Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about
Online ISSN 3007-2387
Print ISSN 3007-2379

Precision Nutrition Powered by Artificial Intelligence, Nutrigenomics and Gut Microbiome Modulation: Future Directions in Personalized Healthcare

Rida Abraiz
Human Nutrition and Dietetics, University of the Punjab Lahore
Email: ridaabraiz439@gmail.com
Maria Hussain
Human Nutrition and Dietetics, University of the Punjab
Email: mariahussain18786@gmail.com
Maheen Haider
Human Nutrition and Dietetics, University of the Punjab
Email: maheenhaider76@gmail.com
Aqsa Fatima
Human Nutrition and Dietetics, University of the Punjab Lahore
Email: aqsafatima3897@gmail.com
Mohammad Hamza
Human Nutrition & Dietetics, University of the Punjab
Email: muhammadhamza2052@gmail.com
Ayesha Sohail Shaukat
Human Nutrition and Dietetics, University of the Punjab
Email: ayeshasohailshaukat@gmail.com
Ameer Jan
University of Makran Email: ameerjan@uomp.edu.pk

Author Details

Keywords: Precision Nutrition, Artificial Intelligence, Nutrigenomics, Gut Microbiome, Multi-Omics Integration, Personalized Healthcare, Machine Learning, Digital Health

Received on 15 May 2026
Accepted on 10 Jun 2026
Published on 20 Jun 2026

Corresponding E-mail & Author*:

Rida Abraiz
Human Nutrition and Dietetics, University of the Punjab Lahore
Email: ridaabraiz439@gmail.com

Abstract

Combining the best of AI, nutrigenomics, and the gut microbiome is redefining nutrition healthcare from a population-based approach to personalized nutrition strategies. This review summarizes the recent progress in multi-omics integration and discusses the hierarchy of the genomic, epigenomic, transcriptomic, proteomic, metabolomic and microbiome levels, which all impact metabolic phenotypes in a unique way and demonstrate the interrelationships between these layers. We will discuss the use of two recently developed machine learning algorithms, transformer and graph neural network, that have been shown to provide high accuracy, typically >90% in clinical applications, to process complex biological data and predict metabolic outcomes. Personalized treatment is already proven to be superior to conventional treatment in weight management, glycemic management, and dietary adherence in landmark clinical trials such as PREDICT, FOOD4ME and PRECISION-HEALTH. Digital health solutions like continuous glucose monitoring and AI-powered apps allow for continuous monitoring of the body and adaptive nutritional planning. With the adoption of digital health tools like continuous glucose monitoring and AI-powered apps, real-time monitoring and adaptive nutrition planning become possible. But to be successful in implementing solutions, issues such as data privacy, cost differences, clinical validation and equitable access must be dealt with. The review offers an in-depth view of the future of precision nutrition within health care systems globally and highlights the necessity to involve various fields of science, such as biologists, computational scientists, clinicians and policymakers.

Introduction

Personalized nutrition is a revolution in current health care, changing the paradigms of nutrition guidelines (population based) to the new ones (personalized nutrition) that are defining the nutritional response of the individual (Ordovas *et al*., 2018). Personal nutrition can be considered as the science of providing dietary recommendations to a specific individual based on their unique genetic, metabolic, microbiome, epigenetic and lifestyle profiles to optimize health benefit and prevent disease, as opposed to the classical one size fits all approach which does not consider inter-individual variability in the metabolism and response to nutrients (Zeisel, 2020; Singar *et al*., 2024). Three major developments, which have never been seen before, contribute to this paradigm shift: unprecedented advances in genomics and multi-omics technologies, advances in artificial intelligence and the recognition that the nutritional needs of the individual are different for every person, due to genetic, metabolic and environmental differences (Berry *et al*., 2020, Guasch-Ferre *et al*., 2025).

The traditional recommendations on food and eating that have been created, including the National Food Pyramid and the Dietary Guidelines for Americans, have been aimed at preventing the occurrence of diseases at the population level and preventing deficiencies of nutrients (Moore, 2020). But there is a lot of inter-individual heterogeneity with regard to the response to a given dietary intervention, as evidenced by the fact that various genetic, epigenetic, metabolic and microbial factors contribute to this heterogeneity (Drabsch and Holzapfel, 2019). For example, people with certain polymorphisms of genes like MTHFR, FTO and APOE have very different impacts on folate supplementation, dietary fat and dietary carbohydrates, respectively (de Toro-Martín *et al*., 2017; Shi *et al*., 2024). This variability presents a challenge to the traditional care and highlights the need for more specific care.

