

Systematic Review with Meta-Analysis

Effects of the Dietary Approach to Stop Hypertension (DASH) diet on cardiovascular risk factors: a systematic review and meta-analysis

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Abstract

The Dietary Approach to Stop Hypertension (DASH) is recommended to lower blood pressure (BP), but its effects on cardiometabolic biomarkers are unclear. A systematic review and meta-analysis of randomised controlled trials (RCT) was conducted to determine the effects of the DASH diet on cardiovascular risk factors. Medline, Embase and Scopus databases were searched from inception to December 2013. Inclusion criteria were as follows: (1) DASH diet; (2) RCT; (3) risk factors including systolic and diastolic BP and glucose, HDL, LDL, TAG and total cholesterol concentrations; (4) control group. Random-effects models were used to determine the pooled effect sizes. Meta-regression analyses were carried out to examine the association between effect sizes, baseline values of the risk factors, BMI, age, quality of trials, salt intake and study duration. A total of twenty articles reporting data for 1917 participants were included in the meta-analysis. The duration of interventions ranged from 2 to 24 weeks. The DASH diet was found to result in significant decreases in systolic BP (-5.2 mmHg, 95% CI -7.0 , -3.4 ; $P < 0.001$) and diastolic BP (-2.6 mmHg, 95% CI -3.5 , -1.7 ; $P < 0.001$) and in the concentrations of total cholesterol (-0.20 mmol/l, 95% CI -0.31 , -0.10 ; $P < 0.001$) and LDL (-0.10 mmol/l, 95% CI -0.20 , -0.01 ; $P = 0.03$). Changes in both systolic and diastolic BP were greater in participants with higher baseline BP or BMI. These changes predicted a reduction of approximately 13% in the 10-year Framingham risk score for CVD. The DASH diet improved cardiovascular risk factors and appeared to have greater beneficial effects in subjects with an increased cardiometabolic risk. The DASH diet is an effective nutritional strategy to prevent CVD.

Key words: Dietary Approach to Stop Hypertension diet; Meta-analyses; Hypertension; Dyslipidaemia; Diabetes; Cardiovascular risk

CVD are the leading cause of mortality worldwide, accounting for 30% of all global deaths⁽¹⁾. Haemodynamic (elevated blood pressure (BP)) and metabolic (hyperlipidaemia and hyperglycaemia) stressors are important cardiovascular risk factors and linked to the onset and progression of atherosclerosis⁽²⁾. Models incorporating risk factors such as age, smoking status, sex, diabetes, BP, and total cholesterol and HDL-cholesterol concentrations have been developed for predicting the risk of cardiovascular events and mortality^(3,4).

Dietary and lifestyle interventions are important behavioural strategies for cardiovascular risk reduction^(5,6). The Dietary Approach to Stop Hypertension (DASH) is a dietary pattern that promotes the consumption of fruits, vegetables, and low-fat dairy products; includes whole grains, poultry, fish, and nuts; and attempts to reduce the intakes of red meat,

sweets, sugar-containing beverages, total fat, saturated fat and cholesterol⁽⁷⁾. Thus, the DASH dietary pattern promotes a higher intake of protective nutrients such as K, Ca, Mg, fibre and vegetable proteins and, at the same time, a lower intake of refined carbohydrates and saturated fat. Furthermore, feeding trials have demonstrated the additive effects of salt restriction on the efficacy of the DASH dietary pattern in reducing BP. The DASH diet is recommended by the American Heart Association for the non-pharmacological management of hypertension⁽⁸⁾. Compared with a typical American diet, the DASH diet has been found to significantly reduce systolic and diastolic BP in hypertensive individuals⁽⁹⁾. Importantly, the beneficial effects of the DASH diet are not limited to BP and some studies have reported significant improvements in insulin sensitivity⁽¹⁰⁾, inflammation⁽¹¹⁾, oxidative stress⁽¹²⁾ and

Abbreviations: ADV, dietary advice; BP, blood pressure; CON, controlled feeding; DASH, Dietary Approach to Stop Hypertension; RCT, randomised controlled trials.

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recognised cardiovascular risk factors including concentrations of fasting glucose⁽¹³⁾ and total cholesterol⁽¹⁴⁾. However, other studies have observed non-significant effects of the DASH diet on BP^(15–17), fasting glucose concentrations^(18,19) and total cholesterol concentrations^(18–20).

We systematically reviewed the evidence from randomised controlled trials (RCT) investigating the effects of the DASH diet on BP (systolic and diastolic) and on the concentrations of glucose and lipids (total cholesterol, HDL, LDL and TAG) in human subjects. We also investigated whether the effects of the DASH diet on each cardiovascular risk factor were modified by methodological (trial design, duration and type of control diet, and dietary Na intake) and phenotypic (systolic and diastolic BP, plasma concentrations of metabolic biomarkers and BMI) characteristics. In addition, we examined the effects of the DASH diet on the 10-year risk for CVD, CHD, myocardial infarction and stroke estimated using the Framingham risk equations⁽³⁾.

Methods

The systematic review was conducted, and its details are reported, according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines⁽²¹⁾. The protocol was registered in the Prospective Register of Systematic Reviews database (registration no. CRD4201007296).

Types of studies

RCT carried out in human subjects were included in the meta-analysis and the specific characteristics and the effects of trial design (including dietary intervention used for the control group, delivery of the nutritional interventions, parallel or cross-over design, run-in period, blinding of the measurement protocols, duration, compliance, randomisation procedure, and use of intention-to-treat analysis) were assessed.

Participants

Publications reporting trials carried out in adult male and female participants (age >18 years) with or without comorbidities (hypertension, diabetes, the metabolic syndrome or gestational diabetes) were included. There were no restrictions with respect to participants' BMI or ethnic background.

Types of interventions

RCT investigating the effects of the DASH diet on cardiovascular risk factors and providing information on the energy and macronutrient contents of both DASH and control interventions were included in the meta-analysis. The minimum duration of the RCT for inclusion in the meta-analysis was 2 weeks. An important inclusion criterion was that the DASH and control diet interventions had to be comparable in terms of energy intake and other lifestyle interventions, e.g. physical activity. In other words, RCT were included only if both control and DASH diet interventions involved a similar degree of energy restriction and/or physical activity to avoid

the confounding effects of changes in body weight on cardiovascular risk factors. In addition, RCT were included if they altered minor components of the DASH interventions (e.g. modified DASH), but retained the core characteristics of the archetypical DASH dietary plan⁽⁷⁾. Examples of DASH dietary plan modifications include reduction of salt intake, increased consumption of lean red meat, and combination with other interventions such as weight loss or physical activity. Similarly, RCT having either a typical dietary pattern or a healthier dietary pattern (healthy diet) as a control were included, provided that these patterns matched the DASH intervention in terms of both energy intake and physical activity level. Finally, RCT were not excluded according to dietary Na intake, as information regarding this variable was not consistently reported across trials; this approach was intended to minimise the risk of publication bias.

Outcome measures

The primary outcomes of the analyses were changes in cardiovascular risk factors including systolic and diastolic BP and concentrations of total cholesterol, glucose, TAG, HDL and LDL.

Search strategy and selection of studies

A literature search of the Medline, Embase and Scopus databases was undertaken from inception to December 2013. The systematic review was restricted to articles published in English. The search was conducted based on predefined search terms (DASH, BP, glucose, diabetes, lipids, cholesterol, metabolic syndrome, insulin resistance, homeostatic model of assessment (HOMA), lipoproteins, HDL and LDL) and using specific building blocks (Boolean terms and truncation) to create algorithms entered into each database. Articles were assessed for eligibility independently by two investigators (M. S. and S. C.). Complete details of the algorithms and selection process are reported in the online supplementary Box S1.

Data extraction and bias measurement

Data extraction was performed independently by two investigators, and a list of the extracted variables is provided in the online supplementary Box S2. Attempts were made to contact the corresponding authors if data were incomplete. The quality of the RCT was assessed using a modified Jadad score against the following criteria: blinding; randomisation procedure; adherence to the interventions⁽²²⁾. As blinding to the dietary interventions was not possible, blinding of the research staff to the measurement protocols contributed to the overall quality score. Scores ranged from 0 (low quality) to 5 (high quality).

Measurement of the treatment effect

The meta-analysis was based on the absolute differences between the DASH and control intervention groups. Baseline and end-of-study mean, standard deviation and sample size for each outcome variable were extracted for each treatment group. Where appropriate, baseline–end-of-study mean

differences, standard deviation values and sample size were used. For cross-over studies, the effect size was calculated as the difference between the DASH and control groups at the end of each intervention. Results presented as medians and interquartile ranges (25th–75th percentiles) were transformed into means and standard deviations using the method proposed by Hozo *et al.*⁽²³⁾.

