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Precision nutrition for cardiometabolic diseases

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Precision nutrition is a vibrant and rapidly evolving field of scientific research and innovation with the potential to deliver health, societal and economic benefits by improving healthcare delivery and policies. Advances in deep phenotyping technologies, digital tools and artificial intelligence have made possible early proof-of-concept research that expands the understanding of within- and between-person variability in responses to diet. These studies illustrate the promise of precision nutrition to complement the traditional 'one size fits all' dietary guidelines, which, while considering broad life-stage and disease-specific nutritional requirements, often lack the granularity to account fully for individual variations in nutritional needs and dietary responses. Despite these developments, however, considerable challenges remain before precision nutrition can be implemented on a broader scale. This Review examines the current state of precision nutrition research, with a focus on its application to reducing the incidence and burden of cardiometabolic diseases. We critically examine the evidence base, explore the potential benefits and discuss the challenges and opportunities ahead.

Nutrition is a key determinant of health, development, well-being and longevity, with changing requirements along the life course[1]. Current dietary guidelines account for some individual differences in nutritional requirements, providing life stage- and disease-specific recommendations[2–5]. However, while 'one size fits all' approaches are broadly effective at a population level, the nutritional needs of many people diverge from population averages[6].

Precision nutrition considers how nutrients, foods and dietary patterns affect nutritional status and health outcomes in the context of differences in dynamic biology, behavior, environment and social determinants of health that occur between and within individuals. Precision nutrition aspires to tailor dietary recommendations to individuals or populations sharing similar characteristics[7], much like the ambitions of precision medicine to deliver medical interventions optimized at the person level[8]. Given the communal nature of food preferences and consumption in households, as well as societal and cultural contexts and the built food environment, precision nutrition shares some features with precision public health, which considers population and subpopulation stratifications for developing policies and interventions to protect and improve the health of specific groups according to their unique needs[9]. At its core, precision nutrition seeks to optimize health by addressing diverse nutritional needs across different demographics. Recognizing the heterogeneity in nutritional needs and dietary responses, the necessity for greater rigor in dietary assessment and the challenge of sustaining long-term adherence to dietary advice, the framework underscores the importance of innovations

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in molecular biology and '-omics', wearable devices and digital technologies[10]. Additionally, it emphasizes the importance of addressing health disparities in nutrition, obesity and cardiometabolic health to ensure equitable access to precision nutrition advancements[11].

This Review provides a critical evaluation of state-of-the-art precision nutrition research and how it can help enhance contemporary nutritional science and improve policy and practice. Although the focus here is on precision nutrition for cardiometabolic diseases, concepts herein transcend disease domains. This Review examines the current readiness of precision nutrition for public health and clinical practice, including implications for translating the efficacy observed in short-term, tightly controlled studies to scalable real-world settings. We also highlight several ongoing precision nutrition initiatives and explore their potential societal implications, including considerations of sustainability and accessibility.

Healthy diets in the era of precision nutrition

Leading global policy-makers and medical organizations develop evidence-based nutritional and dietary guidelines that promote health and well-being and prevent and manage various diseases[2–5]. These guidelines emphasize a varied, balanced diet, with fruits, vegetables, whole grains, legumes, lean animal and plant protein foods, and healthy vegetable oils, while limiting saturated fats, added sugars, alcohol and sodium. Guidelines are often adapted to the life course, from infancy to older adulthood, and consider stages with unique nutritional needs, such as pregnancy and lactation[4]. Increasingly, they also consider the environmental impact of food production[12]. Dietary guidelines form the basis of national and global food and nutrition policies and inform school meals[13] and nutrition support for institutionalized and community-dwelling older populations[14].

Dietary guidelines are also tools for dietitians, clinicians and other healthcare providers, enabling them to assess individual nutritional requirements, design meal plans adapted to individual preferences and cultural traditions, and guide healthy eating[15]. However, dietary guidelines assume that all people within broad population groups benefit similarly from the same recommendations. For example, nutrition therapy for women with gestational diabetes aims to optimize maternal weight gain and improve glycemic control through dietary strategies such as modifying carbohydrate quality and/or quantity[16]. However, metabolic challenge tests in pregnant women show considerable heterogeneity in postprandial responses to the same substrate load or meal[17]. This wide interindividual variability highlights the need for more personalized dietary recommendations.

The challenges for the practical implementation of dietary guidelines are evident from the small proportion of the global adult population consuming the recommended intake of fruits and vegetables[18] and the overall poor-quality diets consumed by many young people[19]. Several barriers impede the adoption of dietary guidelines, including personal preferences, cultural beliefs and limited access to the recommended healthy foods. These issues are further complicated by societal pressures, time and economic constraints, and fluctuating individual-level motivation[20]. By aggressively marketing unhealthy products, the commercial food environment also undermines intentions at the individual level to adhere to the recommendations[21]. Additionally, across different countries, nutrition education is delivered by different healthcare professionals who may not always have the necessary training or resources to effectively promote healthy eating to their patients. This concern has been shared by multiple professional societies, which have called for enhanced nutrition education and training for both current and future healthcare professionals providing nutritional counseling[22,23].

