Comparison of dietary macronutrient patterns of 14 popular named dietary programmes for weight and cardiovascular risk factor reduction in adults: systematic review and network meta-analysis of randomised trials

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ABSTRACT

OBJECTIVE

To determine the relative effectiveness of dietary macronutrient patterns and popular named diet programmes for weight loss and cardiovascular risk factor improvement among adults who are overweight or obese.

DESIGN

Systematic review and network meta-analysis of randomised trials.

DATA SOURCES

Medline, Embase, CINAHL, AMED, and CENTRAL from database inception until September 2018, reference lists of eligible trials, and related reviews.

STUDY SELECTION

Randomised trials that enrolled adults (≥18 years) who were overweight (body mass index 25-29) or obese (≥30) to a popular named diet or an alternative diet.

OUTCOMES AND MEASURES

Change in body weight, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, systolic blood pressure, diastolic blood pressure, and C reactive protein at the six and 12 month follow-up.

REVIEW METHODS

Two reviewers independently extracted data on study participants, interventions, and outcomes and assessed risk of bias, and the certainty of evidence using the GRADE (grading of recommendations, assessment, development, and evaluation) approach. A bayesian framework informed a series of random effects network meta-analyses to estimate the relative effectiveness of the diets.

RESULTS

121 eligible trials with 21 942 patients were included and reported on 14 named diets and three control diets. Compared with usual diet, low carbohydrate and low fat diets had a similar effect at six months on weight loss (4.63 *v* 4.37 kg, both moderate certainty) and reduction in systolic blood pressure (5.14 mm Hg, moderate certainty *v* 5.05 mm Hg, low certainty) and diastolic blood pressure (3.21 *v* 2.85 mm Hg, both low certainty). Moderate macronutrient diets resulted in slightly less weight loss and blood pressure reductions. Low carbohydrate diets had less effect than low fat diets and moderate macronutrient diets on reduction in LDL cholesterol (1.01 mg/dL, low certainty *v* 7.08 mg/dL, moderate certainty *v* 5.22 mg/dL, moderate certainty, respectively) but an increase in HDL cholesterol (2.31 mg/dL, low certainty), whereas low fat (−1.88 mg/dL, moderate certainty) and moderate macronutrient (−0.89 mg/dL, moderate certainty) did not. Among popular named diets, those with the largest effect on weight reduction and blood pressure in comparison with usual diet were Atkins (weight 5.5 kg, systolic blood pressure 5.1 mm Hg, diastolic blood pressure 3.3 mm Hg), DASH (3.6 kg, 4.7 mm Hg, 2.9 mm Hg, respectively), and Zone (4.1 kg, 3.5 mm Hg, 2.3 mm Hg, respectively) at six months (all moderate certainty). No diets significantly improved levels of HDL cholesterol or C reactive protein at six months. Overall, weight loss diminished at 12 months among all macronutrient patterns and popular named diets, while the benefits for cardiovascular risk factors of

WHAT IS ALREADY KNOWN ON THIS TOPIC

A plethora of recommendations have suggested a variety of dietary programmes for weight management and cardiovascular risk reduction, primarily Mediterranean and DASH-style diets

Systematic reviews and meta-analyses of randomised trials have suggested that differences in weight loss between popular named diets are small and unlikely to be of importance to those seeking to lose weight, whereas meta-analyses have yielded conflicting results for cardiovascular risk reduction

Pairwise meta-analyses are limited in examining the relative merit of the range of popular named diets, and no comprehensive comparative effectiveness review, using network meta-analyses of diets for both weight loss and cardiovascular risk factors, has been carried out

WHAT THIS STUDY ADDS

Based on 121 randomised trials with 21 942 patients, low carbohydrate (eg, Atkins, Zone), low fat (eg, Ornish), and moderate macronutrient (eg, DASH, Mediterranean) diets had, compared with usual diet, compelling evidence for modest reduction in weight and potentially important reduction in both systolic and diastolic blood pressure at six months

Weight reduction at the 12 month follow-up diminished, and aside from the Mediterranean diet for LDL reduction, improvements in cardiovascular risk factors largely disappeared

Differences between diets were typically small to trivial and often based on low certainty evidence

all interventions, except the Mediterranean diet, essentially disappeared.

CONCLUSIONS

Moderate certainty evidence shows that most macronutrient diets, over six months, result in modest weight loss and substantial improvements in cardiovascular risk factors, particularly blood pressure. At 12 months the effects on weight reduction and improvements in cardiovascular risk factors largely disappear.

SYSTEMATIC REVIEW REGISTRATION

PROSPERO CRD42015027929.

Introduction

The worldwide prevalence of obesity nearly tripled between 1975 and 2018.[1] In response, authorities have made dietary recommendations for weight management and cardiovascular risk reduction.[2 3] Diet programmes—some focusing on carbohydrate reduction and others on fat reduction—have been promoted widely by the media and have generated intense debates about their relative merit. Millions of people are trying to lose weight by changing their diet. Thus establishing the effect of dietary macronutrient patterns (carbohydrate reduction *v* fat reduction *v* moderate macronutrients) and popular named dietary programmes is important.

Biological and physiological mechanisms have been proposed to explain why some dietary macronutrient patterns and popular dietary programmes should be better than others. A previous network meta-analysis, however, suggested that differences in weight loss between dietary patterns and individual popular named dietary programmes are small and unlikely to be important.[4] No systematic review and network meta-analysis has examined the comparative effectiveness of popular dietary programmes for reducing risk factors for cardiovascular disease, an area of continuing controversy.[5-8]

Proponents of Mediterranean-type and DASH-type (Dietary Approaches to Stop Hypertension) diets suggest that these diets can improve risk factors for cardiovascular disease through weight loss itself and owing to their limited sodium content and claimed anti-inflammatory properties.[9] Systematic reviews and meta-analyses have shown conflicting results for the dietary effect on markers of cardiovascular disease risk, including blood pressure, low density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol, and C reactive protein.[6 8-12] Few reviews have used rigorous meta-analytical techniques to obtain quantitative estimates of the relative effect of different diets.[4 13 14] Systematic reviews have relied on pairwise comparisons. These comparisons have failed to examine direct and indirect clinical trial data by conducting a network meta-analysis, and they have not dealt with the certainty (quality) of evidence using the widely accepted standard, the GRADE (grading of recommendations, assessment, development, and evaluation) approach.[15]

We performed a systematic review and network meta-analysis of randomised controlled trials for improvements in weight loss and cardiovascular risk factors to determine the relative effectiveness and certainty of evidence among dietary macronutrient patterns and popular named dietary programmes for adults who are overweight or obese.

