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Ph.D. értekezések

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The role of dietary fibers and diet composition in the management of metabolic disorders

Ph.D. Thesis

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" Let food be thy medicine and medicine be thy food."

Hippocrates

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1. LIST OF ABBREVIATIONS

2h pp.G - 2-h postprandial glucose level

CrI - Credible intervals

DASH - Dietary approaches to stop hypertension

FBG - Fasting blood glucose

FI - Fasting insulin

FSH - Follicle stimulating hormone

GRADE - The Grading of Recommendations Assessment, Development, and Evaluation

GLP-1 - Glucagon-Like Peptide-1

HbA1c - Hemoglobin A1c

HOMA-IR - Homeostatic Model Assessment of Insulin Resistance

HDL cholesterol - High-Density Lipoprotein Cholesterol

LDL cholesterol - Low-Density Lipoprotein Cholesterol

LH - Luteinizing hormone

MCMC - Markov Chain Monte Carlo

MD – Mean difference

MNT - Medical nutrition therapy

NMA - Network meta-analysis

PCOS - Polycystic ovarian syndrome

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-analyses

RCT - Randomized controlled trial

RoB 2 - Risk-of-bias tool for randomized trials

SCFA - Short-chain fatty acid

SUCRA - The surface under the cumulative ranking curve

T2DM – Type 2 diabetes mellitus

TC - Total cholesterol

TG – Triglyceride

TT - Total testosterone

2. STUDENT PROFILE

2.1. Vision and mission statement, specific goals

My vision is to improve the metabolic health and long-term quality of life of patients affected by metabolic disorders by promoting effective, evidence-based nutritional strategies.

My mission is to raise physicians' awareness of the scientific evidence supporting the role of dietary fiber and overall diet composition in improving metabolic outcomes.

My specific goal is to investigate the role of dietary fibers and diet composition in the management of type 2 diabetes and polycystic ovary syndrome, with the aim of supporting the clinical application of nutritional therapies.

2.2. Scientometrics

Number of all publications:	8
Cumulative IF:	14,1
Av IF/publication:	4,7
Ranking (SCImago):	D1: 3
Number of publications related to the subject of the thesis:	2
Cumulative IF:	9,9
Av IF/publication:	4,95
Ranking (SCImago):	D1: 2
Number of citations on Google Scholar:	168
Number of citations on MTMT:	117
H-index:	3

The detailed bibliography of the student can be found on page 70.

2.3. Future plans

My future plans include strengthening the scientific evidence supporting lifestyle interventions, particularly dietary therapy for patients with impaired carbohydrate metabolism, including those with type 2 diabetes and polycystic ovary syndrome. I aim to contribute to a shift in clinical practice where lifestyle modification becomes the first-line therapy, recognized and recommended by physicians as a standard of care. Furthermore, I intend to promote greater collaboration between medical professionals and dietitians to ensure that patients receive comprehensive, evidence-based nutritional support. In parallel, I aspire to demonstrate to my dietetics students that their future profession not only has a solid place in healthcare, but also holds its ground in the world of science, and can be practiced at the highest academic and clinical standards.

3. SUMMARY OF THE PH.D.

Dietary fibers are a highly researched area in nutritional science, particularly regarding its impact on the gut microbiome. In addition to this, increasing evidence supports its beneficial effects on blood glucose and lipid levels, making it a promising adjunct in the management of metabolic disorders.

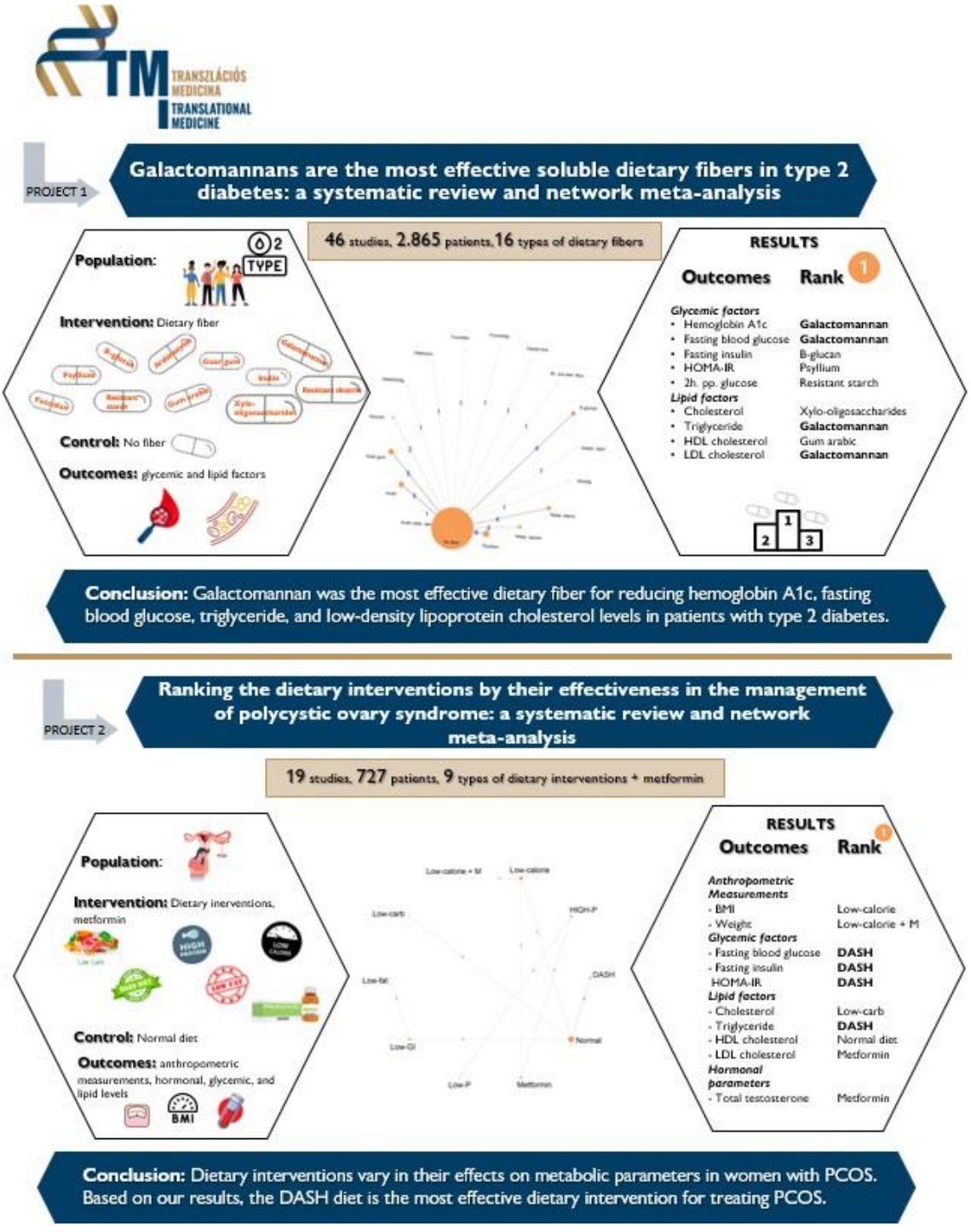
The research initially aimed to explore the role of dietary fiber in women with polycystic ovary syndrome (PCOS), a common endocrine and metabolic disorder affecting women of reproductive age. However, due to the limited number of eligible studies available for meta-analysis in this area, the focus was expanded to include another prevalent disorder of carbohydrate metabolism: type 2 diabetes mellitus (T2DM). Consequently, two network meta-analyses were conducted, one investigating dietary fiber interventions in T2DM, and the other assessing the effectiveness of various dietary patterns in PCOS.

The first network meta-analysis evaluated the comparative effectiveness of 16 types of dietary fibers in patients with T2DM. The findings revealed that galactomannan were the most effective fiber for reducing Hemoglobin A1c (HbA1c), fasting blood glucose, triglycerides, and Low-Density Lipoprotein Cholesterol (LDL cholesterol), highlighting their potential therapeutic value in diabetes management.

The second network meta-analysis investigated various dietary interventions in women with PCOS. Among the dietary interventions, the Dietary Approaches to Stop Hypertension (DASH) diet demonstrated a statistically significant and superior effect on reducing Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and body weight compared to a normal diet, suggesting it may be the most beneficial dietary approach for improving insulin resistance and metabolic health in this population.

Together, these studies support the integration of tailored dietary strategies, including specific fiber types and overall dietary patterns, into the clinical management of metabolic disorders such as T2DM and PCOS.

4. GRAPHICAL ABSTRACT



5. INTRODUCTION

5.1. Overview of the topic

5.1.1. What is the topic?

The focus of my research is to evaluate and rank the effectiveness of various types of soluble dietary fibers on glycemic and lipid parameters in patients with type 2 diabetes, while also providing clinicians an evidence-based guidance on dietary interventions in the lifestyle management of women with PCOS.

5.1.2. What is the problem to solve?

Type 2 diabetes accounts for more than 90% of all diabetes mellitus cases worldwide (1). One of its primary risk factor is obesity. Consequently, the management of type 2 diabetes requires lifestyle modifications, including medical nutrition therapy (MNT) and physical activity, to promote healthy weight loss and achieve optimal glycemic control. MNT recommends reducing energy intake, particularly by lowering overall carbohydrate consumption. Carbohydrate sources should be nutrient-dense and rich in dietary fiber (2). However, current guidelines do not specify which types of dietary fiber are preferred. Therefore, it is important to assess the effects of each fiber type individually.

The International Evidence-based Guideline for the Assessment and Management of PCOS recommends dietary and exercise interventions as the first-line treatment strategy (3). Most women with PCOS are overweight or obese, and even modest weight loss (5-10% of body weight) can lead to significant improvements in metabolic parameters and reproductive function. Weight reduction increases sex hormone-binding globulin (SHBG) levels, enhances ovarian function and fertility, and lowers the risk of miscarriage (4, 5). While achieving a healthy body weight can alleviate symptoms in overweight women with PCOS, there is currently no clear evidence indicating which specific dietary intervention is most effective for reaching this goal.

5.1.3. What is the importance of the topic?

The importance of this topic cannot be overstated. In 2024, an estimated 589 million adults aged 20-79 were living with diabetes, and this number is expected to rise

to 853 million by 2050(6). This rapid increase highlights the importance of developing effective and accessible strategies for prevention and management.

Polycystic ovary syndrome is one of the most common endocrine disorders among women of reproductive age, with a recent meta-analysis estimating a global prevalence of 9.2%(7). PCOS is closely associated with metabolic disturbances such as insulin resistance, obesity, and dyslipidemia, all of which increase the risk of type 2 diabetes and cardiovascular disease. Therefore, investigating the effects of specific dietary components is crucial for formulating evidence-based nutritional strategies in the management of PCOS.

5.1.4. What would be the impact of our research results?

Our findings support evidence-based recommendations for the management of T2DM and PCOS, emphasizing the role of dietary strategies, particularly dietary fiber, as effective alternatives or complementary therapies to pharmacological treatment. Reducing the prevalence and impact of these conditions not only improves individual health outcomes but also alleviates pressure on healthcare systems and enhances overall population well-being.

5.2. Type 2 diabetes

T2DM is a chronic metabolic disorder characterized by insulin resistance and relative insulin deficiency. Unlike Type 1 diabetes, which results from autoimmune destruction of pancreatic β-cells, T2DM develops gradually, often in association with obesity, physical inactivity, and genetic predisposition. It accounts for approximately 90% of all diabetes cases worldwide and is a major public health concern due to its growing prevalence and significant morbidity (1). The pathophysiology of T2DM involves a complex interplay between insulin resistance, particularly in skeletal muscle, adipose tissue, and the liver and progressive β-cell dysfunction in the pancreas. Insulin resistance leads to decreased glucose uptake and increased hepatic glucose production, while β-cell impairment reduces insulin secretion. Over time, this imbalance results in chronic hyperglycemia, which contributes to the development of diabetes-related complications.

Risk factors for T2DM include excess body weight (especially central obesity), physical inactivity, unhealthy dietary patterns, family history of diabetes, advanced age, and certain ethnic backgrounds. Additionally, conditions such as hypertension, dyslipidemia, and PCOS are commonly associated with increased risk. T2DM is associated with a wide range of microvascular and macrovascular complications. These complications significantly impact morbidity, quality of life, and mortality, making early diagnosis and effective management essential. Management of T2DM includes lifestyle modification as the cornerstone of therapy, focusing on weight loss, dietary changes, increased physical activity, and behavioral interventions (2, 8, 9).

5.3. Dietary fiber

The definition of dietary fiber may vary slightly across organizations, one of the most widely accepted descriptions is provided by the Codex Alimentarius (FAO/WHO). According to this definition, dietary fibers are carbohydrate polymers composed of ten or more monomeric units that are not hydrolyzed by endogenous enzymes in the human small intestine. The definition encompasses naturally occurring fibers in foods, fibers extracted or modified from raw food materials with proven physiological benefits, and synthetic carbohydrate polymers that have demonstrated positive health effects (10).

Based on their functional properties and physiological effects, they are typically categorized as soluble and insoluble fibers. Insoluble fibers, mainly found in cereals, have a strong water-binding capacity that enhances satiety and may help prevent overeating. Soluble fibers, present in fruits and vegetables, are often considered prebiotics, as they support the growth of beneficial gut microbes, such as *Lactobacillus* and *Bifidobacterium*, while reducing pathogenic bacteria. Some dietary fibers can be fermented by gut microbiota in the colon, producing short-chain fatty acids (SCFAs). These SCFAs exert beneficial effects on glucose metabolism by enhancing insulin sensitivity, reducing hepatic glucose production, and stimulating the secretion of gut hormones such as Glucagon-Like Peptide-1 (GLP-1) and Peptide YY, which help regulate appetite and glycemic control. SCFAs also influence lipid metabolism by inhibiting hepatic lipogenesis, promoting fatty acid oxidation, and lowering circulating triglyceride and cholesterol levels (11, 12). Together, these mechanisms support the role of dietary fiber in improving dysglycemia and dyslipidemia.

It is also worth mentioning that in the European Union, many types of dietary fiber are used as food additives. These are substances assigned an E number, tested and certified according to specific standards. For example, guar gum (E412), and acacia gum (E414) are commonly used fibers that serve both technological and nutritional functions (13, 14).

5.4. Polycystic ovary syndrome

PCOS is one of the most common (5-18%) abnormalities in women of reproductive age (15). PCOS is usually diagnosed according to the Rotterdam criteria, meaning the presence of two of the following criteria: ovulatory dysfunction, hyperandrogenism, or polycystic ovary morphology (3). PCOS has more clinical manifestations like insulin resistance, hyperinsulinemia (70%), and obesity (80%) (16). PCOS can be categorized into separate 4 phenotypes (A, B, C, and D), depending on the features used in the diagnostic criteria. Characteristics of the phenotypes: A: clinical or biochemical hyperandrogenism (HA) + oligo-anovulation (OA) + polycystic ovarian morphology (PCOM); phenotype B: HA + OD; phenotype C: HA + PCOM; and phenotype D: OD + PCOM. According to the literature, Phenotype A has the highest prevalence (50%-63%)(17). Women with phenotype A appear to be more obese and hirsute, more likely to have insulin resistance, and dyslipidemia compared with other phenotypes (18).

According to the most recent guidelines for the assessment and management of PCOS, lifestyle intervention is regarded as first-line therapy to manage reproductive and metabolic outcomes regardless of phenotype. Obesity seems to exacerbate the clinical features of PCOS, but also weight independent insulin resistance is strongly implicated in the aetiology of PCOS, contributing to the reproductive and metabolic complications (3). Even a 5% weight reduction increases the sex hormone-binding globulin (SHBG) concentration, improves ovarian function and fertility, and reduces miscarriages (5). According to the latest international guideline, in addition to lifestyle intervention, treatment with metformin should also be considered in individuals with a BMI over 25 kg/m^2 (3). Metformin, also known as dimethyl biguanide, is an oral antidiabetic agent. Its principal clinical actions include the inhibition of hepatic glucose production, the enhancement of insulin sensitivity in peripheral tissues, and the reduction of intestinal glucose absorption (4).

PCOS is associated with a range of long-term health consequences, including an elevated risk of developing T2DM, a higher prevalence of metabolic syndrome, infertility, and increased risk of endometrial hyperplasia and cardiovascular disease (3).

5.5. Dietary interventions

A wide range of dietary approaches exists, reflecting diverse nutritional philosophies and health goals. Some interventions primarily aim to reduce total energy intake, thereby promoting weight loss and improving metabolic health. Others focus on altering the ratio of macronutrients, such as increasing protein or reducing carbohydrate or fat intake, in order to influence physiological pathways like insulin sensitivity, satiety, or lipid metabolism. Additionally, there are diets that emphasize the quality and source of macronutrients, encouraging the consumption of whole, minimally processed foods, low-glycemic carbohydrates, unsaturated fats, and lean proteins over their refined or less healthful counterparts. In our second meta-analysis, we summarized the dietary interventions used in the included studies and presented their macronutrient compositions in the following Table 1.

Table 1. Summary of the dietary interventions

Dietary intervention	Carbohydrate %	Protein %	Fat %	Other information
DASH	50-55	15-20	25-30	High in fruits, vegetables and in whole grains. Includes low-fat dairy products, lean protein (especially poultry and fish) Low in saturated fat and cholesterol Reduced sodium intake (typically 1500–2300 mg/day)

				Limits added sugars and red/processed meats Emphasizes potassium, calcium, magnesium
High-P	40	30	30	
Low-calorie	40-55	15-20	30-35	400-600 kcal/day deficit
Low-fat	55	20	25	
Low-GI	40-45	20-30	30-35	GI < 45
Mediterranean	20	35-45	35-45	Similar to DASH, but does not restrict sodium. Greater emphasis on fat quality – mainly from nuts, seeds, and olive oil.
Low-carb	41	19	40	
Low-P	55	15	30	
Metformin	50	25	25	1000-2000 mg metformin/day
Low-calorie + M	40-50	15-20	30-35	400-600 kcal/day deficit + 1000-2000 mg metformin/day
Normal	55	15-20	25-30	

DASH: Dietary approach stop hypertension; Low-calorie + M: Low-calorie diet plus metformin; Low-carb: Low- carbohydrate diet; High-P: High-Protein diet; Low-GI: Low-Glycemic Index diet; Low-P: Low-Protein diet

6. OBJECTIVES

6.1. Study I. - Galactomannans are the most effective soluble dietary fibers in type 2 diabetes: a systematic review and network meta-analysis

The objective of this network meta-analysis (NMA) was to compare the effects of different dietary fibers used as supplementation in the management of type 2 diabetes. The objective was to establish a ranking of these interventions and identify the most effective soluble fiber for improving glycemic (*HbA1c, fasting blood glucose (FBG), fasting insulin (FI), 2-h postprandial glucose level (2h pp. G), HOMA-IR*) and lipid parameters (*total cholesterol (TC), triglyceride (TG), HDL, LDL*) in patients with type 2 diabetes.

6.2. Study II. - Ranking the dietary interventions by their effectiveness in the management of polycystic ovary syndrome: a systematic review and network meta-analysis

The aim of this study was to rank the effectiveness of various dietary and therapeutic interventions used in the treatment of women with PCOS, based on changes in anthropometric parameters (*body weight, Body Mass Index (BMI)*), hormonal markers (*total testosterone (TT) follicle-stimulating hormone (FSH), luteinizing hormone (LH)*), and metabolic outcomes (*FBG, FI, HOMA-IR, TC, TG, HDL, LDL*) observed during the intervention period.

7. METHODS

The systematic reviews and network meta-analyses were conducted in accordance with the PRISMA 2020 guidelines (19) and the methodological recommendations outlined in the Cochrane Handbook for Systematic Reviews of Interventions (20). The study protocol was prospectively registered in the PROSPERO database (Study I.: *CRD42021282984* and Study II.: *CRD42022329961*), and the reviews were carried out in full adherence to the registered protocol.

7.1. Literature search and eligibility criteria

A comprehensive systematic literature search was performed for both studies using major databases. The initial search for Study I was conducted on October 20, 2021, and for Study II on May 2, 2022. The databases searched included MEDLINE (via PubMed), Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL), with Scopus and Web of Science additionally included in the search strategy for Study II. Both searches were later updated, on November 20, 2022, for Study I, and on March 8, 2023, for Study II, however, no further eligible studies were identified during the updates. No restrictions were applied regarding language, publication date, or study characteristics in either case.

The search strategies for both studies were developed around core concepts relevant to their respective research questions. For Study I, the main terms included ("type 2 diabetes") AND ("soluble dietary fiber") AND (random), with the truncation "random" used to identify all variations of randomized study designs. For Study II, the strategy focused on concepts such as polycystic ovary syndrome (PCOS), dietary interventions, metformin treatment, and randomized controlled trials. To maximize sensitivity and ensure comprehensive coverage, both free-text terms and controlled vocabulary (MeSH and EMTREE) were applied in the search development for each study. The complete search strategy is available in the supplementary material of both original articles (21, 22).

Only randomized controlled trials (RCTs) were included in both Study I and Study II. For Study I, eligible trials enrolled adults diagnosed with type 2 diabetes, in which dietary fiber intake was compared to either another type of fiber or to a control group receiving no fiber. Studies were required to report at least one of the following outcomes: HbA1c,

fasting blood glucose (FBG), fasting insulin (FI), 2-hour postprandial glucose (2h-PPG), HOMA-IR, total cholesterol (TC), triglycerides (TG), HDL, or LDL. Trials involving pregnant women or children were excluded.

For Study II, eligible RCTs enrolled women with a diagnosis of PCOS and compared two different dietary interventions or one dietary approach against either a standard diet or metformin. Eligible outcomes included body mass index (BMI), body weight, total testosterone (TT), follicle-stimulating hormone (FSH), luteinizing hormone (LH), in addition to the metabolic outcomes listed in Study I. To minimize confounding, studies were excluded if participants engaged in structured exercise programs or received dietary supplements, as these could act as effect modifiers.

7.2. Selection process and data collection

The bibliographic results for both NMAs were imported into EndNote X9 (Clarivate Analytics, Philadelphia, PA, USA), which was used to remove duplicates and organise records for screening. Two reviewers independently screened titles and abstracts, followed by full-text assessment. The reference lists of all eligible papers were manually searched for additional studies. Inter-rater agreement at both stages was quantified with Cohen's kappa coefficient (23). Disagreements were resolved by discussion with a third reviewer.

From each included trial the reviewers independently extracted: first author, year of publication, study population and period, country, number of centres, participant characteristics (age, sex, diabetes treatment (Study I.), and BMI) number of participants per arm, details of the dietary interventions and control conditions (type and amount of fiber or macronutrient composition of the diet), pre- and post-intervention values, and changes in the specified laboratory outcomes (HbA1c, FBG, FI, 2h-PPG, HOMA-IR, TC, TG, HDL, LDL, BMI, body weight, TT, FSH, LH). Corresponding authors were contacted when data were incomplete.

Study-specific procedures were retained within this common framework:

Study I.: Controls were standardised to "no fibre" when participants received either no supplement or digestible carbohydrates (maltodextrin, glucose, or xylitol). Trials whose control groups received any dietary fibre are summarised only in the qualitative (systematic-review) component.

Study II.: Due to the heterogeneous definitions of dietary approaches, interventions were re-classified into broader categories based on macronutrient distribution and aligned with the EFSA Dietary Reference Values for Nutrients (24). A “normal diet” was defined as ~55 % carbohydrate, 15–20 % protein and 25–30 % fat of total energy intake.

