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PU	Public	x
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

PERSONALISED NUTRITION: OPPORTUNITIES AND CHALLENGES
An introduction to the Food4Me project

Roger J Williams (1893-1988) was an American biochemist who named the b-vitamin folic acid and who discovered the b-vitamin pantothenic acid. In 1950, in an article entitled "Concept of genetotrophic disease" he wrote thus:

> "A genetotrophic disease is one, which occurs if a diet fails to provide sufficient supply of one or more nutrients required at high levels because of the characteristic genetic pattern of the individual concerned. This concept based upon results in genetics and biochemistry is new in medical thought and is believed to be the basis for many diseases, the causation of which is now obscure. Individual patients are far from standardised specimens and medical problems should consistently be considered in terms of the genetically diverse patients, rather than in terms of an absolute normal."

Thus the concept of genetically based personalised health was first envisaged over 6 decades ago but would remain dormant for over half a century. The sequencing of the human genome changed those dynamics and led to a widespread belief that personalised medicine, where therapeutic strategies would be targeted to patients on a genetic basis, was imminent. Soon, the term "personalised nutrition" began to emerge with a belief that the nutritional management of diet-related chronic disease could be considerably improved, based on an individual's genomic data. In 2003, about the time of the release of the human genome, the Institute for the Future at Palo Alto issued a report on personalised nutrition in which they concluded thus:

> "Analysis of the data shows that about one third of American adults are likely to make at least some decisions based on a knowledge of personalized nutrition by 2010. This will create an opportunity for a substantial transformation of the food and nutrition industry in the United States and elsewhere – especially for producers and packagers of foods, retailers, pharmacies, managers of magazines and health reports and health insurance."

Clearly that hasn't happened but it was against such expressed expectations of the potential of personalised nutrition that the European Commission's DG Research issued a call for proposals in FP7, specifically to explore this area in 2009. The Food4Me consortium was then developed and the consortium submitted its proposal in 2010. The submission was successful and the Food4Me consortium began its programme in April 2011 to run until March 2015. The project aimed to explore all elements of personalised nutrition using a multi-disciplinary approach.

At the outset Food4Me recognised that personalised nutrition would operate at three levels each of which could be stand alone or combined: personalised dietary analysis, personalised phenotype analysis and personalised genotype analysis. The design of the proof-of-principle (PoP) study presented some very novel challenges to the consortium, particularly the recruitment of subjects into a study where all contact between researchers and subjects was via the Internet or the postal services. A standard operating procedure (SOP) of some 900

pages was constructed to ensure consistency in a detailed protocol across each of the seven participating centres (Dublin, Reading, Warsaw, Athens, Pamplona, Munich and Maastricht). Two centres started ahead of all others and based on their experience, modifications to the SOP were made and an intense training programme was initiated. The PoP study kicked off in June 2012 and ended in March 2014. Absolutely all objectives, milestones and deliverables were achieved which, given the scale and novelty of the PoP study, remains a credit to all involved.

Food4Me recognised that without a detailed understanding of consumer attitudes to personalised nutrition, any foresight in this field would fall well short of ideal. Thus a very significant part of the work-programme was devoted to probing the opinions of EU consumers. An extensive focus group study was carried out in 9 participating centres leading to the development of a questionnaire that would then be administered to 1,000 subjects in each of these 9 centres. In addition, about 700 of those who actually participated in the PoP undertook this same questionnaire. The outcome is an extremely valuable database, which can now be mined to address the many complex questions that will be asked of consumer attitudes to personalised nutrition. Allied to an understanding of consumer attitudes to personalised nutrition is the need to understand the viability of any personalised nutrition enterprise whether driven by either social or private entrepreneurship. Across a series of workshops with stakeholders from across a wide range of interested sectors, a number of scenarios were developed which will help shape our thinking of the viable alternatives for the creation of a sustainable personalised nutrition offering. This work-package on business models drew on the findings of the consumer research group in developing its final set of scenarios.

Personalised nutrition is largely driven by technology, with regards to what can be measured to best characterise health status and nutritional needs. The efficiency of assessment and delivery of personalised nutrition advice is also technology-dependent. For this reason, exploring the technologies needed in personalised nutrition is a central focus of the project, with a specific work-package dedicated to the theme. The researchers involved set up a Global Network and online knowledge base to establish the most relevant genes in relation to dietary interactions for health outcomes. In addition, the work-package has developed algorithms for the delivery of personalised nutrition advice and has pioneered novel methods for assessing health parameters using very small blood-spot samples.

In the USA, personalised nutrition, specifically personalised nutrition based on genomic data, has come under the scrutiny of regulatory authorities from time to time. In addition, fears are frequently expressed at personalised genomic data becoming available to third parties such as health insurance companies. Thus Food4Me established an ethics and legal work-package devoted entirely to this topic. Several ethical issues have been raised and explored via work-shops and scientific publications. These include the autonomy of consumers, the responsibility of disclosing genetic risk factors (particularly over the Internet) and trustworthiness in relation to data handling and storage. This work-package has completed a report which is a Regulatory Analysis of personalised nutrition, with an emphasis on what legislative reform may be needed to develop the current EU legislative framework in the area.

Finally, the consortium needed to address the issue of communication and not just communication about the workings and outcomes of the project, but communication in general about personalised nutrition. Social media was at the heart of this communication programme as were workshops at high-level scientific conferences throughout the project. An extended deliberative workshop was completed towards the end of the project, to ascertain in face-to-face discussions what consumers thought of the project, its concepts and outcomes. Finally, this White Paper represents the high point of the communication process because it presents all of the detailed studies within Food4Me and all the top line outcomes.

Consumers, industry, regulators, the media and many other stakeholders now have available the most comprehensive analysis ever of personalised nutrition, its opportunities and challenges. As the two who had responsibility for coordinating this project, may we thank all the researchers involved and also thank our project and finance officers at DG Research and Innovation.

Prof Michael J Gibney
Project Coordinator

Dr Marianne Walsh
Project manager

Institute of Food and Health, University College Dublin, Ireland

ABOUT FOOD4ME AND THIS WHITE PAPER

ABOUT FOOD4ME

Food4Me is an EU-funded project under Framework Programme 7. The project started in April 2011 and has run until March 2015. The project aimed to explore all elements of personalised nutrition using a multi-disciplinary approach. The main objectives of the project were to explore the scientific, business and consumer aspects of personalised nutrition, and to determine whether dietary advice, including knowledge of a person's genes, could deliver consumer benefits.

The consortium of partners is shown in Appendix 1.

The project has been delivered through 7 Work Packages:

- **WORK PACKAGE 1: Business and Value Creation Models**
- **WORK PACKAGE 2: Consumer Attitudes to Personalised Nutrition**
- **WORK PACKAGE 3: Technology for Personalised Nutrition**
- **WORK PACKAGE 4: Proof of Principle of Models for the delivery of Personalised Nutrition**
- **WORK PACKAGE 5: Ethical and Legal**
- **WORK PACKAGE 6: Communication**
- **WORK PACKAGE 7: Management**

WHITE PAPER

This White Paper (Deliverable D 6.22 Production of a White Paper on recommendations and policy applications) is a summary of the main outcomes of the work in Food4Me, and their implications. Following an Introduction from the Project Co-ordinators, Professor Michael Gibney and Dr Marianne Walsh of University College, Dublin, Ireland, the White Paper is divided into Chapters that reflect individual Work Packages. Within each Chapter, the research is described, its methodology and results. The implications of the results and how they might translate into practical implications, is discussed, and how they have added to the State of the Art in their respective research fields. Thought is given to what gaps in knowledge still remain, and finally each Work Package chapter reflects on how their research can feed into future Horizon 2020 research calls.

CHAPTERS

1. Personalised Nutrition: opportunities and challenges. An introduction to the Food4Me project

A description of the background to personalised nutrition, the expectations following the sequencing of the human genome, and the potential for personalised nutrition. A summary of the project proposal and the main project objectives and its multi-disciplinary approach.

2. The scientific basis for personalised nutrition - advice and lessons learned from a proof of principle study

This is an overview of Work Package 4, which has been the completion of a Proof-of-Principle (PoP) Randomised Controlled Trial (RCT) on the implementation of personalised nutrition (PN) across seven European centres. The RCT was designed to mimic a real-life internet-based personalised nutrition service and to provide an insight into the effectiveness of PN advice compared with non-personalised "one size fits all" recommendations.

3. Technical developments making personalised nutrition offerings possible

This is an overview of Work Package 3. This Work Package defined a panel of anthropometric and other measurements needed to define the phenotype for the PoP study, did a scouting of emerging technologies for better phenotyping, developed a data base for validated gene-nutrient-health interactions and developed tools such as a meal coding system and a menu-planning module for future applications in personalised nutrition.

4. Consumer attitudes to adoption of personalised nutrition

This is an overview of Work Package 2. The debate about implementation, and subsequent realisation of the public health benefits of personalised nutrition, is dependent on empirical analysis of consumer preferences for its implementation. Research activities in Work Package 2 focused on understanding the specific needs of consumers with respect to personalised nutrition and its delivery to consumers, as well as identification of those factors which prevent consumers taking advantage of personalised nutrition.

5. Communication messages for personalised nutrition service providers

This is part of Work Package 6, as it results in Communication Guidelines. Based on the consumer attitudes research in Work Package 2, the deliberative workshop, and other workshops in the Food4Me project, this chapter describes the concerns or perceptions that consumers have about personalised nutrition, measures to lessen the concerns, and suggested communication advice for the use of personalised nutrition service providers.

6. Business and value creation concepts for personalised nutrition

This is an overview of Work Package 1. Personalised nutrition concepts could potentially improve the value perception of food and its role in health and in society, with the overall objective of achieving a lasting dietary behaviour change at the core of the personalised nutrition system. But for personalised nutrition to succeed, there needs to be a business case, although there

will be a range of different business models. Based on a wide range of inputs from societal, scientific and industrial stakeholders, a systems view of the personalised nutrition concept and its environment was developed.

7. Ethical considerations in relation to personalised nutrition

This is an overview of the ethical part of Work Package 5. It considers the debate about whether the current scientific evidence on gene-diet-health interaction is strong enough for taking an ethically responsible decision to offer personalised nutrition advice. Ethical issues in the fields of nutrition, health care, genetics, and public health were studied, and explored through Workshops. The issues around providing personal health data have been debated. A precautionary approach is advocated, as we make cautious estimations of the risk-benefit balance of personalised nutrition, as well as a respect for autonomy, focusing on personal choice.

8. Legal barriers and requirements

This is an overview of the legal aspects studied in Work Package 5. The objective of this research was to identify and analyse the legal and regulatory framework of relevance for personalised nutrition services in the EU. Applicability of frameworks and resulting barriers and requirements was made by assessing typical business models of personalised nutrition against the requirements currently set up by legal instruments in the EU, or at Member State level.

9. Integrating personalised nutrition - the way forward?

This final chapter paints a vision of what personalised nutrition could deliver. Aspiring to this vision, the chapter summarises the main results and policy implications with respect to the many scientific, technical, legal and ethical hurdles that will arise, and finishes with recommendations for next steps.

Appendix 1: Food4Me PARTNERS

1	University College Dublin	**14**	Wageningen University
2	Ulster University	**15**	LEI-Wageningen University Research
3	Maastricht University	**16**	Philips Netherlands
4	Newcastle University	**17**	Technical University Munich
5	University of Oslo	**18**	NuGO-A Association
6	University of Navarra	**18**	Keller and Heckman
7	Lund University	**20**	Philips UK
8	University of Reading	**21**	Vitas
9	Crème GlobalSoftware Ltd.	**22**	HLK
10	European Food Information Council	**23**	Porto University
11	National Food and Nutrition Institute, Warsaw	**24**	Bio-Sense
12	TNO Quality of Life	**25**	DSM Nutritional Products Ltd
13	Harokopio University, Athens	**26**	University of Bradford

THE SCIENTIFIC BASIS FOR PERSONALISED NUTRITION ADVICE AND LESSONS LEARNED FROM A PROOF OF PRINCIPLE STUDY

An overview of Work Package 4

INTRODUCTION

A major undertaking of the Food4Me project has been the completion of a Proof-of-Principle (PoP) Randomised Controlled Trial (RCT) on the implementation of personalised nutrition (PN) across seven European centres. The RCT was designed to mimic a real-life internet-based personalised nutrition service and to provide an insight into the effectiveness of PN advice compared with non-personalised "one size fits all" recommendations.

RESEARCH METHODOLOGY

- Study design

The Food4Me PoP study was a four arm, internet-based, 6-month RCT conducted across seven European countries, which compared the effects of different levels of personalised nutrition (PN) on health-related outcomes (http://clinicaltrials.gov/show/NCT01530139)[1].

Hypothesis: Providing personalised dietary advice will improve dietary intakes and markers of health, including weight and waist circumference.

- Primary research questions:

Does PERSONALISATION OF DIETARY ADVICE assist and/or motivate participants to eat a healthier diet in comparison with non-personalised, conventional healthy eating guidelines?

Is PERSONALISATION BASED ON INDIVIDUALISED PHENOTYPIC OR GENOTYPIC INFORMATION more effective in motivating participants to make healthy changes, than personalisation based on diet alone?

- Secondary research question:

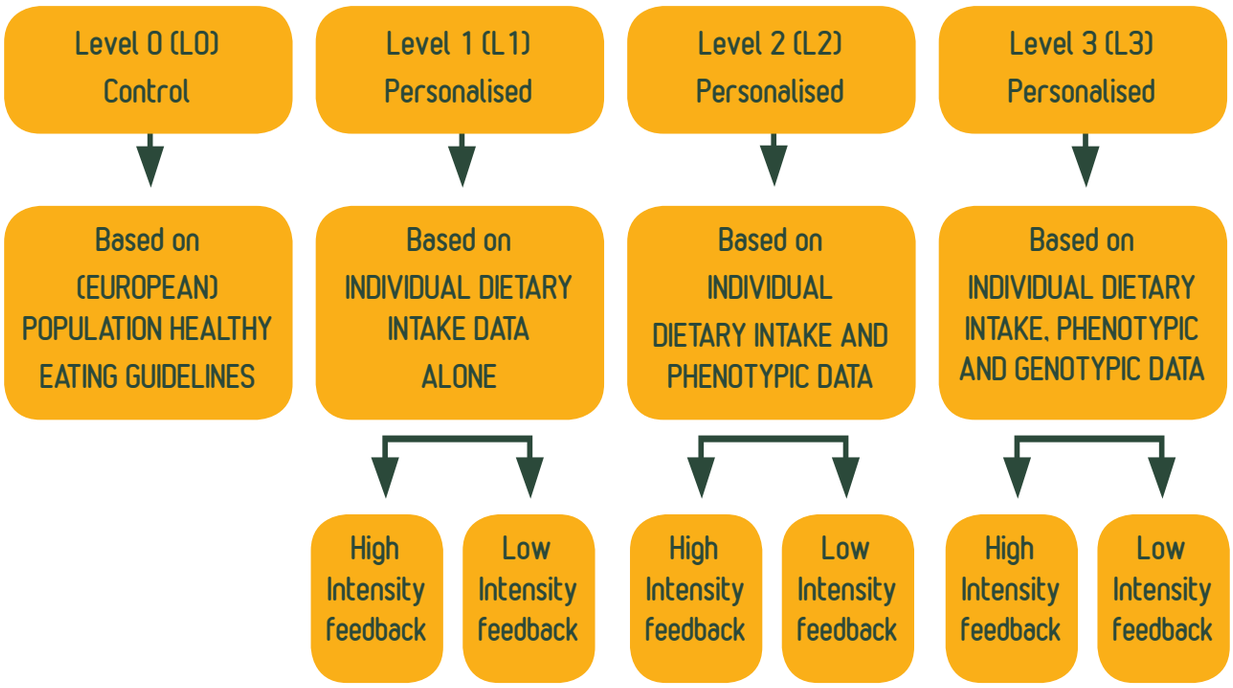
Does
MORE FREQUENT FEEDBACK HELP
PARTICIPANTS TO IMPROVE
their compliance and motivate them to follow a healthier diet and lifestyle in comparison with those receiving less frequent feedback?

INTERVENTION ARMS

To answer the **primary research questions**, participants were randomised to either Level 0 to receive non-personalised dietary advice (control), or *Level 1* (L1), *Level 2* (L2) or *Level 3* (L3) to receive one of three levels of personalised dietary advice. Personalised dietary advice was based on the participant's current diet alone (L1), based on current diet and phenotypic data (L2), or based on dietary advice, phenotypic and genetic data (L3).

Level 1 - Diet	**Current Diet** **Weight, BMI, physical activity**	**Level 1 :** protein, carbohydrates, fats, salt, omega-3, fibre, calcium, iron, vitamin A, folate, thiamine, riboflavin, vitamin B12, vitamin C
Level 2 - Phenotype	**Level 1 + waist circumference + Blood markers**	**Level 1 + waist circumference + blood markers** (glucose, total cholesterol, carotenes, n-3 index)
Level 3 - Genotype	**Level 2 + Genetic markers**	**Level 2 + genetic markers** (MTHFR, FTO, TCF7L2, APOE E4, FADS1 genes)

To answer the **secondary research question**, participants randomised to L1, L2 or L3 were further randomised into *low* (LI) or *high intensity* (HI) intervention groups. LI groups received personalised feedback three times during the intervention (at baseline, month 3 and month 6), whereas HI groups were given personalised feedback five times (at baseline and months 1, 2, 3 and 6). The HI group also had access to an online forum for discussion of topics related to the intervention, had access to personalised recipes and had more personalised feedback on physical activity (PA).



PRIMARY AND SECONDARY OUTCOMES

The primary and secondary outcomes of the study are summarised below.

Primary outcome

Dietary intake at month 6.

Secondary outcome

PA and phenotypic biomarkers at month 6. The latter included obesity-related measures (i.e. body weight, body mass index (BMI) and waist circumference) and blood-based biomarkers (i.e. blood glucose, total cholesterol, carotenoids and fatty-acids).

Interim measure

Interim measures of diet, PA and phenotypic markers were collected at month 3.

RECRUITMENT

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

- **The PoP study recruitment sites were as follows:**

1. National Food and Nutrition Institute Warsaw (Poland)
2. Technical University of Munich (Germany)
3. Maastricht University (The Netherlands)
4. Harokopio University Athens (Greece)
5. University College Dublin (Ireland)
6. University of Navarra (Spain)
7. University of Reading (UK)

RECRUITMENT FLOW CHART

REGISTER ONLINE

Interested individuals registered their details on the Food4Me website **http://www.food4me.org/**

1st SCREENING QUESTIONNAIRE

Age, sex, internet access, pregnancy, food intolerances and allergies

2nd SCREENING QUESTIONNAIRE

Demographic, health, anthropometric and dietary information

SCREENING FFQ

Food Frequency Questionnaire (FFQ) to estimate habitual dietary intakes

ENROLMENT INTO STUDY

Excluded those who were pregnant, lactating, following a prescribed diet or having a food allergy or intolerance or not having access to the internet

BASELINE FFQ DNA AND BLOOD SAMPLE

Participants completed the online FFQ, took anthropometric measurements, started wearing PA monitors and sent buccal swabs and dry blood spot cards to the research team

MONTH 3 FFQ AND PROVIDE BLOOD SAMPLE

Participants in the *high intensity* group also completed the FFQ, anthropometric and PA at Month 1 and Month 2

MONTH 6 FFQ AND PROVIDE BLOOD SAMPLE

Participants were provided with a personalised report (based on diet, phenotype and genotype) regardless of their intervention arm

STUDY DESIGN

ALLOCATION of participants was done by balancing **sex** and **age** ratios. Ratios of no more than 70/30 or 30/70 for males to females and <45 years to >45 years old were permitted.

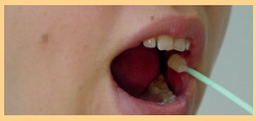
RANDOMISATION to treatment arms was done by country (UK, GRE, ESP, POL, IRE, GER and NL), **sex** (female or male) and **age** (<45 or >45).

ELIGIBLE PARTICIPANTS aged ≥18 years of age were included in the study. To keep the cohort as representative as possible of the adult population a minimal set of exclusion criteria were applied, as depicted below.

PA Monitor

Dietary FFQ

Buccal Swab

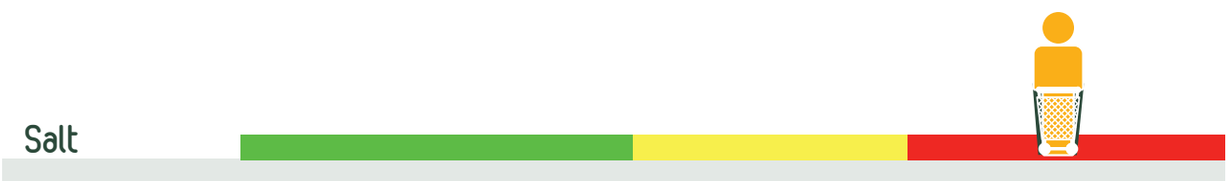


Dry Blood Spot Card

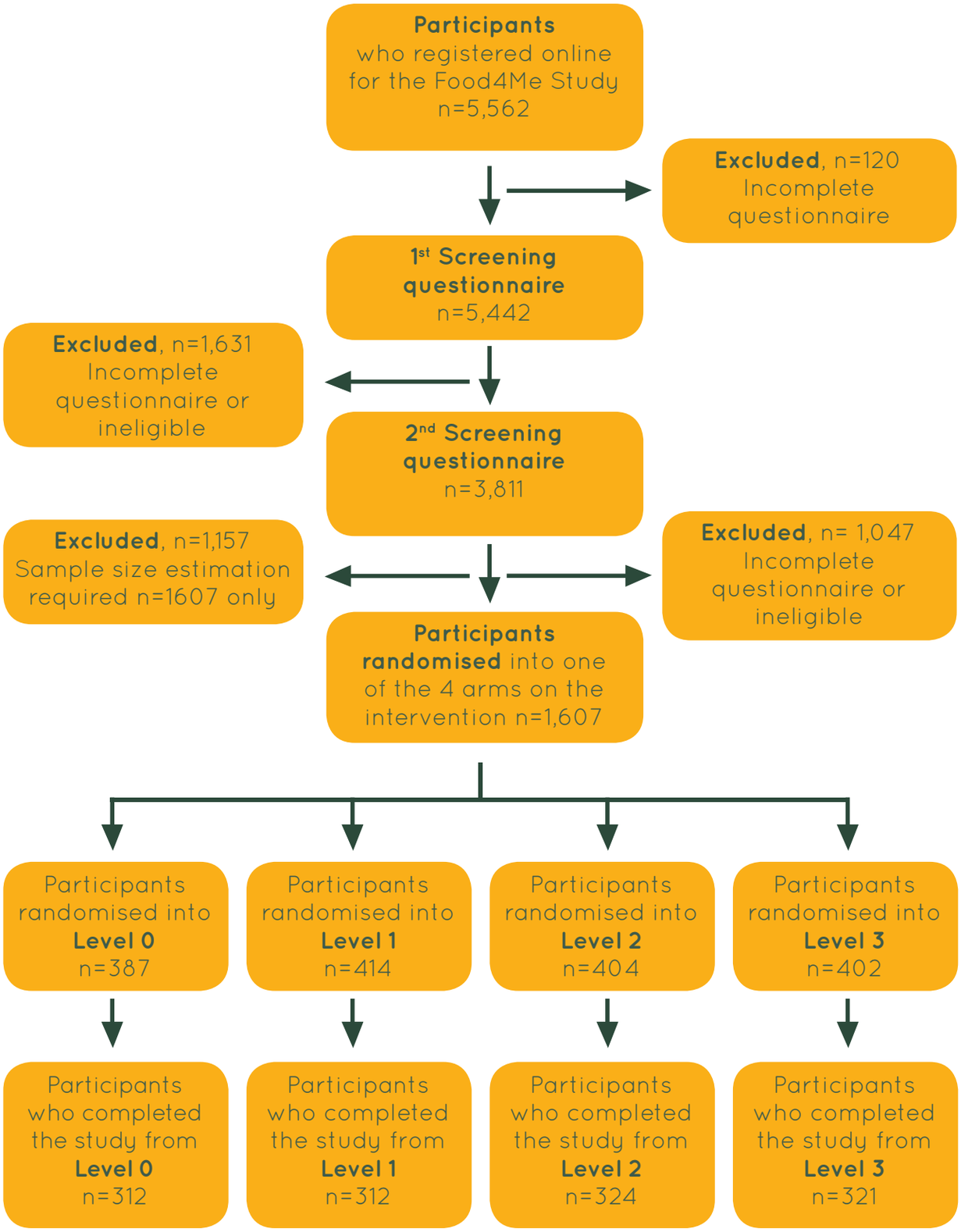
ETHICAL APPROVAL The Research Ethics Committees at each centre delivering the intervention granted ethical approval for the study. Participants completed a **two-stage online consent** process (paper-based for Germany and The Netherlands) prior to submitting personal data and prior to randomisation into the study.

RESULTS

Personalised advice was delivered in the participants' report at baseline and at Month 3. A final personalised report was provided at Month 6 to all participants. Each report provided **three food-based goals.** These goals were selected by ranking all dietary, phenotypic and genotypic markers (as appropriate for the intervention group) based on their risk status (red, amber or green – see below). The cut-off points for each of the nutritional and phenotypic variables were used to derive personalised goals and advice.

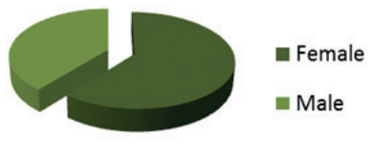


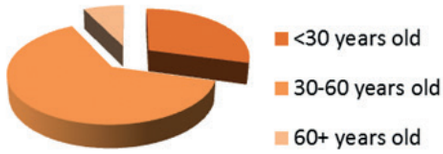
As illustrated below, a total of **5562** individuals registered their name and contact details on the Food4Me website (http://www.food4me.org/). Of the individuals who consented to participate in the study, 65% were female and 64 % were below 45 years of age. A total of **3811** individuals completed the second screening questionnaire. Of these individuals, **one in two adults** were either **overweight or obese**. A total of **1607** participants were randomised into the study.

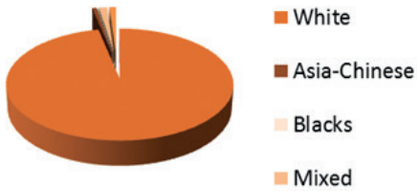


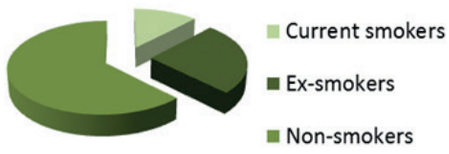
BASELINE CHARACTERISTICS

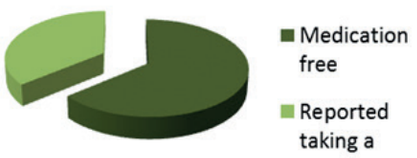
The demographic and anthropometric characteristics of the 1607 individuals randomised into the study are summarised below:

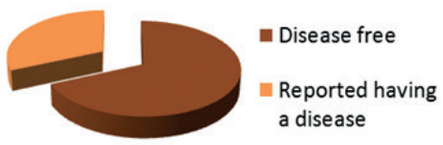








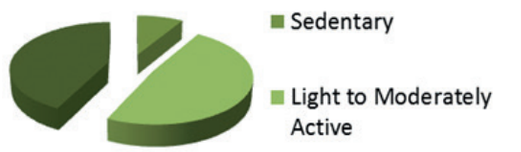




*Diseases were unrelated to nutritional status

1 in **2** adults were overweight or obese

1 in **2** adults were insufficiently active



MAIN OUTCOMES OF THE INTERVENTION

Is
PERSONALISED DIETARY ADVICE MORE EFFECTIVE
than non-personalised advice?

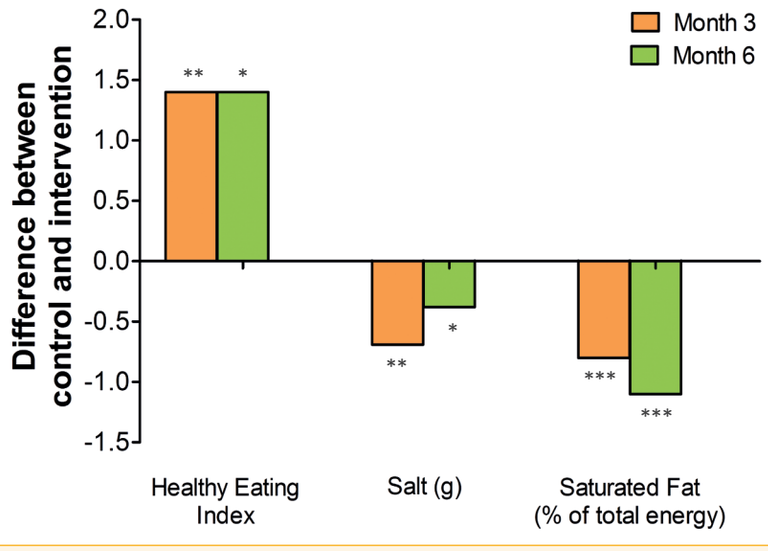
The main dietary outcomes are summarised below. A **Healthy Eating Index (HEI)** was estimated based on a scoring system of the following foods [2]:

Empty calories, fatty acids, proteins, salt, refined grains, whole grains, total fruit, whole fruit, vegetables, greens and beans and dairy products intake.

The HEI is a scoring system designed to evaluate the healthfulness and quality of an individual's diet. These indexes, based on established nutrient requirements and dietary guidelines, can help researchers to evaluate the relevance of an individual's intake of specific foods in a whole diet context [3-5]. Moreover, the scores are easy for clinicians and dietitians to use for monitoring dietary intakes in a clinical setting.

