St George's University Hospitals
NHS Foundation Trust

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CARSK Study

Participant Information Sheet (PIS)

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Study Title: Screening vs not screening for asymptomatic coronary artery disease in patients on kidney transplant wait list (CARSK Study)

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Invitation to participate in the above study:

We would like to invite you to take part in a research study. Before you decide we would like you to understand why the research is being done and what it will involve for you. Please take time to read the following carefully and discuss it with others if you wish. ***We will go through the information sheet with you and answer any questions you have.*** *We'd suggest this should take about 15 minutes.*

Part 1 of the Participant Information Sheet (PIS) tells you the purpose of this study and what will happen if you take part. Part 2 gives you more detailed information about the conduct of the study.

Please ask us if there is anything that is not clear. Take time to decide whether or not you wish to take part.

If you decide to take part, we will ask you to sign a consent form declaring this. We will keep the original form in your study file and give you a photocopy to take home for your own records.

Please turn the page to start reading.

PART 1:

What is the purpose of the study?

We believe that the current strategy of regularly screening for heart vessel blockages and surgically correcting blockages in wait-listed candidates without active symptoms of heart disease is not beneficial compared to an alternative strategy in which patients are investigated for heart vessel blockages only if they develop symptoms. Currently, heart tests are done routinely for patients on kidney transplant wait list without clear evidence that this is beneficial to the patients who don't have any symptoms suggestive of heart vessel blockages. These tests and interventions that may follow are not without risks. They can also lead to unnecessary suspensions from transplant wait lists, delay in getting back on to the list and may reduce the chance of getting a kidney transplant.

This study will only include asymptomatic participants—that is, patients without symptoms or signs of coronary arterial disease (disease affecting heart blood vessels). If you develop any symptoms of coronary artery disease any time during the course of your participation in this study, you will be treated as per standard of care.

The current study is designed to determine which strategy (regular screening or screening only in the presence of symptoms) is more effective in preventing heart attacks in kidney transplant candidates.

This study is important because screening and surgical correction of heart vessel blockages is not currently recommended in patients undergoing other types of surgical procedures. Although the current screening strategy is the standard of care and is intended to prevent heart attacks, it is not proven to be effective and may either be unnecessary or even harmful because there are risks associated with performing coronary angiograms and surgery to correct blockages in heart vessels.

The information we learn from this study will help us determine the best way to care for patients who are on the kidney transplant wait list.

The study is being conducted in 28 transplant centers across Canada, Australia and New Zealand and two centers in the UK. There will be a total of 3,306 participants enrolled into the study.

St George's University Hospitals NHS Foundation Trust are leading this study in the UK. The University of British Columbia, Canada, is leading the study internationally (the "Sponsor").

Why have I been invited?

You have been invited to take part because you are on national kidney transplant wait list and you are over the age of 18 years.

Do I have to take part?

No. It is up to you to decide whether or not to take part. We will describe the study and go through this information sheet. If you do, you will be given this information sheet to keep and asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time or not take part will not affect the standard of care you receive.

What will happen to me if I take part?

Study Procedures

If you choose to participate in this study, you will be assigned by chance (like flipping a coin) to one of two groups**:**

1) Screening at regular intervals during wait-listing according to current standard of care or
2) No regular use of screening tests, unless you develop symptoms suggestive of coronary artery disease (disease affecting heart blood vessels).

This trial is **randomised** as we don't know if routine screening or not screening for aymptomatic coronary artery disease is best for our patients. To find out, we need to compare two different strategies as described above by placing patients in to two groups. To try to make sure the groups are the same to start with, each patient is put into a group by chance (randomly).

If you develop active symptoms suggestive of coronary artery disease, you will be evaluated and treated as you normally would, according to the current standard of care.

Study Visits

If you agree to participate, the study coordinator will conduct a chart review and telephone interview with you every 6 months during the wait-list period up to 5 years. The information collected from you and your health record will include: ethnicity, medical history, test results, hospitalizations, transplantation, outpatient visits, cardiac events, completion of the expected number of screening tests, use of cardiac screening and the reasons for testing.

Studies involving human subjects now routinely collect information on race and ethnic origin as well as other characteristics of individuals because these characteristics may influence how people respond to different medications. Providing information on your race or ethnic origin is voluntary.

