Perspective: Guiding Principles for the Implementation of Personalized Nutrition Approaches That Benefit Health and Function

Sean H Adams,[1] Joshua C Anthony,[2] Ricardo Carvajal,[3] Lee Chae,[4] Chor San H Khoo,[5] Marie E Latulippe,[5] Nathan V Matusheski,[6] Holly L McClung,[7] Mary Rozga,[8] Christopher H Schmid,[9] Suzan Wopereis,[10] and William Yan[11]

[1]Arkansas Children's Nutrition Center and Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [2]Campbell's Soup Company, Camden, NJ, USA; [3]Hyman, Phelps & McNamara, PC, Washington, DC, USA; [4]Brightseed, San Francisco, CA, USA; [5]International Life Sciences Institute North America, Washington, DC, USA; [6]DSM Nutritional Products, Parsippany, NJ, USA; [7]US Army Research Institute of Environmental Medicine, Natick, MA, USA; [8]Academy of Nutrition and Dietetics, Chicago, IL, USA; [9]Department of Biostatistics, Brown University, Providence, RI, USA; [10]Research Group Microbiology & Systems Biology, TNO, Zeist, Netherlands; and [11]Health Canada, Toronto, Ontario, Canada

ABSTRACT

Personalized nutrition (PN) approaches have been shown to help drive behavior change and positively influence health outcomes. This has led to an increase in the development of commercially available PN programs, which utilize various forms of individual-level information to provide services and products for consumers. The lack of a well-accepted definition of PN or an established set of guiding principles for the implementation of PN creates barriers for establishing credibility and efficacy. To address these points, the North American Branch of the International Life Sciences Institute convened a multidisciplinary panel. In this article, a definition for PN is proposed: "Personalized nutrition uses individual-specific information, founded in evidence-based science, to promote dietary behavior change that may result in measurable health benefits." In addition, 10 guiding principles for PN approaches are proposed: *1*) define potential users and beneficiaries; *2*) use validated diagnostic methods and measures; *3*) maintain data quality and relevance; *4*) derive data-driven recommendations from validated models and algorithms; *5*) design PN studies around validated individual health or function needs and outcomes; *6*) provide rigorous scientific evidence for an effect on health or function; *7*) deliver user-friendly tools; *8*) for healthy individuals, align with population-based recommendations; *9*) communicate transparently about potential effects; and *10*) protect individual data privacy and act responsibly. These principles are intended to establish a basis for responsible approaches to the evidence-based research and practice of PN and serve as an invitation for further public dialog. Several challenges were identified for PN to continue gaining acceptance, including defining the health–disease continuum, identification of biomarkers, changing regulatory landscapes, accessibility, and measuring success. Although PN approaches hold promise for public health in the future, further research is needed on the accuracy of dietary intake measurement, utilization and standardization of systems approaches, and application and communication of evidence. *Adv Nutr* 2020;11:25–34.

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Introduction

> We do not know enough about nutrition to identify an "ideal diet" for each individual.
>
> —Dietary Guidelines for Americans reported research gap, 1980 and 1985

Since 1980, the Dietary Guidelines for Americans (DGAs) have been the foundation of nutrition recommendations for the generally healthy population in the United States (1). Although some at-risk subgroups are addressed (e.g., individuals with hypertension), the DGAs represent population-level recommendations and are not intended to provide ideal nutrition guidance for each individual. Recent evidence suggests that personalized approaches may result in quantifiable improvements in dietary behaviors (2) and health outcomes (3) compared with conventional approaches. In 2017, the American Society for Nutrition (4) prioritized the need for more research to advance understanding regarding the role of individual variability in developing

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personalized approaches that can better achieve health outcome goals.

Some aspects of personalized nutrition (PN) are already regularly assessed and utilized in the nutrition field, such as advice based on dietary intake, lifestyle, phenotype, and personal goals. However, a recent surge in technological development across various disciplines has increased the ability to collect, store, and analyze more in-depth individual-level assessment data and, therefore, to deliver individualized information, products, and advice on nutritional needs, food, and diet. Many of the assessment tools used to develop personalized advice have focused on ≥1 individual characteristics such as genetic information, disease status, dietary intake, nutrient status, anthropometrics, physiological state, food preferences, lifestyle, and sensory preference. A number of these assessment tools for personalization are becoming more widely accessible, whereas others involve emerging technologies that are not yet commonplace or validated for clinical relevance. Some examples of personalized tools and information are presented in **Box 1**. An important aspect of PN approaches is the integration of several of these characteristics to deliver individualized nutritional advice, products, or services and drive behavior change. Concurrently, progress has occurred in product innovation, enabling the accessibility of more personalized foods, supplements, or diets customized to nutritional needs, taste, and lifestyle preferences (e.g., products for diets that are lactose free, vegan, gluten free, or low in fat or sodium).

