

This is a pre-copyedited, author-produced pdf of an article accepted for publication in *Public Health Nutrition* following peer review.

The version of record, 'Characteristics of European adults who dropped out from the Food4Me Internet-based personalised nutrition intervention'

K. M. Livingstone, et.al., *Public Health Nutrition*, pp 1-11, November 2016, first published on line on August 5, 2016, is available on line via doi:

<http://dx.doi.org/10.1017/S1368980016002020>

© 2016 The Authors. This manuscript version is made available under the CC-BY-NC-ND 4.0 license <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

Title**Characteristics of European adults who dropped out from the Food4Me internet-based personalised nutrition intervention****Author names**

Katherine M. Livingstone*¹, Carlos Celis-Morales*¹, Anna L. Macready², Rosalind Fallaize², Hannah Forster³, Clara Woolhead³, Clare B. O'Donovan³, Cyril F.M. Marsaux⁴, Santiago Navas-Carretero⁵, Rodrigo San-Cristobal⁵, Silvia Kolossa⁶, Lydia Tsigoti⁷, Christina P. Lambrinou⁷, George Moschonis⁷, Agnieszka Surwiłło⁸, Christian A. Drevon⁹, Yannis Manios⁷, Iwona Traczyk⁸, Eileen R. Gibney³, Lorraine Brennan³, Marianne C. Walsh³, Julie A. Lovegrove², J. Alfredo Martinez⁵, Wim H. Saris⁴, Hannelore Daniel⁶, Mike Gibney³, John C. Mathers¹, on behalf of the Food4Me Study.

Author affiliations

1, Human Nutrition Research Centre, Institute of Cellular Medicine, Newcastle University, Newcastle Upon Tyne, UK (KML, katherine.livingstone@newcastle.ac.uk, CCM, carlos.celis@newcastle.ac.uk; JCM, john.mathers@newcastle.ac.uk)

2, Hugh Sinclair Unit of Human Nutrition and Institute for Cardiovascular and Metabolic Research, University of Reading, Reading, UK (ALM, a.l.macready@reading.ac.uk; RF, r.fallaize@reading.ac.uk; JAL, j.a.lovegrove@reading.ac.uk)

3, UCD Institute of Food and Health, University College Dublin, Belfield, Dublin 4, Republic of Ireland (CBD, clare.odonovan@ucdconnect.ie; HF, hannah.forster@ucdconnect.ie; CW, clara.woolhead@ucdconnect.ie; EG, eileen.gibney@ucd.ie; LB, lorraine.brennan@ucd.ie; MCW, marianne.walsh@ucd.ie; MG, mike.gibney@ucd.ie)

4, Department of Human Biology, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, Maastricht, The Netherlands (CFMM, c.marsaux@maastrichtuniversity.nl; WHMS, w.saris@maastrichtuniversity.nl)

5, Center for Nutrition Research, University of Navarra, Pamplona, Spain; CIBER Fisiopatología Obesidad y Nutrición (CIBERObn), Instituto de Salud Carlos III, Madrid, Spain (SNC, snavas@unav.es; RSC, rsan.1@alumni.unav.es; JAM, jalfmtz@unav.es)

6, ZIEL Research Center of Nutrition and Food Sciences, Biochemistry Unit, Technical University of Munich, Germany (SK, silvia.kolossa@tum.de; HD, hannelore.daniel@tum.de)

7, Department of Nutrition and Dietetics, Harokopio University, Athens, Greece (LT, tsirigoti.lydia@gmail.com; CPL, cplambrinos@gmail.com; GM, gmoschi@hua.gr; YM, manios@hua.gr)

8, National Food & Nutrition Institute (IZZ), Poland (AS, asurwillo@izz.waw.pl; IT, itraczyk@izz.waw.pl)

9, Department of Nutrition, Institute of Basic Medical Sciences, Faculty of Medicine, University of Oslo, Oslo, Norway (CAD, c.a.drevon@medisin.uio.no)

*KML and CCM are joint first-authors

Corresponding author; request for reprints

Professor John C. Mathers

Human Nutrition Research Centre

Institute of Cellular Medicine

Newcastle University

Biomedical Research Building

Campus for Ageing and Vitality

Newcastle upon Tyne

NE4 5PL

UK

john.mathers@newcastle.ac.uk

Tel: +44 (0) 1912081133 Fax: +44 (0) 1912081101

Word count: 3902

Number of Figures: 2

Number of Tables: 4

OSM available

PubMed indexing: Livingstone, Celis-Morales, Macready, Fallaize, Forster, Woolhead, O'Donovan, Marsaux, Navas-Carretero, San-Cristobal, Kolossa, Tsirigoti, Lambrinou, Moschonis, Surwiłło, Drevon, Manios, Traczyk, Gibney, Brennan, Walsh, Lovegrove, Martinez, Saris, Daniel, Gibney, Mathers

Running title: Dropouts from internet-based personalised nutrition intervention

Abbreviations: Body mass index (BMI), Cardiovascular disease (CVD), Food frequency questionnaire (FFQ), Physical activity (PA); Physical activity level (PAL), Personalised

Nutrition (PN), Proof-of-principle (PoP); Randomized controlled trial (RCT), Sedentary behaviour (SB), Socio-economic status (SES); Waist circumference (WC)

Financial support: This work was supported by the European Commission under the Food, Agriculture, Fisheries and Biotechnology Theme of the 7th Framework Programme for Research and Technological Development [265494].

Conflict of interest: None of the authors had a personal or financial conflict of interest.

Authorship: Author responsibilities were as follows: YM, IT, CAD, ERG, LB, JAL, JAM, WHMS, HD, MG and JCM contributed to the research design. JCM was the Food4Me Proof of Principle study leader. CCM, CFMM, HF, CBO, CW, ALM, RF, SNC, RSC, SK, LT, CPL, AS, MCW, ERG, LB and JCM contributed to the developing the Standardised Operating Procedures for the study. CCM, SNC, RSC, CW, CBO, HF, CFMM, ALM, RF, SK, LT, CPL, AS, MCW and JCM conducted the intervention. CCM, CFMM and WHMS contributed to physical activity measurements. KML and CCM wrote the paper and performed the statistical analysis for the manuscript and are joint first authors. All authors contributed to a critical review of the manuscript during the writing process. All authors approved the final version to be published.

Ethical standards disclosure: This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Research Ethics Committees at each University or Research Centre delivering the intervention. The Food4Me trial was registered as a RCT (NCT01530139) at Clinicaltrials.gov. All participants expressing an interest in the study were asked to sign online consent forms at two stages in the screening process. These consent forms were automatically directed to the local study investigators to be counter-signed and archived.

1 **Abstract (words count=248)**

2 **Objective**

3 To characterise participants who dropped out of the Food4Me Proof of Principle study.

4 **Design**

5 The Food4Me study was an internet-based, 6-month, 4-arm, randomized controlled trial. The
6 control group received generalised dietary and lifestyle recommendations, whereas
7 participants randomised to three different levels of PN (personalised nutrition) received
8 advice based on dietary, phenotypic and/or genotypic data respectively (with either more or
9 less frequent feedback).

10 **Setting**

11 Seven recruitment sites: the UK, Ireland, the Netherlands, Germany, Spain, Poland and
12 Greece.

13 **Subjects**

14 Adults aged 18-79 years (*n* 1607).

15 **Results**

16 A total of 337 (21%) participants dropped out during the intervention. At baseline, dropouts
17 had higher BMI (0.5kg/m^2 ; $P<0.001$). Attrition did not differ significantly between
18 individuals receiving generalised dietary guidelines (Control) and those randomized to PN.
19 Participants were more likely to drop out if they received more frequent feedback (OR: 1.81,
20 CI: 1.36-2.41; $P<0.001$), if they were female (1.38, 1.06-1.78; $P=0.015$), less than 45 years of
21 age (2.57, 1.95-3.39; $P<0.001$) and obese (2.25, 1.47-3.43; $P<0.001$). Attrition was more
22 likely in participants who reported an interest in losing weight (1.53, 1.19-1.97; $P<0.001$) or
23 skipping meals (1.75 (1.16-2.65; $P=0.008$), and less likely if they claimed to eat healthily
24 frequently (0.62 (0.45-0.86); $P=0.003$).

25 **Conclusions**

26 Attrition did not differ between participants receiving generalised or PN advice but more
27 frequent feedback was related to attrition for those randomized to PN interventions. Better

28 strategies are required to minimise dropouts among younger and obese individuals in those
29 participating in PN interventions and more frequent feedback may be an unnecessary burden.

30 **Trial registration** – Clinicaltrials.gov NCT01530139

31 **Key Words:** Dropout; personalised nutrition; internet-based; European adults; Food4Me

32 INTRODUCTION

33 Improving diet and physical activity behaviours are important means of lowering risk of non-
34 communicable diseases, promoting healthy ageing and increasing well-being ^(1; 2). Given that
35 the burden of ill health is increasing ^(1; 3), alternative strategies for improving dietary
36 behaviours, based on predictive, personalised, preventative and participatory interventions,
37 may be more effective than conventional “one size fits all” generalised dietary advice ^(4; 5).
38 Personalised nutrition (PN) may be a more effective approach for improving dietary and
39 physical activity behaviours than non-personalised advice ^(5; 6). However, the relevance of the
40 outcomes of PN interventions may be limited if there are systematic socio-demographic or
41 behavioural differences between study completers and dropouts, which may result in specific
42 target groups (e.g. obese individuals) not benefiting from PN. Socio-demographic variables
43 such as age, social class, occupation, and financial factors are key determinants of dropouts in
44 lifestyle-based interventions ^(7; 8), with more recent evidence also suggesting that behavioural
45 characteristics are important predictors of attrition ⁽⁹⁾. Dropouts from dietary and lifestyle
46 interventions may differ considerably from one intervention to another ⁽⁷⁾, with approximately
47 a third of participants dropping out of weight loss interventions ^(10; 11; 12; 13) and 20% from
48 other diet and lifestyle interventions ^(7; 14). For reasons of cost-effectiveness, reach and
49 scalability, internet-based lifestyle interventions are increasingly popular ^(15; 16) although more
50 information is needed on the characteristics of dropouts from such studies. Understanding the
51 determinants of attrition from internet-based PN intervention studies will inform the design of
52 more efficiently targeted lifestyle interventions.