If you have a transplant within 5 years, a chart review will occur at the time of discharge from hospital and an in-person or telephone interview and chart review will be performed 3 months and 12 months after the transplant and your time in the study will be concluded. If you are in the no-regular-screening group and have not received a transplant within 60 months after enrollment, you will go back to regular screening as per standard of care. All

participants will undergo screening in their assigned groups until the date of transplantation or 60 months, whichever occurs first. All participants will be followed for 12 months after the date of transplantation.

Quality of Life questionnaire and Study Diary:
You will be asked to complete 2 Quality of Life questionnaires (EQ-5D-5L and KDQOL-36) at time of enrolment and yearly at time of follow-up visit. The EQ-5D-5L questionnaire is to assess your overall health and well-being and it consists of 5 multiple choice questions. It will take approximately 5-10 minutes to complete it.

Below is an example of the sort of questions you would see on this questionnaire:
MOBILITY

I have no problems in walking about	❑
I have slight problems in walking about	❑
I have moderate problems in walking about	❑
I have severe problems in walking about	❑
I am unable to walk about	❑

The KDQOL-36 also is to assess your overall health, but it focuses more on your kidney disease. You may skip any questions that you do not wish to answer.
This is an example of the sort of questions you would see on the questionnaire:

1. In general, would you say your health is: [Mark an ☒ in the one box that best describes your answer.]

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? [Mark an ☒ in a box on each line.]

	Yes, limited a lot	Yes, limited a little	No, not limited at all
2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
3. Climbing several flights of stairs	☐ 1	☐ 2	☐ 3

The research coordinator will give you a Study Diary where you will be asked to record any event occurring during your participation in the study. This will help us to keep track of any hospitalization or other events that need to be collected for the study.

Your Responsibilities*:*
You will be required to present a wallet card that summarizes the study and procedures to any treating physician who may be considering cardiac investigations for you. You may also be required to contact your research doctor or research team before completing any cardiac screening tests.

Possible Side Effects and/or Risks
The purpose of regular screening for heart vessel blockages is to prevent the development of a heart attack, and therefore it is possible that patients who are not regularly screened may be at increased risk of heart attack. We believe that this risk is similar or lower than the risks of regular screening but will carefully monitor subjects assigned to both screening strategies for any imbalance in heat attacks or related complications between groups.

Your doctor will discuss the risks of this study with you. The study will be monitored by an independent data safety monitoring committee that will ensure the safety of all participants in this study. If there is an increase in adverse events noted in any group, you will be notified and the study may be discontinued.

Expenses and payments
Neither you nor your doctor will be paid for taking part in this study.

What do I have to do?
As described in above section on 'What will happen to me if I take part?'

There is no study medication involved and you can continue all the medications given to you by your doctor as part of your clinical care. You can participate in the study if you are involved in other studies.

What are the alternatives for diagnosis or treatment?
Alternative is to not participate in the study and undergo routine heart tests at regular intervals as per current standard of care

What are the possible disadvantages and risks of taking part?
The purpose of regular screening for heart vessel blockages is to prevent the development of a heart attack, and therefore it is possible that patients who are not regularly screened may be at increased risk of heart attack. We believe that this risk is similar or lower than the risks of regular screening but will carefully monitor subjects assigned to both screening strategies for any imbalance in heat attacks or related complications between groups.

You should discuss the risk of this study with the doctor. The study will be monitored by an independent data safety monitoring committee that will ensure the safety of all participants in this study. If there is an increase in adverse events noted in any group, you will be notified and the study may be discontinued.

What are the possible benefits of taking part?
Currently, heart tests are done routinely for patients on kidney transplant wait list without clear evidence that this is beneficial to the patients who don't have any symptoms suggestive of heart vessel blockages. These tests and interventions that may follow are not without risks. They can also lead to unnecessary suspensions from transplant wait lists, delay in getting back on to the list and may reduce the chance of getting a kidney transplant.

If you participate in the study and get randomized to the arm in which routine tests are not done, that would mean less hospital visits and investigations for you. If you are randomized to the 'standard of care' arm, you will continue to have tests as per usual protocol.

What happens when the research study stops?