BOX 1.
The spectrum of PN: examples of individual-level information and tools that can inform PN approaches

Widely accessible tools	Less accessible tools (special populations, motivated consumers)
Demographic information[1] • Age, sex, life-stage information *Phenotype-based information* • Anthropometrics • Standard clinical biomarkers (e.g., cholesterol, blood glucose, blood pressure) • Biomarkers of nutrient status *Lifestyle-based information and tools* • Personal goals • Physical activity/environment • Preferences, including cultural • Smartphone applications for diet tracking, planning, and behavior change • Wearable devices • Dietary intake assessments	*Gene- and omics-based information and tools* • Genetic testing and counseling • "Omics" testing (transcriptomics, proteomics, metabolomics, microbiome and xenometabolome analyses) *Lifestyle-based information and tools* • Energy intake sensors • Prepared or portioned meal delivery • Fitness testing and exercise training • Metabolic challenge testing (oral-glucose-tolerance tests, mixed macronutrient challenge testing) • Challenge testing for other systems (e.g., immune system, gut microbiota)

[1]This list is not intended to be comprehensive and provides examples only. Accessibility refers to the cost and convenience of obtaining the information or using the tools.

Guiding principles for PN approaches are needed

The lack of a clear definition of PN and of established guardrails for its scientific substantiation creates barriers for examining its credibility to help individuals achieve and sustain their dietary and health goals. To address this gap, the North American Branch of the International Life Sciences Institute (ILSI North America) convened a multidisciplinary panel of scientists in Washington, DC, in June 2018. This panel included individuals from government, industry, nutrition practitioner organizations, research institutes and academia, and regulatory institutions with expertise in computational biology, systems biology, integrative physiology,

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Address correspondence to MEL (e-mail: mlatulippe@ilsi.org).
Abbreviations used: DGAs, Dietary Guidelines for Americans; ILSI North America, North American Branch of the International Life Sciences Institute; PN, personalized nutrition; SES, socioeconomic status.

nutrition assessment and practice, product development, regulatory science, law, nutrigenomics, biostatistics, and other disciplines. The meeting objectives were to *1*) define PN, *2*) identify guiding principles related to PN approaches, *3*) propose steps to overcome barriers to implementation, and *4*) identify research gaps and future research needs.

This Perspective article outlines key outcomes of this discussion and stimulates thinking around what is needed to ensure that PN approaches are designed in such a way that their full potential for health benefit can be reached. For the purposes of this article, guiding principles are considered to be generally agreed-upon fundamental requirements among experts in the field.

Definition of PN

In order to propose guiding principles, it is important to first clarify the scope of PN. The lack of an existing authoritative or universal definition for "personalized nutrition" in the context of rapid innovation has led to confusion about what PN means, from the perspectives of both technology for information gathering and technology for development of foods, ingredients, and dietary recommendations that utilize this information. This is evidenced by the wide variety of product offerings that address PN in the marketplace. The phrase "personalized nutrition" is often used as a catch-all for these new opportunities but other terms, including "precision nutrition," are also used, further contributing to the confusion (5). In parallel with an expanding marketplace, not all of which may be grounded in science, skepticism about the benefits of PN and other individualized approaches to health has surfaced, particularly considering the challenges with causal inference and the complexity of physiological networks in health and disease management (6). Limited evidence directly demonstrates the long-term efficacy of PN approaches compared with population-based advice.

Because confusion partially stems from the many terms related to individualization that are used interchangeably by different groups and for different purposes, it is important to begin with establishing a definition for PN. Ordovas et al. (6) specifically refer to information that can be used to develop targeted advice, products, or services. "Precision nutrition" is more specific to disease intervention (7), and "customized nutrition" has been used in reference to targeting accessibility/delivery options and food preferences. Verma et al. (8) broadened definitions to include dietary habits and physical activity. Regardless of the terms used, all have common core elements: tailoring nutritional recommendations to account for individual variation related to phenotype, genotype, lifestyle behavior (diet, activity, etc.), goals, and preferences. The ILSI North America 2018 panel refined the work of a previous 2017 ILSI North America expert group organized exclusively to develop a pragmatic working definition of PN. The 2018 panel proposes the following definition language:

> Personalized nutrition uses individual-specific information, founded in evidence-based science, to promote dietary behavior change that may result in measurable health benefits.