Precision nutrition offers the potential to enhance dietary guidelines and address these challenges by focusing on three core components: first, targeted dietary recommendations to account for individual or subgroup differences in nutritional requirements for optimal health; second, delivery of dietary advice through the use of digital applications (apps), wearables and other technological advances that make real-time monitoring and personalized feedback possible; and third, assessment and optimization of adherence to dietary advice through digital tools, empowering individuals to make informed dietary choices by simplifying dietary decisions and adapting them to the individuals' competing risk factors, environmental contexts and life events. Cross-cutting themes such as artificial intelligence (AI), behavioral science, stakeholder engagement, health equity, food sustainability and data privacy provide the foundation for achieving these goals (Fig. 1).

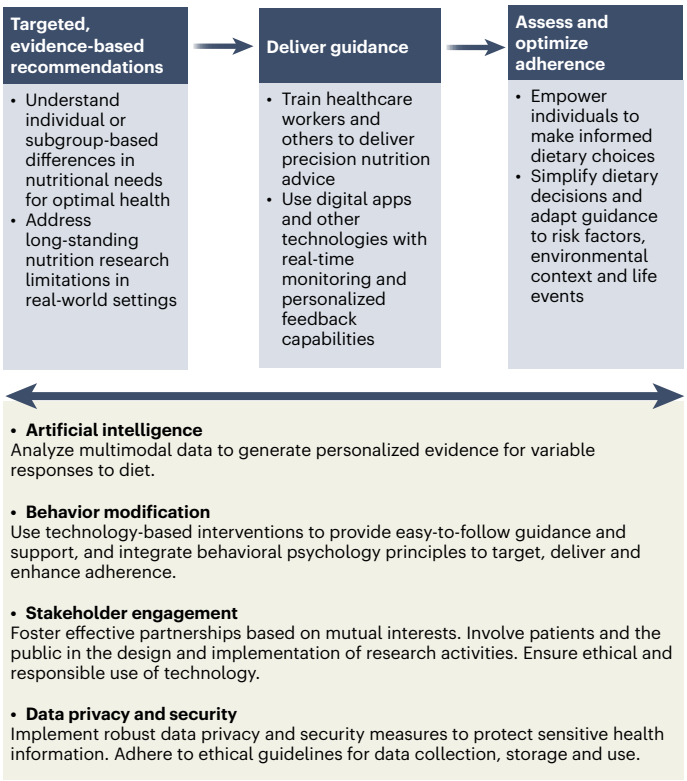

Fig. 1 | Precision nutrition aims to improve the discovery and delivery of, and adherence to, evidence-based dietary recommendations. The three core components of precision nutrition are underpinned by cross-cutting themes, including AI, behavioral science, stakeholder engagement, health equity, food sustainability and data privacy.

Accounting for heterogeneity

At a cellular level, heterogeneity in nutritional needs and responses is attributable to the interaction of nutrients and an individual's biological constituents, such as variation in their DNA, gene expression and regulation factors, gut microorganisms and other biochemical derivatives[24]. Beyond this, behavioral factors such as physical activity levels, meal timing, sleep and circadian rhythms have a critical role in metabolic homeostasis and contribute to large variance in postprandial glucose responses[25,26]. Furthermore, psychosocial, economic, political and cultural factors often influence a person's exposure to factors affecting their food intake and preferences[27]. For precision nutrition to have a clinical and public health impact, analytical approaches must account for the complex interplay of multiple molecular processes with external factors, which vary in intensity and type between individuals and over time.

Gene–environment interactions

An example of genetic adaptation shaping nutritional needs has been observed in the Greenlandic Inuit population[28], whose genomes are

enriched for variants that enhance fatty acid desaturation. As Inuit diets traditionally contain high levels of very-long-chain polyunsaturated fatty acids (PUFAs) such as eicosapentaenoic acid and docosahexaenoic acid, likely owing to exposure to diets rich in fatty marine animals, evolutionary pressures have favored alleles that increase the availability of very-long-chain PUFA precursors such as linoleic acid or α-linolenic acid[28]. Such knowledge can help identify specific gene–diet interactions that influence nutrient bioavailability and metabolism and the risk of developing cardiometabolic complications. For people harboring these genetic variants, for example, the most beneficial diets might be those rich in linoleic acid or α-linolenic acid, common in nuts and seeds.

Beyond single genetic variants, polygenic risk scores—which consider the combined effects of multiple genetic variants—have been proposed for identifying individuals who may respond idiosyncratically to specific diets or nutrients. While interactions between genetic risk for obesity and dietary factors have been observed in the context of weight gain[29,30], evidence supporting similar gene–diet interactions in type 2 diabetes or cardiovascular complications is limited[31–34]. In a meta-analysis of individual participant data, which included data from up to 100,000 individuals across 15 prospective studies with a median follow-up of 12 years, a polygenic score for type 2 diabetes and dietary fat quality were both associated with the development of type 2 diabetes, but no significant interaction between them was observed[34]. Others have used polygenic scores that reflect distinct pathophysiological mechanisms underlying type 2 diabetes to show that the risk of type 2 diabetes attributed to the combination of genetic susceptibility and diet quality is similar to the sum of the risks associated with each factor alone, indicating no evidence of interactions[33]. These findings highlight the importance of integrating polygenic risk scores with additional molecular or phenotypic information to achieve a more comprehensive understanding of how genetic risk and environmental factors shape variable disease risk[35].

