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**Key Evidence for Personalised Nutrition: A Review of Randomised Controlled Trials**

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**Abstract:**

The field of personalised nutrition is growing and is based on the concept that delivering personalised dietary advice will be more effective than generic healthy eating guidelines for individuals to improve their diet and metabolic health. While there is substantial interest in the field, there is also a need to examine the evidence base. The objective of this review was to examine existing literature on the efficacy of personalised nutrition approaches and to identify research gaps and future needs. A literature search was conducted in PubMed for randomised controlled trials published between 2000 and 2025. Studies investigating the effects of personalised nutrition were included, and relevant papers were identified through the reference lists of existing papers. In total, 24 papers were included, with 12 studies investigating personalised nutrition based on current diet, phenotype, and metabolic biomarkers, five studies examining the effects of genotype-based personalised nutrition, and seven studies exploring approaches based on gut microbiome and machine learning algorithms. Overall, evidence from the included studies indicates that personalised nutrition approaches consistently improved dietary quality and led to significant improvements in metabolic markers, including HbA1c, triglycerides, and insulin sensitivity. However, few studies showed significant between-group differences in weight loss, and most studies did not find significant differences in blood pressure. While the results are promising, there are key challenges and research gaps that remain. Some approaches demonstrated potential for targeted improvements, but further high-quality research is needed to confirm their effectiveness and long-term impact. Future research should prioritise longer-term studies, better stratification of responders and non-responders, and cost-effectiveness evaluations to determine where and for whom personalised nutrition adds the most value.



1. INTRODUCTION

Noncommunicable diseases, including obesity, type 2 diabetes, and cardiovascular disease, account for nearly two-thirds of global deaths, with healthier diets being a key recommendation for prevention and management.<sup>1, 2</sup> Despite well-established national dietary guidelines that emphasise the importance of a varied and balanced diet, a substantial proportion of the population continues to fall short of these recommendations, particularly regarding fruit and vegetable intake.<sup>3</sup> This gap between dietary guidance and actual dietary behaviour underscores an urgent need for more effective nutritional strategies to improve public health outcomes.

A promising strategy to address this challenge is personalised nutrition, which tailors dietary advice to individual characteristics and needs, such as metabolic profile, genetics, lifestyle and environmental factors.<sup>4</sup> Growing evidence indicates substantial inter-individual variability in responses to identical meals.<sup>5, 6</sup> Studies like The Personalized Nutrition Project and the Predict 1 study have demonstrated that individuals consuming the same food exhibit markedly different postprandial glycaemic and lipid responses.<sup>6, 7</sup> Consistent with these findings, a recent study reported that seven standardised carbohydrate meals elicited postprandial glycaemic responses that were reproducible within individuals but highly heterogeneous between individuals.<sup>5</sup> This variability in dietary responses is determined by a complex interplay of genetic, metabolic, microbiome, circadian, and behavioural factors, including physical activity, sleep, and meal timing.<sup>8</sup> Harnessing this variability is a promising approach for delivering personalised dietary advice. Concomitant with this is the more widespread use of omics technologies such as metabolomics and metagenomics.<sup>9</sup> Combining these with wearable biosensors and machine learning algorithms is driving a paradigm shift in healthcare, industry and nutritional science.<sup>10</sup>

However, some criticism exists of the field with a number of key questions remaining. An example is the lack of evidence that adherence to the personalised diets compared to adherence to control diets results in improvements in diet and metabolic health parameters. Furthermore, there is no clear indication on the effect size of personalised dietary advice on the outcome variables. Despite these and other concerns there is growing interest in the area and whether it can be moved into clinical practice. As this field of personalised nutrition continues to evolve, rigorous research through randomised controlled trials remains essential to validate emerging interventions and understand their impact on health outcomes. Thus, the objective of this review is to synthesise existing literature on the efficacy of various personalised nutrition approaches and to identify research gaps and future needs in the field.



## 2. METHOD

### 2.1. Search strategy

A search was performed in PubMed for studies published up to June 2025. The inclusion of studies was determined according to the Population, Intervention, Comparison, Outcome and Study (PICOS) framework (**Table S1**). Briefly, human studies ( $\geq 18$  years) that collected personalised information and then used that data to provide dietary advice are included. To find relevant studies, the following key terms were used: "*Personalised nutrition*" OR "*Personalized nutrition*" OR "*Precision nutrition*". Relevant articles were identified through the reference list of the existing papers. The search was restricted to include only randomised controlled trials. Primary and secondary outcomes were extracted from each included study and are presented in summary tables.

## 3. RESULTS

The search yielded 111 articles, of which 33 were excluded based on title or abstract screening. A total of 78 full-text articles were retrieved, and 56 were excluded due to a lack of focus on a personalised nutrition intervention. In total, 24 articles were included in this review. Of the included articles, two relevant papers were found through the reference list of the existing papers. A flow chart of the search and study selection is shown in **Figure S1**. The included studies were grouped into three categories: (1) Studies that delivered personalised nutrition interventions based on one of the following: dietary intake, phenotype data and metabolic biomarkers. (2) Studies that delivered genotype-based personalised nutrition. (3) Studies that employed gut microbiome and machine learning algorithms to deliver dietary advice.

Of the 24 studies included, the sample size varied from 23 to 1607 participants, with an age range of 18 to 80 years. Most studies enrolled generally healthy adults or individuals with overweight, obesity, prediabetes, or metabolic risk factors. Trials were conducted across North America (USA, Canada), Europe (e.g., Denmark, Spain, UK, Ireland, France, Netherlands), Asia (India, Israel), and Australia. Study durations ranged from short-term (2-3 weeks) to longer interventions lasting up to 12 months. Comparator arms typically included standard population-level dietary advice, Mediterranean-style diets, low-fat diets, or general health information. Some used placebo controls (e.g., micronutrient supplementation), while others used non-personalised versions of the same digital tools or dietary programs. Primary outcomes were diverse and included diet quality or adherence scores, weight loss or body composition, glycaemic control (HbA1c, fasting glucose, PPGR), lipid profiles, metabolic biomarkers (e.g., insulin, CRP), and psychosocial outcomes such as health behaviours or perceived control.



