

DELIVERABLE 4.3

Ethical issues relating to
personalised nutrition

Task 4.5

Task leader: UBATH

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Introduction

Stance4Health – Smart Technologies for personAlised Nutrition and Consumer Engagement is a project funded by European Union’s Horizon 2020 research and innovation programme. The objective of Stance4Health is to develop a complete Smart Personalized Nutrition (SPN) service based on the use of mobile technologies as well as tailored food production that will optimise gut microbiota activity and long-term consumer engagement.

Within the Stance4Health project, Work Package 4 (WP 4) engages scholars from the social sciences and the humanities to explore consumer perceptions of personalised nutrition (PN). The focus of WP 4.5 is to define ethical factors influencing the acceptance and uptake of PN. In WP 4.5, we consider both PN in general and gut microbiome-based PN specifically, given the particular focus of the Stance4Health project and the increasing availability of gut microbiome (GM)-based PN to consumers.

Scientific understanding of the viability of PN – whether based on analysis of the GM, or on analysis of other types of personal data, such as genotypic or phenotypic – is constantly evolving. In the specific case of the GM, a plethora of scientific evidence links it to many aspects of human health, both mental (e.g., Foster & Neufeld, 2013) and physical (e.g., Philips et al., 2020; Vivarelli et al., 2019). In contrast to the human genome, the GM is responsive to a number of environmental factors, including diet; meaningful changes to GM composition have been observed even after a relatively short period of altered diet (Spector, 2017), although it is not clear whether these changes can be long-lasting (Klimenko et al., 2018). Although links between GM and health, and diet and GM are evident, important procedural issues, such as quite how the GM interacts with genes and diet to influence health outcomes (e.g., Bligh, Ware, & Squire, 2020) are not fully understood. As a general rule, greater microbial diversity in the gut appears beneficial for the health and lower diversity is associated with poor health and conditions such as obesity, type two diabetes, and coeliac disease (Valdes, Walter, Segal, & Spector, 2018). However, there is no definitive definition of a ‘healthy’ GM, since healthy is dependent upon an individual and their own unique context (Leeming et al., 2021). In sum, whilst many questions remain unanswered, this is a fast moving area and one of significant research interest (Cani, 2018); knowledge about the complex relationship between individuals, their unique collection of microorganisms, and their health is continuously advancing (de Vos, Tilg, Van Hul, & Cani, 2022).

Given that the scientific understanding of GM-based PN is evolving but not yet definitive, it is therefore important to consider the potential ethical issues that could ensue. In the context of inconclusive science around PN based on genetic information, Görman, Mathers, Grimaldi, Ahlgren, and Nordström (2013) outlined two viable if opposing perspectives regarding the viability of PN. Firstly, that the evidence base is simply too immature at this stage for PN to be considered genuinely

useful, and secondly, that PN should be evaluated on a case-by-case basis; for some individuals in some contexts, PN could be appropriate because in specific instances, it will likely be more effective than generalised nutritional advice. From an ethical perspective therefore, they suggest that PN may only be suitable in those cases where there is enough scientific evidence to support it. Although the same argument could legitimately be made about GM-based PN, it is already being commercialised, with several companies offering direct-to-consumer GM-based personalised nutrition services on the internet.

Although a large European study found that PN based on genotypic and phenotypic data did not enhance intervention effectiveness over and above recommendations based on more easily accessible - and arguably much less intrusive - lifestyle information (Celis-Morales et al., 2017), research suggests that consumers are nonetheless fairly well-disposed towards the idea of PN (Ahlgren et al., 2013). However, regardless of how it is perceived by the public, PN raises potential ethical issues, some of which are especially pertinent to commercial situations where consumers are paying for a PN service (Ahlgren, Gorman, & Nordstrom, 2015), given the uncertainty of the scientific evidence and – with companies offering PN situated in an ambiguous position between the medical and the nutritional – the lack of clear and specific regulation in this sphere (Rottger-Wirtz & De Boer, 2021). The aim of WP 4.5, therefore, is to identify ethical factors relating to PN, taking into consideration its existing commercial operationalisation, a phenomenon that seems likely to expand over the coming years.

In advance of the empirical work in WP 4.5, a focus group study was conducted within WP 4.2. The overall aim of this study was to explore and characterise consumer mental models of personalised nutrition. A relatively small part of these discussions was dedicated to exploring ethical issues arising from the consideration of genotypic, phenotypic, lifestyle, and GM-based PN. The intention was to scope out ethical issues, which could then inform the design and development of the empirical studies in WP 4.5. Participants in the WP 4.2 focus group study articulated concerns relating to data protection and privacy, and about the potential for personal data to be misused. More concerns were raised about PN based on genotype than on phenotype, lifestyle, or GM-based PN. This appeared to be informed – at least in part – by prior knowledge or experience of the misuse of genetic data, for example, the potential for genetic information to be shared for purposes not originally agreed to, such as to inform employment decisions. Comments about GM-based PN articulated an interesting lack of concern about microbiome data compared to other types of PN, due to the apparent perception that GM data equated to giving ‘less’ of oneself than would be contained within other types of data:

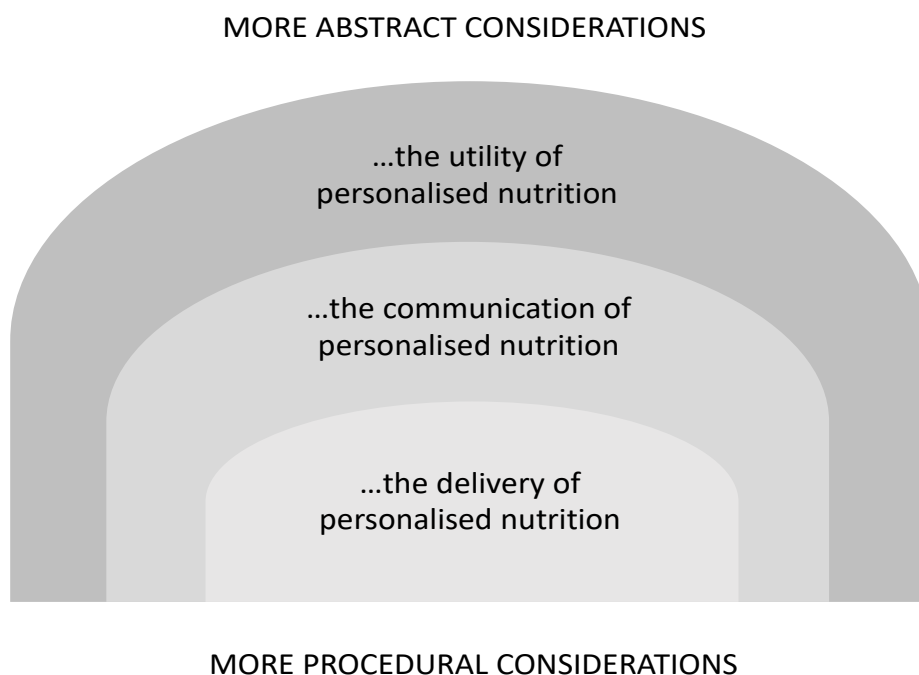
“I feel like this is where I give away the least of myself. I don't have to share my medical history. I don't have to do whatnot.”