Since completion of the human genome project in 2003, the field of nutrigenomics has made significant progress. More than 1247 genetic loci have been associated to nutrient metabolism, food behavior, and dietary responses, across several populations, in a multitude of genome-wide association studies (GWAS) (Westerman *et al*., 2020; Tan *et al*., 2024). With the emergence of COVID-19 and the mounting interest in personalized nutrition, there is growing evidence of the impact that genetic variants in genes such as ACE2, TMPRSS2, and immune-related genes have on the effectiveness of nutrition interventions to support the immune system and prevent diseases (Kapellou *et al*., 2025). There was an increase in the awareness of the consumers along with technological advances and growing clinical evidence regarding the efficacy of precision nutrition that is expected to drive the global precision nutrition market to reach $24.6 billion by 2028, with a CAGR of 10.8% (Singar *et al*., 2024). More than 127 health systems offer precision nutrition services, and more than 50 companies offer recommendations for personalized nutrition based on genetic testing and multi-omics profiling, which has been made easier with the use of electronic health records (EHRs) (Aljasir *et al*., 2024).

Multiple omics layers – genomics, epigenomics, transcriptomics, proteomics, metabolomics and microbiomics – has enabled the understanding of complex biological networks involved in nutrition responses. The advent of new single-cell sequencing methods, real-time metabolomic monitoring, and artificial intelligence has allowed researchers to capture these interactions at a more refined level than ever before and identify specific molecular markers predicting individual response to dietary interventions (Ang and Choo, 2026; Fu *et al*., 2025). New studies are also exploring the role of genetic polymorphisms in the circadian clock genes (CLOCK, PER1, CRY1) in the determination of optimal meal timing and macronutrient distribution, with some evidence that metabolic response to dietary interventions is 34% better when they match the genetic polymorphisms of the circadian clock genes (Fu *et al*., 2025).

The overview compiles the latest evidence on precision nutrition and its clinical relevance, while highlighting the strategies for multi-omics integration, the technological advances and hurdles to implementation, and the future directions. We discuss key clinical trials that illustrate the effectiveness of a personalized strategy, explore the impact of digital health technologies for scaling up precision nutrition, as well as discuss key considerations such as cost-effectiveness, accessibility and ethics. The interdisciplinary approach we have brings in the molecular biology, computational science, clinical medicine and public health to offer a direction to the future of personalized nutrition in health care systems globally.

Omics layers: A systems biology approach

Precision nutrition is evolving and a systems biology perspective is necessary to break down the hierarchical layers of omics, each of which has a unique contribution to metabolic individuality but together interact to create it. Precision nutrition practitioners conduct systematic analysis of several layers of biology, ranging from the genomic to the epigenomic, transcriptomic, proteomic, metabolomic and microbiome layers. These different layers offer the opportunity for different insights regarding individual metabolic phenotypes, and they draw attention to the interconnection of these processes (Aljasir *et al*., 2024; Zeisel, 2020).

Information in the different layers of omics is hierarchical. Genomic variations have been shown to be the main factors determining the basic metabolic capacities of an organism. Any change in the cellular environment is essential for the networks to react and this is achieved by means of epigenetic modifications. The state of the cells at a particular time is shown by the transcriptomic patterns. Proteomic profiles are a measure of pathways that are active at present. Metabolomic signature is dependent on metabolic flux. The function of the microbiome can be used to develop insights into the processes of nutrients and in nutrient bioavailability (Fu *et al*., 2025).

Genomics: The Foundation of Nutritional Variability

Rather, there is a great deal of variation in the genome that impacts the metabolism of nutrients and that can increase the risk of obesity and diabetes (Drabsch and Holzapfel, 2019). SNPs in the genes FTO and TCF7L2 are linked to a greater risk of obesity and alterations in glucose metabolism (de Toro-Martín *et al*., 2017). However, as science in the field of nutrigenomics progresses, the carbohydrate sensitivity has been attributed to a genetic cause, and certain food items with low glycemic index (GI) can be superior for some people, but not so for others (Zeisel, 2020).

Individual gene-targeted dietary treatments have proven to be more effective than general ones for weight loss and glucose management (Matusheski *et al*., 2021). Carriers of mutations in PPARG enjoyed extra advantages from leaner diets of Mediterranean type with higher levels of monounsaturated fat (Ferguson *et al*., 2016). Likewise, people with APOA2 polymorphisms need to reduce saturated fat intake to prevent metabolic diseases (Lagoumintzis and Patrinos, 2023). The results suggest that a nutrigenetic testing approach to obesity and diabetes management could be personalized nutrition therapy (Goni *et al*., 2016).

Table 1: Key Genetic Variants Influencing Dietary Responses and Metabolic Outcomes

Gene	Variant	Dietary Interaction	Metabolic Consequence	Population	Reference
FTO	rs9939609	High carbohydrate intake	Increased obesity risk, impaired glucose metabolism	Multiple populations	De Toro-Martín *et al.*, 2017
TCF7L2	rs7903146	Dietary glycemic load	Type 2 diabetes susceptibility	European, African	Kapellou *et al.*, 2025
APOE	ε4 allele	Saturated fat intake	Increased cardiovascular risk	Global	Ordovas *et al.*, 2018
MTHFR	C677T	Folate supplementation	Neural tube defects, stroke prevention	Multiple populations	Shi *et al.*, 2024
PPARG	Pro12Ala	Monounsaturated fatty acids	Improved insulin sensitivity	Mediterranean	Ferguson *et al.*, 2016
APOA2	-265T>C	Saturated fat consumption	Increased BMI, metabolic syndrome	European, Asian	Lagoumintzis and Patrinos, 2023
CLOCK	rs4580704	Meal timing	Circadian disruption, metabolic syndrome	European	Fu *et al.*, 2025
AMY1	Copy number variation	Starch intake	Carbohydrate metabolism efficiency	Multiple populations	Perry *et al.*, 2007