3.1. Studies delivering personalised advice based on dietary intake, phenotype data and/or metabolic biomarkers

All 12 studies using dietary intake, phenotype data and/or metabolic biomarkers to tailor dietary advice are presented in **Table 1**. A total of five studies used a combination of different data to personalise the dietary advice. A 10-week randomised controlled trial (Preventomics) found that personalised nutrition based on biomarker-driven clustering did not result in significantly greater weight loss or fat mass reduction compared to a standardised diet.<sup>11</sup> Metabolic clusters were primarily defined by metabolomic profiles from blood and urine, with single-nucleotide polymorphism data used as a secondary input. Furthermore, no differences were observed between groups in improvements in insulin resistance or lipid profile. The preventomics e-commerce study involving 193 participants compared two personalised, omics-based Mediterranean diets with a standardised Mediterranean diet.<sup>12</sup> The personalised diets were tailored using integrated data, primarily metabolomics and proteomics, with genetic information used as a complementary factor. Over the 21 weeks, the study observed no significant differences between groups in Mediterranean dietary adherence or clinical health outcomes, including body weight, blood pressure, lipid profiles, glucose levels or inflammatory markers.

The Food4Me study examined delivery of personalised advice at different levels: dietary intake alone, dietary intake plus phenotype, and dietary intake plus phenotype and genotype.<sup>13</sup> Following the six-month intervention period, all three intervention groups showed greater improvements in dietary intake, including reduced consumption of red meat, salt, and saturated fat, as well as higher Healthy Eating Index scores, compared to those receiving standardised dietary advice. However, incorporating phenotypic or genotypic data did not further enhance the effectiveness of the personalised nutrition approach. In an older adult group ( $67.7 \pm 4.8$  years), personalised nutrition tailored using biomarkers, dietary intake and genetic information was compared with generic lifestyle advice.<sup>14</sup> After the nine-week intervention the personalised nutrition group showed improvements in body composition and certain aspects of wellbeing, such as motivation and resilience. However, there were no substantial short-term benefits in overall self-perceived health or well-being compared to the control group. Furthermore, an 18-week randomised controlled trial observed that personalised nutrition advice tailored to each participant's dietary intake, anthropometrics and metabolic biomarkers improved adherence to dietary intake for several food groups compared with generic dietary advice or no advice.<sup>15</sup> Additionally, within the personalised advice group, participants who set specific goals, such as increasing whole-grain and unsalted-nut intake, achieved a significantly greater reduction in LDL-cholesterol levels than those who did not set such goals.

A total of four studies focused predominantly on dietary intake or nutrient status to deliver the personalisation. Personalised micronutrient supplementation based on blood levels of selenium, zinc, and vitamin D did not improve the incidence or severity of upper respiratory tract infections, compared to a placebo group in an 18-week randomised controlled trial.<sup>16</sup> In a 12-week randomised controlled trial, participants were assigned to either a personalised nutrition group receiving dietary feedback, self-monitoring, and dietitian coaching or a control group receiving web-based feedback only.<sup>17</sup> Following the study period, the intervention group





showed greater improvements in dietary intake compared to the control group, including increased consumption of meat, vegetarian alternatives, and dairy, along with reduced intake of energy-dense and nutrient-poor foods. In the EatWellUK study, the effectiveness of personalised nutrition based on dietary intake delivered via a web-based app was compared to standard dietary advice without personalised feedback.<sup>18</sup> The intervention led to significant improvements in diet quality over 12 weeks with increased intake of nuts and legumes, and reduced red and processed meat consumption. At follow-up, 64% of participants reported continuing to follow some of the dietary advice, and 31% remained motivated to improve their diet. In a randomised controlled trial, 127 older adults (50-80 years) received either a precision nutrition strategy featuring personalised food products and digital tools or standard dietary advice.<sup>19</sup> At three-month follow-up, improvements in metabolic health were observed in both groups. However, the precision nutrition approach demonstrated significantly greater reduction in body weight, BMI, blood pressure, HbA1c, and liver function parameters (ALT and AST) compared with standard advice.

The remaining three studies delivered personalised dietary advice based on assessment, predominantly of phenotypic and metabolic data. Using a metatype approach, the Metabodiet study demonstrated that personalised advice improved overall diet quality and led to favourable changes in metabolic health biomarkers, including reduction in total cholesterol, LDL-cholesterol, triacylglycerol and the triglyceride-glucose index, compared with generic advice.<sup>20</sup> The metatype approach classified the intervention group based on four biomarkers (triacylglycerol, high-density lipoprotein-cholesterol, total cholesterol and glucose) and delivered advice based on the metabolic characteristics. In the PERSON study, tailoring diets to tissue-specific insulin-resistance phenotypes significantly improved cardiometabolic health.<sup>21</sup> Muscle insulin-resistant individuals exhibited the most significant response to a low-fat, high-protein, high-fibre diet. In contrast, liver insulin-resistant individuals improved most on a high-monounsaturated fat diet. These targeted diets resulted in greater improvements in insulin sensitivity, fasting insulin, 2-hour glucose and insulin, triacylglycerol, and C-reactive protein independent of weight loss. During a 12-month randomised controlled trial, breast cancer survivors in post-surgical menopause received personalised nutrition based on body composition and inflammation markers, while the control group received no dietary advice.<sup>22</sup> The intervention resulted in significant reductions in insulin and subcutaneous adipose tissue.

### 3.2. Genetic-based personalised nutrition

All five studies presented in **Table 2** focused predominantly on genetic-based personalised nutrition. The NOW study, a 12-month randomised controlled trial involving 140 participants, compared the effects of genetically personalised lifestyle advice with a population-based lifestyle programme.<sup>23</sup> The intervention was tailored to participants' genetic profiles, particularly focusing on FTO gene variants associated with nutrient metabolism, physical activity responsiveness and weight regulation. In contrast to the control group, which exhibited only short-term improvements, the intervention group demonstrated sustained enhancements in attitudes, subjective norms, and perceived behavioural control. These enduring improvements in key psychological constructs were observed alongside significant short- to



mid-term reductions in body fat percentage, as well as improved perceptions of friends and family members healthy eating behaviours (subjective norms). A randomised controlled trial (ASPIRE-DNA) aimed to assess the genetic dietary advice, informed by single-nucleotide polymorphisms, for non-diabetic hyperglycaemia over 26 weeks.<sup>24</sup> At the 6-week stage, fasting plasma glucose levels were not significantly different between the intervention group and the control group (who followed standard dietary advice). However, at 26 weeks follow-up, both the intervention and an exploratory arm (genetic-based dietary advice using an app and wearable device) resulted in a significant reduction in fasting plasma glucose compared to the control group.

