postmenopausal; PTCA, percutaneous intraluminal coronary angioplasty; PUFA, cis-polyunsaturated fatty acids, containing 45% EPA +37.5% DHA; RCT, randomized control trial; RCT-DB, double blinded RCT; RCT-LS, large-scale RCT; RF, risk factors; TC, total cholesterol; TGs, triglicerides.

*Fish oil capsule 1 g, containing EPA 160 mg + DHA 100 mg.

tive protective effect, even in patients already on statin therapy. Numerous RCTs-DB have shown the beneficial effect of omega-3s on TG levels,[93-101] as well as on the overall mortality rate in patients with CAD.[90-92,98,102-105] The reported adverse effects of taking omega-3 fatty acids included gastrointestinal (GI) symptoms, skin rash, and itching.[92,93,106,107] The effects of omega-3 fatty acids on blood lipid levels are summarized in Table 8.

Red yeast rice extract. Red yeast rice extract is a medicinal agent prepared by using *Monascus purpureus* fermented with rice. Lovastatin (monacolin K), the first statin drug, occurs naturally in certain forms of red yeast rice. A number of studies, including 1 meta-analysis,[108] 1 large-scale RCT, and 2 RCTs-DB,[109,110] all support the beneficial effect of red yeast rice on blood lipid profile. A daily capsule of 1 to 2 g red yeast significantly lowered TC, LDL-C, and TGs by 10% to 44%, 7% to 25%, and 7% to 44%, respectively, and increased HDL-C by 0% to 17%. Furthermore, red yeast rice extract reduced the risk of major coronary events and total mortality by 30% to 50% in patients with a previous CAD.[108,111] It has to be pointed out that red yeast rice extract should be used with caution in subjects already on statin therapy, given that the dose of monacolin can vary greatly between products. Reported side effects included GI symptoms, myalgia, and minor creatine kinase and alanine aminotransferase increases.[109,111] The data are summarized in Table 9.

Policosanol. Policosanol is derived from sugar cane. A recent meta-analysis[53] and a majority of RCTs-DB[112-118] found that a daily dose of 5 to 10 mg policosanol produced a 12% to 20% reduction in TC and a 15% to 25% reduction in LDL-C and an 8% to 30% increase in HDL-C.[53] However, its impact on TGs is not consistent.[112-118] Its cholesterol-lowering efficacy has a dose-dependent pattern in the range of 5 to 20 mg daily.[53,113-115,117,118] However, a daily dose above 40 mg did not result in further improvement of the lipid profile.[115] The adverse effects include polyuria, polyphagia, insomnia, and headache.[119] The effect of policosanol on blood lipid levels in clinical trials is summarized in Table 9.

Guggulipid (gum guggul). Guggulipid is a resin produced by the mukul mirth, a tree native to western India. Guggulipid was studied in 2 RCTs-DB that met our inclusion criteria, and their results are contradictory.[120,121] Singh et al. have reported that a daily dose of 100 mg guggulipid significantly reduced serum TC by 11.7% and LDL-C by 12.5%.[120] In contrast, Szapary et al. reported small but significant increases of 4% in serum LDL-C levels.[121] The side effects include GI upset, headache, and skin hypersensitivity reaction.[121] The effects of guggulipid on blood lipid levels in these clinical trials are summarized in Table 10.

Table 9. Effect of red yeast rice extract and policosanol on serum lipid profile in clinical trials

