

# Personalised nutrition and health

**Jose Ordovas and colleagues** consider that nutrition interventions tailored to individual characteristics and behaviours have promise but more work is needed before they can deliver

**D**ietary factors are well recognised contributors to common diseases, including heart disease, stroke, type 2 diabetes and cancer.<sup>1-3</sup> Despite the known link between dietary patterns and disease, interventions to alter dietary habits and to improve public health and wellbeing have had limited impact. Personalisation of interventions may be more effective in changing behaviour<sup>4</sup> that will affect health outcomes.<sup>5</sup> In this article we consider the evidence for personalised nutrition.

## What is personalised nutrition and what is it used for?

There is no agreed definition of personalised nutrition. For the purposes of this review, we define it as an approach that uses information on individual characteristics to develop targeted nutritional advice, products, or services. Gibney et al<sup>6</sup> describe it as an approach that “assists individuals in achieving a lasting dietary behaviour change that is beneficial for health.” Personalised nutrition partially overlaps with

related terms such as precision nutrition, nutrigenomics, nutrigenetics, nutritional genomics, etc (box 1).

The overall goal of personalised nutrition is to preserve or increase health using genetic, phenotypic, medical, nutritional, and other relevant information about individuals to deliver more specific healthy eating guidance and other nutritional products and services (table 1). Personalised nutrition is equally applicable to patients and to healthy people who may or may not have enhanced genetic susceptibilities to specific diseases.

Personalised nutrition can be applied in two broad areas: firstly, for the dietary management of people with specific diseases or who need special nutritional support—for example, in pregnancy or old age, and, secondly, for the development of more effective interventions for improving public health. It has traditionally focused on maximising the benefits and reducing the adverse effects of dietary changes for the individual. However, this focus on the individual may have limited impact on populations. To have a wider impact, it must be deployed at a scale and in a

### Box 1: Descriptors and definitions

In common with other scientific fields in their early development, multiple concepts and descriptors are used in personalised nutrition, sometimes without rigorous definition. In addition to the term personalised nutrition, many other terms are used—for example, precision nutrition, stratified nutrition, tailored nutrition, and individually tailored nutrition. We have attempted to group the descriptors as follows:

- Stratified and tailored nutrition are similar (if not synonymous). These approaches attempt to group individuals with shared characteristics and to deliver nutritional intervention/advice that is suited to each group
- Personalised nutrition and individually tailored nutrition mean similar things and go a step further by attempting to deliver nutritional intervention/advice suited to each individual
- Precision nutrition is the most ambitious of the descriptors. It suggests that it is possible to have sufficient quantitative understanding about the complex relationships between an individual, his/her food consumption, and his/her phenotype (including health) to offer nutritional intervention/advice, which is known to be individually beneficial. The degree of scientific certainty required for precision nutrition is much greater than that required for the other approaches
- Nutrigenetics is an aspect of personalised nutrition that studies the different phenotypic responses (ie, weight, blood pressure, plasma cholesterol, or glucose levels) to a specific diet (ie, low fat or Mediterranean diets), depending on the genotype of the individual
- Nutrigenomics involves the characterisation of all gene products affected by nutrients and their metabolic consequences
- Exposome is the collection of environmental factors, such as stress, physical activity and diet, to which an individual is exposed and which may affect health

As one moves from stratified to personalised to precision nutrition, it becomes necessary to apply more and more dimensions or characteristics to achieve the desired goal. For example, stratification could be undertaken using one, or a few, dimensions such as age, gender, or health status. In contrast, given the complexity of relationships between individual diet and phenotype, deployment of a wide range of dimensions/characteristics, perhaps including “big data” approaches, would be necessary to achieve the goal of precision nutrition. An exception to this broad generalisation is the management of inborn errors of metabolism such as phenylketonuria, where “precision nutrition” can be achieved using information on a single characteristic—that is, genotype.