In a randomised controlled trial of 138 participants, precision nutrition advice, based on genetic risk variants associated with metabolic syndrome and vitamin D metabolism, did not result in greater weight loss compared to standardised dietary advice.<sup>25</sup> Waist circumference decreased more in males in the intervention group, but no other anthropometric or metabolic markers showed significant changes. In a randomised controlled trial, participants who received DNA-based personalised nutrition advice did not exhibit significant dietary changes at 3 months compared to those given standard dietary advice.<sup>26</sup> However, at 12 months, individuals carrying the risk allele of the angiotensin-converting enzyme gene who were advised to limit sodium intake to  $\leq 1500$  mg/day showed a significant reduction in sodium consumption. No significant genotype-specific effects were observed for caffeine. A 12-week randomised controlled trial investigated whether providing females with their personal FADS1 genetic information would influence omega-3 fatty acid intake and blood levels.<sup>27</sup> The control group received general written information about omega-3 fatty acids recommendations. Both groups significantly increased their intake of EPA and DHA; however, receiving genetic information did not lead to greater changes compared to the control group.

3.3. Algorithm-recommended personalised diet

All seven studies presented in **Table 3** employed gut microbiome and machine learning to deliver dietary advice. Notably, four of the seven studies are based on a similar algorithm that emerged from the initial Personalized Nutrition Project.<sup>7</sup> The original algorithm was trained on data from 800 individuals and validated both by cross-validation and in an independent cohort of 100 participants to predict personalised postprandial glycaemic responses. Its utility was further tested in a randomised controlled trial in adults with prediabetes, which algorithm-guided dietary intervention significantly improved glycaemic outcomes compared with a Mediterranean diet.<sup>28</sup> Both diets improved glycaemic control, but the personalised diet led to significantly greater reductions than control diet in daily time spent with glucose above 140 mg/dL (1.3 vs 0.3 h/day) and in HbA1c (0.16% vs 0.08%). No significant difference was observed in glucose tolerance between groups. Using a similar approach in individuals with prediabetes, 156 participants were randomised to either a personalised, algorithm-recommended diet or a standardised low-fat diet.<sup>29</sup> Over six months, both groups showed reductions in glycaemic variability, along with modest declines in HbA1c and improvement in other glucose monitoring metric, including mean glucose and glucose standard deviation. However, no significant between-groups differences were observed for glycaemic outcomes or





HbA1c. Applying the original algorithms to an American population group with the focus on weight loss revealed that the personalised approach did not lead to a significant difference in weight loss compared to a low-fat diet.<sup>30</sup> This highlights the need to ensure that algorithms are trained on the desired outcome and population characteristics to which they are implemented in. Finally, in adults with newly diagnosed type 2 diabetes a personalised postprandial glucose-targeting diet significantly outperformed a standard Mediterranean diet in a two-week crossover trial.<sup>31</sup> In a subsequent six-month intervention with the personalised diet alone, participants showed significant improvements in glycaemic control, insulin sensitivity, and triglyceride levels, with 61% achieving diabetes remission (HbA1c<6.5%). However, this six-month intervention lacked a control diet.

In the ZOE METHODS study, participants were randomised to receive either a personalised dietary program, integrating individual postprandial glycaemic and lipemic responses, microbiome composition, dietary intake and health history delivered via an app, or standard dietary advice over 18 weeks.<sup>32</sup> Following the intervention, the personalised nutrition group exhibited a significant reduction in triglyceride levels, whereas changes in low-density lipoprotein cholesterol were not significant. The personalised program also led to greater reduction in weight, waist circumference, HbA1c and greater improvement in diet quality compared with standard dietary advice, whereas blood pressure and fasting glucose did not differ between groups. In a randomised controlled trial, adults with type 2 diabetes and hyperlipidaemia received either a microbiota-based personalised dietary intervention or standard diabetic dietary advice.<sup>33</sup> The personalised group showed a significant reduction in HbA1c levels. However, only within group comparisons were reported. No significant between group differences were observed for LDL, HDL or triglyceride levels.

#### 4. DISCUSSION

Our comprehensive analysis of the randomised controlled trials investigating approaches to deliver personalised dietary advice has highlighted a large diversity in the approaches used and outcomes measured. Overall, the review indicates that personalising dietary advice consistently improved diet quality and, in some studies also improved metabolic health parameters. However, some key research questions remain to be answered in order to reach strong clear conclusions in relation to precision nutrition and for the field to reach its full potential.

Most of the included studies used an integrated approach, combining several individual-level factors, such as metabolomics, genotyping and phenotyping, to provide personalised dietary advice. While the majority of these studies reported significant improvements when compared with generic approaches, there is a need to understand which information contributed to the improved outcomes. To address the added benefits of each personalised component, future studies should consider incorporating more nuanced and stratified control groups. Many studies combined multiple data types, opening questions about the cost-effectiveness of the approach. The original Food4Me study demonstrated that personalisation based solely on diet was as effective as the approaches incorporating phenotype and genotype.<sup>13</sup> Furthermore, an approach using metabotyping based on common clinical biomarkers demonstrated a clear



benefit on diet quality and metabolic health markers, making it attractive from a cost-effectiveness viewpoint.<sup>20</sup> These findings support the need for the development of simpler, phenotype-driven approaches combined with support by dietitians or nutritionists, as an effective strategy in changing diet and improving metabolic marker outcomes.

