HOPE-c

Hand **O**steoarthritis: investigating **P**ain trajectories and association with biomarkers including **E**strogen **c**ohort

Participant Information Leaflet

Research Ethics Committee Reference: 19/LO/1888
Chief Investigator: Professor Fiona Watt FRCP, PhD. Kennedy Institute of Rheumatology, University of Oxford, Roosevelt Drive, Headington, OX3 7FY

We are inviting people who have hand pain due to osteoarthritis to take part in the HOPE-c research study.

Before you decide on participation, it is important that you understand why this research is being performed and what it would involve. This information leaflet explains the research, the potential benefits and risks of taking part and how information is gathered and used. Please take time to read this information and discuss it with others if you wish. Please contact us if there is anything that is not clear or if you would like more information.

Participation in this study is entirely voluntary.

For study enquiries please visit www.hopecohort.org.uk or contact the study team:
email: ouh-tr.hopecohort@nhs.net
telephone: 01865 612651

What is the purpose of the study?

Hand osteoarthritis is a common condition, however we do not know why people have different experiences of hand pain. We want to:

i) Improve our understanding of what happens to hand pain over time in people with hand osteoarthritis

ii) Find out whether there are factors that can predict why in some people the pain appears to improve, whilst in others it may remain stable or worsen

iii) Study hand pain flare: why do some people experience flares but not others? How does a flare impact on a person's life and are there factors that can help us to predict flares (or prevent them occurring)?

We believe there may be a link with sex hormones (such as estrogens and testosterone) because the condition is more common in women, particularly around the time of the menopause (when periods stop). We know that sex hormones can influence how both men and women sense pain.

Some people tell us that weather conditions affect their joints. In HOPE-c, we will try to understand any links between weather conditions and daily hand pain severity or flares.

Participants in HOPE-c will be asked to score their hand pain severity every day for six months (by mobile phone or on a paper diary) and complete at least five surveys during this time. Participation can be entirely remote, using text message, email and surveys with telephone support available. If you live near our main study sites (Oxford and London) and express an interest in attending study visits, we may offer face-to-face visits when it is safe and feasible to do so (depending on local COVID-19 restrictions).

Who can take part in the study?

- You can participate if you are a man or woman aged over 18 years old, live in the UK and have painful hand osteoarthritis.
- Your hand pain should be only due to hand osteoarthritis, affecting at least two hand joints (small joints of the fingers, the thumb or the base of the thumb) and painful on most days of the month.
- There are some conditions (past or present) that mean you would not be able to join the study. These include:
    - Another cause for hand pain, including any form of inflammatory arthritis (such as rheumatoid arthritis), connective tissue disease (such as lupus), current carpal tunnel syndrome, fibromyalgia or chronic widespread pain that is causing you hand pain
    - If you have psoriasis, you will not be able to take part as it can be linked to a form of arthritis that looks similar to hand osteoarthritis.
- We need to know whether you are participating in another research study. Depending on the nature of the study and what is involved, this may affect whether you could also participate in HOPE-c.
- If you have started or changed any of the treatments listed in the table below, please wait until the relevant time has passed before joining the study.

Within the last four weeks	Within the last three months	Within the last six months
Started a new **pain medication** Changed the dose or stopped your usual **pain medication** Used **steroid tablets** Received a **steroid injection** into any joint that is not in the hand	Received a **steroid injection into the hand** Received a **steroid injection into muscle** (usually at sites such as the buttock or upper arm) Started a new **hormonal** tablet, patch or injection, or changed your usual hormonal treatment Started glucosamine, chondroitin, hand exercises or any other hand therapy	Used a treatment that **weakens the immune system** (for example, chemotherapy for cancer or medications like methotrexate) Experienced **hand surgery** or planning to have hand surgery within the next six months Received an injection of hyaluronic acid (such as Ostenil or Synvisc) into your hand joints

Do I have to take part?

No, participation is entirely up to you. If you decide to take part, you will be asked to complete a consent form. You remain free to withdraw at any time and do not have to give a reason.

What will happen if I decide to take part?

After you give consent to participate, you will be asked to complete at least five surveys at home over six months (online, or paper forms if requested) and score your daily hand pain during this period. The surveys can be completed in your own time and your responses are saved as you progress, so you can take breaks whenever needed.