The HEI score has been associated with a lower risk of major chronic diseases[6]. Several studies have demonstrated an association between the HEI and healthy ageing and wellbeing[7], lower incidence of obesity[8], lower risk of total prostate cancer[9] and a reduced risk of all cause, cardiovascular, and cancer mortality[10].

The graph below illustrates the difference in HEI and is expanded using two examples from the pool of nutrients assessed (salt and saturated fatty acid (SFA) intake) between individuals randomised to receive non-personalised advice (control) and those who received personalised advice (mean of L1, L2 and L3) at both month 3 and month 6. After both 3 and 6 months of the intervention, those randomised to PN had a significantly higher HEI than the control group. Intakes of salt and SFA intake were also significantly lower in the PN group at months 3 and 6 of the intervention compared with the controls. (*, P<0.05; **, P<0.01; ***, P<0.001)



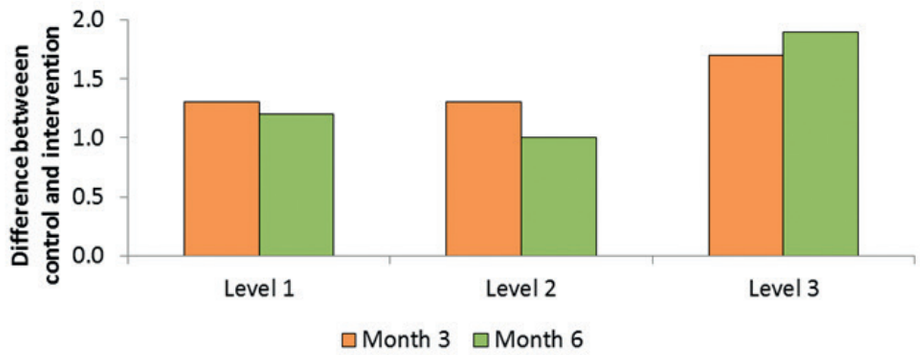
In summary, **participants ate significantly healthier diets after receiving personalised dietary and lifestyle advice** compared with the control group who received non-personalised, population-based advice.

Is
PERSONALISATION BASED ON PHENOTYPE OR GENOTYPE
MORE EFFECTIVE
than personalisation based on diet alone?

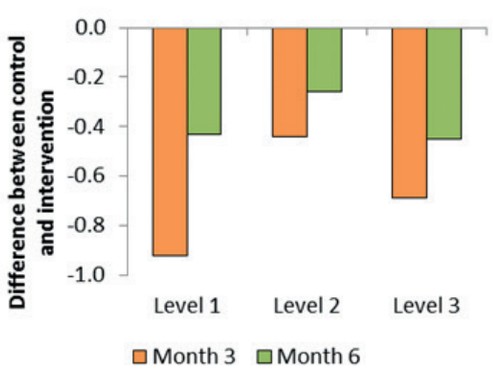
Summarised below are the differences in HEI and the examples of salt intake and SFA intake between individuals randomised to receive non-personalised advice (control) and those who received personalised advice based on either diet alone (L1), phenotype (L2) and genotype (L3) at both month 3 and month 6. After both 3 and 6 months of the intervention, there were no significant differences in HEI or intakes of salt or SFA in individuals who received personalised advice based on their phenotype (L2) and genotype (L3), when compared with advice based on current diet alone.

In summary, **participants who received personalised nutrition advice ate significantly healthier diets** compared with the control, **regardless of whether this personalisation was based on their diet alone, their phenotype or their genotype.** These results indicate a lack of added value from using genomic information to personalise lifestyle-based interventions.

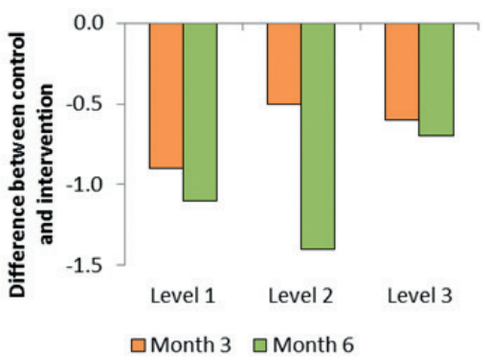
Healthy Eating Index



Salt intake (g)



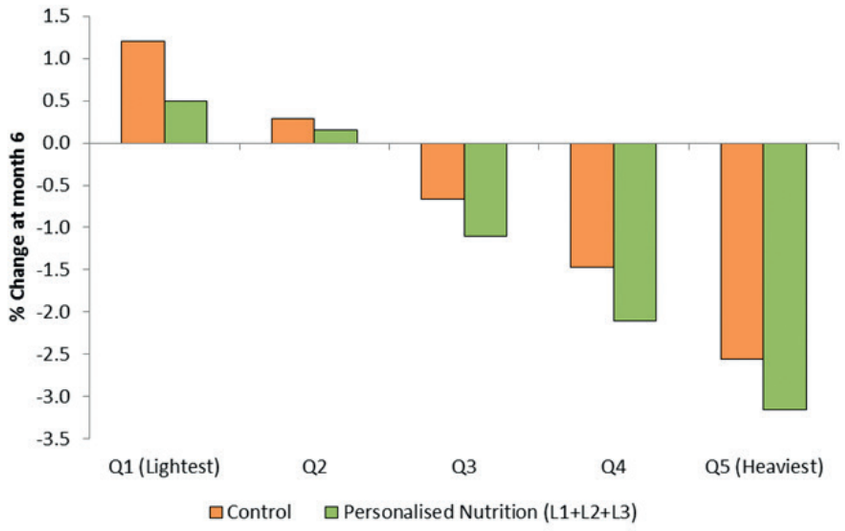
Saturated fat (% of total energy)



Will the
EFFECT OF PN ADVICE ON BODY WEIGHT CHANGE DIFFER BETWEEN INDIVIDUALS
with different starting body weights

The graph below indicates the change in body weight between baseline and Month 6 according to the body weight of individuals at baseline (lightest weight (Q1) to heaviest weight (Q5)). Individuals who were underweight gained over 1% of their body weight, compared with individuals who were overweight or obese, who lost up to 3.5% of their body weight.

Change in body weight between baseline and Month 6



TAKE HOME MESSAGES

IMPLICATIONS OF THE RESULTS

The Food4Me PoP study results have the following implications:

1. With a validation study (n=140) showing high agreement between self-reported and measured anthropometric markers, sex and identity, an internet-based platform can be used to collect reliable and accurate measurements of dietary and anthropometric characteristics.

2. We demonstrated that an internet-based PN intervention can be highly effective in recruiting and retaining participants for at least 6 months across seven European countries.

3. PN advice is effective in improving dietary behaviours compared with conventional, population-based advice.

4. We saw no evidence that adding phenotypic or genotypic data to the information used to develop and deliver PN advice enhanced the effectiveness of the intervention based on analysis of current eating habits.

5. PN advice delivered via the internet offers promise as a scalable and effective route to improving dietary behaviours, which may have important public health benefits.

DEVELOPING THE STATE OF THE ART

The Food4Me PoP study has developed the state of the art by:

Developing the evidence base for, and practical approaches which can be used to implement, three levels of PN advice (based on diet, phenotype and genotype) in large-scale intervention studies designed to improve dietary habits.

Undertaking a pan-European test of the effectiveness of PN in a large representative sample of European adults.

Demonstrating the utility of an Internet-based platform for delivering dietary and lifestyle-based PN advice and for supporting and motivating the public to make sustained improvements in eating patterns.

WHAT GAPS IN KNOWLEDGE STILL REMAIN?

The following areas require further investigation:

1. Are three nutrient-related goals optimum in promoting improvements in diet via internet-delivered PN?

2. Are there additional characteristics (beyond diet, phenotype and genotype), which could be included in PN interventions to improve their effectiveness in changing lifestyle behaviours? For example, characteristics such as current conditions (e.g. diseases), psychological characteristics, socio-economic class and ethnicity.

3. Could more engagement with participants e.g. via social media, enhance motivation and improve behavioural changes?

4. What additional feedback mechanisms e.g. home monitoring of physiological responses, could help motivate participants to make appropriate lifestyle changes?

5. Are the improvements in dietary behaviour, which we observed after 6 months intervention, sustained long-term?

HOW COULD THESE EFFORTS FEED INTO HORIZON 2020 RESEARCH CALLS?

Findings from the Food4Me PoP study will inform future PN interventions and services. The internet-based design of the study will feed into the development of future e-Health services, which are addressed in various Horizon 2020 research calls. These non-invasive, internet-based tools will feature the self-assessment of diet and lifestyle factors and will include the remote collection of biological samples. As a result, future interventions will be able to reach a larger number of individuals and will be a more cost-effective strategy for improving the health and wellbeing of populations than traditional face-to-face interventions. The platform which we have developed could be tailored to address the needs of particular population groups e.g. the overweight and obese or those with particular diet-related diseases such as type 2 diabetes.

In addition, our demonstration that the concept of PN is viable and that it produces bigger and more appropriate changes in diet means that this approach could be a feature of future health care provision and Horizon 2020 research calls. The Food4Me PoP study was the first study to compare the effectiveness of PN advice at the level of diet, phenotype and genotype and to demonstrate that it could be implemented via the internet in multiple European countries. With rates of non-communicable diseases, such as cardiovascular disease and cancer, and obesity at epidemic proportions, the encouraging results from the Food4Me PoP study will stimulate the development and testing of more PN interventions and services to address these societal challenges.

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REFERENCES

1. Celis-Morales C, Livingstone K, Marsaux CM, Forster H, O'Donovan C, Woolhead C, Macready A, Fallaize R, Navas-Carretero S, San-Cristobal R, Kolossa S, Hartwig K, Tsirigoti L, Lambrinou C, Moschonis G, Godlewska M, Surwiłło A, Grimaldi K, Bouwman J, Daly EJ, Akujobi V, O'Riordan R, Hoonhout J, Claassen A, Hoeller U, Gundersen T, Kaland S, Matthews JS, Manios Y, Traczyk I, et al. Design and baseline characteristics of the Food4Me study: a web-based randomised controlled trial of personalised nutrition in seven European countries. Genes Nutr. 2014,1:1-13.

2. Guenther PM, Casavale KO, Reedy J, Kirkpatrick SI, Hiza HAB, Kuczynski KJ, Kahle LL, Krebs-Smith SM. Update of the Healthy Eating Index: HEI-2010. Journal of the Academy of Nutrition and Dietetics. 2013,4:569-80.

3. Kant AK. Dietary patterns and health outcomes. J Am Diet Assoc. 2004,4:615-35.

4. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol. 2002:3-9.

5. Fransen HP, Ocké MC. Indices of diet quality. Curr Opin Clin Nutr Metab Care. 2008,5:559-65.

6. Chiuve SE, Fung TT, Rimm EB, Hu FB, McCullough ML, Wang M, Stampfer MJ, Willett WC. Alternative Dietary Indices Both Strongly Predict Risk of Chronic Disease. The Journal of Nutrition. 2012,6:1009-18.

7. Samieri C, Sun Q, Townsend MK, Chiuve SE, Okereke OI, Willett WC, Stampfer M, Grodstein F. The relation of midlife diet to healthy aging: a cohort study. Annals of internal medicine. 2013,9:584-91.

8. Boggs DA, Rosenberg L, Rodríguez-Bernal CL, Palmer JR. Long-Term Diet Quality Is Associated with Lower Obesity Risk in Young African American Women with Normal BMI at Baseline. The Journal of Nutrition. 2013,10:1636-41.

9. Bosire C, Stampfer MJ, Subar AF, Park Y, Kirkpatrick SI, Chiuve SE, Hollenbeck AR, Reedy J. Index-based Dietary Patterns and the Risk of Prostate Cancer in the NIH-AARP Diet and Health Study. American Journal of Epidemiology. 2013,6:504-13.

10. Reedy J, Krebs-Smith SM, Miller PE, Liese AD, Kahle LL, Park Y, Subar AF. Higher Diet Quality Is Associated with Decreased Risk of All-Cause, Cardiovascular Disease, and Cancer Mortality among Older Adults. The Journal of Nutrition 2014 6:881-9.

TECHNICAL DEVELOPMENTS MAKING PERSONALISED NUTRITION OFFERINGS POSSIBLE

An overview of Work Package 3

1 INTRODUCTION

By definition, any type of service can only be personalised if appropriate information about the individual is available. Personalised nutrition services rely on knowledge of food choices or total food intake usually recorded by food frequency questionnaires and on phenotypic data (such as gender, age, body height, body mass, physical activity). This may also be extended to include other measurements such as blood glucose, or cholesterol levels or blood pressure reflecting the health status. Not required but easily available nowadays is the analysis of the genetic background by profiling single nucleotide polymorphisms (SNPs) or in the future by exome or whole genome sequencing. Collected data in turn need to be evaluated from a health perspective including questions related to weight management as a key motivator and determinant of compliance to these services. Assessment of the individual's life style – particularly dietary habits and physical (in)activity – are the leading themes as they provide the closest link to the nutrition-related chronic diseases like diabetes, coronary heart diseases, or cancers. Possible nutrient deficiencies or at least intakes below the recommendations are also addressed, if identified. Finally, analysis needs to be translated into comprehensible, feasible, and maybe even enjoyable recommendations for life style changes, taking into account identified constraints such as food allergies and intolerances, or simply food dislikes, via questionnaires.

Within this framework and as a pillar in Food4me, work package 3 (WP3) defined a panel of anthropometric and other measurements needed to define the phenotype, did a scouting of emerging technologies for better phenotyping, developed a data base for validated gene-nutrient-health interactions and developed tools such as a meal coding system and a menu-planning module for future applications in personalised nutrition.

2 RESEARCH METHODOLOGY

• 2.1 Data collection

It was the prime responsibility of WP3 to identify and implement data collection approaches that provide valid information about the participant, collected at home, i.e. without any support by experts such as dietitians, nurses, or medical doctors. Work thus included the development of methods for collecting various types of personal data and phenotypic measures and the provision of information material (descriptions, instruction videos) on how to do the measurements for the volunteers in the different countries. In addition, the practicability (ease to use) of the methods, and the validity and coherence of the data collected, was assessed.

2.1.1 Dietary habits and food preferences

Food frequency questionnaires (FFQ) are currently the preferred dietary assessment approach to capture information on long-term food consumption, i.e. dietary habits. The Food4me FFQ

was developed on the basis of the EPIC study FFQ which gathers information on the frequency of the consumption of approximately 150 food items. It was designed as a web-based dietary assessment tool and incorporated into a software system that supports researchers in recruiting and managing study participants, including enrolment, randomisation, and communication. (Fallaize et al. 2014; Forster et al. 2014)

2.1.2 Nutrient intakes

Frequencies of food consumption can be converted into estimates of nutrient intakes, if information on portion sizes and nutritional composition of food items is available. Such data can be obtained from national dietary intake data bases. In the food4me study, an Irish nutrition database (2008-2010 National Adult Nutrition Survey (NANS) database, Forster et al. 2014) was used to form the basis of the food composition data; this was then expanded to be applicable across 7 EU countries. An automated system was designed to convert food intake data into nutrient information in the context of an individual's nutrient requirements.

2.1.3 Anthropometric measures

Anthropometric measures such as body height and body mass, as well as upper leg circumference and the waist-to-hip ratio, were identified as relevant information for phenotyping and for assessing some critical health parameters (for example waist-to-hip ratio as an established risk factor in the metabolic syndrome). In supporting participants of Food4me to provide such data in a valid and consistent way, instruction sheets, demonstration videos, and lists of frequently asked questions (FAQs) with respective answers were developed and made available (Figure 1).

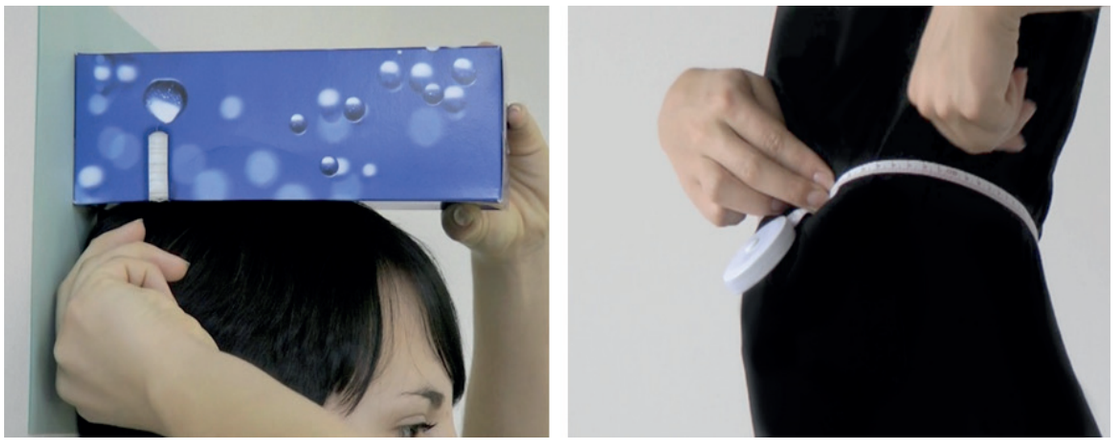

Figure 1: Example instruction pictures provided to participants on how to do anthropometric measurement.

2.1.4 Biomarkers of health

Biomarkers can provide useful additional information on an individual's heath status, independent of any person-related biases (e.g. recall or interviewer biases). Food4me used dried blood spots (DBS) to profile nutrient status and derive some health-related biomarkers such as cholesterol levels. DBS provide a convenient and inexpensive way of collecting blood samples. For this, subjects are asked to use finger-pricks and fill predefined spots on particular filter cards with drops of blood, dry the cards at room temperature, put them in airtight foil (aluminium) bags, and return them by post to the corresponding research centres (Figure 2). The samples were used for measurements of numerous parameters including total cholesterol, selected carotenoids, vitamin D, and a wide variety of fatty acids. (Celis-Morales et al. 2015)

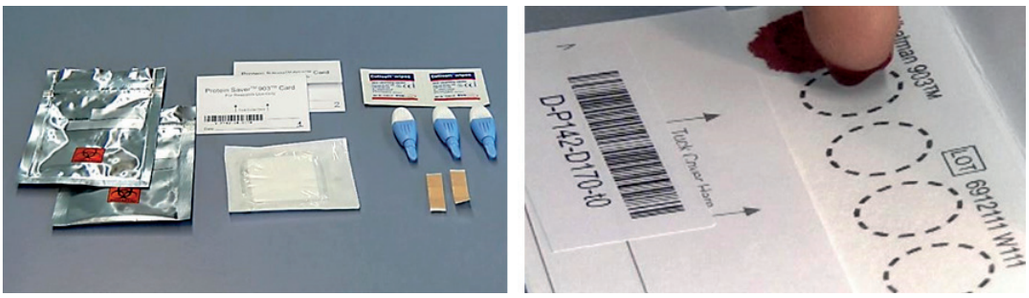

Figure 2: Materials provided to participants for DBS sampling.

2.1.5 Extended phenotyping - scouting for new methods and tools

Classic anthropometric measurements such as determination of body mass and height, or waist-to-hip ratio provide easy, inexpensive and yet sufficiently reliable information for describing an individual's basic phenotypic features. But, in recent years, new electronic tools for more extensive phenotyping have appeared on the market which may prove useful for personalised nutrition services. Such technologies comprise mobile applications (Apps), websites and electronic devices for determining body parameters, self-tracking and lifestyle interventions. The Apps work either independently and show simply the evaluation of data entered by the user, or they interface with an external measuring device connected via Bluetooth or via the charger docking port to a smart-phone that allows the assessment of parameters such as blood pressure, blood glucose concentration, sleep quality, heart rate, energy expenditure, or exercise intensity. For some devices it is claimed that they can determine arterial stiffness, others claim to be able to measure antioxidant status in skin. Other devices with a sensor coupled to a smartphone determine excretion of distinct metabolites in urine to assess vitamin status.

2.1.6 Genotypic information

Genotypic information in Food4me was obtained from buccal cell samples that were provided by subjects using DNA buccal swabs. Participants received detailed instructions on how to collect the sample. The material was used for DNA extraction and genotyping of about 30 SNPs in predefined loci using KASPTM genotyping assays to provide bi-allelic scoring (Celis-Morales et al. 2015).

• 2.2 Data evaluation

When individual data on genetic predisposition (SNP´s) in the context of diet and health are used in personalised nutrition services, a key question is on how valid scientific findings are that link dietary intake and genetic variation to health outcomes. For this purpose, a scientific knowledge base was developed, capturing the current knowledge in the field of nutrition with a particular focus on the interaction of food consumption, nutrient intakes, biomarkers, genetic variation to health. SNP information comprises risk allele frequencies as well as gene symbols and functions. The collected scientific knowledge represented in the data base covers currently 35 food items, 92 biomarkers, 36 genetic variations, 16 different health outcomes, and 180 established interactions based on scientific publications and an expert assessment. The knowledge base is a tool that can be used to define desirable ranges for a multitude of health parameters that may serve as a basis to decide on what dietary changes may be advisable.

• 2.3 Recommendations

The aim of personalised nutrition services is to advise or provide services or products considering a person's individual needs and preferences. In large scale applications, this

approach will become laborious and costly. It might therefore be more efficient to provide services tailored to the needs of "nutritypes" as clusters of persons with similar features (food intake patterns, similar risk factors etc.) rather than to every single individual.

2.3.1 Individualised recommendations

Based on the participants' dietary habits and health parameters, recommendations on advisable dietary changes were developed. Personalised nutrition advice can be given at the level of foods (e.g. your folic acid is low, eat more green leafy vegetables), at the level of recipes (e.g. your folic acid is low, here is a recipe for a spinach pie that will boost your intake) and ultimately at the level of meals (e.g. your folic acid is low, here is a combination of meals for a certain period of time that will help boost your intake).

2.3.1.1 Food and nutrient based recommendations

A set of algorithms was developed to translate phenotypic as well as genotypic data into recommendations for nutrient intake. These algorithms are comprised of a series of decision trees that lead from a specific phenotypic and/or genotypic characteristic to a concise recommendation to alter nutrient intake. These decision trees were developed in an iterative process also taking into account the experiences made within the Proof-of-Principle (PoP) study (see WP 4). Out of these recommender systems, conflicting or at least inconsistent recommendations may originate. A frequent example is to decrease consumption of dairy products for lowering intake of saturated fatty acids and simultaneously recommending an increased intake of dairy when calcium intake is low. Within Food4me, these flaws were systematically identified and eliminated. The decision trees employed in the PoP study have meanwhile been automated using a MySQL database and incorporated into a web interface (Advice4me) that can be used to generate personalised dietary advice. The anthropometric, dietary and genotype data of a participant at a certain measurement moment as collected from the PoP study serves as input for the Advice4me system. Nutrient values outside certain threshold values are automatically flagged and, based on a complex prioritisation approach, three target nutrients are selected. For each of these, the appropriate decision tree is automatically executed resulting in a set of advice codes that are linked to specific diet related messages available in several languages.

2.3.1.2 Recipe based recommendations

A personalised recipe advice system (Recipe4me) was developed which adapted food based dietary recommendations to the individual preferences. It aims at bridging the often seen gap between intentions and execution of behavioural changes in healthy eating. Recipe4me provides guidance in the form of tailored recommendations of recipes based on personalised dietary advice. It is a web-based recommender system and cooking guide offering personalised recipe suggestions. Recipe4me comprises a database of 1100 recipes, which were made available by the partners in the project. Along with each recipe, information is available on nutritional composition, cooking instructions, and preparation time. The recommender picks recipes from the database that are in line with a person's dietary needs and preferences.

2.3.1.3 Meal based recommendations

Finally, dietary recommendations were also developed on the level of meals and overall dietary pattern, aiming at providing personalised nutrition in a more holistic and particularly more user-friendly manner. The menu based recommender system includes a questionnaire assessing an individual's food preferences including favourite dishes but also specific dietary needs (e.g. due to potential intolerances or allergies). Based on such information and on the evaluation of the individual dietary habits, personalised menu plans are produced consisting of different recipes

for a certain period of time. These menu plans are designed to meet the user's individual dietary requirements as well as preferences. Next to a recipe database, meal based recommendations require algorithms to estimate individual dietary needs, to select individually acceptable recipes and to arrange recipes to meals and days using Pure Integer Linear Programming.

2.3.2 Recommendations based on "nutritypes"

Providing personalised nutrition services to "nutritypes" rather than to individuals would allow less demanding processes required to "personalise" recommendations. A prerequisite is that such clusters of metabolically similar individuals can be found and this requires comprehensive phenotyping. This was exemplarily done in an Irish cohort (n=896) using a K-means clustering approach on basis of a wide range of phenotypic parameters (including plasma levels of glucose, LDL-cholesterol, apolipoproteins, or C-reactive protein) and genotypic information. A targeted dietary advice system was developed for each cluster using a decision tree/algorithm approach and these cluster-related recommendations were compared to the individual based recommendations of the persons within each cluster.

3 KEY FINDINGS

Key findings of the various activities under the umbrella of workpackage 3 can be grouped into the following five categories.

• 3.1 Coherence of collected data

The validity of the various types of data remotely collected and provided by the volunteers via the website was evaluated based on their self-consistency across different measurements. Anthropometric data revealed, for instance, that males have a higher waist-to-hip ratio than females (mean values 0.96 vs. 0.82) while both, males and females displayed reasonable median waist circumferences of 0.96 m and 0.81m respectively (Figure 3). The inter quartile ranges imply well compatible waist and hip measurements for the majority of participants of the PoP study. Measurements of body mass index (BMI) and waist circumference also show a rather strong and highly significant correlation ($r = .82$). Significant positive correlations were also found for food consumption data as obtained by FFQ and biomarkers in blood, e.g. consumption of oily fish with blood levels of omega-3 fatty acids ($r = 34$; $p < .0001$) or consumption of fruit and vegetables with blood carotenoid levels ($r = 24$; $p < .0001$).

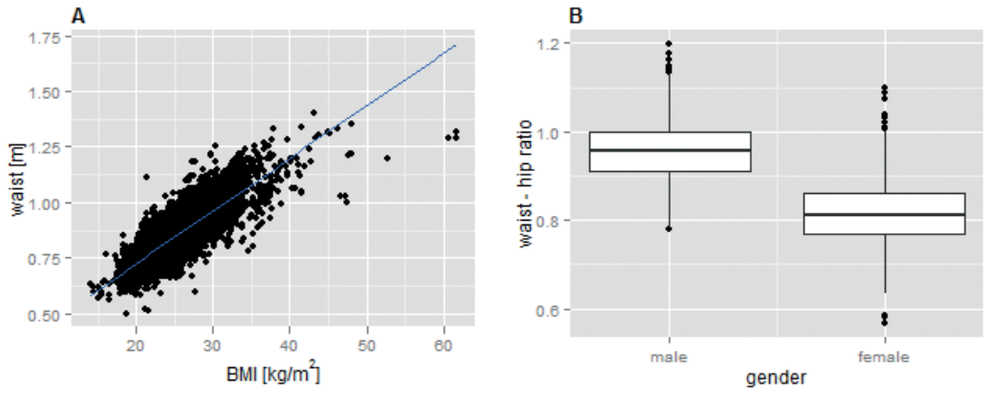

Figure 3: A: Relationships found between self-reported BMI [kg/m2] and waist circumference [m], n = 4021. B: box-whisker plot of waist-to-hip ratios for male and female participants, n = 2310 females, n = 1691 males. All time points accumulated.

• 3.2 Feasibility of self-monitoring

For assessing whether the self-monitoring and reporting including the dried blood spot sampling caused major problems or was felt to be a particular burden, a post-hoc evaluation of the Proof-of-Principle study was performed in three countries. The feed-back provided showed that home-based sampling of phenotypic data was widely accepted by the participants. The vast majority did not feel the need for help in taking the anthropometric measurements (77 %) or collecting blood samples (78 %); and the blood sampling procedure was not considered as very hard (78 %). Moreover, no indication for deterrent effects in participation in similar studies was obtained (81 %) which is important information for future projects.

• 3.3 Scouting for new and emerging phenotyping tools

The scouting for new and emerging phenotyping tools revealed a highly dynamic market of products with rapid appearance of new devices but also with rapid disappearance of others. A key issue is the claimed function, the accuracy and reliability of the devices. Collected data are often questionable since most of the devices have never been tested for validity of claimed output measures and for some even the principles on which measurements are based did not become available for justification of feasibility. Exceptions are some of the widely-used physical activity monitors (PAMs), for which in recent months various scientific papers describe their usefulness and reliability (e.g. Berendsen et al. 2014; Calabró et al. 2014). Most of the PAMs employ built-in accelerators that can recognise the type of physical activity via pattern recognition analysis, and most of them also provide a decent estimation of energy expenditure.

• 3.4 Menu Planning Recommender System

Pure Integer Linear Programming was employed and proved useful to generate a menu plan for the user, on the basis of nutrient-based recommendations but also by taking individual food preferences into account. The developed recommender system is capable of providing a one-week-menu plan either categorising the menus by pattern (i.e. breakfast, main meal, light meal and snacks) or by assigning individual meals and servings to the days of the week.

• 3.5 Identification of "nutritypes"

Three distinctly different "nutritypes" were identified by clustering in the Irish cohort, profiled for a large set of markers. Cluster 1 had the lowest BMI and the lowest levels of the tumor necrosis factor (TNF) alpha (a marker of inflammation). Cluster 2 was identified as the healthiest group having the most favourable levels in relation to markers of metabolic health such as insulin, c-peptide and adiponectin levels. Finally, Cluster 3 was characterised as having the highest body mass and the most "unhealthy" metabolic profile. Those "nutritypes" were than considered as if they were three individuals and respective dietary advice was created and elaborated. A comparison of the advice given to the "nutritypes" with the advice that would have been given to the individuals assigned to those clusters showed a good agreement of both approaches. The average match between messages reached 88%, and for two thirds of the individuals there was even a 100% match between the "nutritype" and the individual dietary advice approach. This indicates great potential for such an approach in a clinical setting by enabling the provision of tailored dietary advice when it may otherwise have been unfeasible.

