[Insert Trust Logo]

Methotrexate Oral Or SubcutanEous for RA

The **MOOSE** Study

IRAS ID: 1006576

Participant Information Sheet

1. You are invited to take part in our research study

Our hospital is working with a team of researchers to find out whether it is better to treat people with newly diagnosed rheumatoid arthritis with methotrexate tablets or with methotrexate injections.

This study is called the MOOSE study and this information sheet is to help you understand why the research is being carried out and what it will involve for you if you decide to take part.

Please take time to read this information and ask us if there is anything that is not clear to you, or you would like more information. It is entirely your decision whether to take part in this study. If you agree to take part, you are free to stop at any time without giving a reason. If you choose not to take part, your care will continue in the usual way.

2. Study summary and purpose

We are studying how to improve the treatment of people with rheumatoid arthritis.

Rheumatoid arthritis (RA) is treated with medicines such as methotrexate that control inflammation and reduce joint damage. In the UK, methotrexate is usually prescribed as tablets that are taken once a week. Some people taking methotrexate tablets may experience side effects such as sickness. To reduce these side effects, a doctor may advise to stop taking methotrexate tablets and use methotrexate injections. These are administered by the patient themselves to an area just below the skin. Similarly, if the RA is not controlled with methotrexate tablets, some doctors may advise patients to take methotrexate injections.

We are conducting this study to find out if methotrexate injections are better than tablets in treating RA in people newly diagnosed with this condition. We don't currently have enough evidence from high quality research to know for sure whether tablets or injections are the best option. We will look at benefits, side-effects, and acceptability of both treatments to patients. We will also look at whether methotrexate injections are cost-effective treatment for use in the NHS.

3. Why have I been invited to take part?

We are inviting 386 people to join the study, who, like you, have recently been told they have RA. We will be asking patients from clinics across the UK to help us with this research.

You've been invited to help because:

- You have recently been diagnosed with RA

- You will be prescribed methotrexate to treat your RA
- Your rheumatologist thinks you are suitable to take part in this study.

4. Do I have to take part?

It is up to you whether you take part in the study. We will talk to you about the study and answer any questions you may have. If you agree to take part, we will ask you to sign a consent form.

Taking part in the study does not affect your access to any other treatments for RA. If you experience side-effects whilst taking your study treatment, this can be stopped and a new treatment prescribed without affecting your participation in the study. There will also be no restrictions on the use of medicines to treat your RA if it flares up.

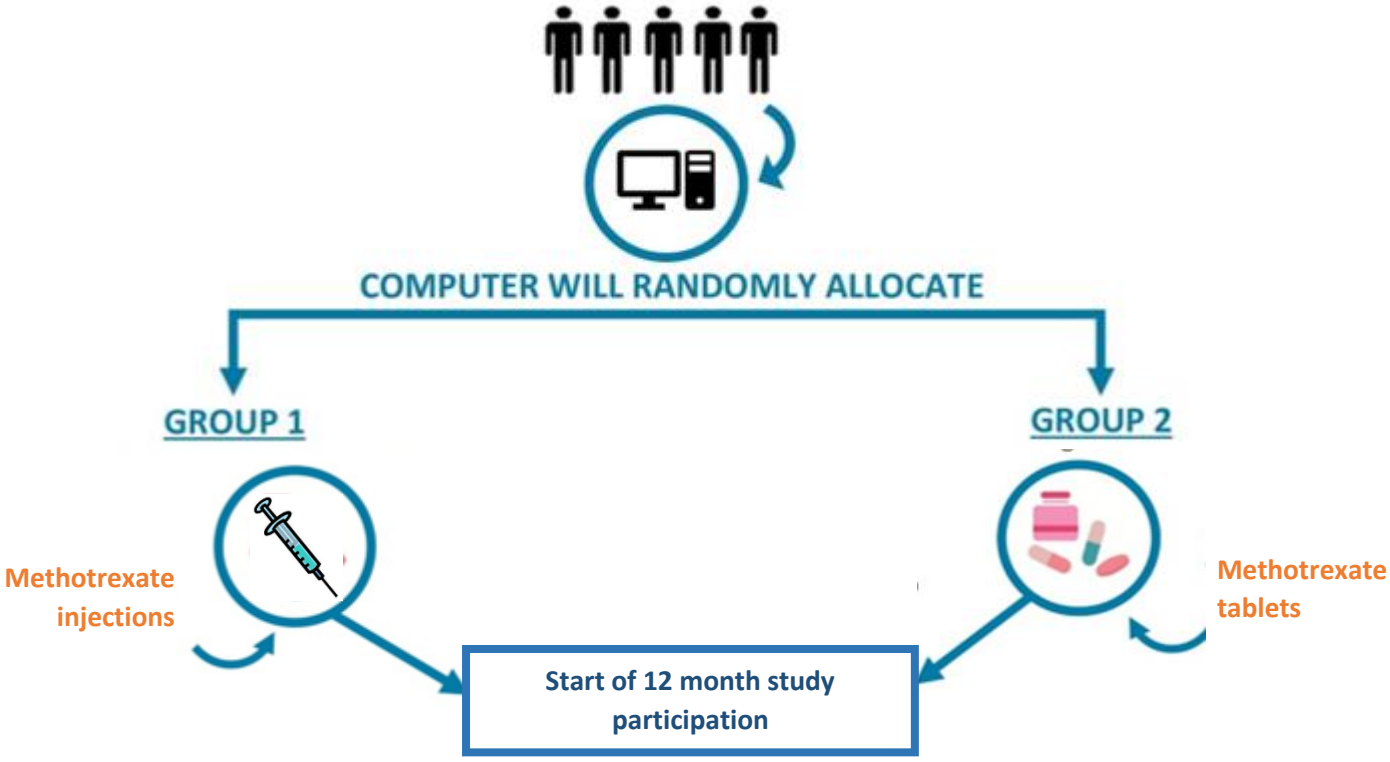
If you choose not to take part in the study, your clinical care will continue as normal.

