Recent advances and current controversies in genetic testing for personalized nutrition

Bibiana Garcia-Bailo and Ahmed El-Sohemy

Purpose of review
Considerable interest in personalized nutrition exists among the general public, policymakers, healthcare organizations and the private sector, but there is also skepticism of its utility. The present review aims to provide a summary of current controversies in the field of nutrigenomics, and to highlight recent research on the potential impact of implementing genetic testing for personalized nutrition in practice.

Recent findings
Numerous companies already offer genetic testing for personalized nutrition based on research developments in nutritional genomics. However, controversy exists over whether genetics contributes to interindividual responses to diet; the utility of single genetic variants versus genetic risk scores; the ability of DNA-based nutritional advice to elicit positive behavior change and health effects; and whether genetic information makes a difference on the type of dietary advice provided. Potential factors contributing to the discrepant viewpoints are discussed.

Summary
Despite the existing controversies, a solid body of evidence demonstrates that genetic testing for personalized nutrition is a powerful tool to guide dietary recommendations to improve health and performance, and to elicit positive behavior change.

Keywords
behavior modification, genetic testing, genetic variation, nutrigenetics, nutrigenomics, personalized nutrition, precision nutrition, response to diet

INTRODUCTION

Since the publication of the first draft sequence of the human genome, research innovations and public interest in personalized health have paved the way for the burgeoning market of consumer genetic testing. Presently, numerous companies offer genetic test kits that provide individuals with ostensibly personalized information about everything from disease risk to athletic ability. One offering with considerable potential to impact health is DNA-based personalized nutrition. Findings from the field of nutritional genomics, which aims to understand why some people respond differently from others to the same foods, beverages and supplements that they consume, now make it possible to develop personalized nutrition strategies for disease prevention and health optimization. With companies seizing upon the opportunity to bring these innovations to consumers, the global market for nutrigenomics-based services is forecast to reach $17 billion USD by 2023 [1].

Recent initiatives from public health agencies and professional organizations indicate that interest in personalized nutrition is not just restricted to the general public and the private sector. For example, the US National Institute of Diabetes and Kidney Diseases, a part of the National Institutes of Health (NIH), hosted a 2-day workshop in early 2021 entitled 'Precision Nutrition: Research Gaps and Opportunities' that showcased, in addition to developments in nutritional genomics research, the NIH's 'All of Us' landmark research program on precision medicine [2▪,3]. This program aims to recruit one million individuals, with the goal of developing an extensive database of health information to substantiate the broad implementation of precision medicine in the US healthcare system. In

Department of Nutritional Sciences, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

Correspondence to Ahmed El-Sohemy, Department of Nutritional Sciences, University of Toronto, 1 King's College Circle, Room 5326A, Toronto, ON, Canada M5S 1A8. Tel: +1 416 946 5776; e-mail: a.el.sohemy@utoronto.ca

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KEY POINTS

- Selection of the appropriate genetic variants is a crucial methodological step for research studies attempting to elucidate how genetic variation impacts dietary responses, health and performance.
- Genetic variation is often associated with downstream omic biomarkers. As genotyping only requires a single, noninvasive sample, genetic testing represents a robust, affordable marker of more complex omic variation that is easy to implement in practice.
- Genetic risk scores are often used to capture the overall contribution of genetic variation to chronic disease risk but their utility in personalized nutrition is limited unless the variants used to build the risk scores are known to impact nutrient metabolism or responses to dietary factors.
- Randomized controlled trials consistently show that DNA-based, personalized nutrition advice is more effective than general advice at modifying behavior, and it is also more effective than personalized advice that does not incorporate genetic information.
- Knowledge of an individual's genotype enables practitioners to provide targeted, personalized recommendations that are more specific, and often more stringent, than general advice, and can better help the individual meet his or her health and performance goals.

addition, the American Nutrition Association and the International Life Sciences Institute have both published proposed definitions for personalized nutrition and outlined steps for its implementation in clinical practice [4▪,5▪].

