

Characteristics of participants who benefit most from personalised nutrition: findings from the pan-European Food4Me randomised controlled trial

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Abstract

Little is known about who would benefit from Internet-based personalised nutrition (PN) interventions. This study aimed to evaluate the characteristics of participants who achieved greatest improvements (i.e. benefit) in diet, adiposity and biomarkers following an Internet-based PN intervention. Adults (n 1607) from seven European countries were recruited into a 6-month, randomised controlled trial (Food4Me) and randomised to receive conventional dietary advice (control) or PN advice. Information on dietary intake, adiposity, physical activity (PA), blood biomarkers and participant characteristics was collected at baseline and month 6. Benefit from the intervention was defined as $\geq 5\%$ change in the primary outcome (Healthy Eating Index) and secondary outcomes (waist circumference and BMI, PA, sedentary time and plasma concentrations of cholesterol, carotenoids and omega-3 index) at month 6. For our primary outcome, benefit from the intervention was greater in older participants, women and participants with lower HEI scores at baseline. Benefit was greater for individuals reporting greater self-efficacy for 'sticking to healthful foods' and who 'felt weird if [they] didn't eat healthily'. Participants benefited more if they reported wanting to improve

Abbreviations: HEI, Healthy Eating Index; PA, physical activity; PN, personalised nutrition; WC, waist circumference.

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their health and well-being. The characteristics of individuals benefiting did not differ by other demographic, health-related, anthropometric or genotypic characteristics. Findings were similar for secondary outcomes. These findings have implications for the design of more effective future PN intervention studies and for tailored nutritional advice in public health and clinical settings.

Key words: Food4Me: Personalised nutrition: Internet-based interventions: European: Adults

Personalised nutrition (PN) approaches offer an alternative and potentially more effective strategy to improve dietary intake^(1,2). PN interventions are tailored to key characteristics of the participant such as current diet, phenotype and genotype⁽³⁾. Although genotype-based personalised interventions designed to change risk behaviours (e.g. smoking and diet) have shown mixed results⁽⁴⁾, recent PN interventions have demonstrated encouraging improvements in dietary behaviours^(2,5-7). Furthermore, Internet-based interventions have the advantage of being scalable and more cost-effective than face-to-face interventions. Evidence from Internet-based nutrition interventions suggests that participants who are most likely to benefit from a nutrition-related intervention are older, female and more highly educated⁽⁸⁾. These are also the characteristics of those who are interested in Internet-based PN interventions⁽⁹⁾. These findings raise the possibility that other population groups may benefit less from Internet-based PN interventions. However, this hypothesis is yet to be examined in a randomised controlled trial, and the characteristics of participants who benefit most from Internet-based PN interventions are unknown. With the use of Internet-based PN interventions increasing^(7,10), understanding the characteristics of individuals who would benefit most from such interventions is imperative for improving the design of PN interventions that are intended to improve diet and health outcomes across the population.

The Food4Me Study was a 6-month, Internet-based, PN intervention conducted in seven European countries that showed that PN advice improved dietary intakes more than generalised dietary advice^(6,7,11,12). The present paper examines the socio-demographic, anthropometric, physical activity (PA)-related, health-related, genotypic and behavioural characteristics of participants who benefited most from this PN intervention based on the change in diet quality and adiposity following the intervention.

Participants and methods

Study design

The Food4Me Study⁽¹³⁾ was a 6-month, four-arm, Internet-based randomised controlled trial conducted in seven European countries, designed to compare the effects of personalised dietary and PA advice with generalised advice in changing dietary and lifestyle behaviours^(6,7,11,14,15). Recruitment included newspapers, radio advertisements and flyers, and participants could participate in the study by registering their details on the Food4Me website⁽¹³⁾. Participants were asked via email to complete online questionnaires and to provide biological samples at baseline and after 3 and 6 months intervention. Participants could interact via email with the dietitians, nutritionists and researchers at each

centre during the 6-month intervention. Participants were randomised to one of the four intervention arms and received either non-personalised, generalised dietary advice (control; level 0), or one of the three levels of PN based on dietary, PA, phenotypic and genotypic data (see below). Behaviour change techniques were included in the study protocol^(11,16). Participants were asked to complete an online FFQ, the Baecke PA questionnaire⁽¹⁷⁾, to wear accelerometers and to provide self-measured anthropometric information, buccal swabs and dry blood spot cards.

Ethics approval and participant consent

Participants (n 1607) were recruited between August 2012 and August 2013. The Research Ethics Committees at each university or research centre delivering the intervention granted ethics approval for the study. The Food4Me trial was registered as a randomised controlled trial (NCT01530139) at ClinicalTrials.gov. Participants signed online consent forms⁽¹¹⁾.

Eligibility criteria

Participants aged ≥ 18 years were included in the study. The following exclusion criteria were applied: (i) pregnant or lactating; (ii) no or limited access to the Internet; (iii) following a prescribed diet for any reason, including weight loss, in the last 3 months and (iv) diabetes, coeliac disease, Crohn's disease or any metabolic disease or condition altering nutritional requirements.

