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Faculty of Medicine & Health Sciences
School of Medicine
Academic Unit of Injury, Inflammation and Recovery Science, Academic Orthopaedics, Trauma and Sports Medicine, Room WC1380, C Floor, West Block, Queen's Medical Centre, Nottingham, NG7 2UH

PARTICIPANT INFORMATION SHEET

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lIfestyle iNterventionS for PaIn ReliEf (The 'INSPIRE' Study)

Research Team: Prof Ana Valdes and Dr Amrita Vijay

We would like to invite you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. One of our team will go through the information sheet with you and answer any questions you have. Please take time to read this carefully and discuss it with others if you wish. Ask us anything that is not clear.

1. What is the purpose of the research?

Previous research has shown that the types of bacteria that reside in your gut as well as the chemicals that they produce have implication on inflammation and pain. Furthermore, mild to moderate exercise has also shown to reduce pain in individuals with knee osteoarthritis via specific pathways.
The purpose of the study is to investigate the effect of consuming a common plant derived dietary fibre on metabolic pain by changing the composition of the bacteria that reside within the gut and the levels of specific molecules called Short chain fatty acids that they produce. In addition, we will investigate the effects of exercise on compounds called endocannabinoids (i.e. cannabis like substances produced by your own body) and the effect these substances have on improving knee pain. In the current study, you will be assigned randomly assigned into a group wherein you will be asked to take a fibre supplement and/or perform a series of routine exercises for a period of 6 weeks.

You have been invited to take part in this research because you are over the age of 18, are willing and able to give informed consent for participation in the study and have a body mass index (BMI) between 20 and 39.9 kg/m2

Unfortunately, you will be unable to take part if any of the following apply:

- Have a psychosocial or gastrointestinal condition (e.g. malabsorptive conditions such as IBS/IBD, coeliac)
- Are taking the following medications: immunosuppressants, anticoagulants, amiodarone and/or perhexiline
- Are currently following or anticipated to commence a specialised commercially available weight loss diet and/or program
- Pregnant or breast feeding
- History or current psychiatric illness
- History or current neurological condition (e.g. epilepsy)

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- If you are undergoing revision, having severe hip OA, inflammatory arteriopathies
- If you are diagnosed with non-OA cause of knee pain (e.g. rheumatoid arthritis)
- Neuropathy or diabetes mellitus
- Having taken part in a research study in the last 3 months involving invasive procedures which included an inconvenience allowance

Please read this information sheet in detail before deciding whether you wish to take part or not. We aim to invite 120 participants like you to take part.

3. Do I have to take part?

No, it is up to you to decide if you want to take part in this research. We will describe the study and go through this information sheet with you to answer any questions you may have. If you agree to participate, we will ask you to sign a consent form and will give you a copy to keep. However, you would still be free to withdraw from the study at any time, without giving a reason and without any negative consequences, by letting the research team know. If you are a student at the University of Nottingham, there would be no disadvantages to your study or to you personally if you decide not to take part in this study, or if you decide to withdraw at any point.

4. What will happen to me if I take part?

A trained researcher will contact you to go over the information sheet, explain the procedures, and go through a pre-screening with you to check if it is safe for you to participate. If you agree to take part in the study, you will be asked to attend two visits at the Queen's Medical Centre, one at the start and one at the end of the study period. During these visits, we will collect blood and faecal samples. We will ask you to complete a series of questionnaires and you will also undergo physical measurements, which will include waist, hip, blood pressure, hand grip strength and physical measurements to assess pain.

We will ask you to join one of these four groups as mentioned below. We will provide you with the allocated study group or access to the exercise scheme on the day of your first visit. You will not know if you are taking a supplement or placebo.

5. What do I have to do?

Please contact us at the email address below if you are willing to participate in the study. You will be required to visit the Queens Medical Centre in Nottingham on two occasions, first at the start of the study and second at the end of the study, which will be after 6 weeks. Both your visits will last approximately 30-45 minutes. The dates of your appointments will be arranged with you at the start of the study. We will send follow up reminders as each visit date approaches.

Before your 1st visit

All we ask is that you attend the unit having fasted overnight. This means no food or drink, except water, from midnight the night before your visit. You will need to have collected a faecal sample using the sample collection kit provided to you prior to both your visits. You will also be required to complete a series of questionnaires prior to your visits (Microsoft forms). This will take about 30 minutes and may require you to find additional information, e.g. what medications you are currently using, and any you have taken in the past, as well as how long have you used them for.