Epigenomics and Transcriptomics: The Dynamic Response Layer

Environmental exposures interact with gene expression through epigenomic changes such as DNA methylation, histone modifications and non-coding RNAs. These changes are responsive to diet, and can regulate the expression of genes associated with metabolic pathways (Fu *et al.*, 2025). Transcriptomic patterns offer live information about the state of the cells and show which genes are actively transcribed depending on the nutrient stimuli.

The temporal aspect of gene expression is especially important to precision nutrition. Genetic polymorphisms of circadian rhythm genes have been shown to strongly affect optimal meal timing and macronutrient intake, with optimal improvements in metabolic parameters after dietary adjustments according to an individual's chronotype genetic profile (Fu *et al.*, 2025). This chronogenomic approach adds accuracy, binding genetic clocks with best feeding times.

Proteomics and Metabolomics: The Functional Readout

Proteomic profiles are an indicator of the pathways that are active and a functional readout of the cell processes that are affected by nutrition. Metabolomic signatures are the result of metabolic flux and are the integration of genetic, epigenetic, and environmental influences in the downstream direction. (Fu *et al.*, 2025) These layers offer the closest possible indication of how a single phenotype might be metabolized.

Metabolomic profiling has proven to be useful in predicting the glycemic response to dietary interventions in particular. Recently, the use of advanced machine learning models and metabolomic data has shown a success rate surpassing 90% when applying the models to predicting individual metabolic responses (Fu *et al.*, 2025). This forecasting ability can be used to create personalized dietary plans that consider specific metabolic profiles.

The Gut Microbiome: A Critical Mediator of Nutritional Response

It was established that the gut microbiome is a key component in modulating nutritional responses, regulating nutrient absorption, and regulating bioactive metabolite production, and also effects energy extraction (Kujawska and Hall, 2026). Diet influences the composition and function of the gut microbiome and dietary interventions in turn influence the metabolic response of the host.

There are species of bacteria which are shown to be linked to better insulin sensitivity and metabolic health, such as *Akkermansia muciniphila* (Gopal *et al.*, 2024). Microbial personalized nutrition has been proven to have a beneficial impact on metabolic outcomes. For instance, in individuals with high abundance of the Prevotella species, increased production of the short-chain fatty acids (SCFAs) is associated with improved glucose metabolism, and these people have better responses to dietary fiber interventions (Kovatcheva-Datchary *et al*., 2015).

Table 2: Gut Microbiome Signatures and Their Implications for Personalized Nutrition

Microbial Signature	Associated Dietary Intervention	Metabolic Impact	Clinical Application	Reference
Akkermansia muciniphila abundance	High-fiber diet	Improved insulin sensitivity, reduced inflammation	Obesity, T2D management	Gopal *et al.*, 2024
Prevotella enrichment	Fiber-rich diet	Enhanced glucose metabolism, SCFA production	Glycemic control	Kovatcheva-Datchary *et al.*, 2015
Bacteroides dominance	Animal fat/protein diet	Increased branched-chain amino acids	Cardiometabolic risk stratification	Rothschild *et al.*, 2018
High microbial diversity	Mediterranean diet	Reduced inflammatory markers	Cardiovascular disease prevention	Jennings *et al.*, 2024
Bifidobacterium abundance	Prebiotic supplementation	Improved gut barrier function	Immune modulation	Sanz *et al.*, 2025
Dysbiosis pattern	Targeted probiotic therapy	Reduced glucose intolerance	T2D prevention	Leshem *et al.*, 2020
Enterotype clustering	Fiber vs. fat adaptation	Personalized dietary response prediction	Precision nutrition algorithms	Song and Shin, 2022

But host genetics and microbiome composition combine to further complicate nutritional responses. The microbiome is mostly influenced by the environment, but host genetic factors also influence the composition and function of the microbiome (Rothschild *et al*., 2018). It is very important to understand these interactions to create truly individual nutritional interventions.

Artificial Intelligence in Precision Nutrition

Precision nutrition, with its application of AI, is a revolutionary development that offers the ability to integrate and interpret multi-omics data, which would have been impossible before. In the field of nutrition research, AI techniques, such as those based on machine learning and deep learning, have shown great potential for predicting the metabolic response of each individual and providing personalized dietary advice (Ang and Choo, 2026; Fu *et al*., 2025).

Machine Learning Approaches for Multi-Omics Integration

The processing of multi-omics data and prediction of metabolic outcomes has been approached by the development of advanced computational models such as transformer and graph neural networks. The accuracy of these models for predicting the individual response to diet interventions has been shown to be over 90% (Fu *et al*., 2025). Combination of multiple omics data types – genomic, metabolomic, and microbiome – allows for more comprehensive and accurate predictions than single omics.

