





Effectiveness of Personalized Nutrition on Management Diabetes Mellitus Type 2 and Prediabetes in Adults: A Systematic Review

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Background: Diabetes mellitus type 2 and prediabetes are diet-related diseases with varied individual responses to routine dietary interventions. Personalized nutrition, a novel approach tailored to individual variability in response to nutrients, may offer improved outcomes.

Purpose: This systematic review analyzed the effectiveness of personalized nutrition compared to control diet for managing diabetes mellitus type 2 and prediabetes.

Methods: A comprehensive search was conducted in Medline, PubMed, and Cochrane CENTRAL for randomized controlled trials (RCTs) published in English up to March 31, 2024. Studies involving humans were screened independently by two reviewers, who also extracted data and assessed study quality using the Risk of Bias 2 tool. The SWiM (Synthesis Without Meta-Analysis) approach was used to summarize effect estimates and combine p-values.

Results: Eight studies, including five RCTs, met the inclusion criteria. Two studies had high risk of bias and another six had some concern bias. Personalized nutrition significantly reduced HbA1c (median mean difference: -0.925% , $p < 0.01$, 4 studies), though the effect was minimal in studies with some concern of bias (-0.035%). Fasting glucose showed no significant change ($p = 0.12$, 2 studies) in prediabetics, while PPGR improved significantly (-14.85 mg/dLxh, $p < 0.01$, 2 studies). Energy intake did not significantly differ ($p = 0.06$). Personalized nutrition reduced body weight (-0.58%) compared to control only when including high-risk studies; this effect was not significant in lower-risk studies ($p = 0.06$). Personalized nutrition also significantly reduced carbohydrate intake (-10.8% of energy, $p = 0.02$) compared to control diet. It also improved gut microbiome diversity and richness from baseline in prediabetics.

Conclusion: Personalized nutrition shows promise in improving HbA1c, PPGR, and reducing carbohydrate intake, with potential effects on body weight, in adults with diabetes mellitus type 2 or prediabetes. Effects on fasting glucose and energy intake remain unclear.

Keywords: personalized nutrition, diabetes mellitus type 2, prediabetes, adults

Introduction

In 2021, the global prevalence of diabetes reached 6.1% of the world's population, with approximately 529 million people, with the majority of them (96%) being diabetes mellitus type 2.¹ Diabetes mellitus type 2 caused 66.3 million Disability-Adjusted Life Years (DALYs) in 2019.² In 2021, the prevalence of prediabetes, specifically impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), was 9.1% (464 million) and 5.8% (298 million), respectively, among adults aged 20–79 years worldwide. By 2045, the global prevalence of IGT and IFG is projected to increase to 10.0% (638 million) and 6.5% (414 million). Additionally, prediabetes can progress to diabetes in up to 50% of cases within 5 years.³ Nutrition plays a key role in managing symptoms and preventing progression of both diabetes and prediabetes.



Nutritional interventions can help maintain glycemic targets, manage body weight, and improve cardiovascular risk factors (such as blood pressure and lipid profile) in people with diabetes and prediabetes.⁴

Recent findings highlight that metabolic responses to diets can vary between individuals.⁵ This variability was evident in a randomized controlled trial involving 609 overweight adults, which demonstrated significant variation in weight loss, with a range of about 40 kg among individuals in both the low-fat and low-carbohydrate diet groups over 12 months.⁶ These differences are thought to be driven by fundamental factors that influence our individual responses to food and the biological effects of its consumption include the human genome, the epigenome, the microbiome, and variations between individuals in environmental exposures and lifestyle habits.⁵

Over the past two decades, a nutritional intervention strategy known as personalized nutrition has emerged. Personalized nutrition has developed based on the understanding that each individual's response to a nutritional intervention can significantly differ.⁴ Personalized nutrition can predict an individual's unique response to a nutrient using machine learning. Personalized nutrition utilizes data based on anthropometry, food composition, metabolism, genotype-phenotype, and microbiome to generate its nutritional recommendation algorithms.⁴

Several randomized controlled trials (RCTs) have been conducted on personalized nutrition in addressing diabetes mellitus type 2 and prediabetes. However, far too little attention has been paid to synthesizing the effectiveness of personalized nutrition compared to a control diet in managing these conditions. Therefore, a systematic review is needed to synthesize the effectiveness of personalized nutrition compared to a control diet in managing diabetes mellitus type 2 and prediabetes.

Methodology

Protocol and Registration

We performed a systematic review following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions⁷ and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 Checklist⁸ ([Supplementary 1](#)), and the Synthesis Without Meta-analysis (SWiM)⁹ ([Supplementary 2](#)). The study protocol has been registered at International Prospective Register of Systematic Reviews (PROSPERO), Number Centre for Reviews and Dissemination (CRD) 42024532817.

Eligibility Criteria

The inclusion criteria for study selection in this systematic review were (detailed on [Supplementary 3](#)):

1. Studies on adults (aged > 18 years) diagnosed with diabetes mellitus type 2 and prediabetes.
2. Studies that apply personalized nutrition interventions to manage diabetes mellitus type 2 and prediabetes. There are some differences in defining the term personalized nutrition, but in this review, personalized nutrition is defined according to the American Nutrition Association, which is a dietary recommendation approach based on individual differences in response to nutrition, nutritional status, eating patterns, meal timing, and environmental exposures. These differences arise due to variations in biochemistry, metabolism, genetics, and microbiome.¹⁰
3. Studies that provide data on the effectiveness of personalized nutrition compared to control diet.
4. Studies published in full-text format in English.
5. Study design using RCTs.

