PROTOCOL

Pilot Clinical Trial on the Effects of Dietary Fibres on Gut Microbiome and Metabolic Profiles in a Transgenerational Cohort

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1. Introduction:

Westernised diets, rich in animal proteins and fats and low in dietary fibres, have become more common around the world in the past 3-4 decades[1]. This trend has been accompanied by a rise in cardiometabolic conditions (diabetes, obesity, heart disease) as well as allergies. However, no causal relationship between these trends has been proven yet. Dietary fibres are complex plant polysaccharides which reach the colon intact; there they are broken down into smaller molecules, such as short-chain fatty acids by the gut bacteria[2]. Examples of short-chain fatty acids include acetate, propionate or butyrate. These molecules end up in the blood stream where they perform a wide range of significant functions, such as appetite regulation, control of colon cells development etc[2,3]. Increased intake of dietary fibres which leads to a diverse gut bacteria composition and consequently increased production of short-chain fatty acids is associated with good health[2]. Examples of health benefits include lower risks of heart disease or type 2 diabetes.

The recommended daily intake of dietary fibre is 30g, nonetheless, the average daily intake is around 15-18g[4,5]. A trend characterised by decreased dietary fibre intake has become more apparent in the past decades in various countries around the world[5,6]. Younger people tended to consume fewer dietary fibres when compared to older people[5,6]. Among younger people, dietary fibres were generally replaced with animal fats and proteins.

A human study indicated that migration from non-Westernised societies (Thailand), where intake of dietary fibres is high, to Westernised societies (USA), where intake of dietary fibre is low, leads to loss of gut bacteria diversity[7]. This loss was associated with increased BMI (body mass index) and these negative effects exacerbated the longer the individuals spent in the USA. Indeed, second generation migrants had lower gut bacteria diversity, higher protein intake and higher BMI when compared to first generation migrants or individuals who remained in Thailand[7]. In addition, a mice study demonstrated that breeding mice on low fibre diets over 4 generations led to 70% of gut bacteria taxa (population) being lost in the fourth generation[8]. None of these studies have explored the impact of these long-term low dietary fibre trends on gut bacteria production of short-chain fatty acids. This is a significant gap given that production of short-chain fatty acids by the gut bacteria influences colon cells development, lipids levels or appetite[3].

Because short-chain fatty acids production is related to the amount of fibre intake, we believe that the current trends in lower fibre intake especially in younger generations

may have led to changes in the functionality of their gut bacteria. Specifically, we hypothesize that production of short-chain fatty acids is lower in younger generations compared to older generations and these dietary habits may also have affected the gut bacteria composition. To our knowledge, no research has been done to demonstrate that this hypothesis is valid or not. Therefore, we would like to test this hypothesis in a cross-over clinical trial where gut bacteria production of short-chain fatty acids, gut bacteria composition, metabolic profiles, glucose, insulin, lipid, gut hormones and inflammatory marker levels will be measured in duos or trios of participants (in direct link) who will take dietary fibre intervention daily for 4 weeks and compare these results with placebo intake over 4 weeks.

We want to investigate this hypothesis in women from 2 or 3 generations in direct link from the same family, such as grandmother, mother and daughter. At birth, mothers transmit gut bacteria to their offspring and therefore the maternal microbiome plays an important role in shaping the early composition of offspring's gut microbiota when compared to fathers. Mother's breast milk also influences the gut microbiome of their offspring in early life. However, there is little information on these maternal influences in the late life of offspring and especially in response to dietary fibre intake. Therefore, we want to determine if there is a transgenerational similarity in gut microbiome composition, metabolic profiles and clinical outcomes in response to 4-week high intake of dietary fibres compared to placebo. This approach (individuals in direct link and female participants across all generations) will allow us to 1) determine if there is a maternal influence on the gut microbiome and responses to dietary fibres of younger generations in late life and 2) have a less heterogenous cohort by focusing on women only which will allow for a better understanding of the data.

