REVIEW

Nutritional Genomics and Direct-to-Consumer Genetic Testing: An Overview

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ABSTRACT

The increasing prevalence in polygenic diseases, such as obesity, cardiovascular disease, and type 2 diabetes, observed over the past few decades is more likely linked to a rapid transition in lifestyle rather than to changes in the sequence of the nuclear genome. In the new era of precision medicine, nutritional genomics holds the promise to be translated into tailored nutritional strategies to prevent and manage polygenic diseases more effectively. Nutritional genomics aims to prevent, treat, and manage polygenic diseases through targeted therapies formulated from individuals' genetic makeup and dietary intake. Direct-to-consumer genetic testing (DTC-GT) has become commercially available to equip individuals with information on their genetic vulnerability to different diseases. This information may potentially prompt behavioral changes against adverse factors. However, scientific evidence behind the clinical recommendations is a matter of continuous debate, and behavioral modifications after disclosing genetic information remain inconclusive. In this review, we provide an overview of nutritional genomics and related nutritional DTC-GT services and discuss whether available data are sufficient to be translated into clinical recommendations and public health initiatives. Overall, the scientific evidence supporting the dissemination of genomic information for nutrigenomic purposes remains sparse. Therefore, additional knowledge needs to be generated, particularly for polygenic traits. *Adv Nutr* 2018;9:128–135.

Keywords: direct-to-consumer genetic testing, nutritional genomics, genomics, gene-diet interaction, precision nutrition

Introduction

Noncommunicable diseases linked to excess calorie intake, sedentary behavior, smoking, and overweight or obesity are the leading cause of death and represent the most significant public health burden (1, 2). The distressing economic backlash and elevated direct and indirect medical costs attributed to these otherwise largely preventable diseases pose a challenge for health care systems and economic development (3). Consequently, efforts to prevent the significant global increase in obesity, type 2 diabetes (T2D), cardiovascular disease (CVD), and their disabling and life-threatening complications are now at the forefront of public health initiatives (4). Thus, disclosing early stages of prevalent diseases and identifying at-risk individuals may have the potential for more effective prevention programs and therapeutic strategies.

Understanding the genetic basis of diseases was presumed to yield improved diagnosis and better-targeted treatments (5). Significant contributions from the Human Genome Project have provided a critical resource on the structure, organization, and function of the complete set of human genes (6). Furthermore, advancements in technologies and analytics, such as genomewide association studies, further enabled the discovery of hundreds of disease-associated genes (7). The growing data generated through genotyping and genetic sequencing have inspired new avenues for polygenic disease prevention, treatment, and cure through characterization and improved understanding of relevant biological pathways (8, 9).

To accelerate the incorporation of genetics into clinical practice, in 2011 the US National Human Genome Research Institute put forth a 20-y plan for translating insights from genomics to medicine (10, 11). The plan was organized around 5 domains extending from basic research to health applications, with an overall aim to advance medical science and to identify novel ways to improve human health. Worth noting is the genomic medicine initiative set in 2015 by former President Barack Obama that laid out a vision for a national

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Abbreviations used: CAD, coronary artery disease; CVD, cardiovascular disease; DTC-GT, direct-to-consumer genetic testing; *FTO*, fat mass and obesity–associated; *PPARG*, peroxisome proliferator–activated receptor γ; RCT, randomized clinical trial; T2D, type 2 diabetes.

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Precision Medicine Initiative in the United States articulated through the All of US research program (12, 13). Precision medicine is an expanded concept stemming from initial efforts to understand the human genome, and it is intended to convey the principle that certain therapeutics or primary preventive strategies may be more effective in subgroups of patients.

Starting in the 2000s, and in parallel with the advancements in genomic medicine, direct-to-consumer genetic testing (DTC-GT) has become commercially available for the purposes of tracking ancestry and providing genetic information for the risk of several diseases, including T2D, CVD, and cancer (14, 15). In addition, DTC-GT has gained popularity particularly among individuals who seek genetic susceptibility–tailored nutritional recommendations. The aim of the present review was to provide an overview of nutritional genomics and related nutritional DTC-GT services and to discuss whether generated scientific knowledge is ready to be utilized and translated into clinical recommendations and public health initiatives.