The exclusion criteria for study selection in this systematic review were (detailed on [Supplementary 3](#)):

1. Studies conducted on children, adolescents, and animal subjects.
2. Diseases unrelated to diabetes mellitus type 2 and prediabetes.
3. Inadequate data in the study.
4. Study designs using qualitative methods, case series, narrative reviews, systematic reviews, and observational studies (cohort, case-control, and cross-sectional studies).

Information Sources and Search Strategy

The study search sources were PubMed, Cochrane CENTRAL, and Medline (Ovid). We searched those published up to March 31, 2024, conducted on humans, with a randomized controlled trial design, and written in English. The literature search strategy was carried out using all Medical Subject Headings (MeSH) terms and text words for each concept in the search, combined with “OR”. Subsequently, the concepts of diabetes mellitus type 2 and prediabetes were merged using “OR” to form the fourth concept. The personalized nutrition concept and the fourth concept were combined using “AND”. A detailed searching strategy is listed in [Supplementary 4](#). The retrieved studies were exported to the EndNote 21 citation manager.

Selection Process

Two reviewers Elisa Fauziyatul Munawaroh (EFM) and Andri Wijayakesuma (AW) independently screened the literature from all sources. In case of disagreement, it was resolved through consensus. A third reviewer, Dani Dani (DD) was involved if consensus could not be reached. The first stage assessed abstracts and titles using Covidence software. The second stage assessed the full texts using Covidence software.

Data Collection Process and Data Items

Two reviewers (EFM and AW) independently extracted data from a subset of the studies (20%). The inter-rater agreement between the two reviewers was high $\geq 95\%$. Any disagreements were resolved by reaching a consensus. Subsequently, EFM extracted data from all included studies. Data extracted onto Table of Study Characteristics included: author, year of publication, country, study design, participant type (age, gender), number of participants, description of the intervention, description of the comparison, intervention and follow-up duration, and measured outcomes.

Study Risk of Bias Assessment

Two reviewers (EFM and AW) assessed the quality of the included studies. In case of disagreement, it was resolved through consensus. If consensus could not be reached, DD was involved. The study quality assessment used Cochrane’s ROB 2 (Risk of Bias 2). ROB 2 consists of five domains of bias that are evaluated: the randomization process, the effect of the intervention, missing data, outcome measurement, and result reporting. The quality assessment results were then classified into high risk, some concerns, or low risk.⁷

Synthesis Methods

1. A meta-analysis was not considered appropriate for this review due to the significant heterogeneity until 99%, suggesting that the studies varied greatly in their participants, interventions, or measurement methods. Despite after we do subgroup analysis the source of heterogeneity could not be explained. A meta-analysis was not considered appropriate for this review also due to the limited number of studies and lacked enough comparable data of the included studies (often 2 RCTs).
2. We used the Synthesis Without Meta-analysis (SWiM) method for synthesis instead of meta-analysis. SWiM was used in this systematic review to examine the quantitative effects of interventions. The synthesis included a structured summary of effect estimates as well as the combination of p values to evaluate the overall statistical significance. P value combining was conducted using Fisher’s method.^{7,9}
3. We analyzed studies by separating the risk of bias. The visually display results used the box and whisker plot.
4. The review includes quantitative data on effect sizes, using the median mean difference (MD) as the measurement. Median MD was calculated for RCTs that provided necessary follow-up data for each outcome.
5. Following standard Cochrane methodology, we created a Table Summary of Findings.⁷ We considered it important to summarize the following outcomes.
 - a. HbA1c (%)
 - b. Fasting Blood Glucose (mmol/L)
 - c. PPGR (mg/dlxh)

- d. Body Weight (%)
- e. Energy Intake (% of energy)
- f. Carbohydrate Intake (% of energy)
- g. Gut Microbiome Richness and Diversity (species)

Certainty Assessment

The quality of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system. The quality of evidence was evaluated by considering the risk of bias, inconsistency, indirectness, imprecision, and publication bias. Each domain was classified as not serious, serious, or very serious, except for the publication bias domain, which was classified as undetected or strongly suspected. GRADEpro Software was used to guide the evidence assessment for each outcome.¹¹ The results of the evidence quality assessment were classified as high, moderate, low, or very low. The results of the evidence quality assessment are presented in the Table Summary of Findings.

Results

Study Selection

The search results from three electronic databases, Medline, Cochrane CENTRAL, and PubMed, yielded 5061 relevant studies ([Supplementary 5](#)). After automatically excluding non-RCTs and duplicates using Covidence software, as well as manual exclusions, 3211 studies remained for the title and abstract screening. Based on title and abstract screening, 3200 studies were excluded, and eleven studies were included for full-text screening. From the full-text screening, three studies were excluded, and eight studies were included for review. Although our review included eight articles, only five distinct RCTs were represented. One RCT was reported in three separate articles: Ben-Yacov et al 2021;¹² Ben-Yacov et al 2023;¹³ Shoer et al 2023.¹⁴ Another RCT was reported in two articles: Kharmats et al 2023¹⁵ and Popp et al, 2022.¹⁶ The remaining three RCTs were each reported in a single article: Joshi et al 2023;¹⁷ Karvela et al 2024,¹⁸ and Rein et al, 2022.¹⁹ [Figure 1](#) presents the PRISMA diagram flow illustrating the selection process of the included studies.

