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Diet in the management of type 2 diabetes: umbrella review of systematic reviews with meta-analyses of randomised controlled trials

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► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjmed-2023-000664).

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Cite this as: *BMJMED* 2023;2:e000664. doi:10.1136/bmjmed-2023-000664

Received: 5 June 2023
Accepted: 29 September 2023

ABSTRACT

OBJECTIVE To systematically summarise and evaluate the existing evidence on the effect of diet on the management of type 2 diabetes and prevention of complications.

DESIGN Umbrella review of systematic reviews with meta-analyses of randomised controlled trials.

DATA SOURCES PubMed, Embase, Epistemonikos, and Cochrane, from inception up to 5 June 2022.

ELIGIBILITY CRITERIA FOR SELECTING STUDIES Systematic reviews with meta-analyses of randomised controlled trials reporting summary effect estimates on the effect of diet on any health outcome in populations with type 2 diabetes were included in the review. Only meta-analyses with randomised controlled trials with the duration of at least 12 weeks were eligible for inclusion. Summary data were extracted by two investigators independently. Summary effect estimates with 95% confidence intervals were recalculated with a random effects model if the information provided was insufficient. Methodological quality was assessed with the A MeaSurement Tool to Assess systematic Reviews (AMSTAR) 2 tool and the certainty of evidence with the Grading of Recommendations Assessment, Development, and Evaluations (GRADE) approach.

RESULTS 88 publications with 312 meta-analyses of randomised controlled trials were included. Methodological quality was high to moderate in 23% and low to very low in 77% of the included publications. A high certainty of evidence was found for the beneficial effects of liquid meal replacement on reducing body weight (mean difference −2.37 kg, 95% confidence interval −3.30 to −1.44; n=9 randomised controlled trials included in the meta-analysis) and body mass index (−0.87, −1.32 to −0.43; n=8 randomised controlled trials), and of a low carbohydrate diet (<26% of total energy) on levels of haemoglobin A_{1c} (−0.47%, −0.60% to −0.34%; n=17 randomised controlled trials) and triglycerides (−0.30 mmol/L, −0.43 to −0.17; n=19 randomised controlled trials). A moderate certainty of evidence was found for the beneficial effects of liquid meal replacement, plant based, Mediterranean, high protein, low glycaemic index, and low carbohydrate diets (<26% total energy) on various cardiometabolic measures. The remaining results had low to very low certainty of evidence.

CONCLUSIONS The evidence indicated that diet has a multifaceted role in the management of type 2 diabetes. An energy restricted diet can reduce body weight and improve cardiometabolic health. Beyond energy restriction, dietary approaches such as plant based, Mediterranean, low carbohydrate (<26% total energy), or high protein diets, and a higher intake of omega 3 fatty acids can be beneficial for cardiometabolic health in individuals with type 2 diabetes.

SYSTEMATIC REVIEW REGISTRATION PROSPERO CRD42021252309.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Type 2 diabetes is a major global health problem that can cause further health complications

⇒ Diet is essential in managing type 2 diabetes and preventing further diabetes related complications

⇒ To provide evidence based dietary recommendations for people with type 2 diabetes, the existing evidence needs to be systematically summarised and evaluated with established tools

WHAT THIS STUDY ADDS

⇒ This umbrella review of systematic reviews with meta-analyses of randomised controlled trials identified the dietary factors that can improve surrogate markers of disease and health in people with type 2 diabetes

⇒ Robust evidence indicated that in addition to energy restriction, dietary approaches, such as plant based, Mediterranean, low carbohydrate (<26% total energy), and high protein diets are beneficial for cardiometabolic health in individuals with type 2 diabetes

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ This study identified the dietary recommendations that can be effective in improving surrogate markers of disease and health in people with type 2 diabetes

⇒ More randomised controlled trials with long term interventions, focusing exclusively on complications related to type 2 diabetes, are needed to provide robust evidence based recommendations for other dietary factors in the management of type 2 diabetes

Introduction

Type 2 diabetes is a major global health problem. In 2021, the International Diabetes Federation estimated that a total of 536.6 million individuals worldwide lived with diabetes, and this number is expected to increase.[1] Type 2 diabetes carries a huge financial burden on health systems and people with diabetes.[2 3] Type 2 diabetes is typically associated with obesity, abnormalities of lipid metabolism, and an increased risk of numerous complications and comorbidities.[4 5] These include cardiovascular and liver disease, kidney disease, diabetes related eye disease, and lower limb amputations.[6 7] Also, people with type 2 diabetes have about a 2.5 times higher risk of all cause mortality than people without diabetes.[8 9]

Lifestyle factors, such as diet, form the basis of the management of type 2 diabetes,[1 4 10] and over the past decades, the effects of different diets on managing type 2 diabetes have been studied. Meta-analyses of randomised controlled trials showed that Mediterranean,[11] vegetarian,[12] and ketogenic diets[13] lowered levels of haemoglobin A_{1c} (HbA_{1c}), whereas a higher intake of dietary fibre[14] and soy isoflavones,[15] and magnesium supplementation[16] improved concentrations of blood lipids. These findings suggest that changes in diet might be important for preventing further complications and progression of disease in individuals with type 2 diabetes. To provide evidence based dietary recommendations, however, the existing evidence needs to be systematically summarised and evaluated based on state-of-the-art approaches.

So far, several umbrella reviews have been conducted summarising the evidence on selected dietary factors and specific outcomes in diabetes.[17–20] None of the previous umbrella reviews, however, included meta-analyses with randomised controlled trials lasting at least 12 weeks,[17–20] not all focused exclusively on people with type 2 diabetes,[18] and not all assessed the certainty of evidence with the Grading of Recommendations Assessment, Development, and Evaluations (GRADE) approach.[19] There is an urgent need to summarise all available evidence on this topic and, most importantly, to assess the certainty of evidence using the GRADE approach. Our aim in this umbrella review was to systematically summarise the most recent evidence on dietary interventions, including dietary patterns, food groups, and dietary supplements, on health outcomes in people with type 2 diabetes. The evidence was derived from systematic reviews with meta-analyses of randomised controlled trials that lasted at least 12 weeks. We also evaluated the certainty of evidence of these effects.