Statistical analysis

A meta-analysis was conducted using the Comprehensive Meta-Analysis 2 software (Biostat). Data are presented as mean differences (in mmHg for BP and in mmol/l for the remaining metabolic risk factors) and 95% CI. The differences were combined across trials using a random-effects model. The paired nature of the cross-over trials was taken into account in the meta-analysis to minimise unit-of-analysis errors and underestimation of the effect size⁽²⁴⁾. Forest plots were generated for graphical presentations of the cardiovascular risk factors. Statistical heterogeneity across the trials was assessed using the I^2 and Q tests according to specific categories (low < 25%, moderate 25–75%, or high > 75%) and significance level ($P < 0.10$), respectively⁽²⁵⁾. Funnel plots and Egger's regression test were used to evaluate publication bias. Additional analyses were conducted to evaluate the impact of potential confounding factors. Sensitivity analyses were conducted to evaluate whether changes in cardiovascular risk factors were influenced by study design (parallel or cross-over), type of control diet (typical diet or healthy diet) and delivery of nutritional interventions (controlled feeding (CON) study or provision of dietary advice (ADV)). Results obtained in individual trials were retrieved from the majority of the articles. However, for some cardiovascular risk factors (i.e. glucose, HDL, total cholesterol, LDL and TAG), results were obtained but not reported in the articles^(16,26,27); in such cases, attempts were made to obtain the required data. Where such attempts failed, RCT were included in the primary meta-analysis by entering into the model a null effect size and the pooled standard error for each of these studies. A sensitivity analysis was conducted to evaluate the influence of these assumptions on the overall estimates by excluding studies with missing information from the models. In addition, results obtained for glucose and TAG in the Lifestyle Interventions for Blood Pressure Control (PREMIER) study⁽²⁶⁾ were reported as geometric mean and 95% CI. The effect of the DASH diet on these two risk factors was not significant, and therefore a null effect and a pooled standard error were entered into the final model. The results of the PREMIER trial (total cholesterol, LDL and HDL)⁽²⁶⁾ and the DASH-Na trial (all risk factors)^(28,29) were stratified by metabolic syndrome diagnosis and dietary Na intake (low, medium or high), respectively, and average values were calculated and entered into the final model. Meta-regression analyses were conducted to evaluate whether changes in the cardiovascular risk factors were influenced by baseline concentrations of outcome variables, study duration (in weeks), sample size, age, BMI, Jadad score and difference in dietary Na intake (mg/d) between the DASH and control intervention groups. A summary of the differences in dietary Na intake for each trial is given in Table S1 (available online).

A mixed-effects meta-regression model (unrestricted maximum likelihood) was used.

Estimated 10-year risk scores for CVD, CHD, myocardial infarction and stroke were calculated using the Framingham CVD risk equation⁽³⁾ incorporating the following: age and pre- and post-intervention mean values for systolic BP and total cholesterol and HDL concentrations. Risk scores were calculated for a non-diabetic population and stratified by sex and smoking status.

Results

Main search

A total of 5395 articles were identified during the primary search and, after the removal of duplicates (n 4562), 833 articles were screened based on titles and abstracts. After screening, sixty-five articles were selected for a full-text review and twenty articles^(9,13–20,26–36) were selected for inclusion in the systematic review. Results for independent groups (men, women; lean, obese) were reported by three trials^(13,19,31), and results obtained for these groups were analysed separately in the meta-analysis. A flowchart depicting the different stages leading to the selection of trials included in the meta-analysis is shown in Fig. 1. Among the trials included in the meta-analysis, four had a cross-over study design^(16,19,31,34) and thirteen had a parallel-group design^(9,13,15,17,28,30,32,33,35,36). The trials were conducted between 1997 and 2013 and included a total of 1917 participants (range: 19–537 participants per study). The duration of the interventions ranged from 2⁽³⁶⁾ to 24 weeks^(13,18). The majority of the trials were conducted in the USA (nine trials)^(9,13,18,19,30–33,36), four in Australia^(16,17,27,35) and three in Iran^(13,15,34). The main characteristics of the trials are given in Table 1.

Participant characteristics

Otherwise healthy individuals with above-optimal BP and stage 1 hypertension were recruited in the majority of the studies. Individuals with the metabolic syndrome were recruited in three trials^(13,19,31) and those with type 2 diabetes in one trial⁽³⁴⁾, and one study was conducted in women with gestational diabetes⁽¹⁵⁾. The baseline average age of participants recruited in each trial ranged from 31 to 60 years. Most trials had an approximately equal sex distribution, but two trials recruited only men⁽¹⁷⁾ or women⁽¹⁵⁾. The mean BMI of the participants ranged from 23 to 37 kg/m² in individual studies^(31,36); BMI was not reported in one study⁽³⁴⁾. Changes in body weight during the trial were not reported in one study⁽¹⁵⁾; five trials either reported adjustment of energy intake to meet energy requirements or mentioned maintenance of body weight during the trial^(16,28,30,31,36).

Nutritional interventions

The DASH diet as originally described in the first DASH trials was prescribed without modification in ten trials^(9,15,16,19,30–34,36)

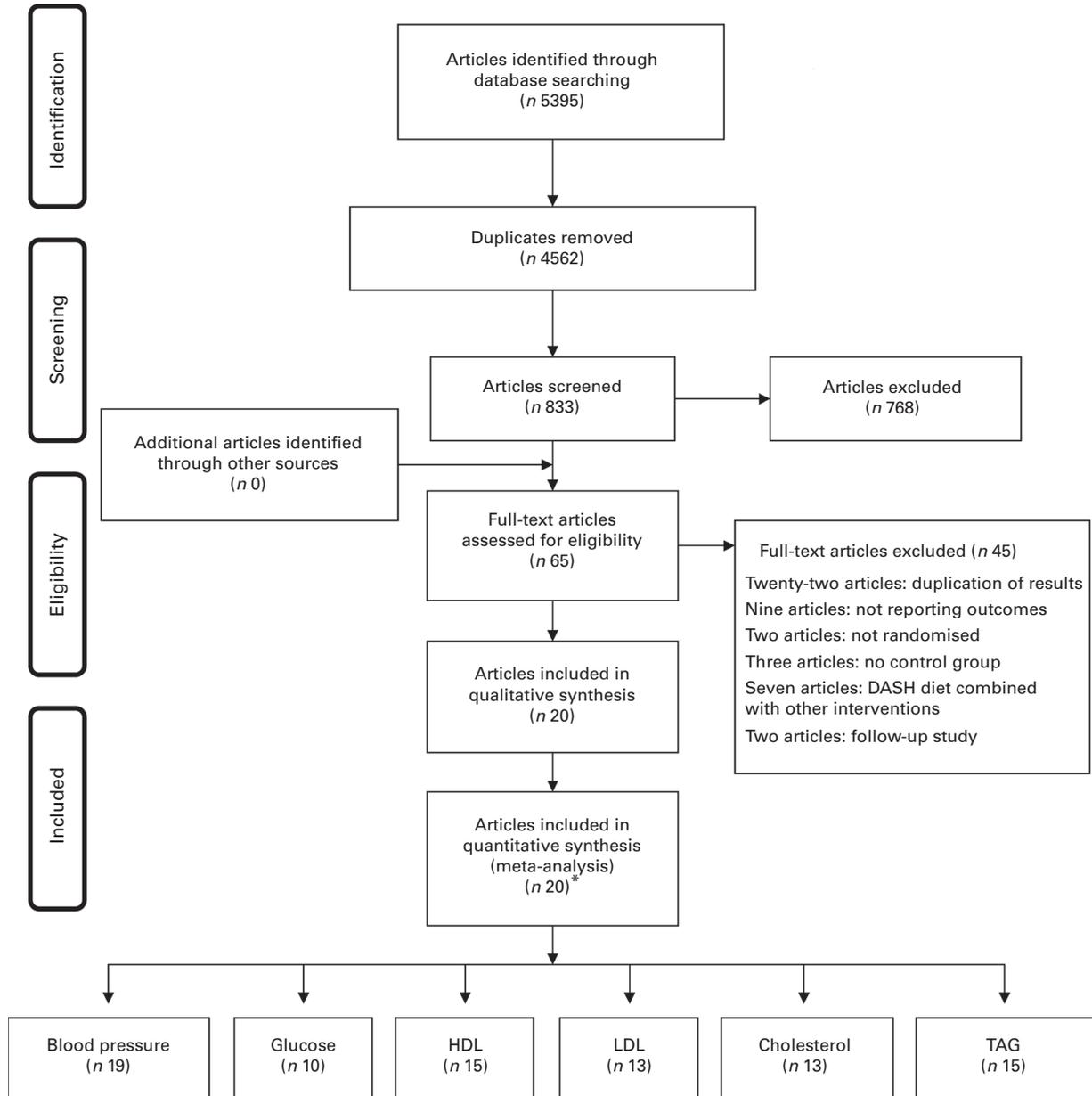


Fig. 1. Flowchart depicting the different stages leading to the selection of trials included in the meta-analysis. * The different number of articles (n) included in the analyses for specific cardiovascular risk factors is related to the selective reporting of the risk factors in each article. The number of articles and number of independent subgroups included in the meta-analysis are given in Table 1. DASH, Dietary Approach to Stop Hypertension.

and five trials modified the DASH dietary plan by incorporating additional components such as dietary energy restriction or physical exercise^(13,17,18,27,35). These protocol variations resulted in between-study differences in the magnitude of weight change. The greatest weight loss was observed in a 24-week trial combining the DASH diet with dietary energy restriction to investigate effects on BP and metabolic risk factors (control group was only energy restricted); both groups exhibited similar levels of body weight loss (approximately 14 kg)⁽¹³⁾. Similarly, the inclusion of an exercise intervention in both groups within a study did not induce differential changes in body weight⁽³⁵⁾. However, the majority of the trials aimed at maintaining stable weight and reported weight changes <1.5 kg during the intervention period.