53 The aim of the present paper was to characterise participants who dropped out of the
54 Food4Me Proof of Principle (PoP) internet-based trial of PN, which was designed to improve
55 dietary and physical activity behaviours. Socio-demographic, anthropometric, dietary,
56 behavioural and health-related characteristics are compared between completers and those
57 who dropped out.

58

59 METHODS

60 Study design

61 The Food4Me PoP study was a 6-month, 4-arm, internet-based, RCT conducted across 7
62 European countries via www.food4me.org ⁽¹⁷⁾. The RCT was designed to emulate a real-life

63 internet-based PN service and aimed to investigate i) whether personalisation of dietary
64 advice assists and/or motivates participants to eat a healthier diet in comparison with non-
65 personalised, conventional healthy eating guidelines and ii) whether personalisation based on
66 individualised phenotypic or genotypic information is more effective in assisting and/or
67 motivating study participants to make, and to sustain, appropriate healthy changes, than
68 personalisation based on diet alone. The Research Ethics Committees at each University or
69 Research Centre delivering the intervention granted ethical approval for the study. The
70 Food4Me trial was registered as a RCT (NCT01530139) at Clinicaltrials.gov. All participants
71 expressing an interest in the study were asked to sign online consent forms at two stages in
72 the screening process.

73

74 **Recruitment and eligibility criteria**

75 Participants were recruited via the Internet to emulate an internet-based PN service. This was
76 aided by local and national advertising of the study via the Internet, radio, newspapers,
77 posters, e-flyers, social media and word of mouth. Recruitment sites were as follows:
78 University College Dublin (Ireland), Maastricht University (The Netherlands), University of
79 Navarra (Spain), Harokopio University (Greece), University of Reading (United Kingdom,
80 UK), National Food and Nutrition Institute (Poland) and Technical University of Munich
81 (Germany). Participants were excluded if they were <18 years of age, pregnant or lactating,
82 had no or limited access to the Internet, were following a prescribed diet for any reason,
83 including weight loss, in the last 3 months or had diabetes, coeliac disease, Crohn's disease,
84 or any metabolic disease or condition altering nutritional requirements such as thyroid
85 disorders (if condition was not controlled), allergies or food intolerances. Participants were
86 incentivised to join the study by receiving a personalised feedback report at month 6 based on
87 their dietary, phenotypic and genotypic information, regardless of their treatment arm
88 allocation.

89

90 **Intervention arms**

91 A total of 1607 participants were randomized to one of four intervention arms. Participants
92 received non-personalised, generalised dietary and physical activity (PA) advice (Control), or
93 one of three levels of PN: Level 1: based on personal current PA + diet alone; Level 2: based
94 on PA + dietary and phenotypic data; Level 3: based on PA + dietary, phenotypic and

95 genotypic data. Participants randomized to levels 1, 2 or 3 were further randomized into “low
96 intensity” or “high intensity” intervention groups. Participants in the low intensity group
97 received personalised feedback three times during the intervention (at baseline, month 3 and
98 month 6), whereas those randomized to the high intensity group received personalised
99 feedback five times during the intervention (at baseline and months 1, 2, 3 and 6). In addition,
100 the high intensity group had access to an online forum for discussion of topics related to the
101 intervention, personalised recipes and had more personalised feedback on PA. Further details
102 of the Food4Me PoP study are provided elsewhere ⁽¹⁷⁾.

103

104 **Personalized feedback report**

105 At baseline, month 3 and month 6, intakes of 5 food groups (fruits and vegetables,
106 wholegrain, low-fat dairy products, oily fish and red meat and processed meat) and 17
107 nutrients were categorized as too high or too low for each participant randomised to PN.
108 Contributing foods were identified and specific messages were developed, according to
109 standardized algorithms, to advise change in intake of those foods. For participants
110 randomized to L2 and L3, feedback also included phenotypic measures (L2) and phenotypic
111 and genotypic data (L3) ⁽¹⁷⁾.

112

113 **Screening questionnaires and dietary intakes**

114 Individuals who were interested in participating in the study completed an online screening
115 questionnaire to collect information on socio-demographic, health and anthropometric
116 characteristics. This questionnaire also included information on dietary habits (e.g. meal
117 skipping) and reasons for interest in participation in the study (e.g. weight loss). Likert scale
118 responses were aggregated into three categories: ‘Disagree’ (‘Completely disagree’ and
119 ‘Disagree’), ‘Neither disagree nor agree’ and ‘Agree’ (‘Agree’ and ‘Completely agree’) and
120 questions relating to frequency of the occurrence into two categories: Often (‘Every day’ and
121 ‘4-6 times per week’) or Rarely (‘1-3 times per week’ and ‘(almost) never’; **Supplemental**
122 **Table 1**).

123 Participants were asked to complete an online food frequency questionnaire (FFQ) to
124 estimate usual dietary intake at screening, baseline (month 0) and at months 3 and 6 (also at
125 months 1 and 2 for the high intensity group only). This FFQ was developed and validated for
126 the Food4Me Study ^(18; 19), and included 157 food items consumed frequently in each of the 7

127 recruitment countries. Intakes of foods, total energy and macronutrients were computed in
128 real time using a food composition database based on McCance & Widdowson's "The
129 composition of foods" ⁽²⁰⁾. Basal metabolic rate (BMR) was estimated using the Oxford
130 equation ⁽²¹⁾. Intakes were assessed using standardised recommendations ⁽¹⁷⁾ for foods and
131 food groups that were integrated and harmonised across 8 European countries (UK, Ireland,
132 Germany, The Netherlands, Spain, Greece, Poland and Norway) ^(22; 23; 24; 25). The following 5
133 food group recommendations were used in the present analysis: eat at least 5 portions of
134 fruits and vegetables every day (operationalised as $\geq 400\text{g}$); eat at least 3 portions of
135 wholegrain products daily ($\geq 50\text{g}$); eat at least 3 portions of low-fat dairy products daily
136 ($\geq 600\text{g}$); eat at least 1 portion of oily fish per week ($\geq 150\text{g}$) and eat fewer than 3 portions of
137 red meat and processed meat per week ($\leq 450\text{g}$) ⁽¹⁷⁾.

138

139 **Socio-demographic and health-related measures**

140 Body weight, height and waist circumference (WC) were self-measured and self-reported.
141 Body mass index (BMI) was estimated from body weight and height. Self-reported
142 measurements were validated in a sub-sample of the participants ($n=140$) and showed a high
143 degree of reliability ⁽²⁶⁾. Participants were sent finger-prick based Dry Blood Spot cards
144 (collected 5 drops equivalent to 150 μl of blood per card) which were completed and returned
145 by post to recruitment centres and used to estimate total blood cholesterol concentrations.
146 Physical activity levels (PALs) and time spent in sedentary behaviours (SB) were estimated
147 from tri-axial accelerometers (TracmorD, Philips Consumer Lifestyle, The Netherlands).
148 Participants self-reported smoking habits and occupation. Based on European classifications
149 of occupations the following groupings were used: "Professional and managerial"
150 (professionals; managers); "Intermediate" (armed forces occupations; technicians and
151 associate professionals; clerical support workers); "Routine and manual" (craft and related
152 trades workers; plant and machine operators and assemblers; service and sales workers;
153 elementary occupations; skilled agricultural, forestry and fishery workers) ^(27; 28). Categories
154 for "Students" and "Retired and unemployed" were added. See Supplemental material for
155 further information on the study design.

156

157 **Statistical analyses**

158 Data were analysed using Stata (version 13; StataCorp, College Station, TX, USA).
159 Screening data (dietary habits, FFQ, reasons for interest in the study, ethnicity, medication
160 use and health characteristics) plus measurements of WC, SB and PAL, which were collected
161 at baseline, were used in the present analysis. Logistic regression and multiple linear
162 regression were used to test for significant differences between categorical and continuous
163 variables, respectively. The Odds Ratio (OR) for dropping out before month 6 was estimated
164 for categorical variables. All analyses were adjusted for baseline age, sex and country.
165 Physical activity outcomes were further adjusted for time spent wearing the accelerometer
166 and season. Sensitivity analyses were performed to estimate ORs for dropping out at the
167 interim time point (month 3). Results were deemed significant at $P<0.05$.

168

169 **RESULTS**

170 A total of 1607 participants were randomized into the study at baseline. As summarised in
171 **Figure 1**, 337 participants (21%) dropped out and 1270 participants completed the 6-month
172 intervention period. Of the 337 participants dropped out, 127 (38%) dropped out before
173 completing baseline measurements and a total of 261 (77%) had dropped out by month 3 (Fig
174 1).

175

176 **Health and lifestyle-related characteristics**

177 Dropouts were on average 6 years younger than completers and were predominantly female
178 (**Table 1**). In addition, dropouts weighed more, had higher BMI and lower WC (Table 1).
179 More participants who dropped out of the study (8%), than those who completed, reported
180 being interested in participating because they wanted to lose weight. No significant
181 differences in occupation classification were observed between completers and those who
182 dropped out. Furthermore, there were no significant differences in the height, PAL, SB or
183 total cholesterol concentrations between groups. The percentage of individuals following a
184 restricted diet, taking medication or presenting with clinically diagnosed diseases did not
185 differ significantly between completers and dropouts (Table 1).