2. Study Hypothesis:

We hypothesize that compared to placebo, the dietary fibre intervention will lead to a higher production of short-chain fatty acids by the older generation's gut microbiota when compared to that of the younger generation which will translate into differential responses of gut microbiota composition, glucose, insulin, lipids, gut hormones and inflammatory markers levels.

3. Study Aim:

Investigate the effects of a dietary fibre blend taken over a 4-week period on the production of short-chain fatty acids by the gut microbiota, microbiota composition and health outcomes (glucose, insulin, lipids, gut hormones and inflammatory markers levels) of individuals from 2 or 3 generations in direct link (grandmother, mother and daughter).

4. Primary Outcome:

Comparison of the change in SCFA production from baseline to the end of the intervention between grandmothers, mothers and daughters between dietary fibre intervention and placebo.

5. Secondary Outcomes:

- Comparison of gut microbiota composition from baseline to the end of the intervention between grandmothers, mothers and daughters between dietary fibre intervention and placebo.
- Comparison of metabolic profiles of urine and stool samples from baseline to the end of intervention between grandmothers, mothers and daughters between dietary fibre intervention and placebo.
- Comparison of blood glucose levels from baseline to the end of intervention between grandmothers, mothers and daughters between dietary fibre intervention and placebo.
- Comparison of blood insulin levels from baseline to the end of intervention between grandmothers, mothers and daughters between dietary fibre intervention and placebo.
- Comparison of gut hormone levels from baseline to the end of intervention between grandmothers, mothers and daughters between dietary fibre intervention and placebo.
- Comparison of blood lipid levels from baseline to the end of intervention between grandmothers, mothers and daughters between dietary fibre intervention and placebo.
- Correlation of 3 days food diary information with gut bacteria production of SCFA among the 2 or 3 generations.

- Correlation of 3 days food diary information with gut bacteria composition among the 2 or 3 generations.
- Correlation of 3 days food diary information with urine metabolic profiles among the 2 or 3 generations.

6. Study methodology:

- Randomised, placebo controlled, double-blinded, cross-over study
- 4 weeks intervention (dietary fibre/placebo) – 4 weeks wash-out – 4 weeks intervention (opposite arm of intervention)

7. Intervention products:

The fibre intervention product will contain in equal proportions inulin, pectin and oat beta-glucan.

The placebo product will contain cellulose.

The intervention products will be sourced from Nestlé.

The fibre intervention and placebo products will be powders stored in sachets that will look identical and identically-packaged and participants will be able to add them to and mix them with their meals. The amount of intervention taken daily will be increased gradually (see below) to allow participants to adapt to the increased intake of dietary fibre and reduce the likelihood of gastrointestinal discomfort.

Both researchers and study participants will be blinded to the order in which the interventions will be given. The blinding process will be conducted by an independent researcher of the study team. This is done in order to avoid any bias when analysing the data. Unblinding of the study interventions will be done by the same researcher who was involved in the blinding process and it will be done at the end of the clinical study which is after the last study visit of the last participant.

Emergency unblinding will only be conducted in medical emergencies when the appropriate management of the participant necessitates knowledge of the treatment, or in the event that expedited reporting to the Research Ethics Committee (REC) of an unexpected and related Serious Adverse Event (SAE) is required. In the event that emergency unblinding of an individual participant is required, authorised members of the research team will follow trial procedures to unblind the participant in question and proceed with expedited reporting if required. Unblinding should only be considered if

management of the participant would differ depending on whether they were on placebo intervention (cellulose) or dietary fibre intervention (fibre mix of inulin, pectin and oat beta-glucan).
Randomization of study participants to the order in which they will receive the intervention products (placebo and dietary fibre) will be done by SealedEnvelope.com
Participants will take the dietary supplements twice daily over 28 days in the order outlined below:
10g/day (5g morning or lunch and 5g dinner) from day 1 to day 4
20g/day (10g morning or lunch and 10g dinner) from day 5 to day 12
30g/day (15g morning or lunch and15g dinner) from day 13 to day 28

After the wash-out period, the same procedure as above will be repeated but participants will consume the opposite arm of the intervention. For example, if in the first four weeks of the intervention period of the study, they consumed the placebo product, in the second four weeks of the intervention period of the study, they will consume the dietary fibre product.

