A pragmatic approach to the investigation of stable chest pain: a UK, multi-centre, randomised trial to improve patient experience, outcomes and NHS cost efficiency (CE-MARC 3)

(Version 1.0; 16th August 2021)

Trial summary sheet

- You are invited to take part in a research trial comparing different ways of investigating patients who have chest pain.

- All tests done in this trial are standard NHS care. The study is simply investigating the best order in which the tests are done.

- The study is funded by the charity Heart Research UK.

- If you consent to take part in the study you will be randomly assigned to one of two groups:

Group 1	**This group will get a cardiac test following UK National Guidelines (NICE). This will usually be a CT coronary angiogram.**
Group 2	**This group will get a test chosen by your doctor according to individual patient risk factors, local availability and expertise**

- The test you have will be reported in the normal way at your hospital and your management will not be altered by participating in this trial.

- There are no extra hospital visits.

  All patients will be followed up and therefore members of the research team will need access to your records during and after trial participation. We will only use information that we need for the research study and everyone involved in this study will keep your data safe and secure, following strict privacy rules.

- You will not benefit directly from taking part in the study.

- You do not have to take part if you do not want to, in which case you would receive standard care instead.

The research team will also be happy to explain the trial in more detail to you in person.

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PATIENT INFORMATION LEAFLET

Version 1.0, 16th August 2021

UK Chief Investigator: Professor JP Greenwood, University of Leeds
Local Principal Investigator: <*insert name and hospital details*>

Dear Patient,
You are being invited to take part in a research trial. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Purpose of the study
There are several tests available to help us find out if chest pain is caused by narrowing of the heart arteries (coronary heart disease). We are trying to establish the best test patients should have first. We hope to find the test strategy that gets each patient to their correct diagnosis as quickly as possible whilst also avoiding unnecessary invasive angiograms.

Why have I been chosen?
This study is looking at people like you, who have been referred to a cardiology clinic with chest pain. We will be asking 4000 people, in several UK hospitals, to take part in this trial.

Do I have to take part?
No. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information leaflet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care that you receive from the NHS.

What will happen to me if I take part?
If you take part in this trial you will be assigned to one of two groups. We call one group '**Standard Care'** and the other group '**Pragmatic Care'**. The choice will be made randomly, like tossing a coin. Neither you nor your doctor can influence what group you will be in. All heart tests in this trial are commonly performed as part of routine NHS care. How the test is done is not being altered for this research trial, it is simply trying to decide the best test to do first.

> **1. Standard Care group:** (2000 out of the 4000 patients will be in this group). If you are allocated to this group your first test will follow UK national guidelines (NICE guidelines). You will probably have a **CT coronary angiogram** as your first test. CT stands for 'computerised tomography' and is a sophisticated type of X-ray. You will lie on a bed inside a scanner and will be asked to hold your breath briefly for the scan to be performed. During the **CT coronary angiogram** you will receive an injection of a contrast dye into a vein in your am. You may also receive an injection of a medicine (a beta-blocker) to slow your heart rate down a little bit. This can help reduce the time you will need to hold your breath for.

What happens next: The CT scan will be reported by a consultant who is an expert in this area in your local hospital. Depending on the result your further treatment will be decided by your own cardiologist.

2. Pragmatic Care group: (2000 out of the 4000 patients will be in this group). You will have an individual assessment of the likelihood of you having coronary artery narrowing. This will be considered along with local expertise and availability when choosing your first cardiac test. This could either be a CT coronary angiogram (described above) or a functional test. Each hospital has different functional tests available and your heart specialist could choose any of these tests: The most commonly used tests are **Stress echo, Stress MRI** or **Myocardial Perfusion Scan** (MPS-SPECT).

Stress Echo takes approximately 60 minutes. You are normally asked to walk on a treadmill and then ultrasound pictures of your heart are taken. Some patients may need a cannula to be inserted in a vein in their arm to give a dye that improves the quality of the pictures.