7.3. Risk-of-bias assessment and quality of evidence

The risk of bias assessment was independently performed in duplicate by two review authors using version 2 of the Cochrane Risk of Bias tool for randomized trials (RoB 2) across all reported outcomes (25). The five key domains evaluated were: the randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of the reported results. Each domain was rated as low risk, some concerns, or high risk of bias. Any disagreements were resolved by consultation with a third independent reviewer.

To assess the certainty of evidence, we applied the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) approach (26). Each outcome and comparison was evaluated independently by two reviewers according to the GRADE criteria. Any discrepancies in judgment were discussed and resolved with the involvement of a third reviewer.

7.4. Synthesis methods

A Bayesian framework was applied to conduct both pairwise and network meta-analyses (NMA), using a random-effects model (27). Consistency was assessed through visual inspection of the network plots. The network was visualized as a graph in which nodes represented different types of dietary fibers in Study I, and types of dietary interventions in Study II. Edges indicated direct comparisons between interventions. The size of each node was proportional to the number of studies investigating the respective fiber type (Study I) or intervention (Study II), while the thickness of each edge reflected the number of trials contributing direct comparisons.

For continuous outcomes, mean differences (MDs) with 95% credible intervals (CrIs) were calculated, representing the Bayesian equivalent of traditional confidence intervals. Model optimisation and posterior sampling were performed using Markov Chain Monte Carlo (MCMC) methods, running four chains with at least 20,000 adaptation iterations to ensure convergence and 40,000 simulation iterations for estimation. Pooled estimates,

combining both direct and indirect comparisons, were summarised in a league table, comparing all interventions with each other and, when applicable, with the control group (no fiber in Study I; normal diet in Study II). Interventions were ranked based on their posterior probabilities, expressed through surface under the cumulative ranking curve (SUCRA) values. These values (ranging from 0% to 100%) reflect the likelihood that an intervention is the most effective or among the most effective ones. For instance, a SUCRA value of 55% indicates a 55% probability that the intervention is the best. Higher SUCRA values correspond to a greater probability of being among the top-ranked options (28).

All analyses were conducted using R software (version 4.1.1) with the BUGSnet package (version 1.1.0) and the JAGS (Just Another Gibbs Sampler) MCMC engine (version 4-12).

Due to the limited number of studies, separate network meta-analyses could not be performed for certain outcomes, such as trials using insoluble fiber as a comparator in Study I, or FSH and LH outcomes in Study II. For the same reason, pairwise comparisons were also not feasible in some cases. These studies, along with those that reported results only as medians without standard deviations, or did not specify the exact type of fiber, were included only in the qualitative synthesis.

8. RESULTS

8.1. Study I.

8.1.1 Search and selection

The systematic search provided 1,605 records. After removing duplicates and screening the remaining entries, 56 studies met the eligibility criteria and were included in the qualitative and quantitative syntheses. The study selection process is illustrated in Figure 1.

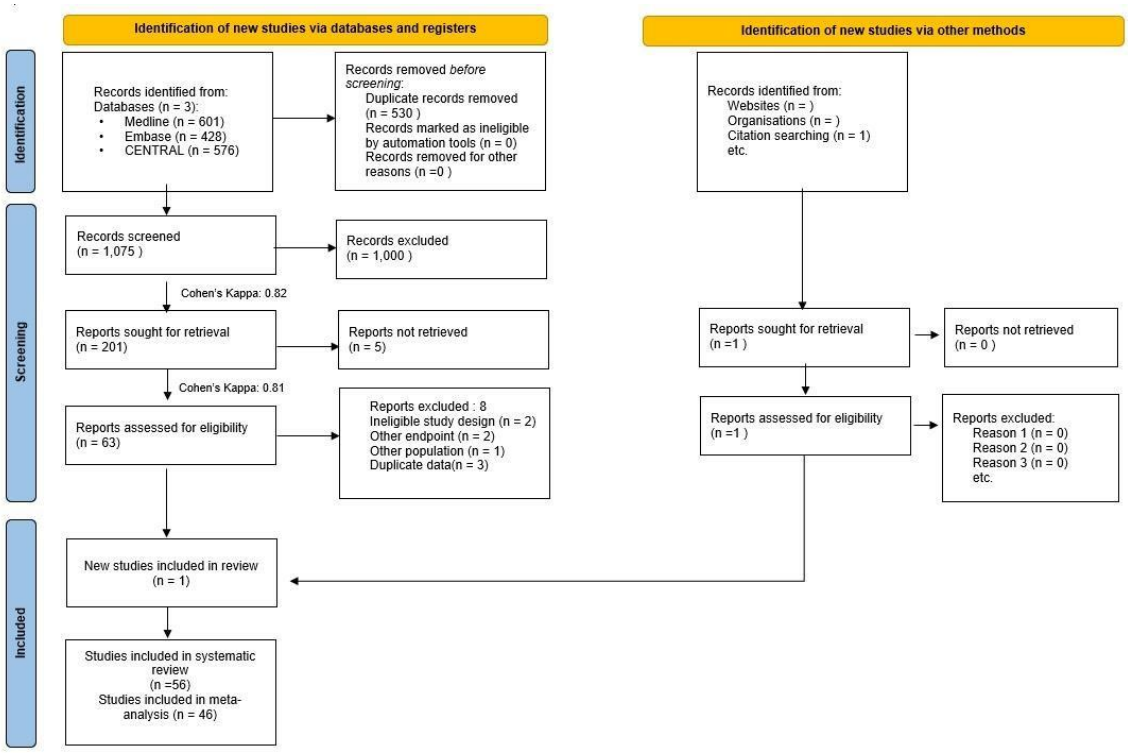


Figure 1. PRISMA Flow Diagram of the screening and selection process for Study I. (21)

8.1.2. Main characteristics of included studies

Baseline characteristics of the included studies are presented in Table 2 (21-65). Altogether, 2,865 participants were enrolled across the trials, which were conducted in 30 countries, with a notable proportion originating from Iran (16 out of 46 studies). Study durations ranged from 30 days to 6 months. In total, 16 different types of dietary fiber interventions were evaluated. Baseline characteristics of studies included only in the qualitative synthesis are provided in Supplemental Table 3 of the original publication (21).

Table 2. Basic characteristics of the included studies (21).

Study, year	Country	Study period	Number of patients	Sex (female%)	Mean age (SD) Intervention /Control group	BMI kg/m^2(SD) Intervention /Control group	Medi cation	Intervention (g/day)	Control	Outcome
Abutair, 2016 (29)	Palestine	8 weeks	40	50	35 <	31.7(2.71)	OAD	Psyllium (10.5)	No fiber	FBG, HbA1C, FI, HOMA IR
Abutair, 2018 (30)	Palestine	8 weeks	40	50	47.5(4.2)	N/A	OAD	Psyllium (11.5)	No fiber	TC, HDL, LDL
Aliasgharzadeh, 2015(31)	Iran	8 weeks	75	100	49.2(8.4)/ 49.6(9.6)	30.8(4)/ 31.8(4.1)	OAD	Resistant dextrin (10)	Maltodextrin	FBG, HbA1C, FI, HOMA IR
Aliasgharzadeh, 2015(32)	Iran	8 weeks	70	100	48.4(9.7)/ 48.5(8.4)	31.8(4.5)/ 30.8(5.2)	OAD	Inulin (10)	Maltodextrin	TC, TG, HDL, LDL
Alles, 1999(33)	the Netherlands	20 days	20	55	56(5.2)/ 62(4.1)[1]	29.4(4.2)/ 27.4(2.2)[1]	OAD (n=17)	Fructooligo saccharides (15)	Glucose	FBG, TC, TG, HDL, LDL
Babiker, 2018(34)	Sudan	12 weeks	100	80	49.9(8.7)/ 50.2(9.3)	27.6(5.4)/ 29.9(6.5)	OAD	Gum arabic (30)	No fiber	TG, HDL
Bodinham, 2014(35)	United Kingdom	12 weeks	17	29	55	31.0(1.3)/ 30.7(1.4)	OAD (n=15)	Resistant dextrin (40)	Amioca	FBG, HbA1C, FI, TG, TC, HDL, LDL
Bonsu, 2012(36)	Canada	12 weeks	36	46	64(5.8)/ 66(11.2)	31(4.5)/ 29.7(4.3)	N/A	Inulin (10)	Xylitol	FBG, HbA1C, TG, TC, HDL, LDL
Cai, 2018(37)	China	12 weeks	371	62	60.9(5.4)/ 60.2(5.8)	27.8(3.5)/ 27.7(3.8)	OAD (n=43)	Inulin, resistant dextrin (6.3)	Placebo	FBG, HbA1C, FI, 2h pp. G, HOMA IR, TG, TC, HDL, LDL

Chearskul,2007(38)	Thailand	4 weeks	20	50	51.4(2.3/ 51(2.2)[1]	26.5(1.2)/ 26.4(1.1)	N/A	Gluco mannan (3)	Placebo	FBG, FI, 2h pp. G, HOMA IR, TG, TC, HDL, LDL
Chen, 2003(39)	Taiwan	4 weeks	22	54	64.2(8.3)/ 52–771	25.5(3.2)	OAD (n=21), insulin (n=1)	Gluco mannan (3)	Placebo	FBG, 2h pp. G, TG, TC, HDL, LDL
Cho, 2005(40)	Korea	8 weeks	42	57	57.2(2.6)/ 57.1(2.9)	23.7(0.4)/ 23.4(0.6)	OAD	Cassia tora (3)	Maltodextrin	FBG, HbA1C, TG, TC, HDL, LDL
Costa, 2019(41)	Brazil	24 weeks	131	75	65(62–71)/ 64(60-71)2	29.8(26.7–33.5)/ 28.9(26.5–33.1)	OAD	Resistant starch (4)	No fiber	TC, HDL, HOMA IR
Cugnet, 2010(42)	France	8 weeks	53	39	61.9(9.1)/ 61.8(7.5)	30.5(4.8)/ 29.1(4.5)	OAD	B glucan (3.5)	No fiber	FBG, HbA1C, TC, HDL, LDL
Dall'Alba, 2013(43)	Brazil	6 weeks	44	61	60.5(9.1)/ 63.6(9.6)	30.2(3.6)/ 29.3(3.6)	OAD	Guar gum (10)	No fiber	FBG, HbA1C, TC, HDL, LDL
Dehghan, 2013(44)	Iran	8 weeks	65	100	47.8(10.1)/ 48.7(9.7)	31.6(0.9)/ 29.9(4.2)	OAD	Inulin (10)	Maltodextrin	FBG, HbA1C, TG, TC, HDL, LDL
Dehghan, 2016(45)	Iran	8 weeks	70	100	48.1(8.7)/ 48.6(9.2)	31.4(3.5)/ 29.9(4.01)	OAD	Inulin (10)	Maltodextrin	FBG, HbA1C, TG, TC, HDL, LDL
Farhangi, 2018(46)	Iran	8 weeks	85	100	49.2(9.6)/ 49.6(8.4)	31.8(4.5)/ 30.8(5.2)	OAD	Resistant dextrin (10)	Maltodextrin	FBG, HbA1C, TG, TC, HDL, LDL
Farhangi, 2020(47)	Iran	8 weeks	70	100	49.5(8.0)/ 48.6 (7.9)	31.5(4.5)/ 32(3.9)	OAD	Inulin (10)	Maltodextrin	FI
Feinglos, 2013/1	United States of America	12 weeks	37	33	61.8(9.4)/ 56.5(9.9)	N/A	OAD	Psyllium (6.8)	Placebo	FBG, HbA1C

Feinglos, 2013/2(48)	United States of America	12 weeks	37	33	64.8(8.4)/ 56.5(9.9)	N/A	OAD	Psyllium (13.6)	Placebo	FBG, HbA1C
Gargari, 2013(49)	Iran	8 weeks	65	100	47.8(0.1)/ 48.7(9.7)	31.6(4.1)/ 29.9(4.2)	OAD	Inulin (10)	Maltodextrin	FI, HOMA IR
Gargari, 2015(50)	Iran	8 weeks	60	100	49.5(8.0)/ 49.6(8.4)	31.5(4.5)/ 30.8(5.2)	OAD	Resistant starch (10)	Maltodextrin	FBG, HbA1C, TG, TC, HDL, LDL
Ghalandari, 2018(51)	Iran	8 weeks	47	65	55.9(8.3)/ 48.8(8.5)	29.7(7.5)/ 28.5(2.5)	OAD	Psyllium (3.1)	No fiber	TG, TC, HDL, LDL
Ghavami, 2018(52)	Iran	6 weeks	46	56	41.5(6.3)/ 42.7(5.9)	27.7(4.6)/ 28.8(4.8)	OAD	Inulin (10)	Starch	FBG, FI, HbA1C, HOMA IR, TG, TC, HDL, LDL
Karimi, 2015(53)	Iran	8 weeks	60	100	49.5(8.0)/ 48.6(7.9)	31.5(4.5)/ 31(4.9)	OAD	Resistant starch (10)	Maltodextrin	HOMA IR, FI
Kondo, 2017(54)	Japan	8 weeks	28	35	68.1(8.7)/ 65.2(6.8)	24.2(3.5)/ 25(3.7)	OAD	Brown rice dietary fiber (4.3)	White rice	FBG, FI, HbA1C, HOMA IR, TG, TC, HDL, LDL
Lalor, 1990(55)	United Kingdom	12 weeks	26	53	58(40-73)2	31.5(5.1)	OAD	Guar gum (15)	Placebo	FBG, TC, TG, HDL, LDL
Li, 2016/1	China	30 days	298	47	59.7(6.1)/ 59(3.9)	26.9(2.7)/ 25.2(0.9)	OAD (n=75), insulin (n=28)	B glucan (2.65)	No fiber	FBG, HbA1C, 2h pp. G, HOMA IR, TG, TC, HDL, LDL
Li, 2016/2(56)	China	30 days	298	47	59.4(6.8)/ 59(3.9)	27.4(2.4)/ 25.2(0.9)	OAD (n=49), insulin (n=24)	B glucan (5.3)	No fiber	FBG, HbA1C, 2h pp. G, HOMA IR, TG, TC, HDL, LDL

Liatis, 2009(57)	Greece	3 weeks	41	43	60.2(8.9)/ 66.5(8.9)	29.6(4.7)/ 27(3.7)	OAD	B glucan (3)	No fiber	FBG, FI, HOMA IR, TG, TC, HDL, LDL
Lotfollahi, 2020(58)	Brazil	6 months	39	N/A	65	N/A	OAD	Resistant starch (4.5)	No fiber	FBG, FI, HOMA IR, TG, TC, HDL, LDL
Lu, 2004(59)	Australia	5 weeks	15	60	60 (2.0)	28.1(0.9)	OAD	Arabino xylan (14-17)	No fiber	FBG, FI, 2h pp. G, TG, TC, HDL, LDL
Luo, 2000(60)	Belgium	4 weeks	10	40	57 (2.0)	28 (1.0)	OAD (n=10)	Fructooligo saccharides (20)	Sucrose	FBG, FI, HbA1C, TG, TC, HDL, LDL
Mclvor, 1986(61)	United States of America	6 months	16	62	49.6(3.0)/ 48.5(2.9)	N/A	insulin	Guar gum (26.4-39.6)	Placebo	TC, TG, HDL, LDL
Meng, 2019(62)	China	12 weeks	70	41	62.8(9.3)/ 61(9.5)	26.4(3.9)/ 25.8(3.6)	OAD, insulin	Resistant starch (17.41)	No fiber	FBG, HbA1C, TG, TC, HDL, LDL
Noureddin, 2018(63)	Iran	12 weeks	54	82	58(7.2)/ 55.9(8.7)	29.3(5.2)/ 28.7(5.9)	OAD	Psyllium (10)	Maltodextrin	FBG, HbA1C, TG, TC, HDL, LDL
Pedersen, 2016(64)	United Kingdom	12 weeks	39	0	56.7(1.6)/ 58.1(1.7)	28(1.1)/ 28.4(0.1)	OAD	Galactooligo saccharides (5.5)	Maltodextrin	FBG, FI, HbA1C, HOMA IR
Peterson, 1987/1	United Kingdom	6 weeks	16	38	60(47-69)	27.3(21.9-36.9)[2]	OAD	Guar gum (7.6)	No fiber	FBG, FI, HbA1C, TG, TC, HDL, LDL
Peterson, 1987/2(65)	United Kingdom	6 weeks	16	38	60(47-69)	27.3(21.9-36.9)[2]	OAD	Guar gum (8.3)	No fiber	FBG, FI, HbA1C, TG, TC, HDL, LDL
Rashid, 2019(66)	Pakistan	12 weeks	64	29	48.5/48.2	32.3(1.5)/ 30.2(1.6)[1]	N/A	Galacto mannan (1)	Placebo	FBG, HbA1C, TG, TC, HDL, LDL

Sakai, 2019(67)	Japan	12 weeks	30	26	59.1(13.2)	25.18(3.9)	N/A	Fucoidan (1.62)	Placebo	FBG, FI, HbA1C, HOMA IR, TG, TC, HDL, LDL
Sartore, 2009(68)	Italy	8 weeks	40	33	61(8.4)/ 60(8)	30.1(3.9)/ 30.5(2.9)	N/A	Psyllium (10.5)	No fiber	FBG, HbA1C, TG, TC, HDL, LDL
Sheu, 2008(69)	Taiwan	8 weeks	26	26,9	64(7.6)/ 67.6(7.9)	25(2.7)/ 25(3.9)	OAD	Xilooligo saccharides (4)	Glucose	FBG, FI, HbA1C, TG, TC, HDL, LDL
Soltanian, 2019(70)	Iran	12 weeks	77	83	58(7.2)/ 55.9(8.7)	29.3(5.2)/ 28.7(5.9)	OAD	Psyllium (10)	No fiber	FBG, HbA1C, TG, TC, HDL, LDL
Tajadadi, 2014(71)	Iran	8 weeks	54	81	52(7.2)/ 53.4(7.5)	29.8(5.7)/ 30.5(4.1)	OAD	Inulin (8.4)	No fiber	FBG, FI, HOMA IR
Uusitupa, 1989(72)	Finland	12 weeks	39	66	58.6(5.4)/ 61.48(6.3)[1]	N/A	OAD	Guar gum (15)	No fiber	FBG, HbA1C, TC, HDL, TG
Zhang,2007/1	China	4 weeks	40	N/A	N/A	N/A	N/A	Resistant starch (30)	No fiber	FBG, 2h pp. G, FI, TG, TC
Zhang, 2007/2(73)	China	4 weeks	40	N/A	N/A	N/A	N/A	Resistant starch (30)	No fiber	FBG, 2h pp. G, FI, TG, TC

N/A: not available; [1]males/females; [2]median (range); OAD: Oral Antidiabetic Drug; FBG: fasting blood glucose; FI: fasting insulin; TG: trygliceride; TC: cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol;

8.1.3. Results of the quantitative analysis

8.1.3.1 Glycemic levels

HbA1c

The network comprised 30 studies involving a total of 1,526 patients (Figure 2. Network). Regarding HbA1c levels, the three most effective interventions were galactomannans (SUCRA: 92.33%), inulin (SUCRA: 69.00%), and xylo-oligosaccharides (SUCRA: 60.45%) (Figure 2. Rankogram). A statistically significant reduction in HbA1c was observed when galactomannans were compared with psyllium (MD: -1.39% [-15.2 mmol/mol]; 95% CrI: -2.54, -0.03) and with no fiber (MD: -1.46% [-16.0 mmol/mol]; 95% CrI: -2.58, -0.33).

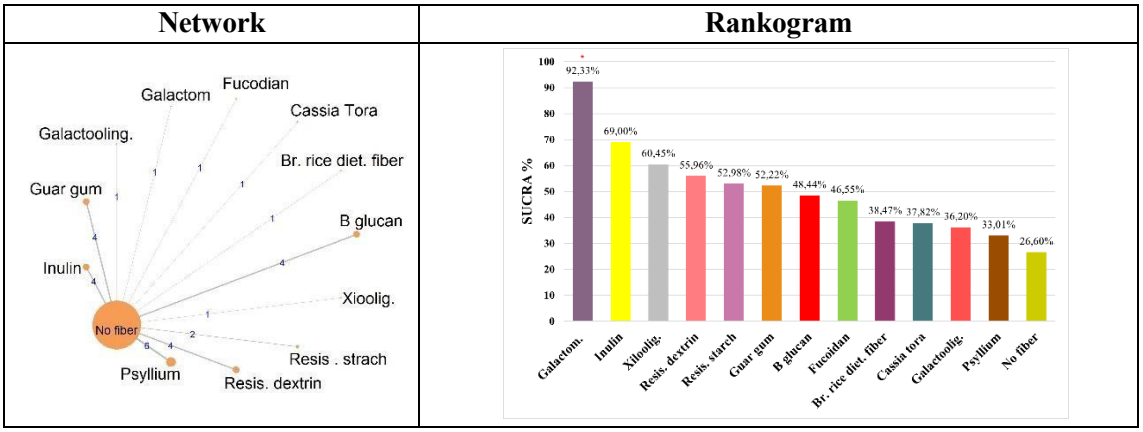


Figure 2. Network plot and rankogram of dietary fibers for HbA1c (21).

Br. rice diet. fibre: Brown rice dietary fibre; Galactom.: Galactomannan; Galactoolig.: Galactooligosaccharide; Resis. dextrin: Resistant dextrin; Resis. starch: Resistant starch; Xiloolig.: Xilooligosaccharide

*Means statistically significant difference was observed when the intervention was compared with another type of fiber or with no fiber.

Fasting blood glucose

A total of 38 studies including 1,819 participants were incorporated into the network for FBG outcomes (Figure 3. Network). Based on SUCRA values, the three most effective interventions were galactomannans (85.92%), resistant starch (85.07%), and psyllium (72.01%) (Figures 3 Rankogram).

Galactomannans showed statistically significant reductions in FBG compared with resistant dextrin (MD: -1.48 mmol/L; 95% CrI: -2.75, -0.03), no fiber (MD: -1.69 mmol/L; 95% CrI: -2.84, -0.59), and Cassia tora (MD: -2.90 mmol/L; 95% CrI: -5.66, -0.25). Resistant starch also significantly outperformed resistant dextrin (MD: -1.46 mmol/L; 95% CrI: -2.70, -0.22), no fiber (MD: -1.66 mmol/L; 95% CrI: -2.72, -0.74), and Cassia tora (MD: -2.87 mmol/L; 95% CrI: -5.70, -0.22). Psyllium was superior to no fiber (MD: -1.20 mmol/L; 95% CrI: -1.83, -0.63), and β-glucans also showed a significant effect compared with no fiber (MD: -0.91 mmol/L; 95% CrI: -1.69, -0.19).

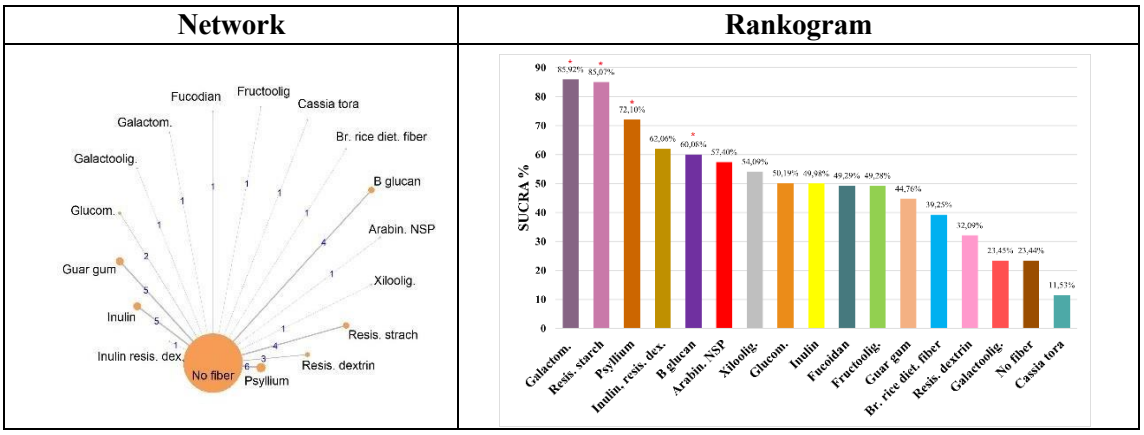


Figure 3. Network plot and rankogram of dietary fibers for FBG (21).

