



Precision Nutrition Redefined: Integrative Molecular Frameworks for Personalized Dietary Interventions

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ABSTRACT

Personalized nutrition represents a transformative paradigm in dietary science, aligning nutritional strategies with individual biological variability to optimize health outcomes and reduce chronic disease risk. This review explores the biochemical, molecular, and technological foundations of personalized nutrition, emphasizing its basis in nutrigenetics, epigenetics, microbiomics, and metabolomics. It examines how genetic polymorphisms, such as SNPs in genes like MTHFR, FTO, and APOE, influence nutrient metabolism and disease susceptibility, necessitating genotype-informed dietary interventions. Epigenetic mechanisms, including DNA methylation and histone modifications, dynamically regulate gene expression in response to dietary inputs and can be targeted through nutrient-specific interventions, especially during critical developmental windows. The gut microbiome is highlighted as a key determinant of individual dietary responses, with personalized modulation through prebiotics and probiotics showing benefits in nutrient absorption, metabolic regulation, and immune function. Metabolomic profiling offers real-time insights into nutrient utilization, enabling the development of biomarker-based dietary plans tailored to individual metabolic phenotypes. Integrating these omics technologies with digital health tools and artificial intelligence has allowed for more accurate and scalable nutrition strategies, paving the way for truly individualized interventions. Despite rapid advancements, the review also addresses major ethical, regulatory, and equity challenges, including concerns about data privacy, accessibility, and the standardization of nutrigenomic practices. It calls for robust multidisciplinary frameworks to ensure responsible implementation and equitable access. Furthermore, emerging areas such as microbiotaderived metabolites, bioactive herbal compounds, circadian-linked nutrient metabolism, and environmental exposures (e.g., microplastics) are discussed as novel biochemical considerations in personalized nutrition. In conclusion, personalized nutrition holds immense potential to revolutionize healthcare by translating molecular insights into actionable, precise, and preventive dietary recommendations. Its successful implementation requires continued innovation, ethical oversight, and a commitment to inclusivity across clinical and public health domains.

KEYWORDS

Personalized nutrition, nutrigenomics, epigenetics, gut microbiome, metabolomics, precision health

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INTRODUCTION

Personalized nutrition represents a transformative approach to dietary planning, emphasizing the customization of nutritional strategies based on an individual's unique biological makeup. This paradigm shift seeks to optimize health outcomes by aligning dietary recommendations with genetic, metabolic, microbiomics, and lifestyle factors. Unlike traditional nutritional guidelines that adopt a generalized "one-size-fits-all" model, personalized nutrition acknowledges the complexity and individuality inherent in human metabolism and health status, enabling more targeted and effective dietary interventions¹.

At the heart of personalized nutrition lies the concept of biochemical individuality, the idea that each individual processes nutrients differently due to inherent genetic, epigenetic, and physiological variations. These differences affect how nutrients are absorbed, metabolized, and utilized, ultimately influencing health and disease risk. For instance, polymorphisms in genes involved in folate or lipid metabolism can significantly alter nutrient requirements from one person to another¹.

The urgency of individualized approaches in nutrition is underscored by global health data that highlights the wide variability in disease burden attributable to dietary risks. The Global Burden of Disease Study revealed that poor diet quality remains one of the leading contributors to morbidity and mortality worldwide, yet these dietary impacts are not uniform across populations¹. This observation supports the need for interventions that are more personalized to individual and population-specific nutritional profiles.

Recent advances in molecular biology and the advent of nutrigenomics have revolutionized our understanding of how diet interacts with the human genome to influence health¹. Nutrigenomics explores the gene-diet interface, offering insights into how specific nutrients modulate gene expression and how genetic variations influence dietary responses. These insights lay the foundation for precision dietary strategies aimed at disease prevention and wellness promotion^{1,2}.

Equally significant is the role of the gut microbiome, which has emerged as a critical determinant of personalized nutrition. The microbiome, a diverse community of trillions of microorganisms residing primarily in the gastrointestinal tract, plays essential roles in nutrient digestion, immune modulation, and metabolic regulation^{1,2}. Interindividual variability in microbiome composition and function contributes significantly to differential responses to the same diet, further validating the personalized nutrition model^{1,2}.

Moreover, nutrigenetics and nutrigenomics offer integrative frameworks to understand how genetic variations (nutrigenetics) and gene-nutrient interactions (nutrigenomics) shape nutrient needs and health outcomes². This dual perspective enables more precise dietary recommendations, helping individuals mitigate genetic predispositions to chronic diseases and optimize health through diet.

The field continues to evolve, with researchers and clinicians exploring the applications of emerging tools and data-driven technologies such as machine learning, digital health platforms, wearable sensors, and Al-driven dietary algorithms to deliver personalized dietary guidance². These tools enhance the scalability, accessibility, and accuracy of personalized nutrition interventions, making them increasingly feasible in clinical and public health settings.

With the growing recognition of the interplay between aging, epigenetics, and dietary needs, personalized nutrition is being explored not just for disease prevention but also for promoting healthy aging and regenerative potential². Epigenetic reprogramming, for instance, shows promise in modulating age-related metabolic decline and improving healthspan in response to tailored nutritional strategies².

As personalized nutrition expands into specialized domains such as precision oncology, its potential to support disease-specific interventions is gaining momentum. Tailoring nutritional plans to the metabolic demands of cancer patients and integrating them with therapeutic regimens are emerging as important strategies in personalized medicine².

Despite these advancements, several challenges and ethical considerations remain. These include issues of data privacy, accessibility, affordability, and the potential for health disparities arising from unequal access to genomic and nutritional technologies³⁻⁵. Additionally, robust regulatory frameworks and evidence-based guidelines are needed to validate and standardize personalized nutrition practices globally.

This review aims to provide a comprehensive overview of the scientific foundations, emerging technologies, and practical considerations underpinning personalized nutrition. It will explore the contributions of genetics, epigenetics, the microbiome, and digital health innovations to the evolving landscape of individualized dietary strategies. Furthermore, the review will critically examine current challenges and propose future directions to harness the full potential of personalized nutrition in improving global health outcomes.

MOLECULAR MECHANISMS OF NUTRIENT REQUIREMENTS

This section explores the biochemical and molecular foundations that determine individual nutrient needs and responses. It delves into genetic, epigenetic, microbiome, and metabolomic influences on nutrient metabolism.

Genetic variability in nutrient metabolism: Genetic variability is a key determinant in how individuals absorb, metabolize, and utilize nutrients. The influence of Single-Nucleotide Polymorphisms (SNPs) on these metabolic processes forms the basis of personalized nutrition, which seeks to align dietary interventions with individual genetic profiles. Differences in genes encoding enzymes, transporters, and receptors can significantly affect nutrient bioavailability, efficacy, and health outcomes³.