Study Characteristics

The study characteristics table is presented in [Table 1](#), and the studies included were conducted in Israel, India, United of Kingdom (UK), and the United States of America(USA). From these eight studies, there were only five clinical trials. Four of the five clinical trials used an individually randomized controlled trial design.^{12,16–18} Only one study used a crossover randomized controlled trial design.¹⁹ The total number of participants was 919 individuals with prediabetes or diabetes mellitus type 2. The five personalized nutrition clinical trials included in this review consistently used clinical data, anthropometric measurements, and blood biomarkers to predict participants' responses to a particular food. In addition to these data, four of the clinical trials also utilized microbiome data.^{12,16–19} However, only one clinical trial used genotype data.¹⁸ The duration of the interventions ranged from 2 weeks to 1 year. The comparisons consisted of a Mediterranean diet, a low-fat diet, and a diet according to recommendations from nutrition experts (medical nutrition therapy).

Risk of Bias in Studies

[Supplementary 6](#) shows the quality assessment results of the eight studies evaluated based on Cochrane Risk of Bias 2. Two studies were rated as having a high risk of bias because the allocation was not concealed,^{17,18} and six were rated as having some concern because of bias due to deviation from intended interventions and reporting results.^{12–16,19}

Results of Synthesis and Certainty of Evidence

Based on [Table 2](#), which summarizes the findings on the effectiveness of personalized nutrition compared to a control diet for managing diabetes mellitus type 2 and prediabetes, the following is the data analysis for each outcome (quantitative synthesis detailed on [Supplementary 7](#)):

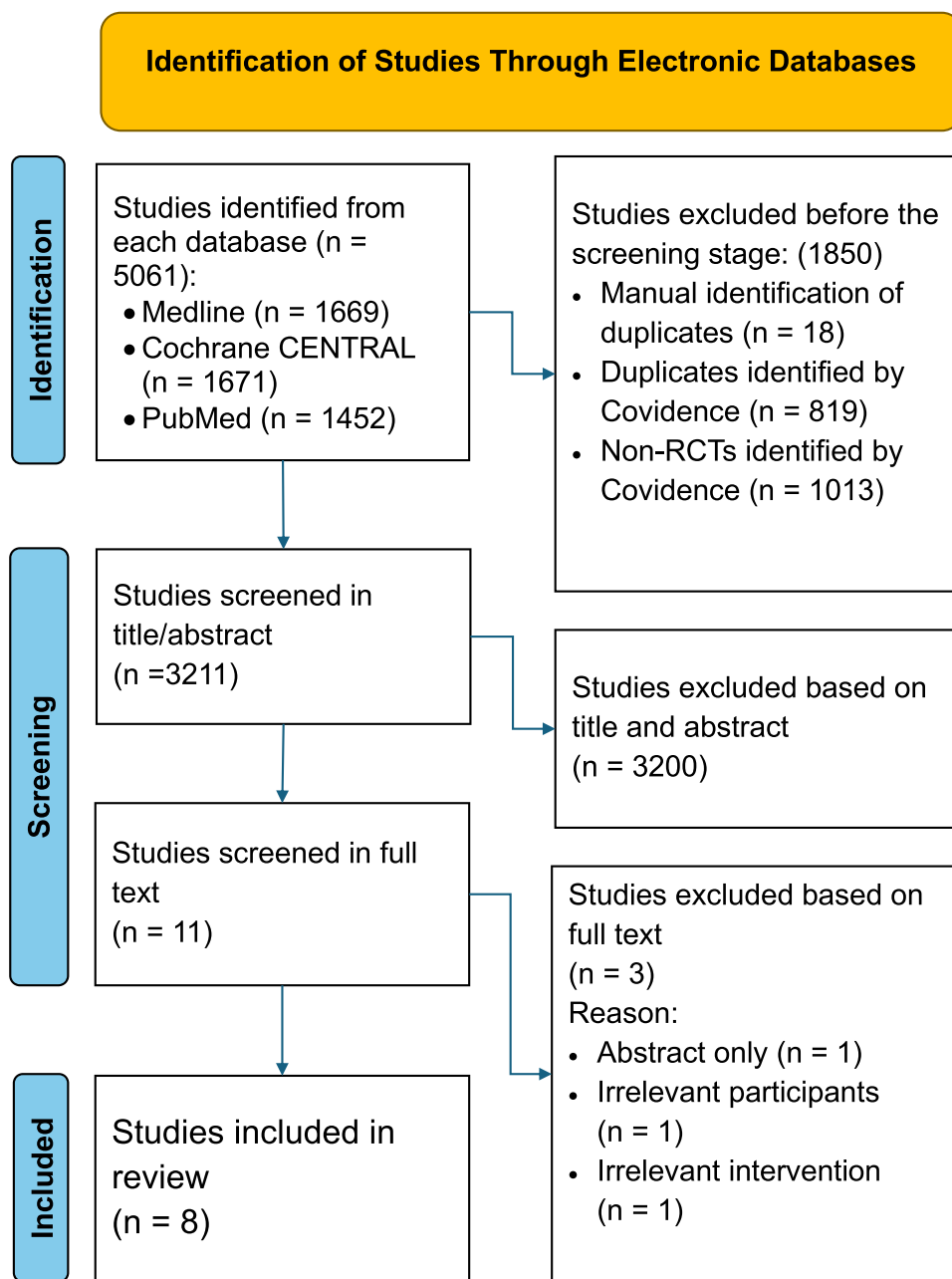


Figure 1 PRISMA Diagram Flow.

Effectiveness of Personalized Nutrition on HbA1c

- The synthesis of the summarized effect estimate of HbA1c values from four studies (Ben-Yacov et al 2021;¹² Joshi et al 2023;¹⁷ Karvela et al 2024;¹⁸ Kharmats et al 2023¹⁵) showed a reduction in HbA1c levels in the personalized nutrition group, with a median mean difference (MD) of -0.925% compared to the control diet in diabetes mellitus type 2 and prediabetes patients. The combined p-value synthesis from these four studies indicated that this reduction was significant ($p < 0.0$, 4 studies) showed in Figure 2.
- When the synthesis was limited to studies with some concerns risk of bias (Ben-Yacov et al 2021;¹² Kharmats et al 2023¹⁵), decreased HbA1c levels in the personalized nutrition group were still observed, with a median MD of -0.035% compared to the control diet in diabetes mellitus type 2 and prediabetes patients. The combined p-value also remained significant ($p < 0.0$, 2 studies) showed in Figure 2.