Randomisation and masking

An urn randomisation scheme was used to allocate individuals to each treatment arm. Participants randomised to level 1 (L1) received personalised dietary advice based on current diet and PA alone, level 2 (L2) received personalised dietary advice based on dietary, PA and phenotypic data and level 3 (L3) received personalised dietary advice based on dietary, PA, phenotypic and genotypic data. Personalised dietary feedback was based on how intakes of specific nutrients compared with recommended intakes, which was then translated into advice on changing intakes of food groups (fruits and vegetables, whole-grain products, fish, dairy products and meat). Personalised phenotypic feedback utilised anthropometric measurements and nutrient- and metabolic-related biomarkers to derive personalised feedback, and specific variants in five nutrient-responsive genes were used to provide personalised genotypic feedback. Personalised advice on PA was based on responses to the Baecke Questionnaire and accelerometer data.

Participants randomised to the control group (L0) received dietary advice based on population-level healthy eating guidelines. This non-personalised dietary advice was derived from

national dietary recommendations in each of the seven European countries and included generalised advice on the food groups listed above. In addition, these recommendations included a generic PA recommendation. Further details of the Food4Me PoP Study are provided elsewhere⁽¹¹⁾.

Personalised feedback report

Participants randomised to L1, L2 and L3 received personalised feedback reports via email at baseline and at months 3 and 6 of the intervention. For those randomised to L1, L2 and L3, algorithms were used to provide participants with three specific top priority food-based dietary goals according to the individual's intakes of foods and nutrients⁽¹⁸⁾. For participants randomised to L2 and L3, the dietary advice was also based on phenotypic data (L2) and phenotypic plus genotypic data (L3)⁽¹¹⁾.

Dietary and anthropometric measures

Participants completed an online FFQ to estimate usual dietary intake at baseline and at months 3 and 6 of the intervention. This FFQ was developed and validated for the Food4Me Study^(19,20) and included 157 food items consumed frequently in each of the seven recruitment countries. Intakes of foods and nutrients were computed in real time using a food composition database⁽²¹⁾.

The Healthy Eating Index (HEI) 2010 was used to assess diet quality according to the 2010 Dietary Guidelines for Americans⁽²²⁾. The HEI included twelve food groups, nine of which assessed adequacy of the diet: (1) total fruit; (2) whole fruit; (3) total vegetables; (4) greens and beans; (5) whole grains; (6) dairy products; (7) total protein foods; (8) seafood and plant proteins and (9) fatty acids. The remaining three groups, refined grains, Na and 'empty calories' (i.e. energy from solid fats, alcohol and added sugars), included dietary components that should be consumed in moderation. Less beneficial food groups were scored such that lower intakes receive higher scores. For all components, higher scores reflected better diet quality. The scores of the twelve components were summed to yield a total score with a maximum value of 100⁽²²⁾. For use in sensitivity analyses, adherence to the Mediterranean diet was estimated based on the fourteen-point criteria. Participants scored 1 point for each of the fourteen criteria they met and 0 for each they did not meet; points were summed to create an overall Mediterranean diet score, ranging from 0 to 14. More details are provided elsewhere^(23,24).

Body weight (kg), height (m) and waist circumference (WC; cm) were self-measured and self-reported. BMI (kg/m²) was estimated from body weight and height. Self-reported measurements were validated in a sub-sample of the participants (*n* 140) and showed a high degree of reliability⁽²⁵⁾.

Study measures

Participants self-reported smoking habits and occupations. Country of residence was treated as dummy variables, such that the odds of benefiting for participants from one country were compared with all other countries. PA level, the percentage of individuals meeting PA recommendations (>150 min moderate PA or >75 min vigorous PA or an equivalent combination of

moderate and vigorous PA per week⁽²⁶⁾) and sedentary time were estimated from triaxial accelerometers (TracmorD, Philips Consumer Lifestyle) and the Baecke PA questionnaire. An online screening questionnaire collected information on meal habits, healthy eating perceptions, self-efficacy for sticking to healthy foods and motivation for participation in the study (online Supplementary Table S1).

Participants collected buccal cell samples at baseline using Isohelix SK-1 DNA buccal swabs and Isohelix dried-capsules. LGC Genomics extracted DNA and genotyped-specific loci using TaqMan genotyping assays to provide bi-allelic scoring of single nucleotide polymorphisms: *FTO* (rs9939609), *MTHFR* (rs1801133), *TCF7L2* (rs7903146), *APOE(e4)* (rs429358 and rs7412) and *FADS1* (rs174546). Dried blood spots were collected for measurements of total cholesterol, carotenoids, omega-3 fatty acid index, thirty-two individual fatty acids and vitamin D (25-hydroxyvitamin D₂ and 25-hydroxyvitamin D₃)^(27–29).

