NIHR | Leicester Biomedical Research Centre

The GENVASC Study

Chief Investigator, Professor Nilesh Samani

At the Heart of Research

Practice Study pack

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Practice Information

The **GENVASC** Study

The purpose of this brief document is to provide some background on the GENVASC Study and to explain what participation would involve for the practice.

Objective: The main purpose of the GENVASC Study is to determine if addition of genetic information can improve risk prediction of coronary artery disease (CAD).

Why is the GENVASC study important? Currently we use risk scores such as Framingham or QRisk2 scores to classify individuals into low (< 10%), medium (10-20%) and high (> 20%) 10-year CAD risk to help target primary prevention measures to those at highest risk. While targeting such individuals is clearly beneficial, because many more subjects are located in the intermediate or low risk categories, although their proportional risk is lower, in absolute terms more events actually occur in these groups. Improving the accuracy of risk categorisation for CAD is therefore a high public health and clinical priority.

Inheritance plays an important role in the aetiology of CAD but a family history is neither a sufficient or accurate surrogate for an individual's genetic risk. The risk to an individual is 4-8 fold higher if a first degree relative has died prematurely of CAD. The heritability of CAD is estimated at around 50%. In some, especially more recent risk scores, a "family history" of CAD is included in the algorithm. However, identifying a positive family history due to inheritance has significant limitations. Family history based on recall can be notoriously inaccurate. Algorithms vary in the age cut-off used to define a positive family history. Furthermore, an individual's family may not be sufficiently large (e.g, no siblings) to assess genetic risk; finally family members could have died from competing causes (e.g. cancer or road traffic accidents) before manifesting CAD, or could have developed CAD but due to a strong lifestyle factor such as heavy smoking.

Recent progress in understanding the genetic basis of CAD: In the last 5 years there has been remarkable progress in identifying individual genetic variants that affect risk of CAD, much of the work being led from Leicester. Currently, over 40 variants (each carried by between 10-80% of the population) have been identified that increase risk of CAD (by between 5-30% per copy of each variant). Individually, the genetic variants do not have sufficient discrimination to individually change risk prediction sufficiently. However, a Genetic Risk Score (GRS) based on combining the variants could be more powerful. Indeed, in a recent study we showed that there was a > 3-fold difference in risk of CAD between those subjects in the highest quintile compared with those in the lowest quintile for a GRS score based on 25 of the initially identified CAD-associated variants. This is similar to or greater than the strength of association seen with other established risk factors such as blood pressure and cholesterol. Addition of further variants as they are discovered to the GRS is likely to further improve its risk prediction potential. ***Therefore, recent discoveries on the basis of CAD now provide a framework for testing whether adding genetic information in the form of a genetic risk score can improve current risk prediction of CAD.***

The NHS Health Check Programme provides an ideal opportunity for testing whether a GRS for CAD can improve risk prediction. To test whether a GRS for CAD could be of clinical benefit requires the assembly of a large cohort of individuals representative of the general population who are: (i) free of overt CAD at recruitment (ii) assessed in a uniform fashion for their CAD risk and who can (iii) provide blood samples for genetic analysis and (iv) be followed up systematically for CVD outcomes. Assembling such a cohort for research purposes only would be hugely expensive. In this context, the recently initiated Department of Health NHS Health Check Programme provides an ideal unique opportunity to establish such a cohort as it specifically targets all individuals in the appropriate age range (40-74 years) free of CVD. The large number of subjects that will be assessed in a systematic manner for cardiovascular risk and who will all have blood samples routinely collected provides an ideal scenario to add a research project at marginal cost and effort that can help determine whether inclusion of genetic information will be useful in predicting CAD risk in clinical practice. Our aim is to recruit in excess of 30,000 participants by March 2022.

The GENVASC Study has received ethical approval and is adopted onto the NIHR portfolio. The GENVASC Study is being led by Professor Nilesh Samani, Professor of Cardiology and run by the NIHR Leicester Biomedical Research Centre based at Glenfield Hospital. Its adoption on the NIHR Portfolio means that we can provide training for staff in the practice and meet support service costs incurred by the practice. Further details on the payment that will be made are given on the collaborative agreement form to be signed by participating practices.