"They would not... I guess the advantage I can see is... the way I understand it is they don't have... for example... to do a dna test, it's just about which bacteria there is inside the intestines, it's not as personalised, well you have this or that intestinal flora, and better eat this and that. It's not DNA, some kind of genes that need to be determined" Marco, Group 1A

"In my case, I would basically do it, but as already mentioned, the question is, is it really meaningful? But if I can see there are certain things... well at least I have fewer data protection concerns compared to DNA samples. So..."

The discussion about ethical issues in the focus groups highlighted concerns around privacy and data security and are aligned to the kinds of ethical concerns common to research ethics. Through analysis of the literature, we identified two additional broad and inter-related strands of ethical issues: those relating to the communication of PN and to the utility of PN. Below, we outline each of the three strands and some issues specific to each and present a diagrammatic representation in Figure 1 below:

Figure 1. Ethical issues relating to PN



1. Ethical issues relating to the delivery of PN

These issues relate to PN at the point of delivery. First, how providing a biological sample, over and above providing lifestyle information, relates to concern about data security and privacy; second, whether delivering advice in person rather than online impacts concern about data security and privacy; and finally, whether consumers give fully informed consent.

1.1 How does providing a biological sample relate to concern about data security and privacy?

This question relates to whether providing a personal biological sample – over and above more easily accessible lifestyle information relating to diet, goals, etc – impacts consumers' concern about data privacy and security. As already noted, some participants in the WP4.2 focus group study seemed more concerned about the security of their data when providing biological (especially genetic) samples, although it should be noted that others did not seem particularly concerned about providing any kind of biological sample.

1.2 Does mode of service delivery impact concern about data security and privacy?

In a qualitative study, Stewart-Knox et al. (2013) found that continuity of care and in-person consultations could potentially allay concerns about data security and privacy. Participants were also happier with the idea of face-to-face over online delivery formats.

1.3 Do consumers understand what they are consenting to?

Given some of the issues outlined in the following 'communication' section and specifically, the issue of communicating scientific uncertainty, there is a question of whether consumers can be said to be giving fully informed consent when they sign up to PN. For example, do customers have a complete understanding of what information is being gleaned from the sample that they are providing, and do they have a full appreciation of the accuracy of any subsequent analysis? Can consenting to e.g., providing a stool/blood/cheek swab sample necessarily be construed as consenting to providing data relating to microbiome/phenotype/genotype? Can one be inferred from the other?

2. Ethical issues relating to the communication of PN

These issues relate to how PN is communicated to potential customers the communication of personalised nutrition to consumers. First, whether the portrayal of the science is accurate – and particularly the extent to which certainty about the underpinning science is articulated – and second, whether products are positioned as medical or lifestyle.

2.1 Is the (uncertain) science being communicated accurately?

The science underpinning personalised nutrition could perhaps be summarised as very promising but not definitive. Gorman et al., (2013) point out that the evidence for genotypic-based personalised nutrition is not (yet) strong enough in most cases. Similarly, the evidence base for microbiota-based personalised nutrition is not yet completely compelling. First, most data come from observational studies, or studies in mice (Fan & Pedersen, 2021). Second, whilst numerous microbial taxa and genes have been identified, a full understanding of how the GM interacts with diet to impact

health has not been achieved (Thomas & Segata, 2019). Third, whilst environmental factors are important, so too are genes. There are many outstanding unknowns about how the GM interacts with the human genome and with diet (Bligh et al., 2020). Finally, some individuals are classified as 'responders' and some 'non-responders', depending on the extent to which their GM responds to dietary intervention (Mills et al., 2019). It is important to understand whether any uncertainty about the science behind PN is being communicated to consumers or whether it is being portrayed as certain and definitive and how these portrayals impact consumers' ethical concerns about and perceptions of PN.

2.2 How is the offering framed?

Another communication issue, somewhat linked to the above, are the ways that companies frame their offering to the consumer. PN products are often portrayed in a rather ambiguous or abstruse fashion, as something in between, or simultaneously 'medical' and 'consumer'. This is important because of the different rules and laws covering medical compared to consumer lifestyle products; regulations are considerably more stringent for medical than consumer lifestyle products (Lucivero & Prainsack, 2015). Discussing genetic testing for PN, Stewart et al., (2018) observe that some companies state that results can be used to inform health, yet also state that information is 'for informational purposes only', advising people to consult their doctor. This paints a picture of companies blurring the line between what might be perceived as medical and what could be seen as consumer lifestyle, raising an important question about transparency and the consequent impact on the ways consumers understand these products. It is important to understand how companies are framing their offering and whether ethical concerns, preferences, perceptions, and ultimately, purchasing decisions are impacted by the notion that commercially available PN is a medical or a lifestyle product.

3. Ethical issues relating to the utility of personalised nutrition

These issues relate to the utility of personalised nutrition. First, the question of whether they have much utility at all, second, the question of for whom they have utility, and finally, the question of whether they should or could have utility for everyone.

3.1 Does PN have utility over and above more general approaches?

It is important to understand how useful PN is, over and above following standard 'sensible' dietary advice or advice given based on relatively simple and more readily available lifestyle information. Findings from one large-scale study (Celis-Morales et al., 2017) suggest that they may not necessarily be more effective. This raises the question of whether it is ethical to take a biological sample from an individual for a service if it does not necessarily deliver better results. Also, whether

consumers nonetheless associate giving a personal sample with greater utility on the basis that if you are 'giving more' by going through the process of collecting a biological sample, you would expect more in return.

3.2 Who benefits from personalised nutrition?

Does collecting samples serve the individual and/or the collective? Chadwick (2004) highlights two ways of thinking about ethics in relation to nutrigenomics: individualism and choice and common and public good. Perhaps paradoxically, greater utility for the former is contingent on the cooperation of the latter, as to make meaningful discernments at the individual level, samples from a section of the much broader population are required. When consumers sign up to PN, are they interested in individual or collective benefit or both? Are they even aware of the collective benefit? Is one perceived more favourably than the other?

3.3 Can everyone who should benefit, have the opportunity to benefit from personalised nutrition?

Arguably, given existing and wide-ranging health disparities along socioeconomic lines, many of those potentially more likely to develop health problems are also those less likely to be able to afford the cost of accessing personalised nutrition services (these retail at around £200-250) if they are sold as commercial products rather than being freely available. Do consumers think that these products should be accessible to all? And how does the pricing of products relate to perceptions of the products and willingness to pay for them?

Empirical studies

Three empirical studies were undertaken within Task 4.5. First, to examine the ways that the GM and GM-based PN are currently being communicated to potential consumers in the commercial arena and to examine the extent to which the science is communicated as certain, we undertook a qualitative analysis of the content of the websites of commercial companies offering direct-to-consumer GM-based PN. Second, to explore issues relating to utility, communication, and delivery of PN, we conducted an experimental survey study. The aim of the study was to explore the extent to which ethical concerns about, along with perceptions of and attitudes toward PN are impacted by a) expression of scientific certainty and b) PN being predicated on the provision of different types of biological sample. Third, the aim of the word association study was to examine participants' immediate responses – and the associated affect rating – to the idea of giving either a urine, blood, or stool sample for the purposes of analysis for PN and to examine whether these responses were impacted by the expression of certainty about the science underpinning PN.

Study 1: Qualitative analysis of consumer websites

Research aim and questions

The aim of this study is to understand how commercial companies are communicating to consumers and to understand the extent to which they present the science underpinning GM-based PN as certain. The research questions are:

RQ1: How is the GM presented?

RQ2: What benefits are claimed, how are these benefit claims given credibility?