Numerous studies have demonstrated that genetic polymorphisms can influence responses to macronutrients such as carbohydrates, fats, and proteins. For example, variations in genes like FTO, APOA2, and TCF7L2 have been associated with altered lipid metabolism, glucose homeostasis, and energy balance, contributing to inter-individual variability in dietary responses³. These insights lay the groundwork for tailoring nutritional strategies to optimize health based on one's genetic composition.

Beyond the direct influence of DNA sequence variation, epigenetic factors also modulate gene expression and metabolic outcomes. Epigenetic modifications such as DNA methylation and histone modification can be influenced by dietary intake and, in turn, regulate metabolic gene activity. This complex interplay between genetic and epigenetic mechanisms underscores the multifaceted nature of nutrient metabolism and highlights the importance of a systems biology approach in personalized nutrition^{1,2}.

A well-studied example of gene-nutrient interaction involves the methylenetetrahydrofolate reductase (MTHFR) gene and folate metabolism. The MTHFR C677T and A1298C polymorphisms have been shown to reduce enzymatic activity, impairing the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, its active form in the methylation cycle³. This inefficiency can lead to elevated plasma homocysteine levels, increasing the risk of cardiovascular disease, neural tube defects, and other health complications. Individuals with these polymorphisms may benefit from increased folate intake or supplementation to counteract these metabolic impairments^{3,4}.

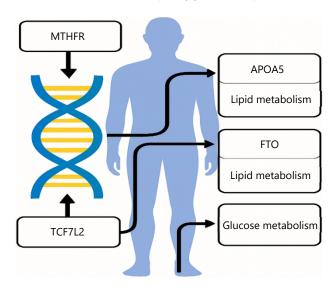


Fig. 1: Genetic pathways influencing nutrient metabolism (self-generated, using canvas and DALL.E image generating tools)

Key genetic pathways involved in nutrient metabolism, highlighting polymorphisms such as MTHFR C677T in folate metabolism and genetic variations affecting lipid and glucose regulation

Recent research also emphasizes the role of SNPs in shaping metabolic responses and dietary needs. Advances in genotyping have allowed for the identification of numerous SNPs that influence nutrient processing and risk of chronic diseases³. Understanding these genetic differences enables the implementation of more precise dietary recommendations that go beyond generalized guidelines³.

In addition, certain genetic polymorphisms have been specifically linked to dietary fat intake and cardiovascular risk. For instance, variants in genes such as APOE, FABP2, and PPARG are associated with differential lipid metabolism and inflammatory responses, thus modifying the impact of dietary fat on individual health³. These findings support the need for genotype-informed dietary fat recommendations to mitigate disease risk^{3,4}.

Figure 1 illustrates how genetic variability plays a pivotal role in nutrient absorption and metabolism, influencing dietary needs and health outcomes^{3,4}. Polymorphisms in MTHFR affect folate metabolism, altering homocysteine levels and increasing susceptibility to cardiovascular diseases^{3,4}. Additionally, variations in lipid metabolism-related genes such as APOA5 and FTO modulate fat utilization and storage, impacting an individual's risk for obesity and metabolic disorders^{3,4}. Genes regulating glucose metabolism, including TCF7L2, contribute to insulin sensitivity and predisposition to type 2 diabetes⁴. Understanding these gene-nutrient interactions enables precision nutrition strategies tailored to genetic profiles⁴.

Epigenetic modifications and nutrient responses: Epigenetic modifications represent a pivotal interface between dietary intake and gene expression, influencing metabolic outcomes without altering the underlying DNA sequence. Among these modifications, DNA methylation and histone modifications are the most extensively studied in the context of nutrition. These biochemical changes serve as molecular switches that regulate gene activity in response to nutrient availability, contributing to the interindividual variability observed in nutrient metabolism and disease susceptibility^{3,4}.

The DNA methylation, particularly at cytosine-phosphate-guanine (CpG) sites, is highly sensitive to dietary inputs. Nutrients such as folate, vitamin B_{12} , methionine, and choline provide essential methyl donors and cofactors for the one-carbon metabolism pathway, directly influencing methylation patterns¹⁵. Alterations in methylation profiles, whether hypermethylation or hypomethylation, can modulate the expression of key metabolic genes and have been linked to the development of obesity, insulin resistance, and cardiovascular disease^{3,4}. Systematic reviews have confirmed that specific dietary patterns, including high-fat or high-sugar diets, can induce epigenetic changes that affect metabolic health^{3,4}.

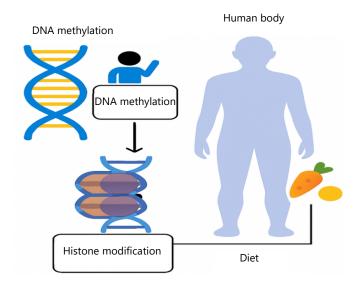


Fig. 2: Epigenetic mechanisms affecting nutrient metabolism (self-generated, using canvas and DALL.E image generating tools)

Key epigenetic modifications, including DNA methylation and histone acetylation, and their impact on gene expression related to nutrient metabolism

Chemical changes to histones, such as acetylation, methylation, and phosphorylation, play a vital role in controlling how tightly DNA is packaged and how accessible genes are for transcription. These histone modifications are highly responsive to changes in nutrient availability and metabolic conditions, thereby influencing the expression of genes involved in metabolic regulation^{3,4}. Nutrient-driven histone acetylation, for example, has been shown to influence lipid metabolism and energy homeostasis.

Maternal nutrition exerts profound epigenetic effects on offspring, especially during critical windows of development such as gestation and early infancy. Early-life nutritional exposures can induce lasting epigenetic marks that are maintained throughout life, a phenomenon referred to as epigenetic programming⁴. Studies in both human and animal models have demonstrated that maternal malnutrition or overnutrition can predispose offspring to chronic diseases through persistent alterations in DNA methylation and histone modification patterns⁴.

Transgenerational epigenetic inheritance further underscores the long-term impact of early nutritional environments. Nutritional insults experienced by one generation may lead to epigenetic reprogramming that affects not only immediate offspring but also subsequent generations^{3,4}. This transgenerational effect highlights the critical importance of maternal and early childhood nutrition in shaping population health trajectories.

Emerging research in nutritional epigenetics offers promising clinical applications, especially within the framework of precision nutrition. By identifying epigenetic biomarkers and nutrient-sensitive genomic regions, it becomes possible to develop targeted dietary strategies tailored to individual epigenetic profiles⁴. These approaches aim to prevent or mitigate disease risk through modifiable lifestyle and dietary interventions, harnessing the plasticity of the epigenome⁴.

