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Effectiveness of personalized nutrition – the German experience

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Summary

An imbalanced intake of nutrients and poor physical activity lead to an increase in risk factors associated with non-communicable diseases (NCDs). Although generic guidelines on a balanced diet are omnipresent, their effect seems to be limited, as the global burden of NCDs rises continuously. Another approach on improving nutritional behavior is the concept of individually tailored advice, i.e. personalized nutrition. In the European online-based proof-of-principle study Food4Me, personalized nutrition was shown to be more effective in inducing a healthier diet than generic guidelines. Advice on phenotypic or phenotypic plus genotypic information, however, did not lead to an enhanced effectiveness compared to advice on diet only. The first aim of this work was to analyze the effectiveness of different levels of personalized nutrition within the German Food4Me cohort.

220 adults were randomized into a control group (L0) receiving generic advice and an intervention group receiving personalized advice (Li) over six months. Li was subdivided into three levels, receiving feedback on their diet (L1), diet and phenotype (L2) or diet, phenotype and genotype (L3). Advice was based on Food Frequency Questionnaires, anthropometry and markers from dried blood spots, and on analyses of five single nucleotide polymorphisms.

At baseline, 53% of the participants were women, the mean age was 44.2 with a range from 18 to 72 years, and the mean BMI was 24.5 kg/m². Between baseline and after six months, Li participants significantly reduced their intake of in total fat (Median L0 = 0.57, Li = -1.76 %E, p = 0.003), monounsaturated fat (0.4, -0.41 %E, p = 0.013), and protein intake (0.03, -0.15 g/kg bodyweight/d, p = 0.004) in contrast to an increase in L0. The opposite effect was significant for the ω3 index measured in blood (-0.11, 0.14%, p = 0.005). Li participants also had a significant greater reduction in the consumption of red meat (-1.64, -9.5 g/d, p = 0.007), energy (-127.45, -338.06 kcal/d, p = 0.005), saturated fat (0.26, -1.38 %E, p = 0.002), and salt (-0.05, -1.14 g/d, p = 0.002), and a significant greater increase in carbohydrate intake (0.24, 1.98 %E, p = 0.003) compared to L0. Comparing levels L0, L1, L2, and L3, the group of L2 was most successful in dietary behavior change in the German cohort. Participants in L2 had a significant greater reduction in energy intake (Observed difference – critical difference = 6.6, p = 0.008), %E coming from saturated (0.5, p = 0.044) and total fat (0.5, p = 0.044), protein (2.4, p = 0.026) and salt (9.5, p = 0.003) compared to L0.

The results indicate that personalized advice was more effective to achieve a healthier dietary behavior that generic advice. The inclusion of advice on the individual's dietary and phenotypic data had the most effective change towards a healthier dietary behavior.

As feedback can be personalized based on certain food items, but also based on recipes and meal plans, the second aim was to develop a showcase of a meal planning tool which delivers individual recipe lists over one week. The mathematical model used, was a linear programming approach. It combines recipes in a way that food preferences of the participant, e.g. likes, aversions, and allergies were optimized and simultaneously, current recommendations on macro- and micro nutrient intake were fulfilled. In qualitative interviews, the tool was evaluated and found suitable especially for single households. In future studies, it should be taken into a real setting for a quantitative analysis of its effectiveness.

Zusammenfassung

Eine unausgewogene Nährstoffzufuhr und geringe körperliche Aktivität führen zu einer Zunahme von Risikofaktoren, die in Zusammenhang mit nicht-übertragbaren Krankheiten stehen. Obwohl generische Empfehlungen zu einer ausgewogenen Ernährung allgegenwärtig sind, scheint ihre Wirkung begrenzt, da die globale Belastung von nicht übertragbaren Krankheiten kontinuierlich steigt. Ein weiterer Ansatz um das Ernährungsverhalten zu verbessern, ist das Konzept der individuell zugeschnittenen Empfehlungen, d.h. die personalisierte Ernährung. In der europäischen, online-basierten Proof-of-Principle-Studie Food4Me wurde gezeigt, dass personalisierte Ernährung effektiver zu einer gesünderen Ernährungsweise führt, als allgemeingültige Regeln. Empfehlungen zu phänotypischen oder phänotypischen plus genotypischen Informationen zeigten jedoch keine verbesserte Wirksamkeit im Vergleich zu Empfehlungen, die nur auf Ernährungsdaten beruhen. Das erste Ziel dieser Arbeit war es, die Effektivität der personalisierten Ernährung in der deutschen Food4Me-Kohorte zu analysieren.

220 Erwachsene wurden in eine Kontrollgruppe (L0), die eine generische Beratung erhielt, und eine Interventionsgruppe, die personalisierte Beratung (Li) über sechs Monate erhielt, randomisiert. Li-Teilnehmern wurde empfohlen, individuell bestimmte Lebensmittel vermehrt oder eingeschränkt zu verzehren. Li wurde in drei Gruppen unterteilt, die personalisierte Empfehlungen zu Ernährung (L1), Ernährung und Phänotyp (L2) oder Ernährung, Phänotyp und Genotyp (L3) erhielten. Die personalisierte Beratung basierte auf Verzehrshäufigkeitsfragebogen, Anthropometrie und Markern aus getrockneten Blutspots, sowie auf Analysen von fünf Einzelnukleotid-Polymorphismen.

Zu Beginn der Studie waren 53% der Teilnehmer Frauen, das Durchschnittsalter lag bei 44,2, im Bereich von 18 bis 72 Jahren und der mittlere BMI betrug 24,5 kg/m². Zwischen Beginn der Studie und nach sechs Monaten reduzierten die Li-Teilnehmer signifikant ihre Aufnahme von Gesamtfett (Median L0 = 0,57; Li = -1,76% E, p = 0,003), einfach ungesättigtem Fett (0,4; -0,41% E, p = 0,013) und der Proteinzufuhr (0,03; -0,15 g/kg Körpergewicht/d, p = 0,004), während die Zufuhr bei den L0-Teilnehmer anstieg. Der entgegengesetzte Effekt war für den im Blut gemessenen ω3 index signifikant (-0,11; 0,14%, p = 0,005). Die Li-Teilnehmer hatten eine signifikant größere Reduktion bezogen auf den Verzehr von rotem Fleisch (1,64; -9,5 g/d, p = 0,007), die Zufuhr von Energie (-127,45; -338,06 kcal/d, p = 0,005), gesättigtem Fett (0,26; - 1,38 %E, p = 0,002) und Salz (0,05; -1,14 g/d, p = 0,002) und eine signifikante größere Zunahme der Kohlenhydratzufuhr (0,24, 1,98 %E, p = 0,003) im Vergleich zu L0. Im Vergleich der Gruppen, L0,

L1, L2, und L3 war die Gruppe L2 in der deutschen Kohorte am effektivsten in der Änderung des Ernährungsverhaltens. Die Teilnehmer von L2 hatten eine signifikant größere Reduktion der Energiezufuhr (beobachtete Differenz (OD) - kritische Differenz (CD) = 6,6; p = 0,008), %E aus gesättigtem Fett (0,5; p = 0,044) und Gesamtfett (0,5; p = 0,044), Protein (2,4; p = 0,026) und Salz (9,5; p = 0,003).

Die Ergebnisse zeigen, dass personalisierte Beratung effektiver war, eine gesündere Ernährung zu erreichen, als die generische Beratung. Die Einbeziehung von Daten zur Ernährung und zum Phänotyp des Individuums hatte die effektivste Veränderung hin zu einem gesünderen Ernährungsverhalten.

Empfehlungen können nicht nur auf bestimmte Lebensmittel bezogen werden, sondern auch auf Rezepte. Daher war das zweite Ziel dieser Arbeit, exemplarisch ein Mahlzeitenplanungstool zu entwickeln, das individuelle Rezepte über eine Woche liefert. Das verwendete mathematische Modell war eine lineare Programmierung. Hierbei wurden Rezepte so kombiniert, dass die Lebensmittelpräferenzen des Teilnehmers, z.B. Vorlieben, Aversionen und Allergien, optimiert und gleichzeitig aktuelle Ernährungsempfehlungen für Makro- und Mikronährstoffzufuhr erfüllt wurden. In qualitativen Interviews wurde das Tool evaluiert und festgestellt, dass es sich besonders für Single-Haushalte eignet. In zukünftigen Studien sollte dieses Tool mittels einer quantitativen Analyse auf seine Wirksamkeit getestet werden.

1. Introduction

1.1. From generic recommendations to personalized nutrition

Nutritional recommendations were initially provided to ensure an adequate intake of nutrients to prevent malnutrition with special emphasis on minerals, trace elements and vitamins. The first concise dietary recommendation was given to crews on ships at the end of the 15th century when the adventurer Jacques Cartier described what was later called scurvy, a disease occurring from ascorbic acid deficiency. It was shown that eating “Anneda tree extract” cured and prevented scurvy. Thus, the recommendation for consuming beverages produced from the Anneda tree were provided to ships’ crews [95].

While for centuries under-nutrition was a key health problem all over the world, the last decades have brought over-nutrition and numerous diseases originating from or promoted by over-nutrition. Recommendations in developed countries nowadays especially target an adequate intake of nutrients and sufficient physical activity to reduce risk factors such as blood pressure, overweight and obesity, hyperglycemia and hyperlipidemia. When established as a chronic condition, these parameters lead to chronic non-communicable diseases (NCD) that are responsible for 52% of global deaths amongst under 70 year olds. With 17.5 million people dying from cardiovascular diseases per year this represents 46.2% of NCD deaths, followed by cancers with 8.2 million (21.7%), respiratory diseases with 4 million (10.7%), and diabetes mellitus with 1.5 million (4%) (Figure 1) [141].

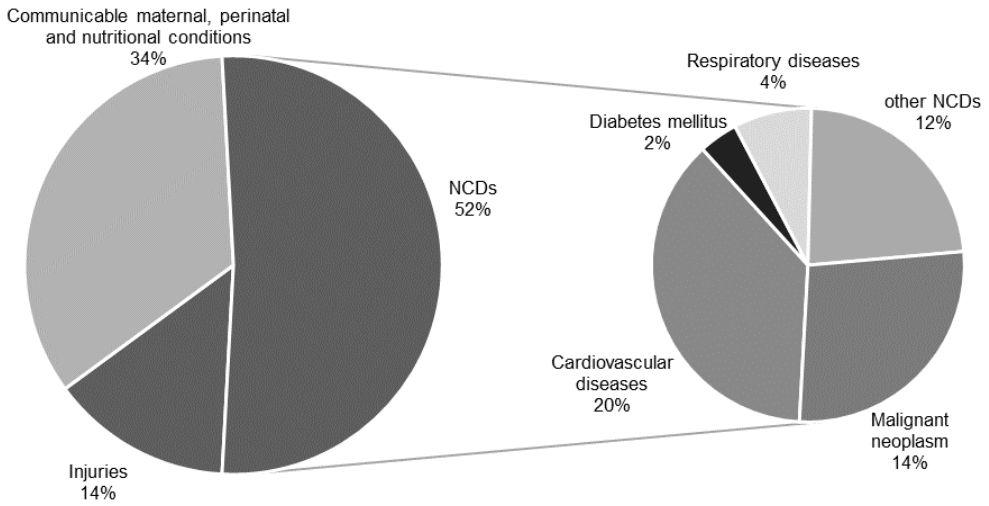


Figure 1: Proportion of global deaths under the age 70 years by cause of death (left) with details on NCDs (right), comparable estimates, 2012 adopted from [141]

Estimations show that 24 to 31% of cancers could be prevented, if risk factors such as poor diet, insufficient physical activity and an unbalanced body composition were eliminated [140] and 80% of diabetes mellitus type II could be prevented by sustaining healthy body weight and maintain sufficient physical activity [77]. Although dietary guidelines, such as the “10 guidelines” of the German Nutrition Society [1] or “10 tips for healthy eating” of the European Food Information Council [47] provide easy-to-understand advice for consumers on how to achieve and maintain a healthy lifestyle, there is low consumption of fruit and vegetables and a high intake of saturated fat, salt and sugar at population levels [142]. This is not only a problem in Germany or central Europe but worldwide. Consequently, the global burden of NCDs rises continuously [141] which contributes substantially to the rise in health care costs. A recent econometrical analysis estimated the healthcare costs in Germany for direct medical treatment originating from unbalanced consumption of fat, salt and sugar to 16.8 billion € (CI 95%: 6.3–24.1 billion €) [98]. The global costs for diabetes were estimated to about 500 billion US$ in 2010 with the perspective to raise to 745 billion US$ in 2030, and for cardiovascular diseases it accounted to about 863 billion US$ in 2010, and is estimated to raise to 1,044 billion US$ in 2030 [14]. The council of European Union institutions, bodies, offices and agencies therefore advices the member states to promote healthy diets and life styles to reduce NCDs [130].

It has been suggested that digitally delivered personalized advices, so-called “personalized nutrition”, may be more effective to achieve a sustainable healthy life style and diet than “one-size-fits-all” approaches, like generic guidelines. This might promote public health, as personalization is assumed to enhance the perceived relevance of nutritional feedback and thus leads to an increased motivation and attention. Higher effectiveness of personalized advice may also be due to the possibility of self-assessment and active participation via social media, as well as due to the selection of individually relevant information [21, 22]. An individual feedback to a person’s diet might also overcome the proposed inability to evaluate the own diet, as most Europeans believe their diet to be healthy enough [85].

1.2. Online-based personalized nutrition on three levels

Conceptually, personalized nutrition may be developed on basis of information collected on the individual’s diet, on basis of the phenotype, and/or based on the individual’s genotype [58].

1.2.1. Dietary level

To assess an individual's diet, several pro- and retrospective dietary assessment tools were developed over the last decades. Classic assessment tools are dietary records, 24-hour recalls, and food frequency questionnaires (FFQs) [13, 131]. Food records are a prospective method, asking the individual to record every food item consumed over a certain period of time. This minimizes the recall bias, i.e. fading memory concerning accuracy or completeness of food consumption, especially in weighing records. However, it relies on a long-term motivation and, because of the prospective recording, the eating patterns might change because of the assessment [131]. For 24-hour recalls, the individual describes his/her dietary intake of the last 24h from memory. This requires less motivation and time than a food record, but as there is a high day-to-day variance in the diet, it may not reflect the overall dietary pattern [13, 131]. FFQs aim at reflecting an individual's usual food intake. They comprise a list of about 100 to 150 food items asking the participant for the frequency and quantity of consumption, usually over a certain period, as of the last month for example. The FFQ is subject to a recall bias [13] and relies on the individual's ability to estimate portion sizes [131]. For large epidemiological studies, however, the FFQ was identified as a simple, cost-effective and time-saving tool [121].

The use of technology facilitates dietary assessment as well as analysis. Next to simply transferring pen and paper to computers and smartphones, more objective measurements using photographs [19, 104] or lightweight, wearable micro-cameras [110] enhance the accuracy and reduce time and costs of dietary assessment. Also, direct transferring of data to the analyst and the possibility of time- and location-independent feedback is more time- and cost-efficient [104]. However, these new and more objective dietary assessment tools still need further examination concerning usability and validity [54].

Several studies have compared more tailored dietary advice to untargeted and generic advice. A systematic review by Harris et al (2011) analyzed 43 intervention studies concerning adaptive e-learning and its potential to improve dietary behavior [68]. Harris described e-learning as 'the use of interactive electronic media'; tailored e-learning therefore was the exchange of individual data and personalized feedback. Tailored e-learning was shown in one study to be successful for increasing fruit and vegetable, decreasing the mean intake of saturated fat intake as well as the mean percentage of energy from fat. There was, however, no evidence that mean intake of fat, dietary fiber, energy intake, and Body Mass Index (BMI) were different comparing e-learning to the control (non-e-learning) group. In contrast, a study by Brug and van Assema (2000) concluded that

computer-based tailored feedback was more effective compared to general advice for motivating people to reduce their fat intake [23].

1.2.2. Phenotypic level

A large variety of tools is available to assess phenotypic parameters in study participants. Cheap and easy to use measurement tapes and scales can be employed for weight, height, hip and waist circumference measurements, as well BMI calculation. Specific questionnaires estimate physical activity, such as the Baecke questionnaire (PAQ) for assessing the Physical Activity Index (PAI) [5]. Next to such manual tools, various other devices exist to objectively measure health parameters, e.g. physical activity monitors and devices for measuring blood pressure, pulse rate or blood oxygen saturation [96, 106]. Many of these are already used in public for crowdsourced research e.g. by the Quantified Self Movement [113]. However, only for a few devices such as blood pressure measurement devices [100, 106] and accelerometers [122, 132] validation studies are available.

Another aspect of phenotyping, but also for objectively estimating food intake, is the analysis of metabolites in blood. A minimal-invasive method for home-based sampling are dried blood spots (DBS). For this, commercially available finger-prick lancets are used to prick the finger pulp. Capillary blood is dropped on filter cards and allowed to air-dry for three to four hours and sent by normal mail for lab analysis. DBS are a cost-efficient and feasible alternative to venipuncture in epidemiological studies [115] and do not require trained medical staff for their collection.

Concerning behavioral change to increase physical activity levels comparing tailored to generic advice, studies report controversial results. In an intervention in six European countries, the intervention group receiving computer based tailored advice reported a higher level of physical activity compared to the control group [18]. The analysis of the European Food4Me Study also showed an increase in physical activity reported in the PAI but not via accelerometer measurements [94]. In contrast, in studies by Bull et al. (1999), Spittaels et al. (2006) and Haerens et al. (2009), computer based tailored advice on exercise was only as effective as generic advice [24, 64, 124]. An internet-based tailored intervention by Papadaki and Scott (2005) combined assessment on dietary and phenotypic level. They found a change in behavior towards a Mediterranean diet in the intervention group with a significant increase of fruit, vegetables and legumes intake, of the monounsaturated fatty acids-saturated fatty acids ratio, and of the plasma high density lipoprotein cholesterol levels compared to a control group receiving only general healthy eating information [109].

1.2.3. Genotypic level

Personalization of nutritional advice cannot only be tailored to an individual's dietary preferences and phenotype; it can also be tailored to the genotype or may include genotypic information [108]. About a decade ago, nutrigenetics emerged as a branch of nutritional science when the human genome was revealed as a blueprint in 2003 [32]. Nutrigenetics analyses the interaction between genome and diet in the context of health and diseases risks and towards better understanding nutrient requirements [103]. Such knowledge may help to refine nutritional advice for individuals which may also increase motivation and compliance for sustained changes in lifestyle [80]. As deoxyribonucleic acid (DNA) is easy to collect, e.g. using buccal cell samples [81], there is a growing number of commercialized offers for personalized nutrition based on genetic analysis [97].

A large number of single nucleotide polymorphisms (SNPs) has been identified over the last two decades that were shown to be associated with the health-disease trajectory. One example is the rs9939609 SNP of the *Fat Mass And Obesity-Associated Gene* (*FTO*). In Europe, the A allele of this SNP has a frequency of 41% with 20% for the homozygotes [45]. Studies suggest that *FTO* might be involved in adipocyte lipolytic activity [136] and amino acid sensing [63]. Carriers of the A allele were associated with an increased BMI and homozygous carriers displayed an even higher BMI than heterozygous individuals [55, 74, 76, 135]. A recent meta-analysis suggests that A-homozygotes were additionally more susceptible to weight-loss during lifestyle intervention compared to non-carriers [143]. Concerning the effectiveness of integrating genetic information to advice regarding body weight management, Meisel et al. (2014) conducted an intervention study. The intervention group received feedback on *FTO* as well as weight control advice, a control group received weight control advice only. Although the readiness to control weight was elevated in the intervention group, there was no difference in actual behavioral changes with regard to body weight [99]. Partly independent from the effect on BMI, this SNP might also increase the risk for diabetes type 2 [70]. The A allele was, however, also discussed as potential protective factor for certain diseases, showing an reduced risk of pancreatic [90], lung [20] and prostate cancer [89] as well as a lower risk of contracting depression [116].

Another SNP identified to interact with diet-related health was rs174546 found in the *Fatty Acid Desaturase 1* (*FADS1*) gene locus. In Europe, the C allele of this SNP has a frequency of 65% with 44% for homozygotes [40]. *FADS1* encodes the delta-5-desaturase, which introduces cis-double bonds into dihomo-γ-linoleic acid 20:3(n-6) (DGLA) and eicosatetraenoic acid (ETA) 20:4(n-3) to generate arachidonic acid 20:4(n-6) (AA) and eicosapentaenoic acid 20:5(n-3) (EPA). Such long-chain polyunsaturated fatty acids

(PUFAs) have numerous functions. Next to their role as energy source, they enhance membrane fluidity and permeability and serve as ligands for transcription factors such as peroxisome proliferator-activated receptor. They are also precursors of pro- and anti-inflammatory mediators. While EPA-derived eicosanoids are attributed to possess a light proinflammatory activity, AA-derived eicosanoids are strongly proinflammatory and participate via this activity in the genesis of cardiovascular diseases and cancers [26]. The T allele of the rs174546 in *FADS1* was associated with lower D5D activity especially for n-6 PUFA substrates. Homozygous T-carriers showed significantly higher serum concentrations of linoleic acid 18:2(n-6) and DGLA than the C homozygotes [16]. In a study by Dumont et al. (2011) high intake of the PUFA α-linolenic acid 18:3 (n-3), a precursor of ETA, was associated with lower cholesterol concentrations in T allele carriers [38].

Another example of nutrient-gene interaction is the SNP rs7903146 in the *Transcription Factor 7-Like 2* (*TCF7L2*) gene. In Europe, the T allele of this SNP has a frequency of 32% with 12% for the homozygotes [44]. *TCF7L2* codes for a transcription factor which might play a role in the regulation of the proglucagon gene expression [61]. The T allele was associated with a higher risk for diabetes type 2 [61, 120] and reduced function in beta-cells [17]. Additionally, a study by Grau et al. (2010) suggests that obese homozygous T-allele carriers are more sensitive to low-fat than to high-fat weight-loss diets [62].

In the *Apolipoprotein E* (*ApoE*) gene, two SNPs rs429358 and rs7412 were identified. The frequencies of the C allele in rs429358 is 16%, for homozygotes it is 2%; in rs7412 for the T allele it is 6% and <1% in Europe [42, 43]. There are four allelic variants for the combination of the two SNPs, ε1 holds C in rs429358 and T in rs7412, ε2 T in both, ε3 T in rs429358 and C in rs7412 (most frequent with >60% [39]), ε4 holds C in both [37]. As for the mechanism, ApoE is a ligand for the low-density lipoprotein receptor as well as for the Apo E specific receptor which are involved in cholesterol regulation [39]. Carriers with at least one *ApoE* ε4 variant had higher and with at least one ε2 lower total cholesterol levels than ε3/ε3 carriers [65]. A study by Hietaranta-Luoma et al. (2014) compared behavioral changes (diet and exercise) of a control group receiving general information on health and gene-diet interaction with an intervention group being informed about the individual *ApoE* genotype. Individuals with risk factors had a statistically greater improve of their intake of unsaturated fat and reduction of saturated fat than the control group. However, this effect was only on short term [72]. Besides for cholesterol levels, *ApoE* ε4 was also associated with higher risks for cardiovascular diseases [39, 87] and Alzheimer's disease [50].

The rs1801133 SNP, also referred to as C677T polymorphism in the *Methylene Tetrahydrofolate Reductase* (*MTHFR*) has a frequency of 37% and of 14% for homozygotes

in Europe [41]. The MTHFR enzyme is involved in the remethylation of homocysteine to methionine and T allele carriers show a mild MTHFR deficiency [88]. The homozygous T allele was associated with higher plasma homocysteine levels and lower serum folate compared to heterozygotes or C homozygotes. In a meta-analysis, Colson et al. (2015) provided evidence that supplementation of folic acid and/or enhanced dietary folate compensate these plasma differences [33]. Concerning disease risks, the percentage of homo- and heterozygous T carriers of this SNP was higher in patients with cardiovascular disease [31]. Furthermore, a relationship between rs1801133, homocysteine and the risk of Alzheimer's disease was suggested in recent studies [75, 112].

1.2.4. Online data collection

Collecting data remotely via the internet provides numerous advantages, like opportunities to recruit very large cohorts at low costs and a reduced response time for whatever sampling is requested [60]. However, in contrast to face-to-face data collection in which samples and data are obtained by trained staff, studies collecting self-reported data via the internet rely on trust that data is entered correctly. There are multiple sources of errors like inaccuracies in following the protocol or mistakes in data entry. Although the occurrence of errors can be reduced beforehand by implementing checks or improving instructions, data cleaning methods are important for picking up erroneous data which passed these beforehand checks or where such checks were not implemented [134]. Subjective choices of whether certain data points are true or erroneous can deliver different results [69]. Objective and systematic screening needs definitions of expected ranges, distributions and relationships to compare the real data set to, e.g. the definition of soft and hard cut offs [8, 133]. After identifying potential errors, editing can be performed by changing, deleting or leaving values unchanged. Impossible values are to be deleted or, if possible may be corrected [134]. For data editing, the 'preponderance' approach can be applied, during which each inconsistent case is examined and the predominantly appearing answer is assigned to the inconsistent case, if in agreement with other values [8].

To address the question, if online-based personalized nutrition on all three levels is advantageous over generic advice to induce a life style change, the European Food4Me Study was designed as online-based randomized control trial in seven European counties with 1269 participants. The aim was to compare the conventional one-size-fits-all to a personalized nutrition approach, involving individual dietary, phenotypic and genotypic data [27]. In the study, feedback was provided as semi-quantitative recommendations, advising the participants to increase or decrease the intake of certain nutrients and food items. The European Food4Me Study confirmed that personalized nutrition based on

participants' dietary data is more effective than a general conventional advice. However, advice on phenotypic or phenotypic plus genotypic information did not lead to an enhanced effectiveness of personalized nutrition [28]. Nevertheless, the reasons for behavior change might differ from country to country, depending on the acceptance of new technology or the weight of genetic information or blood levels.

1.3. Linear programming in nutritional science

Besides semi-quantitative personalized advice, as given in the European Food4Me study [27], advice may also be provided quantitatively by estimating the nutritional requirement and providing suitable amounts of certain food items in a menu plan for an optimal individual diet. 'Optimal' in case of personalized menu plans means meeting the nutritional requirements while on the same time optimizing on an intended purpose. Menu plans mainly either optimize on the minimal costs of a diet or on the maximal acceptance of the diet [126].

In 1945, Stigler published a first attempt on an optimal diet at minimal costs, following the recommendations by the National Research Institute for a moderately physically active man, weighing 154 pounds. His food data base comprised 77 items and for each, the respective price of the year 1939 as well as the amounts of energy, protein and seven minerals and vitamins was given. His aim was to find the cheapest combination of these 77 food items in-line with the national recommendations of the nine nutrients. Using trial and error, he found that a combination of 370lb wheat flour, 57 cans of evaporated milk, 111lb cabbage, 23lb spinach and 285lb dried navy beans would fulfill the nutritional recommendation at the lowest possible price of 39.93$ per year [127].

Stigler's attempt was act on in the following decades, but instead of trial and error, the mathematical model of linear programming was used for solving the problem [6, 35, 123]. Linear Programming is a mathematical system that aims at finding a minimal or maximal solution for an equation considering a set of constraining equations or inequalities. The standard form describing such linear programming problems consists of three parts: An objective linear function, linear constraints and the further constraint of non-negative solutions. In 1947, George Dantzig proposed the Simplex algorithm to solve it [35]. Due to computer technology, more complex calculations were possible and further constraints were introduced to calculate menu plans. Stigler's diet was fulfilling the national nutritional recommendations but palatability was neglected. The importance of a palatable diet was emphasized later on by Smith in 1959, introducing further constraints like minimal and maximal amounts of certain food items and restrictions for combinations of food items [123]. Balintfy refined Smith's attempt on palatability in 1964 by using menu items

rather than food items. The menu items were defined as recipes, i.e. combinations of food items, and he considered the recipes as “palatable per se” [6, p.255]. The menu items had fixed portion sizes and were categorized into the several components of dishes of the day, for example ‘entrée’, ‘salad’, and ‘dessert’ [6]. Balintfy also introduced a new objective function to maximize preferences [7]. Computer-based optimizations on price and nutrients were realized e.g. in school canteens in the United States, or for compiling of personal diets in clinics [56]. In the last decade further constraints on a larger perspective on diet were considered, e.g. stainable diets. Macdiarmid et al. (2012) included constrains into a linear programming model to reduce greenhouse gas emissions, keeping meat and dairy products, but avoiding extra costs for the consumer [92]. Linear programming was also used in the context of malnutrition. Darmon et al. (2002) used this approach not only for identifying limiting nutrients in the diet of Malawian school children, but also whether local food can provide adequat nutrient intake [36]. Santika et al. (2009) provided evidence that it is useful to objectively deliver complementary dietary recommendations for Indonesian infants [117].

2. Project aims

The first aim of the work presented here was to analyze the effectiveness of an online personalized nutrition service in Germany by providing statistical evidence to the following hypotheses:

A. Personalized dietary advice is more effective, i.e. leads to a healthier lifestyle compared to non-personalized, conventional healthy dietary guidelines.

B. The effectiveness of personalized advice increases with the amount of individual data comprised. Dietary advice based on diet, pheno- and genotype is more effective than on diet and phenotype, which again is more effective than dietary information only.

C. Personalization based on genotypic information with reference to risk alleles is more effective than without risk allelles.

D. Detailed messages on a subset of specific nutrients are an effective tool to cause behavior change towards an alteration of diet.

These hypotheses were tested in a German cohort of the Food4Me proof of principle study (Food4Me Study) as a fully internet-delivered home-based personalized nutrition service. It involved three levels of personalized nutrition advice comprising either dietary intake only or including additionally phenotypic and genotypic information.

The second aim was to take the concept of personalized nutrition forward with a recipe advice system. For this, a linear programming approach was used to develop a system with the output of a personal meal plan compiling recipes for the one week. It is optimized not only on the dietary guidelines for the individual with phenotype and genotype, but also taking into account food preferences and aversions. For evaluation, qualitative interviews with former participants of the Food4Me Study were conducted.

3. Material and Methods

3.1. Study Design

The Food4Me Study was an online-based, randomized controlled intervention study, conducted from December 2012 to March 2014. Personalized nutrition was delivered based on food intake, phenotype and genotype. The intervention period for each participant was six months.

3.1.1. Measurement and sampling tools

Individual food intake data was recorded via the evaluated European Food4Me Study FFQ [49, 53], reflecting the participants' diet over one month with 162 preselected food items. In order to calculate the nutrient and energy intake, the individual portion size of each food item was assessed by the participants. To decrease the bias of the portion size estimation, photos of the food item on a standardized plate indicating different portion sizes were provided. Additionally to the food items consumed, data on supplement use were collected. Each FFQ was accompanied by a Baecke questionnaire to estimate the participants' total PAI during the last month, which was performed by the study center at Maastricht University, the Netherlands. The participants also self-measured their anthropometric markers weight, height, waist and hip circumference. Questionnaires and anthropometric data were filled in online by the participants on a password protected online platform.

The physical activity level (PAL) was assessed using the DirectLife triaxial accelerometer TracmorD (Philips Consumer Lifestyle, the Netherlands). As soon as a certain level of activity was reached, successively light up green dots on the device itself gave immediate feedback. Physical activity data from the accelerometer devices were provided via the Philips Consumer Lifestyle partner in the Netherlands.