RQ3: Are any uncertainties about the science underpinning PN articulated or any caveats about the science given?

Method

Ethical approval for the study was granted by University of Bath Psychology Research Ethics Committee (PREC).

To define our inclusion criteria, we followed Adam's definition of PN (Adams et al., 2020). To be included, a company had to present their offering on their website in English and fit the following criteria:

- 1) Individual-specific microbiome information must be provided to the company by the consumer (via stool or other relevant test)
- 2) An evidence-based scientific basis for claims relating to the microbiome test and benefits of performing that test must be articulated
- 3) Dietary advice must be provided post-test
- 4) Benefits of making the recommended dietary changes on the individual's health/wellbeing must be articulated

In June 2021 we conducted Google searches using the following search terms:

- 1) Gut microbiome test personal nutrition
- 2) Personalised nutrition microbiome
- 3) Buy microbiome test
- 4) Best microbiome test

We saved the first ten pages of results for each search. Over the 40 pages of results, we identified 28 sites that met the inclusion criteria. A follow-up search in November 2021 revealed that one of

the initially identified sites was no longer trading, and another was trading under a different name. We examined the relevant pages of each site, selecting text and images pertinent to the research questions. We grouped images and texts into initial codes and then broader categories, using the principles of inductive thematic analysis (Braun, Clarke, Hayfield, & Terry, 2019). We allocated each of the 27 companies a code, to maintain their privacy.

Results

Our intention was to examine the way commercial companies communicate to consumers about the GM, GM-based PN, and how they communicate about the certainty of the science behind GM-based PN.

We identified 27 companies offering GM tests, an analysis of that test, and subsequent provision of dietary / nutritional advice. The 27 companies fit within one of three discrete categories. First, companies exclusively offering personalised nutrition programs on the basis of an analysis of a customer's GM (n=12). Second, companies offering GM analysis and dietary recommendations alongside a range of their own supplements, such as pre- or pro-biotics (n=8). Finally, there were companies that offered a broad range of tests – such as DNA, fertility, or food intolerance – of which a GM test is one (n=7). Our findings in relation to the three research questions are outlined below.

RQ1: How do companies present the GM?

Companies undertook two tasks when presenting the GM: articulating what the GM is and what the GM does. The GM was presented both as small and friendly – as a collection of 'helpful' bugs – and as a vast fighting force, or 'invisible army'. Here, imagery, personification, simplification, and metaphor were used to help make the GM more accessible and relatable.

Meet your invisible army. In the ongoing fight against chronic disease, scientists have begun to turn to an army of unexpected allies – bacteria and other microorganisms.

Company C

Explaining the function of the GM was communicated in simple terms: the GM is the key to good health.

'The intestines are the seat of health' Hippocrates. Company M

Every individual has a unique GM, which can be altered (for the better) by making dietary and lifestyle changes. This improved GM health can then lead to improved health and wellbeing.

A damaged gut microbiome produces an improper imbalance of building blocks, which makes the body more susceptible to health issues. A healthy gut microbiome produces a better balance of building blocks, which protects the body. Company F

RQ2: What benefits are claimed and how are these claims made credible?

A range of claims were made about the benefits of GM-based PN and a variety of resources drawn upon to support these claims. Wide ranging claims about health benefits were made. These were both specific and diffuse and also alluded to the potential for improvements to physical appearance (e.g., improved skin health).

A targeted approach to improving your gut microbiome. Increase energy, support weight loss, optimize health, support emotional health, improve sleep, strengthen immunity. Company F

These claims were made credible in four ways. First, by highlighting the scientific credibility – either of the organisation itself or of individuals (such as academics or medics) affiliated with it; second, by asserting technological and analytic expertise and superiority over other companies operating in the same domain; third, via the use of customer testimonials; and finally, by alluding to media coverage or recognition.

Over the last few years, in excess of \$1.7 billion was spent on gut microbiome research. We've tapped into numerous research publications to bring you the latest science-backed findings. Company I

The best gut health test is one that offers a full spectrum microflora analysis and includes full HD resolution scanning of over 23,000 microbes including probiotics, viruses, phages, and fungi. Think of it like watching your favourite movie, sports team, or show on TV. Would you prefer watching it with 1080p resolution or 5K UHD? Our whole genome sequencing gut test results will show you your bacteria all the way down to the species level, so you know you're getting the best resolution. Company H

RQ3: Are any uncertainties about the science around the GM and diet/health articulated, or any caveats given?

The companies presented their offering in a highly medicalised manner on the main pages of their sites. Although they did not explicitly claim to be offering a medical service, this was heavily inferred by the strong claims that linked dietary changes to better gut health and then to better physical and mental health. Disclaimers were not present on the main pages of companies' websites. In contrast, it was firmly established in disclaimer sections – hard to find because they were usually buried within terms and conditions or located at the bottom of long web pages – that companies were not offering a medical service and that only doctors are able to diagnose medical conditions.

The tests we offer are not intended to diagnose or treat disease, or to substitute for a physician's consultation. Company L

The information Company C provides is for educational and informational use only. The information is not intended to be used by the customer for any diagnostic purpose and is not a substitute for professional medical advice. Company C

Study 2: Experimental survey study

Research Aim and Questions

The aim of this study is to examine the impact of the expression of scientific certainty and type of biological sample required for PN on a range of perceptions towards and ethical concerns about PN. The research questions are:

RQ1: Are ethical concerns, perceptions, attitudes, and intentions towards personalised nutrition impacted by expression of scientific certainty?

RQ2: Are ethical concerns, perceptions, attitudes, and intentions towards personalised nutrition impacted by sample type?

Method

Ethical approval for the study was granted by University of Bath Psychology Research Ethics Committee (PREC).

We recruited a nationally representative sample of 716 UK participants via the Prolific platform. Participants first read through an information form and gave their consent. After answering some demographic questions, participants read a short passage about personalised nutrition based on a type of classification called metabotyping. The manipulation was relatively subtle, but in the certainty condition, definitive language was used (e.g., diet *is* an important contributor; *it is possible* to design targeted dietary advice). In the uncertainty condition, more provisional language was used (e.g., diet *is thought to be* an important contributor; *it may be possible* to design targeted dietary advice). The data of the 261 participants who expressed a view about certainty aligned to the certainty condition they were allocated to were retained for analysis. Of these 261 participants, 48% were male. 183 participants were in the Certainty condition, 79 in the Uncertainty condition.

Immediately following the information relating to the certainty of the science, participants were directed to one of three biological sample conditions, either Urine, Blood, or Stool, to read about providing one of these samples. Here, we adapted NHS guidelines for collecting each of the samples and outlined the process for collecting each type of sample in a series of short steps, from washing hands, to carrying out the sampling procedure, through to packaging and posting it off for analysis. We developed our own scales to cover some of the concepts within our three layers of ethical issues: Delivery, Communication, and Utility. Existing validated scales were selected to measure Attitudes towards Personalised Nutrition, Benefit Perception Associated with Personalised Nutrition, Intention to Adopt Personalised Nutrition, and Perceived Efficacy of Trust and Regulation of Personalised Nutrition (Poínhos et al., 2014). Table 1 details these scales and the items within each.

