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

PARTICIPANT INFORMATION SHEET

Version 3.0, dated 14-Jan-2025

The MEDAL trial team would like to invite you to take part in their research trial. Before you decide, we would like you to understand why the research is being done and what it would involve for you. Please take the opportunity to ask any questions using the contact information at the end of the document.

What is the purpose of this trial?

Low back pain is very common and affects nearly all adults at some point in their lives. Sometimes low back pain can be linked with leg pain, which is sometimes known as sciatica. These can all be very painful and disabling. Many people with these symptoms 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, give the best relief from pain. This trial aims to answer this important question and is the first of its kind. You will be helping the MEDAL team identify the best medications to treat low back pain, which will help tackle one of the biggest health problems in the UK and reduce suffering for people who get low back pain and sciatica in the future.

Why have I been chosen?

We are inviting people aged 18 years and older who currently have low back pain, with or without related leg pain, or sciatica, which they have been experiencing for less than 3 months.

What would taking part involve?

You may have already called your GP practice to book an appointment to discuss your back pain. Your GP might have thought that the MEDAL trial is appropriate for you and sent you a link to this information with access to a summary video. Alternatively, you may have seen a poster advertising this trial and visited our website or been given a paper version of this information sheet.

After reading the patient information sheet and watching the summary video, we would like you to complete a self-assessment questionnaire about your back pain by clicking the link on the website. You will be asked if you consent to completing the questionnaire before starting to answer the questions. The questionnaire should only take a few minutes to complete, and your answers will help us to understand if the MEDAL trial is right for you. If it is, our research nurse will contact you to discuss the trial in more detail, answer any questions that you might have, and if you would like to take part, complete our consent process.

Should you opt in to SMS communication your mobile telephone number and trial number will be shared with a UK-based, GDPR compliant third-party SMS platform to send you text messages for information on the trial and follow ups. Your data will not be used by the third-party for any other purpose.

If you are reading a paper version of this information sheet, please contact our research nurse on this number: 0121 685 4316. The research nurse will go through the self-assessment and eligibility questionnaire with you during that call.

The following lists everything that will happen if you decide to take part in the MEDAL trial.

Self-assessment and Eligibility check: You will complete a self-assessment questionnaire of your pain either online or over the phone with a nurse.

Initial contact: This initial contact may take place on the phone, on a video call or in person at a MEDAL research nurse site and will take roughly 35 minutes. The nurse will check that you are eligible to take part in the study and if relevant may also ask you questions about existing and any potential pregnancy plans. You will have the opportunity to ask for more information about the trial and, if you decide to take part, you will be asked to complete a consent form. We will ask you questions about your medical history, your current health, complete some questionnaires with you, and ask for more details about your pain and how you are managing it.

GP eligibility check: Following the initial contact you will then see your GP at the appointment that you originally booked. Your GP will carry out their routine care, confirm your eligibility to take part in the trial. This could be your regular GP or any other GP within your GP practice. As part of this eligibility check, a pregnancy test may be required, and your GP will also discuss appropriate contraception and further required pregnancy testing whilst taking the medication (even if taking contraception) during MEDAL. This is because some of the medications that you may be prescribed are not recommended during pregnancy. Your GP will discuss this more once you know which treatment plan you have been allocated to. You will be randomly allocated to one of six treatment plans and given a Ladder Information sheet to take away with you. You may also receive a copy by email.

Treatment Plans: Each of these treatment plans is known as a 'ladder' of medication, which starts with a medication that should help your pain. If the starter medication (Step 1) does not help your pain, then there are options within the ladder you are allocated to help improve your pain. This may involve either adding to your medication or trying a different medication within the same ladder. These ladders have been carefully developed with pain and medication experts, and GPs to try and determine which medication ladder is the most effective at controlling your back pain as fast as possible.