For phenotyping, DBS were collected on Protein Saver™ 903R Cards (Whatman, Sanford, USA) with five circles per sampling time point. After disinfection of the finger with a provided swab, the finger was pricked with a lancet. The first drop of blood was discarded, the following drops were placed on the cards without touching the paper. The cards were dried for at least two hours, before storing them with a drying sachet in airtight aluminum bags. They were then send by post to the study center and again forwarded to the partner in Oslo for analysis of glucose, total cholesterol, total carotenoids and ω3

index. Total carotenoids were the sum of concentrations of alpha-carotene, beta-carotene, lutein, zeaxanthin, beta-cryptoxanthin and lycopene. The ω3 index was calculated from the concentrations of EPA, docosapentaenoate acid (DPA) and docosahexaenoate acid (DHA) as shown below:

$$\omega 3 \text{ index } = 1.4473 + 0.8303(\text{EPA} + \text{DPA} + \text{DHA})$$

The material, i.e. cards, finger prick lancets, disinfection swabs, and ω3 index calculations was provided and samples were analyzed by Vitas Ltd, Oslo, Norway.

Buccal cell samples were collected for SNP analysis using SK-1S swabs (Isohelix, United Kingdom) and DNA samples were analyzed for the SNPs rs9939609 in *FTO*, rs174546 in *FADS1*, rs7903146 in *TCF7L*, rs1801133 in *MTHFR*, and rs429358 and rs7412 in *ApoE* using the KASP™ assay, performed by LCG Genomics, Hertfordshire, United Kingdom.

3.1.2. Recruitment and exclusion criteria

Recruitment of volunteers was promoted via newspapers, posters and word of mouth aiming at 220 participants in each study center. In Germany, 788 volunteers signed in to an online platform to pass a standardized online procedure. They were informed about the study procedure and filled in a questionnaire on exclusion criteria as well as a screening FFQ.

To avoid any health disadvantages by taking part, volunteers were excluded if they fulfilled one of the exclusion criteria, i.e. if they

- were under 18 years old
- planned to become pregnant, were pregnant or lactating
- suffered from any metabolic disease or condition altering nutritional requirements, including allergies and intolerances
- gave any hint within the screening questionnaire indicating a risk taking part, e.g. severe depression.

Volunteers were also excluded for other than health risks, i.e. if they

- followed a prescribed diet for any reason in the last three months which would interact with the Food4Me Study intervention
- had no or limited internet access or no postal address any country taking part as the study is conducted via internet and conventional mail
- underreported in the screening FFQ for the second time to avoid unrealistic dietary reporting

After passing the online recruitment procedure, the volunteers gave consent for taking part as participant for the Food4Me Study and additionally signed a paper consent form. Further details on sample size consideration and on the screening process are described elsewhere, as this was performed and predetermined by the European Food4Me Study's operational headquarters, the University of Newcastle [27].

3.1.3. Randomization into groups

After receipt of a signed consent form, the first 220 volunteers which passed the screening were automatically randomized in either the control group (L0, n=51) or into the intervention group (Li, n=169). Li was subdivided into Levels 1 (L1, n=56), Level 2 (L2, n=57) and Level 3 (L3, n=56) on the online platform (Figure 2). The randomization process was controlled in the way to achieve a balanced sex ratio and a mean age of 45 years within the different levels.

- L0: Control group. Participants only received generic dietary feedback.
- L1: Participants received personalized dietary feedback based on their dietary intake data and PAL.
- L2: Participants received personalized dietary feedback based on their dietary intake data, BMI, waist circumference, PAL and blood levels.
- L3: Participants received personalized dietary feedback based on their dietary intake data, their phenotypic data and their genotypic data.

Each of the three intervention groups L1, L2 and L3 was split again in high intensity (L1h, L2h, L3h) and a low intensity groups (L1l, L2l, L3l). High intensity participants received a higher frequency of feedback on dietary intake data and PAL compared to low intensity and generally received more detail on the physical activity data (see 3.1.5).

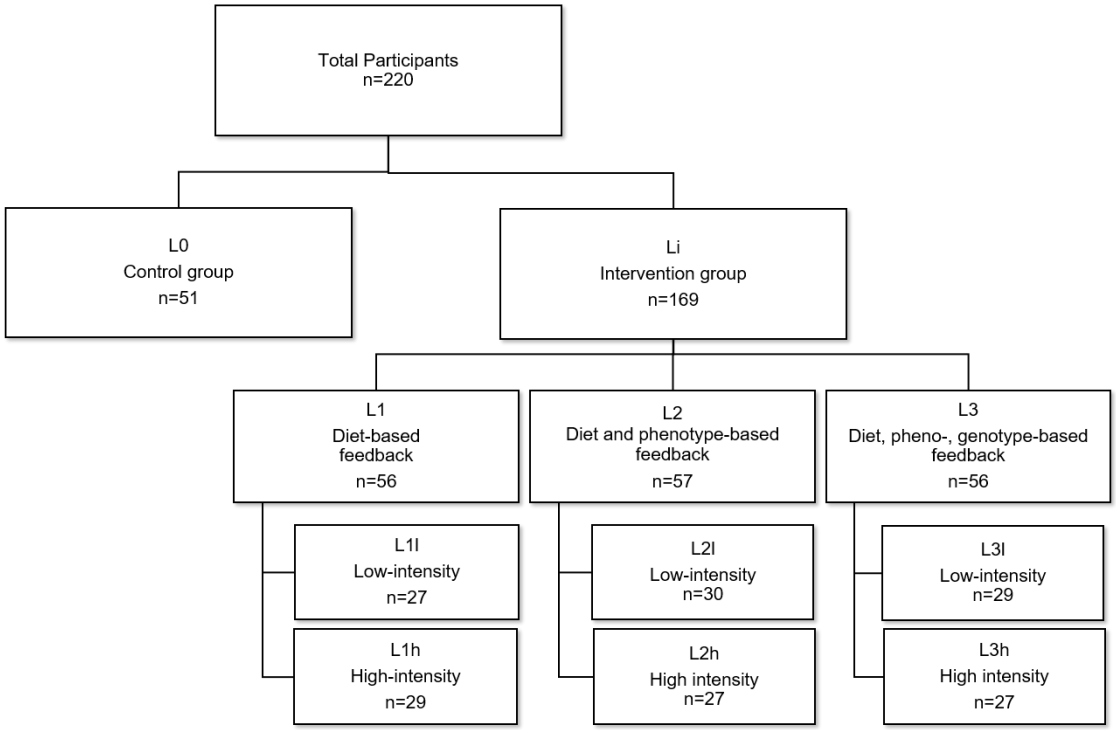


Figure 2: Flowchart of randomization into groups within the Food4Me Study.

3.1.4. Measurement and feedback frequency

Every participant was advised to provide FFQ, PAQ, anthropometric measurements, and DBS on three time points; at the first day of his/her Food4Me study inclusion (t0), three months after t0 (t3) and six months after t0 (t6). DNA samples were collected on t0, only. High intensity participants additionally provided FFQ, PAQ and anthropometric measurements one month (t1) and two months after beginning (t2). Feedback for t0 was given three weeks after data collection, for t1 and t2 two weeks later, for t3 and t6 three weeks later (Figure 3). Materials for anthropometric measurements, sample collection and the accelerometer were sent by postal mail. Digital and paper instruction sheets as well as videos were provided to ensure standardized measurements and sample collection by the participants. Participants were rolled out with an average of 10 persons per week.

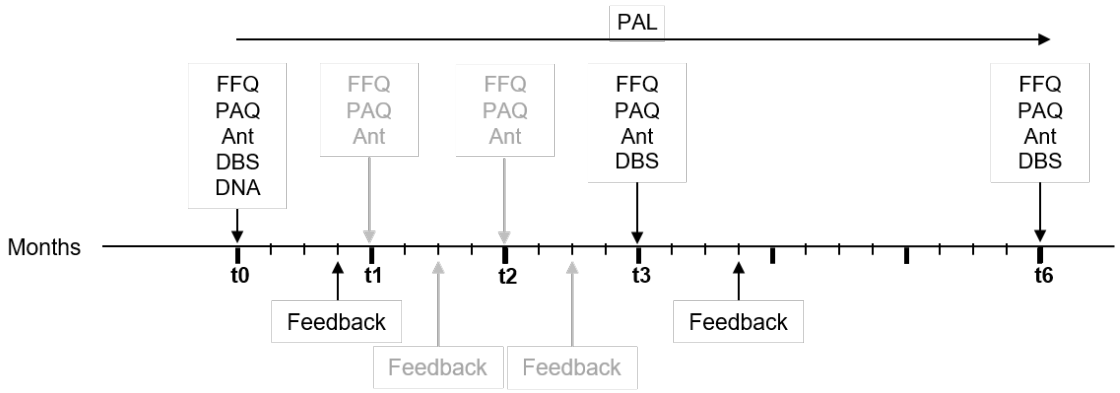


Figure 3: Food4Me Study design. PAL: Physical activity level via accelerometer; FFQ: Food Frequency Questionnaire filled in; PAQ: Physical Activity Questionnaire filled in; Ant: Anthropometrics measured; DBS: Dried Blood Spots collected; DNA: buccal cells collected; grey: only high intensity group.

3.1.5. Feedback reports

The generic feedback for L0 was based on the national dietary recommendations. It aimed at achieving a normal BMI and healthy portions of fruit and vegetables, wholegrain and dairy products, fish, meat, salt and saturated as well as unsaturated fat. It also included physical activity guidelines (see Annex 1).

Personalized dietary feedback reports (see Annex 2) were written using template reports for each level as designed in Microsoft® Word, Microsoft Company, United States, provided by European Food4Me Study.

The feedback reports were structured as follows:

- A message from your nutritionist
- Section 1: How your diet compares to recommendations
- Section 2: Your Physical Characteristics
- Section 3a: Your Nutrient Profile
- Section 3b: Your Blood Profile (L2 and L3 only)
- Section 3c: Your Genetic Profile (L3 only)
- Section 4: Your Personalized Nutrition Advice

The “message from your nutritionist” was a non-scientific 100 to 150 words summary of the following recommendations written manually by the respective nutritionist. The aims of this text were to further personalize the report and to encourage the participants to make changes in their lifestyle. In later reports, this message also compared the progress since the last report.

Section 1 indicated how the portions of the food groups “fruit and vegetables”, “wholegrain”, “dairy”, “oily fish”, and “red meat” in the participants’ diet compared to the Food4Me recommendations. The calculation of the individual portions of those food groups was based on the FFQ data (Table 1).

Table 1: Food groups, reference portion size and portion advice by the European Food4Me Study.

	Reference portion size	**Portion advice**
Fruit & Vegetables	80 g	≥ 5/day
Wholegrain	50 g	≥ 1/day
Dairy	200 g	3/day
Oily Fish	150 g	≥ 1/week
Red meat	150 g	≤ 3/week

Within section 2 of the report, participants received information on their anthropometrics. Their waist circumference, BMI and physical activity level was manually indicated on traffic light coded scales. If the anthropometric parameter was coded in red, the participant’s parameter was either too high or too low, coded in amber it was slightly too high or low and a green color code indicated on optimal value. The classification depended on age and gender of the participant (Table 2). The high intensity participants were additionally provided with a detailed overview of their activity during the last two weeks (see Annex 3).

Table 2: Anthropometrics in traffic light ranges: Color-coded ranges of anthropometrics and physical activity level dependent on age and sex by European Food4Me Study. NA: threshold not defined; m: male, f: female.

	Age	**Sex**	**Intake**				
			Too low (red)	**Slightly too low (amber)**	**Optimal (green)**	**Slightly too high (amber)**	**Too high (red)**
Body Mass Index [kg/m²]	>18	m, f	<18.5	NA	18.5 - <25	25 - <30	≥30
Waist circumference [cm]	>18	m	<102	NA	≥102	NA	NA
		f	<88	NA	≥88	NA	NA
Physical activity index	>18	m, f	<5.5	5.5 - <8.5	≥8.5	NA	NA

Section 3a visualized how their intake of 17 selected macro- and micronutrients compared to the recommendations. The nutrients were also classified in and manually indicated on traffic light scales within the Word-document (Figure 4). The values of the thresholds for all 17 nutrients were based on the recommendation of the Institute of Medicine (Table 3). The nutrient intakes were calculated using the FFQ data and comparing it to the food composition table of the Irish National Adult Nutrition Survey which is based on the McCance and Widdowson's Composition of Foods [53].

For participants of L2 and 3, also the blood markers cholesterol, glucose, ω3 index and carotenoids were classified graphically on a traffic light scale in section 3b (Table 4). For participants in L3, a table reflected whether participants carried or not a risk variant of the five different reference SNPs and explained the effect of the respective risk variant in section 3c. Every SNP was associated with a nutrient, anthropometric or blood marker (Table 5).

Figure 4: Example of the feedback participants received in Section 3 of the feedback report. As shown, the participant's intake of protein is optimal, the intake of carbohydrate slightly too low, and the intake of total fat is slightly too high.

Table 3: Nutrients in traffic light ranges: Color-coded ranges of nutrient intake dependent on age and sex by European Food4Me Study. NA: threshold not defined; m: male, f: female; % E: percentage of total energy intake

Nutrients	**Age**	**Sex**	**Intake**				
			Too low (red)	**Slightly too low (amber)**	**Optimal (green)**	**Slightly too high (amber)**	**Too high (red)**
Total fat [%E]	>18	m, f	<15	15 - <20	20 - <30	30 - <40	≥40
Saturated fat [%E]	>18	m, f	NA	NA	<10	10 - <15	≥15
Monounsaturated fat [%E]	>18	m, f	<10	10 - <15	15 - <20	20 - 30	≥30
Polyunsaturated fat [%E]	>18	m, f	<5	5 - 6	6 - 11	11 - 12	≥12
ω3 fatty acids [%E]	>18	m, f	<0.2	0.2 - <0.6	≥0.6	NA	NA
Carbohydrate [%E]	>18	m, f	<40	40 - <45	45 - <65	65 - <70	≥70
Fiber [g/d]	18 - 50	m	<28	28 - <38	≥38	NA	NA
		f	<15	15 - <25	≥25	NA	NA
	>51	m	<20	20 - <30	≥30	NA	NA
		f	<14	14 - <21	≥21	NA	NA
Protein [g/kg body weight/d]	>18	m, f	<0.52	0.52 - <0.66	0.66 - 2.4	NA	≥2.4
Salt [g/d]	18-50	m, f	NA	NA	<3.75	3.75 - <5.75	≥5.75
	51-70	m, f	NA	NA	<3.25	3.25 - <5.75	≥5.75
	>71	m, f	NA	NA	<3	3 - <3.75	≥5.75
Calcium [mg/d]	18 – 70	m	<600	600 - <800	800 - <2500	NA	≥2500
	18 – 50	f	<600	600 - <800	800 - <2500	NA	≥2500
	>71	m	<800	800 - <1000	1000 - <2500	NA	≥2500
	51	f	<800	800 - <1000	1000 - <2500	NA	≥2500
Iron [mg/d]	>18	m	<4	4 - <6	6 - <45	NA	≥45
	18 - 50	f	<3.15	3.15 - <8.1	8.1 - <45	NA	≥45
	>51	f	<3.5	3.5 - <5	5 - <45	NA	≥45
Vitamin A RE [µg/d]	>18	m	<350	350 - <625	625 - <3000	NA	≥3000
		f	<300	300 - <500	500 - <3000	NA	≥3000
Thiamin [mg/d]	>18	m	<0.8	0.8 - 1	≥1	NA	NA
		f	<0.7	0.7 - <0.9	≥0.9	NA	NA
Riboflavin [mg/d]	>18	m	<0.9	0.9 - <1.1	≥1.1	NA	NA
		f	<0.7	0.7 - <0.9	≥0.9	NA	NA
Folate [µg/d]	>18	m, f	<240	240 - <320	320 - <1000	NA	≥1000
Cobalamin [µg/d]	>18	m, f	<1.6	1.6 - <2	≥2	NA	NA
Ascorbic acid [mg/d]	>18	m	<60	60 - <75	75 - <2000	NA	≥2000
		f	<45	45 - <60	60 - <2000	NA	≥2000

Table 4: Markers in traffic light ranges: Color-coded ranges of markers dependent on age and sex by European Food4Me Study. NA: threshold not defined; m: male, f: female

Marker	Age	Sex	Intake				
			Too low (red)	Slightly too low (amber)	Optimal (green)	Slightly too high (amber)	Too high (red)
Cholesterol [mmol/l]	>18	m, f	NA	NA	<5	5 - <8	≥8
Glucose [mmol/l]	>18	m, f	NA	NA	<5.1	5.1 - <7	≥7
ω3 index [%]	>18	m, f	<4	4 - <8	≥8	NA	NA
Carotenoids [µmol/l]	>18	m, f	<1.3	1.3 - <1.5	≥1.5	NA	NA

Table 5: Genetic feedback: Single nucleotid polymorphisms (SNP), associated nutrient, anthropometric or blood marker and feedback for risk alleles defined by European Food4Me Study.

Genes	SNP rs	Risk alleles	Association	Nutritional effects associated risk variants
Fat mass and obesity associated (*FTO*)	9939609	AA AT	BMI, weight, waist circumference	A specific variation of this gene is associated with a greater need to maintain a healthy body weight and engage in physical activity. A healthy weight combined with exercise may provide added health benefits for these individuals.
Fatty acid desaturase 1 (*FADS1*)	174546	CC	ω3 fatty acids	People with a specific variation of this gene can benefit by increasing their intake of the healthy ω3 fat found in oily fish. Increasing ω3 intake has been associated with an improvement in factors relating to cardiovascular health in these individuals.
Transcription factor 7-like 2 (*TCF7L2*)	7903146	TT CT	Fat intake	A specific variation of this gene is associated with improved weight loss when following a low fat diet compared to other weight loss diets. Reducing dietary fat may enhance weight loss in these individuals.
Apolipoprotein E (*ApoE*)	429358/ 7412	CC/CC CT/CT CT/CC CC/CT	Saturated fat	A specific variation of this gene is associated with a greater need to maintain healthy cholesterol levels. Decreasing saturated fat intake has been associated with an improvement in cholesterol and factors relating to cardiovascular health in these individuals.
Methylenetetrahydrofolate reductase (*MTHFR*)	1801133	TT CT	Folate	People with a specific variation of this gene can benefit by increasing their intake of the vitamin folate. Increasing folate intake (found in green leafy vegetables) has been associated with an improvement in factors relating to cardiovascular health in these individuals.

Section 4 gives detailed messages on individual body weight including feedback on glucose level and *FTO* risk alleles and on three to four so called 'target nutrients' including the markers cholesterol, ω3 index and carotenoids. Individuals were asked to specifically concentrate on these target nutrients to achieve an optimal intake or blood level. They were identified using the traffic light classifications (Table 3, Table 4) of the nutrient intakes or markers and a priority list with the latter divided into three groups (Table 6): Starting at the top of group 1, i.e. cholesterol, it was checked whether this nutrient's intake was classified red. If this was not the case, the nutrient in second place, i.e. ω3 intake or for L2 and L3 ω3 index, was checked for red-classified intake, and so forth. If in none of the nutrients in group 1 the intake was classified as red, the nutrients in group 2 and afterwards in 3 were checked. As soon as the first nutrient with red-classified intake was identified, this was defined as first priority nutrient. The same procedure was repeated for the determination of the second and third priority nutrient. If there were less than three red-classified nutrient intakes, the same procedure was repeated with amber-classified nutrients. When less than three nutrients were amber-classified, in the t0 feedback green classified nutrients were chosen randomly. In the following feedback reports, those nutrients were chosen, which changed from red or amber into a green classification.

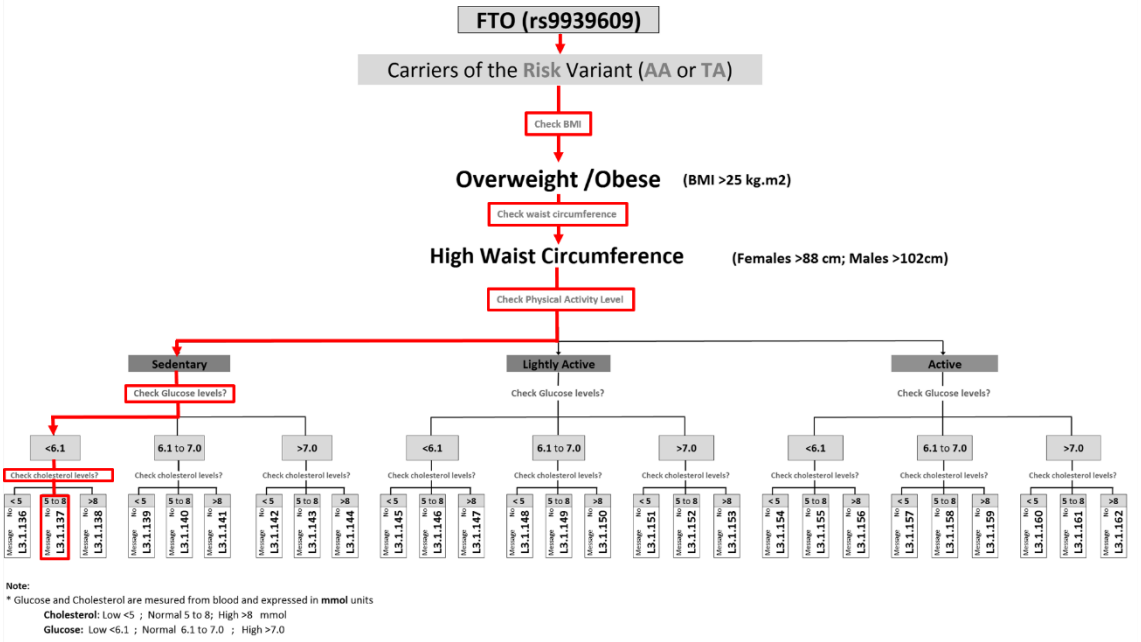
There were two exceptional cases for this procedure: First, if participants in L3 had a risk variant in a SNP, the associated nutrient or blood marker was favored over higher-ranked nutrients with no risk association. Second, to avoid duplication of fat or fat related messages, fats or related markers were allocated to group 1. Thus, as soon as one nutrient was selected from group 1, this group was neglected.

Table 6: Priority list for target nutrient identification. * Nutrients associated with one of the analyzed single nucleotide polymorphisms (see Table 5).# level 1: ω3 intake from food frequency questionnaire, level 2 and 3: ω 3 index from blood

Ranking	Group 1	Group 2	Group 3
1	Cholesterol	Carotenoids	Calcium
2	ω3 intake/index*#	Folate*	Iron
3	Saturated fat*	Fiber	Vitamin C
4	Total Fat*	Salt	Vitamin A
5	Monounsaturated fat	B12	
6	Polyunsaturated fat	Riboflavin	
7		Thiamin	
8		Protein	
9		Carbohydrate	

For reasons of comparison, the personalized messages were compiled of standardized sentences identified by using decision trees. For body weight and each nutrient and level, a specific decision tree was developed involving relevant anthropometric, metabolic and genetic parameters to be considered. Thus, the number and complexity of the decision trees varied from nutrient to nutrient. As an example, the L3 body weight decision tree took into account the participants' alleles in *FTO* (risk allele yes/no), BMI (underweight, optimal, overweight), waist circumference (optimal/high), PAL (sedentary/lightly active/active), glucose (low/optimal/high) and cholesterol level (low/optimal/high). This adds up to 324 different messages that might have been given for body weight in L3. At the end of each tree branch, a message number was indicated. The decision trees were manually executed, the resulting numbers looked up in a messages index (Table 7) and copy-pasted into the feedback report.

Table 7: Example of decision tree with correspondent message. Excerpt from level 3 body weight decision tree, assuming the participant carries a risk variant in the *FTO* gene, is overweight with a high waist circumference, sedentary, with low glucose and slightly elevated cholesterol levels. [red]: indicates the considered parameter for the respective sentence, does not belong to original message. BMI: Body Mass Index



L3.1.137 Your BMI is greater than the recommended healthy range, indicating that you are very overweight for your height [BMI]. Your waist circumference is also higher than recommended. Carrying too much weight around your middle increases your risk of certain diseases including heart disease and cancer [waist circumference]. We recommend reducing your body weight and waist circumference to a healthy normal range because you have a genetic variation that can benefit by reducing these two obesity markers [risk variant FTO]. We strongly recommend that you try to reduce your weight; a weight loss of 0.5-1.0kg (1-2lbs) a week is a realistic goal. Also, your physical activity level is too low; improving your physical activity level will help you to reduce your weight [physical activity]. Your fasting cholesterol level was slightly above the recommended level [cholesterol]. The following list contains suggestions to help you to lose weight: Become more physically active; 60-90 minutes of moderately intense aerobic activities, such as brisk walking, swimming or cycling, on most days of the week is recommended. Reduce your portion sizes. Eat regularly and avoid skipping meals. Avoid snacking on foods high in sugar and fat - swap these for healthier alternatives, such as fruit. Choose low-fat options.

3.2. Data cleaning

Data cleaning was performed by defining cut offs and analyzing summary statistics to detect outliers. Using the preponderance approach, potential erroneous data of the detected outliers were edited or deleted. For all analyses, the software R, version 3.1.1 was used [111].

3.2.1. Outlier detection

As nutritional intake can vary tremendously, hard cut offs were not considered to not prematurely delete data. Also, no cut offs for nutrients intake given in percentage of total energy intake (%E) were considered. For the intake of essential nutrients, a minimum intake was assumed, therefore cut offs were calculated using the thresholds of the traffic light classifications (Table 3, Table 4): minimal soft cut off using 25% of the maximum of the "too low (red)" range and maximal soft cut offs using 200% of the highest value available (Table 8).

Table 8: Soft cut offs for outlier detection within the data cleaning process of Food4Me Study nutrient intake. Minimum and maximum soft cut offs were determined according to gender and age. M: male, f: female.

Nutrients	**Age**	**Sex**	**Cut offs**	
			min	**max**
Calcium [mg/d]	18-70	m	150	5000
	18-50	f	150	5000
	>71	m	200	5000
	51	f	200	5000
Iron [mg/d]	>18	m	1	90
	18-50	f	0.8	90
	>51	f	0.85	90
Vitamin A RE [µg/d]	>18	m	85	6000
		f	75	6000
Thiamin [mg/d]	>18	m	0.2	
		f	0.17	
Riboflavin [mg/d]	>18	m	0.23	
		f	0.17	
Folate [µg/d]	>18	m, f	60	2000
Cobalamin [µg/d]	>18	m, f	0.4	
Ascorbic acid [mg/d]	>18	m	15	4000
		f	12	4000

Additionally, cut offs were defined for age with a minimum of 18 and a maximum of 120 years, body height with 50 and 230 cm, BMI with 15 and 50 kg/m² and waist circumference with 40 and 200 cm, respectively (Table 9). The latter cut offs were arbitrarily estimated as borderline physiological possible. As this was an intervention study and changes are expected, the differences in nutrient intake were not analyzed to perform inlier detection. However, a soft cut off of ±5 cm for body height was defined, as height should not change. As well as was defined a soft cut off of +1 year for age, as participants took part for 6 months.

Table 9: Soft cut offs for outlier detection within the data cleaning process of Food4Me Study anthropometric data. Minimum and maximum soft cut offs were determined according to gender, male (m), and female (f) and according to age.

Anthropometrics	**Age**	**Sex**	**Cut offs**	
			min	**max**
Age [years]		m, f	18	120
Body height [cm]	18-50	f	50	230
Body Mass Index [kg/m²]	>18	m, f	15	50
Waist circumference [cm]	>18	m, f	40	200

3.2.2. Data editing

Values above the soft cut offs were only amended, if the true value could be obtained through comparison with values from other time points applying the preponderance approach. No data cleaning was performed for blood markers, as they were measured using a standardized protocol and no subjective information was required. However, participants with missing data or poorly filled blood spots in t0 or t6 were removed to avoid potentially false data.

Data cleaning with soft cut offs demonstrated that there were no cases exceeding age, height, BMI and waist circumference soft cut offs. Also, there were no differences in age between t0 and t6. For participant H081, there was a height difference of 5 cm between t0 and t6. Taking also the measurement of t3 and the screening questionnaire into account, three measurements were listed with 1.64 m and last one with 1.69 m, indicating a potential erroneous measurement which is why this value was changed to 1.64 m.

For the nutrient data, none of the participants' intake values exceeded the cut offs for vitamin A RE, folate, thiamin, riboflavin, cobalamin, and ascorbic acid intake. For calcium, an intake of 9332 mg/d was observed for participant H052 as an outlier. As changes in nutrient intake were expected over time, calcium intake was not compared

on the various time points to ponder whether this value was realistic, but the distribution of calcium intake was considered. The boxplot of calcium intake at t0 indicated only two outliers close to the upper whisker, in contrast to that of H052 on t6 with about threefold of the next highest outlier. Because of this difference to the next outlier, it was decided to exclude this data point from the analysis (Figure 5). For iron intake, H031 on t6 exceeded the maximal cut off. As for H052 and calcium intake, these outliers are more than threefold higher than the next lower outlier and were therefore not included in the analysis. No further suspicious data were found or had to be edited.

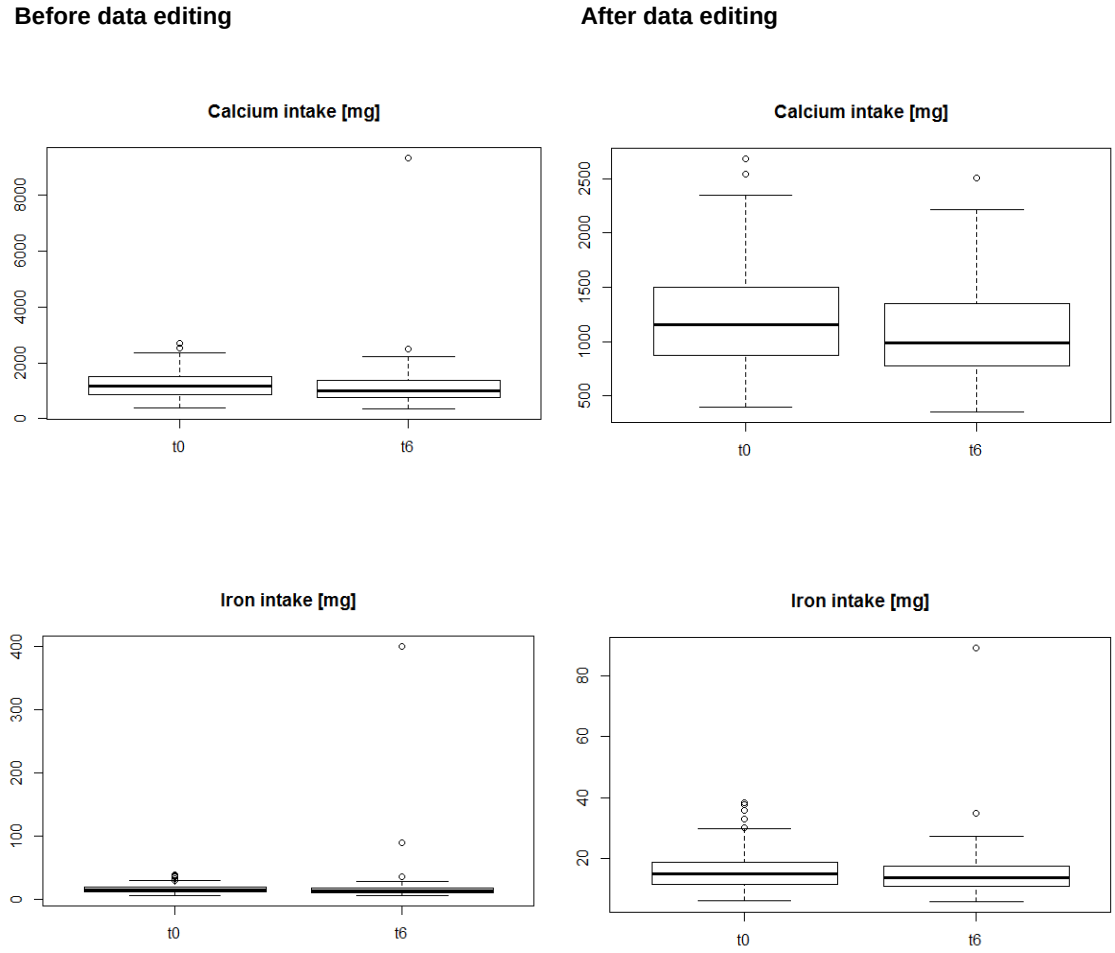


Figure 5: Distribution of calcium and iron intake before and after data editing. Intakes were calculated from FFQs on baseline (t0) and after 6 month (t6). Data cleaning was performed using cut offs and the preponderance approach.