Methods

We searched Medline, Embase, CINAHL (Cumulative Index to Nursing and Allied Health Literature), AMED (Allied and Complementary Medicine Database), and the Cochrane Central Register of Controlled Trials (CENTRAL) from database inception until September 2018. Search terms included extensive controlled vocabulary and keyword searches related to randomised controlled trials, diets, weight loss, and cardiovascular risk factors. Appendix text S1 presents the Medline search strategy. We reviewed reference lists from eligible trials and related reviews for additional eligible randomised controlled trials.

Eligible studies randomised adults (≥18 years) who were overweight (body mass index 25-29) or obese (≥30) to an eligible popular named diet or an alternative active or non-active control diet (eg, usual diet), and reported weight loss, changes in lipid profile, blood pressure, or C reactive protein levels at three months' follow-up or longer.

We categorised dietary treatment groups in two ways: using dietary macronutrient patterns (low carbohydrate, low fat, and moderate macronutrient—similar to low fat, but slightly more fat and slightly less carbohydrate) and according to individual popular

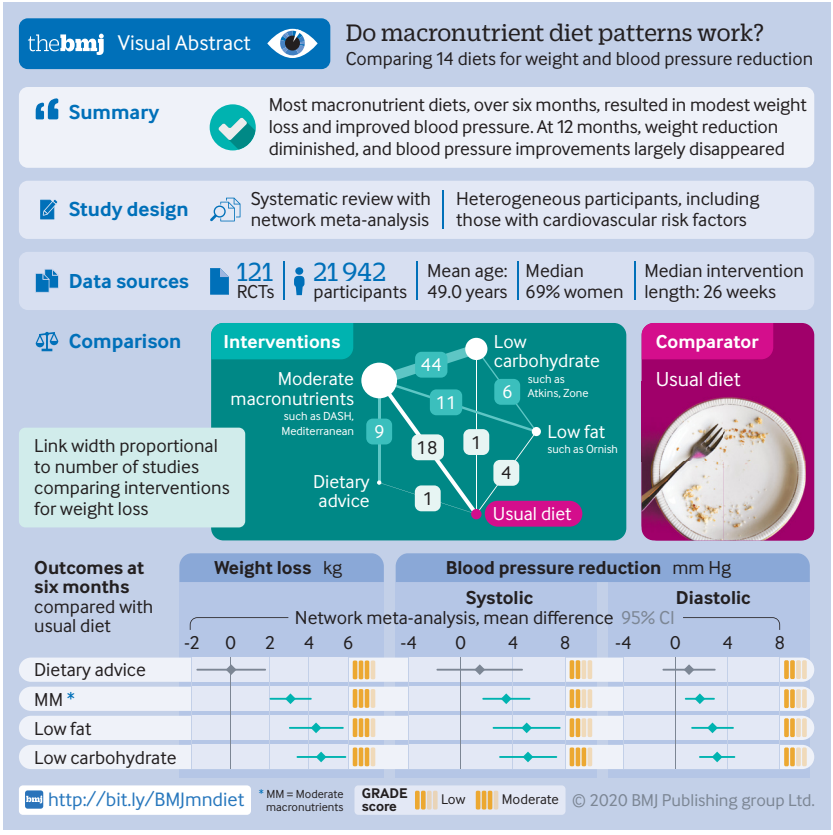

Table 1 | Nutritional patterns based on macronutrient composition

Type of diet	Popular diets*	Carbohydrates, % kcal	Protein, % kcal	Fat, % kcal
Low carbohydrate	Atkins, South Beach, Zone	≤40	Approximately 30	30-55
Moderate macronutrients	Biggest Loser, DASH, Jenny Craig, Mediterranean, Portfolio, Slimming World, Volumetrics, Weight Watchers	Approximately 55-60	Approximately 15	21-≤30
Low fat	Ornish, Rosemary Conley†	Approximately 60	Approximately 10-15	≤20

1 kcal=4.18 kJ.
*A paleolithic diet was reported in two randomised controlled trials (Lindeberg 2007 and Mellberg 2014; appendix table S2), we categorised Lindeberg 2007 as moderate macronutrient based on energy intake (40.2±8.3% carbohydrate, 27.9±6.8% protein, 26.9±6.4% fat). Mellberg, 2014 was categorised as low carbohydrate (30% carbohydrate, 30% protein, 40% fat).
†We categorised Rosemary Conley diet (Truby 2006) as moderate macronutrient (42% carbohydrate, 16% protein, 37% fat).

named dietary programmes.[4] Dietary macronutrient patterns were established by macronutrient content (see table 1). Leading dietary programmes were identified through the explicit naming of the branded or popular diet, the referencing of popular or branded literature, or the naming of a brand as a funder of a randomised controlled trial reporting our target outcomes. The diet was labelled as brand-like when it met the definition of a branded diet but failed to name or reference the brand in the article. For example, dietary programmes that did not refer to Atkins but consisted of less than 40% of kilocalories from carbohydrates per day for the duration of study, or were funded by Atkins, were considered Atkins-like.[16 17] Appendix table S1 presents the characteristics of eligible dietary programmes.

We included dietary programmes with structured advice for daily macronutrient, food, or caloric intake for a defined period (≥3 months). Eligible studies could or could not provide exercise (eg, walking, strength training) or behavioural support (eg, counselling, group support online or in person), and could include meal replacement products, but had to consist primarily of whole foods and could not include drugs.