Methods

This umbrella review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines[21] and the preferred reporting items for overviews of reviews (PRIOR statement) for healthcare interventions.[22]

Literature search

A systematic literature search was conducted in PubMed, Embase, Cochrane, and Epistemonikos, with predefined search terms, from inception to 24 April 2021, with an update on 23 May 2022. None of the studies included in the in 2021 screening were exclusively from Embase, and therefore this database was omitted from the update in 2022. No filters were applied during the literature search process. Online supplemental table S1 shows the detailed search strategies. We also reviewed studies received from PubMed Alert at weekly intervals up to 5 June 2022 and screened the reference lists of all included publications. The literature search originally identified meta-analyses of prospective cohort studies and randomised controlled trials, but for this study, we focused on meta-analyses of randomised controlled trials. The literature screening was conducted by two authors independently. Disagreements were resolved by consensus with a third author.

Eligibility criteria

The systematic reviews with (network) meta-analyses of randomised controlled trials included in our study met the following criteria: the effects of dietary factors (dietary patterns, food groups, and dietary supplements) were investigated; the intervention in randomised controlled trials lasted ≥12 weeks for any health outcome (eg, mortality, incidence of cardiovascular disease, body weight, levels of HbA_{1c}, and heath related quality of life); only individuals with type 2 diabetes were included; effect estimates were reported (eg, for continuous outcomes, mean difference or standardised mean difference with corresponding 95% confidence intervals, or standard error; or for dichotomous outcomes, risk ratio, including hazard ratio or odd ratio, with 95% confidence intervals).

We excluded studies that were not systematic (including narrative reviews), not meta-analyses, not based exclusively on populations with type 2 diabetes, and single study findings. We also excluded publications reporting on alternative dietary treatments or medical nutrition (eg, Chinese medicine, plant extracts, herbs, and Ramadan fasting), and meta-analyses of randomised controlled trials with exclusively active control groups (comparing two intervention arms with each other). We did not exclude studies based on the publication language.

If we identified more than one meta-analysis on the same effect, we chose one meta-analysis for each intervention to avoid inclusion of duplicate results. In this case, we included the meta-analysis with the largest number of randomised controlled trials and participants. If more than one meta-analysis had the same number of randomised controlled trials, we selected the meta-analysis with the largest number of participants. Because we only included meta-analyses that were based on a systematic literature search, we assumed that newer and larger meta-analyses included the same randomised controlled trials as older and smaller meta-analyses looking at the same research question. We always prioritised evidence from direct comparisons over network meta-analyses.

Data extraction

Data were extracted by one author and double checked by a second author. Discrepancies were discussed between the authors, involving a third author if necessary. Data extracted from each publication were name of the first author, publication year, intervention type, comparison, outcome, duration of

Table 1 | Summary of results with high to moderate certainty of evidence from umbrella review of systematic reviews with meta-analyses of randomised controlled trials on diet in the management of type 2 diabetes

Outcomes	Type of dietary intervention	Effect estimates (mean difference, risk ratio, or risk difference (95% CI))	Certainty of evidence*
Changes within the clinically meaningful range			
Body weight (kg)	▶ Liquid meal replacement	−2.37 (−3.30 to −1.44)	High ⊕⊕⊕⊕
	▶ 10% decrease in carbohydrate intake	−1.34 (−1.77 to −0.91)	Moderate ⊕⊕⊕◯
Body mass index	▶ Liquid meal replacement	−0.87 (−1.32 to −0.43)	High ⊕⊕⊕⊕
	▶ Plant based diet	−1.13 (−1.88 to −0.38)	Moderate ⊕⊕⊕◯
Waist circumference (cm)	▶ Liquid meal replacement	−2.24 (−3.71 to −0.76)	Moderate ⊕⊕⊕◯
	▶ Plant based diet	−2.41 (−3.50 to −1.32)	Moderate ⊕⊕⊕◯
Haemoglobin A_{1c} (%)	▶ Low carbohydrate diet (<26% total energy)	−0.47 (−0.60 to −0.34)	High ⊕⊕⊕⊕
Fasting blood glucose (mmol/L)	▶ Liquid meal replacement	−0.63 (−0.99 to −0.27)	Moderate ⊕⊕⊕◯
	▶ Ginger	−1.18 (−1.47 to −0.88)	Moderate ⊕⊕⊕◯
	▶ Psyllium	−1.78 (−2.33 to −1.23)	Moderate ⊕⊕⊕◯
Fasting insulin (μIU/mL)	▶ Liquid meal replacement	−1.97 (−3.88 to −0.07)	Moderate ⊕⊕⊕◯
HOMA-IR	▶ Cocoa	−0.82 (−1.38 to −0.25)	Moderate ⊕⊕⊕◯
	▶ Probiotics	−0.90 (−1.34 to −0.46)	Moderate ⊕⊕⊕◯
	▶ Anthocyanin	−1.08 (−1.86 to −0.30)	Moderate ⊕⊕⊕◯
Triglycerides (mmol/L)	▶ Low carbohydrate diet (<26% total energy)	−0.30 (−0.43 to −0.17)	High ⊕⊕⊕⊕
	▶ Mediterranean diet	−0.41 (−0.72 to −0.10)	Moderate ⊕⊕⊕◯
Total cholesterol (mmol/L)	▶ High protein diet (>25% total energy)	−0.21 (−0.31 to −0.11)	Moderate ⊕⊕⊕◯
	▶ Soy protein	−0.19 (−0.33 to −0.05)	Moderate ⊕⊕⊕◯
	▶ Psyllium	−0.24 (−0.31 to −0.16)	Moderate ⊕⊕⊕◯
Low density lipoprotein cholesterol (mmol/L)	▶ High protein diet (>25% total energy)	−0.10 (−0.18, -0.02)	Moderate ⊕⊕⊕◯
	▶ Low glycaemic index diet	−0.23 (−0.37 to −0.09)	Moderate ⊕⊕⊕◯
	▶ Soy protein	−0.18 (−0.31 to −0.05)	Moderate ⊕⊕⊕◯
High density lipoprotein cholesterol (mmol/L)	▶ Low carbohydrate diet (<26% total energy)	0.06 (0.01 to 0.10)	Moderate ⊕⊕⊕◯
Systolic blood pressure (mm Hg)	▶ Liquid meal replacement	−4.97 (−7.32 to −2.62)	Moderate ⊕⊕⊕◯
Diastolic blood pressure (mm Hg)	▶ Liquid meal replacement	−1.98 (−3.05 to −0.91)	Moderate ⊕⊕⊕◯
Reduced use of drug treatments	▶ Low carbohydrate diet (<26% total energy)	Risk ratio 0.24 (0.12 to 0.35)	Moderate ⊕⊕⊕◯
Changes not within the clinically meaningful range			
Body weight (kg)	▶ Mediterranean diet	−0.25 (−0.99 to 0.49)	Moderate ⊕⊕⊕◯
Body mass index	▶ Almonds	−0.36 (−0.53 to −0.20)	Moderate ⊕⊕⊕◯
Haemoglobin A_{1c} (%)	▶ 10% decrease in carbohydrate intake	−0.11 (−0.17 to −0.04)	High ⊕⊕⊕⊕
	▶ Non-nutritive sweeteners	0.02 (−0.13 to 0.17)	Moderate ⊕⊕⊕◯
Fasting blood glucose (mmol/L)	▶ Almonds	−0.03 (−0.17 to 0.12)	Moderate ⊕⊕⊕◯
QUICKI	▶ Vitamin D	0.02 (0.01 to 0.03)	Moderate ⊕⊕⊕◯
Triglycerides (mmol/L)	▶ 10% decrease in carbohydrate intake	−0.12 (−0.22 to −0.01)	High ⊕⊕⊕⊕
	▶ Moderate carbohydrate diet (<40% total energy)	−0.13 (−0.24 to −0.02)	Moderate ⊕⊕⊕◯
Low density lipoprotein cholesterol (mmol/L)	▶ Liquid meal replacement	0.02 (−0.10 to 0.14)	Moderate ⊕⊕⊕◯
	▶ 10% decrease in carbohydrate intake	−0.03 (−0.08 to 0.02)	Moderate ⊕⊕⊕◯
	▶ Low glycaemic index or glycaemic load diet	−0.26 (−0.43 to −0.09)	Moderate ⊕⊕⊕◯
Non-high density lipoprotein cholesterol (mmol/L)	▶ Liquid meal replacement	−0.02 (−0.11 to 0.07)	Moderate ⊕⊕⊕◯
High density lipoprotein cholesterol (mmol/L)	▶ All types of carbohydrate restriction	−0.04 (−0.08 to −0.00)	Moderate ⊕⊕⊕◯
	▶ Low glycaemic index or glycaemic load diet	−0.02 (−0.07 to 0.03)	Moderate ⊕⊕⊕◯
	▶ Low fat diet (<30% total energy)	0.01 (−0.03 to 0.05)	Moderate ⊕⊕⊕◯
Systolic blood pressure (mm Hg)	▶ All types of carbohydrate restriction	0.03 (−1.77 to 1.84)	Moderate ⊕⊕⊕◯
	▶ Ginger	−0.11 (−1.10 to 0.88)	Moderate ⊕⊕⊕◯
Diastolic blood pressure (mm Hg)	▶ Moderate carbohydrate diet (<40% total energy)	−0.21 (−1.21 to 0.79)	Moderate ⊕⊕⊕◯
Blood urea nitrogen (mg/dL)	▶ Probiotics	−1.22 (−1.94 to −0.51)	Moderate ⊕⊕⊕◯
C reactive protein (standardised mean difference)	▶ Resveratrol	−0.87 (−1.11 to −0.63)	Moderate ⊕⊕⊕◯
Major cardiovascular events	▶ Omega 3 fatty acids	Risk difference 0.94 (0.87 to 1.02)	High ⊕⊕⊕⊕