Current evidence suggests that genotype-based nutrition interventions, when delivered in isolation, have a limited and inconsistent effect on clinical and behavioural outcomes, such as weight loss, dietary intake or metabolic markers.<sup>25, 26</sup> While genetic information may prompt short-term interest or modest dietary adjustments, sustained change appears to require structured support. For instance, studies that included behavioural factors, such as those informed by the Theory of Planned Behaviour or incorporating regular counselling, consistently demonstrated greater improvements in engagement, self-efficacy and longer-term adherence.<sup>23, 24</sup> For example, in one of the studies, participants in the personalised nutrition group who set specific goals, such as increasing whole-grain and unsalted-nut intake, achieved significantly greater reduction in LDL-cholesterol underscoring the added value of structured goal-settings<sup>15</sup>. Moreover, the reviewed trials also indicate that increasing the complexity or breadth of genetic information does not necessarily enhance efficacy, underscoring the importance of targeting gene-diet interactions that are relevant to individual risk profiles. Overall, results indicate that genotype alone is not an effective approach for delivery of personalised nutrition. However, its impact is significantly enhanced when integrated into broader, behaviourally informed personalised nutrition frameworks.

The review provides emerging evidence for the effectiveness of machine learning driven personalised nutrition approaches in improving glycaemic outcomes. Overall, four out of five studies reviewed that specifically targeted glycaemic measures demonstrated significant improvements, including reductions in HbA1c, postprandial glucose, and CGM-derived metrics.<sup>7, 28, 31, 32</sup> This consistency across varied populations and study designs strengthens confidence in the clinical relevance of this approach. The one study that did not report superior glycaemic outcomes compared to a standard dietary intervention still observed within-group improvements<sup>29</sup>, suggesting that factors such as algorithm accuracy, intervention duration, individual variability and the choice of the control group may influence effectiveness. The findings underscore the potential of algorithm-based personalisation to support glycaemic control in individuals at metabolic risk. However, a key question emerging from these studies is which specific input features are most influential in driving improvements in clinical parameters. Identifying the most predictive inputs and understanding their underlying mechanisms could inform algorithm refinement and enable more precise, targeted dietary interventions. Furthermore, there is a need to demonstrate that these machine learning-based algorithms are delivering more than low carbohydrate dietary advice and that individuals receive different patterns of dietary advice. The suitability of these diets for long-term adherence is also lacking.



#### 4.1. Research Gaps and Future Needs in Personalised Nutrition

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Despite significant progress in personalised nutrition research, several critical research gaps and challenges remain. Most studies to date have been conducted in small and relatively homogenous populations, which restricts generalisability across diverse populations. Additionally, many interventions are short-term, often lasting only weeks or months, limiting assessment of long-term efficacy and adherence. This may also partly explain the less consistent findings across the included trials for outcomes such as weight loss and blood pressure, which are influenced by multiple determinants beyond dietary composition and show substantial within and between individual variability.<sup>34</sup> Detecting meaningful between differences in these endpoints may therefore require larger samples size and longer follow up. Furthermore, behavioural and psychological determinants such as motivation, digital literacy, and readiness to change are rarely measured, despite their known influence on dietary adherence.<sup>23</sup> Methodological limitations also include the use of generic control groups, which may not adequately isolate the effects of personalisation. The optimal choice of a comparator group is not easy and may require more than a single control group to adequately capture differential responses. In certain cases, a factorial design or multi-arm trial may be necessary not only to compare personalised dietary approaches with standard dietary advice but also to isolate the effects of individual intervention components and evaluate their potential interactions. Additionally, the reproducibility and long-term stability of algorithm-based dietary advice remain largely untested, raising concerns about their consistency and biological relevance.<sup>7</sup> To be effective, machine learning algorithms need to demonstrate that individuals are receiving truly personalised advice and that it leads to measurable health outcomes. This requires not only tailoring advice to individual characteristics but also subjecting these recommendations to systematic evaluation. Overall, to date the results from published studies reported no adverse effects, suggesting that personalised dietary advice is unlikely to pose long-term risks. However, extended follow-up is necessary to confirm its long-term safety and efficacy. Finally, considerations of sustainability and environmental impact remain largely absent from personalised nutrition frameworks, despite their critical importance for ensuring long-term viability, equitable access, and the resilience of global food systems.

To realise the clinical potential and public health value of personalised nutrition, future research must prioritise rigorous, long-term randomised controlled trials. These studies should assess whether personalised approaches offer advantages over optimised generic diets, such as the Mediterranean or DASH diets, in improving cardiometabolic outcomes. Moreover, future trials must control for intensity of behavioural support and blinding, as unbalanced study designs risk overestimating personalised nutrition benefits due to placebo or engagement effects. A key concern previously raised is that many existing algorithms provide similar advice across individuals, often recommending lower carbohydrate or higher fibre diets, regardless of complex input variables like genotype or microbiome profile<sup>35</sup>, which raises questions about the distinctiveness and reproducibility of personalised nutrition advice. As such, within-subject repeatability testing and comparative effectiveness studies are crucial to validate whether personalised recommendations truly differ between individuals and meaningfully impact outcomes. Most personalised nutritional trials to date lack demographic diversity, with participants skewing towards European and North American ancestry, higher socioeconomic



status, and lower comorbidity profiles. Diverse recruitment, across age, ethnicity, gender, health status, and socioeconomic backgrounds, will be critical for identifying differential responses and ensuring real-world applicability. Consistent with our findings, a previous systematic review reported that interventions relying solely on genotype data produced inconsistent results.<sup>36</sup> This highlights the need for future models to focus on mechanistic insights derived from systems biology and to investigate which combinations of clinical, behavioural, and biological inputs most effectively predict dietary responses. As machine learning algorithms become more central to personalised nutrition, transparency is paramount. The “black box” nature of machine learning models obscures which variables drive dietary recommendations, limiting understanding of key predictive features. Developing interpretable models with clear and reproducible decision pathways will be essential for the broader implementation of personalised nutrition, including its integration into both clinical practice and public health strategies.

**5. CONCLUSION**

In conclusion, personalised nutrition interventions are a promising approach to improving diet-related behaviours and certain health outcomes. Compared to standard dietary advice, personalised strategies, tailored to individual characteristics often led to better adherence to healthy eating and improvements in specific biomarkers. However, the overall benefits compared to standard dietary advice were often small or inconsistent, especially for outcomes like weight loss or long-term health effects. While some personalised methods, particularly those using digital tools and machine learning, show potential for more targeted improvements, further high-quality research is needed to confirm their effectiveness and long-term impact. Future research should prioritise longer-term studies, better stratification of responders and non-responders, and cost-effectiveness evaluations to determine where and for whom personalised nutrition adds the most value.