Notwithstanding the substantial current interest in personalized nutrition and nutritional genomics, skepticism of the field exists, with some healthcare professional organizations questioning the readiness of genetic testing for incorporation into practice. A consensus report by the Academy of Nutrition and Dietetics concluded that, at present, 'there is insufficient evidence from randomized controlled trials regarding the effectiveness of incorporating nutrigenetic testing into nutrition counseling or care [6]' . The conclusion was based on two systematic reviews of randomized, controlled trials on personalized nutrition that were published concurrently with the consensus report [7,8]. As illustrated by a letter to the Editor in response to the publication of the consensus report that highlighted methodological flaws of the systematic reviews [9], the Academy's conclusion was controversial and the debate on whether genetic testing for personalized nutrition is ready for prime time continues. The present review aims to provide a summary of current controversies in the field, and to highlight recent research on the potential impact of implementing genetic testing for personalized nutrition in practice.

CONTROVERSY: DO GENETIC DIFFERENCES CONTRIBUTE TO INTERINDIVIDUAL RESPONSES TO DIET?

The utility of genetic information versus other tools, including both traditional biochemical markers and more novel omics technologies, in guiding personalized nutrition interventions has been a matter of debate [10,11]. Some examples of the controversy, and potential contributing factors to help explain discrepant points of view, are discussed below.

Selection of genetic markers

Postprandial lipid and glycemic responses are independent predictors of cardiometabolic diseases, and evidence over time has shown that genetic variation can help predict variation in postprandial responses across individuals. Recent examples are two genome-wide association studies (GWAS) carried out in the Netherlands Epidemiology of Obesity cohort that have identified single nucleotide polymorphisms (SNPs) predicting postprandial triglycerides and early-phase insulin responses to a liquid mixed meal [12,13]. Despite this evidence, controversy exists surrounding the utility of genetic information for predicting postprandial responses to diet. A recent example of this controversy comes from the PREDICT 1 study [10]. One aim of the study was to evaluate the contribution of different types of data, such as genetic, metabolic and metagenomic (gut microbiome) information, as well as meal context and composition, to interindividual variability in postprandial responses. The study population consisted of approximately 1000 healthy individuals living in the United Kingdom, and a smaller (approximately 100 participants) replication population of persons living in the United States. To explore the genetic contribution to postprandial responses, the authors genotyped participants for SNPs previously found to be associated with postprandial triglyceride and glycemic responses [14,15]. Participants consumed standardized meals varying in macronutrient composition, and their responses to them were quantified. Genetic variation was the second most significant contributor to postprandial glucose after meal composition, demonstrating that individual genetic differences are more important than the gut microbiome for predicting changes in postprandial blood glucose.

However, genetics did not significantly contribute to postprandial triglycerides [10]. Instead, serum lipids and serum glycemic markers were the top contributors to triglyceride and C-peptide responses, respectively. Other significant contributors to both outcomes included anthropometry, gut microbiome composition, blood pressure, etc. [10].

On the basis of the PREDICT 1 study findings, some have argued that genetic variation is not an important predictor of interindividual variability in response to diet. A more accurate interpretation of the study's results, however, would conclude that genetic variation is an important predictor of postprandial glucose, second only after meal composition, but may not contribute as much to postprandial triglycerides. The difference in the ability of genetics to predict glucose versus triglycerides may be partly a result of the distinct physiological mechanisms behind postprandial increases in both biomarkers. However, methodological considerations such as genetic variant selection may also contribute to the observed differences. Indeed, the SNPs chosen to predict postprandial glucose came from a comprehensive meta-analysis of nine GWAS [15]. Meanwhile, the genetic variants selected to predict postprandial triglycerides were based on a single GWAS of triglyceride responses to a high-fat meal, which was different in composition from the meals tested in PREDICT 1, and the markers identified in that study have not been replicated to the extent that the SNPs chosen for postprandial glucose have [15]. As such, it may be premature to conclude that genetics does not predict postprandial triglyceride responses. It is possible that SNPs strongly linked to triglyceride responses were not included in the PREDICT 1 study, and this would explain why genetics appeared to be a weak predictor of postprandial triglycerides in that study – the right genetic variants may not have been analyzed.