- Epigenomics is a branch of genomics concerned with the epigenetic changes (methylation, histone modification, microRNAs) that modify the expression and function of the genetic material of an organism
- Metabolomics is the scientific study and analysis of the metabolites (usually restricted to small molecules, ie, <900 daltons) produced by a cell, tissue, or organism
- Microbiomics is the study of the microbiome, the totality of microbes in specific environments (ie, the human gut)

### KEY MESSAGES

- Personalised nutrition uses information on individual characteristics to develop targeted nutritional advice, products, or services to assist people to achieve a lasting dietary change in behaviour that is beneficial for health
- Personalised nutrition is based on the concept that individualised nutritional advice, products, or services will be more effective than more traditional generic approaches
- This personalisation may be based on biological evidence of differential responses to foods/nutrients dependent on genotypic or phenotypic characteristics, and/or based on current behaviour, preferences, barriers and objectives
- Most of the available evidence in support of personalised nutrition has come from observational studies with risk factors as outcomes, rather than from randomised controlled trials using clinical end points
- The overall consensus is that much research and regulation is required before personalised nutrition can deliver the expected benefits

way that reduces (rather than increases) health disparities. Individuals may also wish to use personalised nutrition to achieve personal goals/ambitions that are less directly related to health—for example, to deal with preferences for, and dislikes of, specific foods, to attempt to achieve a desired body size or shape, or for competitive sports.<sup>7</sup>

#### What are the conceptual bases for personalised nutrition?

Personalised nutrition is based on the idea that individualising nutritional advice, products, or services will be more effective than more generic approaches.

Personalisation can be based on:

- Biological evidence of differential responses to foods/nutrients dependent on genotypic or phenotypic characteristics
- Analysis of current behaviour, preferences, barriers, and objectives and subsequent delivery of interventions, which motivate and enable each person to make appropriate changes to his or her eating pattern.

#### Personalisation based on biological characteristics of the individual

Differences in the response of people to dietary components have been well documented for almost a century.<sup>8–10</sup> This provides the basis, and motivation, for developing personalised nutrition strategies. The trend towards personalisation is the result of: firstly, nutrition research that provides a better understanding of how diet affects health; secondly, new technology that enables better and continuous measurements of markers of individual health and fitness; and thirdly, new analytical tools that interpret this flow of data and transform it into user friendly practical information. Moreover, personal nutrition integrates with the change in bioscience and public health programmes towards preventing rather than mitigating existing disease. Response to food is variable and has multiple forms. These include differential responses in plasma cholesterol concentration to dietary saturated fat intake, food allergies or intolerances (eg, lactose intolerance or gluten sensitivity), or more severe forms such as phenylketonuria and other inborn errors of metabolism. Moreover, personalised nutritional advice may be appropriate for some key factors, such as age (teenager, elderly, child, adult), stage of life (pregnant, lactating, etc), sex, BMI, disease or health status, ethnicity, and cultural or religious backgrounds that dictate particular diets

Nutrigenetics has been defined as “the discipline that studies the different phenotypic response to diet depending on the genotype of each individual.”<sup>11</sup>

It is a classic example of an attempt to characterise the response of an individual to a dietary intervention based on genetic factors. To a large extent, this is based on accumulating evidence of the phenotypic consequences of interactions between interindividual differences in genetic make up and nutrition.<sup>12</sup> Nutrigenetics has evolved from using a unique single nucleotide polymorphism at a candidate gene locus to examine interaction with a specific nutrient (eg, saturated fat) to a more comprehensive whole genome approach analysing interactions with dietary patterns.<sup>13</sup>

More recently, new technology has enabled multiple endogenous and exogenous factors to be studied at the same time and used to predict the response to intervention. These include epigenomics, metabolomics, microbiomics (box 1), and the individual’s environment,<sup>14</sup> also known as the exposome.<sup>15</sup> The ability to measure “everything that matters” is becoming a reality with the increasing availability of fitness trackers, mobile apps, and other devices. These enable individuals to monitor continuously multiple health related factors, such as physical activity, sleep, and vital signs—for example, blood pressure, heart rate, and stress levels. The usefulness of these devices remains controversial.<sup>16–17</sup> However, in theory, such information could be used to develop algorithms that, in combination with genetic and other biological information, may provide a sound basis for personalised recommendations.