4 IMPLICATIONS OF THE RESULTS

The Proof-of-Principle study in Food4me demonstrated that collecting phenotypic and food intake data remotely via the internet is possible and can deliver coherent and high quality data.

The concept of a web-based study was introduced by Hercberg et al. (2010) as a prospective study (still ongoing) with the recruitment of 500,000 study participants in France. This study focuses on the relation of nutrition and health and dietary patterns in a long-term perspective. Despite having less volunteers, Food4Me has taken this concept further by collecting all data and samples remotely, including blood and DNA specimens, for more comprehensive phenotyping and by providing personalised advice.

The advantages of such studies are clear. Collecting all information remotely as well as digitised and with at-home sampling of DNA and biosamples such as DBS has unquestionable advantages, both on grounds of costs as well as of logistics. There is no need to bring study participants into a research facility with the requirement to have a physician or nurse at hand for collecting blood and also for volunteer insurance coverage. Authenticity of the information and biological samples provided has of course to be assured and future studies may include other measures for proving identity (pictures). The huge advantages of DBS are the minimally invasive sampling (which is well accepted), and storage of samples which is easy to do and cheap. The drying process simultaneously provides a high stability of most analytes. DBS analysis can provide information on markers of health, on the nutritional status and can also reveal food intake information with compliance assessment via markers of exposure such as carotenoids or fatty acid patterns. In the future, DBS may also be used as a DNA source for genotyping as it can easily be done from the blood sample. The current limits in using DBS are validation of the measurements, and to ensure that findings are comparable to those of classical venous blood samples. This applies in particular to the biomarkers such as blood cholesterol or blood glucose, with the latter identified as not sufficiently stable in DBS within the Proof-of-Principle study.

The work in Food4me has also demonstrated that nutrient-based recommendations can be translated into food-based recommendations or even a menu-plan by also taking individual likes and dislikes into account. The underlying algorithms of the recommender systems are applicable in future studies dealing with dietary recommendations on different levels. The underlying data processing and recommender algorithms may also be improved by machine learning approaches.

5 DEVELOPING THE STATE OF THE ART

There can be no doubt that all tools developed by and/or employed in the Proof-of-Principle study of Food4me need refinements and extensions. This applies to both the assessment of dietary habits and food intake, as well as the measurements of biomarkers from DBS, but also to the recommender systems development. Tools to collect information, including the electronic devices, need to be validated and this applies in particular to emerging new instruments coupled to smart-phones for measuring for example blood pressure or blood glucose, as well as for other phenotypic features with data transmission into a database or cloud. Since different providers utilise different output routes and formats, the inclusion of multiple devices for online monitoring in future studies is a challenge. Affordability of the devices for inclusion into large scale studies is also a limiting factor. There is still a huge challenge in all diet and lifestyle studies to assess food intake with the necessary precision and without too many constraints such as underreporting using FFQs either in paper or web-based form. A new and promising tool for dietary assessment may be the use of photos taken from individual foods or menus coupled to image analysis to extract information on the type of food and the corresponding volume or weight for calculation of nutrients consumed. This is in development in the framework of the TADA (technology assisted dietary assessment) project under the patronage of Purdue University (see Schap et al., 2014). Despite the current limitations of the various assessment tools, huge interest has been generated by media coverage of the Food4me study, with requests for employment of these tools in other types of research studies or even in commercial applications.

6 WHAT GAPS IN KNOWLEDGE STILL REMAIN?

Despite the fact that we do not know yet the effect sizes caused by changes in food intake and lifestyle following the personalised advice as provided in Food4me, it can be anticipated that such approaches need long term support of participants/customers to generate sustainable changes. Models and studies to test how this can be achieved need to be developed and this may also include novel reward systems to keep up interest and motivate the participation of health insurances or other health care providers, for example.

Despite enormous efforts over the last decade to identify gene variants that define the susceptibility of an individual to a life-style dependent disease, the outcomes of the large-scale profiling studies are rather disappointing. Although a large number of genes and variants have been found (there are for example around 60 genes that carry a susceptibility risk to develop type 2 diabetes mellitus (T2DM)), the effect sizes of each individual gene variant are generally very low. In almost all cases, the risk-variant increases disease risks by only a very few percent. Since there are additive effects of the gene variants, future applications of genotyping in personalised nutrition need to include many more genes for a single disease entity such as T2DM, requiring then also a "staged" risk assessment profile. Although genotyping may not be considered as important for providing individualised nutrition advice, it is obvious that genotyping will become available and affordable for everybody in due time. Moreover, technical developments may make genotyping available for everyone without expert service by portable devices (see Nanopore technologies). In addition to exome or whole genome sequencing that will also be available at low cost or even for free, sequencing of the gut microbiota is also emerging as a service that builds on research suggesting a prominent role of the bacterial population in the human gut in health and disease.

The most critical aspect of genotyping (of whatever specific approach) when included into personalised nutrition programs is that statistically identified population risks are taken to predict an individual's risk and thus its fate. Research for identifying associations between gene variants and nutrition/lifestyle and disease susceptibility is usually done in cohort studies comprising thousands of individuals observed over long time periods. This means that disease-related relative risks can be calculated from the disease trajectories combined with genotyping and those are now projected onto individuals carrying the same gene variants and that is the current weakness in the entire approach. This means that for most of the relevant gene variants, the proof that the recommended changes in diet or lifestyle indeed have beneficial gene-specific effects on health, has not been established. It thus needs many more studies that assess the effects of diet or lifestyle changes on background of individual and preselected genotypes on health outcomes (or intermediate disease biomarkers that relate to health outcomes) in a prospective design. This should be the "guiding principle" for any future research and for providing a more valid basis for personalised nutrition approaches.

7 HOW COULD THESE EFFORTS FEED INTO HORIZON 2020 RESEARCH CALLS?

The tools that have been applied or developed in Food4me (for example, the different knowledge bases, the recommender systems or the DBS measurements) can easily be transferred to similar studies or to other types of personalised nutrition services. Although the Proof-of-Principle study employed only electronic physical activity monitors, it is evident that numerous other devices described above can be very helpful in the future for more comprehensive phenotyping, in particular in settings in which volunteers (or customers) do self-assessment. The numerous offerings for electronic devices meet the growing interest of consumers to observe, monitor and quantify body functions including cognitive performance and mental state. The emerging m- and e-health (health supported by mobile or electronic

devices) domains are vital research areas and are addressed by various Horizon 2020 calls in 2014 and they also include the development of devices, such as mobile devices, that record and report a patient´s health status. Non-invasive or minimally invasive monitoring devices will become important tools in future nutrition research as well, as they allow novel study designs, enable large scale studies without the need to bring volunteers into study units. They also provide an immediate feed-back to the study participant on changes in body functions, that can increase compliance and foster motivation, for example for lifestyle interventions. Undoubtedly, tools developed by and the experiences collected in Food4Me will find their ways into project proposals under Horizon 2020.

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9 REFERENCES

Berendsen BA, Hendriks MR, Meijer K, Plasqui G, Schaper NC, Savelberg HH (2014): Which activity monitor to use? Validity, reproducibility and user friendliness of three activity monitors. BMC Public Health 14:749

Calabró M, Lee JM, Saint-Maurice PF, Yoo H, Welk GJ (2014): Validity of physical activity monitors for assessing lower intensity activity in adults. Int J Behav Nutr Phys Act. 11(1):119

Celis-Morales C, Livingstone KM, Marsaux CF, Forster H, O'Donovan CB, Woolhead C, Macready AL, Fallaize R, Navas-Carretero S, San-Cristobal R, Kolossa S, Hartwig K, Tsirigoti L, Lambrinou CP, Moschonis G, Godlewska M, Surwiłło A, Grimaldi K, Bouwman J, Daly EJ, Akujobi V, O'Riordan R, Hoonhout J, Claassen A, Hoeller U, Gundersen TE, Kaland SE,

Matthews JN, Manios Y, Traczyk I, Drevon CA, Gibney ER, Brennan L, Walsh MC, Lovegrove JA, Alfredo Martinez J, Saris WH, Daniel H, Gibney M, Mathers JC. (2015): Design and baseline characteristics of the Food4me study: a web-based randomised controlled trial of personalised nutrition in seven European countries. Genes Nutr. 10(1): 450

Fallaize R, Forster H, Macready AL, Walsh MC, Mathers JC, Brennan L, Gibney ER, Gibney MJ, Lovegrove JA (2014): Online dietary intake estimation: reproducibility and validity of the Food4me food frequency questionnaire against a 4-day weighed food record. J Med Internet Res. 16(8):e190

Forster H, Fallaize R, Gallagher C, O'Donovan CB, Woolhead C, Walsh MC, Macready AL, Lovegrove JA, Mathers JC, Gibney MJ, Brennan L, Gibney ER (2014): Online dietary intake estimation: the Food4me food frequency questionnaire. J Med Internet Res. 16(6):e150

Hercberg et al. (2010): The Nutrinet-Santé Study: a web-based prospective study on the relationship between nutrition and health and determinants of dietary patterns and nutritional status. BMC Public Health. 10:242

Schap et al. (2014): Merging dietary assessment with the adolescent lifestyle. J Hum Nutr Diet. 27 Suppl 1:82-88Consumer

ATTITUDES TO ADOPTION OF PERSONALISED NUTRITION
Overview of Work Package 2

INTRODUCTION

The debate about implementation, and subsequent realisation of the public health benefits of personalised nutrition, is dependent on empirical analysis of consumer preferences for its implementation. It is also important to recognise that some consumers may be reluctant to adopt personalised nutrition, and understanding barriers to adoption will facilitate the "fine-tuning" of delivery to optimise consumer uptake. Research activities in workpackage 2 focused on understanding the specific needs of consumers with respect to personalised nutrition and its delivery to consumers, as well as identification of those factors (both psychological and pragmatic) which prevent consumers taking advantage of personalised nutrition.

Primary Objective: understand consumer behaviour and preferences with respect to personalised nutrition

The **primary objective was to understand consumer behaviour and consumer preferences** with respect to the implementation of personalised nutrition. The research also aimed to identify which factors related to consumer decision-making will ensure that the benefits of personalised nutrition impact upon both upon the **competitiveness of the European food industry** (for example, in relation to the viability of SMEs or other agrifood industries with interests in exploitation of personalised nutrition) and the health and well-being of the European citizen (for example, the inclusion of personalised nutrition in health policies and other health promotion activities).

Secondary Objective: develop a theoretical model of the factors influencing consumer decisions about personalised nutrition

The secondary objectives were to develop a theoretical model of the factors influencing consumer decision-making regarding personalised nutrition, in particular in relation to the perceived risks and benefits and their influences on expressed behavioural intention, and the identification of consumers' needs, values and preferences regarding provision of personalised nutrition information, including those related to product delivery. It is also important to recognise that consumers are not homogenous with respect to their perceptions, attitudes and health related behaviours. The research aimed to identify differences in consumer preferences in terms of socio-economic factors, cross-cultural preferences, demographic differences and other salient individual difference (gender, other genetic factors, health status, age, income, etc.).

The background of the research relates to the issue of consumer uptake of, and demand for, technological innovations associated with food and the food supply. Consumer acceptance of innovative novel technologies is not a given, and, while consumer choice is central to any discussion of food technology and its application, consumer rejection of nutrigenomics may have concomitant impacts on public health, and result in the commercial failure of a

potentially beneficial technology. Even if putative benefits to individuals and society can be identified, consumer adoption of novel food technologies, including those focused on the improvement of health, should be based on the premise of informed choice. In order to provide this, understanding of the psychological and socio-cultural factors which shape consumers' perception, attitudes and decision-making related to behaviour, is needed. This understanding was provided by the research conducted in WP 2. At the initiation of the food4me project, there was considerable uncertainty associated with the extent to which personalised nutrition will be adopted by consumers, what psychological, cultural and practical factors might prevent consumer adoption and, as a consequence, the long-term potential for positive impact on public health. As the project progressed, consumers potentially began to encounter real examples of Internet-based nutrigenomics products and services. However, experts still disagree on the exact form and future of nutrigenomics-based personalised nutrition, as well as which commercialisation options are likely to be the most viable. The development of effective business models for introducing novel applications of personalisation is dependent on understanding consumer preferences and priorities for application characteristics, following personal experience with emerging applications, under circumstances where such experience is vicarious, or based on the recommendations of health professionals or other information sources.

Public rejection of technologies has frequently resulted in negative consequences for the commercialisation of technologies. In particular, unpredicted events and accidents affecting the public have acted as a signal which has resulted in fear and reluctance to adopt certain technologies, and these have resulted in consumer rejection of the products of these technologies. Perhaps as a consequence, much of the research focused on understanding societal acceptance of technologies has been directed towards risk perception. The usual agrifood application of technology used as an example is the market introduction of the first generation of genetically modified (GM) food crops, which led to polarised GM food debate internationally. The intensive societal discussion that followed was detrimental for the adoption and commercialisation of GM crops and food products at least in some regions of the world. Although the introduction of genetically modified foods is frequently posited as the "normative" societal response to technological innovation in the agrifood sector, public acceptance of technological innovation will occur if perceived benefits outweigh the perceived risks. Occurrence of such events and controversies associated with (agrifood) technologies emphasises the importance of public acceptance in their strategic development, application and commercialisation.

Resistance to technologies and factors influencing public acceptance of technologies have generated wide interest in academia, particularly in the arena of social and behavioural research. Whilst the focus of this research has traditionally been the extent to which peoples' risk perceptions predict acceptance of existing and emerging technologies, more recently benefit perceptions have also been examined. The "trade-off" between risk and benefit perceptions have been shown to be the major factors influencing public acceptance of technologies. Psychological research has focused on how individuals define risks and benefits associated with (different applications of) technologies, and what factors influence these perceptions. Peoples' attitude towards technological risks and benefits are influenced by risk dimensions that have little to do with the possible consequences of the technology. An individual can evaluate a risk cognitively and react to it emotionally. Pesticides, while considered to be the technology driving the "Green Revolution", and contributing to international improvement in food security, are primarily associated with consumer negativity linked to "negative affect", or emotional responses, rather than systematic cognitive evaluation of the issues, although these are also a topic of societal discourse. Cognitive evaluation and emotional response do not necessarily align. Although these two reactions are interrelated, they have different determinants. Exploring these determinants in detail can facilitate our understanding of the socio-psychological process affecting public acceptance of technology.

Understanding the determinants of consumer attitudes towards personalised nutrition needs to take account of how the specific attributes of different types of personalised nutrition application are perceived. For example, at the most "medicalised" level of personalised nutrition, dietary interventions could be developed for groups of individuals with specific genotypes. In contrast, recommendations can also be made based on phenotypical observation of a particular individual, which might be described as a "low level" of medicalisation. An individual's acceptance or rejection of personalised nutrition may be dependent on the level of medicalisation. Indeed, the use and storage of an individual's genetic data is an area which has frequently been the topic of societal discussion and concern. In addition, the application of personalised nutrition may also take into account various factors, which contribute to an individual's phenotype, such as family and personal history, psychological well-being, and environmental, social and lifestyle practices, which may or may not factor in genetic differences, but may independently raise privacy issues. Thus it is also important to consider that the technology associated with nutrigenomics may raise consumer concerns about how human genetics research can compromise the integrity of nature and have a negative impact on privacy, for example, related to the management of DNA banks and how sensitive personal information is handled. It is important that the public expectations and concerns about the potential applications of nutrigenomics are addressed as part of a development and commercialisation strategy. For example, it has been suggested that the commercialisation of nutrigenomics initiatives should align with differences in consumer preferences for different levels of potential "medicalisation". Individual differences in perceptions and attitudes are relevant here. Consumers' attitudes may be more favourable where there is potential for individuals to use the information for their own health benefit. Perceived risk, benefit and control are powerful determinants of consumer acceptance of novel food technologies as are perceptions of disease risk and affective responses to different applications of personalised nutrition. Other potentially influential psychological determinants of consumer attitudes include perceived uncertainty associated with both risk and benefits, normative beliefs, health locus of control, the tendency to exhibit habitual behaviours, trust in risk managers in regulatory institutions and industry, inter alia. To date, systematic analysis of these potential predictors of consumer attitude towards different applications of personalised nutrition has not been addressed, nor has their relative impact been evaluated. The importance of these different factors needs to be taken into account if predictive models of consumer acceptance are to be developed and a communication strategy which targets the information needs of different groups of consumers is to be applied to the facilitation of informed consumer choice. All of these factors were taken into account in the research which was conducted in WP2.

There are also likely to be socio-cultural differences in requirements of personalised nutrition, for example, related to socio-cultural differences in dietary preferences or food choices, which also need to be considered. A potential barrier to adoption of a personalised diet is the extent to which people with potentially different dietary requirements identified by the science of personalised nutrition "share" food in different cultural settings, for example family meals or social events. Other more pragmatic factors related to how people make food choices in the context of their daily lives also need to be considered. For example, the availably of foods "prescribed" by a personalised diet may be limited if an individual is acquiring food outside of the home. A qualitative investigation of potential barriers to, and facilitators of, the adoption of personalised nutrition is likely to yield further information relevant to pragmatic and socio-cultural factors relevant to consumer adoption of personalised nutrition. Such an approach has hitherto been applied only in other areas of food-related consumer behaviour. In comparison to well-formed attitudes about some other recent technological innovations, such as those associated with agricultural biotechnology and GM foods, public opinion on nutrigenomics is in the early stages of societal introduction and as yet uncrystallised. The case of personalised nutrition and nutrigenomics, therefore, also provides a unique opportunity to examine theoretical models of public opinion formation under circumstances consumers are only

beginning to make sense of the potential perceived risks, costs and benefits associated with a specific technological innovation.

Other factors may also be important determinants of consumer uptake of personalised nutrition. As stated previously, the adoption of individualised diets may vary cross-nationally and according to local cultural practices regarding dietary preferences and social activities. However, it is quite possible that these do not influence the psychologically (and theoretically) underpinned determinants of whether an individual adopts personalised nutrition – rather they may represent pragmatic barriers to adoption of individualised diets. For this reason, it is important to compare attitudes and perceptions across populations which are associated with different cultural practices regarding food choices. In this regard, comparing populations within EU member countries is useful, as they share a common regulatory regime, "The European Food Law[1]" regarding food safety standards and implementation, reducing the complexity of potentially influential factors. At the same time, consumers across Europe adopt a wide range of culturally influenced food choices and socially influenced dietary practices.

RESEARCH METHODOLOGY

Taking an overview of the work package, the research was conducted in four main "phases". First, an initial **qualitative** research investigated pan-European consumer perceptions of benefit, risk and cost associated with personalised nutrition, assessed across different levels of medicalisation. The results, together with insights from the theoretical literature, were then used to develop the second, **quantitative** phase of the research. The resulting data were subsequently analysed using structural equation modelling to develop and validate an integrated psychological model of the determinants of consumer attitudes towards personalised nutrition. A systematic analysis of individual differences in consumer preferences for different types of personalised nutrition was also addressed in order that an effective development and commercialisation strategy could target the needs of different consumers. Thus, Food4me moved beyond the state of the art by completing a multi-centre analysis of attitudes and preference across European populations, which allowed systematic comparison of demographic and psychological determinants of consumer acceptance. Additional barriers to consumer uptake (for example, related to lifestyle, pragmatic or domestic factors) were examined regarding prevention or facilitation or the adoption of different levels of personalised nutrition. Third, utilisation of the same quantitative survey instrument at the end of the proof of principle study allowed comparison between psychological factors determining uptake in the general population who had not experienced personalised nutrition service provision, with participants who had been involved in such a service for 6 months. Finally, a deliberative workshop exercise was conducted in collaboration with WP 6 to further unpack consumer preferences for communication strategies about personalised nutrition.

Details of the methodologies applied will now be described.

Study 1. Qualitative research

Focus groups were used for generating data on the basis of their capacity to provide insights into participants' perceptions of, and attitudinal consistency associated with, substantive issues that arise from both individual contributions and interactive exchanges. The use of focus group methodology facilitated the exploratory analysis in the hitherto not well understood area of public opinion towards personalised nutrition. Data were collected in eight European countries: Ireland, University College Dublin (IE); United Kingdom, University of Reading (UK); Spain, University of Navarra (ES); Greece, Harokopio University Athens (GR); The Netherlands,

[1] http://ec.europa.eu/food/food/foodlaw/index_en.htm

Wageningen University (NL); Germany, Technical University Munich (DE); Poland, National Food and Nutrition Institute (PL); and Portugal, University of Porto (PT); University of Oslo (NO). Ethical approval for the research was obtained by each participating institution. A standardised focus group protocol (including focus group composition) was developed by a core of researchers experienced in qualitative research from Ulster, Newcastle, Wageningen and Porto. Two pilot focus groups were conducted in English in Newcastle during September 2011, and the results used to further refine the protocol used in the main study. These data were not used further in the main analysis, to ensure all data had been collected using an identical protocol. About one month prior to the focus groups being held (October 2011), a two day training course was provided to harmonise focus group moderation in all participating centres. The research protocols were translated from English into the national languages of the centres responsible for the data collection and back-translated to ensure consistency in methodology was applied across all the centres. One hundred and twenty six participants were recruited using social research agencies (UK, Spain, the Netherlands, Poland and Portugal) or through distributed flyers and/or posters (Ireland, Greece and Germany). Two focus groups were conducted in each country. Each focus group comprised 6-10 free living, urban dwelling participants. Gender and occupations were mixed within the groups. Individuals who were not healthy (according to their own definition) were excluded. Vulnerable individuals, health professionals with an interest in food or diet, individuals with a background in genomics, nutrigenomics or personalised medicine, individuals who had previously taken part in research related to personalised nutrition, or those who were regular focus group attendees were also excluded. In each centre, one group comprised a mixed age profile (18-65), and one group comprised "older" individuals (30-65), to allow age or cohort specific issues to be investigated. Participant profiles were verified using a questionnaire administered to record sex, age, marital status, household size, number of dependents, and information about occupation. There were no significant differences in the distribution of sex or age group. Marital status did differ across countries, with Germany and Greece having more, and the Netherlands and Poland fewer, single individuals than expected.

Study 2. Development and analysis of survey instrument

The focus group study provided source constructs for development of a predictive model of the intention to adopt personalised nutrition. Within this study perceived personal benefit was identified as a positive attribute of personalised nutrition. Perceived risk and perceived benefit associated with a range of potentially controversial issues, including those located within the health domain, and consumer adoption of ICT services, have been found to be inversely correlated in previous research. Thus it is predictable that the greater the perceived benefit, and the less the perceived risk, individuals associate with personalised nutrition, the greater will be their intentions to adopt it. In the focus group research, negative attitudes were reported to be associated with internet delivery of personal and identifiable genetic information. Although participant negativity did not focus on personalised nutrition per se, participants raised concerns about broad technological issues associated with personal data protection, and trust in regulators, the efficacy of legislation put into place to protect privacy and exploitation of consumer data, and the reliability and motivation of service providers in relation to consumer protection. Potentially, the more individuals trust regulatory systems to optimise consumer protection in relation to nutrigenomics, the greater will be their intentions to adopt personalised nutrition.

The focus group protocols also took account of the potential for different responses in different countries. In particular, the protocol design acknowledged that the adoption of individualised diets may vary cross-nationally and according to local cultural practices regarding dietary preferences and social activities, and this was systematically explored and analysed between the countries involved. These socio-culturally specific factors may represent pragmatic

barriers to adoption of individualised diets and so it was important to compare attitudes and perceptions across populations which are associated with different cultural practices regarding food choices.

However, some psychological factors which potentially influence consumer acceptance of personalised nutrition may be relatively stable across individuals from different cultures. For example, a potentially important determinant of adoption or rejection of personalised nutrition is health locus of control. If people believe that they have control over their own health through their own volitional behaviours, they exhibit a high level of internal health locus of control. The concept of external health locus of control relates to the belief held by some individuals that health status is a matter of chance, or under the control of powerful others. Individuals exhibiting high internal health locus of control may be more likely to adopt personalised nutrition. Similarly, individuals with high levels of perceived self-efficacy (perceived capabilities to perform a desired task) may also exhibit a greater tendency to adopt personalised nutrition. These factors may influence attitude towards personalised nutrition, which, in turn, may influence behavioural intention regarding its adoption or otherwise. Social trust in regulators and service providers may also affect people's tendency to adopt personalised nutrition, as well as perceptions of affordability of services. This would reflect a key finding in the focus group research.

A total of 9381 participants from 9 EU countries (Germany, Greece, Ireland, Poland, Portugal, Spain, the Netherlands, the UK, and Norway) were quota sampled to be nationally representative for each country, on sex, age (18-29, 30-39, 40-54, 55-65 years) and education level (highest level of education completed based on International Standard Classification of Education levels ISCED 0-2, ISCED 3-4, ISCED 5-6). Participants were drawn from an existing panel held by a social research agency. Additional research agencies were subcontracted by the primary agency to supplement panels if needed. A total of 29,450 individuals were contacted, and the overall response rate was 31.9%. Data were collected in February and March 2013, using on-line survey methodology. After reading an introductory text, participants provided informed consent prior to completing the questionnaire. Ethically approved research procedures were noted by the lead academic institution.

In addition, data regarding peoples' willingness to pay (WTP) for personalised nutrition services was included in the survey described above, as well as in the research survey instrument utilised in WP 1 after the WP2 data collection had been finalised. This data enabled assessment of the extent to which different groups of individuals were willing to pay for personalised nutrition services, which is particularly relevant from a business development perspective. At the time of writing, there have already been several initiatives which have attempted to exploit personalised nutrition as a business opportunity (see the chapter on WP 1). It is, however, not clear how much consumers are willing to spend on personalised nutrition services in comparison to existing dietary advice which should deliver health benefits to the entire population, without taking account of individual differences in dietary requirements. It is assumed that the perceived risks and benefits of personalised nutrition which are held by individuals, as well as the perceived benefits of specific personalised nutrition services, will influence the potential success of commercialising a personalised nutrition service. On one hand, assuming behavioural adoption is contingent on perceived benefit of adoption, it could be posited that consumers who perceive greater benefit will be willing to pay more for personalised nutrition services. However, increasing the use of genetic data in personalised nutrition may have a larger effect on increasing risk perception related to potential privacy issues, than on benefit perception related to better advice. This raises the question to what extent the increasing levels of personalisation facilitated by more specific and more privacy sensitive data contribute to the market potential of personalised nutrition services using different levels of data. In particular it raises the question if consumers are willing to pay for the required additional analyses needed

on blood and DNA samples. The two waves of the cross-national surveys (in WP 1 and WP 2) were conducted nine months apart, in February/March 2013 (WP 2) and November/December 2013 (WP 1). In both waves, willingness to pay for a personalised nutrition service was measured next to various other constructs, to predict the potential market for such services. In addition, income was surveyed to investigate to what extent such nutritional service might be adopted across income classes.

In both surveys, data was collected on people's willingness to pay for different personalised nutrition services. In both surveys, the "sensitivity" of the information that the end-user had to provide to receive personalised nutrition advice was varied. Sensitivity of information depended on provision of (1) dietary lifestyle information, (2) lifestyle information and blood samples and (3) dietary lifestyle information, blood samples and DNA samples. The combination of data sets allowed us to answer the following questions:

- To what extent do people differentiate their willingness to pay depending on sensitivity of provided information?
- How much influence does income have on willingness to pay for a personalised nutrition service?
- To what extent do people show a stable willingness to pay over time?

Study 3. Comparisons with participants in the Proof of Principle study

In addition to the studies above, the same survey was administered to participants in the Proof of Principle study being conducted in WP 4. This allowed some comparisons to be made regarding the importance of the psychological factors which determine potential adoption of personalised nutrition in the general population being surveyed in the large survey (who were only expressing their theoretical intentions to adopt personalised nutrition) and those participants who had been recruited into the personalised nutrition trial (who, as self-selected and interested individuals may have been expected to hold more positive attitudes towards personalised nutrition as compared to the general population on recruitment, but none-the-less may have moderated these attitudes positively or negatively after recruitment into the trial, following their allocation to trials focused on different levels of medicalisation of personalised nutrition in WP4). Two analyses were conducted. The first analysis focused on understanding differences in relevant psychological traits between the different levels of personalised nutrition included in the PoP study. The second compared attitudes of the general population with individuals recruited into the PoP study itself.

Study 4. The "citizen's panel"

Finally, a deliberative workshop was set up to produce guidelines on effective communication for people interested in developing and delivering personalised nutrition services. The citizen's panel was held in London in November 2014. Participants (n=22) were recruited by a social research agency according to a sampling frame based upon age, gender, social class and ethnicity that was broadly representative of the wider UK population. Criteria for exclusion included people working in nutrition and genomics related areas or who had taken part in a clinical trial. The deliberative workshop was delivered by OPM Group and took place in one day over a 6 hour time period (10am-4pm) and included the following activity sessions: 1) introducing the topic of personalised nutrition; 2) introducing personalised nutrition; 3) discovering personalised nutrition; 4) data collection for personalised nutrition; 5) reporting personalised nutrition outputs; 6) designing your ideal personalised nutrition service; and 7) message prioritisation. During these sessions and over the course of the workshop, participants

were exposed to several knowledge sources that were used to prompt discussion and deliberation, and enabled the participants to construct, reflect upon and discuss their understanding of personalised nutrition. The knowledge sources included; a formal presentation to the whole group, made by a technical expert, describing personalised nutrition, a technical video clip, information embedded in stimulus materials such as personalised diet reports, examples of devices to collect phenotypic and genotypic data, informal 'round table' interactions facilitated by a trained moderator in small groups of 5-7, and informal interactions between participants during lunch and tea breaks. Participant outputs were captured through a variety of pre-tested media including; audio recordings of discussions, written comments in pre-prepared work books, plans written on flipcharts, and electronic voting system and moderator notes. The data generated throughout this workshop process both complemented and extended an understanding of attitudes and perceptions of personalised nutrition communication.