Arabin. NSP: Arabinoxylan non-starch polysaccharides; Br. rice diet. fibre: Brown rice dietary fibre; Fructoolig.: Fructooligosaccharide; Galactom.: Galactomannan; Galactoolig.: Galactooligosaccharide; Glucom.: Glucomannan; Inulin resis. dex: Inulin with resistant dextrin; Resis. dextrin: Resistant dextrin; Resis. starch: Resistant starch; Xiloolig.: Xilooligosaccharide

*Means statistically significant difference was observed when the intervention was compared with another type of fiber or with no fiber.

Fasting insulin

The network for FI outcome included 21 studies comprising 888 patients (Figure 4. Network). Based on SUCRA values, the top three interventions were β-glucan (73.45%), psyllium (72.10%), and resistant starch (59.48%) (Figure 4. Rankogram). No statistically significant differences were observed in FI changes across the pairwise comparisons of the included dietary fiber interventions.

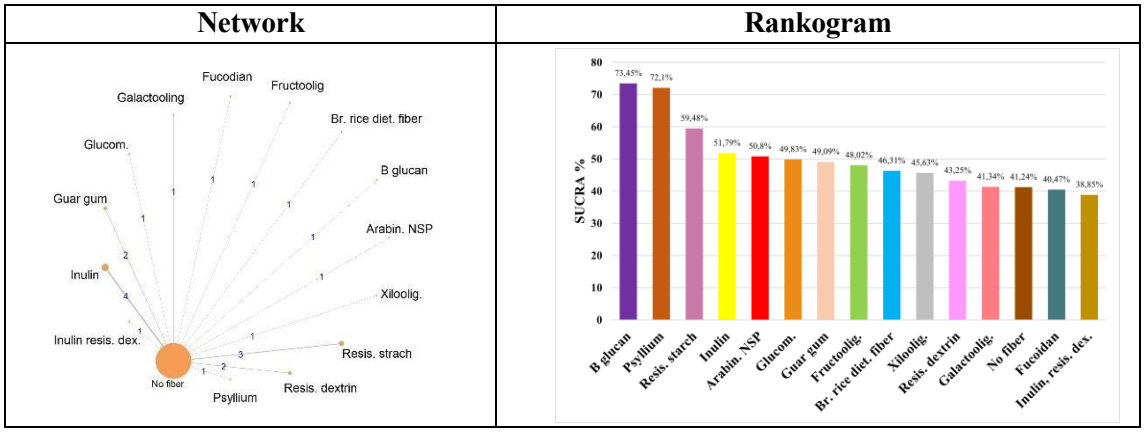


Figure 4. Network plot and rankogram of dietary fiber interventions for fasting insulin outcomes (21).

Arabin. NSP: Arabinoxylan non-starch polysaccharides; Br. rice diet. fibre: Brown rice dietary fibre; Fructoolig.: Fructooligosaccharide; Galactoolig.: Galactooligosaccharide; Glucom.: Glucomannan; Inulin resis. dex: Inulin with resistant dextrin; Resis. dextrin: Resistant dextrin; Resis. starch: Resistant starch; Xiloolig.: Xilooligosaccharide

HOMA-IR

From 15 studies, 977 patients were included in the network (Figure 5. Network). According to SUCRA values, the most effective interventions were psyllium (96.67%), β-glucans (73.05%), and resistant dextrin (63.16%) (Figure 5. Rankogram). Psyllium demonstrated statistically significant improvements in HOMA-IR when compared with multiple interventions, including inulin (MD: -5.33; 95% CrI: -9.92, -0.50), inulin plus resistant dextrin (MD: -5.63; 95% CrI: -10.84, -0.12), resistant starch (MD: -6.10; 95% CrI: -11.91, -0.38), brown rice dietary fiber (MD: -6.17; 95% CrI: -12.03, -0.53), no fiber (MD: -6.29; 95% CrI: -10.53, -2.02), fucoidan (MD: -6.69; 95% CrI: -12.42, -0.70), and galacto-oligosaccharide (MD: -7.44; 95% CrI: -14.32, -0.53).

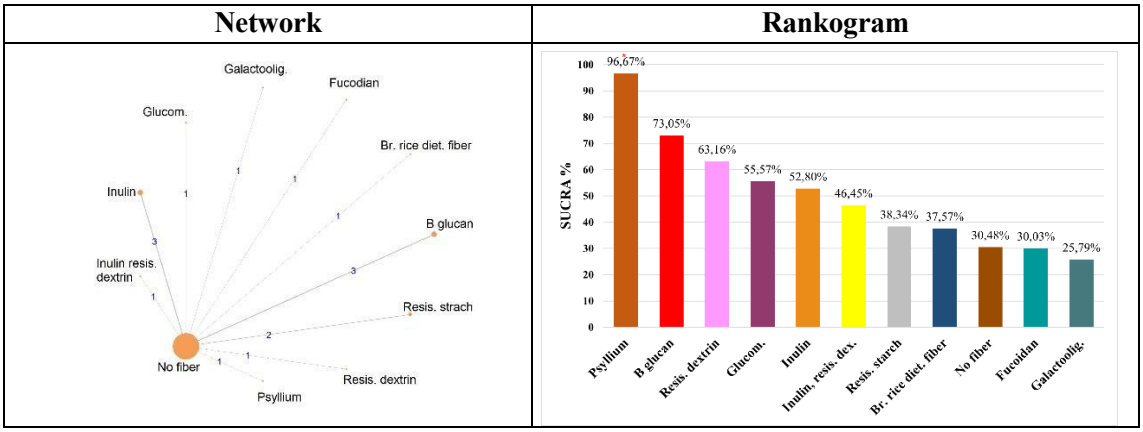


Figure 5. Network plot and rankogram of dietary fiber interventions for HOMA-IR (21).

Br. rice diet. fibre: Brown rice dietary fibre; Galactoolig.: Galactooligosaccharide; Glucom.: Glucomannan; Inulin resis. dex: Inulin with resistant dextrin: Resis. dextrin, Resistant dextrin; Resis. starch: Resistant starch

*Means statistically significant difference was observed when the intervention was compared with another type of fiber or with no fiber.

2-h postprandial glucose level

The network analysis for 2h-PPG included eight studies with a total of 570 patients (Figure 6. Network). Based on SUCRA values, the top-ranked interventions were resistant starch (92.3%), β-glucans (63.48%), and arabinoxylan (51.81%) (Figure 6. Rankogram). A statistically significant reduction in 2h-PPG was observed when resistant starch was compared with no fiber (MD: -5.97 mmol/L; 95% CrI: -10.26, -1.65).

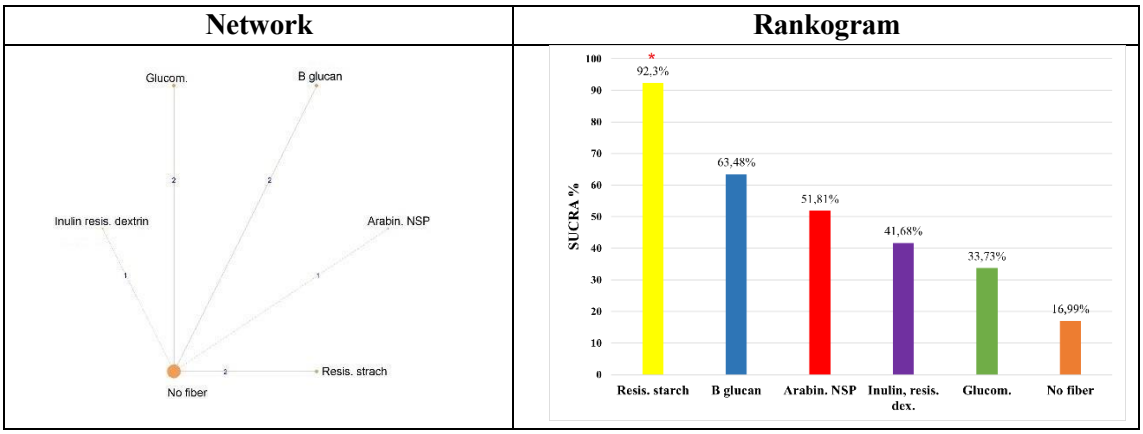


Figure 6. Network plot and rankogram of dietary fiber interventions for 2-hour postprandial glucose level (21).

Arabin. NSP: Arabinoxylan non-starch polysaccharides; Glucom.: Glucomannan; Inulin resis. dex: Inulin with resistant dextrin; Resis. dextrin: Resistant dextrin; Resis. starch: Resistant starch

*Means statistically significant difference was observed when the intervention was compared with no fiber.

8.1.3.2. Lipid profile
Total cholesterol

TC outcome was evaluated across 38 studies comprising 1,817 patients, as shown in Figure 7. Network . According to SUCRA values, the three most effective interventions were xylo-oligosaccharides (84.59%), galactomannans (76.06%), and inulin (70.8%) (Figure 7. Rankogram). A statistically significant reduction in TC was observed when xylo-oligosaccharides were compared with no fiber (MD: -0.95 mmol/L; 95% CrI: -1.86, -0.90).

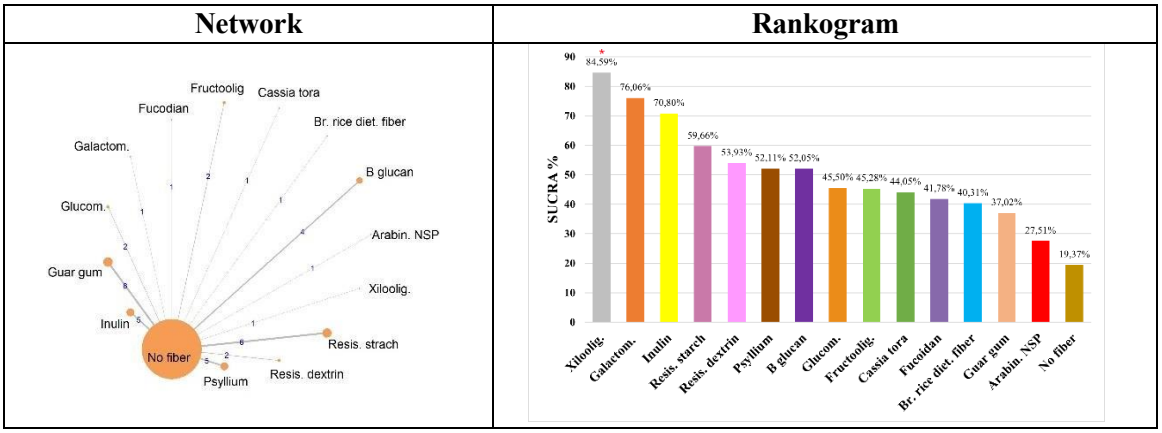


Figure 7. Network plot and rankogram of dietary fiber interventions for total cholesterol (21).

Arabin. NSP: Arabinoxylan non-starch polysaccharides; Br. rice diet. fibre: Brown rice dietary fibre; Fructoolig.: Fructooligosaccharide; Galactom.: Galactomannan; Galactoolig.: Galactooligosaccharide; Glucom.: Glucomannan; Resis. dextrin: Resistant dextrin; Resis. starch: Resistant starch; Xiloolig.: Xilooligosaccharide

*Means statistically significant difference was observed when the intervention was compared with no fiber.

Triglycerides

The network included 34 studies with 1,701 patients (Figure 8. Network). The top three interventions according to SUCRA values were galactomannans (82.77%), xylo-oligosaccharides (78.91%), and inulin (70.83%) (Figure 8. Rankogram). A statistically significant reduction in TG levels was observed when galactomannans were compared with no fiber (MD: -0.57 mmol/L; 95% CrI: -1.06, -0.07).

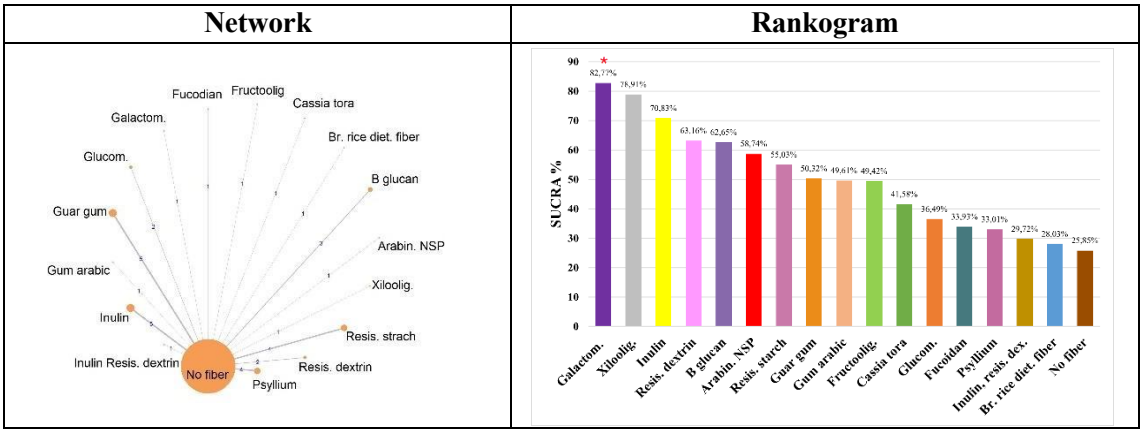


Figure 8. Network plot and rankogram of dietary fiber interventions for triglyceride (21).

Arabin. NSP: Arabinoxylan non-starch polysaccharides; Br. rice diet. fibre: Brown rice dietary fibre; Fructoolig.: Fructooligosaccharide; Galactom.: Galactomannan; Galactoolig.: Galactooligosaccharide; Glucom.: Glucomannan; Inulin resis. dex: Inulin with resistant dextrin; Resis. dextrin: Resistant dextrin; Resis. starch: Resistant starch; Xiloolig.: Xilooligosaccharide

*Means statistically significant difference was observed when the intervention was compared with no fiber.

HDL cholesterol

HDL cholesterol was evaluated across 37 studies, involving a total of 1,851 patients (Figure 9.Network). Based on SUCRA values, the most effective interventions were gum arabic (89.06%), resistant dextrin (83.72%), and inulin (71.92%) (Figure 9. Rankogram). Gum arabic was associated with statistically significant increases in HDL levels compared with no fiber (MD: +0.21 mmol/L; 95% CrI: 0.02, 0.39) and β-glucans (MD: +0.23 mmol/L; 95% CrI: 0.03, 0.42). Similarly, resistant dextrin was significantly more effective than no fiber (MD: +0.16 mmol/L; 95% CrI: 0.02, 0.31) and β-glucans (MD: +0.18 mmol/L; 95% CrI: 0.02, 0.35).

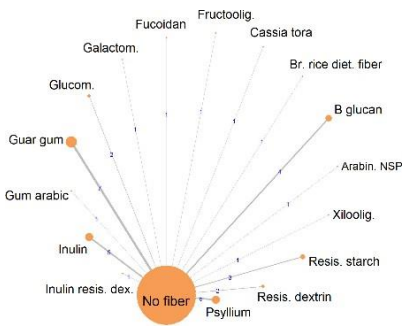
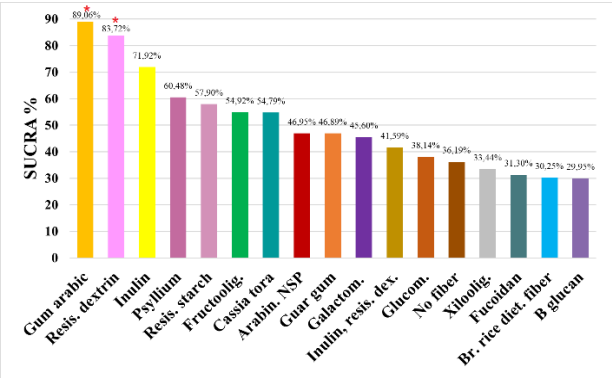
Network	Rankogram
	

Figure 9. Network plot and rankogram of dietary fiber interventions for HDL (21).

Arabin. NSP: Arabinoxylan non-starch polysaccharides; Br. rice diet. fibre: Brown rice dietary fibre; Fructoolig.: Fructooligosaccharide; Galactom.: Galactomannan; Galactoolig.: Galactooligosaccharide; Glucom.: Glucomannan; Inulin resis. dex: Inulin with resistant dextrin; Resis. dextrin: Resistant dextrin; Resis. starch: Resistant starch; Xiloolig.: Xilooligosaccharide

*Means statistically significant difference was observed when the intervention was compared with another type of fiber or with no fiber.

LDL cholesterol

In the analysis of LDL cholesterol, 1,778 patients across 35 studies contributed data (Figure 10. Network). Among the dietary fibers, galactomannans and inulin emerged as the most effective, with SUCRA values of 86.56% and 85.86%, respectively, followed by xylo-oligosaccharides (61.51%) (Figure 10. Rankogram). Both galactomannans and inulin showed statistically significant reductions in LDL levels when compared with no fiber. Galactomannans led to a mean difference of -0.81 mmol/L (95% CrI: -1.53, -0.08), while inulin achieved a similar effect (MD: -0.71 mmol/L; 95% CrI: -1.30, -0.12), supporting their potential clinical utility in lipid management.

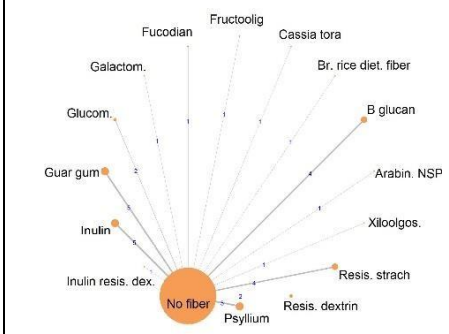
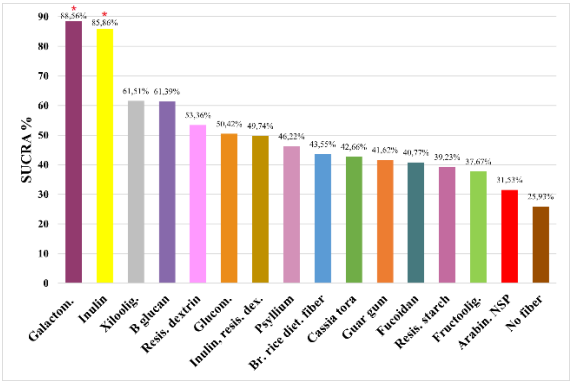
Network	Rankogram
	

Figure 10. Network plot and rankogram of dietary fiber interventions for LDL (21).

Arabin. NSP: Arabinoxylan non-starch polysaccharides; Br. rice diet. fibre: Brown rice dietary fibre; Fructoolig.: Fructooligosaccharide; Galactom.: Galactomannan; Galactoolig.: Galactooligosaccharide; Glucom.: Glucomannan; Inulin resis. dex: Inulin with resistant dextrin; Resis. dextrin: Resistant dextrin; Resis. starch: Resistant starch; Xiloolig.: Xilooligosaccharide

*Means statistically significant difference was observed when the intervention was compared with another type of fiber or with no fiber.

8.1.4. Results of the qualitative analysis

A total of 13 studies were included in the qualitative synthesis. In eight of these, the control group received non-soluble dietary fibers (74-81). Two studies did not specify the type of fiber used (82, 83). and in three trials, some outcomes were reported only as medians rather than means (41, 51, 58). Most studies indicated significant differences in outcomes between soluble and non-soluble fiber groups. Trials with control groups receiving no dietary fiber consistently showed superior results in favor of the dietary fiber intervention. The supplementary appendix of the original article provides an overview of the detailed findings from these RCTs (21).

8.1.5. Risk-of-bias assessment and certainty of evidence

Most studies were judged to have a low risk of bias; however, 17 trials were rated as having “some concerns,” particularly in the domains of randomization process, missing outcome data, and outcome measurement. The certainty of evidence across comparisons ranged from low to high, with the majority of studies rated as having low or moderate

certainty due to imprecision, primarily related to wide credible intervals. No signs of inconsistency were detected across outcomes. A detailed assessment of the risk of bias and certainty of evidence for each study is available in the supplementary material of the original publication (21).

8.2. Study II.

8.2.1 Search and selection

We identified 1,309 records through systematic searching. After removal of duplicates and application of eligibility criteria, 27 studies were deemed suitable for inclusion in the qualitative and quantitative syntheses. The study selection process is illustrated in Figure 11.

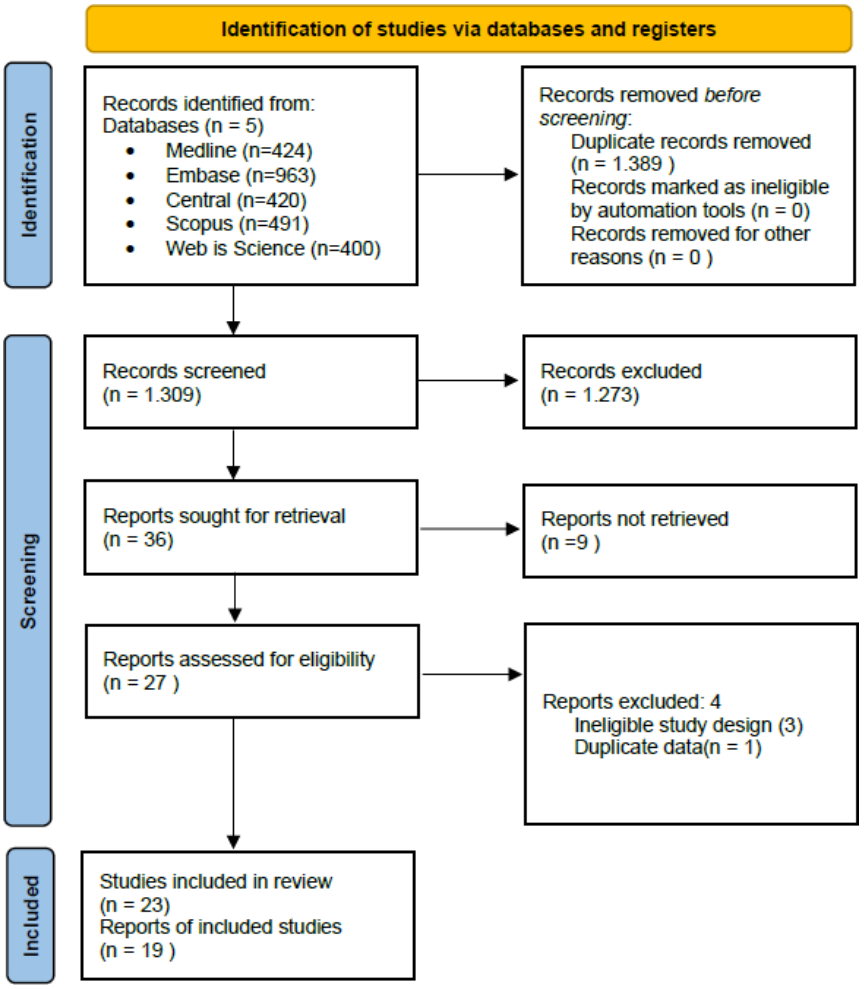


Figure 11. PRISMA Flow Diagram of the screening and selection process for Study II.(22)

8.2.2. Main characteristics of included studies

Baseline characteristics of the studies included in both the quantitative and qualitative syntheses are presented in Table 3. A total of 800 patients were involved across the trials, with study durations ranging from 4 to 24 weeks. The interventions assessed included 10 different dietary approaches and metformin.