Potentially just as important is the belief that easy access to indices of health provided frequently, and in real time, will be a driver for beneficial, and sustained behaviour change. Thus, an individual will acquire data on his/her genotype and multiple phenotypic characteristics on which the personalised nutrition is based. Periodic physiological and biochemical analyses and microbiome tests will enable tracking of their health metrics in response to dietary, and other personalised, behavioural changes in real time. Relatively little has been published on the development and validation of the algorithms for personalised nutrition. The Food4Me Study published algorithms to integrate information based on current diet, phenotypic characteristics, and genotypic characteristics.<sup>18</sup> However, other approaches—for example, using machine-learning<sup>19</sup> or artificial intelligence,<sup>20</sup> might offer additional advantages.

For example, Zeevi et al<sup>21</sup> used the connection between a raised concentration of postprandial blood glucose and the risk of type 2 diabetes risk. They monitored

glucose concentrations in 800 people continuously for 1 week. They then used the variability in glycaemic response to identical test meals to devise a machine-learning algorithm that integrated blood parameters, dietary habits, anthropometrics, physical activity, and gut microbiota to predict an individual’s postprandial glycaemic response to real meals. The predictive algorithm was validated in an independent cohort (n=100). These investigators conducted a small randomised controlled dietary intervention study that suggested that personalised diets may successfully modify raised postprandial blood glucose.

The potential role of microbiome based information in developing personalised nutrition has been emphasised in more recent work from the same group. They used a small intervention study to show that an individual’s glycaemic response to a test meal can be predicted from microbiome data before the intervention.<sup>22</sup> These results highlight the importance of information about individual people in understanding the effects of dietary factors on metabolism and health. The results suggest that interindividual differences in responses to dietary challenges may be particularly informative, but we need evidence from larger scale studies to know whether such personalised interventions based on a “challenge test” offer significant advantages.

This approach was illustrated more recently by Price et al.<sup>23</sup> They collected personal data, including whole genome sequences, clinical tests, blood metabolome and proteome, physical activity, and fecal microbiome, on three occasions over 9 months from 108 people. They used these data to generate correlation networks that disclosed communities of related analytes associated with physiology and disease. They also used some of the personal data (genotype and clinical markers) to implement behavioural coaching to help participants to improve biomarkers of health. This study showed, firstly, that some highly motivated people are willing to collect personal data over extended periods; secondly, that more information can help to confirm existing knowledge about the connectedness of human physiology and to expose new connections; and, thirdly, with intense measurement in highly motivated people, “personalised coaching” may help to change behaviour. However, it is not clear how much of the detailed measurement undertaken in the study was essential in developing the “personalised coaching.” As the participants were self-selected, it is unclear whether this approach would be acceptable to larger populations.

### Personalisation based on analysis of current behaviour, preferences, barriers, and objectives

Most researchers, and other stakeholders in personalised nutrition, have focused on the capture of genotypic or phenotypic characteristics. The implicit assumption is that, the more we can measure, the more effective will be the outcomes of personalisation.<sup>24</sup> There is increasing realisation that, unlike with medication, dietary changes require individuals to make daily, sometimes hourly, choices. The adoption of these lifestyle changes (including but not limited to changes in dietary patterns) is highly dependent on effective collaboration with participants who are being helped to take responsibility for their behaviour, and, ultimately, health. Increasing technology is available that can motivate healthy eating. However, such applications usually adopt a “one-size-fits-all” approach that is biased towards specific cultures or population subgroups. Evidence suggests that it is possible to facilitate a change in behaviour using genetic testing or personalised advice as the catalysts.<sup>25 26</sup> More emphasis is needed to develop behavioural approaches that will best motivate particular individual and cultural groups.