KEY RESULTS

Qualitative research[2]

The results of the focus groups indicated that European consumers may construe personalised nutrition in terms of benefit in terms of potential improvements to both individual and public health. In contrast to other agrifood technologies, perceived risks are more closely linked to general concerns about genetic privacy and data security, and are not specifically linked to personalised nutrition per se. Furthermore, the results suggested that consumer acceptance may be dependent on the development of an efficacious, transparent and trustworthy regulatory framework associated with human genetic technologies, which would apply to other types of application as well. While data privacy was also important for those levels of personalised nutrition which did not involve the sampling of genetic data, most concern expressed by study participants related to the need to ensure that the principle of "genetic privacy" was enshrined in regulation. The results suggested that participants thought that developing trust in service providers is important, in particular for service providers located within the commercial sector rather than in the public health sector. It was also found that a possible barrier to adoption may be represented by optimistic bias, where participants indicated that they thought personalised nutrition services were being developed to benefit individuals at greater risk of disease development than they were personally. This suggested that communication about personalised nutrition might usefully target those individuals who might potentially experience benefits from the adoption of personalised nutrition, but who do not perceive that personalised nutrition will benefit them personally. In particular,this might include younger consumers, for whom the benefits of personalised nutrition will potentially accrue for longer. Communication might also discuss specific benefits for those consumers with existing medical conditions. In addition, focus group participants were concerned that adoption might be difficult, and foods inconvenient to obtain. Communication about personalised

2 Stewart-Knox, B., Kuznesof, S., Robinson, J., Rankin, A., Karen Orr, K., Duffy, M., Poínhos, R. Vaz de Almeida,M.D., Macready, A., Gallagher, C., Berezowska, A., Fischer, A.R.H., Navas-Carretero, S, Riemer, M., Gjelstad,I.M.F, Christina Mavrogianni, C., Frewer, L.J. (2013). Factors influencing European consumer uptake of personalised nutrition.Results of a qualitative analysis. Appetite, 66, 67-74.

nutrition might focus on convenience of adoption, as well as the provision of individually tailored benefits for health and fitness, which were identified as important benefits of adoption by some focus group participants. An important finding was that advice should be tailored to align with people's lifestyles and preferences, including those related to food choices, anonymity, and motivational factors. Cost may also be a factor in determining whether an individual may adopt personalised nutrition. No evidence of cross-cultural differences was found between the countries surveyed in the focus group results, although this issue was analysed further in the survey study.

Main survey

A structural equation model was developed (figure 1) which examined the relationship between perceived risk, perceived benefit, health locus of control, perceived self-efficacy, attitudes towards personalised nutrition, and behavioural intention to adopt personalised nutrition.[3]

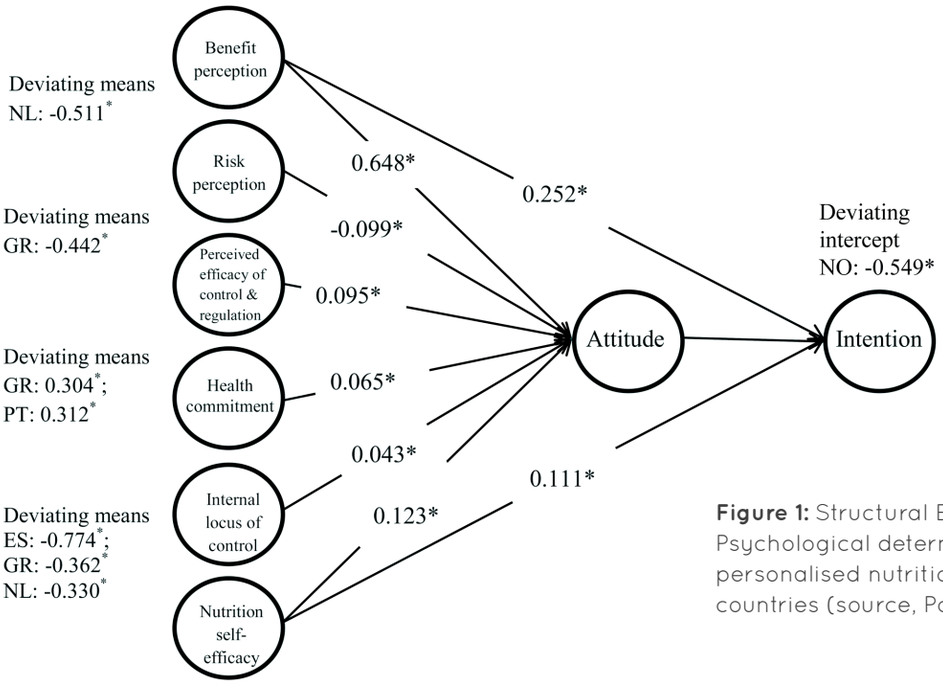

Figure 1: Structural Equation model. Psychological determinants of personalised nutrition in 9 European countries (source, Poinhos et al, 2014).

Betas with 95% CI per country

Paths to Attitude		
- Internal locus of control	[0.023	0.063]
- Health commitment	[0.043	0.087]
- Nutrition self-efficacy	[0.101	0.145]
- Risk perception	[-0.121	-0.077]
- Benefit perception	[0.623	0.674]
- Perceived efficacy of control and regulation	[0.075	0.115]
Paths to Intention		
- Nutrition self-efficacy	[0.089	0.133]
- Benefit perception	[0.223	0.281]
- Attitude	[0.437	0.499]

The psychological factors included in the analysis were chosen to be relatively stable across

3 Poínhos, R., van der Lans, I. A., Rankin, A., Fischer, A. R., Bunting, B., Kuznesof, S., Stewart-Knox, B. and & Frewer, L. J. (2014). Psychological determinants of consumer acceptance of personalised nutrition in 9 European countries.PloS one, 9(10), e110614.

cultures in order to develop a predictive model which was stable across cultures and likely to maintain stability with time. A priori hypotheses about the relationships between the different factors could also be developed, and these were confirmed in the analysis. The extent to which individuals trusted relevant regulatory systems was also assumed to be a good predictor of an individual's intention to adopt personalised nutrition.

The results of the analysis imply that attitudes towards, and adoption of, personalised nutrition appear to be primarily driven by perceptions of benefit, together with the extent to which an individual perceives that adoption of personalised nutrition is achievable (reflected by self-efficacy scores). In addition, the extent to which an individual trusts those regulatory systems associated with consumer protection and personalised nutrition, (in particular in relation to personal genetic data protection), and the extent to which individuals are committed to improving their own health status through their own actions, influences attitudes towards personalised nutrition, and subsequently behavioural adoption. In spite of local socio-economic and cultural factors that may influence the extent to which adoption of personalised nutrition is operationalised by consumers, the research demonstrated that the associations appeared stable across a range of European countries.

- **Willingness to Pay for different types of personalised nutrition service.**

The Willingness to Pay (WTP) data from the WP 1 and WP2 nationally representative population surveys was collated and analysed[4]. The results indicated that a limited group of about 30% of the population is willing to pay more for a personalised nutrition service than for a generic nutrition service, which is currently provided by health professionals. The additional price people are willing to pay for a personalised nutrition service was, however, also somewhat limited. The results suggested that, based on consumer WTP for personalised nutrition services, that additional price of personalised nutrition services over and above standardised nutritional advice should be less than 50% (or 50€) in comparison to generic services. The additional prices people are willing to pay for increasing levels of medicalisation (dietary and blood collection, and dietary and DNA collection) are very small indeed (below 5% of the total price, representing a 5€ difference between increased levels of medicalisation of personalised nutrition). The data in survey 2 was collected about a year after survey 1. Comparative analysis of the WTP data acquired in the first and second waves of data collection suggests that the amount participants are willing to pay for personalised nutrition services was fairly stable when surveyed over this time period, which suggests that people have long term preference regarding what they see as an appropriate price for personalised nutrition services utilising different levels of medicalisation in their "diagnosis" of individualised diets. Perhaps as might be expected, people in the highest income groups report being willing to pay the greatest additional price. This raises a question of whether access to personalised nutrition services should be determined by financial restrictions, which raises ethical issues about access to a healthy life for all, independent of income. Furthermore, equal access to personalised nutrition services will prevent the development of dietary related diseases, reducing the burden of health care costs. It may be an important public health measure to routinely include personalised dietary advice as part of health service provision, health insurance coverage or human resource management programs.

Finally, an analysis of different participant motives for adopting personalised nutrition was applied to the general population data collected in the WP 2 research[5]. Included in the survey

4 Fischer, A.R.H, Berezowska, A., Ronteltap, A. , van der Lans, I.A., van Trijp. H.C,M., Rankin, A., Frewer, L.J., Kuznesof, S., Panzone, I., Poinhos, R., Oliveira, B., Markovina, J. and Stewart-Knox, B. (2014). Food4me Deliverable 2.8 – Report on relationship between consumer attitudes and personalized nutrition.

5 Rankin, A (submitted) Motives for food choice and individual's intention to adopt personalised nutrition. chapter 5. "Factors determining the uptake and effectiveness of personalised nutritional interventions", PhD thesis, Ulster University.

were items included in the "Food choice questionnaire"[6], which assesses people's motivations for making specific food choices. Nine motives have been identified, and include the following; health, mood, convenience, sensory appeal, natural content, price, weight control, familiarity and ethical concern. The extent to which different food choice motives influenced attitudes towards personalised nutrition and intention to adopt personalised nutrition were analysed. The application of structural equation modelling indicated that, of the food choice motives, weight control and mood were the main determinants of both attitudes towards personalised nutrition and high levels of intention to adopt personalised nutrition. Health was also found to be amongst the main predictors of positive attitude towards personalised nutrition but not intention to adopt personalised nutrition. Price, sensory appeal and familiarity were found to be negatively associated with positive attitudes towards personalised nutrition and/or intention to adopt personalised nutrition. From this, it could be concluded that personalised nutrition providers may benefit from taking into consideration the underlying determinants of food choice in potential consumers, to target potential users and tailor communications to be motivationally relevant.

• Comparisons between the general population and study participants recruited into the Proof of Principle Study

A detailed comparative analysis between WP 2 and WP 4 samples is currently in progress. The initial findings derived from the analysis of the WP 2 and WP 4 Proof-of-Principle (PoP) questionnaires will be summarised here.

It was hypothesised that personalised nutrition has the potential to motivate behaviour change[7]**.** However, it is not known if differing levels of personalisation (for example, based on standardised dietary advice related to the phenotype, blood sampling or genetic profiling, as was utilised in the research conducted within Food4me at different levels of "medicalisation") or feedback intensity (embedded in the experimental design of the PoP study in WP 4) will have implications for compliance to personalised nutrition advice. The psychological impact of, and compliance with, personalised nutrition at the 3 levels of personalisation and 2 levels of feedback intensity, was assessed using the questionnaire data collected from the PoP participants in study 4. To summarise, participants (N=1609) were recruited onto the online personalised nutrition 6 month PoP intervention study and randomised into 1 of 4 intervention groups: non-personalised dietary advice (Level 0; control group); personalised dietary advice (Level 1); personalised dietary and phenotypic advice (Level 2); or, personalised dietary, phenotypic and genotypic advice (Level 3). Participants were further randomised into low and high feedback intensity levels. The screening and post-intervention (n=798) questionnaire included validated scales to assess nutrition self-efficacy, health locus of control and habit strength. The results indicated that both younger and female participants, with lower habit strength scores (where a higher habit strength score reflects greater tendency to adopt habitual behaviours) were associated with higher attrition from personalised nutritional interventions.

Both being part of the intervention and the intensity level of feedback had a significant positive time effect upon nutrition self-efficacy score, irrespective of increasing levels of medicalisation associated with the intervention. The impact of being involved in the intervention also had an impact on locus of control, such that external health locus of control scores increased and

6 Steptoe, A., Pollard, T. M., & Wardle, J. (1995). Development of a measure of the motives underlying the selection of food: the food choice questionnaire. Appetite, 25(3), 267-284.

7 Rankin, A. (submitted) Psychological impact of personalised nutritional intervention. "Factors determining the uptake and effectiveness of personalised nutritional interventions", Chapter 6. Ulster University.].

internal health locus of control scores decreased. Although counterintuitive, this result suggests that being involved in the trial resulted in a loss of perceived personal control over personal health. The significant increase in habit strength that was only apparent in Level 1 suggests that personalisation based on current diet may be sufficient to elicitappropriate changes in eating habits. These results suggest that personalised nutritional interventions and services which take into consideration self-efficacy, locus of control and habit in users may be associated with increased compliance to dietary advice. For some individuals, however,increasing levels of personalisation may have a detrimental effect on perceived personal control over health. For example, if health is perceived to be controlled by genetic factors, some individuals may perceive that these are relatively immutable, and cannot be influenced by volitional behaviours or actions. The groups of participants who dropped out of the trial may have had different scores on self-efficacy, locus of control and habit, but these data are unavailable.

The questionnaire data from the same 798 participants was matched to that obtained from socio-demographically similar participants selected from the nationally representative samples included in WP2, who had not been included in the intervention trial. [8]The initial analysis has indicated that participants' attitudes generally became more positive following inclusion in the intervention when compared to the general population sample, as did their perceptions of benefit. However, participants were most positive in the low intensity feedback condition, suggesting that high intensity feedback was less effective than low intensity feedback where participants' responses were concerned, perhaps because the intense feedback became monotonous or overwhelming. Increased medicalisation had little effect on perceptions or attitudes. Some significant country differences were also observed in the intervention participants suggesting that socio-cultural factors may be influencing the pragmatic adoption of personalised diets, although such differences were not observable in the general population sample who had not had direct experience of trying to follow a personalised diet.

• Deliberative Workshop

The results[9] indicated that communication about personalised nutrition services required information to convey the trustworthiness of the service provider. This was potentially determined by expertise, for example, evidence of medical training of the personalised nutrition provider (which included dietitians, nutritionists, nurses and medical doctors), and information that communicated credibly robust systems for handling personal data and maintaining anonymity and privacy of the PN user. Participants also wanted a fast, responsive service that incorporated multiple information delivery methods including personal contact. Potential service providers were identified as both National Health Service (NHS) and private organisations, although participants queried the ability of the NHS to respond in a timely and efficient manner. The results of the deliberative workshop were UK-specific, given that only UK participants were included, and so emphasised the role of the NHS in delivering personalised nutrition. None-the-less, the results supported the conclusions of the surveyand empirical research conducted ealier in the project, in particular in relation to the provider having a health professional background, and in respect to data privacy.

8 Panzone, L. Personal communication.

9 OPM (2015) Food4Me Workshop. Report to European Food Information Council.

IMPLICATIONS OF THE RESULTS

Some recommendations for developing communication about personalised nutrition can be identified:

First, it is likely that people will be primarily interested in receiving information about potential (and personal) **benefits** of adopting personal nutrition. Although benefits (and consumer recognition of these) are a very important determinant of consumer acceptance of personalised nutrition, the form that these take may vary considerably between different consumers, and may need to reflect the individual goals in which consumers are interested.

Second, information about **ease of adoption** of personalised nutrition may convince potential adopters not only of the benefits, but the attainability of these. Thus, while some individuals may be reinforced in their commitment by internet-based coaching, others may prefer a directly personalised approach using meeting with health professionals (see also Stewart-Knox et al, 2013).

Third, **transparent regulations regarding protection of data**, in particular, but not exclusively genetic data, are required. There needs to be evidence of enforcement of these regulations across both the private and public sectors and information about these needs to be communicated to the public. In order to develop trust, it is also necessary to engage with the public regarding the design of legislative infrastructure and subsequent implementation of regulations, a debate which is likely to extend beyond personalised nutrition to other areas of personalised medicine, including regulations designed to promote data protection.

Fourth, it is also important to ensure that the personalised nutrition provider is perceived to be **credible in terms of expertise** - ideally a health professional needs to be involved in the provision of personalised nutrition Information.

Fifth, increasing feedback may not facilitate adoption of personalised nutrition and take up of dietary advice. **Moderately intense feedback** seems to deliver the most positive participant responses, at least for those participants who continued through to the end of the trial. This should be taken into account in the design of personalised nutrition services.

Some additional observations relate to the extent to which people are willing to pay for personalised nutrition services. Only the most affluent participants indicated that they were in any way willing to pay for a personalised nutrition service – and a careful analysis of the costs required to provide such a service, when compared to what even this group is willing to pay, is required to assess whether such personalised nutrition services can be viable financially as a business operation, particularly when blood sampling and DNA testing ae involved in the "diagnosis" of dietary advice, as even more affluent consumers appear unwilling to pay very much for such diagnostic services.

DEVELOPING THE STATE OF THE ART

An important issue is that the results suggest that people's intention to adopt agrifood technologies is not driven by perceived risk alone, but by perceived (personal) benefits. It is possible that governance and regulation needs to take the issue of benefit into account at the technology assessment stage, for example as part of a risk-benefit analysis approach to technological governance, rather than develop governance strategies based on risk assessment in isolation, in line with the current dominant model of technology regulation. The results directly challenge the assumption that the societal response to GM foods represents the normative position in European society to agrifood technologies. Rather, each example of such a technology

needs to be assessed on its own merits, and how society perceives both risks and benefits. The model developed which links risk –benefit perceptions to attitudes towards personalised nutrition, and hence to behavioural adoption, is worthy of further application to other (agrifood) domains.

In addition, the relationships between various psychological constructs and behavioural intention to adopt personalised nutrition appear robust, and may be applied in the future to understand consumers' attitudes to various technological innovations, for example, in the area of personalised medicine or consumer goods produced with the aid of nanotechnologies. Understanding such consumer priorities and preferences early in the technology application trajectory may allow the "fine –tuning" of product design in line with consumer preferences and priorities. Furthermore, as these results have shown, it is unlikely that all consumers will adopt a new technology at the same time, if at all. The models developed in this research can be applied to identify which consumers will adopt the technology, and how much, or if they are willing to pay for the technology. This information can be used to shape the commercialisation trajectory for emerging applications of novel technologies. Thus it can be argued that, although the research conducted in WP 2 of the Food4me project utilised personalised nutrition as a case study, the results have generic applicability to our understanding of the broader area of technology adoption and commercialisation.

WHAT GAPS IN KNOWLEDGE STILL REMAIN?

As a consequence of the researchers' inability to collect attitudinal data from those participants in the PoP study who dropped out, it can only be surmised that these participants held more negative attitudes about personalised nutrition after their inclusion in the trial than before. Further research regarding the psychological factors which resulted in specific participants dropping out of the intervention is required if the delivery of personalised nutrition services in line with consumer expectations is to be further refined. Alternatively it may be that the benefits of personalised nutrition will only ever be appreciated by a subsection within the population, and that for others, inclusion in such dietary interventions will be short-lived.

As consumer exposure to individualised medicine becomes more common, it may also be the case that people will become more positive about the potential benefits of personalised nutrition in particular. Following up these results as time progresses will confirm whether this is indeed the case.

HOW COULD THESE EFFORTS FEED INTO HORIZON 2020 RESEARCH CALLS?

1. Tracking changes in attitudes associated with personalised nutrition in time, as personalised medicine becomes established.

2. As governance and regulation associated with the storage of human genetic data becomes more established, will this facilitate the consumer adoption of personalised nutrition, as well as other applications of personalised medicine. Can legislative changes be used as a "natural experiment"?

3. How might the conclusions feed into the development of research in the area of "responsible research and Innovation" with the H2020 programme, for example through developing formalised models of consumer choice based on perceived risk and benefit and associated attitudes.

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REFERENCES

Poínhos, R., van der Lans, I. A., Rankin, A., Fischer, A. R., Bunting, B., Kuznesof, S., Stewart-Knox, B. and & Frewer, L. J. (2014). Psychological determinants of consumer acceptance of personalised nutrition in 9 European countries.PloS one, 9(10), e110614.

Rankin, A., Stewart-Knox, B., Duffy, M., Kuznesof, S., Fischer, A., de Almeida, M., Gibney, M. & Frewer, L. (2013). Food4me personalised nutrition: What does the consumer want?. In Annals of nutrition and metabolism (Vol. 63, pp. 345-346). Allscwilerstrase 10, CH-4009 Basel, Switzerland, Karger.

Stewart-Knox, B., Rankin, A., Kuznesof, S., Poínhos, R., Vaz de Almeida, M. D., Fischer, A., & Frewer, L. J. (2014). Promoting healthy dietary behaviour through personalised nutrition: technology push or technology pull? Proceedings of the Nutrition Society, 1-6.

Stewart-Knox, B., Kuznesof, S., Robinson, J., Rankin, A., Karen Orr, K., Duffy, M., Poínhos, R. Vaz de Almeida,M.D., Macready, A., Gallagher, C., Berezowska, A., Fischer, A.R.H., Navas-Carretero, S, Riemerh, M., Gjelstad,I.M.F, Christina Mavrogianni, C., Frewer, L.J. (2013). Factors influencing European consumer uptake of personalised nutrition.Results of a qualitative analysis. Appetite, 66, 67-74.

COMMUNICATION MESSAGES FOR PERSONALISED NUTRITION SERVICE PROVIDERS, TO ADDRESS CONSUMER CONCERNS from Work Package 6

Based on consumer attitudes research, the deliberative workshop, and other workshops in the Food4Me project, the table below describes the concerns or perceptions that consumers have about personalised nutrition, measures to lessen the concerns, and suggested communication advice for the use of personalised nutrition service providers.

Concern or perception	Measure to highlight perception, lessen concerns and improve acceptance	Communication advice
What is personalised nutrition (PN)?		
Focus group participants were not entirely clear what PN was, and how could it help an individual - especially if they had no underlying health issues.	Communicate clearly the benefits of PN for both healthy and metabolically challenged individuals, via channels such as articles, leaflets, websites, podcasts, tutorials or videos.	**Explain how PN improves an individual's health profile. Highlight a relatively short-term effort to produce a long-term gain.**
Fast and personalised		
The participants appreciated the speed benefits of PN delivered online. Some (mainly older) participants were hesitant in using internet for PN service, due to technical challenges. Younger people likely more comfortable with an online PN service.	Explain the speed benefits of PN in various media, including articles, leaflets, websites, podcasts, tutorials or videos. Provide IT training where required.	**Highlight the speed in which an individual can submit their details and then obtain personalised nutrition advice. Highlight the simplicity and convenience of internet-service.**
Convenient, possibly unreliable dispatcher		
Focus group participants appreciated the convenience of PN delivered via the post. On the other hand, mistrust was voiced around the reliability of postal service, especially for sending blood and DNA samples.	Explain the convenience benefits of PN in various media, including articles, leaflets, websites, podcasts, tutorials or videos. Provide alternative way of sample / information delivery (e.g. courier service) where postal system is perceived as unreliable.	**Highlight the relative ease of obtaining personalised nutrition results. Emphasise the convenience of sending individual information and receiving personalised nutrition information via the 'guaranteed' post or courier.**
Public vs. commercial offerings		
Interviewees perceived less risk and reported to have more trust in a public health sector or a university/ institutional provider.	Have public/official websites of governments, education bodies and health institutions, etc. endorse the service.	**Give examples of specific government/education/ health institutions that are introducing or supporting personalised nutrition services.**

Concern or perception	Measure to highlight perception, lessen concerns and improve acceptance	Communication advice
Security and information misuse		
Major concerns were expressed related to data handling and online security/ safety. Concerns of misuse that individual health data could be passed onto insurance companies, marketers and even employers. A PN service administered by a local GP or a dietitian was seen as most trustworthy.	Make sure that maximum IT (protocols and software) security measures are undertaken. Provide valid and recognisable security certificates and logos. Allow for secure payment channels (cooperation with online banking such as PayPal).	**Explain that personal information will be kept confidential. Highlight safety and security of the service (explicitly state that data will not be forwarded to any other/third parties outside of the PN service). Positive testimonials from other consumers. Provide endorsements by recognised institutions. Highlight confidentiality of the PN service.Highlight confidentiality of the PN service. Make clear that there is a team of health professionals also behind the internet service.**
Anonymity and privacy		
Anonymity was seen as an advantage, as it would reduce the perceived risk and protect an individual's privacy.	Wherever possible provide detailed information on data protection guidelines. Latest encryption protocols and standards should be employed.	**Explain that personal information will be anonymised.Clearly state why the protection of users' identity is of foremost importance.**
Trust – up to a level		
Misuse of biological material, especially DNA, was seen as a possibility. Genetic testing was often mentioned as a step too far The competency of the "behind the screen" PN individual was questioned.	Provide information of the different steps of the PN analysis and where and why the samples are going to be used. Explain how different types of samples provide different information, to produce a different level/ depth of advice. Give supporting credentials of the PN specialist.	**Clearly explain that the only purpose that the samples will be used for is the PN analysis. Highlight the benefits and importance of genetic testing. Communicate about science and technology as the sheer carriers of progress. Highlight that the service is administered by health professionals.**
Cost - a burden or an assurance?		
A segment of participants believed that a PN service should be provided for free. Alternatively, having to pay for a PN service was seen as a guarantor for a quality service.	Provide an overview of the different steps of the PN programme and where and why costs arise for the provider.	**Provide a selection of cost/ payment options available to the consumer. Highlight that costs will be tailored to the individual, just as their personalised nutrition results will be. Justify that the safety and quality of the service, cannot be given for free. Emphasise value for money.**

Concern or perception	Measure to highlight perception, lessen concerns and improve acceptance	Communication advice
Psychological wellbeing – fear of failure		
PN services were associated with a fear of failure (or of getting uninterested), as signing up and keeping to a programme requires strong motivation and will-power.	Motivate people with key motivation messages. Make available trained and friendly advice via specialists on the phone or online.	**Explain risks to future health if no action is taken. Provide reassurance that support is provided every step of the way.**
Psychological wellbeing – fear of truth		
PN testing was linked to a possibility of identifying serious disease risks.	Provide professional advice and explain pros and cons of knowing one's genetic predispositions.	**Explain risks to future health if no action is taken. Provide reassurance that support is provided every step of the way.Make clear that what is written in genes is not set in stone. One can always influence their health by making better choices.**
Psychological wellbeing – personal contact		
Personal contact was considered important both to motivate and emotionally support an individual, also to prove the legitimacy of the service.	Use personalised letters or emails to directly communicate with individuals. Establish a telephone help line or an online chat service for guidance and explanation.	**Highlight 'personal touch' provided by the PN service. Be transparent who the team are, with profiles, photo, qualifications. Reassure people that operators are an experienced and trained team of specialists. Give positive testimonials from other consumers.**

BUSINESS AND VALUE CREATION CONCEPTS FOR PERSONALISED NUTRITION
Overview of Work Package 1

INTRODUCTION

New scientific advances still face important barriers in becoming accepted and applied by society, even though benefits seem very obvious. There are a multitude of factors at play that may drive or block acceptance for successful uptake of novel business or value creation concepts.

A fundamentally new development such as personalised nutrition is particularly delicate to evaluate because it touches upon two primary human needs; health and food. These are today at the heart of a major societal debate because the growing pressure in public health care results from health issues that are, to a large extent, a consequence of inappropriate dietary behaviour. There is an urgent need to help citizens to adjust their dietary behaviour. Personalised nutrition offers a new approach by advising food choices and eating patterns that fit individual needs and are in line with personal preferences. This should help a person to achieve a lasting dietary behaviour change that supports optimal health.

This inherent link between individual behaviour change and the societal impact of it means that personalised nutrition as a concept is deeply embedded in societal tissue. Its introduction is likely to have significant societal consequences and on the other hand societal changes to cope with this issue are likely to embrace personalised nutrition concepts. That makes value creation models for personalised nutrition interesting but also very challenging. Personalised nutrition concepts need to integrate very different elements such as personal coaching principles and a wide range of new technological tools, from self-sampling diagnostics and wearable lifestyle and food intake monitoring, to mobile interfaces for dietary coaching. Moreover personalised nutrition concepts hold the potential to substantially improve the value perception of food and its role in health and in society.

This requires a fundamental understanding of the system and the dynamics of the personalised nutrition concept. Based on a wide range of inputs from societal, scientific and industrial stakeholders, a systems view of the personalised nutrition concept and its environment were developed. Achieving a lasting dietary behaviour change is at the core of this personalised nutrition system.

In order to explore what value creation models could emerge in the future, it was necessary to explore the possible future societal context in which this is bound to take place. Four scenarios about evolution of the nutrition and health issues in Europe served as a basis to conceive 10 value creation concepts for personalised nutrition. These illustrated very different options in personalised nutrition concepts but also the extent to which these may be inherently linked to changes in our future society.

Since personalised nutrition is just starting to take shape, it is inevitable that many of the aspects described here are still very speculative. However, the insights developed in this research seem to indicate that personalised nutrition may be a trigger for important changes in the way our society deals with health and food behaviours.

1 RESEARCH METHODOLOGY

The process for developing business and value creation models is different from other scientific research performed in this project. The stepwise approach outlined below was based on a combination of field research, systems analysis, scenario planning and creative multi-stakeholder processes, gradually gaining deeper insight into the subject, its elements and its environment.