Table 3. Basic characteristics of the included studies (22)

First author, year	Country	Study period (weeks)	Number of patients	Mean age (SD) Intervention /Control group	BMI kg/m^2(SD) Intervention /Control group	Medication[3]	Intervention	Control	Outcome
Agowska,2021 (84)	Poland	8	35	16.8 (1.3)	>95th percentile	No	Low-calorie	Metformin	Weight, FBG, FI,HOMA-IR
Asemi, 2014 (85)	Iran	8	48	30.7(6.7)/ 29.4(6.2)	29.1(3.2)/ 31.5(5.7)	No	DASH	Normal	BMI,Weight, FBG,FI, HOMA-IR
Asemi, 2015 (86)	Iran	8	48	22.1(3.2)/ 24.7(6.0)	30.3(4.5)/ 28.6(5.8)	No	DASH	Normal	LDL, HDL, TC, TG
Azadi-Yazdi, 2017 (87)	Iran	12	55	32.1(5.9)/ 31.7(6.2)	31.9(4.1)/ 30.2(3.2)	No	DASH	Normal	BMI, Weight, TT
Esfahanian, 2013 (88)	Iran	12	30	20(4.6)/ 21.9(9.3)	34.1(5.4)/ 31.1(3.3)	No	Low-calorie	Metformin	BMI, FBG, FI, HOMA-IR, TT, LDL, HDL, TC, TG
Foroozanfard, 2017 (89)	Iran	12	60	27.1(4.7)/ 25.6(3.7)	32.3(4.6)/ 32.2(3.9)	N/A	DASH	Normal	BMI, Weight, FBG, FI, HOMA-IR, TT, FSH, LH
Galletly, 2007 (90)	Australia	16	27	33(1.2)/ 32(1.2)	37.6(6.4)/ 34.5(5.7)	No	Low-P	High-P	BMI, Weight

Gower, 2013 (91)	United States of America	8	30	31.2(5.8)	31.8(5.7)	No	Low-carb	Normal	FI, HOMA-IR, TT, FSH, LH, LDL, HDL, TC, TG
Marzouk, 2015 (92)	Egypt	24	60	19.3(1.3)/ 20.1(1.8)	36.0(4.7)/ 35.8(4.8)	No	Low-calorie	Normal	BMI, Weight, FBG
Mehrabani, 2012 (93)	Iran	12	49	28.5(5.2)/ 30.5(6.4)	31.1(4.6)/ 31.9(4.0)	No	Low-calorie	Normal	FI, HOMA-IR, TT, FSH, LH, LDL, HDL, TC, TG
Mei, 2022 (94)	China	12	59	27.9(5.3)/ 28.07(7.1)	39.3(2.2)/ 29.5(2.4)	No	Mediterranean	Low-fat	BMI
Moran, 2003 (95)	Australia	16	28	32(1.2)/ 33(1.2)	37.9(1.6)/ 37.7(1.9)	No	High-P	Low-P	FBG, FI, LDL, HDL, TC, TG
Nadjarzadeh, 2021 (96)	Iran	12	32	28.8(6.5)/ 29.4(6.6)	33.9(5.3)/ 32.8(5.3)	No	Low-calorie	High-P	BMI, Weight, TT
Panico, 2014 (97)	Italy	12	14	28.7(4.9)	28.7(4.9)	No	Low-GI	Normal	BMI, Weight, FBG, FI, HOMA-IR, TT, FSH, LH, TC, TG
Qublan, 2007 (98)	Jordan	24	46	31.5(19-38)/ 30.8(20-37)	32.2(29-43)/ 31.9(29-44)	No	High-P	Metformin	FBG, FI, FSH, LH
Sorensen, 2012 (99)	Denmark	24	27	27.7(5.5)/ 28.4(5.8)	30.6(7.8)/ 30.5(8.5)	No	High-P	Normal	BMI, Weight, FBG, TT, LDL, HDL, TC
Stamets, 2004 (100)	United States of America	4	26	29(4)/26(4)	38(4)/37(5)	No	High-P	Low-calorie	Weight, TT, FSH, LH, LDL, HDL, TC, TG
Toscani, 2011 (101)	Brazil	8	18	22.7(5.6)/ 29.5(5.7)	> 25 kg/m2	No	High-P	Low-calorie	Weight, FBG, LDL, HDL, TC

Wong, 2016 (102)	United States of America	24	16	15.4(1.3)/ 16.3(2.2)	36.2(5.3)/ 33.9(4.7)	No	Low-GI	Low-fat	BMI, FBG, FI, TT, TC, TG
Articles in the qualitative synthesis									
Mittal,2020 (103)	India	12	21	33.1 (4.4)/ 34.4 (5.0)	33.7 (4.8)/ 32.2 (5.9)	No	Vegan	Low- calorie	BMI, Weight
Ornstein,2011 (104)	United States of America	12	16	15.8 (2.2)	35.7 (6)	No	Low- carbohydrate	Low-fat	Weight
Sordia-Hernández, 2016 (105)	Mexico	12	37	26.1 (4.1)/ 26.1 (4.7)	N/A	N/A	Low-glycemic	Normal	Weight
Turner-McGrievy ,2014 (106)	United States of America	24	18	27.8 (4.5)	39.9 (6.1)	No	Vegan	Low-calorie	Weight

N/A: not available; 3Medication that might affect the patients' physiology during the intervention (lipid-lowering, anti-obesity, oral antidiabetic drug, hormonal therapy)

DASH: Dietary approaches to stop hypertension; Low-calorie + M: Low-calorie diet plus metformin; Low-carb: Low- carbohydrate diet; High-P: High-Protein diet; Low-GI: Low-Glycemic Index diet; Low-P: Low-Protein diet; FBG: fasting blood glucose; FI: fasting insulin; TG: triglyceride; TC: cholesterol; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; TT: total testosterone; FSH: follicle-stimulating hormone; LH: luteinizing hormone

8.2.3. Results of the quantitative analysis

The structure of the intervention networks corresponding to each outcome is illustrated in Figure 12.

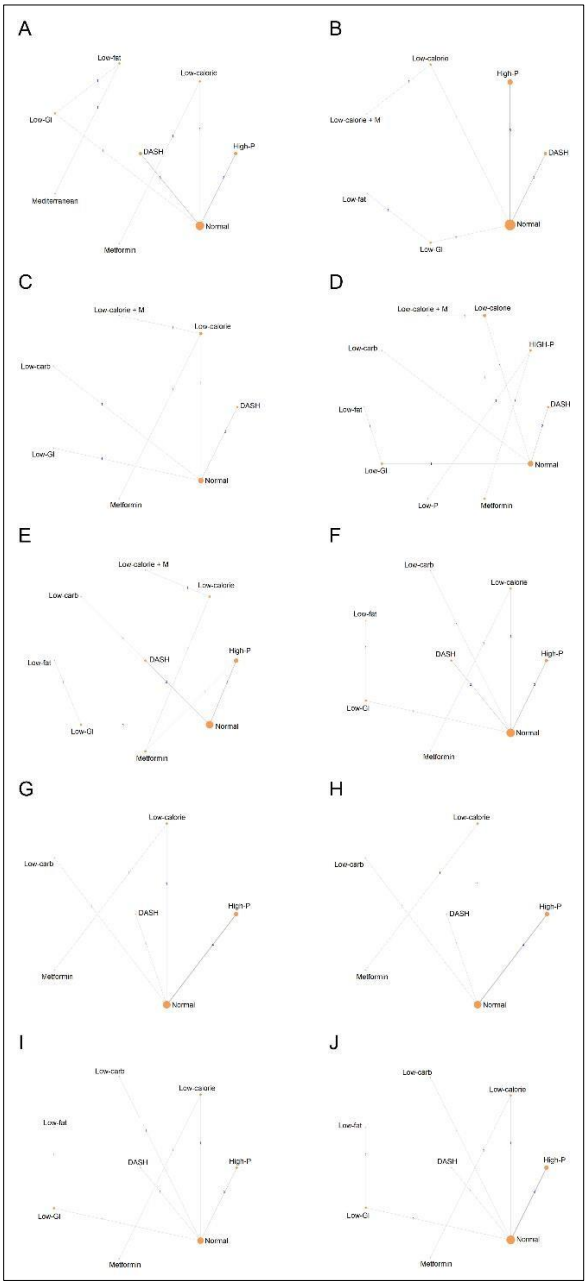


Figure 12. The network interventions regarding each outcomes (22).

The size of the node is proportional to the number of studies. The thickness of the edges is proportional to the number of trials with a direct comparison. **A**: BMI, **B**: Body weight, **C**: HOMA-IR, **D**: FI, **E**: FBG, **F**: TT, **G**: LDL, **H**: HDL, **I**: TG, **J**:TC

DASH: Dietary approaches to stop hypertension; Low-calorie + M: Low-calorie diet plus metformin; Low-carb: Low- carbohydrate diet; High-P: High-Protein diet; Low-GI: Low-Glycemic Index diet; Low-P: Low-Protein diet

8.2.3.1. Anthropometric measures

BMI

The network included 11 studies encompassing 8 interventions and a total of 428 patients for BMI outcome (Figure 12A). The low-calorie diet ranked highest in effectiveness based on SUCRA values (73.58%) (Table 4). No statistically significant differences in BMI change were observed in any of the pairwise comparisons among the interventions included in the network.

Body weight

For body weight, the network included 12 studies investigating 7 interventions with a total of 418 patients (Figure 12B). The combination of a low-calorie diet with metformin was ranked as the most effective intervention based on SUCRA values (73.7%) (Table 4). Statistically significant reductions in body weight were observed in several comparisons: low-fat diet versus low-GI diet (MD = -3.59; 95% CrI: -6.03, -1.08), DASH diet versus high-protein diet (MD = -2.88; 95% CrI: -4.96, -0.89), and DASH diet versus normal diet (MD = -1.67; 95% CrI: -3.20, -0.34).

8.2.3.2. Glycemic levels

HOMA-IR

A total of 286 participants from 7 trials contributed to the HOMA-IR network analysis, covering 7 dietary interventions (Figure 12C). The DASH diet was ranked as the most effective intervention, with a SUCRA value of 80.47% (Table 4). Moreover, the DASH diet showed a statistically significant improvement compared to the normal diet (MD = -1.10; 95% CrI: -2.05, -0.03).

Fasting insulin level

FI outcome were derived from 10 studies including 376 patients and 10 dietary interventions (Figure 12D). Once again, the DASH diet was ranked as the most effective

intervention, with a SUCRA value of 79.73% (Table 4) No statistically significant differences were observed between any of the interventions.

Fasting blood glucose level

The analysis of FBG included 11 studies, 9 interventions, and 372 patients (Figure 12E). Once again, the DASH diet ranked as the most effective intervention for lowering FBG levels, with a SUCRA value of 76.6% (Table 4) However, no statistically significant differences were found in any of the pairwise comparisons among the included interventions.

8.2.3.3. Hormonal measures

Total testosterone level

Total testosterone outcome was assessed across 10 studies involving 8 interventions and 359 patients (Figure 12F). Based on SUCRA values, metformin emerged as the most effective intervention for reducing total testosterone levels (71.28%) (Table 4). For this outcome, similarly to several others, no statistically significant differences were found between the interventions.

8.2.3.4. Lipid levels

LDL cholesterol level

The network of LDL was analysed based on 8 studies, including 6 interventions and a total of 276 patients (Figure 12G). Metformin was ranked as the most effective intervention, with a SUCRA value of 78.08% (Table 4). No statistically significant differences were observed in the pairwise comparisons between the included interventions.

HDL cholesterol level

HDL cholesterol was evaluated across 8 studies, comprising 6 interventions and 276 patients (Figure 12H). Interestingly, the normal diet ranked as the most effective intervention, with a SUCRA value of 65.69% (Table 4) However, as with previous lipid outcome, no statistically significant differences were observed in the pairwise comparisons for HDL levels.

Triglyceride level

Eight studies, with 261 patients, were included in the network (Figure 12I).The DASH diet ranked as the most effective intervention, with a SUCRA value of 82.07% (Table 4). However, consistent with previous outcomes, no statistically significant differences were observed in any of the pairwise comparisons.

Total cholesterol level

Regarding TC level, the network included 10 studies and 8 interventions with 306 patients (Figure 12J). Among the interventions, the low-carbohydrate diet ranked highest in effectiveness with a SUCRA value of 69.68% (Table 4). Again, no statistically significant differences were found between the interventions in the pairwise comparisons.

The relative ranking of dietary interventions for each outcome was determined using SUCRA values and ranking probabilities. It is important to interpret these rankings with caution, as the frequency of interventions varied considerably. For instance, the Mediterranean and low-protein diets demonstrated extreme SUCRA values but were each represented in only a single RCT. The full results are presented in Table 4.

Table 4 Interventions' SUCRA% regarding each outcomes (22).

Dietary approaches	SUCRA %	Anthropometric measurements		Glycemic factors			Lipid factors				Hormonal parameters	Summary ranking
		BMI	Body Weight	HOMA-IR	FBG	FI	TC	TG	HDL	LDL	TT	All outcomes combined
DASH		57.1	53.3*	**80.4***	**76.6**	**79.7**	61.8	**82.1**	61.8	44.4	54.5	64.8
High-P		29.6	17.9	-	50.0	39.3	43.9	53.6	23.6	54.9	18.4	36.8
Low-calorie		**73.6**	69.9	59.1	20.1	67.5	51.8	38.7	56.8	41.5	61.9	54.1
Low-carb		-	-	50.7	73.4	52.9	**69.7**	46.7	55.2	22.5	67.4	54.8
Low-fat		60.1	60.6		51.1	61.2	52.5	43.6	-	-	51.4	54.4
Low-GI		36.6	35.3	32.6	40.4	34.8	53.8	64.1	-	-	44.8	42.8
Low-P		-	-	-	-	16.0	-	-	-	-	-	16.0
Mediterranean		65.6	-	-	-	-	-	-	-	-	-	65.6
Low-calorie + M		-	**74.4**	59.6	31.4	64.5	-	-	-	-	-	57.5
Metformin		38.5	-	30.9	54.5	37.9	23.7	28.5	36.6	**78.1**	**71.2**	44.4
Normal		38.8	35.8	36.6	52.5	46.1	42.6	42.6	**65.7**	58.4	30.1	44.9

SUCRA values range from 0 to 100%. The higher the SUCRA value, and the closer to 100%, the higher the likelihood that intervention is in the top rank or one of the top ranks. The top interventions are in bold text. *Means statistically significant difference was observed when the intervention was compared with normal diet. FBG: fasting blood glucose; FI: fasting insulin; TG: triglyceride; TC: cholesterol; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; TT: total testosterone; DASH: Dietary approaches to stop hypertension; Low-calorie + M: Low-calorie diet plus metformin; Low-carb: Low- carbohydrate diet; High-P: High-Protein diet; Low-GI: Low-Glycemic Index diet; Low-P: Low-Protein diet

8.2.4. Results of the qualitative analysis

Ten studies were reviewed qualitatively due to limitations in the available data. In six of these, insufficient information was reported for FSH and LH outcomes (89, 91, 93, 97, 98, 100). Most studies reported no significant changes in FSH or LH levels following treatment, and no differences were observed between intervention and control groups. In two RCTs, body weight and BMI were reported as percentage changes, which were not included in the statistical analysis (103, 104). Mittal et al. observed a significant reduction in body weight and BMI in the vegan diet group, while Ornstein et al. reported body weight changes that were not statistically significant. In one study, the standard deviation (SD) for post-intervention body weight was not reported (105), although the authors stated that body weight reduction occurred without reaching statistical significance. In a study, data were reported as medians (106). However, the results indicated that participants following a vegan diet lost significantly more body weight than those who followed a low-calorie diet.

8.2.5. Risk of bias assessment and certainty of the evidence

Risk of bias assessments summarised the overall quality of the included studies. Most studies were rated as having some concerns, while three trials showed a high risk of bias, mainly related to the "missing outcome data" domain.

The certainty of evidence for each comparison ranged from low to high, with lower certainty typically attributed to imprecision, such as wide confidence intervals. No inconsistency was detected across any of the outcomes based on the results of the inconsistency tests. Detailed evaluations and supporting materials can be found in the supplementary files of the original publication (22).

9. DISCUSSION

9.1. Summary of findings, international comparisons for Study 1

According to the Dietary Guidelines for Americans, individuals with or at risk for type 2 diabetes are encouraged to consume at least 14 grams of dietary fiber per 1,000 kcal per day, with an emphasis on whole, intact grains (9). The European Association for the Study of Diabetes (EASD) recommends that adults with diabetes aim for at least 16.7 g/1,000 kcal (8). These two recommendations are closely aligned and both exceed the World Health Organization's general population guideline of at least 25 grams of dietary fiber per day (107). All three organizations recognize these as minimum intake levels, noting that higher intakes are associated with greater health benefits. Our Study I contributes to this growing evidence by identifying which of 16 different dietary fibers may be most effective, even when consumed as a supplement. We aimed to examine the role of soluble dietary fibers in the management of T2DM, with a focus on both glycemic and lipid parameters. These biomarkers are not only relevant for short-term metabolic control but also for improving long-term outcomes and reducing the risk of cardiovascular complications.

Galactomannans exerted the most effective on lowering **HbA1c, FBG, TG,** and **LDL** levels in our first NMA. These findings are consistent with those of a 2016 meta-analysis, which also demonstrated reductions in TG and LDL, as well as significant decreases in HbA1c and fasting blood glucose (FBG) following supplementation with fenugreek, whose seeds contain high levels of galactomannan (108). Since the publication of our original article, more recent evidence has emerged that further supports our findings. The researchers reported that fenugreek consumption reduced fasting blood glucose by 3.7 mg/dL and HbA1c by 0.88%, with the reduction in HbA1c reaching statistical significance (109). It is also important to note that the study included in our analysis assessed only FBG and HbA1c from glycemic factors. Therefore, it is possible that galactomannans could also have a beneficial effect on other glycaemic parameters, if these had been evaluated. Galactomannans have been shown to exert anti- diabetic effects through multiple mechanisms. They can prolong gastric emptying time and reduce glucose absorption in the small intestine, thereby slowing carbohydrate metabolism and lowering postprandial blood glucose levels. In addition, they have been reported to stimulate glycogen synthase activity, promoting the replenishment of glycogen stores in the liver and muscle. This regeneration of depleted glycogen may

contribute to reduced pro-inflammatory cytokine production, modulation of pancreatic enzyme activity, and improvement in serum lipid profiles, as well as enhancement of insulin-sensitive carbohydrate metabolic enzymes (109). Galactomannans, the main bioactive component in fenugreek, are polysaccharides composed of galactose and mannose in varying ratios, and are widely used in the food industry as stabilizers and additives. The common dietary sources of galactomannans include guar gum and fenugreek. While in Asian countries galactomannan-rich preparations, are more widely used for traditional medicinal purposes, in Hungary and many Western countries, fenugreek is primarily known and used as a culinary spice only.

Our results indicated that β-glucans were the most effective dietary fiber in reducing **FI** levels when compared with other fiber types. β-glucans are naturally occurring polysaccharides found in a variety of food sources, including oats, barley, mushrooms, and seaweeds. Although in our study β-glucans showed the most pronounced effect only on FI levels, their health benefits have nonetheless been acknowledged by the European Food Safety Authority (EFSA). EFSA has approved health claims stating that β-glucans from oats and barley can contribute to the maintenance of normal blood cholesterol levels and help reduce postprandial glycaemic responses, provided they are consumed in sufficient quantities. To achieve this effect, people need to consume at least 3 grams of oat or barley β-glucan per day (13). Previous research also supports the glycaemic benefits of oat- β-glucan, showing that an intake of 2.5–3.5 g/day for 3–8 weeks in T2DM patients significantly lowered FBG and HbA1c levels (118). The high viscosity of cereal-derived β-glucans slows nutrient absorption in the small intestine, which can lead to improved insulin response and reduced postprandial hyperglycemia. Moreover, β-glucans form a viscous gel that binds bile acids, compounds synthesized from cholesterol, thus preventing their reabsorption. This process leads to increased bile acid excretion and prompts the liver to convert more cholesterol into bile acids, ultimately lowering circulating LDL cholesterol levels. Additionally, β-glucans are fermented by the gut microbiota, producing SCFAs such as propionate, which have been shown to inhibit hepatic cholesterol synthesis, further contributing to their cholesterol-lowering effects (110).

Psyllium demonstrated the strongest effect on lowering **HOMA-IR** in our analysis. Psyllium is a viscous, functional soluble fiber that can delay intestinal transit time, promote satiety, and slow the absorption of glucose, thereby attenuating the postprandial

glycaemic response (121). In addition to its effects on glycemic control, previous studies have also reported favorable outcomes regarding lipid profiles (29, 111).

Resistant starch proved to be the most effective intervention for reducing **2h-PPG** levels in patients with T2DM. The health effects of resistant starch have been widely studied, and multiple types (RS1–RS5) are distinguished based on their structure and resistance to digestion. Among the studies included in our NMA, type 2 resistant starch (RS2), primarily high-amylose maize starch, was the most commonly investigated. Our findings are consistent with previous research demonstrating that RS2 can significantly reduce postprandial glucose levels in individuals with type 2 diabetes, further supporting its potential role in glycemic management (119). Natural dietary sources of resistant starch include grains, seeds, legumes, pasta, potatoes, and unripe bananas (120).

In our study, xylo-oligosaccharides (XOS) were found to be the most effective in reducing **TC** levels. XOS are non-viscous oligosaccharides with primarily prebiotic properties. Their cholesterol-lowering effect is considered to be indirect, largely mediated through modulation of the gut microbiota. This microbial activity may lead to reduced expression of lipogenic enzymes, decreased cholesterol absorption, and enhanced fecal excretion of bile acids and cholesterol, ultimately contributing to improved lipid profiles (69). The concentrations of XOS in natural food sources are relatively low; therefore, to achieve its documented health benefits, consumption through fortified foods or dietary supplements is often considered more advantageous.

According to our findings, gum arabic was the most effective fiber in increasing **HDL** levels. It is a non-viscous, soluble fiber, naturally derived from the dried exudates of Acacia senegal and Acacia seyal. Usually it is used as a food additive, usually as a emulsifier, thickener, and binder. Its mechanism in lipid metabolism is likely similar to XOS (112).

9.2 Summary of findings, international comparisons for Study 2

The aim of the second MNA was to establish a ranking of the interventions used in the treatment of PCOS and to identify which dietary approach was the most effective in improving anthropometric, glycemic, lipid, and hormonal parameters in affected individuals. Current international recommendations for the management of PCOS also highlight the importance of lifestyle interventions. According to evidence-based guidelines, lifestyle modifications- whether exercise alone or a combination of dietary

changes, physical activity, and behavioral strategies - should be recommended to all women with PCOS to support improvements in metabolic health, including central adiposity and lipid profile. At the same time, it is emphasized that there is currently no strong evidence to support the superiority of any specific diet composition over another in terms of anthropometric, metabolic, hormonal, reproductive, or psychological outcomes (3).