Dietary counselling was employed to deliver the nutritional interventions in several trials^(13,15–19,27,31–35). In such cases, a nutritionist/dietitian regularly met with the study participants (weekly, fortnightly or monthly) to instruct them on the specific dietary and lifestyle interventions (DASH or control). In contrast, four studies controlled dietary intake more carefully by providing participants with all their meals^(9,28,30,36). Salt intake was standardised and participants were asked to maintain a record of the non-study foods that they consumed in the latter studies. Trials differed in their attempts to standardise Na intake in the DASH and control intervention groups; five trials reported marginal differences (<210 mg/d) in dietary Na intake^(9,18,27,31,36), eight trials reported differences >300 mg/d (range: 319–2481 mg/d)^(13,15–17,19,32–34) and one trial⁽²⁸⁾

Table 1. Summary of findings from studies included in the meta-analysis

Author (year, country)	Inclusion criteria	Design	Duration (weeks)	Run-in	ITT	Groups	Subjects (n)	Age (years)	Females (n)	Caucasians (n)	BMI (kg/m ²)	Diet	Feeding	Weight loss (kg)	Completion (%)	Risk factors	Jadad* score	
Appel† (1997, USA) ⁽⁹⁾	Age >22 years SBP <160 mmHg DBP: 80–95 mmHg Stop HT drugs	P ^{MC} ‡	8	Yes	Yes	C	154	44	72	48	28	TD	Controlled	-0.1	95	BP ^R ‡	☑	5
						I	151	44	77	53	29	DASH	Controlled	-0.4	99	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	
Sacks† (2001, USA) ⁽²⁶⁾	Age >22 years SBP: 120–159 mmHg DBP: 90–95 mmHg BMI: 18.5–45 kg/m ²	P ^{MC,SS} ‡	12	Yes	Yes	C	204	49	110	81	30	TD	Controlled	NR ^{WS} ‡	95	BP ^R ‡	☑	5
						I	208	47	122	83	29	DASH	Controlled	NR ^{WS} ‡	94	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	
Appel† (2003, USA) ⁽¹⁸⁾	Age ≥25 years SBP: 120–159 mmHg DBP: 80–95 mmHg	P ^{MC} ‡	24	Yes	Yes	C	269	50	154	163	33	HD	Counselling	-4.9	71	BP ^R ‡	☑	5
						I	268	50	174	181	33	M-DASH	Counselling	-5.8	78	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	
Conlin (2003, USA) ⁽³⁰⁾	SBP: 140–179 mmHg DBP: 90–109 mmHg Stop HT drugs	P ^{MC,SL} ‡	8	Yes	Yes	C	28	52	15	10	30	TD	Controlled	NR ^{EI} ‡	100	BP ^{AMB} P‡	☑	3
						I	27	52	15	10	32	DASH	Controlled	NR ^{EI} ‡	100	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	
Lopes (2003, USA) ⁽¹⁹⁾	NW: BMI <25 kg/m ² No MetS§	CO	4	Yes	No	C	12	39	6	6	23	LAO	Counselling	0	100	BP ^R ‡	☑	3
						I	12	39	6	6	23	DASH	Counselling	0	100	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	
Lopes (2003, USA) ⁽¹⁹⁾	OW: BMI >27 kg/m ² MetS§	CO	4	Yes	No	C	12	35	6	6	34	LAO	Counselling	0	100	BP ^R ‡	☑	3
						I	12	35	6	6	34	DASH	Counselling	-1	100	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	
Harsha† (2004, USA) ⁽²⁵⁾	Age >22 years SBP: 120–160 mmHg DBP: 90–95 mmHg	P ^{MC,SS} ‡	8	Yes	Yes	C	193	49	104	110	30	TD	Controlled	NR ^{RP} ‡	95 ^{RP} ‡	BP ^R ‡	☑	5
						I	197	48	116	112	29	DASH	Controlled	NR ^{RP} ‡	94 ^{RP} ‡	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	
Nowson (2004, Australia) ⁽¹⁶⁾	Age >25 years SBP: 120–160 mmHg DBP: 80–90 mmHg	CO	4	Yes	No	C	94	56	38	NR	29	TD	Counselling	NR ^{WS} ‡	97	BP ^R ‡	☑	3
						I	94	56	38	NR	29	DASH	Counselling	NR ^{WS} ‡	97	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	
Nowson (2005, Australia) ⁽¹⁷⁾	Age >25 years SBP ≥120 mmHg DBP ≥80 mmHg BMI: 25–35 kg/m ²	P	12	No	No	C	27	49	0	NR	31	LF¶	Counselling	-4.6	87	BP ^R ‡	☑	3
						I	27	47	0	NR	30	M-DASH¶	Counselling	-4.9	85	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	
Azadbakht (2005, Iran) ⁽¹³⁾	MetS** BMI ≥25 kg/m ²	P	24	Yes	NA	C	11	41††	0	NR	30††	WL¶	Counselling	-14	100	BP ^R ‡	☑	3
						I	11	41††	0	NR	30††	M-DASH¶	Counselling	-15	100	G HDL TC TAG LDL	☑ ☑ ☑ ☑ ☑	

Dietary patterns and cardiovascular risk

Table 1. Continued

Author (year, country)	Inclusion criteria	Design	Duration (weeks)	Run-in	ITT	Groups	Subjects (n)	Age (years)	Females (n)	Caucasians (n)	BMI (kg/m ²)	Diet	Feeding	Weight loss (kg)	Completion (%)	Risk factors	Jadad ^a score
Azadbakht (2005, Iran) ⁽¹³⁾	MetS** BMI ≥ 25 kg/m ²	P	24	Yes	NA	C	27	41††	27	NR	30††	WL¶	Counselling	-12	100	BP ^R ‡	3
						I	27	41††	27	NR	30††	M-DASH¶	Counselling	-14	100	G HDL TC TAG LDL	
Lien† (2007, USA) ⁽²⁶⁾	Age ≥ 25 years SBP: 120–159 mmHg DBP: 80–95 mmHg	P ^{MC} ‡	24	Yes	Yes	C	269	50	154	163	33	HD	Counselling	-4.9	71	BP ^R ‡	5
						I	268	50	174	181	33	M-DASH	Counselling	-5.8	78	G HDL TC TAG LDL	
Nowson (2009, Australia) ⁽²⁷⁾	Age: 45–75 years BMI: 18–35 kg/m ² SBP: 120–159 mmHg DBP: 80–94 mmHg HT diagnosis	P	14	Yes	No	C	49	58	49	NR	30	HD	Semi-controlled	0.8	85	BP ^R ‡	3
						I	46	60	46	NR	29	M-DASH	Semi-controlled	1.1	87	G HDL TC TAG LDL	
Al Solamain (2010, USA) ⁽³¹⁾	Age: 21–49 years NW: BMI < 25 kg/m ² No MetS‡‡	CO	3	Yes	NA	C	15	37	12	10	23	TD	Counselling	NR ^{WS} ‡	83	BP ^R ‡	3
						I	15	37	12	10	23	DASH	Counselling	NR ^{WS} ‡	83	G HDL TC TAG LDL	
Al Solamain (2010, USA) ⁽³¹⁾	Age: 21–49 years OW: BMI > 27 kg/m ² MetS‡‡	CO	3	Yes	NA	C	15	40	12	7	34	TD	Counselling	NR ^{WS} ‡	78	BP ^R ‡	3
						I	15	40	12	7	34	DASH	Counselling	NR ^{WS} ‡	78	G HDL TC TAG LDL	
Blumenthal† (2010, USA) ⁽³²⁾	Age > 35 years BMI: 25–40 kg/m ² SBP: 130–159 mmHg DBP: 85–99 mmHg	P	16	Yes	Yes	C	48	52	34	29	33	TD	Counselling	0.9	98	BP ^R ‡	4
						I	46	52	29	23	33	DASH	Counselling	-0.3	100	G HDL TC TAG LDL	
Blumenthal† (2010, USA) ⁽²⁰⁾	Age > 35 years BMI: 25–40 kg/m ² SBP: 130–159 mmHg DBP: 85–99 mmHg	P	16	Yes	Yes	C	48	52	34	29	33	TD	Counselling	0.9	98	BP ^R ‡	4
						I	46	52	29	23	33	DASH	Counselling	-0.3	100	G HDL TC TAG LDL	
Chen† (2010, USA) ⁽¹⁴⁾	Age > 22 years SBP < 160 mmHg DBP: 80–95 mmHg Stop HT drugs	P ^{MC} ‡	8	Yes	Yes	C	144	44	66	47	28	TD	Controlled	-0.1	95	BP ^R ‡	5
						I	146	44	75	53	29	DASH	Controlled	-0.4	99	G HDL TC TAG LDL	
Malloy-McFall (2010, USA) ⁽³³⁾	Age: 22–60 years SBP: 120–160 mmHg DBP: 80–95 mmHg	P	4	No	No	C	10	38	3	NR	26	TD	Counselling	-0.6	NR	BP ^R ‡	1
						I	10	38	5	NR	34	DASH	Counselling	-1.3	NR	G HDL TC TAG LDL	
Azadbakht (2011, Iran) ⁽³⁴⁾	T2D G ≥ 126 mg/dl (6.993 mmol/l)	CO	8	Yes	No	C	31	NR	18	NR	NR§§	HD	Counselling	-2	70	BP ^R ‡	3
						I	31	NR	18	NR	NR§§	DASH	Counselling	-5	70	G HDL TC TAG LDL	