Current Status of Knowledge

Nutritional genomics: from monogenic to polygenic disease

Nutritional genomics can be considered to be an extension of precision medicine that aims to prevent, treat, and manage diseases through targeted nutritional therapies formulated from individuals' genetic makeup (16, 17). It includes the study of the bidirectional relation between genes and diet and constitutes 2 complementary approaches: *1*) how genetic variation affects the body's nutrient response (nutrigenetics) and *2*) how nutrients affect gene function (nutrigenomics) (18). Nutritional genomics extended definitions, aims, and methodologic challenges are summarized in **Text Box 1**.

TEXT BOX 1 NUTRITIONAL GENOMICS DEFINITION, AIMS, AND METHODOLOGIC CHALLENGES

Nutritional genomics is "the study of how diet may affect the expression of genetic information in an individual, and how an individual's genetic makeup affects the metabolism and response to nutrients and other bioactive components in food" (18).

The aims of nutritional genomics are as follows:

1. Identify genetic variants that may be significant in understanding genetic responses to diet
2. Identify genetic variants associated with diet-related diseases
3. Identify effective dietary strategies to prevent or treat disease
4. Improve dietary guidelines at a population level

Methodologic challenges:

1. Not a complete picture of genetic influences for several polygenic diseases
2. Lack of longitudinal studies integrating genetic, molecular, clinical, phenotypic, and dietary data
3. Dietary intake is not well characterized and results are lacking in replication phases
4. Many genes discovered, but only a few of them seem to have direct connections with metabolic consequences

Despite these challenges, biotechnological companies and laboratories are offering genetic services on the basis of findings from nutritional genomic research. These services include nutrigenomic tests for genetic variants associated with diet-related disease, such as obesity, diabetes, and CVD. Companies may also offer services related to dietary patterns, dietary supplementation, and lifestyle on the basis of genomic test results.

Like the majority of commercially available genetic services, nutrigenomic services are sold as laboratory services, whereby the laboratory uses an in-house protocol to analyze patient or consumer specimens and prepare a report of test results. Unlike in vitro diagnostic "test kits" that are manufactured and labeled with instructions for a specific clinical use by multiple laboratories, DTC-GT laboratory services are not currently regulated by the FDA (except for 23andMe).

Perhaps the best-known examples of the clinical application of nutritional genomics have been in relation to inborn errors of metabolism, which are monogenic diseases resulting from well-characterized, highly penetrant genetic variants, primarily in genetic coding regions that modify critical proteins in a metabolic pathway. Examples of such monogenic diseases include phenylketonuria, galactosemia, and maple syrup urine disease (17–19). In phenylketonuria, individuals carrying a homozygous mutation affecting the phenylalanine hydroxylase gene (*PAH*) function have an inability to effectively metabolize phenylalanine, and consequently, a low-phenylalanine diet is recommended (19). Likewise, the current nutritional treatment for individuals with galactosemia, the partial incapacity to break down galactose due to genetic defects in the gene that encodes for the galactose-1-phosphate uridyl transferase enzyme (*GALT*), is to limit the intake of foods containing galactose (20).

Unlike monogenic diseases, polygenic diseases result from changes in a substantially larger number of genetic loci, whereby each individual locus contributes a small effect on the underlying disease of interest. At least 60 and 100 independent loci contribute to the genetic architecture of coronary artery disease (CAD) and T2D, respectively (21, 22), and the underlying pathology is further influenced by interplay between genetic and environmental factors. For these polygenic diseases, an additional layer of complexity comes into play when considering that the majority of identified loci from relevant genomewide association studies are situated in noncoding genetic regions. In the case of CAD and T2D, ~80% of the identified loci reside in areas with uncharacterized biological function. As a result, there is uncertainty in identifying disrupted biological pathways and, more importantly, disease-relevant tissues where these variants are likely to be differentially expressed (23).

Starting in the late 1990s, hundreds of epidemiologic studies have purported to have identified gene-lifestyle interactions for cardiometabolic diseases, in particular obesity and T2D (24, 25), whereby a lifestyle component or a nutrient

is observed to either attenuate or exacerbate a genetic influence on disease. These early observations have several limitations, including small sample-size studies, imprecise measurement estimates of lifestyle exposures, specifically diet, or self-reported outcomes (25). In addition, the evidence inadequately accounts for the effects of multiple testing on type 1 error (26). Only a few interactions were replicated in independent cohorts (27, 28), and recent efforts to replicate previous interaction findings for T2D risk have failed, casting doubt on the validity and generalizability of the findings (29).