Participants will be asked not to consume any intervention products on the study visit. At the end of study visits 1 and 3, participants will receive 56 sachets of intervention products. At study visits 2 and 4, participants will be asked to bring the empty sachets to assess compliance with the intervention. Throughout the 2 study intervention periods, participants will be asked to complete daily the Intervention Product Reminder sheet whenever they take the intervention product. This will also allow for assessing compliance with the intervention.
Intervention products will be stored in sachets and boxes in the Commonwealth Building of Hammersmith campus, Imperial College London.

8. Participants:

10 duos or trios (20-30 participants) females

Inclusion criteria:

- Any of the following groups of people (in direct descent and from the same family):
    - Grandmother, mother and daughter

  - Mother and daughter
  - Grandmother and granddaughter
- Age 18-85 (inclusive)
- BMI: 18.5-30 kg/m^2 (inclusive)
- Considering themselves healthy

Exclusion criteria:

- Intake of antibiotics in the past 3 months and during the study
- Intake of probiotic supplements in the past month and during the study
- Regular intake of laxatives in the past month and during the study
- Subjects with the following conditions:
  - Inflammatory Bowel Disease (IBD)
  - Irritable Bowel Syndrome (IBS)
  - Coeliac Disease
  - Type ~~II~~ 2 Diabetes
  - Any type of cancer
  - Autoimmune conditions
  - Conditions that affect the liver
  - Conditions that affect the pancreas
- Subjects who require medical intervention in the coming 3 months
- Smokers
- Shift workers
- Gluten intolerance
- Pregnant and lactating women
- Subjects living in care homes
- had weight changes >5% in the preceding 3 months
- Subjects who are unable to give informed consent by themselves
- Subjects who are currently participating in other clinical trials

Support of number of volunteers:

This is a pilot exploratory study in a new area of research and therefore statistical power calculation is not possible.

8.1 Participants' Recruitment

Participants will be recruited through leaflets posted on and distributed at Imperial College London buildings and Imperial College NHS Trusts buildings and the areas surrounding them, using the Imperial College CRF (Clinical Research Facility) healthy volunteers database (an Imperial College CRF where volunteers sign up to the database as they are interested in participating in research studies organised by Imperial College), social media platforms, clinical study advertising platforms, advertising websites, London and Kent newspapers, GP practices, supermarkets, train stations, people's letterboxes in Greater London Area and Kent county. In the case of Imperial College CRF healthy volunteers' database, authorised users of this database will be able to send e-mails to individuals who may fit the eligibility criteria (women, age 18-85, BMI 18.5-30 g/m^2) based on the information these volunteers provide when they sign up for this database. Study adverts will be distributed and posted by members of the research team around tube stations areas part of Greater London Area and Kent county.

9. Study Design:

Individuals who reply to the study advert will receive either by e-mail or post the Participant Information Sheet (PIS) which they will read and then consider whether they wish to participate in the study provided they meet the eligibility criteria. They will be able to get in touch by phone and/or e-mail with a member of the research team and discuss the study. Individuals will be able to ask questions about the study and will be given time (>24h) to decide whether they wish to participate. If they decide to participate, they will agree to attend a health screening visit at NIHR/Wellcome Trust Imperial Clinical Research Facility at Hammersmith Hospital with a member of the research team.

Visit 0- Health screening

Interested duos or trios (grandmother, mother, daughter) will attend the NIHR/Wellcome Trust Imperial Clinical Research Facility at Hammersmith Hospital where they will be able to ask further questions regarding the study. If participants are eligible for the study and are willing to participate, they will sign an informed consent form. They will keep a copy of the consent form and will be explained that they are free to withdraw from the study at any time without giving any explanation.