186

187 **Dietary characteristics**

188 No significant differences in total energy intakes or energy intake (EI) to BMR ratio were
189 identified between individuals who completed the 6-month intervention and those who
190 dropped out (**Table 2**). Completers reported consuming more energy from polyunsaturated
191 fatty acids (PUFA) and less salt than dropouts. Percentage energy intakes from total fat,
192 saturated (SFA) and monounsaturated fatty acids (MUFA), protein and carbohydrate were not
193 significantly different between dropouts and completers (Table 2). The percentage of
194 individuals who met the dietary recommendations for oily fish, wholegrains, red meat, fruit
195 and vegetables, and low-fat dairy products did not differ significantly between completers
196 and dropouts (Table 2).

197

198 **Odds ratios of dropping out by intervention arm**

199 Attrition did not differ significantly depending on whether individuals were randomized to
200 receive generalised dietary guidelines (Control) or any level of PN (L1, L2 or L3; **Table 3**).
201 When levels of PN were grouped together (L1, L2 and L3), there was no significant
202 difference in OR for dropping out between participants who received generalised dietary
203 advice (Control) and those who received PN advice (Table 3). However, when intervention
204 arms were grouped according to whether individuals received high or low intensity feedback,
205 the odds of participants dropping out were higher in those randomised to receive high
206 intensity feedback than low intensity feedback (OR 1.81, 95% CI: 1.36-2.41; $P < 0.001$).

207

208 **Odds ratio of dropping out by socio-demographic and dietary characteristics**

209 Stratification by age revealed that the odds of participants dropping out were higher if they
210 were under 45 y of age than if they were over 45 y (**Table 4**). In addition, the odds of females
211 dropping out were higher than for males. Compared with normal weight individuals, the odds
212 of dropping out were higher in obese individuals. Attrition was not significantly different in
213 overweight compared with normal weight individuals, between non-smokers and current
214 smokers or individuals with low vs. high PAL or low vs. high SB. (Table 4).

215 Compared with the average for all countries, the odds of dropping out were higher in
216 participants from Ireland, whereas the odds in participants from the Netherlands were lower.
217 Attrition was not significantly different for participants from Germany, Greece, Poland, Spain
218 or the United Kingdom when compared with the overall average (Table 4). Being in an
219 intermediate or routine/manual occupation, or being a student or retired/unemployed did not

220 significantly affect the OR of dropping out from the study compared with being in a
221 professional/managerial occupation (Table 4). Baseline diet was not a predictor of drop out.
222 Attrition did not differ significantly between individuals who met the recommendations for
223 oily fish, wholegrains, red meat, fruit and vegetables and low-fat dairy products compared
224 with those who did not (Table 4).

225

226 **Odds ratio of dropping out by behavioural characteristics**

227 As illustrated in **Figure 2**, the odds of dropping out were higher in participants who had
228 signed up to the study with the aim of losing weight [1.53 (1.19-1.97); $P<0.001$]. Attrition
229 was not significantly different if participants had, or had not, signed up with the aim of
230 gaining weight, wanting to know what foods are best for them, wishing to improve their own
231 or their family's health, for wellbeing reasons nor in individuals with an interest in sports
232 performance or preventing a future illness (**Supplemental Table 2**).

233 Odds of attrition were higher if participants ate their main meal away from home [1.33 (1.04-
234 1.72); $P=0.023$] and higher if they regularly skipped meals [1.75 (1.16-2.65; $P=0.008$; Figure
235 2]. ORs for dropping out were not significantly different depending on whether participants
236 prepared a meal from scratch, ate many or few hot meals per day, or spent little time
237 preparing a main meal (Supplemental Table 2).

238 Odds of dropping out were lower if participants reported that they frequently ate healthy
239 [0.62 (0.45-0.86); $P=0.003$] and lower if they reported eating healthy without having to think
240 about it consciously [0.74 (0.56-0.97); $P=0.031$; Figure 2]. Attrition was not significantly
241 different depending on whether participants reported being in control of their health, staying
242 healthy by taking care of themselves, agreed that efforts to improve their health were a waste
243 of time, agreed that there was no use in concerning themselves with their health or felt weird
244 if they did not eat healthily (Supplemental Table 2).

245

246 **Sensitivity analyses**

247 Factors predicting the likelihood of dropping out by month 3 were similar to those observed
248 at month 6. However, odds of early attrition were higher if participants reported having a
249 clinically diagnosed disease (Supplemental Table 2). Furthermore, odds of dropping out in
250 overweight individuals were higher by month 3, compared with normal weight individuals.
251 The odds of dropping out by month 3 were lower in individuals who indicated that they had

252 signed up to the study because they thought it was important to support academic studies, and
253 lower among those who were curious to find out what happened in academic studies
254 (Supplemental Table 2).

255

256 **DISCUSSION**

257 The present study is the first to investigate the socio-demographic, anthropometric, dietary,
258 behavioural and health-related characteristics of participants who dropped out of a 6-month
259 internet-based study of PN. Our main findings suggest that dropouts were more likely to be
260 younger, obese individuals who skip meals more often and were motivated by weight loss.
261 Furthermore, more frequent data collection and PN feedback increased the likelihood of
262 individuals dropping out.

263 The dropout rate observed in the present study is well within the range expected from a
264 traditional face-to-face lifestyle intervention of this duration ⁽²⁹⁾. A recent meta-analysis on
265 the effectiveness of web-based interventions ⁽³⁰⁾ concluded that web-based interventions were
266 as effective as face-to-face interventions in achieving weight loss and that the dropout rate
267 was 21%, which is similar to the dropout rate in our study. However, the studies included in
268 the meta-analysis were heterogeneous, with dropout rates as high as 40% ^(31; 32). Our findings
269 suggest that individuals interested in joining the Food4Me Study for the purpose of losing
270 weight were more likely to drop out. The present study was not designed, or advertised, as a
271 weight-loss study, but rather as a PN intervention aiming to improve diet and physical
272 activity. Thus, some participants may have felt discouraged by their lack of weight loss
273 during the intervention, which has been highlighted as a predictor of attrition in previous
274 obesity-related studies ^(13; 33).

275 Our characterization of dropouts versus completers is broadly similar to previous lifestyle-
276 based intervention studies. We found that younger age and higher BMI were strong predictors
277 of greater attrition, which confirm previous findings ^(34; 35). Older individuals may be more
278 interested in sustained participation due to increased health concerns and heightened
279 perceived susceptibility to disease. Obese individuals are often characterised by poor diet and
280 low levels of physical activity ⁽³⁶⁾, which may make lifestyle changes challenging. In contrast
281 with an earlier report that individuals from lower socio-economic status (SES) are more
282 likely to drop out of lifestyle interventions ⁽⁷⁾, we found no differences in attrition between
283 occupation groups. This may be due to the personalised nature of the Food4Me intervention:
284 recent research suggests that lifestyle interventions may be more effective in individuals with

285 low SES if they use tailored, or personalised, advice based on information about individual
286 physical condition e.g. being overweight or having high cholesterol concentrations ⁽³⁷⁾.
287 However, it may also be due to the higher SES of our participants and that our measure of
288 SES was limited to occupation. We did not identify any difference in health and disease
289 status between completers and those who dropped out. Although some associations between
290 attrition and health-related characteristics have been observed ⁽³⁸⁾, results have been
291 inconsistent ⁽³⁹⁾.

292 Inter-country differences in attrition observed in our analyses may partly be explained by the
293 timing of the interventions. Ireland and the UK were the first centres to commence the
294 Food4Me intervention, and so the higher dropout rates (although not significant for the UK)
295 may be a result of initial teething problems, such as responding to queries from participants,
296 in delivering the intervention, which were resolved when the other centres initiated
297 recruitment. There is no obvious explanation for the significantly lower dropout rate in the
298 Netherlands, but may have been due to centre-to-centre variation in the perseverance of
299 researchers. Attrition was similar for control and PN intervention arms, however, individuals
300 were more likely to drop out if they were in the high intensity feedback group. The burden
301 associated with the higher number of occasions that participants were contacted to complete
302 their FFQs and provide their phenotypic data between baseline and month 3 may explain
303 these results more than receiving more frequent PN feedback per se. Alternatively, although
304 individuals in the high intensity group had access to online discussion forums, personalised
305 recipes and additional PA advice, while those in the low intensity group did not, the
306 perceived value to participants of the more frequent feedback may not have been sufficient to
307 outweigh the added burden of completing extra questionnaires. As a result, further
308 consideration of the nature and frequency of such feedback may be important for future study
309 designs.

310 Our study is the first internet-based PN study to characterise dropouts based on their dietary
311 habits. Although many studies have associated socio-demographic characteristics, such as age
312 and social class, with attrition ^(7; 14), behavioural determinants, such as reasons for
313 participation and dietary habits, require further elucidation ^(8; 40). Improved understanding of
314 these factors may help in tailoring interventions to the needs of participants ⁽⁹⁾ and hence
315 reduce dropout. Furthermore, a systematic review of predictors of dropout in weight loss
316 interventions reported that poor eating habits were associated with higher dropout rates ⁽⁸⁾.
317 We found that participants were more likely to drop out if they skipped meals and if ate their

318 main meal away from home, suggesting that it may be more difficult for individuals with
319 these dietary habits to comply with PN intervention. As a result, future design of PN advice
320 would benefit from incorporating eating behaviour characteristics. Participants in the
321 Food4Me Study were also less likely to drop out if they reported that they often ate healthily,
322 did not have to consciously think about eating healthily and had lower PUFA and higher salt
323 intakes. These findings are consistent with previous studies, where healthier individuals are
324 more interested and willing to participate in and complete lifestyle interventions ⁽⁸⁾. However,
325 participants in the Food4Me PoP study were broadly representative of the European
326 population in terms of obesity prevalence and dietary adequacies, and so would benefit from
327 improved diet and PA ⁽⁴¹⁾. Although psychological determinants of attrition have been studied
328 ^(42; 43), the role of influences such as life stress, motivation and perceived self-efficacy on
329 attrition in a PN intervention is poorly understood ⁽⁴⁴⁾.