What does this mean for your practice and your patients?

As one of our contributing recruitment centres, your team will be asked to invite and recruit NHS Health Check candidates into the GENVASC study at the time of their NHS Health Check.

This includes

- Obtaining consent for use of data and samples.
- GENVASC study participation flagged on NHS Health Check template
- Study samples drawn in conjunction with the routine NHS Health Check clinical samples.
- Study samples bagged and transported using the routine Department of Haemotology & Biochemistry transit arrangements.
- Relevant participant data supplied centrally.

A simple and adaptable recruitment process has been devised, to suit the differing service delivery models in individual practices (Figure 1).

Training and support will be offered through your protected learning time and at a local level by our study team.

Study materials, including a site file folder and local study administration guidance, promotional posters and patient information leaflets will be provided.

Reimbursement will be provided based on the number of participants recruited. The service support costs, £16 per recruit, is based on an approximation of time, (25 minutes), across the potential grades of staff, GP/Nurse/HCA for administration,explanation and consent into the study.

The GENVASC study will not interfere with the primary imperative of the NHS health Check programme. There are no additional treatments or additional information to gather.

We hope that you agree to participate in this simple but important project with potentially major benefit in the future for preventing CAD.

The GENVASC recruitment process

Figure 1 recruitment process

Consultation
Patient attends GP practice for NHS Health Check.

Consent
Invitation to participate in GENVASC & Consent at first point of contact.

Samples
GENVASC study samples requested and drawn in conjunction with NHS Health Check clinical samples.

Sample Transit
Study samples bagged and transported using the routine department of Haematology & Biochemistry transit arrangements.

Data
Participant Data Acquisition.

GENVASC COLLABORATION AGREEMENT REC #12/EM/0208

This constitutes an agreement between (the Practice) .....

at (address) .....

and the NIHR Leicester Biomedical Research Centre, University of Leicester, Glenfield Hospital, Groby Road, Leicester, LE3 9QP.

The Practice agrees to the following:

1. ETHICS AND GOOD CLINICAL PRACTICE

1.1 Abide by the Research Governance Framework 2005, Human Tissue Act 2004 and GDPR 2018.

1.2 Maintain a site file in respect of this project including

1.2.1 Documentation of personnel working on the project

1.2.2 Details of breaches of GCP or the protocol

1.2.3 Retain all original consent forms

2. RECRUITMENT AND SAMPLING

2.1 Invite eligible patients to participate in the project

2.2 Seek informed written consent for participation

2.3 Follow the procedures described in the protocol

2.4 Use the approved Information Sheet, Consent Form and Site File templates provided for the project

3. LOCAL SUPERVISION

3.1 Ensure that all personnel working on the project are appropriately trained and supervised, particularly in Good Clinical Practice, consent and the study protocol and procedures

4. DATA ACCESS

4.1 Permit CCG processes to supply clinical data to the NIHR Leicester Biomedical Research Centre.

4.2 Permit access to inspection or audit by the Research Sponsor or UK authorities to ensure the study is being conducted properly.

The NIHR Leicester Biomedical Research Centre agrees the following:

5. RESOURCES

5.1 The Practice will be paid £16 per participant recruited quarterly in arrears through the Primary Care Research Network

6. TRAINING AND SUPPORT

6.1 Provide training for personnel working on the project, through the Comprehensive Research Network

6.2 Provide, through the Main Site Study Team and the CRN, ongoing support and advice to participating Practices

7. AUTHORISATION

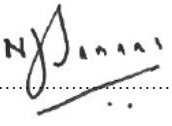
Signed on behalf of the Practice by:

Name..... Signature .....

Role ..... Date .....

Signed on behalf of the by: NIHR Leicester Biomedical Research Centre,

Name **Professor NJ Samani** Signature .....



Role **Chief Investigator GENVASC** Date .....

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University Hospitals of Leicester
NHS Trust

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