The different medication ladders, and how they are prescribed to you, are described below:

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

GP prescriptions: Your GP will issue a prescription for the first step (Step 1) of your medication ladder. If, after a minimum of 3 whole days, you feel that there hasn't been enough improvement in your pain, you will be able to contact your GP practice, via their usual repeat prescription process, to request the next medication on your ladder. You should not need another GP appointment, but if you feel that you do need one, please arrange this as normal. If your pain does not improve or go away, this process of requesting the next medication on your ladder can be repeated until you are on the last step (Step 4) of your medication ladder.

As your pain improves, you will be able to reduce the amount of medication you are taking. How to reduce the medication will vary depending on the medication that you are taking, and we will give you written guidance on this as part of the trial.

If you have reached step 4 of your ladder or the end of the medication period (8 weeks) and the medication is not treating your pain enough, please arrange to see your GP. You are free to see your GP at any point during the trial.

MEDAL MyCap App: All of the questionnaires completed during the trial can be completed using an App called MyCap***,*** which you can download onto your smartphone to access the questionnaires.
During your initial contact, the nurse will discuss the MyCap App and you will receive joining instructions by email after you have been randomised into MEDAL. The App is simple, easy to navigate, and doesn't require any special skills. If you do not have or do not want to use a smartphone, you can complete the questionnaires as an online survey (a link will be sent to you in an email), or we can provide you with paper versions of the questionnaires to complete.

Baseline questionnaire: This is a very short questionnaire that will take no more than 5 minutes to complete. The questions will ask you about your pain and how it affects you.

Daily questionnaire: These questionnaires will be completed daily, and the questions will ask about your pain, any prescribed medication you have taken on that day, along with any other medicines that you have taken and any side effects that you may have experienced. It will also ask about any other ways you have tried to alleviate your pain, such as acupuncture, massage, or physiotherapy and, if you have had any visits to hospital.

You will need to **contact your GP immediately, or attend your nearest accident and emergency department** without delay, if you experience any of the following symptoms, which may indicate that your back problem has become more serious:

- Pain in both legs (bilateral leg pain)
- Numbness around your bottom
- Sudden weakness in one or both legs (with or without foot drop)
- Loss of control of your bladder or bowel or loss of sensation of your bladder

Scheduled follow up: All participants using the MyCap App will be prompted to complete follow up questionnaires at the times below, which refer to the time since joining the MEDAL trial, or paper versions of these questionnaires will be sent to you to complete:

- **4 weeks, 8 weeks and 26 weeks (6 months)** – You will be asked to complete the questionnaire that you completed at your baseline appointment, so that we can see if your pain has improved. At **6 months (26 weeks)**, we will also ask about visits to any NHS service, or any other visits such as private physiotherapy, that you may have had during your time in the MEDAL trial.

If using paper versions of the daily questionnaires, they will need to be returned to the MEDAL trial office every week. We will provide you with freepost envelopes to do this.

If you are unable to complete your follow up questionnaires or return them on time, for any reason at all, a MEDAL trial nurse will contact you to offer help to complete them with you remotely.
Reminders: If you choose to complete questionnaires on the MyCap App or as a survey you will receive email reminders if any questionnaire that is due has not been completed.

Optional interview study: One of our researchers may also contact you to ask if you are still happy to take part in a meeting after 8 weeks from randomisation for you to talk about your experiences in the MEDAL trial. You will only be contacted to arrange a meeting if you initially told us that you are happy to do so. Only a selection of participants who are happy to participate in the qualitative research will be contacted to take part.

Postcards: We will also send you an electronic or paper postcard at 8 weeks of you taking part in the MEDAL trial. We will ask you to write down your thoughts about the trial and send it back to us electronically or in a sealed envelope that we will provide.

Do I have to take part?
No, it is entirely up to you to decide whether or not to take part in the MEDAL Trial. If you decide not to take part, this decision will not affect the care you receive now or in the future.