Evidence also suggests that diet-induced epigenetic modifications are reversible, opening avenues for therapeutic interventions. Dietary interventions such as calorie restriction, phytochemical intake (e.g., polyphenols, curcumin), and microbiota modulation have shown potential in restoring healthy epigenetic signatures⁴. Thus, understanding and leveraging the epigenetic impact of diet is a critical step toward integrating nutrigenomic insights into clinical practice⁴.

Figure 2 describes how epigenetic mechanisms play a crucial role in regulating nutrient metabolism by modifying gene expression without altering the genetic code. Dietary components influence DNA methylation patterns, impacting metabolic pathways and long-term health outcomes. Early-life nutrition can induce transgenerational epigenetic effects, shaping individual nutrient responses and disease predisposition. Advances in nutritional epigenetics pave the way for precision nutrition strategies tailored to individual epigenetic profiles⁴.

Microbiome and nutrient absorption: The human gut microbiome plays a fundamental role in the regulation of nutrient absorption, metabolism, and overall health. Comprising trillions of microorganisms, bacteria, archaea, viruses, and fungi the gut microbiota functions as a metabolic organ that interacts intricately with dietary components to influence host physiology⁵. One of its primary roles is the fermentation of otherwise indigestible dietary fibers into Short-Chain Fatty Acids (SCFAs) such as acetate, propionate, and butyrate, which serve as key energy sources and modulators of immune and metabolic functions⁵.

Beyond energy production, gut microbes participate in the biosynthesis and bioavailability of vitamins, including vitamin K and certain B vitamins, and facilitate mineral absorption. Importantly, the composition and diversity of the microbiota directly influence these metabolic outcomes. Dysbiosis an imbalance in microbial communities has been associated with impaired nutrient utilization, inflammation, and increased risk for metabolic disorders⁵.

Personalized nutrition increasingly incorporates prebiotics and probiotics as precision tools for influencing the gut microbiota toward improved health. Prebiotics, non-digestible compounds that are specifically metabolized by advantageous gut microbes, include substances like inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS)⁵. These compounds encourage the proliferation of beneficial bacteria such as *Lactobacillus* and *Bifidobacterium*, contributing to stronger intestinal barrier function and more efficient nutrient uptake⁵.

In parallel, probiotics live microorganisms that, when administered in adequate amounts, confer a health benefit on the host have been shown to influence digestion, reduce gastrointestinal inflammation, and modulate nutrient bioavailability⁵. Both strategies are increasingly integrated into precision nutrition frameworks aimed at tailoring dietary interventions based on an individual's microbiome profile.

Recent studies also highlight the bidirectional nature of the diet-microbiota relationship. The composition of an individual's microbiota not only responds to dietary changes but can also determine the metabolic fate of specific nutrients and dietary compounds⁶. For instance, polyphenols and other phytochemicals undergo microbial biotransformation in the gut, and the resulting metabolites can exert systemic effects on inflammation and metabolic pathways⁶. This interaction underscores the significance of individual variability in microbiome composition for predicting nutritional responses and optimizing dietary recommendations.

Furthermore, emerging evidence indicates that dietary interventions can lead to sustained alterations in gut microbiota structure and function. Controlled studies have shown that long-term dietary patterns such as high-fiber, plant-based, or Mediterranean diets can increase microbial diversity and functional capacity, thereby improving metabolic health markers⁶. This reinforces the concept that diet is a powerful and modifiable determinant of microbial composition and, by extension, nutrient absorption and overall health.

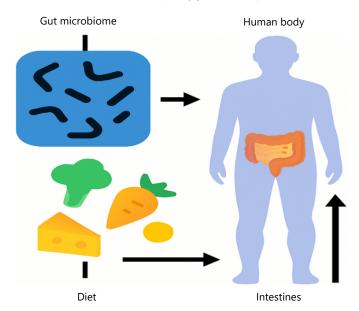


Fig. 3: Microbiome interactions with dietary components (self-generated, using canvas and DALL.E image generating tools)

Key relationships between dietary components, gut microbiota composition, and nutrient absorption, emphasizing the role of probiotics and prebiotics in personalized nutrition

Figure 3 elaborates on the critical role of the gut microbiota in nutrient metabolism, influencing digestion and absorption through complex microbial interactions. Dietary fiber and prebiotics selectively promote beneficial bacterial growth, modulating metabolic functions and overall health. Probiotics contribute to microbiome balance, enhancing nutrient bioavailability and supporting immune function⁶. The integration of microbiome-targeted nutrition into dietary interventions provides personalized approaches to optimize metabolic responses⁶.

Metabolomics and nutrient utilization: Metabolomics, the comprehensive analysis of metabolites in biological systems, has emerged as a powerful tool in the advancement of personalized nutrition. By profiling small-molecule metabolites in biological samples such as blood, urine, and feces, metabolomics enables the identification of distinct metabolic signatures that reflect nutrient intake, metabolic efficiency, and overall physiological status. These metabolic fingerprints provide insights into individual variability in nutrient utilization, revealing biochemical responses that traditional dietary assessments often overlook⁷.

The utility of metabolomics lies in its capacity to bridge the gap between genotype and phenotype, offering real-time information about how the body processes dietary components⁷. This is especially valuable in determining individual nutrient needs and tailoring dietary recommendations based on one's unique metabolic response. For example, the presence or absence of specific metabolites related to amino acid catabolism or lipid oxidation can inform targeted nutritional interventions for individuals with metabolic disorders or suboptimal nutrient assimilation⁷.

Moreover, metabolomics facilitates the identification of biomarkers that can predict dietary responses and health outcomes. These biomarkers such as branched-chain amino acids, ketone bodies, or polyphenol-derived metabolites serve as objective indicators of nutrient intake, metabolic capacity, and disease risk⁷. As such, they are increasingly incorporated into personalized dietary plans aimed at optimizing health, preventing disease, and enhancing nutritional status.

Despite the promise of precision offered by metabolomics, interindividual variability remains a critical consideration. Studies have shown significant differences in metabolic responses to identical diets, even among individuals with similar genetic backgrounds^{7,8}. These variations can be attributed to a complex interplay of factors, including age, sex, gut microbiota composition, physical activity, and pre-existing metabolic conditions. Therefore, metabolomics-based dietary planning must consider this heterogeneity to ensure meaningful and effective interventions^{7,8}.

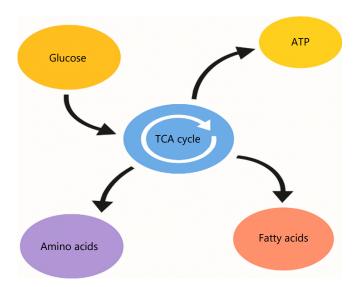


Fig. 4: Metabolic pathways of key nutrients in personalized nutrition (self-generated, using canvas and DALL.E image generating tools)

The biochemical pathways involved in nutrient metabolism, highlighting key metabolomic biomarkers that influence personalized dietary recommendations

Recent advances in high-throughput analytical platforms, such as nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS), have accelerated the integration of metabolomics into precision medicine and nutrition⁸. These technologies allow for high-resolution detection of a wide array of metabolites, enhancing our understanding of metabolic networks and nutrient flux across various physiological states. Additionally, bioinformatic tools now enable the interpretation of large metabolomic datasets, linking metabolic phenotypes with dietary exposures and clinical endpoints⁸.

