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A clinical trial designed to assess the most effective pain-relieving medicines for low back pain with or without leg pain or sciatica

Submission date
08/08/2024

Recruitment status
Recruiting

Registration date
18/10/2024

Overall study status
Ongoing

Last Edited
29/05/2025

Condition category
Musculoskeletal Diseases

[X] 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:
Low back pain, with or without leg pain or sciatica is very common and affects many adults. Unfortunately, it can be very painful and disabling and many of those that suffer take a variety of different pain killing medications to help them cope. It is not clear which medications, either on their own, or in combination with others, gives the best relief from pain. This trial is designed to answer that question.
In order to answer the question of what is the most effective pain relief for low back pain with or without leg pain or sciatica, we have designed a clinical trial to take place in GP surgeries in the UK using analgesic ladders. Analgesic ladders are a combination of analgesic (pain-relieving) medication taken in a step wise fashion, adding to what has already been prescribed in response to how much pain the participant is in. In the MEDAL trial there are six pre-defined analgesic ladders with six steps (i.e. medications) in each ladder. All medications used in the MEDAL trial are already prescribed for low back pain with or without leg pain or sciatica. However, this trial is designed to provide a set way to approach treating this condition which can be applied nationally and provide the most effective pain relief.

Who can participate?
In the MEDAL trial we aim to randomise 3960 adults (18 years or over) with acute low back pain with or without leg pain or sciatica.

What does the study involve?
A participant in the MEDAL trial would start at the bottom step of the ladder (step 1). If their pain is not improved after 3 whole days of taking the medication, the participant can then take the next step of the ladder until they reach step 4. This process continues until the participant feels ‘quite a lot better’ as determined by questions a participant completes daily, up to 8 weeks post randomisation. If the participant is still in pain after 8 weeks, they will return back to standard of care with their GP. We will assess the success of the ladders by asking questions about work, sleep and daily life during and after the medication finishes.

What are the possible benefits and risks of participating?
All medications used in the MEDAL trial are already part of standard of care for the treatment of lower back pain with or without leg pain or sciatica as part of the national formulary and have well characterised safety profiles. As a result, the MEDAL trial is considered a low risk trial.

All participants will be provided a detailed analgesic ladder information leaflet which will be provided by paper and available via the MEDAL trial website. Participants will be able to escalate their medication if their pain is not resolved or de-escalate their medication if their pain has resolved or improved. Participants will be provided with guides on how to do this to help them manage their medication and will be advised to see their GP for additional support if required.
A possible disadvantage of taking part is that the medication ladder the participant is allocated to does not fully address their pain. However, this would be a risk with any medication given by their GP. People with low back pain, with or without leg pain or sciatica, always have a chance of not getting better on medication.
Some people may experience side effects of the medications prescribed. Some people may require further help and treatment for their back pain, which could include the possibility of surgery. The risk of this happening is the same as if their GP were to prescribe pain medication in normal care, outside of the MEDAL trial.
There is not enough evidence for the medications used in this trial to be deemed safe during pregnancy. Therefore, some people will not be able to take part in the trial if they are female and currently pregnant, are planning to become pregnant or are unable to use appropriate contraception whilst in the MEDAL trial.

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

When is the study starting and how long is it expected to run for?
August 2024 to March 2028

Who is funding the study?
Health Technology Assessment programme of the National Institute for Health and Care Research (NIHR)

Who is the main contact?
Birmingham Clinical Trials Unit, medal@trials.bham.ac.uk

Contact information

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1007662

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
ERN_23-1051, CTA 21761/0393/001-0001

Study information

Scientific Title

The pharmacological management of back pain and sciatica in adults: a pragmatic, randomised controlled adaptive platform trial of analgesic ladders

Acronym
MEDAL

Study objectives
Primary objective: To assess which ladder of pain medicine is the most effective in the management and resolution of pain for those with acute low back pain with or without leg pain or sciatica.

Secondary objectives: To assess which ladder of pain medicine is most effective in improving, function, enabling better sleep, facilitating a quicker return to work and/or regular activities, quickly relieves symptoms, and reducing feelings of anxiety and depression.
Also, to compare the cost effectiveness of using different levels of pain relief steps.
This study aims to also understand the opinions and personal encounters of individuals with lower back pain regarding this approach.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/09/2024, South Central - Berkshire Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8233; berkshire.rec@hra.nhs.uk), ref: 24/SC/0280

Study design
Interventional randomized parallel group controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Efficacy

Participant information sheet

Health condition(s) or problem(s) studied
Low back pain with or without leg pain or sciatica

Interventions
MEDAL will be comparing six different analgesic ladders of medication in the management of three different types of LBP and leg pain. Participants will be randomised by their GP to one of six analgesic ladders.
The trial intervention and dosing schedule is based on escalating analgesic ladders over an 8-

week time period from randomisation. All medications used in the analgesic ladders in MEDAL are already part of standard of care.
All randomised participants will start on the bottom step (step 1) of the analgesic ladder and can be escalated up the ladder (to step 4) if symptom improvement is inadequate, on an individual participant basis. Each medication should be taken for at least 3 whole days before contacting GP practice to issue the next step of medication.
At any step of the medication ladder, pain is controlled for 5 days in a row, participants will not need to go up any more steps of the ladder.