We categorised eligible control diets as: usual diet (eg, wait list: participants were instructed to maintain their usual dietary habits), dietary advice (eg, received brochures, dietary materials including dietary guidelines, or consultation with a professional dietician by email or telephone), and low fat diet (≤30% fat with or without advice about lowering calories). We used the usual diet as our reference diet and presented results for the other diets against the reference diet.

Teams of two reviewers independently screened titles and abstracts for possible inclusion. If either reviewer considered a study potentially eligible, reviewers obtained and screened the full text. Reviewers resolved disagreements by discussion and, when necessary, through adjudication by a third reviewer.

Data abstraction and risk of bias assessment

After pilot testing our data extraction forms, teams of two reviewers independently extracted demographic information, experimental and control interventions including exercise and behavioural support, and data on each outcome of interest. We focused on two sets of outcomes: weight loss and related markers of cardiovascular disease risk (systolic blood pressure, diastolic blood pressure, LDL cholesterol, HDL cholesterol, and C reactive protein) at six and 12 month follow-up (±3 months for both periods).

Reviewers assessed the risk of bias for each individual randomised controlled trial independently and in duplicate using the Cochrane risk of bias tool.[18] We assigned individual trials as high risk of bias if one of two key domains, allocation concealment or missing outcome data, was deemed high risk of bias; otherwise, we assigned individual trials as low risk of bias.

Data synthesis and statistical methods

When reported, we used mean change and standard deviations. When authors reported data as measures before and after intervention, we used methods outlined in the Cochrane Handbook to calculate mean change and standard deviations for change.[18] When standard deviations were missing, we estimated them from standard errors, P values, confidence intervals, or graphs. If none of these methods was possible, we derived standard deviations from other studies included in our network meta-analysis using a validated imputation technique.[19] Appendix text S2 presents details of the missing standard deviations imputed for each outcome.

We performed statistical analyses for dietary macronutrient patterns based on five nodes (moderate macronutrients, low carbohydrate, low fat, dietary advice, and usual diet) and for popular named diets based on 17 nodes (14 popular named dietary programmes and three control diets). We used bayesian random effects models to obtain the pooled direct estimates and corresponding forest plots of the available direct comparisons.[20] We assessed heterogeneity between randomised controlled trials for each direct comparison with visual inspection of the forest plots and the I^2 statistic.

We then performed a series of random effects network meta-analyses within a bayesian framework using Markov chain Monte-Carlo simulation methods.[21 22] For each analysis, we used three chains with 100 000 iterations after an initial burn-in of 10 000. We assessed convergence based on trace plots and time series plots. We measured the goodness of model fit by the posterior mean of the overall residual deviance; in a well fitting model the residual deviance should be close to the number of data points included in the analysis.[19] We used vague priors and dealt with the extent of heterogeneity in each network analysis using a common heterogeneity variance (τ); we categorised results as low (from 0.1 to 0.5), moderate (>0.5 to 1.0), and high (>1.0).[23 24] To estimate the precision of the effects, we used 95% credible intervals, by means of the 2.5 and 97.5 percentiles obtained from the simulations.[25] We

used the node splitting method to generate the effect size and credible intervals for the indirect comparison and for the statistical test of incoherence (also known as inconsistency) between direct and indirect estimates.[26] We calculated the ranking probabilities of being the best, second best, and so on for all treatment options and used the surface under the cumulative ranking curve to rank the intervention hierarchy in the network meta-analysis.[27]

We considered two effect modifiers that were modelled as present or absent if they were included in an overall dietary programme: exercise and behavioural support. Exercise was defined as having explicit instructions for weekly physical activities and categorised as exercise or no exercise. Diets with at least two group or individual sessions a month for the first three months were considered to provide behavioural support.[28] We performed a network meta-regression assuming a common coefficient across comparisons to explore the effect of exercise and behavioural support for each outcome.[29] Three sensitivity analyses were conducted by restricting studies to trials with individuals who were overweight or obese, but who were otherwise healthy; those with a low risk of bias; and investigator initiated randomised trials, thus removing trials that were funded partly or wholly by diet companies.

We used the networkplot command of Stata version 15.1 (StataCorp, College Station, TX) to draw the network plots,[30] and WinBUGS version 1.4.3 (MRC Biostatistics Unit, Cambridge, UK) and R version 3.4.3 (R Core Team, Vienna, Austria) with gemtc package for statistical analyses.

Assessing certainty of evidence

We rated the certainty of evidence for each network estimate using the GRADE framework, which classifies evidence as high, moderate, low, or very low certainty. The starting point for certainty in direct estimates for randomised controlled trials is high, but could be rated down based on limitations in risk of bias, imprecision, inconsistency (heterogeneity), indirectness, and publication bias.[15]

We rated the certainty of evidence for each direct comparison according to standard GRADE guidance for pairwise meta-analysis.[31 32] Indirect effect estimates were calculated from available "loops" of evidence, which included first order loops (based on a single common comparator treatment—that is the difference between treatment A and B is based on comparisons of A and C as well as B and C) or higher order loops (more than one intervening treatment connecting the two interventions). We assessed the evidence for indirect and network estimates focusing on the dominant first order loop,[31] rating certainty of indirect evidence as the lowest certainty of the direct comparisons informing that dominant loop. In the absence of a first order loop, we used a higher order loop to rate certainty of evidence and used the lowest of the ratings of certainty for the direct estimates contributing to the loop. We considered further rating down each indirect comparison for intransitivity if the distribution of effect modifiers differed in the contributing direct comparisons.[31]

For the network estimate, we started with the certainty of evidence from the direct or indirect evidence that dominated the comparison and, subsequently, considered rating down our certainty in the network estimate for incoherence between the indirect and direct estimates for imprecision (wide credible intervals) around the treatment effect estimates. When serious incoherence was present, we used, as the best estimate, that with the higher certainty of the direct and indirect evidence.[32] Appendix text S3 presents additional details of the GRADE assessment.

