

Royal Marsden Gynae Unit

BRCA testing learning resources pack (MCG LRP2)

Please read all the information in this pack.

You may also find it useful to return to this information when you are BRCA testing.

You should use the information in conjunction with the e-learning modules MCG ELM1, MCG ELM2, MCG ELM3b and MCG ELM4.

The pack includes the following:

- MCG P2 – Ovarian cancer BRCA testing protocol
- MCG IS1 – BRCA1 and BRCA2 gene testing - Information sheet for patients with cancer
- MCG IS2 – Receiving a normal BRCA1 and BRCA2 test result - Information sheet for patients with cancer
- MCG IS3 – Receiving a BRCA1 and BRCA2 test result that identifies a mutation - Information sheet for patients with cancer
- MCG IS4 - Receiving a BRCA1 and BRCA2 test result that identifies a variant requiring evaluation (VRE) - Information sheet for patients with cancer
- MCG F1 – Consent for genetic testing
- MCG F2 – BRCA gene test request form
- MCG FAQ1 – BRCA1 and BRCA2 gene testing - frequently asked questions for breast and gynae units
- e-learning module 1 (MCG ELM1) summary information
- e-learning module 2 (MCG ELM2) summary information
- Ovarian cancer BRCA testing checklist

Ovarian cancer BRCA testing protocol

Cancer Team

Patient with non-mucinous ovarian cancer

Actions by approved Cancer Team member:

1. Information sheet (MCG IS1) given to patient.
2. BRCA gene testing discussed.
3. Consent (MCG F1) obtained and scanned onto EPR.
4. Blood (2xEDTA) and request form (MCG F2) sent to lab.

More discussion required →

Refer to Genetics

Genetics Team

Result reviewed and interpreted by Genetics Team

NO MUTATION

MUTATION

VARIANT REQUIRING EVALUATION (VRE)

Actions by Genetics:

1. Result and information sheet (MCG IS2) sent to patient.
2. Result sent to Cancer Team.

Actions by Genetics:

1. Result and information sheet (MCG IS3) sent to patient.
2. Result sent to Cancer Team.
3. Genetics appt sent to patient.

Actions by Genetics:

1. Result and information sheet (MCG IS4) sent to patient.
2. Result sent to Cancer Team.
3. Genetics appt sent to patient.

Notes:
For FAQs (MCG FAQ1) see: www.mcgprogramme.com/BRCAtesting

BRCA1 and BRCA2 gene testing

Information sheet for patients with cancer

In most people cancer occurs by chance. In a minority of people with ovarian cancer (about 15%) or breast cancer (about 3%), cancer occurs because they have a mutation in the BRCA1 or BRCA2 gene. BRCA1 and BRCA2 mutations result in increased risks of breast and ovarian cancer. They occur more frequently in women who have both breast and ovarian cancer, those with particular types of cancer, and if there is a strong family history of breast and/or ovarian cancer. It is important to identify if a cancer is due to a BRCA1 or BRCA2 mutation because it provides you and your doctors with information that can help treat your cancer and to reduce your risk of future cancer. It can also provide information for relatives about their risks of cancer.

Why am I being offered this test?

You are being offered a test to look for mutations in BRCA1 and BRCA2 because of your cancer diagnosis.

What are the benefits to me?

Knowing whether or not you carry a mutation in BRCA1 or BRCA2 gives the cancer team more information about your cancer. This can help decisions about the treatments they recommend for you, for example which chemotherapy drugs or surgery would be most suitable. It will also give better information about your risk of developing cancer in the future.

Does having the test have implications for my family?

In most people the test will be normal and we will not find a gene mutation. This would be reassuring for relatives as it would indicate that your cancer was unlikely to be due to hereditary factors that would put them at very high risk of cancer. If your test shows you have a gene mutation, it is possible that some relatives also have the mutation. Relatives would be able to discuss this with a specialist geneticist and have a test if they chose to.

What will happen if NO mutation in BRCA1 or BRCA2 is found?

