Participant Information Sheet

Chief Investigator: Dr Edward Chambers

Increasing gut-derived propionate to improve bone health in postmenopausal women

You will be given a copy of this Information Sheet and a signed copy of your consent form to keep, should you decide to participate in the study.

You are being invited to take part in a research study investigating the effect of gut-derived propionate on bone health markers. Before you decide if you would like to participate, 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 and discuss it with your friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

If you do decide to take part, please let us know beforehand if you have been involved in any other study during the last year. You are free to withdraw at any time without explanation.

Thank you for reading this

WHAT IS THE PURPOSE OF THIS STUDY?

There are >500,000 osteoporotic fractures per year in the UK. Older women (>50 years) have a 2.5-fold increased risk of osteoporotic fractures compared with older men, owing to the profound negative impact of the menopause on bone health. Consequently, there is an urgent need for effective, safe, inexpensive, and widely applicable interventions to prevent osteoporotic fractures in postmenopausal women.

Higher intakes of dietary fibre in postmenopausal women are associated with improved bone health. Dietary fibre is fermented by bacteria that live in the gut and this produces molecules called short chain fatty acids (SCFA). Recent studies have shown that a SCFA called propionate may be effective at improving bone health. Accordingly, interventions that can increase propionate in postmenopausal women may be an effective strategy at improving bone health and preventing osteoporotic fractures. To raise gut-derived propionate we have developed a dietary supplement called inulin-propionate ester (IPE). The objective of this project is test if IPE improves markers of bone health in postmenopausal women.

WHO IS SUITABLE TO PARTICIPATE?

- Post-menopausal females (>5 years post-menopause)
- Non-obese (body mass index (BMI) of 20-30 kg/m^2) - BMI is equal to body weight (kg) divided by height squared (m2))
- Age between 50-75 years (inclusive)
- Non-diabetic

And because you do not have/are:

- Weight change of ≥ 3kg in the preceding 2 months
- Current smokers
- Substance abuse

- Excess alcohol intake
- Cardiovascular disease
- Cancer
- Gastrointestinal disease e.g. inflammatory bowel disease or irritable bowel syndrome
- Kidney disease
- Pancreatitis
- Use of medications likely to interfere with energy metabolism, appetite regulation and hormonal balance, including: anti-inflammatory drugs or steroids, antibiotics, androgens, phenytoin, erythromycin or thyroid hormones.

Any participants with the above conditions would already have an altered pattern of hormones and inflammatory molecules because of their disease process and would therefore give us confounding or misleading results.

We aim to recruit 28 participants in total. It is entirely up to you whether or not to take part. If you do we will ask you to sign a consent form. You are free to withdraw at any time and you do not have to give a reason. A decision either not to take part or to withdraw from the study will not affect the standard of care you receive.

DO I HAVE TO TAKE PART?

You can withdraw from the study at any time and you do not need to give a reason. All of your tissue collected would be withdrawn from the study. Tissue which is not identifiable to the research team may be retained.

WHAT WILL I HAVE TO DO?

If you do decide to participate, the study will consist of 4 separate study visits. We request that you do not start any new diets or intensive exercise regimes (dramatically increase the amount of exercise you do, for example, join a gym) in-between the study visits as this may give us conflicting results.

Visit 1- Health Screening

You will be asked to attend the NIHR Imperial Clinical Research Facility at Hammersmith Hospital where you will be interviewed about your general health. You will have a blood test to confirm that you are non-diabetic and your body weight and height will be recorded. The duration of the study visit would be around 1 hour.

Visit 2 – Week 0 Study Visit

The week before the study visit you will be asked to complete a 7-day food diary and physical activity questionnaire to measure your dietary intake and exercise levels.

On the day before the study visit we will ask you to refrain from strenuous exercise, caffeine and alcohol. You will then be requested to fast overnight (you are allowed to drink water) from 20:00 the evening before the study visit.

On the study day, you will be asked to arrive at the NIHR Imperial Clinical Research Facility at Hammersmith Hospital at approximately 9:00am. A small plastic tube (a cannula) will be inserted into a vein in your arm. This will be in place for the duration of the study day and will be used to

take blood samples at regular intervals without causing you any further discomfort. A total of 100 ml of blood (~20 teaspoons) will be collected at the study visit. Fasting blood samples will be collected and analysed for bone health markers. We will also ask you to provide a urine sample to measure additional bone health markers.

You will then consume a standard breakfast and further blood samples will be taken for 5 hours to measure SCFA, glucose and insulin. During the course of the study day you will be able to read or use electronic devices if you wish.

We will ask you to collect a stool sample to assess SCFA production. You will be asked to provide this sample the day the study visit. You will be provided with a container and detailed instructions on how to do this correctly. The total duration of the study visit will be around 6 hours.

Supplementation period

Following Visit 2 you will undergo an 8-week dietary supplementation period. You will be provided with 10 g sachets containing either:

1. Control

2. IPE

We do not know if the IPE will improve markers of bone health. To find out, we need to compare it to a different dietary intervention. We put people into groups and give each group a different intervention and the results are compared to see if one is better. To try to make sure the groups are the same to start with, each participant is put into a group by chance (randomly). You have a 50:50 chance of receiving the IPE. If you are not in the group taking the propionate ester you will be in the "control" group and will take a dietary fibre called cellulose. The IPE and cellulose are both natural constituents of fruits and vegetables. You and your researcher will not know the nature of the supplement you are taking.