Several important methodologies have been used for precision nutrition with machine learning are:

Supervised Learning for the prediction of metabolic responses using multi-omics features to stratify people into responder/non-responder to specific dietary interventions.

Unsupervised Learning for discovery of novel patterns in high dimensional omics data – identification of metabolic phenotypes that could be optimally treated with different diet strategies.

Deep Learning for modelling complex non-linear interactions between the different layers of the biology, whereby information about relationships between variables can be lost in conventional statistics.

Adaptive dietary recommendations using Reinforcement Learning: adaptation with time based upon individual responses.

Explainable AI to explain model predictions and understand biological factors causing individual responses, key for clinical decisions (Ang and Choo, 2026).

Predictive Models for Personalized Dietary Responses

Individual specific predictive models are a major step forward in precision nutrition. The models incorporate n-of-1 study designs, cutting-edge wearable technology and machine learning algorithms, and center the individual as the primary focus of nutritional decision making (Fu *et al*., 2025; Tilly *et al*., 2021).

Predictive modeling has a number of important applications, such as:

Glycemic Response Prediction: Models trained on the microbiome composition, genetic variants and meal characteristics have been created to predict individualized postprandial glycemic response, which results in the ability to provide personalized carbohydrate recommendations (Zeevi *et al*., 2015; Wu *et al*., 2025).

Lipid Response Prediction: The prediction of response to dietary fat interventions through the combination of genetic and metabolomic data in individuals can be used to provide personalized fat intake recommendations (Masson *et al*., 2003).

Weight Loss Response Prediction: Machine learning models integrating genetic, microbiome and lifestyle information can predict individual responses to weight loss interventions, to optimize intervention selection (Ben-Yacov *et al.*, 2023).
Personalized Timing of Dietary Interventions: Combining genetic variants of genes in the circadian clock pathway with dietary intervention timing allows for individualized meal timing recommendations (Fu *et al.*, 2025).

Table 3: Artificial Intelligence Applications in Precision Nutrition

AI Application	Data Inputs	Methodology	Clinical Outcome	Accuracy	Reference
Glycemic response prediction	Microbiome, genetics, meal characteristics	Gradient boosting, neural networks	Postprandial glucose management	>90%	Zeevi *et al.*, 2015; Wu *et al.*, 2025
Metabolic response prediction	Multi-omics integration	Transformer, graph neural networks	Dietary intervention response	>90%	Fu *et al.*, 2025
Weight loss prediction	Genetics, microbiome, lifestyle	Ensemble learning	Individualized weight management	85-90%	Ben-Yacov *et al.*, 2023
Cardiometabolic risk stratification	Multi-omics, clinical data	Deep learning	Disease prevention targeting	88%	Ang and Choo, 2026
Meal timing optimization	Chronogenetics, meal data	Reinforcement learning	Circadian-aligned nutrition	34% improvement	Fu *et al.*, 2025
Digital health coaching	Real-time CGM, food logs	Natural language processing	Behavioral adherence	Variable	Berry *et al.*, 2020
Microbiome-diet interaction	Metagenomic sequencing	Bayesian inference	Prebiotic/probiotic personalization	Ongoing	Wang *et al.*, 2024

Digital Health Technologies

Digital health technologies can be integrated with personalized nutrition as a transformative way to manage chronic diseases. Continuous glucose monitoring, AI-powered meal planning apps, and mobile health apps facilitate adaptive dietary changes and enhanced disease monitoring (PMC, 2025).
By giving real-time information on the glycemic effect of food choices, people can make more informed decisions about what and when to eat. This information can be used by AI-powered meal planning apps to generate tailored suggestions for nutrition plans to help improve glycemic management while meeting each person's specific tastes and dietary requirements.
Wearable technology, such as smart watches and activity trackers, offers extra data feeds that can be leveraged to deliver personalized nutrition advice, such as activity level, activity trends and sleep quality. These data streams, combined with biological information, can provide comprehensive and dynamic dietary recommendations (PMC, 2025).

Clinical Evidence and Landmark Studies

The corpus of evidence about precision nutrition has expanded exponentially in recent years. Precise nutrition interventions have been shown to be superior to traditional dietary counselling in several outcomes, including weight loss, glycemic control, lipid control and adherence to diet in the long term, in meta-analyses of RCTs (Ordovas *et al*, 2018; Berry *et al*, 2020).

Landmark Clinical Trials

There are some big clinical studies out there that have proven personalized nutrition to be effective:

The PREDICT Study Series: The Personalized Responses to Dietary Composition Trial series has shown the feasibility of and effectiveness of personalized dietary recommendations according to individual biological profiles. The studies have demonstrated that postprandial metabolic responses are significantly different between people who ate the same meal, highlighting the need for personalized approaches (Berry *et al*., 2020).

FOOD4ME Study: This randomized controlled trial (FOOD4ME) compared personalized dietary advice given using genetic information with standard dietary counseling. The results showed that the personalized group experienced significant enhancement in dietary adherence and metabolic effects (Celis-Morales *et al*., 2017).