After the study stops and if you haven't yet received a kidney transplant, you will continue to receive your usual care from your Hospital team with no effect on your transplant wait list status.

What if there is a problem?
Any complaint about the way you have been dealt with or any possible harm you might suffer will be addressed. The detailed information on this is given in part 2.

Will my taking part in the study be kept confidential?
Yes, we will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1. *If the information in Part 1 has interested you and you are considering participation, please read the additional information in part 2 before making any decision.*

COVID-19 Precautions
As you are most likely aware, due to the outbreak of Covid-19 (Coronavirus) St Georges, like other hospitals, is treating Covid-19 patients. We are taking extra steps to ensure both staff and patients are kept safe at all times and to prevent any further spread.

We would like to reassure you that we are taking every step possible to ensure your visit is as safe as possible, as part of this you will be asked to follow our Hospital policy on social distancing and PPE whilst you are here for your visit.

Staff will be adhering to strict cleanliness guidelines and, in some cases, this may mean full PPE.

Please attend for the appointment on your own if at all possible. Do not bring any children or relatives. Exceptions to this are official Carers or a Parent / Guardian of a Paediatric Patient.

Please don't attend if you:

1. Have been informed that you are in a vulnerable group and should not attend hospital (unless specifically instructed by your doctor that the scan is needed)
2. Have a household member, or are yourself, currently experiencing any COVID-19 symptoms

Then you must stay at home and please contact us to let us know so we can postpone your appointment. If you feel your appointment is no longer needed, please let us know.

Further Note:

Routine medical appointments are an exception to social isolation rules.
Unless you have received a shielding letter, or are currently self-isolating due to COVID-19 exposure, you are permitted to travel to your appointment.

If you have concerns, please don't hesitate to contact us (see below for details)

PART 2:

What if relevant new information becomes available?
If this happens, your research doctor might consider you should withdraw from the study. He/She will explain the reasons and arrange for your care to continue. OR If the study is stopped for any other reason, we will tell you and arrange your continuing care.

What will happen if I don't want to carry on with this study?
If you withdraw from the study, you will continue to stay on the transplant wait list and continue with tests and procedures as required by the protocol to stay on the list.

Complaints:
If you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study, then speak with the researchers who will do their best to answer your questions or concerns. The normal National Health
Service complaints mechanisms are also available to you.
PARTICIPATING SITES TO ENTER CONTACT DETAILS FOR LOCAL PALS DEPARTMENT
If you are still not satisfied with the response, you may contact the Joint Research and Enterprise Office at St George's by emailing researchgovernance@sgul.ac.uk

Harm:
In the event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for legal action for compensation against the Sponsor (**the University of British Columbia, Canada [PENDING**]), but you may have to pay your legal costs. The normal NHS complaints mechanism will still be available to you.

Will my taking part in the study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential, and any information about you which leaves the hospital/surgery will have your name, address and any other identifiers removed so that you cannot be recognized.

How will we use information about you?
We will need to use information from you for this research project. This information will include your name, contact details, date of birth, NHS and Hospital number. 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. Your data will have a code number instead.

We will keep all information about you safe and secure.

Some of your information will be sent to Canada and Australia. They must follow our rules about keeping your information safe.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

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. 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 study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?
You can find out more about how we use your information:

SITES TO ENTER LINKS TO RELEVANT PRIVACY NOTICES

For general information on how the NHS uses research data please visit https://www.hra.nhs.uk/information-about-patients/

What will happen to any samples I give?
[PENDING]

Will any genetic tests be done?
No.

What will happen to the results of the research study?
The results of the study will be disseminated locally, shared with transplant groups locally, regionally and nationally. Any presentations or publications with have anonymised data.

Who is organising and funding the research?
The research is being funded by the Canadian National Institutes for Health Research and is being organised internationally by the University of British Columbia, Canada.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee (REC), to protect your interests. This study has been reviewed and given favorable opinion by _____ Research Ethics Committee.

Further Information and Contact Details

If you require specific information about this research project please contact our research team: _____ (Principal Investigator), Tel:_____, Email:_____

You can also discuss your participation with your regular doctor and/or your GP.

You will be given a copy of this information sheet and a copy of the signed consent form to keep. Thank you for considering taking part in this study.