Advancing nutritional genomics in the era of big data, multiomics and artificial intelligence

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This special issue on Clinical Precision Nutrition in the *British Journal of Medicine, Nutrition, Prevention & Health* arrives at a pivotal moment when the integration of genetic information with nutrition science is poised to redefine dietary recommendations and public health policies. The evolving landscape of precision nutrition provides us with a unique opportunity to bridge genetic epidemiology, diet and health outcomes in a meaningful and clinically impactful way.

THE RISE OF NUTRITIONAL GENOMICS

Nutritional genomics has transformed our understanding of why individuals respond differently to the same diet.[1] Since the early 2000s, following the mapping of the human genome, this field has made significant strides, revealing how genetic polymorphisms influence eating behaviours, nutrient metabolism, dietary responses and chronic disease risk. Landmark studies have demonstrated that genetic variation can determine whether a particular diet is beneficial, benign or harmful, yet much of this research has remained within specialised scientific and clinical circles. Despite decades of progress, the integration of these findings into clinical practice and public health guidelines has been slow, limiting their real-world impact. However, the growing recognition that a one-size-fits-all approach to nutrition fails to optimise health has driven research into gene–diet interactions, multiomics integration and precision dietary interventions. Where robust evidence exists across diverse populations, tailoring dietary recommendations to genetic profiles holds promise for improving metabolic health, reducing disease risk and optimising healthspan.

Our research, alongside those of others, has highlighted the significance of gene–diet interactions, particularly in clinical nutrition and cardiometabolic health. Our studies have shown how genetic variation influences the impact of diet on cardiovascular events, hypertension, diabetes risk and kidney function. For example, research on caffeine metabolism has demonstrated that genetic variants in CYP1A2 modify the cardiovascular effects of coffee in opposite directions—beneficial for some, harmful for others—depending on genotype.[2] These insights, which would have been missed without rigorous methodologies that distinguish key metabolic and dietary factors, illustrate why precision nutrition is essential for improving health outcomes.

Gene–diet interactions can be studied using a range of approaches, from agnostic Genome-Wide Association Studies (GWAS) to mechanistic studies focused on specific pathways. Some studies examine single-gene (monogenic) effects, while others use polygenic risk scores to capture cumulative genetic susceptibility. Regardless of the method, clearly defining scientific questions and applying rigorous methodologies is essential to ensuring meaningful and reproducible findings.

Incorporating nutrient intake within broader dietary patterns is particularly valuable in this context, as it provides a more complete understanding of how diet shapes genetic risk for cardiovascular disease (CVD) and mortality. Our research has helped demonstrate that genetic loci such as 9p21 do not act in isolation but interact with dietary patterns to influence metabolic pathways.[3] Notably, we were the first to identify fasting insulin as a potential mechanistic link between 9p21 and dietary patterns on CVD, diabetes, cancer and accelerated aging risk, offering a new perspective on how diet can modulate genetic susceptibility.[4] We also identified sex-specific differences in cardiometabolic risk profiles,[5] accompanied by distinct proteomic signatures[6] that suggests divergent molecular pathways underlying disease susceptibility and dietary response. Previous studies established associations between 9p21 and CVD but did not account for how diet influences this risk through insulin regulation. By integrating dietary patterns with metabolic intermediates, our work moves beyond simplistic gene-disease models and towards more actionable strategies for nutrition intervention and disease prevention.

These findings challenge the broad application of generic dietary guidelines and emphasise the need for more personalised recommendations. Similar research on folate and choline metabolism,[7] omega-3 fatty acids and lipid regulation further reinforces the role of genetics in shaping dietary responses. By understanding these interactions, we can refine nutrition interventions to align with genetic predisposition, paving the way for a more individualised approach to dietary guidance and clinical nutrition therapy.

THE ROLE OF MULTIOMICS IN NUTRITIONAL RESEARCH AND CLINICAL NUTRITION

While genetics plays a crucial role in shaping dietary responses, the integration of multiomics approaches—including genomics, transcriptomics, epigenomics, proteomics and metabolomics—has provided deeper insights into the complex relationship between diet and health. By incorporating multiple layers of biological data, researchers can clarify the mechanisms through which diet influences gene expression, protein synthesis and metabolic pathways, offering a more comprehensive perspective on how nutrition impacts health across different life stages.

Transcriptomics has revealed how dietary components can regulate gene

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expression in a tissue-specific manner, providing a dynamic perspective on how food interacts with our biology beyond static genetic predisposition.[8] Epigenomical studies have demonstrated that dietary factors such as methyl donors and bioactive compounds can modify DNA methylation patterns, influencing gene regulation and disease susceptibility.[9] Proteomics and metabolomics further refine our understanding by identifying biomarkers that reflect real-time metabolic changes in response to dietary interventions. These integrative approaches provide a more precise method of tailoring diets based on individual biochemical and genetic profiles.

