REVIEW

Effects of Popular Diets on Anthropometric and Cardiometabolic Parameters: An Umbrella Review of Meta-Analyses of Randomized Controlled Trials

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ABSTRACT

The prevalence of overweight, obesity, and their related complications is increasing worldwide. The purpose of this umbrella review was to summarize and critically evaluate the effects of different diets on anthropometric parameters and cardiometabolic risk factors. Medline, Embase, Scopus, Cochrane Database of Systematic Reviews, and Web of Science, from inception to April 2019, were used as data sources to select meta-analyses of randomized controlled trials that examined the effects of different diets on anthropometric parameters and cardiometabolic risk factors. Strength and validity of the evidence were assessed through a set of predefined criteria. Eighty articles reporting 495 unique meta-analyses were examined, covering a wide range of popular diets: low-carbohydrate ($n = 21$ articles), high-protein ($n = 8$), low-fat ($n = 9$), paleolithic ($n = 2$), low-glycemic-index/load ($n = 12$), intermittent energy restriction ($n = 6$), Mediterranean ($n = 11$), Nordic ($n = 2$), vegetarian ($n = 9$), Dietary Approaches to Stop Hypertension (DASH) ($n = 6$), and portfolio dietary pattern ($n = 1$). Great variability in terms of definition of the intervention and control diets was observed. The methodological quality of most articles ($n = 65$; 81%), evaluated using the "A MeaSurement Tool to Assess systematic Reviews-2" questionnaire, was low or critically low. The strength of evidence was generally weak. The most consistent evidence was reported for the Mediterranean diet, with suggestive evidence of an improvement in weight, BMI, total cholesterol, glucose, and blood pressure. Suggestive evidence of an improvement in weight and blood pressure was also reported for the DASH diet. Low-carbohydrate, high-protein, low-fat, and low-glycemic-index/load diets showed suggestive and/or weak evidence of a reduction in weight and BMI, but contrasting evidence for lipid, glycemic, and blood pressure parameters, suggesting potential risks of unfavorable effects. Evidence for paleolithic, intermittent energy restriction, Nordic, vegetarian, and portfolio dietary patterns was graded as weak. Among all the diets evaluated, the Mediterranean diet had the strongest and most consistent evidence of a beneficial effect on both anthropometric parameters and cardiometabolic risk factors. This review protocol was registered at www.crd.york.ac.uk/PROSPERO/ as CRD42019126103. *Adv Nutr* 2020;11:815–833.

Keywords: diet, review, meta-analysis, weight, risk factors

Introduction

With the increasing numbers of overweight and obese people worldwide (1), there is a growing public health concern on body size and dietary habits. Current data show that ~42% of adults worldwide have tried to lose weight at some point in life (2). In response to the ubiquity of weight-loss efforts, diets that promise rapid and easy weight loss by limiting certain foods or macronutrients are constantly emerging, attracting public attention, and generating considerable debate. The effectiveness of a diet, however, is measured not only by its ability to induce weight loss in a short time. Several other factors such as their overall nutritional quality and the long-term effects on cardiometabolic risk factors should be carefully considered (3). As reported by both observational and intervention studies, there is supporting evidence for potential causal relations between dietary patterns, health status, and occurrence of chronic degenerative diseases (4, 5).

Numerous epidemiological studies and clinical trials have evaluated the impact of dietary interventions on weight and biomarkers related to metabolic disorders so far (6), and many meta-analyses have been published (5, 7–9). Meta-analyses are powerful tools that can overcome difficulties in performing large-scale randomized controlled trials (RCTs), but are subject to the possibility of bias related to variation in quality and empirical validation. It has been reported that over half of the meta-analyses published are flawed and unnecessary (10), and that the production of poor-quality and redundant meta-analyses can contribute to the spread of misleading dietary concepts (11).

The assessment of the quality and credibility of existing evidence may have implications for both clinical practice and public health. Umbrella reviews are overviews of systematic reviews and meta-analyses that provide a comprehensive and systematic evaluation of the scientific literature available for a specific research topic and offer the possibility to understand the strength of evidence and extent of potential biases (12). To the best of our knowledge, no previous umbrella reviews have assessed the strength and validity of the evidence available on dietary approaches to the treatment of obesity and overweight. Our aim, therefore, was to describe and critically evaluate the impact of different diets and/or dietary patterns on human health, by considering their effects on anthropometric parameters and cardiometabolic risk factors.

Methods

An umbrella review of meta-analyses of RCTs (CRD42019126103) was conducted according to the Joanna Briggs Institute Umbrella Review Methodology (13).

Search strategy

The systematic literature search was independently conducted by 2 authors (DM and DA). Any discrepancy was resolved through consultation with a third independent reviewer (LL). The systematic computerized literature search was performed in the Medline, Embase, Scopus, Cochrane Database of Systematic Reviews, and Web of Science databases, from inception to April 2019. Additional studies were searched by checking references of the identified articles and by consulting experts in the field. The following search terms were used in combination as Medical Subject Headings (MeSH) terms and text words: "diet*" and its variants, with the words "weight," "body mass index," "BMI," "plasma lipids," "cholesterol," "LDL-cholesterol," "HDL-cholesterol," "triglycerides," "glycated hemoglobin," "insulin," "blood pressure," and their variants, and the words "meta-analysis," "systematic reviews," and their variants. A more exhaustive search strategy list, for each database, is provided in **Supplemental Table 1**. The most updated or complete publication was used when >1 article was present for a meta-analysis. If an article presented meta-analyses for >1 health outcome, each of these was included separately. Missing data or additional information were requested from the corresponding authors of the articles.

Data selection

Supplemental Table 2 summarizes the eligibility criteria, following the PICOS (Population, Intervention, Comparison, Outcome, Study design) format. Inclusion criteria were the following: *1*) Population: adults (aged ≥18 y); *2*) Intervention: all diets or dietary patterns; *3*) Comparison: any other dietary intervention; *4*) Outcome: weight, BMI, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, glucose, insulin, glycated hemoglobin (HbA1c), systolic blood pressure, or diastolic blood pressure; *5*) Study design: meta-analyses of RCTs.

Exclusion criteria were the following: *1*) Population: nonadults (aged < 18 y), pregnancy, or postpartum; *2*) Intervention: not a specific diet or dietary pattern; *3*) Outcome: any other outcome outside of the inclusion criteria; *4*) Study design: systematic reviews of RCTs without quantitative analysis, meta-analyses not reporting comprehensive data (e.g., effect sizes and 95% CIs), or meta-analyses of observational studies. The decision to include studies was based on the title, abstract, and full-text screening.

Data extraction and quality assessment

Three independent researchers (AR, MDA, and LB) achieved consensus on which data to extract from each eligible meta-analysis, using a standard form. The following data were extracted: first author and year of publication, number of included studies, intervention diet, control diet, number of subjects assigned to the intervention group, number of subjects assigned to the control group, duration of the intervention, study population, outcomes of interest, effect size measurements, and quality of the studies included in each meta-analysis. Data were grouped according to the type of dietary intervention. Within each diet, outcomes were categorized as follows: body weight (kg), BMI (kg/m^2), total cholesterol (mmol/L), LDL cholesterol (mmol/L), HDL cholesterol (mmol/L), triglycerides (mmol/L), glucose (mmol/L), insulin (μU/mL), HbA1c (%), systolic blood pressure (mm Hg), and diastolic blood pressure (mm Hg). When data were provided in milligrams per deciliter or picomoles per liter, they were transformed into millimoles per liter or micro-International Units per milliliter for consistency of results.

Three authors (CDB, DN, and EM) independently evaluated the methodological quality of the included meta-analyses. Disagreements were resolved by discussion with a fourth investigator (MD). The "A MeaSurement Tool to

The authors reported no funding received for this study.
Author disclosures: LL is employed by Janssen. All other authors report no conflicts of interest. Janssen did not have any role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.
Supplemental Tables 1–7 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/advances/.
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Abbreviations used: AMSTAR-2, A MeaSurement Tool to Assess systematic Reviews 2; DASH, Dietary Approaches to Stop Hypertension; HbA1c, glycated hemoglobin; MeSH, Medical Subject Headings; PI, prediction interval; RCT, randomized controlled trial.

Assess systematic Reviews 2" (AMSTAR-2) questionnaire was used to identify the high-quality meta-analyses (14). This instrument has 16 items in total, with an overall rating based on weaknesses in critical domains. Critical domains were as follows: adequacy of the literature search, risk of bias from individual studies included in the review, appropriateness of meta-analytical methods, consideration of risk of bias when interpreting the results of the review, and assessment of presence of publication bias.

Data analysis

For each unique meta-analysis, we estimated the summary effect and 95% CIs using both fixed-effect and random-effect models (DerSimonian and Laird method). Heterogeneity among studies was evaluated using the I^2 statistic (15). Where I^2 exceeded 50% or 75%, the heterogeneity was considered substantial or considerable, respectively. The 95% prediction interval (PI) was calculated to predict the range of effect sizes that would be expected in a new original study, after accounting for both the uncertainty of the summary effect estimated in the random-effect model and the heterogeneity among individual studies (16). The possible presence of small-study effects was estimated by using Egger's regression asymmetry test (17). We investigated if small studies tended to give larger estimates of effect size than large studies by calculating the SE of the effect size (under the random-effect model) for the largest study of each meta-analysis. The largest study was defined on the basis of the smallest SE. If the P value for Egger's test was <0.10 and the largest study had a smaller effect size than the summary effect size, both criteria for the existence of small-study effects were fulfilled (18). All statistical analyses were conducted using Review Manager (RevMan, version 5.3 for Macintosh; The Cochrane Collaboration) and the statistical package PASW 20.0 for Macintosh (SPSS Inc.).

As previously proposed (19, 20), observed associations were categorized as convincing or not by using the following criteria: significance at $P \leq 0.05$ and $P \leq 0.001$; inclusion of $\geq$2500 or $\geq$5000 total participants; absence of considerable heterogeneity ($I^2 < 50\%$); 95% PI excluding the null value; and absence of small-study effects. Convincing evidence was assigned to associations with a significance of $P \leq 0.001$ for both random- and fixed-effect models, $\geq$5000 total participants, not large heterogeneity between studies ($I^2 < 50\%$), 95% PI excluding the null value, and no evidence of small-study effects (if it could be tested). Highly suggestive evidence was assigned to associations with a significance of $P \leq 0.001$ for both random- and fixed-effect models, $\geq$5000 total participants, and not considerable heterogeneity between studies ($I^2 = 50$–75%). Suggestive evidence was assigned to associations with a significance of $P \leq 0.001$ for the random-effect model and 2500–5000 total participants. Weak evidence was assigned to associations with a significance of $P \leq 0.05$ for the random-effect model. No-evidence was assigned to associations where the significance threshold was not reached ($P > 0.05$).

Results

Search results

The selection process is shown in **Figure 1**, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Initial database and other searches yielded 27,627 articles. After eliminating duplicates, 12,469 articles were excluded on the basis of their title and abstract, and 105 on the basis of full-text assessment. A total of 80 articles (7–9, 21–97) met the inclusion criteria and were included in the analysis, covering a wide range of diets: low-carbohydrate ($n = 21$ articles), high-protein ($n = 8$), low-fat ($n = 9$), paleolithic ($n = 2$), low-glycemic-index/load ($n = 12$), intermittent energy restriction ($n = 6$), Mediterranean ($n = 11$), Nordic ($n = 2$), vegetarian ($n = 9$), Dietary Approaches to Stop Hypertension (DASH) ($n = 6$), and portfolio dietary pattern ($n = 1$).