Afterwards, they will have a blood test to check they are not anaemic or diabetic and height and weight measurements will also be taken. They will also have ~~an electrocardiogram (ECG) and~~ blood pressure ~~will be recorded~~taken. All women of childbearing age will have a pregnancy test. Participants will also be asked to complete, together with the researcher taking consent, a brief questionnaire assessing their eligibility for the study. Specifically, their weight, height, blood pressure, the result of the pregnancy test will be recorded, as well as any information related to family history of disease, or any medication they are currently taking. In addition, personal information, such as their address (for the collection kits to be sent over), GP details, next of kin will be recorded.

They will also be explained how to use the urine and stool collection kits. Fasted urine and stool samples will be collected by study participants on the day when they come for each study visit. If the results of the blood test will make participants eligible for the study, they will be sent by post the urine and stool collection kits which they will use to bring their samples in on the first study visit. If the blood tests results indicate that they are not eligible for the study, participants will be informed (either by phone or e-mail) by a member of the research team that they will not be able to participate in the study because they do not fit the eligibility criteria.

During the health screening visit, participants will also be explained how to complete the 3 days food diary. If the results of the blood test will make participants eligible for the study, they will be sent by post the first 3 days food diary which they will bring filled in with what they ate and drank 3 days before the first study visit. Eligible participants (once the blood tests results will come and indicate that participants are eligible to participate) will also be sent by post a questionnaire related to demography and dietary habits.

Participants will be advised not to start any strenuous physical activities or go on new diets as these may lead to conflicting results. They will also be asked to consume a similar evening meal the day before each study visit (to ensure consistency between study visits), avoid alcohol the day before each study visit and fast overnight (for 12h) before each study visit (drinking water will be fine).

Visits 1, 2, 3 and 4– Study Visits

There is a 4-week gap (28 days +/-4 days) between Study Visits 1 and 2, followed by a 4-week wash-out period (28 days +/-7 days) and then followed by Study Visits 3 and 4 (4-week gap 28 days +/-4 days between Study Visits 3 and 4) (Figure 1).

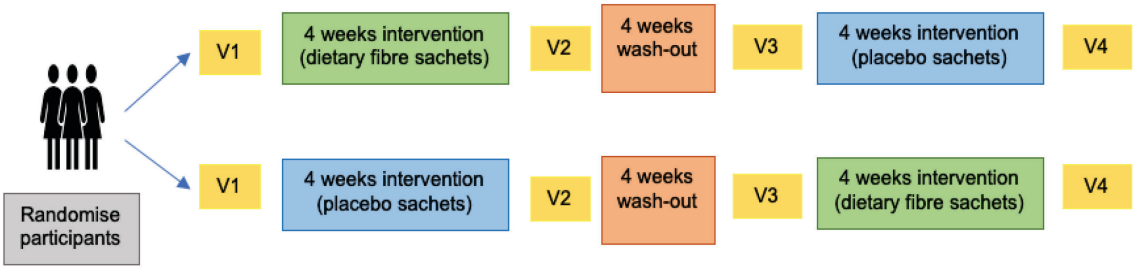

Figure 1. Diagram of study visits; V=study visit

Participants will come fasted at the Study Visits and they will not have consumed any intervention products in the morning. They will bring their stool and urine samples, the 3 days food diaries and the participants questionnaire. They will also undergo a physical examination (body weight, height and fat percentage) and have their blood pressure measured and recorded. Women of childbearing age will have a pregnancy test at the beginning of each study visit. If the pregnancy test result is positive, they will be withdrawn from the study. No more data and samples will be collected from them. All the data and samples that were collected up to their withdrawal will be used in data analysis.

At Study Visits 2 and 4 participants will be asked to complete a Visual Analogue Questionnaire where they will rate how the dietary intervention has affected various gastrointestinal symptoms, such as constipation, bloating, appetite.

At 09:30 an intravenous cannula will be inserted into one arm for blood sampling by an adequately trained doctor, nurse or member of research team under aseptic conditions. Just before 10:00 fasting blood samples will be taken through an intravenous peripheral cannula (-15min and -5min). Participants will then receive a standardised breakfast at 10:00.