Gut microbiome. The gut microbiome may also influence how individuals respond to diet, but the relationship among diet, the gut microbiome and cardiometabolic health is highly complex and multidirectional[36]. Short-term dietary changes and long-term dietary habits both influence microbiome composition. For example, consuming an animal-based diet for 5 days, compared to a plant-based diet, has been shown to decrease species that metabolize plant polysaccharides while increasing bile-tolerant bacteria[37]. In addition, long-term adherence to dietary patterns such as the Mediterranean diet (MedDiet) has also been linked to specific changes in microbiome composition in observational and interventional studies. In an observational study that included 307 generally healthy men, the protective association between the MedDiet and cardiometabolic risk was notably stronger in participants with gut microbiomes depleted of the *Prevotella copri* species[38]. Individuals with overweight or obesity randomized to a MedDiet exhibited increased levels of *Faecalibacterium prausnitzii* and *Roseburia* species, along with reduced levels of *Ruminococcus gnavus* and *Ruminococcus torques* compared to those on a regular diet[39]. Given that the MedDiet is characterized by a high intake of plant-based, minimally processed foods, these findings support the potential relevance of fiber–gut microbiome interactions in precision nutrition for cardiometabolic diseases.

The small intestine's microbiome is relevant in multiple host–microbiome interactions[40], and improving the understanding of the spatiotemporal structure of the human small intestinal microbiome may help extend the role of the microbiome in precision nutrition. Two studies have provided insights into this role, developing active swallowable capsule devices under different pH conditions for sample collection at different locations along the gastrointestinal tract. These studies revealed region-specific microbial communities, metabolomes and proteomes that comprehensively capture the diversity and functional roles of the metagenome[40] and are linked to dietary variation and biosynthesis of short-chain fatty acids[41].

Gut–brain axis. Previous experimental studies in mice have highlighted gut–brain axis circuits involving specific signals from the gut and certain areas of the central nervous system that have a crucial role in regulating eating behavior[42]. In humans, activation of these circuits, driven by short-term signals from the gastrointestinal tract, long-term signals from adipose tissue or external food cues, contributes to the overconsumption of energy-dense foods[43]. Research into the neurobiology of appetite has already informed actionable dietary advice by uncovering how brain mechanisms influence food reward[44], food preferences[45] or food choices[46]. Understanding these neurobiological pathways could help identify relevant groups for risk stratification.

Mapping the molecular and functional profiles of neuronal cells involved in appetite regulation and body weight control is a rapidly advancing field[47], yet progress is hampered by the brain's inherent cellular heterogeneity and the challenges of translating animal research findings to humans. Single-cell or single-nucleus mRNA sequencing offers a promising solution by making possible the identification of cell-specific molecular pathways underlying appetite, both in physiological conditions[48] and in metabolic disease[49]. Although most current studies using these techniques rely on animal models and in vitro systems, new methodologies are paving the way for human application. For example, a study combined single-nucleus sequencing with spatial transcriptomics to construct a detailed spatiocellular atlas of the human hypothalamus, which represents a critical resource for deciphering the neurocircuitry that controls hunger, satiety and energy balance[50]. Integrating this molecular knowledge with behavioral, socioeconomic and environmental information might offer potential next-generation strategies for managing metabolic health[51,52].

Metabotypes. Other studies have used clinical and other physiological characteristics—such as dynamic glycemic responses to an oral glucose tolerance test—to identify individuals more likely to respond differently to certain nutritional interventions. Clinical trials, such as the PERSON study, have provided initial evidence supporting this concept[53]. Findings from this 12-week randomized clinical trial suggest that individuals with insulin resistance due to liver dysfunction will experience the most cardiometabolic benefit from a diet high in monounsaturated fatty acids compared to a low-fat, high-protein and high-fiber diet[53]. While these insights offer a promising avenue for advancing precision nutrition, emerging evidence suggests that the classification of individuals into rigid categories or disease subtypes on the basis of dynamic clinical characteristics may have limited utility as these disease subtypes may represent transient metabolic states, with subtype classifications shifting over time[54,55].