330 The present study had a number of strengths. The Food4Me PoP study included a large
331 number of participants from 7 different European countries. By collecting information on
332 socio-demographics, anthropometric, PA, and dietary intakes as well as information on
333 dietary habits, we had a comprehensive overview of the characteristics of participants who
334 dropped out of an internet-based PN intervention.

335 A limitation of this study is that psychological determinants of attrition were not investigated.
336 Psychological constructs, such as perceived self-efficacy, may affect behaviour change and
337 thus attrition. For example, an individual with a low perceived self-efficacy may be less
338 likely to follow dietary advice and thus be less likely to remain in a dietary intervention ⁽⁴⁵⁾.
339 However, as a PoP study, assessment of psychological determinants was not within the scope
340 of the present study. As a result, the present findings should be interpreted with the
341 understanding that psychological constructs may have played a role in determining attrition
342 and further research into these specific determinants is warranted. A potential limitation of
343 the study is that our data were self-reported via the internet, which may have introduced
344 measurement error. However, the validity of internet-based, self-reported anthropometric data
345 is high ⁽⁴⁶⁾ and has been confirmed in the present study ⁽⁴⁷⁾. Dietary intakes were estimated by
346 a FFQ, which is known to be subject to misreporting error ⁽⁴⁸⁾ but this was minimised by
347 validating our FFQ against a 4-day weighed food record ⁽¹⁹⁾. Occupations were not asked for
348 the purposes of SES and so the specificity of the classification of the occupations could not
349 always be guaranteed. Our study participants were predominantly Caucasian so further

350 research among wider ethnicity groups is required to generalise our findings to other
351 populations.

352 Our findings suggest that future PN interventions would benefit from strategies designed to
353 sustain compliance from younger participants and those who are obese. Importantly, future
354 PN interventions should consider dietary habits e.g. the frequency of meal skipping and
355 eating main meals away from home, and psychological characteristics of their participants to
356 develop strategies to help such participants remain in the study. In addition our finding of
357 higher dropout rate among those completing more FFQs and receiving more frequent
358 feedback suggests that the extra burden of completing additional questionnaires may be
359 detrimental to their compliance with the intervention.

360

361 **Conclusions**

362 Attrition in the Food4Me PN intervention study delivered via the internet was close to the
363 average for other lifestyle-based interventions. There was no difference in dropout rate
364 between those randomized to the Control group (generalised dietary advice) and those
365 randomised to receive PN advice. However, more frequent data collection and PN feedback
366 and behavioural barriers to healthy eating were strong determinants of attrition. Future PN
367 interventions would benefit from improved strategies to minimise dropouts among younger
368 and obese individuals. Findings from this study will be of value to researchers who wish to
369 design and implement internet-delivered PN interventions which have considerable potential
370 to deliver improved lifestyle behaviours and, therefore, benefits for public health.

REFERENCES

1. Ng M, Fleming T, Robinson M *et al.* (2014) Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet* **384**, 766-781.
2. World Health Organization (2014) Global status report on noncommunicable diseases 2014.
3. Sepúlveda J, Murray C (2014) The state of global health in 2014. *Science* **345**, 1275-1278.
4. Hood L, Friend SH (2011) Predictive, personalized, preventive, participatory (P4) cancer medicine. *Nat Rev Clin Oncol* **8**, 184-187.
5. Celis-Morales C, Lara J, Mathers JC (2014) Personalising nutritional guidance for more effective behaviour change. *Proc Nutr Soc* **12**, 1-9.
6. Nielsen DE, El-Sohehy A (2014) Disclosure of Genetic Information and Change in Dietary Intake: A Randomized Controlled Trial. *PLoS ONE* **9**, e112665.
7. Roumen C, Feskens EJM, Corpeleijn E *et al.* (2011) Predictors of lifestyle intervention outcome and dropout: the SLIM study. *Eur J Clin Nutr* **65**, 1141-1147.
8. Moroshko I, Brennan L, O'Brien P (2011) Predictors of dropout in weight loss interventions: a systematic review of the literature. *Obesity Reviews* **12**, 912-934.
9. Huisman S, Maes S, De Gucht VJ *et al.* (2010) Low Goal Ownership Predicts Drop-out from a Weight Intervention Study in Overweight Patients with Type 2 Diabetes. *Int J Behav Med* **17**, 176-181.
10. Bennett GA, Jones SE (1986) Dropping out of treatment for obesity. *J Psychosom Res* **30**, 567-573.
11. Dalle Grave R, Calugi S, Molinari E *et al.* (2005) Weight Loss Expectations in Obese Patients and Treatment Attrition: An Observational Multicenter Study. *Obesity Res* **13**, 1961-1969.
12. Davis M, Addis M (1999) Predictors of attrition from behavioral medicine treatments. *Ann Behav Med* **21**, 339-349.
13. Colombo O, Ferretti VV, Ferraris C *et al.* (2014) Is drop-out from obesity treatment a predictable and preventable event? *Nutrition Journal* **13**, 13.
14. Groeneveld I, Proper K, van der Beek A *et al.* (2009) Factors associated with non-participation and drop-out in a lifestyle intervention for workers with an elevated risk of cardiovascular disease. *International Journal of Behavioral Nutrition and Physical Activity* **6**, 80.
15. Williams G, Hamm MP, Shulhan J *et al.* (2014) Social media interventions for diet and exercise behaviours: a systematic review and meta-analysis of randomised controlled trials. *BMJ Open* **4**.
16. Shuger S, Barry V, Sui X *et al.* (2011) Electronic feedback in a diet- and physical activity-based lifestyle intervention for weight loss: a randomized controlled trial. *International Journal of Behavioral Nutrition and Physical Activity* **8**, 41.
17. Celis-Morales C, Livingstone KM, Marsaux CFM *et al.* (2015) Design and baseline characteristics of the Food4Me study: a web-based randomised controlled trial of personalised nutrition in seven European countries. *Genes Nutr* **10**, 450.
18. Forster H FR, Gallagher C, O'Donovan CB, Woolhead C, Walsh MC, Macready AL, Lovegrove JA, Mathers JC, Gibney MJ, Brennan L, Gibney ER (2014) Online Dietary Intake Estimation: The Food4Me Food Frequency Questionnaire. *J Med Internet Res* **16**, e150.
19. Fallaize R, Forster H, Macready AL *et al.* (2014) Online Dietary Intake Estimation: Reproducibility and Validity of the Food4Me Food Frequency Questionnaire Against a 4-Day Weighed Food Record. *J Med Internet Res* **16**, e190.
20. Food Standards Agency (2002) *McCance and Widdowson's The Composition of Foods*. Sixth summary edition ed. Cambridge: Royal Society of Chemistry.
21. Henry CJK (2005) Basal metabolic rate studies in humans: Measurement and development of new equations. *Public Health Nutr* **8**, 1133-1152.

22. Institute of Medicine (2005) Dietary Reference Intakes for energy, Carbohydrate, Fibre, Fat, Fatty acids, Cholesterol, Protein, and Amino acids
2005. <http://www.nap.edu/openbook.php?isbn=0309085373> (accessed 24th March 2015)
23. Institute of Medicine (2011) Dietary Reference Intakes Tables and Applications
2011. <http://www.iom.edu/Activities/Nutrition/SummaryDRIs/DRI-Tables.aspx> (accessed 24th March 2015)
24. World Health Organisation (2007) *Protein and Amino acid requirements in Human Nutrition. Report of a Joint WHO/FAO/UNU Expert Consultation (WHO Technical Report Series 935)*.
25. World Health Organisation (2010) Food and Agriculture Organisation of the United Nations (FAO) report of an expert consultation on fats and fatty acids in human nutrition. http://www.who.int/nutrition/publications/nutrientrequirements/fatsandfattyacids_humannutrition/en/ (accessed 30th March 2016)
26. Celis-Morales C, Livingstone K, Woolhead C *et al.* (2015) How reliable is internet-based self-reported identity, socio-demographic and obesity measures in European adults? *Genes Nutr* **10**, 1-10.
27. European Commission (2015) European skills, competences, qualifications and occupations. <https://ec.europa.eu/esco/web/guest/hierarchybrowser/-/browser/Occupation> (accessed 1st April 2015)
28. European Commission (2015) Mean annual earnings by sex, age and occupation. http://ec.europa.eu/eurostat/web/products-datasets/-/earn_ses_agt28 (accessed 27th March 2015)
29. Clark F, Jackson J, Carlson M *et al.* (2012) Effectiveness of a lifestyle intervention in promoting the well-being of independently living older people: results of the Well Elderly 2 Randomised Controlled Trial. *Journal of Epidemiology and Community Health* **66**, 782-790.
30. Neve M, Morgan PJ, Jones PR *et al.* (2010) Effectiveness of web-based interventions in achieving weight loss and weight loss maintenance in overweight and obese adults: a systematic review with meta-analysis. *Obesity Reviews* **11**, 306-321.
31. Tate DF, Wing RR, Winett RA (2001) Using internet technology to deliver a behavioral weight loss program. *JAMA* **285**, 1172-1177.
32. Harvey-Berino J, Pintauro S, Buzzell P *et al.* (2004) Effect of internet support on the long-term maintenance of weight loss. *Obesity Reviews* **12**, 320-329.
33. Grossi E, Dalle Grave R, Mannucci E *et al.* (2006) Complexity of attrition in the treatment of obesity: clues from a structured telephone interview. *Int J Obesity* **30**, 1132-1137.
34. Wanner M, Martin-Diener E, Bauer G *et al.* (2010) Comparison of Trial Participants and Open Access Users of a Web-Based Physical Activity Intervention Regarding Adherence, Attrition, and Repeated Participation. *J Med Internet Res* **12**, e3.
35. Susin N, Boff RdM, Ludwig MWB *et al.* (2015) Predictors of adherence in a prevention program for patients with metabolic syndrome. *J Health Psychol.*
36. Mesas AE, Guallar-Castillón P, León-Muñoz LM *et al.* (2012) Obesity-Related Eating Behaviors Are Associated with Low Physical Activity and Poor Diet Quality in Spain. *The Journal of Nutrition* **142**, 1321-1328.
37. Bukman AJ, Teuscher D, Feskens EJM *et al.* (2014) Perceptions on healthy eating, physical activity and lifestyle advice: opportunities for adapting lifestyle interventions to individuals with low socioeconomic status. *BMC Public Health* **14**, 1036.
38. Graffagnino CL, Falko JM, La Londe M *et al.* (2006) Effect of a Community-Based Weight Management Program on Weight Loss and Cardiovascular Disease Risk Factors. *Obesity* **14**, 280-288.
39. Gripeteg L, Karlsson J, Torgerson J *et al.* (2010) Predictors of Very-Low-Energy Diet Outcome in Obese Women and Men. *Obesity Facts* **3**, 159-165.
40. Davis MJ, ME A (1999;) Predictors of attrition from behavioral medicine treatments. *Ann Behav Med* **21**, 339-349.