The PRECISION-HEALTH Initiative: An extensive investigation into the integration of various layers of the omics approaches towards personalized health optimization, with emphasis on the feasibility of multi-omics approach for dietary recommendations in real-world scenarios (Fu *et al*., 2025).

Diabetes and Obesity Management

For diabetes and obesity, in particular, digital health technologies combined with personalized nutrition have demonstrated great promise for diabetes management. Carbohydrate targeting based on genetic polymorphisms like FTO and TCF7L2 has been shown to improve diabetes management (Singar *et al*., 2024). An increase of *Akkermansia muciniphila* in the gut microbiota can be expected to be the most beneficial for those consuming a high fiber diet, because *Akkermansia muciniphila* is linked to increased production of short-chain fatty acids, and insulin sensitivity (Gopal *et al*., 2024).

Diabetes prevention programs (DPPs) have demonstrated the benefits of digital health interventions (DHIs) such as gamification, nudges and remote monitoring for improving behavior adherence (Partridge and Redfern, 2018). Meal planning apps with AI and CGMs give users real-time feedback, enabling them to make adjustments to their diet on the fly (Michel and Burbidge, 2019).

Cardiovascular Disease Prevention

Precision nutrition interventions have been shown to be effective for changing cardiovascular disease risk factors. Genetic and metabolomic profiling may be used to identify individuals that will respond most to certain dietary interventions for lipid control and blood pressure management (Guasch-Ferre *et al*., 2025). The incorporation of microbiome data has also furthered narrowed the focus for cardiovascular risk prediction and intervention (Jennings *et al*., 2024).

Implementation Challenges in Clinical Settings

Although there is strong evidence to support the effectiveness of precision nutrition, there are some challenges to its clinical adoption:

Cost-Effectiveness: The cost of genetic testing, multi-omics profiling, and AI platforms presents questions around cost-effectiveness, especially in resource-limited environments. Economic modeling studies are needed to set the value proposition in various health care settings.

Clinical Validation: Strong clinical validation in a variety of populations is critical for clinical practice guidelines based on evidence. The majority of validation studies have focused on people within European and North American populations and there is limited data from other ethnic groups (Tan *et al*., 2024).

Healthcare Provider Training: Healthcare providers need to be trained to understand and interpret genetic, microbiome and metabolic data to effectively implement precision nutrition. There is a need for training programs to develop this capacity in all aspects of health care.

Privacy Concerns: The ability to collect and combine genetic, microbiome, and clinical information means there are serious privacy issues that will need to be addressed using effective security measures and policy.

Data Privacy: The collection and integration of genetic, microbiome, and clinical data introduces major privacy concerns that require careful security measures and policy safeguards (PMC, 2025)

Gut Microbiome Modulation as a Therapeutic Target

The gut microbiome has become a game-changer therapeutic target for personalized nutrition interventions. Dietary modulation of microbial communities in the gut has potential implications for metabolic health, particularly in terms of composition and function (Kujawska and Hall, 2026; Nisa *et al*., 2025).

Microbiome-Based Interventions

Prebiotic Interventions: Dietary fibers that specifically promote growth of beneficial microorganisms have been found to be effective as a therapeutic intervention for metabolic health. Responses to prebiotic interventions are highly individualistic, depending on the microbial baseline status (Kovatcheva-Datchary *et al*., 2015).

Probiotic Interventions: Live microorganisms that when administered in sufficient quantities, can bring about health benefits. New evidence indicates that individual microbiome composition and host genetic factors affect probiotic interventions (Guizar-Heredia *et al*., 2023).

High fiber dietary interventions: High fiber dietary interventions have been shown to positively affect glucose metabolism but the effect of the intervention is dependent on the presence of specific microbial species that have the ability to produce short-chain fatty acids (SCFAs) (Jennings *et al*., 2024).

5.2. Microbial Metabolites as Biomarkers

Microbiome activity and metabolic health are characterized by microbial metabolites such as short-chain fatty acids, bile acids and tryptophan metabolites. Metabolites production is affected by dietary intake and microbial composition, and targets for personalized nutritional interventions (Sanz *et al*., 2025).

Table 4: Therapeutic Strategies for Gut Microbiome Modulation in Precision Nutrition

Intervention Type	Target Population	Mechanism of Action	Metabolic Outcome	Clinical Evidence	Reference
High-fiber diet	Prevotella-enriched individuals	Increased SCFA production	Improved glucose metabolism	RCTs	Kovatcheva-Datchary *et al*., 2015
Mediterranean diet	Individuals with high microbial diversity	Anti-inflammatory effects	Reduced cardiometabolic risk	Population studies	Jennings *et al*., 2024
Akkermansia	Individual	Improved	Enhanced	Clinical	Guizar-

probiotics	s with low Akkermansia	gut barrier, insulin sensitivity	metabolic health	trials	Heredia *et al*., 2023
Personalized prebiotics	Enterotype-specific formulations	Targeted microbial stimulation	Individualized metabolic benefits	Ongoing	Song and Shin, 2022
Dietary polyphenols	Individuals with specific metabolizing capacity	Gut microbiome-derived metabolites	Cardiovascular protection	Observational	Sanz *et al*., 2025
Fermented foods	General population	Microbial diversity enhancement	Inflammatory modulation	RCTs	Kujawska and Hall, 2026
Resistant starch	Individuals with specific amylase genes	Butyrate production	Glucose homeostasis	Interventional	Perry *et al*., 2007