400 **Conflicts of Interest**

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401 There are no conflicts to declare

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**Table 1:** Personalised Nutrition Interventions based on Dietary Intake, Phenotype, and/or Metabolic Biomarkers

Author, y (Country, study)	Methods (RCT, duration)	Population (N, age, health)	Intervention Group (Approach, delivery)	Control Group (Approach, delivery)	Outcomes (Primary; secondary)	Main Results (Intervention group (PN), control group (CG), $p>0.05$ )
Aldubayan et al., 2022 <sup>11</sup> , Denmark  The Preventomics Study	Parallel, double- blinded, 10 weeks	N=100; 18-65 y., Healthy adults with BMI $\geq 27$ - <40 kg/m <sup>2</sup>	Personalised nutrition based on metabolomics and genotyping, 60% of meals provided, e-health behaviour app with personalised prompts	Generic dietary advice, similar food provided (60%), generic health prompts via app	Fat mass change  Weight loss, metabolic markers	No significant difference between PN and CG: Fat mass $\downarrow$ 2.1 kg (PN) vs $\downarrow$ 2.0 kg (CG), $p=0.77$ .  Body weight $\downarrow$ 3.1 kg (PN) vs. $\downarrow$ 3.3 kg (CG), $p>0.05$ . Both improved insulin resistance and lipid profiles, but differences between groups were not significant.
Calderón- Pérez L. et al. 2024 <sup>12</sup> , Spain  Preventomics E-Commerce Study	Parallel, single- blinded, three arms, 21 weeks	N=193; $\geq 18$ y., Healthy adults	Personalised nutrition based on omics (genetics, metabolomics, proteomics). Personalised Plan: Same personalised advice plus behavioural change support. Delivered via a digital tool for tailored grocery selection	Mediterranean diet recommendations via the same digital tool without personalisation	Diet adherence (MEDAS)  Biometric, dietary habits, metabolic markers	All groups: $\uparrow$ MEDAS scores, but no significant group differences in MEDAS or conventional clinical markers.  No significant dietary habit differences between groups, but the PN groups showed selective biomarker improvements (e.g., inflammation, oxidative stress) compared with CG (FDR<0.05).
Celis-Morales et al, 2017 <sup>13</sup> , Seven European countries  Food4Me	Four- arms, 6 months	N=1607; 18-79 y., mixed health status, 46% overweight or obese	Three levels PN approach: L1: Diet only L2: Diet + phenotype L3: Diet + phenotype + genotype - Delivered via website reports	Standard dietary advice based on European guidelines (L0); also, web based	Dietary intake  Anthropometrics (BMI, WC), blood biomarkers	PN groups: $\downarrow$ red meat (-5.48g/day, $p=0.046$ ), $\downarrow$ salt (-0.65g/day, $p=0.002$ ), $\downarrow$ saturated fat (-1.14% $\downarrow$ energy, $p<0.0001$ ), and $\uparrow$ folate (+29.6 $\mu$ g/day, $p=0.048$ ), and $\uparrow$ Healthy Eating Index (+1.27, $p=0.010$ ). No additional benefit from phenotype or genotype-approach vs. diet only.
Doets et al., 2019 <sup>14</sup> , Netherland	Single- blinded, 9 weeks	N=59; $\geq 60$ y., Healthy older adults	Tailored dietary advice based on metabolic, genetic, dietary, and psychological data; online delivery + behavioural support	Generic advice: national guidelines via leaflet	Self-perceived health  SPPB, anthropometry, grip strength	No significant group differences ( $p >$ 0.05).  Both groups: $\uparrow$ physical performance (SPPB) PN: $\downarrow$ body fat %, $\downarrow$ WC, $\sim$ grip strength GA: $\uparrow$ body fat %, $\sim$ WC, $\sim$ grip strength



Galarregui et al., 2024 <sup>19</sup> , Spain	Parallel-group, 3 months	N=127; 50-80 y., Healthy older adults with overweight or obesity and ≥1 dysglycemia risk factor	Precision nutrition strategy including a personalised Mediterranean-based diet with individualised functional foods + use of a digital mobile app for guidance, support, and monitoring; in-person dietitian consultations	Generic advice: Delivered via online group sessions	Metabolic Health score  Body composition, biochemical markers, QoL (SF-36)	No significant group differences in metabolic health score ( $p>0.05$ ).  Both groups: ↓ triglycerides, ↓ uric acid, ↑ Mediterranean diet adherence, ↓ weight PN: ↓ body fat %, ↓ WC, ↓ HbA1c, ↓ ALT/AST, ↑ QoL (SF-36) CG: ~ body fat %, ~ WC, ~ HbA1c, ~ QoL (SF-36)
Haas et al., 2024 <sup>16</sup> , Germany	Double-blind, placebo-controlled intervention study, 18 weeks	N=59; 18-65 y., Healthy adults	Individualised supplementation based on dried blood spot analysis of selenium, zinc, and vitamin D levels; Delivered as a personalised powder supplement taken daily	Placebo powder (no micronutrients); daily intake	Correction of micronutrient deficits, frequency of URIs, Severity and duration of URIs	PN group normalised micronutrients (vitamin D significant). 16 URIs (9 PN, 7 CG). PN had higher URI severity, but no difference in duration. Overall, no effect on URI incidence or severity.
Hillesheim E. et al., 2023 <sup>20</sup> , Ireland  Metabodiet	Single-blind, Parallel trial, 12 weeks	N=107; 18-65 y., Healthy adults	Personalised nutrition via metabotype framework; dietary advice based on TG, HDL, TC, glucose and personal traits; reports at baseline and week 4	Population-level advice based on national guidelines; same format reports at weeks 0 and 4	Dietary quality (AMED score)  Lipid profile, glucose, insulin, blood pressure	Significant improvements in PN group vs CG ( $p<0.05$ ): PN: ↑AMED +12%, ↓TAG, ↓TC, ↓LDL, ↓TyG index; CG: minor improvements.  No significant weight or BP changes.
Hoevenaars et al., 2020 <sup>15</sup> , France	Parallel trial, 18 weeks (9 wk run in + 9 wk intervention)	N=155; 25-70 y., Healthy adults, BMI 20-35 kg/m <sup>2</sup>	Personalised nutrition based on metabolic, anthropometric and dietary intake data; delivered via web portal with three dietitian phone calls	No advice (habitual lifestyle) or generic dietary guideline leaflet	Nutrition Intake Status (NIS)  LDL cholesterol, other health biomarkers	PN group: ↑ fruits, whole grains, nuts, fish, ↓ added salt and sugar-sweetened beverages compared with controls ( $p<0.05$ ).  Within the PN group, LDL cholesterol decreased significantly more in goal-setters for whole grains and nuts than in non-goal setters. No significant between-group differences in health biomarkers overall.
Rollo M. E. et al., 2020 <sup>17</sup> , Australia	12 weeks	N=50; mean age 39.2 y., Healthy adults	High personalisation (HiP), involving structured video calls plus dietary self-monitoring with text	Low personalisation (LoP), comprising a web-based personalised nutrition feedback report	Diet quality score (ARFS),	HiP group: ↑ overall diet quality (ARFS +5.6 points), ↑ variety in meat, vegetarian options, and dairy, and ↓ energy from unhealthy foods by 7.2%, ↑ core food





