PARTICIPANT INFORMATION SHEET

Investigation of factors underlying heart disease and stroke – the LOLIPOP study
REC Ref: 07/H0712/150. Version 7. 12th December 2012.

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish.

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

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.

Part 1

1. What is the purpose of the study?

Heart attack and stroke are major, common medical problems. We know some of the reasons why heart attack and stroke occur - for example smoking, high blood pressure and high blood fats are all important causes. However, many people develop heart attack or stroke without having any clear reason.

The purpose of this study is to improve our understanding of the causes of heart attack and stroke. We are trying to work out why some people, but not others, develop these health problems. If we are successful, the results of the study will allow us to better identify which people are at risk of heart attack and stroke. Better understanding of the causes of heart attack and stroke may also lead to the development of new treatments for these conditions.

2. Why have I been invited?

We have contacted you because you previously agreed to participate in this research study (the LOLIPOP study). We are now recontacting all 30,000 people who participated in the LOLIPOP study, so that we can get an up-to-date assessment of their health and work out who might have had a problem with heart attack or stroke since we last saw them.

3. Do I have to take part?

Not if you don't want to. It is up to you to decide. We will describe the study and go through this information sheet, a copy of which will be yours to keep. If you agree to take part, we will ask you to sign a consent form. You are free to withdraw at any time, without giving a reason. This would not affect the medical care you receive.

4. What will happen to me if I take part?

You will be asked to attend Ealing Hospital for one visit lasting about one hour.

During the first visit, we will go through this information sheet and explain the study to you ourselves. You will receive a copy of this information sheet, which you can keep. You will also have access to the study protocol, which gives a more detailed and technical view of the study. We will answer any questions you may ask about the study. If you agree to take part, you will be asked to sign a consent form, a copy of which will be yours to keep.

After you have signed the consent form, we will ask you to complete a questionnaire about yourself and your health. This will ask questions about things like medical problems you may have had, admissions into hospital, symptoms of chest or other pain, memory, lifestyle and medications that you may be taking. A member of the research team will be available to help you answer these questions. As part of the research we may need to review your medical notes so that we can confirm the medical details of any suspected health problems that you tell us about. We would like your permission to do this.

Next we will take some measurements from you. These will be measurements of your height, weight, blood pressure and waist size. We will then record an ECG from you. This is a tracing of the heart that simply involves you lying still on a couch for a few minutes.

After that we will take a small blood sample (60mls, approximately 6 tablespoons**)** This will be sent for measurement of blood sugar and blood fats to diagnose diabetes and high blood fats, both risk factors for heart disease. Some of the blood will be stored for future testing, including tests for genetic factors that may lead to heart disease / stroke. More information on this is given in Part 2.

We will also ask you to provide a sample of saliva. In addition we will give you a stool sample swab kit to take home to collect two stool samples on separate days. The research staff will provide instructions along with appropriate appliances and containers to do this. Once collected, the stool samples are to be returned in the post using pre-paid jiffy bags provided by the research team. These samples will be used to study bacteria in your mouth and gut.

Finally, we will ask you to wear a physical activity monitor on your wrist for the next 7 days. The monitor is light weight (equivalent to a £2 coin) and resembles a wrist watch. You should wear it all day and night, but not in water (bath, shower, swimming). We will provide you with a prepaid jiffy bag to return the device to us after 7 days.

After these tests have been carried out, your direct participation is complete. Once we have collated your results we will forward them to you. We shall include a copy for you to give to your GP.

After your visit is over, we would like to continue to monitor your health. This will allow us to work out who has remained well, and who has developed heart attack / stroke. We would therefore like your permission to use any records held by the NHS (hospital or GP) and by the General Register Office to keep in touch with you and to monitor your health status.

Your future treatment will not be affected by participating (or not participating) in this study.

5. Expenses and Payments

We are happy to reimburse your travel expenses to and from Ealing hospital.

6. What will I have to do?

We will ask you to come to Ealing Hospital for a single appointment lasting about one hour. You will need to come fasting (nothing to eat or drink except water for 8 hours prior to the appointment).

At the visit we shall ask you to do the following:

- Read this information sheet, ask us any questions you like, and sign a consent form
- Complete a questionnaire about your health and lifestyle
- Allow us to measure your height, weight and blood pressure
- Lie still on a couch for 5 minutes so that we can record an ECG (heart tracing)
- Allow us to take a small blood sample
- Allow us to take a saliva sample
- Provide two stool samples using a stool sample swab kit
- Wear a wrist watch physical activity monitor for one week.

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

You may experience some mild discomfort from the blood test. No other risks are expected from the appointment.

There is a small chance that your results will show a significant abnormality of which you were unaware. In such circumstances you will be referred to the appropriate specialist in consultation with your GP, if that is what you would like. Such detection has the benefit of starting treatment early, but in a small number of cases may have implications for future employment and insurance.

8. What are the side-effects of any treatment received when taking part

There are no treatments involved in this study

9. Ionizing radiation

There is no radiation involved in this study.