Translating short-term precision nutrition studies into long-term clinical effectiveness

Effectively translating precision nutrition research into meaningful guidance and beneficial clinical outcomes requires the assessment and integration of diverse data types to capture population heterogeneity and identify subgroups. This approach makes tailored nutritional recommendations possible by leveraging individual-level data. Large feeding studies in humans, such as the Personalized Nutrition Project[56] and PREDICT[26], have successfully used this framework to provide valuable insights into individual responses to nutrients, foods and dietary patterns by integrating data from blood biomarkers, diet, anthropometry, physical activity and the gut microbiome. However, before scaling and implementation, it is crucial to validate these frameworks through rigorous clinical trials. Crucially, findings from these clinical studies should be further evaluated in pragmatic studies conducted under

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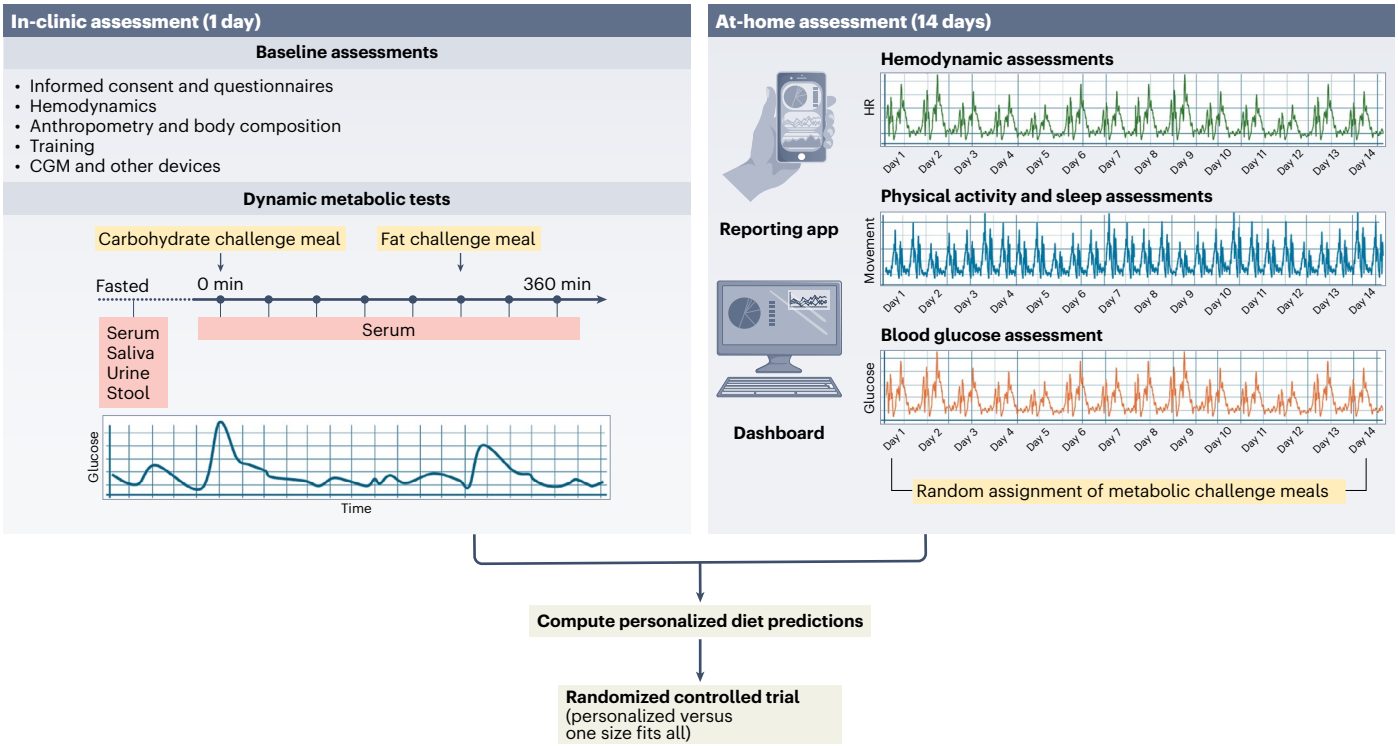

Fig. 2 | Precision nutrition study design framework. Precision nutrition studies typically begin with comprehensive assessments to capture population heterogeneity and identify subgroups that respond differently to dietary interventions. This process involves collecting diverse data types through both in-clinic assessments and at-home assessments. The multidimensional data gathered from these assessments are then integrated and analyzed using advanced machine learning algorithms to predict individualized dietary responses. These predictive models aim to identify beneficial foods or meals tailored to each individual's unique metabolic and phenotypic profile. These predictive frameworks need to be rigorously evaluated through randomized controlled trials to ensure the effectiveness and generalizability of personalized dietary recommendations. In these trials, personalized nutrition guidance is compared against conventional 'one size fits all' dietary approaches to assess the impact on health outcomes. Validating these frameworks through randomized controlled trials is crucial before scaling and broad implementation of precision nutrition strategies. HR, heart rate.

real-world conditions to ensure the feasibility of delivering sustained, long-term health benefits (Fig. 2).

A major limitation in the field is that most precision nutrition studies are short-term investigations, typically lasting only a few weeks or months. Furthermore, there is considerable heterogeneity in study designs, methodologies and results reporting, complicating the synthesis of findings. Bridging the gap between short-term research and long-term clinical effectiveness requires studies to incorporate more extended follow-up periods and standardized protocols for clinical assessments and results reporting to enhance the generalizability of results.