Summary of more and less preferred treatments

To optimise the presentation of results for the 17 diet (14 popular, three control) network meta-analysis, we applied a new approach to summarise the results, establishing different groups of interventions (from the most to the least effective) based on the effect estimates obtained from the meta-analysis and their certainty of evidence.[33] For each outcome, we created three groups of interventions. Firstly, the reference diet (usual diet) and diets that did not differ from the reference (that is, confidence interval crossed mean difference=0), which we refer to as "among the least effective". Secondly, diets superior to the reference, but not superior to any other diet superior to the reference (which we call category 1 and describe as "inferior to the most effective, but superior to the least effective"). Lastly, diets that proved superior to at least one category 1 diet (which we call "among the most effective"). We then divided all three categories into two groups: those with moderate or high certainty evidence relative to the usual diet, and those with low or very low certainty evidence relative to the usual diet.

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, in developing plans for design or implementation of the study, or in the interpretation or write up of results. We did not evaluate whether the studies included in the review involved patients in planning or implementing the study.

Results

Search

The electronic searches yielded 27 238 unique studies, and the grey literature search identified 213 additional studies. Of the total, 1411 were potentially eligible, and 137 articles reporting 121 randomised controlled trials proved eligible (fig 1). Appendix text S4 presents the list of eligible studies.

Study characteristics, risk of bias, and certainty of evidence

Appendix table S2 summarises the characteristics of the 121 randomised controlled trials, which included

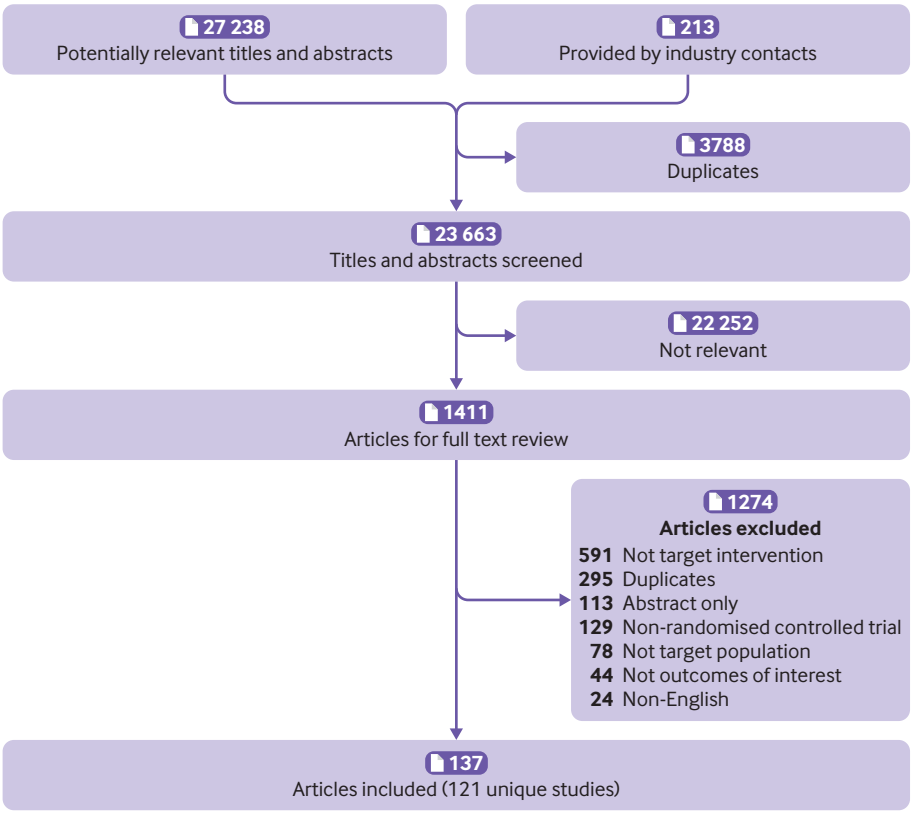

Fig 1 | Flow diagram of literature selection

from 21 to 1269 participants (total 21 942) with a median of mean age of 49.0 years, a median of mean body mass index of 33.0, a median of mean weight of 92.9 kg, a median proportion of women of 69.0%, and a median intervention duration of 26 weeks. Figure 2 provides the network plot of macronutrient consumption patterns and the popular named diets. Appendix figures S1-S6 present the network plot for each outcome, appendix table S3 presents the number of studies and participants for the popular named diets for all outcomes, and appendix table S4 summarises the funding sources and primary and secondary outcomes reported in included trials.

Ninety four randomised controlled trials were at low risk of bias and 27 were at high risk of bias (appendix table S5).

For the outcomes of weight and blood pressure, many comparisons of popular diets versus the reference standard, usual diet, provided moderate certainty evidence. For other outcomes, and for most comparisons of popular diets against one another, results provided only low certainty evidence.