10. Harm to the unborn child

Women of child-bearing age may participate in this study without risk, as the study does not involve treatment, invasive procedures or ionizing radiation.

Women who are pregnant though should defer their research study appointment until 3 months after the baby is born, as pregnancy has a number of effects on blood pressure, blood sugar and blood fats that make the research results difficult to understand.

11. What are the possible benefits of taking part?

The tests may reveal health problems about which you were previously unaware, for example diabetes, high blood cholesterol level, high blood pressure or heart problems. Such detection has the benefit of starting treatment early, which will help you to avoid complications.

We cannot promise the study will help you personally, but the information we get from this study will help improve the prevention and treatment of heart attack and stroke in the wider community, in the future.

12. What will happen next?

We may contact you again to invite you to take part in future studies. You may be asked to participate in these studies on the basis of genetic/biochemical results obtained from your sample as described above and other information given to us or obtained from your medical records. You will be provided with full information regarding each of these studies and will be free to decide whether or not to participate. We closely monitor the number of times you are approached and invited to studies and will ensure that the maximum number of invitations to studies will be 4 each year.

13. What happens when the research study stops?

We plan to follow your health through NHS and General Register Office records over the long term. This may be 20 or more years. Once the research is completed the data and results will be made fully anonymous (ie all personal information removed), and available for use by other researchers. Any remaining blood samples will be destroyed.

14. What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

15. 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.

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.

Part 2

More detail – information you need to know if you still want to take part

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

You are free to withdraw from the study at any time. Please talk to any member of the research team if you wish to withdraw. The research team may ask you why you are leaving the study. Explaining why will help us to design future studies. However, you do not have to give any reasons for your withdrawal if you do not want to.

If you withdraw from the study, we will destroy all your identifiable samples, but we may need to use the data collected up to your withdrawal. For example, where samples and data have been anonymised, we will not know the identity of the person who gave any particular sample. If data has been publicly shared on scientific databases we also will not be able to retrieve it.

2. What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (Professor Kooner and Dr John Chambers can both be contacted on 020 8967 5000). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Ealing Hospital NHS Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

3. Will my taking part in this be kept confidential?

We will keep your information in confidence, and in a way that meets the security criteria set by the Data Protection Act 1988. Professor JS Kooner will act as the custodian of the data.

Your research data will be anonymised (all personal information removed). Only your research doctors will have access to the key matching anonymous numbers with personal information. This means we will only tell those who have a need or a right to know (eg authorised persons such as research regulatory authorities). Wherever possible, we will only send out information that has your name and address removed.

The study is expected to last at least 20 years, and data and samples will be kept for this time. Once the research is completed, the data and results will be made fully anonymous (ie the key matching research data and samples to personal information will be destroyed). The fully anonymised data may be available for use by other researchers.

4. Involvement of your GP.

We would like to inform your GP that you have taken part in the study, but will only do this if you agree. We will also provide you with a copy of your key test results (such as high blood sugar levels requiring treatment) for you to give to your GP if you wish.

5. What will happen to any samples that I give?

As part of this study we wish to store small amounts of blood, urine, stool and saliva for future testing. In addition some of the blood will be stored long term to allow us to study functional impact of genetic variants. We will keep your samples securely and in confidence. Professor JS Kooner will act as the custodian of the samples.

Your samples will be anonymised (all personal information removed). Only your research doctors will have access to the key matching the anonymous samples with personal information. This means we will only tell those who have a need or a right to know (eg authorised persons such as research regulatory authorities). Your samples will be kept in secure databases freezers. They will only be accessible to authorised researchers.

Because technology and analysis tools develop all the time, it isn't possible to give you an exact list of everything that might be done with your samples/information in the future. Our aim is always to work towards the benefit of patients and communities. In doing so, we may feel it is beneficial to work with other hospitals, universities, research institutes, pharmaceutical and bio-technology companies, including organisations in other countries. They may have expertise, technology, and resources unavailable to us, which would be helpful in driving research forward to everyone's benefit. However, we won't share your information with any other organisation unless it is anonymised ie the information can't be traced back to you.

If we find out information which has implications for your future health or healthcare, or which we believe impacts on your interests, we will feed this back to. If you would rather not know, you have the option not to be told. If however your samples/information are put into fully anonymised form, you must understand that it will then no longer be possible to feed back specific results to you and any testing/research done will not be available to you.

The role of an individual sample/set of information in any commercial project is likely to be minimal and impossible to quantify. Therefore it is not possible to trace back any benefit to individual donors and you should regard participation in the project as being for the benefit of the community at large. No financial benefits from exploiting the results of the study will come back to you.

The study is expected to last at least 20 years, and samples will be kept for this time. Once the research is completed, any remaining blood samples will be destroyed.

6. Will any genetic tests be done?

Some of the research and testing on your sample may be genetic in nature as this can be the most powerful way to discover the causes of disease/defects and to treat and deal with these by developing new drugs and treatments. For example we may try to find variants in genes that protect against or increase the risk of heart attack and stroke. This may include "sequencing" the DNA samples to read all the genetic information in it.