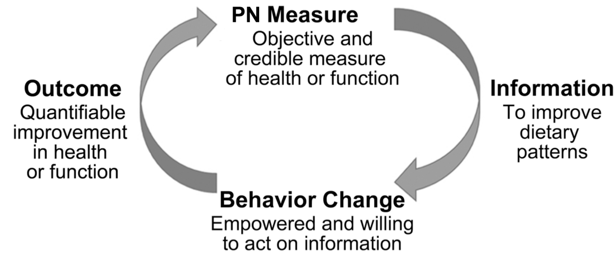

FIGURE 1 Model of PN. An objective and credible (science-based) assessment measure should provide the user with information that can help to improve dietary and lifestyle patterns. The information provided should drive a change in dietary patterns or intake of specific food components, preferentially in conjunction with other lifestyle factors. This change in dietary behavior may result in quantifiable and desirable health outcomes and/or improved function and/or lower disease risk. As health or function improves, repeated assessments are necessary to continue the process and further optimize these factors. For PN to be successful, there needs to be a clear demonstration of long-term health or functional benefit. Regular health, function, and dietary assessments may be necessary to monitor and enable sustained behavior change. PN, personalized nutrition.

The components of this definition are described below and reflected in **Figure 1**:

- *Individual-specific information:* This includes any information that is more specific than population level, such as behaviors, diet history, socioenvironmental factors, phenotype, and genetic and other forms of individualized testing (e.g., blood biomarkers).
- *Founded in evidence-based science:* Supporting scientific evidence is considered adequate for the specified tool if the data, and methods of its collection and analysis, are generally accepted by experts and adhere to well-established principles of scientific substantiation, including rigor and reproducibility. Specifics of the evidence required may vary depending upon the potential benefits and risks of the tools in question. Recently, Grimaldi et al. (9) proposed guidelines for substantiating the effects of genotype-based dietary advice. Leveraging such evidence-grading frameworks will be useful in both the assessment of PN approaches and their communication and implementation.
- *To promote behavior change:* An essential step in PN is that the information provided promotes a change in individual dietary behaviors that may result in health or function improvement [see, e.g., Ory et al. (10) and Wood and Neal (11)]. An important element to consider in behavior change is the sustainability, or longer-term adherence to diet and lifestyle patterns [see, e.g., Foreyt and Goodrick (12)], and the resulting health effects.

- *Measurable health benefits:* Benefits achieved by PN must be measured using validated methods and metrics. Examples of measurable validated measures of health include change in a specific nutrient marker (e.g., improving micronutrient status), weight and body composition (e.g., improving weight status or bone mineral density), or measures of blood glucose control (e.g., improved fasting glucose or hemoglobin A1c). Health has been redefined as the ability of the human body to adapt and self-manage in the face of social, physical, and emotional challenges (13). In other words, health can be considered as the ability to cope with daily or prolonged stressors. The ability to adapt to continuously changing conditions has been termed "phenotypic flexibility" (14) and quantification of the biological response may offer a sensitive way to continuously monitor individual changes in health status (15). This component of the PN definition also captures "function" in terms of phenotype changes that improve quality of life or individual performance (e.g., cognition, mobility, or other outcomes), outside of the classic definition of "health."

Proposed Guiding Principles for the Design and Implementation of PN Approaches

The expert group designed guiding principles for PN approaches considering any individual, authority, or company that is developing, applying, or evaluating options, as well as elements foundational to the scientific substantiation of health benefits. These include, for example, biological plausibility, reproducibility, and validity of data collection, methods, measures, and analysis. Unique to personalization is the interplay of these research elements with rapid advances in technology that include advanced modeling and machine learning. Appropriate application of evidence-based regulatory science and law as well as data management and privacy were also considered as elements required for successful and protective societal implementation. Taken together, these principles help to establish a basis for responsible research approaches and evidence-based practice of PN, with an aim to understand the potential for science-based PN approaches to affect health and function in individuals and the population at large.

The following are a series of proposed guiding principles intended to serve as a starting point for further development and refinement (**Box 2**). Although some of these principles are certainly being used today in clinics and private industry, the guidance presented herein represents a broadly applicable and comprehensive set of principles that are relevant to all PN approaches.