Study characteristics and quality

Table 1 reports the characteristics and methodological quality of the meta-analyses included. There was great variability in terms of definition of the intervention diets: as regards low-carbohydrate diets, for example, some studies defined as "low-carbohydrate" diets containing $\leq$45% of total energy from carbohydrates (23, 28, 34, 36, 38), others diets that included carbohydrates totalling $\leq$26% (33) or even less ($\leq$10%) (26) of the total energy, whereas others did not define the amount of carbohydrates included (22, 24, 25, 27, 31, 32, 35, 40). Similarly, for high-protein diets, in some meta-analyses the high-protein content was defined as $>$20% of total energy (42), in others $>$25% (43) or between 25% and 35% (41, 45), and in others it was not defined at all (8, 25, 44, 46). High variability was also observed among vegetarian diets, where some meta-analyses included lacto-ovo-vegetarian and vegan diets altogether (85, 86, 89–91), whereas others considered lacto-ovo-vegetarian (84, 87, 88) or vegan (87, 88, 92) diets specifically. A consistent heterogeneity was also present for control diets. In fact, most meta-analyses had as "control" any other dietary intervention, without specific indication. The study population was mainly composed of subjects with overweight/obesity or type 2 diabetes. Overweight was defined as a BMI between 25 and 29.9 and obesity as a BMI $\geq$ 30. A greater number of RCTs and a bigger sample size ($\geq$2500 subjects) were observed in meta-analyses on Mediterranean (74–76, 79, 80, 82) and low-carbohydrate (23, 24, 28, 38, 39) diets. Conversely, the number of RCTs and the study population were small ($\leq$500 subjects) in meta-analyses on paleolithic (55, 56), intermittent energy restriction (68–73), Nordic (81, 83), and portfolio dietary patterns (97). The methodological quality of the included meta-analyses, determined by the AMSTAR-2 questionnaire, was moderate-to-high only in 6 meta-analyses on low-carbohydrate diets (7, 26, 27, 36, 37, 39), in 2 meta-analyses on low-glycemic-index/load (58, 64) and vegetarian diets (91, 92), and in 1 meta-analysis on each of low-fat diet (52), intermittent energy restriction (71), Mediterranean diet (9), Nordic diet (83), and portfolio

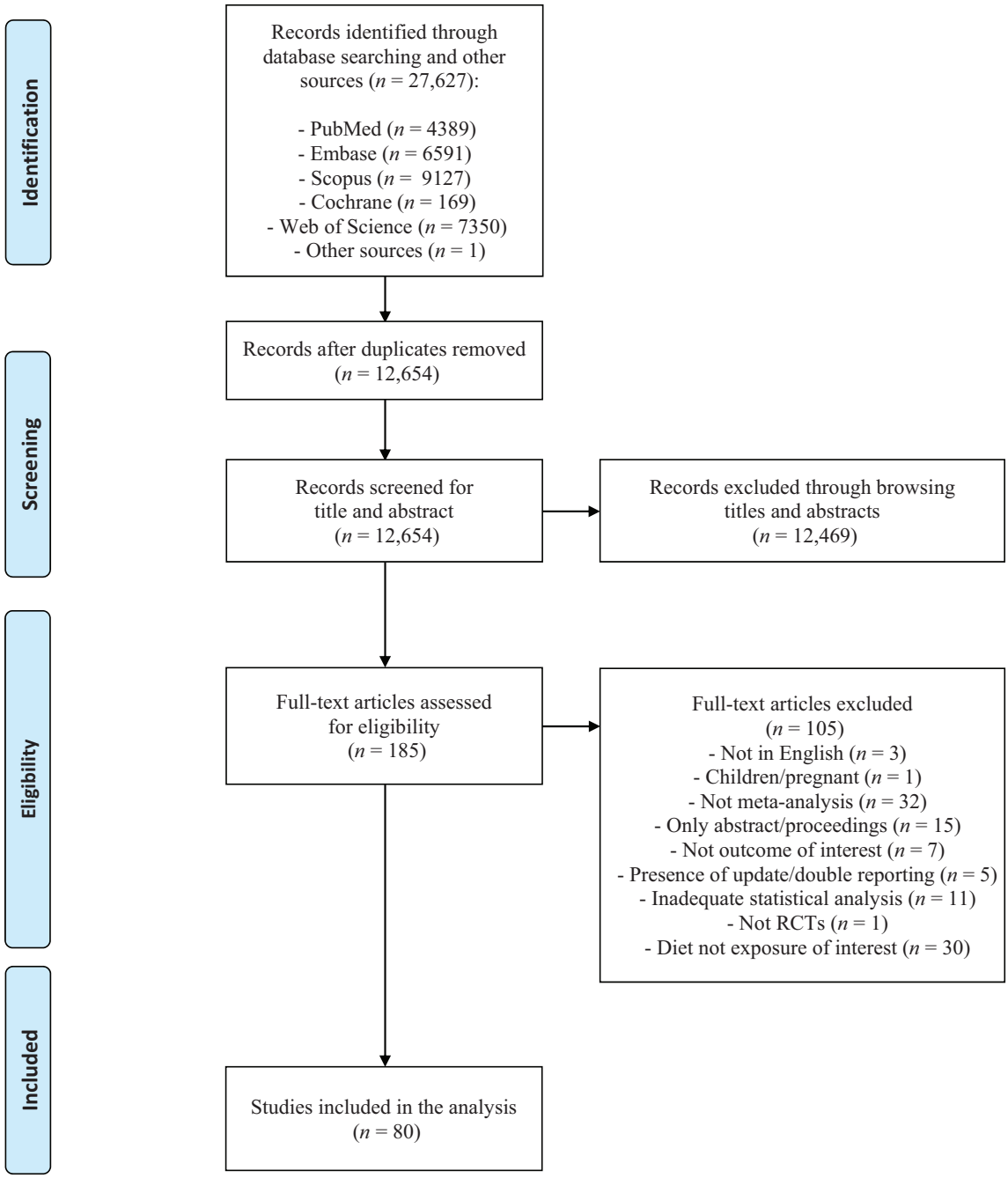

Figure 1 Flow diagram of the study selection process. RCT, randomized controlled trial.

dietary pattern (97). There were no meta-analyses with moderate or high methodological quality for high-protein, paleolithic, and DASH diets. Although most meta-analyses ($n = 73$; 91%) performed a quality/risk of bias assessment using validated tools or criteria set by the authors, only 27 (34%) accounted for risk of bias in individual studies when interpreting/discussing the results of the meta-analysis.

Supplemental Table 3 reports the effects of all the diets studied on body weight and cardiometabolic risk factors. By applying our evidence classification criteria, based on the evaluation of the level of significance for both random- and fixed-effect calculations, the sample size, the heterogeneity, the 95% PI, and the presence of small study effects, only a limited number of meta-analyses provided suggestive evidence and no meta-analyses provided highly suggestive or convincing evidence.

Anthropometric parameters

Figure 2 summarizes the characteristics and the strength of evidence of the meta-analyses of RCTs that evaluated the effects of diets on anthropometric parameters. With regard to body weight, suggestive evidence for a decrease

TABLE 1 Characteristics of meta-analyses of RCTs included in the umbrella review according to dietary interventions[1]

Meta-analyses	Intervention diet	Control diet	*n* Intervention	*n* Control	Study population (age ≥ 18 y)	Duration	Quality/risk of bias assessment	Outcomes	Quality of meta-analyses (AMSTAR-2)
LCs									
Nordmann et al. (21)	LC (≤60 g CHO)	LF (≤30% of TE)	222	225	OW/OB	>6 mo, >12 mo	Criteria set by authors	Weight, TC, LDL-C, HDL-C, TG, SBP, DBP	Critically low
Hession et al. (22)	LC/HP[2]	HC/LF[3]	375	367	OW/OB	>6 mo, >12 mo	Criteria set by authors	Weight, TC, LDL-C, HDL-C, TG, glucose, SBP, DBP	Critically low
Hu et al. (23)	LC (≤45% of TE)	LF (≤30% of TE)	1396	1392	OW/OB	6–24 mo	No	Weight, TC, LDL-C, HDL-C, TG, glucose, insulin, SBP, DBP	Critically low
Santos et al. (24)	LC[4]	Other	2394	4346	OB	3–24 mo	Criteria set by authors	Weight, BMI, LDL-C, HDL-C, TG, glucose, insulin, HbA1c, SBP, DBP	Critically low
Ajala et al. (25)	LC[4]	Other	NA	NA	T2DM	6–12 mo	Cochrane RoB	HbA1c	Critically low
Bueno et al. (26)	VLCKD (≤50 g CHO or ≤10% of TE)	LF (≤30% of TE)	712	703	OW/OB	12–24 mo	Cochrane RoB	Weight, LDL-C, HDL-C, TG, SBP, DBP	High
Naude et al. (27)	LC[4]	Balanced energy-restricted diets	837	872	OW/OB, T2DM	3–6 mo, 12–24 mo	Cochrane RoB	Weight	Moderate
Alexandraki et al. (28)	LC (≤45% of TE)	LF (≤30% of TE)	1548	1543	OW/OB	6 mo, 12 mo	Cochrane RoB	Weight	Critically low
Sackner-Bernstein et al. (29)	LC (≤120 g CHO)	LF (≤30% of TE)	895	902	OW/OB	2–24 mo	No	Weight	Critically low
Fan et al. (30)	LC (≤130 g CHO)	Other	567	569	T2DM	3–48 mo	Jadad scale	Weight, HbA1c	Critically low
Hashimoto et al. (31)	LC[4]	Other	697	719	OW/OB	2–24 mo	AMSTAR	Weight	Critically low
Mansoor et al. (7)	LC (≤20% of TE)	LF (≤30% of TE)	688	681	OW/OB	6–24 mo	Cochrane RoB	Weight, TC, LDL-C, HDL-C, TG, glucose, insulin, SBP, DBP	High
Steckhan et al. (32)	LC[4]	Other	96	90	MetS	1–24 mo	Cochrane RoB	Weight, insulin	Low
Meng et al. (33)	LC (≤26% of TE) or ≤130 g CHO/d	HC (45–60% of TE)	366	368	T2DM	3–24 mo	Jadad scale	Weight, TC, LDL-C, HDL-C, TG, glucose, HbA1c	Critically low
Snorgaard et al. (34)	LC (≤45% of TE)	HC (45–60% of TE)	414	425	T2DM	<12 mo, ≥12 mo	Cochrane RoB	Weight, BMI, LDL-C, HbA1c	Critically low
Huntriss et al. (35)	LC[4]	Other	330	315	T2DM	12 mo	Cochrane RoB	Weight, TC, LDL-C, HDL-C, TG, HbA1c, SBP, DBP	Critically low
Sainsbury et al. (36)	LC (≤45% of TE)	HC (>45% of TE)	NA	NA	T2DM	6 mo, 12 mo	Cochrane RoB	Weight, HbA1c	Moderate
van Zuuren et al. (37)	LC (≤40% of TE)	LF (≤30% of TE)	269	270	T2DM	<2 mo, 2–4 mo, 4–6 mo, >6 mo, 24 mo	Cochrane RoB/ROBINS-I tool	Weight, BMI, LDL-C, HDL-C, TG, glucose, HbA1c, SBP, DBP	Moderate
Gjuladin-Hellon et al. (38)	LC (≤45% of TE)	LF (≤35% of TE)	1680	1678	OW/OB	6–24 mo	Cochrane RoB	TC, LDL-C, HDL-C, TG	Critically low
Korsmo-Haugen et al. (39)	LC (≤40% of TE)	HC (>40% of TE)	1587[5]	NA	T2DM	3–24 mo	Cochrane RoB	Weight, TC, LDL-C, HDL-C, TG, HbA1c, SBP, DBP	High
McArdle et al. (40)	LC[4]	Other	1006	1126	T2DM	3–52 mo	Cochrane RoB	Weight, HbA1c	Critically low

(*Continued*)

TABLE 1 (*Continued*)