41. Livingstone K, Celis-Morales C, Navas-Carretero S *et al.* (2015) Profile of European adults interested in internet-based personalised nutrition: the Food4Me study. *Eur J Nutr*, 1-11.
42. Post A, Gilljam H, Bremberg S *et al.* (2012) Psychosocial Determinants of Attrition in a Longitudinal Study of Tobacco Use in Youth. *The Scientific World Journal* **2012**, 7.
43. Cochrane G (2008) Role for a sense of self-worth in weight-loss treatments: Helping patients develop self-efficacy. *Can Fam Physician* **54**, 543-547.
44. Mutsaerts MAQ, Kuchenbecker WKH, Mol BW *et al.* (2013) Dropout is a problem in lifestyle intervention programs for overweight and obese infertile women: a systematic review. *Hum Reprod* **28**, 979-986.
45. Schwarzer R, Renner B (2000) Social-cognitive predictors of health behavior: Action self-efficacy and coping self-efficacy. *Health Psychol* **19**, 487-495.
46. Pursey K, Burrows LT, Stanwell P *et al.* (2014) How Accurate is Web-Based Self-Reported Height, Weight, and Body Mass Index in Young Adults? *J Med Internet Res* **16**, e4.
47. Celis-Morales C, Forster H, O'Donovan C *et al.* (2014) Validation of Web-based self-reported socio-demographic and anthropometric data collected in the Food4Me Study. *Proc Nutr Soc* **73**, null-null.
48. Macdiarmid J, Blundell J (1998) Assessing dietary intake: Who, what and why of under-reporting. *Nutr Res Rev* **11**, 231-253.

Table 1 Baseline socio-demographic characteristics of participants who completed the intervention and those who dropped out by month 6

	Completers (n=1270)		Dropouts (n=337)		P*
	Mean	SD	Mean	SD	
Age, years	40.8	13.0	34.8	12.3	<0.001
Female, %	57.4		66.8		0.017
Ethnicity					
Caucasian, %	96.9		96.1		0.83
Occupation, %					
Professional and managerial	40.0		34.6		0.53
Intermediate occupations	26.1		25.5		0.98
Routine and manual	9.5		11.1		0.42
Student	14.0		21.2		0.13
Retired	3.0		2.4		0.39
Unemployed	7.4		5.3		0.88
Anthropometrics					
Body weight, kg	74.6	15.7	75.4	17.0	<0.001
BMI, kg/m ²	25.4	4.8	25.9	5.5	<0.001
Waist circumference, cm	85.9	13.7	84.6	14.7	0.015
Height, m	1.7	0.1	1.7	0.1	0.89
Physical activity					
PAL	1.7	0.2	1.7	0.2	0.86
Sedentary behaviour, min/d	747	75.2	732	77.1	0.31
Dietary conditions, %					
Want to lose weight	45.8		53.7		0.002
Restricted diet	6.7		8.3		0.66
Medication use, %					
Prescribed medication	30.5		27.6		0.67
Non-prescribed medication	10.3		7.7		0.32
Health and disease					
Total cholesterol, mmol/L	4.6	1.0	4.3	0.9	0.06
Current smoker, %	11.7		13.7		0.66
Cancer, %	1.6		0.3		0.21
High blood pressure, %	7.9		6.8		0.21
Heart disease, %	1.4		1.2		0.61
Diabetes, %	0.6		0.6		0.61
Blood disorders, %	1.1		0.6		0.29

Values represent means, SD or percentages; BMI, body mass index; PAL, Physical activity level

*, Multiple linear regression and logistic regression were used to test for significant differences between groups in continuous and categorical variables, respectively. Analyses were adjusted for age, sex and country.

Table 2 Baseline dietary characteristics of participants who completed the intervention and those who dropped out by month 6

	Completers (n=1270)		Dropouts (n=337)		P*
	Mean	SD	Mean	SD	
Nutrient intake					
Total energy, kcal/d	2756	1208	2796	1149	0.43
EI:BMR ratio	1.8	0.7	1.8	0.7	0.94
Total fat, % energy	35.5	6.5	35.1	6.5	0.29
SFA, % energy	14.0	3.4	14.1	3.6	0.64
MUFA, % energy	13.6	3.5	13.2	3.2	0.10
PUFA, % energy	5.7	1.5	5.4	1.2	0.002
Protein, % energy	16.9	3.6	17.1	4.1	0.41
Carbohydrate, % energy	46.8	8.2	47.3	8.3	0.70
Sugars, % energy	21.2	6.1	21.0	6.7	0.21
Dietary fibre, g/d	33.2	18.9	33.9	20.6	0.35
Salt, g/d	8.1	4.2	8.6	7.9	0.050
Meeting dietary recommendations, %					
Oily fish	34.7		32.3		0.92
Wholegrains	77.6		75.7		0.74
Red meat	48.0		49.6		0.67
Fruit and vegetables	57.7		56.4		0.66
Low fat dairy	8.0		6.5		0.29

Values represent means, SD or percentages; SFA, saturated fatty acid; MUFA, mono-unsaturated fatty acid; PUFA, poly-unsaturated fatty acid

*, Multiple linear regression and logistic regression were used to test for significant differences between groups in continuous and categorical variables, respectively. Analyses were adjusted for age, sex and country.

Table 3 Odds ratio (OR) of participants dropping out at month 6 by intervention arm

	Odds ratio	95% CI	P*
Control (ref) vs.			
L1 (low and high intensity)	1.40	0.99-1.98	0.05
L2 (low and high intensity)	1.04	0.72-1.48	0.85
L3 (low and high intensity)	1.07	0.75-1.53	0.70
Control (ref) vs. personalised nutrition	1.17	0.87-1.56	0.30
Low (ref) vs. high intensity feedback	1.81	1.36-2.41	<0.001

Values represent the adjusted OR, 95% CI and their corresponding P value. L1, Level 1 – personalised advice based on diet alone, L2, Level 2 – personalised advice based on diet and phenotype, L3, personalised advice based on diet, phenotype and genotype

*, Logistic regression was used to test for significant differences between groups. Analyses were adjusted for age, sex and country.

Table 4 Odds ratio (OR) for participants dropping out at month 6 by baseline socio-demographic characteristics and dietary adequacies

	Odds ratio	95% CI	P*
Under 45 y (ref) vs. over 45 y	2.57	1.95-3.39	<0.001
Male (ref) vs. female	1.38	1.06-1.78	0.015
BMI category (ref normal weight)			
Overweight	1.31	0.91-1.90	0.15
Obese	2.25	1.47-3.43	<0.001
Non-smoker (ref) vs. current smoker	1.11	0.86-1.44	0.41
Country (ref overall average)			
Germany	1.09	0.76-1.56	0.66
Greece	0.90	0.63-1.27	0.54
Ireland	1.62	1.20-2.18	0.002
Netherlands	0.18	0.09-0.35	<0.001
Poland	1.08	0.77-1.50	0.67
Spain	1.06	0.75-1.52	0.73
United Kingdom	1.17	0.85-1.62	0.33
Occupation (ref professional and managerial)			
Intermediate occupations	1.08	0.73-1.59	0.70
Routine and manual	1.22	0.73-2.08	0.45
Student	0.73	0.45-1.17	0.19
Retired or unemployed	1.37	0.75-2.52	0.31
Meeting dietary recommendations (ref not meeting recommendation)			
Fruit and vegetables (≥ 5 portions/day)	1.05	0.82-1.35	0.69
Wholegrains (≥ 50 g/day)	0.93	0.70-1.24	0.63
Red meat (≤ 3 servings/week)	0.93	0.72-1.20	0.56
Oily fish (≥ 1 serving/week)	0.99	0.77-1.31	0.99
Low-fat dairy products (≥ 3 servings/day)	0.77	0.48-1.26	0.30

Values represent the adjusted OR, 95% CI and their corresponding P value.

*, Logistic regression was used to test for significant differences between groups. Analyses were adjusted for age, sex and country

FIGURE LEGENDS

Figure 1 Flow diagram of cumulative dropouts from the Food4Me Proof of Principle Study

Figure 2 Odds ratio (OR) for participants dropping out according to their dietary behaviours and reasons for participation in the study at baseline¹

Values represent the adjusted OR, 95% CI and their corresponding P value.

1, Logistic regression was used to test for significant differences between groups. Models were adjusted for age, sex and country. Variables are dichotomous, reference group (“No/Disagree”).