Define potential users and beneficiaries

Before implementation, evaluate the needs, motivation, and concerns of potential users to determine if PN approaches are appropriate. Current users of PN approaches are often confined to a small percentage of motivated consumers, typically of higher socioeconomic status (SES) (16–18). The definition proposed here is intentionally broad to be inclusive of the various population segments interested in applying individualized dietary approaches/interventions to improve health and function and prevent disease. In fact, if PN is effective in sustaining changes in health, then it is desirable that these tools are accessible and affordable to most people. Evidence suggests that rates of death from noncommunicable diseases are 65% higher globally (19), and the life span is significantly shorter (20), in population groups or countries of lower income and education levels. Achieving sustainable improvements in health using PN at a large scale will require affordable and accessible approaches.

BOX 2.
Ten proposed guiding principles for the design and implementation of PN approaches

1. Define potential users and beneficiaries.
2. Use validated diagnostic methods and measures.
3. Maintain data quality and relevance.
4. Derive data-driven recommendations from validated models and algorithms.
5. Design PN studies around validated individual health or function needs and outcomes.
6. Provide rigorous scientific evidence for an effect on health or function.
7. Deliver user-friendly tools.
8. For healthy individuals, align with population-based recommendations.
9. Communicate transparently about potential effects.
10. Protect individual data privacy and act responsibly.

Use validated diagnostic methods and measures

The diagnostic methods and measurement tools employed to develop supporting evidence should be validated through procedures that are generally accepted by the scientific community as reliable and appropriate. Methods should follow established best practices for analytical measurement [e.g., Brenna et al. (21)], and new measurements should be either validated against reference methods or otherwise established as relevant to a specific health or function benefit.

Maintain data quality and relevance

Decisions about individual data inclusion should consider data integrity and transparency. The confidence in any dietary recommendation is limited by the accuracy and validity of the evidence upon which it is based. With respect to individual data points, decisions for inclusion and exclusion may be more challenging. Ideally, data are considered valid if they meet some quality standard (e.g., complete data collected in a manner free from error and bias, and with validation) or a predefined validity threshold for the measure. Data quality may differ for subjective compared with objective data types, but data quality parameters should still be established a priori as the foundation for inclusion decisions. Information upon which PN approaches are based should consider sources of intra- and interindividual variability. Decisions concerning data quality and relevance for the individual should be transparent and understandable, whether being reviewed by a scientist, health-care professional, or end-user.

Derive data-driven recommendations from validated models and algorithms

Model- and algorithm-based PN advice should be validated to demonstrate acceptable predictive performance. Predictive models of nutrition-related outcomes can be generated using large-scale biological and phenotypic data sets representing individuals across populations (22). These models can be helpful in developing personalized recommendations, based on the predicted outcome for that individual. Models should be validated with a relevant external population to demonstrate an acceptable quantified performance level. For example, in Zeevi et al. (23), a predictive multifactorial model of postprandial blood glucose response to meals was validated on an external data set to demonstrate that predictive performance was consistent with performance in the study, and a small clinical trial was undertaken to assess its performance. Any personalized approach generated from models or algorithms should have a biologically plausible explanation for the intended effect and should ideally be biologically validated. Collections of PN data over time could be used to refine individual advice or to predict health outcomes with artificial intelligence and Bayesian networks. However, risks of sampling and selection bias in such an approach should be carefully assessed, and health-care professionals or others who implement data-driven PN models should be trained in their interpretation.

Design PN studies around validated individual health or function needs and outcomes

Research investigating the efficacy of a PN approach should also include outcomes validated at the individual level. Essential to understanding the potential for personalized approaches to benefit health is designing studies that also allow for detection of individual behavior, health, or function. Studies that account or control for variability inherent to the biological system (e.g., diurnal variation, sex, gut microbiome, physical fitness and sedentary behaviors, circadian rhythm) have a greater potential to detect effects on an individual level. Studies should be adequately powered to detect the outcome of interest.

An *N*-of-1 trial design can also be used to compare individual changes over time. This is an individualized trial in which participants receive each treatment multiple times, usually in a randomized multi-crossover design (24–26). A CONSORT extension has been developed for *N*-of-1 trials (27). Such an approach allows for the estimation of within-person variability, and meta-analyses of *N*-of-1 trials can provide information on the consistency of effects among a larger population as well as provide better predictions of individual health by using information from the population parameters being estimated. Objective health monitoring over time can also be done on several endpoints simultaneously with tools such as the health space visualization (28). Such a composite measure can look at individual changes across a range of disease and health states over time.

