Exploring mechanism of action of dietary fibre on the gut microbiota and metabolites: can we identify responders and non-responders to psyllium and inulin dietary fibres?

Principal Investigator: Prof Anne Kiltie

You are being invited to take part in a research study. Before you decide whether to volunteer, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

Please do not hesitate to contact us (see below) if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

To understand how dietary fibre supplements influence the composition of the gut microbiota, the production of metabolites called short chain fatty acids and the immune system. This will give us important information before we start clinical trials in patients with pelvic cancers.

Why have I been chosen?

You have been chosen because you fulfil our eligibility criteria:

- You have expressed an interest in taking part after seeing the study advertised either on the Rowett Institute website, on social media, in local press, by letter, newsletter or on a public poster or in another way.
- You are aged over 60 years old.

The exclusion criteria for this study are as follows:
Medication exclusion criteria:

- Oral antibiotic use (within the past 3 months due to impact on gut microbiota).
- Anti-coagulants (Warfarin).
- Carbamazepine (epilepsy)

- Digoxin (heart conditions)
- Mesalazine (gut problems)
- Regular use of anti-constipation medication/laxatives.

Medical exclusion criteria:

- Food allergies, self-reported food sensitivity or intolerance.
- Type 1 or Type 2 diabetes.
- Coeliac disease or gluten intolerance.
- Metformin intake.
- Bowel obstruction
- Muscle weakness of the bowel
- Phenylketonuria.

Other exclusion criteria:

- Anyone with unsuitable veins for blood sampling.
- Anyone with chronic constipation (>3 days without defaecation).
- Anyone who is unable to fluently speak, read and understand English.

Do I have to take part?

No. It is up to you to decide whether to take part.
If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form during your first visit, where you will also be able to ask a member of the research team any questions you might have. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What does the study involve?

You will be invited to come to the Rowett Human Nutrition Unit (HNU) for a screening visit where your eligibility for the study will be confirmed and consent paperwork for participation will be completed. Before starting the study, you will be asked to complete questionnaires about your health status and general information.

A total of 42 participants will be included in this study, and each participant will be involved for 74 days. We anticipate the whole study will take 18

months. When you start the 10-week study period, we will provide you with pouches filled with supplements that need to be taken twice daily (details below) for two weeks at a time. You will be asked to attend the HNU on six occasions for test days, each of which lasts approximately 6 hours, where you will be asked to fill in gastrointestinal wellbeing and quality of life questionnaires and provide blood and faecal samples.

What will my role be in this study?

Each participant will be involved for 74 days, divided into 3 blocks of 2 weeks each, with 2 weeks in between the blocks. You will be asked to attend the HNU on six occasions for Test Days, at the beginning and end of each block (+/- 2 days). Each test day lasts approximately 6 hours. During these test days, we provide you with breakfast in the HNU.

On Test Day 1, 3 and 5, you will be provided with pouches containing a powder, and will be asked to take these twice daily for 14 days, until the next Test Day (Test Day 2, 4 and 6), which will be on the last day of each block. It is important to take these pouches twice daily, but in case you do forget to take one, we ask you to return all unused pouches at the next visit.

On a Test Day, we will meet you in the HNU between 7-8am and provide you with breakfast. On Test Day 1, 3 and 5, we will take one blood sample (less than 10ml) 5 hours after eating breakfast. On Test Day 2, 4 and 6, we will take 2 blood samples (less than 10 ml in total) 5 hours after taking the last pouch during breakfast. We will use these blood samples to determine the short chain fatty acid (SCFA) concentration and cytokine levels in your blood. It is not necessary to fast overnight. We will also ask you to bring a faecal sample of less than 28h old to the Test Day, or provide one during the Test Day, which will be used to determine the composition of your gut microbiota, SCFAs, and general gut health. We will also ask you to fill out some questionnaires during the visit, and encourage to bring reading glasses, when necessary.

You will be asked to fill in a 3-day weighed food questionnaire 3 days before each Test Day and fill out a Food Frequency Questionnaire before the study starts and at Test Day 6.

It will not be possible to participate in another study during the study period. You can give permission to be contacted again in the future to take part in any further research for this study or others, but participation in these future studies will be completely up to you. With your consent, the data will be stored for 5 years, and after this period, the samples will be stored into the NHS Grampian Biorepository. If you decide to withdraw from the study, all collected data will be destroyed.

What measurements will be conducted if I take part?

Screening visit (~1hrs):

- Medical screening: you will be asked to complete a health status questionnaire and general information form
- A trained member of the HNU staff will assess the suitability of venous access

Test days (~6hrs):

We will measure you on 6 occasions (Test Day 1, 2, 3, 4, 5 and 6). On these days, we will provide breakfast, to be consumed in the HNU. We will take the following measurements:

- Blood samples- the blood samples will be collected 5 hours after eating breakfast, and will not exceed 10 ml. The samples will be analysed for short chain fatty acid content and cytokines.
    - We will take one blood sample on Test Day 1, 3, and 5
    - We will take two blood samples on Test Day 2, 4 and 6
- Faecal samples: you will be asked to bring in a faecal sample of less than 28h old on each of the Test Days, or, when not needing to go before the test day, on the test day itself. Sample pots and instructions on how to collect these samples will be provided. In some cases, a faecal sample produced 3 days – 28h before the test day can also be collected/ brought to the HNU. A portion of your

faecal sample may be used to test the dietary fibres in a gut model under controlled conditions in the lab.
- A quality of life questionnaire to assess tolerance of interventions.