CI=confidence interval; HOMA-IR=homeostatic model assessment-insulin resistance; QUICKI=quantitative insulin sensitivity check index.

*Assessed with the GRADEpro tool.

the study, number and study design of randomised controlled trials, and number of participants in the intervention groups. Online supplemental table S2 lists the definitions and cut-off values for categorising dietary patterns in terms of the amount of energy derived from macronutrients. We also extracted summary effect estimates (mean difference, standardised mean difference, or risk ratio) with corresponding 95% confidence intervals, the statistical model used (fixed effect or random effects model), a measure of inconsistency between randomised controlled trials (I^2), publication bias, risk of bias, and certainty of evidence (if assessed according to the GRADE approach). Online supplemental table S2 has further details on data extraction.

Assessment of methodological quality and certainty of evidence

The methodological quality of each included publication was assessed with the validated A MeaSurement Tool to Assess systematic Reviews (AMSTAR) 2 by two reviewers independently.[23] Online supplemental table S3 lists a detailed description of the tool, included domains, and grading system.

The certainty of evidence was evaluated with the GRADEpro tool.[24 25] GRADE rates the certainty of evidence as high, moderate, low, or very low. A high certainty of evidence means that it is very likely that the true effect lies on one side of a specified threshold or within a chosen range, a moderate certainty of evidence indicates moderate confidence that the true effect lies on one side of a specified threshold or within a chosen range and further studies might change the results, and low or very low certainty of evidence means that confidence in the meta-evidence available is limited.[26 27] Three reviewers, in pairs of two, independently rated the certainty of the evidence. Online supplemental table S4 lists a detailed description of the grading of the certainty of evidence.

Data analysis

For meta-analyses that used a random effects model and provided I^2 values and forest plots, we extracted the reported summary effect estimates with 95% confidence intervals. For meta-analyses that used a fixed effect model, or did not provide I^2 values or forest plots, we recalculated the mean difference, standardised mean difference, and summary risk ratio with corresponding 95% confidence intervals with the random effects model by DerSimonian and Laird.[28] Information on small study effects and publications bias was extracted from the included publications or, if not reported, was assessed by funnel plots and Egger's test (if ≥10 studies were included).[29 30] Online supplemental table S5 presents further details on the statistical methods. All analyses were conducted with Stata version 14.1.

Patient and public involvement

No patients or public were involved in setting the research question, the design of the study, the interpretation of the results, or the writing of the manuscript. The results of this study will be spread to the public via social media or press release.

Results

Literature search

Of 25 221 publications, 764 eligible articles were retrieved for screening of the full text of the article (online supplemental figure S1). Online supplemental table S6 lists the excluded studies and the reasons for exclusion. We identified 88 eligible publications of systematic reviews with meta-analyses of randomised controlled trials for inclusion in our umbrella review.

Description of published meta-analyses

Online supplemental table S7 presents the characteristics and results of all of the included systematic reviews with meta-analyses of randomised controlled trials. Eighty eight publications, with 310 meta-analyses of randomised controlled trials, investigated the effectiveness of dietary patterns (liquid meal replacement, energy, carbohydrate, and fat restriction, low glycaemic index and glycaemic load, high protein, Mediterranean, plant based, vegetarian, and ketogenic diets, and intermittent fasting), foods (mixed nuts, tree nuts, walnuts, almonds, blueberries and cranberries, olive oil, cocoa products, cinnamon, curcumin, ginger, soy and soy isoflavones, and non-nutritive sweeteners), nutrients (monounsaturated fatty acids, omega 3 fatty acids, α-lipolenic acid, L-carnitine, and salt), micronutrients (magnesium, chromium, and zinc), vitamins (niacin, and vitamins E, C, and D), phytochemicals (anthocyanins, flavonoids, polyphenols, and resveratrol), fibre (psyllium, soluble fibre, and guar gum), and probiotics (online supplemental table S7).