Provide rigorous scientific evidence for an effect on health or function

Statements about an effect of the PN approach should be based on peer-reviewed, published scientific evidence. Ideally, this evidence is analyzed comprehensively in a systematic review. In order to be utilized in clinical or community nutrition practice, PN approaches should demonstrate efficacy in improving nutrition-related health and/or functional outcomes (29), resulting in change that is statistically significant and clinically meaningful. With respect to PN, it is important to note that traditional statistical approaches that pool findings from many individuals to estimate an overall average effect may not capture variations in findings between individuals ("responders" compared with "nonresponders" or phenotypic subgroups), and as a result may yield "null findings" in clinical intervention studies. For example, a weight loss intervention was recently shown to have varying efficacy in 2 identified metabotypes (30). Systematic assessment of the effect of PN approaches should be based on the quality and quantity of studies that report hard outcomes or those known to be associated with hard outcomes. Consideration of biological plausibility and mechanism of action are important criteria.

Deliver user-friendly tools

In alignment with the goal to provide individualized care to a population, tools and approaches should be scaled to the user skill level and degree of understanding. Data capture tools and reporting should consider how the user's education, skill, perception, and experiences affect the data quality and accuracy. The accuracy of test kits, food intake tools, and other measures can only be ensured if they are designed to align with user skill level and if appropriate training and messaging are in place.

As an example, US population expenditures for foods consumed away from home (31) and portion sizes have increased over time (32), suggesting a population shift in food "skill" or lack of portion awareness. Current dietary intake assessment tools (e.g., web- or smartphone-based) rely on self-report of food item portion size to accurately capture and calculate nutrient assessment. Data collected from consumers or subjects that are affected by these shifts are similarly skewed to the current experience. PN providers have a responsibility to instruct users on how to properly use tools and minimize user error, and to develop innovative tools that optimize user-dependent data capture and information delivery. Ideally, providers should also understand how user error could influence results, communicate potential risk to users, and account for how user error may affect recommendations.

For healthy individuals, align with population-based recommendations

Information, advice, or services provided to the generally healthy individual should typically fall within the range of population-based recommendations, such as the DGAs (33). However, because such recommendations are designed to help address gaps for *most* individuals, there is an opportunity for further refinement of recommendations to better meet individual needs while remaining within the broader boundaries of an established evidence-based framework. Any substantial divergence from existing population-level recommendations (e.g., advice that falls outside of recommended ranges) requires significant scientific justification and consistency with accepted standards of clinical practice.

Communicate transparently about potential effects

The PN approach should consider the potential for each piece of individualized information to influence health or deliver a functional benefit. The potential contribution of the PN recommendation to health or function should not be overstated. For example, with some exceptions, the potential of individual genes as the basis of a PN approach to affect health is relatively small (3, 9). Measures should only be included if there is reliable evidence for benefit. Although assigning a quantitative contribution of a marker or model to a health outcome is ideal, this may be misleading on an individual basis. However, relevant communications could be made with respect to population-based studies and known associations of a given marker or model to health outcomes. Communications should be made consistent with applicable regulations. If a measure is being included in a model to help establish an evidence base but does not have a clear link to health or function, this fact should be transparently communicated.

Protect individual data privacy and act responsibly

The approach should incorporate protections for individual data and disclose intentions for data use. As advanced data collection mechanisms become more available and data repositories grow, the predictability of personalized approaches and models can be strengthened. However, protection and use of this individual information is a concern. Security and anonymity of data and protocols to protect information should be transparent to patients/clients of PN approaches with an opportunity for informed consent. A risk-based approach should be taken to identify data privacy risks for the individual. Appropriate actions should be taken to mitigate those risks, including but not limited to adherence to local and international standards (e.g., the European General Data Protection Regulation and ISO 25237 on pseudonymization of health data).

The Future of Privacy Forum (34) is a collaborative of nearly 200 companies that use personal data to some degree. The forum's mission is to develop a policy framework for the collection, protection, sharing, and use of genetic data generated by consumer genetic testing services. Attention to such frameworks will be critical to ensure individual protections as data repositories grow in size and utilization. Also critical to consider are developments in data ownership and "health data cooperatives" that allow for aggregation of health data sets with the aim to learn from the data collected in a responsible way (35).

Challenges

Although PN is gaining more widespread acceptance and implementation, challenges should be recognized and addressed if these emerging approaches are to hold promise for benefiting health.

Defining the health–disease continuum

A significant challenge is defining health and disease risk, particularly on an individualized basis. Health may be considered as a continuum from wellness optimization to functional maintenance to disease risk reduction to disease management. This framework may point to steps in a personalized approach. Measuring functional disruptions occurring earlier in the health–disease pathway can enable intervention before disease develops. Early intervention has the potential to significantly affect health care costs (36). Considering health–disease as a continuum (e.g., overweight–metabolic syndrome, prediabetes–diabetes) allows use of direction and magnitude of change as a marker of benefit. There is no question that nutrition is one piece of a complex set of interactions that determine health or function (the systems approach), such as nutrition interactions with lifestyle, energetics and fitness level, the microbiome, and cognitive health and behavior. Figure 1 considers that a number of factors are integrated or, at minimum, are not ignored in studying or implementing PN approaches that motivate users to adopt appropriate changes in behavior to drive meaningful benefits.