Table 1. Original survey study scales

Name of scale	Source	Question asked	Items	Response
<i>Ethical scales</i>				
Concerns about Delivery	Developed by WP 4.5	If you decided to use a personalised nutrition service to give you dietary advice, how much would you be concerned about...	Whether your data would remain private Whether your data would be stored securely Whether correct consent procedures would be followed Whether your data might be used inappropriately	Four-point scale, from extremely concerned to not at all concerned
Concerns about Communication	Developed by WP 4.5	If you decided to use a personalised nutrition service to give you dietary advice, how much would you be concerned about...	Whether you would be told about all the scientific evidence relating to personalised nutrition Whether uncertainties about the effectiveness of personalised nutrition would be transparently communicated Whether you could believe all the benefit claims being made about personalised nutrition Whether claims about personalised nutrition can be trusted	Four-point scale, from extremely concerned to not at all concerned
Concerns about Utility	Developed by WP 4.5	If you decided to use a personalised nutrition service to give you dietary advice, how much would you be concerned about...	Whether PN is more effective than generalised nutritional advice Whether personalised nutrition advice given would be genuinely beneficial Whether personalised nutrition only benefits those who can afford it Whether everyone who could benefit from personalised nutrition would be able to access it	Four-point scale, from extremely concerned to not at all concerned
<i>Other scales</i>				
Attitude towards personalised nutrition	Adapted from Poinhos et al., 2014	Personalised nutrition is:	Worthless to Valuable Unpleasant to Pleasant Boring to Interesting Bad to Good Untrustworthy to Trustworthy Ineffective to Effective	Five-point scale, where 5 is most and 1 least positive
Benefit perception associated with personalised nutrition	Adapted from Poinhos et al., 2014	Please indicate the extent to which you agree or disagree with the following statements	Personalised nutrition could benefit me personally Personalised nutrition could benefit my family Personalised nutrition could benefit an average member of the society in which I live	Five-point scale, from completely disagree to completely agree

Intention to adopt personalised nutrition	Adapted from Poinhos et al., 2014	Please indicate the extent to which you agree or disagree with the following statements	I intend to adopt personalised nutrition I would consider adopting personalised nutrition I am definitely going to adopt personalised nutrition	Five-point scale, from completely disagree to completely agree
Efficacy of trust and regulation	Adapted from Poinhos et al., 2014	Please indicate the extent to which you agree or disagree with the following statements	I worry that a personalised nutrition diet plan is not effective I worry about how personal biological data might be used by authorities I worry that personal biological data may not be treated confidentially I worry about how my biological data and test results might be stored I worry about how my personal biological data might be used by personalised nutrition providers I worry about how my personal biological data might be used by insurance companies I worry that my personal biological data could be accessed by hackers	Five-point scale, from completely disagree to completely agree

To test the viability of the three ethical scales developed by WP4.5 we conducted an exploratory factor analysis, which indicated a three-factor solution that was similar, but not identical to, our original conceptualisation. Two of the questions originally relating to communication sat across two factors, so were discarded. The remaining ten questions formed three unique factors we renamed ‘PN data security and privacy’, ‘Certainty about PN claims, and ‘Equality of access to PN’. The first factor comprised the four questions that sat within our original ‘Delivery’ measure, and all related to issues around privacy, security, and consent. The second factor comprised two of the original ‘Communication’ and two of the original ‘Utility’ questions and related to certainty about the claims made about PN. The final factor comprised two of the questions within the original ‘Utility’ measure and related to the extent to which PN is or should be accessible to everyone. The final scales used in the study are outlined in Table 2.

Table 2. Scales used in survey study (ethical scales updated post factor analysis)

Name of scale	Source	Question asked	Items	Response
<i>Ethical scales</i>				
PN data security and privacy	Developed by WP 4.5 – post factor analysis	If you decided to use a personalised nutrition service to give you dietary advice, how	Whether your data would remain private Whether your data would be stored securely	Four-point scale, from extremely concerned to

		much would you be concerned about...	Whether correct consent procedures would be followed Whether your data might be used inappropriately	not at all concerned
Certainty about PN claims	Developed by WP 4.5 – post factor analysis	If you decided to use a personalised nutrition service to give you dietary advice, how much would you be concerned about...	Whether you could believe all the benefit claims being made about personalised nutrition Whether claims about personalised nutrition can be trusted Whether personalised nutrition is more effective than general nutritional advice Whether personalised nutrition advice given would be genuinely beneficial	Four-point scale, from extremely concerned to not at all concerned
Equality of access to PN	Developed by WP 4.5 – post factor analysis	If you decided to use a personalised nutrition service to give you dietary advice, how much would you be concerned about...	Whether personalised nutrition only benefits those who can afford it Whether everyone who could benefit from personalised nutrition would be able to access it	Four-point scale, from extremely concerned to not at all concerned
Other scales				
Attitude towards personalised nutrition	Adapted from Poinhos et al., 2014	Personalised nutrition is:	Worthless to Valuable Unpleasant to Pleasant Boring to Interesting Bad to Good Untrustworthy to Trustworthy Ineffective to Effective	Five-point scale, where 5 is most and 1 least positive
Benefit perception associated with personalised nutrition	Adapted from Poinhos et al., 2014	Please indicate the extent to which you agree or disagree with the following statements	Personalised nutrition could benefit me personally Personalised nutrition could benefit my family Personalised nutrition could benefit an average member of the society in which I live	Five-point scale, from completely disagree to completely agree
Intention to adopt personalised nutrition	Adapted from Poinhos et al., 2014	Please indicate the extent to which you agree or disagree with the following statements	I intend to adopt personalised nutrition I would consider adopting personalised nutrition I am definitely going to adopt personalised nutrition	Five-point scale, from completely disagree to completely agree
Efficacy of trust and regulation	Adapted from Poinhos et al., 2014	Please indicate the extent to which you agree or disagree with the following statements	I worry that a personalised nutrition diet plan is not effective I worry about how personal biological data might be used by authorities I worry that personal biological data may not be treated confidentially I worry about how my biological data and test results might be stored	Five-point scale, from completely disagree to completely agree

			<p>I worry about how my personal biological data might be used by personalised nutrition providers</p> <p>I worry about how my personal biological data might be used by insurance companies</p> <p>I worry that my personal biological data could be accessed by hackers</p>	
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Where necessary, scales were reversed prior to conducting the analysis, so that higher numbers always indicated more positive responses, or reduced concern. We conducted a factorial MANOVA in SPSS to determine whether the two independent variables impacted participants' responses to the dependent variables.

Results

A factorial multivariate analysis of variance was performed to investigate the impact of the two independent variables (Certainty – Certain vs Uncertain science - and Biological sample – Urine, Blood, Stool) on the seven dependent variables. Preliminary assumption testing was conducted to check for normality, linearity, univariate and multivariate outliers, homogeneity of variance-covariance matrices, and multicollinearity. No serious violations were observed. There was a statistically significant difference of Certainty on the combined dependent variables, $F(8, 215) = 14.99$, $p = .000$, Wilks' Lambda = .98, partial eta squared = .36. There was a statistically significant difference of Sample on the combined dependent variables, $F(16, 430) = 2.06$, $p = .009$, Wilks' Lambda = .98, partial eta squared = .07. There was no significant interaction effect. As Levene's test was significant for the dependent variables Benefit perception and Intention to adopt, separate t-tests for Certainty and an ANOVA for Sample were carried out for these dependent variables, with readings taken from the unequal variances assumed line.

RQ1: Are ethical concerns, perceptions, attitudes, and intentions towards personalised nutrition impacted by expression of scientific certainty?