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Table 1. Continued

Author (year, country)	Inclusion criteria	Design	Duration (weeks)	Run-in	ITT	Groups	Subjects (n)	Age (years)	Females (n)	Caucasians (n)	BMI (kg/m ²)	Diet	Feeding	Weight loss (kg)	Completion (%)	Risk factors	Jadad* score
Edwards (2011, Australia) ⁽³⁵⁾	Age: 25–60 years SBP: 120–170 mmHg DBP: 80–95 mmHg Stop HT drugs	P	12	No	No	C	25	46	13	NR	30	EX	Counselling	–0.2	NR	BP ^R ‡	3
						I	12	48	6	NR	31	EX-DASH	Counselling	–0.8	NR	G HDL TC TAG LDL	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/>
Lin (2012, USA) ⁽³⁶⁾	Age >22 years BMI: 18.5–40 kg/m ² SBP: 140–159 mmHg DBP: 90–99 mmHg	P	2	Yes	Yes	C	9	42	6	2	37	TD	Controlled	NR ^{El} ‡	90	BP ^R ‡	4
						I	10	46	7	3	31	DASH	Controlled	NR ^{El} ‡	100	G HDL TC TAG LDL	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/>
Asemi (2013, Iran) ⁽¹⁵⁾	Pregnant women GD (24–26 weeks) Age: 18–40 years	P	4	No	No	C	17	29	17	NR	31	TD	Counselling	NR	85	BP ^R ‡	3
						I	17	31	17	NR	29	DASH	Counselling	NR	85	G HDL TC TAG LDL	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/>

ITT, intention to treat; SBP, systolic blood pressure; DBP, diastolic blood pressure; HT, hypertension; P, parallel study design; C, control group; I, intervention group; TD, typical diet; DASH, Dietary Approach to Stop Hypertension; BP, blood pressure; G, glucose; TC, total cholesterol; HD, healthy diet; M-DASH, modified DASH diet; NW, normal weight; MetS, metabolic syndrome; CO, cross-over study design; LAO, low antioxidant; OW, overweight; NR, not reported in the article; LF, low-fat; NA, not applicable; WL, weight loss; T2D, type 2 diabetes; EX, exercise intervention; EX-DASH, DASH diet combined with EX; GD, gestational diabetes. , results reported in the article and included in the meta-analysis; , results not reported in the article.

* The Jadad score ranges from 0 to 5⁽²²⁾. One point was assigned by default to the blinding scale as dietary interventions could not be blind. The other point was assigned based on whether personnel performing the measurements were blind to the interventions.

† The results of the following pairs of publications were obtained from the same trial design: Appel⁽⁹⁾ and Chen⁽¹⁴⁾; Sacks⁽²⁸⁾ and Harsha⁽²⁹⁾; Appel⁽¹⁸⁾ and Lien⁽²⁶⁾; Blumenthal⁽³²⁾ and Blumenthal⁽²⁰⁾.

‡ MC, multicentre study; R, resting BP; SS, stratified by salt intake (three groups, cross-over design); NR^{W/S}, weight not reported in the article, but weight stability of participants mentioned in the 'Results' section of the article; SL, stratified by losartan treatment (cross-over, double blind); NR^{El}, weight not reported in the article, but adjustment of energy intake to maintain body weight mentioned in the 'Methods' section of the article; AMBP, ambulatory 24 h BP; RP, article refers to related publications for details.

§ Inclusion criteria for the study were as follows: (1) OW group (BMI ≥27 kg/m², dyslipidaemic (TAG concentration >150 mg/dl (>1.7 mmol/l) and/or HDL-cholesterol concentration <45 mg/dl (<1.17 mmol/l) for women or <40 mg/dl (<1.04 mmol/l) for men) subjects with high-normal to stage 1 HT (BP 130–159/85–99 mmHg) and twelve lean (BMI <25 kg/m²) normotensives (BP <130/85 mmHg) with normal lipid concentrations.

|| Results obtained for lipids after the intervention period were not provided in the article. A summary of the main findings was provided in the 'Results' section of the article. These results have been included in the meta-analysis.

¶ WL studies including a DASH diet intervention. Studies demonstrated a similar level of energy deficit in the DASH and C groups as shown by the similar WL. The C of these studies have been classified as HD in the meta-analysis.

** Inclusion criteria for the study were as follows: NW (waist:hip ratio <0.80 for women and <0.85 for men, BP <130/85 mmHg, glucose concentration <110 mg/dl (<6.105 mmol/l), TAG concentration <125 mg/dl (<1.4 mmol/l), and HDL concentration >40 mg/dl (>1.04 mmol/l) for men and >45 mg/dl (>1.17 mmol/l) for women) and obese (waist circumference (WC) >101 cm for men and 88 cm for women, BP within 130/85 and 159/99 mmHg, glucose concentration <126 mg/dl (<6.993 mmol/l), TAG concentration >170 mg/dl (>1.9 mmol/l), and HDL concentration <40 mg/dl (<1.04 mmol/l) for men and <50 mg/dl (<1.30 mmol/l) for women).

†† Baseline subjects' characteristics were not reported by sex in the article.

‡‡ Inclusion criteria for the study were as follows: NW (BMI <25 kg/m², WC <102 cm for men and <88 cm for women, blood pressure consistently <130/85 mmHg during all three visits before the first study, fasting glucose concentration <100 mg/dl (<5.550 mmol/l), fasting TAG concentration <125 mg/dl (<1.4 mmol/l), HDL-cholesterol concentration >40 mg/dl (>1.04 mmol/l) for men and >50 mg/dl (>1.30 mmol/l) for women and/or TC/HDL concentration <3.5) and OW (blood pressure in the 130–159/85–99 mmHg range during the three screening visits, BMI >27 kg/m² and WC ≥40 inches (≥102 cm) for men and ≥35 inches (≥88 cm) for women). They also had at least one other risk factor including impaired fasting glucose concentration (100–125 mg/dl; 5.550–6.938 mmol/l), fasting TAG concentration >150 mg/dl (>1.7 mmol/l) or HDL-cholesterol concentration <50 mg/dl (<1.30 mmol/l) for women and <40 mg/dl (<1.04 mmol/l) for men.

§§ Only body weight was reported in the article.

||| Changes in BMI.

Dietary patterns and cardiovascular risk

specifically evaluated the additive effects of a stepwise reduction in dietary Na intake on the BP-lowering effects of the DASH diet (see online supplementary Table S1).

