



**Genetic Cancer Prediction
through Population Screening
GCaPPS**

What is GCaPPS?

Please take the time to read the following information and discuss it with others (your family, friends or other healthcare professional) if you wish. Please ask if there is anything you do not understand or if you would like more information.

GCaPPS is a research study evaluating the feasibility of offering genetic testing to everybody in the population. The aim of this genetic test (a straightforward blood test) is to identify individuals at high risk of developing cancers linked to certain inherited gene alterations.

Background information

Genes are basic units of inheritance. They contain the blueprint of all hereditary information. Genes are made up of building blocks called DNA. Each gene is a short sequence of DNA which corresponds to a unique set of instructions. These instructions are responsible for the characteristics of an individual. Some individuals may have an alteration in their DNA sequence or genetic code. This is called a mutation. Those who carry an alteration in certain specific genes are at a greater risk of developing cancer. Two such genes are known as the BRCA1 and BRCA2 genes (pronounced 'brakka-1' and 'brakka-2'). They repair damaged or defective DNA or genes and protect the body from cancerous changes. You can think of them as acting rather like policemen in the cells.

Individuals carrying an alteration in the BRCA1 and BRCA2 genes have a high risk of developing breast, ovarian and prostate cancer. Each of their children (irrespective of sex) has a 50%, or 1 in 2, chance of inheriting the altered gene. Established early detection and preventive strategies such as screening and

surgery are available to address the cancer risk of these 'at risk' individuals.

Technology to identify 'at risk' individuals who carry an altered gene now exists. This involves a straightforward blood test just like any other blood test. However, at present this test is only available (on the NHS) to individuals who have a strong family history of cancer. In addition, individuals from these families need to take the initiative to contact their doctor. However, many people may be unaware of their family history or may not have relatives who have had cancer. Hence, this strategy fails to identify a large proportion (over 40%) of 'at risk' people.

Special attention needs to be given to some population groups known to include frequent BRCA alterations. These include Ashkenazi Jews and some individuals of Swedish, Norwegian, or Icelandic origin. Up to 1 in 40 Ashkenazi Jewish individuals carry such an alteration in the BRCA 1 and 2 genes and thus are at increased risk. This is around 10-20 times higher than the general (non-Ashkenazi Jewish) population.

There are over a thousand different types of alterations in these genes. However, in the Ashkenazi Jewish population only three alterations have been found to be very common. These three alterations account for 96% of the BRCA-related risk. These have been called 'founder mutations' because they arose in a small isolated group of 'founders' (ancestors), who gave rise to most of the individuals in the present-day Ashkenazi

Jewish population. Two of these alterations are found in the BRCA1 gene and one in the BRCA2 gene.

Genetic testing – which comprises a straightforward blood test - will provide an opportunity to identify 'at risk' individuals carrying founder mutations. This will allow these individuals to choose options of early detection or prevention to minimise their risk of developing cancer.

Questions & Answers

What will the project provide?

GCaPPS will:

- provide genetic counselling and education on the genetic risk of breast, ovarian and prostate cancer;
- provide lifestyle advice on reducing the risk of cancer;
- offer a blood test to identify those individuals who have a BRCA gene alteration (founder mutation) and are therefore at higher risk of developing these cancers;
- offer those found carrying a BRCA alteration, cancer risk reduction and prevention options;
- refer 'at risk' individuals to

genetic clinics to enable them to access early detection and preventive options;

- provide post-test counselling support;
- follow up participants after testing to assess outcomes.

What are the aims of the project?

- This study aims to identify the best method of screening the Ashkenazi Jewish population for individuals at increased risk of genetic cancer.
- This project compares the option of testing everyone with the current practice of testing only

those with a high-risk family history.

- The project hopes to show that the approach of testing everyone would identify more carriers of gene alterations.
- It will also evaluate the acceptability and psychological impact of testing, the effect on quality of life, uptake of preventive options and the cost of such an approach.
- We aim to develop a strategy for prediction and prevention of genetic cancer. Over the long term we hope this will reduce cancers in the community.

When does the project begin and how long will it last?