Table 3 details the univariate effects of Certainty for the dependent variables that met the threshold of $p < .05$. All dependent variables except for one of the ethical variables – equality of access to PN – were statistically significant.

Table 3. Significant Univariate effects of Certainty (at $p < .05$ level)

Dependent variable	Condition	Mean	95% Confidence Interval	
			Lower Bound	Upper Bound
Ethical variables				
Data privacy and security	Certainty	2.46	2.33	2.60
	Uncertainty	2.18	1.95	2.40
Certainty about PN claims	Certainty	2.53	2.41	2.64
	Uncertainty	2.07	1.88	2.27
Other variables				
Attitude toward PN	Certainty	4.19	4.10	4.28
	Uncertainty	3.30	3.15	3.45
Perceived benefit of PN	Certainty	4.28	4.20	4.37
	Uncertainty	3.49	3.30	3.67
Intention to take up PN	Certainty	3.48	3.35	3.59
	Uncertainty	2.44	2.23	2.66
Trust/efficacy of regulation	Certainty	2.96	2.81	3.12
	Uncertainty	2.47	2.21	2.73

Here we can see the differences in the means across the dependent variables for which $p = <0.05$ follow the same pattern, in that they are higher for participants in the Certainty than Uncertainty conditions across these six variables. Participants in the Certainty condition expressed more favourable mean scores in response to all the dependent variables than those in the Uncertainty condition. These mean scores for participants in the Certainty condition indicates they were less concerned about ethical issues and held more positive views towards PN than participants in the Uncertainty condition.

RQ2: Are ethical concerns, perceptions, attitudes, and intentions towards personalised nutrition impacted by sample type (urine, blood, stool)?

Table 4 details the univariate effects of Sample for the dependent variables that met the threshold of $p < .05$. One ethical variable – data privacy and security – and two other variables – attitude towards PN and trust/efficacy of regulation were statistically significant.

Table 4. Significant Univariate effects of Sample (at p <.05 level)

Dependent variable	Sample	Mean	95% Confidence Interval	
			Lower Bound	Upper Bound
Ethical variables				
Data privacy and security	Urine	2.45	2.25	2.65
	Blood	2.05	1.79	2.30
	Stool	2.47	2.24	2.69
Other variables				
Attitude towards PN	Urine	3.72	3.58	3.85
	Blood	3.62	3.45	3.79
	Stool	3.89	3.74	4.04
Trust/efficacy of regulation	Urine	2.75	2.52	2.98
	Blood	2.43	2.14	2.72
	Stool	2.97	2.72	3.23

There were fewer dependent variables with a significance of $p = <0.05$ for the Sample IV than for Certainty IV. Here, a pattern emerges in that those participants in the Stool condition had the lowest concern about data privacy and security and about trust/efficacy of regulation, and the most favourable attitude towards PN of the three conditions. Participants in the Blood condition were more concerned about data security and privacy and trust/efficacy of regulation and the least favourable attitude towards PN. This suggests that concerns relating to issues of trust, privacy, and data security may be reduced in relation to stool samples compared to other types of samples, and particularly blood samples, in line with the comments that were made by participants in the WP 4.2 focus groups.

Study 3: Word association study

Research Aim and Questions

The findings from Study 2 indicated that participants were less concerned about data privacy and security in the Stool condition than participants in the Blood condition. This accords with the comments made in the WP 4.2 focus group, where participants articulated the view that giving a stool sample amounted to giving 'less' of oneself, as it would not contain genes or DNA. The aim of this final study is to understand the impact of the expression of scientific certainty on peoples' spontaneous responses to the notion of giving one of three personal biological samples (Urine, Blood, Stool) for the purposes of PN. The research questions are:

RQ1: What impact does expression of scientific certainty have on the word categories produced and the associated affect ratings?

RQ2: What impact does biological sample have on the word categories produced and the associated affect ratings?

Method

Ethical approval for the study was granted by University of Bath Psychology Research Ethics Committee (PREC).

Participants were first allocated into one of two Certainty conditions and then into one of three Sample conditions. Immediately after reading about how to give one of the three personal biological samples (Urine, Blood, Stool), participants were asked to write the first, second, and third word that came to mind when they thought about giving the biological sample described in the condition they had been allocated to. They were also asked how positive or negative they felt about the three words they provided, from 1 – very negative, to 5 – very positive, with 3 representing a neutral response.

A total of 261 participants were included in the analysis. The words and associated affect ratings were copied into Microsoft Excel for analysis. A breakdown of the number of participants in each condition and the total number of words elicited in each is outlined in Table 5 below:

Table 5. Number of participants and words in each condition

Sample condition	Urine		Blood		Stool	
Certainty condition	Certainty	Uncertainty	Certainty	Uncertainty	Certainty	Uncertainty
n=	62	32	63	18	58	28
words, n=	185	95	188	53	173	83

An initial broad coding of the words that participants provided was conducted. Following this, and over several iterations, words were subject to further lemmatisation, whereby synonyms were grouped together, and the words placed into broader categories of meaning. Members of the research team consulted on category development throughout the process. A total of 21 unique word categories were identified. Counts were performed for each category within each of the six condition permutations. Mean affect ratings for the six condition permutations were also calculated. We examined whether there was a statistically significant impact of certainty and biological sample on the affect ratings by including affect as a dependent variable in the quantitative analysis outlined in the section on Study 2. These are reported in the results section below.

Results

Following lemmatisation, the words elicited in response to reading about providing a personal biological sample were coded into the following 21 discrete word categories, detailed below in Table 6 below.

Table 6. Word categories, descriptors, and exemplars

Category	Description of category. Word...	Exemplar words
Disgust	Indicates repulsion, abhorrence	Disgusting, Gross, Yuk, Nasty
Synonym	Is a synonym for the sample	Poo, Wee, Blood
Straightforward	Refers to ease or simplicity of task	Simple, Easy, Straightforward, Manageable
Convolutd	Suggests the task is onerous or lengthy	Inconvenient, Hassle, Involved, Tedious, Tricky
Worry	Refers to anxiety or nervousness	Worry, Anxious, Nervous
Smell	Refers to odour	Smell, Stink