Furthermore, metabolomics plays an increasingly important role in nutritional epidemiology, where it is employed to validate dietary intake, assess nutrient status, and elucidate diet–disease associations on a population level⁸. In this context, metabolomics strengthens the evidence base for dietary guidelines and supports the development of public health strategies tailored to metabolic subgroups rather than generalized populations⁸.

Figure 4 interprets how metabolomics enables precise assessment of individual nutrient needs by analyzing biochemical markers linked to metabolic health. Variations in metabolic responses to diet arise due to genetic and environmental factors, influencing nutrient utilization and disease risk. Understanding metabolomic signatures allows for tailored dietary interventions that optimize metabolic efficiency . As precision medicine advances, integrating metabolomics into nutritional strategies enhances personalized health outcomes

PERSONALIZED NUTRITION STRATEGIES

Overview: This section explores the application of personalized nutrition, focusing on strategies tailored to individual genetic, epigenetic, microbiome, and metabolic profiles. The goal is to optimize health outcomes by customizing dietary recommendations based on molecular and biochemical individuality.

Precision diets based on genetic profiles: The evolution of precision nutrition has ushered in an era where dietary interventions are increasingly informed by individual genetic profiles. Nutrigenetics the study of how genetic variation influences nutritional response forms a cornerstone of this paradigm, aiming to optimize health outcomes through genetically tailored diets⁹. By identifying Single Nucleotide Polymorphisms (SNPs) associated with nutrient metabolism, disease risk, and food intolerances, clinicians can design personalized dietary plans that surpass one-size-fits-all recommendations.

Table 1: Genetic markers and corresponding dietary recommendations for precision nutrition

	Associated nutrient or	Recommended dietary	
Genetic marker	metabolic pathway	adjustment	Citation's
MTHFR C677T	Folate metabolism	Increase folate intake through	Tanaka <i>et al</i> . ⁹ and
		leafy greens or supplementation	Wang et al. ¹⁰
APOE ε4	Lipid metabolism and	Reduce saturated fat intake;	
	cardiovascular risk	emphasize unsaturated fats	
FTO rs9939609	Obesity and energy regulation	Increase physical activity; emphasize	
		a low-calorie, high-protein diet	
TCF7L2 rs7903146	Glucose metabolism and	Limit refined carbohydrates; adopt	
	type 2 diabetes risk	a Mediterranean-style diet	
CYP1A2*1F	Caffeine metabolism	Limit caffeine intake if slow	
		metabolizer genotype is present	
LCT -13910C>T	Lactose digestion	Opt for lactose-free dairy or plant-based	
	-	alternatives if lactose intolerant	

Table illustrates selected genetic variants and their associated dietary guidance and these markers support the development of targeted nutritional strategies

Genetic screening in the context of nutrition allows for the identification of specific gene variations that affect how the body processes nutrients like fats, sugars, and essential vitamins and minerals. For instance, alterations in the FTO gene are associated with varied reactions to fat consumption, which may influence an individual's susceptibility to obesity. Similarly, mutations in the MTHFR gene can disrupt folate metabolism, thereby affecting cardiovascular health. Such insights make it possible to tailor nutritional plans according to one's genetic makeup, leading to more effective and personalized dietary interventions⁹

Case studies further illustrate the real-world application of genetically based dietary recommendations. For instance, individuals with the APOE $\epsilon 4$ allele associated with lipid metabolism and cardiovascular disease may benefit from reduced saturated fat intake, whereas those with polymorphisms in the TCF7L2 gene, implicated in type 2 diabetes, may respond more favorably to diets lower in glycemic load⁹. These gene diet interactions reinforce the need for evidence-based genetic screening in clinical nutrition practice.

Systematic reviews support the integration of nutrigenetic insights into dietary counseling. They show that individuals who receive genetic-based dietary advice are more likely to adopt and adhere to dietary changes than those given generic nutritional guidance⁹. Moreover, nutrigenetics helps uncover hidden risk factors for diet-related conditions, such as lactose intolerance or gluten sensitivity, which may otherwise remain undetected through phenotypic assessments alone.

The field's growing relevance is also demonstrated by its incorporation into multidisciplinary frameworks, combining genomic, transcriptomic, and metabolomic data to refine personalized recommendations^{9,10}. The convergence of these omics technologies enhances the accuracy and clinical utility of genetic-based diets, creating opportunities for preventative and therapeutic interventions tailored to molecular profiles.

Despite its promise, the implementation of precision diets based on genetic profiles must navigate challenges including genetic privacy, cost, regulatory standards, and the need for robust clinical validation. However, ongoing research continues to elucidate the pathways linking genotype to nutrient response, providing a scientific foundation for more sophisticated personalized nutrition strategies^{9,10}.

Table 1 exemplifies how precision nutrition integrates genetic information to tailor dietary advice and optimize health outcomes. For example, variants such as MTHFR and APOE4 are linked to altered nutrient metabolism and disease susceptibility, necessitating specific dietary adjustments. Such gene-based interventions are increasingly supported by nutrigenetic evidence and omics technologies^{9,10}. This approach represents a pivotal shift toward individualized dietary planning in clinical and public health nutrition.

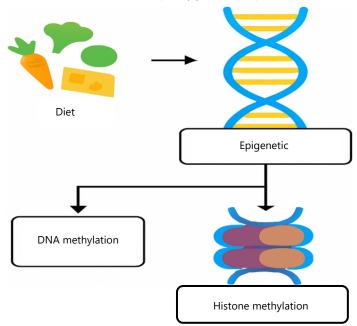


Fig. 5: Epigenetic dietary interventions and nutrient regulation (self-generated, using canvas and DALL.E image generating tools)

Key epigenetic mechanisms, such as DNA methylation and histone modifications, in response to dietary factors influencing gene expression

Epigenetic-based dietary modifications: Epigenetics, the study of heritable changes in gene expression without alteration in the DNA sequence, has become a cornerstone in the evolution of personalized nutrition. Nutritional epigenomics focuses on how specific dietary components can modulate gene activity through epigenetic mechanisms such as DNA methylation, histone modification, and non-coding RNA regulation. These modifications can significantly influence disease susceptibility and health outcomes across an individual's lifespan and even across generations^{9,10}.