The Brain-Gut-Microbiome Axis

The brain-gut-microbiome axis is a bidirectional relationship that impacts eating habits, metabolism and mental wellbeing. This is where brain connectome data becomes valuable, alongside data on the gut microbiome and metabolic profiling, as it provides new opportunities for personalized interventions (Fu *et al*., 2025; Zhang *et al*., 2024).

Recent studies have shown that dietary decisions and metabolic outcomes vary between people and this could be explained by differences in brain network architecture, representing an additional layer of precision nutrition. Combining data from functional brain imaging and metabolic and microbiome profiling could enable more comprehensive and effective personalized interventions (Finn *et al*., 2015; Mueller *et al*., 2013).

Challenges and future directions

Technical Challenges

Data Integration: The integration of different kinds of data such as genomic, microbiome, metabolomic, lifestyle and clinical data is a challenging computational problem. For successful integration and interpretation (Fu *et al*., 2025; Ang and Choo, 2026), data collection and analysis methods need to be standardized.

Scalability: Many existing methods of personalized nutrition are based on very detailed profiling, which is not possible at population level. It is critical to develop cost effective and scalable methods for widespread implementation (PMC, 2025).

Causal Inference: Most of the information on the science of precision nutrition today is correlational, not causal. Randomized controlled trials and longitudinal studies are key for establishing causality, which is crucial for evidence-based clinical practice (Guasch-Ferre *et al*., 2025).

Algorithm Generalization: machine learning models trained in a particular population might not apply to other populations. There is a need for multi-ethnic validation studies to assure equitable application (Tan *et al*., 2024).

Ethical and Societal Considerations

Collection and linkage of sensitive/biological data is an important privacy issue. Enabling data protection mechanisms and informed consent procedures are vital (PMC, 2025).

Health Disparities: Precision nutrition approaches can be used to contribute to health disparities unless they are available to everyone. Equity is a key consideration and strategies are necessary to ensure that it is realized (Tan *et al*., 2024).

Genetic determinism: When communicating genetic risk information, it is important to avoid becoming "deterministic" or "stigmatizing". Healthcare professionals need to be educated on communicating genetic and omics information (Kohlmeier *et al*., 2016).

Regulatory Frameworks

There is a need for clinical guidelines to standardize the implementation of precision nutrition and ensure quality of healthcare, for this purpose, evidence-based clinical guidelines are required. Professional organizations are starting to create these guidelines (Ordovas *et al*., 2018).

Direct-to-Consumer Services: There are regulatory concerns with the growing numbers of direct-to-consumer genetic testing and personalized nutrition services. These services should be monitored to ensure that they are giving accurate, evidence-based recommendations (PMC 2025).

Future Directions

Large, Longitudinal and Multi-Ethnic Cohorts: Establishment of large, longitudinal cohorts consisting of multiple ethnic groups will be important for validating and improving precision nutrition approaches across various populations (Tan *et al*., 2024; Ang and Choo, 2026).

Integration to EHR: Connecting omics data to EHRs would help to translate precision nutrition into routine clinical practice, so that it could be used by providers in their care plans (PMC, 2025).

Explainable AI: The ability to develop AI models that are explainable and can offer clinical interpretation of their predictions is key to clinical trust and decision making (Ang and Choo, 2026).

Causal Validation: RCTs and n-of-1 designs are necessary to validate the causal effects of precision nutrition interventions and determine mediators of individual response (Guasch-Ferre *et al*., 2025).

To translate precision nutrition into real-world healthcare practice, implementation science research on the implementation of precision nutrition, precision nutrition cost-effectiveness, and integration of precision nutrition in clinical workflows is needed (Ordovas *et al*., 2018).

Conclusion

Precision nutrition is a paradigm shift in healthcare, rather than a single-size-fits-all approach to nutrition, it is an approach that takes into account the individual's biological profile and creates a customized strategy. The intersection of gut microbiome science, nutrigenomics, and AI has led to new insights and breakthroughs into the effects of dietary interventions on individual gut microbes and their associated complex networks. The integration of artificial intelligence, nutrigenomics, and gut microbiome science has ushered in a new era of understanding and prediction regarding the interactions between dietary interventions and specific gut microbes and networks. By integrating data from multiple ‘omics' (genomic, metabolomic and microbiome), the multi-omics integration offers a comprehensive view of each individual's metabolic phenotype, which can be used to guide personalized dietary advice.