5. What would taking part involve?

If you agree to take part, you will be asked to attend appointments in person at your usual rheumatology clinic. You will be involved with the study for 12 months from receiving your prescribed treatment to your last follow-up.

The first clinic appointment
After you have signed your consent form, a nurse will ask you some questions about you, your arthritis symptoms, examine you and take a 5ml blood sample. You will be asked to answer a questionnaire relating to your treatment and overall wellbeing. If you are of childbearing potential you will be asked to take a pregnancy test during this visit.

Your medicine
You will be prescribed either methotrexate injections, that you will be able to use at home, or tablets. As nobody knows which treatment is best, your treatment will be allocated using a process called randomisation. This means you will have an equal chance of having the methotrexate injections or the methotrexate tablets. Randomisation is used as it creates groups of patients that are similar except for the treatment received. This will enable a fair comparison of the different treatments so we can assess at the end of the study which one is best for future patients. Neither you, the doctors or the research team can choose which group you will go in, as this could result in the groups being unequal and the findings unreliable.



Your local care team will talk to you about the treatment you've been offered, arrange prescriptions, and will tell you when and how to take your treatment.

Following your progress

People newly diagnosed with RA are seen by their rheumatology team regularly to get their treatment adjusted. Depending on local arrangements, these visits occur at approximately monthly intervals until the RA is well controlled. At these visits, the dose of methotrexate may be changed, and new treatments may be started. After this, the hospital visits are less frequent, for example occurring once every six to twelve months.

If you take part in the study, we will also ask you to return to the clinic for up to three study visits around 3 months, 6 months and 12 months after starting your methotrexate. We will work with your local research team to make sure these visits coincide with your usual clinic visits where possible.

When you return to the clinic 3 months after starting methotrexate, the nurse will assess your RA (including with a blood test) and provide your rheumatologist with a score that tells them whether your RA is getting better or worse. This score, along with your personal experience of using the treatment will be used to help us assess how effective your medication is at treating RA symptoms.

You will have another study visit at 6 months after starting your methotrexate. This visit will be slightly longer (approx. 60 minutes in total) as you will also be asked to answer some questionnaires relating to your treatment and overall wellbeing, in addition to your usual RA assessment.

Although there will not be any travel reimbursement for attending the study visits, you will receive a £25 shopping voucher at your initial appointment, and again at the 6 months visit. This is to thank you for the time taken to fill in the initial questionnaires and to attend appointments that are not usually part of your NHS care.

12 months after starting your methotrexate you will have your final study assessments, and we will ask you to complete some questionnaires. These will be the same as those you answered during your first appointment.

We will also send you a brief questionnaire enquiring about any side-effects of methotrexate 1 month and 2 months after you join the study. We may use a combination of email/phone call/text message to contact you if the questionnaires have not been completed.

At the study visits at 3, 6 and 12 months, your joints will be checked by a clinician that does not look after you usually. The clinician will not know that you are currently taking or previously took methotrexate as either a tablet or as an injection. Knowing whether you've been taking methotrexate tablets or injections may affect the results of their assessment, so please do not share this information with them at the month 3, 6, and 12 study visits.