			personalised message feedback		Energy intake from healthy and unhealthy foods	intake and ↓ takeaway consumption, with significant changes in 12 dietary variables vs. 1 in the LoP group.
Sturgeon K. et al., 2018 <sup>22</sup> , USA	12 months	N=35; 18-55 y., BRCA1/2+ breast cancer survivors, surgically induced menopause before age 45	Personalised nutrition-based phenotype and biomarkers (Subcutaneous adipose tissue, insulin levels and TNF-alpha): - Web-based lifestyle modification combining dietary changes and exercise; personalised guidance.	No dietary advice, maintained usual activity	Fasting insulin, inflammatory markers, body composition  Correlations between biomarkers and body fat	PN: ↓ fasting insulin; ↓ SAT; VAT unchanged; ↓ TNFα; IL-6 unchanged. CG: ↑ fasting insulin; no significant changes in other measures.  Correlation: 10% reduction on TAT associated with 9% decrease in insulin.
Trouwborst I. et al., 2023 <sup>21</sup> , the Netherlands,	Parallel, double- blinded, 12 weeks	N=242; 40-75 y., adults with overweight or obesity with tissue-specific insulin resistance - either muscle insulin resistance (MIR) or liver insulin resistance (LIR)	PhenoDiet Group B: - MIR: low-fat, high-protein, high-fibre (LFHP) diet - LIR: high-monounsaturated fatty acid (HMUFA) diet Weekly dietary counselling, isocaloric diets, food provision	PhenoDiet Group A: - MIR: HMUFA diet - LIR: LFHP diet Same counselling and food support as intervention group	Disposition Index  Fasting insulin, 2h glucose, insulin, HOMA- IR, Matsuda index, MISI, CRP, TAG, body fat, liver fat, glucose variability, QoL	No significant difference in disposition Index between groups ( $p=0.109$ ).  Greater improvements in PN vs CG for: Fasting insulin, 2h glucose/insulin, HOMA-IR, Matsuda index, MISI (all $p<0.05$ ). CRP ( $p=0.034$ ), TAG ( $p=0.028$ ). Similar weight and liver fat reduction in both groups. No significant difference in glycaemic variability or quality of life ( $p>0.05$ ).
Zenun F. et al., 2022 <sup>18</sup> , UK	Single- blinded, 12 weeks	N=210; ≥ 18 y., Healthy adults	Personalised nutrition via the eNutri web app; automated, tailored advice based on m- AHEI diet quality score, with feedback on top 3 weakest components, BMI, and physical activity	Generic advice based on UK guidelines; delivered via the same app without personalisation during the intervention	Change in diet quality (m- AHEI),  BMI, Physical activity	PN: ↑ diet quality score by + 3.5 points ( $p=0.003$ ); ↑ nuts and legumes ( $p=0.04$ ) and ↓ red/processed meat ( $p=0.04$ ); No significant change in BMI or overall, physical activity.

566 **Abbreviations:** AMED, Alternate Mediterranean Diet Score; ARFS, Australian Recommended Food Score; BMI, body mass index; CG, control group; CRP,  
567 C-reactive protein; eNutri, electronic nutrition (app); FI, fasting insulin; FPG, fasting plasma glucose; GA, generic advice; HbA1c, glycated haemoglobin; HDL,  
568 high-density lipoprotein; HiP, high personalisation; HMUFA, high-monounsaturated fatty acid diet; HOMA-IR, homeostatic model assessment of insulin  
569 resistance; IL-6, interleukin 6; LFHP, low-fat, high-protein, and high-fibre diet; LIR, liver insulin resistance; LDL, low-density lipoprotein; LoP, low  
570 personalisation; MEDAS, Mediterranean Diet Adherence Screener; MIR, muscle insulin resistance; MISI, muscle insulin sensitivity index; m-AHEI, modified



571 Alternate Healthy Eating Index; NIS, Nutrition Intake Status; PN, personalised nutrition; QoL, quality of life; TAT, total adipose tissue; SF-36, 36-Item Short  
 572 Form Health Survey; SPPB, Short Physical Performance Battery; TAG, triacylglycerol; TC, total cholesterol; TG, triglycerides; TNF $\alpha$ , tumour necrosis factor  
 573 alpha; TyG index, triglyceride-glucose index; URI, upper respiratory infection; VAT, visceral adipose tissue.