Two clinical trials have attempted to examine the long-term benefits of personalized dietary advice over general dietary advice in real-life conditions[57,58]. One study, involving 225 adults with impaired fasting glucose, compared a personalized, algorithm-derived postprandial diet to a MedDiet for 6 months with an additional 6 months of follow-up[57]. Although the personalized diet group showed slightly greater improvements in glycemic measures (mean hemoglobin A1c change at 6 months: −0.16% versus −0.08%, with between-group differences ranging from −0.02% to −0.14%), the effect size was modest, and the lower carbohydrate content of the personalized diet may have independently contributed to the observed benefits. Another trial randomized 347 participants to receive either a personalized dietary program or general dietary advice in an 18-week app-based program[58]. The personalized group saw statistically significant reductions in triglycerides (one of the primary outcomes) and many secondary outcomes, including body weight, waist circumference and hemoglobin A1c levels, but not low-density lipoprotein cholesterol (one of the two prespecified primary outcomes). However, a key limitation was the greater intensity of the personalized intervention delivery, which involved more frequent contact with study staff, potentially skewing the results in favor of the personalized approach[59].

Despite the varied approaches in precision nutrition clinical trials, a common feature is the development of predictive algorithms for detrimental glycemic responses to certain foods or diets, based on continuous glucose monitors (CGMs). These algorithms integrate multiple data sources and have excellent correlation with observed responses. However, their current reliance on data from short-term measurements limits their effectiveness, as dietary requirements and metabolic responses are dynamic and influenced by factors such as weight changes, physical activity, metabolic status and environmental conditions[52]. To enhance effectiveness and real-world translation, predictive models must adapt over time. Furthermore, there is skepticism about the real-world applicability of AI-driven dietary recommendations, particularly for complex phenotypes such as food choices[60]. To overcome this, future systems should incorporate frequent assessments of psychosocial factors, dynamically adjusting recommendations on the basis of these inputs.

Increasing precision and accuracy in nutrition research

Maximizing the potential of precision nutrition necessitates addressing the long-standing limitations of nutrition research in free-living settings. Key among these limitations is how diet is assessed. Traditional dietary assessment methods, such as food-frequency questionnaires, 24-hour recalls and diet diaries, are designed and validated for specific timeframes (for example, habitual diet over the past year or the past 24 h), which may lack the specificity needed by many precision nutrition

tools that rely on inputs of acute dietary exposures[61]. Because misreporting is often correlated with a person's body weight, underpinned by stigma and other complex cognitive and behavioral factors[62], associations of dietary intake with obesity and related complications are vulnerable to bias.

Dietary biomarkers offer a useful complementary approach to self-reported methods by providing objective dietary intake estimates[63], although currently validated biomarkers are insufficient to cover all relevant nutrients, foods or dietary patterns. High-throughput metabolomic profiling has emerged as a powerful approach to identifying biomarkers for various dietary exposures. A randomized cross-over trial mapped 19 urinary metabolites to four distinct dietary patterns, which were subsequently used to test associations of diet with disease traits[64]. The findings were replicated in independent cohorts[65], suggesting their potential as reliable indicators of dietary patterns. Similarly, a metabolic signature associated with self-reported adherence to the MedDiet in the PREDIMED trial was associated with future cardiovascular events in separate US cohorts[66]. In another study, a lipid metabolic signature that reflects dietary replacement of saturated fats with plant-based monounsaturated fats and PUFAs was associated with reduced risk of cardiovascular complications and helped identify participants who particularly benefited from a MedDiet[67].

Despite their potential, widespread clinical and public health implementation of dietary biomarkers faces substantial challenges. In many cases, especially in large-scale observational studies, the identification of dietary biomarkers is prone to confounding and error owing to individual differences in clinical, behavioral and genetic variability[68]. For example, caffeine is a robust biomarker of coffee and tea intake, but genetic variation in *CYP1A2* influences caffeine metabolism rates[69]. While some dietary biomarkers reflect acute intake, circulating metabolites are also affected by long-term adherence to dietary patterns, making it challenging to untangle whether the metabolites are the cause or consequence of specific dietary exposures. Furthermore, biomarkers often reflect the consumption of food groups rather than specific foods, and biomarkers for key nutrients, such as carbohydrate and dietary fiber intake, are yet lacking or might even not exist, limiting their usefulness for developing tailored recommendations[68]. A comprehensive roadmap for improving the use of food intake biomarkers in dietary assessment has been proposed[63]. Strategies include using diverse biological samples and collection time points, distinguishing between food groups and considering the effects of food processing methods. Standardized sampling and biospecimen storage conditions are also essential for the effective use of food intake biomarkers.

A promising approach to improving the accuracy of dietary assessment involves integrating multiple methodologies, such as image-based food-logging apps and wearable devices, alongside advanced analytical tools. In this context, a transformer-based computational model trained on >10 million CGM measurements from 10,812 adults, combined with dietary data collected by a mobile app in real-world settings, has been shown to robustly infer dietary intake on the basis of observed glucose patterns and vice versa[70]. The generalizability of this approach has been validated across 19 external cohorts, encompassing diverse ethnicities, age groups and metabolic conditions and different CGM brands[70]. The integration of CGM and diet data with AI-driven models could potentially represent a major advancement in dietary assessment. Future efforts should focus on expanding multimodal data collection, refining AI-based food tracking and incorporating additional metabolic biomarkers to optimize precision nutrition strategies further.