3.3. Statistics

Two different approaches were applied for the determination of “effectiveness”. The first used the actual measured values to determine if there were differences between beginning and end of the study comparing intervention and control. The second considered the color classification of the specific variable, analyzing the change into a healthier color range comparing intervention to control. Analyzed variables were energy and nutrient intakes calculated from the FFQ, food groups, anthropometric data, PAI and blood parameters. For all statistical analyses the software R, version 3.1.1 was used [111]. P-values < 0.05 were considered significant.

3.3.1. Values approach

Concerning hypothesis A, personalized advice is more effective than non-personalized advice, delta t6-t0 of every variable in every participant was compared between Li and L0. As the majority of the variables did not meet the assumption of normal distribution using the Shapiro-Wilk test in the two groups L0 and Li, the non-parametric Wilcoxon’s rank-sum test was performed with the respective variable as outcome and the level as predictor. The relationship between carbohydrate and monounsaturated fatty acid intake was tested using Spearman’s r, as data were not normally distributed in the Shapiro Wilk test.

Concerning hypothesis B, effectiveness of personalized advice increases with the amount of individual data comprised, L0, L1, L2, and L3 were compared to each other. The assumption of homogeneity of variances were met in every variable except red meat intake as tested using the Fligner-Killeen test. However, normal distribution of the residuals after performing ANOVA was not confirmed by the Shapiro-Wilk test in the majority of variables. Therefore, the Kruskal-Wallis test was used for analysis, again with the respective variable as outcome and the level as predictor. Post hoc, the Wilcoxon rank-sum test was performed on all possible comparisons.

Concerning hypothesis C, personalized advice with reference to risk alleles is more effective than without, the tests above were also applied to compare L0, L1, L2 and L3 with risk factor SNP´s (L3r) and L3 without risk factor within a certain SNP (L3n). All five SNPs were analyzed separately, using accompanied variables (Table 5).

3.3.2. Classification approach

To analyze if participants improved the variables’ color classification, again L0 to Li (Hypothesis A), and L0, L1, L2 and L3 (Hypothesis B), as well as L0, L1, L2, L3n and L3r (Hypothesis C) were compared to each other. For this, the values of the variables were

classified into the different colors green, amber and red and again for t0 and t6. Then, the colors of each variable in each participant on t0 were compared to those on t6 by testing, if there was an improvement towards a healthier color (red to amber, red to green or amber to green) or if there was no improvement (red to red, amber to amber, amber to red, green to amber, green to red). Participants with optimal intake (green in t0 and t6 L0) were not included in the analysis. L0 to Li, and L0, L1, L2 and L3, as well as L0, L1, L2, L3n and L3r respectively, were compared using the Pearson's χ^2 test with the improvement of a variable (yes, no) as first categorical variable and the level as second categorical variable. The odds ratio was calculated as effect size. A post-hoc test was performed using Bonferroni correction for comparing L0, 1, 2, and 3, as well as L0, L1, L2, L3n and L3r.

3.3.3. Effect of target nutrients

The feedback reports included three to four target nutrients, for which detailed information was provided to the participants. To test hypothesis D on successful changes in these targets nutrients, the difference for each nutrient between previous and subsequent feedback report was calculated, i.e. the difference between reports on t0 and t3, and on t3 and t6 for low intensity participants; on t0 and t1, t1 and t2, t2 and t3, and on t3 and t6 for high-intensity participants. Afterwards, a new factor variable was created, stating whether a certain nutrient was a target nutrient in the first feedback report and a second variable reporting whether the participant was in a high or a low-intensity group. Because of these three variables "level", "high/low" and "target nutrient y/n" a multifactorial ANOVAs for each target nutrient was applied, with the latter three variables as predictors and the calculated difference in the target nutrient as outcome variable. As post hoc test, Tukey's Honestly Significant Difference (HSD) test was applied.

4. Results

4.1. Baseline characteristics

After data cleaning, the participants' data were analyzed concerning their characteristics at t0 (Table 10). Participants were 18 to 72 years old, with a mean of 44.2 years; 52.9% were women and with over 98% a large majority of the participants had a white-European ethnic background. Summary statistics revealed a mean BMI of 24.5 kg/m² (SD 3.97 kg/m²) for the participants, 27.8 % were pre-obese, 8.5 % obese and 17.6% central obese. Central obesity in women was defined as a waist circumference >88 cm, and in men >102 cm. 57% of the participant stated in the PAI to be moderately active and 40% to be active. Measurements of the PAL generally showed a higher inactivity compared to the PAI with only 25% being active and 65% moderately active. 8% of the participants were smokers. The participants had a mean energy intake of 2514 kcal (SD 893.14 kcal) and dairy products, saturated fat and salt intake as well as ω3 index in blood were those with the lowest percentage in the optimal range (Table 1, Table 3, Table 4) at baseline (Table 11).

Table 10: Baseline characteristics of the Food4Me Study participants. n=176 if not stated otherwise. Central obesity: waist circumference in women >88 cm, in men >102 cm, n=175; PAI: Physical activity index, inactive <5.5, moderately acitve 5.5 to 8.5, active >8.5; PAL: Physical Activity Level measured by Direct-Life triaxial accelerometer (TracmorD), inactive <1.5, moderately active 1.5 to 1.8, active >1.8, n= 157. In mean with standard deviation (SD) or percentage of participants.

	mean (SD) or %		**%**
Sex: female [%]	52.9	**Weight classification [%]**	
Age [years]	44.2 (13.4)	Underweight (BMI <18.5)	2.3
Age range [years]	18 - 72	Normal weight (BMI 18.5 to <25)	61.4
Smoker [%]	8.0	Pre-obese (BMI 25 to <30)	27.8
Ethnicity [%]		Obese (BMI ≥30)	8.5
White	98.3	Central obesity	17.6
Asien/Black/others	0	**Physical Activity [%] PAI/PAL**	
Mixed	1.7	Inactive	3.4 / 8.9
Anthropometrics		moderately active	56.8 / 65.6
Height [m]	1.75 (0.1)	active	39.8 / 25.5
Weight [kg]	75.4 (15.1)		
BMI [kg/m²]	24.5 (3.97)		
Waist circumference [cm]	85.4 (13.9)		

Table 11: Baseline dietary intake of Food4Me Study participants. SD: standard deviation; %E: percentage of total energy intake; Food groups and nutrients: n=176, Cholesterol and ω3 index: n=174, Glucose: n=172, Carotenoids: n=168, optimal intake see Tables 1, 3, 4.

	Mean (SD)	**% optimal intake**
Energy intake [kcal/d]	2514 (893.14)	
Food groups		
Fruit & Vegetables [g/d]	635.44 (396.14)	72
Wholegrain [g/d]	162.52 (125.98)	89
Dairy [g/d]	292.1 (199.8)	6
Oily Fish [g/d]	15.34 (16.95)	25
Red Meat [g/d]	60.32 (47.86)	55
Nutrients		
Total fat [%E]	37.11 (5.56)	34
Saturated fat [%E]	15.3 (3.17)	3
Monunsaturated fat [%E]	13.76 (2.54)	23
Polyunsaturated fat [%E]	5.93 (1.35)	40
ω3 fatty acids [%E]	0.61 (0.14)	50
Carbohydrate [%E]	45.79 (6.73)	57
Fibre [g/d]	29.22 (13.28)	46
Protein [g/kg BW/d]	1.28 (0.44)	96
Salt [g/d]	7.04 (2.72)	6
Calcium [mg/d]	1217.09 (435.65)	82
Iron [mg/d]	15.66 (5.99)	97
Vitamin A RE [µg/d]	1535.44 (779.87)	90
Thiamin [mg/d]	3.34 (5.41)	98
Riboflavin [mg/d]	2.82 (3.46)	96
Folate [µg/d]	370.97 (209.94)	50
Cobalamin [µg/d]	18.84 (87.99)	98
Ascorbic acid [µg/d]	194.91 (189.26)	88
Marker		
Cholesterol [mmol/l]	4.99 (1.02)	52
Glucose [mmol/l]	3.92 (0.78)	99
ω3 Index [%]	5.5 (0.85)	1
Carotenoids [µmol/l]	1.78 (0.77)	56

4.2. Drop-out and compliance

Out of 788 German volunteers that signed in, 220 were randomized into the study. 176 participants completed the study, which adds up to a 20% drop out rate. 12 drop outs were counted before the t0 FFQ, followed by 19 drop outs before t3 and 13 drop outs between t3 and t6. 137 participants provided a full data set of all analyzed variables on t0 and t6. Reasons for the exclusion of the participants were one pregnancy (2.3%), three times moving to a different country (6.8%), one later on diagnosed diabetes mellitus type

2 and one surgery after which the participants was not able to work on the computer any more (4.5%). The study was voluntarily discontinued by four participants stating that it took too much time to continue (9.1%). Three participants were disappointed, one explicitly stated because of weight gain instead of weight loss, another because of inaccurate measurements of the accelerometer (6.8%). The majority of the drop outs did not fill in their FFQs anymore and would not answer to reminder mails, therefore the reason for their discontinuing is unknown (70.5%) (Figure 6).

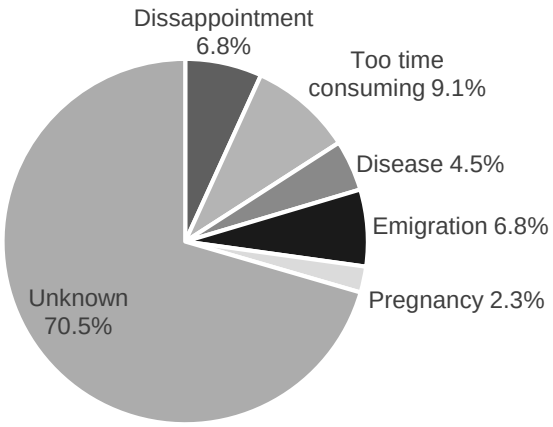


Figure 6: Drop out reasons during the Food4Me Study. n = 44

Generally, in each of the three levels, the low-intensity group always showed a higher mean percentage of completed measurements (86%, 88%, 87%) compared to the high-intensity (80%, 71%, 83%). Participants in L2 high-intensity had the lowest mean percentage of data collected comparing target with actually completed measurements (71%); in contrast, L2 low-intensity with the highest (88%).

Of the 826 FFQs that should have been filled in by the 220 participants during the six months study period, 715 (88%) were actually completed (Table 12, Figure 7). The highest percentage of completed FFQs was obtained in the L3 low-intensity group with 93% and the lowest in the L2 high-intensity group with 79%. Anthropometric measurements were similarly successful as the FFQ with a mean of 87% for waist circumference, weight and height. The FFQ accompanied PAQs were filled in by in 697 of 826 cases which sums up to 84%. There was less compliance for carrying of the accelerometer. Only in 71% of the cases, enough data was provided to calculate the participants' PAL. Lowest collection of PAL values were in L2 high-intensity, where only 77% of the recruited participants still had enough data to calculate their PAL.

Concerning the compliance of DBS collection, cards were filled with 2,628.5 of 3,300 blood spots (80%) to be analyzed for glucose, cholesterol, carotenoids and ω3 index. Out of the 583 cards, which were handed in, 2,332 analyses that should have been performed to quantify the blood markers. 6 measurements of cholesterol, 18 of glucose, 28 of carotenoids, and 7 of ω3 index could not be analyzed due to poorly filled cards. This adds up to 2273 (97%) successfully handled cards and measurements.

Every participant who filled in the FFQ at t0 also provided a buccal cell sample. Out of these 208 buccal cell samples handed in, 5 SNPs were analyzed for feedback reasons, so out of 1040 analyses to be performed, 1031 (99%) results were actually received.

Table 12: Completion of data collection by level and intensity. x axis: h: high intensity, l: low intensity. FFQ: Food Frequency Questionnaire; Ant: Anthropometric measurements (height, weight, waist circumference); PAQ: Physical Activity Questionnaire; PAL: Physical Activity Level measured by DirectLife triaxial accelerometer (TracmorD).

		L0	**L1h**	**L1l**	**L2h**	**L2l**	**L3h**	**L3l**	**mean**
FFQ	target	153	145	81	135	90	135	87	
	actual	131	121	74	107	82	119	81	
	%	85.6	83.4	91.4	79.3	91.1	88.1	93.1	87.5
Ant	target	153	145	81	135	90	135	87	
	actual	131	121	74	107	81	119	81	
	%	85.6	83.4	91.4	79.3	90.0	88.1	93.1	87.3
PAL	target	153	145	81	135	90	135	87	
	actual	102	106	62	87	66	99	63	
	%	66.7	73.1	76.5	64.4	73.3	73.3	72.4	71.4
PAQ	target	153	145	81	135	90	135	87	
	actual	128	119	71	104	78	117	80	
	%	83.7	82.1	87.7	77.0	86.7	86.7	92.0	85.2
DBS	target	765	435	405	405	450	405	435	
	actual	608	344.5	329	279	387.5	322	358.5	
	%	79.5	79.2	81.2	68.9	86.1	79.5	82.4	79.6
	Mean of %	80.22	80.24	85.64	71.12	88.42	83.14	86.6	

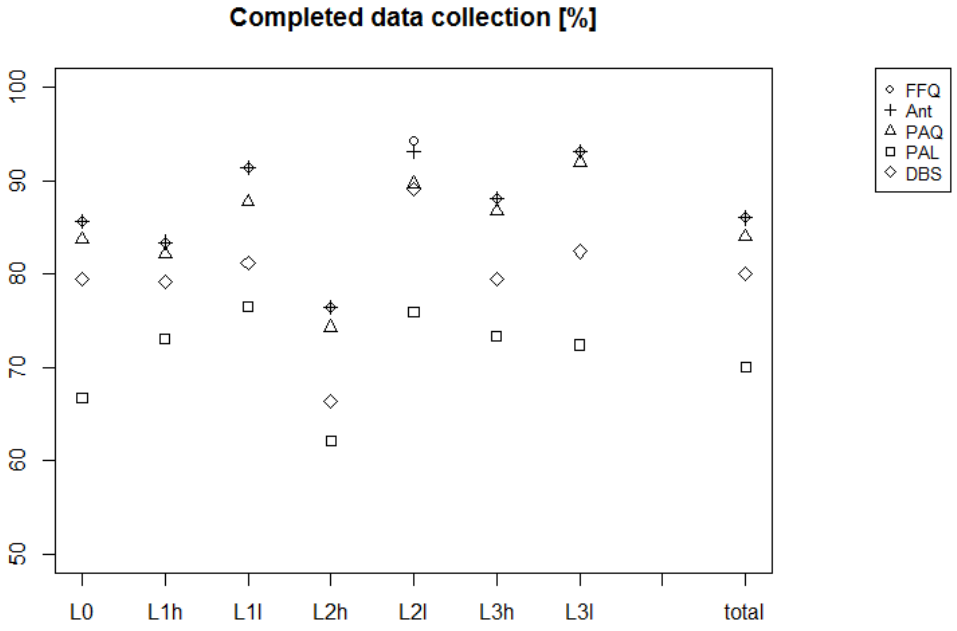


Figure 7: Completion of data collection in % by level and intensity. x axis: h: high intensity, l: low intensity. FFQ: Food Frequency Questionnaire; Ant: Anthropometric measurements (height, weight, waist circumference); PAQ: Physical Activity Questionnaire; PAL: Physical Activity Level measured by DirectLife triaxial accelerometer (TracmorD).

4.3. Values approach

4.3.1. Personalized compared to non-personalized advice (L0 vs. Li)

Hypothesis A states that personalized dietary advice leads to a healthier lifestyle compared to non-personalized conventional advice based on healthy dietary guidelines. To provide evidence for this, Li was compared to L0 concerning the difference between t0 and t6 of all dietary, phenotypic and genotypic variables (Table 13). Compared to the control group, Li participants had a significant greater reduction in red meat intake (Median L0 = -1.64 vs. Li = -9.5 g/d), energy intake (-127.45 vs. -338.06 kcal/d) and intake in saturated fat (0.26 vs -1.38 %E), and salt (-0.05 vs -1.14 g/d) between t0 and t6 (Figure 8). There were significantly differences with an increase in the control group and a simultaneous decrease in the intervention group for total fat (0.57 vs -1.76 %E), monounsaturated fat (0.4 vs. -0.41 %E), and protein intake (0.03 vs. -0.15 g/kg bodyweight/d). The opposite was significant for the ω3 index in blood (-0.11 vs. 0.14 %) (Figure 9). Furthermore, Li participants had a significantly greater increase of their carbohydrate as %E compared to L0 participants (0.24 vs. 1.98 %E) (Figure 9). However, the effect sizes of all significant cases were small compared to Cohen's criteria [51]. It was unexpected that monounsaturated fat was decreased instead of increased. This might be due to the

effort to reduce fat and increase in carbohydrates, as there is a significant negative relationship between carbohydrate and monounsaturated fat intake with Spearman's ρ = -0.66, $p < 0.01$.

Table 13: Comparison of control and intervention group concerning the difference between t0 and t6 for food and nutrient intake, anthropometrics and markers in the Food4Me Study. L0: control group, n∈ [27;41]; Li: intervention groups Li, n∈ [94;135]. Statistical analysis was performed using Wilcoxon's rank-sum test. Mdn: Median; r: effect size. Grey background: variables with $p < 0.05$.

	Mdn L0	Mdn Li	W	p	r
Food groups					
Fruit & Vegetables [g]	10.71	29.50	2541	0.429	-0.06
Wholegrain [g]	-13.71	-6.00	2520	0.387	-0.07
Dairy [g]	6.39	-24.18	3119	0.219	-0.09
Oily Fish [g]	4.14	0.00	3016	0.386	-0.07
Red meat [g]	-1.64	-9.50	3536	0.007	-0.20
Nutrients					
Energy [kcal]	-127.45	-358.06	3567	0.005	-0.21
Total fat [% E]	0.57	-1.76	3611	0.003	-0.22
Saturated fat [% E]	-0.26	-1.38	3661	0.002	-0.24
Monunsaturated fat [% E]	0.40	-0.41	3478	0.013	-0.19
Polyunsaturated fat [% E]	0.40	0.10	3029	0.361	-0.07
ω3 fatty acids [% E]	0.05	0.04	2893	0.662	-0.03
Carbohydrate [% E]	0.24	1.98	1927	0.003	-0.22
Fibre [g]	-2.07	0.17	2569	0.488	-0.05
Protein [g/kg BW]	0.03	-0.15	3581	0.004	-0.21
Salt [g]	-0.05	-1.14	3672	0.002	-0.24
Calcium [mg]	-88.90	-151.20	3155	0.151	-0.11
Iron [mg]	-0.68	-1.32	3074	0.250	-0.09
Vitamin A RE [µg]	3.18	-84.54	3199	0.131	-0.11
Thiamin [mg]	-0.09	-0.20	2554	0.456	-0.06
Riboflavin [mg]	-0.04	-0.21	3070	0.291	-0.08
Folate [µg]	-21.79	-29.38	2934	0.561	-0.04
Cobalamin [µg]	0.05	-0.41	3148	0.184	-0.10
Ascorbic acid [mg]	-15.50	1.40	2438	0.250	-0.09
Anthropometrics					
Bodyweight [kg]	-0.10	-1.00	3208	0.124	-0.12
BMI [kg/m²]	-0.07	-0.33	3173	0.156	-0.11
Waist circumference [cm]	0.00	0.00	3123	0.184	-0.10
Physical activity					
Physical activity index	0.25	0.38	2151	0.299	-0.08
Physical activity level	0.02	-0.05	1556	0.075	-0.13
Marker					
Cholesterol [mmol/l]	-0.61	-0.18	2308	0.362	-0.07
Glucose [mmol/l]	-0.48	-0.49	2450	0.713	-0.03
ω3 Index [%]	-0.11	0.14	1828	0.005	-0.21
Carotenoids [µmol/l]	-0.04	-0.19	2497	0.644	-0.03

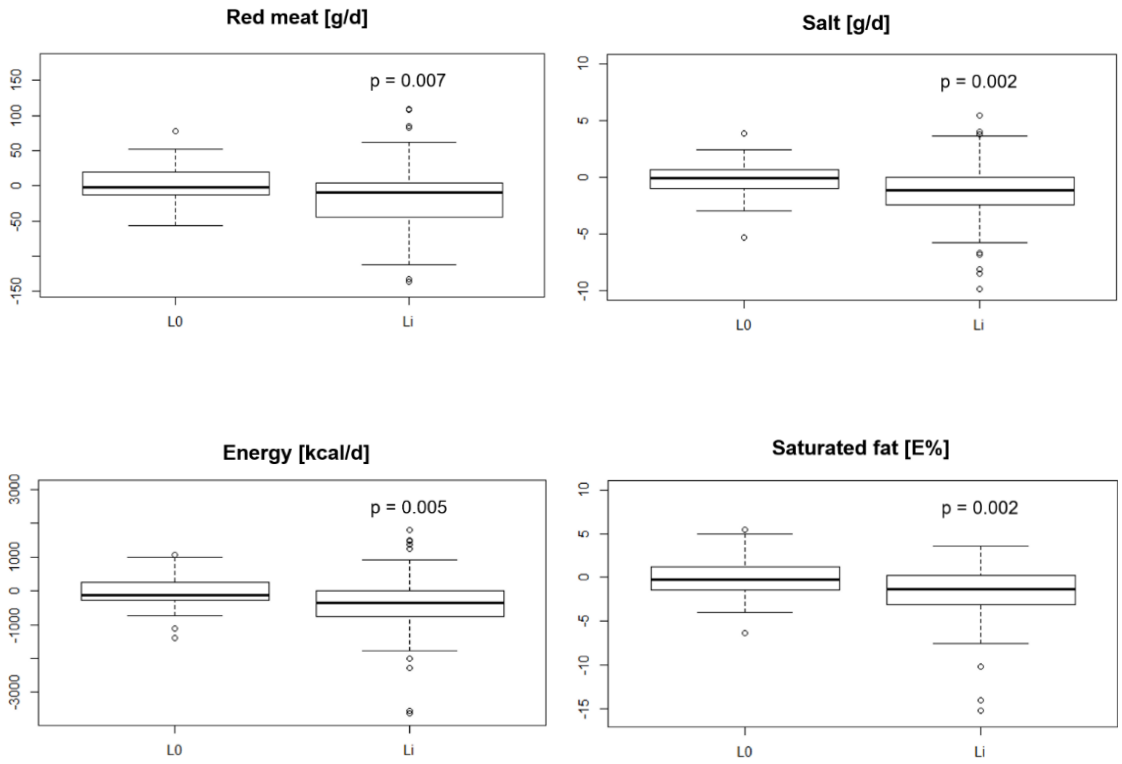


Figure 8: Comparison of control and intervention group concerning the difference between t0 and t6 for red meat, energy, saturated fat and salt intake. L0: control group, n = 41; Li: intervention groups Li, n = 135. Statistical analysis was performed using Wilcoxon's rank-sum test

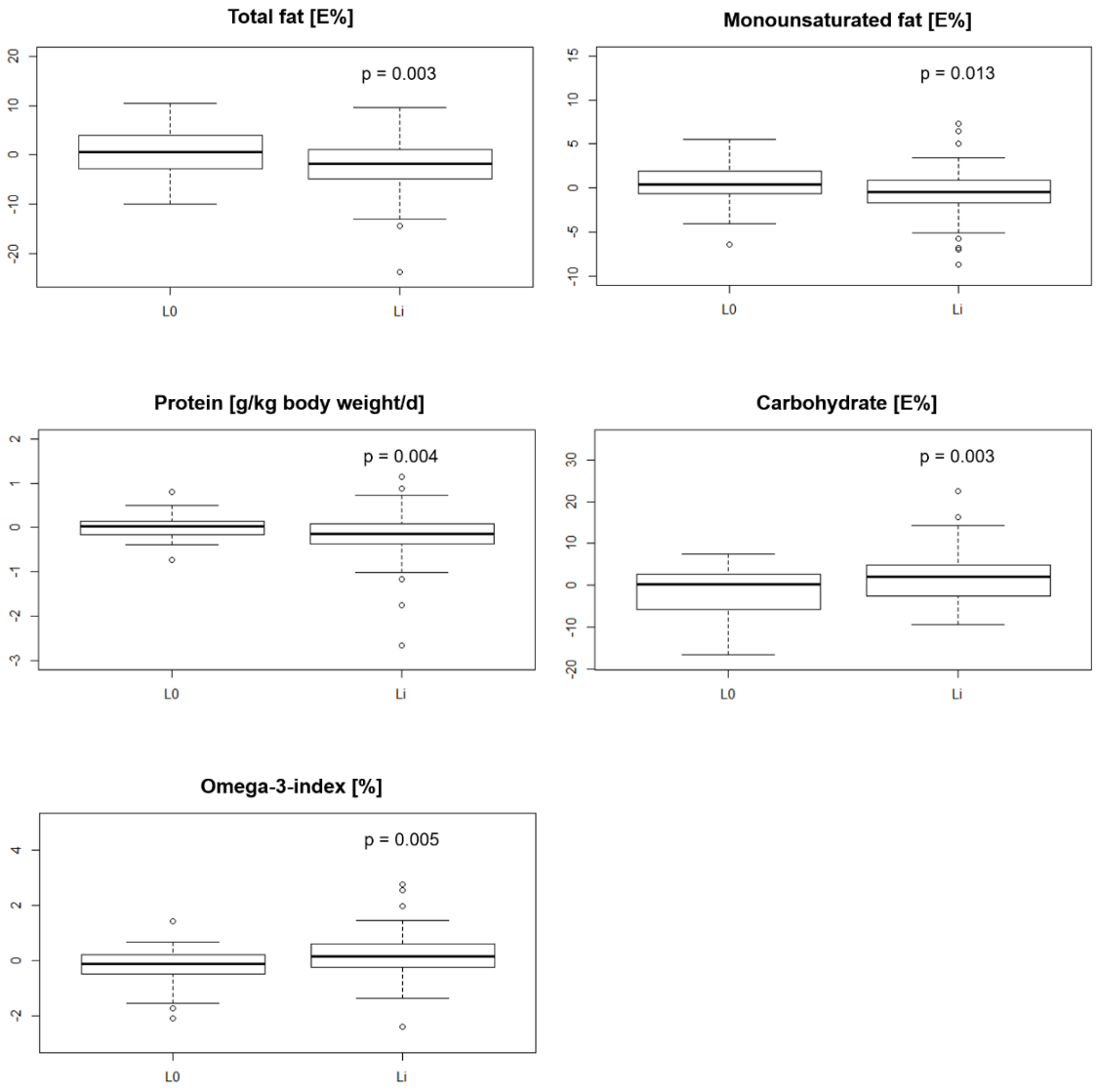


Figure 9: Comparison of control and intervention group concerning the difference between t0 and t6 for, monounsaturated fat, protein, carbohydrate intake as well as ω3 Index. L0: control group; n∈ [40;41]; Li: intervention groups Li, n∈ [130;135]. E%: Energy %. Statistical analysis was performed using Wilcoxon's rank-sum test.

4.3.2. Effectiveness according to amount of individual data (L0 vs. L1 vs. L2 vs. L3)

Hypothesis B states that the effectiveness of personalized advice increases with the amount of individual data comprised. To statistically support this, the difference of t6 and t0 in L0, L1, L2 and L3 were compared among each other, concerning the different nutrients, pheno- and genotypic markers.

There were significant differences for red meat $H(3) = 8.75$, energy $H(3) = 10.68$, total fat $H(3) = 8.95$, saturated fat $H(3) = 10.10$, carbohydrate $H(3) = 8.73$, protein $H(3) = 9.16$, salt $H(3) = 12.50$, and ω3 index $H(3) = 8.87$ between the different levels (Table 14). Post hoc tests indicated significant differences between each comparison of L0, 1, 2, and 3, if the observed difference (OD) was higher than the critical difference (CD) comparing the mean ranks. These post hoc comparisons revealed that there were only significant differences between L0 and any intervention level, but none in-between the different intervention levels. The reduction between t0 and t6 was significantly higher in L1 compared to L0 regarding saturated fat (OD-CD=1.6), and for the same comparison there was a significant increase in ω3 index in blood (OD-CD=0.5). There were significantly greater reductions in L2 compared to L0 for energy (OD-CD=6.6), total fat (OD-CD=0.5), saturated fat (OD-CD=0.5), protein (OD-CD=2.4) and salt (OD-CD=9.5) (Table 15, Figure 10). Although the Kruskal-Wallis test resulted in p-values of < 0.05 for red meat and carbohydrate intake, post hoc comparisons did not find significant differences within levels.

Thus, only comparisons between L0 and intervention levels showed significant differences or trends, but none among the intervention levels themselves. Most significant differences were found comparing L0 and L2, but no trend or significant difference was observed for the comparison of L0 and L3. However, there was no differentiation in L3 between non-risk and risk-allele-carriers, although risk allele carriers were thought to be more susceptible and coherent to personalized nutrition.

Table 14: Comparison of control and three intervention groups concerning the difference between t0 and t6 for food and nutrient intake, anthropometrics and markers in Food4Me Study. L0: control group, n∈ [27;41]; L1: Level 1, n∈ [33;44]; L2: Level 2, n∈ [30;45]; L3: Level 3, n∈ [31;46]. Statistical analysis was performed using Kruskal-Wallis test. Grey background: variables with p <0.05.

	Medians				χ^2	**p**
	L0	**L1**	**L2**	**L3**		
Food groups						
Fruit & Vegetables [g]	10.71	96	-1.96	13.21	5.76	0.124
Wholegrain [g]	-13.71	7.41	-11.36	-5.73	1.09	0.779
Dairy [g]	6.39	-8.77	-34.21	-58.7	5.11	0.164
Oily Fish [g]	4.14	0	0	0.2	1.13	0.770
Red meat [g]	-1.64	-4.62	-11.64	-11.64	8.75	0.033
Nutrients						
Energy [kcal]	-127.45	-260.8	-492.37	-256.12	10.68	0.014
Total fat [% E]	0.57	-1.65	-2.59	-1.64	8.95	0.030
Saturated fat [% E]	-0.26	-1.66	-1.55	-1.28	10.10	0.018
Monunsaturated fat [% E]	0.4	-0.27	-0.1	-0.65	6.95	0.074
Polyunsaturated fat [% E]	0.4	0.23	0.12	-0.13	4.59	0.204
ω3 fatty acids [% E]	0.05	0.03	0.06	0.03	0.56	0.905
Carbohydrate [% E]	0.24	2	2.06	1.59	8.73	0.033
Fibre [g]	-2.07	1.57	-0.6	0.52	1.19	0.755
Protein [g/kg BW]	0.03	-0.15	-0.13	-0.15	9.16	0.027
Salt [g]	-0.05	-0.94	-1.6	-0.89	12.50	0.006
Calcium [mg]	-88.9	-74.56	-159.68	-187.95	3.83	0.281
Iron [mg]	-0.68	-0.07	-2.05	-0.43	3.87	0.276
Vitamin A RE [µg]	3.18	-52.8	-103.14	-53.74	3.11	0.374
Thiamin [mg]	-0.09	-0.22	-0.3	-0.09	2.60	0.457
Riboflavin [mg]	-0.04	0	-0.44	-0.22	6.63	0.085
Folate [µg]	-21.79	-20.9	-32.43	-19.14	0.63	0.890
Cobalamin [µg]	0.05	0.01	-1.3	-0.8	6.67	0.083
Ascorbic acid [mg]	-15.5	5.36	7.22	-17.7	4.01	0.260
Bodyweight [kg]	-0.1	-0.85	-0.9	-1	3.18	0.365
BMI [kg/m²]	-0.07	-0.28	-0.33	-0.34	2.16	0.540
Waist circumference [cm]	0	0	-0.01	-0.01	2.24	0.524
Physical activity index	0.25	0.38	0	0.44	4.28	0.232
Physical activity level	0.02	-0.12	-0.04	-0.04	6.87	0.076
Cholesterol [mmol/l]	-0.61	-0.37	-0.17	-0.11	1.70	0.636
Glucose [mmol/l]	-0.48	-0.3	-0.42	-0.64	1.34	0.721
ω3 Index [%]	-0.11	0.25	0.01	0.19	8.87	0.031
Carotenoids [µmol/l]	-0.04	-0.35	-0.17	-0.06	4.99	0.173

Table 15: Post hoc comparison of control and three intervention groups concerning the difference between t0 and t6 for nutrient intake, anthropometrics and markers in the Food4Me Study. L0: control group, n∈ [27;41]; L1: Level 1, n∈ [33;44]; L2: Level 2, n∈ [30;45]; L3: Level 3, n∈ [31;46]. Statistical analysis was performed using Kruskal-Wallis test and post hoc Wilcoxon rank-sum test on all possible comparisons, with the difference of observed difference (OD) - critical difference (CD). Grey background marks variables with significant values (OD>CD) $p<0.05$.