Author (year)	Participants N	Sex	Characteristics	Design	Duration	Intervention	Daily dose (g)	Results (Δ%) TC	LDL-C	TG	HDL-C
Red yeast rice extract											
Liu (2006)[108]	9625	M/F	Hyperlipidemia	Meta	4-24 wk	Red yeast rice capsule	1.2-3.15	−14.2	−16.2	−17.8	+11.0
Becker (2009)[151]	62	M/F	Hyperlipidemia*	RCT	24 wk	Red yeast rice capsule	3.6	−15.0	−20.0	NS	NS
Lu (2008)[111]	4870	M/F	Hyperlipidemia	RCT-LMC	4.5 y	Red yeast rice capsule	0.6	−13.0	−20.0	−14.0	+4.2
Lin (2005)[110]	79	M/F	Hyperlipidemia	RCT-DB	00-8 wk	Red yeast rice capsule	1.2	−21.5	−27.7	−15.8	NS
Heber (1999)[109]	83	M/F	Hyperlipidemia	RCT-DB	12 wk	Red yeast rice capsule	2.4	−16.8	−22.3	−13.3	NS
Policosanol											
Chen (2005)[53]	1528	M/F	Hyperlipidemia	Meta	8 wk-2 y	Policosanol	0.005-0.04	−16.2	−23.7	NS	+10.6
Berthold (2006)[152]	143	M/F	Hyperlipidemia	RCT-DB	12 wk	Policosanol	0.01-0.08	NS	NS	NS	NS
Lin (2004)[153]	58	M/F	Hyperlipidemia	RCT-DB	4 wk	Policosanol	0.02	NS	NS	NS	NS
Castano (2002)[113]	589	M/F	Hyperlipidemia	RCT-DB	1 y	Policosanol	0.005-0.01	−15.4	−20.5	−11.9	+20.1
Castano (2001)[115]	89	M/F	Hyperlipidemia	RCT-DB	6 mo	Policosanol	0.02	−15.6	−27.4	−12.7	+17.6
							0.04	−17.3	−28.1	−15.6	+17.0
Mirkin (2001)[118]	56	F	Hyperlipidemia-PM	RCT-DB	8 wk	Policosanol	0.005	−12.9	−17.3	NS	NS
							0.01	−19.5	−26.7	NS	+7.4
Castano (2000)[114]	244	F	Hyperlipidemia-PM	RCT-DB	12 wk	Policosanol	0.005	−12.6	−17.7	NS	+16.5
							0.01	−16.8	−25.4	NS	+29.3
Mas (1999)[117]	437	M/F	Hyperlipidemia	RCT-DB	8 wk	Policosanol	0.005	−13.0	−18.2	NS	+15.5
							0.01	−17.4	−25.6	−5.2	+28.4
Crespo (1999)[116]	53	M/F	DM-type 2	RCT-DB	12 wk	Policosanol	0.01	−14.0	−20.4	NS	+7.5
Canetti (1995)[112]	69	M/F	Hyperlipidemia	RCT-DB	2 y	Policosanol	0.01	−18.0	−25.0	NS	−21.0

DM, diabetes melitis; F, women; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, men; Meta, meta-analysis; M/F, men and women; NA, not available; NS, not significant; PM, postmenopausal; RCT, randomized control trial; RCT-DB, double blinded RCT; RCT-LMC, large-scale and multicentre randomized control trial; TC, total cholesterol; TGs, triglicerides.

*Hyperlipidemia intolerant to statin therapy because of myalgias.

Garlic (*Allium sativum*). A number of RCTs-DB have shown that garlic supplement in a daily dose of 600 to 1000 mg was ineffective in lowering lipid profile in patients with hypercholesterolemia.[122-128] Although a few meta-analyses have suggested that the major effect of garlic in the forms of powder, tablet, oil, or extract on blood lipid levels was a mild to moderate reduction of TC (3% to 12%),[129-132] there was no significant effect on other components of the lipid profile. The adverse effects included GI symptoms, headaches, and garlic smell. The effects of garlic on blood lipid levels are summarized in Table 10.

Others. Other identified supplements, such as chromium,[133] vitamin C,[134,135] artichoke extract (*Cynara cardunculus*),[136] magnesium-pyridoxal-phosphate-glutamate,[137] tocotrienols,[138] and absorbitol,[139] did not show any significant effects on serum lipid profile. Their efficacy and safety remain uncertain.

Table 10. Effect of guggulipid and garlic on serum lipid profile in clinical trials