In a recent review, we cover multiple aspects of omics applications directly to clinical settings, much of which can be ready to use and integration with clinical populations.[3]

MICROBIOME RESPONSES DRIVEN BY DIET AND HOST GENOTYPE

The gut microbiome plays a central role in mediating nutrient signalling, bile acid turnover and inflammatory pathways that underlie many chronic diseases and ageing processes. While diet is a potent and modifiable driver of microbiome composition and function, recent evidence confirms that host genetics also shapes which microbial functions emerge in response to dietary intake. Large-scale cohort studies now show that common host genetic variants—particularly at loci such as ABO, LCT and FUT2—influence not only microbial taxa but also structural variants within microbial genomes that control nutrient utilisation pathways.[10 11] For example, *Faecalibacterium prausnitzii* strains possessing host-linked gene clusters for glycan metabolism appear only in individuals with compatible secretor genotypes, meaning the host's genetic expression of mucosal glycans directly governs microbial functional capacity.

Diet remains an essential lever in this equation. Controlled feeding studies have demonstrated that high-fibre or plant-based diets can shift microbial gene expression and metabolite output within days, including impacts on short-chain fatty acid production and host glycaemic responses. However, these functional effects are not uniform across individuals. Recent multiomic profiling has shown that diet-induced microbial shifts yield different cardiometabolic trajectories depending on host genotype, reinforcing the view that precision nutrition must move beyond taxonomic classification toward individualised functional targeting.[12]

Further support comes from experimental studies in gnotobiotic animal models, where host genotype—not maternal inheritance or diet alone—has been shown to direct the long-term structure and activity of the microbiome.[10 13] Meanwhile, emerging reviews emphasise that microbiome-guided nutrition must account for genetically modulated microbial activity, rather than treating the gut microbiome as a passive reflection of dietary intake.[14] Taken together, these findings suggest that clinical nutrition interventions must target microbiome function, not just composition, and that both dietary strategies and therapeutic outcomes will vary based on an individual's genetic capacity to support specific microbial responses. As clinical precision nutrition evolves, the integration of host genotyping, microbial metabolomics and targeted dietary modulation will be essential for advancing from general dietary advice to mechanism-informed interventions.

THE IMPACT OF ARTIFICIAL INTELLIGENCE AND LARGE LANGUAGE MODELS

The integration of artificial intelligence (AI) and large language models (LLMs) into clinical nutrition and genomics is transforming the way we analyse complex biological data and implement precision nutrition strategies. AI-driven algorithms can process vast datasets from GWAS, metabolomics and dietary assessments, identifying gene–diet interactions that would be difficult to detect using traditional statistical approaches.[15] Machine learning models enhance risk prediction by integrating polygenic risk scores, metabolic markers and lifestyle factors, allowing for more refined dietary recommendations tailored to an individual's genetic profile. LLMs further accelerate research by synthesising vast bodies of literature, automating data extraction from clinical trials and assisting in real-time clinical decision-making. In clinical settings, AI-driven tools can personalise nutrition therapy by predicting metabolic responses to specific diets, optimising dietary interventions for chronic disease management and translating genomic insights into actionable recommendations. As these technologies continue to advance, integrating AI with multiomics approaches has the potential to revolutionise precision nutrition, making personalised dietary guidance more accessible and effective for both clinicians and patients. However, ensuring the validity and ethical application of these models requires robust validation, transparency in data sources and continued collaboration between computational scientists, clinicians, nutrition professionals and geneticists.

IMPLEMENTATION AND CLINICAL INTEGRATION

The successful implementation of precision nutrition will depend not only on advances in technology, but also on the development of scalable, context-specific frameworks that align with the priorities and constraints of each area of clinical nutrition practice. As multiomics platforms, continuous glucose monitoring (CGM) and AI-enabled analytics become more widely available, their integration must be guided by robust cost-effectiveness analyses and tailored to the clinical realities of specific populations. In our recent work on the nutritional management of diabetes in patients undergoing peritoneal dialysis, we discuss how integrated multiomics and AI can inform individualised dietary strategies and improve glycemic control in a population with uniquely complex metabolic demands.[16] Such population-specific applications highlight that implementation challenges are not uniform: the infrastructure, data modalities and clinical decision pathways required for kidney care differ markedly from those needed in oncology nutrition, metabolic disorders or maternal health.