Table 1 Table of Study Characteristics

No.	Author, Year of Publication	Country	Study Design	Participant Characteristics (n)	Intervention Description	Comparison Description	Outcome Reported
1	Ben-Yacov et al 2021 ¹²	Israel	Biphasic, randomized controlled trial, single-blind	Prediabetes (n = 225): Age 50 ± 7 years, 58% women, Body Mass Index (BMI) 31.3 ± 5.8 kg/m ² , HbA1c 5.9 ± 0.2%, Fasting blood glucose 114 ± 12 mg/dl	Personalized postprandial targeting (PPT) diet. This diet recommendation integrates data from self-reported dietary tracking using a smartphone app, gut microbiome data from metagenomic shotgun sequencing of stool samples, and clinical data from continuous glucose monitoring, blood biomarkers, and anthropometry. Duration intervention: 6 months, Follow-up: 6, 12 months.	Mediterranean diet. Recommends whole grain bread, grains, legumes, low-fat dairy products, fish, poultry, olive oil, fruits, and vegetables. This diet does not recommend sweet foods, fried foods, snacks, fatty and processed meats, and high-fat dairy products. Diet composition: 45–65% of energy intake from carbohydrates, 15–20% from protein, and <35% from fat, with <10% from saturated fat.	<ul style="list-style-type: none"> • Time spent with glucose above 140 mg/dL • HbA1c • 2-hour postprandial glucose • Average glucose from CGM (Continuous Glucose Monitoring) • Fasting blood glucose • HOMA-Insulin Resistance • Fructosamine • 5-hour postprandial glucose response (PPGR) excursion • Total cholesterol • Triglycerides • HDL (High-Density Lipoprotein) • LDL (Low-Density Lipoprotein) • ALT (Alanine Aminotransferase) and AST (Aspartate Aminotransferase) activity, liver ultrasound, fatty liver index) • Blood pressure • Body weight • Body composition
2	Ben-Yacov et al, 2023 ¹³	Israel	Biphasic, randomized controlled trial, single-blind	Prediabetes (n = 200): 58% women, BMI 31.3 ± 5.8 kg/m ² , HbA1c 5.9 ± 0.2%, Fasting blood glucose 114 ± 12 mg/dl	PPT diet that recommend integrates data from self-reported dietary tracking using a smartphone app, gut microbiome data from metagenomic shotgun sequencing of stool samples, and clinical data from continuous glucose monitoring, blood biomarkers, and anthropometry. Duration: intervention: 6 months, Follow-up: 6, 12 months.	Mediterranean diet. Recommends whole grain bread, grains, legumes, low-fat dairy products, fish, poultry, olive oil, fruits, and vegetables. Does not recommend sweet foods, fried foods, snacks, fatty and processed meats, and high-fat dairy products. Diet composition: 45–65% of energy intake from carbohydrates, 15–20% from protein, and <35% from fat, with <10% from saturated fat.	<ul style="list-style-type: none"> • Macronutrient and fiber intake • Gut microbiome diversity • Diet adherence • Time with glucose above 140 mg/dL • Average glucose from CGM • Body weight • BMI • Basal metabolic rate • Body fat percentage

3	Joshi et al, 2023 ¹⁷	India	Open-label randomized controlled trial	Newly diagnosed Diabetes mellitus type 2 (n = 319)	Digital Twin Personalized nutrition predicting postprandial glycemic response using Digital Twin Technology. This diet recommendation integrates food nutrition data, clinical conditions, and laboratory profiles. Patients were also recommended to walk 5000 steps daily for three months, followed by 1000 steps per day in the following month. Additionally, resistance exercise for 20 minutes three times a week, 7–8 hours of sleep, and daily meditation were recommended. Duration: 1 year. Follow-up: 1 year.	Standard care receiving dietary recommendations based on individual assessment of current dietary patterns, preferences, and metabolic goals. Standard care followed a low-calorie diet with reductions in saturated fats, starches, and added sugars. Also recommended is physical activity, including 150 minutes of moderate-to-high intensity aerobic activity per week, 3 days per week, and strength training 2–3 sessions per week.	<ul style="list-style-type: none"> ● HbA1c ● Mean amplitude of glycemic excursions (MAGE) ● HOMA2-Insulin resistance ● Reduction in diabetes medication usage ● Body weight ● BMI ● Waist circumference ● Diabetes remission ● Liver score ● Visceral adiposity
4	Karvela et al, 2024 ¹⁸	UK	Open-label randomized controlled trial	Prediabetes (n = 148): Age 58 ± 11 years, 69% women, BMI 30.4 ± 6.9, HbA1c 6–6.4%	Deoxyribonucleic Acid (DNA)-personalized nutrition using genetic biomarkers, phenotype, and nutrient intake profile to determine diet recommendations. Duration: 26 weeks. Follow-up: 6, 12, and 26 weeks.	Standard care using dietitian recommendations according to healthy dietary guidelines, specifically the NICE (National Institute for Health and Care Excellence) guidelines.	<ul style="list-style-type: none"> ● Fasting blood glucose ● 2-hour postprandial blood glucose ● HbA1c ● Dietary intake (energy, salt, carbohydrates, fat, saturated fat)
5	Kharmats et al, 2023 ¹⁵	USA	Parallel group clinical trial	Prediabetes or controlled Diabetes mellitus type 2 (n = 204)	Personalized diet using a machine learning algorithm to estimate postprandial glycemic response to food. Recommendations integrate data from anthropometry, blood tests (eg, HbA1c), lifestyle based on questionnaire responses, and microbiome quantity. Duration: intervention: 6 months. Follow-up: 6 months.	Low-fat diet recommends total fat intake <25% of total energy and saturated fat <7% of total energy.	<ul style="list-style-type: none"> ● Glycemic variability: MAGE, average glucose from CGM, continuous overall net glycemic action (CONGA) ● HbA1c ● Adverse effects
6	Popp et al, 2022 ¹⁶	USA	Parallel group clinical trial	Prediabetes or controlled Diabetes mellitus type 2 (n = 204): Age 58 ± 11 years, 66.8% women, BMI 33.9 ± 4.8 kg/m ² , HbA1c 5.8 ± 0.6%	Personalized diet using a machine learning algorithm to estimate postprandial glycemic response to food. Recommendations integrate data from anthropometry, blood tests (eg, HbA1c), lifestyle based on questionnaire responses, and microbiome quantity. Duration: intervention: 6 months. Follow-up: 6 months.	A low-fat diet recommends a total fat intake of <25% of total energy and saturated fat of <7% of total energy.	<ul style="list-style-type: none"> ● Percentage weight loss ● Body composition: fat mass, body fat percentage, lean mass ● Adaptive thermogenesis (difference between measured and estimated resting energy expenditure) ● Dietary intake (carbohydrates, fats, protein) ● Physical activity ● Adherence to counseling and self-monitoring