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575 **Table 2:** Personalised Nutrition Interventions based on Genetic

Author, y (Study, country)	Methods (RCT design, duration)	Population (N, age, health)	Intervention Group (Genotype assessed, delivery)	Control Group (Approach, delivery type)	Outcomes (Primary, secondary)	Main results (Intervention group (PN), control group (CG), $p > 0.05$ )
Horne J.R. et al., 2020 <sup>23</sup> , Canada,  NOW trial	Parallel- group, pragmatic, cluster, 12 months	N=140; $\geq 18$ y., Adults with BMI $\geq 25$ kg/m <sup>2</sup> ; predominantly middle-aged, Caucasian females	Genetic-based advice (FTO rs9939609) integrated into Group Lifestyle Balance (GLB+LGx), plus personalised genomics report and dietitian counselling	Standard population- based advice	Theory of Planned Behaviour: attitudes, subjective norms, perceived behavioural control	PN: $\uparrow$ attitudes, $\uparrow$ subjective norms, $\uparrow$ perceived behavioural control (sustained); $\uparrow$ perceptions of family support for PA/nutrition; $\downarrow$ fat intake; improved body composition ( $p < 0.05$ ). CG: Short-term improvements only; effects diminished by 12 months. No significant differences in weight or physical activity levels between groups.
Karvela M. et al., 2024 <sup>24</sup> , UK,  ASPIRE-DNA study	Open-label, three arms (Control, Intervention, Exploratory), Follow-up: 26 weeks	N=148; mean 59 y., Adults with non- diabetic hyperglycaemia	Genotype assessed: SNPs linked to T2DM, obesity, cholesterol, hypertension (e.g. rs7903146, rs699); Delivery: dietitian-guided sessions or self-guided app with wearable device	Standard advice, dietitian counselling without DNA personalisation	Change in fasting plasma glucose (FPG) at 6 weeks  FPG, HbA1c, weight, BMI, BP, cholesterol, glucose tolerance, dietary intake	No significant difference in FPG at 6 weeks ( $p = 0.28$ ). At 26 weeks: FPG significantly reduced in PN group ( $-0.019$ mmol/L, $p = 0.01$ ) and Exploratory ( $-0.021$ mmol/L, $p = 0.006$ ) vs CG. HbA1c reduced in PN group ( $-0.038$ mmol/mol, $p = 0.04$ ); no significant change in Exploratory ( $p = 0.4$ ). Small effect on progression to T2DM ( $p = 0.06$ ). Weight and BMI changes were not statistically significant.
McCarthy et al., 2023 <sup>25</sup> , USA	Two-arm prospective, non-blinded 12 weeks	N=107; mean age 31, active- duty military personnel at risk for MetS	Genotype-advice, incorporating 80 SNPs across 70 genes linked to metabolic syndrome and vitamin D metabolism. Delivered by dietitians through six weekly	Standardised educational materials on MetS prevention (no counselling) + app	Weight change  Body composition, BP, serum biomarkers,	No significant weight difference between groups, $p = 0.27$ .  MetS prevalence $\downarrow$ (27% $\rightarrow$ 17.8%, $p = 0.05$ ); WC $\downarrow$ more in intervention





			sessions (in-person/telehealth) + app		MetS criteria, app adherence	males ( $p=0.015$ ); other outcomes no significant difference.
Nielsen D.E. and El-Sohemy A. et al., 2014 <sup>26</sup> , Canada	Double-blinded, parallel group, 12 months	N=138; 20-35 y., Healthy adults	Genotype-advice based on: CYP1A2, GSTT1, GSTM1, TAS1R2, ACE; Delivery: via email	General dietary recommendations with no genetic info; email delivery	Changes in dietary intake of caffeine, vitamin C, added sugars, sodium	At 12 months, sodium intake was significantly reduced in the ACE risk genotype group (~287.3 mg/day vs. control 129.8 mg/day, $p=0.008$ ). No significant changes in other nutrients or among non-risk genotypes ( $p>0.05$ ).
Roke K. et al., 2017 <sup>27</sup> , Canada	Parallel-arm, 12 weeks	N=57; females 18-25 y., healthy, not using omega-3 supplements	FADS1 (rs174537); received personal genetic info + general omega-3 dietary info	Non-genotype-based advice	Dietary EPA+DHA intake  RBC %EPA/DHA, omega-3 awareness	Both groups ↑EPA + DHA intake ( $p=1\times10^{-4}$ ); no significant difference between groups ( $p>0.05$ ); PN group ↑awareness and perceived usefulness.

576 **Abbreviations:** TPB, Theory of Planned Behaviour; PN, Personalised Nutrition; CG, Control Group; BMI, Body Mass Index; RCT, Randomised  
577 Controlled Trial; PA, Physical Activity; FPG, Fasting Plasma Glucose; HbA1c, Haemoglobin A1c; BP, Blood Pressure; T2DM, Type 2 Diabetes Mellitus;  
578 MetS, Metabolic Syndrome; WC, Waist Circumference; SNP, Single Nucleotide Polymorphism; EPA, Eicosapentaenoic Acid; DHA, Docosahexaenoic  
579 Acid; RBC, Red Blood Cell; %EPA/DHA, Percentage of EPA and DHA in RBCs; GLB, Group Lifestyle Balance; LGx, Lifestyle Genomics; DNA,  
580 Deoxyribonucleic Acid; y, Year; N, Number (sample size); FTO, Fat Mass and Obesity-Associated Gene; rs9939609, SNP in FTO gene; rs7903146, SNP  
581 in TCF7L2 gene (linked to T2DM); rs699, SNP in AGT gene (linked to BP); CYP1A2, Cytochrome P450 1A2; GSTT1, Glutathione S-transferase Theta-1;  
582 GSTM1, Glutathione S-transferase Mu-1; TAS1R2, Taste Receptor Type 1 Member 2; ACE, Angiotensin-Converting Enzyme; FADS1, Fatty Acid  
583 Desaturase 1; rs174537, SNP in FADS1 gene.