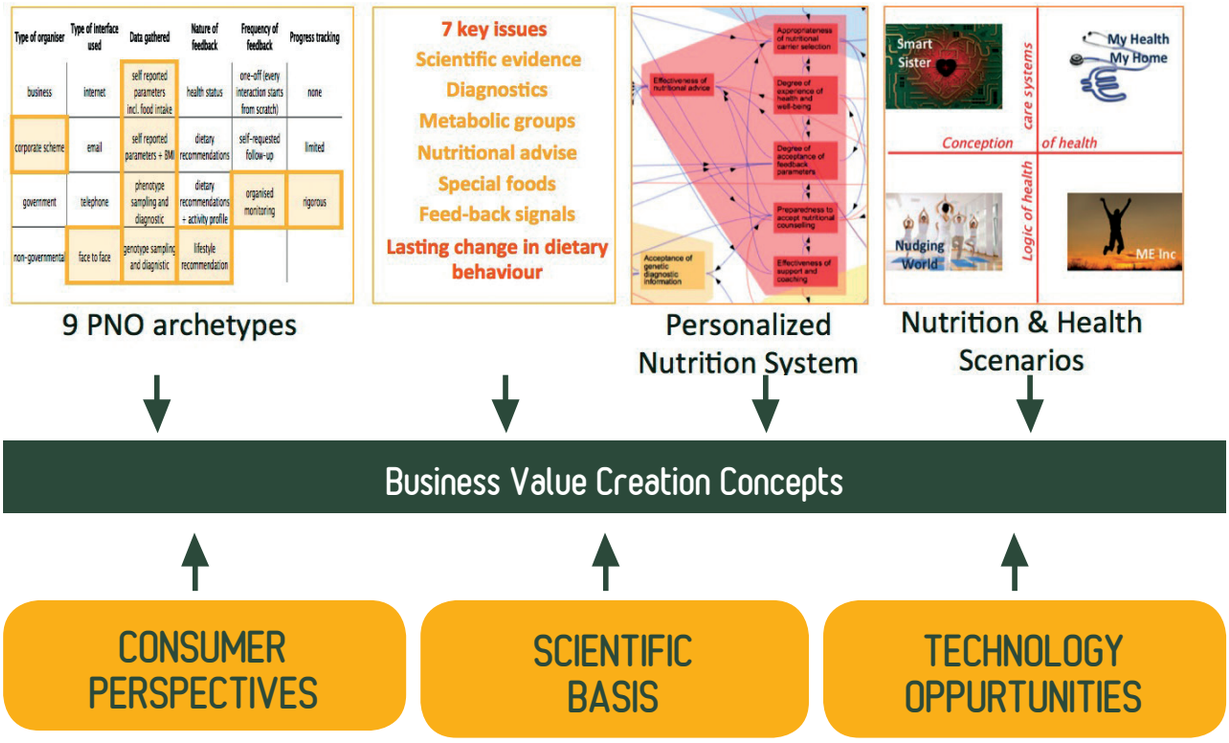


Figure 1: The research process to develop and assess business and value creation models.

1.1 Market analysis of existing personalised nutrition offerings

An inventory of existing business propositions involving some form of personalised nutrition or a similar type of service in Europe, India, Japan and Australia was obtained by an internet and trade press search. This sample was analysed to identify the possible key differentiating characteristics between the offerings and the basic business model archetypes.

1.2 Societal and business stakeholder analysis

Perceptions about personalised nutrition were collected from a wide stakeholder field, including societal, policy and industrial stakeholders, through extensive interviews (by phone or face to face) organised as open-ended conversations. Identifying the key statements and clustering related statements resulted in a set of elements that form the basis for a generic activity model for a personalised nutrition business approach. It also enabled the identification of 7 critical issues that need to be addressed in the development of any personalised nutrition approach.

1.3 A systems view of personalised nutrition

The inherent complexity of a personalised nutrition approach was explored by creating a systems view in the form of an influence diagram that visualised the main drivers and how they interact in shaping the environment in which a personalised nutrition approach is embedded. This "system map" was developed in a co-emerging process in parallel with the analysis of the

outcome of the multi-stakeholder interviews. The modelling process starts by trying to identify the core variables that constitute the 'central engine' of the system. Step by step, other drivers influencing these core variables are then added to the system map and the logical context starts to build up. Variable definitions are gradually refined during the process to arrive at a more accurate description of the environment of the personalised nutrition system.

1.4 Future scenarios about health and nutrition

Future scenarios were designed to provide insight about possible future environments in which personalised nutrition business models could emerge and operate. The two questions driving the scenario building were:

- How will the issues around nutrition and health impact our society and the future business and regulatory environment?

- What opportunities for economic and societal value creation will exist in this vast and complex arena and how can personalised nutrition contribute to this?

In a facilitated and structured scenario planning process, a group of about 25 representatives from a variety of industrial, societal and academic backgrounds participated in three consecutive workshops to design four scenarios. Each scenario was described in detail in terms of a storyline, key events, food consumption patterns and health care sources, as well as business, regulatory, ethical and information environments. A final assessment explored the possibility for personalised nutrition to emerge in these scenarios.

1.5 Business model development

The aim was to explore which novel business and value creation concepts based on personalised nutrition may be possible and useful in the future.

Two interactive creative sessions were held with a limited group of participants, selected from those participating in the future scenario planning and reinforced with representatives from a wide range of industries, such as food, wellness, health, diagnostics, medical and pharmaceutical players. As a basis for the creative process, an overview was presented of all the insights so far available on personalised nutrition, from the market analysis, the stakeholder interviews, the systems view and the scenarios, as well as the first results from the other work packages of the project dealing with consumer, technological, legal and ethical aspects. In the first session the creative space was left entirely open to the participants, whereas the second session more specifically explored business model concepts that may emerge within the boundaries of each of the four future scenarios.

The Osterwalder business model canvas was used to describe the concepts. Business model concepts were analysed for:

- fit within each of the four scenarios

- capacity to overcome the 7 critical issues for development

- sustainability of the concept in the long run

1.6 Economic evaluation

A first estimate of the economic value of personalised nutrition has been based on desk research, taking into account the previous analyses combined with consumer insights and

experience from the development of health and nutrition related businesses over the last 20 years. It includes estimating the cost and value of a personalised nutrition service as well as the potential market and the degree of penetration. This is then considered within the broad societal context of health care costs and prevalence of diet-related diseases to determine the possible contribution of personalisation in providing a solution to these issues.

2 KEY FINDINGS

• 2.1 Existing business model archetypes

The present market is characterised by a flurry of commercial offerings, many of which could be considered rather opportunistic, simple and sometimes doubtful or misleading in nature. Advice is typically based on very limited data, probably because of the cost to collect and diagnose, and hence the advice is quite basic, limited to nutritional elements, food choices and in some cases a meal plan. The scientific evidence for the advice is often unclear. Many offerings appear to be a means for selling health foods, supplements, diet coaching services or monitoring apps and devices. This is a typical pattern for the early stages of an emerging market and holds major risks for consumer disappointment in the quality of such novel services. This environment of purely commercial opportunism puts the few more extensive offerings, which are obviously also more expensive, under an enormous pressure to survive as some premature cessations have shown.

This market analysis resulted in identifying 9 business model archetypes, each of which can be described by various combinations of the following 6 key differentiating features:

Type of organiser	Type of interface used	Type of data gathered	Nature of feedback	Evolution tracking	Frequency of feedback
business corporate government NGO	internet email telephone face to face	self reported +BMI phenotyping genotyping	health status, food & diet plan activity profile lifestyle	none limited rigorous	one-off self-requested organised - monitoring

Figure 2: Six key differentiating features of business model archetypes.

The majority of current offerings are organised by small companies, use the internet as their main interface, work on the basis of self-estimated and self-reported inputs from consumers and focus on dietary and lifestyle advice based on dietary intake profiles. Regular feedback and progress tracking are not commonly provided by the offerings. It is clear that future business model concepts will need to leverage many more of the above options in order to be perceived of sufficient quality and reliability.

• 2.2 Seven critical issues to implement personalised nutrition

The combined perceptions of a wide range of stakeholders revealed 7 important concerns to address when operationalising a personalised nutrition approach. These have obviously been noted from the perspective of today's environment and therefore can be seen as a set of criteria that need to be fulfilled to facilitate introduction and/or acceptance of personalised nutrition approaches in the future.

2.2.1 There is still doubt about the strength of the scientific evidence for personalising dietary advice

This is a concern shared by many, including those in scientific communities, industries and society. It relates especially to the need and possible usefulness of using individual genetic

information to produce the advice but it also relates to concerns that the existing knowledge about biomarkers can be insufficient. Such measures are key in tracking progress when implementing the advice. An underlying reason for this concern is the fact that currently used research models have not been designed to deliver proof of efficacy on an individual level, but only on a research cohort level. In general there was a feeling that adding more scientific arguments in health and nutrition advice might be counter-productive to achieve dietary behaviour change. This may be particularly the case in providing genetic information, which may be counterintuitive for those with a fatalistic view i.e. they can't change their genes so it is beyond their control.

2.2.2 Making diagnostics feasible and reliable is a huge barrier

Extensive diagnostic testing such as that required for personalised nutrition, is perceived to be a major cost barrier for any business model aimed at general use. While it was postulated that health professionals would have to be involved in the execution and distribution of the diagnostics, they were also perceived to be the most critical in adopting it because of concerns about quality, reliability and usefulness of such diagnostics.

2.2.3 Providing nutritional advice at an individual level is not realistic, it should be delivered at a nutritype level.

There was significant doubt that it was possible and even useful to develop nutritional advice at an individual level. It was suggested that it could be possible to identify large groups of individuals (nutritypes) having very similar metabolic profiles for which similar nutritional advice could be generated. However individual analysis would still be needed to identify to which nutritype an individual belongs. Providing nutritional advice on a nutritype level therefore would not take into account any individual preferences or limitations in terms of food choice, eating patterns and psycho-social factors that would influence adopting a dietary behaviour change.

2.2.4 Personalising food products is economically not feasible

Mass customisation of foods is perceived to be economically impossible and will at most consist of special product ranges designed to fit the largest nutritypes. Moreover health-related claims on food products can be a regulatory nightmare and impossible without strong clinical trial evidence and intellectual property protection. Also decades of changing product/diet recommendations with doubtful health benefits have made the market wary of new health and nutrition related product innovation.

2.2.5 There is a need for economic feedback signals to adopt a healthier lifestyle

Without an economic stimulus, it will be difficult to trigger a change in diet and lifestyle. The economic benefit is complex to assess and therefore defining assessment measures will be difficult. Private health care actors are expected to lead this initiative because authorities until now have shown little drive to change public health care systems. Also it could be expected that the pharmaceutical industry would be a strong adversary to personalised nutrition based on food and not dietary supplements. A harmonised approach in Europe will face important barriers due to regional and cultural differences.

2.2.6 Providing and delivering useful dietary advice at a personal level is the most controversial issue in implementing a personalised nutrition approach

There is doubt that consumers, especially those who need it most, may be hard pressed to seek such professional advice due to ignorance, confusion or fear. Even if they do, it may still be very difficult to provide good personalised dietary advice due to inaccurate or incomplete reporting

of their behaviour and the social environment, thus limiting the effectiveness of the advice. The underlying reason for advising a dietary behaviour change is to 'prevent' disease, however the health care logic in our societies is still dominated by the 'curative' approach.

2.2.7 Personalised nutrition is about achieving a lasting dietary behaviour change

Food as a vector to deliver health is not self-evident. Health is not the most compelling factor for consumers when choosing food, therefore dietary behaviour changes that benefit health are difficult to achieve. Moreover, the perception of food as a vector of health is hampered by several factors:

- lack of understanding about food, its constituents and its preparation
- a decline in the social aspect of eating
- a perceived low value as a result of low pricing, abundance and ubiquitous availability
- extremely confusing and conflicting information streams on food and health
- the perceived inefficacy of dieting

Therefore the main role of personalised nutrition is not to improve nutritional advice or to make it more accessible, but to facilitate a process that will help an individual in achieving a lasting dietary behaviour change that results in experiencing better health. This points to the importance that coaching will have to play.

2.3 The personalised nutrition system: a systems perspective on achieving a lasting dietary behaviour change

The previous insights were consolidated into a personalised nutrition system. It was visualised in the form of an influence diagram (Figure 3) that shows the causal relationships between societal, economic, technical, psychological and biological drivers that affect a personalised nutrition approach. Groups of related drivers are highlighted in the map.

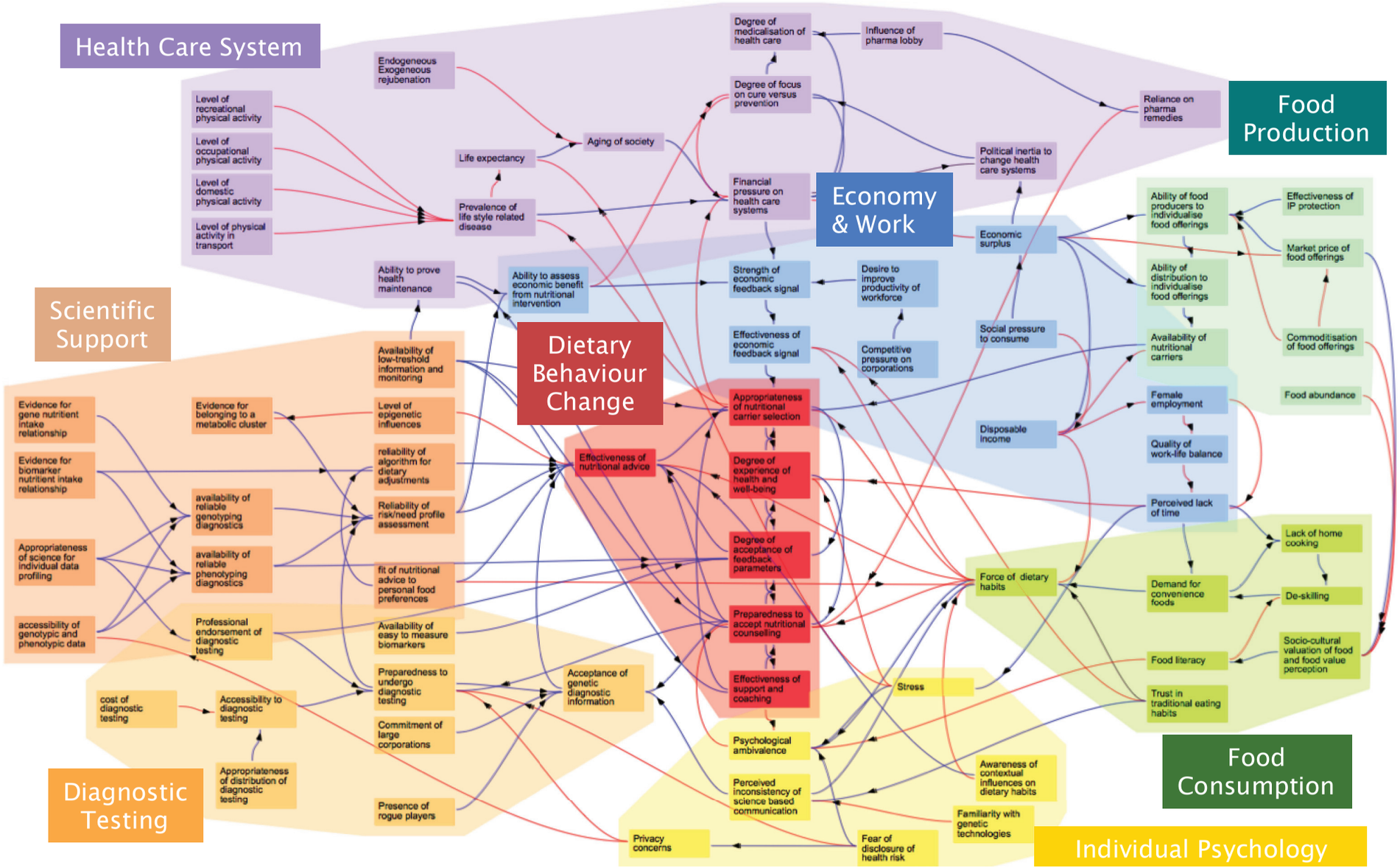


Figure 3: The personalised nutrition system map.

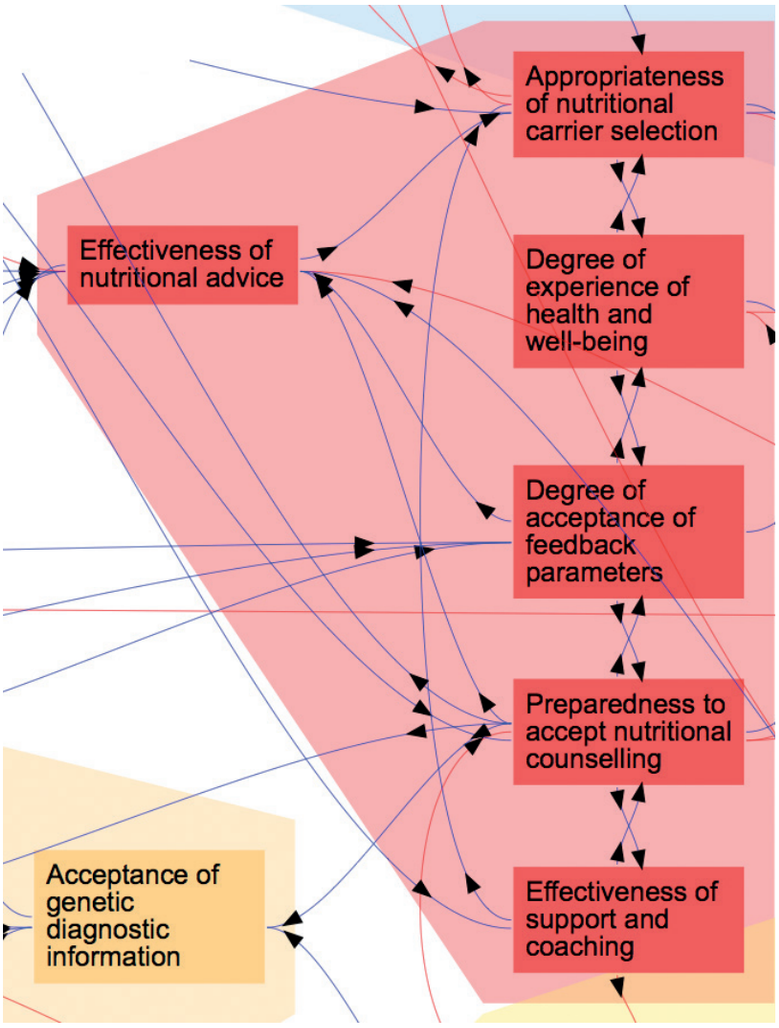


Figure 4: The core engine of the personalised nutrition system: achieving lasting dietary behaviour change.

The "core engine" of the system consists of a set of key activities enabling an individual to achieve a lasting dietary behaviour that is appropriate for his/her individual health and well-being.

The map shows that 6 drivers can be considered key leverage points because they are influenced by many other drivers and transfer these on to many other parts of the system, in particular to the core engine of the system. These are:

- The **effectiveness of support and coaching** in nutritional counselling
- The **financial pressure on health care systems**, which feeds into the central engine via the effectiveness of the economic feedback signal
- The **force of dietary habits** keeping people from adopting healthier dietary alternatives
- The **level of psychological ambivalence** experienced by people in deciding dietary and lifestyle choices (food, exercise)
- The **acceptance of genetic diagnostic information** making the use of genetic information useful in driving dietary behaviour change
- The **reliability of the risk/need profile assessment** which is the basis for proper nutritional counselling

• 2.4 Approaches for personalisation of dietary advice

In a personalised nutrition offering, the advice is, by definition, tailored to the individual. Our insights point to three different approaches for individualisation:

• The **basic assessment of the metabolic profile**. Individualisation at this level means that individual physical characteristics, biomarkers and DNA need to be collected and analysed in order to establish to which nutritype the individual belongs. This allows a set of basic nutritional recommendations to be provided, that fit everyone in this nutritype and therefore are NOT yet individual recommendations.

• **Assessment of individual food preferences and desired eating patterns.** Here the nutritional advice is individualised by translating it into recommended food choices and meals that take individual dietary and food preferences into account.

• **Defining individual preferences with regard to the coaching process** (interface, tools, frequency, follow-up). This tailors the advice to fit the specific individual psycho-social factors that present relevant barriers for change.

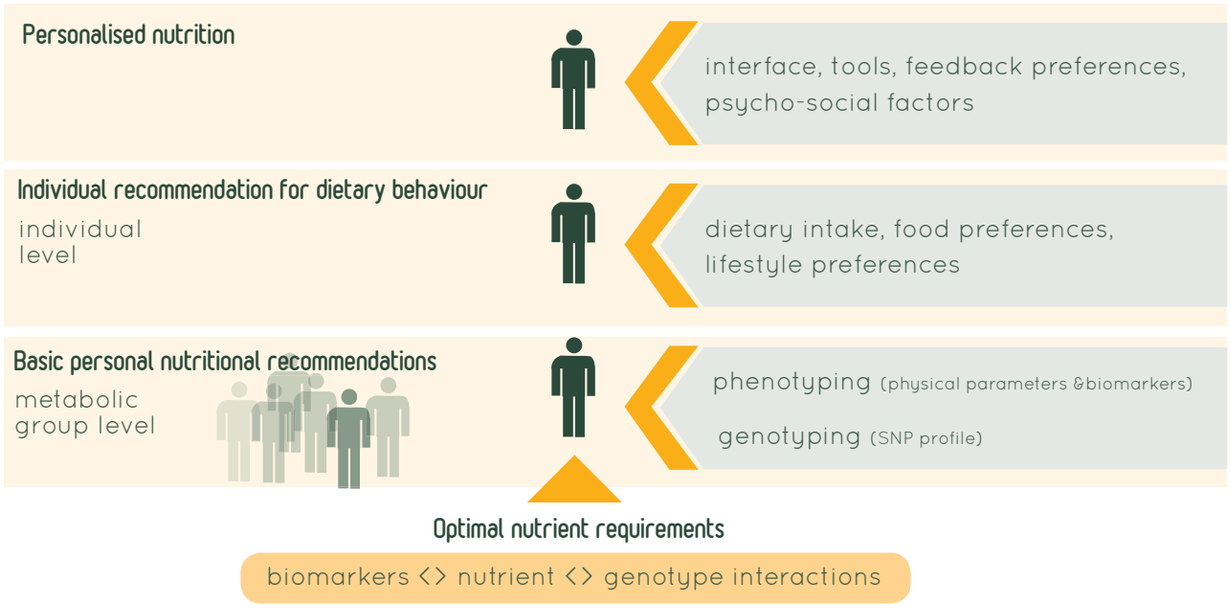


Figure 5: Three approaches for personalised dietary advice.

Thus effective personalised nutrition offerings preferably include all three approaches of personalisation. At present, most commercial offerings focus only on the second approach, thus missing a sound data basis and disregarding the sensitivities of how to deliver the advice.

2.5 NUTRITION AND HEALTH ISSUES WILL BE RESHAPING OUR SOCIETIES

Four future scenarios were developed based on an agreed space defined by the following two axes: the "logic of health care systems" and the "conception of health":

The scenarios show that our society will be significantly reshaped in order to deal with the growing nutrition and health issues. Although there has been no particular role assumed for personalised nutrition in designing the scenarios, it transpired that personalised nutrition approaches are likely to emerge in each of the scenarios where they can potentially be a major driver of change.

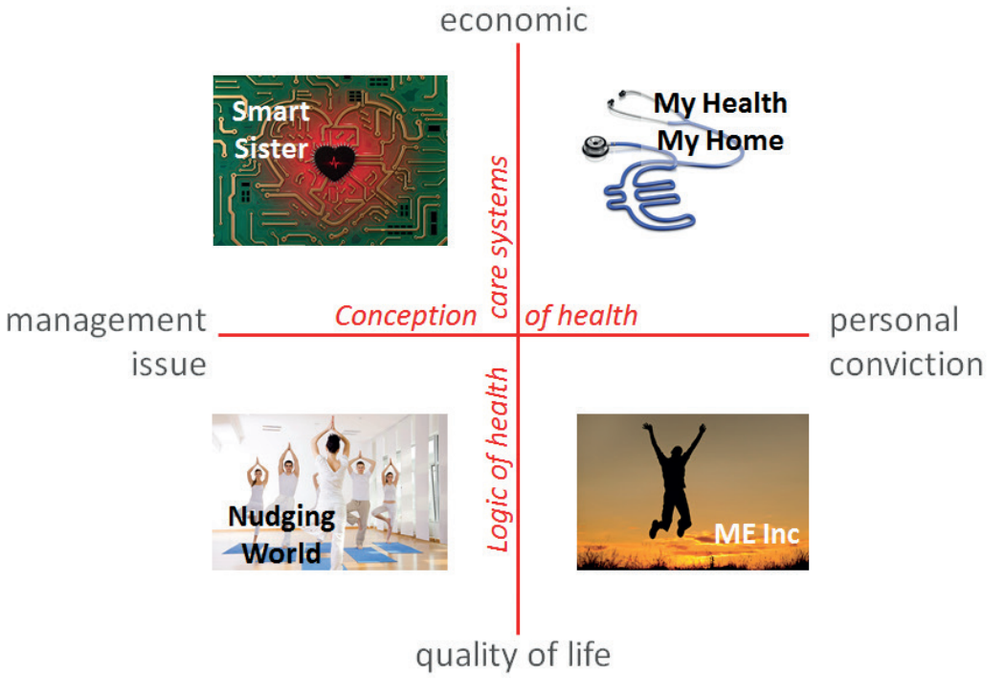


Figure 6. The 4 scenarios in the Food4Me scenario space as defined by its two axes.

The scenarios have fundamentally different dynamics as shown by comparison of three key characteristics:

Scenario	Dominant logic	Key activity	Governance type
Super Sister	Efficiency	Monitoring	Hierarchy
My Health My Home	Private Health Asset Management	Investing	Responsible Autonomy
Me INC	Manifesting Values	Choosing	Heterarchy
Nudging Society	Health Commons Management	Stewarding	Responsible Collectivity

Table 1. Comparison of three key characteristics of the scenarios.

Scenarios were used to explore which personalised nutrition offerings (PNOs) may materialise within these possible contextual environments. They provided both an inspirational background against which business models can be developed, and a set of contexts in which they can be tested and evaluated.

2.6 BUSINESS MODEL CONCEPTS: EMERGING, NETWORKED AND COMMUNITY DRIVEN

Conceiving business model concepts for personalised nutrition transpired to be more difficult than expected. When given full creative freedom, there was a natural tendency to focus on the immediate future and this revealed that the present societal context was severely limiting the scope and novelty of the ideas. The six ideas developed in this way concentrated on alternative retail formats (distribution focus), services and tools directed to child health (target focus) as well as local community-driven health services (organisation focus), each of which was not very different from known business models. The ideas were not felt to be major commercial opportunities, nor were they believed to achieve significant dietary behaviour change in a large population group.

However business models specifically conceived within the four future scenario environments, were vastly different and were felt to be much more conceptual and far-reaching in terms of potential and impact. They shared the following characteristics:

• Gradually emerging as various elements are being added over time to strengthen the scope and reach of the service

• Networked operations rather than single companies or organisations, indicating that personalised nutrition offering is the combination of a group of actors each adding different elements and channels to the concept

• Public and private partnerships, triggered by either public or private initiatives

• Distributed profit centres as many actors are involved: sometimes it is hard to differentiate between a societal service (cost focus) and a business (profit focus)

• The origin or initiative that triggers the development is often hard to define and transition dynamics appear to play a rather important role in the emergence

• The key role of an integrator driving the concept using different types of actors

The potential role of personalised nutrition businesses as integrators between many players is illustrated below:

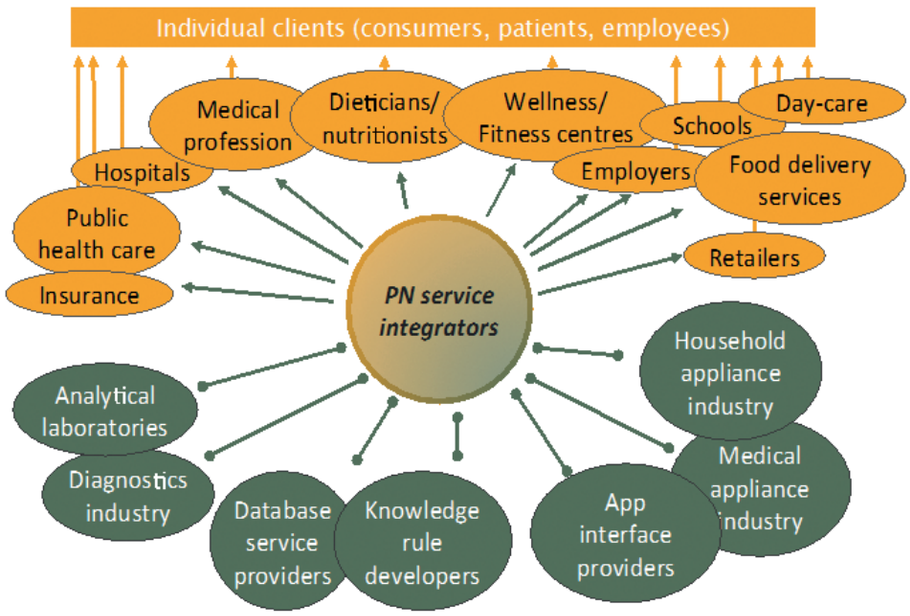


Figure 7: Personalised nutrition service providers as integrators between societal and business actors.

• 2.7 Societal relevance and potential impact

The system map, the scenarios and the business model concepts all point to the fact that personalised nutrition as a concept is deeply embedded in societal tissue. Its introduction is therefore likely to have profound societal consequences but vice versa, societal changes aimed at resolving the nutrition and health issues are likely to result in personalised nutrition approaches. Especially the business models conceived in the context of the 4 future scenarios show how important societal evolution and personalised nutrition approaches are intertwined.

An important societal consequence of personalised nutrition is that individual responsibility for important health aspects is made very explicit and with that the responsibility for the societal consequences of ill health. This will undoubtedly result in a shift in the perception of health and

the logic of health care structures in our society. This raises important ethical issues, especially with regard to the risk for social injustice should not everyone have access to the service or with regard to right to personal freedom of choice, in particular when such choices result in negative health impacts which has repercussions on society as a whole.

• 2.8 Significant economic potential

The development of personalised nutrition approaches is an opportunity that emerges at the confluence of the following three important driving forces in society:

• the **technological and scientific capability** to understand how food and dietary behaviour influences individual health and to assess individual risk for disease, which allows us to make nutritional recommendations more effective, appealing and more convenient to implement and to follow up in daily life.