(Continued)

Table I (Continued).

No.	Author, Year of Publication	Country	Study Design	Participant Characteristics (n)	Intervention Description	Comparison Description	Outcome Reported
7	Rein et al, 2022 ¹⁹	Israel	Single-center randomized crossover trial	Newly diagnosed Diabetes mellitus type 2 (n = 23): Age 53.5 ± 8.9 years, BMI 30.8 ± 7.4 kg/m ² , HbA1c 6.8 ± 0.4%	PPT diet predicting glycemic response based on blood test results (HbA1c, fasting blood glucose, and hemoglobin), gut microbiota quantity, anthropometric data (such as body weight and waist circumference), health condition questionnaire, and dietary components. Duration: 2 weeks. Follow-up: 2 weeks and 6 months.	The Mediterranean diet recommends whole grain bread, grains, legumes, low-fat dairy products, fish, poultry, olive oil, fruits, and vegetables. Not recommended foods include commercial bread products, sweets and pastries, fried foods and snacks, fatty and processed meats, and high-fat dairy products. Mediterranean diet composition: 45–65% of energy intake from carbohydrates, 15–20% from protein, and <35% from fat, with <10% from saturated fat.	<ul style="list-style-type: none"> ● Fructosamine ● PPGR ● Glucose measurements from CGM: hourly duration for glucose levels above 140, 150, 160, 170, 180 mg/dl, and glucose fluctuation
8	Shoer et al, 2023 ¹⁴	Israel	Biphasic, randomized controlled trial, single-blind	Prediabetes (n = 225): 58% women, BMI 31.3 ± 5.8 kg/m ² , HbA1c 5.9 ± 0.2%, Fasting blood glucose 114 ± 12 mg/dl	PPT diet that recommend integrates data from self-reported dietary tracking using a smartphone app, gut microbiome data from metagenomic shotgun sequencing of stool samples, and clinical data from continuous glucose monitoring, blood biomarkers, and anthropometry. Duration: intervention: 6 months, Follow-up: 6, 12 months.	Mediterranean diet. Recommends whole grain bread, grains, legumes, low-fat dairy products, fish, poultry, olive oil, fruits, and vegetables. Does not recommend sweet foods, fried foods, snacks, fatty and processed meats, and high-fat dairy products. Diet composition: 45–65% of energy intake from carbohydrates, 15–20% from protein, and <35% from fat, with <10% from saturated fat.	<ul style="list-style-type: none"> ● Gut microbiome diversity ● Gut microbiome quantity ● Serum metabolites ● Cytokines

Table 2 Summary of Findings on the Effectiveness of Personalized Nutrition Compared to Control Diet for Managing Diabetes Mellitus Type 2 and Prediabetes