Baseline visit (1st visit)

1. Blood sample collection: Fasting blood samples will be collected by a trained member of staff as soon as you arrive at the clinical research unit.
2. Basic physical measurements: Hip/waist ratios and blood pressure measurements will be taken. We will also measure hand grip strength using a hand-held dynamometer.
3. Pain outcome measurements: This will include standard tests to measure pain sensitivity and threshold.
4. Stool sample collection: You will be asked to provide a stool sample (collected by you at home either the night before or on the day of your visit)
5. Questionnaires: You will be requested to fill in a set of online questionnaires relating to your diet and lifestyle. The set of questionnaires will be sent to prior to first visit. A simple calendar with dates of your intervention period may also be provided to you to record whether you take the supplements or do the exercise routine as instructed and to record any side effects.

Dietary supplements

1. After your first visit, you will be asked to take a dietary fibre supplement or a dummy (placebo) for a total period of 6 weeks. The supplement/ dummy will be provided to you for the duration of the 6 weeks. You will be required to take 20g of the supplement on a daily basis for 6 weeks. The fibre supplement can be added to your daily diet by adding to water, juice, smoothies, yogurts etc.

2. You will also be contacted via email regularly to ensure you have been taking the recommended daily intake of either the fibre supplements or placebo correctly. To record compliance on a daily basis, you may be asked to tick under each day to confirm the recommended dosage has been taken and also record any side effects.

Exercise program

1. After your first visit you will be asked to follow an exercise routine for a total period of 6 weeks. These exercises can be accessed online using Joint Academy- An app-based exercises platform (Joint Academy®). The programme consists of a mixture of open and close chain exercises, a combination of concentric, eccentric and

focusing on the global strength of legs including the muscles around the hips and knee joints as well as balance enhancement exercises. The app will be free to use for upto 12 weeks from the start of the programme. The app will charge a fee if you wish to continue using the app post the 12-week period.
2. You will also be contacted via the app to ensure you have been following the exercise program correctly.

Diet and Exercise program

1. After your first visit you will be asked to take a dietary fibre supplement and follow an exercise routine for a total period of 6 weeks. Progress will be monitored by regular contact via email or the app to ensure the programme is running smoothly.

Follow up (2nd visit)

At the end of the 6-week dietary supplement and/or exercise period, you will be booked in for your second and final visit to the study facility. Similar to your first visit, you will be instructed to bring with you a faecal sample and to complete the last set of online questionnaires either the day before or on the day of your visit. Fasting blood samples will be collected along with anthropometric measurements.

6. What is being tested?

In this study, we are testing the effect of the dietary fibre and/ or exercise, in improving metabolic health by not only modulating the composition and function of the bacteria residing in your gut but also altering the levels of specific molecules called endocannabinoids have shown to reduce pain. Dietary fibres used in this study are soluble complex carbohydrates which are naturally found in fruits or plants like chicory root, apples, leeks and a variety of other fruit and vegetables. Further, short exercise routines can improve pain levels by releasing endocannabinoids, which are cannabis like substances produced by our bodies and have anti-inflammatory effects.

If you agree to participate, you will be given dietary fibre supplements, an exercise routine or a placebo. The study group based on the intervention will be provided to you by the research team.

7. Are there any risks in taking part?

You should not experience any side effects whilst taking part in this study.
You may feel slight discomfort when the blood sample is being taken, but this should subside soon afterwards. With an increased intake of fibre, some people may become constipated or experience bloating but this can be avoided by ensuring that you drink enough water throughout the day.

The exercise routine has been well received in previous studies and like any other online exercise app, it poses minimal risks.

None of the other tests performed such as blood pressure measurements, waist to hip ratio measurements will cause you any harm.

If you face any adverse side effects during the course of the study please inform the study team immediately on the contact numbers provided below.

8. Are there any benefits in taking part?

The results from your participation along with others in this study might help our understanding of how diet and exercise may help reduce knee pain in those suffering from OA.

9. Will my time be reimbursed?

You will be reimbursed for your travel expenses.

10. What will happen to any samples I give?

All samples provided will be safely stored in appropriate facilities within the University of Nottingham. We would also like to seek your consent so that any remaining samples may be stored and used in possible future research – this is optional (please indicate you agree to this on the consent form). The samples will be stored with a code unique to you and securely at the University of Nottingham under the University's Human Tissue Research Licence (no 12265).