If you do decide to take part in the MEDAL trial, you will be asked to sign a consent form. Even if you provide consent to take part, you are still free to withdraw at any time afterwards. You can withdraw by contacting the MEDAL trial team by email at Medal@trials.bham.ac.uk. However, we will use any data collected up to the point of withdrawal (even if incomplete), unless a specific request to withdraw the data is made.

How would my treatment group be decided?
The decision regarding which medication ladder you will be allocated to is random and automatically made by a computer programme at Birmingham Clinical Trials Unit at the University of Birmingham.

Like when rolling dice, you will have an equal chance of being allocated to one of the six medication ladders that have been developed by experts. Allocating people in a random way is very important because it is the best way to compare different treatments fairly.

It is important to remember that everyone who takes part in the MEDAL trial, whichever treatment they receive, is providing an equally valuable contribution.

What are the possible benefits of taking part?
The medication you receive within the MEDAL trial should help your back pain to improve. You could also be helping us to improve the treatment and care for other people with low back pain and sciatica.
The findings from this study could provide valuable scientific guidance so that GPs can offer the most effective medication options for those with acute low back pain and sciatica.

What are the possible disadvantages and risks of taking part?
We don't anticipate disadvantages or risks in taking part in this trial as your GP will have ensured that the medications are safe for you to take. All the medications being used in the MEDAL trial are already in common use in the UK and are regularly prescribed to treat low back pain with or without leg pain or sciatica.

A possible disadvantage of taking part is that the medication ladder you are allocated to does not fully address your pain. This would be a risk with any medication you were given by your GP. People with low back pain, with or without leg pain or sciatica, always have a chance of not getting better on medication.

One of the reasons that the MEDAL trial is needed is to find the best medications to treat back pain. 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 your GP were to prescribe you 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. Accordingly, you will not be able to take part in the trial if you are female and currently pregnant, are planning to become pregnant or are unable to use appropriate contraception whilst in the MEDAL trial. You might also need a pregnancy test to take part for safety and regulatory reasons if you are not using contraception. If you inadvertently become pregnant while on treatment within the MEDAL trial, you must notify your trial doctor immediately.

If during your participation in the MEDAL trial, it is identified that you may be at risk of harm to yourself, or others local safeguarding procedures will be followed and confidentiality may be breached in order to inform your healthcare team.

Who is organising and funding this trial?

The MEDAL trial is being led by Professor Adrian Gardner and Dr Toby Helliwell, along with other researchers at the University of Birmingham. They are working in partnership with Birmingham Clinical Trials Unit (BCTU) and with patients, GPs, and other health care professionals across England. The MEDAL trial is funded by the Health Technology Assessment programme (Ref: NIHR151008) of the National Institute for Health and Care Research (NIHR), which is the research arm of the NHS.

Have patients and the public been involved in this trial?

A group of patient advisors with lived experience of low back pain and sciatica have helped to develop this research and the questions that are being asked in the trial. This group will also be advising the research team as the trial progresses to ensure that the patient's perspective is taken into account at all times. For example, patient advisors were involved in reviewing this Participant Information Sheet. There is also a patient who is a member of a separate committee that oversees the running of the trial, called the Trial Steering Committee.

Who has reviewed the trial?

This trial has been approved by the Medicines and Healthcare products Regulatory Agency (MHRA). All research in the NHS is carefully looked at by an independent group of people, called a Research Ethics Committee (REC), to protect your interests and to ensure safety and

ethically conducted research. This trial has been reviewed and given a favourable opinion by South Central - Berkshire Research Ethics Committee.

Involvement of General Practitioner

You may have been invited to take part in the MEDAL Trial through your registered GP practice. Regardless of how you have been invited to take part, we will ask for your permission to inform your GP of your participation in this trial.

In addition, the trial questionnaires ask some questions about your well-being. All answers to these questionnaires will be held in the strictest confidence. However, if we have concerns for your well-being, or the wellbeing of others, we are duty bound to inform your GP and/or other healthcare professionals to make sure we can look after you in the best way possible.

What if something goes wrong?