Author (year)	Participants N	Sex	Characteristics	Design	Duration	Intervention	Daily dose (g)	Results (Δ%) TC	LDL-C	TG	HDL-C
Guggulipid											
Szapary (2003)[121]	103	M/F	Hyperlipidemia	RCT-DB	8 wk	Guggulipid	3-6 g	NS	+10.0	NS	NS
Singh (1994)[120]	61	M/F	Hyperlipidemia	RCT-DB	24 wk	Guggulipid	0.1 g	−11.7	−12.5	−12.0	NS
Garlic											
Reinhart (2009)[129]	1683	M/F	Hyperlipidemia	Meta	2 wk-1 y	Garlic powder/oil/ extract	0.6-1.2	−3.2	NS	−6.5	NS
Stevinson (2000)[131]	1518	M/F	Hyperlipidemia	Meta	8-24 wk	Garlic powder	0.6-0.9	−5.8	NS	NS	NS
Silagy (1994)[130]	952	M/F	Hyperlipidemia	Meta	4 wk-6 mo	Garlic powder	0.6-0.9	−12.0	NS	−12.4	NS
Warshafsky (1993)[132]		M/F	Hyperlipidemia	Meta	8-24 wk	Garlic powder/tablet	0.6-0.9	−9.0	NA	NA	NA
Zhang (2006)[128]	3411	M/F	Hyperlipidemia	RCT-DB	3.3-7.3 y	Aged garlic extract	0.2	NS	NS	NS	NS
						steam-distilled garlic oil	0.001				
Tanamai (2004)[127]	116	M	Healthy	RCT-DB	3-6 mo	Garlic tablet	0.5	NS	NS	NS	NS
Satitvipawee (2003)[125]	136	M/F	Hyperlipidemia	RCT-DB	12 wk	Garlic tablet	0.0056	NS	NS	NS	NS
Gardner (2001)[14]	51	M/F	Hyperlipidemia	RCT-DB	12 wk	Garlic powder	0.5-1.0	NS	NS	NS	NS
Superko (2000)[126]	50	M/F	Hyperlipidemia	RCT-DB	12 wk	Garlic powder	0.9	NS	NS	NS	NS
Isaacsohn (1998)[123]	50	M/F	Hyperlipidemia	RCT-DB	12 wk	Garlic powder	0.9	NS	NS	NS	NS
Neil (1996)[124]	115	M/F	Hyperlipidemia	RCT-DB	24 wk	Garlic powder	0.9	NS	NS	NS	NS
Mader (1990)[154]	261	M/F	Hyperlipidemia	RCT-DB	16 wk	Garlic powder	0.8	−12.0	NS	−17.0	NS

Meta, meta-analysis; RCT-DB, double-blinded randomized controlled trial.

Table 11. Level of evidence and size of treatment effect for dietary interventions

Level of Evidence	Size of treatment effect			
	Class I	Class IIa	Class IIb	Class III
	Benefit >>> risk Little or no conflicting evidence	Benefit>> risk Some conflicting evidence; additional studies with focused objectives needed	Benefit ≥ risk More conflicting evidence; additional studies with broad objectives needed	Risk ≥ benefit No additional studies needed
Level A Multiple populations (3–5) evaluated Data derived from multiple RCTs or meta-analyses	Fully recommend Soy protein High-fibre diet Phytosterols Whole grain foods Low-fat diet Mediterranean diet Portfolio diet Omega-3 fatty acids	Reasonable to recommend Policosanol Red yeast rice extract	Probably not recommend Guggulipid	Cannot recommend Garlic
Level B Limited populations evaluated Data derived from single RCT or nonrandomized studies	Might be useful Nuts Green tea Red wine High-carbohydrate diet High-protein diet	Might be useful	Not recommended	Not recommended Chromium MPPG Vitamin C Tocotrienols Absorbitol
Level C Very limited population evaluated Only consensus opinion of experts, case studies, or standard of care	Might be useful	Not recommended	Not recommended	Not recommended

MPPG, magnesium-pyridoxal-phosphate-glutamate; RCT, randomized controlled trial.

Discussion

There are growing numbers of available dietary changes and supplements that claim to be beneficial for management of dyslipidemia. Following our search and inclusion criteria, a total of 22 different dietary interventions were identified. Some of the dietary interventions have been claimed to reduce TG and LDL-C levels by 5% to 20% and 10% to 30%, respectively. It is important to analyze the level of evidence for these dietary interventions and their efficacy in order to provide proper suggestions for their use. According to the American College of Cardiology and the AHA clinical practice guidelines,[140] the level of evidence can be classified as A, B, or C on the basis of the quality of studies and populations being evaluated, and the size of treatment effect can be classified as class I, IIa, IIb, and III (Table 11). Recommendations are based on the level of evidence and size of treatment effect. For example, interventions with level A evidence and class I effect are fully recommended. In contrast, interventions with level A evidence and class III effect cannot be recommended.

The level of evidence and size of treatment effect for each individual dietary intervention derived from the studies meeting our inclusion criteria are summarized in Table 11. Given the level A evidence and class I effect, daily ingestion of the following is fully recommended: either 30 to 50 g soy protein powder or 50 to 100 mg isoflavones, 5 to 15 g soluble fibre diet, 1 to 3 g phytosterols, 60 g uncooked oatmeal, and 1 to 2 g omega-3 fatty acids, as well as the AHA Step I and Step II diets, the Med-diet, and the Portfolio diet. The daily consumption of 50 to 80 g nuts, 200 to 300 mL red wine (depending on gender), and diets with high carbohydrate and high protein is effective in improving the lipid levels and can be recommended given the level B evidence and class I effect. Supplementation with a daily dose of 5 to 20 mg policosanol and 1 to 2 g red yeast rice extract can be reasonably recommended considering the level A evidence and class IIa effect. Supplementation with guggulipid shows level A evidence with class IIb effect; therefore, it probably cannot be recommended. Supplements of garlic, chromium, vitamin C, magnesium-pyridoxal-phosphate-glutamate, tocotrienols and absorbitol cannot be recommended, given their class III effect. Each dietary intervention's recommended daily dose, reported effects on lipid profile, side effects, level of evidence, and size of lipid-lowering effect derived from the reviewed studies are summarized in Table 12.