Biomarkers in the health–disease continuum

Because disease outcomes may take years to manifest, evaluating true changes in health over a short period of time is a major challenge not only to PN but to all interventions. For this reason, surrogate markers of disease risk and health status are useful. Examples include short-term (days to weeks) changes in blood lipids, blood pressure, body weight, or fitness level. Moving forward, there are many opportunities to further characterize and integrate outcome measures and models for determining the efficacy of PN.

Health may be characterized by the ability to continuously adapt in varying circumstances where multiple mechanisms of systems flexibility are involved. Additional biomarkers are needed to more fully quantify systems flexibility, opening the door to real lifestyle-related health optimization, self-empowerment, and related PN products and services (37). Characterization of biomarker response will also allow for choosing the most relevant markers, further increasing accessibility of PN platforms by targeting relevant health states or function for the individual. To this end, the development and application of a standardized metabolic stress test, evaluated with multibiomarker panels that act as composite descriptors of physiological processes, has been suggested for health quantification (15).

Approaches from the field of machine learning may enable discovery of new biomarkers of health and their interrogation may help define states along the health–disease continuum. Methods such as feature selection have proven effective in interrogating high-dimensional biological data to identify and develop biomarkers of disease (38). In addition, data fusion techniques are actively being researched to merge diverse data sets and multiomics technologies to increase the ability to detect predictors of specific biological phenomena (39).

Regulatory considerations

In the realm of nutrition, moving from population-based to individual-targeted mechanisms and claims may be novel to many regulators. Regulators will need to consider this new paradigm, while also aligning with the well-accepted population-based guidance currently in place. Regulators and scientific assessment bodies will also need to consider new realms of science for which the evidence is just now emerging (e.g., microbiome-related health and function effects).

In some jurisdictions, existing principles and frameworks can be adapted for regulation of PN approaches, with allowances for the type of product or service, and for claims of intended effect. Thus, regulation may be claims based, product based, and/or service based. The core qualities of existing regulations can be applied to PN to ensure data quality, use of validated biomarkers, and evidence of a link to a health benefit.

In the United States and Canada, a variety of PN products and services are already being marketed, sometimes in combination. These include biomarker analysis, DNA analysis, questionnaires, dietary supplements (a type of food under US law), food delivery, and nutrition counseling. These products and services are subject to regulation under several federal and state laws that govern product formulation, manufacture, and promotion, as well as licensing of health-care providers and protection of health-related information.

Depending on the regulatory categorization of a product, it might require premarket review and approval or might be subject only to postmarket enforcement. However, even products that are subject only to postmarket enforcement cannot be marketed with any claim that is false or misleading. Regulators should enforce existing law as it applies to PN products and services. Because multiple regulatory challenges currently exist within the field of PN, collaboration with industry and health stakeholders will be necessary to develop a regulatory framework that enables PN products to access markets while achieving health protection objectives.

Affordability, acceptance, and accessibility of PN approaches in the marketplace

As commonly conceived, many products and services marketed under the PN umbrella are at a price point outside of what the majority of the population can afford. In addition, although the goal of many PN methods is to optimize health or function, individuals who are of low SES face significant barriers even to basic health care. Yet it may be argued that those least able to afford PN may benefit the most, because disease burden prevalence tends to inversely track with income level (40). Furthermore, there may be a need to tailor communication or to establish partnerships (e.g., with trained health-care professionals) to support information provision and behavior change across the entire spectrum of the population that differs in education, background, access, and SES. There may be external barriers for key populations (e.g., living in a "food desert" or in areas that lack a safe outside space for exercise) or cultural barriers to sharing medical information (41).

Measuring success

Most success measures have been defined in the context of health policy targeted to populations. In the case of PN, success will be defined, in part, at the individual level. In some cases, self-defined needs may not align with population-based needs. For example, consumer desires are often very "in the moment" (e.g., a perception of "more energy now" or "better memory"). These are legitimate targets but may not help address longer-term population health opportunities, such as a reduction in rates of cardiovascular disease.

