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Personalized nutrition: aligning science, regulation, and marketing

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Abstract

Interest in personalized nutrition among researchers and industry has grown rapidly in recent years and shows no signs of abating. In this paper, we discuss the growth of the personalized nutrition market, the evidence for the approach, and the regulatory landscape for personalized nutrition products. We found that regulatory gaps have led to market growth of products with unknown efficacy that are making bold, and possibly unsubstantiated, claims. As personalized nutrition products and related treatments continue to enter the market without regulation, unreliable products may cause consumers financial, psychological, and physical harm. Stronger regulation will help engender trust in these products among consumers and ensure their safety and effectiveness.

Key words: personalized nutrition; precision nutrition; regulation; US Food and Drug Administration.

Introduction

In 1892, Dr. T.M. Rotch published an article in the *Journal of the American Medical Association* in which he described modifying cow's milk to produce individualized fat, sugar, and protein content.[1] "It is merely a matter of mathematic calculation to combine [skimmed milk and cream] in such proportions as to produce a mixture in the percentage of fats and albuminoids prescribed by the physician" (p. 57).[1] He claimed that 7 studied infants digested their individualized formulas well, "while what agreed with one produced serious symptoms in another" (p. 57).[1]

Over a century later, the potential for creating foods tailored to particular individuals continues to be explored and, in some cases, promoted, although now the movement has a name—personalized nutrition—defined as an approach to dietary advice that utilizes individual attributes drawn from genetic, serologic, and microbiome testing as well as questionnaires to develop personalized nutritional recommendations.[2-4] For example, Everlywell offers a food sensitivities blood test and recommends temporarily eliminating certain foods from the diet based on the results.[5]

Proponents of personalized nutrition assert that population-based approaches to dietary recommendations have had limited impact because they have failed to take interindividual differences into account.[2] Proponents argue that increasing or reducing consumption of particular foods in response to the results of a survey or diagnostic test allows for the development of more personalized and, it is argued, more effective recommendations.[2]

The claimed benefit of personalized nutrition derives from the frequent inability to predict who in a population will respond to a given intervention; personalized nutrition, in effect, claims that it can identify the likely responders who can then be offered treatment in a manner that better balances benefits against risks and costs, while sparing adverse effects in likely nonresponders. This paper discusses the growth of the personalized nutrition market, the evidence for the approach, and the regulatory landscape for personalized nutrition–related products.

The growth of the personalized nutrition market

Personalized nutrition and the associated commercialized direct-to-consumer products are based on recent exciting scientific developments in a number of fields and appear to have expanded rapidly in recent years, although information on the size of the personalized nutrition market is relatively scarce. According to Precedence Research, a market research firm, the global personalized nutrition market was valued at $12 billion in 2022 and is projected to be worth almost $50 billion by 2032.[6] Industry analysts estimate that there were about 12 personalized nutrition companies in 2012, a number that grew to nearly 400 in 2021.[7]

The number of research publications on the topic has clearly grown, from 12 in 2016 to almost 400 in 2023 (Figure 1), although some of this growth may reflect general acceptance of standardized terminology.[8] In May 2020, the National Institutes of Health (NIH) released its 2020–2030 Strategic Plan for NIH Nutrition Research, which "presents a bold, unifying vision emergent as 'Precision Nutrition'" (p. 4).[9] A new $170 million NIH-funded randomized crossover trial—Nutrition for Precision Health, Powered by the All of Us Research Program—will recruit 10 000 participants and examine their phenotypic, metabolomic, and microbiome responses to various diet combinations.[10,11]