You can make an appointment to see your GP at any time during the trial or when the trial stops should you so wish.

If you have a concern about any aspect of this trial, you should ask to speak to the researchers who will do their best to answer your questions. Please contact the MEDAL trial team by email at MEDAL@trials.bham.ac.uk or by phone 0121 414 8528.

If you remain unhappy and wish to complain formally, you can do this by contacting your local Patient Advice and Liaison Service (PALS), which offers confidential advice, support and information. Details can be obtained from: https://www.nhs.uk/nhs-services/hospitals/what-is-pals-patient-advice-and-liaison-service/

If you have any questions or concerns about taking part in research you can also contact NHS England: Tel: 0300 311 2233, email: england.contactus@nhs.net

Are there any costs to participating?

Funds are not available to pay you to take part in the trial. Medication prescribed on each step of your treatment ladder will be collected from your pharmacy in the usual way that you collect other prescriptions. If you pay for prescriptions, you may wish to consider a prescription prepayment certificate. Please discuss this with your local pharmacy or GP. However, you will be offered a £10 gift voucher after attending the initial appointment, and a £15 gift voucher after your 8 weeks follow up data collection is complete, to say thank you for your time.

What happens if new information becomes available?

Sometimes we get new information about the treatments being studied. If this happens, a member of the research team will tell you and discuss whether you should continue in the

trial. If your GP is happy for you to continue in the trial, you will have the option to decide whether you wish to continue. If this happens, a member of the research team may ask you to re-sign a consent form if you decide that you want to continue. If you decide not to carry on, a member of the research team will make arrangements for your standard clinical care to continue with your GP. If, however, a member of the research team considers that you should withdraw from the trial, they will explain the reasons and arrange for your standard clinical care to continue, again with your own GP.

What happens when the research trial stops?
Throughout the trial, and once the research trial stops, your routine care will continue as usual with your GP practice.

What will happen to the results of the research trial?
After the trial has finished and we have reviewed the results, the main findings will be shared with the research sites and GP practices involved in the trial. The results will also be available on the MEDAL trial website:
https://www.birmingham.ac.uk/research/bctu/trials/primary-care/medal
The results of this trial will be shared at medical conferences and through publication in academic journals, which are read by many health professionals around the world. You will not be individually identified in any way in any posters, reports or publications where data is being shared with third parties either as part of this study or further research.

How will my personal data be kept secure?
The University of Birmingham take great care to ensure that personal data is handled, stored, and disposed of confidentially and securely. Our staff receive regular data protection training, and the University has put in place organisational and technical measures so that personal data is processed in accordance with the data protection principles set out in data protection law.

Any physical paperwork containing identifiable data will be kept in an access-controlled and secured room inside a locked filing cabinet.

In relation to this project, all questionnaire answers that you provide for the trial will be kept anonymous and stored in a protected computer database on physically secure servers at the University of Birmingham. This database will be password protected and accessible only by certain members of the research team on a need-to-know basis.

How long will my personal data be kept?
Your data will be retained for up to 25 years after the end of the trial at the University of Birmingham. If you withdraw from the trial, we will keep the information we have already

obtained but, to safeguard your rights, we will use the minimum personally identifiable information possible.

How will we use information about you?

We will need to use information from you and your medical records for this research trial. This information will include your NHS number, name, age, contact details, medical history and health information. 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. You and your data will have a trial number instead.

We will keep all information about you safe and secure.

Once we have finished the trial, we will use the data to check the results. We will write our reports in a way that no-one can work out that you took part in the trial.

What are your choices about how your information is used?

- You can stop being part of the trial 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 trial, you will have the option to take part in future research using your data saved from this trial.

Will my taking part in this study be kept confidential?

All information collected about you for this trial will be subject to the General Data Protection Regulation and Data Protection Act 2018 for health and social care research and will be kept strictly confidential.

How will we use information about you?