Analgesic Ladders:
Ladder A
Step 1: Naproxen 500mg twice daily (with food)
Step 2: Add Co-codamol 30/500 2 tablets 4 times daily
Step 3: Add Amitriptyline 10mg at night
Step 4: Stop Amitriptyline 10mg and start Amitriptyline 25mg at night
Ladder B
Step 1: Naproxen 500mg twice daily (with food)
Step 2: Add Co-codamol 30/500 2 tablets 4 times daily
Step 3: Stop Co-codamol 30/500 and add Tramadol 100mg 4 times daily
Step 4: Add Gabapentin 300mg Day 1 once daily, Day 2 twice daily, Day 3 3 times daily
Ladder C
Step 1: Naproxen 250mg twice daily (with food)
Step 2: Stop Naproxen 250mg and add Naproxen 500mg twice daily (with food)
Step 3: Add Amitriptyline 10mg at night
Step 4: Stop Amitriptyline 10mg add Amitriptyline 25mg at night
Ladder D
Step 1: Co-codamol 30/500 2 tablets 4 times daily
Step 2: Add Naproxen 500mg twice daily (with food)
Step 3: Add Amitriptyline 10mg at night
Step 4: Stop Amitriptyline 10mg Add Gabapentin 300mg Day 1 once daily, Day 2 twice daily, Day 3 3 times daily
Ladder E
Step 1: Co-codamol 30/500 2 tablets 4 times daily
Step 2: Stop Co-codamol 30/500 Add Tramadol 100mg 4 times daily
Step 3: Add Amitriptyline 10mg at night
Step 4: Stop Amitriptyline 10mg Add Pregabalin 50mg Three times daily
Ladder F
Step 1: Co-codamol 15/500 2 tablets 4 times daily
Step 2: Stop Co-codamol 15/500 add Co-codamol 30/500 2 tablets 4 times daily
Step 3: Add Amitriptyline 10mg at night
Step 4: Stop Amitriptyline 10mg Add Amitriptyline 25mg at night

If pain decreases, (controlled for 5 days in a row) medication can be reduced and then stopped in conjunction with the de-escalation guide provided to participants and if necessary, their GP.

Intervention Type
Drug

Pharmaceutical study type(s)
Dose response, Pharmacoeconomic, Therapy

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Amitriptyline, Co-Codamol [Codeine Phosphate, Paracetamol], Naproxen, Gabapentin, Pregabalin, Tramadol

Primary outcome measure
The primary end point will have been reached when, using the Patient Global Impression of Change (PGIC) pain scale, the self-assessment scores reach 4 points or more (going from 'no improvement' to at least 'quite a lot better') for 5 days in a row. Daily measurements will be collected until 8 weeks after randomisation. The PGIC scale ranges from -5 to +5, with 0 indicating no change. Higher positive numbers show improvement, while negative numbers indicate worsening.

Secondary outcome measures
Outcomes collected daily for 8 weeks are:
1.The intensity of pain using the Numerical Rating Scale (NRS) of pain. Score of 0 to 10 (10 is the worst pain you can imagine)
2.The number and type of any serious side effects
Outcomes measured at 4, 8 weeks and 26 weeks after randomisation are:
3. Patient self-assessment of resolution of symptoms
4.The level of back-related function and disability of daily activities using the Oswestry Disability Index (ODI).
5. If their pain has disturbed their sleep in the past week (Yes/No).
6. Percent overall work impairment using the Work Productivity and Activity Impairment (WPAI) scale.
7. Mental health using the Depression, Anxiety and Positive Outlook Scale (DAPOS).
8. Health-related quality of life using the EQ-5D-5L.
9. Relapse of pain. Determined by asking if pain has relapsed after the end of the medication.
10. Admission to hospital related to the back pain/leg pain/sciatica or the medications given.
We will also record and report descriptively, but without making formal comparisons:
11. The number and type of side effects / adverse events
12. The type, and quantity, of other treatments undertaken on top of the medication in the trial (physical, topical, other medications/analgesics etc.)

Overall study start date
05/08/2024

Completion date
30/03/2028

Eligibility

Key inclusion criteria
1. Aged 18 years or over
2. A clinical diagnosis of acute low back pain +/- low back related leg pain, or sciatica of no more than 3 months duration
N.B. This includes individuals with an acute flare up of back and/or leg pain on the background of low-grade symptoms – numerical rating scale (NRS) for pain of ≤ 3 - and in the preceding one

month have not had severe pain requiring substantial use of analgesia.
3. Must understand spoken and written English
N.B. If unable to write in English for themselves, they must have someone in their home who can understand written English to help with consent and data capture.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
3,960

Key exclusion criteria
1. More than 3 months of pain symptoms in this episode of pain
2. Other previously diagnosed spinal pathology (e.g., scoliosis, kyphosis, spondylolisthesis, spinal stenosis, systemic inflammatory disease)
3. Inability to take any of the medications to be used in the study for any reason (specified co-morbidities, drug interactions, known allergies)
4. Neurological deficit requiring an urgent surgical assessment (e.g., cauda equina syndrome or 'foot drop')
5. Clinical suspicion (red flags) or known diagnosis of spinal malignancy, infection, or fracture
6. History of drug misuse
7. Currently taking regular analgesia (not including paracetamol and ibuprofen that could be bought over the counter) that has been prescribed by a health care professional
8. Already enrolled in another clinical trial
9. Onset of pain following significant trauma, such as a road traffic collision
10. Ongoing litigation for spinal or musculoskeletal pain
11. Currently pregnant or intending to become pregnant in the next 8 weeks
12. Currently breastfeeding
13. Undergoing active chemotherapy for cancer
14. Listed on a palliative care register at a general practice or hospital

Date of first enrolment
01/05/2025

Date of final enrolment
31/01/2028

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
University of Birmingham

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Sponsor type
University/education

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ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care 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
Peer reviewed scientific journals
Conference presentation
Publication on website
Other publication

Intention to publish date
30/03/2029

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date