It is anticipated that the project will begin in the autumn of 2008. There will be an initial pilot phase which will screen 1,000 individuals. This may take up to one year. This will be followed by the core phase of the project which hopes to screen 9,000 individuals and this may take up to three years. Individuals tested will be followed up for up to three years to ascertain the impact of testing.

Who can participate?

You may take part if you are over the age of 18 years and have four Ashkenazi Jewish grandparents.

The GCaPPS team at the Coordinating Centre at University College London (UCL) will assess and confirm your eligibility for you.

What do I have to do to take part in the project?

You will need to register your interest by informing the GCaPPS team at UCL. You may already have done so by sending the reply slip attached to the study pamphlet. In case this has not been done, you can do so by filling in the slip at the end of this leaflet and sending it (Freepost) to the GCaPPS team at the following address (you do not need to attach a stamp to the envelope):

“Freepost RRYB-GZET-UXCK,
GCaPPS,
University College London,
GCRC
London W1T 7DN”

Alternatively you can send an email gcapps@ucl.ac.uk or letter (postal address on page 12) regarding your intention to register along with your name, address, age and telephone number to the GCaPPS team.

You will need to undergo a genetic counselling session with a genetic counsellor. This will be organised for you by the GCaPPS team. The counselling session(s) and

additional educational materials provided will help you decide if you wish to undergo genetic testing and participate in the study. Following counselling if you decide to go ahead you will need to sign a consent form in order to participate in the study.

Prior to seeing the counsellor you will be asked to complete a baseline questionnaire. This will be done at the counselling centre. You will also be sent a family history form prior to your appointment. You will need to fill in this form and bring it to give to the genetic counsellor at the appointment. It is important you fill in the form beforehand as this information will be used in the counselling session.

How do I make an appointment to see the counsellor?

The GCaPPS team will contact you and send you an appointment after you have registered your interest.

What if I do not know whether all four of my grandparents were of Ashkenazi Jewish descent?

We appreciate that many people may not be sure if all four grandparents were of Ashkenazi Jewish descent. Self-reported Ashkenazi Jewish origin on both sides as far as can be ascertained

may be the best you can do. There is no means to confirm this and neither is this necessary. You can still join the study even if you are unsure if all your grandparents were of Ashkenazi Jewish descent. However, if individuals are aware that one or more of their grandparents were definitely not Ashkenazi Jews, they would be excluded from the study and not be eligible for testing.

Do I have to undergo testing?

No, you do not have to take part if you do not wish to. Participation is completely voluntary. Even if you decide to take part and change your mind later, you are free to withdraw from the project at any time and you do not have to give a reason. This will not affect any future care you receive. In addition should you change your mind after providing a blood sample, you can still opt out of having the genetic test if you inform the GCaPPS study team of your decision within three weeks of providing the blood sample.

Can I take part even if I do not want to get tested?

We are interested in hearing from all eligible individuals even if they feel they do not want to take the test. If eligible you will be invited to attend the counselling sessions.

You can decide if you wish to get tested after counselling.

What happens if I decide not to take part?

We will ask you to fill in a form to assess the counselling you received and your reasons for not undergoing testing. This too is completely voluntary. You do not have to fill in this form if you do not wish to.

Is there any cost for having the test done?

No, there is no cost for joining the study or having the test done.

Where will I be tested?

Facilities for screening or testing will be available at a number of centres in the community. You can choose to undergo counselling and testing at any centre convenient for you. Testing consists of a straightforward blood test (like any other blood test). The names and addresses of the centres are listed at the end of the leaflet.

There isn't any cancer in my family – should I still undergo testing?

Although having a strong family history of cancer increases the likelihood of carrying a gene alteration, up to 4 in 10 individuals carrying the gene alteration may

have no family history of cancer. Screening only those with family history may thus miss a number of individuals at risk. Therefore, it is still worth taking the test even if you do not have a family history of cancer.

How confidential is the genetic test?

The genetic test will be absolutely confidential. Any information provided will be stored on a secure username/password protected database. Your GP will be informed that you have agreed to take part (unless you request otherwise). Your participation in the study and all the information you supply will be treated as confidential and not released to anyone else outside the study.

What are the potential benefits of joining the project?