Another example of inadequate selection of genetic variants comes from the DIETFITS study [16]. DIETFITS was a large randomized, controlled trial examining the effects of a genotype-guided low-carbohydrate diet, compared with a typical low-fat diet, on weight loss. The authors reported that genetic variation did not interact with macronutrient content of the diet to affect weight loss, and popular media headlines promoted this as evidence that DNA-based personalized nutrition elicits no more successful weight loss responses than general advice. However, an examination of published supplementary data from the DIETFITS study indicates that there was considerable variability in response to the study diets, suggesting an important role for individual factors, such as genetic variation, in explaining the wide range of weight loss responses [16]. Furthermore, the rationale for genetic variant selection for DIETFITS is unclear. The SNPs chosen for analysis appear to have come from unpublished research, making it difficult to ascertain their validity as potential predictors of weight loss responses [16]. Indeed, the three SNPs used to predict response to a low-fat or low-carbohydrate diet have never been associated with weight loss response to either low-fat or low-carbohydrate diets in any study. Meanwhile, genetic variants that have been extensively researched, such as SNPs within *FTO*, and are well known to mediate the association between dietary macronutrients and body composition, were excluded from the research. Given all of this, a more appropriate conclusion for the DIETFITS study may be that the SNPs selected for analysis failed to account for differences in weight loss across study participants.

Taken together, PREDICT 1 and DIETFITS offer evidence that selection of the right genetic markers for analysis is crucial, and can lead to erroneous conclusions if the wrong variants are chosen. Indeed, PREDICT 1 indicates that whenever robust, extensively replicated SNPs are chosen, as was the case for only postprandial blood glucose, genetic variation is an important contributor to certain outcomes [10].

Utility of genetics versus other omics

Technical developments in systems biology have led to a rapidly growing body of research on how variation at different levels of the omics spectrum impacts individual responses to diet. Indeed, PREDICT 1 is one example of research incorporating different omics tools, and other recent studies have examined the association between various omics and variation in responses to diet [17–20]. Although variation across the omics spectrum undoubtedly helps explain why some individuals respond differently from others to the same dietary exposures, it is important to point out that genetic variation often is closely associated with downstream epigenetic, proteomic, metabolomic and even metagenomic variation. As genetic variation can be measured easily and economically from a single, noninvasive bodily fluid or cheek cell sample, genetic testing represents a robust, affordable marker of more complex omic variation that is easy to implement in practical settings and on a large scale. A recent example of genetic variation underlying downstream omics effects comes from a study that used a sophisticated multiomics approach to elucidate the mechanism behind a well studied gene–diet interaction involving *APOA2*, saturated fat intake, and obesity [17]. The authors used methylomics to

identify different DNA methylation patterns in individuals with the risk genotype for rs5082, and found that these methylation differences occurred only with saturated fat intakes above the study population median of 22 g/day. Using transcriptomics, the authors then determined that the observed differences in methylation resulted in lower expression of the *APOA2* gene in CC homozygotes than TT homozygotes. They then used a metabolomics approach to examine whether lower expression of the gene, and subsequent limited production of the APOA2 protein, resulted in different concentrations of metabolites in the pathways affected by APOA2. These results indicated differences between the genotypes in several pathways implicated in lipid and amino acid metabolism, which have been linked to appetite and energy balance [17]. Overall, this study highlights the profound implications of the interaction between one SNP and one nutrient on physiological pathways that affect obesity risk. Furthermore, it underscores the fact that to identify individuals who may be at a greater risk of obesity with a higher saturated fat intake, a simple genetic test for *APOA2* rs5082 is all that is required. This option is arguably easier to implement in practice than more complex and invasive omics testing.