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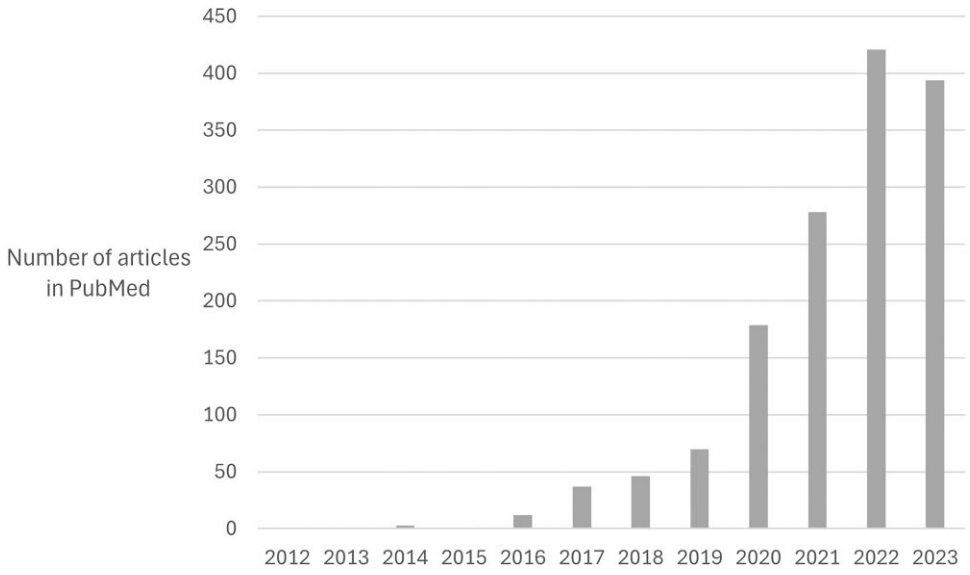

Figure 1. Number of articles produced by a search for "personali? ed nutrition" OR "individuali? ed nutrition" OR "precision nutrition" in PubMed (2012–2023). Source: Authors' analysis of data produced by a search for "personali? ed nutrition" OR "individuali? ed nutrition" OR "precision nutrition" in PubMed from 2012 through 2023.

Interest in personalized nutrition was preceded by the nascent field of precision medicine, which expanded in the 1990s with the Human Genome Project. But, even with the Precision Medicine Initiative announced under President Barack Obama,[12] the intense interest in the potential of precision medicine did not deliver a plethora of quick clinical advances. In practice, as 1 recent review[13] has noted, precision medicine has focused primarily on genetic factors. Some of these applications have shown some success, notably in rare diseases, conditions with clear genomic linkages, especially with single mutations, and in specific applications (eg, using genomics to avoid rare and serious adverse drug reactions). But there is less evidence to suggest that precision medicine is useful in complex diseases and at a large scale. For complex diseases related to diet, such as diabetes and cardiovascular disease, genome-wide association studies have undermined the hypothesis that a few gene variants are responsible for most disease incidence. Although additional research may demonstrate more relationships between genetic factors and disease, in many instances, the predictive tools we have long relied on, such as family history and weight, can still be as effective as genetic screening for complex diseases.

Companion diagnostics approvals can be used as a proxy measure for the growth of precision medicine over time. Eighty percent of approved companion diagnostics—defined by the Food and Drug Administration (FDA) as a medical device "which provides information that is essential for the safe and effective use of a corresponding drug or biological product"[14]—were approved in the last decade, but all but 6 were for use in cancer treatment (Figure 2). This suggests that this important aspect of precision medicine has grown, but only recently, underlying the sometimes-halting progress in these fields.

The evidence for a personalized nutrition approach

As with precision medicine, it is not inherently the case that a personalized approach to nutrition will be preferable to a population-based one. To show the efficacy of the approach, there should be at least some demonstration randomized controlled trials (RCTs) comparing a personalized with a more population-level approach that examine disease outcomes, not merely biomarkers or dietary behaviors.