Study quality

The following factors were considered while determining the quality of studies included in the meta-analysis: type of dietary intervention; study design; compliance monitoring; measurement protocols. On occasion, some important information was missing or incomplete, e.g. intakes of energy, macronutrients and micronutrients, and there was large variability in the assessment of compliance with the dietary interventions with respect to monitoring changes in body weight and physical activity levels. An important aspect of the nutritional interventions was the inclusion of a run-in period (both parallel and cross-over studies) and/or a washout period (cross-over studies). Specifically, a run-in period (duration: 1–4 weeks) was included in twelve trials^(9,13,16,18,19,27,28,30–32,34,36) and a washout period (duration: 2 and 4 weeks) was included in two cross-over trials^(16,34). There was considerable variability in the effectiveness of monitoring compliance with the dietary interventions, which was influenced by the intervention protocol (e.g. CON study *v.* provision of ADV). Urinary or plasma mineral and electrolyte concentrations (i.e. Mg, Na, K, phosphate and Ca) were measured in eleven trials to evaluate the adherence to the dietary interventions^(9,16–19,27,28,30–32,36). Only seven trials reported whether the personnel involved in the collection of outcome data were unaware of participants' diet assignment^(9,15,18,28,32,34,36).

Meta-analysis results and estimated CVD risk

The DASH diet resulted in significant decreases in systolic BP (-5.2 mmHg, 95% CI -7.0 , -3.4 , $P < 0.001$; Fig. 2(a)) and diastolic BP (-2.6 mmHg, 95% CI -3.5 , -1.7 , $P < 0.001$; Fig. 2(b)) and in the concentrations of total cholesterol (-0.20 mmol/l, 95% CI -0.31 , -0.10 , $P < 0.001$; Fig. 2(d)) and LDL (-0.10 mmol/l, 95% CI -0.20 , -0.01 , $P = 0.03$; Fig. 2(f)). The pooled effect of the interventions was not significant for the concentrations of glucose (-0.19 mmol/l, 95% CI -0.39 , -0.17 , $P = 0.07$; Fig. 2(c)), HDL (0.003 mmol/l, 95% CI -0.05 , 0.05 , $P = 0.95$; Fig. 2(e)) and TAG (-0.005 mmol/l, 95% CI -0.06 , 0.05 , $P = 0.87$; Fig. 2(g)). There was no change in the estimates for glucose, HDL, LDL, total cholesterol and TAG concentrations after the exclusion of trials^(16,26,27) with missing information (see online supplementary Table S2). The DASH diet resulted in highly significantly lowered BP when the analyses were stratified by the type of intervention (CON^(9,28,30,36) and ADV^(13,15–19,27,31–35)) and by the type of the control diet (typical diet^(9,15,16,28,30–33,36) and healthy diet^(13,17–19,27,34,35)), albeit the decline in systolic BP was greater when a typical diet was used as the control intervention (see online supplementary Table S3). Using the Framingham risk equations⁽³⁾, it was estimated that the concomitant changes in BP and cholesterol concentrations elicited by the DASH diet would

lead to a reduction of approximately 13% in the estimated 10-year risk for CVD (see online supplementary Fig. S1).

Meta-regression analysis

Reductions in systolic and diastolic BP following randomisation to the DASH diet were greater in participants with higher BP or BMI at baseline. For each mmHg increase in baseline systolic and diastolic BP, the effect size for both BP variables increased by about 0.1 mmHg. Similarly, baseline BMI was directly associated with changes in both systolic BP ($\beta - 0.1$ (SE 0.06) mmHg, $P = 0.02$) and diastolic BP ($\beta - 0.1$ (SE 0.04) mmHg, $P < 0.001$) (Table 2). Differences in dietary Na intake between the DASH and control intervention groups were not associated with changes in systolic and diastolic BP as well as with glucose and lipid concentrations (Table 2).

Publication bias and heterogeneity

Funnel plots generated for all the cardiovascular risk factors revealed an overall symmetric distribution for BP (systolic and diastolic) and for total cholesterol, glucose, HDL and LDL concentrations, indicating the absence of publication bias (see online supplementary Fig. S2). In addition, Egger's regression test for these risk factors was not significant (see online supplementary Table S4). In contrast, funnel plots generated for TAG concentrations revealed some asymmetry, which was confirmed by a significant Egger regression test ($P = 0.01$). The heterogeneity of the models was high for systolic BP ($I^2 = 76.0\%$) and HDL concentrations ($I^2 = 75.6\%$), whereas the lowest value was observed for TAG concentrations ($I^2 = 0\%$; online supplementary Table S4).

Discussion

Summary of the main results

DASH diet interventions resulted in significant improvements in systolic and diastolic BP along with significant reductions in total cholesterol and LDL concentrations. However, these interventions did not affect TAG, glucose and HDL concentrations. The responses of both systolic and diastolic BP to the DASH diet were greater in participants with higher BP or BMI at baseline. The responses appeared to be independent of differences in dietary Na intake. Importantly, measures of the effectiveness of the DASH diet were not modified by the type of study design or feeding protocol and the characteristics of control diet.

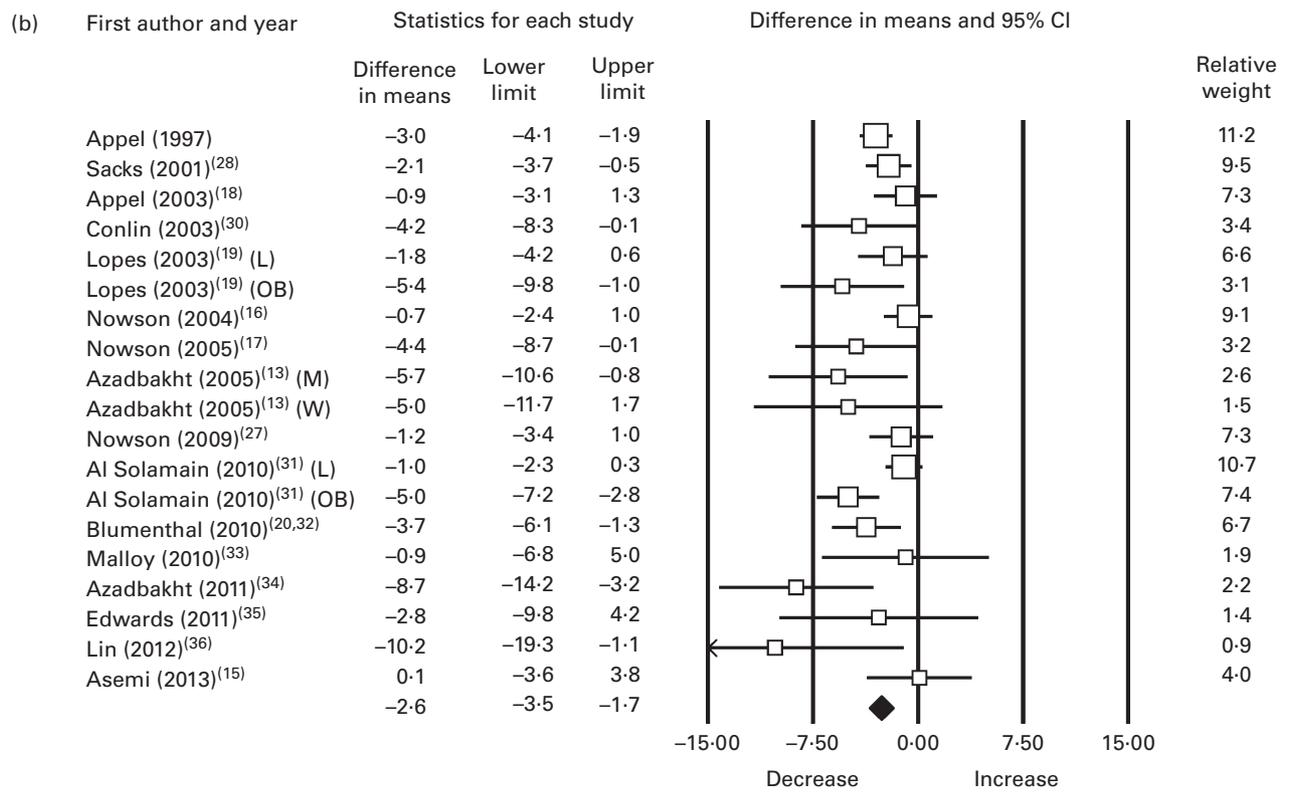
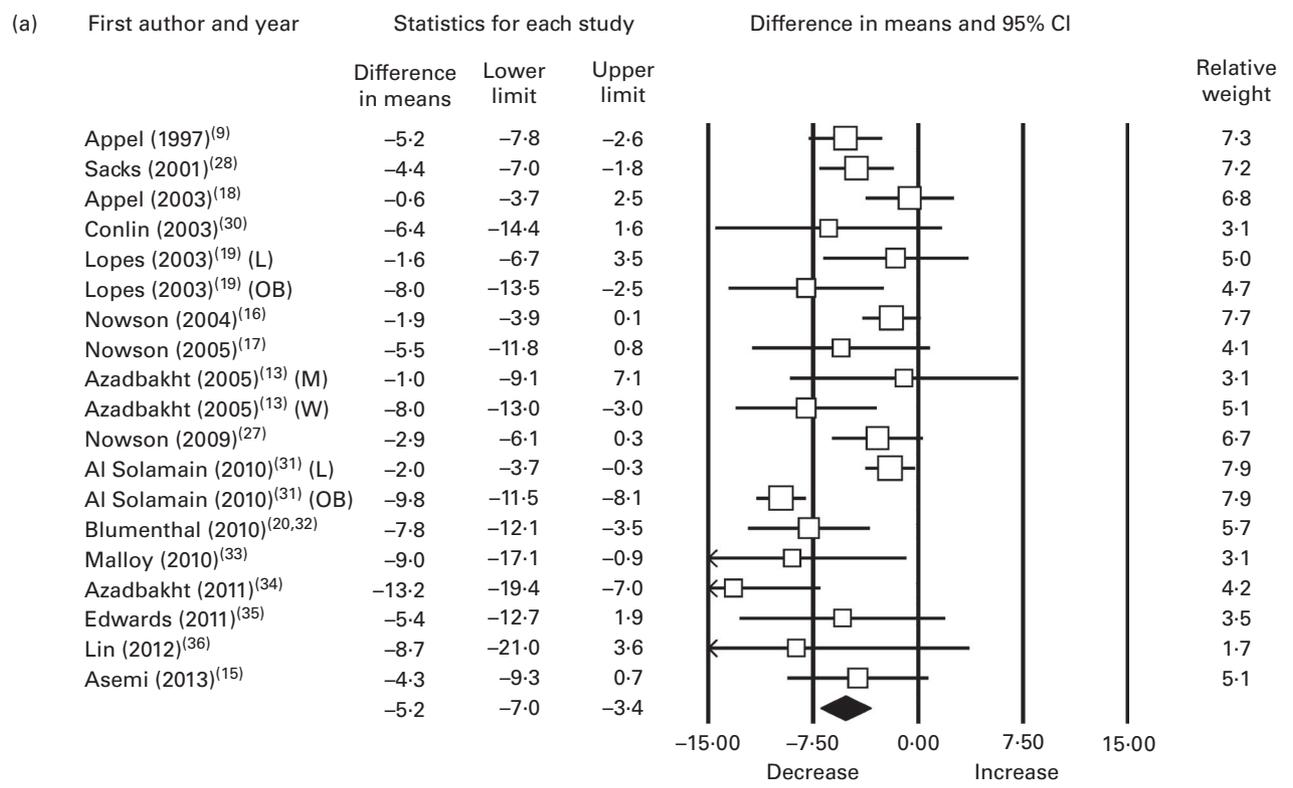
Study quality and applicability of evidence

