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Effect of dietary fibre and exercise on knee pain

Submission date
19/08/2025

Recruitment status
No longer recruiting

Registration date
20/08/2025

Overall study status
Completed

Last Edited
19/08/2025

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
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 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.

Who can participate?
You have been invited to take part in this research because you experience pain in or around a knee on most days for more than 3 months and a doctor has told you have knee osteoarthritis, 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) • 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. We aim to invite 120 participants like you to take part.

What does the study involve?
If you take part, you'll be asked to attend two study visits (one at the beginning and one at the end of the 6-week period) at the Clinical Sciences Building, City Hospital, Nottingham. At these visits, we'll collect blood and stool samples, take some physical measurements, and ask you to complete questionnaires. You'll then be randomly assigned to one of four groups: fibre

supplement, exercise programme, both fibre and exercise, or placebo. The aim is to see how these different approaches affect knee pain and health markers.

What are the possible benefits and risks of participating?
Taking part may not directly help your knee pain, but your involvement could improve understanding of how diet and exercise affect pain in people with osteoarthritis. This may help develop better treatments in the future. The risks are small: you may feel mild discomfort when blood is taken, and fibre can sometimes cause bloating or constipation (which usually settles if you drink enough water). The exercise programme is safe and commonly used but, like any exercise, may cause some muscle soreness.

Where is the study run from?
The study is being run from the University of Nottingham, with participant visits held at the Clinical Sciences Building, City Hospital, Nottingham (UK).

When is the study starting and how long is it expected to run for?
April 2022 to February 2025

Who is funding the study?
UK Medical Research Council (MRC)

Who is the main contact?
Professor Ana M. Valdes, ana.valdes@nottingham.ac.uk

Contact information

Type(s)
Public, Scientific

Contact name
Dr Afroditi Kouraki

Contact details
University of Nottingham
Academic Rheumatology,
Clinical Sciences Building
Hucknall Road
Nottingham
United Kingdom
NG5 1PB
+44 115 8231676
afroditi.kouraki1@nottingham.ac.uk

Type(s)
Principal Investigator

Contact name
Prof Ana Valdes

Contact details

University of Nottingham
Academic Rheumatology,
Clinical Sciences Building
Hucknall Road
Nottingham
United Kingdom
NG5 1PB
+44 115 8231676
ana.valdes@nottingham.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT05670314

Secondary identifying numbers
473-0322

Study information

Scientific Title
Molecular signatures of endocannabinoid induced pain relief in humans: lifestyle interventions, systemic and localised changes. lIfestyle iNterventionS for PaIn ReliEf (INSPIRE)

Acronym
INSPIRE

Study objectives
1. To assess the magnitude of the effect of prebiotic supplementation (inulin) side by side with physiotherapy exercise versus placebo (maltodextrin) on knee pain
2. To assess the combined effects of exercise and prebiotic inulin supplementation (synergistic effect) over six weeks
3. To elucidate the molecular pathways involved in pain relief induced by exercise and gut microbiome modulation in individuals with painful knee osteoarthritis

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 29/04/2022, University of Nottingham Faculty of Medicine and Health Sciences (Faculty Hub, Room E41, E Floor, Medical School, Queen's Medical Campus, Nottingham University Hospitals, Nottingham, NG7 2UH, United Kingdom; -; FMHS-ResearchEthics@nottingham.ac.uk), ref: 473-0322

Study design
2x2 factorial intervention trial

Primary study design
Interventional

Secondary study design
2x2 factorial randomized controlled trial

Study setting(s)
Community

Study type(s)
Efficacy

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Knee Osteoarthritis (OA)

Interventions
Participants identified as having knee arthritis are 1:1:1:1 randomised to web-based Physiotherapy-supported Exercise (PSE), inulin, PSE and inulin or placebo and usual care. Researchers assessing outcomes were blinded to the interventions and participants were blinded to the dietary intervention. However, blinding for the PSE intervention was not feasible since participants were informed if they were assigned to one of the PSE groups or not.

PSE intervention: the study uses a digitally delivered physiotherapy platform known as Joint Academy (JA) (https://www.jointacademy.com/gb/en/) as a previous RCT from our group demonstrated promising results with this platform. The JA company has granted permission for this study to be carried out using their platform. The standardised PSE intervention includes tailored intensity levels and combines concentric and eccentric exercises with open- and closed-chain movements to strengthen the legs, including the hip and knee muscles, and improve balance. The programme also includes educational sessions on OA fundamentals, treatment, symptom self-management, and healthy lifestyle benefits. Participants receive an email with a link to the online platform and log-in instructions. The PSE intervention, lasting 6 weeks, begins after log-in and a kick-off call with a personal physiotherapist with participants expected to engage daily

Prebiotic intervention: Inulin fibre (20g) in powder form (commonly found in root vegetables such chicory) is randomly allocated to eligible participants. They are instructed to mix it into breakfast cereal, smoothies, yogurt, or a drink of their choice.