We identified 6 recent RCTs (10 articles), all of which compared only biomarkers or dietary behaviors in personalized nutrition and standard-care groups; none examined disease outcomes (Appendix A; to access the Appendix, click on the Details tab of the article online). While 3 of the 6 RCTs showed improvements in at least 1 biomarker[15,16] or dietary outcome,[17-20] the magnitude of the improvements was generally modest. For example, 2 articles from the same study reported increases in diet quality indices of +0.28 on a 0–14-point scale[17] and +1.27 on a 0–100-point scale.[18] One of the 2 studies that examined blood glucose outcomes reported small effects (−0.08% for glycated hemoglobin [HbA1c] and −0.97 h/d on time with glucose >140 mg/dL),[16] while the other reported no benefit.[21] The results of these studies suggest a potential benefit of personalized nutrition advice on dietary intake with a less certain impact upon biomarkers and no demonstrated benefit to date on health outcomes.

The regulatory landscape for personalized nutrition products

There is no regulatory framework specific to the rapidly emerging area of personalized nutrition as it includes products that fall within FDA's purview in addition to practices that do not. Companies that provide tailored dietary guidance based on questionnaires are not regulated by FDA, while those that utilize medical devices and sell dietary supplements are overseen by different regulatory frameworks within FDA. This fragmented, and generally weak, regulatory environment has created a perfect storm of lack of regulation that may lead consumers to believe that the claimed health-promoting potential of various personalized nutrition approaches exceeds what the evidence supports.

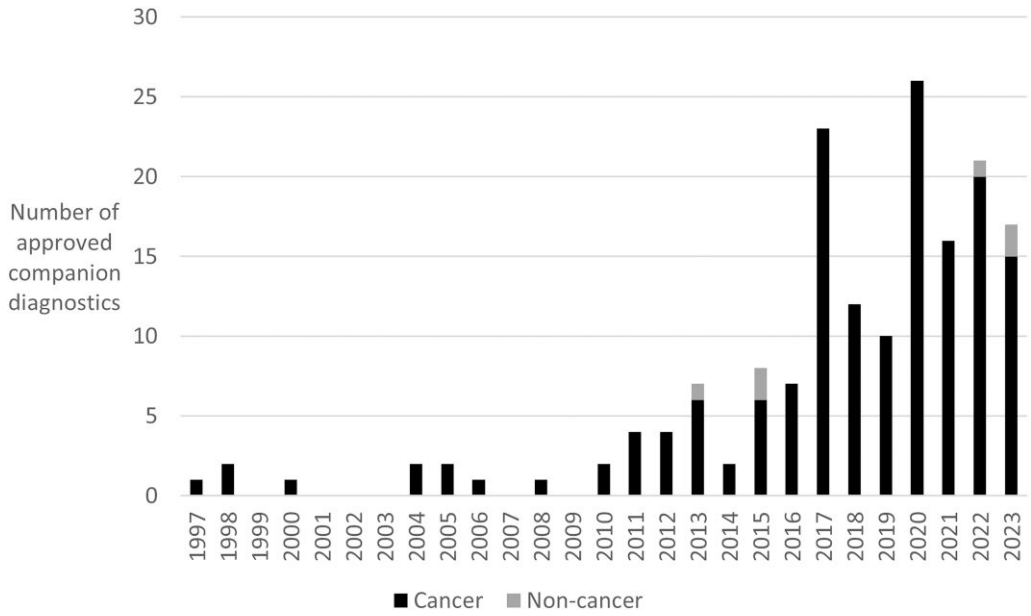

Figure 2. Number of Food and Drug Administration (FDA)–approved companion diagnostics by year of approval (1997–2023). Source: Authors' analysis of data from US FDA's list of cleared or approved companion diagnostic devices (in vitro and imaging tools) (available from: https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools).