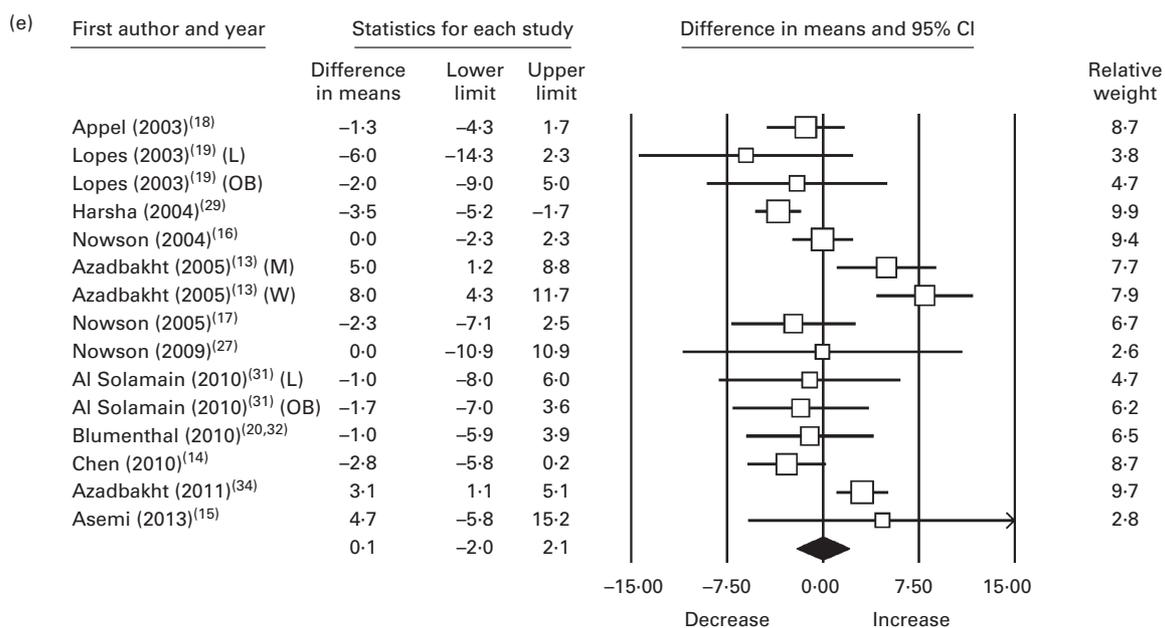
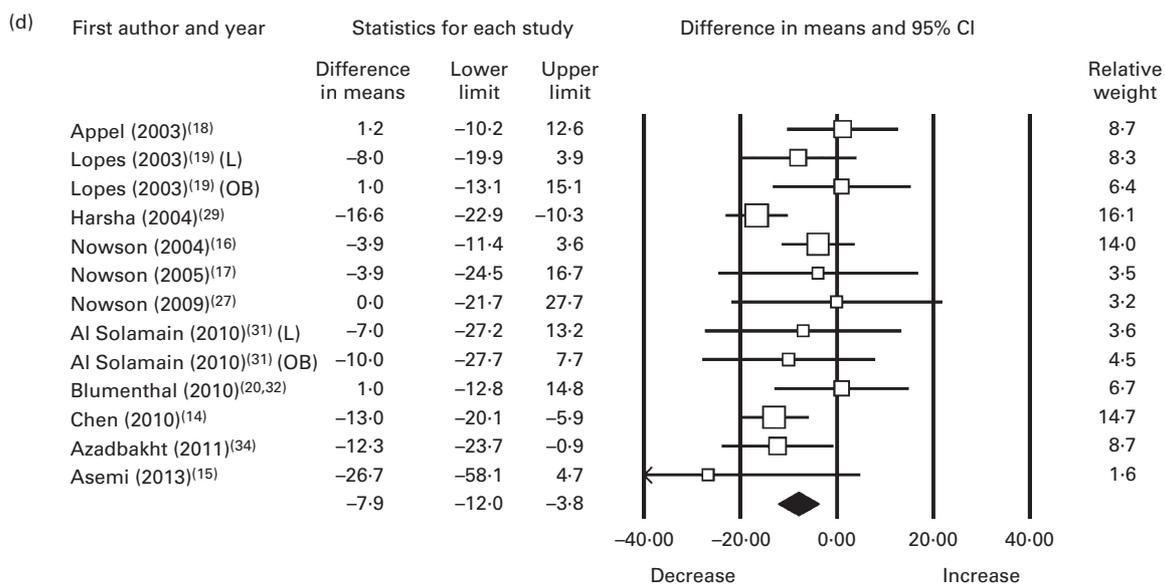
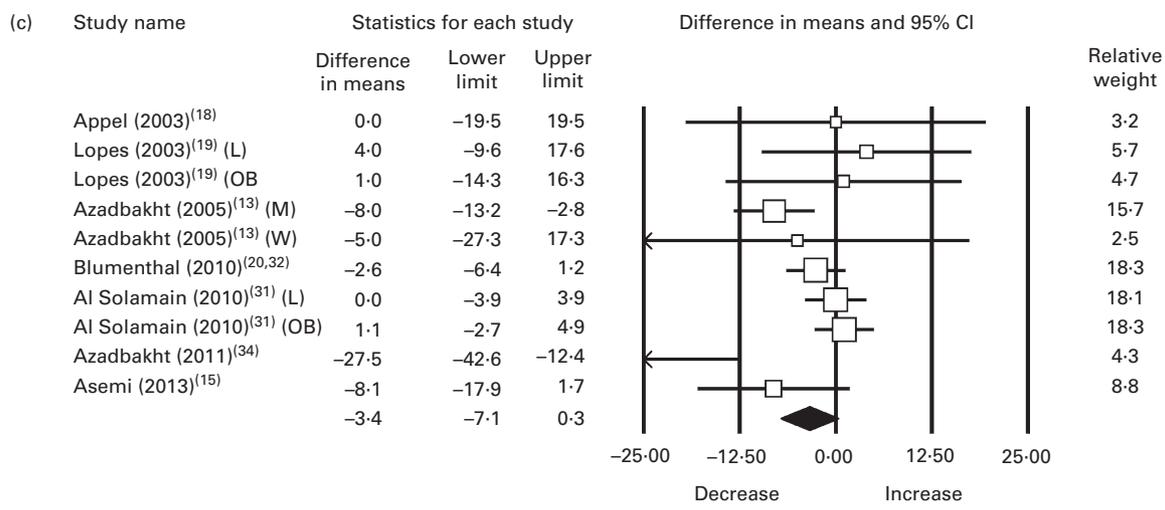
In general, the quality of the trials was good (median Jadad score ≥ 3). Most trials provided a summary of the randomisation process and evidence of adherence to the study protocols and to the dietary interventions. Compliance appeared to be superior in controlled interventions^(9,28,30,36). Less-controlled trials (those based on ADV) and longer-duration trials tended to report greater dropout rates^(13,15–19,27,31–35). The stratification of the meta-analysis by the type of dietary