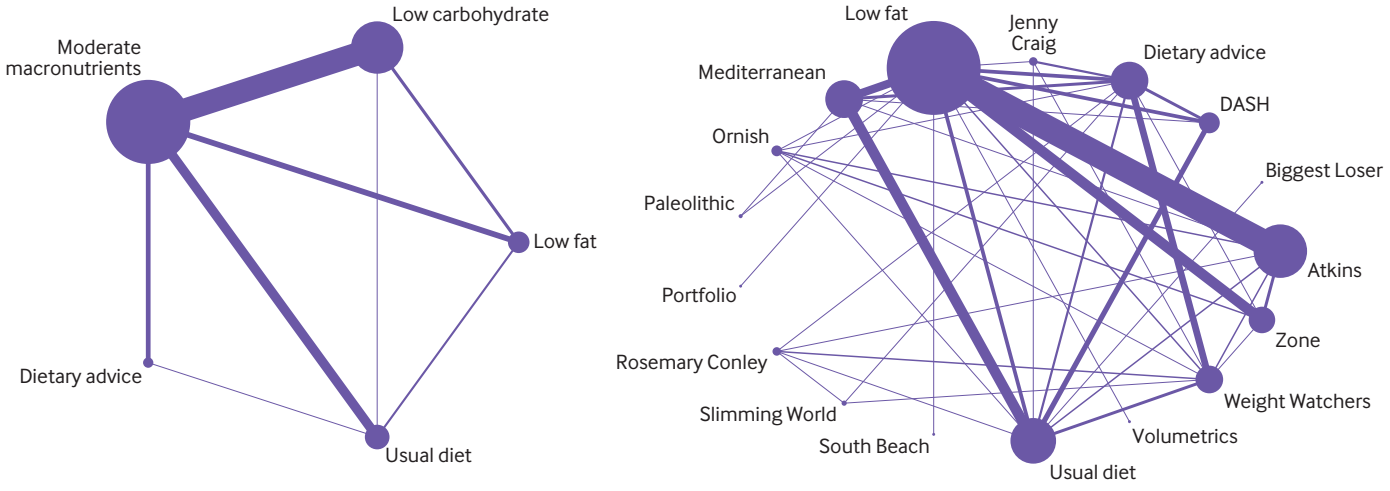

Fig 2 | Network plots of all included studies for macronutrient patterns and popular named diets

Dietary macronutrient patterns

Appendix tables S6-S11 present GRADE assessments for all outcomes at six months (±3 months), with the number of included randomised controlled trials, sample size, I^2, direct estimates, indirect estimates, intransitivity, and incoherence assessment. Much of the evidence was judged as moderate certainty, rated down most often because of serious inconsistency. Compared with a usual diet, low carbohydrate diets had median differences in weight loss of 4.63 kg (95% credible interval 3.42 to 5.87; moderate certainty; fig 3), a reduction in systolic blood pressure of 5.14 mm Hg (3.01 to 7.32; moderate certainty; fig 4), a reduction in diastolic blood pressure of 3.21 mm Hg (1.89 to 4.53; low certainty; fig 4), an increase in HDL cholesterol of 2.31 mg/dL (0.68 to 3.87; low certainty; fig 5), and a reduction in LDL cholesterol of 1.01 mg/dL (−2.96 to 4.96 mg/dL; low certainty; fig 5). Low fat diets had estimated effects similar to those of low carbohydrate diets for weight loss (fig 3) and blood pressure (fig 4), but a greater effect on LDL cholesterol reduction (7.08 mg/dL; moderate certainty; fig 5). Based on moderate to low certainty evidence, moderate macronutrient diets had slightly smaller effects than low carbohydrate diets on weight loss (fig 3), blood pressure (fig 4), and HDL cholesterol increase (fig 5), but a greater effect on LDL cholesterol reduction (fig 5). Appendix table S12 presents the network meta-analysis results for C reactive protein, showing no statistically significant differences between diets.

At the 12 month (±3 months) follow-up, the estimated average weight loss of all dietary macronutrient patterns compared with usual diet was 1 to 2 kg less, generally with low certainty evidence (appendix table S13). We found no significant differences between the macronutrient dietary patterns and usual diet for systolic and diastolic blood pressure, LDL cholesterol, and C reactive protein reductions, except low fat and moderate macronutrients, which each showed significant adverse reductions in HDL cholesterol (−2.90 mg/dL, −2.81 mg/dL, respectively; appendix tables S12, S14, and S15).

Appendix tables S16-S25 present sensitivity analyses showing that the findings were similar to those of the primary analyses. Network meta-regression accounting for both exercise and behaviour support also showed similar results (appendix tables S26-S28).

Individual popular named diets

Appendix tables S29-S34 present the GRADE assessment details for all outcomes at six months (±3 months). Figure 6 and appendix table S35 summarise the results for all outcomes at six months in comparison with a usual diet, organised by GRADE certainty of evidence.

Weight loss

Appendix table S36 presents the league table of weight loss at six months. Among the diets with high or moderate certainty evidence relative to usual diet, Jenny Craig and Atkins proved the most effective popular named diets, whereas Volumetrics, paleolithic, low fat, Zone, Weight Watchers, Rosemary Conley, DASH, Ornish, and Mediterranean were inferior to the most effective but superior to the least effective diet interventions. The Biggest Loser, Slimming World, and dietary advice were the least effective diet interventions (fig 6, appendix table S35). Among the diets with only low or very low certainty evidence relative to usual diet, South Beach might be the most effective (fig 6).

All named diets, except a paleolithic diet, decreased their estimated effects at the 12 month follow-up by, on average, 1.5 kg compared with the six month follow-up (appendix tables S36 and S37).

Systolic blood pressure

Appendix table S38 presents the league table of reduction of systolic blood pressure at six months. Among the diets with moderate certainty evidence relative to a usual diet, paleolithic was probably the most effective, whereas Atkins, DASH, Portfolio, low fat, Zone, and Mediterranean were probably inferior to the most effective, but superior to the least effective,

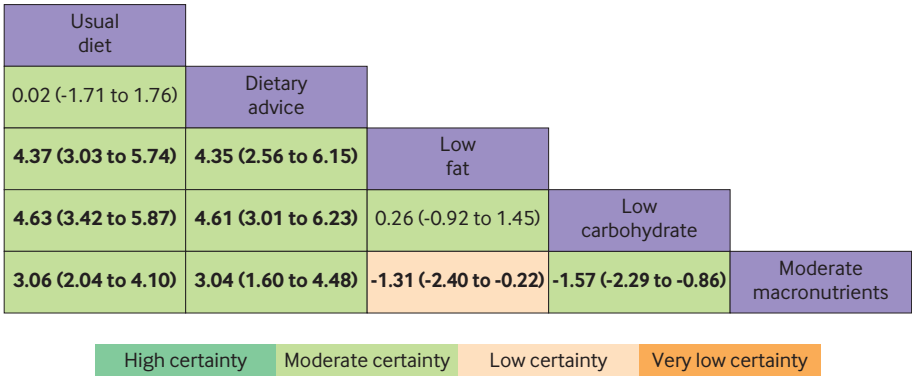

Fig 3 | Macronutrient pattern network meta-analysis results with corresponding GRADE (grading of recommendations, assessment, development, and evaluation) certainty of evidence for six month weight loss (kg). Values correspond to difference in median weight loss between column and row at six months, for positive values the diet indicated in the column is favoured (eg, low fat had a median weight loss of 4.37 kg at six months compared with usual diet). Values in bold indicate a statistically significant treatment effect