Our results demonstrated considerable heterogeneity across the different outcomes. However, the DASH diet showed statistically significant effects on body weight and HOMA- IR. In addition, based on SUCRA percentages, the DASH diet ranked highest for **HOMA- IR, FI, FBG**, and **TG** outcomes. We also observed that calorie restriction was associated with favorable effects on **body weight** reduction, suggesting its potential as an effective dietary strategy in the management of PCOS-related obesity. These results are consistent with a previous meta-analysis including 19 trials (1,193 women with PCOS), which suggested that both the DASH diet and calorie-restricted diets are likely to be optimal for reducing insulin resistance and improving body composition in women with PCOS (113). The DASH diet, in particular, may exert beneficial effects on glycemic control by enhancing β-cell function, lowering glucose and HbA1c levels, and improving insulin sensitivity (114).

Our analysis indicates that the Mediterranean diet may be an effective dietary intervention for reducing **BMI**. However, this finding is based on limited evidence, as only one trial included in the analysis specifically assessed the effects of the Mediterranean diet. This diet is a promising and widely studied dietary pattern, associated with numerous health benefits across a range of chronic conditions, including cardiovascular disease, type 2 diabetes, and metabolic syndrome. It is characterized by a high intake of fruits, vegetables, whole grains, legumes, nuts, and olive oil; moderate consumption of fish and poultry; low consumption of red and processed meats; and a moderate intake of red wine during meals. Its balanced and nutrient-rich composition contributes to anti-inflammatory and antioxidant effects, as well as improved metabolic outcomes. Due to its cultural, historical, and nutritional significance, the Mediterranean diet was inscribed on the UNESCO Representative List of the Intangible Cultural Heritage of Humanity in 2010 (115).

For the **TC** outcome, the low-carbohydrate diet proved to be the most effective

intervention. This result is particularly interesting considering the macronutrient composition of the diet, characterized by higher fat and lower carbohydrate intake, yet still associated with improvements in lipid profiles. The authors of the included study suggest that these changes are likely mediated by weight loss achieved during the intervention (91).

In terms of **LDL** and **TT** levels, treatment with metformin was found to be the most effective based on SUCRA rankings, outperforming all dietary interventions. For **HDL** levels, however, none of the dietary interventions demonstrated greater effectiveness compared to the standard diet. These findings suggest that dietary modifications alone may not exert a sufficiently strong effect to achieve statistically significant changes in certain outcomes. While improvements in body weight and glycemic parameters appear to be more readily attainable through diet, changes in lipid and hormonal markers are less consistently observed and may require additional or combined interventions. Similar findings were reported in another NMA, where the authors concluded that interventions combining diet, exercise, and weight-lowering medications were among the most effective in improving hormonal profiles, particularly in reducing testosterone levels (116).

9.2. Strengths

To our knowledge, these were the first network meta-analyses to evaluate the effects of soluble dietary fibers in type 2 diabetes (Study I) and to rank dietary interventions in women with PCOS (Study II). A major strength of Study I is its large sample size (2,865 participants) and the inclusion of 16 different types of dietary fiber, enabling comprehensive comparisons. Study II stands out for covering most clinically relevant parameters in PCOS and for identifying a potentially beneficial dietary approach to support clinical decision-making. Both studies employed rigorous and transparent methodology, contributing to the robustness and credibility of the findings.

9.3. Limitations

Despite the strengths, both studies have several limitations. First, the number of direct comparisons was limited, reducing the strength of head-to-head evidence. In Study I, the formulations and dosages of fiber supplements varied across trials, and background factors such as participants' diets, medications, and physical activity levels were often not controlled. The choice of placebo also differed, with some studies used sugar instead of maltodextrin, potentially influenced metabolic outcomes.

In Study II, limitations included the small overall sample size and variability in participants' age and ethnicity, which is particularly relevant given that PCOS phenotypes and clinical presentations may differ across populations. Most trials lacked information on the specific PCOS phenotype, which may have influenced treatment response. Additionally, the duration of interventions varied across studies, and the practicality of implementing certain diets, such as the DASH diet, may differ depending on cultural and environmental factors.

10. CONCLUSIONS

Although dietary fiber intake is widely promoted in national nutrition guidelines, recommendations rarely specify fiber types. Based on our findings, galactomannans appear to be the most beneficial soluble dietary fiber in the management of type 2 diabetes, demonstrating consistent improvements across multiple glycemic and lipid outcomes. These results support galactomannans as a promising adjunctive therapy for patients with type 2 diabetes.

In the context of PCOS, effective dietary management remains a challenge due to heterogeneous evidence. Our network meta-analysis suggests that the DASH diet may be the most effective option for improving metabolic and hormonal parameters, particularly in patients who cannot tolerate metformin. Notably, diets that focus on improving food quality and reducing total energy intake, without altering macronutrient ratios, were generally more effective than macronutrient-modifying approaches, such as high-protein diets.

Together, these findings highlight the importance of evidence-based, targeted dietary strategies in managing both type 2 diabetes and PCOS.

11. IMPLEMENTATION FOR PRACTICE

Considering that most of the patients with type 2 diabetes are advised to limit their daily carbohydrate intake, reaching the recommended 35-40 grams of fiber per day through diet alone can be difficult. This is especially true since the richest sources of fiber, such as whole grains, legumes, and fruits, also contain significant amounts of simple carbohydrates. Vegetables are an exception but are often consumed in insufficient quantities. Therefore, fiber supplementation should be more strongly recommended by both diabetologists and dietitians as a practical and effective adjunct to medical therapy in the management of type 2 diabetes.

In the case of PCOS, where no specific dietary protocol has been universally accepted, our findings provide clear guidance for clinical practice. Highlighting the DASH diet as a beneficial and well-tolerated adjunct dietary strategy, particularly for patients who are unable to tolerate metformin due to gastrointestinal side effects, or as a potential means of facilitating glycaemic and hormonal control with lower pharmacologic doses.

Our results may support dietitians in developing evidence-based, individualized dietary strategies for patients with metabolic disorders. As effective dietary counseling by qualified professionals plays a key role in managing metabolic disorders, our findings contribute valuable guidance for clinical nutrition practice (117).

12. IMPLEMENTATION FOR RESEARCH

There is a clear need for more randomized controlled trials with larger sample sizes and longer follow-up periods to confirm and extend current findings. Based on our results, there are differences in the effects of certain types of fiber, so it is worth examining the different fiber types individually. High-quality, long-term studies are particularly needed to evaluate the clinical effects of newer soluble fibers (e.g.: xylo-oligosaccharides), as well as to explore the potential of non-soluble dietary fibers in improving glycemic and lipid parameters in patients with type 2 diabetes. Additionally, given that our first planned meta-analysis could not be conducted due to the limited number of eligible studies, further research on the role of dietary fibers in polycystic ovarian syndrome is also needed. The potential benefits of fiber supplementation in related metabolic and endocrine disorders, such as obesity and PCOS, should be systematically investigated to inform future dietary guidelines and therapeutic strategies.

13. IMPLEMENTATION FOR POLICYMAKERS

In both type 2 diabetes and polycystic ovary syndrome, dietary therapy plays a central role in improving clinical outcomes. Therefore, it is essential that health policies explicitly emphasize the involvement of dietitians as key members of the multidisciplinary care team. Physicians should be encouraged to refer patients to qualified dietitians for individualized nutrition counseling, particularly when initiating or modifying dietary interventions. Integrating dietitians more systematically into standard care pathways may not only improve health outcomes but also reduce healthcare costs by preventing complications and reducing the need for pharmacological or hospital-based interventions.

Ultimately, investing in dietary intervention is more cost-effective than treating advanced diseases.

14. FUTURE PERSPECTIVES

In the coming years, dietary therapy is expected to play an increasingly central role in the management of metabolic and endocrine disorders. Research into specific fiber types and structured dietary interventions, such as galactomannans in type 2 diabetes and the DASH diet in PCOS, highlights the potential of nutrition-based strategies to improve clinical outcomes beyond standard pharmacological care. As interest in the gut microbiome continues to grow, the metabolic effects of dietary fibers, particularly their impact on blood glucose and lipid levels, are also expected to gain increasing attention. With accumulating evidence, these interventions may soon become integral components of first-line therapy, offering effective, well-tolerated, and sustainable options for long-term disease management.

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16.1. Publications related to the thesis

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D1, IF: 6,5

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16.2. Publications not related to the thesis

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18.PUBLICATIONS

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Original Research Article

Galactomannans are the most effective soluble dietary fibers in type 2 diabetes: a systematic review and network meta-analysis

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A B S T R A C T

Background: Soluble dietary fibers are known to reduce the levels of blood glucose and lipids in patients with type 2 diabetes mellitus (type 2 diabetes). Although several different dietary fiber supplements are utilized, to our knowledge, no previous study has ranked their efficacy yet.

Objectives: We performed this systematic review and network meta-analysis to rank the effects of different types of soluble dietary fibers.

Methods: We performed our last systematic search on November 20, 2022. Eligible randomized controlled trials (RCTs) included adult patients with type 2 diabetes and compared the intake of soluble dietary fibers with that of another type of dietary fiber or no fiber. The outcomes were related to glycemic and lipid levels. The Bayesian method was used to perform a network meta-analysis and calculate the surface under the cumulative ranking (SUCRA) curve values to rank the interventions. The Grading of Recommendations Assessment, Development, and Evaluation system was applied to evaluate the overall quality of the evidence.

Results: We identified 46 RCTs, including data from 2685 patients who received 16 types of dietary fibers as intervention. Galactomannans had the highest effect on reducing the levels of HbA1c (SUCRA: 92.33%) and fasting blood glucose (SUCRA: 85.92%). With regard to fasting insulin level, HOMA-IR, β-glucans (SUCRA: 73.45%), and psyllium (SUCRA: 96.67%) were the most effective interventions. Galactomannans were ranked first in reducing the levels of triglycerides (SUCRA: 82.77%) and LDL cholesterol (SUCRA: 86.56%). With regard to cholesterol and HDL cholesterol levels, xylo-oligosaccharides (SUCRA: 84.59%) and gum arabic (SUCRA: 89.06%) were the most effective fibers. Most comparisons had a low or moderate certainty of evidence.

Conclusions: Galactomannans were the most effective dietary fiber for reducing the levels of HbA1c, fasting blood glucose, triglycerides, and LDL cholesterol in patients with type 2 diabetes. This study was registered at PROSPERO as ID CRD42021282984.

Keywords: dietary fiber, glycemic factors, lipid levels, ranking, galactomannan, β-glucan, resistant starch, inulin, xylo-oligosaccharides

Introduction

Diabetes mellitus (DM) is one of the greatest and rapidly increasing global health burdens of the 21st century. It has been estimated that 537 million adults will live with DM in 2022, projected to reach 643 million by 2030 and 783 million by 2045. Type 2 diabetes accounts for >90% of all DM cases worldwide [1].

One of the main risk factors for type 2 diabetes is obesity. Therefore, the management of this disease demands lifestyle changes, including medical nutrition therapy (MNT) and physical activity, to reach a healthy weight and achieve proper glycemic control. MNT suggests reducing energy intake, including decreased overall consumption of carbohydrates [2]. Carbohydrate intake should contain nutrient-dense sources that are high in fibers. However, no specific recommendations have been

Abbreviations used: 2h pp. G, 2-h postprandial glucose level; CrI, credible interval; DM, diabetes mellitus; FBG, fasting blood glucose; FI, fasting insulin; GRADE, Grading of Recommendations Assessment Development and Evaluation; MD, mean difference; MNT, medical nutrition therapy; NMA, network meta-analysis; SUCRA, the surface under the cumulative ranking; TC, total cholesterol; TG, triglyceride.

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made related to the preferred types of dietary fibers to be consumed; therefore, it is essential to evaluate each dietary fiber separately.

Fibers are carbohydrate polymers, which are neither digested nor absorbed in the small intestine of humans. Traditionally, dietary fibers are classified as water-soluble and insoluble forms, referring to their utilization in food products and their physiologic effects. Water-insoluble fibers are present in cereals and have a high water-binding capacity, thus facilitating satiety and preventing overeating. Water-soluble fibers are present in fruits and vegetables and are often considered prebiotics, which refers to their ability to increase the number of beneficial microbes (e.g., *Lactobacillus* and *Bifidobacteria*) while decreasing the number of pathogens in the human gut [3–5]. High dietary fiber intake has a prebiotic effect on SCFA-producing microbial species. SCFAs have shown pleiotropic effects in different targets that improve glucose metabolism. However, it is also important to emphasize that the consumption of more fibers than the optimal dose can have side effects, including bloating, constipation, and diarrhea [6].

A previous systematic review and meta-analysis published in 2021 examined the effectiveness of soluble dietary fibers. The authors' findings demonstrated that supplemental soluble dietary fibers improved glucose metabolism and BMI (in kg/m^2) in patients with type 2 diabetes. However, different soluble dietary fibers can show a wide variety in their daily effective dose, impact on gut microflora, and metabolic parameters [7]. In contrast to soluble dietary fibers, insoluble fibers have no significant effect on cholesterol concentrations or glycemic control; instead, they are used as a placebo in studies [8]. Therefore, the present study aimed to rank the effects of different types of soluble dietary fibers on glycemic and lipid factors in patients with type 2 diabetes.

Methods

We report our systematic review and network meta-analysis based on the recommendation of the PRISMA 2020 guideline [9], whereas we followed the Cochrane Handbook [10]. The study protocol was registered on PROSPERO (CRD42021282984), and we fully adhere to it.

Eligibility criteria

The inclusion criteria specified any randomized controlled trials (RCTs) that included adult patients diagnosed with type 2 diabetes and compared the intake of soluble dietary fibers with that of another type of dietary fiber or no fiber reported at least 1 of the following outcomes: HbA1c, fasting blood glucose (FBG), fasting insulin (FI), 2-h postprandial glucose level (2h pp. G), HOMA-IR, total cholesterol (TC), triglyceride (TG), HDL, and LDL. Studies involving pregnant women or children were excluded.

Information sources

Our systematic search was conducted on October 20, 2021, in 3 scientific databases: MEDLINE (via PubMed), Embase, and Cochrane Central Register of Controlled Trials (CENTRAL). No language or other filters were applied. We updated the systematic search on November 20, 2022, and could not find any new eligible articles.

Search strategy

During the systematic search, the main concept was (type 2 diabetes) AND (soluble dietary fiber) AND random*. The entire search key is found in Supplemental Table 1.

Selection process

After duplicates were excluded, the title and abstract of the remaining studies were screened, and the full text was finally screened by 2 independent authors (AEJ and DG). We calculated the Cohen kappa coefficient to measure the agreement between 2 raters at the 2 levels of the selection process (title and abstract as well as full text) [11]. Any disagreements were resolved by a third review author (BT). Additional articles were searched manually and identified from the reference lists of the eligible articles based on the review of full text (RJ).

Data collection

Two authors (AEJ and DG) independently collected data from the eligible articles. A third independent author (RJ) resolved all disagreements. The following data were extracted from each eligible article: first author, year of publications, study population, study period, country, number of centers, patient characteristics (age, sex distribution, treatment of diabetes, and BMI), number of patients allocated to the study arm, type and amount of dietary fibers in the intervention and control groups, preinterventional and postinterventional values, and changes in laboratory parameters according to our outcomes. We contacted the corresponding authors for articles for which data were not fully available. In the case of articles in foreign languages, we asked a specialist to translate them. The details of the soluble and nonsoluble fiber groups can be found in Supplemental Table 2. Furthermore, we accepted only those studies in which the control group did not get dietary fibers as a supplement to their normal diet. Therefore, we standardized the controls to "no fiber" when the patients did not receive any supplementation or received maltodextrin, glucose, or xylitol. These carbohydrates are not dietary fibers because they can be digested or absorbed in the human body. Studies in which the control group received dietary fibers are presented in the systematic review section of our manuscript.

Risk-of-bias assessment and quality of evidence

The risk-of-bias assessment was conducted in duplicate (AEJ and DG) using version 2 of the Cochrane Risk of Bias tool for randomized trials for all outcomes [12]. The 5 main domains assessed were randomization process, deviation from the intended intervention, missing outcome data, measurement of the outcome, and selection of the reported results. These were scored as having a low risk, with some concerns, or a high risk of bias. A third review author (RJ) resolved any disagreement between the assessors.

To evaluate the evidence certainty, we followed the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) recommendation [13]. Each assessment criteria for each outcome and comparison were evaluated by 2 independent review authors (AEJ and DG). Any dissidents were resolved by a third party (RJ).

Synthesis methods

The Bayesian method was used to perform pairwise meta-analyses and network meta-analyses (NMAs) using the random-effects model. The consistency examination was ruled out based on visual inspection of plots. The network was depicted using a graph, with the nodes representing dietary fiber types and the edges representing direct comparisons. The size of the node is proportional to the number of studies. The thickness of the edges is proportional to the number of trials, as determined using a direct comparison. We used mean difference (MD) for continuous data with 95% credible intervals (CrIs). We

optimized the model and generated posterior samples using the Monte-Carlo method running in 4 chains. We set at least 20,000 adaptation iterations to get convergence and 40,000 simulation iterations. The network estimates (pooled estimates of direct and indirect data) of each intervention were presented in comparison with those of no fiber and each other in a league table. The interventions were ranked based on their posterior probability by calculating the surface under the cumulative ranking (SUCRA) curve values. The cumulative probabilities of each treatment were expressed as a single value between 0% and 100%. Ranking probabilities allow easy-to-interpret conclusions with their application ("intervention A has a 55% chance of being the best"). The higher the percentage or SUCRA value is, the higher the probability of the intervention is, being in the top rank or one of the top ranks. All calculations were performed using the R package (version 4.1.1) BUGSnet (version 1.1.0) along with the Markov Chain Monte-Carlo engine JAGS (version 4-12).

Because of the small number of articles, a separate NMA was not possible with studies in which insoluble dietary fibers were the control. For the same reason, pairwise comparisons could also not be performed. These articles are included only in the systematic review section. Studies that did not report the type of fiber and presented data only in medians are also reported in the qualitative synthesis section.

Results

Search and selection

Altogether, 1605 studies were identified by our systematic search. After duplicate records were removed and the remaining records were selected, we identified 56 eligible studies for qualitative and quantitative synthesis. The selection process is shown in Figure 1.

Main characteristics of included studies

The baseline characteristics of the enrolled analyses are detailed in Table 1 (14–58). The total number of involved patients was 2865. The RCTs were conducted in 30 countries, and there were a vast number of trials from Iran (16/46). The study duration varied from 30 d to 6 mo. With regard to intervention, a total of 16 dietary fibers were assessed in the trials. The baseline characteristics of the articles included for qualitative synthesis are detailed in Supplemental Table 3.

Quantitative synthesis

The network interventions regarding each outcome are presented in Figure 2.

Ranking of interventions

The relative ranking of the different dietary fibers for each outcome was estimated using ranking probabilities and SUCRA. The results are shown in Table 2.

Glycemic levels

HbA1c

The network included 30 studies, with 1526 patients (Figure 2A). In terms of HbA1c, galactomannans (SUCRA: 92.3%), inulin (SUCRA: 69%), and xylo-oligosaccharides (SUCRA: 60.4%) were ranked as the 3 most effective interventions (Table 2, Supplemental Figures 1 and 2). A statistically significant difference was observed in the HbA1c% level when galactomannans were compared with psyllium (MD: −1.39% [−15.2 mmol/mol]; 95% CrI: −2.54, −0.03) and no fiber (MD: −1.46% [−16.0 mmol/mol]; 95% CrI: −2.58, −0.33) (Supplemental Table 4).

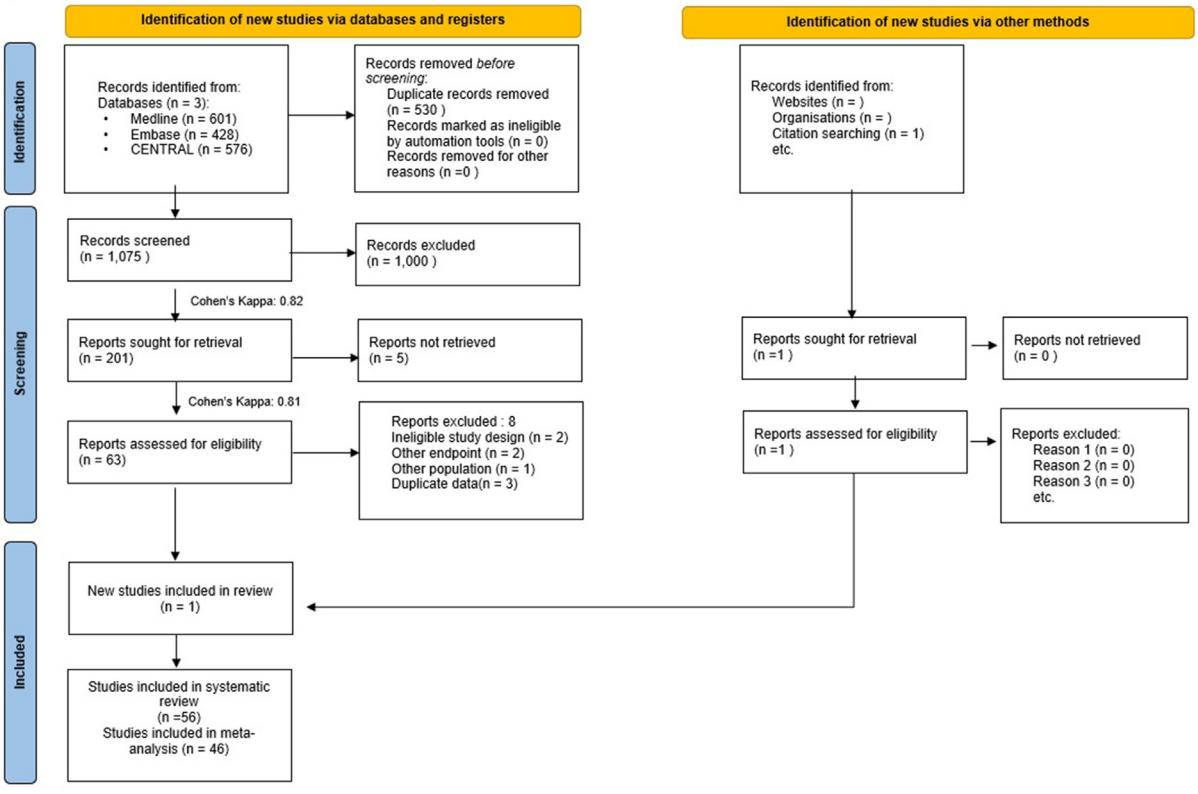

FIGURE 1. PRISMA 2020 flowchart representing the study selection process.