CONTROVERSY: ARE SINGLE GENETIC VARIANTS AS USEFUL AS GENETIC RISK SCORES?

As common noncommunicable diseases tend to be complex and multifactorial in etiology, many rightly argue that the contribution of single genetic variants to disease risk is negligible. However, the ensuing conclusion that genetic tests for personalized nutrition focusing on single genetic variants are far too crude to provide meaningful information can be countered by the evidence to date. As the previously mentioned study on *APOA2* (rs5082), saturated fat intake and obesity risk makes evident, a single genetic variant interacting with one nutrient can have profound effects on risk of chronic diseases like obesity, an observation that has been replicated in at least six distinct populations representing different ethnic groups [17,21,22].

Despite compelling evidence from studies like the one mentioned above, some researchers and practitioners believe that genetic risk scores, which combine multiple genetic variants into an algorithm to predict overall risk, are superior to single markers. Indeed, in recent years, the field of nutritional genomics has adopted the use of genetic risk scores in research studies. An important consideration when using genetic risk scores is that, although it is true that many genetic variants can affect disease risk, this does not necessarily translate into multiple genetic variants modifying the effect of a dietary factor on disease risk. There are various examples of studies that have examined how diet modifies genetic risk for given diseases. For example, a recent analysis of data from the Nurses' Health Study reported that a higher intake of fruit and vegetables ameliorated a person's genetic risk of obesity, as calculated based on 77 markers previously associated with BMI [23]. Another recent study of participants of the UK Biobank examined the association between a plant-based dietary pattern, genetic risk and cardiovascular disease [24]. Their findings suggested that plant-based diets ameliorate cardiovascular disease risk, regardless of genetic susceptibility [24].

Although both of these studies are examples of how genetic risk scores can add to our understanding of the relationship between diet and disease, it is important to point out that it remains unclear whether any of the variants included in the genetic risk scores modify the metabolism of any dietary components. This limits their utility as part of genetic tests for personalized nutrition as no truly focused, actionable recommendations for dietary intake can be built upon them. They simply show that prudent dietary advice is associated with a lower risk of disease among those with an increased genetic susceptibility. Yet, in most cases, even those without a genetically increased risk of disease also benefit from the same prudent dietary advice. As such, providing the same prudent dietary advice, regardless of genetic profile, is not consistent with the goals of personalized nutrition. A more suitable approach to capture gene–diet interactions of potential practical utility using polygenic scores would be to build genetic algorithms that include variants known to impact metabolism of specific dietary factors.

CONTROVERSY: DOES DNA-BASED PERSONALIZED NUTRITION ELICIT BEHAVIOR CHANGE TO A GREATER EXTENT THAN GENERAL ADVICE?

One of the controversies on genetic testing for personalized nutrition revolves around its utility for behavior modification [25]. Although some studies show that personalized advice of any kind is better than general advice at changing food intake habits [26], studies that have specifically examined the effects of genetic information on behavior change consistently show that DNA-based advice is more effective than general advice at modifying behavior, and also more effective than personalized advice that does not incorporate genetic information [27].

The first randomized, controlled trial to compare the effects of providing DNA-based advice versus general dietary advice on behavior found that DNA-based advice resulted in successful, sustained dietary behavior change [28]. Research since then has confirmed these findings. For example, the Nutrigenomics, Overweight/Obesity and Weight Management (NOW) NOW trial evaluated the effect of a nutrigenomics-informed lifestyle year-long intervention versus a population-based intervention on dietary adherence, dietary intake and body weight [29▪▪,30▪]. All participants were included into the Group Lifestyle Balance (GLB) Program, formerly called the Diabetes Prevention Program, which is considered a gold standard intervention for weight management and diabetes risk reduction. In addition, the control group received population-based dietary advice, and the treatment group received DNA-based dietary advice. The specific areas of recommendation included intake of total energy, protein, saturated fat, monounsaturated fat, polyunsaturated fats, total unsaturated fat, total fat and sodium; and participants were also informed about snacking behavior. Dietary intake was assessed at baseline, 3, 6 and 12 months. The authors reported a sustained behavior change that was specific to the group receiving DNA-based advice only [29▪▪]. Regarding body weight, the group receiving DNA-based advice lost a greater relative body fat percentage at 6 months, although this differenced was attenuated to nonsignificant by the 12th month [31▪▪].

