ISRCTN55059760 https://doi.org/10.1186/ISRCTN55059760

The IN RESPOND study

Submission date
01/04/2015

Recruitment status
No longer recruiting

Registration date
02/04/2015

Overall study status
Completed

Last Edited
17/05/2023

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Osteoarthritis (OA) is the most common disease affecting the joint. It can develop in any joint but it most often affects those that carry weight, such as the hips, spine and knees. It is caused by damage in and around the joint that can't be fully repaired. Some of the cartilage (the protective layer covering the bones at the joint that ensures the joint moves smoothly) can become damaged or lost, leading to swelling (inflammation), pain and stiffness. Typical symptoms also include a deep, aching pain which can spread (radiate)from the affected joint, loss in the range of movement possible in the joint and the development of hard, bony, growths. Sufferers may also feel like their joints are crunching or grinding when they use them and find that they give way when weight is put on them. It is a long-term condition that can get worse over time. Treatment options include regular (sometimes prescribed) exercise, losing excess weight, drug treatments (such as painkillers and anti-inflammatories) and surgery. Knee osteoarthritis is the most common cause of knee pain and there are few treatments available that really work. For the most common type of knee osteoarthritis, the type affecting the inner (medial) side of the knee, special wedge insoles that fit inside the shoe have been recommended because they reduce the load (a force that is put on a weight bearing joint during activity) across the medial side of the knee. However, previous studies have shown that, on average, they don't reduce knee pain. The studies of loading have found that the wedge's effect on medial load is extremely inconsistent and, for many people, the wedge can increase or worsen load. Furthermore, osteoarthritis in the knee cap may get worse if medial load is reduced. Bone marrow lesions (or BMLs) are bruises to the bone and are common in knees with OA. These lesions occur in areas where there is increased stress on bone due to misalignment of the knee. BMLs are strongly associated with the progression of osteoarthritis and pain. Targeting BMLs for treatment means attempting to correct the misalignment therefore reducing stress on the bone. An approach to reduce knee loading with insoles should therefore, also reduce the number of these medial bone bruises. Here, we want to investigate the effect of wedge insoles on medial knee osteoarthritis. We will compare wedge insoles with a placebo, a neutral shoe insole, evaluating pain and also examining whether the reduction in medial load leads to a reduction in bone bruising that can be seen and measured on an MRI scan.

Who can participate?
People aged 40-85 with knee OA

What does the study involve?
Patients will be randomised into two groups:
Treatment group A
Patients will be required to attend 4 appointments over a period of 24 weeks and are asked to test two different shoe insoles as treatments for their knee osteoarthritis. Patients will wear the first insole for 8 weeks followed by a gap of 8 weeks where no insoles are worn. Finally patients will be asked to wear the second insole for another 8 weeks. Walking tests and MRI scans will also be carried out at the study visits.
Treatment group B
Patients will be required to wear one insole for 8 weeks only and undertake walking tests at the study visits.

What are the possible benefits and risks of participating?
Benefits: Patients may see a reduction in knee pain by wearing the interventional wedge, they will recieve a pair of insoles at the end of the study and they will be reimbursed for their time at each of the 4 study visits.
Risks: Some participant may be required to have a screening x-ray to assess eligibility. The amount of radiation for a knee X-ray is very small, so the risk of harm is negligible.
As part of the research, patients will be involved in investigations such as gait analysis and MRI scans, which are not part of routine care. These are safe procedures. Although there will be a time commitment required from the patients there are no expected risks by taking part in the study .

Where is the study run from?
University of Manchester (UK)

When is the study starting and how long is it expected to run for?
April 2015 to January 2017

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Ms Suzanne Carter

Contact information

Type(s)
Scientific

Contact name
Ms Suzanne Carter

Contact details
University of Manchester
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M13 9PL

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
18701

Study information

Scientific Title
The effect of lateral wedge INsoles on pain in individuals with medial knee osteoarthritis who biomechanically RESPOND

Acronym
IN RESPOND

Study objectives
To determine whether, when treated with a lateral wedge insole, individuals with painful medial knee osteoarthritis experience a reduction in medial biomechanical loading, which reduces knee pain compared with treatment with a neutral insole

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West – Preston, 09/03/2015, 15/NW/0158

Study design
Randomised; Interventional; Design type: Not specified, Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied

Topic: Primary Care, Musculoskeletal disorders; Subtopic: Musculoskeletal (all Subtopics), Musculoskeletal disorders; Disease: Musculoskeletal, All Diseases

Interventions
1. Lateral Wedge: Participants will be required to wear a lateral wedge in their shoes for a period of 8 weeks
2. Placebo: Participants will be asked to wear a neutral insole for a period of 8 weeks
Follow Up Length: 6 month(s); Study Entry : Registration and One or More Randomisations

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
-

Primary outcome measure
Knee pain using Numerical Rating Scale – Last Week (Patient perceived Pain/Discomfort overall in the last week) question.