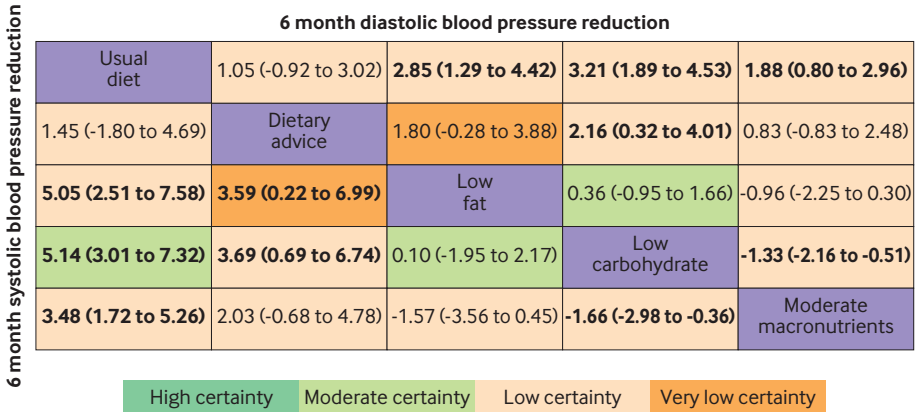

Fig 4 | Macronutrient pattern network meta-analysis results with corresponding GRADE (grading of recommendations, assessment, development, and evaluation) certainty of evidence for six month systolic blood pressure (SBP) and diastolic blood pressure (DBP) reduction (mm Hg). Values correspond to difference in median DBP reduction (above, right of macronutrient patterns) and SBP reduction (below, left of macronutrient patterns) between column and row at six months (eg, low fat had a median DBP reduction of 1.80 and a median SBP reduction of 3.59 compared with dietary advice). Values in bold indicate a statistically significant treatment effect

diets. The Biggest Loser and Ornish proved the least effective diets. Among the diets with only low or very low certainty evidence relative to usual diet, Jenny Craig might be the most effective (fig 6, appendix table S35).

Effects for all popular named diet programmes had decreased at the 12 month follow-up compared with the six month follow-up. No statistically significant differences were found between popular named diets and a usual diet (appendix tables S38 and S39).

Diastolic blood pressure

Among the diets with moderate certainty evidence relative to a usual diet, Atkins proved the most effective popular named diet at six months, whereas DASH, low fat, and Zone were probably inferior to the most effective, but superior to the least effective, diets. Paleolithic, Biggest Loser, Mediterranean, and Ornish proved the least effective diets. Among the diets with only low or very low certainty evidence relative to a usual diet, Jenny Craig might be the most effective (fig 6, appendix tables S35 and S38). We found no statistically significant differences between popular named diets and usual diet at the 12 month follow-up (appendix table S39).

Blood lipoproteins

Among the diets with moderate certainty evidence relative to usual diet, the Mediterranean diet proved the most effective popular named diet for LDL cholesterol reduction; Ornish, DASH, Biggest Loser, low fat, and dietary advice were probably no better than usual diet. Among the diets with only low or

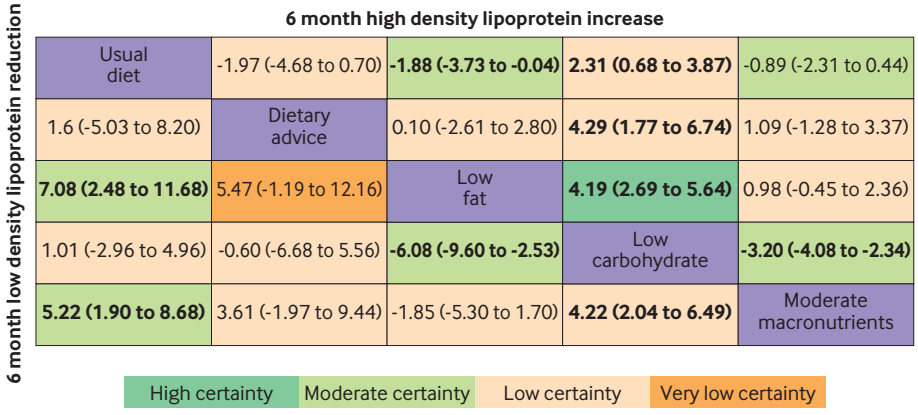

Fig 5 | Macronutrient pattern network meta-analysis results with corresponding GRADE (grading of recommendations, assessment, development, and evaluation) certainty of evidence for reduction in low density lipoprotein (LDL) cholesterol and increase in high density lipoprotein (HDL) cholesterol (mg/dL) at six months. Values correspond to difference in median HDL cholesterol increase (above, right of macronutrient patterns) and LDL cholesterol reduction (below, left of macronutrient patterns) between column and row at six months (eg, low fat had a median HDL cholesterol increase of 0.10 mg/dL and a median LDL cholesterol reduction of 5.47 mg/dL at six months compared with dietary advice). Values in bold indicate a statistically significant treatment effect