TABLE 1
Basic characteristics of the included studies

Study, y	Country	Study period	Number of patients	Sex (female %)	Mean age (SD) Intervention/control group	BMI, kg/m^2 (SD) Intervention/control group	Medication	Intervention (g/d)	Control	Outcome
Abutair et al. [14], 2016	Palestine	8 wk	40	50	>35	31.7 (2.71)	OAD	Psyllium (10.5)	No fiber	FBG, HbA1c, FI, HOMA-IR
Abutair et al. [15], 2018	Palestine	8 wk	40	50	47.5 (4.2)	N/A	OAD	Psyllium (11.5)	No fiber	TC, HDL, LDL
Aliasgharzadeh et al. [16], 2015	Iran	8 wk	75	100	49.2 (8.4)/49.6 (9.6)	30.8 (4)/31.8 (4.1)	OAD	Resistant dextrin (10)	Maltodextrin	FBG, HbA1c, FI, HOMA-IR
Aliasgharzadeh et al. [17], 2015	Iran	8 wk	70	100	48.4 (9.7)/48.5 (8.4)	31.8 (4.5)/30.8 (5.2)	OAD	Inulin (10)	Maltodextrin	TC, TG, HDL, LDL
Alles et al. [18], 1999	the Netherlands	20 d	20	55	56 (5.2)/62 (4.1)[1]	29.4 (4.2)/27.4 (2.2)[1]	OAD ($n = 17$)	Fructo-oligosaccharides (15)	Glucose	FBG, TC, TG, HDL, LDL
Babiker et al. [19], 2018	Sudan	12 wk	100	80	49.9 (8.7)/50.2 (9.3)	27.6 (5.4)/29.9 (6.5)	OAD	Gum arabic (30)	No fiber	TG, HDL
Bodinham et al. [20], 2014	United Kingdom	12 wk	17	29	55	31.0 (1.3)/30.7 (1.4)	OAD ($n = 15$)	Resistant dextrin (40)	Amioca	FBG, HbA1c, FI, TG, TC, HDL, LDL
Bonsu and Johnson [21], 2012	Canada	12 wk	36	46	64 (5.8)/66 (11.2)	31 (4.5)/29.7 (4.3)	N/A	Inulin (10)	Xylitol	FBG, HbA1c, TG, TC, HDL, LDL
Cai et al. [22], 2018	China	12 wk	137	62	60.9 (5.4)/60.2 (5.8)	27.8 (3.5)/27.7 (3.8)	OAD ($n = 43$)	Inulin, resistant dextrin (6.3)	Placebo	FBG, HbA1c, FI, 2h pp. G, HOMA-IR, TG, TC, HDL, LDL
Chearskul et al. [23], 2007	Thailand	4 wk	20	50	51.4 (2.3)/51 (2.2)[1]	26.5 (1.2)/26.4 (1.1)	N/A	Glucomannan (3)	Placebo	FBG, FI, 2h pp. G, HOMA-IR, TG, TC, HDL, LDL
Chen et al. [24], 2003	Taiwan	4 wk	22	54	64.2 (8.3)/52–77[1]	25.5 (3.2)	OAD ($n = 21$), insulin ($n = 1$)	Glucomannan (3)	Placebo	FBG, 2h pp. G, TG, TC, HDL, LDL
Cho et al. [25], 2005	Korea	8 wk	42	57	57.2 (2.6)/57.1 (2.9)	23.7 (0.4)/23.4 (0.6)	OAD	*Cassia tora* (3)	Maltodextrin	FBG, HbA1c, TG, TC, HDL, LDL
Costa et al. [26], 2019	Brazil	24 wk	131	75	65 (62–71)/64 (60–71)[2]	29.8 (26.7–33.5)/28.9 (26.5–33.1)	OAD	Resistant starch (4)	No fiber	TC, HDL, HOMA-IR
Cugnet et al. [27], 2010	France	8 wk	53	39	61.9 (9.1)/61.8 (7.5)	30.5 (4.8)/29.1 (4.5)	OAD	β-glucan (3.5)	No fiber	FBG, HbA1c, TC, HDL, LDL
Dall'Alba et al. [28], 2013	Brazil	6 wk	44	61	60.5 (9.1)/63.6 (9.6)	30.2 (3.6)/29.3 (3.6)	OAD	Guar gum (10)	No fiber	FBG, HbA1c, TC, HDL, LDL
Dehghan et al. [29], 2013	Iran	8 wk	65	100	47.8 (10.1)/48.7 (9.7)	31.6 (0.9)/29.9 (4.2)	OAD	Inulin (10)	Maltodextrin	FBG, HbA1c, TG, TC, HDL, LDL
Dehghan et al. [30], 2016	Iran	8 wk	70	100	48.1 (8.7)/48.6 (9.2)	31.4 (3.5)/29.9 (4.01)	OAD	Inulin (10)	Maltodextrin	FBG, HbA1c, TG, TC, HDL, LDL
Farhangi et al. [31], 2016	Iran	8 wk	85	100	49.2 (9.6)/49.6 (8.4)	31.8 (4.5)/30.8 (5.2)	OAD	Resistant dextrin (10)	Maltodextrin	FBG, HbA1c, TG, TC, HDL, LDL
Farhangi et al. [32], 2020	Iran	8 wk	70	100	49.5 (8.0)/48.6 (7.9)	31.5 (4.5)/32 (3.9)	OAD	Inulin (10)	Maltodextrin	FI
Feinglos et al. [33], 2013	United States of America	12 wk	37	33	61.8 (9.4)/56.5 (9.9)	N/A	OAD	Psyllium (6.8)	Placebo	FBG, HbA1c
	United States of America	12 wk	37	33	64.8 (8.4)/56.5 (9.9)	N/A	OAD	Psyllium (13.6)	Placebo	FBG, HbA1c
Gargari et al. [34], 2013	Iran	8 wk	65	100	47.8 (0.1)/48.7 (9.7)	31.6 (4.1)/29.9 (4.2)	OAD	Inulin (10)	Maltodextrin	FI, HOMA-IR

(*continued on next page*)

TABLE 1 (*continued*)

Study, y	Country	Study period	Number of patients	Sex (female %)	Mean age (SD) Intervention/control group	BMI, kg/m^2 (SD) Intervention/control group	Medication	Intervention (g/d)	Control	Outcome
Gargari et al. [35], 2015	Iran	8 wk	60	100	49.5 (8.0)/49.6 (8.4)	31.5 (4.5)/30.8 (5.2)	OAD	Resistant starch (10)	Maltodextrin	FBG, HbA1c, TG, TC, HDL, LDL
Ghalandari et al. [36], 2018	Iran	8 wk	47	65	55.9 (8.3)/48.8 (8.5)	29.7 (7.5)/28.5 (2.5)	OAD	Psyllium (3.1)	No fiber	TG, TC, HDL, LDL
Ghavami et al. [37], 2018	Iran	6 wk	46	56	41.5 (6.3)/42.7 (5.9)	27.7 (4.6)/28.8 (4.8)	OAD	Inulin (10)	Starch	FBG, FI, HbA1c, HOMA-IR, TG, TC, HDL, LDL
Karimi et al. [38], 2016	Iran	8 wk	60	100	49.5 (8.0)/48.6 (7.9)	31.5 (4.5)/31 (4.9)	OAD	Resistant starch (10)	Maltodextrin	HOMA-IR, FI
Kondo et al. [39], 2017	Japan	8 wk	28	35	68.1 (8.7)/65.2 (6.8)	24.2 (3.5)/25 (3.7)	OAD	Brown rice dietary fiber (4.3)	White rice	FBG, FI, HbA1c, HOMA-IR, TG, TC, HDL, LDL
Lalor et al. [40], 1990	United Kingdom	12 wk	26	53	58 (40–73)[2]	31.5 (5.1)	OAD	Guar gum (15)	Placebo	FBG, TC, TG, HDL, LDL
Li et al. [41], 2016	China	30 d	298	47	59.7 (6.1)/59 (3.9)	26.9 (2.7)/25.2 (0.9)	OAD ($n = 75$), insulin ($n = 28$)	β-glucan (2.65)	No fiber	FBG, HbA1c, 2h pp. G, HOMA-IR, TG, TC, HDL, LDL
	China	30 d	298	47	59.4 (6.8)/59 (3.9)	27.4 (2.4)/25.2 (0.9)	OAD ($n = 49$), insulin ($n = 24$)	β-glucan (5.3)	No fiber	FBG, HbA1c, 2h pp. G, HOMA-IR, TG, TC, HDL, LDL
Liatis et al. [42], 2009	Greece	3 wk	41	43	60.2 (8.9)/66.5 (8.9)	29.6 (4.7)/27 (3.7)	OAD	β-glucan (3)	No fiber	FBG, FI, HOMA-IR, TG, TC, HDL, LDL
Lotfollahi et al. [43], 2020	Brazil	6 mo	39	N/A	65	N/A	OAD	Resistant starch (4.5)	No fiber	FBG, FI, HOMA-IR, TG, TC, HDL, LDL
Lu et al. [44], 2004	Australia	5 wk	15	60	60 (2.0)	28.1 (0.9)	OAD	Arabinoxylan (14-17)	No fiber	FBG, FI, 2h pp. G, TG, TC, HDL, LDL
Luo et al. [45], 2000	Belgium	4 wk	10	40	57 (2.0)	28 (1.0)	OAD ($n = 10$)	Fructo-oligosaccharides (20)	Sucrose	FBG, FI, HbA1c, TG, TC, HDL, LDL
McIvor et al. [46], 1986	United States of America	6 mo	16	62	49.6 (3.0)/48.5 (2.9)	N/A	insulin	Guar gum (26.4-39.6)	Placebo	TC, TG, HDL, LDL
Meng et al. [47], 2019	China	12 wk	70	41	62.8 (9.3)/61 (9.5)	26.4 (3.9)/25.8 (3.6)	OAD, insulin	Resistant starch (17.41)	No fiber	FBG, HbA1c, TG, TC, HDL, LDL
Noureddin et al. [48], 2018	Iran	12 wk	54	82	58 (7.2)/55.9 (8.7)	29.3 (5.2)/28.7 (5.9)	OAD	Psyllium (10)	Maltodextrin	FBG, HbA1c, TG, TC, HDL, LDL
Pedersen et al. [49], 2016	United Kingdom	12 wk	39	0	56.7 (1.6)/58.1 (1.7)	28 (1.1)/28.4 (0.1)	OAD	Galacto-oligosaccharides (5.5)	Maltodextrin	FBG, FI, HbA1c, HOMA-IR
Peterson et al. [50], 1987	United Kingdom	6 wk	16	38	60 (47–69)	27.3 (21.9–36.9)[2]	OAD	Guar gum (7.6)	No fiber	FBG, FI, HbA1c, TG, TC, HDL, LDL
	United Kingdom	6 wk	16	38	60 (47–69)	27.3 (21.9–36.9)[2]	OAD	Guar gum (8.3)	No fiber	FBG, FI, HbA1c, TG, TC, HDL, LDL
Rashid et al. [51], 2019	Pakistan	12 wk	64	29	48.5/48.2	32.3 (1.5)/30.2 (1.6)[1]	N/A	Galactomannan (1)	Placebo	FBG, HbA1c, TG, TC, HDL, LDL
Sakai et al. [52], 2019	Japan	12 wk	30	26	59.1 (13.2)	25.18 (3.9)	N/A	Fucoidan (1.62)	Placebo	FBG, FI, HbA1c, HOMA-IR, TG, TC, HDL, LDL

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Sartore et al. [53], 2009	Italy	8 wk	40	33	61 (8.4)/60 (8)	30.1 (3.9)/30.5 (2.9)	N/A	Psyllium (10.5)	No fiber	FBG, HbA1c, TG, TC, HDL, LDL
Sheu et al. [54], 2008	Taiwan	8 wk	26	26,9	64 (7.6)/67.6 (7.9)	25 (2.7)/25 (3.9)	OAD	Xylo-oligosaccharides (4)	Glucose	FBG, FI, HbA1c, TG, TC, HDL, LDL
Soltanian and Janghorbani [55], 2019	Iran	12 wk	77	83	58 (7.2)/55.9 (8.7)	29.3 (5.2)/28.7 (5.9)	OAD	Psyllium (10)	No fiber	FBG, HbA1c, TG, TC, HDL, LDL
Tajadadi et al. [56], 2014	Iran	8 wk	54	81	52 (7.2)/53.4 (7.5)	29.8 (5.7)/30.5 (4.1)	OAD	Inulin (8.4)	No fiber	FBG, FI, HOMA-IR
Uusitupa et al. [57], 1989	Finland	12 wk	39	66	58.6 (5.4)/61.48 (6.3)[1]	N/A	OAD	Guar gum (15)	No fiber	FBG, HbA1c, TC, HDL, TG
Zhang et al. [58], 2007	China	4 wk	40	N/A	N/A	N/A	N/A	Resistant starch (30)	No fiber	FBG, 2h pp. G, FI, TG, TC
	China	4 wk	40	N/A	N/A	N/A	N/A	Resistant starch (30)	No fiber	FBG, 2h pp. G, FI, TG, TC

2h pp. G, 2-h postprandial glucose; FBG, fasting blood glucose; FI, fasting insulin; N/A, not available; OAD, oral antidiabetic drug; TC, cholesterol; TG, triglyceride.

[1] Males/females.

[2] Median (range).

FBG

From 38 studies, 1819 patients were included in the network (Figure 2B). In terms of FBG level, galactomannans (SUCRA: 85.92%), resistant starch (SUCRA: 85.07%), and psyllium (SUCRA: 72.01%) were ranked as the 3 most effective interventions (Table 2, Supplemental Figures 3 and 4). A statistically significant difference was observed in the changes in the FBG level when galactomannans were compared with resistant dextrin (MD: −1.48 mmol/l; 95% CrI: −2.75, −0,03), no fiber (MD: −1.69 mmol/l; 95% CrI: −2.84, −0.59), and *Cassia tora* (MD: −2.90 mmol/l; 95% CrI: −5.66, −0.25); resistant starch was compared with resistant dextrin (MD: −1.46 mmol/l; 95% CrI: −2.70, −0.22), no fiber (MD: −1.66 mmol/l; 95% CrI: −2.72, −0.74), and *Cassia tora* (MD: −2.87 mmol/l; 95% CrI: −5.70, −0.22); psyllium was compared with no fiber (MD: −1.20 mmol/l; 95% CrI: −1.83, −0.63); and β-glucans were compared with no fiber (MD: −0.91 mmol/l; 95% CrI: −1.69, −0.19) (Supplemental Table 5).

FI

The network included 21 studies, with 888 patients (Figure 2C). With regard to FI level, β-glucans (SUCRA: 73.45%), psyllium (SUCRA: 70.44%), and resistant starch (SUCRA: 59.48%) were ranked as the 3 most effective interventions (Table 2, Supplemental Figures 5 and 6). No statistically significant difference was observed in the changes in FI in the pairwise comparisons of the different dietary fibers included in the network (Supplemental Table 6).

HOMA-IR

From 15 studies, 977 patients were included in the network (Figure 2D). In terms of HOMA-IR, psyllium (SUCRA: 96.67%), β-glucans (SUCRA: 73.05%), and resistant dextrin (SUCRA: 63.16%) were ranked as the 3 most effective interventions (Table 2, Supplemental Figures 7 and 8). A statistically significant difference was observed when psyllium was compared with inulin (MD: −5.33; 95% CrI: −9.92, −0.50), inulin plus resistant dextrin (MD: −5.63; 95% CrI: −10.84, −0.12), resistant starch (MD: −6.10; 95% CrI: −11.91, −0.38), brown rice dietary fiber (MD: −6.17; 95% CrI: −12.03, −0.53), no fiber (MD: −6.29; 95% CrI: −10.53, −2.02), fucoidan (MD: −6.69; 95% CrI: −12.42, −0.70), and galacto-oligosaccharide (MD: −7.44; 95% CrI: −14.32, −0.53) (Supplemental Table 7).

2h pp. G

Eight studies, with 570 patients, were included in the network (Figure 2E). With regard to 2h pp. G level, resistant starch (SUCRA: 92.3%), β-glucans (SUCRA: 63.48%), and arabinoxylan (SUCRA: 51.81%) were ranked as the 3 most effective interventions (Table 2, Supplemental Figures 9 and 10). A statistically significant difference was observed when resistant starch was compared with no fiber (MD: −5.97 mmol/l; 95% CrI: −10.26, −1.65) (Supplemental Table 8).

Lipid profile

Cholesterol

The network included 38 studies, with 1817 patients (Figure 2F). In terms of TC level, xylo-oligosaccharides (SUCRA: 84.59%), galactomannans (SUCRA: 76.06%), and inulin (SUCRA: 70.8%) were ranked as the 3 most effective interventions (Table 2, Supplemental Figures 11 and 12). A statistically significant difference was observed when xylo-oligosaccharides were compared with no fiber (MD: −0.95 mmol/l; 95% CrI: −1.86, −0.9) (Supplemental Table 9).

Triglycerides

Thirty-four studies, with 1701 patients, were included in the network (Figure 2G). With regard to TG level, galactomannans (SUCRA: 82.77%), xylo-oligosaccharides (SUCRA: 78.91%), and inulin (SUCRA: 70.83%) were ranked as the 3 most effective interventions (Table 2, Supplemental Figures 13 and 14). A statistically significant difference was observed when galactomannans were compared with no fiber (MD: −0.57 mmol/l; 95% CrI: −1.06, −0.07) (Supplemental Table 10).

HDL cholesterol

From 37 studies, 1851 patients were included in the network (Figure 2H). In terms of HDL level, gum arabic (SUCRA: 89.06%), resistant dextrin (SUCRA: 83.72%), and inulin (SUCRA: 71.92%) were ranked as the 3 most effective interventions (Table 2, Supplemental Figures 15 and 16). A statistically significant difference was observed when gum arabic was compared with no fiber (MD: 0.21 mmol/l; 95% CrI: 0.02, 0.39) and β-glucans (MD: 0.23 mmol/l; 95% CrI: 0.03, 0.42) and resistant dextrin was compared with no fiber (MD: 0.16 mmol/l; 95% CrI: 0.02, 0.31) and β-glucans (MD: 0.18 mmol/l; 95% CrI: 0.02, 0.35) (Supplemental Table 11).

LDL cholesterol

The network included 35 studies, with 1778 patients (Figure 2I). With regard to LDL level, galactomannans (SUCRA: 86.56%), inulin (SUCRA: 85.86%), and xylo-oligosaccharides (SUCRA: 61.51%) were ranked as the 3 most effective interventions (Table 2, Supplemental Figures 17 and 18). A statistically significant difference was observed when galactomannans were compared with no fiber (MD: −0.81 mmol/l; CrI: −1.53, −0.08) and inulin was compared with no fiber (MD: −0.71 mmol/l; 95% CrI: −1.30, −0.12) (Supplemental Table 12).

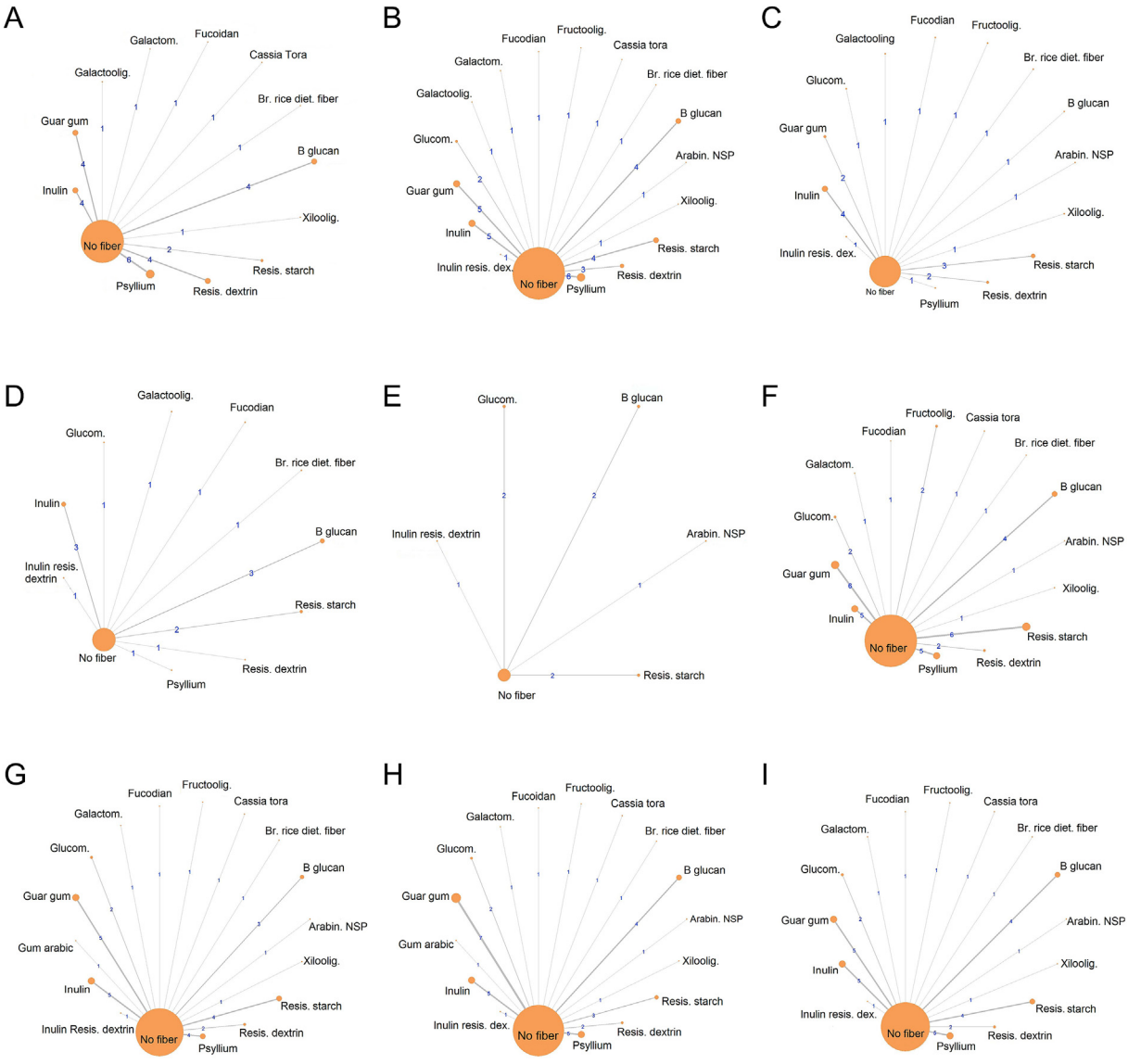

FIGURE 2. The network interventions regarding each outcome. HbA1c (A), fasting blood glucose (B), fasting insulin (C), HOMA-IR (D), 2-h postprandial glucose level (E), total cholesterol (F), triglyceride (G), HDL (H), and LDL (I). The size of the nodes is proportional to the number of studies evaluating each intervention, and the thickness of the edges is proportional to the number of each direct comparison. Arabin. NSP, arabinoxylan nonstarch polysaccharides; Br. rice diet. fiber, brown rice dietary fiber; Fructoolig., fructo-oligosaccharide; Galactom., galactomannan; Galactoolig., galacto-oligosaccharide; Glucom., glucomannan; Inulin resis. dex, inulin with resistant dextrin; Resis. dextrin, resistant dextrin; Resis. starch, resistant starch; Xiloolig., xylo-oligosaccharide.

Qualitative synthesis

Thirteen studies were included for qualitative synthesis. In 8 articles, nonsoluble dietary fibers were used as a control [59–66]. In 2 studies, the dietary fiber type was not specified [67, 68]. Furthermore, in 3 RCTs, some data were published only as median instead of mean [26, 36, 43]. Most of the studies reported that there were significant differences between the soluble and nonsoluble dietary fiber groups. RCTs in which the control group did not receive any dietary fiber had significantly better results in the dietary fiber group. Detailed results of these RCTs are summarized in Supplemental Tables 13 and 14.

Risk-of-bias assessment and certainty of evidence

The study- and domain-level risk-of-bias assessments for each outcome separately have been described in **Appendix A**. Most studies carried a low risk; however, there were some concerns in 17 trials. In these trials, the "randomization process," "missing outcome data," and "measurement of the outcome" domains were considered as having some concerns or with a high risk of bias. Detailed results can be found in Supplemental Figures 19–40. The certainty of evidence ranged between low and high for each comparison. Most studies had a low or moderate certainty of evidence because of wide CIs. Detailed results of the GRADE assessment can be found in Supplemental Tables 15–32. The inconsistency test did not suggest any inconsistencies for any outcomes (Supplemental Figures 41–49).