Meta-analyses	Intervention diet	Control diet	*n* Intervention	*n* Control	Study population (age ≥ 18 y)	Duration	Quality/risk of bias assessment	Outcomes	Quality of meta-analyses (AMSTAR-2)
HPs									
Santesso et al. (8)	HP[4]	LP	1158	1160	Different health status	>1 mo	No	Weight, BMI, TC, LDL-C, HDL-C, TG, glucose, insulin, HbA1c, SBP, DBP	Critically low
Wycherley et al. (41)	HP (25–35% of TE)	LP (12–18% of TE)	494	516	Different health status	1–13 mo	Cochrane RoB	Weight, TC, LDL-C, HDL-C, TG, glucose, insulin, SBP, DBP	Critically low
Ajala et al. (25)	HP4[4]	Other	72	65	T2DM	6–12 mo	Cochrane RoB	HbA1c	Critically low
Dong et al. (42)	HP (>20% of TE)	LP (15–20% of TE)	NA	NA	T2DM	1–6 mo	Criteria set by authors	Weight, TC, LDL-C, HDL-C, TG, glucose, HbA1c, SBP, DBP	Critically low
Schwingshackl and Hoffmann (43)	HP (≥25% of TE)	LP (≤20% of TE)	533	599	Different health status	12–24 mo	Cochrane RoB/Jadad scale	Weight, TC, LDL-C, HDL-C, TG, glucose, insulin, HbA1c, SBP, DBP	Critically low
Clifton et al. (44)	HP[4]	LCD	1681	1811	Different health status	13–52 mo	Cochrane RoB	Weight, TC, LDL-C, HDL-C, TG, glucose, insulin, HbA1c, SBP, DBP	Critically low
Johansson et al. (45)	HP (25–30% of TE)	Other	451	414	Different health status	0.8–2 mo	Criteria set by authors	Weight	Critically low
Zhao et al. (46)	HP[4]	LP	520	539	T2DM	1–24 mo	Cochrane RoB	Weight, BMI, TC, LDL-C, HDL-C, TG, glucose, insulin, HbA1c, SBP, DBP	Critically low
LFs									
Astrup et al. (47)	Reduced fat[4]	Other	1101	869	Nondiabetic	2–12 mo	No	Weight	Critically low
Avenell et al. (48)	LF[4]	Other	665	688	OW/OB	12 mo	Criteria set by authors	Weight	Critically low
Schwingshackl and Hoffmann (49)	LF (≤30% of TE)	Other, HF (>30% of TE), LC (<50 g CHO), LGI/LGL, MUFA	3793	4249	OW/OB	>3 mo	Cochrane RoB/Jadad scale	TC, LDL-C, HDL-C, TG	Critically low
Wu et al. (50)	LF (≤30% of TE)	Usual diet	900	636	Women	1–12 mo	Jadad scale	TC, LDL-C, HDL-C, TG	Critically low
Boaz et al. (51)	LF (≤30% of TE)	LC (≤45% of TE)	569	592	OW/OB	1–8.7 y	No	Weight	Critically low
Hooper et al. (52)	LF (≤30% of TE)	HF (>30% of TE)	22,316	31,331	Different health status	0.5–8 y	Cochrane RoB	Weight, BMI, TC, LDL-C, HDL-C, TG, SBP, DBP	High
Tobias et al. (53)	LF[4]	Other, HF, LC, usual diet	NA	NA	Different health status	1–10 y	Cochrane RoB	Weight	Low
Steckhan et al. (32)	LF[4]	Other	116	111	MetS	1–24 mo	Cochrane RoB	Weight	Low
Lu et al. (54)	LF (≤30% of TE)	HF (>30% of TE)	NA	NA	OW/OB	2–24 mo	Cochrane RoB/Jadad scale	TC, LDL-C, HDL-C, TG, SBP, DBP	Low
Paleolithic diet									
Manheimer et al. (55)	Paleolithic	Other	73	64	MetS	0.5–6 mo	Cochrane RoB	HDL-C, TG, glucose, SBP, DBP	Low
Ghaedi et al. (56)	Paleolithic	Other	115	98	Different health status	0.5–24 mo	Cochrane RoB	Weight, BMI, TC, LDL-C, HDL-C, TG, SBP, DBP	Low

(*Continued*)

TABLE 1 (*Continued*)

Meta-analyses	Intervention diet	Control diet	*n* Intervention	*n* Control	Study population (age ≥ 18 y)	Duration	Quality/risk of bias assessment	Outcomes	Quality of meta-analyses (AMSTAR-2)
LGI/LGLs									
Opperman et al. (57)	LGI[4]	HGI	206	200	Different health status, T2DM	<6 mo	Criteria adapted from the Cochrane EPOC Group	TC, LDL-C, HDL-C, TG, HbA1c	Critically low
Thomas et al. (58)	LGI/LGL[4]	HGI/HGL	82	81	OW/OB	1.3–6 mo	Criteria set by authors	Weight, BMI, TC, HDL-C, TG, glucose, insulin	High
Thomas and Elliott (59)	LGI[4]	HGI	238	219	T2DM	1–6 mo	Criteria set by authors	HbA1c	Critically low
Ajala et al. (25)	LGI/LGL[4]	Other	181	172	T2DM	6–12 mo	Cochrane RoB	HbA1c	Critically low
Fleming and Godwin (60)	LGI[4]	HGI	107	105	OW/OB	<3 mo	US Preventive Services Task Force Quality Rating Criteria	TC, LDL-C, HDL-C, TG	Critically low
Goff et al. (61)	LGI[4]	HGI	733	679	Different health status, T2DM	>1 mo	Jadad scale	TC, LDL-C, HDL-C, TG	Low
Schwingshackl and Hoffmann (62)	LGI/LGL[4]	HGI/HGL	913	857	Different health status	6–17 mo	Cochrane RoB	Weight, TC, LDL-C, HDL-C, TG, glucose, insulin, HbA1c, SBP, DBP	Critically low
Wang et al. (63)	LGI[4]	HGI	421	409	T2DM	<36 mo	Jadad scale	HbA1c	Critically low
Clar et al. (64)	LGI[4]	HGI	NA	NA	CVD	>3 mo	Cochrane RoB	Weight, BMI, TC, LDL-C, HDL-C, TG, SBP, DBP	High
Evans et al. (65)	LGI/LGL[4]	HGI/HGL	NA	NA	Healthy adults	<18 mo	Cochrane RoB	SBP, DBP	Low
Ojo et al. (66)	LGI[4]	HGI	291	283	T2DM	<22 mo	Cochrane RoB/CASP RCT Checklist	Glucose, HbA1c	Critically low
Zafar et al. (67)	LGI[4]	Other	3333	3241	OW/OB	<26 mo	Cochrane RoB	Weight, BMI, TC, LDL-C, HDL-C, TG, glucose	Low
IER									
Alhamdan et al. (68)	ADF	VLCD	91[5]	NA	OW/OB	2–3 mo	Downs and Black checklist	Weight	Critically low
Headland et al. (69)	IER	CER	230	216	Different health status	>12 mo	Cochrane RoB	Weight	Critically low
Cioffi et al. (70)	IER[6]	CER	343	222	Different health status	2–6 mo	Cochrane RoB	Weight, TC, LDL-C, HDL-C, TG, glucose, insulin, HbA1c, SBP, DBP	Critically low
Harris et al. (71)	IER[7]	Ad libitum/CER[8]	180	137	OW/OB	3–12 mo	Cochrane RoB	Weight	Moderate
Harris et al. (72)	IER[7]	Ad libitum/CER[8]	161	126	OW/OB	3 mo	JBI SUMARI	Weight, TC, LDL-C, HDL-C, TG, glucose, insulin	Critically low
Roman et al. (73)	IER	CER	329	337	OW/OB	3–13 mo	Cochrane RoB	Weight	Critically low

(*Continued*)

TABLE 1 (*Continued*)

Meta-analyses	Intervention diet	Control diet	*n* Intervention	*n* Control	Study population (age ≥ 18 y)	Duration	Quality/risk of bias assessment	Outcomes	Quality of meta-analyses (AMSTAR-2)
MDs									
Esposito et al. (74)	MD	Other	1937	1588	Different health status	1–60 mo	Jadad scale	Weight, BMI	Critically low
Kastorini et al. (75)	MD	Other	2202	1903	OW/OB	1–48 mo	Criteria set by authors	HDL-C, TG, glucose, SBP, DBP	Critically low
Nordmann et al. (76)	MD	LF (≤30% of TE)	1641	1009	OW/OB	24 mo	Criteria set by authors	Weight, BMI, TC, LDL-C, HDL-C, glucose, insulin, SBP, DBP	Critically low
Ajala et al. (25)	MD	Other	308	280	T2DM	6–12 mo	Cochrane RoB	HbA1c	Critically low
Huo et al. (77)	MD	Other	568	521	T2DM	1–48 mo	Cochrane RoB	Weight, BMI, TC, LDL-C, HDL-C, TG, glucose, insulin, HbA1c, SBP, DBP	Critically low
Esposito et al. (78)	MD	Other	395	278	Different health status	1–60 mo	Cochrane RoB	HbA1c	Low
Garcia et al. (79)	MD	Other	3262[5]	NA	Different health status	1–52 mo	Cochrane RoB	HDL-C, TG, glucose, SBP, DBP	Low
Gay et al. (80)	MD	Other	5148	5013	Different health status	6–48 mo	Cochrane RoB	SBP, DBP	Critically low
Ndanuko et al. (81)	MD	Other	310	225	Different health status	2–24 mo	Cochrane RoB	SBP, DBP	Critically low
Nissensohn et al. (82)	MD	Other	5226	5111	OW/OB	24 mo	Cochrane RoB	SBP, DBP	Critically low
Rees et al. (9)	MD	Other	692	662	Primary/secondary prevention	≥3 mo	Cochrane RoB	TC, LDL-C, HDL-C, TG, SBP, DBP	High
Nordic diet									
Ndanuko et al. (81)	Nordic	Other	306	NA	Different health status	2–24 mo	Cochrane RoB	SBP, DBP	Critically low
Ramezani-Jolfaie et al. (83)	Nordic	Typical/Danish diets	513[5]	NA	Different health status	0.5–6 mo	Cochrane RoB	TC, LDL-C, HDL-C, TG, SBP, DBP	High
VGTs									
Yokoyama et al. (84)	VGT, LOV	Non-VGT	210	195	Different health status	1.5–13 mo	No	SBP, DBP	Critically low
Yokoyama et al. (85)	VGT	Non-VGT	120	174	T2DM	1–18.5 mo	Cochrane RoB	Glucose, HbA1c	Critically low
Barnard et al. (86)	VGT	Non-VGT	689[5]	NA	Different health status	3–26 mo	Cochrane RoB	Weight	Low
Huang et al. (87)	VGT, LOV, VGN	Non-VGT	1151[5]	NA	Different health status	2.3–24 mo	Jadad scale	Weight	Critically low
Wang et al. (88)	VGT, LOV, VGN	Non-VGT	785[5]	NA	Different health status	2.3–24 mo	Cochrane RoB	Weight, TC, LDL-C, HDL-C, TG	Critically low
Yokoyama et al. (89)	VGT	Non-VGT	1329[5]	NA	Different health status	>1.5 mo	Jadad scale	TC, LDL-C, HDL-C, TG	Critically low
Picasso et al. (90)	VGT	Non-VGT	350	339	Different health status	1.5–18.5 mo	Cochrane RoB	HDL-C, TG, glucose, SBP, DBP	Low
Viguiliouk et al. (91)	VGT	Non-VGT	329	337	T2DM	1–18.5 mo	Cochrane RoB	Weight, BMI, LDL-C, HDL-C, TG, glucose, HbA1c, SBP, DBP	Moderate
Lopez et al. (92)	VGN	Non-VGN	1078[5]	NA	Different health status	0.8–18.5 mo	Cochrane RoB	SBP, DBP	High

(*Continued*)

TABLE 1 (*Continued*)