Taken together, these studies underscore the utility of genetic testing for personalized nutrition as a powerful tool to elicit behavior change. The findings of the NOW trial also suggest that DNA-based advice may lead to faster improvements in body composition than general advice [31▪▪]; this is not only encouraging for individuals who are attempting to lose weight but it may have clinical utility in situations where accelerated weight loss is necessary, including many nonelective surgical procedures.

CONTROVERSY: DOES GENETIC INFORMATION MAKE A DIFFERENCE ON THE TYPE OF DIETARY ADVICE PROVIDED?

One additional controversy surrounding genetic testing for personalized nutrition involves the view that having genetic information does not affect the specific dietary advice provided, as individuals are counseled to adhere to public health recommendations for a specific aspect of their diet, regardless of their genetic profile. This assumption is incorrect. One example comes from research on the effects of genetic variation in *CYP1A2*, caffeine metabolism and various health and performance-related outcomes, where individuals who are slow caffeine metabolizers based on their *CYP1A2* genotype experience different effects after caffeine consumption than fast metabolizers [32]. Indeed, the largest randomized controlled trial to date on caffeine and athletic performance highlights the importance of considering genotype when providing caffeine recommendations [33,34,35▪]. Caffeine, which is a widely used ergogenic aid, exerted different effects on athletes depending on their *CYP1A2* genotype, with fast metabolizers experiencing significant improvements in endurance performance as indicated by a cycling time trial, whereas slow metabolizers actually performed worse after caffeine supplementation [33,34]. The implications of these findings for caffeine recommendations in practical settings are evident: some individuals could be advised to consume caffeine for enhanced athletic performance whereas others should be advised to avoid caffeine before endurance events.

Another example of genetic variation impacting recommendations for a specific nutrient comes from research on *FTO* genotype and weight loss responses to diets varying in macronutrient composition. Indeed, results from the POUNDS LOST trial indicate that the *FTO* variant rs1558902 modifies weight loss responses to a high-protein diet [36]. Among carriers of the T allele, participants lost about 2% of their fat mass regardless of the protein content of their diet. Meanwhile, at the end of the 2-year trial, AA homozygotes lost 220% more body fat on the high-protein diet compared with the low-protein diet [36]. These findings have been replicated by several studies, including in different ethnic groups and in observational study designs and randomized, controlled trials [37,38]. Findings from the Food4Me study, a large trial on the effects of personalized nutrition recommendations on various health outcome, also showed that *FTO*-based advice resulted in greater weight loss [39]. Taken together, these results have important implications for dietary weight loss recommendations. Knowing a person's *FTO* genotype allows healthcare providers to guide the individual towards a high-protein diet if they carry the response allele; meanwhile, carriers of the T allele would be better counseled to adhere to a less restrictive, more macronutrient-balanced hypocaloric diet for weight loss.

CONCLUSION

Despite controversies regarding not only its readiness for incorporation into practice, but its overall utility, a solid body of research evidence clearly demonstrates that genetic testing for personalized