Limited reproducibility of research findings, due to variations in study design, dietary exposures and analytical methods, is a persistent challenge in nutrition research[71]. Often, the inconsistencies in findings across studies can be attributed to different contexts of food intake and analytic approaches[72]. For example, replacing refined carbohydrates with similar amounts of saturated versus unsaturated fats has different implications for cardiovascular disease risk[73]. Other discrepancies can be related to study design, in which results from small clinical interventions examining the effects of diet on intermediate risk factors are synthesized with results of incident disease outcomes reported in large-scale epidemiological studies[74]. As in other scientific disciplines[75], evidence from nutrition research should follow a systematic progression from efficacy and proof-of-concept studies to real-world effectiveness studies. Proof-of-concept studies are critical for generating evidence through an improved understanding of the mechanisms through which diet causally affects health. This is particularly relevant in current precision nutrition studies, in which predictive algorithms often lack a strong mechanistic foundation. Developing a comprehensive framework that combines the power of algorithms with underlying biological mechanisms is critical not only to reveal more effective diets but also to bridge the gap between scientific discovery and translation[76].

An innovative approach for elucidating the molecular mechanisms underlying differential nutritional response is through recall-by-genotype studies. This design involves enrolling participants with juxtaposed genetic characteristics that are hypothesized to underpin the differential metabolic effects of diet. The design is highly efficient, allowing deeper phenotyping within a study cohort than is typically feasible in standard trials[77]. The *PPARG* Pro12Ala missense variant, for instance, is the most extensively investigated genotype in these studies[78]. The *PPARG* gene encodes a nuclear receptor that binds long-chain PUFAs and other ligands, which have key roles in metabolic regulation. Another recall-by-genotype study focused on individuals with heterozygous loss-of-function mutations in the melanocortin 4 receptor gene (*MC4R*), a critical regulator of appetite and body weight[79]. Compared to lean and weight-matched controls, individuals with *MC4R* deficiency displayed a markedly higher preference for high-fat foods but a lower preference for high-sucrose options[80].

Enhancing precision and accuracy in nutrition research requires a strong commitment to diversity. Historically, large-scale nutrition clinical trials have predominantly enrolled participants of non-Hispanic white backgrounds from Europe and the USA, often with middle to high socioeconomic status[81]. As a result, dietary recommendations derived from these studies may not be broadly applicable, potentially exacerbating nutritional and health disparities. To mitigate this risk, precision nutrition research must prioritize diversity from the outset, ensuring that dietary guidance is grounded in evidence generated from the appropriate target populations. Early engagement of key stakeholders, including individuals for whom an intervention is intended, community groups, policy-makers, healthcare providers and research funding bodies, is essential to aligning research with real-world challenges and facilitating its practical application.

Precision nutrition in the real world

Understanding the temporal patterning of behavioral factors, their contextual determinants and their effects on intermediate health outcomes is important when developing strategies to promote health and prevent or manage cardiometabolic diseases. Figure 3 illustrates how precision nutrition might be leveraged in real-world conditions, whereby multimodal information about an individual at a given time is leveraged to generate specific nutritional and behavioral guidance, with personalized delivery strategies. By adapting these interventions to specific life stages and individual needs, precision nutrition aims to empower individuals to make more informed decisions about their diet and prevent health deterioration.

Digital technologies, including mobile apps and web-based platforms, have emerged as powerful tools for capturing diet and behavior and are a critical element in precision nutrition. These technologies offer several potential advantages over traditional food-logging methods or face-to-face interventions, including remote accessibility, scalability, long-term tracking, real-time feedback or integration

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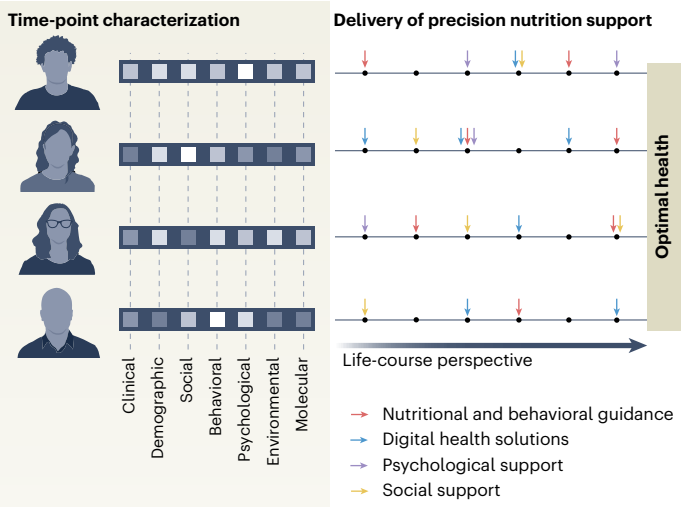

Fig. 3 | Paths toward optimal health through precision nutrition. Each individual presents a unique 'barcode-like' profile at any given time, reflecting the combination of clinical, demographic, social, behavioral, psychological, environmental and molecular influences at play at that point in their life (left). Precision nutrition leverages this information to deliver tailored interventions, combining specific nutritional and behavioral guidance with personalized delivery strategies (right). These delivery strategies encompass psychological support, digital health solutions and social support.

with social media and health data platforms[82,83]. A systematic review and meta-analysis comparing the efficacy of mobile dietary apps on nutritional outcomes showed a significantly greater decrease in energy intake when an app was used in the context of self-monitoring than with no app usage[84]. Another systematic review assessing the efficacy of smartphone apps in promoting weight loss found that individuals using dietary self-monitoring apps experienced greater weight loss than the control group, with a modest average weight loss of 1 versus 0.4 kg, after a median follow-up of 8 weeks[85].