Secondary outcome measures
1. Structural end point: volume of BMLs in the medial TF compartment on MRIs
2. Other measures of knee pain: pain on nominated activity using NRSNA : Numerical Rating Scale - Nominated Activity (patient nominated aggravating activity causing most pain) and KOOS pain and other subscales; physical activity over 1 week (based on activity monitoring); rescue analgesia
3. Physical function: KOOS subscales and SF12
4. Structural outcomes: BMLs in the whole knee

Overall study start date
01/12/2014

Completion date
18/07/2017

Eligibility

Key inclusion criteria
1. Age 40-85
2. Global pain based on NRS ≥ 4
3. Kellgren and Lawrence grades 2 – 4 on AP or PA view xray
(weight bearing, if possible) within the last 2 years of screening. Also, they need to have definite medial narrowing and NOT definite lateral narrowing and evidence (osteophyte +/or definite sclerosis) of OA. And patellofemoral osteoarthritis on xray must be less severe than medial OA and cannot be KL3 or higher in patellofemoral joint
4. On clinical examination, medial joint line tenderness and without significant tenderness at the medial or lateral patellar facets, nor pain on patellar compression tests (which would indicate predominantly PF joint disease and are exclusion findings)

5. Stable medication regimen for 3 months (e.g. if the patients are using NSAIDs there should be no change)
6. Willing to wear insoles for at least 4 hours per day

Participant type(s)
Patient

Age group
Adult

Lower age limit
40 Years

Upper age limit
85 Years

Sex
Both

Target number of participants
Planned Sample Size: 86; UK Sample Size: 86; Description: see recruitment notes

Total final enrolment
83

Key exclusion criteria
1. Pain is more localised to the patellofemoral joint on examination than medial joint line
2. A history of high tibial osteotomy or other realignment surgery or total knee replacement on the affected side.
3. Knee Arthroscopy within at least 6 months
4. Intraarticular injection or visco supplementation injection into the treatment knee in the last 3 months.
5. Inflammatory arthritis including Rheumatoid Arthritis, psoriatic arthritis
6. Diabetic Neuropathic pain, fibromyalgia
7. Foot and ankle problems that will contraindicate the use of the footwear load modifying interventions.
8. Severe coexisting medical morbidities.
9. Unable to walk unaided and have to rely on a stick, crutch or frame
10. BMI greater than 35 (since the gait laboratory cannot perform accurate measurements and the MRI knee coil may not fit these patients)
11. Currently use, or have used, orthoses of any description prescribed by a Podiatrist or Orthotist within the last 2 months.
12. Unable to take in, understand or retain the information provided regarding the study procedures.
13. Inability to walk for 100 metres without stopping, as they may be unable to complete the full testing protocol.
14. Contraindication to MRI such as, but not limited to:Metal implants which prohibit safe use of MRI scan including cochlear implants / metal objects in the body including, knee prosthesis , cardiac or neural pacemakers,

hydrocephalus shunts, intrauterine device or coil, claustrophobia, inability to lie in the MRI for up to 1 hour.
15. Planned surgery or knee replacement in next 6 months

Date of first enrolment
20/04/2015

Date of final enrolment
13/01/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Manchester
Oxford Road
Manchester
United Kingdom
M13 9PL

Study participating centre
The Wellcome Trust Clinical Research Facility
Grafton Street
Manchester
United Kingdom
M13 9WL

Sponsor information

Organisation
University of Manchester

Sponsor details
Oxford Road
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Sponsor type
University/education

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
We intend to publish the results of the study via peer reviewed scientific journals, internals reports, and conference presentations. We estimate publications will take place for about a year after the trial end (March 2017), however we aim to present abstracts/posts at OARSI April 2017. These will further be developed into Journal publications.

Intention to publish date
18/07/2018

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from [matthew.parkes@manchester.ac.uk]. Please note this will only happen after publication of papers.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2019		Yes	No
Other publications	Secondary analysis	18/04/2020	17/05/2023	Yes	No
HRA research summary			28/06/2023	No	No