There may be benefits in moving from a decision framework based on health professionals’ perspectives of effectiveness to one of shared decision making. An intervention based on shared decision making between the provider and the recipient becomes personalised and may increase acceptance and adherence. In this regard, the Food4Me Study stands out. It

was a randomised controlled trial (RCT) involving >1600 participants from seven European countries, which showed that personalised nutrition was more effective than a conventional one-size-fits-all approach as control (box 2).<sup>27</sup> A limitation of the study is that no information is available on outcomes beyond 6 months. However, findings from an earlier systematic review and meta-analysis suggest that, if changes are apparent at 6 months, they are likely to be sustained for at least a year.<sup>28</sup>

None the less, many questions remain, and the conceptual framework underpinning this type of personalisation is poorly defined.

### Implementation challenges

Personalised nutrition has raised expectations similar to the excitement that has surrounded other scientific developments in their early stages. Scientists working in this area have expressed concerns about overpromising,<sup>29 30</sup> individually<sup>31 32</sup> as well as through institutional guidelines and statements.<sup>33-38</sup> Highest expectations arise from the suggestion that genetic information might be used to define personalised dietary recommendations. For example, the Academy of Nutrition and Dietetics states that “nutritional genomics provides insight into how diet and genotype interactions affect phenotype. The practical application of nutritional genomics for complex chronic disease is an emerging science and the use of nutrigenetic testing to provide dietary advice is not ready for routine dietetics practice.” The consensus is that much research

is needed before personalised nutrition can deliver the expected benefits.<sup>36</sup>

*Gaps in the evidence base*—Firstly, most studies, many of which are nutrigenetic, have used retrospective or observational approaches. Those studies that have used interventions are small and have focused on intermediate biomarkers. Only a few reports have studied gene-diet interactions in large, randomised, long term dietary intervention studies with clinical events as endpoints.<sup>39 40</sup> Stronger evidence for causality may come from well designed dietary RCTs that use prospective genotyping when randomising participants to treatments, as in the FINGEN Study<sup>41</sup> (box 3). The latter study investigated the effects of supplementation with fish oil on cardiovascular risk markers. For the design and implementation of an RCT, such an approach is much less complex than trials involving whole foods or which attempt to change eating patterns. Randomised controlled trials are essential to providing proof of concept and to giving scientific credibility to the concept of personalised nutrition. We envisage that ethical providers will build delivery systems in which elements of the system are evidence based but for which it would be difficult or impossible to test the whole system with an RCT.

*Applying evidence for populations to individuals*—Most of our evidence in populations is probabilistic. The personalised nutrition approach wants to use this evidence for individuals. To take a simple example, there is evidence that an interaction between a variant in *APOA2* and intake of saturated fatty acids has an effect on obesity and, by extrapolation, on the risk of cardiovascular disease.<sup>42 43</sup> Lowering saturated fatty acid intake in those carrying this variant would be expected to lower obesity and thus the risk of cardiovascular disease in populations. However, for individuals, there is no guarantee of any benefit. This is because, in common with most health outcomes, the risk of cardiovascular disease is multifactorial and includes the effects of stochastic factors. Available evidence allows us to predict mean outcomes from a given intervention and genotype, but it is impossible to predict health outcomes for individuals. Thus, the current interest is in studies that measure multiple parameters at the same time. Alternatively, others have advocated single subject studies in personalised nutrition.<sup>44</sup> Single subject, or n-of-1, trials can potentially assess the usefulness of personalised interventions by integrating emerging technology and biomarkers.<sup>45</sup> Analytical approaches to n-of-1 studies are being developed in related fields—for example, health

#### Box 2: Food4Me Study

The Food4Me Study<sup>27</sup> is the largest randomised controlled trial to have investigated the efficacy of personalised nutrition.