This is the most likely outcome, as most women with cancer do not have a mutation in BRCA1 or BRCA2. This would be reassuring in suggesting you are unlikely to be at high risk of developing another, new cancer in the future. The cancer team will be able to use this information in their management decisions. Very occasionally mutations in other genes can be involved in causing breast or ovarian cancer. Also new discoveries are



being made all the time. If a new gene test becomes available in the future the genetics team may be able to do the test using the sample you have already provided and would send the result to you and the cancer team. If your doctors think other genetic factors might be involved in your cancer they can ask the genetics clinic to send you an appointment to evaluate this, if you have not already had an appointment with genetics.

What will happen if a BRCA1 or BRCA2 mutation is found?

Your cancer team will use the information in their management decisions. The genetics team will send you an appointment to discuss the results and address any questions you have. They will also discuss what the test result means for your future risk of cancer, your options for future screening and measures to reduce these risks. They will evaluate your family history and can provide information for the appropriate family members should they wish to consider testing to see if they have inherited the mutation. Any relatives can be referred to a Genetics Unit, either at the Royal Marsden or more locally to them, to discuss this further.

What will happen if the test result is unclear?

Very occasionally (<1%) we find a gene change, known as a 'variant', that needs further assessment before we can decide if it is linked to why you have had cancer. If this occurs, the genetics team will send you an appointment to explain the result and to discuss with you what further information and/or tests would be helpful to find out if the variant is linked to your cancer.

Do I have to have the test?

No, having this test is optional. Your decision will not affect the standard of care you receive from the hospital or doctor, which will be based on the available information.

What if I am not sure if I want to have the test?

We would recommend for you to have further discussions with a specialist member of the genetics team.

What will happen next if I say yes?

If you decide to have the test, you will be asked to sign a consent form. A blood sample will be taken for the test.

How will I receive the results of the test?

The genetics team will send you and your cancer team the results of the test by post. The results may take up to 8 weeks, but will usually be within 4-6 weeks.

Will my information be confidential?

All data collected about you will be held under the provisions of the 1998 Data Protection Act and stored in secure files. The only people who will know your identity are the hospital staff and a few trained staff reporting the results who are bound by a professional duty to protect your privacy.

If you have any questions please contact the Royal Marsden Cancer Genetics Unit on 0208 661 3375 or cancergenetics@rmh.nhs.uk



Receiving a normal BRCA1 and BRCA2 test result

Information sheet for patients with cancer

You had a BRCA1 and BRCA2 gene test because you have had cancer.

The test result is normal.

No BRCA1 or BRCA2 mutation (gene change) was identified in your blood sample.

What does this result mean for me?

This means we have not found a BRCA1 or BRCA2 mutation which would put you at high risk of developing another cancer. The cancer team will discuss if this normal result has any implications for your cancer management.

A normal result is common. In most women with breast and/or ovarian cancer no mutation in BRCA1 or BRCA2 is found. If you have a strong family history of breast and/or ovarian cancer, or a strong family history of other cancers, or if you developed cancer at an unusually young age, it may be helpful to look into things further. The genetics or cancer team will discuss this with you, if appropriate.

Very occasionally mutations in other genes can be involved in causing breast or ovarian cancer. Also new discoveries are being made all the time. If a new gene test becomes available the genetics team may be able to do the test using the sample you have already provided and they will send the result to you and your cancer team.

What does this result mean for my relatives?

This result is good news for your relatives, as it means they are unlikely to be at high increased risk of developing breast and/or ovarian cancer themselves. You may wish to share this result with them.

All women are eligible to have mammograms from 47 years in the National Breast Screening Programme. Depending on the family history, some women may be eligible for mammograms from 40 years, even if there has been a normal BRCA1 or BRCA2 gene test in the family. There is currently no known effective form of ovarian screening. If a woman has multiple relatives with ovarian cancer removal of the ovaries is sometimes considered.

If any of your relatives wish to discuss their own risks of cancer further they should speak with their GP who can refer them for further discussions at a Family History or Genetics clinic.

If you have any further questions, please contact the Royal Marsden Cancer Genetics Unit on 0208 661 3375 or cancergenetics@rmh.nhs.uk



Receiving a BRCA1 and BRCA2 test result that identifies a mutation

Information sheet for patients with cancer

You had a BRCA1 and BRCA2 gene test because you have had cancer.