Meta-analyses	Intervention diet	Control diet	*n* Intervention	*n* Control	Study population (age ≥ 18 y)	Duration	Quality/risk of bias assessment	Outcomes	Quality of meta-analyses (AMSTAR-2)
DASH diet									
Shirani et al. (93)	DASH	Other	815	813	Different health status	0.8–6 mo	No	Glucose, insulin	Critically low
Saneei et al. (94)	DASH	Other	1281	1280	Different health status	0.5–6.5 mo	Criteria set by authors	SBP, DBP	Critically low
Siervo et al. (95)	DASH	Other	964	964	Different health status	0.5–6 mo	Jadad scale	TC, LDL-C, HDL-C, TG, glucose, SBP, DBP	Critically low
Gay et al. (80)	DASH	Other	NA	NA	Different health status	6–48 mo	Cochrane RoB	SBP, DBP	Critically low
Ndanuko et al. (81)	DASH	Other	1399	1399	Different health status	2–24 mo	Cochrane RoB	SBP, DBP	Critically low
Soltani et al. (96)	DASH	LCD	1291	1291	Different health status	2–13 mo	Cochrane RoB	Weight, BMI	Low
Portfolio dietary pattern[9]									
Chiavaroli et al. (97)	Portfolio	Energy-matched diets	439[5]	NA	Dyslipidemia	1–6 mo	Cochrane RoB	Weight, TC, LDL-C, HDL-C, TG, SBP, DBP	High

[1] ADF, alternate day fasting; AMSTAR, A MeaSurement Tool to Assess systematic Reviews; CASP, Critical Appraisal Skills Programme; CER, continuous energy restriction; CHO, carbohydrates; Cochrane RoB, the Cochrane risk-of-bias tool for randomized trials; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; EPOC, Effective Practice and Organisation of Care; HbA1c, glycated hemoglobin; HC, high-carbohydrate diet; HDL-C, HDL cholesterol; HF, high-fat diet; HGI, high-glycemic-index; HGL, high-glycemic-load; HP, high-protein diet; IER, intermittent energy restriction; JBI SUMARI, Joanna Briggs Institute's System for the Unified Management, Assessment, and Review of Information critical appraisal tool; LC, low-carbohydrate diet; LCD, low-calorie diet; LDL-C, LDL cholesterol; LF, low-fat diet; LGI/LGL, low-glycemic-index/low-glycemic-load diet (total fat >30% of daily energy consumption, CHO <50% of daily energy consumption, and low-glycemic-index foods); LOV, lacto-ovo-vegetarian diet; LP, low-protein diet; MD, Mediterranean diet; MetS, metabolic syndrome; MUFA, high-MUFA diet (total fat >30% of daily energy consumption and MUFA >12% of daily energy consumption); NA, not available; OB, obese; OW, overweight; RCT, randomized controlled trial; ROBINS-I, Risk of Bias In Non-randomized Studies of Interventions; SBP, systolic blood pressure; TC, total cholesterol; TE, total energy; TG, triglyceride; T2DM, type 2 diabetes mellitus; VGN, vegan diet; VGT, vegetarian diet; VLCD, very-low-calorie dieting (<800 kcal/d); VLCKD, very-low-carbohydrate ketogenic diets (≤50 g/d of CHO or ≤10% of daily energy from CHO).
[2] Low-carbohydrate (≤60 g/d of CHO)/ketogenic diets (<40 g/d of CHO).
[3] Low-fat (≤30% of daily energy from fat)/high-carbohydrate conventional diets, energy restricted.
[4] As defined by the investigators of each trial.
[5] Number of total participants.
[6] IER defined as 75% energy restriction on "fast" days, with a maximum cutoff of 500 and 660 kcal/d for females and males, respectively.
[7] IER defined as consumption of ≤800 kcal on ≥1 d, but no more than 6 d in 1 wk.
[8] Control defined as "ad libitum" diet (no intervention) or advice to continuously follow a reduced-calorie diet of ∼25% of estimated daily energy requirements.
[9] Portfolio dietary pattern was defined as including the following components: 1–3 g plant sterols/d, 15–25 g viscous fibers/d (from oats, barley, psyllium, legumes, eggplants, and okra), 35–50 g plant protein/d, and 25–50 g nuts/d.

WEIGHT	Articles, *n*	Quality of articles (AMSTAR-2)	Unique meta-analyses, *n*	N of studies in each meta-analysis *median (range)*	N of participants in intervention group *median (range)*	N of participants in control group *median (range)*	Strength of evidence ratings
Low-carbohydrate	19	12 CL; 1 L; 3 M; 3 H	31	8 (2–28)	359 (88–2394)	357 (80–4346)	13% 42% 45%
High-protein	7	7 CL	7	16 (6–40)	520 (451–1681)	539 (414–1811)	57% 43%
Low-fat	6	3 CL; 2 L; 1 H	15	11 (2–45)	665 (116–22,316)	688 (111–31,331)	7% 53% 40%
Paleolithic	1	1 L	1	6	115	98	100%
Low-GI/GL	4	1 CL; 1 L; 2 H	4	17 (4–88)	913 (82–3104)	857 (81–3023)	50% 50%
IER	6	5 CL; 1 M	6	6 (4–10)	230 (161–343)	216 (126–337)	17% 83%
Mediterranean	3	3 CL	3	6 (6–15)	1641 (492–1937)	1009 (365–1588)	67% 33%
Vegetarian	4	2 CL; 1 L; 1 M	4	9 (6–13)	271 (NA)	278 (NA)	100%
DASH	1	1 L	1	10	1291	1291	100%
Portfolio	1	1 H	1	7	NA	439*	100%
BMI							
Low-carbohydrate	3	2 CL; 1 M	7	2 (2–11)	91 (40–766)	88 (39–1589)	43% 57%
High-protein	2	2 CL	2	12 (8–16)	341 (242–440)	348 (248–447)	50% 50%
Low-fat	1	1 H	1	10	18,483	27,220	100%
Paleolithic	1	1 L	1	3	65	56	100%
Low-GI/GL	3	1 L; 2 H	3	11 (2–43)	512 (24–1000)	471 (24–918)	67% 33%
Mediterranean	3	3 CL	3	6 (6–12)	1590 (520–1590)	1009 (500–1571)	67% 33%
Vegetarian	1	1 M	1	6	310	321	100%
DASH	1	1 L	1	6	1157	1157	100%

FIGURE 2 Summary and strength of evidence of meta-analyses of randomized controlled trials evaluating anthropometric parameters in adults. Green = suggestive evidence; orange = weak evidence; grey = no evidence. *Number of total participants. AMSTAR, A MeaSurement Tool to Assess systematic Reviews; CL, critically low; DASH, Dietary Approaches to Stop Hypertension; GI, glycemic index; GL, glycemic load; H, high; IER, intermittent energy restriction; L, low; M, medium; NA, not available.

in body weight was observed for low-carbohydrate, low-fat, Mediterranean, and DASH diets. The mean difference between intervention and control diets in meta-analyses reporting suggestive evidence ranged from −0.98 to −7.05 kg for low-carbohydrate diets (23, 24, 28), from −1.75 to −2.24 kg for the Mediterranean diet (74, 76), was −1.54 kg (95% CI: −1.97 to −1.12 kg) for low-fat diets (52), and −1.42 kg (95% CI: −2.03 to −0.82 kg) for the DASH diet (96). Weak or no evidence was reported for high-protein, paleolithic, low-glycemic-index/load, and vegetarian diets, as well as for intermittent energy restriction and portfolio dietary pattern. When the outcome BMI was analyzed, suggestive evidence was observed only in 1 meta-analysis (52) on low-fat diets (mean difference: −0.50; 95% CI: −0.74 to −0.26) and in 2 meta-analyses on the Mediterranean diet (74, 76) (mean difference: −0.57; 95% CI: −0.93 to −0.21 and mean difference: −0.56; 95% CI: −1.01 to −0.11, respectively).

Lipid profile

Figure 3 summarizes the characteristics and the strength of evidence of the meta-analyses of RCTs that evaluated the effects of diets on lipid profile. With regard to total cholesterol, suggestive evidence for a difference between intervention and control diets was reported for low-fat (mean difference: −0.20 mmol/L; 95% CI: −0.29 to −0.11 mmol/L) (52), low-glycemic-index/load (mean difference: −0.14 mmol/L; 95% CI: −0.22 to −0.09 mmol/L) (67), and Mediterranean (mean difference: −0.19 mmol/L; 95% CI: −0.27 to −0.11 mmol/L) (76) diets. Meta-analyses evaluating LDL cholesterol reported suggestive evidence for low-fat (mean difference: −0.08 mmol/L; 95% CI: −0.12 to −0.04 mmol/L) (49) and low-glycemic-index/load (mean difference: −0.14 mmol/L; 95% CI: −0.22 to −0.07 mmol/L) (67) diets. Meta-analyses evaluating HDL cholesterol reported suggestive evidence for low-carbohydrate (mean difference: 0.02–0.08 mmol/L) (23, 24, 38), low-fat (mean difference: −0.06 mmol/L; 95% CI: −0.09 to −0.03 mmol/L) (49), and Mediterranean (mean difference: 0.03 mmol/L; 95% CI: 0.01–0.05 mmol/L) (75) diets. Finally, suggestive evidence for triglycerides was reported in meta-analyses comparing low-carbohydrate with other dietary interventions (mean difference: −0.34 mmol/L; 95% CI: −0.36 to −0.31 mmol/L) (24) or low-fat diets (mean difference: −0.14 mmol/L; 95% CI: −0.18 to −0.11 mmol/L) (23, 38), in 1 meta-analysis (44) comparing high-protein with low-calorie diets (mean difference: −0.18 mmol/L; 95% CI: −0.30 to −0.07 mmol/L), and in 1 meta-analysis (49) comparing low-fat with other dietary