24 month follow up

It is possible that we will complete a 24 month follow up study to find out whether oral methotrexate or methotrexate injections continue to be the most effective treatment for your RA, in the long term. With your permission, this can be done by reviewing your medical notes. Your usual care team or research staff at your local hospital would review your hospital records. You can decide whether or not you want to take part in the 24 month follow up, and you will not need to return to the clinic for this.

GP Involvement

With your permission, we will inform your GP about your participation in this study. If you become pregnant whilst you are taking part in the study we will inform your GP of the pregnancy, and advise that you follow the direction of your clinical care team and GP if this should occur. We may also contact your GP to follow up on your health status, if the study documents are not returned as requested and we are unable to contact you.

Treatment Acceptability Discussions

A small group of people taking part in the study (20 in total) will have the opportunity to share their experiences of using methotrexate during one to one discussion with a member of the research team. We would like to discuss experiences of using methotrexate when people first start treatment and again 8-9 months after starting treatment. This is an optional part of the study and we will ask if you are happy to be contacted about this part of the study in your consent form.

If you agree, we will send some additional information and a separate consent form nearer the time. You may, or may not, be one of the people asked to share your experience with the researchers. If you are invited, you can still opt out of this part of the study if you later decide that you don't want to take part. This would not affect your involvement in the rest of the study.

If invited, the first discussion will take place around 4 weeks after your first clinic visit. You will be asked about your understanding and thoughts on your arthritis diagnosis and the methotrexate treatment you are using. We will speak to you again near the end of the study to find out about your experiences with your treatment whilst in the study for example if things have changed over time and why. These discussions will take place over the phone or over video call depending on your preference.

6. What are the possible benefits of taking part?

We do not know if taking part in the study will directly benefit you, but the information we collect from this study will help us better understand methotrexate treatments and may help us improve treatment for people with RA in the future.

7. What are the possible disadvantages and risks of taking part?

With all medicines, some people experience side effects. The most common side effects of methotrexate are nausea, vomiting, loss of appetite, tummy pain, bloating, diarrhoea, and mouth ulcers. Both methotrexate injections and tablets are recommended as treatments for RA, and there is no evidence that methotrexate injection causes more side-effects than tablets. Whether you take part in the study or not, you will still be given advice by your rheumatology team on the use of methotrexate and what to do if you experience any side effects. A full list of your treatment side effects and contraindications will be provided as part of the patient information leaflet, included with your allocated methotrexate treatment. Please read this carefully.

Your methotrexate should only be taken once a week, as prescribed. Taking too much methotrexate can cause serious side effects. If you have taken more than your prescribed dose you should call 111 or go to 111.nhs.uk for advice. In rare cases serious allergic reactions can occur, that may need immediate treatment in hospital. In an emergency, call 999 or go to your nearest hospital A&E. Methotrexate should be stored separately, away from any daily medications that you take, and in a safe place where children cannot gain access.

You must not become pregnant whilst taking methotrexate or for at least six months after you stop taking methotrexate.

If you are of childbearing potential you must use highly effective contraception during this time. You will have the opportunity to talk with your local team about effective contraceptive methods, which include; established use of the combined oral pill, injected or implanted hormonal methods; placement of an intrauterine device (IUD) or intrauterine system (IUS); true abstinence; or vasectomised partner.

If you are male, and have a partner of childbearing potential, your partner must not become pregnant whilst you are taking methotrexate, or for 6 months after you stop taking methotrexate. You must use effective contraception during this time. You will have the opportunity to talk with your local team about effective contraceptive methods, which include; established use of oral, injected or implanted hormonal methods; placement of an intrauterine device (IUD) or intrauterine system (IUS); condom or occlusive cap (diaphragm or cervical/vault caps) with spermicide; true abstinence; or vasectomy.

8. What if there is a problem?

If you have concerns or questions about any aspect of this study, you should ask to speak to the local researchers. Their contact details are at the end of this information sheet.
If any questions remain you can contact the study coordinating centre:
Tel: 0115 823 1604, contactable Monday to Friday: 9:00 – 16:00
Email: moose@nottingham.ac.uk

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure via your local Patient Advisory and Liaison Service (PALS)
<insert Local PALS details>.
In the event that something does go wrong and you are harmed during the study and this is due to someone's

negligence then you may have grounds for a legal action for compensation against the University of Nottingham but you may have to pay your legal costs. The normal NHS complaints mechanism will still be available to you.

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

You are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw we will no longer collect any information about you or from you but the information already collected will not be erased and this information may still be used in the project analysis.

10.How will information about me be used?

Researchers at the Nottingham Clinical Trials Unit (part of the University of Nottingham), University of Sheffield and University of Keele will need to use information from you, your medical records, and your rheumatologist for this research project.