The criteria for measuring success in a targeted PN intervention, such as duration and magnitude of specific effects and convergence with population-based guidance, may require further development. However, one clear measure of success is the rate of long-term compliance with an appropriate intervention. This is where personal intervention strategies offer unique promise (2). The ability to help consumers objectively and repeatedly track changes in health needs or function should provide greater motivation for compliance, ultimately driving better outcomes. This implies that the intervention is providing value through a meaningful impact on health or function. Both short-term benefits and long-term progress will be important to demonstrate success at the level of the consumer as well as at the population level (an aggregate of individual outcomes). Likewise, for the organization offering the PN intervention, a sustainable business model for delivery of the program is usually the end goal and is necessary for its continued availability to consumers.

Research Gaps and Opportunities for the Future

The current state of assessing dietary intake and nutritional status

Most current food and dietary intake assessment tools are subjective, being based on individual dietary recall (e.g., food records, FFQs), and have well-documented limitations (42–46). More recently, efforts have aimed to advance objective dietary assessment tools such as "apps" or remote photography [see, e.g., Martin et al. (47)]. However, the limitations of any collected information should still be recognized when used as part of an integrated assessment

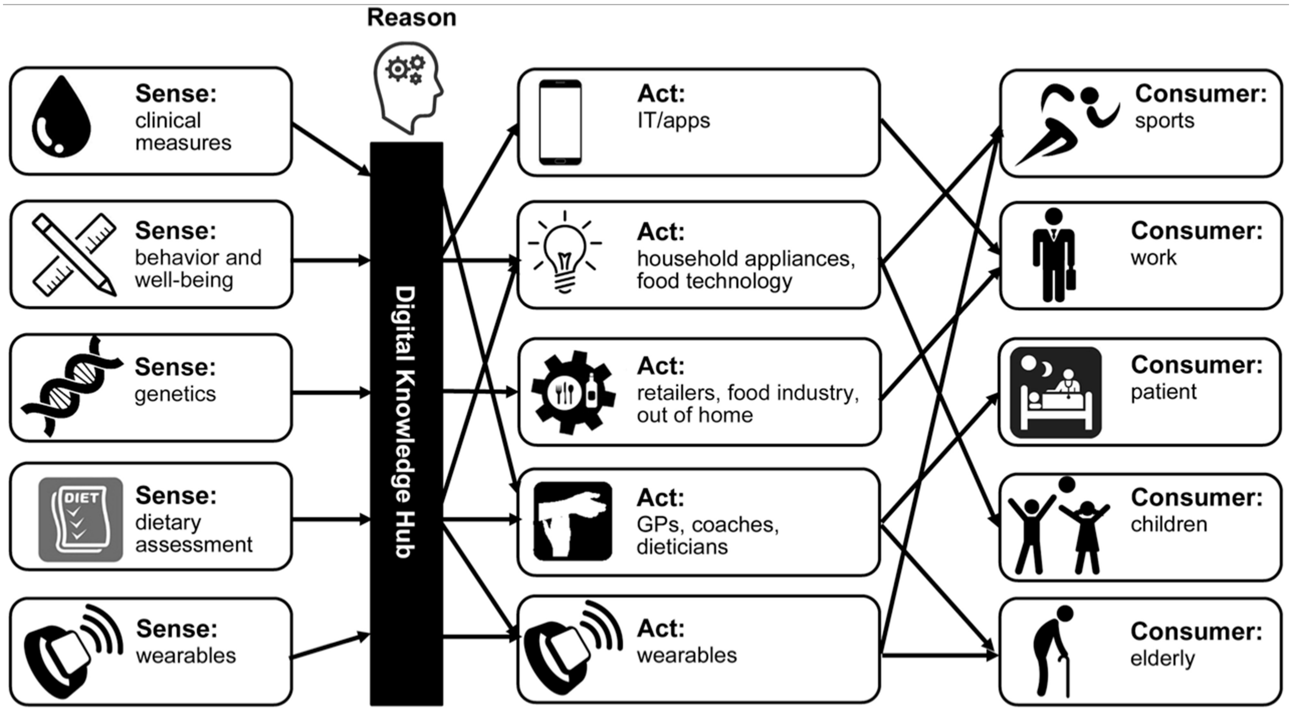

FIGURE 2 Example of a digital knowledge hub in the area of personalized nutrition. GP, general practitioner; IT, information technology.

that generates recommended dietary changes. In the past decade, the field of nutrition has increasingly moved toward dietary patterns as predictors of health outcomes (e.g., Healthy Eating Index), replacing a focus on individual nutrients or foods (48, 49). The best tools for capturing and interpreting dietary pattern information are yet to be defined; however, when used correctly, food intake tools may enable relative comparisons over time. More challenging may be collection of eating behavior and other behavior-change data, which is critical to an iterative PN approach that leads to real health benefit.

