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Review

Nutrigenomics in personalized obesity treatment: A systematic review

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ABSTRACT

Background: Obesity represents a multifactorial chronic disease for which conventional dietary interventions often yield heterogeneous outcomes. Nutrigenomics investigates gene–nutrient interactions to support personalized nutritional strategies. This systematic review sought to assess the existing clinical evidence regarding the efficacy of nutrigenomic-based interventions for the individualized treatment of obesity, concentrating on metabolic, inflammatory, and genetic outcomes.

Methods: A systematic review was conducted in accordance with the PRISMA 2020 guidelines and prospectively registered in the international registry of prospective systematic reviews (PROSPERO). Electronic searches were conducted in PubMed, Scopus, OVID, ScienceDirect, LILACS, and EBSCO to find clinical trials published before July 31, 2025. Eligible studies included adults with overweight or obesity undergoing genotype-based or personalized nutritional interventions compared with standard care. Methodological quality was assessed using the Cochrane Risk of Bias tool (RoB 1.0).

Results: Twenty-one clinical studies were included. Overall, nutrigenomic interventions yielded excellent or comparable results in terms of weight control, body composition, and metabolic parameters compared to traditional nutritional recommendations. Genetic polymorphisms related to energy metabolism,

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particularly Fat Mass and Obesity-Associated (FTO), have been shown to modulate individual responses to dietary interventions. In addition, biologically active substances and personalized diets have been associated with improved inflammatory biomarkers and the expression of obesity-related genes.
Conclusion: Nutrigenomics is a promising approach in the field of precision nutrition for the treatment of obesity. Personalized dietary strategies based on genetic profiles may improve treatment efficacy and metabolic outcomes; however, heterogeneity among studies underscores the need for further well-planned and standardized clinical trials.
Trial registration PROSPERO: (CRD420251248769).

1. Introduction

Obesity is a chronic progressive disease characterized by excessive fat accumulation and accompanied by a wide range of metabolic, cardiovascular, and inflammatory complications [1,2]. Its etiology is multifactorial and involves complex interactions between environmental factors, lifestyle, and genetic predisposition. Despite advances in the field of dietetics and clinical recommendations, traditional dietary interventions often yield mixed and unstable results, underscoring the need for more personalized therapeutic approaches. Interindividual variability in response to weight loss is partly explained by genetic differences that influence energy metabolism, appetite regulation, adipogenesis, and inflammatory pathways [3,4]. Since the completion of the Human Genome Project, increasing attention has been paid to understanding the influence of genetic variations on responses to diet [5]. In this context, nutrigenomics has become an important discipline in the field of precision nutrition, which aims to clarify how nutrients and biologically active components of food regulate gene expression and how genetic polymorphisms influence individual metabolic responses to food.

Single nucleotide polymorphisms (SNPs) represent one of the most common forms of genetic variation and have been associated with differential susceptibility to obesity and related metabolic disorders. Variants in genes involved in energy balance, lipid metabolism, and inflammatory regulation—such as *Fat Mass and Obesity-Associated* (*FTO*), *Peroxisome Proliferator-Activated Receptor Gamma (PPARγ)*, *Leptin gene* (*LEP)* and *Beta-2 Adrenergic Receptor gene (ADRB2)* — have been extensively investigated for their potential role in modulating dietary effects on body weight and metabolic outcomes [6–8]. These results suggest that dietary interventions tailored to genetic profiles could improve treatment efficacy compared to dietary recommendations aimed at the entire population. In addition to genetic variability, nutrigenomics also includes the epigenetic and transcriptomic mechanisms through which dietary habits and biologically active substances influence metabolic pathways. Diets rich in unsaturated fatty acids, polyphenols, fiber, and other functional components have been shown to modulate gene expression, reduce mild inflammation, and improve metabolic homeostasis in obese individuals. These mechanisms provide a biological rationale for personalized dietary strategies focused on both genetic predisposition and molecular regulation. These findings suggest that dietary interventions tailored to genetic profiles may improve treatment effectiveness compared with population-based nutritional recommendations. Beyond genetic variation, nutrigenomics also encompasses epigenetic and transcriptomic mechanisms through which dietary patterns and bioactive compounds influence metabolic pathways. Diets rich in unsaturated fatty acids, polyphenols, fiber, and other functional components have demonstrated the capacity to modulate gene expression, reduce low-grade inflammation, and improve metabolic homeostasis in individuals with obesity. Such mechanisms provide a biological rationale for personalized nutritional strategies targeting both genetic predisposition and molecular regulation [9,10].

Although enthusiasm surrounding nutrigenomics has grown substantially, clinical evidence remains heterogeneous, and the translational application of genetic-based nutrition in obesity management is still evolving. While some clinical trials report favorable outcomes using nutrigenomic-guided interventions, others show modest or inconsistent effects, reflecting differences in study design, genetic panels, intervention duration, and outcome measures [11,12]. Therefore, a critical review of existing clinical data is necessary to clarify the efficacy and limitations of nutrigenomic approaches.