intervention (CON *v.* ADV) did not modify the effects on BP. Although there is evidence for greater changes in total cholesterol, HDL and LDL concentrations in controlled trials, this finding should be treated with caution as only two studies

included in the sensitivity analysis used the CON trial approach. The lack of a significant association between changes in BP and dietary Na intake is unanticipated. However, the results may require a cautious interpretation in consideration of differences





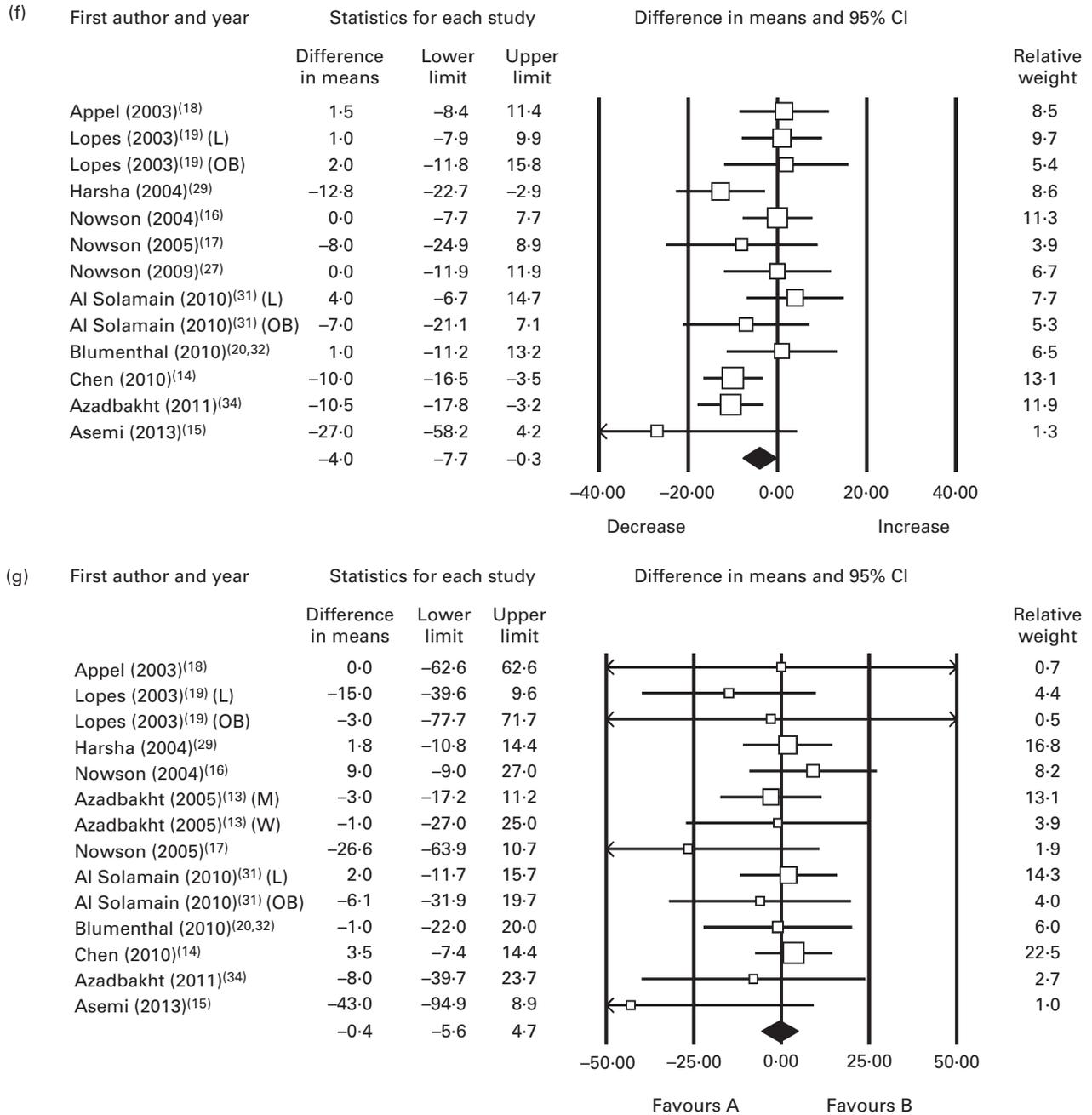


Fig. 2. Forest plots of randomised clinical trials investigating the effects of DASH diet interventions on (a) systolic and (b) diastolic blood pressure (mmHg), (c) glucose (mg/dl) and lipid profile (in mg/dl) ((d) total cholesterol, (e) HDL, (f) LDL and (g) TAG). A random-effects model was used to obtain the pooled mean differences for each metabolic component. L, lean; OB, overweight and obese; M, men; W, women. SI conversion factors: to convert glucose to millimol per litre, multiply by 0.0555; HDL-, LDL- and total cholesterol to millimol per litre, multiply by 0.0259; TAG to millimol per litre, multiply by 0.0113.

between the trials with regard to dietary Na intake in both DASH and control intervention groups, assessment of dietary Na intake (dietary intake or 24 h urinary excretion assessment) and type of dietary intervention (CON or ADV).

The primary outcome of the trials was change in systolic or diastolic BP, and subgroup analyses were conducted to determine the effects on other cardiovascular risk factors^(14,26,29,32). Most of the clinical trials using the DASH diet targeted the primary prevention of hypertension and

chronic metabolic diseases, although, more recently, the DASH diet has been used in studies aiming to prevent progression and complications in other conditions including heart failure⁽³⁷⁾ and uncontrolled asthma⁽³⁸⁾. Prospective cohort studies have found that adherence to a DASH-style diet is associated with a lower risk of CHD and stroke⁽³⁹⁾.

The effectiveness of the DASH diet as a nutritional strategy for the prevention and management of hypertension was confirmed and its significant beneficial effects on other

cardiovascular risk factors including total cholesterol and LDL concentrations were revealed in this meta-analysis. Taken together, these changes are expected to translate into a reduction of approximately 13% in the 10-year Framingham risk scores for CHD, myocardial infarction and stroke. The analysis highlights the beneficial effects of higher

consumption of unrefined carbohydrates, fruits and vegetables and lower consumption of saturated fat on the risk of primary heart disease. However, the efficacy of the DASH diet in reducing the risk of complications, reoccurrence of major cardiovascular events, and mortality in patients with more severe heart conditions is currently not known.

Table 2. Summary of the results of the meta-regression analyses investigating the association of the individual cardiovascular risk factors with covariates that may modify the results of the meta-analysis* (Regression coefficients (β) with their standard errors)