Outcomes included anthropometric, glycaemic, and lipid markers, blood pressure, kidney, liver, and inflammation parameters, as well as quality of life, reduced use of drug treatments, constipation, and major cardiovascular events. The number of participants in meta-analyses of randomised controlled trials ranged from 44 to 28 199, and intervention time from 12 weeks to 96 months. In total, 293 of the included meta-analyses were pairwise meta-analyses and 17 were network meta-analyses,[12 31] and 15% of the meta-analyses included ≥10 randomised controlled trials. Publication bias was detected for 2.2% of the results of meta-analyses of randomised controlled trials, but 59.4% of meta-analyses included ≤5 studies (online supplemental table S7).

Methodological quality was rated as high for 18% (n=16), moderate for 5% (n=4), low for 22% (n=19), and critically low for the remaining 55% (n=49) of publications (online supplemental table S8). The

Reference	Intervention	Outcome	No of trials	No of participants	Mean difference (95% CI)	Mean difference (95% CI)	I² (%)	Certainty of evidence
Noronha 2019	Liquid meal replacement	Body weight (kg)	9	931		-2.37 (-3.30 to -1.44)	84	High
Ajala 2013	Mediterranean diet	Body weight (kg)	3	2077		-0.25 (-0.99 to 0.49)	83	Moderate
Jayedi 2022	10% decrease in carbohydrates	Body weight (kg)	17	1838		-1.34 (-1.77 to -0.91)	0	Moderate
Noronha 2019	Liquid meal replacement	Body mass index	8	817		-0.87 (-1.32 to -0.43)	89	High
Austin 2021	Plant based diet	Body mass index	3	173		-1.13 (-1.88 to -0.38)	80	Moderate
Ojo 2021	Almonds	Body mass index	6	210		-0.36 (-0.53 to -0.20)	0	Moderate
Noronha 2019	Liquid meal replacement	Waist circumference (cm)	5	448		-2.24 (-3.71 to -0.76)	74	Moderate
Austin 2021	Plant based diet	Waist circumference (cm)	2	191		-2.41 (-3.50 to -1.32)	0	Moderate

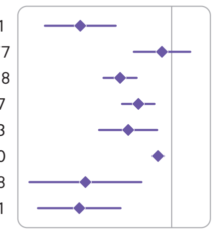

Figure 1 | Effect of different dietary factors on anthropometric measures (body weight, body mass index, and waist circumference) in people with type 2 diabetes.[32–36] Results from meta-analyses of randomised controlled trials with high to moderate certainty of evidence. CI=confidence interval

most common reasons for downgrading the methodological quality were missing study protocol, inappropriate methods for the search strategy (literature search only by one investigator, search strategy not shown, or included reports restricted to the English language), and lack of evaluation or discussion, or both, of the effect of risk of bias on the results.

Evidence for the effect of diet on managing type 2 diabetes: meta-analyses of randomised controlled trials

The certainty of evidence was rated as high for seven (2%), moderate for 40 (13%), low for 120 (39%), and very low for 143 (46%) outcomes (online supplemental tables S9–S32). Table 1 summarises the results of the meta-analyses with high to moderate certainty of evidence and with clinically meaningful changes. Figures 1–6 show the summary effect estimates of the included meta-analyses of randomised controlled trials with high and moderate certainty of evidence. Online supplemental figures S2–S10 show the results of meta-analyses of randomised controlled trials with low and very low certainty of evidence.

Anthropometric measures

The certainty of evidence was high for the efficacy of liquid meal replacement on clinically relevant reductions in body weight and body mass index (figure 1). Liquid meal replacement reduced body weight by 2.37 kg (95% confidence interval −3.30 to −1.44; I^2=84%; n=9 randomised controlled trials) and body mass index by 0.87 (−1.32 to −0.43; I^2=89%; n=8 randomised controlled trials) compared with a control diet.[32] Plant based diets also effectively reduced body mass index by 1.13 (−1.88 to −0.38; I^2=80%; n=3 randomised controlled trials) with moderate certainty of evidence.[33]

Moderate certainty of evidence was found for a reduction in waist circumference after liquid meal replacement (−2.24 cm, 95% confidence interval −3.71 to −0.76; I^2=74%; n=5 randomised controlled trials) and plant based diets (−2.41 cm, −3.50 to −1.32; I^2=0%; n=2 randomised controlled trials).[32,33] Improvement in anthropometric measures was also seen for a decrease in carbohydrate intake of 10%,[34] adherence to a Mediterranean diet,[35] and increased intake of almonds,[36] but effect estimates were small and not clinically relevant (figure 1). The certainty

Reference	Intervention	Outcome	No of trials	No of participants	Mean difference (95% CI)	Mean difference (95% CI)	I² (%)	Certainty of evidence
Goldenberg 2021	Low carbohydrates (<26% total energy)	HbA_{1c} (%)	17	747		-0.47 (-0.60 to -0.34)	NR	High
Jayedi 2022	10% decrease in carbohydrates	HbA_{1c} (%)	13	1222		-0.11 (-0.17 to -0.04)	37	High
Lohner 2020	Non-nutritive sweeteners	HbA_{1c} (%)	2	252		0.02 (-0.13 to 0.17)	0	Moderate
Noronha 2019	Liquid meal replacement	Fasting blood glucose (mmol/L)	9	891		-0.63 (-0.99 to -0.27)	70	Moderate
Ojo 2021	Almonds	Fasting blood glucose (mmol/L)	6	224		-0.03 (-0.17 to 0.12)	0	Moderate
Ebrahimzadeh 2022	Ginger	Fasting blood glucose (mmol/L)	4	252		-1.18 (-1.47 to -0.88)	0	Moderate
Xiao 2020	Psyllium	Fasting blood glucose (mmol/L)	3	193		-1.78 (-2.33 to -1.23)	64	Moderate
Noronha 2019	Liquid meal replacement	Insulin (µIU/mL)	6	586		-1.97 (-3.88 to -0.07)	22	Moderate
Chen 2022	Cocoa	HOMA-IR (units)	2	128		-0.82 (-1.38 to -0.25)	0	Moderate
Fallah 2020	Anthocyanins	HOMA-IR (units)	2	218		-1.08 (-1.86 to -0.30)	0	Moderate
Zhang 2022	Probiotics	HOMA-IR (units)	7	503		-0.90 (-1.34 to -0.46)	14	Moderate
Zou 2021	Vitamin D	QUICKI (units)	3	178		0.02 (0.01 to 0.03)	66	Moderate