Statistical analysis

All statistical analyses were performed using Stata (version 15; StataCorp). Data were analysed based on intention-to-treat of all individuals randomised into the intervention. Multiple imputations by chained equations and fully conditional specification methods, including augmentation, were used to address missing data for all outcomes. A total of twenty imputed data sets were used based on recent literature and the percentage of missing data. Given that adjustment for multiple comparisons may increase the risk of type 2 error⁽³⁰⁾, no adjustment for multiple comparisons was included.

The sample size was estimated *a priori* using Minitab® (version 16.1.0) based on data for *n*-3 fatty acids and glucose concentrations in European adults. To address the primary aim of the Food4Me intervention, a sample size of 326 was planned for each of the four intervention arms. This would enable detection of 0.22 SD differences in the main outcomes with 80% power and $\alpha = 0.05$. Assuming that the population standard deviation for omega-3 fatty acid index was 1.5 units and for glucose was 1.05 mmol/l, a total sample of 1280 was estimated as sufficient to detect a difference of 0.33 units for *n*-3 PUFA and 0.23 mmol/l glucose post-intervention. Allowing for a potential 20% drop out, recruitment was targeted at 1540 participants (220 participants per centre)⁽⁷⁾.

For our primary objective, participants randomised to L1, L2 or L3 of the intervention were identified as benefiting from the intervention if their HEI at month 6 was $\geq 5\%$ better than that at baseline. For our secondary outcomes, details for each definition of benefit are summarised in online Supplementary Table S2. Briefly, benefit was defined as: (i) $\geq 5\%$ reduction in body weight and/or WC, (ii) $\geq 5\%$ increase in omega-3 index, (iii) $\geq 5\%$ increase in carotenoids, (iv) $\geq 5\%$ reduction in cholesterol, (v) $\geq 5\%$ reduction in sedentary time and (vi) $\geq 5\%$ increase in PA at month 6. Cut points of 5% were based on recent literature, where a change of $\geq 5\%$ in body weight was identified as clinically significant^(14,31). Logistic regression analyses, using multiple imputation estimation commands, were employed to examine associations between benefiting from the intervention

(independent variable) and participant characteristics (dependent variables). Logistic regression analyses were also used to examine associations between benefiting from the intervention (independent variable) and participant characteristics (dependent variable) among participants randomised to L0 of the intervention only. An interaction effect between the characteristic and study arm (control *v.* PN) was included in the model to determine whether characteristics of benefit differed between the control and intervention groups. Analyses were adjusted for baseline age (continuous), sex, country (categorical), intervention arm (categorical) and baseline values of the outcome (i.e. HEI, WC and body weight). PA outcomes were further adjusted for accelerometer wear time at baseline (continuous) and season (categorical). Correlations between behavioural characteristics were explored using Pearson's correlation coefficients.

As a sensitivity analysis, any impact of regression towards the mean in our estimate of change in HEI was evaluated by including a correction factor in our models according to the following equation $x_{adj} = \bar{x} + p(x - \bar{x})^{(32)}$. Benefit from the intervention (i.e. change in HEI and body weight/WC at month 6) was also treated as a continuous variable. To determine whether findings were robust for different measures of diet quality, benefit was defined according to the change in Mediterranean diet score (continuous).

Results

A total of 1607 participants were randomised into the intervention and 1270 of these completed the intervention (Fig. 1). For the purposes of this analysis, only individuals who were randomised into L1 (*n* 414), L2 (*n* 404) and L3 (*n* 402) were included in the main analyses (*n* 1220). Data were imputed for individuals who dropped out between baseline and month 6 (online Supplementary Tables S3 and S4).

The distributions of change in HEI, body weight and WC are shown in Fig. 2, with the proportion of participants benefiting from the intervention by country shown in Table 1. The country with the highest proportion of participants benefiting based on the primary outcome (HEI) was Spain, whereas Greece and the Netherlands had the greatest proportion of participants with improvements in secondary outcomes (body weight and WC; Table 1).

Baseline socio-demographic, anthropometric, health behaviour and biological characteristics of participants according to whether they benefited more from the PN intervention are shown in Table 2. The odds of benefiting were higher in women than in men. Older participants and participants with lower baseline HEI scores had higher odds of benefiting. The characteristics of individuals benefiting did not differ by other health-related, anthropometric or genotypic characteristics (Table 2).

Behavioural characteristics of participants benefiting from the PN intervention are shown in Table 3. The odds of a participant benefiting more from the intervention at month 6 were higher among those who reported greater self-efficacy for 'sticking to healthful foods' and who 'felt weird if [they] didn't eat healthily' (HEI only), which were correlated (r 0.25, P < 0.0001).

Participants had a higher odds of benefiting if they were interested in improving their health, wanted to know what foods are best for them and frequently ate healthily (HEI only). The characteristics of individuals who benefited more from the intervention did not differ by other healthy eating habits or perceptions (Table 3). Baseline socio-demographic, anthropometric, health-related and behavioural characteristics of participants randomised to L1, L2 and L3 of the intervention associated with benefiting from the PN intervention at month 6 according to each definition of benefit (HEI, weight loss/WC reduction, PA, sedentary time, cholesterol, carotenoids, omega-3 index) are shown online Supplementary Tables S5 and S6. Few participant characteristics were comparable across definitions.