Recent interest has focused on direct assessment of individual nutritional status, because this would be expected to respond to the recommended changes in dietary intake. However, these assessments also present challenges. In some cases, variation may arise owing to a lack of standardization in clinical measurement techniques (e.g., for vitamin D) (50). For other micronutrients, there is a lack of consensus on reference ranges for biomarkers of nutrient status, and the best indicator of status has not been agreed upon for some nutrients (51). Further, there are few reliable noninvasive measures of nutrient status. There is an opportunity for further research in these fields, especially considering the disparate phenotypes and populations around the world, which may display significant variance in "reference ranges" for any given biomarker linked to health or function.

The potential of systems approaches

Biology is a system. Within a system, one change may result in a cascade of events with related consequences. Therefore, any specific measurement and resulting recommendation should be made with a systems-based perspective in order to accurately promote and detect changes to health. This also implies the need for repeated measures because changes in health and lifestyle can affect multiple markers and necessitate a change in the best application of PN for the individual. The use of integrated, systems-based approaches limits reliance on a single measure as a predictor and therefore helps manage error associated with that single measure.

Development of a transparent digital interdisciplinary knowledge ecosystem would assist with systems-based understanding and decision-making to translate individual measurement data into individualized advice, products, or services. Such a system (**Figure 2**) should use a multilevel organization of knowledge—that is, capture information related to *1*) the input, i.e., the individual-level markers being measured (blood markers, single nucleotide polymorphisms, anthropometrics, nutrient status, behavior); *2*) how these markers are related to each other (pathways, process, organ, health, disease); and *3*) the output, i.e., the personalized nutritional advice or product (food, nutrient, compound, supplement). Based on this information, experts can design decision rules that guide which nutritional recommendations or what dietary advice to provide to each individual (22).

The Quisper Association (52) is currently exploring whether such a digital knowledge ecosystem can be created by delivering scientifically validated data, knowledge rules, tools, and services (resources) for PN services to clients, thereby bridging the gap between suppliers of multidisciplinary science essential for PN and stakeholders offering PN services and products.

As the body of available consumer health data increases, the potential to develop algorithms to deliver actionable, individually tailored nutrition recommendations with predictable health outcomes becomes a closer reality. However, defining specific thresholds for success through data modeling is important to ensure that personalized approaches may benefit health. It will also be important to develop agreed-upon rules for inclusion or exclusion of data in such a system, because many different contextual elements may inform whether a new source of data can improve the decision quality of a system.

Application and communication of the evidence

A significant knowledge gap is understanding how to feed information from sophisticated analyses back to users who lack technical training. Ideally, PN tools can be described in such a way as to demonstrate the evidence base. This would include explicit mention of the tested health outcome, report of the percentage of and absolute number for the test population shown to have benefited, and a description of the subject group such that it can be generalized to the free-living target population. An example of communicating the data that support a weight loss approach or tool might be as follows: "The recommended nutrition plan has been shown to result in a 5% average weight loss in 80% of consumers as tested on more than 500 individuals with a BMI range of 20–30 kg/m^2." This could also be further refined by information specific to the individual based on subgroups within the broader population of consumers with similar traits (e.g., based on age, sex, ethnicity, genotype, or phenotype). Challenges will remain in linking what a patient wants to know and act upon with what the science can support and for the time being, "Individual results may vary."

Conclusions

PN offers the opportunity to help users increase compliance with dietary guidelines, shifting the paradigm of nutrition recommendations and delivery from population-based to individualized. This Perspective article identifies 10 guiding principles to consider when developing and implementing PN approaches. These principles are presented to the scientific community as a starting point and an invitation for further refinement. The goal in beginning this discussion is to eventually arrive at principles that are generally accepted by authorities that evaluate nutrition science and develop recommendations. The collective principles can also serve as a guide for companies or organizations that target PN delivery to individuals or populations. It is foreseeable that future iterations of the DGAs will expand options for personalization as our understanding of the "ideal diet for each individual" advances (53). The principles presented in this article could support such expansion. New PN tools have the potential to increase access to high-quality nutrition advice, enabling adherence to dietary and lifestyle goals and thus reducing disease risk and long-term health care costs.

As the field matures, these guiding principles will be developed and adapted to ensure the validity and reliability of interventions. Critical to any approach is the recognition that biological systems are dynamic and integrative. In summary, science-based PN—coupled to an innovative policy/regulatory environment plus greater consumer awareness—promises a new frontier in nutrition that could optimize health and function across the entire population.

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