No	Outcome and Follow-Up (First Author, Year)	Patients (Studies), N	Certainty (GRADE)	Comments
1.	HbA1c (%) Follow-up: range 26 weeks to 1 year (Ben-Yacov et al 2021; ¹² Joshi et al 2023; ¹⁷ Karvela et al 2024; ¹⁸ Kharmats et al 2023 ¹⁵)	Total: 676 (4 RCTs) Diabetes Mellitus (DM) Type 2 and Prediabetes	⊕⊕○○ Low ^{a,b}	Personalized nutrition significantly reduces HbA1c levels compared to the control diet ($p < 0.0$, 4 studies). Personalized nutrition lowers HbA1c levels with a median mean difference of -0.925% compared to the control diet. When limited to studies with some concern of bias, the p-value remains significant ($p < 0.0$, 2 studies). However, the reduction in HbA1c levels in the personalized nutrition group is minimal, with a median mean difference of -0.035% compared to the control diet.
2.	Fasting Blood Glucose (mmol/L) Follow-up: mean 6 months (Ben-Yacov et al 2021; ¹² Karvela et al 2024 ¹⁸)	285 (2 RCTs) Prediabetes	⊕⊕○○ Low ^{a,c}	Personalized nutrition did not significantly reduce fasting blood glucose compared to the control diet ($p = 0.12$, 2 studies).
3.	Postprandial Glucose Responses-PPGR (mg/dLxh) Follow-up: range 2 weeks to 6 months (Ben-Yacov et al 2021; ¹² Rein et al 2024 ¹⁹)	248 (2 RCTs) DM Type 2 and Prediabetes	⊕⊕○○ Low ^{b,c}	Personalized nutrition resulted significantly in a greater reduction in PPGR compared to the control diet ($p < 0.0$, 2 studies), with a median mean difference of -14.85 mg/dLxh.
4.	Body Weight (%) Follow-up: mean 6 months (Ben-Yacov et al 2021; ¹² Joshi et al 2023; ¹⁷ Popp et al 2022 ¹⁶)	741 (3 RCTs) DM Type 2 and Prediabetes	⊕⊕○○ Low ^{a,b}	In studies with mixed risk of bias (including some concerns and high-risk bias), personalized nutrition significantly reduced body weight compared to the control diet ($p < 0.0$, 3 studies). The median mean difference in body weight reduction was -0.58% in favor of personalized nutrition. But, when limited to studies with some concern of bias, no significant differences in body weight change were observed when the results of personalized nutrition were compared with the control diet ($p = 0.06$, 2 studies).
5.	Energy Intake (% of energy) Follow-up: mean 6 months (Ben-Yacov et al 2021; ¹² Popp et al 2022 ¹⁶)	287 (2 RCTs) DM Type 2 and Prediabetes	⊕○○ Very Low ^{b,c,d}	No significant differences in change of energy intake were observed when the results of personalized nutrition were compared with those of the control diet ($p = 0.06$, 2 studies).
6.	Carbohydrate Intake (% of energy) Follow-up: mean 6 months (Ben-Yacov et al 2021; ¹² Popp et al 2022 ¹⁶)	287 (2 RCTs) DM Type 2 and Prediabetes	⊕○○ Very Low ^{b,c,d}	Personalized nutrition significantly reduced carbohydrate intake with median mean difference of -10.8% of energy compared to the control diet compared to control diets ($p = 0.02$, 2 studies).
7.	Gut microbiome richness and diversity (species) Follow-up: mean 6 months (Ben-Yacov et al 2021; ¹² Ben-Yacov et al 2023; ¹³ Shoer et al 2023 ¹⁴)	200 (1 RCT) Prediabetes	⊕⊕○○ Low ^c	Compared to baseline, personalized nutrition significantly increased gut microbiome richness and diversity. Meanwhile, the control diet only showed a significant impact on gut microbiome diversity.

Notes: Certainty of the Evidence (GRADE):

⊕⊕⊕⊕ = High certainty: Very confident that the true effect lies close to the estimate of the effect.

⊕⊕⊕○ = Moderate certainty: Moderately confident in the effect estimate; the true effect is likely to be close but may be substantially different.

⊕⊕○○ = Low certainty: Limited confidence in the effect estimate; the true effect may be substantially different.

⊕○○○ = Very low certainty: Very little confidence in the estimate; the true effect is likely substantially different.

Reason for downgrading the certainty: ^aConcerns regarding allocation concealment and selective outcome reporting. ^bHigh clinical heterogeneity among included studies. ^cSmall sample size. ^dWide confidence intervals.

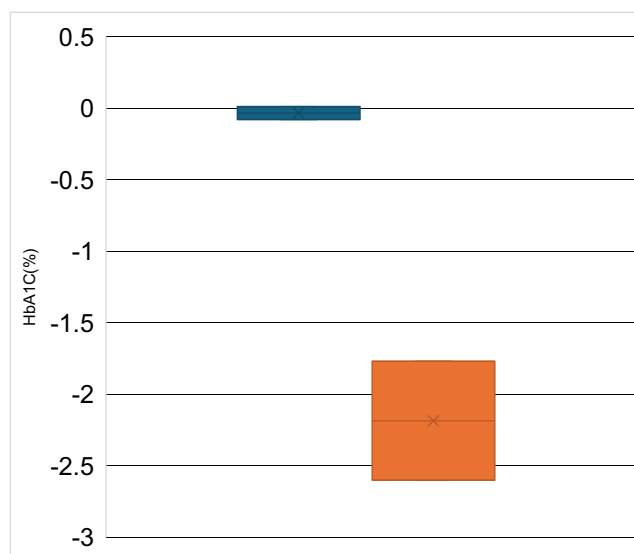


Figure 2 Box-and-whisker plots of estimate of mean differences for HbA1c and separately by the risk of bias. Data mean differences HbA1c of some concern risk bias studies (Blue). Data mean differences HbA1c of high-risk bias studies (Orange).

Effectiveness of Personalized Nutrition on Fasting Blood Glucose

- The synthesis results using the p-combining from both studies (Ben-Yacov et al, 2021¹² and Karvela et al, 2024¹⁸) found that personalized nutrition did not significantly reduce fasting blood glucose compared to control diet in prediabetes patients ($p = 0.12$, 2 studies).
- The synthesis was limited to studies with some concerns risk of bias (Ben-Yacov et al 2021¹²) found that personalized nutrition also did not significantly reduce fasting blood glucose compared to control diet in prediabetes patients.

Effectiveness of Personalized Nutrition on PPGR

- The synthesis results using the p-combining from both studies (Ben-Yacov et al, 2021¹² and Rein et al, 2022¹⁹), which are some concern risks of bias studies, found that personalized nutrition significantly reduces PPGR compared to control diet in diabetes mellitus type 2 and prediabetes patients ($p < 0.0$, 2 studies).
- The synthesis of the summarized effect estimates of PPGR values from two studies (Ben-Yacov et al, 2021¹² and Rein et al, 2022¹⁹), showed personalized nutrition reduces postprandial glucose response (PPGR) with a median mean difference of -14.85 mg/dlxh compared to the control diet in diabetes mellitus type 2 and prediabetes patients.