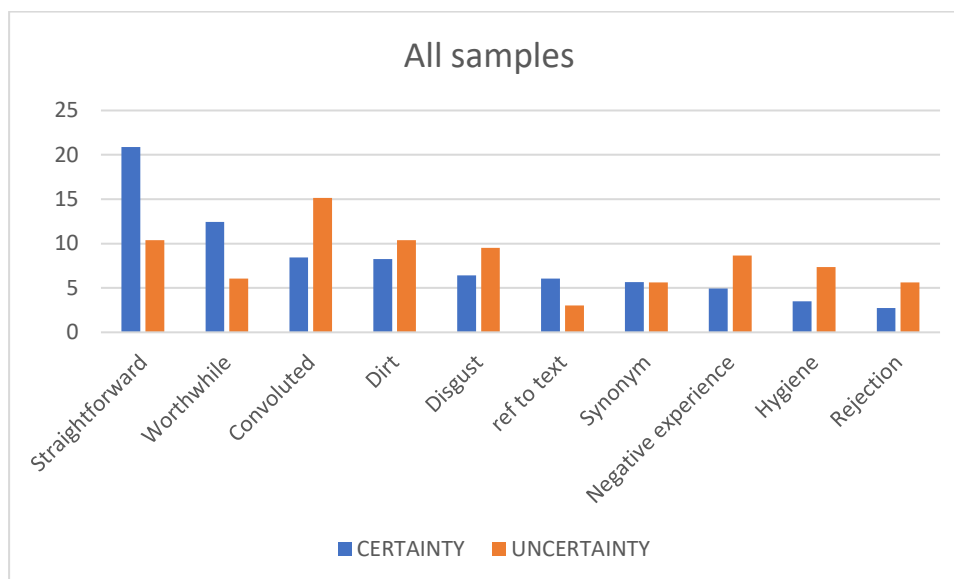
Hygiene	Refers to aspects of hygiene and sterility	Contamination, Sterile, Unhygienic, Cleanliness
Dirt	Is a descriptor of dirt or mess	Messy, Wet, Sloppy, Dirty, Wee on hands
Intrusive	Indicates procedure is intrusive or (too) personal	Embarrassing, Vulnerable, Private, Intrusive
Negative experience	Refers to negative experience	Awkward, Uncomfortable, Weird, Unpleasant
Rejection	Indicates unwillingness to carry out procedure	No way, No, Never, Too much
Reference to text	Refers to the instructions in the sample condition	Spoon, Post, Spatula, Mid-stream, Lancet
Worthwhile	Suggests process is useful or beneficial	Helpful, Necessary, Interesting, Good
Reference to experience	Refers to previous experience / familiarity with procedure	Diabetes, Covid, Bowel cancer test, Used to it
Needle	Refers to needles	Needle, Prick
Pain	Refers to pain	Pain, Ouch, Painful
Science	Refers to science or medicine	Science, Lab, Scientific, Doctors
Health	Refers to health or wellbeing	Health, Healthy
Privacy	Refers to privacy or privacy concerns	Privacy, Confidentiality, DNA access, Biological ID
Novel	Refers to newness or innovation	New, Innovative, Modern
Other	Cannot be assigned to any other code	N/A, Cost, Trying, When

RQ1: What impact does expression of scientific certainty have on the word categories produced and the associated affect ratings?

Some categories (e.g., Straightforward, Convuluted, and Worthwhile) were present in relatively large number across all the sample conditions. Others were solely, or much more highly represented in only one condition (e.g., Worry, Pain, and Needle were almost exclusively associated with the Blood condition, Smell with the stool condition). Across all three sample conditions, there was a difference in the prevalence of the different categories, depending on whether participants were in the Certainty

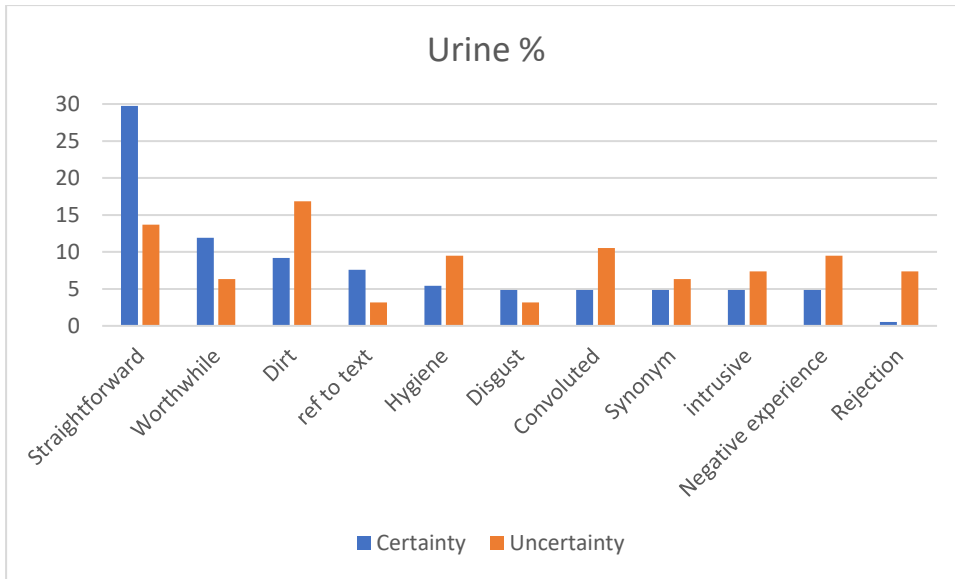
or Uncertainty conditions. In general – albeit this phenomenon was rather less pronounced in the stool than in the other conditions – the categories with more positive connotations, such as Straightforward and Worthwhile, featured more frequently in the Certainty than in the Uncertainty condition. Conversely, categories with more negative connotations, such as Disgust and Convolved, featured more frequently in the Uncertainty than in the Certainty condition. When the science was presented as certain, therefore, participants gave more positive responses to the idea of providing any kind of personal biological sample for the purposes of PN, whereas when the science was presented as less certain, rather less positively connoted responses were given. Category frequencies for Certainty and Uncertainty across all sample conditions, where responses accounted for at least 5% of total responses in either the Certainty or Uncertainty condition are shown in Figure 2 below.

Figure 2. Category frequency in Certainty and Uncertainty conditions – all sample types



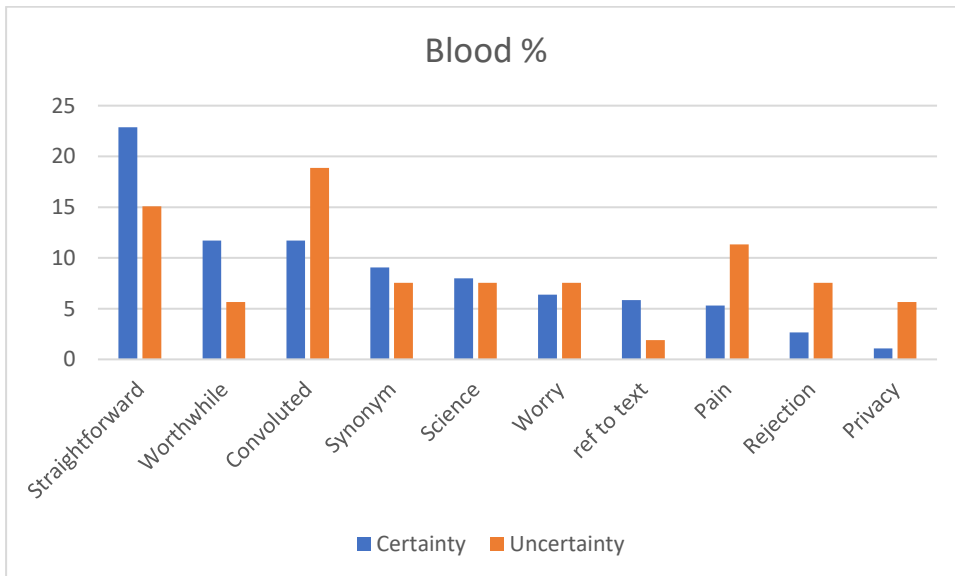
Breaking the differences between categories elicited in the Certainty conditions down further by sample type for those in the Urine condition, we see that in the Certainty condition, elicitations in the Straightforward category accounted for 30% of all responses. This is far lower in Uncertainty condition at less than 15%, where Dirt is the largest single category, and the frequency of categories with more negative connotations (e.g., Negative experience, Dirt, Convolved) is higher than in the Certainty condition. This is shown in Figure 3 below.