	L0.L1	L0.L2	L0.L3	L1.L2	L1.L3	L2.L3
Food groups						
Fruit & Vegetables [g]	-7.9	-26.5	-27.2	-9.7	-5.4	-24.0
Wholegrain [g]	-22.9	-23.2	-17.4	-28.1	-23.2	-22.6
Dairy [g]	-28.4	-12.9	-11.2	-11.6	-9.9	-26.6
Oily Fish [g]	-23.5	-17.4	-22.5	-22.5	-27.7	-22.9
Red meat [g]	-12.5	-0.9	-0.7	-17.0	-16.8	-28.1
Nutrients						
Energy [kcal]	-10.9	6.6	-6.6	-11.1	-24.3	-14.9
Total fat [% E]	-4.9	0.5	-2.3	-23.3	-26.1	-25.3
Saturated fat [% E]	1.6	0.5	-3.9	-27.3	-22.6	-23.6
Monunsaturated fat [% E]	-9.5	-9.0	-0.9	-28.1	-20.1	-20.3
Polyunsaturated fat [% E]	-26.3	-19.5	-11.0	-16.1	-7.6	-19.9
ω3 fatty acids [% E]	-23.9	-28.8	-22.5	-23.5	-27.3	-22.1
Carbohydrate [% E]	-2.3	-0.9	-3.7	-27.2	-26.7	-25.2
Fibre [g]	-17.8	-26.5	-23.7	-19.6	-22.1	-25.5
Protein [g/kg BW]	-8.9	2.4	-3.1	-17.4	-22.9	-22.5
Salt [g]	-6.3	9.5	-4.0	-13.0	-26.4	-14.6
Calcium [mg]	-24.3	-12.2	-11.4	-16.4	-15.6	-27.3
Iron [mg]	-24.7	-8.7	-22.3	-12.8	-26.5	-14.2
Vitamin A RE [µg]	-11.7	-13.4	-20.6	-26.7	-19.1	-20.8
Thiamin [mg]	-22.4	-28.1	-14.5	-20.8	-20.7	-12.9
Riboflavin [mg]	-25.9	-7.0	-19.0	-3.1	-15.2	-16.0
Folate [µg]	-26.4	-20.6	-24.3	-22.9	-26.6	-24.3
Cobalamin [µg]	-27.7	-4.0	-19.2	-5.0	-20.2	-12.9
Ascorbic acid [mg]	-9.6	-18.8	-26.9	-19.2	-10.8	-19.9
Anthropometrics						
Bodyweight [kg]	-14.3	-20.2	-10.6	-22.4	-25.0	-18.7
BMI [kg/m²]	-16.4	-18.1	-13.9	-26.6	-26.2	-24.2
Waist circumference [cm]	-21.3	-14.8	-14.8	-22.0	-22.0	-27.8
Physical activity						
Physical activity index	-15.2	-26.2	-12.0	-13.2	-24.2	-9.9
Physical activity level	-0.9	-16.2	-15.6	-8.6	-8.8	-23.4
Marker						
Cholesterol [mmol/l]	-24.0	-23.1	-14.6	-27.2	-18.7	-19.9
Glucose [mmol/l]	-24.2	-25.2	-19.1	-21.0	-22.3	-15.9
ω3 Index [%]	0.5	-8.7	-1.5	-18.9	-25.5	-20.8
Carotenoids [µmol/l]	-10.8	-26.8	-23.2	-9.8	-6.2	-23.6

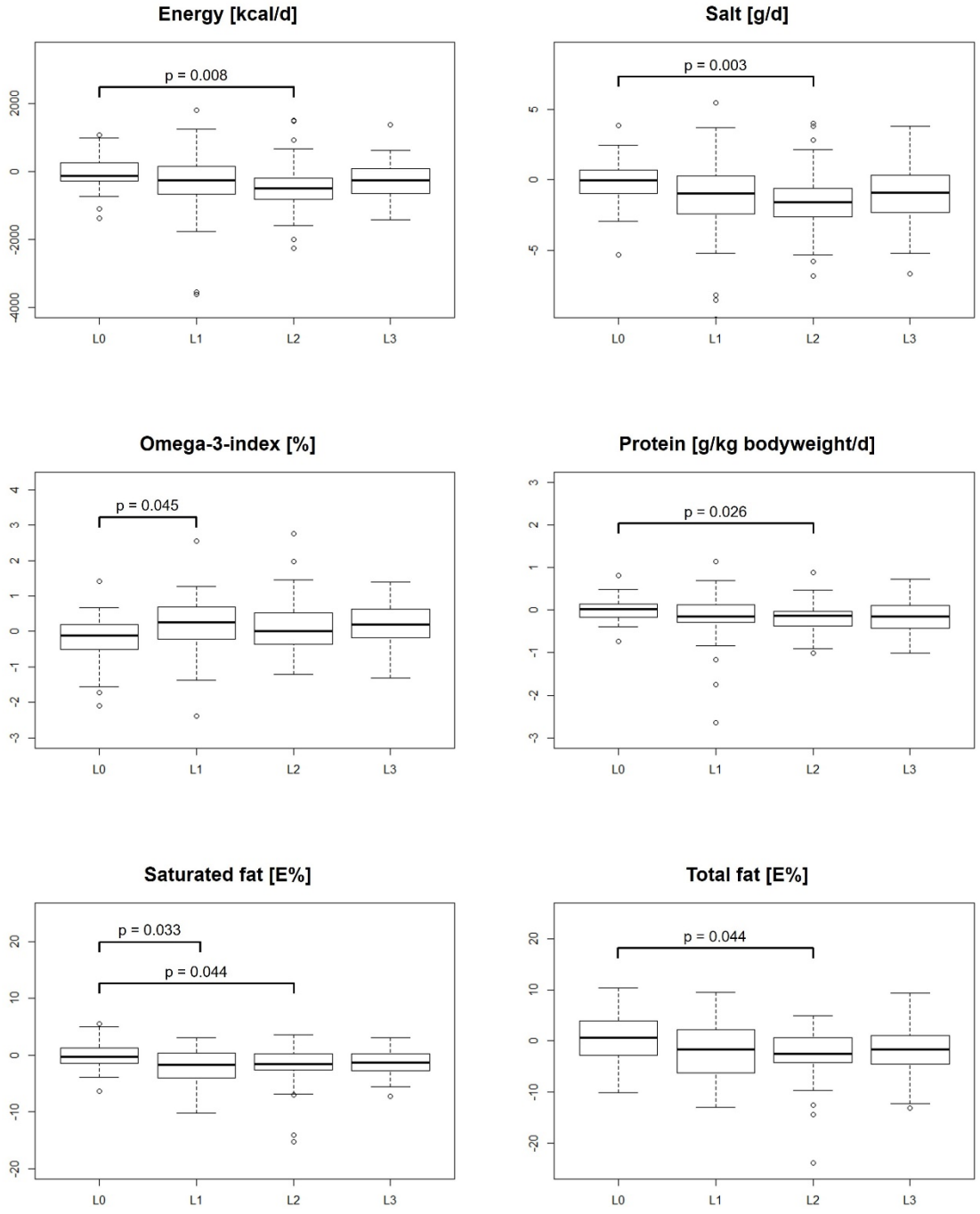


Figure 10: Comparison of control and intervention group concerning the difference between t0 and t6 for saturated and total fat, energy, protein and salt intake and ω3 index in the Food4Me Study. Change of food intake was calculated by subtracting baseline FFQ data from final FFQ data six months later. L0: control group, n∈ [40;41]; L1: Level 1, n∈ [42;44]; L2: Level 2, n∈ [42;45]; L3: Level 3, n∈ [45;46]. E%: Energy %. Statistical analysis was performed using Kruskal-Wallis test and post hoc, the Wilcoxon rank-sum test on all possible comparisons.

4.3.3. Personalized advice with existence compared to absence of risk alleles (L0 vs. L1 vs. L2 vs. L3n vs. L3r)

To assess the effectiveness of personalized nutrition for participants with and those without risk alleles in the selected genes, the participants of L3 were assigned to non-risk allele-carriers L3n and risk-allele-carriers L3r for each analysis. For each of the five SNPs, the different levels L0, L1, L2, L3n and L3r were compared to each other concerning the respective nutrient influenced by the SNP using the delta between t0 and t6. Within the *FADS1*-analysis, the ω3 index showed significant difference H(4) = 10.11, within the *TCF7L2*-analysis saturated fat H(4) = 9.97 and ω3 index H(4) = 9.65, and within the *ApoE*-analysis saturated fat H(4) = 13.79 (Table 14). The post hoc test revealed one significant different comparison for saturated fat in the *ApoE*-analysis between L3r and L0 (OD-CD=1.6) (Table 17, Figure 11).

However, several post hoc comparisons showed only small differences between OD and CD. Thus, to discover trends, differences were analyzed concerning significance of $p < 0.1$. For the *FADS1*-analysis, ω3 index between L0 and L1 as well as between L0 and L3r were significant; for *TCF7L2* between L0 and L2 for total and saturated fat, between L0 and L1 for saturated fat and the ω3 index, and for *ApoE* between L0 and L1, 2 and 3r for saturated fat (Table 17).

Thus, no trend or significant difference was observed for the comparison of L0 and L3n and the only significant comparison was found between L0 and L3r. Most trends were observed with levels involving phenotypic information.

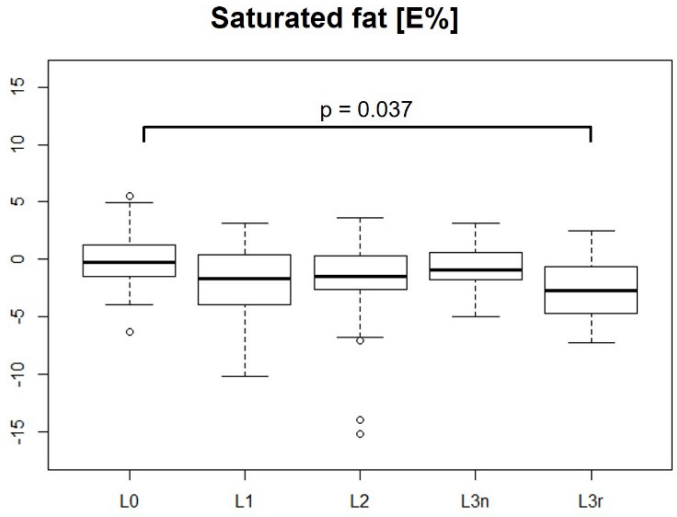


Figure 11: Post hoc comparison of control and three intervention groups with split L3 concerning the difference between t0 and t6 for saturated fat associated with a SNP in *ApoE* in the Food4Me Study. L0: control group, n = 41; L1: Level 1, n = 44; L2: Level 2, n = 45; L3n: Level 3 without risk factor, n = 33, L3r: Level 3 with risk factor, n = 12. E%: Energy %. Statistical analysis was performed using Kruskal-Wallis test and post hoc the Wilcoxon rank-sum test on all possible comparisons.

Table 16: Comparison of control and three intervention groups with split L3 concerning the difference between t0 and t6 for food and nutrient intake, anthropometrics and markers which are associated to SNPs in certain genes in the Food4Me Study. L0: control group, n = 41; L1: Level 1, n = 44; L2: Level 2, n = 45; L3n: Level 3 without risk factor, n∈ [11;33], L3r: Level 3 with risk factor, n∈ [12;34]. Statistical analysis was performed using Kruskal-Wallis test. Grey background: variables with p <0.05.

	Medians					**χ^2**	**p**
	L0	**L1**	**L2**	**L3n**	**L3r**		
FTO							
Bodyweight [kg]	-0.10	-0.85	-0.90	-1.20	-0.50	3.20	0.524
BMI [kg/m²]	-0.07	-0.28	-0.33	-0.52	-0.17	2.57	0.632
Waist Circumference [cm]	0.00	0.00	-0.01	0.00	-0.01	2.18	0.703
FADS1							
ω3 fatty acids [% E]	0.05	0.03	0.06	0.02	0.05	1.60	0.809
ω3 index [%]	-0.11	0.25	0.01	-0.06	0.33	10.11	0.039
MTHFR							
Folate [µg/d]	-21.79	-20.90	-32.43	-14.58	-32.67	1.65	0.799
TCF7L2							
Total fat [% E]	0.57	-1.65	-2.59	-3.15	-1.51	8.87	0.064
Saturated fat [% E]	-0.26	-1.66	-1.55	-0.84	-1.28	9.97	0.041
Monounsaturated fat [% E]	0.40	-0.27	-0.10	-0.51	-0.68	7.35	0.119
Polyunsaturated fat [% E]	0.40	0.23	0.12	-0.09	-0.13	5.26	0.261
ω3 fatty acids [% E]	0.05	0.03	0.06	-0.02	0.05	2.73	0.603
Cholesterol [mmol/l]	-0.61	-0.37	-0.17	-0.13	-0.10	1.75	0.781
ω3 Index [%]	-0.11	0.25	0.01	0.35	0.12	9.65	0.047
ApoE							
Saturated fat [% E]	-0.26	-1.66	-1.55	-0.89	-2.69	13.79	0.008
Cholesterol [mmol/l]	-0.61	-0.37	-0.17	-0.02	-0.41	2.21	0.697

Table 17: Post hoc comparison of control and three intervention groups with split L3 concerning the difference between t0 and t6 for food and nutrient intake, anthropometrics and markers which are associated to SNPs in certain genes in the Food4Me Study. L0: control group, n = 41; L1: Level 1, n = 44; L2: Level 2, n = 45; L3n: Level 3 without risk factor, n∈ [11;33], L3r: Level 3 with risk factor, n∈ [12-34]. Statistical analysis was performed using Kruskal-Wallis test and post hoc Wilcoxon rank-sum test on all possible comparisons, with the difference of observed difference (OD) - critical difference (CD). Grey background marks variables with significant values (OD>CD) p<0.05. Framed values indicate significance for p<0.1.

	L0.L1	**L0.L2**	**L0.L3n**	**L0.L3r**	**L1.L2**	**L1.L3n**	**L1.L3r**	**L2.L3n**	**L2.L3r**	**L3n.L3r**
FTO										
Bodyweight	-16.2	-22.1	-19.5	-19.0	-24.1	-33.8	-33.2	-27.6	-27.0	-38.9
BMI	-18.2	-19.9	-19.2	-26.0	-28.2	-31.5	-31.4	-29.5	-33.2	-31.6
Waist Circumference	-23.1	-16.6	-25.0	-22.9	-23.7	-32.2	-30.1	-38.7	-32.6	-40.2
FADS1										
ω3 fat acids	-25.6	-30.5	-22.4	-36.7	-25.2	-27.2	-32.8	-22.1	-36.3	-28.7
ω3 Index	-1.3	-10.5	-19.4	-2.0	-20.5	-23.2	-30.7	-32.3	-21.2	-22.9
MTHFR										
Folate	-28.1	-22.4	-40.0	-23.5	-24.7	-36.9	-25.8	-31.2	-31.1	-31.5
TCF7L2										
Total fat	-6.7	-1.4	-17.1	-8.2	-24.8	-40.7	-31.7	-40.8	-30.0	-44.9
Saturated fat	-0.2	-1.2	-23.2	-11.0	-28.9	-33.5	-26.0	-34.5	-27.0	-43.4
Monounsaturated fat	-11.3	-10.8	-20.2	-3.3	-29.6	-39.2	-22.2	-39.5	-22.4	-38.6
Polyunsaturated fat	-27.9	-20.9	-20.9	-16.5	-17.5	-17.7	-13.2	-30.0	-25.5	-40.4
ω3 fat acids	-25.4	-30.3	-20.5	-33.9	-25.0	-25.4	-28.3	-20.3	-33.1	-22.5
Cholesterol	-25.4	-24.6	-28.8	-19.3	-28.6	-33.1	-23.4	-34.2	-24.5	-44.0
ω3 Index	-1.3	-10.4	-6.8	-10.7	-20.3	-35.5	-26.7	-26.1	-29.8	-31.5
ApoE										
Saturated fat	-0.3	-1.3	-18.3	1.6	-29.0	-17.2	-28.6	-18.2	-27.3	-14.6
Cholesterol	-25.6	-24.8	-15.9	-35.5	-28.8	-20.0	-39.8	-21.1	-41.0	-39.5

4.4. Classification approach

4.4.1. Personalized compared to non-personalized advice (L0 vs. Li)

Nutrient intake and blood levels were classified in a traffic light system for easy identification, which nutrients were in an optimal, intermediate or poor range. In over 90% of the participants, blood glucose level and estimated intakes of thiamin, riboflavin, cobalamin and protein were in an optimal range, i.e. classified green at t0 as well as t6. Less than 10% on the other hand, had an optimal blood ω3 index or salt and saturated fat (as %E) intake (Table 18). Comparing L0 to Li, there was a significant association between the level affiliation and a shift into a healthier class for saturated fat, $\chi^2(1) = 7.72$, with 12.2% of the participants in L0 versus 34.8% in Li switching classes. There was also a significant association for carbohydrate, $\chi^2(1) = 9.52$ with 12.5% changing towards a healthier class in L0 and 47.9% in Li. A third significant association was found for monounsaturated fat, $\chi^2(1) = 7.22$, with 27.8% for L0 and 10% for Li. This seems to represent the fact that the odds of changing color towards a healthier diet were 3.83 (95% confidence interval (CI): 1.36-13.35) times higher for saturated fat, and 6.34 (CI: 1.68-36.05) times higher for carbohydrate, if participants were in the intensity group. For monounsaturated fat, the odds ratio was 0.29 (CI: 0.1-0.84), which indicates that the odds of changing color towards a healthier diet were higher, if participants were in the control group (Figure 12).

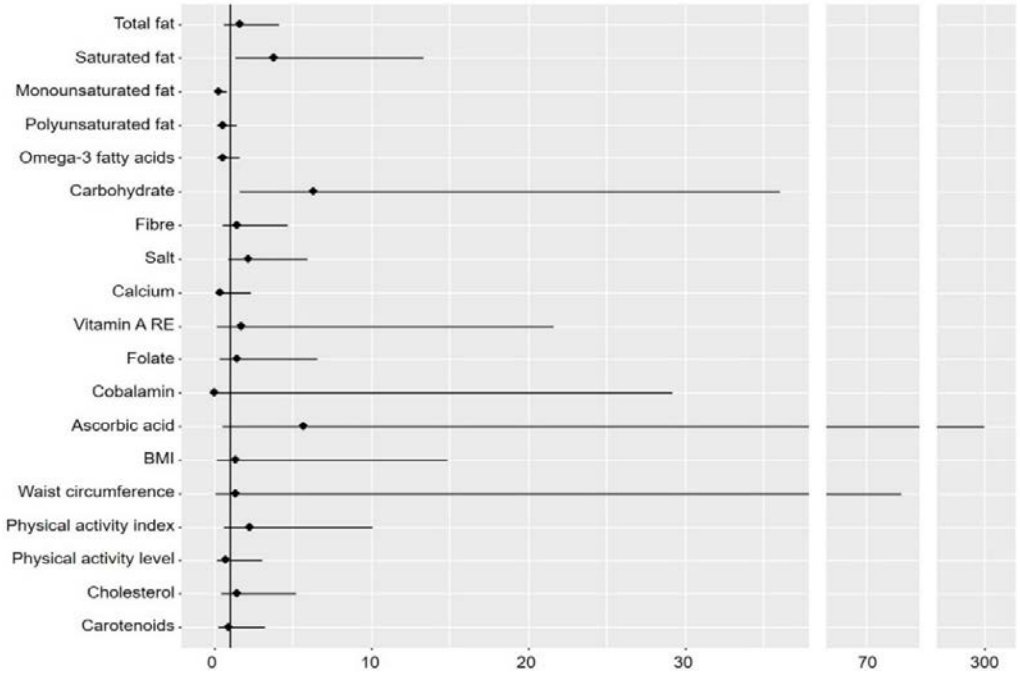


Figure 12: Odds ratios and confidence intervals of comparison of control and intervention group concerning the change into healthier classification for food and nutrient intake, anthropometrics and markers in the Food4Me Study. L0: control group; Li: intervention group. Statistical analysis was performed using Pearson's χ^2. <1: in favor for L0; >1 in favor for Li. For n see Table 18.

Table 18: Comparison of control and intervention group concerning the change into healthier classification for food and nutrient intake, anthropometrics and markers in the Food4Me Study. n Li: number of participants in intervention group; no: no change towards a healthier class; yes: change towards a healthier class; optimal intake %: percentage of participants with classification in optimal range on t0 and t6. Statistical analysis was performed using Pearson's χ^2. OR: odds ratio, CI: confidence interval. Grey background: variables with $p < 0.05$.

	n L0		n Li		optimal intake %	χ^2	p	OR	CI
	no	yes	no	yes					
Nutrients									
Total fat	22	11	52	43	27.30	1.43	0.232	1.65	0.68 - 4.21
Saturated fat	36	5	86	46	1.70	7.72	0.005	3.83	1.36 - 13.35
Monounsaturated fat	26	10	108	12	11.40	7.22	0.007	0.29	0.10 - 0.84
Polyunsaturated fat	12	12	71	39	23.90	1.77	0.184	0.55	0.20 - 1.48
ω3 fatty acids	15	12	58	28	35.80	1.27	0.260	0.61	0.23 - 1.62
Carbohydrate	21	3	38	35	44.90	9.52	0.002	6.34	1.68 - 36.05
Fibre	20	7	57	30	35.20	0.69	0.407	1.50	0.53 - 4.69
Protein	1	0	4	6	93.80	1.32	0.251		
Salt	33	8	86	46	1.70	3.43	0.064	2.20	0.90 - 5.97
Calcium	7	4	46	11	61.10	1.56	0.211	0.42	0.09 - 2.33
Iron	2	0	7	4	92.60	1.05	0.305		
Vitamin A RE	5	2	13	9	83.50	0.34	0.558	1.70	0.21 - 21.63
Thiamin	2	0	6	3	93.80	0.92	0.338		
Riboflavin	1	0	4	6	93.80	1.32	0.251		
Folate	20	4	74	22	31.80	0.44	0.506	1.48	0.43 - 6.59
Cobalamin	0	1	4	2	96.00	1.56	0.212		
Ascorbic acid	6	1	11	11	83.50	2.79	0.095	5.68	0.54 - 300.03
Anthropometrics									
BMI	17	2	48	8	57.40	0.17	0.677	1.41	0.25 - 14.93
Waist circumference	13	1	37	4	68.60	0.09	0.769	1.40	0.12 - 74.44
Physical activity									
Physical activity index	21	4	57	25	34.40	2.04	0.154	2.29	0.67 - 10.11
Physical activity level	17	5	66	15	14.90	0.20	0.658	0.77	0.22 - 3.11
Marker									
Cholesterol	15	6	50	30	40.60	0.58	0.447	1.49	0.48 - 5.23
Glucose	0	0	0	2	98.80				
ω3 Index	40	0	127	2	0.60	0.63	0.428		
Carotenoids	19	6	62	18	34.80	0.02	0.876	0.92	0.29 - 3.24

4.4.2. Effectiveness according to amount of input data (L0 vs. L1 vs. L2 vs. L3)

Comparing L0, L1, L2, and L3 amongst each other, there was a significant association between level affiliation and shift into a healthier class for saturated fat $\chi^2(3) = 8.19$, and carbohydrate intake $\chi^2(3) = 11.51$, as well as for ascorbic acid $\chi^2(3) = 8.06$ (Table 19). After Bonferroni correction, only L0 compared to L1 in carbohydrate was significantly different; within L0 12.5% of the participants changed in to a healthier class, in L1 60.0%, in L2 39.1% and in L3 46.7% (Figure 13).

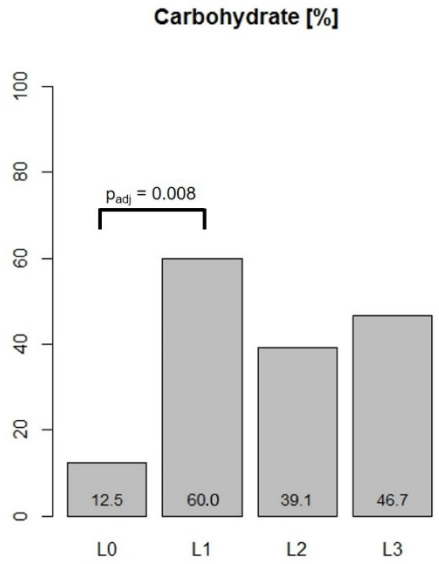


Figure 13: Comparison of control and three intervention groups concerning the change into healthier class for carbohydrate intake. Numbers in bars: % of participants changed in to a healthier classification comparing t0 to t6. Statistical analysis was performed using Pearson's χ^2 with post hoc Bonferroni correction. For n see Table 19.

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Table 19: Comparison of control and three intervention groups concerning the change into healthier classification for food and nutrient intake, anthropometrics and markers in the Food4Me Study. n L0, n L1, n L2, n L3: sample size in control group and levels 1, 2 and 3; no: no change towards a healthier color; y: yes, change towards a healthier color. Statistical analysis was performed using Pearson's χ^2 with post hoc Bonferroni correction. Grey background: variables with p <0.05.

	n L0		n L1		n L2		n L3		χ^2	p	adj p between levels					
	n	y	n	y	n	y	n	y			L0.L1	L0.L2	L0.L3	L1.L2	L1.L3	L2.L3
Nutrients																
Total fat	22	11	15	14	16	14	21	15	1.75	0.625	1	1	1	1	1	1
Saturated fat	36	5	27	16	28	16	31	14	8.19	0.042	0.068	0.073	0.244	1	1	1
Monounsaturated fat	26	10	35	5	37	4	36	3	7.60	0.055	0.889	0.439	0.191	1	1	1
Polyunsaturated fat	12	12	22	15	22	15	27	9	4.25	0.236	1	1	0.347	1	1	1
ω3 fatty acids	15	12	20	11	18	11	20	6	2.77	0.428	1	1	0.888	1	1	1
Carbohydrate	21	3	8	12	14	9	16	14	11.51	0.009	0.008	0.294	0.053	1	1	1
Fibre	20	7	16	10	20	7	21	13	2.00	0.573	1	1	1	1	1	1
Protein	1	0	1	3	2	1	1	2	2.60	0.458	1	1	1	1	1	1
Salt	33	8	30	12	29	15	27	19	5.10	0.164	1	0.899	0.223	1	1	1
Calcium	7	4	12	7	17	1	17	3	7.16	0.067	1	0.324	1	0.254	0.931	1
Iron	2	0	2	3	0	1	5	0	7.37	0.061	1	1	1	1	1	1
Vitamin A RE	5	2	3	2	6	3	4	4	0.85	0.839	1	1	1	1	1	1
Thiamin	2	0	2	1	1	1	3	1	1.34	0.720	1	1	1	1	1	1
Riboflavin	1	0	2	4	1	1	1	1	1.59	0.662	1	1	1	1	1	1
Folate	20	4	21	9	25	4	28	9	2.79	0.424	1	1	1	1	1	1
Cobalamin	0	1	0	2	3	0	1	0	7.00	0.072	1	1	1	0.600	1	1
Ascorbic acid	6	1	4	5	4	0	3	6	8.06	0.045	0.871	1	0.361	0.629	1	0.420
Anthropometrics																
BMI	17	2	13	1	16	3	19	4	1.02	0.796	1	1	1	1	1	1
Waist circumference	13	1	8	1	16	1	13	2	0.65	0.886	1	1	1	1	1	1
Physical activity																
Physical activity index	21	4	16	13	18	5	23	7	6.72	0.081	0.230	1	1	0.849	0.620	1
Physical activity level	17	5	21	4	21	7	24	4	1.37	0.713	1	1	1	1	1	1
Marker																
Cholesterol	15	6	12	11	17	11	21	8	2.93	0.403	1	1	1	1	0.943	1
Glucose	0	0	0	0	0	1	0	1								
Ω3 Index	40	0	41	1	42	1	44	0	2.00	0.572	1	1	1	1	1	1
Carotenoids	19	6	22	2	21	8	19	8	3.96	0.266	1	1	1	0.549	0.483	1

4.4.3. Personalized advice with and without reference to risk alleles (L0 vs. L1 vs. L2 vs. L3n vs. L3r)

L3 was assessed for groups without or with reference to a certain SNP and risk allele respectively. There were significant differences between the groups concerning saturated fat intake in the *ApoE* analysis $\chi^2(4) = 14.82$, and monounsaturated fat intake in the *TCF7L2* analysis $\chi^2(4) = 10.96$ (Table 20). Bonferroni correction revealed that in both cases there were significant differences between L0 and L3r for *ApoE* and *TCF7L2* gene variants respectively (Figure 14).

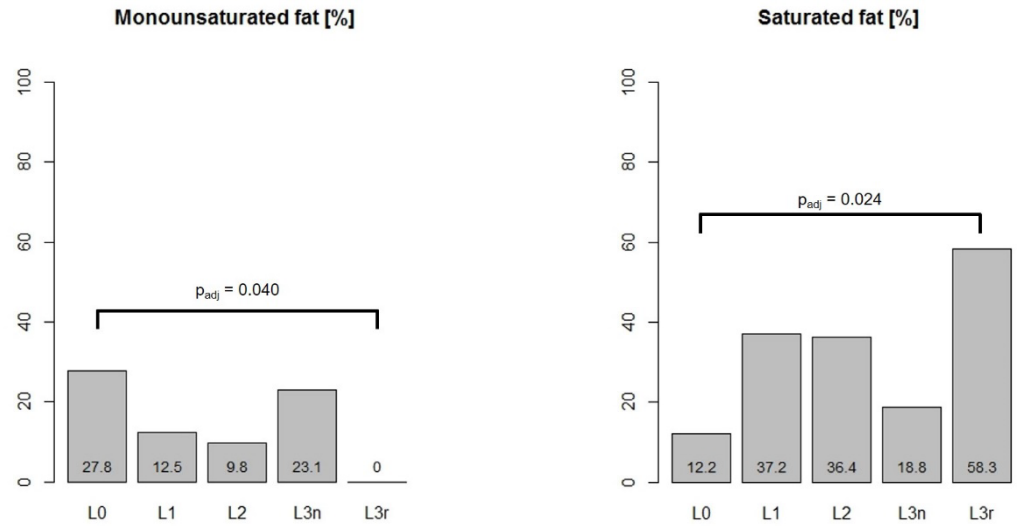

Figure 14: Comparison of control and three intervention groups with split L3 concerning the difference between t0 and t6 for monounsaturated fat intake associated with a SNP in *TCF7L2* and saturated fat associated with a SNP in *ApoE*. Numbers in bars: % of participants changed in to a healthier classification comparing t0 to t6. Statistical analysis was performed using Pearson's χ^2 with post hoc Bonferroni correction. For n see Table 20.