The objective of this systematic review was to synthesize and critically evaluate the available clinical data on personalized nutritional and dietary interventions for the treatment of obesity, with a particular focus on metabolic, inflammatory, and genetic outcomes. By combining the results of recent clinical studies, this review aims to define the directions for future research and support the development of more precise and effective nutritional strategies in the treatment of obesity.

2. Methods

2.1. Study design and reporting guidelines

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines13 and was prospectively registered in the international registry of prospective systematic reviews (PROSPERO) with registration number CRD420251248769. The completed PRISMA checklist is provided as a supplementary file.

Due to substantial clinical and methodological heterogeneity among the included studies, a quantitative synthesis (meta-analysis) was not performed. Therefore, the findings are presented through a structured narrative synthesis, in accordance with PRISMA recommendations for reviews without statistical pooling.

2.2. Eligibility criteria

Eligibility criteria were defined a priori using the PICOS framework (Participants, Interventions, Comparators, Outcomes, Study design).

Participants

Studies including adults aged $\geq$18 years with overweight or obesity (body mass index [BMI] $\geq$25 kg/m^2) were eligible.

Interventions

Interventions involving nutrigenomics, personalized nutrition, or genotype-based **nutritional strategies**, including dietary interventions and supplementation guided by genetic or molecular profiling.

Comparators

The options include conventional dietary interventions, standard nutritional guidelines, placebo, or usual care.

Outcomes

Primary and secondary outcomes included.

- Body weight and body composition;
- Metabolic parameters (lipid profile, glucose metabolism);
- Inflammatory biomarkers;
- The study focuses on gene expression, epigenetic markers, or nutrigenomic-related outcomes.

Study design

Only **clinical trials**, including randomized controlled trials and prospective or retrospective observational clinical studies, were included.

Exclusion criteria

Studies involving children, adolescents, pregnant women, animals, narrative reviews, editorials, case reports, letters to the editor, and studies that did not report relevant metabolic, inflammatory, or nutrigenomic outcomes were excluded.

2.3. Information sources and search strategy

A comprehensive literature search was conducted in the following electronic databases: PubMed, Scopus, OVID, ScienceDirect, LILACS, and EBSCO.

The search covered studies published in English or Portuguese over the last 10 years, up to July 31, 2025. Controlled vocabulary terms (MeSH/DeCS) and free-text keywords were combined using Boolean operators ("AND", "OR", "NOT").

The main search terms included.

- *Obesity*
- *Nutrigenomics*
- *Precision Nutrition*
- *Precision Medicine*

Filters were applied to identify clinical trials. Reference lists of included studies were also manually screened to identify additional relevant articles.

2.4. Study selection

Study selection was performed by a single reviewer in three sequential stages.

1. Removal of duplicate records;
2. Screening of titles and abstracts;
3. Full-text assessment for eligibility.

To mitigate the potential selection bias inherent in screening conducted by a single reviewer, the records were verified by a senior investigator to ensure accuracy and methodological rigor.

2.5. Data extraction

Data extraction was conducted by a single reviewer using a standardized extraction form. The following information was collected from each included study.

- Author(s) and year of publication;
- Country and study population;
- Study design and sample size;
- Type of nutrigenomic or personalized nutritional intervention;
- Comparator group;
- Duration of intervention;
- Primary and secondary outcomes;
- Main findings.

In cases of missing or inconsistent data, information reported by the study authors was considered final. When outcomes were reported using multiple measures, the most comprehensive continuous data were prioritized.

2.6. Risk of bias assessment

The methodological quality and risk of bias of the included studies were assessed using the Cochrane Risk of Bias Tool (RoB 1.0) [13], implemented through Review Manager (RevMan) version 5.4.

The following domains were evaluated.

1. Random sequence generation;
2. Allocation concealment;
3. Blinding of participants and personnel;
4. Blinding of outcome assessment;
5. Incomplete outcome data;
6. Selective reporting;
7. There are other potential sources of bias.

Each domain was classified as low risk, unclear risk, or high risk of bias, according to Cochrane Handbook criteria. Risk of bias assessment was conducted after study inclusion and did not serve as an exclusion criterion.

2.7. Data synthesis

Given the heterogeneity in study design, interventions, populations, and outcome measures, meta-analysis was not feasible. A structured narrative synthesis was therefore performed.

Studies were grouped according to.

- Type of nutrigenomic intervention (genotype-based diets, bioactive compound supplementation, personalized nutritional counseling);
- Population characteristics;
- Duration of intervention;
- Outcomes assessed.

Comparisons across studies were conducted to identify consistent patterns, divergences, and potential sources of heterogeneity. No additional statistical transformations, imputation methods, or meta-regression analyses were applied.

3. Results

3.1. Study selection

The literature search identified a total of 523 records across the electronic databases. After removal of 146 duplicate records, 377 studies remained for title and abstract screening. Of these, 111 records were excluded for not meeting the predefined eligibility criteria.

Subsequently, 266 articles were assessed for full-text eligibility. Following detailed evaluation, 245 studies were excluded due to the following reasons: non-clinical trial design, lack of nutrigenomic or personalized nutritional interventions, inappropriate population, absence of relevant outcomes, insufficient intervention duration, or incomplete data reporting.