When stratified by PN intervention arm, odds of benefiting were higher with higher age in L2 (OR 1.05, 95% CI 1.01, 1.08) and L3 (1.02, 95% CI 1.00, 1.06), with being female in L2 (3.75, 95% CI 1.57, 8.96), and with being a participant in the Netherlands in L3 (3.19, 95% CI 1.41, 7.22). Odds were higher in participants who reported with being able to stick to healthy foods even if they had to re-think their way of nutrition (4.96, 95% CI 1.55, 15.81) in L1 and even if they had to try several times until it worked in L1 (22.69, 95% CI 1.64, 313.2) and L2 (4.96, 95% CI 1.55, 15.81). Odds of benefiting were also higher in participants who wanted to know what foods are best for them in L2 (5.46, 95% CI 1.88, 15.90) and in those who reported frequently eating healthily (3.04, 95% CI 1.30, 7.11) in L3. Odds of benefiting were lower in participants in Germany (0.32, 95% CI 0.12, 0.88) in L3. No other significant differences by PN arm were observed.

When the analyses were restricted to participants randomised to generalised (non-personalised) dietary advice (L0), the odds of benefiting from the intervention were lower in *APOE* (rs429358) risk carriers (OR 0.53 (95% CI 0.32, 0.91), P = 0.020) but higher among individuals reporting being in control of their own health (OR 1.71 (95% CI 1.01, 2.91), P = 0.047) and wanting to gain weight (OR 0.17 (95% CI 0.03, 0.99), P = 0.049). All other characteristics were consistent with those of participants randomised to PN. There was no interaction between participant characteristic and study arm (control *v.* PN) on extent of benefit (change in HEI), with the exception of the *MTHFR* risk allele and participants who wanted to improve their health. HEI improved in participants randomised to PN advice who were carriers of the *MTHFR* risk allele (coefficient 0.08, SE 0.39, P = 0.043) and who wanted to improve their health (coefficient 0.08, SE 0.38, P = 0.038) compared with those in the control arm who were not carriers of the *MTHFR* risk allele and did not want to improve their health, respectively.

Sensitivity analyses

The pattern of results was similar when change in HEI and body weight/WC at month 6 was treated as a continuous outcome (data not shown). The characteristics of participants benefiting most from the PN intervention were similar when benefit was defined using Mediterranean diet (data not shown) and when results for benefit (defined by HEI) were adjusted for regression towards the mean (data not shown).