Nevertheless, important advancements with adequately powered investigations are more possible through large research infrastructures such as the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium (30) and other large biorepositories, such as the UK Biobank (31). By attaining adequate statistical power, interaction analyses have yielded more plausible and convincing findings (32–35). For example, it was observed that self-reported adherence to a healthy dietary pattern modified the association between obesity genetic susceptibility and anthropometric traits (BMI and BMI adjusted for waist-to-hip ratio) in a study including ~68,000 individuals of European descent from 18 cohort studies (35). Moreover, an analysis of 120,000 individuals from the UK Biobank observed that high-risk obesogenic environments and behaviors interacted with genetic susceptibility to obesity by modulating BMI (36).

Robust evidence of the differential impact of dietary intake on polygenic traits, based on single genes, stems from post hoc analyses of well-powered and designed randomized clinical trials (RCTs). For example, the effect of dietary fat intake on glycemic and anthropometric traits was observed to be dependent on Pro12Ala variants at PPAR-γ (*PPARG*) (37). The *PPARG* interaction has been validated and replicated in other independent studies, and more importantly, the underlying molecular mechanism of action, specifically the regulation of adipocyte differentiation, lipolysis, and insulin sensitivity that explains the interaction, is biologically sound (38, 39). Results from a post hoc analysis in the PREvencion con DIeta MEDiterranea (PREDIMED) trial showed that individuals carrying the transcription factor 7-like 2 (*TCF7L2*)–increasing T2D risk genotype improved intermediate CVD risk factors and had a lower incidence of stroke when consuming a Mediterranean diet in comparison to a low-fat diet (40). Other RCTs, including the US Diabetes Prevention Program, the POUNDS Lost trial, and the Look AHEAD trial, have further evaluated the interaction between *TCF7L2* and dietary intake or lifestyle interventions with conflicting findings, likely because of the heterogeneity among these interventions (41–43).

Other studies have also focused on an aggregate of genetic variants, rather than individual genetic variants, to better capture genetic susceptibility. This approach was made possible with genomewide genetic data. For example, whether the intake of sugar-sweetened beverages interacts with BMI genetic susceptibility on changes in BMI was tested with the use of a Genetic Risk Score for obesity comprising 32 BMI-increasing variants. Preliminary findings were observed in ~10,000 individuals from the Nurses' Health Study and the Health Professionals Follow-Up Study and later replicated in 21,740 women from the Women's Genome Health Study (44). The interaction analysis suggested that the odds and risk of obesity were more pronounced with higher intakes of sugar-sweetened beverages (44). A different analysis in the same 3 cohorts identified a significant interaction between fried-food intake and the obesity Genetic Risk Score (45). In another remarkable study that included ≤50,000 participants from 3 prospective cohorts, both genetics and lifestyle were observed to drive CAD risk, but no evidence of an interaction between dietary and other lifestyle factors on CAD based on genetic susceptibility was observed (46).

DTC-GT

Due to the increasing knowledge of population-scale genetic variation, DTC-GT genotyping companies have found an opportunity to encourage people to obtain their own genetic information. This growing market has been made possible by scalability of genotyping platforms and people's interest in taking a proactive role in their health care (47). In general, DTC-GT companies provide information on the risk of monogenic disorders, such as intolerance and sensitivity panels (caffeine and lactose), macronutrient and energy metabolism (e.g., FA oxidation), weight management and obesity, and vitamins and mineral requirements. Several companies further offer nutritional coaching and personalized meal deliveries as well as other lifestyle panels such as exercise performance. Although some companies reveal on their web pages the nutrition-related genes included in their analyses (typically ranging from 9 to 88 genes), this information and other details linking genes to nutrition-related traits and advices are often unavailable.

DTC-GT and behavior change

One of the main interests for delivering genetic information is the belief that if individuals understand their genetic background, they will be more prompt to change their unhealthy behaviors. However, recent studies that evaluated the response of DTC-GT consumers to their own genetic susceptibilities and DTC-GT efficacy in motivating positive lifestyle changes presented conflicting results. A large longitudinal cohort study in 2037 customers from the Scripps Genomic Health Initiative measured the effects of DTC-GT with regard to the susceptibility of developing 18 common conditions on behavioral, physiologic, and clinical effects. Findings from the study indicated no changes in any measurable short-term physiologic health outcome (i.e., anxiety symptoms), dietary intake, or exercise before and after genomic information delivery (48). In addition, findings from a study in 1042 customers, who used 23andMe or Pathway Genomics for evaluating cancer risk and who completed baseline and 6-mo surveys, suggested that most adults receiving reports with elevated cancer risk (based on selected genetic variants)

did not significantly change their diet, exercise, advanced-care planning, or cancer-screening behaviors, compared with those who received reports suggesting that they were at average or lower risk (49).