Stress MRI takes approximately 40 minutes to complete. You lie in a short 'tunnel', which holds a large magnet. Short bursts of magnetic fields and radio waves from the MRI scanner allow images to be created. During the scan, you will have an injection of MRI contrast medication. You will also have an injection of medication (Adenosine), which is a drug to increase the blood flow to your heart. This medication is used routinely in many heart tests.

Myocardial Perfusion Scan (SPECT) is carried out on two separate days and each visit takes approximately 2 hours. On one day pictures of the heart will be taken at rest, and on a second day after injection of a medication (Adenosine) to increase the blood flow to your heart. On both days you will also have an injection of a radioactive dye into the blood, which is taken up by the heart muscle. One hour after the injection, pictures of the heart are taken with a special camera that slowly moves around you while you lie on a bed with one arm raised above your head. Taking these pictures takes approximately 20 minutes.

What happens next: Your heart scan will be reported by a consultant who is an expert in this area in your local hospital. Depending on the result your further treatment will be decided by your own cardiologist.

Health Questionnaires

If you agree to participate in this part of the study, you may be invited to complete three simple health questionnaires when you join the study, after six months, and at twelve months. This can all be done remotely via mobile phone or email and should take no longer than 20 minutes each time.

Follow–up: No extra hospital visits are required. As part of the study we would like to find out how you are getting on after 12 months. We may telephone you to ask you some simple questions about your health. With your permission we may also look at your hospital records, request access to your GP records, central NHS records and/or use information from NHS Digital for up to 10 years after study completion.

It is very helpful if we can continue to track your health over the long term. NHS Digital allows us to access health information about you with your permission. In order to this we are seeking your permission to provide NHS Digital with some of your personal details (including your name, date of birth, address and NHS number) and with this information they will be able to provide us with simple health information about you beyond the 12 month follow up period of this study, for a period of up to 10 years. It is very important to understand the long term health condition of patients to find out if the treatments we are giving are effective. Information will be provided to NHS Digital in strict confidence and will be kept securely and will not be released to a third party.

What are the possible disadvantages and risks of taking part?

If you take part in this trial, you may have a CT scan or a myocardial perfusion scan. You may also have a coronary angiography procedure. These procedures are all part of your routine clinical care; you will not undergo any additional procedures.

These procedures all use ionising radiation to form images of your body and provide your doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure. The chances of this happening to you are the same whether you take part in this study or not.

Benefits to you
We cannot promise the study will directly benefit you, but the information we get from this study might help the treatment of future patients. If you take part in the trial you will have more contact with us, and have more opportunities to ask questions and be informed about your health, which some patients find helpful.

Expenses
You will not be asked to undergo any extra tests or hospital visits as a result of taking part in this trial, so you will incur no extra expenses.

Will my taking part be kept confidential?
All information collected about you during the course of the study will be kept strictly confidential. This information will be coded and securely stored electronically on the University of Leeds secure servers, and on paper, under the provisions of the 2018 Data Protection Act. The data collected will be coded and your personal details (Name, NHS Identifier, date of birth and address) will be kept in a separate secure database at Clinical Trials Research Unit at University of Leeds to permit longer term record linkage for 10 years after the study has finished. Individual participating NHS hospitals/Trusts, on behalf of the University of Leeds (sponsor), will keep identifiable information about you and your contact details for the purpose of the study for 20 years after the study has finished.

We may contact the NHS Digital or other central NHS UK bodies at a later stage for information which they hold on your health status. This means some of your personal data will be shared with NHS Digital. Any information exchanged between us and NHS Digital will be subject to strict data protection laws.

With your permission, your data may also provide a resource for future studies. If any information from this trial is used to develop new research, data protection laws will be observed and strict confidentiality maintained. Any information about you which leaves the hospital will have your name and address removed so that you cannot be identified. Your data and or images may be sent to institutions in the UK, the European Economic Area or outside the EEA. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research. Ethical approval will be obtained for any future studies involving your data. With your consent we may also wish to contact you in the future about new studies you may wish to participate in. We will never give your personal details to any researchers outside of our department.