Laboratory-developed tests

Many personalized nutrition approaches are dependent upon an initial "diagnosis" (eg, intolerance of a specific food or presence of a genetic characteristic or microbiome profile), thus placing diagnostic devices at the core of the nascent field. Laboratory-developed tests (LDTs) are a type of in vitro diagnostic (IVD) that is developed and used in a single laboratory ("send-out tests") as opposed to other IVDs that are used in multiple laboratories and conventionally manufactured and marketed as medical devices.[22,23] The FDA has historically not regulated LDTs despite its authority to do so, because early tests were relatively simple and used on a small number of patients.[23,24] Over time, the market has grown in size and complexity and FDA, along with researchers,[25] has identified several problematic tests.[23]

For well over a decade,[26] FDA tried to regulate these tests and Congress repeatedly failed to act on introduced legislation on this topic.[27] Recently, FDA finalized a rule asserting risk-based agency jurisdiction over LDTs.[28] However, the rule grandfathers in many existing tests, has been challenged in court by the American Clinical Laboratory Association,[29] and may be vulnerable due to a recent Supreme Court decision that prohibits agencies from acting on questions with major economic or political significance without explicit statutory authority.[30]

General wellness devices

In 2016, FDA issued a General Wellness Guidance that applies to all medical devices, including LDTs and IVDs.[31] The guidance clarified FDA's thinking on the regulation of "wellness" products that may meet the definition of a medical device, with a focus on the rapidly expanding market for digital health products and applications.[31] It did not address personalized nutrition products per se, but stated that FDA would not regulate low-risk wellness products (ie, those that are not invasive or implanted) with an intended use that relates to "maintaining or encouraging a general state of health" (p. 3)[32] or relates a healthy lifestyle to reducing the risk or impact of certain diseases or conditions.[32]

Companies can claim, for example, that their product "tracks activity [and] sleep patterns and promotes healthy sleep habits, which, as part of a healthy lifestyle, may help reduce the risk for developing type 2 diabetes" (p. 5),[32] but they cannot claim that it will treat or prevent a disease itself. A recent example of such a product in the personalized nutrition space is Lumen's device, which uses a CO_2 sensor that consumers blow into to determine if their body is using fat or carbohydrate to produce energy.[33] Using these exhalation data, the company provides personalized meal and exercise plans as part of their monthly membership to help customers lose weight. The company website claims that Lumen is "scientifically proven to meet the gold standard of metabolism measurement…in multiple validation studies,"[33] but provides inadequate validation data.[34-36] This exemption from regulation of an entire difficult-to-define category of products provides a relatively wide berth for potentially false, misleading, or poorly substantiated claims.

Dietary supplements

Dietary supplements were not regulated as a category until the 1990s. In the 1970s and 1980s, reports of serious harm from supplements, including instances of L-tryptophan supplements causing eosinophilia-myalgia syndrome, caught the attention of FDA.[37] The 1994 Dietary Supplement Health and Education Act (DSHEA) was passed, resulting in FDA regulation of dietary supplements as foods, not drugs.[38] The dietary supplement market has grown from about 4000 products when DSHEA was enacted to approximately 95 000 products today,[39] and many personalized nutrition companies offer dietary supplements.

Claims related to foods

Companies often make bold claims for personalized nutrition. For example, Viome invites consumers to "discover the best

foods, supplements, and probiotics for your health with advanced RNA-based testing for your microbiome, addressing root causes and supporting overall wellness and longevity."[40]

Generally, FDA regulates 3 types of claims made on food products—health claims, nutrient content claims, and structure/function claims[41]—with the first and third most relevant to personalized nutrition. Health claims assert that a food or food component can reduce the risk of a disease or condition and require "significant scientific agreement" and FDA approval prior to marketing.[42] Structure/function claims characterize the role of a nutrient or ingredient in affecting the normal structure or function of the body, but do not claim benefits in the diagnosis, treatment, or prevention of a disease that is not a "nutrient deficiency disease."[43,44] Structure/function claims do not require prior FDA approval, but manufacturers must notify FDA of their use and certify that they can substantiate the claims.[45] There is no requirement that companies submit evidence supporting their substantiation claim.[46] While FDA can request dietary supplement manufacturers to substantiate their claims, its requests are not always granted.[47] The FDA sends many warning letters to supplement companies whose products explicitly or implicitly link an ingredient to the diagnosis, prevention, or treatment of a disease, as such claims are reserved for drugs and devices (unless specifically authorized by FDA as a health claim) and thus constitute drugs being marketed without approval.[41,48] These carefully selected warning letters represent only a fraction of the apparent violations in this space; FDA does not have a comprehensive list of all supplements currently on the market and manufacturers can introduce new ingredients by a self-certification system without FDA knowledge.[49,50] These provisions have led to a broad lack of oversight over dietary supplements,[51] including those sold by personalized nutrition companies. Although personalized nutrition companies currently focus on dietary supplements, concerns around claims apply equally to foods, which could also be offered in response to test results.