The influence of maternal diet on epigenetic programming during critical developmental windows is a compelling example of how early-life nutrition shapes long-term health. Nutrients such as folate, choline, and vitamin B12 are key methyl donors involved in one-carbon metabolism, which is essential for proper DNA methylation during embryogenesis. Studies have shown that inadequate maternal intake of these nutrients can lead to permanent epigenetic alterations in offspring, predisposing them to chronic diseases like obesity, diabetes, and cardiovascular disorders^{9,10}.

Beyond developmental programming, epigenetic modifications continue to play a pivotal role in adult health and disease prevention. Emerging evidence highlights that bioactive dietary compounds such as polyphenols, isothiocyanates, and omega-3 fatty acids can influence epigenetic markers and gene expression profiles associated with inflammation, oxidative stress, and carcinogenesis^{9,10}. For example, sulforaphane from cruciferous vegetables and Epigallocatechin Gallate (EGCG) from green tea have been shown to modulate histone acetylation and DNA methylation patterns that suppress oncogenic pathways¹⁰.

Such insights provide a framework for personalized dietary interventions aimed at reversing or attenuating disease-related epigenetic signatures. This includes designing diet plans tailored to an individual's epigenetic profile, thereby enhancing the efficacy of preventive and therapeutic strategies¹⁰. Notably, epigenetic plasticity offers a window of opportunity for modifying gene expression through dietary modulation, especially in the early stages of disease or before clinical manifestation¹⁰.

In cancer biology, epigenetics is increasingly recognized as a dynamic and reversible target. Aberrant epigenetic silencing of tumor suppressor genes is a hallmark of many cancers, and dietary interventions rich in epigenetically active compounds offer a non-pharmacological approach to reactivating these protective genes¹⁰. The interplay between diet and the epigenome is therefore not only preventive but also potentially therapeutic, particularly in complex diseases like cancer and neurodegenerative disorders¹⁰.

Recent systematic reviews have further consolidated the role of personalized epigenetic diets in clinical settings. They highlight how interindividual variability in epigenetic responsiveness to nutrients underscores the need for customized dietary protocols. Integrating epigenetic biomarkers into routine nutritional assessments may soon become a standard practice in precision health, allowing for more accurate, sustainable, and individualized dietary strategies¹⁰.

Figure 5 highlights the pivotal role dietary components play in shaping epigenetic modifications that regulate metabolic processes¹⁰. Maternal nutrition influences DNA methylation, impacting fetal development and long-term health outcomes¹⁰. Epigenetic interventions, including targeted nutrient intake, have been explored for disease prevention through precise gene expression regulation Advances in nutritional epigenetics provide new opportunities for personalized nutrition strategies aimed at optimizing health¹⁰.

Microbiome-targeted nutrition: The gut microbiome plays a pivotal role in human health by influencing digestion, immune function, and metabolic regulation. With the advancement of precision nutrition, microbiome-targeted dietary interventions are gaining traction as a promising strategy for individualized healthcare. These interventions utilize knowledge of the host's microbial composition to design dietary plans that optimize health outcomes and reduce disease risk¹¹.

One emerging application of this approach involves the personalized use of probiotics and prebiotics. Unlike conventional interventions, which apply broad-spectrum supplementation, personalized strategies are tailored to an individual's microbiota profile. This personalization aims to correct microbial imbalances, enhance the growth of beneficial microbes, and improve host metabolic responses¹¹. Specific probiotic strains can be selected to counteract dysbiosis, while custom-designed prebiotics can selectively stimulate advantageous microbial communities that support gut and systemic health¹¹.

Microbiome diversity has also been shown to significantly influence individual dietary responses. In a landmark study, inter-individual variability in glycemic responses to the same foods was attributed to differences in gut microbial composition, underscoring the importance of microbiota profiling in personalized nutrition¹². These findings suggest that universal dietary guidelines may fail to account for the nuanced interplay between diet and the microbiome, thus limiting their effectiveness for many individuals.

Further research has demonstrated that incorporating microbiome data into dietary planning enhances the precision of nutritional interventions. Tools such as metagenomic sequencing and microbial metabolite analysis are now employed to refine these strategies. This enables clinicians and nutritionists to predict how an individual's microbiota will respond to specific dietary components, leading to more effective and sustainable health outcomes¹².

Moreover, continued exploration into the diet-microbiome axis has revealed its role not only in metabolic diseases but also in immune-mediated conditions and neurological health. Personalized microbiome-based nutrition holds promise in preventing and managing conditions such as obesity, type 2 diabetes, inflammatory bowel disease, and even depression. These insights represent a significant paradigm shift in dietary science from generalized dietary advice to microbiome-informed, personalized interventions¹².

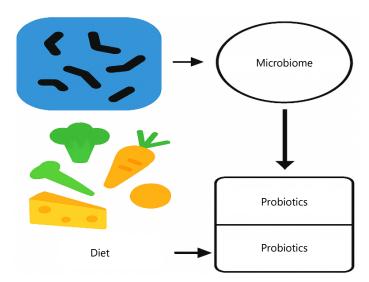


Fig. 6: Microbiome-based dietary strategies for personalized nutrition (self-generated, using canvas and DALL.E image generating tools)

Figure illustrates how gut microbiota influences nutrient metabolism, highlighting the role of probiotics and prebiotics in modulating dietary responses and overall health

Figure 6 visualizes the pivotal role of the gut microbiome in nutrient absorption and metabolic regulation, with microbial diversity shaping individual responses to diet. Probiotics enhance beneficial bacterial populations, improving digestion and immune function. Prebiotics selectively stimulate microbiota activity, optimizing metabolic efficiency and disease prevention. Understanding microbiome-nutrient interactions enables precision dietary interventions to support personalized health outcomes¹².

METABOLOMICS-DRIVEN DIETARY RECOMMENDATIONS

Metabolomics the comprehensive analysis of small-molecule metabolites in biological systems has emerged as a powerful tool in the personalization of nutrition. By capturing the real-time metabolic state of an individual, metabolomics provides a molecular fingerprint that reflects both genetic predispositions and environmental influences, such as diet, lifestyle, and microbiome activity. This approach enables a more dynamic and responsive framework for tailoring dietary interventions to individual metabolic needs.

The integration of metabolomic profiling into nutritional science allows for the identification of biomarkers associated with metabolic health, nutrient status, and disease risk. These biomarkers can guide the formulation of personalized dietary recommendations that aim to optimize metabolic outcomes. For instance, metabolites related to lipid metabolism, amino acid turnover, and gut-derived compounds have been used to stratify individuals and predict differential responses to specific dietary components¹³.

One of the most notable applications of metabolomics in personalized nutrition involves predicting postprandial glycemic responses. In a pivotal study, individualized glucose responses to identical meals were found to vary significantly, influenced by both baseline metabolite profiles and lifestyle factors¹³. Such data challenge the validity of one-size-fits-all dietary guidelines and reinforce the potential of metabolomics in crafting precise nutritional plans.