The project will provide information regarding genetic risk of cancer through a simple blood test. It will provide counselling to help you decide if you would like to get tested. It will provide the opportunity to find out if you are at a high or low risk of developing cancers linked with BRCA alterations. This might provide the opportunity to reduce uncertainty and alert relatives. If found to be 'high risk' you will be able to

opt for increased surveillance or preventive measures. You will also get information on lifestyles aimed at reducing risk of cancer. This may, over the long term, help reduce the number of people developing cancer in the community.

What will happen to me if I take part? What does becoming involved entail?

After receiving counselling and signing a consent form, you will be asked to have a simple blood test.

Participants who have provided a sample will be divided into two groups. In the first group (Systematic Screening group) everyone will undergo testing. In the second group (Family History group) only those who have a high risk of cancer based on family history will undergo testing. It may take 1-3 months to receive the test results.

A health questionnaire will be sent to you 7 days, 3 months, 1 year, 2 years and 3 years after you receive your test result. You need to fill this in and send it back by Freepost.

With your permission the research team will also request that relevant information regarding your future medical care be sent to them by the Office of National Statistics (ONS).

Can I choose which group I wish to belong to?

No, it is important for the study that people are randomly assigned to the two groups. This will be decided by a computerised programme.

What if I am allocated to the Family History group and do not undergo testing but wish to do so?

In this case you will get the opportunity to undergo testing at the end of the study if you choose.

Are there any situations where I will not be eligible for testing or participating in the study even if I am over 18 and have four Ashkenazi Jewish grandparents?

If you have undergone testing for the three Ashkenazi Jewish founder mutations before joining the project, this will not be provided again in the study. If a first degree relative such as your mother, brother or sister is already known to carry a BRCA founder mutation you will not be allocated to either of the two arms of the study. However, you can still opt for testing and the GCaPPS team will offer full support and refer you to the clinical genetic units.

What happens if I test positive?

A positive result indicates that you have inherited one of the three common BRCA gene alterations found in Ashkenazi Jews. This suggests that you are at a higher risk of developing breast, ovarian or prostate cancer.

If you test positive you will see a genetic counsellor, who will help guide you and explain your options of managing your risk of developing cancer. This includes:

- lifestyle advice
- medical prevention
- screening: Yearly surveillance programmes starting at 30-35 years are available for early detection of breast cancer. You can decide to join ongoing research trials for early detection of ovarian and prostate cancer.
- surgical prevention: Surgery to remove breast tissue or tubes and ovaries can prevent cancer.

The genetic counsellor will inform your GP and ensure that you are referred to a specialist genetic unit for further counselling and follow-up. You will be able to see relevant specialists and access these preventive options through the genetics clinic. The GCaPPS team

will also keep in touch with you over the following three years.

What happens if I test negative?

If you test negative it is very likely that you have a low risk of developing cancer i.e. you are not high risk. Your risk is the same as the rest of the general population. You should continue to have cancer screening just as everyone else does (such as mammogram screening for breast cancer for women over 50). You will still be followed up by the GCaPPS team over the next three years.

If you test negative for the three Ashkenazi Jewish founder mutations but fulfill certain 'high-risk' criteria related to multiple cancers in the family, you will be referred to a specialist genetics unit. The clinical genetics team will offer further advice and look for any additional rare gene alterations that may exist. The chance of finding another rare BRCA gene alteration is very small.

What are the disadvantages or drawbacks of taking part?

Some people who receive positive genetic test results may feel frightened or sad or upset about their test result, or guilty about

passing altered genes to their children and rarely may even feel depressed. This is something to discuss with your counsellor if you are worried. Most available scientific information (obtained from high-risk families) suggests a negative test result is associated with reduced cancer worry and anxiety, and a positive test result usually does not lead to adverse psychological consequences. However, the long term psychological effects of testing, especially on quality of life, are not known. This study hopes to answer these questions.

The study tests for three gene alterations (founder mutations). In the Ashkenazi Jewish population, these three alterations are responsible for most of the cancer risk related to the BRCA gene. The chance of carrying a BRCA gene alteration apart from these three is very small. This possibility has been reported to vary between 0% and 4% in individuals who have a strong family history of cancer and have tested negative for the three alterations. The opportunity of testing for a rare alteration will also be provided through referrals to genetic clinics. This will be available to individuals who have a strong family history of cancer and have tested negative for the founder mutations.