In the end, this systematic review included 21 clinical studies that met the inclusion criteria. The PRISMA flow diagram (Figure 1) illustrates the complete study selection process.

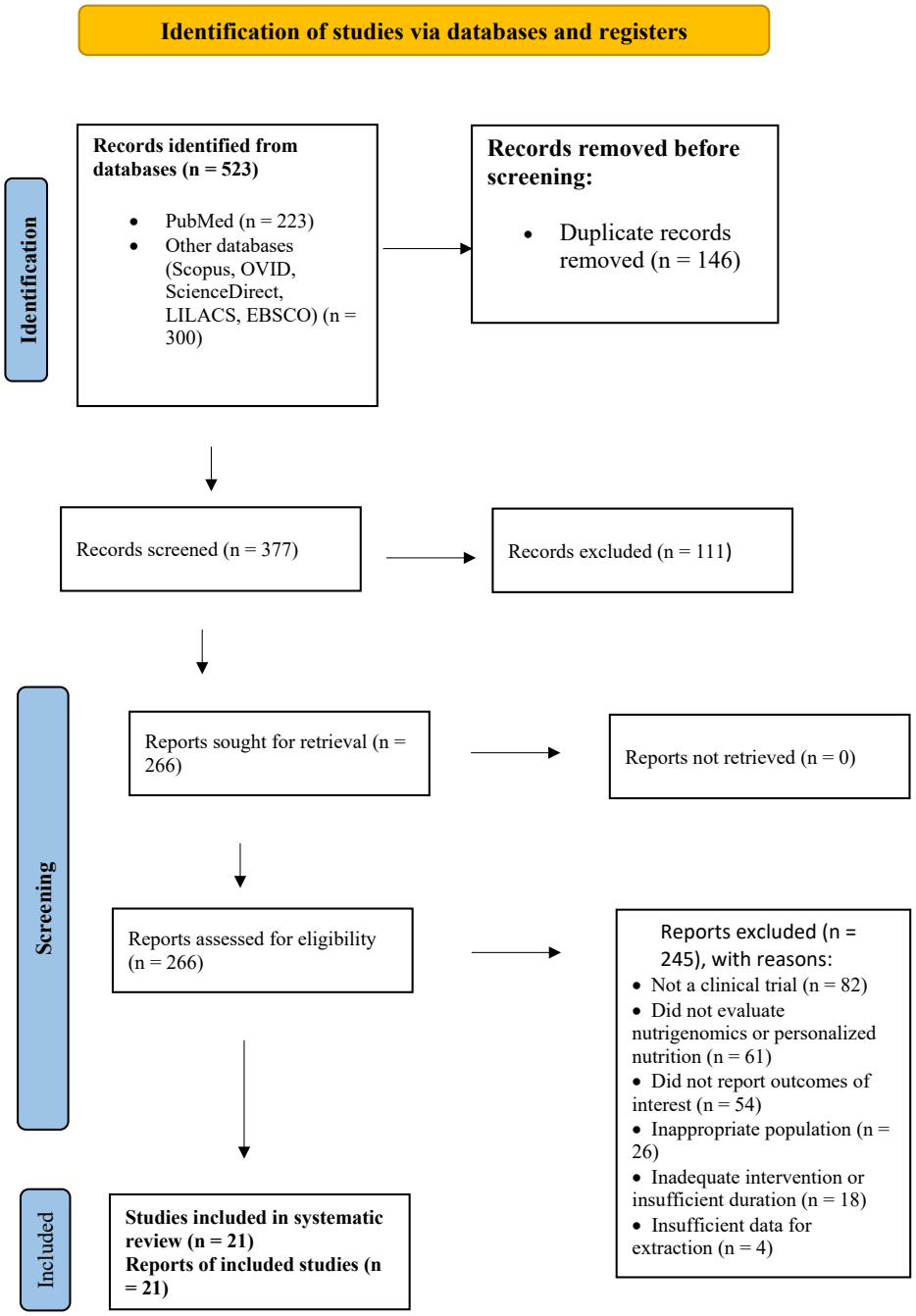


Figure 1. PRISMA 2020 flow diagram illustrating the study selection process.