• the **need to address the huge societal burden of health care** budgets as a consequence of the obesity and chronic disease prevalence, which is essentially due to inappropriate food habits and lifestyles. Health care systems are bound to adapt to cope with costs but this raises the question of social responsibility of the individual to maintain individual health.

• the **desire for individualisation and freedom of choice** requires empowerment of individuals to make appropriate choices, which are particularly difficult in a complex and emotional domain such as food and health. User-friendly tools that enable individuals to access and understand the required information will have to be made available.

Personalised nutrition dynamics are facilitated by a strong technological drive: diagnostic and monitoring tools bring a continued awareness of the personal health status; nutrigenomics and biomarkers make dietary advice more reliable, effective and easier to monitor and mobile interfaces enable instant informed decision making.

It is clear that with the important prevalence of obesity and chronic diseases in our society, there is a large potential market for personalised nutrition services. A rough cost calculation shows that a single personalised nutrition consultation could vary between EUR 40 to 400 and if it would appeal only to 10% of the population needing advice, the market value would still be worth EUR 6 to 18 billion. From a societal perspective, the value would however be a multiple of that because personalised nutrition would contribute substantially to reducing health care costs and increasing economic efficiencies.

3 IMPLICATIONS OF THE RESULTS

Personalised nutrition is a complex but promising concept because its essential goal is to contribute to achieving lasting dietary behaviour change. It therefore holds the potential to relieve the current pressure on our health care budgets and thus to bring significant benefits to the entire society. However, the introduction of personalised nutrition services is not likely to be a regular business development process but will rather require transition dynamics in which societal changes and business model developments co-occur. Thus public-private partnerships are most likely the best form to take developments in personalised nutrition forward. Given the important ethical issues that may arise, policy makers will be required to clear the way for such developments by assuring that regulatory frameworks are in place to guarantee privacy of data in addition to freedom of choice. Without this, there is a significant risk for personalised nutrition services to be misused for commercial reasons or by societal actors to exert improper influences on population.

The networked structure of personalised nutrition approaches will require many different actors to be involved and to co-develop their own services for personalised nutrition integrators (tools, diagnostics, interpretation algorithms) or on the basis of the services from personalised nutrition integrators which can be attached to a wide range of other commercial services (shops, restaurants, wellness and sport centres, medical services, leisure, education, etc.).

There will be a need for scientific coherence in the personalised advice that is generated, because different scientific interpretations of the data at hand will be counterproductive exactly in the same way as contradictory food and dietary advice has caused much confusion until now. One of the approaches that may help to achieve this is the development of initiatives such as QuaLiFY (www.qualify-fp7.eu) which aims to create a uniform platform for PN service providers where scientifically validated knowledge rules are made available for individual data interpretation and food/meal/ recipe advice.

Finally our insights also point to the possibility for a significant change in the perception of the value of health in society. Whereas today health is typically defined as the absence of disease and thus focuses on preventing the onset of disease (pathogenesis), the concept of personalised nutrition offers possibilities to enhance health (salutogenesis). Possible outcomes might be improved metabolic health, greater performance, higher resistance, slower aging, etc. which lead to a higher degree of personal fulfilment as defined in Maslow's pyramid.

These insights are believed to provide potential actors with an excellent basis to set-up more successful initiatives in personalised nutrition services.

4 DEVELOPING THE STATE OF THE ART

The Food4me project has been unique in exploring business model and value creation concepts at a very early stage of a major scientific development and to integrate insights from this process with emerging insights on scientific, technical, consumer, legal and ethical aspects as the project progressed. It is also exceptional to have applied this in the area of nutrition and health where the scientific and technical research is more often confronted with delicate individual and societal issues.

The use of applied systems thinking such as system maps and scenario planning represents a novel way to approach business model development. By exploring the underlying logic of the system and dynamics of the future contextual environment, the creative process to develop business model concepts resulted in fundamentally novel business development scenarios. This approach seems to be particularly useful when dealing with issues that are embedded in very complex environments where many factors and actors interact with each other. The use of a system map to visualise this complexity is an additional strength and helps to come to grips with the contextual environment.

5 WHAT GAPS IN KNOWLEDGE STILL REMAIN?

Due to the nature of this research, which is based on soft systems thinking rather than hard scientific evidence, the findings and conclusions are inherently uncertain, despite the fact that they were obtained through rigorous analysis and with the contribution from a wide range of stakeholder representatives. Significant gaps still exist when it comes to the evaluation of the economic potential due to the lack of accurate cost and value estimates for the various elements in a personalised nutrition service. This will only be possible once real life experience in a commercial environment is available.

With regard to the value of a personalised nutrition offering, there is still much uncertainty to what extent such services will or can be included in public health care systems or whether they will be the domain of private health insurances. In this respect, the variety of European health care systems will make it necessary to differentiate assumptions by country.

When it comes to the role of society and government to take steps to introduce personalised nutrition concepts in society, it will be important to explore the scenario dynamics and business model concepts in relation to available data on health economics, thus considering to elaborate models for economic return when implementing personalised nutrition. This analysis will be necessary as a basis to build the economic arguments that will drive policy decisions to enhance the environment in which personalised nutrition concepts can take shape.

Given the likelihood that personalised nutrition developments will follow a transition dynamic, it would be very useful to explore how the insights about transition dynamics in organisations and societies could inform the next steps that could be taken with regard to personalised nutrition.

6 HOW COULD THESE EFFORTS FEED INTO HORIZON 2020 RESEARCH CALLS?

The application of system thinking and the variety of methodologies utilised in this research are generally applicable and useful in exploring and understanding the dynamic nature of any complex system, particularly when embedded in societal contexts such as is the case for so-called "wicked problems" like climate change, sustainable energy and urbanisation – societal problems difficult to solve. The combination of system map design and scenario planning offers a powerful tool to develop the basic insights that can be a starting point for business development and or policy development. It is also a tool for language creation to discuss the issue at hand.

Given the strong focus of Horizon 2020 on societal challenges and in particular on health and wellbeing, our insights on personalised nutrition systems and business development concepts are of direct importance in any further research looking into alternative health care systems, notably e-health and m-health approaches in which personalised nutrition can be readily included.

7 ACKNOWLEDGEMENTS

Jo Goossens of Bio-Sense, Brussels, Belgium, was WP 1 leader and wrote this chapter.

We wish to thank the entire Food4Me team for the wonderful experience and contribution to our work, but in particular the colleagues from LEI and University of Wageningen who participated in this work package but reported their main findings as part of the consumer chapter (Consumer attitudes towards adoption of personalised nutrition).

Special thanks are extended to all the participants in the scenario and business model workshops for their motivation and interest to contribute. These included many project partners, representatives from industrial, societal and academic organisations as well as independent experts.

8 REFERENCES

Goossens J (2014): Exploring future opportunities and barriers for business model concepts in personalized nutrition. Archives of Public Health 72 (suppl.1.): K5

Goossens J (2013): Future Scenarios about Personalised Nutrition in Europe. http://www.food4me.org/images/banners/food4me_brochure_final_28_06.pdf

Ronteltap A, van Trijp H, Berezowska A, Goossens J (2013): Nutrigenomics-based personalised nutritional advice: in search of a business model? Genes Nutr.8 (2): 153-163

ETHICAL CONSIDERATIONS IN RELATION TO PERSONALISED NUTRITION
An overview of Work Package 5, with respect to ethics

INTRODUCTION

Ethics is the analysis of normative dimensions of human relations and experiences. Such analyses are often based upon basic values related to normative ethical theories. One of the aims of ethics is to discuss arguments and suggest solutions to relational situations, real or imagined, and not least to suggest solutions to complex dilemmas. Our use of ethics as a research tool in this project is an example of applied ethics, also commonly labelled practical ethics. We have started by examining the situation where the practice of personalised nutrition is introduced in the near future. We have then related this understanding to values and normative standpoints that can be drawn from human experiences already analysed in ethical theory.

RESEARCH METHODOLOGY

Personalised nutrition services are related to several fields, such as nutrition, health care, genetics, and public health. In order to deal with ethics in relation to personalised nutrition, we explored ethical issues arising in varying fields while focusing on those aspects that constitute the specific and ethically relevant differences that distinguish personalised nutrition from other health services. One specific characteristic is that personalised nutrition services require personal health data, which qualifies as sensitive information, in order to advise the consumer on how to manage their health. Since a person gives personal data to an institute or company, aspects of trust and trustworthiness become significantly important as well as issues regarding consumer or patient protection. The patient or consumer has to assess the potential benefits of using the service and the risks related to sending in personal health or life-style data. Other characteristics are the focus on prediction and prevention of health problems, as well as the individualising approach to health management and, indirectly, individual responsibility for one´s own health. However, these general characteristics of personalised nutrition vary between

different types of services for personalised nutrition. Therefore, general ethical issues have to be carefully distinguished from specific personalised nutrition services. It matters, for example, what kind of health data are used (e.g. physiological information, genetic information etc.), whether a service requires individual DNA information, or whether a service is based exclusively on direct to consumer (DTC) tools.

• Ethical Dilemmas

Sometimes new information or options for action creates situations where we are unsure about what choice to make, or where all the alternatives for action we identify seem problematic, but for different reasons. This is what we commonly call ethical dilemmas. What dilemmas can be identified related to the introduction of personalised nutrition? Ethics tries to cast light on ethical dilemmas by identifying values and responsibilities discussed in ethical theory. In work package five, we have discussed values and societal or personal responsibilities that may be involved. In some cases it has been possible to give specific advice as a result of ethical reflection.

• Identification and Mapping of the Ethical Issues

THEMES FOR ETHICAL ANALYSIS

Do we know enough?
Commercialisation
Food and Health
Values at stake

One of the objectives of Food4Me work package five included identification and mapping of the ethical issues related to personalised nutrition. We identified four issues, or themes, as in need of further ethical analysis: State of the art of personalised nutrition – do we know enough?; Commercialisation; Food and health; and Values at stake. In October 2011 we also hosted a two-day workshop in Lund, Sweden, targeting these themes. Speakers and participants consisted of both researchers within the Food4Me project, researchers external to the project, and stakeholders representing health insurance companies, patient organisations, professional dietitians' associations, and food and beverage companies.

Below we will present the key questions and results included in the analyses conducted within each theme.

KEY RESULTS

The objectives of Food4Me work package five included a baseline assessment of the ethical and legal aspects of personalised nutrition at the start of the project, as well as a final assessment at the end of the project, taking into account results achieved in other work packages. The initial assessment made a number of ethical issues visible, most of them relating to the consumer of personalised nutrition services. These issues often concern values such as autonomy, trustworthiness, and consumer protection. The results depicted below indicate that many of these questions remain unsolved, and in some cases they seem to be neglected in relation to the services offered by Internet companies. However, the aim of both the baseline assessment at the start of the project and the final assessment at the end of the project was not to provide definitive guidelines or specific advice, although this has been done in some cases. Instead, the primary objective has been to point out major opportunities and challenges for further analysis and discussion.

• THEME 1: State of the art of personalised nutrition – Do we know enough?

A fundamental and debated question concerns whether or not the current scientific evidence regarding the different gene-diet-health interactions is sufficient for taking an ethically responsible decision to offer personalised nutritional advice to consumers. On the one hand, there is a widespread belief that there are many more studies, in different areas, needed to be done. According to this view, the scientific evidence for personalised nutritional advice is quite limited, and more research regarding, for example, behavioural and motivational aspects is also needed. On the other hand, in specific cases of gene-diet interactions, individuals could benefit from following personalised rather than general dietary recommendations. According to this view, personalisation of dietary recommendations is both possible and ethically justified in some instances and should, therefore, be made available for consumers to use.

In light of these opposing views, an ethically sound and responsible way forward is suggested to make use of the precautionary principle, which is often used in situations where we only have limited (or no) knowledge of the possible consequences following different alternatives of action. The precautionary principle can be understood in different ways, and we suggest it to be understood in line with what is considered as "prudent housekeeping". It is suggested that, in good housekeeping, it is appropriate to underestimate incomes (benefits), while overestimating expenses (risks). This will result in cautious estimations of the balance between risks and benefits, while also allowing an appropriate modification of this balance as scientific research is conducted further. Arguing from a precautionary approach, we suggest that personalised dietary advice should be offered only when there is strong scientific evidence for health benefits, followed by stepwise evaluation of unforeseen behavioural and psychological effects.

However, this raises questions about *how* to deliver these recommendations, yet another ethically significant issue to be handled. To give advice based on genetic analyses could be perceived as telling people what they ought to do and, thus, runs the risk of involving a certain amount of paternalism, i.e. an attitude of superiority. From an ethical perspective, paternalism poses a questionable way of dealing with situations where advice and recommendations are given to individuals in order for them to improve certain areas of their lives. Not only from an ethical, but also from a psychological perspective, alternative approaches involving respect for individual integrity as well as individual autonomy, can be seen as more viable.

In the article "Do we know enough? A scientific and ethical analysis of the basis for genetic-based personalized nutrition", questions like these are raised and elaborated in part by confronting two opposing expert opinions with each other.

• THEME 2: Commercialisation

Consumers often have a positive attitude to the option of receiving personalised nutritional advice based upon genetic testing in order to better manage their health, and a variety of companies are presently marketing different kinds of personalised nutrition services over the Internet. Given the current state and amount of scientific evidence for these kinds of services, this raises important ethical (as well as legal) questions.

Psychological and behavioural studies indicate that consumer acceptance of a new technology is primarily explained by the end user's rational and emotional interpretation as well as moral beliefs. Results from such studies indicate that personalised nutrition must create true value for the consumer. Also, the freedom to choose is crucial for consumer acceptance.

Studies have shown that current direct-to-consumer services for personalised nutrition often suffer from a questionable level of truthfulness and an imbalance between far-reaching promises of the effects of personalised advice and contrasting disclaimers of the companies'

services. Since consumers often show an interest in these kinds of services, and also are willing to pay a certain amount of money for it, this could pose a threat to their ability to make informed and autonomous decisions in relation to the services offered, as well as a threat to different aspects of consumer protection.

We have discussed the possibilities of offering consumers personalised nutritional advice over the Internet (by ways of direct-to-consumer genetic tests) in an ethically and legally safe and sound manner securing different aspects of consumer protection. Such aspects include recommendations that are useful, easily understood and valid, as well as safe handling of genetic and other health information and honest marketing methods that enable the potential consumers to make well-informed decisions as to whether or not to make use of the service offered. From an ethical point of view, consumer protection is crucial and we argue that caution must be taken when putting nutrigenomic-based tests and advice services on the market in order to prevent harm.

In relation to legal regulation, personalised nutrition poses a distinctive phenomenon, located on the borderline between nutrition and medicine. Current regulation in this area is perceived as incomplete and, therefore, we argue that there is a need to carefully examine personalised nutrition services on the Internet in order to develop guidelines and rules that safeguard privacy, consumer protection, and safety.

These questions are further developed and discussed in the article "Consumers on the Internet: ethical and legal aspects of commercialization of personalized nutrition".

• Theme 3: Food and health

In human life, food is not only perceived as nourishment and a means for health. Our choice of food is deeply influenced by cultural traditions. A meal is often an important aspect of our social life. Today, food is also to an increasing extent an expression of personal choice. What to eat, with whom and in what kind of context, denotes an important aspect of one´s identity. This means that food is a carrier of values that shape our behaviour.In the context of personalised nutrition, however, food is predominantly seen as a tool for achieving good health.

We explored different connotations of the concept of food and how these might be affected by personalised nutrition. In people's daily lives, various factors have an influence on the actual food consumption pattern. Factors such as the cultural understanding of what is good food, traditional dishes, the social context, availability and affordability influence what people eat. We argue that even if the scientific and health related approach to food is predominant in personalised nutrition, this perspective should be seen as complementary to the social and cultural aspects of food.

The feasibility of personalised dietary advice is therefore likely to depend in part on its compatibility with local food traditions, seasons and social patterns.

Factors such as the cultural understanding of what is good food, traditional dishes, the social context, availability and affordability influence what people eat.

Likewise, the concept of health has been discussed as playing an important role for the way in which personalised nutrition is perceived. The concept of health in itself can be understood in a variety of ways, most of them associated with either a holistic or a biostatistical interpretation. The biostatistical concept of health focuses on survival, while the holistic interpretation focuses on ability as a precondition for health. We suggest that in relation to personalised nutrition, a holistic and individualistic understanding of health and illness has advantages compared to a reductionist biostatistical theory. This may reinforce the benefits of the individualistic approach of personalised nutrition, while also allowing an understanding of health in subjective terms.

For personalised nutrition services, this should imply that the personalisation also affects the idea of health. Different people have different preferences and varying levels of ambition with regard to their health. The holistic connotation of health relates to wellbeing and thus widens the term beyond biomarkers. Consequently, different people in varying life-stages and situations will be motivated by different concepts of what health means for them when receiving and applying life-style and dietary advice. From an ethical perspective, personalised nutrition therefore seems promising, when contributing to the promotion of personal preferences with regard to health. This could imply that certain groups in society are less likely to use and benefit from personalised nutrition, which could be remedied by preventive medical programs focusing on equity and the society as a whole.

In "Food and health: individual, cultural, or scientific matters?" these issues are raised and elaborated further.

• THEME 4: Values at stake

In light of the individualising objective of personalised nutrition, it is of relevance to consider which ethical values might be at stake. One such core value identified is autonomy. We have discussed autonomy in relation to other values of relevance for personalised nutrition, such as responsibility and trustworthiness. As a consequence of the individualising focus, personalised nutrition has the potential to empower the individual who makes use of such services, but may also work the other way around, by attributing exaggerated individual responsibility for health. This can be said to constitute the **DILEMMA OF INDIVIDUALISATION.**

When personalised nutritional advice based on personal health data and personal health risks is available to the consumer, this information could be considered valuable, since there is reason to expect it to be more precise and accurate than traditional population based advice. Thus, better information could facilitate more informed decision making processes and, in this way, enhance individual autonomy. However, when knowledge on personal health risks, as well as information and advice about how to manage these personal risks, is available, individual responsibility and liability might increase as a consequence. If one knows how to improve one's health, but chooses not to follow the advice given – how will this affect that person? In societies where increasing health care costs are an object of policy makers' concerns, there is a risk of individuals being confronted with increased expectations to be compliant with advice regarding healthy nutrition and life style. Thus, technologies such as personalised nutrition services could be said to both contribute to enhanced as well as weakened autonomy. That is, personalised nutrition has the potential to strengthen as well as weaken individual autonomy.

Individualisation also affects the concept of responsibility. Not all people are equal with respect to their abilities or preferences concerning responsibility for health and this poses yet other ethical issues worthy of recognition. From an ethical perspective there might be good reasons to motivate different health policies for promoting individual responsibility in a proactive way. However, according to our understanding, this should be separated clearly from retroactive accountability for bad health.

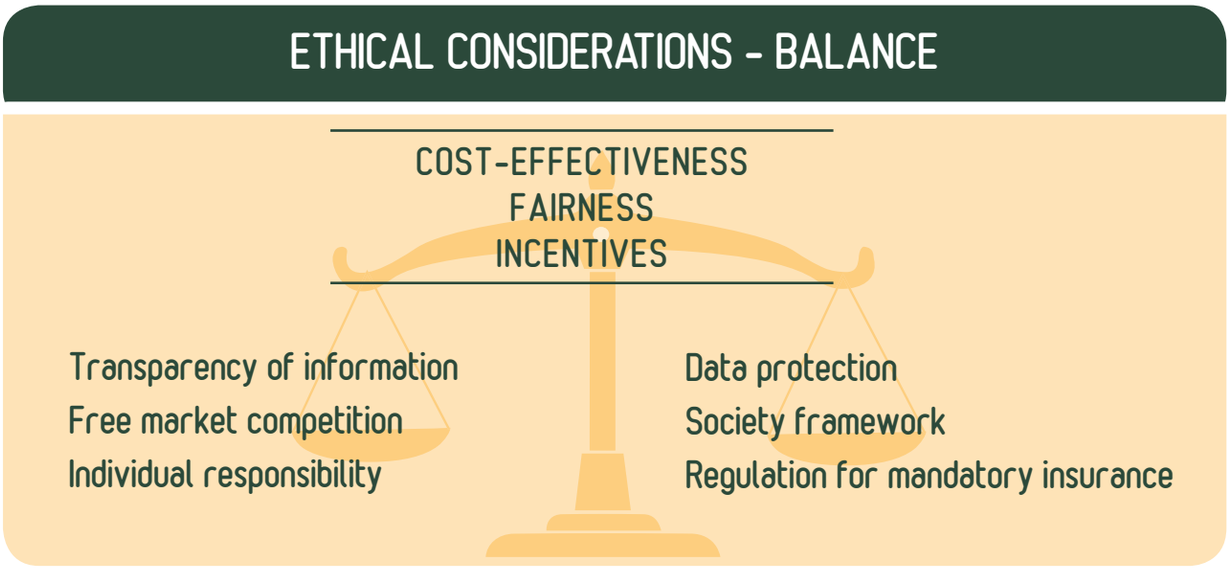
A discussion of different values at stake in relation to the implementation of personalised nutrition can be found in the article "Values at stake: autonomy, responsibility, and trustworthiness in relation to genetic testing and personalized nutrition advice".

In addition to the results presented above, there is ongoing work on several ethical questions raised during the work in the Food4Me project. One of these is an ethical analysis of possible future scenarios identified in Food4Me for distribution of personalised nutrition services. How will personalised nutrition services within these different scenarios affect social relations, values, and justice? Such possible effects will be discussed from a perspective of social ethics.

Another study (publication in progress) addresses issues of solidarity, integrity, and justice in relation to personalised nutrition and the function of health insurances within the scope of compulsory health insurance. We analyse how increasing applications of personalisation in diagnosis and treatment, and consequently of health risk analysis and management, might challenge current systems of solidarity within compulsory health insurance. Will increasing knowledge of individual risks change our view on how health care costs should be shared in the future? Will emerging possibilities to manage individual risks by a corresponding, adjusted lifestyle, influence our view on how we ascribe responsibility for health?

Other questions currently examined relate to consumer protection issues.

IMPLICATIONS OF THE RESULTS



As mentioned above, the objective within work package 5 has not been to produce a set of definitive guidelines either for future research within the area of personalised nutrition or the societal implementation of the concept. However, we have pointed out a number of areas in which important ethical issues arise. As personalised nutrition services are already on the market, it is crucial that these issues are recognised and dealt with in a proper manner in order for the services to be both effective and safe for the individual consumer to use.

HOW COULD THESE EFFORTS FEED INTO HORIZON 2020 RESEARCH CALLS?

The research conducted within work package 5 of Food4Me is well suited to be used and, in some cases, to be further developed within a range of Horizon 2020 research calls, mainly the

ones related to part 16 of the work programme, "Science with and for Society", and also through the Responsible Research and Innovation package. Many of the topics brought up, discussed and processed within Food4Me´s work package 5 relate to societal, legal and ethical challenges concerning consumers and society and address issues of empowerment, trustworthiness, online health services, individual vs societal health responsibility, insurance issues, consumer protection etc. These are also issues related to a range of the topics of Horizon 2020 research calls, for example: Self-management of health and disease and patient empowerment (PHC-27-2015), Public procurement of innovative eHealth services (PHC-29-2015), Self-management of health and disease and decision support systems based on predictive computer modelling used by the patient him or herself (PCH-28-2015) and Advancing active and healthy ageing with ICT: Early risk detection and intervention (PHC-21-2015). The knowledge developed within Food4Me regarding issues like this is can provide a good basis for further research within Horizon 2020

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REFERENCES

Ahlgren, Jennie; Nordgren, Anders; Perrudin, Maud; Ronteltap, Amber; Savigny, Jean; van Trijp, Hans; Nordström, Karin; Görman, Ulf (2013). "Consumers on the Internet: ethical and legal aspects of commercialization of personalized nutrition"; Genes & Nutrition, 8:4, 349-355, Springer Verlag

Görman, Ulf; Mathers, John C.; Grimaldi, Keith A.; Ahlgren, Jennie; Nordström, Karin (2013) "Do we know enough? A scientific and ethical analysis of the basis for genetic-based personalized nutrition"; Genes & Nutrition, 8:4, 373-381, Springer Verlag

Nordström, Karin; Coff, Christian; Jönsson, Håkan; Nordenfelt, Lennart; Görman, Ulf (2013). "Food and health: individual, cultural, or scientific matters?";Genes & Nutrition, 8:4, 357-363, Springer Verlag

Nordström, Karin; Juth, Niklas; Kjellström, Sofia; Meijboom, Franck L. B.; Görman, Ulf (2013). "Values at stake: autonomy, responsibility, and trustworthiness in relation to genetic testing and personalized nutrition advice"; Genes & Nutrition, 8:4, 365-372, Springer Verlag

LEGAL BARRIERS AND REQUIREMENTS
Work Package 5: Legal

INTRODUCTION

The purpose of the research was to identify and analyse the legal and regulatory framework of relevance for 'personalised nutrition' (PN) offerings in the European Union (EU).

The concept of personalised nutrition typically refers to the activity of adjusting personal dietary counselling and advice to information from genetic tests, combined with knowledge received from current and future development in nutritional genomics.

For conducting the research, it was assumed that a service provider, that may be based within or without the EU, offers 'PN advice' to 'customers' in different EU countries. The potential customers find the information about the service offered on the internet, at the consulting room of their general practitioners, at the gym, on TV, etc. The service provider may involve different categories of professionals, from doctors of medicine to sports trainers, etc.

The offering aims at delivering recommendations concerning diet, but possibly also regarding physical activity and lifestyle in general. The advice is based on the information provided by the customers with regard to their lifestyle, dietary habits and food intake. The offering also gives the possibility to provide an even more 'customer tailored advice' which would be based on body dimensions, analysis of blood samples and the analysis of the DNA of the customer (using nutrigenomics). It is up to the customer to choose what would be the basis for the advice they will receive.

The PN advice may be delivered to healthy people wanting to change their diet or lifestyle; but it foresees providing an age or disorder related advice as well. The service is typically provided via the Internet, i.e. through a website using a computer or through an application using a mobile device, where the customer establishes an account secured with a password. The customer may also be contacted by the offering through email, telephone and possibly in person. Before the contract with the customer is signed, the customer is briefed on the details of the service. This includes information on the option of providing the advice on the basis of diet and lifestyle (level 1), phenotypic (level 2) and genetic data (level 3), as well as details regarding the way the data concerning him or her will be handled. The customer chooses the option of the PN advice most suitable for them, and gives consent to the handling of their personal data. The customer will deliver such information by filling in an online questionnaire. Also, if the customers wish to be consulted on the basis of the phenotypic and genetic information, they will be requested to collect the blood and buccal samples at home. To do so, the customer will use medical devices which will be sent to them by the service via post. Following the instructions of use sent to the customer together with the devices and the information on the website of the service, the customer will provide the service with the data.

On the basis of the information provided by the consumer, the PN advice will be generated and delivered to the customer via their account and/or through email. If the option with inclusion of the genetic information has been chosen, the customer will be informed on the dispositions towards certain disorders, if any. The advice may include a food shopping list, diet plan for a certain period of time, inclusion of specific food products in the diet, consumption of food

products designed specifically for the needs of the particular consumer, recipes, physical activity recommendation, etc. The customer will be contacted on a regular basis in order to get feedback on his/her progress in improving their diet and lifestyle in accordance with the PN advice. Also, the customer will be asked to repeat the measurements in order to assess the changes in the body dimensions and in the levels of certain nutrients in the blood.

RESEARCH METHODOLOGY

By contrast with population-based nutritional advice, PN triggers additional legal issues related to the rights of individuals

The determination of the relevant legal and regulatory frameworks applicable to PN and the resulting barriers and requirements has been made by assessing typical business models of PN against the requirements currently set up by legal instruments that have been or will soon be adopted at EU or at Member State level, and in light of international instruments where they exist.

To this effect:

- While compiling the legal framework relevant for PN, both 'hard law' and 'soft law' were considered, at international, EU and national level.

- With regard to international law, the research addressed the relevant instruments where EU law was not addressing the domains of interest, and identifying areas where international law is susceptible to fill the gap.

- The research analysed national law in place in the EU Member States in situations where EU law does not provide satisfactory harmonisation and/or where the legislative competence is in the remit of the Member States.

- In several domains of relevance for PN, the EU legislation is currently being revised and it was therefore not possible to analyse in sufficient depth the impact of these changes given that the proposed provisions are still under intensive discussions.

KEY RESULTS

1. Neither the EU nor its Member States have legal instruments specifically dealing with PN. Instead, due to its nature and characteristics, PN falls within the ambit of several legal instruments, and the determination of which legal instruments are susceptible to apply to any specific PN offering necessitates reviewing the different components of the offered service.

Unlike human genetics in general, the legal issues surrounding the use of gene testing in the context of nutritional advice have been largely unexplored so far, both at international level and in the EU.

By contrast with population-based nutritional advice, PN triggers additional legal issues related to the rights of individuals. Notably, conducting genetic testing and collecting sensitive data requires consent of the person concerned; tests have to be safe, i.e. they have to be provided in accordance with the quality standards; data has to be protected according to the policy established for this purpose, access to it should be restricted; etc.

At international level, EU countries can only be bound by international instruments if they have signed/ratified them themselves or if the EU has the competence to sign/ratify them as

an international entity. As a result, very few instruments addressing certain components of PN offerings can be considered as 'hard law' creating enforceable obligations and rights for the EU countries. Rather, there are several pieces of 'soft law' not directly enforceable but bearing relevance for the matter.

While healthcare is the responsibility of the Member States, the interactions it involves with people (e.g. professionals and patients), goods (e.g. foods, pharmaceuticals and devices) and services (e.g. provided by health care funders and providers) are nevertheless subject to EU law and policy so as to guarantee freedom of movement across borders.