Insurance issues: Questions have been raised regarding the impact of a positive test on insurance and employment. Currently in the UK a concordant between the British government and the Association of British Insurers (ABI) provides a moratorium on the use of predictive genetic test results, by all insurers until 2014. Insurance companies are not allowed to ask for predictive genetic test information. The moratorium includes the caveat that 'customers will not be asked to disclose any predictive or diagnostic genetic test result acquired as a part of clinical research'. However, at present it is unknown whether this moratorium will persist after 2014. You can obtain more information from:

http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4105905

or via a link on the GCaPPS website.

Employment issues: It has been suggested that testing may adversely effect employment. The new UK Employment Practices Code advises that employers should not use genetic testing to obtain information that is predictive of a worker's future general health, nor

insist that a worker discloses the results of a genetic test. It states that employers should not make employment conditional on an individual taking a genetic test. You can obtain more information from:

http://www.ico.gov.uk/upload/documents/library/data_protection/detailed_specialist_guides/employment_practices_code.pdf

or via a link on the GCaPPS website.

Some individuals may feel that undergoing genetic testing is discriminatory and testing positive may lead to social exclusion or poor marriage prospects. The issue of marriageability may be particularly relevant for some sections of the Jewish community where arranged marriages are the norm. It is extremely important for individuals to carefully consider all implications including the issue of future marriage prospects before they decide to participate in this research study.

You must feel free to discuss this or any other questions with the study team.

Sample storage

With your permission, a portion of your blood taken at your genetic test and some extracted DNA will be stored in our serum, plasma and DNA bank for research purposes under the custodianship of Professor Ian Jacobs, at UCL.

The stored blood, DNA and tissue may be used for future research studies, which may include genetic analysis. These studies will not be of direct benefit to you, but we hope will benefit others in the future. In order to ensure that your personal information remains confidential, your blood, DNA and tissue samples will be anonymously coded. Only the GCaPPS research team will be able to trace a sample back to you. Other researchers using your samples will not be able to tell from whom samples were obtained. If you are concerned about the use of your samples in any future research study, please do discuss this with a member of the GCaPPS team or the person recruiting you into the study.

You do not have to agree to allow the GCaPPS team to store your samples for use in future studies. If you do not wish to give permission for your samples to be used in future studies, this will not in any way affect your participation,

testing or any future care you receive. You are free to withdraw your consent for use of your samples for research purposes at any time. Any future research will have to seek the permission of a Research Ethics Committee. It is possible that research may include researchers working for commercial companies. You can take part in the GCaPPS study even if you do not wish any of your samples to be used for future research.

What if I decide to withdraw from the study after joining it?

You are free to withdraw from the study at any time, through personal choice or without giving any reason for doing so. In addition should you change your mind after providing a blood sample, you can still opt out of having the genetic test if you inform the GCaPPS study team of your decision within three weeks of providing the blood sample.

Who are the doctors/scientists involved in the project?

The project will be run by health professionals under the leadership of Professor Ian Jacobs and coordinated by University College London. It is the result of collaborative work with a number of leading doctors and scientists both in the UK and overseas.

The investigators are: Prof. Ian Jacobs (Dept. Gynaecological Oncology, UCL, UK), Dr Usha Menon (Dept. Gynaecological Oncology, UCL, UK), Dr Ranjit Manchanda (Dept. Gynaecological Oncology, UCL, UK), Dr Sue Gessler (Dept. Gynaecological Oncology, UCL, UK); Prof. Jane Wardle (Health Behaviour Unit, Dept. of Epidemiology and Public Health, UCL, UK); Dr Saskia Sanderson (NHGRI, National Institutes of Health, Bethesda, USA); Prof. Ian Tomlinson (Clinical Genetics, LRI, CRUK); Prof. Alistair McGuire (Health Economics, Department of Social Policy, London School of Economics, UK); Prof. Uziel Beller (Dept. of Gynecology, Shaare Zedek Medical Center, Faculty of Medicine, The Hebrew University of Jerusalem, Israel).