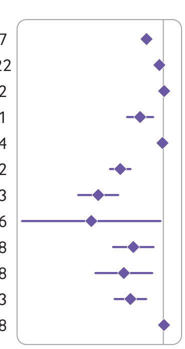

Figure 2 | Effect of different dietary factors on glycaemic measures in people with type 2 diabetes.[14,32,34,36–41,61,62] Results from meta-analyses of randomised controlled trials with high to moderate certainty of evidence. CI=confidence interval; HbA_{1c}=haemoglobin A_{1c}; HOMA-IR=homeostatic model assessment-insulin resistance; NR=not reported; QUICKI=quantitative insulin sensitivity check index

Reference	Intervention	Outcome	No of trials	No of participants	Mean difference (95% CI)	I² (%)	Certainty of evidence
Goldenberg 2021	Low carbohydrates (<26% total energy)	Triglycerides (mmol/L)	19	860	-0.30 (-0.43 to -0.17)	NR	High
Jayedi 2022	10% decrease in carbohydrates	Triglycerides (mmol/L)	13	1423	-0.12 (-0.22 to -0.01)	69	High
Neuenschwander 2019	Mediterranean diet	Triglycerides (mmol/L)	NMA	271	-0.41 (-0.72 to -0.10)	NA	Moderate
Korsmo-Haugen 2019	Moderate carbohydrates (<40% total energy)	Triglycerides (mmol/L)	16	1391	-0.13 (-0.24 to -0.02)	57	Moderate
Yu 2020	High protein	Total cholesterol (mmol/L)	10	968	-0.21 (-0.31 to -0.11)	73	Moderate
Baranska 2021	Soy protein or isoflavone	Total cholesterol (mmol/L)	4	597	-0.19 (-0.33 to -0.05)	0	Moderate
Xiao 2020	Psyllium	Total cholesterol (mmol/L)	2	174	-0.24 (-0.31 to -0.16)	0	Moderate
Noronha 2019	Liquid meal replacement	Low density lipoprotein cholesterol (mmol/L)	9	891	0.02 (-0.10 to 0.14)	68	Moderate
Jayedi 2022	10% decrease in carbohydrates	Low density lipoprotein cholesterol (mmol/L)	13	1901	-0.03 (-0.08 to 0.02)	9	Moderate
Ojo 2019	Low glycaemic index	Low density lipoprotein cholesterol (mmol/L)	5	422	-0.23 (-0.37 to -0.09)	8	Moderate
Neuenschwander 2019	Low glycaemic index or glycaemic load	Low density lipoprotein cholesterol (mmol/L)	NMA	446	-0.26 (-0.43 to -0.09)	NA	Moderate
Yu 2020	High protein	Low density lipoprotein cholesterol (mmol/L)	12	1036	-0.10 (-0.18 to -0.02)	78	Moderate
Baranska 2021	Soy protein or isoflavone	Low density lipoprotein cholesterol (mmol/L)	4	556	-0.18 (-0.31 to -0.05)	0	Moderate
Noronha 2019	Liquid meal replacement	Non-high density lipoprotein cholesterol (mmol/L)	9	891	-0.02 (-0.11 to 0.07)	29	Moderate
Silverii 2020	All types of carbohydrate restriction	High density lipoprotein cholesterol (mmol/L)	17	913	-0.04 (-0.08 to -0.00)	24	Moderate
Goldenberg 2021	Low carbohydrates (<26% total energy)	High density lipoprotein cholesterol (mmol/L)	16	647	0.06 (0.01 to 0.10)	NR	Moderate
Neuenschwander 2019	Low glycaemic index or glycaemic load	High density lipoprotein cholesterol (mmol/L)	NMA	430	-0.02 (-0.07 to 0.03)	NA	Moderate
Neuenschwander 2019	Low fat (<30% total energy)	High density lipoprotein cholesterol (mmol/L)	NMA	2264	0.01 (-0.03 to 0.05)	NA	Moderate

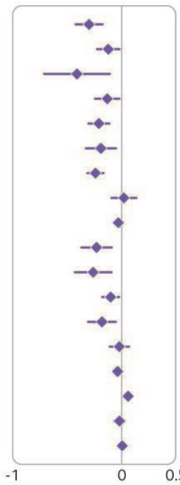

Figure 3 | Effect of different dietary factors on blood lipid measures in people with type 2 diabetes.[14 15 31 32 34 37 42–44 63] Results from meta-analyses of randomised controlled trials with high to moderate certainty of evidence. CI=confidence interval; NA=not available; NR=not reported; NMA=network meta-analysis

of evidence for the effect of other dietary factors was low to very low (online supplemental figure S2).

Glycaemic markers

A low carbohydrate diet (<26% total energy) produced a clinically relevant reduction in levels of HbA_{1c} of 0.47% (95% confidence interval −0.60% to −0.34%; I^2 not reported; n=17 randomised controlled trials) with a high certainty of evidence (figure 2).[37] HbA_{1c} levels were also reduced after a decrease in carbohydrate intake of 10%,[34] but the effect estimate was small and not clinically relevant.

A moderate certainty of evidence was found for reduced concentrations of fasting blood glucose after liquid meal replacement (−0.63 mmol/L, 95% confidence interval −0.99 to −0.27; I^2=70%; n=9 randomised controlled trials), and supplementation with ginger (−1.18 mmol/L, −1.47 to −0.88; I^2=0%; n=4 randomised controlled trials) and psyllium (−1.78 mmol/L, −2.33 to −1.23; I^2=64%; n=3 randomised controlled trials).[14 32 38] Liquid meal replacement reduced insulin concentrations by 1.97 μIU/mL (−3.88 to −0.07; I^2=22%; n=6 randomised controlled trials), with moderate certainty of evidence.[32] Supplementation with cocoa, probiotics, and anthocyanins decreased the homeostatic model assesment-insulin resistance (HOMA-IR) index with moderate certainty of evidence by −0.82 units (−1.38 to −0.25; I^2=0%; n=2 randomised controlled trials), −0.90 units (−1.34 to −0.46; I^2=14%; n=7 randomised controlled trials), and −1.08 units (−1.86 to −0.30; I^2=0%; n=2 randomised controlled trials), respectively.[39–41] The certainty of evidence for the effect of other dietary factors was low to very low (online supplemental figure S3).