On the other hand, other observational studies have suggested that leveraging disease-specific genetic predisposition information may motivate more effective weight management and be perceived as more useful than standard dietary advice. An online survey of 1048 customers investigated whether the interpretation of DTC-GT genetic testing results affected customer behavior and health care use. The survey showed that after DTC-GT, 16% of the customers indicated changes to a medication or supplement regimen, one-third reported being more careful about their diet, and 14% reported increases in amounts of exercise (50). However, this survey study lacked a comparison group. Another small online survey in 275 individuals observed that only 27% of DTC-GT consumers reported positive or neutral health behavior changes, such as a "healthier diet" or "more exercise," as a consequence of their tests (51).

To the best of our knowledge, only a few RCTs have been conducted to compare the effects of providing genotype-based dietary advice with general recommendations on behavioral outcomes. The Food4Me Study is an RCT investigating whether providing personalized dietary advice based on *1*) current dietary intake, *2*) current dietary intake and phenotype, or *3*) current dietary intake, phenotype, and genotype leads to improved compliance with dietary intake recommendations and health outcomes compared with standard nutritional recommendations. Findings from the 6-mo study provided no evidence that including genotypic information enhanced the effectiveness of personalized nutrition advice (52). Instead, the study observed a modest improved adherence to a Mediterranean dietary pattern with the addition of DNA-based dietary advice (53). However, whether these results are generalizable to individuals of different demographic characteristics remains unexplored.

The Toronto Nutrigenomics and Health Study randomly assigned 149 participants to either intervention (genotype-based personalized dietary advice) or control (general dietary advice) groups. Although ∼90% of participants in the intervention group agreed that the dietary recommendations they received were useful and expressed interest to follow up with further recommendations, only ∼10% of participants in the intervention group reported feeling uneasy about learning their genetic information. Because study staff were not blinded to the intervention, the findings may have been affected (52). In another RCT including 569 healthy middle-aged adults randomly assigned to receive standard lifestyle advice alone to reduce T2D risk (group 1) or in combination with genetic risk (group 2) or an additional risk estimated from phenotypic characteristics (group 3), it was observed that complementary genetic (group 2) and phenotypic (group 3) information did not provide added benefit on physical activity or other health behaviors (53).

Limitations, Research Needs, and Health Implications

Evaluating DTC-GT in nutritional genomics

Given the stronger and consistent evidence mapping monogenic traits and diseases, and the direct causal relation between genetic variation and the outcome, DTC-GT nutritional genomics is likely to be more reliable for monogenic rather than polygenic traits. For example, for alcohol flushing reactions, a monogenic disorder due to alcohol dehydrogenase enzyme deficiency, the predictive power of a test including an rs671 variant in the alcohol dehydrogenase gene (*ALDH2*) is likely to be relevant. (It is likely to be relevant, but currently not commonly assessed by DTC-GT companies.) The same can be applied to other monogenic disorders in which genetic variability is known to result in a defective key enzyme, such as those responsible for breaking down lactose or caffeine in cases of primary hypolactasia or caffeine sensitivity, respectively.

However, DTC-GT in nutritional genomics may not be as helpful for polygenic traits and diseases. An illustration is the fat mass and obesity–associated (*FTO*) locus, which confers the largest genetic effect on obesity (54). Homozygote individuals for the BMI-increasing allele at rs9939609 weighed ∼3 kg more than noncarriers and had a 1.67-fold higher risk of obesity compared with their counterparts not carrying the risk allele (54). Consequently, the *FTO* locus is included in the majority of DTC-GT genetic panel algorithms. Although significant interactions have been observed between several dietary components and *FTO* in relation to obesity, including a Mediterranean dietary pattern (55), fat and carbohydrate intake (56, 57), frequency of alcohol consumption (58), or added salt among other dietary components (58), there is a lack of consensus with regard to tailored nutritional recommendations for weight management in individuals harboring this genetic variant (59). In addition, difficulties in understanding *FTO* function, regulation, and interplay with other genetic and nongenetic factors (60) can obscure potential translational findings. Thus, how to best manage weight and overall health when carrying the *FTO* obesity-predisposition alleles in terms of macronutrient distribution remains unknown.