The study asked two key questions:

- Is personalised nutrition more effective in changing diet than a conventional one-size-fits-all approach?
- Does the basis used for personalisation matter? (With particular interest in the benefit of personalisation based on phenotypic and genotypic characteristics)

After 6 months, the answer was clear. Personalisation of dietary advice assisted and/or motivated consumers to eat a healthier diet and follow a healthier lifestyle (in comparison with “impersonal” (conventional) dietary advice). The Healthy Eating Index was used as the global measure of “healthfulness” of eating patterns and change was measured after 3 and 6 months.

Personalisation based on analysis of current diet was more effective in assisting and/or motivating study participants to make, and to sustain, appropriate healthy changes to their usual (habitual) diet and lifestyle. However, there was no evidence of any additional benefit from using more sophisticated, and expensive, bases for personalisation, such as phenotypic and genotypic information.

The Food4Me Study was implemented as an internet based intervention to emulate commercial personalised nutrition aids. The intervention was delivered to >1600 adults in seven European countries and used several new approaches to collection and validation of data and biological samples.<sup>47-58</sup> This study provides a model for the use of the internet in delivering personalised interventions. It demonstrates the opportunities to scale up and to make potentially significant cost effective improvements in public health.

**Box 3: Personalised nutrition****Strengths**

- Interindividual variability in response to dietary factors is a real phenomenon
- Some studies have shown that personalisation results in greater improvements in diet than universal approaches
- Personalisation may foster sustained change in behaviour
- The personalised nutrition approach mirrors the rise in personalised, or precision, medicine, which is likely to drive scientific developments beneficial for personalised nutrition, and, therefore, public health

**Weaknesses**

- Scientific evidence for personalised nutrition is mostly based on observational studies with a low level of reproducibility
- The theoretical basis for personalised nutrition is underdeveloped
- The factors responsible for interindividual differences in response to dietary factors, their persistence over time within the same individual, and their heritability are mostly unknown<sup>59</sup>
- There are few well-designed randomised controlled trial that demonstrate the efficacy and safety of personalised nutrition
- Most commercial offerings in the personalised nutrition area are based on direct to consumer tests that are unregulated and have limited published evidence of benefit

**Personalised nutrition in the marketplace**

The potential market for personalised nutrition is huge. Firstly: as indicated above, it applies to both diseased and healthy people; secondly, eating is a daily activity, and thus opportunities for personalisation are continuous; thirdly, through personalisation a person may feel able to enhance or maintain health. Most commercial personalised nutrition interventions are provided directly to the consumer through the internet. The reliability of the evidence used by such companies is uncertain.<sup>52 53</sup> The business has developed without regulatory oversight, defined standards, and consumer protection.<sup>54</sup> Moreover, there are no educational resources or guidelines for how the outcomes of research into personalised nutrition should be implemented. To protect the public, advice should be based on robust scientific evidence. A framework for testing evidence for the scientific validity of nutrigenetic knowledge has been published.<sup>38</sup> It is intended to be used for developing transparent and scientifically sound advice to the public founded on nutrigenetic tests. This is based on the assumption that scientifically valid, properly regulated information delivered through the internet will be less expensive and more pervasive and may help to reduce health inequalities.

**Suggestions for the future**

Advancement of personalised nutrition will be facilitated by a number of factors. Firstly, the development of a strong theoretical basis, including identification of the most important individual characteristics on which to base personalisation. Secondly, the evidence for efficacy and cost effectiveness from well designed intervention studies. Thirdly, the introduction of a regulatory framework designed to protect the public and to give confidence to health professionals and policy makers. This will require a substantial increase in the scientific evidence. This implies:

- More robust study designs ranging from RCTs enrolling participants based on pre-selected genotypes, to n-of-1 trials and aggregated n-of-1 trials. Such research will benefit from multidisciplinary research teams, comprising, for example, behavioural psychologists, computer scientists, biomedical scientists, and nutritionists.
- Integration of other “omics” to provide greater mechanistic interpretation of the evidence. This is likely to include emphasis on epigenomics, metabolomics, and microbiomics. In this respect, proof of principle of the role of the microbiome in shaping interindividual variability in response to diet has been established.