Effectiveness of Personalized Nutrition on Body Weight

- Based on the results, the p-combining from Ben-Yacov et al, 2021;¹² Joshi et al 2023¹⁷ and Popp et al, 2022¹⁶ that are some concern risks of bias and high-risk bias studies, personalized nutrition significantly reduced body weight compared to the control diet ($p < 0.0$, 3 studies). The median mean difference in body weight reduction was -0.58% in favor of personalized nutrition.
- But, when limited to studies with some concern of bias (Ben-Yacov et al, 2021¹² and Popp et al, 2022¹⁶) personalized nutrition did not significantly reduce body weight in diabetes mellitus type 2 and prediabetes compared to control diet ($p = 0.06$, 2 studies).

Effectiveness of Personalized Nutrition on Energy Intake

- The synthesis results using the p-combining method from both studies (Ben-Yacov et al 2021;¹² Popp et al 2022¹⁶) showed that personalized nutrition did not significantly reduce energy intake compared to the control diet in diabetes mellitus type 2 and prediabetes ($p = 0.06$, 2 studies).

Effectiveness of Personalized Nutrition on Carbohydrate Intake

- The synthesis results using the p-combining method of two studies (Ben-Yacov et al 2021;¹² Popp et al 2022¹⁶) concluded that personalized nutrition was significantly reduced by carbohydrate intake compared to control diets ($p = 0.02$, 2 studies) in diabetes mellitus type 2 and prediabetes.
- The synthesis of the summarized effect estimates of carbohydrates intake from two studies (Ben-Yacov et al 2021;¹² Popp et al 2022¹⁶) showed personalized nutrition reduces carbohydrate intake with a median mean difference of -10.8% of energy compared to the control diet in diabetes mellitus type 2 and prediabetes patients.

Effectiveness of Personalized Nutrition on Gut Microbiome

- The one study (Ben-Yacov et al 2021;¹² Ben-Yacov et al 2023;¹³ Shoer et al 2023¹⁴) concluded that personalized nutrition significantly increased gut microbiome richness and diversity compared to baseline in prediabetes patients ($p = 0.007$). Meanwhile, the control diet only showed a significant impact on gut microbiome diversity in prediabetes patients ($p = 0.18$).

Discussion

The goal of a nutritional intervention in diabetes mellitus type 2, according to the American Diabetes Association (ADA) guidelines, is to improve HbA1c levels, blood pressure, and cholesterol, achieve and maintain target body weight, and prevent diabetes complications.²⁰ Elevated HbA1c significant challenges for individuals with diabetes mellitus type 2. These factors serve as key indicators for assessing glycemic control.²¹ Personalized nutrition significantly reduces HbA1c levels compared to control diets with a median mean difference of -0.925% – 0.035% in diabetes mellitus type 2 and prediabetes. The significant reduction in HbA1c in personalized nutrition is likely due to personalized nutrition significantly reduced carbohydrate intake, with a median mean difference of -10.8% compared to control diets. This is consistent with other randomized controlled trial studies, which state that HbA1c levels in a low-carbohydrate diet (8.5%) decreased significantly ($p < 0.05$) compared to those in a low-fat diet (4%) for 3 months.²¹

Personalized nutrition also significantly reduces PPGR, with a median mean difference of -14.85 mg/dlxh. This suggests that personalized nutrition effectively modulates glycemic responses after meals. This aligns with its primary goal of improving short-term glucose metabolism in diabetes mellitus type 2 and prediabetes.

The reduction in HbA1c is consistent with a decrease in PPGR but does not align with a reduction in fasting blood glucose levels. The difference in effects between HbA1c and fasting blood glucose may be due to HbA1c being more influenced by postprandial blood glucose than fasting blood glucose. This is because the participants recruited in the studies are controlled prediabetes and diabetes mellitus patients. This is supported by the study by Monnier and Colette, which found that in controlled diabetes patients (with low HbA1c), postprandial glucose is more dominant in affecting HbA1c. Conversely, in uncontrolled diabetes patients (with high HbA1c), fasting blood glucose is more dominant. Specifically, the study found that in patients with HbA1c less than 7.3% , postprandial glucose contributes about 70% to the effect on HbA1c. In contrast, in patients with HbA1c greater than 10.2% , the contribution of postprandial glucose drops to 30% , making fasting blood glucose a more dominant factor.²²

Weight loss in diabetes mellitus type 2 and prediabetes aims to improve clinical benefits and reduce disease progression. The weight loss target for diabetes is 5% , while for prediabetes it is $7\text{--}10\%$.²⁰ The combined analysis of studies with varying levels of bias-including those with some concerns and high risk – show that personalized nutrition statistically significantly reduce body weight compared to control diets. The median mean difference in body weight reduction was -0.58% in favor of personalized nutrition. This suggests that while there is some indication that

personalized nutrition may be effective in promoting weight loss. However, this finding should be interpreted with caution as it involves studies with a high risk of bias.