Another major concern for polygenic phenotypes is that nutritional recommendations based on single variants may also have an effect on multiple other physiologic processes and can interact with several genes to modulate the risk of several diseases in various directions. As an illustration, the Pro12Ala variant at *PPARG* has been found to interact with fat intake to modulate glycemic response and weight loss (37). However, despite clinical studies supporting the relation between *PPARG* and metabolic diseases (61), there is a lack of consensus on the optimal amount of fat intake according to *PPARG* genotype. Thus, there is a clinical need to generate sufficient knowledge to be able to confidently establish true cutoffs according to genotype. In addition, given that multiple risk alleles contribute to polygenic traits, the interaction among genes and biological compensatory mechanisms, such

as enhanced genetic expression resulting from certain thresholds of exposure (62), can further complicate tailored genetic recommendations with the current body of evidence.

Hence, in polygenic diseases, current DTC-GT dietary recommendations should integrate information from a complete set of variants reliably associated with risk of disease as well as variants for which interactions with dietary factors have been shown. Dietary recommendations should be provided based not only on these interactions but also on validated nutritional strategies for the prevention and management of disease outcomes to which the individual is genetically predisposed (63).

DTC-GT: current clinical implications

A pressing and timely question is whether we are ready for precision medicine and precision nutrition implications. The benefit of DTC-GT for nutritional genomics purposes should not be ignored, particularly for traits with highly penetrant alleles, whereas insufficient evidence for and understanding of polygenic diseases resulting from low-penetrant alleles limits its benefit for those diseases. Given the limited current biological knowledge on polygenic diseases and inconsistent findings in gene-diet interaction studies for polygenic diseases, DTC-GT dietary advice remains questionable. Most of what has been documented so far for those diseases does not show that the precision nutrition approach is clinically valuable. However, other areas of biomedicine, mostly cancer research, are more amenable to the integration of early findings from precision medicine (64, 65).

Ultimately, DTC-GT may be considered a novel tool for clinicians, health care providers, and consumers to learn about genetic susceptibility to diseases, and thus theoretically offer an opportunity to manage risk and reinforce beneficial behaviors that can counter genetic vulnerability (e.g., smoking cessation on lung cancer genetic risk) (66). Clinicians need to be trained to be able to accurately interpret genetic information with caution because significant gaps in the current scientific evidence remain, particularly for polygenic traits.

It is also important to consider the effect magnitude of interactions, considering that a significant gene-lifestyle interaction may not be clinically meaningful. It is worth noting that few interactions have been replicated across different ethnicities (27), whereas most other research has been routinely restricted to individuals of European ancestry, either to reduce heterogeneity observed in multiethnic analyses (67) or by necessity if the gene of interest is more prevalent among that population. Basing recommendations for Europeans on findings made in other ethnicities, and vice versa, might be meaningless. However, the use of ethnicity-specific genetic variants, thanks to genotyping and sequencing investigations in diverse populations, is emerging as a way to partition polygenic disease heterogeneity (68). For example, a nonsense polymorphism in the TBC1 domain family member 4 (*TBC1D4*) locus, which increases 2-h glucose and increases T2D risk 10-fold, has a minor allele frequency of 17% in Inuit populations, but is almost nonexistent in other groups (69). Similarly, a scan of Inuit genomes showed genetic and physiologic adaptations to a diet rich in PUFAs, showing protective effects of these variants [Fatty acid desaturase (*FADS*) locus] in cardiovascular phenotypes in an Inuit population but not in European-descent individuals (70). Thus, if DTC-GT companies were to use this information, they would need to limit their recommendation to Inuit-descent individuals.

Another challenge of DTC-GT companies is determining the most appropriate format in which the data should be returned to consumers. For example, the provision of raw genetic data (uncommon) or qualitative information (e.g., variant presence compared with absence or "clinical interpretation" of the data) may be confusing, uninformative, and potentially misleading. In addition, privacy and protection of genomic data and consent with regard to storing and using genetic and nongenetic information for further research and development represents a legal and ethical gap.