Online Supporting Material

Supplemental Table 1. Screening questionnaire on dietary habits and reasons for interest in the study

Question	Response options	Aggregated response
How often do you eat your main meal away from home?	Never or up to once/ month Two to three times/ month	Rarely Often
How many hot or cooked meals do you normally eat per day?	Once per week Twice or more/ week	
How often do you prepare a meal "from scratch"?	Every day 4-6 times per week 1-3 times per week	Often Rarely
Do you skip meals and replace them with snacks?	(Almost) never	Often Rarely
How much time on average do you spend preparing a main meal?	Less than 10 min 10-20 min 20-30 min Up to an hour Over an hour	Less than 30 min More than 30 min
I can be as healthy as I want to be	Completely disagree	Disagree
I am in control of my health	Disagree	Neither disagree nor agree
I can pretty much stay healthy by taking care of myself	Neither disagree nor agree Agree	agree Agree
Efforts to improve your health are a waste of time	Completely agree	Note that the option 'Neither disagree nor agree' was excluded in the data analysis
I am bored by all the attention that is paid to health and disease prevention		
What's the use of concerning yourself about your health - you'll only worry yourself to death		
Eating healthily is something I do frequently		
I eat healthily without having to consciously think about it		
I feel weird if I don't eat healthily		
I'm interested in personalised nutrition	No	No
I want to know what foods are best for me	Yes	Yes
I want to lose weight		
I want to gain weight		
I want to improve my family's health		
I want to improve my health		

Online Supporting Material

Supplemental Table 2. Odds ratio of participants dropping out by dietary habits and reasons for interest in the study

Question	Odds ratio	95% CI	P*
Eat your main meal away from home often (ref rarely)	1.33	1.04-1.72	0.023
Normally eat many hot or cooked meals eat per day (ref rarely)	1.06	0.82-1.37	0.67
How often do you prepare a meal "from scratch" (ref often)	1.03	0.79-1.34	0.82
Do you skip meals and replace them with snacks (ref rarely)	1.75	1.16-2.65	0.008
Time spent preparing a main meal (ref less than 30 min)	0.96	0.75-1.24	0.78
I can be as healthy as I want to be (ref disagree)	0.95	0.62-1.44	0.79
I am in control of my health (ref disagree)	0.87	0.58-1.29	0.48
I can pretty much stay healthy by taking care of myself (ref disagree)	0.91	0.50-1.65	0.75
Efforts to improve your health are a waste of time (ref disagree)	1.65	0.78-3.48	0.19
I am bored by all the attention that is paid to health and disease prevention (ref disagree)	1.30	0.58-2.94	0.53
What's the use of concerning yourself about your health - you'll only worry yourself to death (ref disagree)	1.31	0.74-2.33	0.35
Eating healthily is something I do frequently (ref disagree)	0.62	0.45-0.86	0.003
I eat healthily without having to consciously think about It (ref disagree)	0.74	0.56-0.97	0.031
I feel weird if I don't eat healthily (ref disagree)	1.04	0.77-1.41	0.81
I'm interested in personalised nutrition (ref no)	0.94	0.71-1.24	0.65
I want to know what foods are best for me (ref no)	0.86	0.64-1.15	0.31
I want to lose weight (ref no)	1.53	1.18-1.97	0.001
I want to gain weight (ref no)	1.32	0.60-2.95	0.49
I want to improve my family's health (ref no)	0.96	0.72-1.28	0.77
I want to improve my health (ref no)	0.99	0.77-1.28	0.97
I want to improve my wellbeing (ref no)	1.23	0.96-1.6	0.11
I want to improve my sports performance (ref no)	1.09	0.85-1.41	0.49
I want to prevent a future illness (ref no)	1.08	0.84-1.39	0.55
I have a family history of diet-related illness (ref no)	0.81	0.52-1.25	0.34
I think it is important to help academic studies (ref no)	0.80	0.62-1.03	0.09
I am curious to find out what happens in these studies (ref no)	0.82	0.64-1.05	0.11
I can manage to stick to healthful foods: even if I need a long time to develop the necessary routines (ref no)	0.99	0.61-1.62	0.98
I can manage to stick to healthful foods: even if I have to try several times until it works (ref no)	0.76	0.45-1.30	0.31
I can manage to stick to healthful foods: even if I have to rethink my entire way of nutrition (ref no)	1.16	0.80-1.68	0.43
I can manage to stick to healthful foods: even if I do not receive a great deal of support from others when making my first attempts (ref no)	0.76	0.55-1.05	0.10

Online Supporting Material

I can manage to stick to healthful foods: even if I have to make a detailed plan (ref no)	0.81	0.56-1.15	0.24
---	------	-----------	------

Values represent the adjusted OR, 95% CI and their corresponding P value.

*, Logistic regression was used to test for significant differences between groups. Models were adjusted for age, sex and country. Variables are dichotomous.

Supplementary Methods

The following text is an excerpt from the full manuscript detailing the study design and baseline characteristics of the Food4Me randomized controlled trial (RCT) (1) and has been republished with the kind permission of Springer-Verlag.

Study design

The Food4Me Proof of Principle (PoP) study was a four-arm, web-based RCT conducted across seven European countries, which compared the effects of different levels of personalised nutrition (PN) on health-related outcomes. The intervention was designed to emulate a real-life web-based PN service, and the study aimed to answer the following primary research questions:

- Does personalisation of dietary advice assist and/or motivate participants to eat a healthier diet in comparison with non-personalised, conventional healthy eating guidelines?
- Is personalisation based on individualised phenotypic or genotypic information more effective in assisting and/or motivating study participants to make, and to sustain, appropriate healthy changes, than personalisation based on diet alone?

To answer these research questions, we used an hierarchical study design in participants randomised to a control group (Level 0) or to one of 3 PN interventions with increasingly complex bases for personalised dietary advice (Levels 1–3), i.e. randomisation was to one of the following treatment groups for a 6-month period:

- Level 0 (L0): (control group): non-personalised dietary advice based on (European) population healthy eating guidelines.
- Level 1 (L1): personalised dietary advice based on individual dietary intake data alone.
- Level 2 (L2): personalised dietary advice based on individual dietary intake and phenotypic data.
- Level 3 (L3): personalised dietary advice based on individual dietary intake, phenotypic and genotypic data.

The secondary research question of the study was as follows:

- Does more frequent feedback help participants to improve their compliance and motivate them to eat a healthier diet and follow a healthier lifestyle in comparison with those receiving less frequent feedback?

To answer this secondary research question, participants randomised to Levels 1, 2 or 3 were further randomised into “low-intensity” or “high-intensity” intervention groups:

- Low intensity: personalised feedback given three times during the intervention (at baseline, month 3 and month 6).
- High intensity: personalised feedback given five times during the intervention (at baseline and months 1, 2, 3 and 6). In addition, the “high-intensity” group had access to an online forum for discussion of topics related to the intervention, had access to personalised recipes and had more personalised physical activity (PA) feedback.

Primary and secondary outcomes

The primary outcome of the study was dietary intake at months 3 and 6. The secondary outcomes included PA and phenotypic biomarkers at months 3 and 6. The latter included obesity-related measures (i.e. body weight, body mass index (BMI) and waist circumference) and blood-based biomarkers (i.e. blood glucose, total cholesterol, carotenoids and fatty acids).

Recruitment

Participants were recruited via the Internet to emulate a web-based PN service. This was aided by local and national advertising of the study via the Internet, radio, newspapers, posters, e-flyers, social media and word of mouth.

Recruitment into the Food4Me intervention trial was carried out using identical standardised protocols in seven European recruitment centres. Based on sample size calculations (see below for further details), we aimed to recruit a total of 1,540 study participants (i.e. 220 participants per country). The PoP study recruitment sites were as follows: University

College Dublin, Ireland; Maastricht University, the Netherlands; University of Navarra, Spain; Harokopio University, Greece; University of Reading, UK; National Food and Nutrition Institute, Poland; and Technische Universität München, Germany.

Eligibility criteria

Participants aged ≥ 18 years of age were included in the study. To keep the cohort as representative as possible of the adult population, the following minimal sets of exclusion criteria were applied:

- Pregnant or lactating;
- No or limited access to the Internet;
- Following a prescribed diet for any reason, including weight loss, in the last 3 months;
- Diabetes, coeliac disease, Crohn's disease, or any metabolic disease or condition altering nutritional requirements such as thyroid disorders (if condition was not controlled), allergies or food intolerances.

Exclusion based on prescribed diet or specific diseases was to avoid the theoretical risk that participating in the study could be disadvantageous to the individual.

Ethical approval and participant consent

The Research Ethics Committees at each University or Research Centre delivering the intervention granted ethical approval for the study. An application for the Norwegian arm of the study administered by the University of Oslo was not approved by the local ethics committee.

Prior to participation, an information sheet was provided to all potential volunteers who completed an online informed consent form before submitting personal data. This signed online consent form was automatically directed to the study coordinator to be counter-signed and archived. A second online informed consent form was completed before randomisation to the intervention study only for participants who met the inclusion criteria. A two-step consenting process was applied to permit collection of socio-demographic and dietary information for those interested in participating in PN even if they were ineligible for enrolment in this study, e.g. because of prescribed diets or food allergies. All Ethical

Committees accepted an online informed consent procedure, except for the Netherlands and Germany whose ethics committees requested an additional written informed consent form for each participant recruited into the study. This hard copy consent form was returned by the participant to the respective recruitment centre.