Blood lipids

The certainty of evidence was high for a decrease in carbohydrate intake of 10% and low carbohydrate diet (<26% total energy) to lower concentrations of triglycerides by 0.12 mmol/L (95% confidence interval −0.22 to −0.01; I^2=69%; n=13 randomised controlled trials) and 0.30 mmol/L (−0.43 to −0.17; I^2 not reported; n=19 randomised controlled trials), respectively (figure 3).[34 37] Moderate carbohydrate restriction (<45% total energy) and a Mediterranean diet reduced concentrations of triglycerides by −0.13 mmol/L (−0.24 to −0.02; I^2=57%; n=16 randomised controlled trials) and −0.41 mmol/L (−0.72 to −0.10; I^2 not available;

Reference	Intervention	Outcome	No of trials	No of participants	Mean difference (95% CI)	I² (%)	Certainty of evidence
Noronha 2019	Liquid meal replacement	Systolic blood pressure (mm Hg)	7	754	-4.97 (-7.32 to -2.62)	53	Moderate
Silverii 2020	All types of carbohydrate restriction	Systolic blood pressure (mm Hg)	14	905	0.03 (-1.77 to 1.84)	8	Moderate
Ebrahimzadeh 2022	Ginger	Systolic blood pressure (mm Hg)	2	166	-0.11 (-1.10 to 0.88)	0	Moderate
Noronha 2019	Liquid meal replacement	Diastolic blood pressure (mm Hg)	7	754	-1.98 (-3.05 to -0.91)	15	Moderate
Korsmo-Haugen 2019	Moderate carbohydrates (<40% total energy)	Diastolic blood pressure (mm Hg)	12	944	-0.21 (-1.21 to 0.79)	0	Moderate

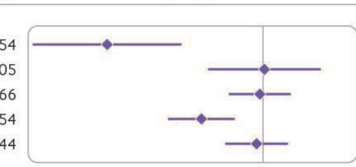

Figure 4 | Effect of different dietary factors on blood pressure in people with type 2 diabetes.[32 38 42 63] Results from meta-analyses of randomised controlled trials with high to moderate certainty of evidence. CI=confidence interval

Reference	Intervention	Outcome	No of trials	No of participants	Summary risk ratio (95% CI)	I² (%)	Certainty of evidence
Goldenberg 2021	Low carbohydrates (<26% total energy)	Reduced use of drug treatments (risk difference)	7	240	0.24 (0.12 to 0.35)	NR	Moderate
Shen 2022	Omega 3 fatty acids	Major cardiovascular events (relative risk)	3	28 199	0.94 (0.87 to 1.02)	20	High

Figure 5 | Effect of different dietary factors on risk reduction in people with type 2 diabetes.[37 45] Results from meta-analyses of randomised controlled trials with high to moderate certainty of evidence. CI=confidence interval; NR=not reported

network meta-analysis), respectively, with moderate certainty of evidence.[31 42] A moderate certainty of evidence was found for reduction in total cholesterol concentrations after a high protein diet (mean difference −0.21 mmol/L, −0.31 to −0.11; I^2=73%; n=10 randomised controlled trials), supplementation with psyllium (mean difference −0.24 mmol/L, −0.31 to −0.16; I^2=0%; n=2 randomised controlled trials), and soy protein (mean difference −0.19 mmol/L, −0.33 to −0.05; I^2=0%; n=4 randomised controlled trials).[14 15 43]

The certainty of evidence was moderate for the low density lipoprotein cholesterol lowering effect of a low glycaemic index diet (mean difference −0.23 mmol/L, 95% confidence interval −0.37 to −0.09; I^2=8%; n=5 randomised controlled trials), a high protein diet (mean difference −0.10 mmol/L, −0.18 to −0.02; I^2=78%; n=12 randomised controlled trials), and a higher intake of soy protein (mean difference −0.18 mmol/L, −0.31 to −0.05; I^2=0%; n=4 randomised controlled trials).[15 43 44] A low carbohydrate diet (<26% total energy) might increase concentrations of high density lipoprotein cholesterol with moderate certainty of evidence (mean difference 0.06 mmol/L, 0.01 to 0.10; I^2 not reported; n=16 randomised controlled trials).[37] Evidence for the effect of other dietary factors was low to very low (online supplemental figure S4).

Blood pressure

Liquid meal replacement diets reduced both systolic and diastolic blood pressure by 4.97 mm Hg (95% confidence interval −7.32 to −2.62; I^2=53%; n=7 randomised controlled trials) and 1.98 mm Hg (−3.05 to −0.91; I^2=15%; n=7 randomised controlled trials), respectively, with moderate certainty of evidence (figure 4).[32] Evidence for the effect of other dietary factors was low to very low (online supplemental figure S5).

Other outcomes

A high certainty of evidence was found for supplementation with omega 3 fatty acids and risk of major cardiovascular events, but the 95% confidence interval was imprecisely estimated and the risk reduction was marginal (figure 5; summary risk ratio 0.94, 0.87 to 1.02; I^2=20%; n=3 randomised controlled trials).[45] A low carbohydrate diet (<26% total energy) reduced the use of drug treatments by an additional 24 per 100 individuals (risk difference 0.24, 0.12 to 0.35; I^2 not reported; n=7 randomised controlled trials, moderate certainty of evidence).[37] Probiotic supplements reduced concentrations of blood urea nitrogen, a marker of kidney function (mean difference −1.22 mg/dL, −1.94 to −0.51; I^2=0%; n=4 randomised controlled trials). Supplementation with resveratrol reduced concentrations of C reactive protein (standardised mean difference −0.87, −1.11 to −0.63; I^2=0%; n=3 randomised controlled trials), with moderate certainty of evidence (figure 6).[46 47] Evidence for the effect of other dietary factors was low to very low (online supplemental figures S2–S10).

Discussion

Main findings

In this umbrella review, we included 88 publications, with 310 meta-analyses of randomised controlled trials for different dietary factors and health outcomes, mainly surrogate markers of disease and health, in populations with type 2 diabetes. We found a high certainty of evidence and clinically important changes for liquid meal replacement diets in reducing body weight and body mass index, as well as for a low carbohydrate diet (<26% total energy) in lowering levels of HbA_{1c} and triglycerides. A moderate certainty of evidence with clinically important changes was found for plant based diets and reduced anthropometric measures; liquid meal replacement diets, and supplementation with

Reference	Intervention	Outcome	No of trials	No of participants	Mean difference (95% CI)	I² (%)	Certainty of evidence
Abdollahi 2021	Probiotics	Blood urea nitrogen (mg/dL)	4	316	-1.22 (-1.94 to -0.51)	0	Moderate
Hosseini 2020	Resveratrol	C reactive protein (SMD)	3	298	-0.87 (-1.11 to -0.63)	0	Moderate

Figure 6 | Effect of different dietary factors on other outcomes in people with type 2 diabetes.[46 47] Results from meta-analyses of randomised controlled trials with high to moderate certainty of evidence. CI=confidence interval; SMD=standardised mean difference fibre, ginger, anthocyanins, or probiotics improved glycaemic measures; and a high protein diet, soya, or fibre improved blood lipids. For other results, no clinically relevant differences were found or the certainty of evidence was low or very low.