The University of Birmingham is the Sponsor for this trial and will act as the data controller. This means that the University of Birmingham are responsible for looking after your information and using it properly. The University of Birmingham and the NHS will keep identifiable information about you for 25 years after the trial has finished, to allow the results of the trial to be verified, if needed. Information which we collect from you for use in this research will include your:

Full name
Date of birth
Telephone contact number

Email address
Postal address
Ethnicity
Sex

Your data will have a unique trial number and all information will be kept safe and secure. The research team will identify you by your unique trial number, and in routine communication between members of the research team, you will only be identified by trial number, initials and partial date of birth.

All information collected by the Sponsor, including the transcript of your interview, will be securely stored at the qualitative research team's office at the University of Birmingham on paper and electronically. Only authorised personnel, who manage the trial or audit the data collection process, will be able to access information that identifies you.

What are your choices about how your information is used?

Individuals from the University of Birmingham and regulatory organisations may look at your trial records to check the accuracy of the research trial. The trial team at your hospital will pass information collected from you to the University of Birmingham.

From time to time, we may be asked to share the trial data we have collected with researchers running other studies on back pain within our organisation and also in other organisations so that they can perform analysis on the data to answer other important questions about back pain. These organisations may be universities, NHS organisations or companies involved in health research and may be in this country or abroad. Any such request is carefully considered by the trial researchers and will only be granted if the necessary procedures and approvals are in place. It will not be used to make decisions about future services available to you, such as insurance.

We will ask for your permission to keep your contact details (name, gender, date of birth, post code and NHS number) at BCTU to allow us to find out about your long-term health without automatically having to contact you. This information will be only shared with NHS digital.

Your rights under GDPR

All individuals who have access to your information have a duty of confidentiality to you. Under the provisions of the General Data Protection Regulation (GDPR) 2018, you have the right to know what information the research team has recorded about you. If you wish to view this information, or find more about how we use this information, please contact the University of Birmingham's Data Protection Officer at the address below.

Where can you find out more about how your information is used?

If you would like more information on your rights, would like to exercise any right or have any queries relating to our processing of your personal data, or if you wish to make a complaint about how your data is being or has been processed, please contact:

The Data Protection Officer, Legal Services, The University of Birmingham, Edgbaston, Birmingham B15 2TT
Email: dataprotection@contacts.bham.ac.uk
Telephone: +44 (0)121 414 3916

Sponsorship, Insurance and Indemnity

The University of Birmingham is the sponsor of this trial. The University of Birmingham has in place Clinical Trials indemnity coverage for this trial which provides cover to the University of Birmingham for harm which comes about through the University's, or its staff's, negligence in relation to the design or management of the trial and may alternatively, and at the University of Birmingham discretion provide cover for non-negligent harm to participants.

With respect to the conduct of the trial at Site and other clinical care of the patient, responsibility for the care of the patients remains with the NHS organisation responsible for the Clinical Site and is therefore indemnified through the NHS Litigation Authority.

The University of Birmingham is independent of any pharmaceutical company and as such it is not covered by the Association of the British Pharmaceutical Industry (ABPI) guidelines for participant compensation.

Contact for further information

Please visit our website at:
https://www.birmingham.ac.uk/research/bctu/trials/primary-care/medal.
If you have any questions, or would like any further information, please contact the MEDAL trial team at Birmingham Clinical Trials Unit by email at MEDAL@trials.bham.ac.uk

If you have any questions or concerns about your healthcare, you can also contact the Patient Advice and Liaison Service (PALS), which offers confidential advice, support and information on https://www.nhs.uk/nhs-services/hospitals/what-is-pals-patient-advice-and-liaison-service/

If you have any queries about the processing of your personal data, please contact dataprotection@contacts.bham.ac.uk for the attention of the Data Protection Officer.

Thank you for taking the time to read this information sheet and for considering taking part in this trial.

Contact Information

If you would like more information or have any questions about the MEDAL trial you can email the trial team on: MEDAL@trials.bham.ac.uk or call: 0121 414 8528

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