nutrition is a powerful tool to guide dietary recommendations to improve health and performance, and to elicit positive behavior change. Efforts to more clearly and comprehensively report gene–diet interactions in the research literature will enable greater transparency and more successful knowledge translation for widespread incorporation of personalized nutrition into healthcare practice [40▪]. Ongoing research efforts, together with considerable interest from public health organizations, are increasing and strengthening the nutrigenomics knowledge base that informs the development of DNA-based recommendations. Given the strong public interest and large market size of the personalized nutrition field, ample opportunities to harness the power of personalized nutrition for health and performance must be matched by a robust understanding of the science behind genetic tests for personalized nutrition. As the consensus report by the Academy of Nutrition and Dietetics concluded, dietitians and other nutrition and healthcare professionals must stay abreast of developments in this rapidly evolving field [6]. Incorporating nutritional genomics into the curricula of dietetics and other healthcare professional training programs, and developing opportunities for continuing education among practitioners, are required to ensure the adequate, evidence-based incorporation of personalized nutrition into practice for maximum benefit. To that end, organizations, such as Dietitians of Canada and the American Nutrition Association have now developed training programs in nutritional genomics that are targeted specifically towards healthcare professionals [41,42].

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Conflicts of interest

B.G.-B. is the Director of Research and Development of Nutrigenomix Inc. A.E.-S. is the Founder and Chief Science Officer of Nutrigenomix Inc. and holds shares in the company.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ▪ of special interest
- ▪▪ of outstanding interest

1. Market Research Future. Global Nutrigenomics Market – Trends & Forecast, 2017-2023. 2017.
2. ▪ National Institute of Diabetes and Digestive and Kidney Diseases. Precision Nutrition: Research Gaps and Opportunities Workshop. 2021. Available at: https://www.niddk.nih.gov/news/meetings-workshops/2021/precision-nutrition-workshop. (Accessed 21 January 2021)

This NIH-sponsored workshop brought together key opinion leaders and researchers in the field of nutritional genomics, and the entire conference contents are freely available for viewing.

3. National Institutes of Health. All of Us Research Program. Available at: https://allofus.nih.gov/. (Accessed 21 January 2021)
4. ▪ Adams SH, Anthony JC, Carvajal R, *et al.* Perspective: guiding principles for the implementation of personalized nutrition approaches that benefit health and function. Adv Nutr 2019; 11:25–34.

This article represents the consensus effort of personalized nutrition thought leaders brought together into a multidisciplinary panel by the International Life Sciences Institute (ILSI). The aim of the article is to define the term 'Personalized Nutrition' and create guiding principles for its implementation in practice.

5. ▪ Bush CL, Blumberg JB, El-Sohemy A, *et al.* Toward the definition of personalized nutrition: a proposal by the American Nutrition Association. J Am Coll Nutr 2020; 39:5–15.

This article puts forth a proposed definition for personalized nutrition and its implications for practice that was developed by the American Nutrition Association.