584 **Table 3:** Personalised Nutrition Interventions based on Gut Microbiome and Machine Learning Algorithms

<b>Author, y</b> (Study, country)	<b>Methods</b> (RCT design, duration)	<b>Population</b> (N, age, health)	<b>Intervention Group</b> (Approach, delivery)	<b>Control Group</b> (Approach, delivery)	<b>Outcomes</b> (Primary, secondary)	<b>Main results</b> (Intervention group (PN), control group (CG), $p>0.05$ )
Ben-Yacov et al., 2021 <sup>28</sup> , Israel	Single-blind; 6-month intervention + 6-month follow-up	N=225; 18-65 y., Adults with prediabetes	Personalised PPGR diet using machine learning algorithm (integrated clinical and gut microbiome features); delivered via app + dietitian support	Mediterranean diet based on standard guidelines; delivered via menu + dietitian support	Change in CGM-measured time with glucose >140 mg/dL and HbA1c  OGTT, lipids, fructosamine, weight, FLI, others	PN showed greater improvements: time >140 mg/dL decreased by -1.3 h/day in PN vs -0.3 h/day in CG, ( $p<0.001$ ), HbA1c decreased by -0.16% in PN vs -0.08% in CG), ( $p=0.007$ ).  No significant difference in OGTT ( $p=0.8$ ). Other secondary outcomes, including triglycerides, HDL, and FLI favoured PN (all $p<0.05$ ).
Bermingham KM et al., 2024 <sup>32</sup> , USA  The ZOE METHOD study	Parallel group, 18 weeks	N=347; 41-70 y., Generally healthy adults with overweight or obesity	Personalised dietary program using postprandial glucose, triglycerides, microbiome, and health history; delivered via ZOE mobile app	Standard care dietary advice; delivered via leaflet, video, online resources	LDL-C and triglycerides,  Weight, waist circumference, HbA1c, diet quality, microbiome composition	In the PN group, triglycerides were significantly reduced ( $p=0.016$ ), with no significant between-group difference in LDL-C ( $p=0.521$ ).  Improvements in secondary outcomes (e.g., weight, WC, HbA1c, diet quality) were greater in PN than CG. No significant between groups differences for insulin, fasting glucose or BP: $p>0.05$ .
Kallapura et al., <sup>33</sup> 2024, India	Prospective, open-label, parallel group study, with two arms, 3 months	N=30; 42-65 y., Adults with type 2 diabetes and or/and hyperlipidaemia	A microbiome-based targeted personalised diet; in-person + remote guidance.	Diabetic nutritional guidance	HbA1c,  CRP, BP, lipid profile, microbiota changes	PN group: HbA1c ↓ from 8.30% to 6.67% ( $p<0.001$ ); CRP ↓ 20%; BP ↓ (significant only in subgroup); and gut diversity increased. CG: HbA1c ↓ from 8.24% to 7.32% ( $p=0.15$ ); less change in CRP/BP. Lipids changes were not significant in either group ( $p>0.05$ )





Kharmats A.Y. et al. 2023 <sup>29</sup> , USA	6 months	N=156; 18-80 y., Adults with BMI $\geq 27$ kg/m <sup>2</sup> and prediabetes or moderately controlled T2D	Personalised diet guided by a machine learning algorithm, with mobile app feedback including meal scores based on predicted PPGR	Standardised low-fat diet, (<25% energy from fat), same app without PPGR-based personalisation	Glycaemic variability (MAGE)  HbA1c, other CGM metrics	No significant difference between PN and CG ( $p>0.92$ ). Both groups had reductions in MAGE and HbA1c, but no between-group differences.
Popp C. et al., 2022 <sup>30</sup> , USA  The Personal Diet Study	Parallel-group, 6 months	N=269; 18-80 y.; BMI: 27-50 kg/m <sup>2</sup> ; prediabetes or moderately controlled T2D	Personalised diet tailored to predict and minimise PPGR using a machine learning algorithm (clinical data, anthropometrics, gut microbiome); delivered via mobile app + counselling	Standardised low-fat diet (<25% of energy from fat); same app and counselling without PPGR personalisation	% Weight loss,  Changes in body composition, resting energy expenditure, adaptive thermogenesis	No significant difference in % weight loss between PN (-3.26%) and CG (-4.31%); $p=0.16$ .  No group differences in body composition or thermogenesis; REE increased more in CG (+92.3 kcal/d; $p=0.05$ ).
Rein M. et al., 2022 <sup>31</sup> , Israel	Crossover trial; 2-week crossover + 6-month single-arm follow-up	N=23 (short-term), N=16 (6-month); mean age $53.5 \pm 8.9$ ; newly diagnosed T2M, no diabetes medications	Personalised postprandial-targeting diet using a machine learning algorithm predicting individual glycaemic responses based on clinical and microbiome data; menus delivered digitally, meals self-prepared	Mediterranean diet, based on standard guidelines for T2M; menus delivered digitally, meals self-prepared	Blood fructosamine (short-term), HbA1c (6-month) CGM-based metrics (mean glucose, time>140 mg/dL), fasting glucose, insulin, HOMA-IR, lipids, body composition, microbiome	PN significantly outperformed CG in lower mean glucose, PPGR, and fructosamine (all $p<0.001$ ).  In a 6-month single arm follow-up, PN led to reductions in HbA1c (-0.39%, $p<0.001$ ), FPG ( $p=0.02$ ), and triglycerides ( $p<0.001$ ) and 61% achieved diabetes remission.
Zeevi D. et al., 2015 <sup>7</sup> , Israel  The Personalized Nutrition Project	Blinded, two-arm crossover; 1-week profiling + 2x1-week intervention	N=26; 18-70 y.; non-diabetic adults, some prediabetes	Personalised diets based on an algorithm predicting PPGR. Delivered via pre-designed meals tailored to individual glycaemic profiles	Control group received expert selected diets based on measured PPGRs (profiling week) to elicit lower vs higher PPGR.	PPGR, variability in glucose response, gut microbiota composition	PN (algorithm) significantly reduced PPGR on the lower predicted diet compared to higher predicted diet in 10/12 participants ( $p<0.05$ ); Expert arm showed a comparable within participant difference (8/14, $p<0.05$ ); Overall, glucose variability improved ( $p<0.05$ ) and gut microbiota changes were observed.

585 **Abbreviations:** BMI, Body Mass Index; BP, Blood Pressure; CG, Control Group; CGM, Continuous Glucose Monitoring; CRP, C-Reactive Protein; FLI, Fatty  
586 Liver Index; HbA1c, haemoglobin A1c; LDL-C, Low-Density Lipoprotein Cholesterol; MAGE, Mean Amplitude of Glycaemic Excursions; N, Number of  
587 Participants; OGTT, Oral Glucose Tolerance Test; PN, Personalised Nutrition; PPGR, Postprandial Glucose Response; RCT, Randomised Controlled Trial;  
588 T2D, Type 2 Diabetes; TGs, Triglycerides

No primary research results, software or code have been included and no new data were generated or analysed as part of this review

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