This information will include your initials, NHS or CHI number, name and contact details. The researchers at the Nottingham Clinical Trials Unit will use this information to do the research or to check your records to make sure that the research is being done properly. Your contact details will be used by the Nottingham Clinical Trials Unit to try and get in touch with if you haven't attended your follow up appointments. Researchers from the University of Keele will have access to your name and contact details for the purpose of contacting you for the treatment acceptability discussions (if you choose to participate in these). Researchers at the University of Sheffield will have access to medication data that is anonymised so they will not be able to identify you from the data they receive. We will also need this information if we need to follow up your medical records as part of the research, where we may need to ask the Government services that hold medical information about you (such as NHS England, the Office for National Statistics, among others) to provide this information to us. By signing the consent form you agree to the above.
This information will be kept strictly confidential, stored on a password protected database at the University of Nottingham.

People who do not need to know who you are will not be able to see your name or contact details, your data will have a code number instead. All information about you will be kept safe and secure.

Once the study has finished, the data will be kept for a minimum of 10 years. Results will be checked and you will be told what happened in the study (unless you tell us you do not want to know). Reports will be written in a way so that no-one can work out that you took part in the study.

In accordance with Sponsor, Government and funder policies we may share anonymised research data with researchers in other Universities and organisations, including those in other countries. Sharing research data is important to understand the bigger picture in particular areas of research.

As an optional addition to the study, you may also agree to have your name and telephone number shared with Esendex, our text messaging provider and their sub-processors. This will be used to send you text message reminders about the study and study questionnaires whilst you are participating in the study. Once your participation has ended you will no longer be contacted but Esendex will retain the data for two years or until the end of the study (whichever occurs first).

11.What are your choices about how your information is used?

You can stop being part of the study 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. Under UK Data Protection laws the University is the Data Controller (legally responsible for the data security) and the Chief Investigator of this study is the Data Custodian (manages access to the data). This means we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited as we need to manage your information in specific ways to comply with certain laws and for the research to be reliable and accurate. To safeguard your rights we will use the minimum personally – identifiable information possible.

After 10 years your data collected during the study will be disposed of securely. You will also have the option to take part in future research using your data saved from this study. If you do not wish for your contact details to be kept for a copy of the study results to be sent to you, these will be disposed of securely at the end of the study.

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

You can find out more about how we use your information:

- at **www.hra.nhs.uk/information-about-patients/** and **www.hra.nhs.uk/patientdataandresearch**
- at https://www.nottingham.ac.uk/utilities/privacy/privacy-information-for-research-participants.aspx and http://www.nctu.ac.uk/data-protection/data-protection.aspx
- by asking one of the research team
- by sending an email to moose@nottingham.ac.uk
- by calling the Nottingham Clinical Trials Unit on 0115 823 1604

13.Who is organising and funding this study? How has it been approved?

The study is being organised by the University of Nottingham (the Sponsor) and coordinated by the Nottingham Clinical Trials Unit (NCTU). The funding for the trial is provided by the National Institute of Health Research Health Technology Assessment (NIHR HTA 13271). Professor Abhishek, Professor of Rheumatology is the Chief Investigator of this study. All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by a South Central - Berkshire Research Ethics Committee.

Patients who have previously been treated for rheumatoid arthritis and have been treated with methotrexate have helped us plan and design this study. Patients' representatives are also involved in the teams that oversee the running of the study and a Patient Advisory Group has worked with us to create the patient documentation.

14.What if relevant new information becomes available?

We may get new information about rheumatoid arthritis or methotrexate during the study. If this happens your research doctor will tell you about this new information and discuss whether you should continue in the study. If you decide not to carry on, your research doctor will make arrangements for your care to continue as normal. If you decide to continue in the study you may be asked to sign a new Informed Consent Form.

15.What will happen to any samples I give?

The blood samples taken whilst you are participating in the research will be used to assess the severity of your RA. The sample will be analysed at your local hospital. Samples will be labelled with your date of birth,

NHS or CHI number, date of collection, and hospital number. Collection, storage and destruction of all blood samples will be as per the usual practice in your local NHS hospital.

16.What happens at the end of the study?

When the study ends, your treatment will continue as usual. Any change to your treatment will be decided by you and your rheumatologist. If you withdraw from the study, we will need to keep and use the data collected up to your withdrawal. At the end of the study the results will be published in scientific medical journals and presented at conferences. You will not be identified in any publication. We will send you a newsletter with a summary of the study findings, unless you ask us not to.

17.How to contact us

Contact details of your local care team:

- <insert contact details here>