TC	Articles, *n*	Quality of articles (AMSTAR-2)	Unique meta-analyses, *n*	N of studies in each meta-analysis *median (range)*	N of participants in intervention group *median (range)*	N of participants in control group *median (range)*	Strength of evidence ratings
Low-carbohydrate	8	6 CL; 2 H	10	7 (3–15)	287 (137–1469)	287 (131–1468)	70% 30%
High-protein	6	6 CL	6	15 (8–24)	446 (351–682)	469 (365–686)	17% 83%
Low-fat	4	2 CL; 1 L; 1 H	1	10 (3–29)	466 (214–3793)	423 (211–4249)	13% 62% 25%
Paleolithic	1	1 L	1	6	115	98	100%
Low-GI/GL	7	3 CL; 2 L; 2 H	9	13 (3–73)	233 (66–2820)	224 (65–2696)	11% 67% 22%
IER	2	2 CL	2	6 (3–8)	201 (108–294)	163 (83–243)	100%
Mediterranean	3	2 CL; 1 H	6	6 (2–7)	506 (220–1641)	393 (221–1009)	17% 33% 50%
Nordic	1	1 H	1	5	NA	513*	100%
Vegetarian	2	2 CL	2	14 (10–18)	NA	NA	100%
DASH	1	1 CL	1	13	926	926	100%
Portfolio	1	1 H	1	7	NA	439*	100%
LDL-C							
Low-carbohydrate	12	8 CL; 1 M; 3 H	19	7 (2–22)	250 (29–1911)	246 (30–3223)	42% 58%
High-protein	6	6 CL	6	14 (9–25)	446 (261–790)	469 (269–786)	17% 83%
Low-fat	4	2 CL; 1 L; 1 H	8	12 (4–26)	900 (251–3408)	653 (247–3877)	13% 62% 25%
Paleolithic	1	1 L	1	5	101	83	100%
Low-GI/GL	6	3 CL; 2 L; 1 H	8	13 (4–73)	267 (107–2820)	255 (105–2696)	13% 62% 25%
IER	2	2 CL	2	5 (2–8)	198 (102–294)	159 (75–243)	100%
Mediterranean	3	2 CL; 1 H	5	4 (2–7)	384 (210–1388)	258 (179–752)	25% 75%
Nordic	1	1 H	1	5	NA	513*	100%
Vegetarian	3	2 CL; 1 M	3	7 (6–17)	304 (NA)	315 (NA)	100%
DASH	1	1 CL	1	13	926	926	100%
Portfolio	1	1 H	1	7	NA	439*	100%
HDL-C							
Low-carbohydrate	11	7 CL; 1 M; 3 H	17	7 (2–22)	284 (32–1911)	285 (33–3223)	18% 64% 18%
High-protein	6	6 CL	6	14 (9–27)	490 (282–779)	535 (299–776)	50% 50%
Low-fat	4	2 CL; 1 L; 1 H	8	12 (4–28)	900 (251–3341)	653 (247–3825)	13% 37% 50%
Paleolithic	2	2 L	2	5 (4–6)	94 (73–115)	81 (64–98)	50% 50%
Low-GI/GL	7	3 CL; 2 L; 2 H	8	14 (3–80)	161 (66–3307)	155 (65–3013)	25% 75%
IER	2	2 CL	2	5 (2–8)	198 (102–294)	159 (75–243)	100%
Mediterranean	5	3 CL; 1 L; 1 H	8	6 (2 –29)	494 (220–2202)	397 (221–1903)	25% 75%
Nordic	1	1 L	1	5	NA	513*	100%
Vegetarian	4	2 CL; 1 L; 1 M	4	9 (4–17)	317 (305–329)	314 (291–337)	50%
DASH	1	1 CL	1	15	964	964	100%
Portfolio	1	1 H	1	7	NA	439*	100%
TG							
Low-carbohydrate	11	7 CL; 1 M; 3 H	17	7 (2–20)	330 (32–1859)	315 (33–3388)	18% 70% 12%
High-protein	6	6 CL	6	14 (10–29)	575 (240–1503)	584 (250–1535)	17% 50% 33%
Low-fat	4	2 CL; 1 L; 1 H	8	12 (4–28)	900 (251–3249)	653 (247–3727)	13% 37% 50%
Paleolithic	2	2 L	2	5 (4–6)	94 (73–115)	81 (64–98)	100%
Low-GI/GL	7	3 CL; 2 L; 2 H	8	15 (3–86)	206 (66–3333)	200 (65–3241)	13% 87%
IER	2	2 CL	2	5 (2–8)	198 (102–294)	159 (75–243)	100%
Mediterranean	4	2 CL; 1 L; 1 H	5	7 (2–29)	506 (220–2202)	393 (221–1903)	80% 20%
Nordic	1	1 H	1	5	NA	513*	100%
Vegetarian	4	2 CL; 1 L; 1 M	4	9 (5–19)	331 (312–350)	323 (320–339)	100%
DASH	1	1 CL	1	14	937	915	100%
Portfolio	1	1 H	1	7	NA	439*	100%

FIGURE 3 Summary and strength of evidence of meta-analyses of randomized controlled trials evaluating lipid profile in adults. Green = suggestive evidence; orange = weak evidence; grey = no evidence. *Number of total participants. AMSTAR, A MeaSurement Tool to Assess systematic Reviews; CL, critically low; DASH, Dietary Approaches to Stop Hypertension; GI, glycemic index; GL, glycemic load; H, high; HDL-C, HDL cholesterol; IER, intermittent energy restriction; L, low; LDL-C, LDL cholesterol; M, medium; NA, not available; TC, total cholesterol; TG, triglyceride.

	Articles, *n*	Quality of articles (AMSTAR-2)	Unique meta-analyses, *n*	N of studies in each meta-analysis *median (range)*	N of participants in intervention group *median (range)*	N of participants in control group *median (range)*	Strength of evidence ratings
GLUCOSE							
Low-carbohydrate	6	4 CL; 1 M; 1 H	11	5 (2–16)	196 (70–1315)	200 (48–3210)	36% 64%
High-protein	6	6 CL	6	13 (9–22)	416 (281–513)	440 (299–576)	17% 83%
Paleolithic	2	2 CL	2	5 (2–7)	180 (102–258)	150 (75–225)	100%
Low-GI/GL	4	2 CL; 2 H	4	8 (2–84)	447 (55–2937)	430 (54–2781)	25% 75%
IER	2	2 CL	2	5 (2–7)	180 (102–258)	150 (75–225)	100%
Mediterranean	4	3 CL; 1 L	4	12 (6–23)	1357 (260–1641)	1009 (342–1139)	25% 75%
Vegetarian	3	1 CL; 1 L; 1 M	3	4 (3–6)	110 (105–167)	108 (107–163)	33% 67%
DASH	2	2 CL	2	10 (9–10)	635 (454–815)	635 (457–813)	100%
INSULIN							
Low-carbohydrate	4	2 CL; 1 L; 1 H	4	9 (3–12)	586 (96–941)	579 (90–2478)	25% 50% 25%
High-protein	5	5 CL	5	11 (9–22)	304 (177–503)	311 (193–583)	60% 40%
Low-GI/GL	2	1 CL; 1 H	2	7 (2–11)	316 (55–577)	305 (54–555)	50% 50%
IER	2	2 CL	2	4 (2–6)	165 (102–228)	124 (75–173)	50% 50%
Mediterranean	2	2 CL	2	5 (5–5)	328 (238–418)	365 (319–411)	100%
DASH	1	1 CL	1	6 (6–15)	1641 (492–1937)	1009 (365–1588)	100%
HbA1c							
Low-carbohydrate	10	7 CL; 2 M; 1 H	16	8 (2–25)	348 (21–1006)	342 (21–1126)	75% 25%
High-protein	6	6 CL	6	5 (2–13)	72 (46–458)	65 (41–475)	67% 33%
Low-GI/GL	6	5 CL; 1 H	6	5 (3–15)	227 (167–421)	213 (147–409)	67% 33%
IER	1	1 CL	1	4	174	162	100%
Mediterranean	3	2 CL; 1 L	3	3 (3–9)	395 (308–568)	280 (278–521)	67% 33%
Vegetarian	2	1 CL; 1 M	2	7 (5–8)	162 (120–204)	187 (174–200)	100%

FIGURE 4 Summary and strength of evidence of meta-analyses of randomized controlled trials evaluating glycemic profile in adults. Green = suggestive evidence; orange = weak evidence; grey = no evidence. AMSTAR, A MeaSurement Tool to Assess systematic Reviews; CL, critically low; DASH, Dietary Approaches to Stop Hypertension; GI, glycemic index; GL, glycemic load; H, high; HbA1c, glycated hemoglobin; IER, intermittent energy restriction; L, low; M, medium.

interventions (mean difference: 0.09 mmol/L; 95% CI: 0.04–0.15 mmol/L).

Glycemic profile

Figure 4 summarizes the characteristics and the strength of evidence of the meta-analyses of RCTs that evaluated the effects of diets on glycemic profile. With regard to glucose, suggestive evidence for a difference between intervention and control diets was reported only for Mediterranean diet (mean difference: −0.37 mmol/L; 95% CI: −0.41 to −0.33 mmol/L) (79). On the other hand, 1 meta-analysis (24) comparing low-carbohydrate diets (as defined by the investigators of each trial) with other dietary interventions reported suggestive evidence for insulin (mean difference: −2.24 μU/mL; 95% CI: −2.66 to −1.82 μU/mL). Weak or no evidence was reported by all the meta-analyses evaluating HbA1c.

Blood pressure

Figure 5 summarizes the characteristics and the strength of evidence of the meta-analyses of RCTs that evaluated the effects of diets on systolic and diastolic blood pressure. Suggestive evidence for a difference between intervention and control diets was reported for low-carbohydrate, Mediterranean, and DASH diets. In particular, evidence from 1 meta-analysis (24) comparing low-carbohydrate diets (as defined by the investigators of each trial) with other dietary interventions (mean difference: −4.81 mm Hg; 95% CI: −5.33 to −4.29 mm Hg), 4 meta-analyses (75, 76, 79, 80) on the Mediterranean diet (ranging from −0.37 to −2.35 mm Hg), and 2 meta-analyses (81, 94) on the DASH diet (ranging from −2.63 to −6.74 mm Hg) were graded as suggestive.

Evaluation of methodological quality, bias, heterogeneity, and strength of evidence

Detailed information on the evaluation of the methodological quality of included meta-analyses and the assessment of the quality and/or risk of bias of original studies as reported by the authors of the meta-analyses is summarized in **Supplemental Tables 4** and **5**. Detailed information on the assessment of the strength of evidence is reported in **Supplemental Tables 6** and **7**.

	Articles, *n*	Quality of articles (AMSTAR-2)	Unique meta-analyses, *n*	N of studies in each meta-analysis *median (range)*	N of participants in intervention group *median (range)*	N of participants in control group *median (range)*	Strength of evidence ratings
SYSTOLIC BP							
Low-carbohydrate	9	5 CL; 1 M; 3 H	14	6 (2–22)	233 (79–2170)	238 (74–4482)	7% 7% 86%
High-protein	6	6 CL	6	12 (5–22)	420 (106–587)	455 (124–599)	17% 83%
Low-fat	2	1 L; 1 H	2	10 (9–10)	2527 (NA)	2632 (NA)	50% 50%
Paleolithic	2	2 L	2	5 (4–6)	94 (73–115)	81 (64–98)	50% 50%
Low-GI/GL	3	1 CL; 1 L; 1 H	3	13 (10–16)	814 (NA)	762 (NA)	100%
IER	1	1 CL	1	6	243	211	100%
Mediterranean	8	6 CL; 1 L; 1 H	10	5 (2–25)	971 (76–5226)	617 (75–5111)	30% 40% 30%
Nordic	2	1 CL; 1 H	2	3.5 (3–4)	NA	399 (306–492)*	100%
Vegetarian	3	1 CL; 1 L; 1 M	3	7 (4–11)	305 (210–306)	291 (195–317)	33% 67%
DASH	4	4 CL	4	14 (4–19)	1281 (1039–1399)	1280 (1057–1399)	50% 50%
Portfolio	1	1 H	1	7	NA	439*	100%
DIASTOLIC BP							
Low-carbohydrate	9	5 CL; 1 M; 3 H	14	6 (2–22)	222 (79–2170)	225 (74–4482)	8% 23% 69%
High-protein	6	6 CL	6	11 (6–19)	382 (106–587)	405 (124–599)	17% 83%
Low-fat	2	1 L; 1 H	2	10 (9–10)	2527 (NA)	2632 (NA)	100%
Paleolithic	3	2 L	3	5 (4–6)	94 (73–115)	81 (64–98)	50% 50%
Low-GI/GL	3	1 CL; 1 L; 1 H	3	13 (10–16)	805 (NA)	755 (NA)	33% 67%
IER	1	1 CL	1	5	168	171	100%
Mediterranean	8	6 CL; 1 L; 1 H	10	4 (2–25)	971 (76–5226)	617 (74–5111)	30% 50% 20%
Nordic	2	1 CL; 1 H	2	3.5 (3–4)	NA	399 (306–492)*	100%
Vegetarian	3	1 CL; 1 L; 1 M	3	7 (4–11)	305 (210–306)	291 (195–317)	33% 67%
DASH	4	4 L	4	14 (4–19)	1281 (1039–1399)	1280 (1057–1399)	50% 50%
Portfolio	1	1 H	1	7	NA	439*	100%

FIGURE 5 Summary and strength of evidence of meta-analyses of randomized controlled trials evaluating blood pressure in adults. Green = suggestive evidence; orange = weak evidence; grey = no evidence. *Number of total participants. AMSTAR, A MeaSurement Tool to Assess systematic Reviews; BP, blood pressure; CL, critically low; DASH, Dietary Approaches to Stop Hypertension; GI, glycemic index; GL, glycemic load; H, high; IER, intermittent energy restriction; L, low; M, medium; NA, not available.