If you experience a flare or change in your hand symptoms, we will ask you to complete an additional survey (up to 3 times during the study). At the end of six months, we will ask whether you would like to be contacted again after two years and five years for further assessment. This is to study how your symptoms have changed over time.

If you have previously had a hand X-ray, we will ask for your permission to use this in our research. If you agree to this, we will call to get further information about the scan and your NHS number.

Optional face-to-face appointments: If you live near Oxford or London, we may offer optional face-to-face appointments. At these appointments, we will examine your hands, take blood tests and may perform a hand X-ray. At the first face-to-face visit, you will be asked to sign an additional consent form and have further tests (including a hand X-ray, if this has not been performed within the last 12 months), which can take up to 40 minutes in addition to the usual visit time.

If you attend face-to-face visits, we will follow current recommendations to keep you and our research team safe during the COVID-19 pandemic. These precautions are likely to include ensuring you and your close contacts have not got symptoms of COVID-19, wearing appropriate personal protective equipment (PPE) and increased cleaning of rooms and equipment. However, the exact processes will depend on recommendations at the time of your visit.

	What will happen?
Pre-screening Online form or Telephone call *5 minutes*	To initially assess whether you can take part, we will ask you questions about your hand problem and your health.
Giving Consent Online form or Telephone call *10 minutes*	Completion of a consent form to give a record of your permission to participate in this research study.
Visit 1: Screening Online form or Telephone call *5 minutes*	A more detailed assessment of whether you can take part. You will be asked questions about your health, medical treatments and your hand symptoms.
Visit 2: Baseline Online form or Telephone call *45 minutes* *Face to face visits only:* *up to 1 hour additional time*	• Health and medication review • Assessment of pain and other aspects of your hand osteoarthritis • Completion of study questionnaires • Optional: submission of hand photographs At face-to-face appointments: • Examination of the hands • Blood test (30mls, approximately 2 tablespoons) • Hand X-ray (if you have not had one within the last 12 months)
Start scoring daily hand pain severity: continue until the Week 26 visit (approximately 6 months)	
Visit 3: Week 1 Online form or Telephone call *20 minutes* *Face to face visits only:* *up to 1 hour additional time*	• Health and medication review • Assessment of pain and other features of hand osteoarthritis • Completion of study questionnaires At face-to-face appointments*: • Examination of the hands • Blood test (30mls, approximately 2 tablespoons) • Optional: Hand ultrasound (available at the Oxford site) and recording sound emissions from hand joints
Visit 4 a/b/c: Flare/Change visits Online form or telephone call *30 minutes* *Face to face visits only:* *up to 1 hour additional time*	• Up to three additional assessments for participants who experience a flare or change in hand symptoms during the study • Health and medication review • Assessment of pain and other features of hand osteoarthritis • Completion of study questionnaires • Optional: submission of hand photographs At face-to-face appointments*: • Examination of the hands • Blood test (30mls, approximately 2 tablespoons) • Optional test: Hand ultrasound (available at the Oxford site) and recording sound emissions from hand joints
Visit 5: Week 13 Online form or Telephone call *25 minutes*	• Health and medication review • Assessment of pain and other features of hand osteoarthritis • Completion of study questionnaires
Visit 6: Week 26 Online form or telephone call *45 minutes* *Face to face visits only:*	• Health and medication review • Assessment of pain and other features of hand osteoarthritis • End of 'core study' questions • Completion of study questionnaires • Confirm consent for optional follow-up at Year 2 and Year 5 • Optional: submission of hand photographs

up to 40 minutes additional time	<u>At face-to-face appointments*</u>: • Examination of the hands • Blood test (30mls, approximately 2 tablespoons) • Optional test: Recording of sound emissions from hand joints
End of daily hand pain severity scores	
Optional Visit 7 (Year 2) and Visit 8 (Year 5) Online form or telephone call *40 minutes* <u>*Face to face visits only*</u>*:* *up to 1 hour additional time*	• Health and medication review • Assessment of pain and other features of hand osteoarthritis • Completion of study questionnaires • Optional: submission of hand photographs <u>At face-to-face appointments</u>: • Examination of the hands • Blood test (30mls, approximately 2 tablespoons) • Hand X-ray (if needed) • Optional test: Recording of sound emissions from hand joints

**If you attend a face-to-face appointment for this first time, we may request a hand X-ray if you have not had one in the previous 12 months.*

More about the study

- **Questionnaires:** We will ask you about hormonal symptoms, pain (throughout the body and in the hand) and how arthritis affects your hand function, mood and overall well-being. These questionnaires can be completed at home using a secure emailed link, or as a paper-based questionnaire pack if you prefer this.