6. Braakhuis A, Monnard CR, Ellis A, Rozga M. Consensus Report of the Academy of Nutrition and Dietetics: incorporating genetic testing into nutrition care. J Acad Nutr Diet 2020; 121:545–552.
7. Ellis A, Rozga M, Braakhuis A, *et al.* Effect of incorporating genetic testing results into nutrition counseling and care on health outcomes: an evidence analysis center systematic review-part II. J Acad Nutr Diet 2020; 121:582.e17–605.e17.
8. Robinson K, Rozga M, Braakhuis A, *et al.* Effect of incorporating genetic testing results into nutrition counseling and care on dietary intake: an evidence analysis center systematic review-part I. J Acad Nutr Diet 2020; 121:553.e3–581.e3.
9. Horne JR, Vohl MC. Response to the Consensus Report of the Academy of Nutrition and Dietetics: incorporating genetic testing into nutrition care. J Acad Nutr Diet 2020; 120:1959–1960.
10. Berry SE, Valdes AM, Drew DA, *et al.* Human postprandial responses to food and potential for precision nutrition. Nat Med 2020; 26:964–973.
11. Loos RJF. From nutrigenomics to personalizing diets: are we ready for precision medicine? Am J Clin Nutr 2019; 109:1–2.
12. Ibi D, Noordam R, van Klinken JB, *et al.* Genome-wide association study of the postprandial triglyceride response yields common genetic variation in LIPC (Hepatic Lipase). Circ Genom Precis Med 2020; 13:e002693.
13. Li-Gao R, Carlotti F, de Mutsert R, *et al.* Genome-wide association study on the early-phase insulin response to a liquid mixed meal: results from the NEO Study. Diabetes 2019; 68:2327–2336.
14. Wojczynski MK, Parnell LD, Pollin TI, *et al.* Genome-wide association study of triglyceride response to a high-fat meal among participants of the NHLBI Genetics of Lipid Lowering Drugs and Diet Network (GOLDN). Metabolism 2015; 64:1359–1371.
15. Saxena R, Hivert MF, Langenberg C, *et al.* Genetic variation in GIPR influences the glucose and insulin responses to an oral glucose challenge. Nat Genet 2010; 42:142–148.
16. Gardner CD, Trepanowski JF, Del Gobbo LC, *et al.* Effect of low-fat vs low-carbohydrate diet on 12-month weight loss in overweight adults and the association with genotype pattern or insulin secretion: the DIETFITS Randomized Clinical Trial. JAMA 2018; 319:667–679.
17. Lai CQ, Smith CE, Parnell LD, *et al.* Epigenomics and metabolomics reveal the mechanism of the APOA2-saturated fat intake interaction affecting obesity. Am J Clin Nutr 2018; 108:188–200.
18. Lai CQ, Parnell LD, Smith CE, *et al.* Carbohydrate and fat intake associated with risk of metabolic diseases through epigenetics of CPT1A. Am J Clin Nutr 2020; 112:1200–1211.
19. Bisanz JE, Upadhyay V, Turnbaugh JA, *et al.* Meta-analysis reveals reproducible gut microbiome alterations in response to a high-fat diet. Cell Host Microbe 2019; 26:265.e4–272.e4.
20. Posma JM, Garcia-Perez I, Frost G, *et al.* Nutriome-metabolome relationships provide insights into dietary intake and metabolism. Nat Food 2020; 1:426–436.
21. Corella D, Tai ES, Sorli JV, *et al.* Association between the APOA2 promoter polymorphism and body weight in Mediterranean and Asian populations: replication of a gene-saturated fat interaction. Int J Obes (Lond) 2011; 35:666–675.
22. Basiri MG, Sotoudeh G, Alvandi E, *et al.* APOA2-256T>C polymorphism interacts with saturated fatty acids intake to affect anthropometric and hormonal variables in type 2 diabetic patients. Genes Nutr 2015; 10:464.
23. Wang T, Heianza Y, Sun D, *et al.* Improving fruit and vegetable intake attenuates the genetic association with long-term weight gain. Am J Clin Nutr 2019; 110:759–768.
24. Heianza Y, Zhou T, Sun D, *et al.* Genetic susceptibility, plant-based dietary patterns, and risk of cardiovascular disease. Am J Clin Nutr 2020; 112:220–228.
25. Calabro GE, Sassano M, Tognetto A, Boccia S. Citizens' attitudes, knowledge, and educational needs in the field of omics sciences: a systematic literature review. Front Genet 2020; 11:570649.
26. Hoevenaars FPM, Berendsen CMM, Pasman WJ, *et al.* Evaluation of food-intake behavior in a healthy population: personalized vs. one-size-fits-all. Nutrients 2020; 12:2819.