Placebo Group: Participants in the control placebo group continue with their usual self-management (community setting) and receive maltodextrin (10g) daily in powder form (commonly found in corn, potatoes and rice), with similar consumption instructions as inulin.

At the first visit, both groups receive pre-measured weekly pots containing either supplement or placebo, along with scoops. Participants are instructed to take 2 scoops totalling 10g/day of

maltodextrin or 3 scoops totalling to 20g/day of inulin daily for 6 weeks, depending on their assigned group.

Intervention Type
Mixed

Primary outcome measure
Pain measured using the Numerical Rating Scale (NRS) at baseline (1st visit) and at 6 weeks (2nd visit)

Secondary outcome measures
1. Functional capacity is measured using the 30-second Sit-to-Stand Test (30CST) at baseline and 6 weeks
2. Functional mobility is measured using the Timed Up and Go Test (TUG), averaged over three trials, at baseline and 6 weeks
3. Muscle strength is measured using handgrip dynamometry on the dominant hand, averaged over three trials, at baseline and 6 weeks
4. Pain sensitisation is measured using Temporal Summation (TS) via quantitative sensory testing (QST) at baseline and 6 weeks
5. Pain sensitisation is measured using Pressure Pain Detection Threshold (PPT) via quantitative sensory testing (QST) at baseline and 6 weeks
6. Inflammatory protein levels are measured using Olink cytokine assay panels for IL-6, TNF, and IFN-γ at baseline and 6 weeks
7. Gut microbiome diversity is measured using the Shannon Diversity Index derived from shotgun metagenomic sequencing of stool samples at baseline and 6 weeks
8. Short-chain fatty acid levels are measured using mass spectrometry for butyric acid and acetic acid in serum at baseline and 6 weeks
9. Serum endocannabinoid levels are measured using mass spectrometry for Anandamide (AEA) and 2-arachidonoylglycerol (2-AG) at baseline and 6 weeks
10. Pain-related gene expression is measured using RNA sequencing of whole blood samples at baseline and 6 weeks

Overall study start date
27/04/2022

Completion date
25/02/2025

Eligibility

Key inclusion criteria
1. On the day of the first visit they report having any pain in or around a knee on most days for more than 3 months with a self-reported diagnosis of OA
2. Willing and able to give informed consent for participation in the study
3. Aged>18 years
4. Body mass index (BMI) between 18.5 and 39.9 kg/m²

Participant type(s)
Patient

Age group

Adult

Lower age limit
19 Years

Upper age limit
100 Years

Sex
Both

Target number of participants
120

Total final enrolment
171

Key exclusion criteria
1. Psychosocial or gastrointestinal disorders (e.g. malabsorptive conditions such as IBS/IBD, coeliac)
2. Taking immunosuppressants, anticoagulants, amiodarone and/or perhexiline
3. Following or anticipated to commence a specialised commercially available weight loss diet and/or programme
4. Pregnant or breastfeeding
5. History or current psychiatric illness (including clinical depression)
6. Diagnosed with a neurological condition (e.g. epilepsy)
7. Already undergone a total knee replacement
8. Severe hip OA (were on a waiting list for a total hip arthroplasty)
9. Diagnosed with inflammatory arthropathies
10. Diagnosed with non-OA cause of knee pain (e.g. rheumatoid arthritis)
11. Diagnosed with neuropathy or diabetes mellitus
12. Taken part in a research study in the last 3 months involving invasive procedures or an inconvenience allowance

Date of first enrolment
05/07/2022

Date of final enrolment
25/02/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

Nottingham University Hospitals NHS Trust - City Campus
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Sponsor information

Organisation
University of Nottingham

Sponsor details
Research and Innovation
University of Nottingham
E-Floor, Yang Fujia Building
Wollaton Road
Nottingham
England
United Kingdom
NG8 1BB
-
sponsor@nottingham.ac.uk

Sponsor type
University/education

Website
http://www.nottingham.ac.uk/

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal.

Intention to publish date
25/02/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Afroditi Kouraki, afroditi.kouraki1@nottingham.ac.uk

IPD sharing plan summary
Available on request