- **Daily hand pain score:** You will be asked to rate your daily hand pain at home for the duration of the core study (until the Week 26 visit, approximately 6 months). You can choose one of two different ways of scoring hand pain: using your mobile phone or a study paper diary.

    - *Phone-based:* If you have a smartphone and give consent to receive text messages, you will receive a text message every day (at 6 pm) until your Week 26 study visit. The message contains a secure web link which you will need to open on your phone. The link will take you to a web page which will ask you to do following:

        - Rate your average hand pain for the last 24 hours from 0 to 10.
        - Check boxes: tell us if a new episode of flare or change in your hand symptoms has started or ended
        - Optional free-text box: to record any information that you feel may be relevant (for example, heavy work with hands such as gardening or a change in medications)
        - Optional location: to tell us if you are away from home overnight or longer. This will allow us to match the local weather conditions to your daily pain severity.

    - *Paper-based:* You can opt to record daily hand pain severity on a study paper diary, as well as the start/end of a new episode of flare/change in hand symptoms, any information that you feel is relevant and travel away from home (as above). We ask that you contact us by telephone or email as soon as you experience a new episode of flare/change in hand symptoms.

- **Blood tests (face-to-face visits only)**: We will take blood tests to measure your sex hormone levels, markers of inflammation and (only if you agree) perform a specific DNA test for a gene that has been associated with severe symptoms in hand osteoarthritis. The individual results of these tests will not be shared with you. This is because we have only a limited understanding of the links between these experimental tests and symptoms at present and would not be able to interpret these results for you.

  In some cases, we may need to request blood tests to rule out other forms of arthritis. We will let you know if this is the case and will discuss these results with you.

Can I take other treatments during the study?

- Yes. You should continue your usual treatments during the study and can start any new treatments if you wish. We ask that you tell us about any changes to your treatments when you complete study surveys.

- We need your treatments to be stable for a short period of time before you start the study (see below). This is to ensure that your hand pain severity is at the usual level for you at the Baseline assessment.

Other important considerations

- **Hormonal questionnaires**. Men and women will receive separate questionnaires to assess their hormonal symptoms. Some of these questions ask about sexual symptoms (such as sexual desire). You will complete the questionnaires yourself and the results will be stored securely, along with your other study information. If you are concerned about any of these questions, please speak to a member of the study team, or simply miss them out in the questionnaire.

- **Mood and psychology questionnaires**. To assess the impact of pain on mood, we will ask you to complete questionnaires about low mood, anxiety, anger and how you cope with pain. You will complete these questionnaires yourself (and can skip questions if you prefer), however if we identify any new mood symptoms that we feel may benefit from attention from your GP or another healthcare team, we will discuss this with you.

- **Blood testing (face-to-face visits only).** When having your blood taken, minor bruising at the needle puncture site may occur in some people. Please tell us if you are worried about having blood taken.

- **Hand X-rays (face-to-face visits only).** If you have not had an X-ray of your hands within the last 12 months, this may be requested at your first face-to-face visit and at the optional Year 2 and Year 5 visits. X-rays use ionising radiation which can cause cell damage that may, after many years or decades, turn cancerous. We are all at risk of developing cancer during our lifetime. The normal risk outside of this study is that this will happen to about 1 in 2 people at some point in their life. The dose of ionizing X-rays in a hand X-ray is extremely small. Having all three X-rays as part of taking part in this study is equivalent to a few hours of natural background radiation that we experience here in the UK during our daily lives. If you are a woman with a chance of being pregnant, we will request a urine pregnancy test to exclude this before performing a hand X-ray.

What are the possible benefits of taking part?