Table 20: Post hoc comparison of control and three intervention groups with split L3 concerning the change into a healthier class for food and nutrient intake, anthropometrics and markers as associated with preselected SNPs. n L0, n L1, n L2, n L3: sample size in control group and levels 1, 2 and 3; L3n: Level 3 without target nutrient, L3r: Level 3 with target nutrient; no: no change towards a healthier color; yes: no change towards a healthier color. Statistical analysis was perfomed using Pearson's χ^2 with post hoc Bonferroni correction. Grey background: variables with p <0.05.

	n L0		**n L1**		**n L2**		**n L3n**		**n L3r**		**χ^2**	**p**	**adj p between levels**									
	n	**y**	**n**	**y**	**n**	**y**	**n**	**y**	**n**	**y**			**L0.L1**	**L0.L2**	**L0.L3n**	**L0.L3r**	**L1.L2**	**L1.L3n**	**L1.L3r**	**L2.L3n**	**L2.L3r**	**L3n.L3r**
FTO																						
BMI	17	2	13	1	16	3	5	3	14	1	5.31	0.257	1	1	1	1	1	1	1	1	1	1
Waist circumference	13	1	8	1	16	1	5	1	8	1	0.78	0.941	1	1	1	1	1	1	1	1	1	1
FADS1																						
ω3 fatty acids	15	12	20	11	18	11	13	4	7	2	2.78	0.596	1	1	1	1	1	1	1	1	1	1
Ω3 Index	40	0	41	1	42	1	22	0	21	0	1.98	0.740	1	1	1	1	1	1	1	1	1	1
MTHFR																						
Folate	20	4	21	9	25	4	8	3	19	6	2.90	0.574	1	1	1	1	1	1	1	1	1	1
TCF7L2																						
Total fat	22	11	15	14	16	14	7	6	13	8	1.98	0.740	1	1	1	1	1	1	1	1	1	1
Saturated fat	36	5	27	16	28	16	9	4	22	8	8.34	0.080	0.113	0.122	1	1	1	1	1	1	1	1
Monounsaturated fat	26	10	35	5	37	4	10	3	24	0	10.96	0.027	1	0.732	1	0.040	1	1	1	1	1	0.368
Polyunsaturated fat	12	12	22	15	22	15	7	4	19	5	4.66	0.324	1	1	1	0.687	1	1	1	1	1	1
ω3 fatty acids	15	12	20	11	18	11	8	1	11	5	3.47	0.482	1	1	1	1	1	1	1	1	1	1
Cholesterol	15	6	12	11	17	11	7	3	13	4	3.34	0.502	1	1	1	1	1	1	1	1	1	1
Ω3 Index	40	0	41	1	42	1	13	0	29	0	1.95	0.744	1	1	1	1	1	1	1	1	1	1
ApoE																						
Saturated fat	36	5	27	16	28	16	26	6	5	7	14.82	0.005	0.113	0.122	1	0.024	1	1	1	1	1	0.226
Cholesterol	15	6	12	11	17	11	14	5	7	2	3.55	0.471	1	1	1	1	1	1	1	1	1	1

4.5. Effect of target nutrients

The feedback report for the participants involved specific recommendations on three to four so called 'target nutrients'. These were either nutrients or markers that the individual should especially target. As a help to achieve that, detailed information was provided. Within all feedback reports between t0 and t6, a total of 1904 target nutrient recommendations were included. Salt was defined most frequently as prime target (23.2 % of the cases), followed by saturated fat (20.8%) and folate intake (19.0%). Least frequently defined target nutrients were iron (0.2%), retinol (0.2%) and thiamin (0.1%). Blood glucose level was not identified as a target (Table 21). Each recommendation for a certain target nutrient had a direction; either to increase, to decrease or to maintain the intake. For total and saturated fat, salt and cholesterol, 76 to 100% of the recommendations were to decrease the intake or marker. In contrast, for unsaturated fats, carbohydrate, fiber, vitamins, carotenoids and calcium, the recommendations were mainly directed to increase the intake.

Table 21: Frequency and direction of target nutrient recommendations. Total number of target nutrients recommended on all time points n = 1904. Freq: number of recommendations as target nutrient, %TN: percentage of target nutrient recommendations (100% = 1904). % increase/maintain/decrease: % of recommendations to increase/maintain/decrease the intake.

	Freq	**%TN**	**% increase**	**% maintain**	**% decrease**
Total fat	76	4.9	0	24	76
Saturated fat	321	20.8	0	1	99
Monounsaturated fat	50	3.2	100	0	0
Polyunsaturated fat	60	3.9	100	0	0
ω3 fatty acids & index	165	10.7	99	1	0
Carbohydrate	52	3.4	100	0	0
Fiber	164	10.6	100	0	0
Protein	7	0.5	43	0	57
Salt	358	23.2	0	0	100
Calcium	101	6.5	94	2	4
Iron	3	0.2	33	0	67
Vitamin A RE	3	0.2	67	0	33
Thiamin	1	0.1	100	0	0
Riboflavin	5	0.3	100	0	0
Folate	293	19.0	88	11	1
Cobalamin	6	0.4	100	0	0
Ascorbic acid	20	1.3	100	0	0
Cholesterol	65	4.2	0	0	100
Glucose	0				
Carotenoids	154	10.0	100	0	0

To analyze the effectiveness of these target nutrient recommendations, the difference for each target nutrient between the previous and subsequent feedback report was calculated. If this difference matched the direction of the specific recommendation, the recommendation was classified as effective in changing the behavior towards a healthier diet. For this analysis, only the recommendations of t0, t1, t2 and t3 were taken into account (n = 1228), as behavior changes following the final recommendations of t6 was not recorded. Target nutrient recommendations were most effective for increasing carbohydrate intake and a similar high effectiveness was found for increasing poly- (79%) and monounsaturated fats in the diet (78%). Also the recommendation of an increase in calcium (74%) and ω3- fatty acids (67%), as well as a decrease in total fat (70%), cholesterol (69%) and salt (67%) intakes were realized (Table 22).

Table 22: Percentage of behavior change to the recommended direction for each nutrient. Target nutrients with a frequency of >20 (see Table 21).

	Direction	**% behavior change**
Total fat	Decrease	69.7
Saturated fat	Decrease	64.4
Monounsaturated fat	Increase	78.4
Polyunsaturated fat	Increase	79.1
ω3 fatty acids & index	Increase	67.5
Carbohydrate	Increase	80.0
Fiber	Increase	58.7
Salt	Decrease	67.3
Calcium	Increase	73.7
Folate	Increase	64.5
Cholesterol	Decrease	69.2
Carotenoids	Increase	59.3

The effect of recommending target nutrients on the corresponding nutrients or blood values was as well statistically tested by calculating the difference for each nutrient between previous and subsequent feedback report with level, intensity and target nutrient as predicting variables. There were significant effects on recommending target nutrients on the corresponding intake levels or blood values; For total fat $F(1, 410) = 4.98$, saturated fat $F(1,410) = 14.55$, monounsaturated fat $F(1,410) = 25.69$, polyunsaturated fat $F(1,410) = 5.70$, carbohydrate $F(1,410) = 17.78$, dietary fiber $F(1,410) = 8.99$, salt $F(1,410) = 33.67$, total cholesterol $F(1,194) = 8.31$, and total carotenoids intakes $F(1,179) = 12.34$, with $p<0.05$ (Table 23, Figure 16).

Table 23: Effects of recommending a target nutrient, level affiliation and high/low-intensity affilitation. p- values for the comparison of changes between two subsequent FFQ concerning recommending the variable as target nutrient, intensity affiliation, level affiliation and interactions of the three factors. TN: target nutrient, hl: high/low affiliation, Lvl: Level affiliation. Statistical analysis was performed using multifactorial ANOVA.

Target Nutrient	Lvl	hl	TN	Lvl:hl	Lvl:TN	hl:TN	Lvl:hl:TN	DF
Total fat	0.626	0.216	0.026	0.583	0.114	0.120	0.593	410
Saturated fat	0.803	0.063	<0.001	0.880	0.390	0.455	0.338	410
Monounsaturated fat	0.873	0.259	<0.001	0.676	0.656	0.300	0.329	410
Polyunsaturated fat	0.770	0.944	0.017	0.441	0.977	0.991	0.898	410
ω3 fatty acids & index	0.714	0.532	0.065	0.658	0.448	0.518	0.055	410
Carbohydrate	0.933	0.143	<0.001	0.641	0.015	0.840	0.767	410
Fiber	0.912	0.382	0.003	0.731	0.511	0.421	0.777	410
Salt	0.865	0.846	<0.001	0.607	0.452	0.454	0.975	410
Calcium	0.696	0.350	0.09	0.499	0.893	0.809	0.543	410
Folate	0.892	0.691	0.135	0.983	0.913	0.270	0.349	410
Cholesterol	0.060	0.720	0.004	0.368	0.462	0.023	0.705	194
Carotenoids	0.734	0.791	0.001	0.111	0.862	0.373	0.613	179

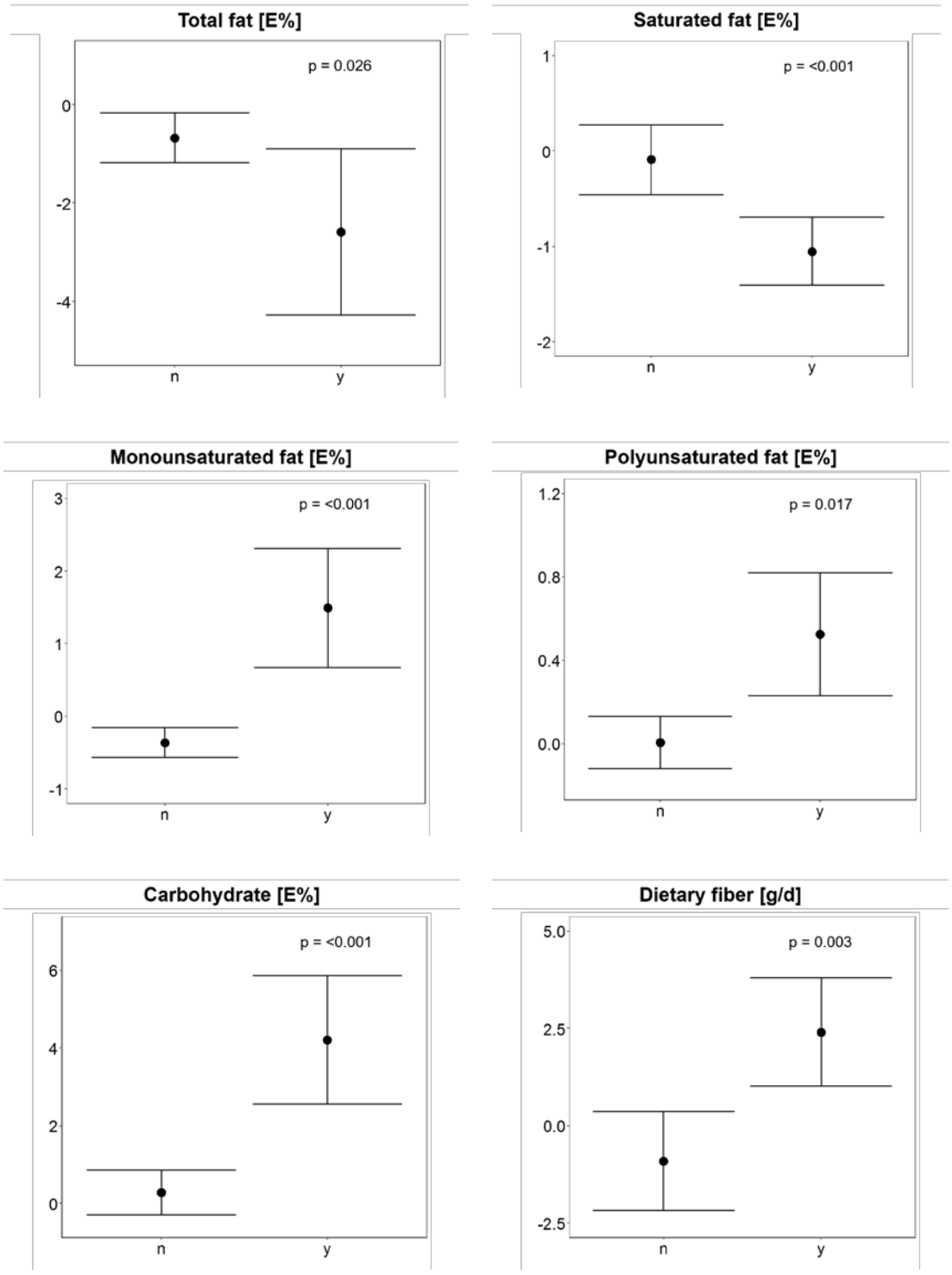

Figure 15: Effect of recommending a nutrient or biomarker as target nutrient (Part I). Comparison of differences in nutrient intake and biomarker values between two subsequent FFQ concerning recommending the variable as target nutrient, n: nutrients not recommended as target nutrient; y: nutrient recommended as target nutrient. Statistical analysis was performed using multifactorial ANOVA, mean ± SE.

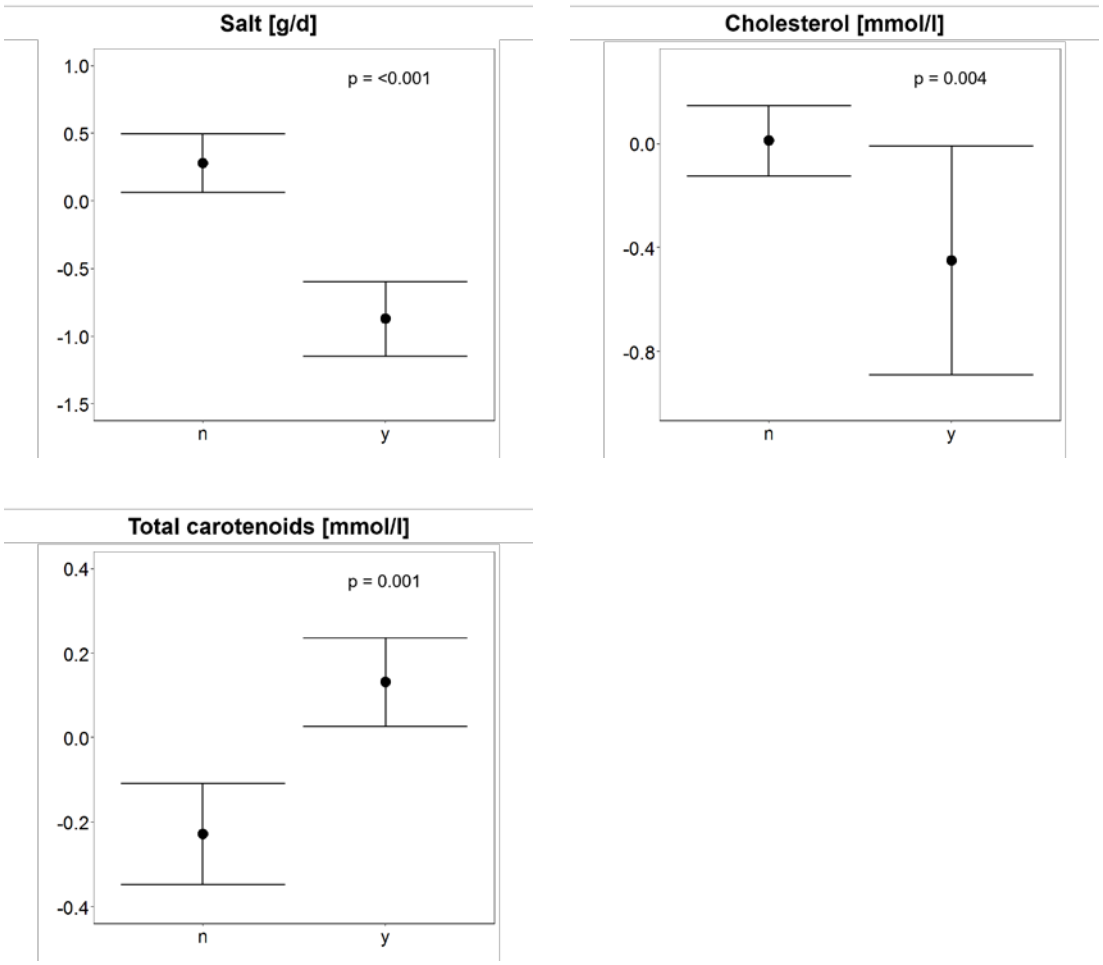

Figure 16: Effect of recommending a nutrient or biomarker as target nutrient (Part II). Comparison of differences in nutreint intake and biomarker values between two subsequent FFQ concerning recommending the variable as target nutrient, n: nutrients not recommended as target nutrient; y: nutrient recommended as target nutrient. Statistical analysis was performed using multifactorial ANOVA, mean ± SE.

There was neither a significant main effect of the level affiliation, nor of the high or low-intensity affiliation. The analysis of the interaction concerning level and target nutrient revealed significant results for carbohydrate intake $F(1,410) = 4.25$ and for the interaction of high/low intensity and target nutrient for total cholesterol $F(1,194) = 5.22$. Post hoc tests for the interactions of level and target nutrient showed that L2 participants with carbohydrate as target nutrient had a significantly greater increase with almost 10% increase in intake (Mean = 9.58 %E, SD = 5.45) compared to L1 (0.31 %E ± 5.87), L2 (0.11 ± 6.52) and L3 (0.40 ± 4.59) without this target nutrient as well as compared to L3 with this target nutrient (2.08 ± 4.79). Post hoc tests for interactions of high/low-intensity and target nutrient indicated that high-intensity participants with cholesterol as target nutrient had a significant greater reduction of their cholesterol level (-1.20 mmol/l ± 0.66) compared to high (0.09 mmol/l ± 0.94) as well as low-intensity participants (-0.02 mmol/l ± 0.91) without this target nutrient (Figure 17).

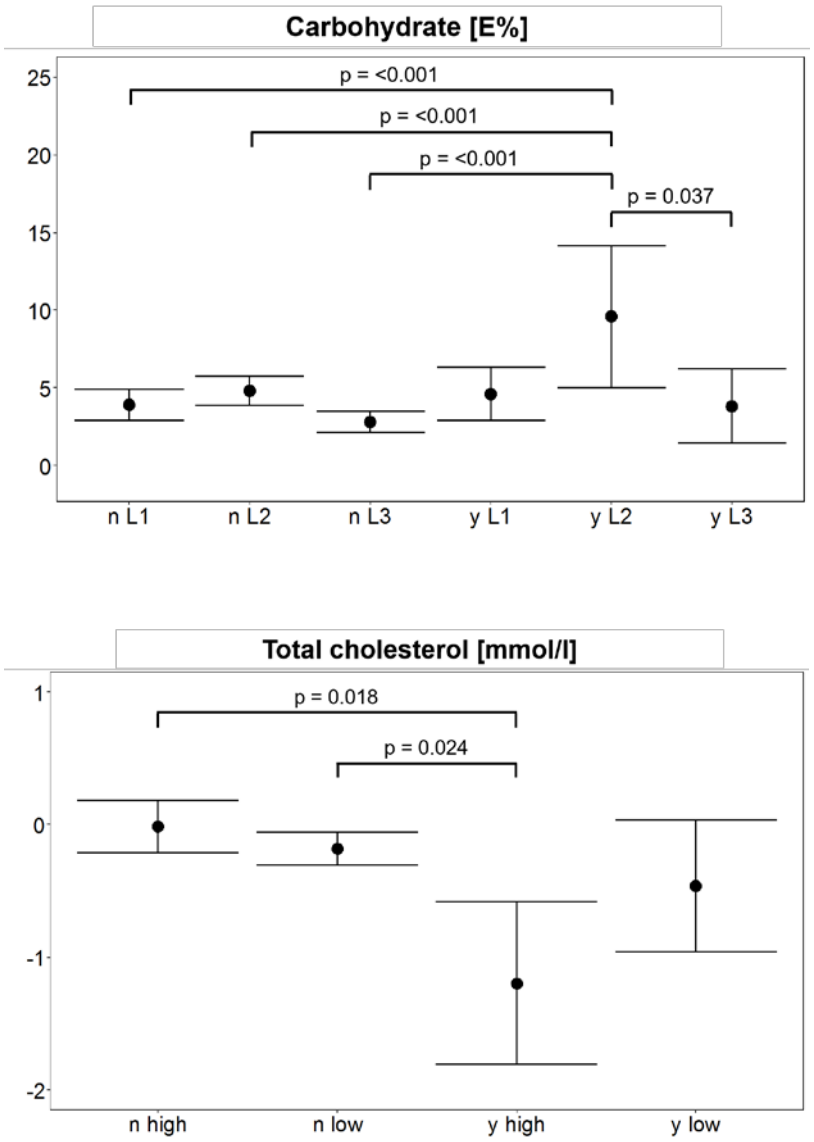

Figure 17: Interaction of recommending target nutrients and level as well as intensity affiliation. Comparison of differences between two subsequent FFQs. TN: as target nutrient recommended; n: not recommended; y: recommended; L: Level, high/low: intensity affiliation. Statistical analysis was performed using multifactorial ANOVA, mean ± SE

5. Discussion

The Food4Me Study collected dietary intake data as well as information on phenotype and genotype to test the effectiveness of personalized nutrition in an online-based system. The present thesis summarizes the approaches and findings in the German subcohort and discusses this in the context of the pan-European findings.

5.1. Baseline characteristics

The mean BMI of 24.5 kg/m² of the German Food4Me participants was slightly lower than the mean of the population based on national statistics that reports 25.9 kg/m² [57]. Around 28% of the participants were pre-obese and 8.5% obese, while in national statistics 36.7% are pre-obese and 15.7% obese [57]. As BMI is inversely associated with the social economic status [129] the study participants probably had a higher social economic status compared to the German Population. While smoking is also inversely associated with the socio economic status [138], this hypothesis was supported by the relatively low number of smokers with 8% in the German Food4Me study compared to 32.7% in the general population [119].

Concerning the physical activity levels, participants reported it in a PAQ and an accelerometer, which measured activity during the 6 months study period. According to the accelerometer findings, 25% were very and 66% moderately active, in contrast to 40% defined as very and 57% as moderately active in the self-reported PAQ. The difference between accelerometer and PAQ within the study might be due to an overestimation of the physical activity in the questionnaire or due to an underestimation of certain activities by the accelerometer. Such underestimation especially occurred during activities with a static torso, e.g. weight training and during ascending movement, which the accelerometer cannot distinguish from movements on the flat [94]. The validation of the TracmorD as used in the Food4Me Study was affirmed only in overweight and obese adults [132], as well as in pre-school children [122] and might therefore have led to data underestimating real activity. However, a national survey match quite well with the accelerometer data with around 25% of the participants defined as very active. For the 41% defined as moderately active, national survey data do not match with neither PAL nor PAI in the Food4Me Study [84]. The results on physical activity again indicate that Food4Me participants might have a healthier lifestyle at baseline than the general population. Future studies should thus not only employ accelerometers but other devices such as heart rate monitors and other multi-sensor systems [2, 30] to have an independent assessment that prevents an over- or underestimation of physical activity.

Based on the food intake data at t0, the study cohort had higher consumption of fruit and vegetables (635 g/d) than findings of the results of the German National Nutrition Survey II (NVS II) from 2015, with a mean of 218 g/d for fruits and 237 g/d of vegetables. Data of the Food4Me Study were slightly higher compared to NVS II concerning milk products (Food4Me 292, NVS II 256 g/d). Meat and Fish intake was not comparable, as the NVS distinguished neither between red and white meat nor between oily and non-oily fish [71].

Overall, German participants seemed to have a higher socio economic status and a healthier lifestyle than the mean reported for Germany. This may also depend on the recruitment procedure - which was via an advertisement in “Süddeutsche Zeitung” – with a readership that might not represents the “average German”. The characteristics of the German participants therefore do not match with the overall finding within the European Food4Me study that volunteers participating in such internet-based personalized nutrition studies generally represent the adult population [27]. Future studies should secure a more equal distribution across the educational and socioeconomic levels by incorporating also relevant questions into the screening procedure.

5.2. Drop-out rate and overall compliance

The drop-out rate in the German study section was 20% which is comparable to the estimated drop-out rate of the European Food4Me Study [27] and the mean drop-out rate across the entire Food4Me study with 21% [91].

Several of the methods and devices used in Food4Me were tested for usability and compliance. Concerning completing of measurements, low-intensity participants generally showed a higher compliance rate than high-intensity participants, with L2 low-intensity showing the highest percentage of completed measurements while time consuming additional FFQs at t1 and t2 in the high intensity group reduced compliance again. To improve the handling and accuracy of food intake data collection, future studies may introduce immediate audio recording [128, 131] or even test objective measurements such as image taking and analysis [137, 144]. The compliance for wearing the accelerometer was the lowest of all measurement and data collection approaches. This might be due to the fact that participants had to wear it every day throughout the study which might have been too demanding. Also, it was discussed that participants gave more focus on the dietary part of the study [94].

Next to dietary, anthropometric and physical activity data, blood samples for lab-based analyses were as well collected by the participants in form of DBS. This minimal-invasive method of blood sampling showed a high compliance, as 80% of all expected blood spots

were indeed sampled. Food4Me participants were collecting samples properly allowing 97% of the samples analyzed. This finding is in-line with a Norwegian study analyzing handling of DBS, where 93% out of 3,263 DBS cards could be analyzed for at least one blood marker [115]. In Food4Me glucose, carotenoids, cholesterol and polyunsaturated fatty acids were analyzed but also vitamin D [73]. However, DBS allow also other vitamins or xenobiotics to be analysed and even antibodies against viruses, e.g. Epstein-Barr, Rubella, dengue and human immunodeficiency virus [86] have been determined from DBS. This makes DBS a valuable tool for health status monitoring – even in developing countries. Collecting buccal cell samples did also not cause any problems, as every participant filling in the first FFQ also provided a DNA sample and 99% of the analysis were successful.

5.3. Values and classification approach

The effectiveness of online-based personalized nutrition advice was analyzed comparing the mean of the intervention group to the respective control group, considering nutrient intake, consumption of certain food items, blood levels of markers as well as anthropometrics and physical activity data.

In comparison to the control group (L0) participants in the intervention group (Li) reduced their intake of red meat, salt, protein and energy, and had a significantly lower %E of total, saturated and monounsaturated fat in t6 compared to t0. Additionally, %E coming from carbohydrates and the ω3 index in blood was significantly higher. As the mean of total fat, saturated fat and salt was too high compared to the Food4Me recommendations, and the mean of %E of carbohydrate and the ω3 index in blood was too low, the direction of change in most of the analyzed variables was heading towards a healthier diet. Unexpected was the reduction for monounsaturated fat within the Food4Me intervention group. As the mean at t0 was with 13.76 below the optimal range of 15 to 20 %E, an increase within Li was the expected outcome. As the macronutrients were not analyzed as absolute intake data but as % of energy, this result might be caused by the participants' general attempt to reduce fat intake and increase carbohydrate consumption; there is a significant negative relationship between the increase in carbohydrate intake and the decrease in monounsaturated fatty acid intake. It is of course especially demanding for participants to reduce saturated fat, increase unsaturated fat and at the same time to increase carbohydrate intake.

As the participants receive nutrient intake data or blood levels classified in red, amber or green, it was also analyzed, whether the participants successfully achieved a healthier classification in the course of the study. The odds for changing into a healthier color were

in favor for Li for saturated fat and carbohydrate. The result for monounsaturated fat from the values approach was reproduced in the classification approach, as the odds were in favor for the L0.

Findings of the German study group were similar to data reported from those in other countries with the effects of the intervention to cause significantly lower intake of salt and %E derived from saturated fat. However, the European Food4Me study additionally showed a significantly lower intake in red meat and significantly higher intake in folate [28]. A Dutch study with 347 participants comparing computer-generated personalized feedback to general nutritional information on fat, vegetable and fruit intake come to similar findings and conclusions as the present study. After the intervention, the mean fat score of the personalized feedback group was significantly lower than that of the control group. But there was no significant difference between intervention and control group concerning fruit and vegetable consumption [23]. A systematic review including 43 intervention studies about adaptive e-learning and its potential to improve dietary behavior also compared the intake of certain nutrients and food items between intervention and control groups [67]. But here, the main outcome showed no reduction of total fat, saturated fat and energy intake caused by the intervention. In contrast to the Food4Me study and the Dutch study, the servings of fruit and vegetables were significantly increased in the intervention group. This increase in servings though, would still not meet the recommendations [67]. Within the Food4Me study and across countries, the mean fruit and vegetable intake at baseline was already within with the recommendations.

In line with the current findings, several studies demonstrated that computer-based tailored advice on exercise was only as effective as general advice [24, 64, 124]. In Food4Me across Europe, however, an increase in physical activity reported in the PAQ but not via PAL measurements was observed [94]. For the German cohort, it has to be considered, though, that it was a relatively small sample size compared to the entire European Food4Me study cohort with more than 1,200 participants.

Overall, the results of the current study confirm that personalized advice was significantly more effective that generic advice. This generalized finding is in line with several other studies that show higher effectiveness of personalized nutrition advice over generalized advice. Concerning the application of personalized nutrition in Germany, the “12. Ernährungsbericht” of the German Nutrition Society confirms that changes as found in the Li group in the Food4Me study would, when applied to the general population, improve the overall diet quality. Intake of energy and meat consumption in Germany is generally too high, the percentage of energy derived from carbohydrates is too low compared to fat intake and within total fat, the proportion of saturated fat is too high compared

to unsaturated fat. Those would change accordingly when the Food4Me approach would be applied [125].

For analyzing the effectiveness of different levels of personalized nutrition, the intervention group was split into three levels, receiving personalized information about diet only (L1), diet and phenotypic measures (L2), and diet, phenotype and genotype information (L3). Compared to the L0, participants in L1 had a significantly greater reduction in %E derived from saturated fat and, although they did not have information on their blood levels, in the ω3 index in blood. Participants in L2 had a greater reduction in energy, %E coming from saturated and total fat, as well as in protein and salt compared to the control group. These significant differences could however not be confirmed in assessing the changes towards a healthier diet based in the color classification. However, there was a significant difference in %E from carbohydrate in L1 compared to L0 for changing into a healthier color class. Across the entire European Food4Me study cohort no significant differences between the different levels of personalization were found [28].

In the German cohort, the L2 strategy was the most promising. Participants changed in five nutrients and food items compared to the control group. Taking the overall compliance into account, L2 low-intensity was at the same time the most compliant group. These findings also argues that inclusion of additional dietary and/or phenotypic measurements might even improve compliance and outcome, but not a higher frequency of data collection and advice. What might be considered in future analysis are alcohol, processed meat and added sugars as targets for change. Especially sugar sweetened beverages are shown to be associated with weight gain, increased risks for type 2 diabetes and cardiovascular disease [93] and thus the German Society of Obesity recommends to reduce sugar sweetened beverage consumption [12]. The Food4Me feedback already considered red meat and recommended to consume less than 450g per week. Processed meat, on the other hand, was not included, though studies have shown an association of processed, but not red meat with coronary heart disease and diabetes mellitus [10, 101]. A third food-item to be considered in future studies is alcohol intake as a major risk factor for hypertension and premature mortality [82, 83].