A first step in developing guidelines for using genotype based advice in personalised nutrition has been proposed by the

psychology, and may be suitable for use in personalised nutrition.<sup>46</sup>

**Effect on health disparities**—The use of most new technology (such as n-of-1 trials) for predicting and measuring the response to specific dietary changes may be prohibitively expensive if deployed at scale.<sup>5</sup> This may increase health disparities. The challenge for research will be to define the minimum set of measurements/biomarkers that predicts individual response to personalised nutrition.

**Encouraging shared decision making**—Face-to-face consultations with a health professional or lifestyle coach might enable shared decision making, but is relatively expensive. In the Food4Me Study, personalisation was implemented by nutrition researchers<sup>52 47</sup> using decision trees. This guided the personalised advice and ensured that it was standardised across study sites. This process could be used to build algorithms that “tailor” the advice/support offered to an individual, based on preferences, barriers, ambitions, etc. Such algorithms can also incorporate techniques for behaviour change to help maximise the (health) benefit.<sup>48</sup> These algorithms could be automated and could operate in “real time” using the internet. They provide an opportunity for large scale, cost effective shared decision making that may minimise possible increases in health disparities.

**Is personalised nutrition more effective than alternative approaches?**

Despite studies supporting personalised nutrition, most evidence has come from observational studies with risk factors as outcomes, rather than from RCTs using clinical end points.

There are two key related questions. Firstly, can personalised nutrition produce

greater, more appropriate and sustained changes in behaviour than conventional approaches? Secondly, do these changes result in better health and wellbeing?

We have limited information that the answer to the first of these questions is yes.<sup>27 49</sup> However, evidence for the usefulness of communicating genetic risks of a disease itself on risk-reducing health behaviour is weak.<sup>50</sup> A recent systematic review studied genetic testing and lifestyle behaviour change. It concluded that behaviour change can be facilitated using genetic testing as the catalyst. The authors argued that to promote such change the theory of planned behaviour should be deployed when communicating the results of genetic testing.<sup>26</sup>

The second question remains unanswered. No personalised nutrition study has been carried out at a large scale, in an appropriate population group and over a sufficiently long time. For this reason, and because of the importance of lifestyle change for large sections of the population, other investigators advocate a universal, rather than targeted, approach to lifestyle intervention for disease prevention and treatment.<sup>51</sup> The logistical complexity, practical challenges, and financial costs of nutrition intervention studies with disease risk as outcomes are large and likely to be increased in personalised nutrition interventions. Thus further testing will probably use outcomes such as changes in diet, adiposity, or established biomarkers of disease such as blood pressure, HbA<sub>1c</sub>, or cognitive function. In addition, there are major opportunities to test the usefulness of personalised nutrition in the response to disease management and treatment. This would be cost effective and logistically feasible.