Postprandial blood samples will be taken at 15, 30, 45, 60, 90, 120 180 and 240 minutes after having the standardised breakfast to measure gut hormones, ~~lipids,~~ glucose, and insulin ~~and inflammatory marker~~ levels. 10ml of blood samples will be

taken at each sampling point, and therefore 100ml (10 x 10ml) during each study visit will be taken (Figure 2).

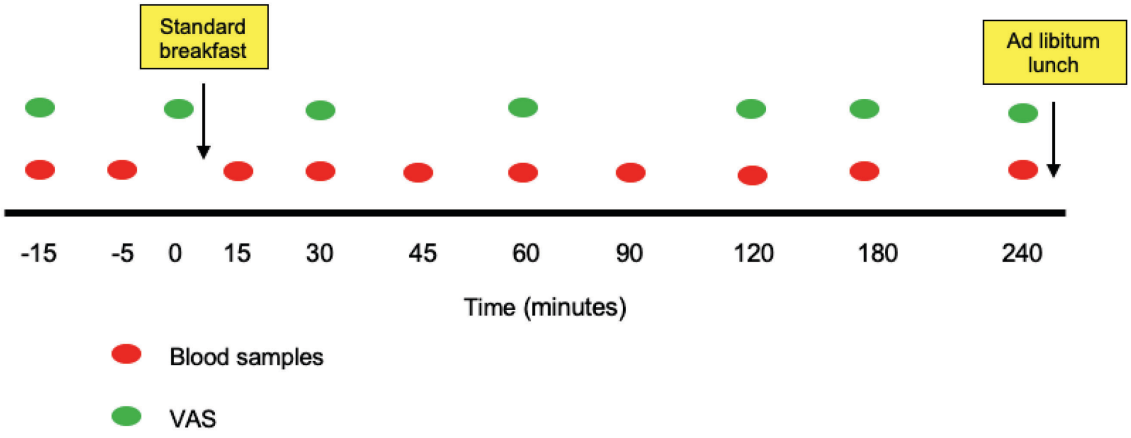

Figure 2. Diagram of Study Visit protocol; VAS=Visual Analogue Scale

Appetite and wellbeing will be assessed at the following timepoints (Figure 2): -15, 0, 30, 60, 120,180 and 240 minutes using a visual analogue scale (VAS).

After the last sampling point, the canula will be removed and participants will be given an ad libitum standardised lunch which participants will be allowed to eat until they feel comfortably satiated. This will allow us to determine whether the long-term intake of the dietary intervention product had any impact on participants' appetite when compared to baseline. The bowl with pasta will be weighed before and after they had the meal to determine how much food the participants consumed.

At the end of Study Visits 1 and 3, participants will receive 56 sachets with intervention products as outlined in section 7. At study visits 2 and 4 participants will bring the empty intervention sachets and completed Intervention Product Reminded sheet to assess compliance with the intervention.

10. Samples storage and analysis

Samples will be stored in -80°C or -20°C freezers during the clinical trial until ready to be analysed. Samples will be stored in pseudonymised form. Upon enrolment and after signing the informed consent form, each participant will receive an enrolment I.D. that will keep their identity confidential.

Samples analysis will be carried out at Imperial College laboratories. Blood test (that assess participant's eligibility) and urine analysis for pregnancy test will be analysed

immediately. Stool, urine and blood samples collected during the study visits will be stored in freezers until ready to be analysed and then safely disposed. Samples may need to be transported abroad to carry out the same analyses described below. If this happens, samples will be transported securely and safely. Samples will be transported in pseudonymised form. At the end of the clinical trial and after all desired analyses were conducted, the remainder samples will be kept under the authority of Imperial Healthcare Tissue Bank for 10 years for any future ethically approved research studies in accordance with the Human Tissue Act except for samples whose participants did not consent to this on their consent form. In this instance, these will be safely disposed of.