Table 1
Characteristics of the included studies

Author (Year)	Country/ Population	Study design	Sample size (n)	Nutrigenomic/ Nutritional intervention	Comparator	Duration	Main outcomes
Hernando-Redondo *et al.* (2025)	Spain/Older adults at high cardiovascular risk	Randomized clinical trial	240	Mediterranean diet enriched with olive oil or nuts; hypocaloric Mediterranean diet plus physical activity	Low-fat diet or ad libitum Mediterranean diet	12 months	Gene expression related to cholesterol efflux (ABCA1, ABCG1)
Galekop *et al.* (2025)	Poland and United Kingdom/Adults with overweight or obesity	Randomized controlled trial	319	Personalized nutrition plan based on genetic and metabolic profiling (PREVENTOMICS)	Standard lifestyle intervention	4 months	BMI, quality of life, cost-effectiveness
Razmpoosh *et al.* (2024)	Iran/Women with overweight or obesity	Double-blind placebo-controlled trial	46	Nigella sativa oil supplementation (2000 mg/day)	Placebo	8 weeks	Inflammatory gene expression, insulin, leptin
Rundle *et al.* (2023)	United Kingdom/ Adults with overweight or obesity	Randomized controlled trial	72	Energy-restricted diet (20%) combined with healthy dietary pattern (DASH)	Habitual diet	12 weeks	Insulin sensitivity, phenotypic flexibility, metabolomics
Schutte *et al.* (2022)	Netherlands/Adults with abdominal obesity	Randomized controlled trial	100	High-quality hypocaloric diet rich in MUFA, omega-3 fatty acids, and fiber	Low-quality hypocaloric diet or habitual diet	12 weeks	Weight loss, hepatic fat, adipose tissue transcriptomics
Aldubayan *et al.* (2022)	Denmark/Adults with overweight or obesity	Randomized controlled trial	100	Personalized dietary intervention based on metabolic and genetic clustering	Generic dietary advice	10 weeks	Body weight, fat mass, waist circumference
Pérez-Díaz-del-Campo *et al.* (2022)	Spain/Adults with NAFLD and obesity	Randomized controlled trial	86	Personalized FLiO diet based on genetic risk score (95 SNPs)	American Heart Association diet	6 months	Fatty Liver Index, metabolic markers, body composition
Han *et al.* (2022)	South Korea/Adults with obesity	Randomized controlled trial	400	Diet enriched with legumes replacing refined carbohydrates	Habitual diet	12 weeks	Body weight, adiponectin, oxidative stress markers
Michielsen *et al.* (2022)	Netherlands/Adults with overweight or obesity	Randomized controlled crossover trial	20	Fish oil supplementation (3.7 g/day omega-3)	Fenofibrate or placebo	6 weeks	Plasma metabolomic profile
Kanoni *et al.* (2021)	Greece, Italy, Serbia/ Adults with NAFLD and obesity	Randomized controlled trial	98	Mastiha supplementation (2.1 g/day) with gene–nutrient interaction analysis	Placebo	6 months	Inflammatory and antioxidant markers
Lisboa *et al.* (2020)			48			8 weeks	

(*continued on next page*)

Table 1 (*continued*)

Author (Year)	Country/ Population	Study design	Sample size (n)	Nutrigenomic/ Nutritional intervention	Comparator	Duration	Main outcomes
	Brazil/Women with overweight or obesity and MTHFR polymorphism	Randomized controlled trial		High-folate vegetable intake	Low-folate vegetable intake		Homocysteine, inflammatory biomarkers
Horne *et al.* (2020)	Canada/Adults with overweight or obesity	Randomized controlled trial	140	Lifestyle intervention plus nutrigenomic counseling (12-gene panel)	Standard lifestyle intervention	12 months	Body weight, body fat percentage
Di Renzo *et al.* (2018)	Italy/Adults	Randomized clinical trial	188	Mediterranean diet evaluated according to FTO rs9939609 genotype	No specific dietary intervention	4 weeks	Body weight, body composition
Lowry *et al.* (2018)	Canada/Adults with metabolic syndrome	Randomized controlled trial	159	Lifestyle intervention with genetic risk stratification (17 SNPs)	Baseline comparison	12 months	Continuous metabolic syndrome score
McMorrow *et al.* (2018)	Ireland/Adolescents with overweight or obesity	Randomized controlled trial	70	Anti-inflammatory supplement (omega-3, vitamins C/E, green tea, lycopene)	Placebo	8 weeks	Insulin resistance, DNA methylation
Santamarina *et al.* (2018)	Brazil/Adults with obesity	Randomized placebo-controlled trial	27	Juçara pulp supplementation (5 g/day)	Placebo	6 weeks	Epigenetic markers, fatty acid profile
Ramos-Lopez *et al.* (2018)	Spain/Adults with overweight or obesity	Randomized controlled trial	107	Moderate high-protein diet according to PPARGC1A genotype	Low-fat diet	4 months	Lipid profile, body weight

Abbreviations: BMI stands for body mass index, DASH for Dietary Approaches to Stop Hypertension, MUFA for monounsaturated fatty acids, NAFLD for non-alcoholic fatty liver disease, and SNP for single nucleotide polymorphism.

3.2. Characteristics of included studies

Table 1 summarizes the main characteristics of the included studies. The studies were published between 2018 and 2025 and involved diverse populations across multiple countries, including Europe, Asia, the Middle East, and South America.

Sample sizes ranged from 20 to 400 participants, and the duration of interventions varied from 4 weeks to 12 months. The study populations consisted predominantly of adults with overweight or obesity, with some studies focusing on specific subgroups, such as individuals with non-alcoholic fatty liver disease, metabolic syndrome, or high cardiovascular risk.

Interventions included.

- Genotype-based or nutrigenomic-guided dietary counseling;
- Personalized dietary patterns (e.g., Mediterranean diet variants);
- Supplementation with bioactive compounds (e.g., polyphenols, omega-3 fatty acids);
- The program offers integrated lifestyle interventions that incorporate genetic or molecular profiling.

Comparator groups typically consisted of standard dietary recommendations, placebo, or conventional lifestyle interventions.