You may not benefit directly from taking part in this study. We do not know what the outcome will be, which is why we are conducting the research. Sometimes, we detect conditions that would otherwise have been undetected, for example another form of arthritis or low mood, or may give you advice about your hand osteoarthritis. In this situation, we will involve your GP with your permission. Joining the study can therefore have indirect health benefits.

The study will give us useful information which may benefit others with this condition in the future.

Will my General Practitioner/family doctor (GP) be informed of my participation?

We will ask for your permission to contact your GP if we need further information about your medical background and (if you are attending face-to-face visits) give them information about the study.

Will my taking part in the study be kept confidential?

Your identity as a participant in this study will be kept confidential. Responsible members of the Sponsor (University of Oxford) and the host NHS Trust may be given access to data for monitoring and audit of the study to ensure we are complying with regulations. If you attend face-to-face visits, we will ask for your permission to access your medical records for use in the study.

To help keep your information confidential, any information recorded about you in this study and your sample results will be stored securely using a unique study identification code. If you give (optional) consent, this data may, in certain circumstances, be passed on to collaborators working with us in organisations other than the University of Oxford. This may include research collaborators and commercial organisations. Information will only be passed to other researchers and organisations in a format that does not identify you.

If you take part in recording of sound emissions from your hand joints, this audio recording will include your study code and no other personal details. The microphone used to record sound emissions has been specially modified for this purpose. Hand photographs will be used to look at changes in appearance over time and may be used when we discuss our research, for example at conferences and in research papers. These images can potentially identify participants who have unique features (such as tattoos, rings or scars). You can contact us at any point during this time if you change your mind about us using sound recordings or photographs.

What will happen to the samples I give?

- Blood samples will be sent to hospital laboratories and to our research unit, the Kennedy Institute of Rheumatology. These blood samples will be used for tests that include measurement of sex hormone levels, markers of inflammation and (only if you agree) DNA testing.

  Samples sent to the hospital laboratory will be labelled in the usual way as for normal clinical testing (with your name and hospital number) and destroyed once the requested tests are complete. Samples sent to the Kennedy Institute laboratories will be labelled with only your study code and the date the sample was taken; these will be frozen and stored for future analysis in batches during the study or within 12 months of the end of the study.

- If you agree to DNA testing but we are unable to take a blood sample, we may send you a kit to collect saliva at home and send it back to us in stamped addressed envelope (with appropriate safety precautions).

- We will ask for your consent to transfer any remaining blood and saliva samples at the end of the study for indefinite storage in a registered biobank. From here, your de-identified samples may be used by local researchers and in ethically approved research projects in hospitals, universities, non-profit institutions or commercial laboratories worldwide. In this scenario, your samples would only be provided in a de-identified (anonymous) way, however, your DNA is unique to you so can never be completely anonymous.

- For women of child-bearing age, we may need to perform urine tests to exclude pregnancy before a hand X-ray. This urine sample will be destroyed immediately after testing.

What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the data controller and is responsible for looking after your information and using it properly.

We will be using information from you and your medical records to undertake this study and will use the minimum personally identifiable information possible. Your responses to the web-based pre-screen will not be stored. We will keep research data (including potentially identifiable hand photographs and a copy of your consent form) for 15 years after the end of the study; all other identifiable information about you will be destroyed within 2 years after the study has finished. However, if your blood samples have been transferred to a biobank, your consent form will be held until the samples have been used-up or destroyed.

The study team will use your name, phone number, email address and (only if you wish to receive documents by post) home address to contact you about the research study and oversee the quality of the study. They will keep your email address (or postal address, if you prefer) for up to 2 years after the study has finished, destroying this information once we have sent you a summary of our research results. In certain circumstances (and only with your permission), the study team may use your NHS number or other medical record number to access your medical records, to check eligibility or other details relevant to the study, to contact your GP or receive copies of your hand X-rays from your local clinic or hospital.

Even if you do not continue to take part, we will continue to hold information on you which you have provided and use this for research for the duration of the study, unless you ask us not to.

If you consent to be contacted for future research, your details will also be stored separately – please see below for further details.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be

limited for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rights

You can find out more about how we use your information by contacting ouh-tr.hopecohort@nhs.net. Please see the section on Confidentiality (Page 6) for further information.

Will I be reimbursed for taking part?

You will not receive payments for participating in the study.