Despite these potential benefits, there are critical knowledge gaps and challenges that need to be addressed in the field of digital health applications for dietary advice. First, many nutrition apps fail to consider the unique needs of specific communities, neglecting factors such as language availability, digital literacy and culture-specific health literacy. Addressing this challenge requires prioritizing digital literacy within target populations and clearly defining responsibility for effective and fair implementation[86]. Although evidence supporting the efficacy of culturally adapted digital interventions remains limited, the MINISTOP app in Sweden—developed to help prevent obesity in children—provides a promising model[87,88]. Adapted to Somali- and Arabic-speaking immigrant families, MINISTOP has managed to recruit a study population in which 24% of the children had two foreign-born parents[87], a population notoriously difficult to reach through traditional clinical studies. The app has been linked to reduced sugary drink consumption among children and increased parental support for a healthy lifestyle[88]. MINISTOP is now being implemented in Swedish child healthcare. Similar mobile health interventions are currently being developed and evaluated among pregnant Indigenous women in Australia[89] and underserved adult populations with uncontrolled blood pressure in the USA[90].

Real-world data are essential for understanding how individuals interact with and respond to food cues and diets in everyday settings. Unlike the controlled conditions of clinical trials and the participation of highly motivated participants, real-world data capture the complexities of actual food choices, reflecting the diverse factors outlined in the socio-ecological model, such as individual preferences, social norms, local food environments and health policies. The ChooseWell program in the USA exemplified how personalized approaches, informed by insights from behavioral economics, can leverage workplace environments to influence food choices[91]. Through strategies such as traffic-light labeling and product placement, the program demonstrated improved effectiveness, sustainability and scalability of health promotion efforts in the workplace[91,92]. In addition, outcome data from the ChooseWell program provided insights into the subgroups of individuals more likely to benefit from population-wide strategies by showing that those with a higher genetic predisposition toward carbohydrate preference were more likely to buy healthier products[46]. These findings illustrate how a combined population health and individualized approach might work by identifying those who may need additional support for making more healthy food purchases.

Looking forward

Precision nutrition faces several key challenges that also highlight crucial areas for future research. Developing more robust predictive models is paramount, requiring sophisticated integration of multiomics data with behavioral, social and environmental factors to generate more accurate dietary recommendations. This necessitates further research into the psychological and social determinants of dietary behavior, informing the development of tailored interventions and digital platforms that provide personalized, adaptive support, accounting for individual needs and evolving life circumstances[93]. Advanced analytical techniques are needed to extract meaningful insights from complex and often noisy real-world data, including information gleaned from wearable devices such as CGMs, mobility data, food purchase records and social media activity. Addressing ethical considerations related to data privacy, security and potential discrimination is essential, demanding the establishment of clear guidelines for data collection, storage and use, especially when sensitive health information is held by companies that may not endure in the long term. Furthermore, the cost-effectiveness of precision nutrition interventions must be thoroughly evaluated before widespread implementation. Finally, integrating sustainability principles into precision nutrition approaches is critical. This requires developing standardized metrics for assessing the environmental impact of dietary recommendations and exploring policy interventions, such as subsidies or incentives, that support the adoption of both healthy and sustainable dietary choices. Research should also investigate how precision nutrition can optimize food systems, from production and distribution to consumption, benefiting both human health and planetary sustainability[94].

Several precision nutrition initiatives are underway to tackle the complexities of personalizing nutrition at scale. For instance, the National Institutes of Health leads efforts to revolutionize nutrition science through the Nutrition for Precision Health cohort, part of the larger 'All of Us' research program (https://commonfund.nih.gov/nutritionforprecisionhealth). The study is structured into three modules. Module 1 involves approximately 8,000 participants to assess self-selected dietary patterns, nutritional status and physiological responses to a liquid mixed-meal challenge. Modules 2 and 3 focus on controlled dietary intervention trials, with module 2 conducted in community settings and module 3 within domiciled settings with regulated eating, exercise and sleep routines. By prioritizing the inclusion of historically underrepresented populations and promoting sustained participant engagement, this study aims to address diversity and social equity in precision nutrition, generating knowledge applicable to specific subgroups and circumstances. Furthermore, the study uses complementary dietary assessment methods, including food-frequency questionnaires, 24-hour dietary recalls and smart glasses to improve the accuracy of dietary assessments.