Several case studies and systematic reviews have documented successful metabolomics-based dietary interventions. These include personalized weight loss programs, cardiovascular risk reduction strategies, and targeted nutritional therapies for metabolic disorders¹³. In these cases, real-time metabolic data enabled clinicians to monitor intervention effectiveness and adjust recommendations accordingly, thereby enhancing compliance and clinical outcomes.

Table 2: Metabolomic biomarkers and dietary recommendations

Metabolomic biomarker	Associated health condition or trait	Dietary recommendation	Citations
Branched-Chain	Insulin resistance and increased	Reduce intake of red meat and dairy;	Villanueva et al. ¹³
Amino Acids (BCAAs)	type 2 diabetes risk due to disrupted	emphasize plant-based protein	Francino and
	glucose metabolism	sources	Henares ¹⁴
Trimethylamine-N-oxide	Elevated cardiovascular disease risk	Limit consumption of choline-rich	
(TMAO)	linked to microbial metabolism of choline	foods such as eggs, liver, and red mea	t
Urinary Polyphenol	Reflective of antioxidant intake and	Encourage high intake of polyphenol-	
Metabolites	gut microbiome activity	rich fruits, vegetables, and whole grains	
Citrate	Indicator of acid-base imbalance and	Prioritize alkaline-forming foods like	
	risk of metabolic acidosis	leafy greens, citrus, and root vegetable	es
Acylcarnitine's	Sign of mitochondrial overload and	Balance macronutrient intake and avoi	d
	inefficient fatty acid oxidation	excessive saturated fats and caloric sur	plus

Table illustrates key metabolomic biomarkers linked to health conditions and the personalized dietary strategies they inform. Each biomarker is mapped to specific nutritional adjustments supported by metabolomics research

Moreover, the growing body of evidence underscores metabolomics as a cornerstone in the evolving paradigm of precision nutrition. The use of this technology facilitates the dynamic adjustment of dietary recommendations in response to changes in an individual's internal metabolic environment^{13,14}. It also supports longitudinal monitoring and early detection of metabolic derangements before they manifest clinically, enabling truly preventative nutritional care^{13,14}.

Recent advances in analytical platforms and computational modeling have accelerated the clinical applicability of metabolomics. Integrating metabolomic data with genomics, microbiome, and lifestyle information creates a holistic profile of the individual, empowering healthcare providers to deliver dietary interventions with unprecedented precision ^{13,14}.

Table 2 outlines how advancements in metabolomics have enabled the identification of biomarkers that predict individual responses to dietary intake, thus supporting personalized nutrition strategies. For instance, elevated BCAAs correlate with insulin resistance¹⁴, while TMAO is associated with cardiovascular risk¹⁴. Polyphenol metabolites reflect antioxidant consumption¹⁴, citrate indicates acid-base imbalance¹⁴, and acylcarnitine's reveal mitochondrial dysfunction¹⁴. These findings underscore the role of metabolic profiling in tailoring effective and condition-specific dietary interventions.

FUTURE PERSPECTIVES AND CHALLENGES

Overview: This section explores the advancements, ethical considerations, and obstacles in the field of personalized nutrition. As technology evolves, integrating genetic, epigenetic, microbiome, and metabolomic data into dietary recommendations presents both opportunities and challenges.

Technological advances in personalized nutrition: The future of personalized nutrition is being revolutionized by rapid technological advancements, particularly in artificial intelligence (AI), machine learning (ML), and systems biology. These technologies are enhancing the ability to generate, analyze, and interpret complex datasets, enabling a more tailored approach to individual dietary recommendations.

Al and ML have emerged as pivotal tools in predicting individualized responses to diet by integrating a broad spectrum of biological and lifestyle data. These technologies can identify patterns and correlations within large datasets that are beyond the scope of traditional statistical models, allowing for more nuanced dietary planning¹⁵. By leveraging machine learning algorithms trained on clinical, genetic, metabolic, and behavioral data, practitioners can offer precise and predictive nutrition strategies that align with personal health goals and risk profiles.

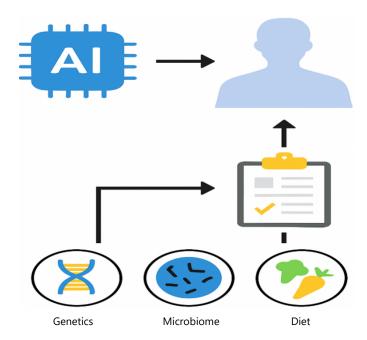


Fig. 7: Al-driven personalized nutrition framework (self-generated, using canvas and DALL.E image generating tools)

The integration of AI and machine learning in personalized nutrition, highlighting their role in dietary recommendations and multi-omics data analysis

Building on this, systematic reviews have emphasized the increasing role of Al-driven tools in clinical and research settings for personalized nutrition. These tools support automated nutrient tracking, adaptive dietary coaching, and real-time health feedback, thus bridging the gap between data acquisition and actionable nutritional guidance¹⁵. Notably, wearable technologies have further augmented these capabilities by providing continuous and non-invasive monitoring of physiological and biochemical parameters, such as heart rate variability, blood glucose levels, and sleep patterns¹⁵. Such real-time data streams feed directly into Al systems to deliver dynamic and context-aware dietary recommendations.

In addition to AI innovations, the integration of multi-omics data including genomics, transcriptomics, proteomics, metabolomics, and microbiomics has become central to the precision nutrition framework. This holistic data convergence facilitates a more comprehensive understanding of individual nutritional needs and disease susceptibilities^{15,16}. Systems medicine, as an interdisciplinary approach, supports the synthesis of these complex data layers into coherent, personalized health strategies that extend beyond nutrition to encompass overall wellness.

Furthermore, emerging frameworks built on integrated multi-omics platforms are now being designed to inform dietary recommendations with unprecedented resolution. These frameworks consider molecular signatures, microbiota composition, and metabolic phenotypes simultaneously, thus enabling precise interventions that reflect the individual's unique biological context^{15,16}. This integrated strategy signifies a shift from reactive to proactive nutrition, where diet is not only a tool for managing disease but also a means of optimizing health and preventing illness.

Figure 7 delineates how artificial intelligence and machine learning are transforming personalized nutrition by analyzing genetic, metabolic, and dietary data¹⁶. Advanced computational models enhance predictive capabilities, allowing for precise dietary interventions based on individual health profiles¹⁶. Wearable technologies and multi-omics integration enable continuous monitoring of nutrient metabolism, optimizing personalized dietary recommendations¹⁶. The convergence of AI with nutritional science paves the way for precision medicine approaches, tailored to unique biological responses¹⁶.