Intervention design

Eligible and consenting participants were allocated to one of the four arms of the study, which included three intervention groups receiving different levels of personalised nutritional advice (L1: dietary data only; L2: dietary and phenotypic data; and L3: dietary, phenotypic and genotypic data) and the control group (L0), receiving conventional, non-personalised advice. To address our secondary research question, participants in levels L1, L2 and L3 were allocated into “low-” or “high-” intensity groups (see next section for details of the randomisation methods). At the end of the study (month 6), all participants received a personalised report which contained dietary, phenotypic and genotypic information and which summarised changes in their individual dietary intake and phenotypic measures between baseline and month 6 of the intervention.

Randomisation

Participants were randomised to one of the seven treatment groups (control group (L0), L1 high intensity, L1 low intensity, L2 high intensity, L2 low intensity, L3 high intensity and L3 low intensity) in combination with stratified randomisation by country (UK, Greece, Spain, Poland, Ireland, Germany and the Netherlands), sex (female or male) and age (<45 or ≥45 years) equally allocated to each treatment using an urn randomisation scheme (2).

Intervention groups

Level 0 (“control group”)

Following baseline measures, participants randomised to the control group (L0) received non-personalised dietary advice based on conventional population healthy eating guidelines. This non-personalised dietary advice was based on national dietary recommendations in each of the seven European countries participating in the Food4Me PoP Study which were integrated to produce a coherent set of recommendations suitable for Europe-wide use. These

“standardised” recommendations included advice on energy intake to optimise BMI and on the consumption of fruits and vegetables, whole-grain products, fish, dairy products, meat, type of fat and salt. In addition, these recommendations included a generic PA recommendation. An advice leaflet was delivered via the web and also attached to an e-mail, which was sent to participants at baseline and at month 3 of the study.

Level 1 (“diet group”)

Following baseline measures, participants randomised to L1 received feedback on how their intakes of specific food groups (fruits and vegetables, whole-grain products, fish, dairy products and meat) compared with guideline amounts. In addition, personalised dietary advice based on their reported dietary intake at baseline and month 3.

Level 2 (“diet + phenotype group”)

Following baseline measures, participants randomised to L2 received personalised dietary advice based on their dietary intake (as for L1) and also on their baseline phenotypic data. The phenotypic feedback was based on anthropometric measurements and nutrient- and metabolic-related biomarkers.

Level 3 (“diet + phenotype + genotype group”)

Participants randomised to L3 received personalised dietary advice based on their dietary intake plus phenotypic and genotypic data collected at baseline. The genotypic feedback was based on specific variants in five nutrient-responsive genes selected specifically for the study.

Personalised feedback report

Participants randomised to L1, L2 and L3 received personalised feedback based on decision trees developed to provide a structured, evidence-based protocol for delivering tailored advice. This advice was based on dietary, PA, phenotypic and genotypic information as appropriate for each intervention group. In each case, intakes were compared with recommended intakes and determined to be adequate, high or low. If intakes were categorised as too high or too low, contributing foods were identified and specific messages were

developed to advise change in intake of those foods. Full details of these decision trees will be published elsewhere. Protocols for the decision trees were standardised across the seven recruitment centres and translated into the language of each country. Nutritionists and dietitians implementing the decision trees were trained to ensure consistency in the PN advice given throughout the study, and, across all seven countries, these staff participated in frequent teleconferences (every 1–2 weeks) to resolve issues and to share best practice.

The participants' reports contained information on how their health-related characteristics compared with recommendations. Estimations of healthy behaviours were explained using a three-colour sliding scale: green representing "Good, no change recommended", amber representing "Improvement recommended" and red representing "Improvement strongly recommended". For the genotype-based information, risk was indicated using "Yes" or "No" according to whether the participant did, or did not, carry the higher risk variant for each of the five nutrient-related genes. Finally, each report contained a personalised message from the dietitian/nutritionist to the participant. This message provided tailored advice for body weight and PA, and included specific nutrition-related goals derived from dietary, phenotypic and/or genotypic markers (according to the participants' intervention group). Based on patient-centred counselling models for facilitating dietary change (3), a total of three nutrient-related goals were provided. These goals were selected by ranking all dietary, phenotypic and genotypic markers (as appropriate for the intervention group) based on their risk status (red, amber or green). The cut-off points for each of the nutritional and phenotypic variables were used to derive personalised goals and advice.

Behavioural change techniques

Explicit behaviour change techniques (BCT) were integrated into several aspects of the intervention and used to support, encourage and enhance dietary and lifestyle changes. The BCT and their conceptual framework were derived from work by Michie et al. on smoking cessation and dietary behaviour change (4, 5). The BCT categories used in the Food4Me PoP study were as follows: (1) behaviour and motivation, (2) behaviour and self-regulatory capacity/skills, (3) interaction and delivery, (4) interaction and information gathering and (5) interaction and communication.

Study measures

Participants consented to self-report all their measures via the Internet and to send requested biological samples (Dry Blood Spot cards and buccal swabs) by conventional mail, using prepaid, stamped addressed envelopes provided by the research team. To ensure that procedures were similar in all recruiting centres, standardised operating procedures were prepared for all study procedures (see below), and researchers underwent centralised training. In addition, to enable participants to collect and report the required information and to collect, process and dispatch the necessary biological samples correctly, participants were provided with detailed instructions online, including pictures and video demonstrations of all procedures, in their native language.

First screening questionnaire

Participants who consented to take part in the study completed an online screening questionnaire that included basic socio-demographic and health statistics, and information about Internet access, pregnancy and lactation, prescribed diets, food intolerance and allergies (used as exclusion criteria). Persons who were deemed unsuitable for the study, e.g. because of inadequate Internet access, pregnancy or use of a therapeutic diet, received formal e-mail notification that they did not match the inclusion criteria for the study and were thanked for their time.

Second screening questionnaire

Eligible participants for inclusion in the RCT completed a second online questionnaire, which collected more detailed socio-demographic, health and anthropometric data, as well as detailed information on food choices and dietary habits using a Food Frequency Questionnaire (FFQ) developed and validated specifically for this study (see below). Following assessment of this information, participants considered suitable for inclusion in the intervention study were asked to complete a second online consent form, which was sent to the study coordinator to be signed and archived. Potential participants considered unsuitable for the intervention study, e.g. through non-compliance in completion of the screening FFQ, received formal notification that they did not match the inclusion criteria for the study and were thanked for their time.

Anthropometric measurements

Body weight, height and upper thigh, waist and hip circumferences were self-measured and self-reported by participants via the Internet. Standardised instructions on how to perform these measurements were provided in printed and digital format (i.e. a video clip available on the Food4Me website in the languages of each of the seven recruitment countries).

Participants were instructed to measure body weight without shoes and wear light clothing using a home or commercial scale and to measure height barefoot using a standardised measuring tape provided by Food4Me. Waist circumference was measured at the mid-point between the lower rib and the iliac crest using the same tape measure. Hip circumference was measured at the widest point around the greater trochanters, while the upper thigh circumference was measured midway between the iliac crest and the knee.

Food Frequency Questionnaire (FFQ)

Habitual dietary intake was quantified using an online-FFQ, developed for this study which included food items consumed frequently in each of the seven recruitment countries. The Food4Me online-FFQ has been validated against a 4-day weighed food record, and the agreement between methods varied, with correlations ranging from .23 (vitamin D) to .65 (protein, % total energy) for nutrient intakes and .11 (soups, sauces and miscellaneous foods) to .73 (yogurts) for food group intake (6, 7). Intakes of foods and nutrients were computed in real time using a food composition database based on McCance & Widdowson's "The composition of foods" (8).

Metabolic markers

Finger-prick blood samples were collected by participants using a collection pack provided by Vitas Ltd, Oslo, Norway. To help with blood collection, participants had access to an online video demonstration with instructions and frequently asked questions. Each participant was asked to fill two Dry Blood Spot cards (equivalent to five drops of blood or to 150 µl of blood per card) at each collection time point. When the ten blood spots were filled, participants were instructed to dry the cards at room temperature for at least 2 h, but not longer than 4 h, before samples were put in an airtight aluminium bag with drying sachet and returned by post to the corresponding recruiting centre. The centres shipped the samples to

Online Supporting Material

Vitas (Vitas Ltd, Norway) and DSM (DSM Nutritional Products Ltd, Switzerland) for measurements of glucose, total cholesterol, carotenoids, n-3 fatty acid index and 32 other fatty acids (by Vitas), and vitamin D (25-OH D2 and 25-OH D3) (by DSM).

Genotypic analyses

Buccal cell samples were collected by participants at baseline using Isohelix SK-1 DNA buccal swabs and Isohelix Dri-capsules and returned by post to each recruiting centre for shipment to LCG Genomics (Hertfordshire, UK). LCG Genomics undertook DNA extraction and genotyping of the five loci used for derived personalised advice. These loci were analysed using KASPTM genotyping assays to provide bi-allelic scoring of single nucleotide polymorphisms (SNPs) and insertions and deletions at specific loci.

Physical activity

PA patterns were determined using a PA monitor—the DirectLife triaxial accelerometer for movement registration (TracmorD) (Philips Consumer Lifestyle, the Netherlands)—and a self-reported Baecke PA questionnaire (9) which was completed online. The accelerometer-based monitor (Philips DirectLife Activity Monitor, the Netherlands) was posted to each participant. Online video demonstrations as well as digital and printed instructions were provided at baseline. Participants were instructed to wear the monitor throughout the six-month intervention and to upload their PA data fortnightly via an online interface.

Sample size consideration

A power calculation was conducted a priori using Minitab® (version 16.1.0) and data for n-3 fatty acids and glucose concentrations in adult European populations. To address our primary research questions, and based on the resources available for the intervention, a sample size of $n = 326$ participants for each of the four intervention arms was planned. This allows us to detect differences of 0.22 SD in our main outcomes with 80 % power and $\alpha = 0.05$. Assuming that the population standard deviation (SD) for n-3 fatty acid index is 1.5 units and for glucose is 1.05 mmol l⁻¹, a total sample of $n = 1,280$ participants was estimated as sufficient to detect a real differences of 0.33 units for n-3 PUFA and 0.23 mmol l⁻¹ glucose post-intervention. Allowing for a potential 20 % drop out, we aimed to recruit 1,540 participants into the study (220 participants per centre).