Because technology and analysis tools develop all the time, it isn't possible to give you an exact list of everything that might be done with your samples/information in the future. We will not contact you directly about these individual genetic studies, as this would be impractical given the numbers of persons participating in the research.

Our aim is always to work towards the benefit of patients and communities. In doing so, we may feel it is beneficial to work with other hospitals, universities, research institutes, pharmaceutical and bio-technology companies, including organisations in other countries. They may have expertise, technology, and resources unavailable to us, which would be helpful in driving research forward to

everyone's benefit. We will not your information with any other organisation unless it is anonymised ie the information can't be traced back to you.

There is a small chance that we may find out information from the genetic tests which has implications for your future health or healthcare or which we believe impacts on your interests. Such detection has the benefit of starting treatment early, but in a small number of cases may have implications for future employment and insurance. If you would rather not know the results of these tests, you have the option not to be told. If you would like to know the results, then we will feed them back to, and you will be referred to the appropriate specialist in consultation with your GP, if that is what you would like. If your samples/information have been put into fully anonymised form, you must understand that it will then no longer be possible to feed back specific results to you.

7. What will happen to the results of the research study?

If you wish, you will receive an individual report of medically relevant results from your tests. If you would rather not know, you have the option not to be told.

We plan to publish the overall results of the completed study in medical journals. You will not be identified in any publications.

The results of the research may also be shared through open access (public) scientific databases, including internet databases (www.HapMap.org is an example of such an approach). This will enable other researchers to use the data to investigate other important research questions. The results will be anonymised by removing all traditional identifying information (eg name, address, date of birth, NHS numbers).

8. Risks of personal identification from genetic data

We may generate lots of genetic information about the people whose samples are studied. This information may be put in open access scientific databases, available on the Internet to anyone who wants to look at it. Although only experts will know how to interpret this information, there is a small chance that somebody could figure out how to connect you with the information from the study of the sample you give; the information could then be used to discriminate against you or your family members. Currently, we believe this could happen only if somebody knew that you had given a sample to be studied for this project and did one of the following:

- Got another sample from you, found an expert to test that sample, and then compared the genetic information from that test with the genetic information in the scientific databases.
- Found an expert to compare the genetic information about you in the scientific databases with information known to have come from you (or from a family member) included in some other database developed by someone else for some other purpose.
- Found an expert to look in the scientific databases for a particular genetic variation known (or someday found) to be associated with a disease or trait that you have or carry, that others know about or can see, and that is very rare.

Any of these things would require that the person trying to link the information to you knew that you participated in the project. For this reason, to minimize these risks, you may wish to limit the number of people you tell about your participation.

As technology advances, there may be new ways of linking information back to you that we cannot foresee now. Also, we cannot always foresee the results of research, so new risks may come up in the future that we cannot predict now. We believe that the benefits of learning more about human genetic variation and how it relates to health and disease outweigh the current and potential future risks, but this is something that you must judge for yourself.

9. Risks to community

The names of the ethnic or geographic groups the samples came from will be included in the scientific databases. In future studies, researchers may find that certain metabolic or genetic variations appear more often in people from your group than in people from other groups, and that these variations are more common in people with a certain disease. This may make some people look down on your group unfairly. Some people may use the information from the scientific databases, or from future studies using the scientific databases, to exaggerate differences between groups for prejudiced or other bad reasons. Others may use the information to downplay differences between groups, to say that all people's genes are about the same, so we don't need to respect the special concerns of different groups. Biology does not provide a reason for prejudice, but discrimination does exist. We will work to make sure that the ethnic or geographic identity of your community is described as carefully as possible - in the sample collection, in the scientific databases, and in articles that project researchers write based on this research, but we cannot completely control how this information is described in publications that others write.

10. Who is organising and funding the research?

The research is organised by Professor Kooner and Dr Chambers. The research is funded by the British Heart Foundation, the Medical Research Council, and grants have also been submitted to the Wellcome Trust and the National Institute for Health Research. Additionally, we hold unrestricted grants from the Pharmaceutical Industry. Your doctors will not receive any payment for including you in the study.

11. Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee to protect your safety, rights, well-being and dignity. This study has been reviewed and given favourable opinion by the St Mary's Hospital Research Ethics Committee.

12. Further information and contact details

For general information about research, please see

MRC Clinical Trials Unit (http://www.ctu.mrc.ac.uk/TakePart.asp). This provides useful advice for potential participants in research.

For further information about this research project, or if you are unhappy with any aspect of the study, please contact:

Professor Jaspal S Kooner, Consultant Cardiologist, Ealing Hospital, Uxbridge Road, Middx UB1 3HW, telephone 020 8967 5000, fax 020 8967 5007.

Dr John Chambers, Consultant Cardiologist, Ealing Hospital, Uxbridge Road, Middx UB1 3HW, telephone 020 8967 5000, fax 020 8967 5007.