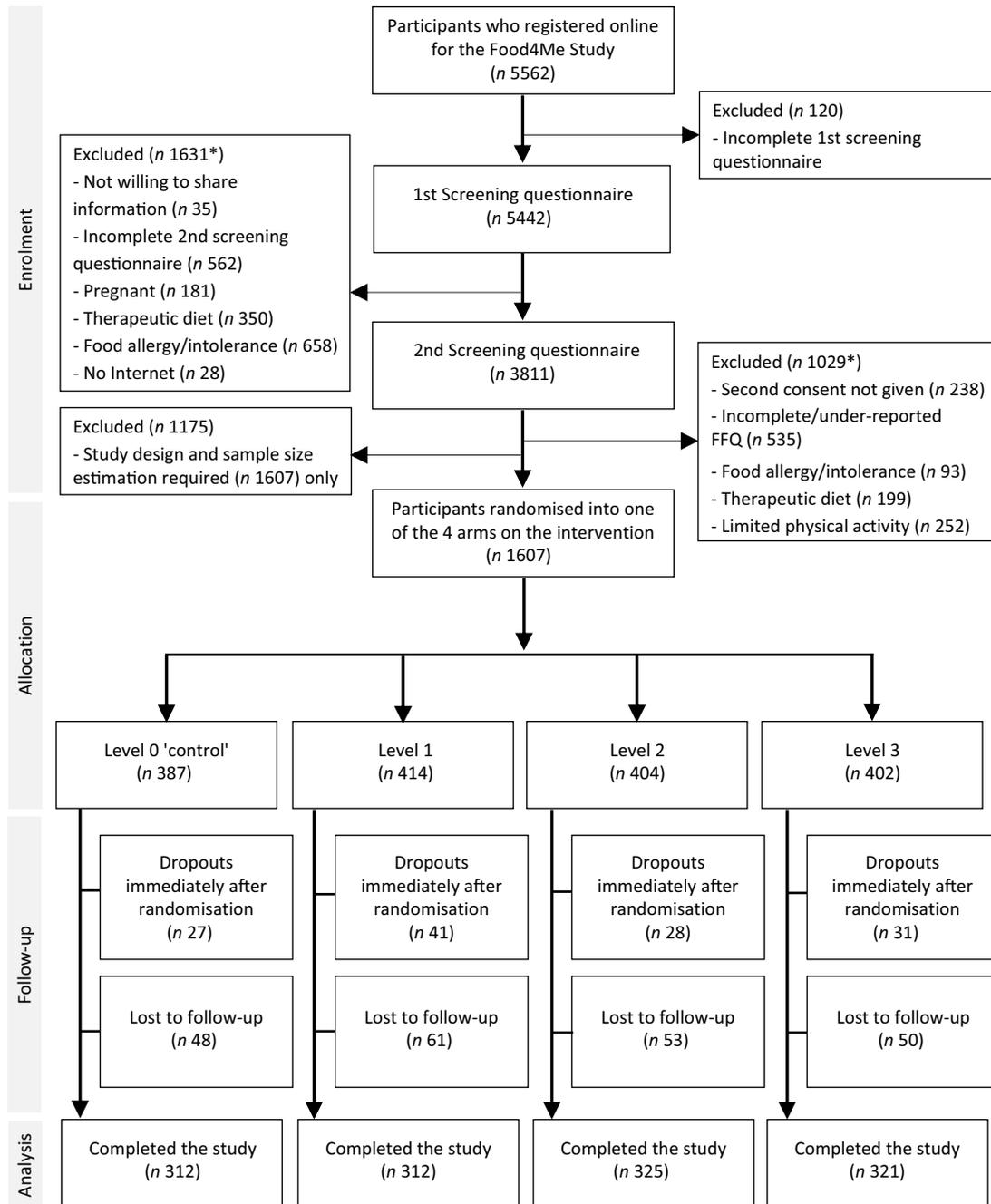


Fig. 1. CONSORT diagram of participants included in the Food4Me Study.

Discussion

This study aimed to characterise the participants benefiting most from a 6-month, Internet-based PN intervention. Our main findings are that older participants, women and those with less healthy diets at baseline benefited most from PN advice. The odds of benefiting did not differ by weight status, genetic risk or socio-economic position. These findings confirm the need to enhance the effectiveness of PN interventions in certain groups, for example, young men and those with unhealthier eating perceptions/motivations. These individuals may require

additional tailoring of PN advice using individual characteristics that were not investigated in this study. Nonetheless, since many participant characteristics did not affect the extent of benefit, our findings suggest that most population groups would benefit from PN advice.

To the best of our knowledge, no previous studies have investigated the characteristics of individuals benefiting most from an Internet-based PN intervention. Studies have shown that women, older individuals and generally healthier individuals are more likely to participate in nutrition interventions⁽³³⁾, including Internet-based interventions⁽³⁴⁾. This may be due to a greater

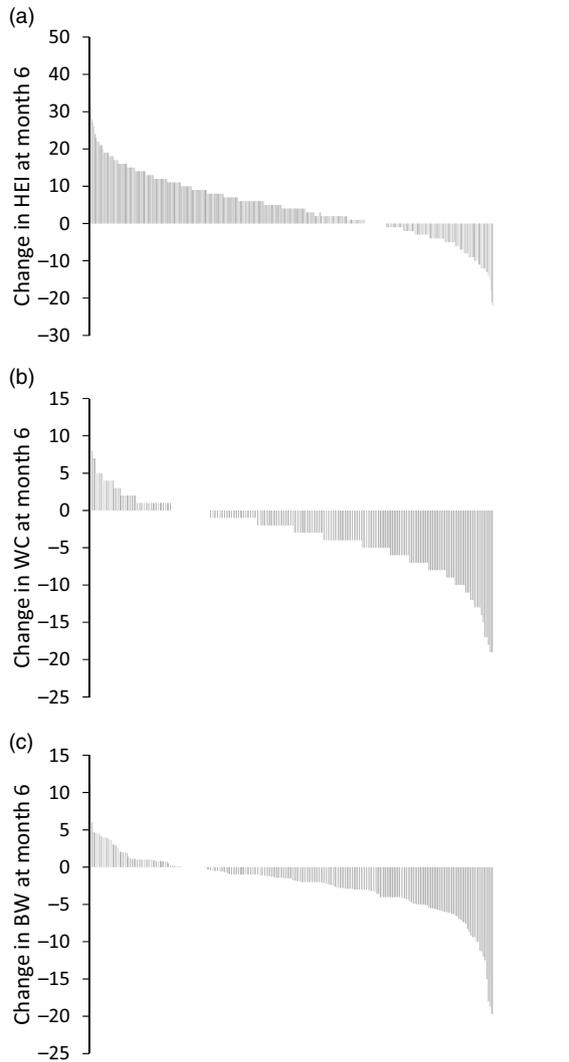


Fig. 2. Distribution of change among Food4Me participants in (a) Healthy Eating Index (HEI); (b) waist circumference (WC) and (c) body weight (BW). Participants achieving a greater than 5% improvement in HEI and BW/WC at month 6 are in light grey.