Comparison with existing dietary guidelines

Dietary interventions based on energy restriction for weight loss are the focus of current guidelines for the management of type 2 diabetes.[48–53] Clinically important weight loss of 5-10% can improve insulin sensitivity, glycaemic control, blood pressure, and dyslipidaemia.[48 49 53] Also, the guidelines suggest that low calorie meal replacement plans are relatively easy to adhere to and allow for clinically significant weight loss in people with type 2 diabetes.[48 50 53] We found a reduction in body weight of 2.4 kg after at least 12 weeks of liquid meal replacement diet.

Current guidelines for type 2 diabetes recommend vegetarian or plant based diets and Mediterranean diets for reducing body weight.[48 49 52] Our umbrella review confirmed the beneficial effect of plant based diets on reducing body mass index and waist circumference. Also, some of the current guidelines conclude that short term low carbohydrate interventions have a beneficial effect on anthropometric measures, but no clear recommendations exist for the amount of carbohydrates that should be restricted.[48 49] Our study showed that a decrease in body weight was greater in interventions with low (<26% total energy) or very low (<15% total energy) carbohydrate intake than in interventions with moderate (<45% total energy) carbohydrate intake for at least 12 weeks.

We found a low certainty of evidence for the effects of a Mediterranean or plant based diet on glycaemic measures. Our findings of the beneficial effect of low carbohydrate diets on levels of HbA_{1c}, however, are in line with current guidelines.[49 50] Increased intake of dietary fibre is emphasised in all guidelines, and our results are consistent with the positive effect of fibre rich foods, especially psyllium supplements, on fasting blood glucose levels.[49 53] Adding to the current guidelines, we identified a moderate certainty of evidence for the beneficial effects of ginger supplements, as a plant, capsule, or powder, on fasting blood glucose levels, and the potential importance of polyphenols or polyphenol rich products (eg, cocoa) on HOMA-IR.

Our umbrella review supports evidence of the beneficial effects of a Mediterranean diet on triglyceride levels, but we found only a low certainty of evidence for its effect in reducing levels of high and low density lipoprotein cholesterol. In agreement with current guidelines, we also found beneficial effects of low carbohydrate and low glycaemic index diets on levels of triglycerides and low and high density lipoprotein cholesterol, and of higher fibre intake on levels of total cholesterol.[48–50 53] Current Canadian, German, and European guidelines recommend no change in protein intake, which for most people with normal kidney function is 15-20% and 10-25% of total energy.[48 50 53] Thus our findings of a beneficial effect of a high protein diet (>25% total energy) on levels of total cholesterol and low density lipoprotein cholesterol provide novel evidence in this context. A previous meta-analysis, however, showed that the health benefits are from an increased intake of plant based rather than animal based protein sources.[54] Furthermore, our study provides evidence of the beneficial effects of soy proteins on levels of total cholesterol and low density lipoprotein cholesterol. Pulses are considered a good alternative to meat and a good source of fibre and are therefore recommended for controlling levels of blood lipids.[48 50]

In common with current guidelines, we found insufficient evidence to recommend reducing total fat intake to improve cardiometabolic measures in people with type 2 diabetes.[48 50] American and European guidelines recommend a higher intake of monounsaturated and polyunsaturated fatty acids to improve glucose metabolism, but the evidence supporting this recommendation, according to our results, is weak.[49 53] We found that studies of supplementation with monounsaturated or polyunsaturated fatty acids showed improvements in levels of HbA_{1c} and insulin, and in HOMA-IR, but the estimates were imprecisely estimated and the number of participants included was small (≤800). Also, a subgroup analysis comparing different doses of omega 3 fatty acid supplements was performed in one meta-analysis,[45] and a stronger risk reduction of major cardiovascular events was seen in the group receiving >3 g/day of omega 3 fatty acids, whereas no precisely estimated effect was found in the group receiving lower doses. This finding might explain the observed effect of omega 3 fatty acids on the incidence of major cardiovascular events in people with type 2 diabetes in our umbrella review. Moreover, a recent systematic review and meta-analysis of randomised controlled trials with an intervention duration of at least 3.9 years showed that supplementation with omega 3 fatty acids reduced cardiovascular events in people with type 1 and type 2 diabetes (risk ratio 0.93, 95% confidence interval 0.90 to 0.97; n=8 randomised controlled trials). The effect was marginal but precisely estimated.[55]

Strengths and limitations

Our study has several strengths. Our umbrella review included meta-analyses of all possible dietary interventions and their effect on many health outcomes in populations with type 2 diabetes. We summarised the evidence from randomised controlled trials that lasted at least 12 weeks, giving a more reliable assessment of the effectiveness of the interventions. We recalculated the results of meta-analyses that used a fixed effect model, or did not provide I^2 values or forest plots, to ensure valid meta-estimates with 95% confidence intervals to provide an evaluation of the certainty of evidence based on the GRADEpro approach. Finally, we detected gaps in the evidence that indicate the need for future research.

The main limitation of our umbrella review was that recently published randomised controlled trials not yet included in systematic reviews and meta-analyses were not considered in our report.[56–58] Also, we did not explore subgroup analyses (eg, by sex, race, or duration of diabetes) or sensitivity analyses (eg, excluding studies with a high risk of bias). We used the DerSimonian and Laird approach[28] for recalculation of extracted estimates with the random effects meta-analyses, but the Hartung and Knapp method might perform better in terms of more adequate error rates, especially when the number of studies was small.[59]

In terms of the limitations of the publications included in our umbrella review, studies of interventions lasting at least 12 weeks provide more reliable estimates than shorter trials, but these studies do not represent long term interventions. Also, the number of randomised controlled trials in most meta-analyses was small (13 meta-analyses with ≥10 randomised controlled trials). Consequently, the number of participants was also low (n<800 for 83% of meta-analyses of randomised controlled trials). This limitation was one of the main reasons for downgrading the certainty of evidence because of imprecision. Other reasons for downgrading the certainty of evidence were the high risk of bias in the randomised controlled trials and inconsistency of the results. Furthermore, the methodological quality of most included publications was low to very low.