3.3. Risk of bias assessment

The methodological quality and risk of bias of the included studies were assessed using the Cochrane Risk of Bias Tool (RoB 1.0). Overall, most studies demonstrated a low risk of bias across the majority of assessed domains.

Regarding random sequence generation, the majority of trials adequately described randomization procedures and were classified as having a low risk of selection bias. Allocation concealment was clearly reported in several studies; however, a subset of trials did not provide sufficient methodological detail and were therefore rated as having an unclear risk of bias for this domain.

Blinding participants and personnel was adequately addressed in most randomized controlled trials, particularly those involving dietary supplementation or placebo-controlled designs. Nevertheless, some studies presented a high or unclear risk of performance bias due to the inherent challenges of blinding in dietary and lifestyle interventions. Similarly, blinding to outcome assessment was judged as low risk in most studies, although a few trials lacked explicit reporting.

Incomplete outcome data were generally well managed, with most studies reporting low attrition rates or appropriately addressing missing data, resulting in a low risk of attrition bias. Selective reporting was considered low risk across the included studies, as predefined outcomes were consistently reported. No major concerns related to other sources of bias were identified.

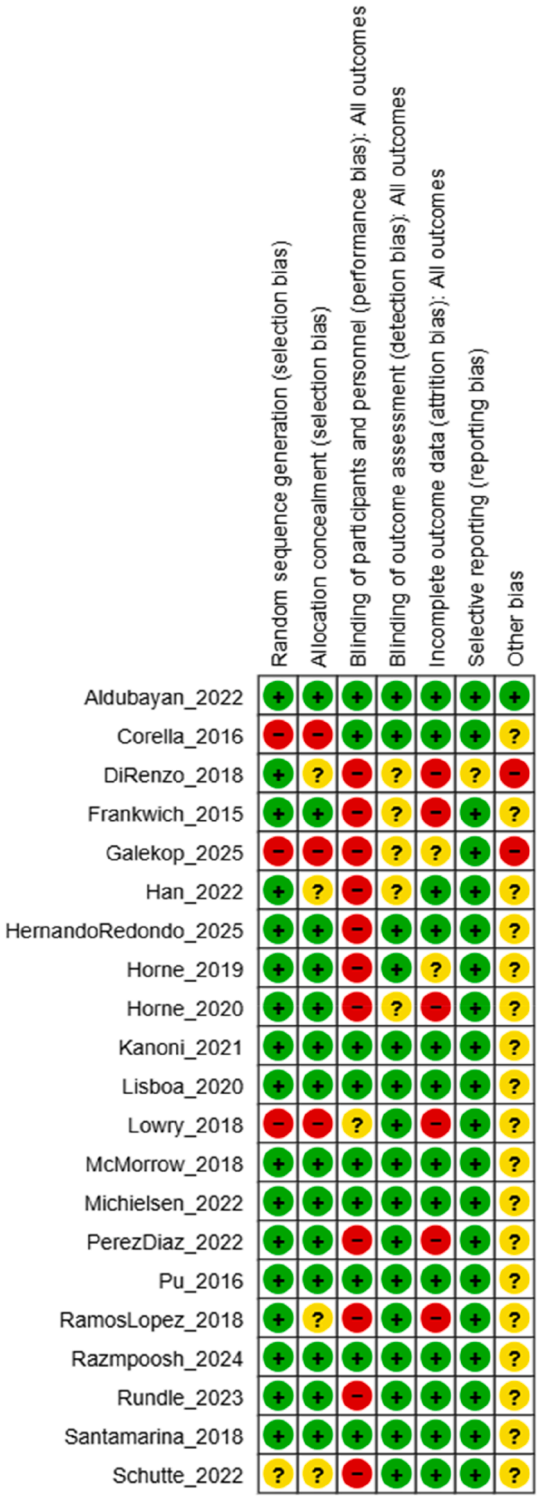
A summary of the risk of bias assessment for each included study is presented in Figure 2.

3.4. Effects of nutrigenomic-based interventions

3.4.1. Anthropometric and body composition outcomes

Most included studies reported improvements in body weight, BMI, or body composition following nutrigenomic-based or personalized nutritional interventions. Several trials demonstrated greater reductions in body weight or fat mass in intervention groups compared with standard dietary approaches, while others reported comparable effects between groups.

Interventions tailored according to genetic variants or metabolic profiles appeared to enhance individual responsiveness to dietary strategies, particularly in studies incorporating personalized counseling or genotype-informed dietary modifications.


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias): All outcomes
Blinding of outcome assessment (detection bias): All outcomes
Incomplete outcome data (attrition bias): All outcomes
Selective reporting (reporting bias)
Other bias
Aldubayan_2022
Corella_2016
DiRenzo_2018
Frankwich_2015
Galekop_2025
Han_2022
HernandoRedondo_2025
Horne_2019
Horne_2020
Kanoni_2021
Lisboa_2020
Lowry_2018
McMorrow_2018
Michielsen_2022
PerezDiaz_2022
Pu_2016
RamosLopez_2018
Razmpoosh_2024
Rundle_2023
Santamarina_2018
Schutte_2022

3.4.2. Metabolic and inflammatory outcomes

Multiple studies reported improvements in metabolic parameters, including lipid profile, insulin sensitivity, and glucose metabolism. Additionally, several interventions were associated with reductions in inflammatory biomarkers, such as interleukins, tumor necrosis factor-alpha, and oxidative stress markers.