Concerning the phenotypic measurements, numerous health parameters could be measured to fine-tune the recommendations. Particularly interesting are biomarkers that are indicating the transition from healthy to disease state and that are reversible by changing dietary intake. Blood pressure, for example, could serve as an additional parameter, as there is evidence that it might be lowered by a diet rich in fruits and vegetables and reduced in fat [3] and sodium [114]. LDL/HDL cholesterol and HbA1c, too, might be proper biomarkers for personalized nutrition, as carbohydrate restriction for example was

discussed for beneficially modifying HDL and LDL [139] and an elevated HbA1c was shown to be improved by adopting a Mediterranean diet [46].

As there are studies that suggest that inclusion of personal risks increases compliance, it was expected in Food4Me that genotypic information would increase adherence to recommendations [80]. Therefore, the L3 group was split into L3 with risk factor communication as compared to L3 without risk factor definition for each SNP. Including genetic analysis into a personalized nutrition strategy, however, does not seem to motivate participants further to follow advice, as there were controversial results. From the five SNPs analyzed, participants in L3 with risk alleles in *ApoE* showed a significantly greater reduction in saturated fat intake compared to L0. This was confirmed by the analysis of the color classification, as participants in the L3 *ApoE* risk group changed significantly more often into a healthier color regarding saturated fat intake. For monounsaturated fat however, L3 participants with risk allele reference in *TCF7L2* changed significantly less frequently into a healthier color compared to the control group. This matched with the overall finding that changes in monounsaturated fat intake is preferentially found in the control group as discussed before.

Arkadianos et al. analysed a group of 24 variants in 19 genes comparing a control group receiving standard dietary information and an intervention group with modification in diet based on genetic background. They showed a significant difference between the groups for lowering fasting glucose to less than 100mg/dl in the group receiving a “genetic-based diet”. The intervention group had also a significantly greater loss of BMI compared to the control group with a BMI gain [4]. Another randomized controlled trial revealed that participants with the risk allele in the gene encoding A*ngiotensin I Converting Enzyme* (*ACE*) and the recommendation to reduce sodium intake were more compliant than the control group receiving general advice without genetic information [105]. The lack of similar effects in the present German cohort of Food4Me might be due to low sample size, but even across all study centers no major effects of genotypic information was found [28]. Within Food4Me at the pan-European level it was also explicitly demonstrated that knowledge about the *MTHFR* risk alleles did not have an impact on folate intake [107].

It is of course not only a scientific but also an ethical issue to refer to genetic variants and risk alleles. Certain SNPs which are associated with the response to certain nutrients and thus appear suitable for personalized nutrition advice are also associated with severe diseases. SNPs in *ApoE* for example are linked to moderately increased LDL-cholesterol and increased triglyceride levels [79, 118], but also to Alzheimer’s disease [34]. The latter information can easily be found by any person using the web search engine google.de and the keyword ‘ApoE4’ (date of access 02.01.2017), as out of the first 10

hits, the connection to an elevated risk for Alzheimer's disease is mentioned six times in the title. So, although providing specific genotypic information might appear beneficial, only few SNPs-diet-interactions have been identified and in any case, unexpected behavioral and psychological effects have to be considered [59]. This uncertainty was also one of the reasons for the ethics committee in Norway to disapprove the proposal for participation in the Food4Me study.

5.4. Effect of target nutrients

The feedback reports of the Food4Me study did not only differ in amount of information, but also in specific target nutrients which where explicitly recommended to change, as well as in the frequency of feedback reports. Thus, next to the comparison of the different levels of personalization, an analysis of the impact of the latter two aspects was also performed. The three most frequently recommended target nutrients were salt, saturated fat and folate. This is again in line with the "12. Ernährungsbericht" of the German Nutrition Society, stating that the proportion of saturated versus unsaturated fat is too high and dietary folate intake is too low in the German diet [125]. Although the most frequently recommended target nutrient during this study was salt, it cannot be concluded that this was the most important nutrient for change, because of the very low optimal range. The recommendations for salt intake in Food4Me was, dependent on the age, 3.75 to 3 g/d. This maximal recommended salt intake was equivalent to the minimal recommendation of the IOM with 3 g/d.

However, participants with salt as defined target nutrient significantly reduced salt intake compared to those without reference to this target nutrient. This holds also true for %E of total and saturated fat, as well as for cholesterol levels in blood. Participants with the target nutrients of mono- and polyunsaturated fatty acids, carbohydrate, dietary fiber and carotenoids on the other hand were able to significantly increase their intake and blood level, respectively. In every case, the direction of change for these nutrients was as anticipated from the given advice and thus successful in changing the eating behavior towards a healthier diet.

Whether participants were in the high or low intensity group was only of relevance for the cholesterol level in blood. Here, only participants in the high-intensity group had a significantly stronger reduction in cholesterol level compared to high and low without target nutrient. As a summary, recommendations on specific target nutrients are an effective tool to cause a behavior change towards a more healthy diet.

The target nutrients were mainly identified based on food intake data. The underlying food composition database for the food items covered by the FFQ was therefore most critical for the identification of the relevant nutrients for change. Within Food4Me, the nutritional composition data calculation was based on Irish and UK databases [53], although the Bundeslebensmittelschlüssel (BLS) would be more appropriate for German cohorts [25]. There are, however, attempts being made to validate and harmonize food composition databases across European countries to overcome differences of country-specific food compositions in international studies, e.g. by the EuroFIR project. This project aimed at developing a standard for sampling procedures, analytical methods and calculation procedures, data sources and quality criteria for food composition [9].

5.5. Strengths and limitations of the approaches

Conceptually Food4Me included two main innovative aspects. It was the first study that developed and tested a personalized nutrition service based on dietary intake assessment as well as by including phenotypic and genotypic information. Data and sample collection was carried out exclusively home-based by the participants themselves, without the need for a medical expert or a visit at the study center. Several health related markers such as BMI, blood ω3 index, cholesterol and glucose levels were thus remotely determined. At the beginning of the study, standard operating procedures and protocols were defined across all study centers. The reliability of internet-based, self-reported anthropometric and demographic data were tested in subsets of participants across the European cohort [29]. However, home-based data and sample collection are always prone to underreporting and collecting erroneous samples and data [59]. A data cleaning exercise was thus included to detect and delete unfeasible and erroneous values. Only three amendments were made. As food intake intrinsically varies substantially and anthropometric measurements are prone to underreporting, future studies might improve data quality by introducing certain checks and boundaries for weight, height, waist and hip measurements when assessing those online. To further improve the food intake assessment, a warning should show up when implausibly high or low values are entered.

As a unique approach and as a test of feasibility, a modeling approach was employed to assess whether food intake data combined with selected genotypic information can predict measured markers in blood correctly. This was possible on basis of the data collected in Food4Me. The prediction modeling was performed for concentrations of DGLA, AA, EPA, DHA, and DPA in capillary whole blood from the DBS cards across the European Food4Me cohort (n = 1,607). Models were created and tested based on selected food items and the rs174546 genotypes in *FADS1* with confounders such as physical

activity, gender, age, BMI, and smoking. Food items from records were selected using multiple hypothesis testing and bootstrapped LASSO. Among others, fish, pizza, chicken, and cereals were found as especially tightly associated with the PUFA levels in blood. For model development, the data of t0 was used and their predictive power was tested using t6 data. Based on these approaches 26 to 43% of the variability in the PUFA DBS concentrations was explained for the t0 data set and 22 to 33% variation was explained in the t6 data set [66].

A major limitation within the Food4Me project was the manual generation of the individual feedback given to the participants. A major improvement – in particular for upscaling into even larger cohorts - would be the automation of the feed-back based on the classification of nutrient intake into the traffic light system, as well as the filtering of target nutrient information via decision trees. Another limitation in the present study cohort was that it did not match the German general population in a variety of parameters. This was probably due to the unintentional recruitment of participants with higher education which this addresses the recruitment strategies. Although the Food4Me study included dietary, phenotypic and genetic data, the nutritional needs were and could not be determined for every participant. Recommendations given were solely based on dietary reference values of the IOM. Such values were estimated from population-based studies, considering age and gender distribution [48]. A next step into personalization is therefore to determine the nutritional need of individuals, including persons suffering from chronic diseases. In the project as carried out only nutrient-based recommendations with some minor references to individual food items were provided. It is, however, suggested to focus on food- and dietary pattern-based recommendations rather than on specific nutrients, as they are easier to realize and the food matrix also in known to influence the metabolic response [78, 102, 131]. Additionally, the present study neither involved personal likes and dislikes, allergies or intolerances, nor did it consider any diseases or family history of diseases. Food4Me generally provided qualitative suggestions for improvement, which might be challenged, especially concerning the optimal balance of carbohydrate, mono-, polyunsaturated and saturated fat intakes. Future concepts might include not only such qualitative recommendations but even propose recipes considering food preferences and an optimal combination of nutrients.

Development of a Meal Planning Tool

6. Material and Methods

6.1. Design

The meal planning tool (MPT) was based on Food4Me results of a qualitative study aiming at understanding the consumers perceptions and desires in personalized nutrition. In 16 focus groups, consumers discussed different offers and concepts for personalized nutrition services. As an outcome, it was defined that personalized nutrition should have a focus on life style changes in contrast to a sheer weight loss program. To achieve this, advice on exercise, shopping lists as well as tailoring the advice to the consumers' needs and preferences were seen as very valuable features [11].

In the MPT, output was defined as a meal plan for one week that comprised the recipes for breakfasts, main meals and light meals as well as at least seven recipes for snacks. The recipes were combined to meet the users' estimated nutrient and energy requirements over one week when one portion of each recipe was consumed. The estimations were based on nutrient intake gradations used in the Food4Me Study. Furthermore, five servings of fruit and vegetables per day were included. Simultaneously, the user's preferences were taken into account to increase compliance and enable easier the behavioral changes in the user's everyday life. Food preferences reflected the individual´s likes or dislikes of foods due to taste, religious or personal ethical concerns as well as physiological reasons like intolerances or allergies.

The MPT provided the optimal recipe combination in two versions. The first version listed the recipes according to meals. The second distributed the recipes equally to the days of the week, ensuring that one breakfast, one main meal, one light meal and at least one snack was offered every day. The tool was developed based on linear programming with constraints for fruit and vegetable portions, as well as nutrient and energy intakes to meet the individually defined target range for the user and an optimization concerning personal preferences.

6.2. Input data

The MPT required a recipe database, the users' food preferences and the estimation of the users' nutrient and energy requirements.

6.2.1. Recipe database

The recipe database used included recipes collected by Food4Me researchers within the "Recipe4Me" database. Additional recipes were compiled using the BLS as a German food composition database [2]. The recipe database contained in total 3869 recipes. Each recipe provides information on nutrient and energy content, a standard portion size and a classification to a certain meal type. The considered nutrients and food constituents are carbohydrate, protein, total fat, saturated fat, mono- and polyunsaturated fat, ω3 fatty acids, salt, fiber, retinol, thiamin, riboflavin, folate, cobalamin, ascorbic acid, calcium, iron, and energy. The number of fruit and vegetable portions was listed per recipe. Additionally, each recipe was categorized to a meal type as breakfast, main meal, light meal, or snack. Snacks involve side dishes like salads, fruits, and sweets. As the MPT was developed using also the BLS and was tested with German participants, the categorizing needed to fulfil also German culinary and customs such as no fish as a breakfast meal [52].

6.2.2. Individual preferences

Dietary preferences of the users were determined by means of a preference questionnaire (Figure 18). In the first part of the questionnaire, users have to choose food items or ingredients, which must be excluded from meals, because of intolerances, allergies or for other (religious) reasons. This included nuts, peanuts, soy, gluten, cow milk, lactose, shellfish, fish, egg, pork, beef, animal products and alcohol. The ingredients and food items listed in the second part of the questionnaire mainly focused on certain eating behaviors and should, but not explicitly had to be ex- or included. Users could tick the boxes to exclude dairy, high fat dairy, added sugar, oily fish, red meat or gluten. They were also able to include recipes with low total fat, low saturated fat, low salt content or recipes as a source of high fiber, as well as only vegetarian or vegan recipes. Vegetarian was defined as ovo-lacto-vegetarian. Vegan did not include any animal product. In the last section of the preference questionnaire, users stated most and least favorite dishes or food items, such as "Spaghetti bolognese" or "Asparagus". If a vegetarian user also ate fish, any kind of fish dish or just "fish" could be stated in the text fields for favorite dishes and was then included into the meal plan as acceptable item. As optional user choice, favorite dishes could be included up to seven times per week.

6.2.3. Individual nutrient and energy requirements

The users' individual nutrient requirements could only be estimated based on age, gender, BMI and Estimated Energy Requirement (EER). Taking these estimations into account, the target ranges of nutrients to be met within the users' meal plan were calculated based on the Food4Me optimal intake (Table 3). For the calculation see 6.3.2.1.

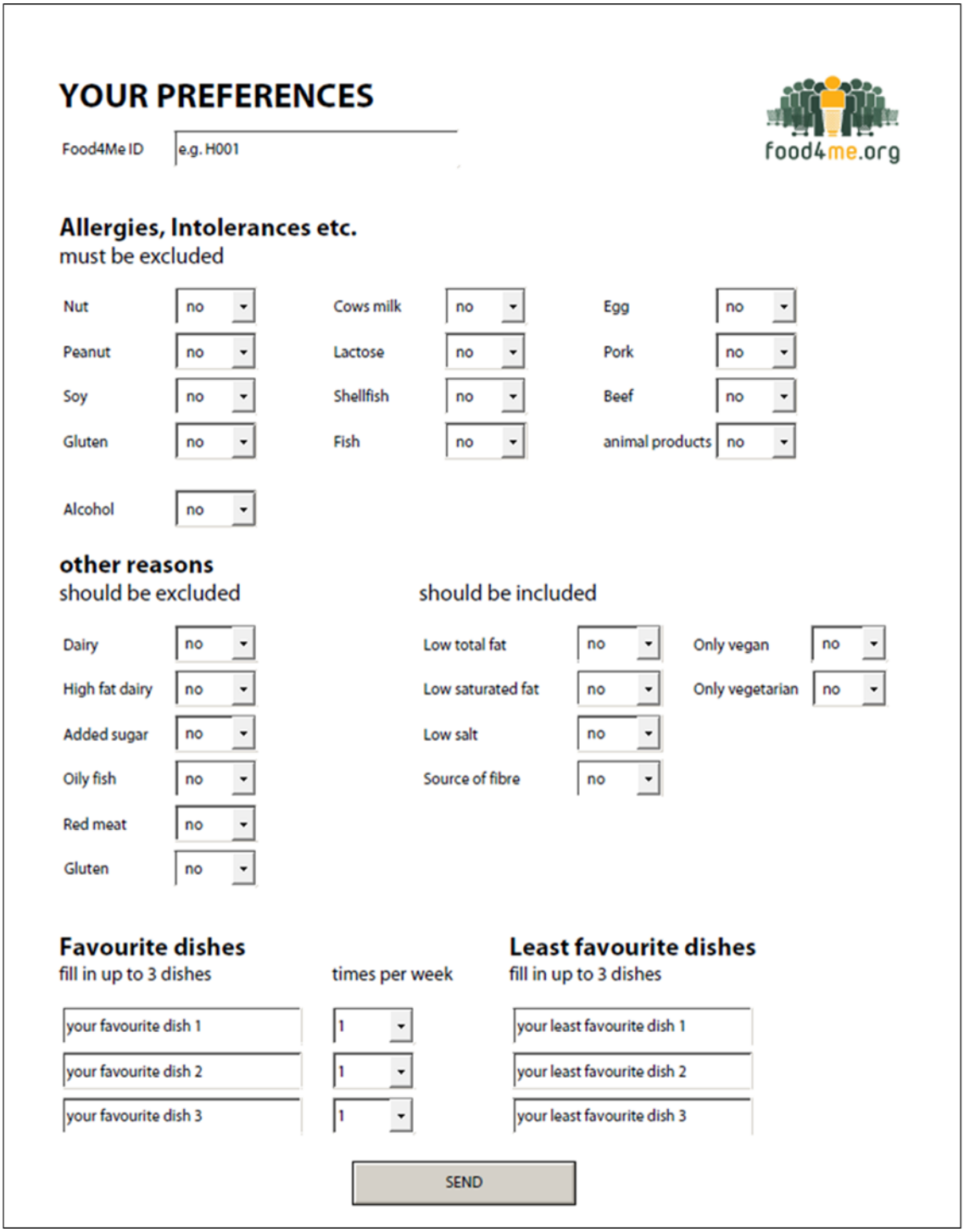

Figure 18: Preference Questionnaire

6.3. Mathematical model

The mathematical model used is an integer linear minimization, consisting of a linear objective function and linear constraints.

6.3.1. Objective function

The objective function was defined as a linear equation to be minimized containing all recipes from the recipe database as variables. The solution vector x, $x \in \mathbb{N}_m$, $m =$ number of recipes within the recipe data base, was derived as the minimum of the following equation:

$$f(x) = \sum_{i=1}^{m} \mathrm{p_i} x_\mathrm{i}$$

with $\mathrm{p_i}$ being the preference for recipe $\mathrm{i}, \mathrm{i} = 1, \ldots, \mathrm{m}$.

The objective function of the MPT required the preference vector p as well as the solution vector x. The preference vector p was the numerical classification of each recipe according to the users' preferences. It could take values of 1, 100 or 1000. As the MPT was a minimization, the lower the preference value, the higher the probability that the recipe was taken into account for the solution of the problem. These values were determined empirically.

For programming the numerical classification, a preference data frame was generated, with the recipe names as rows and the food items of the preference questionnaire as columns. If a recipe contained a respective food item, the cell states "TRUE", otherwise "FALSE"; e.g. every recipe containing nuts was set to "TRUE" within the column "Nuts" (Table 24, first recipe).

Subsequently, the different data of the users' preference questionnaire were used to generate a preference value for each recipe. The default preference value for all recipes was 100 (Table 24, second recipe). If a food item from the questionnaire was set as "must be excluded", all the recipes with "TRUE" for this item were deleted from the data-frame. If e.g. "Nuts" must be excluded, the recipe was deleted (Table 24, first recipe). It was assumed that users who are not gluten sensitive would not choose products that explicitly state "gluten free". Therefore, users not confirming "Gluten must be excluded" did not receive any recipes that explicitly stated "gluten free" in the recipe name; those recipes were also deleted from the data frame. In this case, "Pasta gluten free with pesto"

was deleted (Table 24, third recipe). The same applied for “Lactose” or “Dairy” and “lactose free” as well as for “Low in Fat” and the declaration “0 % fat”.

If users ticked items from the questionnaire which should be excluded, the preference value of those recipes with “TRUE” for this item were set to 10 times higher as the default value, i.e. 1000. This reduced the probability to be taken into account for the minimization. Vice versa, if items at the section “should be included” were ticked, all recipes stating “FALSE” for these items were also set to 1000. If e.g. dairy should be excluded, the preference for “Bread with margarine and cheese” was set to 1000 (Table 24, fourth recipe).

Least favorite dishes were deleted, the preference values of the favorite dishes were set to 1 (Table 24, fifth recipe). If there was more than one recipe containing the favorite foods, as many recipes as stated in the associated “times per week” were randomly chosen and set to 1.

If users filled in conflicting statements within the questionnaire, items that must be excluded had a higher priority than favorite and least favorite dishes, which again had a higher priority than items that should be ex- or included. An example for conflicting statements would be as follows. If users would like to reduce their dairy intake, they ticked “dairy” as “should be excluded” and the preference value of the recipe “Cereals with milk, strawberries and nuts” was set to 1000, as it contains dairy. If users were simultaneously allergic to nuts, they ticked “nuts” as “must be excluded” and the recipe was deleted from the data frame, as “must be” has a higher priority than “should be”. If additionally “strawberries” was stated as favorite dish, the recipe “Cereals with milk, strawberries and nuts”, was still not taken into account as recipe, as “must be” had a higher priority than favorite food items. If nuts would not have been ticked as “must be excluded”, preference value of the recipe would be changed from 1000 to 1, as favorite food items had a higher priority than “should be”.

Table 24: Excerpt from the preference data frame with 5 exemplary recipes. Columns: preference items from the preference questionnaire. P: Preference values, if P=delete: recipe deleted from the data frame. The recipes are checked for each preference item, stating “TRUE” if they contain the preference item and “FALSE” otherwise. Assumptions for this example: must be excluded: Nuts should be excluded: Dairy, Favorite dish: “Spaghetti bolognese”.

Recipe name	Dairy	Gluten	Peanut	Nuts	Fish	Fiber	P
Cereals with milk, strawberries, nuts	TRUE	TRUE	FALSE	TRUE	FALSE	TRUE	delete
Bean stew with beef	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	100
Pasta gluten free with pesto	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	delete
Bread with margarine and cheese	TRUE	TRUE	FALSE	FALSE	FALSE	TRUE	1000
Spaghetti bolognese	FALSE	FALSE	FALSE	FALSE	TRUE	FALSE	1

The result of the MPT’s linear minimization process were portions of recipes, stated in the solution vector x. Each recipe could occur either not at all or once per week. Therefore, only integer solutions of 0 or 1 were accepted. This way, unrealistic numbers of portions like 0.2 portions of Spaghetti bolognese were avoided. The only exception was, if an explicit number was stated in the food preference questionnaire for a favorite recipe or food item; in this case, $x_i \in \{0, 1, \ldots, 7\}$.

6.3.2. Linear constraints

Constraints were given in form of linear equations or inequalities. These were based on the matrix (n_{ji}), with $n \in \mathbb{R}^{q \times m}$, $q =$ number of considered nutrients, $m =$ number of recipes, with n_{ji} being the content of nutrient j in recipe i. For each considered nutrient, the sum of the product of this matrix and the solution vector x was on the left hand side of the inequality. The mathematical operator was named constraint type and the constraining value Right Hand Side coefficient (RHS). The RHS were defined as the users’ estimated nutrient and energy requirements.

$$\sum_{i=1}^{m} n_{ji} x_i \ \leq \wedge \geq \wedge = \ \mathrm{RHS}$$

Further constraints were the number of each meal type snacks, breakfast, light meal and main meal as well as of certain food items like fruit and vegetables. While the frequency of the meal types was fixed, the nutrient and energy requirements were estimated for each participant individually. The intake of nutrients and energy was estimated as a target range and not given as a concrete value. Consequently, for each nutrient, two RHS values were defined as the minimum and the maximum threshold of this target range. This implicated that the respective constraint types were greater than or equal to the minimum threshold and lower than or equal to for the maximum threshold.

6.3.2.1. Estimated nutrient requirements

To obtain the target ranges for each of the 17 considered nutrients, the current intake of the nutrients was calculated from the users' FFQ data and classified in a traffic light system as red, amber or green as used in the Food4Me study (Table 3).

The target range always included the next healthier class. If the current nutrient intake of the users was in the amber classification, the target range was the green class. If the intake was too low and therefore in the red classification, the target range was a combination of the amber too low plus green classification. The amber classification was also into account, as the users behavior change might be less radical and therefore easier to realize. Vice versa, if it the intake was too high and therefore also in the red classification, the target range is the amber too high plus green classification.

It was decided in Food4Me to select three to four target nutrients as the most important items to be changed by the participant. Those were explicitly addressed in the recommendations. To emphasize their importance within the MPT, their intake was always set to be within the green classification.

The calculations of the target range of each nutrient were programmed in three consecutive steps. (1) Import of age and gender of the user to define the classifications and their thresholds. (2) Combination of the thresholds to pairs i.e. the user specific thresholds of the ranges low red, low amber, green, high amber and high red. The main output was the threshold within which the current nutrient intake of the user was found. (3) Definition of the target ranges.

To illustrate these three consecutive steps, data of participant H014 from the Food4Me study are used exemplarily and the calculations of the target ranges of saturated and total fat, dietary fiber and protein are chosen as examples (Figure 19). Participant H014 was a 47 year old woman (1). The function *built.sub* returned intake thresholds matching a 47 years old female. (2) Based on her FFQ, a saturated fat intake of 24.1 E% and a total fat intake of 49,6 E% intake was calculated. For saturated and total fat, the calculation function *built.Lvl* returned the red classification with 15 to 100 E% and 40 to 100 E%, respectively. As the dietary fiber intake was 17.2 g/d, *built.Lvl* returned the amber classification with 15 to 25 g/d, and for protein with 0.9 the green classification with 0.66 to 2.4 g/kg bodyweight/d. (3) As the participant's intake for dietary fiber was classified as amber and for protein green, the defined MPT thresholds calculated by the function *built.reclvl* were in both cases those of the green classification 25 and 1000 g/d dietary fiber and 0.66 and 2.4 g/kg body weight protein/d. In the case of total fat, the intake of

participant H014 was in the red class, therefore MPT used the amber and green classification as target range, i.e. 20 E% as minimum and 40 E% as maximum thresholds. Saturated fat was one of the priority nutrients of participant H014, therefore, the MPT provided recipes with 0 to 10 E% intake from saturated fat, i.e. with the green classification.

Macronutrient intake as %E and g/kg bodyweight were recalculated into absolute amounts as g/d which again were then added up to g/week.

```
Saturated fat [% Energy]

> built.sub ("SATFAT1")
NA NA 0 10 15 100
> built.Lvl ("SATFAT1")
[15,100)
Levels:[0,10)[10,15)[15,100)
> built.reclvl ("SATFAT1")
0 10

Total fat [% Energy]

> built.sub ("TOTALFAT1")
0 15 20 35 40 100
> built.Lvl ("TOTALFAT1")
[40,100)
Levels: [0,15) [15,20) [20,35) [35,40) [40,100)
> built.reclvl ("TOTALFAT1")
20 40

Dietary fibre [g]

> built.sub ("DF")
0 15 25 1000 NA NA
> built.Lvl ("DF")
[15,25)
Levels: [0,15) [15,25) [25,Inf)
> built.reclvl ("DF")
15 Inf

Protein [g/kg bodyweight]

> built.sub ("PROTEIN")
0.00 0.52 0.66 2.40 NA 100.00
> built.Lvl ("PROTEIN")
[0.66,2.4)
Levels: [0,0.52) [0.52,0.66)[0.66,2.4) [2.4,Inf)
> built.reclvl ("PROTEIN")
0.66 2.40
```

Figure 19: Example for the output of the commands built.sub, built.Lvl and built.reclvl for H014 female, aged 47 years, for total fat, saturated fat (priority nutrient), dietary fibre and protein. Output of commands in blue. built.sub output: 6 matching thresholds for each nutrient dependent on age and gender. built.Lvl output: thresholds of the range within which the user's current nutrient intake lies, Levels: user specific thresholds of the ranges, built.reclvl output: menu planning tool RHS minimum and maximum thresholds, NA: range thresholds not defined, Inf: infinity.

6.3.2.2. Estimated energy requirements

Next to nutrient intake, the MPT implemented restrictions for the total energy intake per week. The optimal energy intake for a user was calculated dependent on the BMI and EER of the user. Underweight users with a BMI of less than 18.5 kg/m² should gain weight, therefore, the constant c_d = 500 kcal/day was added to their EER to meet their optimal energy intake per day. Pre-obese and obese users with a BMI greater than or equal to 25 kg/m² should lose weight, therefore the constant c_d was subtracted from their EER [12]. The energy intake was multiplied by d_w = 7 to obtain the energy intake per week. It was decided that constant c_w = 1000 kcal per week above or below the optimal intake was still an acceptable range. This way, overweight users could lose weight and underweight users could gain weight. The RHS for energy intake were calculated as follows

Underweight	$\mathbf{RHS_{min} = (EER + c_d)d_w - c_w}$ $\mathbf{RHS_{max} = (EER + c_d)d_w + c_w}$
Normal weight	$RHS_{min} = EER\ d_w - c_w$ $RHS_{max} = EER\ d_w + c_w$
Pre-obese and obese	$RHS_{min} = (EER - c_d)d_w - c_w$ $RHS_{max} = (EER - c_d)d_w + c_w$

As an example, participant H014 had a BMI of 28.4 kg/m² (pre-obese) and an EER of 2126 kcal/d. The lower RHS was calculated as 1483 kcal/day and the upper as 1769 kcal/d.

6.3.2.3. Meal types and food items

The MPT also defined restrictions for the number of certain types of meals and food items to reach an equal distribution over the day and week, respectively. The recipes were categorized into meal types according to their suitability to be served as breakfast, e.g. cereals or toast with jams, as light meal, e.g. soups or salads, or as main meal, e.g. meat with side dishes. All of those were listed with seven portions per week. The category snacks was listed with at least seven portions per week. As fruit and vegetable consumption was one of the most important dietary factor [15], the minimum intake is defined to include at least 35 portions per week i.e. a mean of five portions per day. This restriction was also inserted into the MPT as RHS.

6.3.3. System of constraints

The system of constraints comprised all the constraints (see 6.3.2) with constraint types, and the vector RHS, i.e. the minimum and maximum thresholds of the 17 nutrients, the minimum and maximum threshold of energy intake and the restrictions to the number of certain meal types.

In the example H014, the system was created as follows (Table 25). The saturated fat content of recipe 1 was multiplied with the unknown number of portions of recipe 1, the saturated fat content of recipe 2 was multiplied with the unknown number portion of recipe 2, and likewise for all recipes. These products were summed up. The solution vector *x* was then calculated in a way that this sum was to be lower than the maximum threshold (RHS) of 126 g/week. The next part was created likewise, but the sum of the products was to be greater than the minimum threshold of 0 g/week. This was repeated for all nutrients and the energy intake. The constraints concerning the number of certain meal types were developed likewise.

Assuming that recipe 1 was assigned to “Breakfast”, 1 was multiplied to the unknown number of portions of recipe 1. Assuming that recipe 2 was not assigned to “Breakfast”, 0 is multiplied to the unknown number of portions of recipe 1. These products are again summed up and the unknown number of portions was calculated in a way that this sum is to be equal to 7.

Table 25: Excerpt of the system of constraints H014. T: Term of constraints: $\sum_{i=1}^{m} \boldsymbol{n_{ji} x_i}$ with n_{ji}: content of nutrient j in recipe i, x_i: number of portions of recipe i, m: number of recipes within recipe database. *: Constraints unnecessary, but listed for the sake of completeness

J	**Constraints**	
Saturated fat [g/week]	$T \geq 0$ *	$T \leq 126$
Total fat [g/week]	$T \geq 253$	$T \leq 506$
Fiber [g/week]	$T \geq 105$	$T \leq \infty$ *
Energy intake [kcal/week]	$T \geq 10{,}381$	$T \leq 12{,}376$
Number of breakfasts	$T = 7$	
Number of light meals	$T = 7$	
Number of main meals	$T = 7$	
Number of snacks	$T = 7$	
Number of fruit and vegetables	$T = 35$	

The system of constraints was solved by calculating x with a minimal solution for the preferences meeting all constraints. The MPT provided two versions of a personalized meal plan, as list (Figure 20) and as a structured week plan (Figure **21**).