We will reimburse the cost of SMS messages to score hand pain if this is not included in your mobile phone contract. We will not be able to reimburse costs related to data usage on your smartphone if this is not included in your mobile phone package. In this case, please use Wi-Fi whilst at home and abroad, or we can offer a paper diary instead.

If you attend face-to-face appointments, you will be reimbursed for reasonable travel expenses for travelling to and from the hospital for all visits which are just for the study (this does not cover routine trips to NHS clinic appointments during this time). Your travel costs will be reimbursed based on the receipts you provide, so please keep all your travel receipts and tickets and give these to the study nurse, or a record of your mileage. Unfortunately, we cannot pay for the travel of others who accompany you.

Participation in future research

We would like to ask permission to contact you to discuss participation in future ethically approved studies. If you agree, your contact details would be added to the OsteoArthritis Research Voluntary Interested List (OARVIL) held by Professor Fiona Watt's team at the Centre for Osteoarthritis Pathogenesis Versus Arthritis in Oxford. Only Professor Watt's team in Oxford would have access to your contact details and would only contact you about research relevant to you. You are under no obligation to participate in any subsequent studies. You can ask for your details to be removed from OARVIL at any point. If you agree to your details being held on OARVIL, we will retain a copy of your consent form until your details are removed from our database.

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

- You should contact the research team using the contact details below. Your participation in this research study is entirely voluntary and you are entitled to withdraw at any time.
- The clinical information and samples we have already obtained from you will continue to be used in this study, unless you specifically request otherwise.

What happens at the end of the study?

- If there are any results that affect your medical care, we will contact your GP if you have given us permission to do this.
- We will send you a summary of what we have found in this study and also publish this on our website within 2 years of the last participant completing their last study visit.
- A summary of the results will be made available on department website (NDORMS), Twitter account and via media releases.

- We will publish the research in a scientific medical journal and present the findings at medical conferences. This can potentially take several years. Any information we publish, in any format, will never reveal your identity or contain any information that could be linked to you specifically. Any identifying features on hands such as jewellery, or quotes would be masked ahead of publication.

- Some of the research being undertaken may also contribute to the fulfilment of a PhD project for members of our study team. Results from this study may help future research studies in osteoarthritis.

What if there is a problem?

- The University of Oxford, as Sponsor of the study, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity also operates in respect of any clinical treatment which is provided as part of the study.

- If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, please contact Professor Fiona Watt, Honorary Consultant Rheumatologist, 01865 612651, email: ouh-tr.hopecohort@nhs.net or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480, or the head of CTRG, email: ctrg@admin.ox.ac.uk.

- The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study. If you wish to contact the PALS team, please contact the service at the details below:

    - For Oxford University Hospitals NHS Trust on 01865 738126, or email PALS@ouh.nhs.uk

    - For Imperial College Healthcare NHS Trust 020 3313 0088 or email imperial.PALS@nhs.net.

How have patients and the public been involved in this study?

As part of the preparation for planning this study, six individuals with hand osteoarthritis attended a patient discussion group and discussed with us:

- The purpose of the study and the research questions we should aim to answer
- Their experience of hand pain flare and the features we should capture
- Our plan for how we carry out the study visits, including some of the approaches we are using to measure pain in this study
- Some of the questionnaires that we should use, in particular on frustration/anger during a flare and a male hormonal questionnaire
- Their opinion on how often we should have participant assessments and the tests that we will carry out

Patients were also involved in reviewing this participant information leaflet and the consent form.

Who is organising and funding the study?

The study is sponsored by the University of Oxford and led by Professor Fiona Watt. The study is run by a team based at the University of Oxford. The charity Versus Arthritis (versusarthritis.org) is funding this study. The study also benefits from resources including staff time provided by the NIHR Biomedical Research Centre and the Centre for Osteoarthritis Pathogenesis Versus Arthritis, which is based in Oxford. Neither your doctor nor the study team will benefit financially from you taking part in this study.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by the London-Riverside Research Ethics Committee.

Further information and contact details:

If you are interested in taking part in this study or would like more information, please contact the HOPE-c study team by **email:** ouh-tr.hopecohort@nhs.net or **telephone:** 01865 612651

Thank you for considering taking part.