Studies involving bioactive compound supplementation demonstrated modulation of inflammatory pathways and metabolic regulation, suggesting a potential mechanistic link between dietary components and gene-related metabolic responses.

3.4.3. Gene expression and genetic modulation

A subset of studies evaluated gene expression, epigenetic markers, or gene–diet interactions. Polymorphisms in genes associated with energy balance and adiposity—particularly *FTO*—were frequently reported as modulators of weight loss response and metabolic outcomes.

Some interventions demonstrated changes in gene expression related to lipid metabolism, inflammation, and mitochondrial function, supporting the biological plausibility of nutrigenomic-guided dietary strategies.

4. Discussion

Impact of genetic variability on weight loss

This systematic review synthesizes current clinical evidence on nutrigenomic-based and personalized nutritional interventions for obesity management. Overall, the findings suggest that nutrigenomic-guided strategies may provide incremental benefits compared with conventional dietary approaches, particularly by addressing interindividual variability in metabolic responses, body composition, and inflammatory status. Although effect sizes varied across studies, the available evidence supports the biological plausibility of precision nutrition as a complementary approach in obesity care [11,12,14].

Across the included studies, genetic variability emerged as a recurrent factor influencing dietary response Polymorphisms in genes related to energy metabolism and adiposity, notably *FTO*, were frequently associated with differences in weight loss and body composition outcomes [7,8,15]. These observations are consistent with prior large-scale observational studies and meta-analyses indicating that genetic variants may modulate both obesity susceptibility and responsiveness to lifestyle interventions. Importantly, several trials included in this review indicate that targeted dietary strategies may attenuate, at least in part, genetic risk, reinforcing the notion that genetic predisposition does not necessarily translate into deterministic clinical outcomes [16].

Additional evidence from personalized nutrition trials reinforces the role of genetic and metabolic variability in obesity treatment. Biomarker-based and genotype-guided interventions have demonstrated favorable effects on body weight, body composition, and metabolic outcomes, supporting the concept that individualized nutritional strategies may improve responsiveness to weight-loss interventions [17–21].

Role of bioactive compounds

In addition to genetic polymorphisms, nutrigenomic interventions emphasizing dietary patterns rich in bioactive compounds were associated with favorable metabolic and inflammatory profiles. Diets with more unsaturated fatty acids, polyphenols, dietary fiber, and certain micronutrients were linked to better insulin sensitivity, lipid metabolism, and inflammatory markers [3,4,22]. These findings are in line with mechanistic evidence suggesting that specific dietary components can

Figure 2. Risk of bias summary of the included studies according to the Cochrane Risk of Bias Tool (RoB 1.0).
Green (+): low risk of bias; Red (−): high risk of bias; Yellow (?): unclear risk of bias, according to the Cochrane Risk of Bias Tool (RoB 1.0). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

influence gene expression and intracellular signaling pathways involved in inflammation, mitochondrial function, and adipogenesis [12]. Such molecular effects may partially explain the clinical benefits observed in personalized nutrition interventions.

Additional studies evaluating bioactive compounds have reported beneficial effects on inflammatory pathways, oxidative stress, and metabolic regulation. Interventions involving legumes, mastiha, folate-rich dietary approaches, and omega-3 supplementation demonstrated improvements in biomarkers associated with obesity and metabolic dysfunction, highlighting the relevance of diet–gene interactions in personalized nutrition [23–26].

Clinical implications

From a clinical perspective, the translation of nutrigenomics into routine obesity management remains an evolving area. Lifestyle interventions combining hypocaloric diet, physical activity, and behavioral counseling constitute the established foundation of obesity treatment, consistently yielding 5–10% weight loss when delivered with adequate intensity and follow-up [2,9]. While these standard approaches improve cardiometabolic parameters broadly, interindividual variability in treatment response remains a recognized challenge, partly attributable to genetic differences in energy metabolism, appetite regulation, and adipogenesis [3,4].

Evidence from controlled clinical trials also suggests that dietary quality, energy restriction, and personalized lifestyle interventions can improve metabolic flexibility, cardiometabolic health, and weight-management outcomes. These findings support the integration of precision nutrition approaches into conventional obesity care while maintaining lifestyle modification as the cornerstone of treatment [27–29].

In this context, nutrigenomic-guided strategies have emerged as a promising complement to conventional lifestyle interventions. Genetic variants such as those in the *Fat Mass and Obesity-Associated* (*FTO*) and *Melanocortin-4 Receptor* (*MC4R*) genes have been shown to modify responses to macronutrient composition and energy-restricted diets, suggesting that tailoring dietary recommendations to individual genetic profiles may enhance fat loss, glycemic control, and treatment adherence compared with population-based guidelines [7,8,30,31]. Similarly, epigenetic mechanisms and gut microbiota composition — modulated by dietary fiber, polyphenols, and Mediterranean-style dietary patterns — represent additional biological layers through which personalized lifestyle interventions may exert differential metabolic effects [30–32].