If you withdraw consent from further study follow-up, or if you were to become incapacitated, any data collected about you up to that point will remain on file and will be included in the final study analysis.

For more information on the use of your personal data for clinical research please refer to the following sources:
University Privacy notice: https://ris.leeds.ac.uk/privacy-notice/
University DPO: dpo@leeds.ac.uk
HRA information on patient data use in research: https://www.hra.nhs.uk/information-about-patients/

What will happen to the results of the research study?
When the study is complete the results will be published in a medical journal, but no individual patients will be identified. If you would like a copy of the published results, please ask your doctor.

Indemnity/Compensation
If you are harmed as a direct result of taking part in this trial, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds to a legal action. Regardless of this, if you have any

cause to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you.

The research organisation
This is a research project of the Leeds Institute for Cardiovascular and Metabolic Medicine at the University of Leeds and the *<insert local hospital name>*, in collaboration with the Clinical Trials Research Unit at the University of Leeds. It is being funded by Heart Research UK.

Who has reviewed the study?
The study has been reviewed and approved both by the <*insert details when known*> Research Ethics Committee and by your hospital Trust's Research and Development Office. More details can be provided, on request, by your study doctor.

For further information please contact:
1) <*insert local hospital lead research nurse name, email and telephone*>
2) <*insert local hospital principal investigator name, email and telephone*>

If you would like independent general advice about participating in clinical research, please discuss this with your Clinical Care Team.

Thank you for taking time to read this information leaflet.

CONSENT FORM v 1.0, 16th August 2021

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CI: Professor John Greenwood

Patient Study Number: …….. Patient Initials.....

NHS number: ..... Date of Birth: ……

	Please Initial Each Box
I have read the Patient Information Sheet dated 6th August 2021 (version 1.0) for the above study and I have had the opportunity to ask questions and discuss the research study and I am satisfied with the answers to my questions.	
I understand that my participation is voluntary and I am free to withdraw from the study at any time without giving a reason.	
I understand that data collected in this trial will be stored on a computer system at Leeds University, and, after my personal details have been removed, may be sent to participating study centres and may be available to researchers at other institutions in the UK, the EEA, and countries outside the EEA (e.g. USA).	
I understand that relevant sections of my medical notes and data collected during the trial (including personal data) may be looked at by individuals from the University of Leeds, the Clinical Trials Research Unit, from regulatory authorities, or by the local research team, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
I understand that information held by the NHS, by my General Practitioner, and information held and managed by NHS Digital and other central UK NHS bodies, may be used to provide information about my health status. I give permission for this information to be obtained from NHS Digital, the NHS Central Register and/or my GP if necessary. To do this, I understand that my details (including my name, address, NHS number and date of birth) will be shared by Leeds University with NHS Digital.	
I agree to follow-up information from NHS and Government health records being collected on my future wellbeing and treatment where relevant to this trial for up to 10 years and for clinical and personal data to be stored for up to 20 years.	
If I were to lose capacity or withdraw consent for further follow-up I understand that data already collected will be kept and used for the purposes of the trial.	
I agree to take part in this research trial and that the general results of the trial will be made available to the medical community most likely through publication in a reputable medical journal.	
I am willing to be contacted again in the future with regard to potentially taking part (without any obligation) in further related research studies.	

I agree to a copy of this consent form being sent to the Clinical Trials Research Unit (University of Leeds).	
I agree to completing optional, self-assessed quality of life questionnaires if invited to. *Please complete the Contact Details form with your preferred method of contact (SMS or email).	

Signature.....

Name (block capitals)..... Date.....

Signature of researcher.....

Name (block capitals).....Date.....

Original copy to be retained by the researcher
1 copy for the patient
1 copy to be filed in the medical records (paper notes or electronic version)