Personalized nutrition strategies have shown to be effective in clinical trials, such as the improvement of metabolic outcomes like glycemic control, weight management, and adherence to dietary guidelines. Digital health technologies like continuous glucose monitoring and precision nutrition tools with AI have made it possible to monitor the body's physiology in real time and make dynamic nutrition adjustments, making precision nutrition more accessible to everyday clinical care.

But there are big obstacles to overcome. Challenges such as data integration, scalability, and algorithm generalization need to be overcome. Ethical issues like privacy of data, health differences and genetic determinism need to be taken into consideration. The regulations need to change as well so that the precision nutrition services are available and of a high quality.

These are areas that need further investigation in future studies to validate the cohorts, embed precision nutrition into EHRs, create explainable AI models, and research on implementation science. To reach the full potential of precision nutrition to revolutionize global healthcare systems, there is a need for interdisciplinary collaboration between biologists, computational scientists, clinicians and policymakers.

Precision nutrition will need to be technically accessible, clinically validated, and take into consideration personal preferences and situations for its successful implementation. In 2028, the global precision nutrition market is expected to be worth $24.6 billion, signaling the increasing understanding of the potential of tailored solutions to combat the growing burden of the diet-related chronic diseases. AI-driven nutrition, nutrigenomics, and gut microbiome manipulation presents a promising opportunity for improved, more sustainable, and more inclusive healthcare for everyone.

References

Aljasir, S., N.M.S. Eid, E.V. Volpi and I. Tewfik. 2024. Nutrigenomics-guided lifestyle intervention programmes: A critical scoping review with directions for future research. Clin. Nutr. ESPEN 64:296-306.

Ang, M.Y. and S.W. Choo. 2026. The nutri-exposome intelligence framework: Integrating multi-omics, machine learning, and digital nutrition for precision chronic disease prevention. Nutrients 18:1826.

Ben-Yacov, O., A. Godneva, M. Rein *et al*. 2023. Gut microbiome modulates the effects of a personalised postprandial-targeting (PPT) diet on cardiometabolic markers: A diet intervention in pre-diabetes. Gut 72:1486-1496.

Berry, S.E., A.M. Valdes, D.A. Drew *et al*. 2020. Human postprandial responses to food and potential for precision nutrition. Nature Medicine 26:964-973.

Celis-Morales, C., K.M. Livingstone, C.F.M. Marsaux *et al*. 2017. Effect of personalized nutrition on health-related behaviour change: Evidence from the Food4Me European randomized controlled trial. Int. J. Epidemiol. 46:578-588.

De Toro-Martín, J., B. Arsenault, J.P. Despres and M.C. Vohl. 2017. Precision nutrition: A review of personalized nutritional approaches for the prevention and management of metabolic syndrome. Nutrients 9:913.

Drabsch, T. and C. Holzapfel. 2019. A scientific perspective of personalised nutrition. Nutrients 11:2288.

Ferguson, L.R., R. De Caterina, U. Görman *et al*. 2016. Guide and position of the International Society of Nutrigenetics/Nutrigenomics on personalised nutrition: Part 1—Fields of precision nutrition. J. Nutrigenet. Nutrigenomics 9:12-27.

Finn, E.S., X. Shen, D. Scheinost *et al*. 2015. Functional connectome fingerprinting: Identifying individuals using patterns of brain connectivity. Nat. Neurosci. 18:1664-1671.

Fu, Y., K. Zhang, Z. Miao, G. Yang, Y. Huang and J.S. Zheng. 2025. Advancing precision nutrition through multimodal data and artificial intelligence. Cell Metab. (in press).

Gopal, R., R. Nagpal, B.H. Arjmandi and N.S. Akhavan. 2024. *Akkermansia muciniphila* in metabolic health: Mechanisms and therapeutic potential. Nutrients 16:1456.

Guasch-Ferre, M., C. Wittenbecher, M. Palmnäs *et al*. 2025. Precision nutrition for cardiometabolic diseases. Nature Medicine 31:1444-1453.

Guizar-Heredia, R., C. Martínez-Carrillo and O. Cruz-Cruz. 2023. Gut microbiome-based personalized nutrition: Current evidence and future directions. J. Microbiol. Biotechnol. 33:1101-1112.

Jennings, A., T. Kühn, N.P. Bondonno *et al*. 2024. The gut microbiome modulates associations between adherence to a Mediterranean-style diet, abdominal adiposity, and C-reactive protein in population-level analysis. Am. J. Clin. Nutr. 119:136-144.

Kapellou, A., E. Salata, D.M. Vrachnos, S. Papailia and S. Vittas. 2025. Gene-diet interactions in diabetes mellitus: Current insights and the potential of personalized nutrition. Genes (Basel) 16:578.

Kohlmeier, M., R. De Caterina, L.R. Ferguson *et al*. 2016. Guide and position of the International Society of Nutrigenetics/Nutrigenomics on personalised nutrition: Part 2—Ethics, challenges and endeavors of precision nutrition. J. Nutrigenet. Nutrigenomics 9:28-46.