While genetic testing and personalized dietary recommendations may enhance patient engagement and adherence in selected populations, the incremental clinical benefit of broad genetic panels over standard lifestyle interventions [11,12,33] is still under investigation. Several studies reported modest improvements when compared with conventional approaches, suggesting that nutrigenomic strategies should be viewed as adjuncts rather than replacements for established dietary and lifestyle guidelines [32,34,35]. Furthermore, barriers to implementation — including cost, accessibility, standardization of genetic testing, and the ethical use of genomic data — must be carefully addressed prior to large-scale adoption [2,9,36]. The integration of digital tools such as mobile applications, wearables, and artificial intelligence-driven platforms may facilitate the scalable delivery of personalized lifestyle interventions in clinical practice, though robust evidence supporting their combined use with nutrigenomic data remains limited [34,36].

Limitations

Despite the potential advantages highlighted, the current evidence base is characterized by substantial heterogeneity [11,12]. Marked variability was observed across study designs, genetic panels, intervention durations, dietary components, and outcome measures. In addition, many studies were limited by relatively small sample sizes and short follow-up periods, which may restrict the assessment of long-term clinical effectiveness. Methodological challenges that are inherent to dietary intervention trials, such as difficulties in blinding and the potential for selection bias, further limit the robustness of the findings [4]. Collectively, these factors precluded the conduct of a quantitative meta-analysis and warrant cautious interpretation of reported effect sizes.

Future perspectives

Future investigations should focus on adequately powered randomized controlled trials employing standardized nutrigenomic protocols, longer follow-up periods, and clinically meaningful endpoints. The integration of multi-omics approaches, such as transcriptomics, metabolomics, and epigenetics, may offer more profound insights into the mechanisms underlying diet–gene interactions in obesity [37]. Additionally, greater harmonization of outcome measures across studies would facilitate future quantitative syntheses and strengthen the overall evidence base supporting precision nutrition strategies.

5. Conclusions

This systematic review indicates that nutrigenomic-based and personalized nutritional interventions represent a promising approach for obesity management, particularly in addressing interindividual variability in metabolic and inflammatory responses. The available clinical evidence suggests that dietary strategies informed by genetic and molecular profiles may enhance treatment effectiveness and support more targeted nutritional care.

However, substantial heterogeneity across interventions, genetic markers, and outcome measures limits definitive conclusions regarding the magnitude of clinical benefit. While nutrigenomics should not be viewed as a replacement for established lifestyle and dietary recommendations, it may serve as a valuable complementary tool within precision nutrition frameworks.

Further high-quality, standardized clinical trials are required to consolidate evidence, clarify mechanisms, and support the integration of nutrigenomic strategies into routine obesity treatment.

Protocol registration

This systematic review protocol was prospectively registered in the *International Prospective Register of Systematic Reviews* (PROSPERO) under the identifier **CRD420251248769**.

CRediT authorship contribution statement

Fabrício Bastos Fernandes: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing – original draft, Visualization, Project administration.

Antonio Ruben da Silva Maia Júnior: Validation, Formal analysis, Writing – review & editing.

Bennett Barroso de Carvalho: Investigation, Data curation, Writing – review & editing.

Lucas de Almeida Santana: Validation, Formal analysis, Writing – review & editing.

Matheus Silva Alves: Investigation, Data curation, Writing – review & editing.

Arannadia Barbosa Silva: Conceptualization, Methodology, Validation, Writing – review & editing, Supervision.