In Europe, the Precision Nutrition Challenge investigates the causal relationships among diet, the microbiome and glycans, focusing on personal signatures that influence disease outcomes rather than just

factors associated with intermediate risk factors (https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/horizon-eic-2023-pathfinderchallenges-01-03). The challenge also integrates food production and technologies, working to identify suitable food ingredients, food components and technological processes relevant to precision nutrition applications. In Denmark, the Danish Precision Health Initiative is currently enrolling participants to investigate how dietary, behavioral and environmental factors interact with biology in the transition from health to disease, using deep phenotypic assessments in real-world settings (https://delphi.ku.dk). This longitudinal study, with 10,000 participants, emphasizes precision and accuracy in measurements and consists of a comprehensive baseline assessment and a 14-day continuous health monitoring period, including the use of wearable devices and a mobile phone app to track activity, vital signs, sleep, food intake, blood pressure and glucose levels. In Sweden, the SCAPIS2-Home study aims to dissect the determinants of interpersonal metabolic responses to whole and refined grains as part of high- or low-carbohydrate and high- or low-fat meals and repeated dietary challenges administered at home. The study, which is still recruiting participants and is expected to be completed in 2027, further aims to link interindividual variation in postprandial metabolic responses to atherosclerosis, liver fat, prediabetes and long-term disease outcomes in 4,300 individuals (https://www.scapis.org).

In low- and middle-income countries (LMICs), precision nutrition is emerging as a potential strategy to combat malnutrition and improve health by enhancing the accuracy of data collection and analysis. The Swiss Food & Nutrition Valley (a public–private partnership that also includes stakeholders such as academic institutions) has established the Precision Nutrition for LMICs Working Group, dedicated to advancing nutrition equity in these regions[95]. Initial efforts included an expert opinion survey among nutrition leaders who live or work in an LMIC, followed by a workshop to determine essential prerequisites, including funding, resources, awareness, training and culturally relevant tools, for successful precision nutrition implementation. These ongoing initiatives represent critical steps in generating the evidence base to sustain precision nutrition strategies, incorporating psychosocial factors and real-world dietary behaviors. They also emphasize inclusivity, precision and long-term engagement, which are vital for addressing the diverse needs of global populations.

The precision nutrition field is rapidly advancing, drawing considerable attention and investment. A number of public–private partnerships between academia and small to medium-sized enterprises[96,97] have commercial products available and are also engaging in further research with extensive data collection and sophisticated machine learning algorithms to uncover individual metabolic responses to various foods. While the commercialization of precision nutrition reflects a growing societal interest in more effective, personalized health management strategies, it is important to recognize that the field remains in a nascent stage. Many precision nutrition companies make claims supported only partially by scientific evidence, and their products are often inaccessible to those who may need them most. For precision nutrition to thrive, it requires a strong commitment and collaboration that prioritizes long-term impact over short-term profits and involves a wide range of stakeholders working at the intersection between individual and population health.

Conclusions

While the long-term benefits of precision nutrition are still unknown, its potential impact on the implementation of dietary interventions and their efficacy on health outcomes is increasingly recognized by researchers and stakeholders. Advances in molecular biology and '-omics' technologies, wearable and digital technologies, and AI, as well as a deeper understanding of human behavior, societal contexts and health disparities in nutrition and cardiometabolic diseases, are accelerating progress in this field. Robust research approaches in precision nutrition contribute to the growing evidence base for the development of valid and scalable tailored dietary recommendations rooted in individual needs and responses. Enabled by sensors, rapid and affordable molecular analysis of accessible samples, and digital technology, precision nutrition can enhance real-time monitoring and deliver personalized feedback, ultimately empowering individuals to make sustainable dietary choices that adapt to their evolving food environments, social contexts and life circumstances.

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Author contributions

M.G.-F. and J.M. take responsibility for the integrity and accuracy of the work. M.G.-F., C.W., M.P., P.W.F., R. Landberg, J.L.S. and J.M. designed the research. M.G.-F., P.W.F., J.L.S. and J.M. wrote the first draft of the manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors approved the final version of the manuscript. The corresponding authors attest that all listed authors meet the authorship criteria and that no others meeting the criteria have been omitted.

Competing interests

M.G.-F. is the principal investigator of a grant funded by the International Nut Council (INC). R. Landberg is the founder of the Nordic Rye Forum—a platform for collaboration on rye and health between universities, institutes and industry. R. Landberg is a member of the scientific panel of the Lantmännen Research Foundation and Arla Food and Health. R. Landberg is a recipient of research grants from the Lantmännen Research Foundation, Lantmännen, Barilla, Oatly and Arla for specific projects. P.W.F. is a member of the scientific advisory board of and has received consulting honoraria from Zoe Ltd. He was a senior investigator in the PREDICT1 trial. J.L.S. has received consulting fees from the World Health Organization and the University of Bergen. This work was done outside these roles, and the opinions expressed herein do not necessarily reflect those of the World Health Organization or the University of Bergen. J.L.S. is the founder of BabelFisk, which provides consulting services in health sciences and public and global health; she was also Deputy Editor of *Nature Medicine* until December 2023, and all work on the current Review was done after she left employment at Springer Nature.

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