Kovatcheva-Datchary, P., A. Nilsson, R. Akrami *et al*. 2015. Dietary fiber-induced improvement in glucose metabolism is associated with increased abundance of Prevotella. Cell Metab. 22:971-982.

Kujawska, M. and L.J. Hall. 2026. Microbe–diet interactions and personalized nutrition. Annu. Rev. Food Sci. Technol. 17:3.1-3.21.

Lagoumintzis, G. and G.P. Patrinos. 2023. Nutrigenomics: A new era of personalized nutrition. Clin. Chem. Lab. Med. 61:1501-1512.

Leshem, A., T. Segal and E. Elinav. 2020. The gut microbiome and individual-specific responses to diet. mSystems 5:e00324-20.

Masson, L.F., G. McNeill and A. Avenell. 2003. Genetic variation and the lipid response to dietary intervention: A systematic review. Am. J. Clin. Nutr. 77:1098-1111.

Matusheski, N.V., A. Caffrey, L. Christensen *et al*. 2021. Precision nutrition: A review of current approaches and future directions. Nutr. Rev. 79:894-910.

Michel, M. and A. Burbidge. 2019. Digital health and personalized nutrition: The convergence of technology and wellness. J. Nutr. Sci. 8:e15.

Moore, J.B. 2020. From personalised nutrition to precision nutrition: The future of dietary guidance. Proc. Nutr. Soc. 79:143-150.

Mueller, S., D. Wang, M.D. Fox *et al*. 2013. Individual variability in functional connectivity architecture of the human brain. Neuron 77:586-595.

Nisa, P., A.V. Kirthi and P. Sinha. 2025. Microbiome-based approaches to personalized nutrition: From gut health to disease prevention. Folia Microbiol. 70:961-978.

Ordovas, J.M., L.R. Ferguson, E.S. Tai and J.C. Mathers. 2018. Personalised nutrition and health. BMJ 361:bmjk2173.

Partridge, S.R. and J. Redfern. 2018. Strategies to engage adolescents in digital health interventions for obesity prevention. J. Adolesc. Health 63:617-624.

Perry, G.H., N.J. Dominy, K.G. Claw *et al*. 2007. Diet and the evolution of human amylase gene copy number variation. Nat. Genet. 39:1256-1260.

PMC. 2025. Personalized nutrition in the era of digital health: A new frontier for managing diabetes and obesity. Food Sci. Nutr. 13:e71006.

Rothschild, D., O. Weissbrod, E. Barkan *et al*. 2018. Environment dominates over host genetics in shaping human gut microbiota. Nature 555:210-215.

Sanz, Y., J.F. Cryan, M. Deschasaux-Tanguy, E. Elinav, R. Lambrecht and P. Veiga. 2025. The gut microbiome connects nutrition and human health. Nat. Rev. Gastroenterol. Hepatol. 22:534-555.

Shi, Y., Z. Zhang, B. Wang *et al*. 2024. Effect of plateletcrit and methylenetetrahydrofolate reductase (MTHFR) C677T genotypes on folic acid efficacy in stroke prevention. Signal Transduct. Target. Ther. 9:110.

Singar, S., R. Nagpal, B.H. Arjmandi and N.S. Akhavan. 2024. Personalized nutrition: Tailoring dietary recommendations through genetic insights. Nutrients 16:2673.

Song, E.J. and J.H. Shin. 2022. Personalized diets based on the gut microbiome as a target for health maintenance: From current evidence to future possibilities. J. Microbiol. Biotechnol. 32:1497-1505.

Tan, P.Y., J.B. Moore, L. Bai, G. Tang and Y.Y. Gong. 2024. In the context of the triple burden of malnutrition: A systematic review of gene-diet interactions and nutritional status. Crit. Rev. Food Sci. Nutr. 64:3235-3263.

Tilly, P., R. Vieira and B. Roos. 2021. Perspective: Application of N-of-1 methods in personalized nutrition research. Adv. Nutr. 12:579-589.

Wang, T., Y. Fu, M. Shuai *et al*. 2024. Microbiome-based correction for random errors in nutrient profiles derived from self-reported dietary assessments. Nat. Commun. 15:9112.

Westerman, K., Q. Liu, S. Liu *et al*. 2020. A gene-diet interaction-based score predicts response to dietary fat in the Women's Health Initiative. Am. J. Clin. Nutr. 111:893-902.

Wu, Y., B. Ehlert, A.A. Metwally *et al*. 2025. Individual variations in glycemic responses to carbohydrates and underlying metabolic physiology. Nature Medicine 31:2232-2243.

Zeevi, D., T. Korem, N. Zmora *et al*. 2015. Personalized nutrition by prediction of glycemic responses. Cell 163:1079-1094.

Zeisel, S.H. 2020. Precision (personalized) nutrition: Understanding metabolic heterogeneity. Annu. Rev. Food Sci. Technol. 11:71-92.

Zhang, R., B. Zhang, C. Shen *et al*. 2024. Associations of dietary patterns with brain health from behavioral, neuroimaging, biochemical and genetic analyses. Nat. Ment. Health 2:535-552.