The test result has shown that you have a mutation (gene change) in either the BRCA1 or BRCA2 gene. The exact details of the mutation are given in the test report.

BRCA1 or BRCA2 mutations result in increased risks of breast and ovarian cancer, and occasionally other cancers. Therefore this result provides an explanation for why you developed cancer.

Your cancer team will discuss with you if this result has implications for your cancer treatment and/or follow-up.

This result has implications for your future health and potentially for your relatives. An appointment has been made for you in the Genetics clinic to discuss these issues further. At the appointment you will be able to discuss your future risks of cancer and your options for cancer screening and measures to reduce the risk of cancer. The potential implications for relatives will also be discussed. The processes by which your relatives can have discussions themselves to decide if they wish to have testing will be explained.

You may find it helpful to read the information booklet “A Beginner’s Guide to BRCA1 and BRCA2” which gives more detailed information. This can be downloaded from www.royalmarsden.nhs.uk/brca

If you need to discuss anything urgently prior to your appointment, or wish to alter the date of your appointment, please contact the Royal Marsden Cancer Genetics Unit on 0208 661 3375 or cancergenetics@rmh.nhs.uk



Receiving a BRCA1 and BRCA2 test result that identifies a variant requiring evaluation (VRE)

Information sheet for patients with cancer

You had a BRCA1 and BRCA2 gene test because you have had cancer.

The test result has shown that you have a gene change (variant) in either the BRCA1 or BRCA2 gene that requires further evaluation.

At the moment, we do not have enough information to decide if this variant is linked to why you have had cancer.

Variants in the BRCA1 and BRCA2 genes are common, and most do not cause cancer. Very occasionally, we find a variant that requires further assessment before we can decide if it leads to an increased risk of cancer. In some cases, we may need to do further blood tests to help us find out more about the impact of the variant.

We have made an appointment for you in the Genetics clinic to discuss your result further. At the appointment we will explain in more detail about the result and any further tests that may be required. We will also discuss the process and timeframe for deciding if the variant is likely to be linked to your cancer.

It is important for us to have as much information as possible when we see you. We have enclosed a family history questionnaire with your letter, and would be very grateful if you would fill this in and return it to us before we see you in clinic.

If you need to discuss anything urgently prior to your appointment, or wish to alter the date of your appointment, please contact the Royal Marsden Cancer Genetics Unit on 0208 661 3375 or cancergenetics@rmh.nhs.uk



Consent for Genetic Testing

| | |
|---|--|
| THE ROYAL MARSDEN NHS FOUNDATION TRUST Patient / parental agreement to investigation | Patient's surname/family name |
| | Patient's first names |
| | Date of birth |
| | Responsible health professional |
| | Job title |
| | NHS number (or other identifier) |
| See overleaf for: (1) Special Requirements (2) Information provided and (3) Consent policy | <input type="checkbox"/> Male <input type="checkbox"/> Female |

Statement of health professional (to be filled in by health professional with appropriate knowledge of proposed procedure, as specified in consent policy)

The purpose of these investigations is to help establish the causes of cancer and/or risk of cancer for you. The results may also provide information which may be helpful for other family members. We have provided written information outlining the risks and benefits of these investigations. During the consultation and/or through written information we have discussed the following issues related to gene testing and you have agreed to the numbered statements indicated below. If you have further questions please contact the genetics team on **0208 661 3375** or **The Royal Marsden, Cancer Genetics Unit, Downs Road, Sutton, SM2 5PT**

Please circle as appropriate

| | | | | |
|---|--|-----|----|-----|
| 1 | I agree to the testing of | Yes | | |
| 2 | I understand that the test results will be put on the electronic patient records at the Royal Marsden NHS Foundation Trust. | Yes | | |
| 3 | I understand the sample will be stored in case new gene tests become available. | Yes | | |
| 4 | I understand that additional tests may be undertaken on the stored sample, if indicated, and I will be informed of any relevant results. | Yes | | |
| 5 | I agree that the test results can be made available to doctors looking after family members, on request. | Yes | No | N/A |
| 6 | I agree to the sample being used anonymously for research. | Yes | No | |

Additional issues discussed:

Signature: _____ Print name: _____ Date: _____
(Patient / Parent / Guardian / Relative)

To be completed if individual identified above is deceased:
 I agree to the above genetic tests and sharing of information on behalf of my relative.
 Relationship to patient: _____

Signature: _____ Print name: _____ Date: _____
(Clinician)

To be retained in patient's notes

The following information leaflet / consultation letter(s) have been provided:

- (version no. _____)
- (version no. _____)

Special requirements (e.g. other language/other communication method):

.....