In meta-analyses of randomised controlled trials, a high risk of bias caused by lack of blinding of participants to the dietary intervention is a concern. For dietary interventions based on health promoting changes in diet (eg, advice on a Mediterranean diet, where participants are actively instructed and encouraged to change their diet), however, blinding to the intervention might not be feasible. Furthermore, low compliance with the assigned dietary regimens and high dropout rates were commonly seen in randomised controlled trials, especially for low carbohydrate and ketogenic diets,[60] potentially resulting in underestimation of their actual effect. For example, one meta-analysis found greater clinically significant weight loss in those with greater adherence than in those with lower adherence to a very low carbohydrate diet,[37] and another meta-analysis reported inadequate compliance with the ketogenic diet, as assessed by urinary measurements of ketones.[13] Systematic reviews of other dietary interventions lacked a description of compliance with the intervention. Also, study arms did not always receive isocaloric diets, making it difficult to differentiate between the effects of change in dietary patterns, foods, or nutrients on the reduction in energy intake. Some of the meta-analyses conducted subgroup analyses, however, and did not find differences when calories were restricted or matched with controls in the trials.[33 34 37]

Study implications

Robust evidence exists that in people with type 2 diabetes, liquid meal replacements decrease energy intake and thus body weight. For people who prefer a dietary approach, plant based or carbohydrate restricted diets are also effective in reducing anthropometric measure. Other dietary regimens, such as a ketogenic diet or intermittent fasting, reduced body weight, but the certainty of evidence was low or very low.

Many dietary interventions effectively improved glycaemic measures, but the certainty of the evidence was robust only for liquid meal replacement diets and restricting carbohydrates. Intake of fibre rich foods, polyphenols, probiotics, and ginger was also beneficial for glycaemic control. For control of blood lipids, a low carbohydrate (<26% total energy), Mediterranean, or high protein diet is recommended for people with type 2 diabetes, with the advice to change the protein source to plant based alternatives. Energy restriction was the only effective approach in reducing blood pressure with robust evidence. Restriction of salt intake also showed beneficial effects, but the certainty of evidence was very low and thus recommendations cannot be made from the current body of evidence.

For clinical outcomes, robust evidence exists only for a low carbohydrate diet and reduction in the use of drug treatments. For other outcomes, including kidney function parameters, inflammatory markers, liver enzymes, and patient relevant outcomes (eg, remission of diabetes, health related quality of life, and incidence of cardiovascular disease), meta-analyses are already available, but the certainty of evidence was rated as low or very low, and definitive conclusions on these findings cannot be drawn. In summary, people with type 2 diabetes can be advised to reduce their energy intake if they have obesity or overweight, decrease their carbohydrate intake, or increase their consumption of foods from plant sources (especially plant based proteins) or from Mediterranean-style diets (foods high in polyunsaturated fatty acids, such as fish and nuts, or foods high in polyphenols, such as fruit, vegetables, and legumes).

To strengthen the certainty of evidence for many of the findings on diet and the management of type 2 diabetes and its complications, future studies with a low risk of bias are needed. More randomised controlled trials should investigate the effects of long term (at least six months) dietary interventions, as well as considering isocaloric comparisons between intervention and control arms. Also, more research on dietary patterns (eg, DASH (dietary approaches to stop hypertension), Nordic, and portfolio diets), fasting approaches, single foods (eg, dairy products, fish, or meat), and single nutrients (eg, specific fatty acids) is needed. Finally, future systematic reviews and meta-analyses should follow current guidelines for conducting and reporting on included studies (eg, reports should be transparent about the methods used and critically examine the effect of risk of bias on meta-findings).

Conclusions

In this umbrella review, we identified the dietary factors with robust evidence of health benefits, expressed as surrogate disease and health markers in people with type 2 diabetes. An energy restricted diet can reduce body weight and improve cardiometabolic health. In addition to energy restriction, dietary approaches, such as a plant based, Mediterranean, low carbohydrate (<26% total energy), or high protein diet, are beneficial for cardiometabolic health in individuals with type 2 diabetes. For evidence based recommendations of the effectiveness of other dietary factors in the management of type 2 diabetes, more randomised controlled trials and systematic reviews with meta-analyses focusing on long term interventions are needed.

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Acknowledgements We thank Andrew Reynolds, Department of Medicine, University of Otago, Dunedin, New Zealand; Grace Austin, Hunter Medical Research Institute, University of Newcastle, New Lambton, Australia; Likun Ma, Department of Cardiology, the First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China; Eunyoung Kim, Evidence-Based and Clinical Research Laboratory, Department of Health, Social, and Clinical Pharmacy, College of Pharmacy, Chung-Ang University, Seoul, Republic of Korea; Kaijian Hou, Endocrine Department, Longhu Hospital, First Affiliated Hospital of Shantou University Shantou City, China; Shaun Mason, School of Exercise and Nutrition Sciences, Deakin University, Melbourne, Victoria, Australia; Jean-Philippe Drouin-Chartier, Department of Nutrition, Harvard T H Chan School of Public Health, Boston, MA, USA; and Sakineh Shab-Bidar, Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran, for sending additional data needed for the meta-analysis.

Contributors SS designed the research. ES and TS conducted the literature search and literature screening. ES and TS extracted the data. ES, AS-P, and TS assessed the methodological quality of the included publications. ES, SS, and LS evaluated the certainty of evidence. ES, JB, and SS analysed the data and wrote the first draft of the paper. All authors interpreted the data, read the manuscript, and approved the final version. ES and SS are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria were omitted. Transparency: The lead authors (the manuscript's guarantors) 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 have been explained.

Funding The German Diabetes Centre is funded by the German Federal Ministry of Health and the Ministry of Innovation, Science, Research, and Technology of the State North Rhine Westphalia. This study was also supported in part by a grant from the German Federal Ministry of Education and Research to the German Centre for Diabetes Research. The funders had no role in considering the study design or in the collection, analysis, interpretation of data, writing of the report, or decision to submit the article for publication.

Competing interests All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/ and declare: support from the German Federal Ministry of Health and the Ministry of Innovation, Science, Research, and Technology of the State North Rhine Westphalia, and the German Federal Ministry of Education and Research for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval Not required because only (secondary) data from published studies were used.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. All data are available upon reasonable request. All data for this study were extracted from published meta-analyses, all of which are available and accessible.

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► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjmed-2023-000664).