Breakfast

- Cereals with milk and banana
- Porridge oats with yoghurt, banana and flaxseeds
- Porridge oats with yoghurt and banana
- Porridge oats with low-fat yoghurt and banana
- Cereals with yoghurt banana
- Cereals with milk, and apples
- Porridge with yoghurt and apples

Light meal

- Fennel soup
- Pumpkin soup with cider
- Artichoke soup
- Fried porcini with tomatoes
- Avocado soup
- Salad with chicken
- Beetroot with apples and lemon dressing

Main meal

- Pizza with mozzarella and tomatoes
- Rice pudding with fruits
- Chickpea strew with vegetables
- Eel with tomatoes
- Rice pudding with dried fruits
- Pasta with tomato-anchovy-souce
- Pizza quattro stagioni

Salads, fruits and desserts

- Endive with oil dressing
- Salad with sweet-sour-dressing
- Chichoree salad with lemon dressing
- Endive with yoghurt dressing
- Raw vegetables

- Sweet cottage cheese with pineapple
- Sweet cottage cheese with apples
- Sweet cottage cheese with banana and raspberry topping
- Cherry desert
- Milksoup with pears
- Milksoup with fruits
- Macaroon cake
- Poppy seed and apple cake
- Apples with caramel topping
- Baked apple dumpling

Figure 20: Example of a meal plan as list

Monday	Tuesday	Wednesday	Thursday
Cereals with milk and banana	Porridge oats with yoghurt and banana	Porridge with yoghurt and apples	Cereals with yoghurt banana
Rice pudding with dried fruits	Pumpkin soup with cider	Rice pudding with fruits	Fried porcini with tomatoes
Pizza quattro stagioni	Pasta with tomato-anchovy-souce	Artichoke soup	Eel with tomatoes
Chichory salad with lemon dressing	Endive with yoghurt dressing	Milk soup with pears	Endive with oil dressing
Cherry desert	Sweet cottage cheese with pineapple		Sweet cottage cheese with apples

Friday	Saturday	Sunday
Porridge oats with low-fat yoghurt and banana	Cereals with milk, and apples	Porridge oats with yoghurt, banana and flaxseeds
Avocado soup	Salad with chicken	Beetroot with apples and lemon dressing
Apples with caramel topping	Poppy seed and apple cake	Macaroon cake
Chickpea strew with vegetables	Fennel soup	Pizza with mozzarella and tomatoes
Salad with sweet-sour-dressing	Baked apple dumpling	Raw vegetables
Milk soup with fruits		Sweet cottage cheese with banana and raspberry topping

Figure 21: Example of a meal plan as a structured week plan

7. Results from qualitative interviews

Four qualitative interviews were conducted with former participants of the Food4Me Study. The participants were asked to give their opinion on the concept and structure of such menu plans and also on their personalized meal plans provided as a list and as week plan. These plans were generated using the data the participant provided during the Food4Me study and the data from the preference questionnaire, they were asked to fill in. The overall concept was considered to be realizable for people having time for cooking and time to eat regularly as well as people living in a single household. Problems were detected for employees without timed lunch breaks and regular ends of the working day as well as canteen visitors. If the meals were purchasable as single portions and ready to eat, more people might be able to realize such plans. The plans were also considered to be hard to realize for families.

In comparison to the Food4Me recommendations, the interviewees mentioned several advantages and disadvantages. Following a detailed plan was rated as advantageous as an easy-to-use concept, which additionally does not need critical thinking about healthy cooking. The meal plan was appreciated as particularly useful for persons with several and/or severe dietary restrictions. Also, it might bring more variety into a person's diet, if she or he usually sticks to only a few recipes to be prepared. But the rigorous restriction to such menu plan was also seen as disadvantageous, as it limits the freedom of choice and does not leave room for spontaneous shopping or regional choice. Thus, the idea evolved, whether wild-cards should be used within the plan. Such wild-cards would replace a defined recipe with the nutrient values of an average meal. Users could replace the wild-card with a recipe of her or his own choice. This idea got positive feedback and it was recommended to be integrated into the plan. However, the wild-cards were also assessed as too abstract.

After discussing the general concept, the interviewees were also asked to evaluate their personal meal plans. All of them rated their main meals as very tasty and easy to realize, except for one participant who stated that some rare ingredients as mutton is hard to find in a small town. There was less satisfaction with the snacks and light meals, because of different eating behaviors, e.g. one interviewee mainly had raw fruits as snack, another only bread and coffee, a third a general dislike of cakes. Comparing the list to the week plan, the list appeared to be more suitable as there is still some freedom of choice granted. A week plan, however, might be easier to follow.

8. Discussion

The MPT was programmed to combine recipes to a menu plan, considering the estimated nutrient requirements and the certain meal types optimizing on preferences and is based on data collected in the Food4Me Study.

Early attempts on menu planning by the use of linear programming emphasized that palatability is crucial for the acceptance of the plans. The MPT considered aspects discussed by Smith and Balintfy on palatability [6, 123], using recipes instead of food items and classifying the recipes to certain meal types. Although the MPT did not consider costs, it was optimized on preferences.

During the qualitative interviews, several aspects were proposed to improve the MPT such as the time needed for cooking. This aspect would be a further constraint and could easily be incorporated into the MPT, as long as the corresponding data is available for each recipe. Also, the unavailability of certain food items in the region was mentioned but that may easily be overcome by e-commerce applications. The aspect of canteen food which cannot be added to the current version of the MPT but if canteens would provide their recipes (for a week for example), they could also be added to the recipe data base and listed on the meal plans.

As the MPT was considered to be suitable mainly for single households and not for families, one add-on might be the option for adding data of several members of a family. The system should be able to list e.g. main meals on household bases including all preferences of the family members. However, with the inclusion of further constraints, complexity of the optimization increases. Therefore, it is crucial to also increase the number and variety of recipes to still find a solution. One possibility of the enlargement of the recipe database is to include user generated recipes, like on various web-based recipe portals, e.g. chefkoch.de.

The MPT was created as a showcase and shall be taken now into a real setting to collect experience and improve the tool in an iterative manner.

9. Conclusion and outlook

The data collected in the German cohort within the framework of Food4Me demonstrates that personalized nutrition is a successful strategy to achieve behavior change towards a healthier diet. The methods of home-based data and sample collection, i.e. FFQ, anthropometrics with tape and scale, accelerometer, DBS and buccal swabs were easy to use and shown to be handled by the participants. Personalized recommendations were more effective in causing a dietary behavioral change than generic recommendations. Personalized advice not only on diet but also on blood levels including specific target nutrients seems to be the most promising strategy for sustained changes towards a healthier diet. Although genetic testing may be included, it is not required and may be balanced when used for ethical disadvantages for the participants. Additionally to an individual feedback on diet and phenotype, personalization can be extended to include food preferences, diseases and the family history of diseases. The delivery of individual feedback can be personalized not only by reference to food items but also by providing recipes or meal plans. A learning was that participants should not be overloaded with data collection tasks as this reduces the compliance.

The Food4Me expert-generated personalized nutrition recommendations are the basis for a subsequent project in the Enable cluster at TUM within which an interdisciplinary team of nutritionists and information scientists explore automated algorithmic recommender approaches for personalized nutrition [93]. The main objective is to analyze the effect of personalized algorithmic food and recipe recommendations based on food preferences, dietary and phenotypic data. The recommendations will be developed using expert knowledge but also implementing crowd-sourced user-knowledge.

The Program of Accompanying Research for Agricultural Innovation is a second currently ongoing interdisciplinary project involving nutritionist, agriculture economists and information scientists applying some of the Food4Me techniques in rural West- and East Africa. The overall aim is to analyze the nutritional status and test the effects of automated expert knowledge on nutritional behavior and nutrient-sensitive agriculture.

10. Ethics and funding

All procedures were in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards; trial registration NCT01530139.

This project received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration; contract nº 265494.

11. List of abbreviations

AA	Arachidonic acid
ACE	Angiotensin I converting enzyme
ApoE	Apolipoprotein E
BLS	Bundeslebensmittelschlüssel
BMI	Body Mass Index
CD	Critical difference
CI	Confidence interval
DNA	Desoxyribonucleic acid
DBS	Dried blood spot
DGLA	Dihomo-γ-linoleic acid
DHA	Docosahexaenoate acid
DPA	Docosapentaenoate acid
%E	Energy percentage
EER	Estimated Energy Requirement
EPA	Eicosapentaenoic acid
ETA	Eicosatetraenoic acid
f	Female
FADS1	Fatty Acid Desaturase 1
FFQ	Food frequency questionnaires
Food4Me Study	German Food4Me proof of principle study
FTO	Fat Mass And Obesity-Associated Gene
HSD	Tukey’s Honestly Significant Difference
L*h	Level* high intensity
L*l	Level low intensity
L*n	Level* without risk factor within a certain SNP
L*r	Level* with risk factor within a certain SNP
L0	Control group Level 0
L1	Level 1
L2	Level 2
L3	Level 3
Li	Intervention group (Level 1+2+3)
m	Male
MPT	Meal planning tool
MTHFR	Methylene Tetrahydrofolate Reductase
NCD	Non-communicable chronic diseases
NVS	Nationale Verzehrsstudie II

OD	Observed difference
PAI	Physical Activity Index
PAL	physical activity level
PAQ	Baecke questionnaire
PUFA	Polyunsaturated fatty acid
RHS	Right Hand Side coefficient
SD	Standard deviation
SNP	Single nucleotide polymorphisms
t0	Study start, timepoint 0
t1	1 month after study start, timepoint 1
t2	2 month after study start, timepoint 2
t3	3 month after study start, timepoint 3
t6	6 months after study start, timepoint 6
TCF7L2	Transcription Factor 7-Like 2

* used as wildcard character

12. List of figures

13. List of tables

14. References

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Annexes

1. Feedback Level 0

Essen Sie abwechslungsreich, vorrangig eine pflanzenbasiert mit viel Obst, Gemüse, Vollkornprodukten und Fisch. Schränken Sie die Zufuhr von rotem Fleisch, Salz, Lebensmitteln mit zugesetztem Zucker und energiereichen Lebensmittelprodukten ein.

Eine abwechslungsreiche Ernährung könnte der beste Weg sein, die Gesundheit zu erhalten und zu verbessern und sichert zudem eine optimale Nährstoffzufuhr.

Achten Sie auf eine ausgeglichene Balance zwischen Energiezufuhr und Energieverbrauch.

Die Energiezufuhr über Lebensmittel und Getränke und der Energieverbrauch durch körperliche Aktivität sollten ausgeglichen sein, um das Körpergewicht in einem normalen Rahmen zu halten.

Für übergewichtige Personen wird empfohlen, die körperliche Aktivität zu steigern und gleichzeitig weniger Energie über Lebensmittel aufzunehmen.

Essen Sie mindestens 5 Portionen Obst und Gemüse pro Tag.

Essen Sie mindestens 5 Portionen Obst (inklusive Beeren) und Gemüse pro Tag. Das sind insgesamt wenigstens 400 g, da eine Portion etwa 80g entspricht (das wiederum entspricht etwa der Größe Ihrer Faust oder einem mittelgroßen Apfel) Essen Sie eine Vielzahl von Früchten und Gemüsen verschiedener Farben (rot, grün, gelb, weiß, violett und orange).

Alles Gemüse und Obst, ob frisch, aus Dosen, gefroren oder gekocht, gebacken oder gebraten kann als Teil der empfohlenen Zufuhr miteinbezogen werden. Bitte wählen Sie Produkte aus, denen kein Zucker zugesetzt wurde.

Getrocknete Früchte können als Teil Ihrer Zufuhrempfehlungen miteinbezogen werden, aber die Portionsgröße sollte halbiert werden. Ein Glas Saft oder Fruchtshake, genauso wie Hülsenfrüchte können in die täglichen 5 Portionen integriert werden.

Kartoffeln werden bisher nicht in die 5 Portionen eingerechnet. Allerdings können Kartoffeln allgemein Teil einer ausgewogenen Ernährung sein. Nüsse werden ebenfalls nicht in die 5 Portionen pro Tag einbezogen, aber ein moderater Verzehr von Nüssen (ungefähr 20g pro Tag, also z.B. 20 Mandeln) kann in eine ausgewogene Ernährung integriert werden. Alle Nüsse sollten ungesalzen sein.

Essen Sie jeden Tag Vollkornprodukte.

Essen Sie mindestens 50g Vollkorn täglich, z. B. durch den Verzehr von zwei Scheiben Vollkornbrot, einer kleinen Portion Vollkorn-Müsli oder einer Portion Vollkorn-Pasta oder braunem Reis.

Essen Sie 2 Portionen Fisch pro Woche. Eine Fischmahlzeit sollte aus fettem Seefisch bestehen.

Essen Sie 2 Portionen Fisch pro Woche. Eine Portion Fisch sind ungefähr 150g. Sowohl magerer als auch fetter Fisch können hierzu gezählt werden, eine Portion sollte aber aus fettem Seefisch bestehen.

Fisch in einer Hauptmahlzeit kann durch Fisch als Brotbelag ersetzt werden. Drei Brote mit Fischbelag (50g) entsprechen einer Hauptmahlzeit.

Zu fetten Seefischen zählen Hering, Sardinen, Heilbutt, Makrele, Forelle, Lachs und Thunfisch. Magere Fische sind Dorsch und Seelachs.

Essen Sie 3 Portionen Milchprodukte pro Tag.

Essen Sie drei Portionen fettarmer Milchprodukte pro Tag. Eine Portion ist ein großes Glas Milch (200ml), ein kleiner Becher Joghurt (150g) oder 3 Scheiben Hartkäse (30g).

Fettarme Milchprodukte sind gesünder. Der Verzehr von Milchprodukten mit einem hohen Anteil gesättigter Fette, wie Sahne, fetter Käse und Butter sollte eingeschränkt werden.

Essen Sie mageres Fleisch und magere Fleischprodukte und begrenzen Sie Ihre Zufuhr an rotem und verarbeitetem Fleisch.

Mageres Fleisch und magere Fleischprodukte sind für viele Menschen eine wichtige Quelle für viele verschiedene Nährstoffe. Ein moderater Verzehr von magerem Fleisch kann daher in die normale Ernährung aufgenommen werden.

Sie sollten jedoch versuchen, nicht mehr als 500g rotes Fleisch (Rind, Schwein, Lamm und Ziege) pro Woche zu essen. Das sind ungefähr 3 Hauptmahlzeiten pro Woche mit ca. 150g Fleisch (z.B. eine Scheibe oder ein Burger). Beachten Sie, dass zu den 500g auch Aufschnitt gezählt wird.

Versuchen Sie, weniger verarbeitetes Fleisch, wie geräucherte, gesalzene oder mit Nitraten oder Nitriten haltbargemachte Produkte zu essen. Dazu zählen beispielsweise Würste, Schinken, Salami und Speck.

Benutzen Sie Öl oder pflanzliche Margarine mit ungesättigten Fetten.

Kochen Sie mit Pflanzenölen.

Entscheiden Sie sich für Öle oder Margarine mit einem hohen Anteil ungesättigter Fette (z.B. Raps-, Oliven-, Soja- und Walnussöl) und einem möglichst geringen Anteil gesättigter Fette (z.B. Palmöl oder tierische Fette)

Schränken Sie den Gebrauch von Butter ein, da diese einen hohen Anteil gesättigter Fette und einen geringen Anteil mehrfach ungesättigter Fette hat. Butter und tierische Fette enthalten außerdem Cholesterin, das in Pflanzen nicht vorkommt.

Obwohl Sie eher weniger Lebensmittel mit hohem Energiegehalt essen sollten, liefern Ihnen pflanzliche Öle mehrfach ungesättigte Fette und fettlösliche Vitamine. Daher sollten diese auch Teil Ihrer Ernährung sein.

Als Getränk wird Wasser empfohlen.

Wasser sollte einen großen Teil Ihrer Flüssigkeitszufuhr ausmachen.

Wenn Sie Alkohol trinken, sollten es nicht mehr als zwei Drinks für Männer und nicht mehr als einer für Frauen sein. Eine Portion ist beispielsweise ein Glas Wein, eine Flasche Bier oder ein kleines Glas Spirituosen.

Essen Sie wenige Produkte mit hohem Energiegehalt.

Schränken Sie den Verzehr von Lebensmitteln mit hohem Energiegehalt ein. Dies sind Lebensmittel mit viel Fett, Öl und zugesetztem Zucker, wie Süßigkeiten und Fast Food.

Diese Lebensmittel können ab und zu in kleinen Mengen gegessen werden (z.B. eine Hand voll). Sie sind jedoch nicht zum Stillen von Hunger bestimmt, sondern für den Appetit.

Essen Sie wenig Salz.

Schränken Sie den Verzehr von Salz (Natriumchlorid) ein. Sie sollten nicht mehr als 6g Salz (= 2,4g Natriumchlorid) pro Tag essen. Dies entspricht ungefähr einem halben Teelöffel. Denken Sie daran, dass ein Großteil dieser Menge meist bereits in Lebensmitteln vorhanden ist.

Verarbeitete Lebensmittel und Fertiggerichte haben oft einen hohen Salzgehalt, rohe Zutaten enthalten wesentlich weniger Salz.

Versuchen Sie, beim Zubereiten oder Verzehr von Speisen kein Salz hinzuzugeben. Probieren Sie andere Würzmethoden, wie Kräuter oder Gewürze statt Salz.

Seien Sie mindestens 30 min. pro Tag körperlich aktiv.

Ihr Ziel sollte sein, zumindest moderat körperlich aktiv zu sein. Dies erreichen Sie, wenn Sie mindesten 30 min. am Tag schnell Spazierengehen. Das können Sie auch ich Ihren Alltag einbinden, z.B. im Haushalt oder um von einem Ort an den anderen zu gelangen.

Wenn sich Ihre Fitness verbessert hat, versuchen Sie, täglich mindestens 60 Minuten moderat aktiv zu sein oder 30 min. anstrengenden Sport zu treiben.

2. Feedback Level 3 – low intensity

food4me.org

PERSONALISIERTER ERNÄHRUNGSBERICHT FÜR:

002	Max Mustermann

Ihr Food4Me Ernährungswissenschaftler: Silvia Kolossa

Bericht Nr.: 1

Datum: 26. April 2013

Ihr Bericht zur personalisierten Ernährung basiert auf Informationen, die Sie für das food4me Projekt zur Verfügung gestellt haben, unter anderem Ihr Ernährungsfragebogen, Ihre Messungen, Ihre Blutproben und Ihre DNA -Probe. In diesem Bericht finden Sie folgende Informationen:

1

food4me.org

Eine Mitteilung Ihres Ernährungswissenschaftlers

Lieber Herr Mustermann,

Ihre Angaben zeigen, dass Sie bei Ihrer Ernährung schon vieles richtig machen. So essen Sie beispielsweise viel Obst und Gemüse und haben dadurch eine gute Versorgung mit Vitaminen, Mineralstoffen und Spurenelementen.

Sie haben jedoch etwas Übergewicht. Aufgrund Ihrer genetischen Veranlagung würden Sie ganz besonders von einem gesunden Körpergewicht profitieren. Versuchen Sie daher, ein Körpergewicht von unter 85 kg zu erreichen und zu halten. Hierzu sollten Sie entweder Ihre Energiezufuhr („Kalorienaufnahme") reduzieren oder Ihren Energieverbrauch in Form körperlicher Aktivität erhöhen – oder am besten beides kombinieren. Sie könnten zum Beispiel Vollmilch durch fettarme Milch und Sahnejoghurt durch Joghurt mit geringerem Fettgehalt ersetzen. Hierdurch würden Sie nicht nur Ihre Energiezufuhr verringern, sondern gleichzeitig auch die Aufnahme an gesättigten Fettsäuren reduzieren. Und Sie sollten Ihren Weinkonsum einschränken – Sie nehmen täglich ca. 500 kcal allein in Form von Alkohol zu sich! Zur Steigerung Ihrer körperlichen Aktivität bietet es sich beispielsweise an, noch öfter das Fahrrad zu benutzen.

Hier finden Sie Ihre Hauptziele, auf die Sie sich konzentrieren sollten:

- Reduzieren Sie Ihr Körpergewicht langfristig auf einen Wert unter 85 kg.
- Schränken Sie Ihre Aufnahme an gesättigten Fettsäuren ein.
- Reduzieren Sie Ihren Salzkonsum.
- Steigern Sie den Verzehr von komplexen Kohlenhydraten.

Wir haben Ihnen in Teil 4 dieses Berichts einige Ratschläge zusammengestellt, die Ihnen helfen, diese Ziele zu erreichen.

Um direkt zu Ihrer personalisierten Ernährungsempfehlung (Teil 4) zu gelangen, klicken Sie hier.

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Teil 1: Ihre Ernährung im Vergleich zu den derzeitigen Empfehlungen

Lebensmittelgruppe	Ihre durchschnittliche Anzahl an Portionen	Empfehlung
Obst und Gemüse 	6,5 pro Tag	Mindestens 5 pro Tag
Vollkornprodukte	unter 50g pro Tag	Mindestens 50g pro Tag
Milchprodukte 	4 pro Tag	3 pro Tag
Fetter Seefisch 	1 pro Woche	Mindestens 1 pro Woche
Rotes Fleisch 	5 pro Woche	Nicht mehr als 3 pro Woche

Für weiterführende Informationen zu Ernährungsempfehlungen und Portionsgrößen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

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Teil 2: Ihre körperlichen Kenngrößen

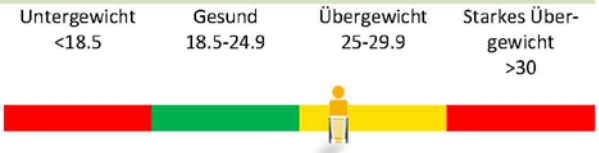
Basierend auf den Messungen Ihres Körpers und der körperlichen Aktivität, die Sie uns mitgeteilt haben, wurden Ihre Kenngrößen bewertet:

Ihr Körpergewicht und Body Mass Index

Ihre Körpergröße: 1,85 m

Ihr Körpergewicht: 88,7 kg

Ihr BMI: 25,9 kg/m^2



BMI = Body Mass Index. Dies ist ein Hinweis darauf, wie gesund Ihr Körpergewicht bezogen auf Ihre Körpergröße ist.

Ihr Taillenumfang: 100 cm

Ihre allgemeine körperliche Aktivität:

von Ihrem Aktivitätsfragebogen

Für weiterführende Informationen zu Ernährungsempfehlungen und Portionsgrößen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

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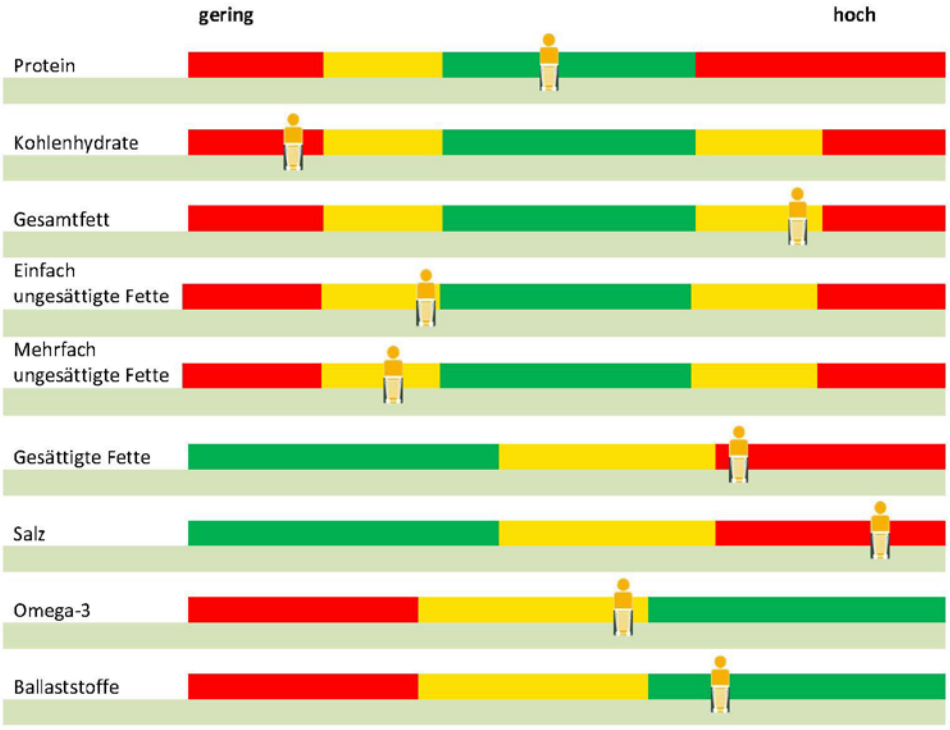
Teil 3a: Ihr Ernährungsprofil

Dieser Teil des Berichts zeigt Ihre durchschnittliche tägliche Zufuhr ausgewählter Nährstoffe, Ballaststoffe, Vitamine und Mineralien im Vergleich zu den internationalen Empfehlungen des „Institute of Medicine", angepasst an Ihr Alter und Ihr Geschlecht.

- Gut, Änderungen nicht nötig
- Verbesserung empfohlen
- Verbesserung dringend empfohlen
- Ihre Zufuhr; Ziel ist es, im grünen Bereich zu liegen



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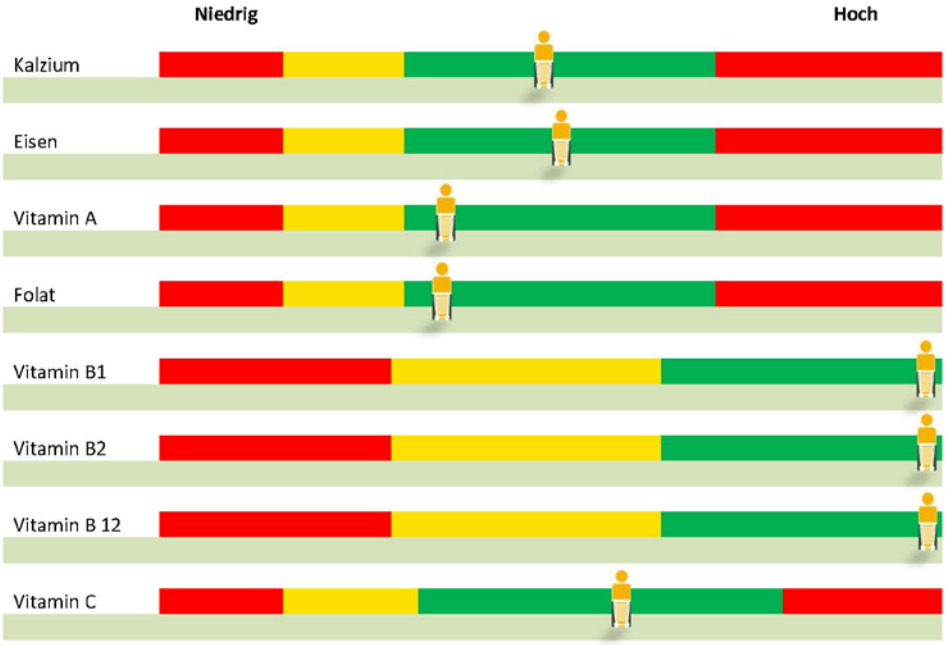
Ihre Vitamin und Mineralienzufuhr



Für weiterführende Informationen zu diesen Nährstoffen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

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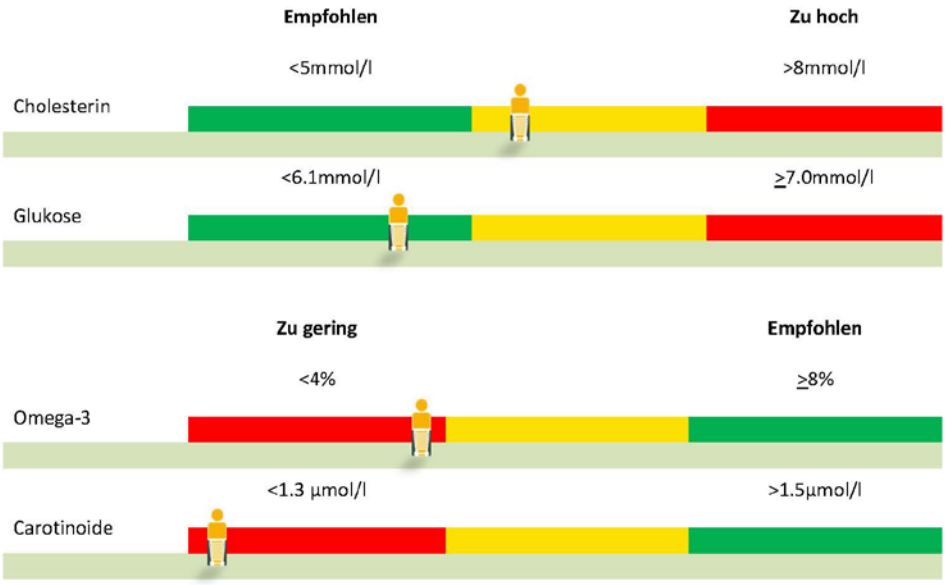
Teil 3b: Ihr Blutprofil

Die folgenden Ergebnisse basieren auf Ihren Blutproben. Diese stellen die wichtigsten ernährungsabhängigen Marker in Ihrem Blut dar, die wir in dieser Studie auswerten.



Für weiterführende Informationen zu diesen Nährstoffen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

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Teil 3c: Ihr genetisches Profil

Menschen haben ca. 25.000 Gene, 99,9% davon sind bei allen Menschen absolut identisch. Wir interessieren uns für die Gene, die sich von Mensch zu Mensch unterscheiden und den Einfluss, den manche dieser Unterschiede auf die Gesundheit und den Bedarf an bestimmten Nährstoffen haben.

Wir haben fünf Gene ausgewertet, die in Zusammenhang mit Ernährung stehen. Es gibt unterschiedliche Variationen dieser Gene in der Bevölkerung. Ernährungswissenschaftler haben Hinweise darauf entdeckt, dass bestimmte Variationen von Nutzen sein könnten, wenn mehr oder weniger bestimmter Nährstoffe verzehrt werden. Neben jedem Gen wird kurz die Verbindung zur Ernährung erläutert.

Gene	Einfluss der Ernährung in Zusammenhang mit einigen Variationen dieses Gens	Haben Sie genetische Variationen, die durch Ernährung beeinflusst werden kann?
MTHFR	Personen mit einer bestimmten Variation dieses Gens können von einer erhöhten Folsäurezufuhr profitieren. Eine erhöhte Zufuhr von Folsäure (vorhanden in grünem Blattgemüse) wird mit einer Verbesserung bestimmter Faktoren gebracht, die in Zusammenhang mit kardiovaskulärer Gesundheit stehen.	Nein
FTO	Eine bestimmte Variation dieses Gens steht in Zusammenhang mit einer erhöhten Notwendigkeit, ein gesundes Körpergewicht zu halten und körperlich aktiv zu sein. Ein gesundes Gewicht und Sport können diesen Personen zusätzlichen gesundheitlichen Nutzen einbringen.	Ja
TCF7L2	Eine bestimmte Variation dieses Gens steht in Zusammenhang mit verbessertem Gewichtsverlust, wenn, verglichen mit anderen Diäten, auf eine fettarme Ernährung geachtet wird. Eine Verringerung des Fettgehalts in der Nahrung kann bei diesen Personen zu einem größeren Gewichtsverlust führen.	Ja
ApoE(e4)	Eine bestimmte Variation dieses Gens steht in Zusammenhang mit einer größeren Notwendigkeit, einen gesunden Cholesterinspiegel zu halten. Eine Verringerung der Zufuhr gesättigter Fettsäuren steht in Zusammenhang mit einer Verbesserung des Cholesterinspiegels und bestimmter Faktoren bezüglich der kardiovaskulären Gesundheit dieser Personen.	Ja
FADS1	Personen mit einer bestimmten Variante dieses Gens können profitieren, indem sie Ihre Zufuhr an gesunden omega-3-Fettsäuren aus fettem Seefisch erhöhen. Eine erhöhte Zufuhr von omega-3-Fettsäuren steht in Zusammenhang mit bestimmten Faktoren bezüglich der kardiovaskulären Gesundheit dieser Personen.	Nein

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

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Teil 4: Ihre personalisierte Ernährungsempfehlung

Ihre Empfehlungen zu Gewicht und körperlicher Aktivität

Obwohl Ihr BMI größer ist als die derzeitigen Empfehlungen, ist Ihr Taillenumfang in Normalbereich. Ein gesunder BMI-Wert ist wichtig für Sie, da Sie aufgrund Ihrer Gene besonders davon profitieren, wenn Ihr Körpergewicht im Normalbereich liegt. Der BMI ist ein geeigneter Kennwert, der einen Überschuss oder ein Defizit an Körperfett in einer normalen Bevölkerung anzeigt. Dies trifft jedoch nicht auf sehr muskulöse Personen zu, da diese keine typische Körperzusammensetzung haben. Obwohl Sie körperlich aktiv sind, entspricht dies noch nicht den derzeitigen Empfehlungen. Wenn Sie ca. 0,5 - 1 kg Gewicht pro Woche verlieren und regelmäßig Sport treiben, verlieren Sie Fett, erhalten aber Ihre Muskelmasse.