Who is funding the project?

The project is currently funded by the The Eve Appeal charity which supports groundbreaking research into gynaecological cancers and by Boots as part of their ongoing support of The Eve Appeal.

Who has reviewed the study?

The study has been reviewed and approved by the National Research Ethics Service (NRES) ICH/GOSH Research Ethics Committee. The Research Ethics Committee consists of healthcare professionals and

members of the public with no connection to the study.

What will happen to the results of the study?

The results of this study will not be known for some time, but will be made available using scientific and medical publications that anyone can access. You will not be personally identified in any such publications.

What happens when the research study stops?

When the research study stops, if you have been detected as carrying a BRCA gene alteration you will continue to be followed up at the regional genetic clinics. You will continue to receive full support and can opt for early detection and risk-reducing or preventative measures through these genetic clinics.

It is hoped that if this approach to testing for cancer predisposition is shown to be effective the NHS will develop a programme to offer it, but this is not guaranteed.

What if something goes wrong?

If you have any concerns or questions you should initially contact the GCaPPS team who will do their best to answer your questions. The contact details

are provided at the end of this information booklet. If there is something that you are unhappy with and wish to complain formally, you can do this through the Research Governance Sponsor of this study by writing to: Joint UCLH/UCL Biomedical Research Unit, R&D Directorate (Maple House), Rosenheim Wing, Ground Floor, 25 Grafton Way, London WC1E 5DB quoting reference 08/H716/29. All communication will be treated in strict confidence.

Every care will be taken to ensure your safety during the course of the study. However, UCL has special (no-fault) insurance arrangements in place in the unlikely event that something unforeseen goes wrong and you are harmed as a result of taking part in the research study. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal NHS complaints mechanisms will be available to you.

Where can I get further information about the project?

GCaPPS

Email: gcapps@ucl.ac.uk

Write to: GCaPPS,
c/o GCRC, Institute for Women's Health,
1st Floor, Maple House,
149 Tottenham Court Road,
London W1T 7DN.

Information is also available on the GCaPPS website:

www.gcapps.org.uk

The Eve Appeal

Website: www.eveappeal.org.uk/gcapps

For free impartial information please contact:

Ovacome

Email: ovacome@ovacome.org.uk

Website: www.ovacome.org.uk

Tel: 020 7299 6654

Helpline: 0845 3710554

Individuals with special needs.

If you have any special communication needs please let the GCaPPS team know. Every effort will be made to provide any special assistance required. Contact details for the GCaPPS team are listed above.

Counselling Centres:

- **Boots,**
32-34, The Broadway. Mill Hill,
London NW7 3LH
- **Norwood Hackney Family Centre,**
85a Lordship Road, London
N16 0QY (Tel: 020 8800 2777)
- **Agudas Israel Housing Association,**
Fradel Lodge, Schonfeld Square
Home, 1 Schonfeld Square,
Lordship Road, London N16 0QQ
(Tel: 020 8802 3819)
- **Redbridge Community Centre,**
Sinclair House, Woodford Bridge
Road, Ilford, Essex IG4 5LN

The project is supported by:

Boots



The Eve Appeal



Jewish Care

JEWISH CARE

Norwood

NORWOOD
CHILDREN & FAMILIES FIRST

Ovacome

ovacome
the ovarian cancer support network

Liberal Judaism (Rabbi Danny Rich)

liberal judaism

Movement for Reform Judaism (Rabbi Tony Bayfield)

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Academic Study Group on Israel & the Middle East

Supporting individuals: Rabbi Dr M Jacobi, Dr Marlena Schmool

and many others

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Reply Slip Please complete and return this slip in an envelope to the Freepost address:

Freepost RRYB-GZET-UXCK, GCaPPS, University College London, GCRC, London W1T 7DN

*I would like to attend a genetic counselling session / participate in the GCaPPS project. (please tick)

*Name: _____ *Age: _____

† Address: _____

† Email: _____

† Telephone: _____ † Mobile: _____

*Signature: _____ *Date: _____

*Essential items † At least one of these methods of contact is essential