**Table 1 | Different levels of recommendation for women (not pregnant or lactating)**

Global recommendation	Personalised dietitian recommendation based on an individual's history and preferences	Personalised recommendation based on individual history, preferences, and genetic information
<b>Zn (8 mg/day):</b> Consume a wide variety of foods containing zinc. Red meat and poultry provide the majority of zinc in the American diet. Other good food sources include beans, nuts, certain types of seafood, whole grains, fortified breakfast cereals, and dairy products	Recommendations vary according to age, sex, pregnancy and lactation (2-13 mg). Personalisation will account for these individual characteristics. In addition, consideration should be given to: <ul style="list-style-type: none"> <li>• People who have had gastrointestinal surgery, such as weight loss surgery, or who have digestive disorders, such as ulcerative colitis or Crohn's disease. Both these conditions can decrease the amount of zinc that the body absorbs and increase the amount lost in the urine</li> <li>• Vegetarians, because they do not eat meat, which is a good source of zinc. Also, the beans and grains they typically eat contain compounds that prevent complete absorption of zinc by the body. For this reason, vegetarians might need to eat as much as 50% more zinc than the recommended amounts</li> <li>• Older infants who are breastfed because breast milk contains insufficient zinc for infants aged &gt;6 months. Infants taking formula receive sufficient zinc. Older infants who do not take formula should be given foods that contain zinc, such as pureed meats</li> <li>• Alcoholics, because alcoholic beverages decrease the amount of zinc absorbed by the body and increase the amount lost in the urine. Also, many alcoholics eat a limited amount and variety of food, so they may not get enough zinc</li> <li>• People with sickle cell disease, because they might need more zinc</li> </ul>	SLC30A8: Carriers of the A allele at the rs11558471 SLC30A8 (zinc transporter) variant need supplements containing zinc in addition to a healthy diet to maintain proper glucose homeostasis. <sup>55</sup> Knowledge of this genetic information will trigger a recommendation for Zn supplementation
<b>Dietary fat and cholesterol:</b> Choose a diet low in fat, saturated fat, and cholesterol	Use fats and oils sparingly. Use the nutrition facts label to help you choose foods lower in fat, saturated fat, and cholesterol Eat plenty of grain products, vegetables, and fruits Choose low fat milk products, lean meats, fish, poultry, beans, and peas to get essential nutrients without substantially increasing calories and intake of saturated fat	TCF7L2: For carriers of the T allele at the TCF7L2-rs7903146 polymorphism a Mediterranean diet reduces its adverse effect on cardiovascular risk factors and incidence of stroke, but not so a low fat diet. Therefore carriers of the T allele will be recommended to: <ul style="list-style-type: none"> <li>• Eat primarily plant based foods, such as fruits and vegetables, whole grains, legumes, and nuts</li> <li>• Replace butter with healthy fats such as extra virgin olive oil</li> <li>• Use herbs and spices instead of salt to flavour foods</li> <li>• Limit red meat to a few times a month</li> <li>• Eat fish and poultry at least twice a week</li> <li>• Drink red wine in moderation (optional)<sup>59</sup></li> </ul>
<b>Vitamin B2 (riboflavin):</b> Consume the appropriate recommended dietary allowance (RDA) from a variety of foods	Recommendations vary according to age, sex, pregnancy, and lactation (0.3-1.6 mg/day) Personalisation will take account of these individual characteristics. In addition, consideration should be given to: <ul style="list-style-type: none"> <li>• Vegetarian athletes, as exercise produces stress in the metabolic pathways that use riboflavin</li> </ul> People who are vegan or consume little milk, or both, are also at risk of riboflavin inadequacy	MTHFR: Carriers of the TT genotype at the MTHFR C677T polymorphism are at higher risk of hypertension, which may not reach targets (systolic blood pressure <120 mmHg) with medication. However, they particularly benefit from riboflavin supplementation (~1.6 mg/day) <sup>56</sup> SLC52A3: Brown-Vialetto-Van Laere syndrome is caused by mutations in the SLC52A3 gene, which encodes the intestinal riboflavin transporter. As a result, these patients have riboflavin deficiency. Riboflavin supplementation can be life saving in this population <sup>57</sup>

Food4Me consortium.<sup>38</sup> It will be important for research and regulatory communities to evaluate the proposed guidelines. This may lead to the development of more generic guidelines that could be valuable for national (and international) regulators. However, given the diversity of approaches to personalised nutrition, it is likely to be difficult to agree on the principles for such generic guidelines. Experience shows that commercial providers are keen to proceed before the scientific evidence is established. This would be unimportant if the commercial offerings were harmless. However, inappropriate dietary change may harm the consumer's health and finances. It will be important to find ways of curbing the more extravagant claims, which are likely to tarnish the emerging science of personalised nutrition.

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