Zusätzlich ist Ihr Cholesterinspiegel leicht erhöht.

Hier sind einige Vorschläge, wie Sie einen gesunden BMI erreichen können:

- Werden Sie aktiver. Um weiter Gewicht zu verlieren wird empfohlen, 60 bis 90 Minuten moderaten Sport, wie schnelles Gehen, Fahrradfahren oder Schwimmen, an den meisten Tagen der Woche zu treiben. Dies hilft Ihnen außerdem, Ihren Cholesterinspiegel zu senken.
- Verkleinern Sie Ihre Portionsgrößen.
- Essen Sie regelmäßig und versuchen Sie, keine Mahlzeit auszulassen.
- Vermeiden Sie Zwischenmahlzeiten mit viel Zucker und Fett – tauschen Sie diese gegen gesündere Alternativen wie Obst.
- Entscheiden Sie sich für fettarme Produkte.

Ihre Ernährungsziele

Da es sehr schwierig ist, alle Nährstoffprofile auf einmal zu verbessern, haben wir Ihre wichtigsten Ernährungsziele herausgesucht, auf die Sie sich bis zur nächsten Datenerfassung konzentrieren können.

Nährstoff	Quellen	Ziele und Tipps
Gesättigte Fettsäuren	Butter und harte Margarine, Vollmilchprodukte, Gebäck und Kuchen, verarbeitete Fleischprodukte Gesättigte Fettsäuren verzehren Sie vor allem mit **1. Vollmilch und Käse** **2. Butter**	<u>Wie Sie Ihre Zufuhr an gesättigten Fettsäuren verringern können:</u> Sie haben bestimmte Gene, für die es nützlich ist, wenn Sie gesättigte Fette in gesunden Mengen essen und einen normalen Cholesterinwert haben. Wir empfehlen Ihnen, weniger gesättigte Fette zu essen, da dies hilft, Ihren leicht erhöhten Cholesterinspiegel zu senken. Entscheiden Sie sich für fettarme Milchprodukte statt vollfetter Produkte und achten Sie auf Ihre Portionsgrößen. Statt Vollmilch (3,5% Fett) fettarme Milch (1,5% Fett) zu trinken, spart Ihnen pro Liter rund 20g Fett

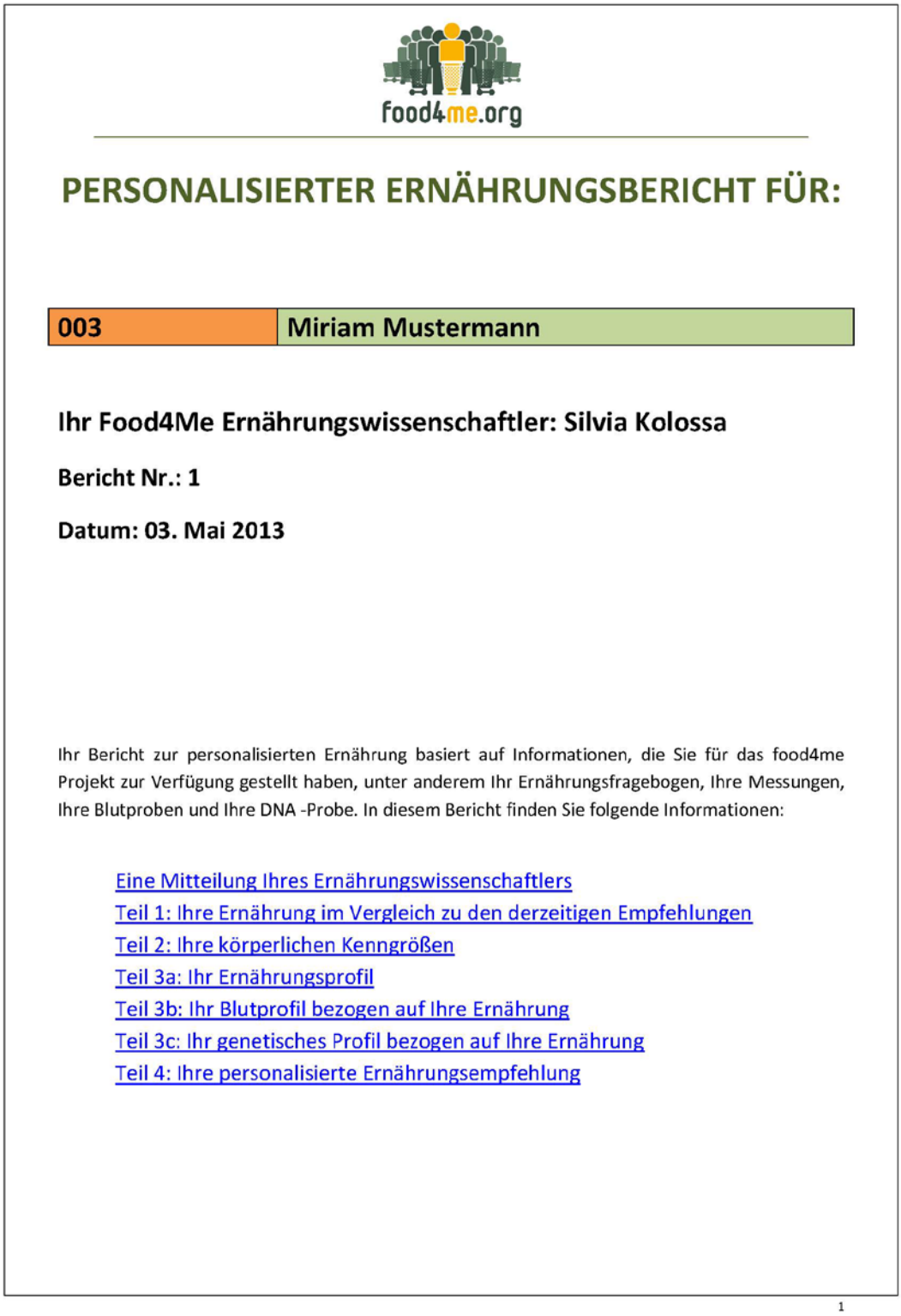
		und rund 170kcal. Nehmen Sie statt Butter gesündere ungesättigte Fette, wie Sonnenblumen-, Oliven- oder Rapsöl und fettarme Brotaufstriche. Entscheiden Sie sich für gesündere Fette, wie fetten Seefisch, Nüsse und Samen oder ungesättigte Öle, wie Olivenöl.
Salz	Geräucherte und verarbeitete Lebensmittel, wie Fleisch, Pizza, Fertiggerichte und Suppen Salz verzehren Sie vor allem mit 1. **Wurst und Fleischwaren** 2. **Brot**	Wie Sie Ihre Salzzufuhr verringern können: Essen Sie weniger verarbeitete Fleischprodukte; tauschen Sie Salami, Schinken und Speck gegen Putenbrust, Rind oder Huhn. Passen Sie bei geräuchertem Fleisch und Fisch auf – diese Lebensmittel enthalten sehr viel Salz. Brot enthält viel "verstecktes" Salz. Vergleichen Sie beim nächsten Einkauf die Salzmenge der Produkte und entscheiden Sie sich für eines mit wenig Salz. Reduzieren Sie die Menge an Salz, die Sie zum Kochen verwenden – probieren Sie Gewürze wie Knoblauch, Zitrone, Ingwer, Chili oder schwarzen Pfeffer statt Salz.
Kohlenhydrate	Komplexe Kohlenhydrate: Brot, Nudeln, Reis, Müsli, Obst und Gemüse, Kartoffeln, Hülsenfrüchte Einfache Kohlenhydrate: Haushaltszucker, Honig, Softdrinks, Süßwaren	Wie Sie Ihre Kohlenhydratzufuhr verbessern können: Stärkehaltige Lebensmittel wie Brot, Nudeln, Kartoffeln und Reis sollten die Grundlage Ihrer Mahlzeiten und Snacks sein. Versuchen Sie, diese Produkte möglichst abwechslungsreich in Ihren Speiseplan aufzunehmen. Sie sind gelangweilt, weil Sie immer das gleiche essen? Probieren Sie unterschiedliche Brot- oder Brötchensorten, Wraps oder Fladenbrote. Entscheiden Sie sich für Vollkornprodukte, wann immer dies möglich ist, da diese reichlich Ballaststoffe enthalten. Essen Sie nur ab und zu zuckerhaltige Lebensmittel, so vermeiden Sie Karies.

Für mehr Informationen zu jedem Nährstoff, Quellen und empfohlenen Portionsgrößen nutzen Sie Ihren persönlichen Login auf der Food4me-Website. Für mehr Informationen zu Alkohol, klicken Sie bitte hier, für Empfehlungen zum Rauchen, klicken Sie bitte hier.

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

Falls Sie Fragen zu Ihrem Bericht haben, kontaktieren Sie bitte Ihre Food4me Wissenschaftler unter food4me@tum.de

3. Feedback Level 3 – high intensity



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PERSONALISIERTER ERNÄHRUNGSBERICHT FÜR:

003	Miriam Mustermann

Ihr Food4Me Ernährungswissenschaftler: Silvia Kolossa

Bericht Nr.: 1

Datum: 03. Mai 2013

Ihr Bericht zur personalisierten Ernährung basiert auf Informationen, die Sie für das food4me Projekt zur Verfügung gestellt haben, unter anderem Ihr Ernährungsfragebogen, Ihre Messungen, Ihre Blutproben und Ihre DNA -Probe. In diesem Bericht finden Sie folgende Informationen:

1

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Eine Mitteilung Ihres Ernährungswissenschaftlers

Liebe Frau Mustermann,

Sie haben eine ausgewogene Ernährung, nur wenige Ihre Nährstoffe liegen im roten Bereich, herzlichen Glückwunsch! Außerdem treiben Sie Sport, das ist sehr gut für Ihre Gesundheit. Dennoch sind Sie stark übergewichtig, das heißt Sie nehmen mehr Energie auf, als Sie wieder abgeben. Versuchen Sie langsamer zu essen, viel zu trinken und auf Ihr Sättigungsgefühl zu achten. Fragen Sie sich, warum Sie gerade essen; Frust oder Langeweile? Versuchen Sie, sich feste Zeiten einzurichten, in denen Sie Pause machen und etwas essen; die kleinen Snacks zwischen durch sollten Sie vermeiden, oder durch Gemüse oder Obst ersetzen. Nehmen Sie grundsätzlich kleinere Portionen und warten Sie einige Minuten, bevor Sie sich eine weitere Portion nehmen. Wenn Sie satt sind, stellen Sie den Rest Ihres Essens konsequent in den Kühlschrank. Leere Teller sollten für Sie keine Priorität haben, sondern das Sättigungsgefühl. Vermeiden Sie fettreiche Lebensmittel; Sie sind Trägerin einer bestimmten Genvariante, bei der eine fettreduzierte Diät zu einem höheren Gewichtsverlust führen kann, als bei anderen Diäten. Sie haben angegeben, dass Sie bereits versuchen Gewicht zu verlieren, das ist sehr gut! Weniger Gewicht und mehr Bewegung sind nicht nur für Ihren Cholesterinwert gut, sondern helfen Ihnen auch, Ihren guten Blutzuckerwert zu erhalten.

Hier finden Sie Ihre Hauptziele, auf die Sie sich konzentrieren sollten:

- Gewichtsreduktion auf einen normalen Body Mass Index
- Weniger Salz
- Mehr Kalzium
- Mehr omega-3-Fettsäuren

Wir haben Ihnen in Teil 4 dieses Berichts einige Ratschläge zusammengestellt, die Ihnen helfen, diese Ziele zu erreichen.

Um direkt zu Ihrer personalisierten Ernährungsempfehlung (Teil 4) zu gelangen, klicken Sie hier.

Teil 1: Ihre Ernährung im Vergleich zu den derzeitigen Empfehlungen

Lebensmittelgruppe	Ihre durchschnittliche Anzahl an Portionen	Empfehlung
Obst und Gemüse 	5,5 pro Tag	Mindestens 5 pro Tag
Vollkornprodukte	Knapp unter 50g pro Tag	Mindestens 50g pro Tag
Milchprodukte 	1,5 pro Tag	3 pro Tag
Fetter Seefisch 	1 pro Woche	Mindestens 1 pro Woche
Rotes Fleisch 	1 pro Woche	Nicht mehr als 3 pro Woche

Für weiterführende Informationen zu Ernährungsempfehlungen und Portionsgrößen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

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Teil 2: Ihre körperlichen Kenngrößen

Basierend auf den Messungen Ihres Körpers und der körperlichen Aktivität, die Sie uns mitgeteilt haben, wurden Ihre Kenngrößen bewertet:

Ihre Wertung

Ihr Körpergewicht und Body Mass Index

Ihre Körpergröße: 1,75 m

Ihr Körpergewicht: 105 kg

Ihr BMI: 34,3 kg/m^2

Untergewicht	Gesund	Übergewicht	Starkes Übergewicht
<18.5	18.5-24.9	25-29.9	>30

BMI = Body Mass Index. Dies ist ein Hinweis darauf, wie gesund Ihr Körpergewicht bezogen auf Ihre Körpergröße ist.

Gesund	Größer als die Empfehlungen
< 88 cm	> 88 cm

Ihr Taillenumfang: 110 cm

Für weiterführende Informationen zu Ernährungsempfehlungen und Portionsgrößen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

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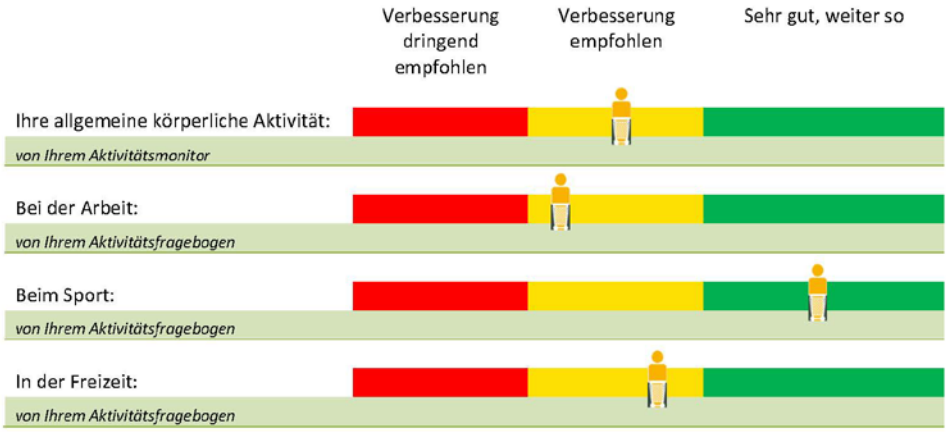
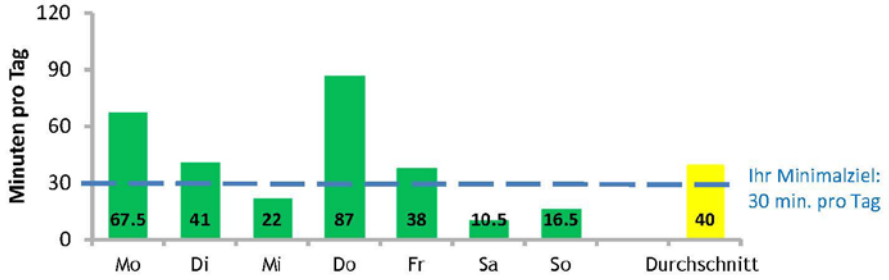
Wie körperlich aktiv Sie sind:



Wie aktiv waren Sie?

Ihre moderate bis anstrengende Bewegung pro Woche: **283 Minuten**



Diese Grafik zeigt, wie aktiv Sie in einer Woche waren. Um Ihre Gesundheit zu erhalten, sollte Ihr Ziel sein, **mindestens 30 Minuten** pro Tag an fünf Tagen der Woche aktiv zu sein oder mindestens **150 Minuten moderaten bis anstrengenden** Sport in der Woche zu treiben.

Für weiterführende Informationen zu Ernährungsempfehlungen und Portionsgrößen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

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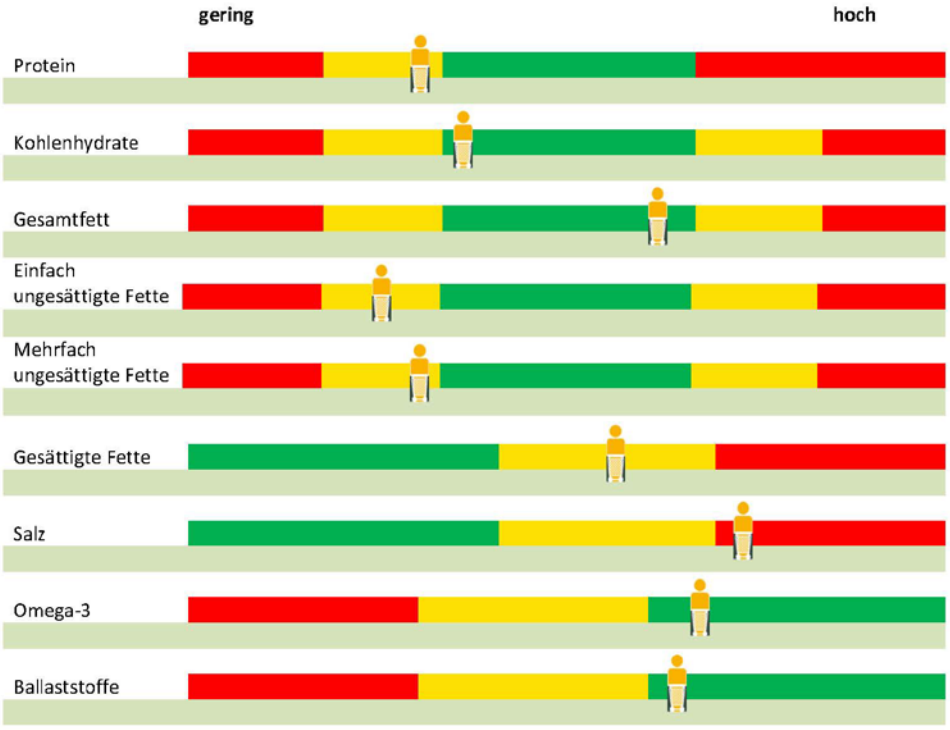
Teil 3a: Ihr Ernährungsprofil

Dieser Teil des Berichts zeigt Ihre durchschnittliche tägliche Zufuhr ausgewählter Nährstoffe, Ballaststoffe, Vitamine und Mineralien im Vergleich zu den internationalen Empfehlungen des „Institute of Medicine", angepasst an Ihr Alter und Ihr Geschlecht.

- Gut, Änderungen nicht nötig
- Verbesserung empfohlen
- Verbesserung dringend empfohlen
- Ihre Zufuhr; Ziel ist es, im grünen Bereich zu liegen



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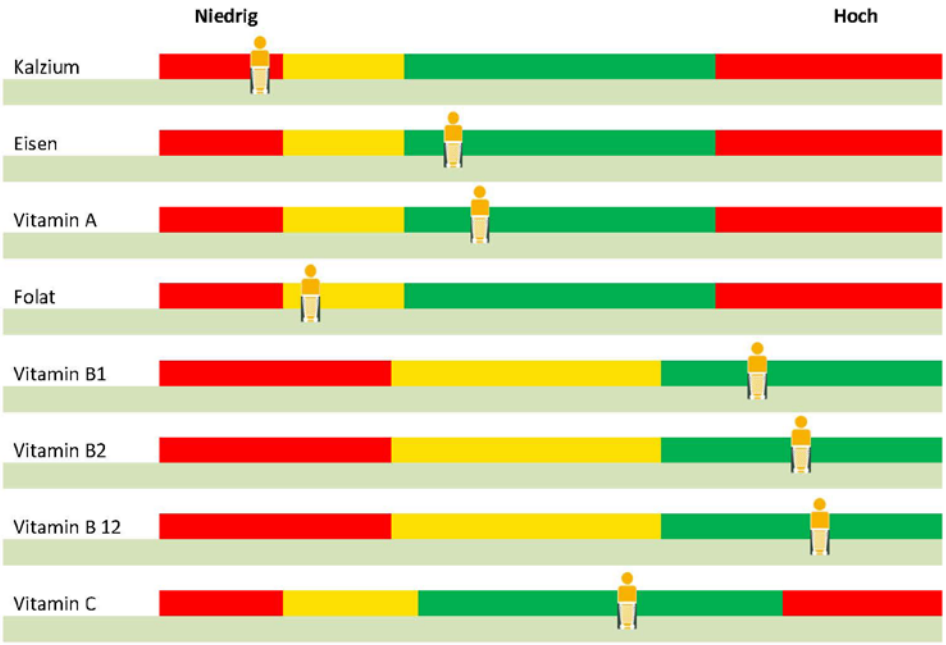
Ihre Vitamin- und Mineralstoffzufuhr

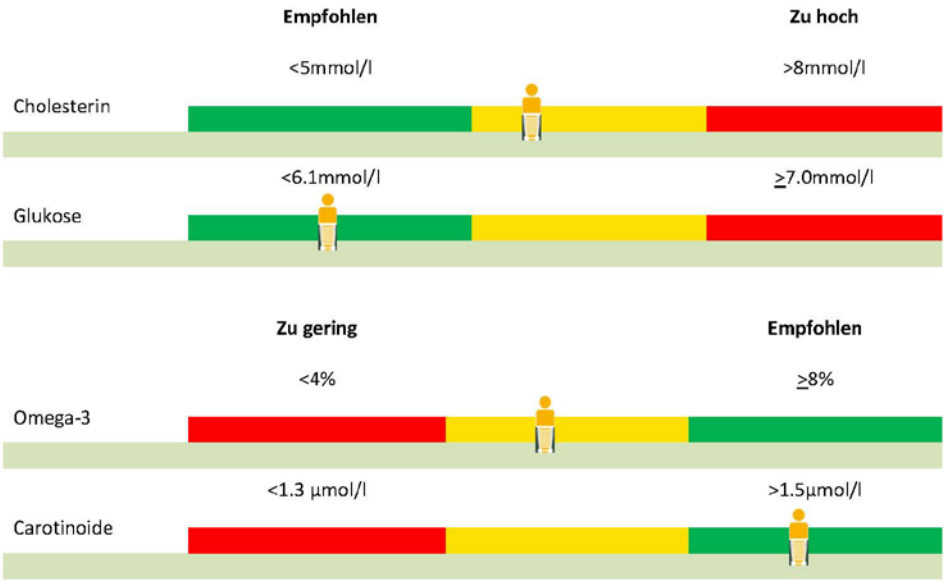


Für weiterführende Informationen zu diesen Nährstoffen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

Teil 3b: Ihr Blutprofil

Die folgenden Ergebnisse basieren auf Ihren Blutproben. Diese stellen die wichtigsten ernährungsabhängigen Marker in Ihrem Blut dar, die wir in dieser Studie auswerten.



Für weiterführende Informationen zu diesen Nährstoffen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

Teil 3c: Ihr genetisches Profil

Menschen haben ca. 25.000 Gene, 99,9% davon sind bei allen Menschen absolut identisch. Wir interessieren uns für die Gene, die sich von Mensch zu Mensch unterscheiden und den Einfluss, den manche dieser Unterschiede auf die Gesundheit und den Bedarf an bestimmten Nährstoffen haben.

Wir haben fünf Gene ausgewertet, die in Zusammenhang mit Ernährung stehen. Es gibt unterschiedliche Variationen dieser Gene in der Bevölkerung. Ernährungswissenschaftler haben Hinweise darauf entdeckt, dass bestimmte Variationen von Nutzen sein könnten, wenn mehr oder weniger bestimmter Nährstoffe verzehrt werden. Neben jedem Gen wird kurz die Verbindung zur Ernährung erläutert.

Gene	Einfluss der Ernährung in Zusammenhang mit einigen Variationen dieses Gens	Haben Sie genetische Variationen, die durch Ernährung beeinflusst werden kann?
MTHFR	Personen mit einer bestimmten Variation dieses Gens können von einer erhöhten Folsäurezufuhr profitieren. Eine erhöhte Zufuhr von Folsäure (vorhanden in grünem Blattgemüse) wird mit einer Verbesserung bestimmter Faktoren gebracht, die in Zusammenhang mit kardiovaskulärer Gesundheit stehen.	ja
FTO	Eine bestimmte Variation dieses Gens steht in Zusammenhang mit einer erhöhten Notwendigkeit, ein gesundes Körpergewicht zu halten und körperlich aktiv zu sein. Ein gesundes Gewicht und Sport können diesen Personen zusätzlichen gesundheitlichen Nutzen einbringen.	ja
TCF7L2	Eine bestimmte Variation dieses Gens steht in Zusammenhang mit verbessertem Gewichtsverlust, wenn, verglichen mit anderen Diäten, auf eine fettarme Ernährung geachtet wird. Eine Verringerung des Fettgehalts in der Nahrung kann bei diesen Personen zu einem größeren Gewichtsverlust führen.	ja
ApoE(e4)	Eine bestimmte Variation dieses Gens steht in Zusammenhang mit einer größeren Notwendigkeit, einen gesunden Cholesterinspiegel zu halten. Eine Verringerung der Zufuhr gesättigter Fettsäuren steht in Zusammenhang mit einer Verbesserung des Cholesterinspiegels und bestimmter Faktoren bezüglich der kardiovaskulären Gesundheit dieser Personen.	ja
FADS1	Personen mit einer bestimmten Variante dieses Gens können profitieren, indem sie Ihre Zufuhr an gesunden omega-3-Fettsäuren aus fettem Seefisch erhöhen. Eine erhöhte Zufuhr von omega-3-Fettsäuren steht in Zusammenhang mit bestimmten Faktoren bezüglich der kardiovaskulären Gesundheit dieser Personen.	ja

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

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Teil 4: Ihre personalisierte Ernährungsempfehlung

Ihre Empfehlungen zu Gewicht und körperlicher Aktivität

Ihr BMI ist höher als die derzeitigen Empfehlungen. Dies bedeutet, dass Sie, verglichen mit Ihrer Größe, zu viel wiegen. Auch Ihr Taillenumfang größer als die derzeitigen Empfehlungen. Zu viel Gewicht um Ihre Mitte erhöht Ihr Risiko für bestimmte Krankheiten, wie Erkrankungen des Herzens und Krebs. Wir empfehlen Ihnen, Ihr Körpergewicht und Ihren Taillenumfang auf ein gesundes Maß zu reduzieren, da Sie bestimmte Gene haben, für die es nützlich ist, wenn diese beiden in einem gesunden Bereich liegen. Wir empfehlen Ihnen dringend, Gewicht zu verlieren. Eine Gewichtsreduktion von ca. 0,5 - 1 kg pro Woche ist ein realistisches Ziel. Obwohl Sie Sport treiben, wird Ihnen eine Steigerung Ihrer körperlichen Aktivität helfen, Gewicht zu verlieren. Zusätzlich ist Ihr Cholesterinspiegel leicht erhöht.

Die folgende Liste enthält Vorschläge, die Ihnen helfen, Gewicht zu verlieren:

- Werden Sie aktiver. Um weiter Gewicht zu verlieren wird empfohlen, 60 bis 90 Minuten moderaten Sport, wie schnelles Gehen, Fahrradfahren oder Schwimmen, an den meisten Tagen der Woche zu treiben. Dies hilft Ihnen außerdem, Ihren Cholesterinspiegel zu senken.
- Verkleinern Sie Ihre Portionsgrößen
- Essen Sie regelmäßig und versuchen Sie, keine Mahlzeit auszulassen
- Vermeiden Sie Zwischenmahlzeiten mit viel Zucker und Fett - tauschen Sie diese gegen gesündere Alternativen wie Obst
- Entscheiden Sie sich für fettarme Produkte

Ihre Ernährungsziele

Da es sehr schwierig ist, alle Nährstoffprofile auf einmal zu verbessern, haben wir Ihre wichtigsten Ernährungsziele herausgesucht, auf die Sie sich bis zur nächsten Datenerfassung konzentrieren können.

Nährstoff	Quellen	Ziele und Tipps
Salz	geräucherte und verarbeitete Lebensmittel, wie Fleisch, Pizza, Fertiggerichte und Suppen Salz verzehren Sie vor allem mit **1. Suppen und Soßen** **2. Fleisch und Fisch**	<u>Wie Sie Ihre Salzzufuhr verringern können:</u> Versuchen Sie, wenig oder nicht gesalzene Produkte zu kaufen. Vergleichen Sie beim nächsten Einkauf die Salzmenge der Produkte und entscheiden Sie sich für diejenigen mit wenig Salz. Essen Sie weniger verarbeitete Fleischprodukte; tauschen Sie Salami, Schinken und Speck gegen Putenbrust, Rind oder Huhn. Passen Sie bei geräuchertem Fleisch und Fisch auf - diese Lebensmittel enthalten sehr viel Salz. Reduzieren Sie die Menge an Salz, die Sie zum Kochen verwenden - probieren Sie Gewürze wie Knoblauch, Zitrone, Ingwer, Chili oder schwarzen Pfeffer statt Salz.

Kalzium	Milchprodukte, wie Milch, Joghurt und Käse; grünes Gemüse und Dosenfisch, wie Sardinen oder Lachs	Wie Sie Ihre Kalziumzufuhr verbessern können: Essen Sie mehr Milchprodukte, da diese die reichhaltigste Quelle für Kalzium sind und kaufen Sie, wenn möglich, fettarme Milchprodukte. Ihr Ziel sollte sein, mindestens 3 Portionen fettarmer Milchprodukte pro Tag zu essen. Nehmen Sie für Ihr Müsli fettarme Milch oder Joghurt. Ein gesunder Nachtisch ist ein fettarmer Joghurt mit frischen Früchten. Versuchen Sie vermehrt grünes Gemüse zu essen, wie Broccoli, Kohl und Kraut.
Omega-3-Fettsäuren	fetter Seefisch, wie Lachs, Makrele, Sardinen, frischer Thunfisch	Wie Sie Ihre Zufuhr von omega-3-Fettsäuren verbessern können: Obwohl Sie offenbar ausreichend omega-3-Fettsäuren zu sich nehmen, wird dies durch Ihre Blutwerte nicht bestätigt. Sie liegen knapp unterhalb der derzeitigen Empfehlungen. Wir empfehlen Ihnen, mehr omega-3-reiche Lebensmittel zu essen, da Sie bestimmte Gene haben, für die es nützlich ist, wenn Sie die Zufuhr dieses gesunden Nährstoffs erhöhen. Sie sollten immer versuchen, mindestens 2 Portionen Fisch pro Woche zu essen, davon mindestens 1 mit fettem Seefisch.

Für mehr Informationen zu jedem Nährstoff, Quellen und empfohlenen Portionsgrößen nutzen Sie Ihren persönlichen Login auf der Food4me-Website.

Für mehr Informationen zu Alkohol, klicken Sie bitte hier, für Empfehlungen zum Rauchen, klicken Sie bitte hier.

*Sie können außerdem in unserem **Forum** mit anderen Teilnehmern über Ernährungsthemen diskutieren.*

Um an den Anfang des Berichts zu gelangen, klicken Sie hier.

Falls Sie Fragen zu Ihrem Bericht haben, kontaktieren Sie bitte Ihre Food4me Wissenschaftler unter food4me@tum.de