27. El-Sohemy A. Only DNA-based dietary advice improved adherence to the Mediterranean diet score. Am J Clin Nutr 2017; 105:770.
28. Nielsen DE, El-Sohemy A. Disclosure of genetic information and change in dietary intake: a randomized controlled trial. PLoS One 2014; 9:e112665.
29. ■■ Horne JGJ, O'Connor C, Seabrook J, Madill J. Enhanced long-term dietary change and adherence in a nutrigenomics-guided lifestyle intervention compared to a population-based (GLB/DPP) lifestyle intervention for weight management: results from the NOW randomised controlled trial. BMJ Nutr Prev Health 2020; 3:49–59.
This study presents results from the NOW Trial, a randomized controlled trial, which showed that individuals living with overweight or obesity, enrolled into a weight management program and following the guidelines of the gold standard behavioral intervention Group Lifestyle Balance/Diabetes Prevention Program (GLB/DPP), exhibited more positive behavior changes when they received DNA-based personalized advice in addition to the GLB/DPP recommendations than when they received only the GLB/DPP advice.
30. ■ Horne JR, Gilliland JA, Vohl MC, Madill J. Exploring attitudes, subjective norms and perceived behavioural control in a genetic-based and a population-based weight management intervention: a one-year randomized controlled trial. Nutrients 2020; 12:3768.
This study examined the attitudes and perceptions of behavioral control of participants of the NOW Trial, a randomized controlled trial examining the effects of providing DNA-based advice on weight loss and health behavior change. Study participants in the DNA-based, personalized nutrition group showed changes in attitudes and behavioral control in the long-term, compared with participants in the control group, whose attitudes and behavioral control only changed in the short term.
31. ■■ Horne JR, Gilliland JA, O'Connor CP, *et al.* Change in weight, BMI, and body composition in a population-based intervention versus genetic-based intervention: the NOW Trial. Obesity (Silver Spring) 2020; 28:1419–1427.
This study reported weight loss outcomes of the NOW Trial, a randomized controlled 485 trial that compared DNA-based nutrition advice versus the gold standard population-based lifestyle program. Participants who received personalized advice lost a greater relative percentage of body fat at 3 and 6 months than those in the control group, although the differences were no longer significant at 12 months.
32. Doepker C, Lieberman HR, Smith AP, *et al.* Caffeine: friend or foe? Annu Rev Food Sci Technol 2016; 7:117–137.
33. Guest N, Corey P, Vescovi J, El-Sohemy A. Caffeine, CYP1A2 genotype, and endurance performance in athletes. Med Sci Sports Exerc 2018; 50:1570–1578.
34. Guest NS, Corey P, Tyrrell PN, El-Sohemy A. Effect of caffeine on endurance performance in athletes may depend on HTR2A and CYP1A2 genotypes. J Strength Cond Res 2020. [Epub ahead of print]
35. ■ Guest NS, Horne J, Vanderhout SM, El-Sohemy A. Sport nutrigenomics: personalized nutrition for athletic performance. Front Nutr 2019; 6:8.
This article is a comprehensive review of research developments and potential practical implications of nutrigenomics for sports performance.
36. Zhang X, Qi Q, Zhang C, *et al.* FTO genotype and 2-year change in body composition and fat distribution in response to weight-loss diets: the POUNDS LOST Trial. Diabetes 2012; 61:3005–3011.
37. Merritt DC, Jamnik J, El-Sohemy A. FTO genotype, dietary protein intake, and body weight in a multiethnic population of young adults: a cross-sectional study. Genes Nutr 2018; 13:4.
38. Antonio J, Knafo S, Kenyon M, *et al.* Assessment of the FTO gene polymorphisms (rs1421085, rs17817449 and rs9939609) in exercise-trained men and women: the effects of a 4-week hypocaloric diet. J Int Soc Sports Nutr 2019; 16:36.
39. Celis-Morales C, Marsaux CF, Livingstone KM, *et al.* Can genetic-based advice help you lose weight? Findings from the Food4Me European randomized controlled trial. Am J Clin Nutr 2017; 105:1204–1213.
40. ■ Horne JR. Strengthening the reporting of nutritional genomics research to inform knowledge translation in personalized nutrition. Lifestyle Genom 2021; 1–6. [Epub ahead of print]
This article proposes a set of guidelines on the reporting of nutrigenomics research findings to facilitate their incorporation into practice.
41. Dietitians of Canada. 2021. Available at: https://www.dietitians.ca/. (Accessed 21 February 2021)
42. American Nutrition Association. 2021. Available at: https://theana.org/. (Accessed 21 February 2021)