Covariates	β	SE	Q (df = 1)	P
Systolic BP (mmHg; n 19)				
Baseline systolic BP (mmHg)	- 0.1	0.06	5.1	0.02
Duration (weeks)	0.08	0.1	0.6	0.43
Age (years)	0.1	0.1	1.0	0.30
BMI (kg/m ²)	- 0.5	0.2	5.9	0.01
Total sample size (n)	0.007	0.004	2.4	0.12
Jadad score	1.0	0.7	1.7	0.18
Dietary Na intake (mg/d)	0.006	0.001	0.1	0.67
Diastolic BP (mmHg; n 19)				
Baseline diastolic BP (mmHg)	- 0.1	0.04	12.7	< 0.001
Duration (weeks)	- 0.006	0.06	0.01	0.91
Age (years)	0.03	0.05	0.3	0.56
BMI (kg/m ²)	- 0.2	0.1	6.0	0.01
Total sample size (n)	0.002	0.002	1.1	0.28
Jadad score	0.2	0.4	0.4	0.52
Dietary Na intake (mg/d)	- 0.0001	0.0007	0.05	0.81
Glucose (mmol/l; n 10)				
Baseline glucose concentration (mmol/l)	- 0.0167	0.0056	12.5	< 0.001
Duration (weeks)	- 0.0167	0.0056	6.4	0.01
Age (years)	- 0.0033	0.0167	0.1	0.72
BMI (kg/m ²)	0.0056	0.0222	0.09	0.76
Total sample size (n)	0.0002	0.0006	0.03	0.86
Jadad score	0.0500	0.1110	0.22	0.63
Dietary Na intake (mg/d)	0.0002	0.0001	4.6	0.03
HDL (mmol/l; n 15)				
Baseline HDL concentration (mmol/l)	- 0.0104	0.0021	19.4	< 0.001
Duration (weeks)	0.0052	0.0026	3.9	0.04
Age (years)	- 0.0026	0.0026	0.7	0.39
BMI (kg/m ²)	0.0026	0.0104	0.2	0.67
Total sample size (n)	- 0.0003	0.0001	3.7	0.05
Jadad score	- 0.0544	0.0078	40.5	< 0.001
Dietary Na intake (mg/d)	- 0.0001	0.0001	3.3	0.06
LDL (mmol/l; n 13)				
Baseline LDL concentration (mmol/l)	- 0.0008	0.0026	0.05	0.81
Duration (weeks)	0.0026	0.0078	0.3	0.58
Age (years)	0.0026	0.0078	0.2	0.66
BMI (kg/m ²)	- 0.0078	0.0130	0.4	0.54
Total sample size (n)	- 0.0002	0.0003	0.5	0.47
Jadad score	- 0.0233	0.0440	0.3	0.56
Dietary Na intake (mg/d)	0.0001	0.0001	0.2	0.62
Total cholesterol (mmol/l; n 13)				
Baseline total cholesterol concentration (mmol/l)	0.0010	0.0026	0.09	0.76
Duration (weeks)	0.0104	0.0078	1.6	0.19
Age (years)	0.0078	0.0078	0.9	0.32
BMI (kg/m ²)	0.0207	0.0181	1.5	0.21
Total sample size (n)	- 0.0002	0.0003	0.5	0.47
Jadad score	- 0.0466	0.0440	1.0	0.31
Dietary Na intake (mg/d)	- 0.0002	0.0001	0.02	0.86
TAG (mmol/l; n 15)				
Baseline TAG concentration (mmol/l)	- 0.0007	0.0006	1.5	0.21
Duration (weeks)	- 0.0007	0.0034	0.02	0.86
Age (years)	0.0011	0.0045	0.1	0.77
BMI (kg/m ²)	- 0.0045	0.0090	0.4	0.52
Total sample size (n)	0.0001	0.0001	1.0	0.29
Jadad score	0.0237	0.0237	1.0	0.33
Dietary Na intake (mg/d)	0.0001	0.0001	2.4	0.12

BP, blood pressure.

* A mixed-effects meta-regression model (unrestricted maximum likelihood) was used.

The majority of the trials were conducted in the USA and there was a lack of RCT investigating the effects of the DASH diet in European populations. One clinical trial was conducted in the UK, but it was excluded from the main meta-analysis because the allocation to the dietary interventions was not randomised⁽⁴⁰⁾. These findings suggest that the evidence on the applicability and acceptability of the DASH diet in populations outside the USA is limited, and this warrants further investigation⁽⁴¹⁾.

Potential biases in the review process

This meta-analysis has some limitations. First, all such meta-analyses are based on retrospective analytical inference using data reported in peer-reviewed journals from original studies that may not have been designed primarily to investigate the risk factors considered in this meta-analysis. However, our clear delineation of the research questions and inclusion and exclusion criteria, the comprehensive search strategy used and the objective assessment of the quality of the trials may have minimised bias and increased the validity of the findings. The suitability of the extracted studies for meta-analysis is confirmed by the absence of significant publication bias for most risk factors. Significant publication bias was observed for only TAG concentrations.

In some articles, relevant information was either not reported or described only in the text^(16,26,27). All studies with missing numerical information reported a non-significant effect of the DASH diet on risk factors for which data were missing. These trials were included in the main analyses where the missing data were imputed by assigning a null effect to each non-significant result. This conservative approach was implemented to avoid potential inflation of the effect size. A subsequent analysis, after exclusion of these trials, revealed a marginal modification of the effects of the interventions. In some trials, the DASH diet was used in combination with restriction of energy or Na intakes or with attempts to increase physical activity. Such trials were included in the main meta-analysis provided that the absence of the DASH diet was the only intervention difference when compared with the control group so that any effect on the cardiovascular risk factors of interest could be ascribed to the DASH diet.

Biological mechanisms

The DASH dietary pattern involves increased consumption of whole-grain cereals, dietary fibre, unsaturated fatty acids and vegetable proteins compared with typical Western diets⁽⁸⁾. In addition, it involves lower salt intake and promotes the consumption of foods rich in vitamins (vitamin C and folate), minerals (K, Ca, Mg and P), amino acids (arginine) and other substances with biological activity in human cells (flavonoids and inorganic nitrate)^(8,36,42). All these factors may contribute to the significant beneficial effects of the DASH diet on cardiovascular risk factors; the putative mechanistic links between altered intakes of these substances

and changes in cardiovascular and metabolic functions have been reviewed extensively⁽⁴³⁾. Briefly, the multi-organ protective effects of the DASH diet may be due to the combined effects of these molecules on multiple physiological mechanisms including the modification of antioxidant capacity⁽⁴⁴⁾, inflammatory response⁽¹¹⁾, hepatic function⁽¹¹⁾, coagulation⁽¹¹⁾, natriuresis⁽⁴⁵⁾, sympathetic activation⁽³⁵⁾, endothelial function⁽³²⁾ and gluco-insular control⁽¹⁰⁾.

The effects of the DASH diet may be related to the high intake of inorganic nitrate and its role in the non-enzymatic generation of NO⁽⁴⁶⁾. Hord *et al.*⁽⁴²⁾ have estimated that the nitrate-rich foods in a DASH dietary plan (including leafy vegetables, raw or cooked vegetables, vegetable juice and fruits) would result in the consumption of approximately 1200 mg nitrate/d. Our group has recently demonstrated a significant effect of inorganic nitrate supplementation on systolic BP (-4.4 mmHg, $P < 0.001$) and diastolic BP (-1.1 mmHg, $P = 0.06$)⁽⁴⁶⁾.

Agreements and disagreements with previous results

The DASH dietary pattern shares some dietary features with the Mediterranean dietary pattern including higher consumption of vegetables and fruits, whole grains, fish and nuts⁽⁴⁷⁾. The Prevención con Dieta Mediterránea trial has recently reported significant beneficial effects of a Mediterranean diet supplemented with extra-virgin olive oil or nuts on multiple cardiovascular and metabolic risk factors and primary prevention of CVD⁽⁴⁸⁾. A recent meta-analysis of clinical studies has shown that adherence to a Mediterranean dietary pattern improves HDL concentrations ($+0.03$ mmol/l), TAG concentrations (-0.07 mmol/l), systolic BP (-2.3 mmHg) and diastolic BP (-1.5 mmHg) and glucose concentrations (-0.21 mmol/l)⁽⁴⁹⁾. The DASH diet appears to have a greater effect on BP than the Mediterranean diet, but the results of these meta-analyses confirm that adherence to either dietary pattern improves multiple cardiovascular risk factors substantially⁽⁴⁷⁾.

Conclusions

The DASH dietary plan has been recommended by several US health organisations as an effective nutritional strategy for the prevention and management of elevated BP^(8,50). This systematic review and meta-analysis of RCT investigating the effects of DASH diet interventions revealed that the mean change in cardiometabolic markers would yield a reduction of approximately 13% in the 10-year Framingham risk score for cardiovascular events. This finding reinforces the evidence that DASH diet interventions could make a significant contribution to the prevention of CVD beyond the well-known BP-lowering effects.

Future studies should include identification of the biological pathways activated in individuals eating the DASH diet that are most influential in lowering CVD risk and investigation of the nutrient–nutrient and gene–diet interactions responsible for inter-individual difference in responsiveness to the DASH diet. Findings from such studies may help to

inform the design of more effective personalised nutritional interventions for CVD prevention.

Supplementary material

To view supplementary material for this article, please visit <http://dx.doi.org/10.1017/S0007114514003341>

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The authors' contributions are as follows: M. S. and J. C. M. conceived the systematic review; S. C. and M. S. searched and collected the data; J. L. acted as a third reviewer during the different phases of the systematic review; M. S. analysed the data and wrote the manuscript. All authors contributed to subsequent analyses, interpretation of the results and the final revision of the manuscript.

The corresponding author (M. S.) is the guarantor for the manuscript and had full access to all the data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

None of the authors has any conflicts of interest to declare.

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