Diet *v* usual diet	Weight loss (kilograms)	Systolic blood pressure reduction (mm Hg)	Diastolic blood pressure reduction (mm Hg)	Low density lipoprotein reduction (mg/dL)	High density lipoprotein reduction (mg/dL)	C-reactive protein reduction (mg/dL)
Atkins	5.46	5.14	3.30	-2.75	3.41	0.64
Zone	4.07	3.46	2.33	-2.89	-0.33	0.27
DASH	3.63	4.68	2.84	3.93	-1.90	NA
Mediterranean	2.87	2.94	1.03	4.59	-0.61	0.25
Paleolithic	5.31	14.56	3.85	7.27	-2.52	0.52
Low fat	4.87	3.95	2.22	1.92	-2.13	0.33
Jenny Craig	7.77	7.86	7.81	0.21	-2.85	0.19
Volumetrics	5.95	2.93	1.95	7.13	-0.13	NA
Weight Watchers	3.90	2.80	1.03	7.13	-0.88	0.87
Rosemary Conley	3.76	2.39	1.44	7.15	-2.04	NA
Ornish	3.64	0.69	0.20	4.71	-4.87	1.11
Portfolio	3.64	5.97	3.98	21.29	-3.26	-0.37
Biggest Loser	2.88	3.17	2.20	3.90	-0.01	NA
Slimming World	2.15	NA	NA	NA	NA	NA
South Beach	9.86	NA	NA	-0.64	0.36	NA
Dietary advice	0.31	0.58	0.40	-2.01	-1.71	-1.15

"Among the most effective" with moderate to high certainty
"Inferior to the most effective/superior to the least effective" with moderate to high certainty
"Among the least effective" with moderate to high certainty
"Maybe among the most effective" with very low to low certainty
"Inferior to the most effective/superior to the least effective" with very low to low certainty
"Maybe among the least effective" with very low to low certainty
"Maybe worse than usual diet"

Fig 6 | Summary of results of popular named diets network meta-analysis for all outcomes at six months. The number is the point estimates of effect in comparison with usual diet

very low certainty evidence relative to a usual diet, Portfolio might be the most effective (fig 6, appendix tables S35 and S40).

No popular named diets showed a statistically significant increase in HDL cholesterol at the six month follow-up (fig 6, appendix tables S35 and S40). Similar, but smaller, results were found at the 12 month follow-up for both LDL and HDL cholesterol (appendix table S41).

C reactive protein

We found no statistically significant differences between popular named diets and usual diet (fig 6, appendix tables S35 and S42). Similar results were found at the 12 month follow-up (appendix table S43).

Additional analyses

Appendix figure S7 presents the results of mean surface under the cumulative ranking curve values for all outcomes at six months. We did not perform network meta-regressions and sensitivity analyses for C reactive protein because of the limited number of eligible randomised controlled trials. Network meta-regressions for the other five outcomes showed that none of the regression factors (behavioural support and exercise, risk of bias, clinical population, and funding support) had statistically significant effects. Appendix tables S44-S57 present the results of network meta-regressions and sensitivity analyses.

Adverse events

Twenty two (18.2%) of the 121 randomised controlled trials, of which 12 evaluated low carbohydrate diets, reported adverse events. One trial reported a statistically significant higher risk of headaches at three months (25% *v* 8%; P=0.03) in the group receiving a low fat diet (n=73) than in the group with a low carbohydrate diet (n=75), but no significant differences at six and 12 months.[34] Another trial reported a statistically significant increase in the risk of several adverse effects at six months in the group assigned to a low carbohydrate diet (n=60) than in those assigned to a low fat diet (n=60), including constipation (68% *v* 35%; P=0.001), headache (60% *v*

40%; P=0.03), halitosis (38% *v* 8%; P=0.001), muscle cramps (35% *v* 7%; P=0.001), diarrhoea (23% *v* 7%; P=0.02), general weakness (25% *v* 8%; P=0.01), and rash (13% *v* 0%; P=0.006).[35] Study authors did not assess the likelihood that the diet was plausibly responsible for the adverse events.

Discussion

Our network meta-analysis quantifies the comparative effectiveness of three dietary macronutrient patterns based on 14 popular named dietary programmes for both weight and related cardiovascular risk factors at six and 12 months using the GRADE approach. Evidence of low to moderate certainty showed that all three dietary macronutrient patterns (low carbohydrate, low fat, and moderate macronutrient) were associated with larger reductions in body weight (fig 3) and blood pressure than a usual diet (fig 4); reductions with moderate macronutrient diets were slightly smaller than with the other two macronutrient patterns. Effects on weight were less at 12 months than at six months (between 4 and 5 kg reductions relative to usual diet at six months, about 3 kg at 12 months). Based on moderate certainty evidence, both low fat and moderate macronutrient diets are likely to reduce LDL cholesterol relative to usual diets at six months. All these changes were potentially important based on the importance threshold we specified in advance (weight loss 2 kg, systolic blood pressure 3 mm Hg, diastolic blood pressure 2 mm Hg, LDL cholesterol 5 mg/dL; appendix text S3). Macronutrient diet related improvements in both blood pressure and blood lipids disappeared almost completely at 12 months.

Of the popular named diets, Atkins, DASH, and Zone had the highest certainty evidence and the most consistent effects for reduction in weight and blood pressure at six months; an unnamed diet, low fat, performed similarly to the named diets (fig 6). Only the Mediterranean diet showed a statistically significant difference compared with usual diet in LDL cholesterol reduction (fig 6). Estimated effects at the 12 month follow-up for weight loss and cardiovascular risk factor improvements diminished for all popular named diets, except for the Mediterranean diet. None of the diets were associated with a statistically significant increase in HDL cholesterol or reduction in C reactive protein at either the six or 12 month follow-up.

Network meta-analyses showed that although there were statistically significant differences between some dietary patterns, these differences were generally small at six months and negligible at 12 months. For example, low carbohydrate dietary patterns resulted in an estimated difference in weight loss of 1.57 kg (95% credible interval 0.86 to 2.29), a reduction in systolic blood pressure of 1.66 mm Hg (0.36 to 2.98), and a reduction in diastolic blood pressure of 1.33 mm Hg (0.51 to 2.16) compared with moderate macronutrient dietary patterns at six months (fig 3, fig 4, and fig 5).