The collected samples (stool, urine and blood) will be analysed for: gut microbiota composition (from stools) through 16S rRNA sequencing and qPCR (quantitative Polymerase Chain Reaction); metabolites produced by the gut microbiota (from stools and urine) thorough NMR (Nuclear Magnetic Resonance), GC-MS (gas chromatography coupled with mass spectrometry), LC-MS (liquid chromatography coupled with mass spectrometry), blood glucose, insulin, gut hormones (PYY and GLP-1), inflammatory markers (C reactive protein) and lipid levels.

11. Statistical Analysis

Statistical tests, such as ANOVA (Analysis of Variance) and t-tests (paired and unpaired) will be used to compare different groups: study participants groups, dietary fibre groups and placebo groups. Correlation analysis (Pearson and/or Spearman) and linear models will be used to analyse the relationship between gut bacteria taxa, short-chain fatty acids levels, metabolites levels, food diary information and demographics. Statistical significance levels will be $p<0.05$.

Various platforms will be used to analyse the data. Gut microbiome composition will be analysed using 16S rRNA sequencing on Illumina MiSeq and statistical analyses will be performed in R. Species diversity and richness will be calculated and statistical tests include t-tests and Mann-Whitney U tests, statistical significance $p<0.05$. Species diversity and richness and their changes from baseline between grandmother, mother and offspring will be compared. Data from placebo and dietary fibre intervention will be compared.

Short-chain fatty acids (SCFA) production from stool samples will be measured using GC-MS (Gas Chromatography coupled with Mass Spectrometry). T-tests (paired and/or unpaired) and ANOVA tests will be used to determine whether there are significant differences in SCFA production between grandmothers, mothers and offspring from baseline to end of intervention. Data from placebo and dietary fibre intervention will be compared. Significance levels will be $p<0.05$.

NMR analysis will be done on urine and stool samples to examine and compare metabolic profiles between grandmothers, mothers and offspring and their changes from baseline to end of intervention. Multivariate data analysis, such as Principal Component Analysis will be used to examine and compare if there are chemicals that differentiate the profiles of grandmothers, mothers and offspring at baseline and at the end of intervention. Analyses will be done using the following software R, Matlab, Simca and Prism GraphPad.

Food diaries will be coded using the Dietplan software which will offer insight into participants dietary habits such as their macronutrient intake. The data will be analysed using ANOVA, t-tests in R and Prism GraphPad to examine potential differences and similarities between participants.

The PhD student will be assisted by Dr Carine Blanchard in analysing the data. She will only have access to anonymised data.

12. Withdrawal Criteria and Adverse Events

Withdrawal Criteria

The safety of the study participants takes priority. Any significant adverse event (as assessed by the researchers) will halt the study and the ethics committee and sponsor will be informed as per standard protocol. All adverse events will be recorded and investigators will review each adverse event as it arises. In addition, participants will be free to withdraw at any time and are not required to give a reason.

If one or two participant(s) of the study group decide(s) to withdraw or need(s) to be withdrawn from the study, the other participant(s) from the group can still continue to participate.

The researcher can withdraw the participant on any of the following grounds:

- Participant’s request

- Participant is lost to follow-up
- Participant no longer fulfils the eligibility criteria during the study duration (e.g. participant becomes pregnant etc.)
- Participant develops a condition or illness that interferes with participant's ability to take part in the study
- The investigator reserves the right to withdraw participants in the interest of participant's safety and welfare
- The participant loses capacity to consent.

All data and samples that have been collected up to the withdrawal point will be analysed and used in the study. After withdrawal from the study, no more samples and data will be collected from the participant.

Adverse Event (AE): Any untoward medical occurrence in a patient or clinical study subject.

Serious Adverse Event (SAE): Any untoward and unexpected medical occurrence that:

- results in death
- is life- threatening – refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it was more severe.
- requires hospitalisation, or prolongation of existing inpatients' hospitalisation.
- results in persistent or significant disability or incapacity
- is a congenital abnormality or birth defect

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

Reporting Procedures

All adverse event should be reported. Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

Non-serious AEs

All such events, whether expected or not, should be recorded.