The advancement of personalised nutrition will require a robust theoretical framework, rigorous evidence from genotype-informed and n-of-1

trials, and integration of multiomics data—including epigenomics, metabolomics and microbiomics—to ensure scientific validity, clinical relevance and regulatory confidence. Moreover, as omics-informed approaches increasingly generate sensitive personal health data, rigorous attention to data governance, privacy protections and ethical use is paramount. Equally critical is the early and sustained professional development of dietitians and clinical nutritionists—ensuring competency in interpreting genomic, proteomic, metabolomic and microbiome data, and in integrating digital tools and clinical decision support systems into practice. At present, precision nutrition is deployed through highly variable models—ranging from CGM-guided glycaemic modulation and behaviourally anchored apps to microbiome-informed and gene-based dietary frameworks. Without consensus on minimal data requirements, validation protocols and standardised clinical endpoints, the field risks fragmentation. To advance both scientific integrity and clinical utility, discipline-specific consensus frameworks are urgently needed to define best practices, promote interoperability and ensure that precision nutrition delivers meaningful benefit across diverse settings and patient populations.

CURRENT ADVANCES AND KNOWLEDGE GAPS

Recent advancements in genomics and bioinformatics have accelerated our ability to identify novel gene–diet interactions. Multiomics approaches integrating genomics, transcriptomics, proteomics and metabolomics are revealing previously unrecognised pathways that mediate the effects of diet on health. Large-scale biobank studies, such as the UK Biobank and Nurses' Health Study, have provided invaluable data, revealing complex interactions between diet, genetics and chronic disease risk over time. However, while these advances are promising, there are still significant knowledge gaps that must be addressed to fully harness the potential of precision nutrition.

One major challenge is ensuring the reproducibility and validity of gene–diet interactions across diverse populations. Many existing studies have primarily focused on populations of European ancestry, limiting the generalisability of findings. Given the significant variability in dietary habits, cultural influences and genetic diversity across global populations, there is a pressing need for more inclusive research that represents a broader spectrum of ethnic backgrounds. Additionally, sex differences in metabolic responses to diet and genetic predisposition to disease remain underexplored, necessitating further investigation into how biological sex influences nutritional genomics outcomes.

The translation of genetic discoveries into clinical practice remains a significant challenge. While genetic testing has become more accessible, its integration into routine dietary counselling is still limited due to the need for stronger evidence on efficacy and cost-effectiveness. Clinicians require well-validated decision-making frameworks and skillsets to implement genomic information in a meaningful way, ensuring that precision nutrition recommendations lead to measurable health benefits. Ethical considerations surrounding the use of genetic and multiomics data in dietary counselling must also be carefully navigated to prevent genetic determinism and misuse of information in commercial settings.

CALL FOR CONTRIBUTIONS

This special issue aims to address these challenges by bringing together pioneering research in nutritional genomics and multiomics applications in precision nutrition. We invite original research articles, systematic reviews and commentaries that explore how genetic, transcriptomic, epigenetic, proteomic, metabolomic and metagenomic data can be leveraged to develop more tailored nutritional interventions in human studies. Contributions exploring the role of gene–diet interactions in chronic disease prevention and management, the integration of multiomics approaches in dietary and metabolic biomarker research, and the clinical implementation of personalised nutrition strategies are encouraged. Research that examines ethnic and sex-specific differences in gene-diet responses, the application of AI and machine learning in diet and genomics, and the ethical, regulatory and public health considerations in precision nutrition are also of great interest.

Expanding the scope of this issue to include multiomics perspectives will provide a more holistic view of how nutrition interacts with biology to influence health. The integration of these approaches represents the next frontier in precision nutrition, offering unparalleled opportunities for refining dietary guidelines and developing personalised strategies for disease prevention.

THE FUTURE OF PRECISION NUTRITION

As our understanding of genetics and multiomics in nutritional responses continues to grow, the next decade holds immense promise for the implementation of precision nutrition strategies in both clinical and public health settings. The expansion of biobanks, longitudinal cohort studies and technological innovations in omics research will provide new insights into the mechanisms underlying dietary effects on human health. The increasing interest in AI-driven approaches for integrating complex datasets will further enhance our ability to identify individualised nutritional recommendations that optimise health outcomes.

However, realising the full potential of precision nutrition will require interdisciplinary collaboration among researchers, clinicians, policy-makers and industry stakeholders. The ability to translate genomic discoveries into actionable dietary guidance will depend on rigorous validation, robust clinical trials and ethical frameworks

that prioritise accessibility and equity in precision nutrition applications.

I am honored to serve as the Guest Editor for this special issue and warmly invite you to contribute to building the scientific evidence base for clinical precision nutrition. Together with Founding Editor-in-Chief Dr. Martin Kohlmeier, we look forward to your submissions and to advancing the field through rigorous, impactful scholarship. This special issue serves as a platform to foster dialogue, disseminate cutting-edge research, and inspire the next generation of scientists in nutritional genomics and multi-omics research. We look forward to receiving high-quality contributions that will propel the field forward and help shape the future of personalized nutrition.

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