Figure 6 depicts a summary of the results reported in the meta-analyses of RCTs included. Among all the diets evaluated, only the Mediterranean diet showed significant beneficial effects (i.e., reduction for all the outcomes except for HDL cholesterol, for which an increase is considered as beneficial) for all the parameters analyzed, without evidence of detrimental effects (i.e., increase for any of the outcomes except for HDL cholesterol). **Figure 7** reports a forest plot with the summary effect for each outcome evaluated. When for an outcome overlapping meta-analyses existed, we retained the meta-analysis with the highest methodological quality as determined by the AMSTAR-2 questionnaire. When the overlapping meta-analyses had the same methodological quality, we reported the meta-analysis with the largest number of studies.

Discussion

The present is the first umbrella review providing a comprehensive overview and a critical evaluation of the effects of different popular diets on body weight and cardiometabolic risk factors. The overall analysis comprised 80 different meta-analyses of RCTs that evaluated low-carbohydrate, high-protein, low-fat, paleolithic, low-glycemic-index/load, intermittent energy restriction, Mediterranean, Nordic, vegetarian, DASH, and portfolio dietary patterns. Over 80% of the meta-analyses included showed low methodological quality and the strength of evidence, assessed using evidence classification criteria, was generally weak. Notably, the Mediterranean diet was the only diet that demonstrated significant and beneficial effects for all the parameters analyzed, without evidence of potential adverse effects.

Over the past few decades, a wide range of dietary strategies have been promoted to reduce body weight. Some of these diets have been characterized by the modulation of macronutrients (e.g., low-carbohydrate, high-protein, and low-fat diets), whereas others focused on dietary patterns as a whole (e.g., Mediterranean, Nordic, vegetarian, DASH, and portfolio dietary models). To date, several meta-analyses including dietary intervention trials have been published, but to the best of our knowledge no umbrella reviews evaluating

FIGURE 6 Summary of the results reported in meta-analyses of randomized controlled trials in adults according to dietary interventions. Green = evidence of a beneficial effect (i.e., lowering for all outcomes except HDL-C); grey = evidence of no effect; red = evidence of a detrimental effect (i.e., increasing for all outcomes except HDL-C). The size of the circles reflects the number of unique meta-analyses available. BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension; ER, energy restriction; GI, glycemic index; GL, glycemic load; HbA1c, glycated hemoglobin; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; TC, total cholesterol; TG, triglyceride.

the strength of evidence for such meta-analyses have been performed.

In the present umbrella review, the largest number of meta-analyses was found for low-carbohydrate diets. Their definition varied greatly, and cutoffs ranged from 50 to 130 g/d, or 26–45% energy from carbohydrates. Four meta-analyses (33, 34, 36, 39), conducted on participants with type 2 diabetes, compared low-carbohydrate with high-carbohydrate diets, reporting no significant effects on weight. The other meta-analyses compared low-carbohydrate with low-fat diets (7, 21–23, 28, 29, 37) or other dietary interventions (24, 27, 30–32, 35, 40), reporting contrasting results. Evidence of a significant reduction in body weight was observed, especially in the short term (6 mo) and in studies with more extreme carbohydrate restriction. When the follow-up period or the amount of carbohydrates increased, the effect was attenuated. As to the other parameters, we observed weak or suggestive evidence of an improvement in glycemic profile and blood pressure, and conflicting results for lipid profile, with an increase in total and LDL cholesterol reported in 12 meta-analyses. The detrimental effects of low-carbohydrate diets on lipid parameters may be related to the fact that people on low-carbohydrate diets tend to eat less vegetables and fruits rich in micronutrients and fiber, and more animal-derived foods (98).

As for high-protein diets, they are one of the most popular weight-loss strategies. Several mechanisms have been proposed to explain their supposed superiority over conventional weight-loss diets, including higher satiety and an increase in energy expenditure (99). Our analysis showed that the quality of published meta-analyses on high-protein diets is critically low and the number of participants is relatively small. Weak or no evidence of a reduction in anthropometric parameters and blood pressure was reported, whereas data on lipid and glycemic profiles were discordant. Increased saturated fat and lower fiber intake can potentially contribute to the observed increase in LDL cholesterol, glucose, and HbA1c, questioning the safety of high-protein diets in the long term.

With regard to low-fat diets, the proportion of fat in the present umbrella review was $\leq$30% of energy intake, according to the dietary recommendations from the WHO Healthy Diet Fact Sheet. Suggestive evidence of weight and BMI reduction was reported in the meta-analysis by Hooper et al. (52), which included the Women's Health Initiative Dietary Modification Trial and compared low-fat with high-fat diets. The other meta-analyses comparing low-fat with high-fat (53), low-carbohydrate (51, 53), and other dietary interventions (32, 47, 48, 53) reported weak or no evidence. As to the lipid profile, low-fat diets resulted in a greater reduction in total and LDL cholesterol than high-fat diets or other dietary interventions, but also in a significant worsening of HDL cholesterol and triglycerides. This negative effect is probably determined by the type of fat and the quality of carbohydrates consumed (100).

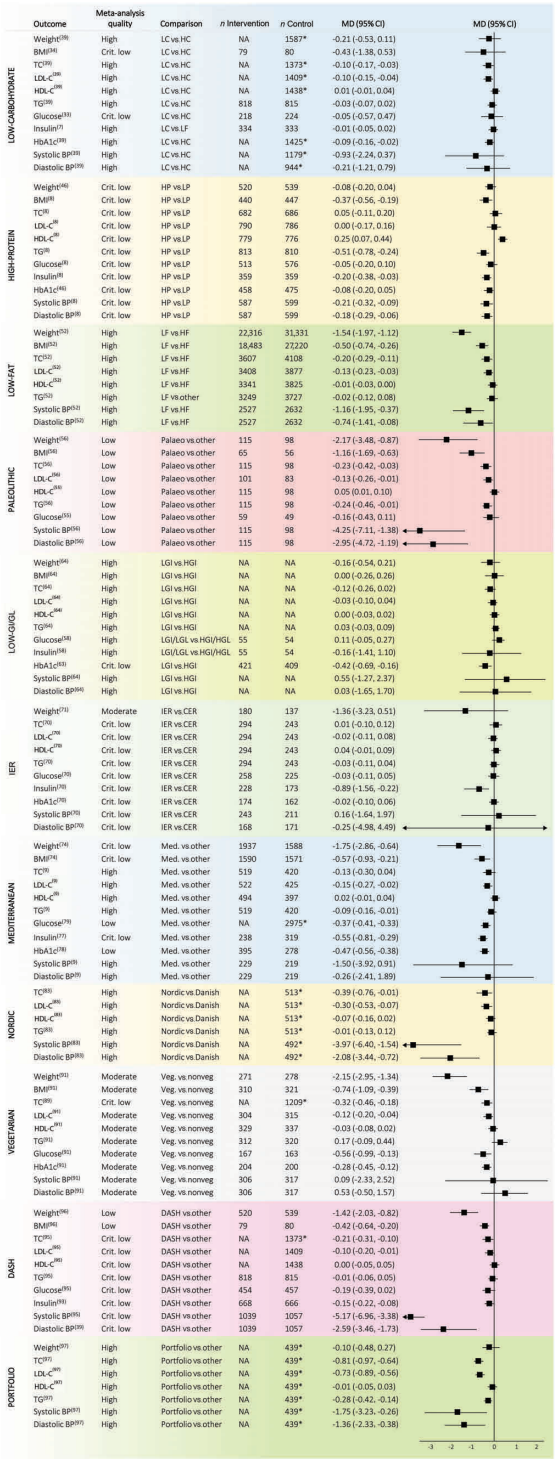

FIGURE 7 Forest plot of all nonoverlapping meta-analyses of randomized controlled trials in adults according to dietary interventions. *Number of total participants. BP, blood pressure; CER, continuous energy restriction; Crit., critically; DASH, Dietary Approaches to Stop Hypertension; HC, high-carbohydrate; HDL-C, HDL cholesterol; HF, high-fat; HGI, high-glycemic-index; HGL, high-glycemic-load; HP, high-protein; IER, intermittent energy restriction; LC, low-carbohydrate; LDL-C, LDL cholesterol; LF, low-fat; LGI, low-glycemic-index; LGL, low-glycemic-load; LP, low-protein; MD, mean difference; Med., Mediterranean; NA, not available; TC, total cholesterol; TG, triglyceride; Veg., vegetarian.

The most consistent findings were observed in studies that included dietary patterns such as the Mediterranean and DASH diets. Both dietary patterns are high in fruits, vegetables, fish, and nuts, and indexes measuring adherence to these diets have been associated with lower risk of cardiovascular events, diabetes, and cancer in epidemiological studies (5, 20). In the present analysis, the Mediterranean diet showed suggestive evidence of a reduction in weight, BMI, total cholesterol, glucose, and blood pressure, and weak evidence of an improvement in LDL and HDL cholesterol, triglycerides, insulin, and HbA1c. No meta-analyses reported detrimental effects. The DASH diet, on the other hand, reported suggestive evidence of a beneficial effect on weight and blood pressure, and weak evidence for BMI and total cholesterol. With regard to the other dietary patterns, the evidence was less consistent, because most studies had a limited sample size and many meta-analyses were of low methodological quality. We found weak evidence of an improvement in total, LDL cholesterol, and blood pressure with the Nordic diet; weak evidence of an improvement in anthropometric parameters, total and LDL cholesterol, glucose, HbA1c, and blood pressure with vegetarian diets; and weak evidence of an improvement in total and LDL cholesterol, triglycerides, and blood pressure with the portfolio dietary pattern. Altogether, these results corroborate observational findings indicating that dietary patterns that emphasize vegetables, fruits, whole grains, and plant-based protein, and limit sugar, sodium, and red and processed meat, are consistently associated with decreased risk of cardiovascular and metabolic diseases (20, 101).

As to the other popular diets studied, the present umbrella review showed many criticisms. For the paleolithic diet, a weight-loss plan based upon the premise of consuming only foods available during the Stone Age (102), the number of participants was very small and the follow-up was short. In addition, extensive publication bias, selective outcome reporting, and potential conflict of interests were detected. With regard to intermittent energy restriction, a dietary approach that has gained greater popularity as a way for losing weight alternative to conventional weight-loss diets, our systematic literature search led to the identification of 6 meta-analyses of RCTs published in the last 3 y. Intermittent energy restriction includes diverse interventions such as alternate day fasting, the 5:2 diet, and longer cyclic periods of restricting energy intake or fasting, interchanged by periods of ad libitum energy intake. The number of clinical trials and participants, however, was very small, most studies were performed by the same authors, and the follow-up was generally short. With the exception of a meta-analysis that reported weak evidence of a greater reduction in insulin (70), all the other meta-analyses evaluating weight, lipid profile, glucose metabolism, and blood pressure reported no evidence of a superiority of intermittent energy restriction over continuous energy restriction.

The present umbrella review has several limitations. First of all, the included meta-analyses showed relevant differences in terms of populations, methods, duration of interventions,

study quality, and definition of intervention and control diets. Most meta-analyses included studies conducted on participants with overweight/obesity or other diseases, and this should be considered before extending these results to the general population. In any case, the choice of the diet should be made via a critical approach, by considering the effects of the diet on all the factors that may have a role in the development of the disease. Second, despite the relatively high number of meta-analyses published, a limited number of clinical trials were available for many diets evaluated. Third, when multiple meta-analyses of RCTs existed for an outcome, often the results were not concordant in terms of direction of effect and/or statistical significance. Such a difference in the final results could be explained mainly by the framing of the question and differences in the inclusion criteria, comparisons, populations, and statistical methods used. Lastly, as with any other systematic review, an umbrella review is dependent on the reporting of the included meta-analyses and does not account for potential omissions or overlapping of original studies.