Serious AEs (SEAs)

An SAE form should be completed and faxed to the Chief Investigator within 24 h. However, relapse, death and hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs.

All SAEs should be reported TBC Research Ethics Committee where in the opinion of the Chief Investigator the event was:

- 'related', i.e. resulted from the administration of any of the research procedures; and
- 'unexpected', i.e. an event that is not listed in the protocol as an expected occurrence.

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES SAE form for non-IMP studies. The Chief Investigator must also notify the Sponsor of all SAEs.

Local investigators should report any SAEs as required by their Local Research Ethics Committee, Sponsor and/or Research & Development Office.

Contact details for reporting SAE:

Contact details for reporting SAEs
jrco@imperial.ac.uk
CI email (and contact details below)
Fax: xxx, attention xxx
Please send SAE forms to: xxx

Professor Gary Frost through his secretary Mon to Fri 9 am-5 pm: 020 75942739.

Incidental Findings

Incidental findings are defined as results that are outside the original purpose for which a test or procedure was conducted. Incidental findings can be either "anticipatable" or "unanticipatable." An anticipatable incidental finding is one that is known to be associated with a test or procedure. Anticipatable incidental findings need not be common or even likely to occur—their defining characteristic is that the possibility of finding them is known. Unanticipatable incidental findings include findings that could not have been anticipated given the current state of scientific knowledge.

All such incidents will be reported to the participants and recorded in participant's file document. The Chief Investigator, and clinical care team of the clinical trial will also be informed of this. If the incidental finding affects the wellbeing and welfare of the participant, they will be assessed immediately by a trained clinician part of the hospital.

13. Regulatory Issues

Ethics Approval

The Study Coordination Centre has obtained approval from the Research Ethics Committee (REC) and Health Research Authority (HRA). The study must also receive confirmation of capacity and capability from each participating NHS Trust before accepting participants into the study or any research activity is carried out. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

Informed Consent

Consent to enter the study must be sought from each participant only after a full explanation has been given, an information leaflet offered, and time allowed for consideration. Signed participant informed consent should be obtained. The right of the participant to refuse to participate without giving reasons must be respected. After the participant has entered the study the clinician remains free to give alternative treatment to that specified in the protocol at any stage if he/she feels it is in the participant's best interest, but the reasons for doing so should be recorded. In such cases, the participants remain within the study for the purposes of follow-up and data analyses. All participants are free to withdraw at any time from the study without giving reasons and without prejudicing further treatment.

Confidentiality

The Chief Investigator will preserve the confidentiality of participants in the study and is registered under the Data Protection Act. To ensure this is done accordingly, each participant at the time of informed consent will be allocated a unique screening number/code before undergoing any screening procedures. The study management team, together with all clinical site team, will comply with all aspects of the Data Protection Act **201**8. All information collected will be kept confidential, and consent forms (containing participants' full names) will be held entirely separate to another data.

All data collection forms will be pseudonymised with either a temporary I.D. or enrolment I.D and stored at ICHT in a locked filing cabinet, with restricted access, and disposal arrangements of participant personal and clinical data.
Participants will not be identifiable in the results of the study. The samples collected will also be pseudonymized with enrollment ID and study visit number.

Indemnity

Imperial College holds negligent harm and non-negligent harm insurance policies, which apply to this study.

Sponsor

Imperial College London will act as the main sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

Funding

This research project is part of a grant funded by the Nestle Research and Development. Participants will be reimbursed for their time: £400 will be awarded for completion of this study (£100 per study visit).

Audits and Inspections

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the UK Policy Framework for Health and Social Care

14. Publication Policy

The findings of the research will be published in open-access, peer-reviewed journal, relevant gut microbiome and nutrition conferences and PhD thesis. In addition, the study team will be collaborating with participants and professional groups to disseminate the findings via multiple media channels such as participants association publications, print and broadcast media.

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