By nature, a PN offering involves the provision of services to the consumers. Accordingly, for services provided to consumers that are based in the EU, the offerings will have to comply with the legal requirements that are applicable in the EU to service providers. For providers that are not established in the EU, it must be determined whether the law of the country of the EU consumer ("country of destination") or that of the vendor outside the EU ("country of origin") should apply.

2. As a service contract, a PN offering will be subject to the provisions of Directive 2006/123/EC on services in the Internal Market unless it is regarded as a healthcare service, in which case, notably, the provisions of Directive 2011/24/EU on the application of patients' rights in cross-border healthcare will apply.

The classification of the PN offering as healthcare or not is dependent on the status of the various professionals involved in the Member State where they are established. Such classification has a significant impact on the legal provisions applicable to the related PN contract of service. Indeed, while in the case of healthcare services, EU provisions are limited to patient's' rights in cross-border situations, non-healthcare services are subject to pretty detailed harmonised rules guaranteeing the protection of consumers in all circumstances. In this sense, the legislation applicable to PN as a service has turned out to be very fragmented and to result in legal uncertainty with regard to (1) the protection of the consumer and (2) the resulting obligations of PN providers depending on the status of the professionals involved in the PN offering.

While PN offerings have to comply with the EU legal requirements that are applicable to service providers, which specific legal instruments will apply will depend on whether the offering is, or is not, regarded as a heath care service. Indeed, although **Directive 2006/123/EC on services in the Internal Market** contains provisions enabling the exercise of the freedom of establishment of service providers and the free movement of services throughout the EU and should therefore apply to PN offerings, that Directive excludes from its scope: *(f) healthcare services whether or not they are provided via healthcare facilities, and regardless of the ways in which they are organised and financed at national level or whether they are public or private.* At the same time, **Directive 2011/24/EU on the application of patients' rights in cross-border healthcare** set specific rules for facilitating the access to cross-border healthcare and to promote cooperation between Member States in the health care area.

2.1 Conditions for a PN offering to be regarded as a healthcare service

Per Directive 2011/24/EU on the application of patients' rights in cross-border healthcare, any PN offering that (1) involves health care professionals (defined as: *a doctor of medicine, a nurse responsible for general care, a dental practitioner, a midwife or a pharmacist within the meaning of Directive 2005/36/EC, or another professional exercising activities in the healthcare sector which are restricted to a regulated profession as defined in Article 3(1)(a) of Directive 2005/36/EC, or a person considered to be a health professional according to the legislation of the Member State of treatment)* and (2) is intended to assess, maintain or restore patients'

state of health, including the prescription dispensation and provision of medicinal products and medical devices, will be regarded as a health care service.

On that basis, while it is clear that doctors of medicine, nurses responsible for general care, dental practitioners, and midwifes or pharmacists will always be regarded as healthcare professionals, taking a global approach for determining whether PN offerings are healthcare or not under EU law will be very challenging, almost impossible with regard to the notion of professionals *'exercising activities in the healthcare sector which are restricted to a regulated profession as defined in Article 3(1)(a) of Directive 2005/36/EC, or any person considered to be a health professional according to the legislation of the Member State of treatment':* the status of each individual PN offering is to be assessed on a case by case basis, taking into account the status of the various professionals involved in the Member State where they are established (qualification in the country of origin or recognition of qualification in the country of establishment).

2.2 Legal barriers and requirements applicable to PN offerings that are not a health care service

In that case, PN offerings will be potentially subject to the provisions of Directive 2006/123/EC on services in the internal market; the Directive 2011/83/EU on consumer rights; the Directive 2000/31/EC on e-commerce; the Directive 2005/29/EC on unfair business to consumer commercial practices; and to the legislation in place at national level setting up the requirements applying to the professionals involved in the PN offering. Of specific relevance to PN offerings:

2.2.1 Directive 2006/123/EC on services in the Internal Market

This Directive relates to the exercise of the freedom of establishment of service providers and the free movement of services. It regulates services supplied by providers established in an EU Member State: it defines 'service' as any self-employed economic activity, normally provided for remuneration. As already noted, healthcare services (as defined in Directive 2011/24/EU on the application of patients' rights in cross-border healthcare) are not within the scope of that 'internal market'. The Directive lays down requirements regarding the information that has to be provided to the recipient of the services, and it requires the Member States to set up points of single contact, through which service providers can deal with administrative procedures and formalities.

2.2.2 Directive 2011/83/EU on consumer rights

The aim of that Directive is the approximation of national legislation of Member States concerning contracts concluded between consumers and traders which also include the so-called 'distance contracts' (defined as: *any contract concluded between the trader and the consumer under an organised distance sales or service-provision scheme without the simultaneous physical presence of the trader and the consumer, with the exclusive use of one or more means of distance communication up to and including the time at which the contract is concluded*).

10 All pictures in this chapter have been sourced from the European Commission websites.

The Directive does not apply to contracts for health care whether or not they are provided via healthcare facilities. Also, Member States may decide not to apply the Directive to off-premises contracts for which the payment to be made by the consumer does not exceed EUR 50. The Directive does not prevent traders from offering consumers contractual arrangements which go beyond the protection provided in the Directive.

The Directive contains a list of core information to be provided by traders prior to the conclusion of consumer contracts, i.e. details on the identity of the trader, the price, the payment arrangements, the guarantee, and the duration of the contract if applicable. Member States may add on further national information requirements. It also provides for specific information requirements applicable to distance contracts, including contracts concluded by electronic means and placing the consumer under an obligation to pay.

The Directive gives the consumer the right to withdraw from the contract within 14 days after the conclusion of the contract. The consumer, when withdrawing from the contract, is to use the model withdrawal statement (given in Annex IB to the Directive)/ or any other unequivocal statement.

2.2.3 Directive 2000/31/EC on certain legal aspects of information society services, in particular electronic commerce, in the internal market (e-commerce Directive)

The aim of this Directive is to ensure the free movement of information society services between the Member States. It refers to the definition of the information society service provided in Directive 98/34/EC, i.e. *any service normally provided for remuneration, at a distance, by electronic means and at the individual request of a recipient of services*. Under Article 3, providers of information society services are subject to the legislation of the Member State in which they are established. The Directive defines a provider's place of establishment as the place in which a service provider effectively pursues an economic activity using a fixed establishment for an indefinite period.

The e-commerce Directive establishes a list of (1) information that the provider of the service has to make available and accessible at any time to the recipient of the service, and (2) information to be provided to the recipient of the service clearly, comprehensibly and unambiguously, prior to placing an order.

The Directive requires that commercial communications, as well as the person on whose behalf the communication is made, are clearly identifiable. In case a Member State allows for unsolicited commercial communications by electronic mail, such communications have to be identifiable clearly and unambiguously as such, as soon as it is received by the recipient. Also, the national legislation should give the recipient of such unsolicited communication a possibility to opt-out, i.e. to remove their name from the list of receivers of such communication. According to the Directive, Member States should permit commercial communications by members of regulated professions. Such communications should be in compliance with professional rules.

2.3 Legal barriers and requirements applicable to PN offerings that are a health care service

Health care legislation in the EU has a fundamental contradiction at its core: On the one hand, the Treaty, as the definitive statement on the scope of EU law, states explicitly that health care is the responsibility of the Member States; on the other hand, as Member State health care involves interactions with people (e.g. professionals and patients), goods (e.g. foods, pharmaceuticals and devices) and services (e.g. provided by health care funders and providers), all of which are granted freedom of movement across borders by the same Treaty, many national health activities are in fact subject to EU law and policy.

Bottom line therefore, if regarded as a health care service, the PN offering will only be subject to EU harmonised provisions when it is offered in a cross-border situation in relation to the protection of a patient's rights. By contrast, when PN service is offered without the cross-border element, e.g. by healthcare professionals established in the same country as the consumer/patient, only the national provisions related to healthcare will apply.

Similar to the situation for non-healthcare services, consumers/patients seeking PN services considered as healthcare in Europe expect to have a good understanding of their individual rights in a number of key areas, such as obtaining sufficient information on diagnosis; informed consent to treatment; privacy protection and access to their health data; or mechanisms to file complaints and to redress harm.

However, comparing the different healthcare legislation in place in the EU Member States is very difficult due to the lack of available and comparable information.

The European Observatory on Health Systems and Policies (EOHSP) supports and promotes evidence-based health policy-making through comprehensive and rigorous analysis of the dynamics of health care systems in Europe.

Various studies are of useful interest when comparing the different health care systems in the EU. From one of them, it is clear that although common values and principles in health care exist, the way in which quality and safety of healthcare are defined and implemented is still largely determined by national law and differs widely from country to country. As an illustration of this divergence, the EU is currently working on various initiatives in relation to patient safety and quality of care to organise an effective exchange of best practice in the field and to propose sustainable EU co-operation in the future.

2.3.1 The EU role is restricted to cross-border healthcare services

The freedom to receive health services throughout the EU must be accompanied by guarantees of quality and security. In order to make an informed choice, patients must be able to access all the information they require regarding the conditions under which they will receive healthcare in another EU Member State and the conditions under which they will be reimbursed once they return home. While the challenges are slightly different in the case of PN offerings considered as healthcare (notably with regard to the possibility of reimbursement), the guarantees of quality and security are also of great importance to PN.

2.3.2 Rules applicable to PN offerings pursuant to Directive 2011/24/EU on the application of patients` rights in cross-border healthcare

The aim of the Directive is to provide rules for facilitating the access to cross-border healthcare and to promote cooperation between Member States in the health care area. This goal is to be achieved with respect to national competencies in organising and delivering healthcare. The Directive applies to the provision of healthcare to patients, regardless of how it is organised, delivered and financed. It therefore applies to any PN offering falling under the definition of healthcare.

While it is essential to determine whether the patient being treated is entitled to reimbursement for the services received in the context of cross-border telemedicine, the matter is not critical in the same way in the context of cross-border PN offerings. The Directive provides that, in principle, the Member State of affiliation of the patient shall reimburse the costs of cross-border healthcare, if the healthcare in question is among the benefits to which the insured person is entitled in the Member State of affiliation.

Although it is not anticipated that PN offerings would be part of the reimbursed healthcare system in the vast majority of the EU countries in the short term, it is quite plausible to assume that PN offerings could be an important tool for the prevention of certain diseases and could therefore in the longer term be reimbursed by the health care system, notably via private insurance. The research noted that this could match the objectives of the Europe 2020 strategy (in particular the EU Health Strategy "Together for Health") aiming to turn the EU into a smart, sustainable and inclusive economy promoting growth for all – one prerequisite of which is a population in good health.

Although Directive 2011/24 does not solve all legal issues related to the provision of cross-border health services in the EU, it establishes Member States' responsibilities in relation to the quality and security of health care that are also of great importance to PN:

• Rights are established to ensure that the essential information on prices, quality and safety of care are accessible to the patient to ensure informed decision.

• The Member State of treatment (in case of PN offerings provided via distance means - where the service provider is established) organises and provides the healthcare. It is responsible for ensuring the quality and the safety of the healthcare provided, in particular by implementing **control mechanisms**. It also ensures the **protection of personal data and equal treatment** for patients who are not nationals of its country.

2.3.3 Potential impact on PN offerings of the EU initiatives in the area of eHealth and mHealth

eHealth
Better Healthcare for Europe

The use of Information and Communication Technologies (ICT) in health care is more and more common. Already in its 2004 eHealth Action Plan, the European Commission had addressed the issue of the so called 'eHealth'. The Directive on consumers' rights in cross-border health care created the 'eHealth network', i.e. a voluntary network connecting national authorities responsible for eHealth. eHealth should be understood as the use of ICT in health products, services and processes combined with organisational change in healthcare systems and new skills, in order to improve health of citizens, efficiency and productivity in healthcare delivery, and the economic and social value of health. eHealth covers the interaction between patients and health-service providers, institution-to-institution transmission of data, or peer-to-peer communication between patients and/or health professionals. The objective of the eHealth network is to allow the citizens to benefit from the eHealth services and applications, to draw up guidelines regarding the use of medical data and to support Member States in cross-border data transfers.

As a result, the European Commission (EC) intends to be more and more active in addressing the eHealth. In December 2012 the EC presented another eHealth Action Plan. The document contains several actions that the Commission commits itself to take in order to continue the development of eHealth in the EU. The Action Plan points out the growth of the mobile health and wellbeing market and the rapid increase in the number of software applications for mobile devices. As stated in the document, the health and well-being applications require a legal regulation in order to ensure their quality and transparency. Accordingly the Commission adopted in 2014 a Green Paper on such applications. In addition the Commission consulted the public on the said Green Paper in order to understand the need for next Commission actions. The discussion on the topic will continue in several events organised by the Commission in 2015.

The 2012 eHealth Action Plan has been accompanied by a Commission Staff Working Document (SWD) on the application of the existing EU legal framework to telemedicine. Telemedicine should be understood as providing health care services through the use of ICT in situations where the health professional and the patient are not in the same location. The SWD presents different situations where telemedicine raises legal concerns. The Commission applies to those issues existing EU legislation on cross-border health care, on medical devices and medicinal products and on data protection.

Finally the Commission plans to address in the future the problem of health data protection and to cooperate with third countries in the eHealth area.

3. THE CHALLENGE OF DATA PROTECTION

A key aspect of the PN offerings is the legitimate processing by the PN offering provider (as the data controller) and possibly other sub-contractors (as data processor acting on behalf of the PN offering provider) of information which relate to the physical health of individuals including phenotype (level 2) or genotype (level 3). Given the 'on line' nature of the PN offerings, the determination of the legal provisions guaranteeing the protection of personal health data is facing the challenges brought by the rapid and recent technological developments and globalisation of data flows.

The current EU data protection rules – mainly dated before the Internet came into widespread use and intended to protect the right to privacy - already set specific rights for data subjects and obligations for data controller/processor that are directly applicable to personal data processed in the context of the PN offerings.

If the data processed in the context of PN offerings are to a great extent health data, the processing of which is subject to special conditions, a distinction is made between the genetic ones (level 3 of PN offerings) and the others in the data protection framework, given the importance to create the trust in an online economic environment.

Recalling that:

• Article 16(1) of the Treaty on the Functioning of the European Union (TFEU), as introduced by the Lisbon Treaty which entered into force in December 2009, establishes the principle that everyone has the right to the protection of personal data concerning him or her. Moreover, Article 16(2) TFEU allows the adoption of rules relating to the protection of individuals with regard to the processing of personal data by Member States when carrying out activities which fall within the scope of Union law. It also allows the adoption of rules relating to the free movement of personal data, including personal data processed by Member States or private parties.

• Article 8 of the Charter of Fundamental Rights of the EU enshrines protection of personal data as a fundamental right just after the right to privacy in the catalogue of freedoms of the individual (Article 7 of the Charter).

• Art. 6(1) of the Treaty on European Union (TEU) incorporates the Charter into EU primary law, and the European Court of Justice of the EU now refers to data protection as a fundamental right.

In other words, EU primary law now furnishes two legal bases for the new fundamental right to data protection as well as a new EU competence to legislate this area. The proposed new Regulation on Data Protection directly results from these new legal bases.

3.1 Data Protection challenges faced by PN offerings

The data protection challenges identified in connection with the development of PN offerings mirror the overall challenges linked to technological developments and globalisation identified by the Commission in its impact assessment.

Obviously, PN offerings benefit from the development of the internet which greatly facilitates and increases the scale of data collecting and sharing, across geographical and virtual borders. Therefore, most of the PN services are likely to be provided online; generally accessible regardless of the geographic location of user and service provider, and the operation of the service includes the transfer of personal data across borders.

The result is that personal data today can be processed more easily - and on an unprecedented scale - by both private companies and public authorities, which increases the risks for individuals' rights and challenges their capacity of keeping control over their own data. Moreover, there are wide divergences in the way Member States have transposed and enforced the current Data Protection Directive, so that in reality the protection of personal data across the EU cannot be considered as equivalent throughout the EU Member States.

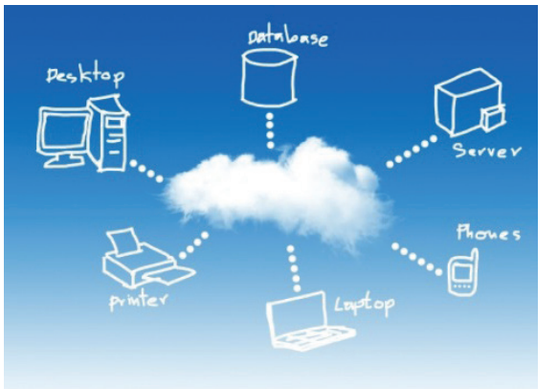
Although it is not anticipated that Member States do, in practice, block the flow of personal data to or from another Member State, these differences raise the compliance costs related to data processing and transfer operations between Member States.

As the Directive leads to the simultaneous application of national laws where the controller is established in several Member States, PN offering providers (data controllers) operating across borders need to spend time and money (for legal advice, to prepare the required documents etc.) to comply with different, and sometimes contradictory, obligations, such as the different requirements for notifications of data processing to Data Protection Authorities. This may discourage some PN businesses (notably small and medium-sized enterprises) from offering services which would require cross-border transfers of data within the EU.

Last but not least, PN offerings may involve the processing of very sensitive data such as genetic data. However, the current framework does not address the particular risk raised by the processing of genetic data.

3.2 Key changes introduced by the Commission Proposal for a General Data Protection Regulation of relevance for PN

The EC has proposed in January 2012 a Regulation reforming the EU data protection legislation. The reform consists mainly of a draft Regulation setting out a general EU framework for data. The proposal is currently being discussed by the two EU co-legislators, the European Parliament and the Council of the EU.



In essence, the form of a Regulation has been chosen as a legal instrument. Its direct applicability in all EU Member States is intended to reduce legal fragmentation and to provide greater legal certainty by introducing a harmonised set of core rules. This should generally lower the cost associated with the processing of sensitive data in the context of PN services offered to EU customers.

3.2.1 Territorial scope

As per the initial Proposal by the Commission, the territorial scope of the legislation would be clarified, so that it applies to the processing of personal data of subjects residing in the EU: whether the data controller is established or not in the EU would no longer matter.

The European Parliament introduced amendments to the effect that the Regulation would apply to controllers or processors whethertheprocessingtakesplace in the EU or not. Also, the Parliament dropped the requirement of the data subject residence in the EU: the Parliament suggested that the Regulation should apply to processing of personal data of data subjects in the EU by a controller or processor not established in the EU, where the processing activities are related to the offering of goods or services to such data subjects in the EU, irrespective of whether a payment by the data subject is required, or the monitoring of such data subjects.

The Commission agreed with those amendments, underlying however that in the second case, i.e. when the processor or controller are not established in the EU, the Regulation applies *regardless* of whether the processing takes place within the EU or not.

In addition, in a partial general approach on specific aspects announced by the Council on 10 October 2014, the Council confirmed the requirement of the designation of a representative of a controller not established in the EU, if this controller is processing personal data of data subjects residing in the EU. The controller should designate a representative, unless the processing it carries out is occasional and unlikely to result in a risk for the rights and freedoms of data subjects, taking into account the nature, scope, context and purposes of the processing or the controller is a public authority or body.

3.2.2 Definition of 'personal data'

The Regulation amends the definition of 'personal data' to include an explicit reference to 'genetic identity' of an identifiable person. A single and consistent definition of 'data subject's consent' is introduced referring to the criterion 'explicit' in order to avoid confusing parallelism with 'unambiguous' consent (Article 7 of the Data Protection Directive). Also, it introduces new key definitions for the protection of sensitive data: 'genetic data', 'biometric data' and 'data concerning health'. (Art. 4)

3.2.3 Consent

The conditions for consent to be valid as a legal ground for lawful processing of the data are further clarified (Art.7), placing explicitly the burden of proof on the controller, introducing the right to withdraw such consent at any time and losing its validity when the purpose ceases to exist or as soon as the processing of personal data is no longer necessary for carrying out the purpose for which they were originally collected.

3.2.4 Prohibition of processing 'sensitive data' and its exceptions

Article 9 sets out a general prohibition for processing sensitive categories of personal data, including explicitly genetic data and the exceptions from this general rule. As in Article 8 of the current Data Protection Directive, the prohibition can be lifted where the data subject has given consent to the processing of those personal data, except where Union law or Member State law provide that this prohibition may not be lifted by the data subject. Differences between the Member States may therefore subsist under the Regulation.

The explicit inclusion of genetic data as a special category of personal data requiring specific safeguards ("sensitive data") would bring about an important positive impact for PN consumers as it should address the particular concern that genetic data is properly and securely dealt with in all Member States.

Additional exceptions from this prohibition would be introduced in relation to:

- The processing of data concerning health (Art. 81), including where such processing is necessary for reasons of public health, such as ensuring high standards of quality and safety, inter alia for medicinal products or medical devices.

- The processing for scientific research purposes (Art. 83) on the condition that:

  the purpose of the research cannot be otherwise fulfilled by processing data which does not permit, or no longer permits, the identification of the data subject;

  data enabling the attribution of information to an identified or identifiable data subject is kept separately from the other information under the highest technical standards, and all necessary measures are taken to prevent unwarranted re-identification of the data subjects.

3.2.5 Other requirements

The Proposal also contains provisions on information requirements, the data subject's right of access to their personal data, the data subject's right to erasure, a limit to profiling, the obligation for controllers and processors to maintain documentation of the processing operations under their responsibility. It also introduces the obligation of controllers and processors to carry out a data protection impact assessment prior to risky processing operations (Art. 33). Those operations are subject to mandatory consultation by the supervisory authority prior to the processing (Art. 34).

3.2.6 Harmonised enforcement

The draft Regulation also sets harmonised rules for enforcement so that, as opposed to the current situation where businesses are supervised by a different authority in each Member State where they are established, there would be only one responsible data protection authority – the national authority of the Member State in which the company has its main establishment.

3.2.7 Legislative process

To become law, the proposal must be approved by the Council and the Parliament. The first reading of the Regulation in the plenary of the European Parliament took place on 12 March 2014. We are awaiting now the reading of the Regulation in the Council.

Obviously, the Regulation is of great interest for many different stakeholders. Therefore, it is expected that the final Regulation will undergo several amendments compared to the initial Commission's proposal.

At this stage, the practical impact of an increased level of protection of data subject's rights, notably with regard to sensitive data may result in new obstacles for the development of PN offerings depending on the final wording of the provisions. However, it can already be anticipated that the harmonised approach would bring about positive impacts for PN companies who process genetic data, as they could enjoy legal certainty for this processing in all Member States and would only have to deal with a single national data protection authority in the EU country where they have their main base.

Also, the objective to improve personal data protection for individuals appears achieved in this proposal, hence increasing trust by the PN consumers/users. The level of trust, however, will depend of the consumers' awareness of their rights given by the new legislation. Finally, from the PN offering stand point the proposed legislation is expected to facilitate the processing of data by the providers across the EU.

4. DEVICES USED IN THE DELIVERY OF PN SERVICES MAY BE SUBJECT TO THE LEGAL REQUIREMENTS APPLICABLE TO MEDICAL DEVICES OR IN VITRO DIAGNOSTIC (IVD) MEDICAL DEVICES

PN offerings may involve the use of various devices, alone or in combination, notably products for the collection of specimens (mainly blood and buccal cells) to be performed by the consumer himself (self-testing), software to process the data or to assist in determining the appropriate recommendations for diet and lifestyle and self-monitoring solutions (e.g. Activity Monitor).

As a matter of principle, devices used in PN offerings must have a medical purpose to be qualified as medical device; only the intended purpose as described by the manufacturer of the device is relevant for its qualification and classification, irrespective of how it may be called. It could be argued that PN offerings have generally not a medical purpose as described in the definition of medical device notably *diagnosis, prevention, monitoring, treatment or alleviation of disease as commonly interpreted. The devices used in the PN context are intended to provide 'lifestyle' services* and might be considered as not covered by the rules applicable to medical devices although they can indeed improve health and contribute to the prevention of diseases.

Importantly, the medical purpose remains unclear and it currently leads to different interpretation on the qualification of the devices used in the context of PN offerings ('lifestyle services') within the EU.

For instance, the Human Genetics Commission noted in its 2003 report the definitive interpretation from the UK Medical Devices Agency that *lifestyle tests are within scope because it sought to measure a physiological state, namely the presence of SNPs in particular metabolic genes and hence the activity of certain metabolic pathways.*

While there should ideally be a very broad interpretation of the medical purpose in the definition of medical device as they apply to lifestyle testing kits or services, the situation remains unclear under the current definition of medical device. Similarly, while in case of doubt the industry should be encouraged to agree to voluntarily comply with the medical devices legislation and submit to the CE mark process (themanufacturer'sdeclarationthattheproductmeetstherequirements of the applicable EC directives), there is no guarantee yet that all operators in the sector will do so, creating therefore a situation of legal uncertainty in the EU.

Even though a given device that does not fall under the definition of medical device, or is excluded by the scope of the Directives, may be subject to other Community and/or national legislation, this alternative framework does arguably not provide the same level of safety, quality and accuracy of the tests as set by the medical devices legislation.

Further, when a device is considered to have a medical purpose, it is not automatically covered by the medical device definition. And, to be qualified as an IVD medical device, devices must first fulfil the definition of a medical device.

Given the speed of technological developments and the development of mobile solutions in a health context, preventive and self-monitoring solutions via mobile devices ('mHealth'), such as mobile phones, personal digital assistants (PDAs), and other wireless devices, are also growing rapidly, such as health and fitness applications. The current legal framework is not clear with regard to its application to these new devices. There is therefore a need to develop guidance in this area to clarify who is responsible under the medical device legislation: the App distributors as a sales channel? The manufacturer of the phone that a medical App runs on although the phone is not intended for use as a medical device?The medical App writer? As stated in the Commission eHealth Action Plan, the health and well-being applications require a legal regulation in order to ensure their quality and transparency. As a step forward the Commission adopted in April 2014 a Green Paper on such applications.

4.1 The Directive 93/42 EEC [11] on medical devices provides rules for placing on the market and putting medical devices into service in the EU

4.1.1 Definitions

The Directive defines 'medical device' as: *any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:*

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception,
- and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

4.1.2 Requirements

The Directive lays down the general requirements medical devices have to comply with, i.e. the safety of the device, its design and construction, as well as its suitability for its purpose.

The Directive groups medical devices in Classes: I, IIa, IIb and III. The higher the classification, the greater the level of assessment required by the national notified body (which ensures that conformity assessment procedures are completed according to the relevant criteria).

11 Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, (OJ L 169, 12.7.1993, p. 1)

It is the intended purpose of the device that determines the classification and not the particular technical characteristics. Considerations for classification include the duration of contact with the body, degree of invasiveness and local versus systemic effect[12].

Irrespective of the class of the device, all devices must:

- Meet the essential (technical and labelling) requirements, including the requirements regarding the information to be supplied by the manufacturer;
- Evaluate clinical efficacy and any side effects, if applicable, by means of a pre-clinical and clinical evaluation;
- Be subject to the reporting requirements under the medical device vigilance system;
- Be CE marked (except accepted exemptions);
- Be registered with the competent national authority where the manufacturer (or the authorised representative) has a registered place of business.

4.2 Directive 98/79/EC provides rules for the marketing of *in vitro* diagnostic (IVD) medical devices

4.2.1 Definitions

The Directive defines IVD medical devices as: *any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment, or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information:*

- *concerning a physiological or pathological state, or*
- *concerning a congenital abnormality, or*
- *to determine the safety and compatibility with potential recipients, or*
- *to monitor therapeutic measures.*

Specimen receptacles are considered to be in vitro diagnostic medical devices. 'Specimen receptacles' are those devices, whether vacuum-type or not, specifically intended by their manufacturers for the primary containment and preservation of specimens derived from the human body for the purpose of in vitro diagnostic examination.

Products for general laboratory use are not in vitro diagnostic medical devices unless such products, in view of their characteristics, are specifically intended by their manufacturer to be used for in vitro diagnostic examination;

Also, the Directive provides for a definition of devices for self-testing: *Any device intended by the manufacturer to be able to be used by lay persons in a home environment.*

4.2.2 Requirements

The Directive lists essential requirements applicable to *in vitro* medical devices, which in a large extent are comparable to the essential safety requirements applicable to all medical devices (including CE marking).

12 Commission Guidance document: classification of medical devices. Version: June 2010.

In addition, the Directive provides for rules directed to **devices for self-testing**. Users of IVD for self-testing ('self-tests') will not have the benefit of a healthcare professional at hand to advise them how to perform the test or to analyse and interpret the results. It is therefore vital that self-tests are suitable for lay use.

This will include aspects affecting its suitability for non-professional users in such a way as to:

- ensure that the device is easy to use by the intended lay user at all stages of the procedure, and

- reduce as far as practicable the risk of user error in the handling of the device and in the interpretation of the results.

Devices for self-testing must, where reasonably possible, include user control, i.e. a procedure by which the user can verify that, at the time of use, the product will perform as intended.

Also, the devices for self-testing have to bear specific particulars into the official language(s) of the Member State in which the device for self-testing reaches its final user.