Discussion

The present NMA was performed to compare dietary fibers as food supplements in the treatment of type 2 diabetes. The aim was to assemble a rank order of the interventions and determine the most effective soluble fibers in controlling glycemic and lipid parameters in patients with type 2 diabetes. Our NMA, including 46 RCTs, with 2865 patients, showed that soluble dietary fibers can influence metabolic parameters to varying degrees.

The consumption of dietary fibers should be at least 14 g daily per 1000 kcal energy intake [3]. European countries show an average intake quite close to this recommendation, with ~20 g/d of fibers for men and 18–20 g/d for women [4]. For many consumers, it is difficult to take the recommended amount of fibers with food. Dietary fibers can be used as supplementation, and in this case, it is easier to take the recommended amount.

Dietary fibers are nondigestible carbohydrates with various structures, molecule sizes, and metabolic effects. Polysaccharides (i.e., cellulose, galactomannans, glucomannans, gum arabic, resistant starch, and inulin), especially those with a branched structure (galactomannans, glucomannans, gum arabic, and resistant starch), have a high water-binding capacity. By absorbing the water content of foods and drinks consumed, they can swell even in the stomach and, thus, increase satiety and delay gastric emptying. Therefore, regular consumption of these fibers can help patients to decrease the amount of consumed food, resulting in weight loss. Dietary fibers with a higher molecular weight are often called viscous fibers, indicating that these molecules can increase the viscosity of contents in the intestinal lumen and hinder the migration of nutrients to the intestinal walls. Therefore, their regular consumption decreases the absorption of several nutrients such as glucose, lipids, cholesterol, vitamins, and minerals. Human enzymes do not digest dietary fibers; however, in some cases (i.e., inulin, oligosaccharides, etc.), they can be fermented by microbes in the human gut. Fermentation results in the growth of beneficial microbes that produce vitamins and SCFAs that promote the absorption of minerals [69].

In a previous meta-analysis, Xie et al. [7] demonstrated that supplemental soluble dietary fibers were beneficial in improving HbA1c, FBG, FI, HOMA-IR, fructosamine, and 2h pp. G levels as well as BMI compared with a control diet in patients with type 2 diabetes. In addition, a daily dosage of 7.6–8.3 g was recommended for managing the glycemic level and BMI. The results of another meta-analysis demonstrated a reduction in HbA1c by 0.58% (6.2 mmol/mol), FBG by 0.82 mmol/l, and HOMA-IR by 1.89 following the intake of viscous fibers at a median dose of ~13.1 g/d compared with those following the intake of a control [70]. According to the present analysis, galactomannans had the highest effect on reducing the HbA1c and FBG levels in the patients with type 2 diabetes. This type of dietary fiber was also investigated in a meta-analysis in 2016. The authors' results showed that galactomannans could significantly reduce the HbA1c and FBG levels [71]. The potential mechanisms are selective reduction in glucose levels and fat absorption, inhibition of glucose transport, direct stimulation of insulin secretion from islet β cells, increased insulin sensitivity, improved oxidative stress, modulation of the glucagon-like peptide-1 hormone, and delayed gastric emptying [72]. Galactomannans are polysaccharides made from galactose and mannose in varying proportions and are commonly used in foods as additives and stabilizers. The common sources of galactomannans include guar gum and fenugreek [73]. Our results showed that β-glucans were the most effective dietary fiber for FI level compared with other fibers. β-glucans can be found in various food products such as oat, barley, mushrooms, and seaweeds. They have numerous effects on the human body, depending on its diverse structures. Their effects are also intensively studied, especially in the case of oat products, which are easily accessible sources of β-glucans. In a previous NMA, the authors aimed to estimate and rank the effects of whole grains and brans on controlling blood lipid levels. Their results showed that oat bran, a good source of soluble fibers, seemed to be the most effective intervention for TC and LDL-C reductions. In contrast, oat was ranked second based on a cumulative ranking analysis [69]. These results are controversial to our results because β-glucans were ranked in the top 3 interventions in terms of the glycemic parameters, and the SUCRA values were much lower for the lipid factors. In our NMA, oat products served as β-glucan sources. The delayed absorption effect because of the high viscosity of β-glucans in cereals can improve insulin response and decrease postprandial hyperglycemia [74]. On the basis of our results, in terms of HOMA-IR, psyllium had the highest effect on reducing this index, although psyllium is a viscous, functional soluble fiber that could delay intestinal transit time and lead to a feeling of fullness, retarding the entry of glucose into the bloodstream and decreasing the postprandial rise in blood glucose. Insulin requirements could be lower [14]. Resistant starch was the most effective intervention in terms of reducing the 2h pp. G level in patients with type 2 diabetes. The natural sources of resistant starch are grains, seeds, legumes, pasta, potatoes, and unripe bananas [75].

A recent meta-analysis demonstrated that prebiotics reduced TC and LDL concentrations in adult patients who were overweight or had obesity, with decreased TG and increased HDL concentrations compared with those with a placebo in adult patients with diabetes and those who were overweight or had obesity [76]. As for TG and LDL levels, galactomannans were the most effective dietary fibers in the present analysis. These NMA results are consistent with those of Gong et al. [71], who showed that galactomannans could significantly reduce HbA1c, and FBG levels. Moreover, it could decrease TG and LDL

TABLE 2
Interventions' surface under the cumulative ranking percentage regarding each glycemic and lipid factor.

Dietary fibers	SUCRA %	Glycemic factors					Lipid factors				Summary ranking
		HbA1c	FBG	FI	HOMA-IR	2h. pp. G	TC	TG	HDL	LDL	All outcomes combined
Arabin. NSP		-	57.4	50.8	-	**51.81**	27.51	58.74	46.95	31.53	46.39
β-glucan		48.44	60.08[1]	**73.45**	**73.05**	**63.48**	52.05	62.65	**29.95**	61.39	**58.06**
Br. rice diet. fiber		38.47	39.25	46.31	37.57	-	40.31	28.03	30.25	43.55	37.97
Cassia tora		37.82	**11.53**	-	-	-	44.05	41.58	54.79	42.66	38.74
Fructoolig.		-	49.28	48.02	-	-	45.28	49.42	54.92	37.67	47.43
Fucoidan		46.55	49.29	40.47	30.03	-	41.78	33.93	31.3	40.77	39.27
Galactom.		**92.33**[1]	**85.92**[1]	-	-	-	**76.06**	**82.77**[1]	45.6	**88.56**[1]	**60.83**
Galactoolig.		36.2	23.45	41.34	**25.79**	-	-	-	-	-	31.70
Glucom.		-	50.19	49.83	55.57	33.73	45.5	36.49	38.14	50.42	44.98
Guar gum		52.22	44.76	49.09	-	-	37.02	50.32	46.89	41.62	45.99
Gum arabic		-	-	-	-	-	-	49.61	**89.06**[1]	-	49.61
Inulin		**69**	49.98	51.79	52.8	-	**70.8**	**70.83**	**71.92**	**85.86**[1]	**62.45**
Inulin, resis. dex.		-	62.06	**38.85**	46.45	41.68	-	29.72	41.59	49.74	44.30
Psyllium		33.01	**72.1**[1]	**72.1**	**96.67**[1]	-	52.11	33.01	60.48	46.22	49.49
Resis. dextrin		55.96	32.09	43.25	**63.16**	-	53.93	63.16	**83.72**[1]	53.36	52.13
Resis. starch		52.98	**85.07**[1]	**59.48**	38.34	**92.3**[1]	59.66	55.03	57.9	39.23	51.80
Xiloolig.		**60.45**	54.09	45.63	-	-	**84.59**[1]	**78.91**	33.44	**61.51**	55.67
No fiber		**26.6**	23.44	41.24	30.48	**16.99**	**19.37**	**25.85**	36.19	**25.93**	**27.34**

2h pp. G, 2-h postprandial glucose; Arabin. NSP, arabinoxylan nonstarch polysaccharides; Br. rice diet. fiber, brown rice dietary fiber; FBG, fasting blood glucose; FI, fasting insulin; Fructoolig., fructo-oligosaccharide; Galactom., galactomannan; Galactoolig., galacto-oligosaccharide; Glucom., glucomannan; Inulin resis. dex., inulin with resistant dextrin; Resis. dextrin, resistant dextrin; Resis. starch, resistant starch; SUCRA, surface under the cumulative ranking; TC, cholesterol; TG, triglyceride Xiloolig., xylo-oligosaccharide.

[1]The top 3 dietary fibers are highlighted with red and the least effective are highlighted with blue.

[2]Means statistically significant difference was observed when the intervention was compared with no fiber.

levels. In our NMA, galactomannans were ranked first for all 4 factors. Xylo-oligosaccharides proved to be the most effective in decreasing TC levels. A decline in cholesterol level might also occur because oligosaccharides could decrease the expression of enzymes required for fatty acid synthesis, reduce the absorption efficiency of cholesterol, and increase the excretion of fecal bile acid and cholesterol [54]. According to our results, gum arabic proved to be the most effective in increasing HDL levels. It is a nonviscous, soluble fiber. Naturally occurring gum can be extracted from hardened exudates of the plants *Acacia seyal* and *Acacia senega*, and it is used as a food additive, usually as a emulsifier, thickener, and binder [77].

Strengths and limitations

To our knowledge, this study is the first NMA to assess the effect of soluble dietary fibers in patients with type 2 diabetes. The major strengths of this study are that it included 2865 participants and 16 dietary fibers. Besides, we employed a rigorous methodology.

As for the limitations of the present study, first, the number of direct comparisons was low. Secondly, in the included studies, the dietary fiber supplementation was in doses and formulations that may have influenced its effect on the glycemic and lipid levels. Furthermore, the involved patients could have had various background diets, medications, and lifestyles, including sport activities. In most cases, maltodextrin was the placebo; however, some trials used sugar, which could have strongly affected the result.

Implications for practice and research

Our findings have public health implications in terms of the use of dietary fibers as a supplement besides their use as medical therapy for the management of type 2 diabetes. More RCTs with higher sample sizes are needed. Additionally, further long-term and high-quality RCTs are needed to explore the effectiveness of newer soluble fibers (e.g., xylo-oligosaccharides) or initiate investigations using nonsoluble dietary fibers in controlling glycemic and lipid levels in patients with type 2 diabetes. As for our results, the beneficial effect of dietary fibers should be assessed on other diseases, including glycemic and lipid disorders such as obesity and polycystic ovarian syndrome.

In summary, we have already shown that the implementation of research results into everyday practice is essential and brings major health and economic benefits (PMID: 34312557 and PMID: 32438747). Many countries include recommended levels of total fiber intake as part of the nutrition policy; however, specific fiber types are rarely mentioned. On the basis of our results, galactomannans should be emphasized in the treatment of type 2 diabetes. Moreover, galactomannans showed significant results in almost all outcomes compared with no fiber, representing a promising alternative additional therapy for patients with type 2 diabetes.

CRediT author statement

The authors' responsibilities were as follows – AEJ: conceptualization, project administration, methodology, formal analysis, writing – original draft; DG: conceptualization, data curation – review & editing; BT: conceptualization, formal analysis, visualization, writing – review & editing; NG: conceptualization, formal analysis, visualization, writing – review & editing; PH: conceptualization; review & editing; EMH: conceptualization; review & editing; PÁD: conceptualization; review & editing; PN: conceptualization; review & editing; NÁ: conceptualization; review & editing; RJ: conceptualization, formal analysis, visualization, data curation, writing – original; supervision; all authors: certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the

concept, design, analysis, writing, or revision of the manuscript; all authors: read and approved the final manuscript.

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Author disclosures

The authors report no conflicts of interest.

Data Availability

Data described in the manuscript, code book, and analytic code will be made publicly and freely available without restriction at Supplementary material.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajcnut.2022.12.015.

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Reproductive Health

REVIEW

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Ranking the dietary interventions by their effectiveness in the management of polycystic ovary syndrome: a systematic review and network meta-analysis

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Abstract

Introduction Polycystic ovary syndrome (PCOS) is a common condition in women, characterised by reproductive and metabolic dysfunction. While dietary approaches have been evaluated as a first-line treatment for patients with PCOS, there is limited evidence to support preference for a specific dietary composition. This systematic review and network meta-analysis was performed with the objective of comparing different dietary interventions in terms of positive impact. Metformin, the currently preferred treatment, was also compared.

Methods The latest systematic search was performed on the 20th of March, 2023. Eligible randomised controlled trials (RCTs) included patients with PCOS and compared the dietary approach with another intervention or a standard diet. Outcomes were expressed via anthropometric measurements and hormonal, glycemic, and lipid levels. The Bayesian method was used to perform a network meta-analysis and to calculate the surface under the cumulative ranking curve (SUCRA) values in order to rank the dietary interventions. The overall quality of the evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation system.

Results 19 RCTs were identified, comprising data from 727 patients who were variously treated with 10 types of dietary interventions and metformin. The Dietary Approaches to Stop Hypertension (DASH) diet was the most effective in reducing Homeostatic Model Assessment of Insulin Resistance (SUCRA 92.33%), fasting blood glucose (SUCRA 85.92%), fasting insulin level (SUCRA 79.73%) and triglyceride level (SUCRA 82.07%). For body mass index (BMI), the most effective intervention was the low-calorie diet (SUCRA 84.59%). For weight loss, the low-calorie diet with metformin (SUCRA 74.38%) was the most effective intervention. Metformin produced the greatest reductions in low-density lipoprotein cholesterol (SUCRA 78.08%) and total testosterone levels (SUCRA 71.28%). The low-carb diet was the most effective intervention for reducing cholesterol levels (SUCRA 69.68%), while the normal diet (SUCRA 65.69%) ranked first for increasing high-density lipoprotein cholesterol levels.

Conclusion Dietary interventions vary in their effects on metabolic parameters in women with PCOS. Based on our results, the DASH diet is the most effective dietary intervention for treating PCOS.

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Keywords Diet, Insulin resistance, Obesity, And weight loss

Introduction

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine diseases in women of reproductive age. Depending on the population studied and the diagnostic criteria used, prevalence ranges from 5 to 18%. [1]. The Rotterdam Criteria, established in 2003, is the most widely used, based on which the diagnosis of PCOS can be declared if at least 2 of the following 3 conditions are met: 1. Oligo-/amenorrhea or anovulation; 2. Laboratory- or clinically-proven hyperandrogenism; 3. A polycystic ovary is visible on an ultrasound image. Common symptoms of the syndromic disorder include: hyperandrogenism, hirsutism, irregular menstruation cycle, and infertility [2], causing significant reduction in quality of life for affected women [3]. Although the specific causes of PCOS are still unknown, insulin resistance (IR) has been identified as a significant etiological factor. Due to abnormal insulin receptor function and signaling, defective insulin receptor shape, or high amounts of insulin-binding antibodies, IR is associated with impaired insulin sensitivity in bodily tissues [4]. Additionally, obesity is commonly, though not always, observed in PCOS patients. It is also observed that being overweight increases the chance of developing PCOS [5].

Several interventions (pharmacological, nonpharmacological, or surgical) are available for reducing PCOS symptoms [6]. Metformin is an insulin sensitiser commonly used in PCOS patients with IR; however, gastrointestinal side effects limit its use as a first-choice for long-term treatment [7]. On the basis of recent results, inositols may have a beneficial effect on PCOS outcomes, but further research is needed [8, 9]. The International Evidence-based Guideline for the Assessment and Management of PCOS suggests dietary and exercise therapies as the first line of management [10]. The majority of women with PCOS are overweight or obese, and even a small weight reduction (5–10% of body weight) can significantly improve metabolic parameters and reproductive function. Weight reduction increases the sex hormone binding globulin (SHBG) concentration, improves ovarian function and fertility, and reduces miscarriages [11, 12].

Although achieving an ideal body weight improves symptoms in overweight women with PCOS, there is no clear evidence to determine which dietary intervention is best for achieving this goal [13, 14]. Currently, the most commonly used diet types are: low-calorie, low-carbohydrate, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean diets for treating PCOS. This study aims to rank the effectiveness of the diets and treatment options used in the therapy of women with PCOS, by comparing anthropometric (e.g.: body weight) changes, hormonal (e.g.: total testosterone level) changes, and metabolic (e.g.: fasting blood sugar level, blood fat levels) changes measured during the intervention period. The main goal of the study is to provide clinicians with clear, evidence-based information about dietary interventions in lifestyle management in women with PCOS.

Methods

This systematic review and network meta-analysis (NMA) is based on the PRISMA 2020 guideline and Cochrane *Handbook* recommendation [15]. The study protocol was registered on PROSPERO (CRD42022329961), and is adhered to fully.

Eligibility criteria

The inclusion criteria specified any RCTs that included women with diagnosed polycystic ovary syndrome, and that compared two dietary approaches or one dietary approach to either a normal diet or metformin. Included RCTs reported at least one of the following outcomes: BMI, weight, total testosterone (TT), follicle-stimulating hormone (FSH), luteinizing hormone (LH), fasting blood glucose (FBG), fasting insulin (FI), HOMA-IR, total cholesterol (TC), TG, HDL, and LDL. Studies were excluded if patients performed exercise alongside their diet or were given dietary supplements to avoid potential effect modifiers.

Information sources

Our systematic search was conducted on the 2nd of May, 2022. It was updated on the 8th of March, 2023, in five scientific databases: MEDLINE (via PubMed), Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and Web of Science. No language or other filters were applied.

Search strategy

During the systematic search, the main concept was (PCOS) AND (dietary interventions) AND (metformin) AND random*. In order to increase the number of potentially relevant articles, besides the free-text words, we used MeSH and EMTREE terms. The entire search key can be found in the Additional file 1: Material.

Selection process

After duplicate studies had been removed, the remaining studies were examined by title and abstract and then by full text by two independent authors (AEJ, MPS). To assess the rate of agreement between two raters at the two stages of the selection process (title and abstract and full text), we calculated Cohen's kappa coefficient [16]. The third review author (BT) settled any disputes. The reference lists of additional articles were located via a manual search of the full texts of the eligible articles (RJ).

Data collection

Data were independently collected by the two authors from the eligible articles (AEJ, MPS). All conflicts were resolved by a third independent author (RJ). The following data were extracted from each eligible article: the first author, the year of publication, study population, study period, country, number of centres, patient characteristics (age and BMI), number of patients allocated to the study arms, the types of dietary interventions used in the intervention and control groups, pre- and post-interventional values, and the change of the laboratory parameters according to our outcomes. In any case that required data were not completely available for a given article, the corresponding authors were contacted. Not all the dietary approaches were defined; for this reason, we created larger intervention groups based on the percentage of macronutrients. The different dietary approaches were standardised according to European Food Safety Authority (EFSA) Dietary Reference Values for Nutrients [17]. A normal diet was considered to be a daily energy intake of 55% carbohydrate, 15–20% protein, and 25–30% fat. The details of the dietary interventions can be found in Additional file 1: Table S2.

Risk of bias assessment and quality of evidence

The risk of bias assessment was conducted in duplicate (AEJ, MPS) using Version 2 of the Cochrane Risk of Bias (RoB 2) Tool for all outcomes [18]. The five key domains evaluated were the randomisation process, deviation from the intended intervention, missing outcome data, outcome measurement, and selection of the reported results. Assigned to these domains were the categorisations: "low risk," "some concerns", or "high risk of bias." Any disagreements among the assessors were resolved by a third review author (RJ).

We followed the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) recommendation when evaluating the certainty of the evidence [19]. Two independent review authors (AEJ, MPS) evaluated each assessment criterion for each outcome and comparison. Any disputes were settled by a third party (RJ).

Synthesis methods

Network meta-analyses was conducted with the random effects model using a Bayesian method [20]. The consistency examination was ruled out by a visual inspection of plots. The network is depicted in a graph, with the nodes representing diet types and the edges representing direct comparisons. The size of the node is related to the number of studies. The thickness of the edges is proportional to the number of trials with a direct comparison. Mean difference (MD) was used for continuous data with 95% credible intervals (the interpretation of the Bayesian 95% confidence interval) (95% CrI). The model was optimised and posterior samples generated using the Monte-Carlo methods running in four chains. At least 20.000 adaptation iterations were set for convergence, and 40.000 simulation iterations. The network estimates (pooled estimates of direct and indirect data) of each intervention were presented in comparison with each other in a league table. The surface under the cumulative ranking (SUCRA) curve values was used to rank the interventions according to their posterior probability. The cumulative probabilities of each treatment were expressed by a single value between 0 and 100%. Ranking probabilities allow for easy-to-interpret conclusions ("Intervention A has a 55% probability of being the best"). The probability that the intervention will be in the top rank or in one of the top ranks increases with a higher percentage or SUCRA value [21]. All calculations were performed with R (V. 4.1.1) package BUGSnet (V. 1.1.0), along with the Markov Chain Monte Carlo engine JAGS (V. 4-12).

Due to the small number of publications, a separate network meta-analysis for FSH and LH outcomes was not possible. The FSH and LH levels results presented in these articles are included only in the systematic review part. The qualitative synthesis also includes studies that only provided data as medians and did not report SD.

Results

Search and selection

A total of 1309 studies were identified as a result of the systematic search. 27 studies were found to be eligible for the qualitative and quantitative synthesis after removal of duplicate records. The selection process is shown in Fig. 1.

Main characteristics of included studies

The baseline characteristics of the articles in the quantitative and qualitative synthesis are detailed in Table 1. The total number of involved patients is 800. The study

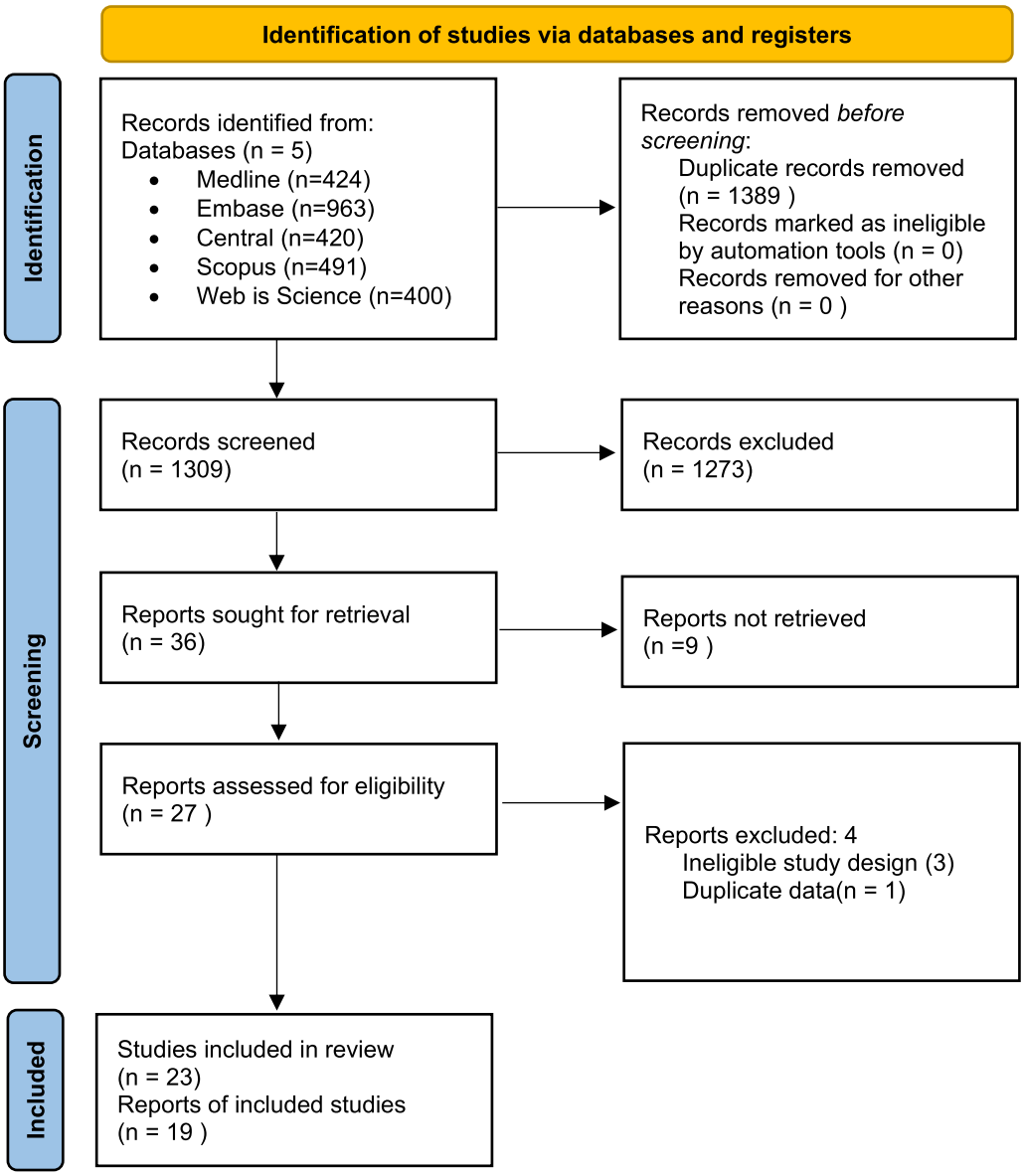

Fig. 1 PRISMA 2020 flowchart representing the study selection process

duration varied from 4 to 24 weeks. As interventions, 10 dietary approaches and metformin were assessed in the trials.