Table 3: Ethical considerations in personalized nutrition

Ethical consideration	Description	Implication	Citations
Privacy of genetic data	Collection and storage of genomic	Robust safeguards are needed	Tsolakidis et al. ¹⁷
	and metabolic data raise concerns	to protect individuals from	and Arowora et al.18
	over consent and data misuse	discrimination or unauthorized acces	S
Informed consent	Understanding complex omics-based	Clear, accessible consent protocols as	re
	interventions requires enhanced	are essential to uphold autonomy	
	communication of risks and benefits		
Equitable access	High costs and technological disparities may	Policies should address affordability	
	limit access to precision nutrition services	and inclusion for underserved popula	ations
Cultural sensitivity	Dietary recommendations must respect	Failure to consider cultural norms may lead	
	cultural and individual food preferences	lead to non-adherence	
Social stigmatization	Labeling individuals based on metabolic	Ethical frameworks should prevent no	utritional
	or genetic risk may lead to social bias	profiling from reinforcing inequality	

Table outlines the major ethical and social challenges in the application of personalized nutrition. Issues span data privacy, equitable access, affordability, and potential for discrimination

Ethical and social considerations: As personalized nutrition becomes increasingly integrated into healthcare and wellness frameworks, critical ethical and social considerations have emerged. These concerns revolve primarily around issues of data privacy, equitable access, affordability, and the broader societal implications of applying genetic and metabolic profiling for dietary guidance.

One of the foremost ethical challenges is the privacy and security of personal health data, particularly genetic and metabolic information. The acquisition and analysis of such intimate biological data raise concerns about data misuse, unauthorized access, and potential discrimination by insurers or employers¹⁷. While personalized nutrition aims to empower individuals with tailored dietary recommendations, the sensitivity of genomic and metabolomic data necessitates stringent data governance policies to safeguard individual autonomy and confidentiality.

Beyond privacy, the application of genome editing technologies in health-related domains including personalized nutrition has sparked intense bioethical debates. Institutions such as the Nuffield Council on Bioethics have highlighted how interventions involving genome profiling may influence reproductive decisions and societal norms, raising questions about consent, heritability, and the potential for unintended social stratification¹⁷. When such technologies are employed within personalized nutrition paradigms, similar concerns about consent, equity, and intergenerational implications must be carefully evaluated.

Furthermore, systematic reviews have underscored the social challenges of implementing personalized nutrition on a broad scale. These include disparities in digital literacy, differential access to omics-based health services, and cultural perceptions of health and nutrition¹⁷. For instance, while affluent populations may readily adopt personalized nutrition technologies, marginalized communities may lack access due to financial constraints or infrastructural limitations, thereby exacerbating existing health inequities.

From an ethical standpoint, some scholars argue that personalized nutrition must align with principles of justice and beneficence. As the field advances, it is imperative to ensure that innovations do not create a nutritional divide between those who can afford precision interventions and those who cannot ^{17,18}. This perspective calls for policy frameworks that support subsidized access, promote education, and foster inclusivity in the design and implementation of personalized nutrition tools.

Additionally, the use of predictive analytics in personalized dietary recommendations introduces the risk of nutritional determinism, where individuals are reduced to their biological profiles without consideration of personal agency or environmental contexts. Scholars have emphasized the importance of maintaining a balance between data-driven recommendations and individual choice^{17,18}. Ethical implementation must therefore integrate participatory approaches that empower individuals while respecting cultural, social, and psychological dimensions of eating behavior.

Table 3 illustrates the growing ethical and social concerns associated with the implementation of precision nutrition as it becomes more integrated into clinical and public health practice. Key issues include genetic data privacy, equitable access, and the potential for stigmatization¹⁸. There are increasing calls for the establishment of robust governance frameworks that ensure informed consent, safeguard against misuse of genetic data, and promote inclusive access to personalized nutrition interventions¹⁸. Moreover, challenges such as affordability and cultural sensitivity may hinder widespread adoption¹⁸. Addressing these ethical dimensions is essential for maintaining public trust, promoting fairness in healthcare delivery, and realizing the full potential of personalized nutrition¹⁸.

Regulatory frameworks and standardization: As personalized nutrition gains traction within the domains of healthcare and public health, regulatory clarity and standardization have become critical. The scientific and commercial advancements in this field necessitate frameworks that both safeguard consumer interests and promote evidence-based innovation.

Presently, regulatory policies addressing personalized nutrition are fragmented and often insufficient in scope. Despite growing interest from stakeholders, there remains a lack of unified international regulations that specifically govern the collection, interpretation, and application of individualized dietary advice. The European Food Safety Authority (EFSA), one of the few bodies to provide guidance, has emphasized that any health claims linked to genetic or phenotypic information must be substantiated with robust scientific evidence to ensure validity and consumer protection¹⁹. However, this position still leaves significant gaps regarding operational standards for digital health tools and nutrigenomic applications.

The development of standardized methodologies for nutrigenomic research remains an unmet priority. Inconsistent study designs, variability in genetic markers assessed, and the absence of agreed-upon metrics for evaluating dietary outcomes have hindered reproducibility and regulatory assessment. A systematic review of current practices revealed substantial heterogeneity in data reporting, analytic approaches, and biomarker validation, all of which challenge the generalizability of findings and the formation of regulatory consensus¹⁹.

Ethical and legal considerations also intersect with regulatory design. As Chih $et\ a^{19}$. have noted, personalized nutrition must navigate complex issues related to informed consent, data security, risk communication, and the delineation of professional responsibilities. These dimensions call for multidimensional regulatory frameworks that address not only scientific rigor but also consumer autonomy and trust.

Efforts to establish a harmonized regulatory landscape are beginning to emerge. Recent literature advocates for the creation of an integrated framework that bridges nutrigenomic science, clinical application, and public health policy. Such a framework would standardize protocols for sample collection, bioinformatics pipelines, and personalized dietary recommendations. Moreover, it would support credentialing mechanisms for nutrition professionals using genomic data, thereby ensuring consistency and accountability across practice settings^{19,20}.

The need for global alignment is further reinforced by the transnational nature of digital health platforms offering direct-to-consumer personalized nutrition services. Regulatory bodies must contend with the challenge of overseeing cross-border data usage and commercially driven algorithms that may not meet established scientific or ethical thresholds. As such, regulatory models should evolve in tandem with technological advancements while maintaining transparency, reproducibility, and consumer safety as core principles^{19,20}.