Because meta-analyses have become an indispensable tool in clinical application for evidence-based decision making, it is extremely important to define and carefully standardize the criteria and the strategies to adopt. Although the number of meta-analyses included in the present umbrella review is high, their methodological quality appears to be mainly low or critically low. More efforts are needed to improve the quality of published articles and further research on the effects of popular diets on anthropometric and cardiometabolic parameters is needed before firm conclusions can be drawn. This will facilitate the understanding, meaning, and applicability of findings in clinical practice.

In conclusion, through a systematic and comprehensive search we were able to include a vast number of meta-analyses that assessed the effects of different popular diets on weight and cardiometabolic risk factors. Among all the diets and dietary patterns evaluated, the Mediterranean diet had the strongest and most consistent evidence, with no meta-analyses reporting detrimental effects. Suggestive evidence of an improvement in body weight and blood pressure was also reported for the DASH diet. Low-carbohydrate, high-protein, low-fat and low-glycemic-index/load diets, on the other hand, showed beneficial effects on weight loss, but also potential risks of unfavorable lipid, glycemic, or blood pressure parameters. The strength of evidence for the other diets evaluated was weak or not statistically significant. Overall, these findings highlight the strengths and limitations of most popular diets, confirming that the best results, in terms of weight and cardiometabolic risk amelioration, are obtained with balanced dietary patterns such as the Mediterranean diet.

Acknowledgments

The authors' responsibilities were as follows—MD and FS: designed the study protocol; DM, DA, and LL: conducted the systematic literature search; CDB, DN, and EM: performed the quality assessment; AR, MDA, and LB: performed the data extraction; MD and GP: performed the statistical analysis; MD, GP, CF, MG, and JG: wrote the first draft of the manuscript; FS: critically reviewed the manuscript and contributed important intellectual content; MD: is the guarantor of the paper; and all authors: contributed to writing and reviewing the manuscript and read and approved the final manuscript.

References

1. GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016;388:1659–724.
2. Santos I, Sniehotta FF, Marques MM, Carraça EV, Teixeira PJ. Prevalence of personal weight control attempts in adults: a systematic review and meta-analysis. Obes Rev 2017;18:32–50.
3. Wirt A, Collins CE. Diet quality – what is it and does it matter? Public Health Nutr 2009;12:2473–92.
4. GBD 2017 Diet Collaborators. Health effects of dietary risks in 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2019;393:1958–72.
5. Rodríguez-Monforte M, Sánchez E, Barrio F, Costa B, Flores-Mateo G. Metabolic syndrome and dietary patterns: a systematic review and meta-analysis of observational studies. Eur J Nutr 2017;56:925–47.
6. Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, Golan R, Fraser D, Bolotin A, Vardi H, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med 2008;359:229–41.
7. Mansoor N, Vinknes KJ, Veierød MB, Retterstøl K. Effects of low-carbohydrate diets vs. low-fat diets on body weight and cardiovascular risk factors: a meta-analysis of randomised controlled trials. Br J Nutr 2016;115:466–79.
8. Santesso N, Akl EA, Bianchi M, Mente A, Mustafa R, Heels-Ansdell D, Schünemann HJ. Effects of higher- versus lower-protein diets on health outcomes: a systematic review and meta-analysis. Eur J Clin Nutr 2012;66:780–8.
9. Rees K, Takeda A, Martin N, Ellis L, Wijesekara D, Vepa A, Das A, Hartley L, Stranges S. Mediterranean-style diet for the primary and secondary prevention of cardiovascular disease. Cochrane Database Syst Rev 2019;3:CD009825.
10. Ioannidis JP. The mass production of redundant, misleading, and conflicted systematic reviews and meta analyses. Milbank Q 2016;94:485–514.
11. Barnard ND, Willett WC, Ding EL. The misuse of meta-analysis in nutrition research. JAMA 2017;318:1435–6.
12. Aromataris E, Fernandez R, Godfrey CM, Holly C, Khalil H, Tungpunkom P. Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. Int J Evid Based Healthc 2015;13:132–40.
13. Aromataris E, Fernandez R, Godfrey C, Holly C, Khalil H, Tungpunkom P. Chapter 10: Umbrella reviews. In: Joanna Briggs Institute Reviewer's Manual [Internet]. Aromataris E, Munn Z (Editors). The Joanna Briggs Institute; 2017. Available from: https://reviewersmanual.joannabriggs.org/.
14. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358:j4008.
15. Cochran WG. The combination of estimates from different experiments. Biometrics 1954;10:101–29.
16. Riley RD, Higgins JP, Deeks JJ. Interpretation of random effects meta-analyses. BMJ 2011;342:d549.

17. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.
18. Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, Carpenter J, Rücker G, Harbord RM, Schmid CH, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ 2011;343:d4002.
19. Belbasis L, Bellou V, Evangelou E, Ioannidis JP, Tzoulaki I. Environmental risk factors and multiple sclerosis: an umbrella review of systematic reviews and meta-analyses. Lancet Neurol 2015;14:263–73.
20. Dinu M, Pagliai G, Casini A, Sofi F. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomised trials. Eur J Clin Nutr 2018;72:30–43.
21. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS, Brehm BJ, Bucher HC. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors. Arch Intern Med 2006;166:285–93.
22. Hession M, Rolland C, Kulkarni U, Wise A, Broom J. Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. Obes Rev 2009;10:36–50.
23. Hu T, Mills KT, Yao L, Demanelis K, Eloustaz M, Yancy WS, Jr, Kelly TN, He J, Bazzano LA. Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. Am J Epidemiol 2012;176:S44–54.
24. Santos FL, Esteves SS, Costa Pereira A, Yancy WS, Jr, Nunes JPL. Systematic review and meta-analysis of clinical trials of the effects of low carbohydrate diets on cardiovascular risk factors. Obes Rev 2012;13:1048–66.
25. Ajala O, English P, Pinkney J. Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes. Am J Clin Nutr 2013;97:505–16.
26. Bueno NB, Vieira de Melo IS, Lima de Oliveira S, da Rocha Ataide T. Very-low-carbohydrate ketogenic diet vs. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials. Br J Nutr 2013;110:1178–87.
27. Naude CE, Schoonees A, Senekal M, Young T, Garner P, Volmink J. Low carbohydrate versus isoenergetic balanced diets for reducing weight and cardiovascular risk: a systematic review and meta-analysis. PLoS One 2014;9:e100652.
28. Alexandraki I, Palacio C, Mooradian AD. Relative merits of low-carbohydrate versus low-fat diet in managing obesity. South Med J 2015;108:401–16.
29. Sackner-Bernstein J, Kanter D, Kaul S. Dietary intervention for overweight and obese adults: comparison of low-carbohydrate and low-fat diets. A meta-analysis. PLoS One 2015;10:e0139817.
30. Fan Y, Di H, Chen G, Mao X, Liu C. Effects of low carbohydrate diets in individuals with type 2 diabetes: systematic review and meta-analysis. Int J Clin Exp Med 2016;9:11166–74.
31. Hashimoto Y, Fukuda T, Oyabu C, Tanaka M, Asano M, Yamazaki M, Fukui M. Impact of low-carbohydrate diet on body composition: meta-analysis of randomized controlled studies. Obes Rev 2016;17:499–509.
32. Steckhan N, Hohmann CD, Kessler C, Dobos G, Michalsen A, Cramer H. Effects of different dietary approaches on inflammatory markers in patients with metabolic syndrome: a systematic review and meta-analysis. Nutrition 2016;32:338–48.
33. Meng Y, Bai H, Wang S, Li Z, Wang Q, Chen L. Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: a systematic review and meta-analysis of randomized controlled trials. Diabetes Res Clin Pract 2017;131:124–31.
34. Snorgaard O, Poulsen GM, Andersen HK, Astrup A. Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes. BMJ Open Diabetes Res Care 2017;5:e000354.
35. Huntriss R, Campbell M, Bedwell C. The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials. Eur J Clin Nutr 2018;72:311–25.
36. Sainsbury E, Kizirian NV, Partridge SR, Gill T, Colagiuri S, Gibson AA. Effect of dietary carbohydrate restriction on glycemic control in adults with diabetes: a systematic review and meta-analysis. Diabetes Res Clin Pract 2018;139:239–52.
37. Van Zuuren EJ, Fedorowicz Z, Kuijpers T, Pijl H. Effects of low-carbohydrate compared with low-fat-diet interventions on metabolic control in people with type 2 diabetes: a systematic review including GRADE assessments. Am J Clin Nutr 2018;108:300–31.
38. Gjuladin-Hellon T, Davies IG, Penson P, Baghbadorani RA. Effects of carbohydrate-restricted diets on low-density lipoprotein cholesterol levels in overweight and obese adults: a systematic review and meta-analysis. Nutr Rev 2019;77:161–80.
39. Korsmo-Haugen HK, Brurberg KG, Mann J, Aas AM. Carbohydrate quantity in the dietary management of type 2 diabetes: a systematic review and meta-analysis. Diabetes Obes Metab 2019;21:15–27.
40. McArdle PD, Greenfield SM, Rilstone SK, Narendran P, Haque MS, Gill PS. Carbohydrate restriction for glycaemic control in type 2 diabetes: a systematic review and meta-analysis. Diabet Med 2019;36:335–48.
41. Wycherley TP, Moran LJ, Clifton PM, Noakes M, Brinkworth GD. Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials. Am J Clin Nutr 2012;96:1281–98.
42. Dong YJ, Zhang ZL, Wang PY, Qin LQ. Effects of high-protein diets on body weight, glycaemic control, blood lipids and blood pressure in type 2 diabetes: meta-analysis of randomised controlled trials. Br J Nutr 2013;110:781–9.
43. Schwingshackl L, Hoffmann G. Long-term effects of low-fat diets either low or high in protein on cardiovascular and metabolic risk factors: a systematic review and meta-analysis. Nutr J 2013;12:48.
44. Clifton PM, Condo D, Keogh JB. Long term weight maintenance after advice to consume low carbohydrate, higher protein diets: a systematic review and meta-analysis. Nutr Metab Cardiovasc Dis 2014;24:224–35.
45. Johansson K, Neovius M, Hemmingsson E. Effects of anti-obesity drugs, diet, and exercise on weight-loss maintenance after a very-low-calorie diet or low-calorie diet: a systematic review and meta-analysis of randomized controlled trials. Am J Clin Nutr 2014;99:14–23.
46. Zhao WT, Luo Y, Zhang Y, Zhou Y, Zhao TT. High protein diet is of benefit for patients with type 2 diabetes: an updated meta-analysis. Medicine 2018;97:e13149.
47. Astrup A, Grunwald GK, Melanson El, Saris WHM, Hill JO. The role of low-fat diets in body weight control: a meta-analysis of *ad libitum* dietary intervention studies. Int J Obes 2000;24:1545–52.
48. Avenell A, Brown TJ, McGee MA, Campbell MK, Grant AM, Broom J, Jung RT, Smith WC. What are the long-term benefits of weight reducing diets in adults? A systematic review of randomized controlled trials. J Hum Nutr Diet 2004;17:317–35.
49. Schwingshackl L, Hoffmann G. Comparison of effects of long-term low-fat vs high-fat diets on blood lipid levels in overweight or obese patients: a systematic review and meta-analysis. J Acad Nutr Diet 2013;113:1640–61.
50. Wu L, Ma D, Walton-Moss B, He Z. Effects of low-fat diet on serum lipids in premenopausal and postmenopausal women: a meta-analysis of randomized controlled trials. Menopause 2014;21:89–99.
51. Boaz M, Raz O, Wainstein J. Low fat vs. low carbohydrate diet strategies for weight reduction: a meta-analysis. J Obes Weight Loss Ther 2015;5:273.
52. Hooper L, Abdelhamid A, Bunn D, Brown T, Summerbell CD, Skeaff CM. Effects of total fat intake on body weight. Cochrane Database Syst Rev 2015;8:CD011834.
53. Tobias DK, Chen M, Manson JE, Ludwig D, Willett W, Hu FB. Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: a systematic review and meta-analysis. Lancet Diabetes Endocrinol 2015;3:968–79.
54. Lu M, Wan Y, Yang B, Huggins CE, Li D. Effects of low-fat compared with high-fat diet on cardiometabolic indicators in people with overweight and obesity without overt metabolic disturbance: a systematic review and meta-analysis of randomised controlled trials. Br J Nutr 2018;119:96–108.