Quantitative synthesis

The network interventions regarding each outcome are presented in Fig. 2.

Ranking of interventions

Using ranking probabilities and the surface under the cumulative ranking curves, the relative ranking of the various dietary interventions for each outcome was calculated. The frequency of the different interventions must be considered since the Mediterranean and the low-protein diets had extreme SUCRA %, however, they were only in 1–1 RCTs. Results are shown in Table 2.

Anthropometric measures

Regarding BMI, the network included 11 studies with 8 interventions and 428 patients (Fig. 2A). The low-calorie diet (SUCRA 73.58%) was ranked as the most effective intervention (Table 2, Additional file 1: Figure S1-S2). No statistically significant difference was observed in the change of BMI with the pairwise comparisons of the

Table 1 Basic characteristics of the included studies

First author, year	Country	Study period (weeks)	Number of patients	Mean age (SD) Intervention /Control group	BMI kg/m^2 (SD) Intervention /Control group	Medication[1]	Intervention	Control	Outcome
Agowska, 2021 [48]	Poland	8	35	16.8 (1.3)	> 95th percentile	No	Low-calorie	Metformin	Weight, FBG, FI, HOMA-IR
Asemi, 2014 [49]	Iran	8	48	30.7 (6.7)/29.4 (6.2)	29.1 (3.2)/31.5 (5.7)	No	DASH	Normal	BMI, Weight, FBG, FI, HOMA-IR
Asemi, 2015 [50]	Iran	8	48	22.1 (3.2)/24.7 (6.0)	30.3 (4.5)/28.6 (5.8)	No	DASH	Normal	LDL, HDL, TC, TG
Azadi-Yazdi, 2017 [51]	Iran	12	55	32.1 (5.9)/31.7 (6.2)	31.9 (4.1)/30.2 (3.2)	No	DASH	Normal	BMI, Weight, TT
Esfahanian, 2013 [39]	Iran	12	30	20 (4.6)/21.9 (9.3)	34.1 (5.4)/31.1 (3.3)	No	Low-calorie	Metformin	BMI, FBG, FI, HOMA-IR, TT, LDL, HDL, TC, TG
Foroozanfard, 2017 [22]	Iran	12	60	27.1 (4.7)/25.6 (3.7)	32.3 (4.6)/32.2 (3.9)	N/A	DASH	Normal	BMI, Weight, FBG, FI, HOMA-IR, TT, FSH, LH
Galletly, 2007 [52]	Australia	16	27	33 (1.2)/32 (1.2)	37.6 (6.4)/34.5 (5.7)	No	Low-P	High-P	BMI, Weight
Gower, 2013 [23]	United States of America	8	30	31.2 (5.8)	31.8 (5.7)	No	Low-carb	Normal	FI, HOMA-IR, TT, FSH, LH, LDL, HDL, TC, TG
Marzouk, 2015 [53]	Egypt	24	60	19.3 (1.3)/20.1 (1.8)	36.0 (4.7)/35.8 (4.8)	No	Low-calorie	Normal	BMI, Weight, FBG
Mehrabani, 2012 [24]	Iran	12	49	28.5 (5.2)/30.5 (6.4)	31.1 (4.6)/31.9 (4.0)	No	Low-calorie	Normal	FI, HOMA-IR, TT, FSH, LH, LDL, HDL, TC, TG
Mei, 2022 [54]	China	12	59	27.9 (5.3)/28.07 (7.1)	39.3 (2.2)/29.5 (2.4)	No	Mediterranean	Low-fat	BMI
Moran, 2003 [55]	Australia	16	28	32 (1.2)/33 (1.2)	37.9 (1.6)/37.7 (1.9)	No	High-P	Low-P	FBG, FI, LDL, HDL, TC, TG
Nadjarzadeh, 2021 [56]	Iran	12	32	28.8 (6.5)/29.4 (6.6)	33.9 (5.3)/32.8 (5.3)	No	Low-calorie	High-P	BMI, Weight, TT
Panico, 2014 [27]	Italy	12	14	28.7 (4.9)	28.7 (4.9)	No	Low-GI	Normal	BMI, Weight, FBG, FI, HOMA-IR, TT, FSH, LH, TC, TG
Qublan, 2007 [25]	Jordan	24	46	31.5 (19–38)/30.8 (20–37)	32.2 (29–43)/31.9 (29–44)	No	High-P	Metformin	FBG, FI, FSH, LH
Sorensen, 2012 [57]	Denmark	24	27	27.7 (5.5)/28.4 (5.8)	30.6 (7.8)/30.5 (8.5)	No	High-P	Normal	BMI, Weight, FBG, TT, LDL, HDL, TC
Stamets, 2004 [26]	United States of America	4	26	29 (4)/26 (4)	38 (4)/37 (5)	No	High-P	Low-calorie	Weight, TT, FSH, LH, LDL, HDL, TC, TG
Toscani, 2011 [58]	Brazil	8	18	22.7 (5.6)/29.5 (5.7)	> 25 kg/m^2	No	High-P	Low-calorie	Weight, FBG, LDL, HDL, TC
Wong, 2016 [59]	United States of America	24	16	15.4 (1.3)/16.3 (2.2)	36.2 (5.3)/33.9 (4.7)	No	Low-GI	Low-fat	BMI, FBG, FI, TT, TC, TG
Articles in the qualitative synthesis									
Mittal, 2020	India	12	21	33.1 (4.4)/34.4 (5.0)	33.7 (4.8)/32.2 (5.9)	No	Vegan	Low-calorie	BMI, Weight
Orstein, 2011	United States of America	12	16	15.8 (2.2)	35.7 (6)	No	Low-carbohydrate	Low-fat	Weight

Table 1 (continued)

First author, year	Country	Study period (weeks)	Number of patients	Mean age (SD) Intervention /Control group	BMI kg/m^2 (SD) Intervention /Control group	Medication[1]	Intervention	Control	Outcome
Sordia-Hernández, 2015	Mexico	12	37	26.1 (4.1)/26.1 (4.7)	N/A	N/A	Low-glycemic	Normal	Weight
Turner-McGrievy, 2014	United States of America	24	18	27.8 (4.5)	39.9 (6.1)	No	Vegan	Low- calorie	Weight

N/A: not available; [1]Medication that might affect the patients' physiology during the intervention (lipid-lowering, anti-obesity, oral antidiabetic drug, hormonal therapy)

DASH, Dietary approaches to stop hypertension; Low-calorie + M, Low-calorie diet plus metformin; Low-carb, Low- carbohydrate diet; High-P, High-Protein diet; Low-GI, Low-Glycemic Index diet; Low-P, Low-Protein diet; FBG: fasting blood glucose; FI: fasting insulin; TG: triglyceride; TC: cholesterol; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; TT: total testosterone; FSH: follicle-stimulating hormone; LH: luteinizing hormone

included different interventions in the network (Additional file 1: Table S3).

Regarding weight, the network 12 studies with 7 interventions and 418 patients (Fig. 2B). The low-calorie diet with metformin (SUCRA 73.7%) was ranked as the most effective intervention (Table 2, Additional file 1: Figure S3-S4). A statistically significant difference was observed when the low-fat diet was compared with low-GI (MD = − 3.59, 95% CrI: − 6.03; − 1.08); DASH diet with high-protein diet (MD = − 2.88 95% CrI: − 4.96; − 0.89) and with normal diet (MD = − 1.67 95% CrI: − 3.2; − 0.34) (Additional file 1: Table S4).

Glycemic levels

Regarding HOMA-IR, the network included 7 studies and interventions with 286 patients (Fig. 2C). For this outcome, the DASH diet (SUCRA 80.47%) was the most effective intervention (Table 2, Additional file 1: Figure S5-S6). Furthermore, this type of diet produced a statistically significant difference compared to the normal diet (MD = − 1.10 95%-os CrI: − 2.05; − 0.03) in terms of HOMA-IR change (Additional file 1: Table S5).

Regarding FI level, the network included 10 studies and interventions with 376 patients (Fig. 2D). The DASH diet (SUCRA 79.73%) was the most effective based on the SUCRA values regarding FI level (Table 2, Additional file 1: Figure S7-8). There was no statistically significant difference between the interventions (Additional file 1: Table S6).

Regarding FBG level, the network included 11 studies, 9 interventions, and 372 patients (Fig. 2E). Based on the SUCRA values, the DASH diet (SUCRA 76.6%) was ranked the most effective dietary intervention for decreasing FBG levels (Table 2, Additional file 1: Figure S9-S10). No statistically significant difference was observed in the change of FBG with the pair-wise comparisons of the included different interventions in the network (Additional file 1: Table S7).

Hormonal measures

Regarding total testosterone levels, the network included 10 studies, 8 interventions, and 359 patients (Fig. 2F). Metformin (SUCRA 71.28%) was observed to be the most effective based on the SUCRA values regarding total testosterone levels (Table 2, Additional file 1: Figure S11-S12). No significant difference could be established between the interventions (Additional file 1: Table S8).

Lipid levels

The network of LDL and HDL levels included 8 studies, 6 interventions, and 276 patients (Fig. 2G, H). Metformin (SUCRA 78.08%) was the most effective intervention regarding LDL (Additional file 1: Figure S13-S14), while the normal diet (SUCRA 65.69%) was observed to be the most effective intervention regarding HDL levels (Additional file 1: Figure S14-S15). No statistically significant difference was observed in the change of LDL or HDL with the pairwise comparisons of the included interventions in the network (Additional file 1: Table S9–10).

Regarding TG level, 8 studies and interventions with 261 patients were included in the network (Fig. 2I). The DASH diet (SUCRA 82.07%) was the most effective intervention, and with the pair-wise comparisons of the included different interventions (Additional file 1: Figure S17-S18), no statistically significant difference was observed in the change of TG level (Additional file 1: Table S11).

Regarding TC level, the network included 10 studies and 8 interventions with 306 patients (Fig. 2J). For this outcome, the low-carb diet (SUCRA 69.68%) was the most effective intervention (Additional file 1: Figure S19-S20). No statistically significant difference was observed

Fig. 2 The network interventions regarding each outcomes. The size of the node is proportional to the number of studies. The thickness of the edges is proportional to the number of trials with a direct comparison. **A**: BMI, **B**: Weight, **C**: HOMA-IR, **D**: FI, **E**: FBG, **F**: TT, **G**: LDL, **H**: HDL, **I**: TG, **J**: TC. DASH, Dietary approaches to stop hypertension; Low-calorie + M, Low-calorie diet plus metformin; Low-carb, Low- carbohydrate diet; High-P, High-Protein diet; Low-GI, Low-Glycemic Index diet; Low-P, Low-Protein diet

Table 2 Interventions' SUCRA% regarding each outcomes

Dietary approaches		Anthropometric measurements		Glycemic factors			Lipid factors				Hormonal parameters	Summary ranking
		BMI	Weight	HOMA-IR	FBG	FI	TC	TG	HDL	LDL	TT	All outcomes combined
DASH	SUCRA %	57.1	53.3[2]	**80.4**[2]	**76.6**	**79.7**	61.8	**82.1**	61.8	44.4	54.5	64.8
High-P		29.6	17.9	–	50.0	39.3	43.9	53.6	23.6	54.9	18.4	36.8
Low-calorie		**73.6**	69.9	59.1	20.1	67.5	51.8	38.7	56.8	41.5	61.9	54.1
Low-carb		–	–	50.7	73.4	52.9	**69.7**	46.7	55.2	22.5	67.4	54.8
Low-fat		60.1	60.6		51.1	61.2	52.5	43.6	–	–	51.4	54.4
Low-GI		36.6	35.3	32.6	40.4	34.8	53.8	64.1	–	–	44.8	42.8
Low-P		–	–	–	–	16.0	–	–	–	–	–	16.0
Mediterranean		65.6	–	–	–	–	–	–	–	–	–	65.6
Low-calorie + M		–	**74.4**	59.6	31.4	64.5	–	–	–	–	–	57.5
Metformin		38.5	–	30.9	54.5	37.9	23.7	28.5	36.6	**78.1**	**71.2**	44.4
Normal		38.8	35.8	36.6	52.5	46.1	42.6	42.6	**65.7**	58.4	30.1	44.9

SUCRA values range from 0 to 100%. The higher the SUCRA value, and the closer to 100%, the higher the likelihood that intervention is in the top rank or one of the top ranks. The top interventions are in bold text. [2]Means statistically significant difference was observed when the intervention was compared with normal diet

FBG: fasting blood glucose; FI: fasting insulin; TG: triglyceride; TC: cholesterol; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; TT: total testosterone;

DASH, Dietary approaches to stop hypertension; Low-calorie + M, Low-calorie diet plus metformin; Low-carb, Low- carbohydrate diet; High-P, High-Protein diet; Low-GI, Low-Glycemic Index diet; Low-P, Low-Protein diet

in the effects of the interventions (Additional file 1: Table S12).

Qualitative synthesis

Ten studies were included in the qualitative synthesis. In six articles, there were insufficient data regarding FSH and LH level outcomes [22–27]. Most studies reported no significant differences in FSH and LH values after the treatment. Additionally, there were no significant differences between the intervention and control groups. In two RCTs, the weight and BMI changes were measured in terms of percentage, which was not used in statistical analysis [28, 29]. Mittal et al. demonstrated a significant change in weight and BMI in the vegan group. Ornstein et al. showed that there was a weight change, but it was not statistically significant. One article did not report SD value for weight after the intervention time [30]. The authors reported that there was a change in patients' weight but it was not statistically significant. In the fourth article, the data were in median [31]. The results show that vegan participants lost significantly more weight than patients in the low-calorie diet group.

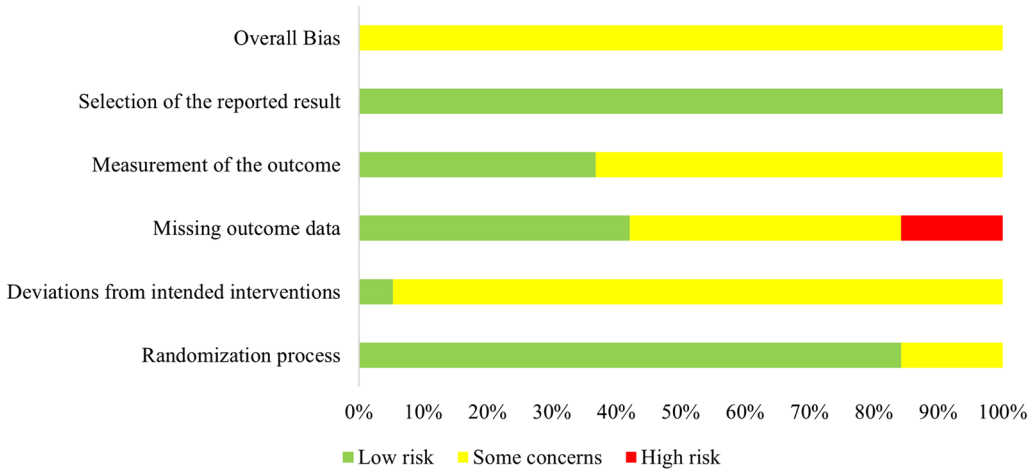

Fig. 3 Overall quality of included studies

Risk of bias assessment and certainty of the evidence

Risk of bias assessments reporting overall quality of included studies are presented in Fig. 3. Domain and study levels for each outcome separately can be found in the Additional file 1: Material. A majority of studies carried some concerns, while there were some high-risk points in 3 trials. The "missing outcome data" domain was considered as a high bias risk in these trials. Detailed results are found in Additional file 1: Figure S21-S40. For each comparison, the level of certainty of evidence ranged from low to high. Low certainty of evidence was mostly due to wide confidence intervals. Additional file 1: Table S13–23 contain the results of the GRADE assessment. No inconsistent results were indicated by the inconsistency test for any of the results. (Additional file 1: Figure S41-S49).

Discussion

The purpose of this study was to create a ranking of the interventions used in treatment of PCOS and to identify which dietary intervention was most beneficial in regulating anthropometric, glycemic, lipid, and hormonal parameters in patients. Our NMA, including 19 RCTs with 708 patients, showed that different dietary interventions could influence anthropometric and metabolic parameters in PCOS.

Our results show that the DASH diet had a statistically significant, superior effect on reducing HOMA-IR and weight compared to the control normal diet, among the studied dietary interventions in women with PCOS. In measuring the severity of IR, HOMA-IR is a more reliable indicator than fasting insulin levels. Our results are consistent with a previous meta-analysis which included 19 trials (1193 women with PCOS) and indicated that the DASH diet and the calorie-restricted diet were likely to be optimal for reducing IR and improving body composition in women with PCOS. The DASH diet may have a positive impact on glycemic management by increasing β-cell function, decreasing high glucose and HbA1c levels, and improving insulin sensitivity [34–37]. Furthermore, the DASH diet provides high fibre intake, which is crucial for patients with metabolic disorders [38]. Various clinical trials have suggested that the DASH diet, either alone or combined with other lifestyle changes, can be effective in treating several diseases aside from hypertension [36].

We also found that a calorie-restricted diet is likely to be an effective option for losing weight. Low-calorie diets have been associated with weight loss that results in decreased fat mass and preserved lean body mass [39]. Abdominal fat has a strong association with insulin resistance, hyperandrogenism, and PCOS. Previous research has shown a correlation between the return of ovulation and the reduction of abdominal obesity. The improvement of metabolic and reproductive risk is significantly impacted by the observed reduction in abdominal fat [40].

Our analysis shows that the Mediterranean diet is an effective dietary intervention for reducing BMI. However, due to a limited number of studies, only one trial evaluated the effects of the Mediterranean diet.

For patients with IR, the recommendations prefer those diets in which the ratio of macronutrients is the same as that of normal dietary recommendations [42–44]. The beneficial effects of the balanced diets are proved in our NMA, since the high protein diet produced lower results (SUCRA 36.8%) compared to the normal diet (SUCRA 44.93%) or the DASH diet (SUCRA 64.78%). This is also supported by the fact that among the many dietary interventions, those which primarily aim to achieve desired results by changing the ratio of macronutrients (for example low-carbohydrate diet, low-fat diet) did not achieve a statistically significant difference compared to other dietary interventions.

In the treatment of PCOS, metformin is the currently preferred metabolic treatment [45]. The present NMA of drug therapy effectiveness could only examine a small group of cases (n = 39), and our results showed that metformin was the most effective intervention for decreasing total testosterone levels.

Strengths and limitations

This study, to our knowledge, is the first network meta-analysis to rank the impact of dietary interventions in PCOS patients. The major strengths of this study are that it includes most of the relevant parameters in PCOS and benefits from a rigorous methodology. Furthermore, this study established an advantageous dietary intervention as a suggestion for clinicians in the treatment of PCOS. The main limitation of this study is the small number of direct comparisons and the low number of patients participating in the trials. The involved patients in the RCTs varied in age and ethnicity, to our knowledge, PCOS may present differently in different ethnicities and populations. In addition there is limited information in the included trials about the specific PCOS phenotype of the patients. PCOS phenotype may also influence the results. Another limitation in evaluating the data is presented by the different durations of the interventions. When analysing the results, it is important to consider each country's environment and food habits. DASH diet can be difficult to implement in some countries.

Implications for practice and research

For the purposes of addressing new questions and providing greater clarity, more RCTs with larger case numbers

are needed, and with longer follow-up times. With regard to informing practice, our results provide clear and useful guidance for clinicians concerning the beneficial effects of the DASH diet in the treatment of PCOS.

Conclusion

It has been shown that implementing research results into everyday practice is essential and brings major health and economic benefits [46, 47]. Normalising weight and metabolic and hormonal parameters is important in treating PCOS but determining which dietary intervention should be preferred is complicated by a lack of clear evidence. Based on our results, the DASH diet should be preferred in the treatment of PCOS, especially in patients unable to tolerate the gastrointestinal side effects induced by metformin. In addition, a notable observation was that diets that avoid changing the ratio of macronutrients (for example, the DASH diet), and rather reduce the daily amount of calories and change the quality of the food, were generally more effective in reducing symptoms than those diets which aim to change the ratio of macronutrients (for example, a protein-rich diet).

Abbreviations

BMI	Body mass index
CrI	Credible intervals
DASH	Dietary approaches to stop hypertension
FBG	Fasting blood glucose
FI	Fasting insulin
FSH	Follicle stimulating hormone
GRADE	The Grading of Recommendations Assessment, Development, and Evaluation
LH	Luteinizing hormone
MD	Mean difference
NMA	Network meta-analysis
PCOS	Polycystic ovarian syndrome
RCT	Randomised controlled trial
RoB 2	Risk-of-bias tool for randomised trials
SUCRA	The surface under the cumulative ranking curve
TC	Total cholesterol
TT	Total testosterone

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12978-024-01758-5.

Additional file 1: PRISMA NMA Checklist; Searchkey; Summary of the dietary interventions; and Rankogram, Surface under the cumulative ranking (SUCRA) curves, League table, Risk of bias assessment, Assessment of certainty of evidence, Investigations of inconsistency of all outcomes.

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Author contributions

A.E.J.:conceptualization, project administration, methodology, formal analysis, writing – original draft; M.P.S.: conceptualization, formal analysis, visualization, writing – review & editing; B.T.:conceptualization, formal analysis, visualization, writing – review & editing; N.G.:conceptualization, formal analysis, visualization, writing – review & editing; P.H.:conceptualization; review & editing; P.N.:conceptualization; review & editing; F.B.: conceptualization; review & editing; N.Á.: conceptualization; review & editing; R.J.: conceptualization, formal analysis, visualization, data curation, writing – original; supervision. All authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the manuscript's concept, design, analysis, writing, or revision.

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Available of data and materials

All data described in the manuscript, and data supporting the results, will be made publicly and freely available without restriction in the Additional file 1: material.

Declarations

Ethics approval and consent to participate

Ethics approval and participants consent are not required because this study is a meta-analysis based on the published studies.

Competing interests

None to declare.

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