Beyond FDA, the Federal Trade Commission (FTC) oversees product advertising by identifying false or misleading advertising, a standard used for all products regardless of their risk or relevance to the medical system,[52] other than prescription drug advertisements, which are regulated by FDA.[53] In December 2022, FTC released an updated Health Products Compliance Guidance that emphasized that, in general, companies need to support health-related claims with high-quality RCTs in humans that demonstrate clinically meaningful results.[54] The impact of this guidance remains unclear.

The consequences of poor oversight

The current complex and nebulous state of regulation for personalized nutrition–related products, coupled with FDA's limited resources, has predictably facilitated market growth of products with expansive claims, but unproven accuracy and clinical utility. Moreover, except where personalized nutrition might lead to the prescribing of a drug or device, the potential harms of these products derive, in part, from the lack of a health care provider intermediary (in contrast to precision medicine where such intermediaries are common), leaving the interpretation of results and resultant therapeutic decisions in the hands of potentially self-interested sellers or patients themselves.

Inappropriate claims can place a company at risk of a class action lawsuit for a false or misleading claim or of enforcement action by FDA, as in the case of 23andMe, Inc, in 2013 for making claims about the prevention and mitigation of disease for its genetic test.[55] Federal oversight is therefore in industry's interest in that such oversight could help ensure that claims are accurate, which would promote consumer confidence in personalized nutrition products, while reducing the prevalence of improperly manufactured products or those claiming unproven benefits, which have the potential to discredit this emerging field.

Equity considerations

As more resources are used to study the effectiveness of personalized nutrition interventions, it is possible that future research will demonstrate benefits of the approach. However, such benefits may be limited to a small number of patients and consumers. Inherent in defining a likely responder subset is a reduction in target population size. For rare genetic variants, for example, this could produce very small markets. As markets shrink, commercial interest could diminish. In the alternative, as recent experience in the orphan-drugs sector has demonstrated, companies facing limited patient populations have implemented extremely high prices for treatments.[56] This suggests a potential niche private market that provides boutique services primarily to the rich. Indeed, the personalized nutrition company Viome offers its Full Body Health Solutions for $199 per month (minimum: 3 orders), which includes its Full Body Intelligence Test and personalized supplements, probiotics, and prebiotics.[57] Yet, it remains unclear whether insurance companies would cover sometimes-expensive personalized nutrition diagnostics and treatments, leaving patients to foot the bill. To the extent that personalized nutrition products are based on solid evidence, this will result in diminished access for those who might benefit from the products most.

Conclusion

The scientific and market interest in personalized nutrition show no signs of abating. Although the underlying science is promising, unreliable products and unsupported claims have the potential to cause financial, psychological, and physical harm to consumers. Until regulatory bodies address the existing regulatory gaps and are provided with adequate resources to exercise those authorities, consumers will continue to encounter products that are, at times, a waste of money and, at worst, harmful to their health. As a first step, FDA should acknowledge precision nutrition products as a category deserving concerted attention and create a risk-based framework for assuring that their benefits outweigh their risks.

Supplementary material

Supplementary material is available at *Health Affairs Scholar* online.

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Conflicts of interest

Please see ICMJE form(s) for author conflicts of interest. These have been provided as supplementary materials.

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