Researchers other than current team, who ran the first study, including researchers working outside the University, may carry some of these future studies out. Any samples or data used will be anonymised, and you will not be identified in anyway. If you do not agree to this any remaining samples will be disposed of in accordance with the Human Tissue Authority's codes of practice.

11. What happens to the data provided?

We will follow ethical and legal practice, and all personal information about you will be handled in confidence.

If you join the study, some parts of the data collected for the study will be looked at by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant.

All information which is collected about you during the course of the research will be kept strictly confidential, stored in a secure and locked office, and on a password protected database. Any information about you which leaves the institution will have your name and address removed (anonymised) and a unique code will be used so that you cannot be recognised.

Your personal data (address, telephone number) will be kept for five years after the end of the study, so that we can contact you about the findings of the study and possible follow-up studies (unless you advise us that you do not wish to be contacted). All other data (research data) will be anonymous and will be kept securely for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team will have access to your personal data.

We would also like to seek your consent so that the research data you have given may be stored and used in possible future research during and after 7 years– this is optional (please indicate you agree to this on the consent form).

We would like your permission to use anonymised data in future studies, and to share our research data (e.g. in online databases) with other researchers in other Universities and organisations both inside and outside the European Union. This would be used for research in health and social care. Sharing research data is important to allow peer scrutiny, re-use (and therefore avoiding duplication of research) and to understand the bigger picture in particular areas of research. All personal information that could identify you will be removed or changed before information is shared with other researchers or results are made public.

12. What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time without giving a reason. If you withdraw we will no longer collect any information about you or from you but we will keep the information that has already been collected and stored as we are not allowed to tamper with study records. This information along with others in the study may still be used in the final study analyses.

13. Who will know that I am taking part in this research?

Data will be used for research purposes only and in accordance with the General Data Protection Regulations. Any electronic data will be anonymised with a code as detailed above. Electronic storage devices will be encrypted while transferring and saving of all sensitive data generated in the course of the research. All such data are kept on password-protected databases sitting on a restricted access computer system and any paper information (such as your consent form, contact details and any research questionnaires) would be stored safely in lockable cabinets in a swipe-card secured building and would only be accessed by the research team.

Under UK Data Protection laws the University is the Data Controller (legally responsible for the data security) and the Chief Investigator of this study (named above) is the Data Custodian (manages access to the data).

You can find out more about how we use your personal information and to read our privacy notice at:

https://www.nottingham.ac.uk/utilities/privacy.aspx/

Designated individuals of the University of Nottingham may be given access to data for monitoring and/or audit of the study to ensure we are complying with guidelines.

With your consent, we will keep your personal information on a secure database in order to contact you for future studies, as detailed above.

Anything you say during a visit will be kept confidential, unless you reveal something of concern that may put yourself or anyone else at risk. It will then be necessary to report to the appropriate persons.

14. What will happen to the results of the research?

The results of this study may be published in scientific literature and may also be presented at scientific meetings.
All such data will be presented anonymously, so that none of the participants can be identified. The results of this study may also be written up as part of an educational qualification, e.g. a PhD or Masters Dissertation.
We will also provide you with a summary of the results if you wish.

15. Involvement of the General Practitioner/Family doctor (GP)

All the procedures outlined above are being carried out for research purposes only, and your GP will not be informed of your participation in the study. However, if any concerns are raised, we will advise the participants to see their GP.

16. Who has reviewed this study?

All research in the University of Nottingham is looked at by an independent group of people, called a Research Ethics Committee who protect your interests. This study has been reviewed and given favourable opinion by the Faculty of Medicine & Health Sciences (FMHS) Research Ethics Committee.

17. Who is organising and funding the research?

This research is being organised by Prof Ana M. Valdes at the University of Nottingham and is being funded by the MRC (Medical Research Council).

18. What if there is a problem?

If you have a concern about any aspect of this study, you should contact the Chief investigator via e-mail: ana.valdes@nottingham.ac.uk. The full contact details of the research team are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you should then contact the FMHS Research Ethics Committee Administrator, Faculty Hub, Medicine and Health Sciences, E41, E Floor, Medical School, Queen's Medical Centre Campus, Nottingham University Hospitals, Nottingham, NG7 2UH or via E-mail: FMHS-ResearchEthics@nottingham.ac.uk.

19. Contact Details

If you would like to discuss the research with someone beforehand (or if you have questions afterwards), please contact:

Prof Ana M. Valdes
School of Medicine
Email: ana.valdes@nottingham.ac.uk

Thank you for taking the time to read this information sheet.