Figure 3. Category frequency in Certainty and Uncertainty conditions – Urine



In the Blood condition, shown in Figure 4 below, Straightforward is the category with the highest frequency for participants in the Certainty condition, Convoluted has the highest frequency for participants in the Uncertainty condition. Overall, categories with more negative connotations account for a larger proportion of the responses in the Uncertainty condition than the Certainty condition; Convoluted, Pain, and Rejection account for well over a third of responses in the Uncertainty conditions.

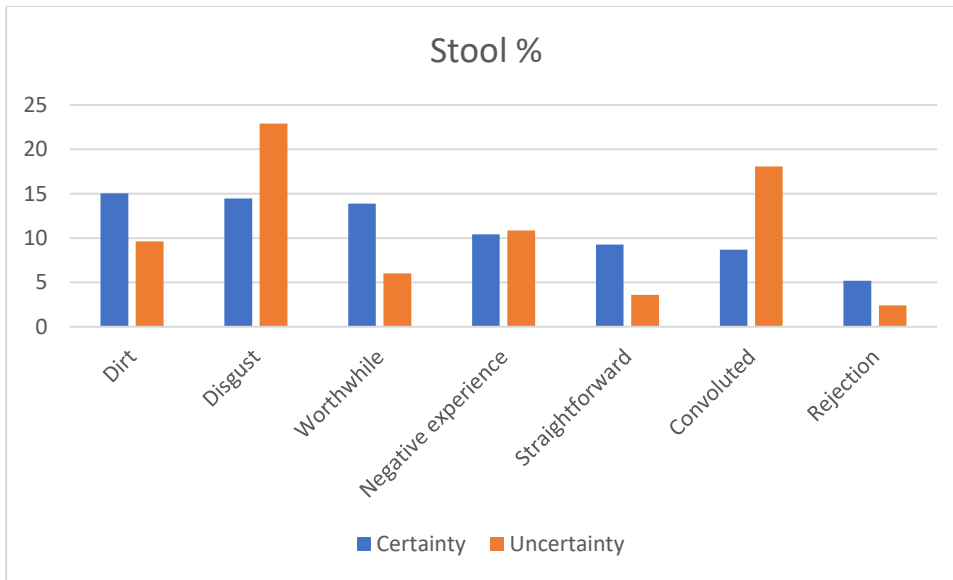
Figure 4. Category frequency in Certainty and Uncertainty conditions – Blood



Finally, in the Stool condition, shown in Figure 5 below, there is a less of a marked difference between category frequencies in the Certainty and Uncertainty conditions compared to the Urine and Blood sample conditions, although there are still some differences to observe. In the Certainty

condition, word categories are more evenly distributed, with the more ‘positive’ categories – Straightforward and Worthwhile – accounting for a higher proportion of responses than in the Uncertainty condition. On the other hand, the Uncertainty condition is more dominated by ‘negative’ categories: Disgust, Convoluted, and Negative experience account for around half of responses, compared to around a third in the Certainty condition.

Figure 5. Category frequency in Certainty and Uncertainty conditions – Stool



Expression of certainty also had an impact on the mean affective response to the words provided. There was a statistically significant difference between the means for the participants in the Certainty condition and participants in the Uncertainty condition – see Table 7 below. The mean affect score for participants in the Certainty condition was 3.23 – more positive than neutral – and in the Uncertainty condition 2.50 – more negative than neutral.

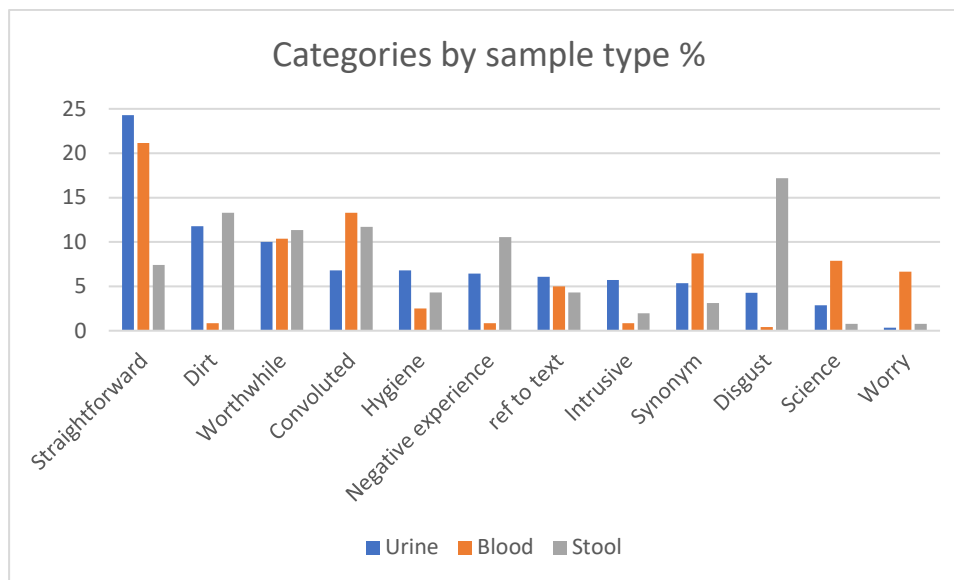
Table 7. Significant Univariate effect of Certainty (at p < 0.5 level)

Dependent variable	Condition	Mean	95% Confidence Interval	
			Lower Bound	Upper Bound
Affective response to sample provision	Certainty	3.23	3.07	3.36
	Uncertainty	2.50	2.24	2.76

RQ2: What impact does biological sample have on the word categories produced and the associated affect ratings?

There were some clear differences in the frequencies of the produced word categories across the three conditions, shown in Figure 6 below. Categories are included where responses accounted for at least 5% of total responses in any of the three sample conditions.

Figure 6. Category frequencies by sample condition



Here we can see that Straightforward is the category with by far the highest frequency for both Urine and Blood. The frequency for Straightforward in the Stool condition is far lower, with higher frequencies for categories such as Disgust, Negative experience, and Dirt. This leads to the conclusion that whilst the idea of giving blood and urine samples provokes some negative responses, they are nonetheless associated with more favourable notions than the idea of giving a stool sample. There was a statistically significant difference between the means of the affect ratings for the three types of samples – see Table 8 below. With a mean score for Urine of 3.01 and for Blood 3.00, these two sample types evoke a neutral mean affect rating. However, the mean for participants in the Stool condition is 2.58, which is more negative than neutral.

Table 8. Significant Univariate effect of Sample (at $p < 0.5$ level)

Dependent variable	Condition	Mean	95% Confidence Interval	
			Lower Bound	Upper Bound
Affective response to sample provision	Urine	3.01	2.78	3.24
	Blood	3.00	2.71	3.29
	Stool	2.58	2.32	2.84

Conclusions and Implications

Here we summarise the conclusions of each of the separate studies, before considering the implications of the findings taken together and suggesting potential directions for further investigation.

The brief discussions of ethical considerations in the focus group study conducted within WP 4.2 hinted at slightly heightened concern around genetic PN compared to lifestyle PN, with less concern about phenotypic PN, although this could perhaps reflect participants not fully understanding the nuances of what the different types of personal data contain. GM-based PN did not appear to raise particular or unique ethical concerns, with a few participants suggesting that giving a GM sample would equate to giving 'less' of yourself than other types of samples. This raises the question of whether giving a GM sample may be perceived as more palatable to consumers, at least from the point of view of data privacy and security, than providing what may be understood to be more 'personal' genetic material.