Lifestyle modification remains the cornerstone of treatment of dyslipidemia. Dietary supplements, along with dietary changes, provide an additional cost-effective treatment for patients with dyslipidemia, especially for those who are intolerant of lipid-lowering medications. The efficacy of lowering lipid levels has been observed in healthy and/or overweight individuals, patients with diabetes, and women in menopause in addition to patients with dyslipidemia. Therefore, dietary interventions can be an effective regimen for people who want to improve their cholesterol levels. In addition to improving lipid profiles, some of the interventions, such as the Med-diet, red yeast rice, and omega-3 fatty acid supplementation, have been shown to confer significant cardiovascular protection that is probably not related to their influence on lipid levels.[34,98,105,111,141]

This review article has several limitations. First, the data were derived from studies meeting our search and inclusion criteria and published between 1990 and 2009. Secondly, the population included in the present study mostly contains whites and Asians. These studies underrepresent Africans. Furthermore, the reported lipid-lowering effects of dietary inter-

Table 12. Summary of dietary interventions' daily dose, effects on lipid profile, side effects, level of evidence, and size of treatment effect derived from the reviewed studies

Dietary intervention	Daily dose	Effects on lipid levels	Side effects	Level of evidence	Size of treatment effect
Soy protein powder	30-50 g	↓ TC by 2%-10%	None	Level A	Class I
Isoflavones	50-100 mg	↓ TC by 2%-10% ↓ LDL-C by 3%-11%	None	Level A	Class I
Soluble fibre	5-15 g	↓ TC and by 2%-12% ↓ LDL-C by 5%-20%	None	Level A	Class I
Uncooked oatmeal	60 g	↓ TC by 4%-6% ↓ LDL-C by 2%-6%	None	Level A	Class I
Plant sterols	1-3 g	↓ TC by 2%-13% ↓ LDL-C by 4%-13%	None	Level A	Class I
AHA Step I and Step II diets		↓ TC and LDL-C by 5%-10%	None	Level A	Class I
Mediterranean diet		↓ TC and LDL-C by 5%-15% ↑ HDL-C by 3%-15%	None	Level A	Class I
Portfolio diet		↓ TC and LDL-C by 10%-20%	None	Level A	Class I
Omega-3 fatty acids	1-2 g	↓ TG level by 3%-9%	GI symptoms, skin rash/itching	Level A	Class I
Nuts	50-80 g	↓ LDL-C by 5%		Level B	Class I
Green tea extract	1.2 g	↓ TC by 2.3% ↓ LDL-C by 10% ↓ TG by 6%	None	Level B	Class I
Red wine	300 mL for men 200 mL for women	↑ HDL-C by 13%	None	Level B	Class I
High-carbohydrate diet	50%-60% of total energy (not > 60%)	↓ TC, LDL and TGs by 5%-10%	None	Level B	Class I
High-protein diet	25% of total energy	↓ TC, LDL, and TGs by 5%-10%	None	Level B	Class I
Policosanol	5-20 mg	↓ TC by 12%-20% ↓ LDL-C by 15%-25% ↑ HDL-C by 8%-30%	Polyuria, polyphagia, insomnia, headache	Level A	Class IIa
Red yeast rice extract capsule	1-2 g	↓ TC by 44% ↓ LDL-C by 7%-25% ↓ TGs by 7%-44% ↑ HDL-C by 0%-17%	GI symptoms, myalgias, elevation of AKP and ALT	Level A	Class IIa
Guggulipid	100 mg	↓ TC by 11.7% ↓ LDL-C by 12.5%	Headache, GI symptoms, skin hypersensitivity reaction	Level A	Class IIb
Garlic powder/tablet/extract	600-1000 mg	None	GI symptoms, headaches, smell	Level A	Class III

AHA, American Heart Association; GI, gastrointestinal; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TGs, triglicerides.

ventions are derived from different studies. We are not able to exclude the confounding factors among these studies. Therefore, these limitations should be considered for the interpretation of this review article.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca, and at doi:10.1016/j.cjca.2010.12.077.