References

1. Celis-Morales C, Livingstone KM, Marsaux CFM, Forster H, O'Donovan CB, Woolhead C, Macready AL, Fallaize R, Navas-Carretero S, San-Cristobal R, et al. Design and baseline characteristics of the Food4Me study: a web-based randomised controlled trial of personalised nutrition in seven European countries. *Genes Nutr* 2015;10(1):450. doi: 10.1007/s12263-014-0450-2.
2. Wei LJ, JM. L. Properties of the urn randomization in clinical trials. *Control Clin Trials* 1988;9(4):345-64.
3. Rosal MC, Ebbeling CB, Lofgren I, Ockene JK, Ockene IS, Hebert JR. Facilitating Dietary Change: The Patient-Centered Counseling Model. *J Am Diet Assoc* 2001;101(3):332-41. doi: [http://dx.doi.org/10.1016/S0002-8223\(01\)00086-4](http://dx.doi.org/10.1016/S0002-8223(01)00086-4).
4. Michie S, Hyder N, Walia A, West R. Development of a taxonomy of behaviour change techniques used in individual behavioural support for smoking cessation. *Addict Behav* 2011;36(4):315-9. doi: <http://dx.doi.org/10.1016/j.addbeh.2010.11.016>.
5. Michie S, Ashford S, Sniehotta FF, Dombrowski SU, Bishop A, DP. F. A refined taxonomy of behaviour change techniques to help people change their physical activity and healthy eating behaviours: the CALO-RE taxonomy. *Psychol Health* 2011;26(11):1479-98.
6. Forster H FR, Gallagher C, O'Donovan CB, Woolhead C, Walsh MC, Macready AL, Lovegrove JA, Mathers JC, Gibney MJ, Brennan L, Gibney ER. Online Dietary Intake Estimation: The Food4Me Food Frequency Questionnaire. *J Med Internet Res* 2014;16(6):e150.
7. Fallaize R, Forster H, Macready LA, Walsh CM, Mathers CJ, Brennan L, Gibney RE, Gibney JM, Lovegrove AJ. Online Dietary Intake Estimation: Reproducibility and Validity of the Food4Me Food Frequency Questionnaire Against a 4-Day Weighed Food Record. *J Med Internet Res* 2014;16(8):e190. doi: 10.2196/jmir.3355.
8. Food Standards Agency. McCance and Widdowson's *The Composition of Foods*. Sixth summary edition ed. Cambridge: Royal Society of Chemistry, 2002.
9. Baecke J, Burema J, Frijters J. A short questionnaire for the measurement of habitual physical-activity in epidemiological-studies. *Am J Clin Nutr* 1982;36(936-942).

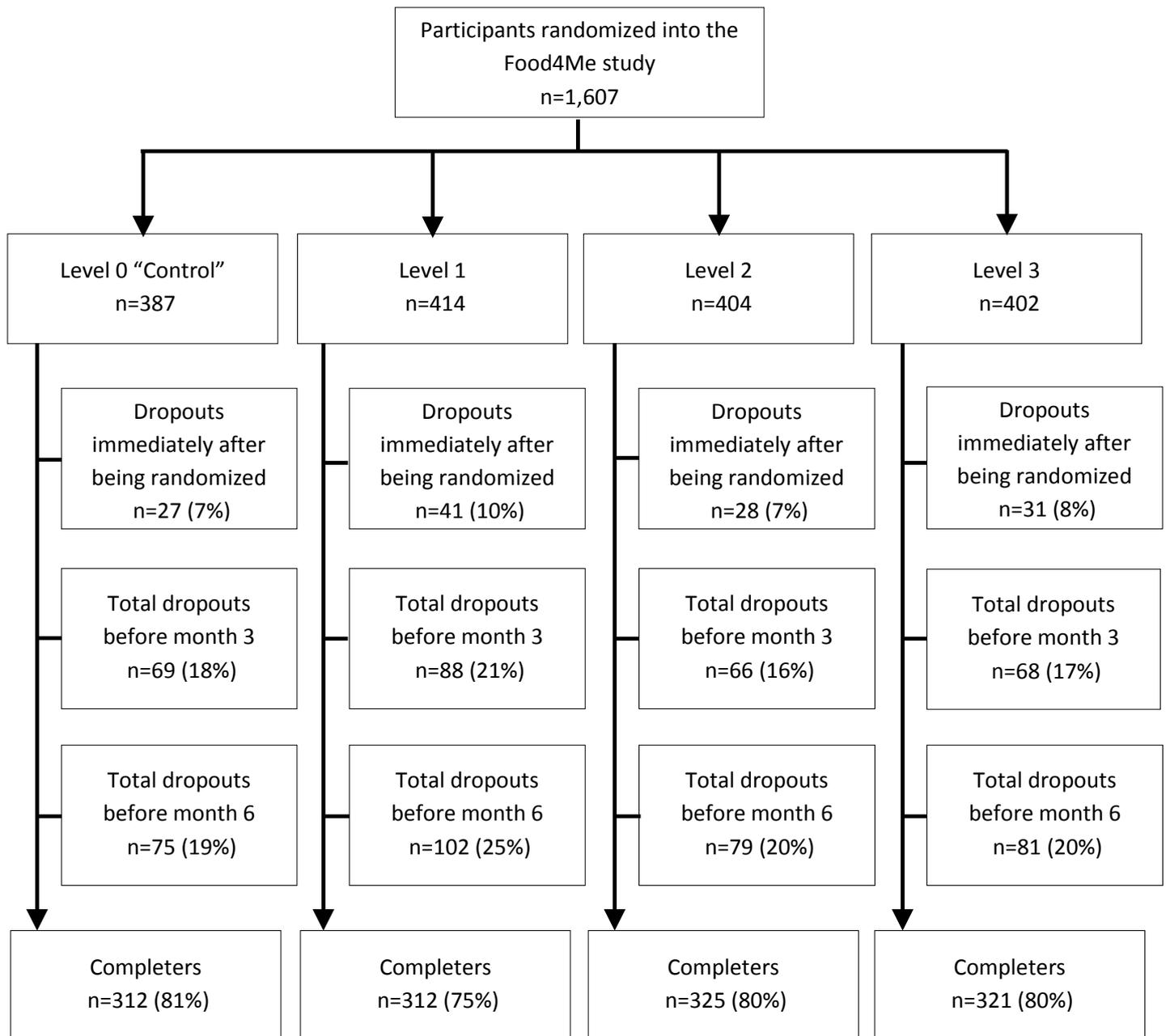


Figure 1

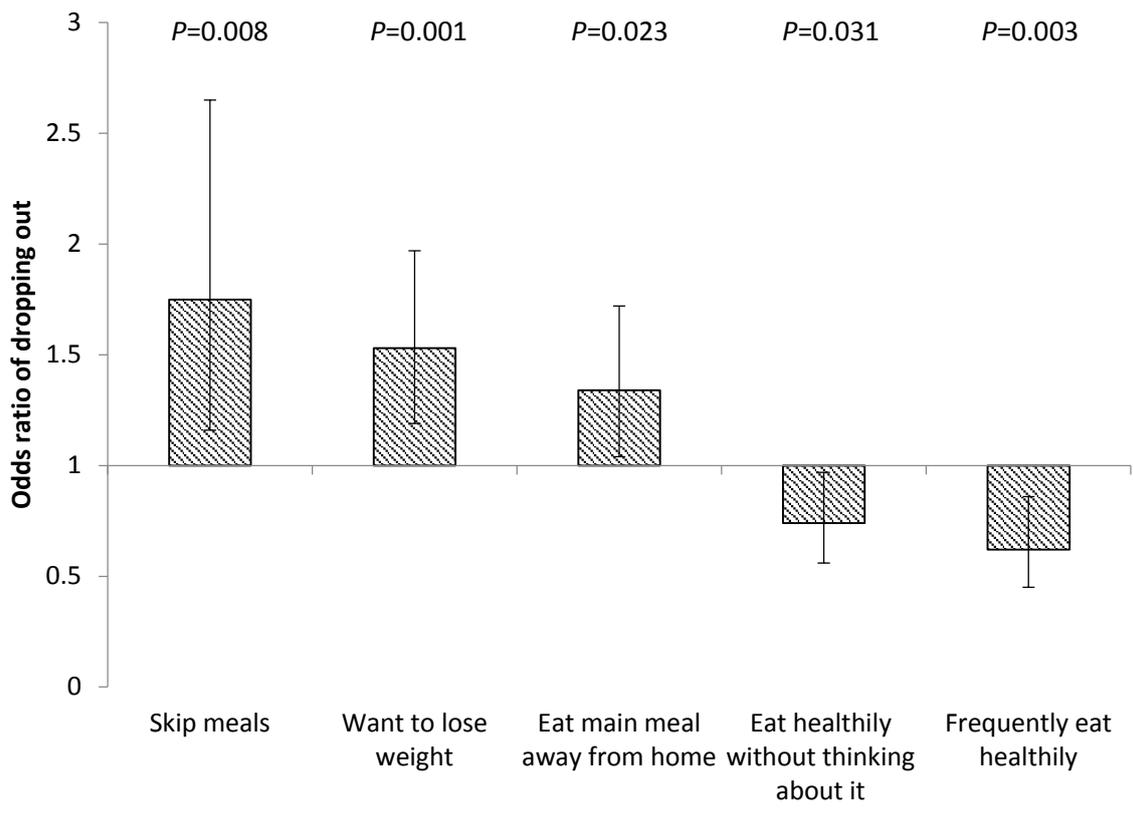


Figure 2