desire to lose weight among women and older adults being more time rich than younger adults. In addition, individuals with greater motivation to be healthy and to participate in nutrition interventions may be more knowledgeable about the benefits of healthy eating⁽³⁵⁾. Similarly, of the 5662 individuals who expressed an interest in participating in the Food4Me Study, 65% were women⁽⁹⁾. Nonetheless, these individuals were broadly representative of the wider European population in terms of need to improve dietary and PA behaviours⁽⁹⁾ and were not skewed towards individuals who were already healthy (i.e. the worried well). In addition, in the Food4Me Study, individuals who met fewer recommendations at baseline⁽³⁶⁾ and who had lower self-perception of healthy eating habits⁽³⁷⁾ showed greatest improvement in diet following the intervention. In the present analysis, despite the odds of benefiting being higher in participants with better self-reported healthy eating perceptions and motivations, the odds of benefiting from PN advice were lower in those with higher HEI at baseline. The proportion

of participants benefiting most appeared to differ by country, which suggests that there may be opportunities to tailor PN advice to different cultural norms.

To a large extent, the characteristics of participants benefiting from the control intervention were similar to those of participants benefiting most from the PN intervention. If this is a true effect, it implies that participants who benefit from PN advice are comparable with those who received general dietary advice. Moreover, it suggests that benefit extends beyond those receiving the intervention. This confirms our observed effect of the intervention on improvements in diet, where participants in the control group showed modest improvements in their diet as a result of participating in the intervention⁽⁷⁾. Where there were differences between treatment arms, reduced power in the control arm could have influenced these findings.

The effects of the intervention on adiposity markers (benefit from the intervention was defined as $\geq 5\%$ weight loss or WC reduction) showed a somewhat different range of participant characteristics compared with those benefiting more in respect of HEI. This may be that those who needed to lose weight were different from the general population. Moreover, the study has shown large individual variation in changes in health behaviours following a PN intervention. Such inter-individual variation is common in (dietary) intervention studies. For example, in the DIETFITS weight loss intervention study, individual body mass changes ranged over approximately 40 kg within each treatment group with some participants losing 30 kg over 12 months and others gaining 10 kg body weight⁽³⁸⁾. Such inter-individual variation is one of the major challenges that PN approaches aim to address. With better understanding of the participant characteristics that lead to no (or adverse) responses to interventions, there is scope to refine the personalisation process and to develop intervention features that improve the target behaviours.

This study had a number of strengths. The Food4Me Study is the largest randomised controlled trial on the effectiveness of PN advice in European adults to date; it used a rigorous design and it investigated change in health-related outcomes sustained to 6 months. We applied multiple imputations to our analyses; thus, limiting bias associated with missing data and the robustness of our findings was confirmed through extensive sensitivity analyses. The pattern of results remained consistent regardless of whether benefit was defined as binary or continuous change in HEI or any of the secondary definitions and following adjustment for regression towards the mean in HEI.

A limitation of our study is that data were self-measured and self-reported via the Internet. Nonetheless, the accuracy of Internet-based, self-reported anthropometric data has been confirmed in the Food4Me Study⁽²⁵⁾. Dietary intakes may be subject to misreporting error, which was minimised by validation of the FFQ against a 4-d weighed food record⁽²⁰⁾. Since 97% of our study participants were Caucasians, research in wider ethnicity groups is required to generalise our findings to other populations. Our sample is a self-selected group of individuals who may be more health conscious than the general population. However, participants interested in joining the study were similar to the wider population of European adults, who would benefit from improved diet and PA⁽⁹⁾. In addition, although the cut-off points for defining benefit were based on previous

Table 1. Proportion of participants (%) randomised to a personalised nutrition intervention arm (level 1, 2 or 3) benefiting from the intervention by country* (Percentages)

	Total (n493)	Germany (n63)	Greece (n47)	Ireland (n64)	NL (n121)	Poland (n62)	Spain (n69)	UK (n67)
Healthy Eating Index	56.8	57.1	48.9	57.8	61.2	58.1	60.9	47.8
BW and/or WC	27.0	20.6	36.1	21.9	31.4	19.4	30.4	26.9
Physical activity	21.5	19.1	19.2	20.3	22.3	17.7	30.4	19.4
Sedentary time	38.5	42.9	34.0	32.8	40.5	45.2	43.5	28.4
Cholesterol	46.7	50.8	29.8	46.9	52.1	35.5	34.8	67.2
Carotenoids	42.2	30.2	34.0	39.1	52.9	53.2	31.9	43.3
Omega-3 index	51.9	42.9	53.2	59.4	63.6	41.9	47.8	44.8

NL, The Netherlands; BW, body weight (kg); WC, waist circumference (cm).

* Benefit was defined as a $\geq 5\%$ improvement in the outcomes from baseline to month 6.