The same small differences between diets at six months and even smaller and uncertain differences at 12 months apply to the popular named diets. For instance, Atkins resulted in an estimated difference in weight loss of only 1.38 kg (95% credible interval 0.15 to 2.62) and an LDL cholesterol reduction of −0.15 mg/dL (−4.92 to 4.63 mg/dL) compared with the Zone diet at the six month follow-up (appendix tables S36 and S40). Figure 6 highlights instances in which differences exist, all of which are small or even trivial, with the corresponding certainty of the underlying evidence.

Strengths and limitations of this review

Strengths of this review include our use of network meta-analysis, thus taking advantage of both direct and indirect comparisons to generate the most robust estimates possible of weight and cardiovascular risk factors for both dietary macronutrient patterns and individual popular named diets. We used explicit eligibility criteria; conducted a comprehensive literature search developed with an experienced librarian; performed duplicate assessment of study eligibility, risk of bias, and data extraction; summarised the data using a transparent statistical analysis including network meta-regression accounting for potential effect modifiers (eg, exercise and behavioural support); applied the GRADE approach to rate certainty of evidence; presented tables of results highlighting certainty of evidence; and used an innovative classification scheme enhancing the transparency of the relative effects of the named diets across multiple outcomes (fig 6). Furthermore, to reduce the heterogeneity between studies, we used three categories for control diets: usual diet, dietary advice, and low fat diet; the low fat diet proved to have moderate certainty evidence supporting weight and blood pressure reductions, similar to the named diets. We conducted sensitivity analyses by restricting them to studies assessed as low risk of bias, studies focusing on otherwise healthy populations, and studies without diet company (industry) support. All analyses provided results similar to those of our primary analysis, further supporting the robustness of our results.

Our review has some limitations. Firstly, many comparisons provided only low certainty evidence, primarily because of inconsistency and imprecision, but also because of risk of bias. The paucity of direct comparisons between popular named diets contributed to the low certainty evidence: 14 popular named diet programmes included 407 paired comparisons across six outcomes, of which only 59 made direct comparisons, and, of these, only 22 included more than one study. Secondly, our ability to deal with publication bias was limited given the paucity of direct comparisons. For example, only two of 136 comparison groups (Atkins *v* low fat, and Zone *v* low fat) had more than 10 studies for the outcome weight loss. Thirdly, we did not involve patients in either the planning or the conduct of the study. Fourthly, considerably fewer trials reported our target outcomes at the 12 month follow-up, and most of the evidence was low to very low certainty (appendix tables S58-S63). Fifthly, adherence to diets was generally not reported, and

could have been low, particularly at 12 months. If this is the case, our results describe what is likely to happen for average adherence by patients. Full adherence would probably yield larger effects in improvement of weight loss and cardiovascular risk factors. If the weight loss achieved at six months continued at 12 months, it is uncertain whether the improvements in cardiovascular risk factors would also be maintained. Future studies, therefore, could usefully examine how to achieve longer term adherence to diets. Lastly, participants in randomised trials are always a select population. Selection could be more important in dietary trials than in trials in which effects are less tied to individual behaviour. Whether trial non-participants would be more, or less, adherent to the popular named diets is, however, a matter of speculation.

Comparison with other studies

Our review examined weight loss and cardiovascular risk factors among dietary macronutrient patterns and popular named diets using new network meta-analysis methods and the GRADE approach to summarise the certainty of evidence. In comparison with our previous network meta-analysis that examined weight loss alone,[4] we included three additional popular diets (DASH, Portfolio, Mediterranean). Altogether, we included 73 additional randomised controlled trials, resulting in almost three times the number of participants included in the previous trial.

Consistent with our previous review, results indicated that almost all dietary patterns and popular named diets showed a minimally clinical important weight loss of 2.0 kg compared with a usual diet for up to 12 months, with the differences among diets, for the most part, small and often trivial.[4] Our findings are also consistent with the 2014 joint guidelines from the American Heart Association, the American College of Cardiology, and The Obesity Society, concluding that evidence was inadequate to recommend any particular diet.[3] Similar to another recent review,[36] our results showed that the Atkins diet probably achieves the largest weight loss, although the gradient of weight or cardiovascular risk factor improvement relative to other diets is small. For reduction of cardiovascular risk, recent dietary guidelines from the US and Canada, and the EAT Lancet commission have recommended plant based diets.[37-39] To the extent that short term results might have implications for long term cardiovascular outcomes, our findings do not support this conclusion: rather, they suggest that omnivorous based diets (eg, Atkins, Zone) have a similar effect to diets that tend to be higher in plant based foods (eg, Ornish, DASH, Mediterranean).

Conclusions

Compared with usual diet, moderate certainty evidence supports modest weight loss and substantial reductions in systolic and diastolic blood pressure for low carbohydrate (eg, Atkins, Zone), low fat (eg, Ornish), and moderate macronutrient (eg, DASH, Mediterranean) diets at six but not 12 months. Differences between diets are, however, generally trivial to small, implying that people can choose the diet they prefer from among many of the available diets (fig 6) without concern about the magnitude of benefits.

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Contributors: BCJ, GDCB, and BS conceived the study. BCJ, GDCB, CLH, BS, LG, BRdC, RTT, and GHG designed the study protocol. TA-W, BS, and BCJ designed and performed the search strategy. BS, LG, CLH, RK, KQ, HYK, MK, WA, SD, DZ, and AN screened abstracts and full texts, extracted data, or judged risk of bias of included studies. LG, AS, AN, and BRdC performed the data analysis. LG, BCJ, BS, GHG, JT, and KY designed and performed the GRADE assessment. LG, BS, and BCJ wrote the first draft of the manuscript. LG, BS, GDCB, CLH, RTT, GHG, and BCJ provided administrative, technical, or material support. BCJ, GDCB, BS, BRdC, and GHG supervised the study. All authors interpreted the data analysis and critically revised the manuscript. BCJ and LG are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Ethical approval: Not required.

Data sharing: All data are freely available within the appendices. No additional data available.

The manuscript's guarantors (BCJ and LG) affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Dissemination to participants and related patient and public communities: We plan to disseminate the results to relevant patient communities through the media relations department of our institutions.

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Web appendix: Supplementary material