55. Manheimer EW, Van Zuuren EJ, Fedorowicz Z, Pijl H. Paleolithic nutrition for metabolic syndrome: systematic review and meta-analysis. Am J Clin Nutr 2015;102:922–32.
56. Ghaedi E, Mohammadi M, Mohammadi H, Ramezani-Jolfaie N, Malekzadeh J, Hosseinzadeh M, Salehi-Abargouei A. Effects of a paleolithic diet on cardiovascular disease risk factors: a systematic review and meta-analysis of randomized controlled trials. Adv Nutr 2019;10:634–46.
57. Opperman AM, Venter CS, Oosthuizen W, Thompson RL, Vorster HH. Meta-analysis of the health effects of using the glycaemic index in meal-planning. Br J Nutr 2004;92:367–81.
58. Thomas D, Elliott EJ, Baur L. Low glycaemic index or low glycaemic load diets for overweight and obesity. Cochrane Database Syst Rev 2007;3:CD005105.
59. Thomas DE, Elliott EJ. The use of low-glycaemic index diets in diabetes control. Br J Nutr 2010;104:797–802.
60. Fleming P, Godwin M. Low-glycaemic index diets in the management of blood lipids: a systematic review and meta-analysis. Fam Pract 2013;30:485–91.
61. Goff LM, Cowland DE, Hooper L, Frost GS. Low glycaemic index diets and blood lipids: a systematic review and meta-analysis of randomised controlled trials. Nutr Metab Cardiovasc Dis 2013;23:1–10.
62. Schwingshackl L, Hoffmann G. Long-term effects of low glycemic index/load vs. high glycemic index/load diets on parameters of obesity and obesity-associated risks: a systematic review and meta-analysis. Nutr Metab Cardiovasc Dis 2013;23:699–706.
63. Wang Q, Xia W, Zhao Z, Zhang H. Effects comparison between low glycemic index diets and high glycemic index diets on HbA1c and fructosamine for patients with diabetes: a systematic review and meta-analysis. Prim Care Diabetes 2015;9:362–9.
64. Clar C, Al-Khudairy L, Loveman E, Kelly SAM, Hartley L, Flowers N, Germanò R, Frost G, Rees K. Low glycaemic index diets for the prevention of cardiovascular disease. Cochrane Database Syst Rev 2017;7:CD004467.
65. Evans CEL, Greenwood DC, Threapleton DE, Gale CP, Cleghorn CL, Burley VJ. Glycemic index, glycemic load, and blood pressure: a systematic review and meta-analysis of randomized controlled trials. Am J Clin Nutr 2017;105:1176–90.
66. Ojo O, Ojo OO, Adebowale F, Wang XH. The effect of dietary glycaemic index on glycaemia in patients with type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Nutrients 2018;10:373.
67. Zafar MI, Mills KE, Zheng J, Peng MM, Ye X, Chen LL. Low glycaemic index diets as an intervention for obesity: a systematic review and meta-analysis. Obes Rev 2019;20:290–315.
68. Alhamdan AB, Garcia-Alvarez A, Alzahrnai AH, Karanxha J, Stretchberry DR, Contrera KJ, Utria AF, Cheskin LJ. Alternate-day versus daily energy restriction diets: which is more effective for weight loss? A systematic review and meta-analysis. Obes Sci Pract 2016;2:293–302.
69. Headland M, Clifton PM, Carter S, Keogh JB. Weight-loss outcomes: a systematic review and meta-analysis of intermittent energy restriction trials lasting a minimum of 6 months. Nutrients 2016;8:354.
70. Cioffi I, Evangelista A, Ponzo V, Ciccone G, Soldati L, Santarpia L, Contaldo F, Pasanisi F, Ghigo E, Bo S. Intermittent versus continuous energy restriction on weight loss and cardiometabolic outcomes: a systematic review and meta-analysis of randomized controlled trials. J Transl Med 2018;16:371.
71. Harris L, Hamilton S, Azevedo LB, Olajide J, De Brún C, Waller G, Whittaker V, Sharp T, Lean M, Hankey C, et al. Intermittent fasting interventions for treatment of overweight and obesity in adults: a systematic review and meta-analysis. JBI Database System Rev Implement Rep 2018;16:507–47.
72. Harris L, McGarty A, Hutchison L, Ells L, Hankey C. Short-term intermittent energy restriction interventions for weight management: a systematic review and meta-analysis. Obes Rev 2018;19:1–13.
73. Roman YM, Dominguez MC, Easow TM, Pasupuleti V, White CM, Hernandez AV. Effects of intermittent versus continuous dieting on weight and body composition in obese and overweight people: a systematic review and meta-analysis of randomized controlled trials. Int J Obes 2019;43:2017–27.
74. Esposito K, Kastorini CM, Panagiotakos DB, Giugliano D. Mediterranean diet and weight loss: meta-analysis of randomized controlled trials. Metab Syndr Relat Disord 2011;9:1–12.
75. Kastorini CM, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB. The effect of Mediterranean diet on metabolic syndrome and its components. A meta-analysis of 50 studies and 534,906 individuals. J Am Coll Cardiol 2011;57:1299–313.
76. Nordmann AJ, Suter-Zimmermann K, Bucher HC, Shai I, Tuttle KR, Estruch R, Briel M. Meta-analysis comparing Mediterranean to low-fat diets for modification of cardiovascular risk factors. Am J Med 2011;124:841–51.
77. Huo R, Du T, Xu Y, Xu W, Chen X, Sun K, Yu X. Effects of Mediterranean-style diet on glycemic control, weight loss and cardiovascular risk factors among type 2 diabetes individuals: a meta-analysis. Eur J Clin Nutr 2015;69:1200–8.
78. Esposito K, Maiorino MI, Bellastella G, Chiodini P, Panagiotakos D, Giugliano D. A journey into a Mediterranean diet and type 2 diabetes: a systematic review with meta-analyses. BMJ Open 2015;5: e008222.
79. Garcia M, Bihuniak JB, Shook J, Kenny A, Kerstetter J, Huedo-Medina TB. The effect of the traditional Mediterranean-style diet on metabolic risk factors: a meta-analysis. Nutrients 2016;8:168.
80. Gay HC, Rao SG, Vaccarino V, Ali MK. Effects of different dietary interventions on blood pressure. Hypertension 2016;67: 733–9.
81. Ndanuko RN, Tapsell LC, Charlton KE, Neale EP, Batterham MJ. Dietary patterns and blood pressure in adults: a systematic review and meta-analysis of randomized controlled trials. Adv Nutr 2016;7: 76–89.
82. Nissensohn M, Román-Viñas B, Sánchez-Villegas A, Piscopo S, Serra-Majem L. The effect of the Mediterranean diet on hypertension: a systematic review and meta-analysis. J Nutr Educ Behav 2016;48:42–53.e1.
83. Ramezani-Jolfaie N, Mohammadi M, Salehi-Abargouei A. The effect of healthy Nordic diet on cardio-metabolic markers: a systematic review and meta-analysis of randomized controlled clinical trials. Eur J Clin Nutr 2019;58:2159–74.
84. Yokoyama Y, Nishimura K, Barnard ND, Takegami M, Watanabe M, Sekikawa A, Okamura T, Miyamoto Y. Vegetarian diets and blood pressure: a meta-analysis. JAMA Intern Med 2014;174: 577–87.
85. Yokoyama Y, Barnard ND, Levin SM, Watanabe M. Vegetarian diets and glycemic control in diabetes: a systematic review and meta-analysis. Cardiovasc Diagn Ther 2014;4:373–82.
86. Barnard ND, Levin SM, Yokoyama Y. A systematic review and meta-analysis of changes in body weight in clinical trials of vegetarian diets. J Acad Nutr Diet 2015;115:954–69.
87. Huang RY, Huang CC, Hu FB, Chavarro JE. Vegetarian diets and weight reduction: a meta-analysis of randomized controlled trials. J Gen Intern Med 2015;31:109–16.
88. Wang F, Zheng J, Yang B, Jiang J, Fu Y, Li D. Effects of vegetarian diets on blood lipids: a systematic review and meta-analysis of randomized controlled trials. J Am Heart Assoc 2015;4:e002408.
89. Yokoyama Y, Levin SM, Barnard ND. Association between plant-based diets and plasma lipids: a systematic review and meta-analysis. Nutr Rev 2017;75:683–98.
90. Picasso MC, Lo-Tayraco JA, Ramos-Villanueva JM, Pasupuleti V, Hernandez AV. Effect of vegetarian diets on the presentation of metabolic syndrome or its components: a systematic review and meta-analysis. Clin Nutr 2019;38:1117–32.
91. Viguiliouk E, Kendall CWK, Kahleová H, Rahelić D, Salas-Salvadó J, Choo VL, Mejia SB, Stewart SE, Leiter LA, Jenkins DJ, et al. Effect of vegetarian dietary patterns on cardiometabolic risk factors in diabetes: a systematic review and meta-analysis of randomized controlled trials. Clin Nutr 2019;38:1133–45.

92. Lopez PD, Cativo EH, Atlas SA, Rosendorff C. The effect of vegan diets on blood pressure in adults: a meta-analysis of randomized controlled trials. Am J Med 2019;132:875–883.e7.
93. Shirani F, Salehi-Abargouei A, Azadbakht L. Effects of Dietary Approaches to Stop Hypertension (DASH) diet on some risk for developing type 2 diabetes: a systematic review and meta-analysis on controlled clinical trials. Nutrition 2013;29:939–47.
94. Saneei P, Salehi-Abargouei A, Esmaillzadeh A, Azadbakht L. Influence of Dietary Approaches to Stop Hypertension (DASH) diet on blood pressure: a systematic review and meta-analysis on randomized controlled trials. Nutr Metab Cardiovasc Dis 2014;24: 1253–61.
95. Siervo M, Lara J, Chowdhury S, Ashor A, Oggioni C, Mathers JC. Effects of the Dietary Approach to Stop Hypertension (DASH) diet on cardiovascular risk factors: a systematic review and meta-analysis. Br J Nutr 2015;113:1–15.
96. Soltani S, Shirani F, Chitsazi MJ, Salehi-Abargouei A. The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. Obes Rev 2016;17:442–54.
97. Chiavaroli L, Nishi SK, Khan TA, Braunstein CR, Glenn AJ, Blanco Mejia S, Rahelić D, Kahleová H, Salas-Salvadó J, Jenkins DJA, et al. Portfolio dietary pattern and cardiovascular disease: a systematic review and meta-analysis of controlled trials. Prog Cardiovasc Dis 2018;61:43–53.
98. Elidottir AS, Halldorsson TI, Gunnarsdottir I, Ramel A. Dietary intake and cardiovascular risk factors in Icelanders following voluntarily a low carbohydrate diet. PLoS One 2016;11:e0156655.
99. Westerterp-Plantenga MS, Nieuwenhuizen A, Tomé D, Soenen S, Westerterp KR. Dietary protein, weight loss, and weight maintenance. Annu Rev Nutr 2009;29:21–41.
100. Forouhi NG, Krauss RM, Taubes G, Willett W. Dietary fat and cardiometabolic health: evidence, controversies, and consensus for guidance. BMJ 2018;361:k2139.
101. Satija A, Bhupathiraju SN, Spiegelman D, Chiuve SE, Manson JE, Willett W, Rexrode KM, Rimm EB, Hu FB. Healthful and unhealthful plant-based diets and the risk of coronary heart disease in US adults. J Am Coll Cardiol 2017;70:411–22.
102. Konner M, Eaton SB. Paleolithic nutrition: twenty-five years later. Nutr Clin Pract 2010;25:594–602.