When focusing only on studies with some risk of bias, personalized nutrition did not lead to a significant reduction in body weight among individuals with diabetes mellitus type 2 or prediabetes. This is reinforced by the study by Rein et al, 2022, which found no significant difference in weight loss between high- and low-adherence groups to personalized nutrition.¹⁹ Moreover, this review found no significant reduction in energy intake between personalized nutrition and control groups, which may explain the lack of substantial weight loss. In line with other personalized nutrition studies, the Food4Me study conducted on healthy adults in Europe showed no significant difference in body weight after 6 months between the personalized and non-personalized diets groups.²³ The Preventomics study, conducted on overweight and obese individuals, also showed that personalized nutrition after ten weeks did not significantly affect weight loss compared to the control diet.²⁴

The previous systematic review mentioned that nutritional interventions can improve metabolic parameters in type 2 diabetes mellitus by improving gut microbiota.²⁵ One of the RCTs in this review further assessed the effectiveness of personalized nutrition on gut microbiota conditions in prediabetic patients. The study found that personalized nutrition, when compared to baseline, significantly increased gut microbiome richness and diversity. Meanwhile, the control diet only showed a significant impact on gut microbiome diversity.^{12–14} Although further investigation is still needed, the study mentioned that two bacterial species, UBA11774 sp003507655 (from the Lachnospiraceae family) and UBA11471 sp000434215 (from the Bacteroidales order), mediated the personalized nutrition for clinical improvements in HbA1C, triglycerides, and HDL.¹³

Personalized nutrition aligns with some goals of nutritional interventions for diabetes mellitus type 2 and prediabetes, such as significantly reducing HbA1c, PPGR level, carbohydrate intake and a possible reduction in body weight compared to control diets as well as significantly increased gut microbiome richness and diversity compared to baseline. However, personalized nutrition does not significantly affect fasting blood glucose in individuals with prediabetes, nor does it significantly affect energy intake in individuals with diabetes mellitus type 2 and prediabetes, compared to control diets. The partial achievement of intervention goals may be because machine learning algorithms in personalized nutrition mainly predict glucose response. This approach may overlook other metabolic responses, which are crucial for clinical improvement and disease progression in prediabetes and diabetes mellitus type 2.²³ So, an essential aspect for future research is that personalized nutrition is expected to predict glycemic responses and other metabolic responses comprehensively.

The strengths of this review are: first, the selection of studies and quality assessment were conducted by two independent reviewers. Second, the search strategy was carried out across three electronic databases. However, the limitations of this review include the fact that only studies published in English were included and this synthesis was not based on a meta-analysis. Therefore, caution is needed when interpreting these pieces of evidence.

The quality of evidence in this review ranges from low to very low, so interpreting the results should be done with caution. Several factors contribute to this. First, two studies were categorized as high risk of bias due to allocation processes not being adequately concealed, potentially leading to selection bias. Second, inconsistency is often rated as serious due to high heterogeneity among studies. Third, some studies frequently categorize imprecision as serious due to small sample sizes.

The studies were conducted in Israel, the United States, the United Kingdom, and India. This may limit generalizability as populations in other countries might have different genetic, lifestyle, cultural, and diabetes mellitus type 2 or prediabetes characteristics. Additionally, these studies primarily involved participants with controlled prediabetes or diabetes mellitus type 2, so the findings may not be generalized to individuals with uncontrolled diabetes mellitus type 2. Furthermore, studies on the effectiveness of personalized nutrition on fasting blood glucose and gut microbiomes parameters were only conducted in prediabetic patients, thus limiting generalizability to other patient groups.

Conclusion

This systematic review found that personalized nutrition interventions in individuals with diabetes mellitus type 2 and prediabetes yielded favorable effects on some glycemic outcomes, particularly HbA1c, postprandial glucose response

(PPGR), reduction in carbohydrate intake and a possible reduction in body weight compared to control diets. Additionally, one study demonstrated improvements in gut microbiome richness and diversity compared to baseline. These results suggest that personalized nutrition may be a useful in glycemic management for people at risk of or living with diabetes. However, no significant effect of personalized nutrition was found on fasting blood glucose in individuals with prediabetes, nor on energy intake in individuals with diabetes mellitus type 2 and prediabetes. This may be due to the current design of personalized nutrition algorithms, which are primarily focused on optimizing glycemic control rather than broader metabolic outcomes. Overall, health-care professionals and policymakers may increasingly consider integrating personalized nutrition approaches into diabetes clinical guidelines and management programs.

The overall certainty of evidence in this review was rated from low to very low, largely due to some studies were categorized as high-risk bias, heterogeneity and small sample sizes. Future synthesis should aim to address these limitations by conducting larger, high-quality trials with standardized interventions and outcome measures to better evaluate the efficacy and applicability of personalized nutrition in diverse clinical settings.

Abbreviations

ADA, American Diabetes Association; ALG, Academic Leadership Grant; ALT, Alanine Aminotransferase; APC, Article Processing Charge; AST, Aspartate Aminotransferase; AW, Andi Wijayakesuma; BMI, Body Mass Index; CGM, Continuous Glucose Monitor; CONGA, Continuous Overall Net Glycemic Action; CRD, Centre for Reviews and Dissemination; DALYs, Disability-Adjusted Life Years; DD, Dani Dani; DM, Diabetes Mellitus; DMDH, Dewi Marhaeni Diah Herawati; DNA, Deoxyribonucleic Acid; EFM, Elisa Fauziyatul Munawaroh; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; HbA1C, Hemoglobin A1C; HDL, High-Density Lipoprotein; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; LDL, Low-Density Lipoprotein; MAGE, Mean Amplitude Of Glycemic Excursion; MD, Mean Difference; MeSH, Medical Subject Headings; NICE, National Institute for Health and Care Excellence; PPGR, Postprandial Glucose Response; PPT, Personalized Postprandial Targeting; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO, International Prospective Register of Systematic Reviews; RCTs, Randomized Controlled Trials; ROB 2, Risk Of Bias 2; SWiM, Synthesis Without Meta-Analysis; UK, United of Kingdom; USA, United States of America.

Data Sharing Statement

The original contributions presented in the study are included in the [supplementary material](#), further inquiries can be directed to the corresponding author.

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Disclosure

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