Advances in nutritional genomics and DTC-GT for the future

Nutritional genomics is a novel, growing field. Further evidence is needed for gene-environment interactions before conclusive recommendations can be made. For example, current gene-environment interactions, particularly those recommendations for polygenic traits included in DTC-GT algorithms, should be rigorously re-evaluated. That re-evaluation encompasses the following: *1*) replicating findings in other independent cohort studies, as was recently attempted by Li et al. (29), including replication in populations of different ethnicities; *2*) assessing whether the recommendation corresponding to the interaction has other effects on the body; and *3*) determining whether the magnitude of interaction has clinically significant effects. Dietary behavior is complex, and accurate assessment of intake requires robust tools that adequately capture diversity in dietary composition. The recognized need for accurate data on dietary exposures has resulted in the development of technology-driven methods for this purpose, including mobile phone applications, that might facilitate tracking food consumed, including capturing photographic images for the identification and quantification of foods consumed (71). These innovations hold promise for contributing to improved dietary assessment given that inconsistent and imprecise dietary intake analysis limits the strength of such correlations.

Improvement in genotyping coverage by whole-genome sequencing, which facilitates genomewide interaction studies, may help identify clinically relevant interactions in an agnostic manner (72). In addition, improvement in genetic imputation algorithms and the incorporation of other genotyping resources and parameters such as expression quantitative trait loci or structural variation information will inevitably result in major leaps in the field.

Nevertheless, genetic advancements should also be in parallel with improvements in nutritional assessment to reduce error in dietary exposure and heterogeneity across studies resulting from differences in assessment tools. In this sense,

other improvements in wearable technology for lifestyle characterization and reliable measurement of comprehensive environmental exposures, as well as the integration of nutritional genomics with other omics, including epigenomics, metabolomics, or metagenomics, may drive major leaps in the field as shown in a recent pilot investigation (73). Of note is the work led by researchers from the Weizmann Institute of Science, which showed that monitoring individual responses to different foods integrated with health variables and microbiome composition may enable personalized nutrition plans for improving postprandial glucose or the rate of postdieting weight regain (74–76). The research technology from these studies was licensed to DayTwo, which offers a consumer-based product to predict glycemic response to foods. Furthermore, nutritional genomic RCTs are needed to better characterize interactions and to validate the necessity of DTC-GT. In addition, the trials should further include other 'omics to understand how genetics respond in the context of other environmental pressures (10). And as the science advances, DTC-GT companies should upgrade their products and methods accordingly.

DTC-GT from a public health perspective

DTC-GT for nutritional genomic applications is among the latest topics in nutrition. The growing interest has been made possible given the social changes in medicine and health perception, in which patients want to be involved in making decisions with regard to their health (77). From a public health perspective, the integration of the information that will be generated through the use of this multidimensional data in public health messages needs to be targeted to diverse audiences, from the general population to high-risk individuals. As technologies mature, and DTC-GT for nutritional genomic purposes incorporates more robust information in its algorithms, they will undoubtedly yield a huge increase in disease-prevention opportunities (78). This knowledge will likely transform the practice of medicine and related social and environmental determinants of health policies (12, 79). However, the added value of new tools and approaches to public health practice needs to be evaluated and fine-tuned. Public health efforts so far have tackled important concerns, such as increasing added sugar intake, childhood obesity, and physical inactivity, through public education and other active strategies (80). Those strategies should be accompanied, but not replaced, by more targeted efforts in order to identify individuals who are susceptible of a disease before its onset on the basis of susceptibility profiles that also include genetics.

Conclusions

Scientific evidence supporting the dissemination of genomic information to consumers remains sparse. Thus, to consider genetic testing as a means for health improvement, it is crucial to have a greater understanding of the relevance of genetics in optimizing human health, delaying disease onset, reducing disease severity, and improving quality of life. Genetic information is complex, and its interpretation is probabilistic, depending on many factors such as health status, family health history, ethnic background, and more. For years, the field of genetic counseling has sought to develop scientifically valid processes of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease. Nutritional genomics holds the promise to be translated into tailored nutritional recommendations on the basis of genetic susceptibility to polygenic diseases, and genetic testing should play a key role in this approach. However, more accurate methods for measuring dietary intake, genetic susceptibility, and the interplay between them could lend better assessment of population health and the development of personalized interventions and public policies.

Finally, the integration of other layers of omics information, such as metabolomics, transcriptomics, epigenetic modifications, and gut microbiota composition, is likely to provide a more comprehensive body of evidence on the interplay between dietary intake and genetic susceptibility. Although the initial drive toward precision nutrition has begun, more work is underway to develop a robust scientific framework for its implementation into practical solutions to benefit individuals and societies alike.

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