4.3 TAKING INTO ACCOUNT THE VARIOUS GUIDANCE DOCUMENTS PUBLISHED BY THE COMMISSION, THE FOLLOWING CLASSIFICATION WOULD APPLY TO SOME OF THE DEVICES THAT MAY BE USED IN PN OFFERINGS IF CONSIDERED TO HAVE A MEDICAL PURPOSE

	Medical device?	*In vitro* diagnostic (IVD) Medical Device?
Specimen receptacles: blood collection tubes or filter paper, DNA collection tubes for buccal swab (including kits with swab)	**Yes**	**Yes** (mainly self-tests subject to additional specific requirements)
Products used to obtain specimen: needles, mouthtubes, swabs etc	**Yes**	**No**
Software combining medical/ nutritional knowledge and algorithms with consumer specific data intended to provide the professionals and/ or user with recommendations for diet and lifestyle **(Decision Support System)**	**Yes**	**No**
Software intended only to store, archive and transfer consumer data related to his health **(Information System)**	**No**	**No**
Software intended to transfer electronic information (Communication System)	**No**	**No**

	Medical device?	*In vitro* diagnostic (IVD) Medical Device?
Software intended for the analysis and interpretation of blood/buccal specimen **(Interpretation of Raw Data)**	**Yes**	Yes if it is specifically intended to be used together with an IVD to enable it to be used in accordance with its intended purpose No (accessory to the IVD) if only necessary to render raw data obtained from an IVD
Software intended for archiving consumer results or for transferring results from the environment to the PN advice provide **(Home Care Monitoring)**	**No**	**No**

4.4 Proposed new Regulations on medical devices and IVD medical devices

Medical devices

Per the proposed **new framework for medical devices** that has been reviewed in the research, the situation of devices used for the purpose of providing 'lifestyle services' would change. Tests providing information about the predisposition to a medical condition or a disease (genetic tests as well as other tests measuring the physiological state such as e.g. glucose or cholesterol level in blood in the context of 'lifestyle services') should fall within the scope as soon as they provide information about the predisposition to a medical condition or a disease and therefore participate in the prevention of disease. Regarding the potential impact of these new requirements on PN, the use of genetic testing may be restricted to PN offerings involving health professionals entitled under the applicable national legislation to prescribe such test after a personal consultation and may be prohibited from advertising to consumers. Such provisions would obviously have a significant impact on the development of PN, notably in its level 3 (genetic tests), and would lead to the automatic classification of a large number of business models as healthcare.

The proposed Regulation is still under discussion by the EU legislators and significant amendments to the proposal were suggested by the European Parliament at first reading. The vote in plenary took place on 2 April 2014 and adopted the text that had been referred back to the committee at the 22 October 2013 plenary session. It is already anticipated that a second reading will be necessary to reach an agreement between the Parliament and the Council. The Council has confirmed that the work on its position will continue in 2015.

IVD medical devices

Among others, the proposed Regulation amends the definition of IVD medical devices, to cover medical devices used for DNA-testing. Also, it defines devices for genetic testing as: *in vitro diagnostic medical device, the purpose of which is to identify a genetic characteristic of a person which is inherited or acquired during prenatal development.* The proposed Regulation provides specification regarding devices for self-testing, including *testing services offered by means of information society services. Another important aspect is the introduction of the concept of novel devices which are devices incorporating technology (the analyte, technology or test platform) not previously used in diagnostics, or existing devices which are being usedfor a new intended purpose for the first time.* The proposed Regulation contains specific definition and requirements for 'devices for near patient testing': these include devices intended to perform testing outside a laboratory environment by a healthcare professional not necessarily a laboratory professional, generally near to, or at the side of, the patient, and will be regulated in a similar way to self-test devices. Finally the Regulation states that each manufacturer and authorised representative will require a person responsible for regulatory compliance.

The proposed Regulation is still under discussion by the EU legislators. Significant amendments have been discussed by the European Parliament already at first reading. The vote in plenary took place on 2 April 2014.The Council confirmed that the work on its position will continue in 2015.

4.5 Impact of these proposed new texts on the devices used in PN offerings

First and foremost, the harmonisation of the rules through Regulations has the potential to solve most of the implementation differences between the Member States and should notably harmonise their respective approach with regard to genetic testing.

The proposed definition of medical device as amended by the European Parliament at first reading does change the situation with regard to **devices used for the purpose of providing 'lifestyle services'** by including the term 'prediction' among the purposes of medical devices and the idea of the indirect medical purpose. Also, the amendment of the IVD medical device definition clearly covers tests providing information about the predisposition to a medical condition or a disease. Arguably, genetic tests as well as other tests measuring the physiological state (such as e.g. glucose or cholesterol level in blood in the context of 'lifestyle services') would now fall within the definition of medical device as soon as they provide information about the predisposition to a medical condition or a disease and therefore participate in the prevention of disease. Also, they are covered by the IVD Regulation.

The proposal brings direct-to-consumer **(DTC) internet-based testing services** (whether for genetic tests or other types of tests) within the scope of the new regulation. Although the proposal does not make clear that DTC internet-based testing services are 'devices for self-testing', they are arguably subject to the conformity assessment requirements for that class of device, including the need to carry out studies of the test in use by its intended users, and the need to provide user information in the language(s) of member states of intended users. These requirements will directly apply to DTC PN offerings involving genetic tests or blood tests.

The classification of **certain IVD as 'prescription only'** is not addressed in the proposal. This leaves unaffected national laws which require that certain devices may only be supplied on a medical prescription. However, the European Parliament introduced an amendment to the text, requiring that Class D and C devices for genetic testing would require medical prescription. The Commission agreed with this amendment. Also, some restrictions are enshrined in international guidelines that have the support of many Member States such as e.g. OECD guidelines on quality assurance in Molecular Genetic Testing and Council of Europe's additional protocol

on genetic testing. In that regard, the proposed amendment 268 by the European Parliament states that certain devices may only be supplied on a medical prescription, particularly Class D devices (high risk) and Class C devices in the following categories: (a) devices for genetic testing; (b) companion diagnostics. If such provision is adopted as is, this would restrict the use of genetic testing in PN offerings to offerings involving health professionals entitled under the applicable national legislation to prescribe such test after a personal consultation.

Also, the new rules would subject the use of a genetic test to **genetic counselling and informed consent.**

Last, as proposed by the Parliament, the **DTC advertising** of devices classed as prescription only (notably devices for genetic testing) will be illegal. The Commission did not agree on this amendment. We still need to wait for the final result of the discussion between the EU legislative bodies. In any case, such a ban would be an additional burden to PN offerings. Indeed, any PN offerings involving the use of genetic testing could no longer be advertised to consumers directly, hence significantly limiting its marketing development.

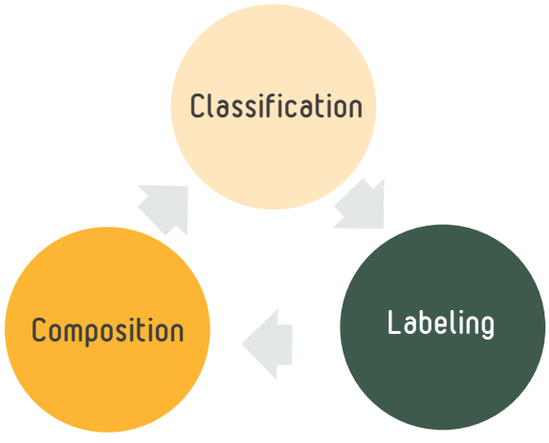
5. OTHER ASPECTS

5.1 Conflicts of law and jurisdiction issues

The relevant implications of the existing law regulating the **conflicts of law and jurisdictions** both at EU or international level, have been addressed in the research. When the PN offerings are provided by actors established within the EU territory, the existing EU frameworks appear sufficient to address the potential conflicts. However, when the PN providers are located outside the EU, determination of the competent jurisdiction and the applicable law is subject to the rules on private international law and have been revealed to be very complex. The current international framework is arguably insufficient to adequately protect the consumer.

5.2 Food law

Regarding the impact of **food law** on PN, irrespective of the model and concept chosen for the development, production and distribution logistics of foods delivered in the context of a PN offering, and ranging from self-choice in shops, over foods for target groups (from healthy consumers to patients) right up to customised production and delivery systems, the food products susceptible to be recommended or delivered will be covered extensively by the provisions that apply 'horizontally' to all foods and food ingredients.



Source – Keller and Heckman

Also they will be subject to the specific provisions applicable to the category to which such food or food ingredient belongs, if any, recognising that the degree of personalisation of the food will itself impact the regulatory classification of that food. This food law framework, although not addressing 'personalised food' as such, appears sufficient to protect the consumers in the various aspects of the food (notably composition and labelling).

Regarding the potential impact of the medicinal product legislation, it has been noted that the personalisation of food products may result in situations where the food product could be classified as medicinal product (either by function or by presentation). The classification

of personalised foods as medicinal products would result in disproportionate pre-marketing requirements given the various levels of counselling, coaching and support of the consumer (depending on the level of PN) that should typically be part of a PN offering.

IMPLICATIONS OF THE RESULTS

The determination of the status of the personalised nutrition offering as 'healthcare or not' will have a significant impact on the legal provisions

The determination of the status of the PN offering as **'healthcare or not'** will have a significant impact on the legal provisions applicable to the related contract of service. If regulated as a conventional business to consumer service contract, the consumer rights appear well protected in a harmonised way by the various EU legal instruments in place. If, however, the PN offering is regulated as a healthcare service, the patient rights will vary from one Member State to another, subject to harmonised rules when the PN offerings is provided in a cross-border situation. Therefore, the determination of the status of each individual PN offering, taking into account the status of the various professionals involved in the Member State where they are established, will be a critical step in the development of PN offerings.

The impact of the **personal data** regulatory frameworks on the field of PN, is that there are wide divergences between Member States, so that in reality the protection of personal data across the EU cannot be considered as equivalent today. It results in important obstacles to the processing of health data; the explicit consent of the consumer may not be sufficient in some Member States. Also, the current framework does not address the particular risks raised by the processing of very sensitive data, such as genetic data, that is an important aspect of PN. It is anticipated that the contemplated new framework should improve personal data protection for individuals, hence increasing trust in the PN consumers/users and facilitating the processing of data by the providers across the EU. On the other hand, while positive impacts for PN companies who process genetic data are anticipated as they could enjoy more legal certainty for processing sensitive data (including genetic data) in all Member States, the practical impact of an increased level of protection of data subject's rights, notably with regard to genetic data may also result in new obstacles for the development of PN, depending on the final wording of the provisions.

So shaped, the regulatory frameworks that apply to PN raise both conceptual and practical issues resulting from the dichotomy in the EU legal framework between medical versus non-medical purposes. As a new type of business offerings connected to the concept of 'lifestyle' or 'wellbeing', PN cannot by definition fit into this framework. The applicable framework has therefore turned out to be fragmented, creating an important source of legal uncertainty requiring a high degree of specification in the definition of the PN offering to determine which parts of the legislation applies. Some effort should therefore be made at EU level to reflect this new category of health related offerings, which are not clearly pursuing medical nor purely nutrition purposes, but rather 'in-between'. The role of the EU should be pivotal both to guarantee the protection of the consumers and the promotion of innovation in the field of PN by (1) defining such 'lifestyle'/'well-being' purposes and (2) coordinating the adjustment of the various legal frameworks to reflect this new concept.

DEVELOPING THE STATE OF THE ART

Similar to the situation from the beginning of the research, i.e. year 2011, the PN offering remains

innovative and difficult to embrace for the EU legislator. It does not fit in the existing legal framework, and it will not be covered by any specific legal act in the near future. The reasons for that are numerous. The EU legislator has no competences to regulate health care and surely it is not the intention of any of the Member States to change this situation. Also, it has been the policy of the EU for many years to issue legislation setting up horizontal standards applicable to a wide range of products, and not detailed rules specific to only one type of precisely described products or services. In line with this idea seems to be the most recent policy of the European Commission of 'Better Regulation' aiming at less regulation and more flexibility.

On the other hand, the EU legislator is more and more active within the area of eHealth and mHealth. Several actions by the European Commission show interest in such new types of services and products. Several contacts with the Commission about PN offerings at the occasion of the research have revealed a genuine interest and even greater conviction of the importance of its emerging m- and eHealth activities.

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KEY REFERENCES

1. Deliverable 5.2 "Personalised nutrition offering in the EU: Applicable legal frameworks and regulatory issues: An overview". Keller and Heckman LLP (Partner 21) April 2014.

2. European Observatory on Health Systems and Policies – Cross-border health care in the European Union. Mapping and analysing practices and policies http://www.euro.who.int/en/about-us/partners/observatory/studies/cross-border-health-care-in-the-european-union.-mapping-and-analysing-practices-and-policies.

3. European Commission – Patient Safety and Quality of Healthcare, Actions at EU level, Background Paper for a Public Consultation, November 2013, http://ec.europa.eu/health/patient_safety/docs/ps_qc_cons2013_background_en.pdf.

4. European Commission on telemedicine for the benefit of patients, healthcare systems and society, COM(2008)689 final. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0689:FIN:EN:PDF.

5. Commission Communication eHealth Action Plan 2012-2020 COM(2012) 736 final.

6. Green Paper on mobile health (mHealth) SWD(2014) 135 final.

7. Commission Staff Working Document on the applicability of the existing EU legal framework to telemedicine services SWD(2012) 414 final.

8. Proposal for a Regulation on the protection of individuals with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation) COM(2012) 11 final.

9. Genes direct: Ensuring the effective oversight of genetic tests supplied directly to the public (A report by the Human Genetics Commission, March 2003) http://www.hgc.gov.uk/genesdirect/genesdirect_full.pdf.

10. Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes, Strasbourg, 27.XI.2008: http://conventions.coe.int/Treaty/en/Treaties/Html/203.htm.

INTEGRATING PERSONALISED NUTRITION the Way Forward

INTRODUCTION

It is an understatement to say that our modern societies are struggling with the rise of health care budgets. An important component of that problem is the inappropriateness of food choices and eating patterns across a large part of the population which has resulted in a continuous rise of diet-related chronic diseases. The 'obesity epidemic' and the wide ramification of its effects on many subsequent health issues is the ultimate expression of the 'size' of this problem. Solutions are needed urgently but we are confronted with the fact that many people find it very difficult to choose foods and adopt eating and life-style patterns that support overall health. Especially fostering a behaviour change that is sustainable, i.e. with little to no risk for a relapse to 'old habits', seems to be one of the toughest problems to solve. The basic underlying reason for this is that we are 'genetically' hardwired to maximise food intake but in a world of abundant food supply, it requires a continuous and conscious effort to balance intake according to needs. There are hundreds of other factors complicating food choices and contributing to the psychological ambivalence about our dietary behaviour.

For decades, societal and industrial actors have been designing and offering all kinds of solutions to help people make better dietary choices: from better recommendations by refining the food pyramid, to 'light foods' to 'natural' supplement cocktails and from highly specialised slimming formula to functional foods enriched in health promoting ingredients and with promising health claims. These significant business opportunities were eagerly exploited by the industry, but the investment hardly resulted in overall healthier dietary behaviour and did not alleviate the societal health care burden to any significant extent.

Personalised nutrition is emerging as a new concept that offers new perspectives for an effective alternative approach, because it focuses exactly on the crucial issue of achieving a lasting individual behaviour change. It enhances the chance that dietary recommendations are more effective and more easily achievable in the context of daily life by assuring that:

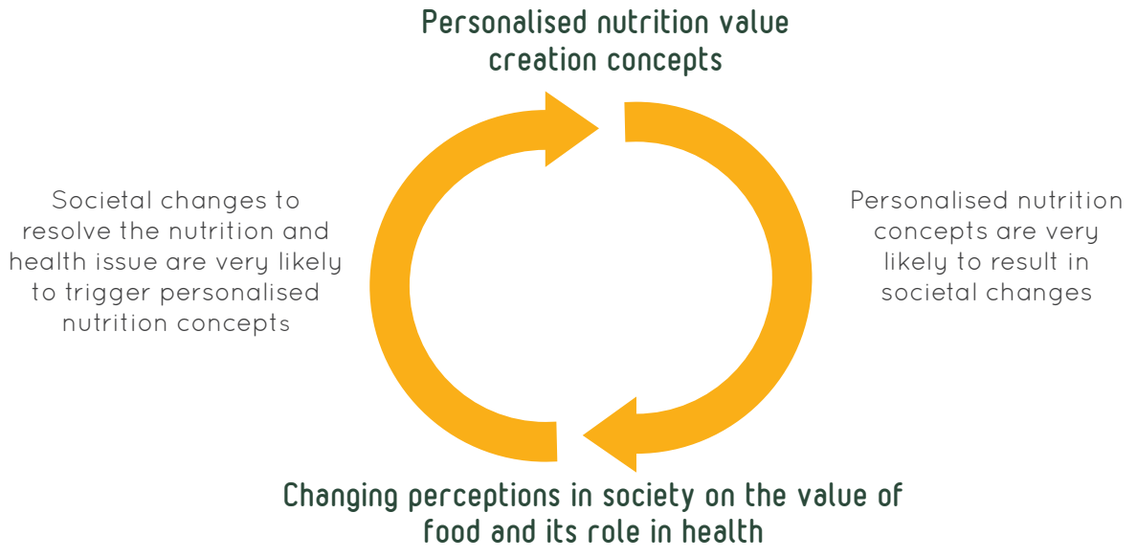
- nutritional recommendations fit the specific individual metabolic profile as determined by detailed diagnostic testing
- dietary advice is provided with insight into personal food and lifestyle preferences
- the advice is delivered, followed up and checked for efficacy in a way that fits the personal, psychological and societal context

Moreover, personalised nutrition can be beneficial to everyone, whether already diagnosed to be at risk or perfectly healthy. It is an approach that helps everyone to reach the health condition that is individually aspired to.

Food4Me has shown that such an approach can be feasible and effective. The mere fact that an individual receives dietary recommendations on a personal basis is already enough to positively

affect dietary behaviour. The effectiveness is however almost twice as high when the advice is also more personalised by basing it on individual dietary behaviour. So far adding biomarker and/or genetic information into the advice could not be shown to result in greater effectiveness, but more detailed analysis will help us to understand why that is and how to further enhance the effectiveness.

Given that dietary behaviour and the whole nutrition and health issue is deeply rooted in our societal tissues, the introduction of personalised nutrition is likely to have a major societal impact. Vice versa, societal changes that are aimed at resolving the nutrition and health issue are likely to embrace such opportunities as offered by the personalised nutrition concept.



The following offers a vision of why and how personalised nutrition could contribute in transforming our societies in the future and which important technical, scientific, legal and ethical questions will need to be addressed to make this possible. The conclusions offer some recommendations for the steps to take this development further.

A VISION

The four future scenarios developed in the Food4Me project show that there will be vast societal changes as Europe tries to cope with the growing nutrition and health problem. But whatever solutions are being considered in this changing societal context, personalised nutrition as a useful and valuable concept to drive dietary behaviour change is very likely to play a role. It is possible that personalised nutrition may either be driving these societal changes or it may rather emerge as a useful solution in response to societal changes as they take shape. This will depend on the one hand how fast technical, scientific and regulatory hurdles can be resolved to allow for a commercial introduction and on the other hand how strong the political motivation is to tackle the nutrition and health issue and to include it as part of the public health care system. Whereas a government-led initiative would be logical given the size and urgency of the problems, it seems unlikely because of the sheer complexity of organising a personalised nutrition offering and the inherent reluctance of authorities to confront the vested interests for changing such complex systems as public health care. A commercial service seems the most likely approach to start the introduction of personalised nutrition, but it will only appeal to a particular segment of the population, notably the early adopters and health seekers. Extending it to a wider population and in particular to those that need it most, will require a transition process with stepwise societal changes that stimulate the adoption of personalised nutrition. Both economic incentives as well as social pressure on inappropriate dietary behaviour will help

to drive this gradual change. Public-private partnerships may be the best approach to trigger such a transition.

Delivering a full personalised nutrition service requires the integration of a wide range of elements, from biomarker, genotype and dietary diagnostics to scientific interpretation algorithms, and from mobile interfaces and wearable monitoring devices, to app development and big-data handling. Many different industries will thus be involved as suppliers of equipment, tools and services, which are then integrated by personalised nutrition providers. Obviously consumers/citizens will be the end-user of the service, but they will probably not be served directly by a personalised nutrition provider. Instead, a wide range of other players are likely to integrate a personalised nutrition offering together with their own services: e.g. private insurers, hospitals, day-care centres, employers, schools, retailers, wellness and fitness centres, etc. The largest group of users will probably be the healthcare professionals, nutritionists and dietitians because they are perceived by consumers to be the most trustworthy to deliver such advice. Their need for using the service of personalised nutrition provider lies in the fact that the underlying consolidated scientific evidence would have become too complex to master. Personalised nutrition providers will therefore be integrators in a complex network of actors. Although some of them are likely to focus on direct to consumer services, the majority of the services will focus more on business to business (organisation) relationships.

Since good health is a human right and societies must ensure all health care options to be available to everyone, there will be a moment that personalised nutrition will become an integral part of public health services. However this will also depend on health economics, meaning that the cost effectiveness of personalised nutrition will need to be proven. There are important ethical considerations in terms of privacy and freedom of choice as well as social justice that need to be considered before taking such an important step.

A wide diversity in access to personalised nutrition is essential and in line with the principle of 'personalisation' which means that everyone can get and tailor the service according to personal preferences. However society will also have to consider that not everyone may care as much about health and hence the assumed societal responsibility in maintaining individual health may not be subscribed to by everyone. Overall it can be assumed that over time a majority of the population will benefit from personalised nutrition and the societal burden of diet-related health problems will be reduced significantly.

The introduction of personalised nutrition will also be driven by a wide range of new technological solutions. They will not only allow us to measure ourselves in terms of health and performance but also assist us in making dietary choices on an on-going basis such as with family meal planners, mobile shopping assistants, home-delivered personal food or meal ingredients, intelligent kitchens, etc. A ubiquitous network with mobile devices will enable us to consult the best possible options and will trigger us to maintain a healthier lifestyle on all levels and at all moments. Generation after generation, the habit of self quantification and mobile advice on food and health will spread as was the case for financial services, mobile phones and GPS.

In the longer term, our society will have fundamentally changed its perception of food and its role in health. With the acceptance of individual responsibility for health and the technologies that enable us to execute this on a continuous basis, there will be a growing feeling of being in control and hence the overall attitude towards diet and health will become much more positive. For the majority it will be enough to be reassured that health risks are under control, turning health into a manageable asset. But a growing number of citizens may see personalised nutrition as the perfect opportunity to realise optimal health, thus shifting the concept of health from achieving basic vital goals to a means for self-realisation.

There may also be a fundamental change in health insurance, at least for the diet-related health aspects. Personalised nutrition will lift the veil of ignorance about individual diet-related health risks and as diet-related health becomes controllable, it puts the responsibility of health maintenance with the individual. Thus the principle of risk sharing as is the case in health insurance will no longer be applicable in general. For non-controllable health risks, the principle of risk-sharing will continue to exist, as well as for the most vulnerable population that may be unable to adopt or understand individual health maintenance.

With health taking a more prominent place in the future, individual health related information will become an important value asset. New societal structures will emerge to guarantee the privacy and protection of the data as well as the freedom of choice in health maintenance.

THE WAY FORWARD

Aspiring to the vision above, there will be many scientific, technical, legal and ethical hurdles to be taken.

• Scientific hurdles

Food4Me has shown the validity of the principle of personalised nutrition as a means to contribute to a dietary behaviour change. However in order to provide solid dietary advice for the wide variety of diet-related health aspects, it is clear that there is a lot more scientific evidence required.

This is particularly true with regard to the use of genetic information as a basis for personalised nutrition advice. Only a limited number of genes have been sufficiently characterised in terms of genetic variation and their impact on metabolism to allow a reasonably accurate interpretation. It will require a huge undertaking to do the same for the majority of genes involved in nutrition related health, especially for very complex systems such as body weight control or metabolic syndrome type of health issues.

There is also a need for more detailed biomarkers to allow a full characterisation of the exact metabolic condition of an individual and how this predisposes to a particular health risk. Easily measurable biomarkers are also needed to measure the effectiveness of the advice and to provide feedback that allows behaviour to be steered towards health goals.

The above may not even be enough to address all health aspects because there is in addition the microbiome (genetics of gut bacteria) and the epigenome (cellular genetics) that also influence our metabolic responses to diet. For example, the role of epigenetics in body weight control has already been scientifically documented, but it is still far from completely understood.

On the other hand, the early introduction of personalised nutrition services will be needed to grow the body of evidence on the relationship between genetic patterns, metabolic conditions and dietary behaviour. Unless this happens, scientific progress based on clinical and intervention studies will be much slower. Initiatives such as the Nutrition Research Cohort by the Nutrigenomics organisation (NUGO) will definitely be instrumental in speeding up the scientific understanding.

• Technical hurdles

Technical hurdles may appear less prominent than scientific ones, but there is still a need to integrate a wide range of information and big data networks, mobile monitoring and feedback devices as well as countless tools that help us to interface with the advice to implement

personalised nutrition in daily life. It demands extremely sophisticated algorithms to combine all these elements and probably some standardisation will be required to assure general applicability across the variety of systems and actors involved.

One of the most important technical challenges is to make diagnostics available, reliable and affordable to provide useful feedback on progress against health goals. This will require simple and easily applicable solutions that can be incorporated almost without hesitation in daily life. Probably the most difficult aspect to implement in this respect is dietary intake measurement, for which there are many but unfortunately still rather inconvenient methods.

Implementing personalised nutrition in daily life will also require much more sophisticated tools that convert nutritional advice into food and meal recommendations, taking into account personal preferences. Meal planner tools, both for individuals, families and occasional groups, both for use at home and in an out-of-home setting, will definitely be needed to properly execute personalised nutrition advice.

• Legal hurdles

Personalised nutrition will require a significant effort to create a regulatory space in which the role of food on health needs to be clearly recognised and controlled. At the moment, European legislation regarding health is fragmented and covers various aspects separately: health data, medical devices, medicinal products.

Both a curative logic and a highly medical perspective, which comes from the historical strength of medical and pharmaceutical research, dominate the regulatory approach to health. For personalised nutrition there will be a need to define a specific regulatory framework focussing rather on preventive health and on the possibility for non-medical approaches, i.e. recommendations for health maintenance through dietary advice and nutritional interventions. Today European regulations are very restrictive with regard to health messages in relation to food products, but hopefully the question of diet-related health messages will be more acceptable. Recent initiatives on e-health and m-health seem to be promising.

There will also be a need to strengthen the rules for safety and privacy of personal health data as more and more actors will become involved. Consumers will first have to be convinced that the necessary regulations are in place because they are particularly concerned about potential misuse by commercial companies, insurers, employers and authorities, or about the risk of personal data being hacked.

However, whatever regulatory changes are needed, the greatest difficulty in Europe will be to overcome the important cultural differences and national legislative barriers which are particularly present in the health care arena. The idea of promoting “codes of conduct”, rather than hard legislation in the area of health and wellbeing services, is an interesting alternative that will promote early market development without stifling innovative approaches.

• Ethical hurdles

Some of the most pressing hurdles for a broad acceptance of personalised nutrition in society are of an ethical nature.

While personalised nutrition offers a means to empower people to gain better control over their health, there may also be negative effects if you know you are at a higher than average risk of the potential of getting a diet-related health problem. This raises questions about the freedom of choice whether or not to know about individual health risks and how to respect that fundamental right in a health care system.

Personalised nutrition also offers a means to cost effective health care and health insurance. However today's health insurance approach that is based on a principle of solidarity, i.e. sharing protection against unforeseeable risk, will be difficult to maintain when risk assessment becomes individualised. This raises questions about how to organise solidarity and on the other hand how to preserve social justice and fairness in a common health insurance system. Important choices will need to be made about how to balance individual interests with the common good. Possibly a new stratification of health risks, between controllable (diet-related) and non-controllable risks, needs to be defined as a new basis for the solidarity principle. For health risks and health maintenance that can be assessed individually, the notion of shared risks and benefits will be no longer applicable.

Finally, the high degree of personalisation of the service raises the question of trustworthiness of the providers, both with regard to competence and the technical ability to deliver appropriate advice and coaching as well as motivation (moral integrity). Ethical standards will be important for providers to establish themselves in the market.

All these issues need to be thoroughly reflected upon by all the stakeholders in order to set clear ethical and moral standards for all personalised nutrition services.

• The consumer challenge

The biggest challenge is obviously to convince consumers/citizens to start using a personalised nutrition service.

Food4me has shown that consumers are interested to adopt a service that will help them make healthier dietary choices and that they do perceive the benefit for their health, but there are a lot of concerns that may prevent them from doing so.

The most prominent concern is about the safety and privacy of personal data, especially when these are to be exchanged over a digital interface. The same is true for sending diagnostic samples over the mail.

Another important concern is the trust in the provider, be it a private or public service. Consumers see health professionals as the most appropriate interface to get personalised nutrition advice as opposed to offerings from a commercial service. Companies will therefore need to find ways to include health professionals in their business models.

While feedback is important to all consumers, it is vital to strike the right balance between empowerment and freedom of use. A too intensive feedback may be counterproductive.

It is striking that most of the concerns are related to the way the service is organised rather than to the principle and perceived benefit of personalised nutrition. The format in which a personalised nutrition service is provided will have to deal with those concerns. Obviously, there will be vast differences between consumers and hence there is a need for a wide range of offerings to accommodate the very different wishes and personal preferences of consumers.

RECOMMENDATIONS FOR FURTHER STEPS

First and foremost the scientific evidence needs to be further developed further to assure that the relationship between nutrition and genes (SNPs), biomarkers, metabolism and health is substantiated further. While the principle has been proven, there is a large set of genes for which the evidence is completely lacking.

There is an important role for the H2020 program to assure that these research lines are prominently taken up in future calls.

Also the algorithms to derive nutritional recommendations on the basis of genes and biomarkers need to be elaborated further. This will finally lead to the characterisation of a number of frequently found metabolic profiles for which the nutritional advice will be more or less identical.

Converting nutritional advice into dietary behaviour patterns, meal plans and food choices also requires further work to assure that these plans are perfectly suitable and amenable to a variety of situations in daily life. Without such useful plans, the adoption of personalised nutrition will remain difficult and uncertain in impact.

It is important for all stakeholders in the area of personalised nutrition to start considering the creation of ethical standards and a code of conduct in order to reduce potential criticism in the early phases of introduction in society. Uncertainty about the purpose and the moral integrity of the actors involved will otherwise quickly generate adverse reactions that may be difficult to counter once they have been in the public domain.

Policy makers need to reflect on the recommendations from the Food4me project and take them into consideration in the development of novel regulations for e-health and m-health.

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