Table 2. Baseline socio-demographic, anthropometric, health-related and genotypic characteristics of participants randomised to levels 1, 2 and 3 of the intervention, and multivariable adjusted odds ratios of benefiting from the personalised nutrition intervention at month 6 as defined by extent of improvement in Healthy Eating Index (HEI) (n493)* (Mean values and standard deviations or percentages; odds ratios and 95 % confidence intervals)

	Total	No benefit	Benefit	Odds of benefiting†		P
				OR	95 % CI	
HEI score				0.89	0.86, 0.91	<0.001
Mean	50.0	54.6	46.5			
SD	9.54	8.07	9.11			
Demographics						
Age (years)				1.03	1.01, 1.04	<0.002
Mean	43.9	43.0	44.6			
SD	13.0	13.3	12.7			
Female (%)	55.6	54.5	56.4	1.64	1.07, 2.50	0.023
Occupation (%)						
Professional and managerial	43.6	42.3	42.9	1.09	0.73, 1.64	0.67
Intermediate occupations	25.2	23.5	26.4	1.06	0.66, 1.69	0.82
Routine and manual	8.32	7.98	8.57	1.04	0.50, 2.16	0.91
Country (%)						
Germany	12.8	12.7	12.9	0.67	0.37, 1.21	0.19
Greece	9.53	11.3	8.21	0.72	0.36, 1.42	0.33
Ireland	13.0	12.7	13.2	1.08	0.59, 1.97	0.80
The Netherlands	24.5	22.1	26.4	1.62	1.01, 2.60	0.044
Poland	12.6	12.2	12.9	0.59	0.30, 1.15	0.12
Spain	14.0	12.7	15.0	1.39	0.78, 2.48	0.26
UK	13.6	16.4	11.4	0.85	0.48, 1.53	0.60
Anthropometrics						
Body weight (kg)				1.00	0.98, 1.01	0.81
Mean	75.0	74.6	75.3			
SD	14.8	14.3	15.1			
BMI (kg/m ²)				1.02	0.97, 1.07	0.16
Mean	25.5	25.1	25.8			
SD	4.45	3.89	4.83			
Waist circumference (cm)				1.00	0.98, 1.02	0.66
Mean	86.4	85.6	87.0			
SD	12.8	12.4	13.0			
Health behaviours						
PAL				1.60	0.48, 5.35	0.45
Mean	1.75	1.75	1.76			
SD	0.18	0.17	0.18			
MVPA				1.00	0.99, 1.01	0.99
Mean	45.8	47.1	44.8			
SD	30.5	31.4	29.8			
Sedentary behaviour (min/d)				1.00	0.99, 1.01	0.95
Mean	758	756.6	758.8			
SD	70.6	71.7	69.9			
Current smoker (%)	8.11	7.04	8.93	1.03	0.46, 2.31	0.84
Medication use (%)	33.5	31.9	34.6	0.96	0.62, 1.47	0.84
Genotype‡						
FTO (rs9939609)	70.4	72.3	68.9	0.91	0.59, 1.41	0.67
FADS1 (rs174546)	42.8	42.3	43.2	0.91	0.60, 1.36	0.63

Table 2. (Continued)

	Total	No benefit	Benefit	Odds of benefiting†		P
				OR	95 % CI	
<i>TCF7L2</i> (rs7903146)	48.9	49.8	48.2	0.96	0.64, 1.44	0.85
<i>APOE</i> (rs429358)	27.4	30.1	25.4	0.95	0.61, 1.48	0.81
<i>APOE</i> (rs7412)	12.6	13.6	11.8	0.72	0.39, 1.32	0.29
<i>MTHFR</i> (rs1801133)	55.6	57.3	54.3	1.01	0.67, 1.52	0.96

Level 1, participants received personalised nutrition advice based on their current diet; level 2, participants received personalised nutrition advice based on their current diet and phenotype; level 3, participants received personalised nutrition advice based on their current diet, phenotype and genotype; PAL, physical activity level; MVPA, moderate to vigorous physical activity.

* Multiple logistic regression was used to test for differences in characteristics between individuals who benefited most and the remaining participants, respectively. Analyses were adjusted for age, sex, country, intervention arm (except when used as the dependent variable) and baseline values of the outcome (i.e. HEI). PAL, MVPA and sedentary behaviour were additionally adjusted for time wearing the accelerometer and season.

† More benefit: $\geq 5\%$ increase in HEI from baseline to month 6; less benefit: $< 5\%$ increase in HEI from baseline to month 6.

‡ Probability carrier of minor allele.

Table 3. Baseline behavioural characteristics of participants randomised to levels 1, 2 and 3 of the intervention and multivariable adjusted odds ratios of benefiting from the personalised nutrition (PN) intervention at month 6 as defined by improvement in Healthy Eating Index (HEI) (n 493)* (Odds ratios and 95 % confidence intervals)