Other measurements (not during test days)
- You will be asked to complete a Food Frequency Questionnaire before the first Test day starts and on Test Day 6.
- You will be asked to complete 3-day weighed food diaries 3 days before each test day to record habitual fibre intake. We will explain to you how to do this.
- You will be asked to complete the gastrointestinal wellbeing questionnaire on the day you produce the faecal sample.

What are the supplements that are tested?

We are testing 3 different supplements, one in each 2-week block: inulin, psyllium + inulin, and a placebo (maltodextrin). Inulin and psyllium are dietary fibres, commonly found in oats, nuts, vegetables and fruits. Maltodextrin is a carbohydrate. The supplements will be provided in pouches. The contents of the pouches can be dissolved in a glass of water, orange juice, etc. and need to be consumed twice daily, around breakfast and dinner. Inulin will be provided in pouches of 8 g, psyllium plus inulin pouches will consist of 3.5g psyllium and 8g inulin, and the placebo pouches will consist of 8g maltodextrin. You will start with half-doses for the first three days of each block as run-in periods to improve tolerability. We encourage you to drink plenty during the study, and not to alter your usual diet.

What are the side effects of any treatment received when taking part?

These supplements could have possible side effects. If you suffer any of these symptoms, we ask you to report them on the next Test Day or by contacting the study team (details below). Contact us immediately using the contact card we will provide you with if the experienced side effects are serious and unblinding is necessary.

Possible side effects of inulin are:

- Flatulence
- Abdominal bloating and discomfort
- Soft stool or diarrhoea
- Increase in gastroesophageal reflux

Possible side effects of psyllium husk powder are:

- Difficulty breathing
- Stomach pain
- Difficulty swallowing
- Skin rash
- Itching
- Nausea
- Vomiting

Possible side effects of the placebo (maltodextrin) are:

- Belching, nausea, bloating, flatulence
- Weight gain
- Gastrointestinal symptoms (gas, gurgling sounds, diarrhoea/watery faeces)
- Allergic reactions (cramping, skin irritations)

What are the possible benefits of taking part in the study?

Although there are no direct benefits to you for taking part, on completion of the study you will receive a written report of a selection of your own results (dietary intake), which you may find interesting. You will receive £75 as a gratuity for completing the study.

What are the possible disadvantages and risks of taking part?

It is possible that you could get one of the above-mentioned side effects from the supplements. Blood sampling may result in minor bruising or irritation at the cannulation site. If we find blood in your faeces, we will inform you and your GP (with your consent).

What if there is a problem?

If you have a complaint or a concern at any time during the study that you have been unable to resolve with the Investigator, Ms Merel van den Haak (01224 438756, r01mv22@abdn.ac.uk), you may contact Dr Frank Thies (Chair of the Human Studies Management Committee). You can be assured that he will be a sympathetic listener and that your concerns will be treated seriously. He can be contacted by email: f.thies@abdn.ac.uk. The University carries indemnity insurance for any harm or adverse event and Dr Thies can be contacted for more information about this.

Adverse event/ emergency

In case of serious side effects, e.g. breathing difficulties, please call 999. If it is necessary to know which fibre you are taking (e.g. in A&E), please contact Gary Cooper (01224 438654) or Graham Horgan (01224 438678). If unavailable, please phone the HNU number (01224 438785) to let you or the doctors looking after you know which fibre you are currently taking. We will provide you with a small, laminated card with the contact details.

Who has reviewed the study?

This study has been reviewed and approved by the Human Studies Management Committee of the Rowett Institute of Nutrition and Health and the Rowett Institute Ethics Panel.

Who is organising and funding the research?

The study is organised by the university of Aberdeen and funded by the charity Friends of ANCHOR. Friends of ANCHOR has multiple cancer wards and clinics within Aberdeen Royal Infirmary, and funds multiple pilot research projects that play a critical role in the future of cancer management.

Will my taking part in this study be kept confidential?

All data collected from you will be coded to ensure your anonymity and you will not be identifiable in any publication of results from this study. Only your screening paperwork will have record of your name. All the data will be held in locked cabinets, in locked offices, on secured shared drives and/or on password protected computers/memory sticks. All data will be stored for a maximum of 10 years, after which it will be destroyed.

Anonymised samples will be stored until the study has been completed and, with your consent, for a further 5 years to allow for potential additional analysis in future ethically reviewed and approved studies. After this period, all samples will be transferred to the NHS Grampian Biorepository, where the samples can be used for future ethically approved studies. The results of this study are planned to be published within 3 years.

The University of Aberdeen is the sponsor for this study based in the United Kingdom. We will be using information from you to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Aberdeen will keep identifiable information about you for 10 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways for the research to be reliable and accurate. If you withdraw from the study, we will destroy the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible. You can find out more about how we use your information http://www.abdn.ac.uk/privacy.

Contacts for study

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Thank you for having taken the time to read this information sheet and for your interest in the study. If you do decide to take part in the study, you will be given a copy of this information sheet and a consent form to sign and date at the HNU.