If you experience any problems from taking the supplement an independent researcher who can access information about the group you are in will assess you and if necessary will ask you to stop taking the supplement and withdraw you from the trial.

You will be asked to add a 10 g sachet into with your normal diet every day for the 8-week supplementation period. The IPE and cellulose are soluble powders that you can easily mix into your food and drink. You are not being asked to change your diet or lifestyle in any other way. We request that you do not start any new diets or intensive exercise regimes in-between the study visits as this may give us conflicting results. You will receive a weekly telephone call during the 8-week supplementation period to monitor compliance and any side-effects. Dietary fibre supplements can cause mild gastrointestinal side-effects, including stomach bloating and flatulence.

Visit 3- Week 2 Follow-up Visit

On the day before the study visit we will ask you to refrain from strenuous exercise, caffeine and alcohol. You will then be requested to fast overnight (you are allowed to drink water) from 20:00 the evening before the study visit.

On the study day, you will be asked to arrive at the NIHR Imperial Clinical Research Facility at Hammersmith Hospital at approximately 9:00am. A blood sample (20 ml of blood) will be taken to

measure changes in bone health markers. You would also be asked to provide a urine sample. The duration of the study visit would be around 1 hour.

Visit 4- Week 8 Follow-Up Visit

This will be identical to Visit 2. The standard breakfast would also contain 10 g IPE or 10 g control depending on your supplementation group.

WILL I GET PAID FOR PARTICIPATING?

You will be reimbursed for any inconvenience caused due to the study. You will receive £50 for completing each study visit (excluding study visit 1). You would therefore receive payment of £150 for completing the entire study. Reimbursement will be made by bank transfer. Following completion of the study you will be sent an electronic payment form to complete and you will need to provide bank account details. The completed form will then need to be sent to the Imperial College Finance Division (details provided on payment form) who will process the study payment. The collection, storage and security of this personal information will comply with General Data Protection Regulation (GDPR).

WHAT IF SOMETHING GOES WRONG?

'Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Dr Edward Chambers; e.chambers@imperial.ac.uk ; 0778361040). The normal National Health Service mechanisms are also available to you such as the local Patient Advice Liaison Services (PAL; pals@imperial.nhs.uk; 020 3313 0088). If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team'

WHAT ARE THE POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART?

In the event that we discover something about your health that you were unaware of, for example if your blood tests are abnormal, we would immediately inform you of this and inform your GP so that you can be referred to an appropriate specialist. If you require more urgent assessment we would arrange this for you immediately within the hospital.

Some of the procedures in this study, such as the recording of your weight, height and blood pressure present no risk to you. Other procedures, such as taking blood samples, can cause mild discomfort. The risks of taking a blood sample include: slight discomfort when the needle is inserted and possible bruising and a localised infection. These procedures will only be carried out by experienced doctors under aseptic conditions to minimise all these risks.

Your GP will be informed that you are taking part in this study. They will be notified in the event of any side effects from taking the supplement or from any of the clinical procedures performed in the study. If you have insurance, you will need to inform your insurance company if anything goes wrong during the course of the study.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

There is no guarantee that you will experience a clinical benefit from taking part in the trial. We cannot promise the study will help you but the information we get might help reduce osteoporotic fractures in the future.

WHAT IF NEW INFORMATION BECOMES AVAILABLE?

Sometimes during the course of a research project, new information becomes available about the intervention being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw your research doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form. Also, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study.

We may also discover incidental findings as part of the trial. For example, blood tests may indicate high blood glucose levels and possible diagnosis of diabetes. This information would be reported to your GP to arrange follow-up care.

WHAT HAPPENS WHEN THE RESEARCH STOPS?

A final study report will be produced summarising the information we have learned. This will be anonymous. The results will be made available to you and/or you GP at your request, if you have any problems following the result, then you can contact one of the research doctors on the numbers provided.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

Imperial College London is the sponsor for 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. Imperial College London will keep your personal data for 10 years after the study has completed in relation to primary research data.

We will need to use information from you for this research project. This information will include your

- Initials
- NHS number
- Name
- Contact details
- Bank details for study payment

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

LEGAL BASIS

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part

in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study.
Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

INTERNATIONAL TRANSFERS

There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (**EC**) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient organisation that incorporates EC approved standard contractual clauses that safeguard how your personal data is processed.

SHARING YOUR INFORMATION WITH OTHERS

For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we will share your personal data with certain third parties.

- Other College employees, agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you. If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to the chief investigator (e.chambers@imperial.ac.uk)
- by ringing us on 07786361040

COMPLAINT

If you wish to raise a complaint on how we have handled your personal data, please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). The ICO does

recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

WHO HAS REVIEWED THIS STUDY?

This study was reviewed by Health Research Authority (HRA). This study was given a favourable ethical opinion for conduct in the NHS by London - South East Research Ethics Committee

CONTACT FOR FURTHER INFORMATION

Dr Edward Chambers	e.chambers@imperial.ac.uk	07786361040