	Total	No benefit	Benefit	OR of benefiting†		P
				OR	95 % CI	
Meal habits						
Often eat main meal away from home	34.3	32.9	35.4	1.08	0.69, 1.66	0.55
Often skip meals and replace them with snacks	6.09	4.69	7.14	0.78	0.33, 1.93	0.62
Often prepare a meal 'from scratch'	30.8	28.2	32.9	0.93	0.59, 1.45	0.74
Often eat hot or cooked meals	28.4	29.6	27.5	1.12	0.71, 1.75	0.63
Spend a lot of time preparing a main meal	43.8	45.5	42.5	1.08	0.72, 1.62	0.72
Healthy eating perceptions						
Believe I am in control of my health	71.6	70.9	72.1	1.16	0.74, 1.82	0.51
Can stay healthy by taking care of myself	86.6	85.5	87.5	1.17	0.65, 2.10	0.61
Efforts to improve health are a waste of time	2.43	2.35	2.50	0.71	0.18, 2.83	0.63
Bored by attention paid to health and disease	1.42	0.94	1.79	1.29	0.19, 8.87	0.79
There's no use of being concerned about health	5.27	3.29	6.79	1.45	0.53, 3.83	0.46
Frequently eating healthily	76.3	77.9	75.0	1.74	1.05, 2.89	0.033
Eat healthily without thinking about it	44.6	47.0	42.9	1.01	0.67, 1.51	0.97
Feel weird if don't eat healthily	47.7	47.4	47.9	1.67	1.10, 2.55	0.017
Self-efficacy for sticking to healthful foods						
Even if I need time to develop the routines	93.1	92.0	93.9	2.35	1.33, 4.14	0.006
Even if I have to try several times until it works	96.4	94.4	97.9	2.45	1.25, 4.78	0.009
Even if I have to rethink my way of nutrition	85.8	83.6	87.5	1.74	1.14, 2.46	0.010
Even if I do not receive support from others	87.2	87.8	86.8	1.22	0.80, 1.87	0.36
Even if I have to make a detailed plan	88.4	86.9	89.6	1.30	0.83, 2.04	0.27
Motivation for participating in the study						
Interested in personalised nutrition	75.7	78.4	73.6	1.19	0.74, 1.92	0.47
Want to know what foods are best for him/her	79.3	76.5	81.4	1.83	1.11, 3.02	0.018
Want to lose weight	43.4	39.0	46.8	1.38	0.91, 2.10	0.13
Want to improve my family's health	27.6	25.8	28.9	0.98	0.63, 1.54	0.93
Want to improve my health	55.8	50.7	59.6	1.52	1.06, 2.28	0.047
Want to improve my well-being	54.8	52.6	56.4	1.31	1.87, 1.97	0.19
Want to improve my sports performance	35.7	36.2	35.4	1.40	0.90, 2.16	0.14
Want to prevent a future illness	60.0	56.8	62.5	1.37	0.91, 2.07	0.13
Have a family history of diet-related illness	8.92	7.98	9.64	1.35	0.67, 2.75	0.41
Think it is important to help academic studies	69.6	68.1	70.7	1.36	0.88, 2.12	0.17
Curious to find out what happens in PN studies	47.1	45.1	48.6	1.24	0.83, 1.86	0.30

Level 1, participants received PN advice based on their current diet; level 2, participants received PN advice based on their current diet and phenotype; level 3, participants received PN advice based on their current diet, phenotype and genotype; PAL, physical activity level; MVPA, moderate to vigorous physical activity.

* Multiple logistic regression was used to test for differences in characteristics between individuals who benefited most and the remaining participants, respectively. Analyses were adjusted for age, sex, country, intervention arm (except when used as the dependent variable) and baseline values of the outcome (i.e. HEI). PAL, MVPA and sedentary behaviour were additionally adjusted for time wearing the accelerometer and season. For the purposes of this table, phrasing of characteristics has been paraphrased from the original questionnaire (see online Supplementary Table S1).

† Benefit: $\geq 5\%$ increase in HEI from baseline to month 6; no benefit: $< 5\%$ increase in HEI from baseline to month 6.

research⁽³¹⁾, the clinical relevance of a 5 % in outcome measures warrants further investigation. The present analyses require replication in a larger study, which would provide more statistical power, particularly for testing subgroup differences in

benefit. Moreover, while analyses were adjusted for appropriate confounders, we cannot discount the possibility of residual confounding. Given that analyses were not adjusted for multiple testing, the risk of type 1 error is higher and so results should be

interpreted with this in mind. Finally, although we included outcomes for seven different health-related biomarkers, future PN interventions may wish to consider the impact of PN on the gut microbiota and on other markers of health⁽³⁹⁾.

These findings have implications for the design of more effective future PN intervention studies and tailored nutritional advice in the public health or clinical settings. Future studies should consider ways of tailoring PN advice to improve efficacy in certain population groups such as young men. Nonetheless, with many characteristics, such as weight status and occupation, being unrelated to extent of benefit in the Food4Me Study, our findings suggest that most population groups will benefit from PN advice. Further improvements in the design, delivery and efficacy of PN interventions will support integration of PN strategies into public health policies.

In conclusion, older individuals, women and those with less healthy diets at baseline were likely to benefit most (i.e. improve their diet and achieve weight loss, where appropriate) from PN advice. Our findings confirm the need to enhance the effectiveness of PN interventions in certain groups, for example, young men. The odds of benefiting did not differ by weight status, genotype or socio-economic position. Since few characteristics affected the degree of benefit from the PN intervention, our findings suggest that PN approaches may be widely applicable.

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Supplementary material

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