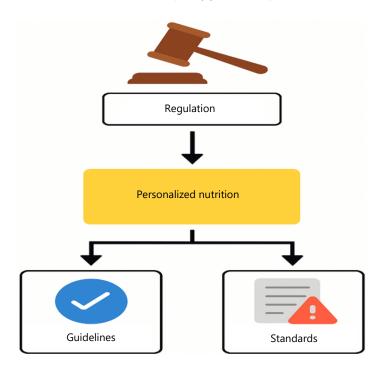


Fig. 8: Regulatory pathways for personalized nutrition (self-generated, using canvas and DALL.E image generating tools)

Key regulatory frameworks guiding personalized nutrition, emphasizing the need for standardized guidelines in nutrigenomics and policy development

Figure 8 expresses the importance of developing robust regulatory frameworks to ensure scientific validity, ethical compliance, and consumer protection in personalized nutrition²⁰. The standardization of nutrigenomic research is essential for harmonizing global policies and enhancing clinical applicability²⁰. Ethical and legal considerations shape the formulation of personalized dietary recommendations while safeguarding public health²⁰. A unified and transparent regulatory framework not only supports innovation in precision nutrition but also addresses emerging challenges in health policy and implementation²⁰.

Future research directions: The evolving fields of nutrigenomics and metabolomics hold considerable promise for advancing personalized nutrition by uncovering novel molecular mechanisms and biomarkers that dictate individual responses to diet. As research increasingly integrates multi-omics technologies, future breakthroughs are expected to enhance the precision of dietary recommendations, optimizing health outcomes on a personalized level²¹. Multi-omics approaches, combining genomics, transcriptomics, proteomics, and metabolomics data, provide a comprehensive understanding of the complex biological interactions underlying nutrition-related phenotypes and disease susceptibilities, thereby enabling tailored interventions with greater efficacy²¹.

Emerging trends in personalized dietary interventions emphasize the convergence of Artificial Intelligence (AI) and Machine Learning (ML) with nutritional science. These computational tools are transforming data analysis, enabling dynamic and adaptive dietary recommendations that respond to real-time physiological and lifestyle inputs. The integration of AI-driven algorithms with high-dimensional biological data promises to revolutionize personalized nutrition by facilitating predictive modeling, optimizing intervention strategies, and enhancing user engagement²¹.

Furthermore, the future of personalized nutrition research is marked by a shift from static, one-size-fits-all dietary guidelines to highly individualized nutrition plans that account for genetic variability, metabolic states, microbiome composition, and environmental factors. This paradigm shift advocates for longitudinal studies and well-designed clinical trials to validate personalized interventions and assess their long-term benefits on metabolic health and chronic disease prevention^{21,22}.

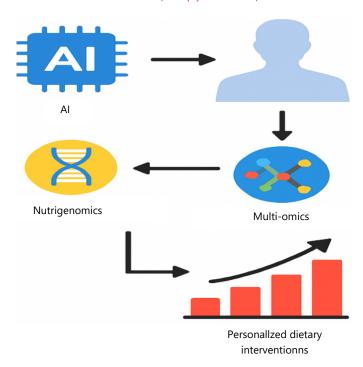


Fig. 9: Future roadmap for personalized nutrition research (self-generated, using canvas and DALL.E image generating tools)

Emerging trends in nutrigenomics and metabolomics, showcasing how Al-driven technologies and multi-omics integration are advancing personalized dietary interventions

Significant attention is also being directed toward refining the usability and accessibility of personalized nutrition technologies. Future research must address challenges related to data privacy, ethical implementation, and equitable access to ensure that advancements benefit diverse populations globally. Collaborative efforts among researchers, clinicians, policymakers, and technology developers will be essential to build robust frameworks that support the sustainable translation of personalized nutrition from bench to bedside and beyond^{21,22}.

Figure 9 demonstrates how the future of personalized nutrition is being shaped by rapid advancements in AI and machine learning, which enable more precise dietary recommendations tailored to individual genetic and metabolic profiles²². Breakthroughs in nutrigenomics continue to reveal complex genenutrient interactions, providing the foundation for more effective, precision-guided nutritional strategies²². The integration of multi-omics technologies including genomics, microbiomics, and metabolomics facilitates comprehensive health assessments and personalized interventions²². Moving forward, interdisciplinary collaborations will play a critical role in refining predictive models and translating research into clinical and public health solutions²².

Integrative biochemical and computational perspectives in personalized nutrition: Emerging research continues to broaden the scientific foundation of personalized nutrition by incorporating complex biochemical and computational insights. Notably, microbiota derived metabolites have been shown to exert profound effects on host metabolic regulation, immune signaling, and neurotransmission processes now recognized as essential modulators of individual dietary responses and nutritional status²³. Parallel investigations have identified microplastics as environmental contaminants capable of disrupting biochemical pathways linked to metabolism and systemic health, thereby posing a potential barrier to achieving optimal personalized dietary outcomes²⁴.

Additionally, biochemical mechanisms underlying sleep regulation, closely tied to circadian rhythms, hormonal control, and nutrient metabolism, are gaining prominence as integral factors influencing personalized dietary interventions²⁵. These pathways underscore the need for precision strategies that accommodate chronobiological variability in nutritional planning.

Bioactive compounds derived from traditional medicinal herbs are also increasingly explored for their therapeutic potential in modulating gene expression, enzyme activity, and immunometabolic pathways. Their integration into culturally responsive personalized nutrition models offers promising avenues for individualized health optimization²⁶.

Furthermore, the application of Artificial Intelligence (AI) in biochemistry and biomedical research is accelerating the capacity to analyze multidimensional biological data, predict dietary responses, and design more effective and adaptive nutritional interventions. These computational approaches represent a transformative addition to the personalized nutrition paradigm.

CONCLUSION

In summary, personalized nutrition offers a paradigm shift in dietary science by aligning nutritional strategies with individual genetic, epigenetic, microbiomics, and metabolic profiles. This integrative approach enables more precise, effective, and preventative health interventions. Advances in multi-omics technologies and digital tools have enhanced the feasibility and scalability of personalized nutrition. However, ethical, regulatory, and accessibility challenges must be addressed to ensure equitable implementation. Continued interdisciplinary research is essential to refine predictive models and clinical applications. Ultimately, personalized nutrition holds transformative potential to improve health outcomes and reduce the global burden of diet-related diseases.

SIGNIFICANCE STATEMENT

This article provides a comprehensive and integrative analysis of the biochemical mechanisms that form the foundation of personalized nutrition a rapidly emerging discipline that seeks to align dietary interventions with individual biological variability. By synthesizing insights from genetics, epigenetics, microbiomics, and metabolomics, the review highlights how personalized dietary strategies can optimize health outcomes, prevent chronic diseases, and support healthy aging. The manuscript also explores the transformative role of digital health technologies and artificial intelligence in advancing precision nutrition, while addressing critical ethical, regulatory, and equity considerations. This work contributes significantly to the evolving landscape of nutrition science by offering a multidimensional framework for translating molecular data into individualized, actionable, and ethically sound nutritional guidance in both clinical and public health settings.

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