Anivaldo Pereira Duarte Junior: Conceptualization, Methodology, Validation, Writing – review & editing, Supervision.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] World Health Organization (WHO). Obesity and overweight [Internet]. Geneva: WHO; 2022 [cited 2025 Apr 29]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.
[2] Brasil. Ministério da Saúde. Boletim Epidemiológico de Obesidade, vol. 55; 2024 (07). Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/edicoes/2024/boletim-epidemiologico-volume-55-no-07.pdf.
[3] Marcum JA. Nutrigenetics/nutrigenomics, personalized nutrition, and precision healthcare. Curr Nutr Rep 2020;9(4):338–45.
[4] Peña-Romero AC, et al. The future of nutrition: nutrigenomics and nutrigenetics in obesity and cardiovascular diseases. Crit Rev Food Sci Nutr 2018;58(17):3030–41.
[5] National Human Genome Research Institute. An overview of the human Genome Project [internet]. 2016 [cited 2024 Nov 6]. Available from: https://www.genome.gov.
[6] Locke AE, et al. Genetic studies of body mass index yield new insights for obesity biology. Nature 2015;518:197–206.
[7] Frayling TM, et al. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. Science 2007;316(5826):889–94.
[8] Dina C, et al. Variation in FTO contributes to childhood obesity and severe adult obesity. Nat Genet 2007;39(6):724–6.
[9] Sonnenburg JL, Bäckhed F. Diet–microbiota interactions as moderators of human metabolism. Nature 2016;535:56–64.
[10] Lee YS, et al. Inflammation is necessary for long-term but not short-term high-fat diet-induced insulin resistance. Diabetes 2011;60(10):2474–83.
[11] Gardner CD, et al. Effect of low-fat vs low-carbohydrate diet on 12-month weight loss in overweight adults and the association with genotype pattern or insulin secretion: the DIETFITS randomized clinical trial. JAMA 2018;319(7):667–79.
[12] Frankwich KA, et al. Differences in weight loss between persons on standard balanced vs nutrigenetic diets in a randomized controlled trial. Clin Gastroenterol Hepatol 2015;13(9):1625–1632.e1.
[13] Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions. 2nd ed. Chichester: Wiley-Blackwell; 2011.
[14] De Lorenzo A, et al. Why primary obesity is a disease? J Transl Med 2019;17(1):169.
[15] Kilpeläinen TO, et al. Physical activity attenuates the influence of FTO variants on obesity risk: a meta-analysis. Plos Med 2011;8(11):e1001116.
[16] Peña-Romero AC, et al. Nutrigenomics and nutrigenetics in obesity and cardiovascular diseases. Crit Rev Food Sci Nutr 2018;58(17):3030–41.
[17] Aldubayan MA, et al. A double-blinded, randomized, parallel intervention to evaluate biomarker-based nutrition plans for weight loss: the PREVENTOMICS study. Clin Nutr 2022;41(8):1834–44.
[18] Galekop MMJ, et al. Cost-effectiveness of personalised nutrition in adults with overweight and obesity: PREVENTOMICS studies in Poland and the UK. J Hum Nutr Diet 2025;38(3):e70071.
[19] Di Renzo L, et al. Influence of FTO rs9939609 and Mediterranean diet on body composition and weight loss: a randomized clinical trial. J Transl Med 2018;16(1):308.
[20] Horne JR, et al. Change in weight, BMI, and body composition in a population-based intervention versus genetic-based intervention. Obesity (Silver Spring) 2020;28(8):1419–27.
[21] Lowry DE, et al. Variants in APOA5 and ADIPOQ moderate improvements in metabolic syndrome. Lifestyle Genomics 2018;11(2):80–9.
[22] Hernando-Redondo J, et al. Mediterranean diet modulates gene expression of cholesterol efflux receptors in high-risk cardiovascular patients. Mol Nutr Food Res 2025;69(13):e70050.
[23] Han Y, et al. Adiponectin and 8-epi-PGF2α as intermediate influencing factors in weight reduction after legume consumption. Br J Nutr 2022;127(2):257–65.
[24] Michielsen CCJR, et al. Comparative analysis of the effects of fish oil and fenofibrate on plasma metabolomic profiles. Mol Nutr Food Res 2022;66(2):e2100192.
[25] Kanoni S, et al. Nutrigenetic interactions modulate antioxidant and anti-inflammatory status in NAFLD. Front Immunol 2021;12:683028.
[26] Lisboa JVC, et al. Food intervention with folate reduces TNF-α and interleukin levels in overweight women with MTHFR polymorphism. Nutrients 2020;12(2):361.
[27] Rundle M, et al. Diet-induced weight loss and phenotypic flexibility among healthy overweight adults: a randomized trial. Am J Clin Nutr 2023;118(3):591–604.
[28] Schutte S, et al. Diverging metabolic effects of two energy-restricted diets differing in nutrient quality. Am J Clin Nutr 2022;116(1):132–50.
[29] Wharton S, et al. Obesity in adults: a clinical practice guideline. CMAJ 2020;192:E875–91.
[30] Farzand A, et al. Nutrigenomics of obesity: integrating genomics, epigenetics, and diet– -microbiome interactions for precision nutrition. Life 2025;15:1658. https://doi.org/10.3390/life15111658.
[31] Mansour S, et al. Precision nutrition unveiled: gene–nutrient interactions, microbiota dynamics, and lifestyle factors in obesity management. Nutrients 2024;16(5):581. https://doi.org/10.3390/nu16050581.

[32] Ramos-López O, Milton-Laskíbar I, Martínez JA. Precision nutrition based on phenotypical traits and the (epi)genotype: nutrigenetic and nutrigenomic approaches for obesity care. Curr Opin Clin Nutr Metab Care 2021;24(4):315–25. https://doi.org/10.1097/MCO.0000000000000754.
[33] Gkouskou K, et al. A genomics perspective of personalized prevention and management of obesity. Hum Genomics 2024;18:57. https://doi.org/10.1186/s40246-024-00570-3.
[34] Liu X, Xu M, Wang H, Zhu L. Integrating precision medicine and digital health in personalized weight management: the central role of nutrition. Nutrients 2025;17:2695. https://doi.org/10.3390/nu17162695.
[35] Kucher S, et al. Impact of lifestyle modification interventions on metabolic syndrome and obesity in adults. Wiad Lek 2025;78(9):1857–65. https://doi.org/10.36740/wlek/212515.
[36] Voruganti VS. Precision nutrition: recent advances in obesity. Physiology 2022;37(6):341–54. https://doi.org/10.1152/physiol.00014.2022.
[37] Page MJ, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.