Our analysis of the websites of companies providing GM-based PN on the internet found that companies explained the nature of the gut microbiome and the benefits of GM-based personalised nutrition in simple and relatable ways, so that the inherently complex proposition is made clear and understandable to the consumer. Several strategies were used to bolster the credibility of the companies and the technological insights they claim to offer. Of some concern – in the context of science that is not fully established – and could not be described as 'certain' – is the finding that companies presented the science underpinning GM-based PN as if it were certain and without caveat, at least on the main pages of their websites. Here, claims about the benefits of GM-based personalised nutrition and the superiority of their analytic technology were made unequivocally; uncertainty was absent. In contrast, explicit caveats were made in difficult-to-find disclaimer sections, buried in lengthy terms and conditions or at the bottom of long web pages. This mirrors an incongruence previously identified by Ahlgren et al. (2013), between the wide ranging promises made about potential positive outcomes arising from other forms of PN, and the content contained in disclaimer sections on PN websites. As already noted, PN is not subject to the more stringent regulations applied to medical products, with some arguing that regulations should be tightened (for review, see Saukko, 2013). In the light of our findings about the way GM-based PN is being communicated to potential consumers in the commercial sphere, we considered it important to explore the impact of the expression of certainty on consumers' perceptions of PN.

Given the findings from the previous study, we employed a 2 x 3 experimental survey study to examine the impact of the expression of certainty on seven dependent variables, to understand whether these factors impact consumers' concerns about various ethical factors, and their

perceptions of and intentions and attitudes towards PN. We also examined whether the provision of different types of biological sample had an impact on these variables. We found that there were main effects of both certainty and sample type on the dependent variables, but no interaction effect. Looking at the significant dependent variables separately, there were statistically significant differences between scores for participants in the Certainty and Uncertainty conditions for all but one of the dependent variables (the equality of access to PN variable was not significant). In each case, scores were higher in the Certainty condition than the Uncertainty condition, indicating that communicating the science as certain results in reduced ethical concerns about and more positive perceptions of PN. For the biological sample manipulation, there were also statistically significant differences for three dependent variables: PN data privacy and security; Trust/efficacy of regulation; and Attitude to PN. Participants in the Stool condition reported lower concern regarding privacy and security and trust and regulation, and had the most positive attitude score when compared to the other sample conditions, and in particular the Blood condition.

To explore potential differences in the way people responded spontaneously to the idea of giving a personal biological sample for the purposes of PN, and whether these responses were impacted by the science behind PN being explained as certain or uncertain, we conducted a word association study. We found that across all three sample conditions there was a difference in the frequencies of words elicited in the Certainty compared to the Uncertainty condition. This suggested that a relatively small manipulation of certainty impacted participants' frame of reference, with many more positively-connoted words appearing in response to the Certainty than Uncertainty condition. There was also a difference in category frequencies across the three sample conditions, with participants in the Stool condition reporting more words with negative connotations overall than those in both the Urine and Blood conditions.

There were also differences in the affect ratings participants associated with the words they produced. Both Certainty and Sample type had a statistically significant impact on the produced affect ratings. Ratings for participants in the Certainty condition were higher than for those in the Uncertainty condition. Ratings for participants in the Urine and Blood conditions were higher than for those in the Stool condition.

Ethical issues relating to the delivery of PN

Ethical issues relating to the delivery of PN are those most closely associated with point of use and concern issues relating to consent, data management, and data privacy. The focus group study found that some participants expressed concern about the privacy and security of their data. This concern was expressed more in relation to genotypic and lifestyle PN than to phenotypic. This may reflect a view that there is less of a privacy and security risk associated with providing phenotypic data compared to lifestyle and genetic information in that it is less relatable back to an individual, or

perhaps, a reduced understanding of the nature of these data. In the survey study, communicating the science as certain led to reduced concerns about this issue. Providing a stool sample led to reduced concerns compared to providing a blood sample.

Ethical concerns relating to the communication of PN

Ethical issues relating to the communication of PN are those concerning how PN is communicated to the public and their consequent perceptions of PN. The findings from both the experimental survey and word association studies suggest that perceptions towards PN are more favourable and ethical concerns relating to data security and privacy and certainty around benefit claims are reduced when the science is presented as certain than when it is presented as uncertain, despite the relative subtlety of the manipulation we employed. This raises the question of whether commercial companies should make more accurate representations of the science and if and how they might be compelled to do so.

Ethical concerns relating to the utility of PN

Although this concept was less directly explored in the empirical studies conducted within WP 4.5, it remains an important ethical consideration in relation to PN, particularly as PN becomes more available to consumers in the commercial sphere. One finding pertaining to the utility of PN, from the experimental survey study, is that there was no effect of certainty or of sample on responses to questions about the utility of PN. These questions related specifically to the issue of whether personalised nutrition is or should be available to everyone, or only those who can afford it. There are two possible explanations for this. First, that the issue does not raise concern because people consider it self-evident that PN should be available to all who could benefit for it. Or second, that it is simply not an issue that people feel is relevant or worthy of concern. This merits further investigation, particularly as PN has been the subject of some criticism in relation to this issue, in that it may have the undesirable effect of widening already-existing health inequalities, such as the prevalence of obesity across socio-economic classes. Chatelan, Bochud, and Frohlich (2019) argue that PN may address only causes of cases rather than causes of incidence. Whilst the former relates to individual cases of obesity, the latter relates to the broader factors in society, such as poverty, educational inequalities, and the so-called 'obesogenic environment' (Swinburn, Egger, & Raza, 1999). Extending this argument to the focus and purpose of commercialised PN, it would seem feasible that such paid-for services might address causes of cases rather than causes of incidence and thus contribute to expanding social and health existing inequalities. Further, there is the question of the extent to which PN is more effective than generalised nutritional approaches, and for whom it may or may not be effective. Thus far, studies indicate that the effectiveness of PN based on genetic or phenotypic information, over and above general nutritional advice, may be rather minimal (e.g., Jinnette et al., 2021).

Summary

The work conducted here has shown first, that although the science cannot be accurately described as certain, that commercial companies selling direct-to-consumer PN based on the GM on the internet are presenting the science as if it were certain on the main pages of their websites. Disclaimers are made, but these are hidden away, typically in lengthy terms and conditions sections. Given this finding, we then sought to understand how expression of certainty impacts perceptions of PN, both in terms of spontaneous responses and more considered responses to survey questions. We found that in both cases, responses were more favourable when participants were told the science behind PN was certain than when it was couched in a more tentative way.

We also found that the idea of giving a stool sample was perceived more negatively than giving a blood or urine sample, yet in relation to ethical issues pertaining to trust, regulation, data security, and data privacy, providing a stool sample was perceived more positively. This suggests that it may be useful to unpick the nuances between stool sample provision – perceived by participants in the word association study as rather onerous and distasteful – and provision of material contained within a stool sample – which provoked less concern than other types of samples in the survey study.

From an ethical perspective, provision of a sample per se and provision of the material contained within a particular type of sample raise slightly different issues. The provision of material contained within a sample raises concerns relating to delivery of PN, specifically data security and privacy. Asking people to provide a biological sample raises concerns relating to the utility and communication of PN; whether the evidence base is robust enough to warrant asking consumers to provide samples via what could be deemed to be onerous collection procedures and whether individuals are fully appraised of the scientific evidence base when deciding whether to provide a sample. The separation of sample provision and sample material raises the issue of whether, when communicating about providing stool samples for the purpose of GM-based PN, it is beneficial to focus on the nature of the data, rather than dwelling on the nature of the procedure.

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