.....

Guidance to health professionals (to be read in conjunction with consent policy)

This form

This form documents the patient’s agreement (or that of a person with parental responsibility for the patient) to go ahead with the investigation you have proposed. It is only designed for use where the patient is expected to remain alert throughout and where an anaesthetist is not involved in their care.

Consent forms are not legal waivers – if patients, for example, do not receive enough information on which to base their decision, then the consent may not be valid, even though the form has been signed. Patients also have every right to change their mind after signing the form.

Who can give consent

Everyone aged 16 or more is presumed to be competent to give consent for themselves, unless the opposite is demonstrated. If a child under the age of 16 has “sufficient understanding and intelligence to enable him or her to understand fully what is proposed”, then he or she will be competent to give consent for himself or herself. Young people aged 16 and 17, and legally ‘competent’ younger children, may therefore sign this form for themselves, if they wish. If the child is not able to give consent for himself or herself, some-one with parental responsibility may do so on their behalf. Even where a child is able to give consent for himself or herself, you should always involve those with parental responsibility in the child’s care, unless the child specifically asks you not to do so. If a patient is mentally competent to give consent but is physically unable to sign a form, you should complete this form as usual, and ask an independent witness to confirm that the patient has given consent orally or non-verbally.

When NOT to use this form (see also ‘This form’ above)

If the patient is 18 or over and lacks the capacity to give consent, you should use form 4 (form for adults who lack the capacity to consent to investigation or treatment) instead of this form. A patient lacks capacity if they have an impairment of the mind or brain or disturbance affecting the way their mind or brain works and they cannot:

- understand information about the decision to be made
- retain that information in their mind
- use or weigh that information as part of the decision-making process, or
- communicate their decision (by talking, using sign language or any other means).

You should always take all reasonable steps (for example involving more specialist colleagues) to support a patient in making their own decision, before concluding that they are unable to do so.

Relatives cannot be asked to sign a form on behalf of an adult who lacks capacity to consent for themselves, unless they have been given the authority to do so under a Lasting Power of Attorney or as a court appointed deputy.

Information

Information about what the investigation will involve, its benefits and risks and the alternatives to the particular test proposed, is crucial for patients when making up their minds about investigations. The courts have stated that patients should be told about ‘significant risks which would affect the judgement of a reasonable patient’. ‘Significant’ has not been legally defined, but the GMC requires doctors to tell patients about ‘serious or frequently occurring’ risks. In addition if patients make clear they have particular concerns about certain kinds of risk, you should make sure they are informed about these risks, even if they are very small or rare. You should always answer questions honestly. Sometimes, patients may make it clear that they do not want to have any information about the options, but want you to decide on their behalf. In such circumstances, you should do your best to ensure that the patient receives at least very basic information about what is proposed. Where information is refused, you should document this overleaf or in the patient’s notes.

The law on consent

See the Department of Health’s Reference guide to consent for examination or treatment for a comprehensive summary of the law on consent (also available at www.dh.gov.uk/consent).

To be retained in patient’s notes

BRCA GENE TEST REQUEST FORM

| | | | | | | |
|---|--------------------------|---|--------------------------|----------|--------------------------|--|
| PATIENT DETAILS FIRST NAME(S): <hr/> SURNAME: <hr/> RMH HOSPITAL NUMBER: <hr/> DATE OF BIRTH: <hr/> GENDER: <table border="0" style="display: inline-table; vertical-align: top;"> <tr> <td>NHS:</td> <td><input type="checkbox"/></td> </tr> <tr> <td>PRIVATE:</td> <td><input type="checkbox"/></td> </tr> </table> | | NHS: | <input type="checkbox"/> | PRIVATE: | <input type="checkbox"/> | REASON FOR TEST Cancer Type: <input type="checkbox"/> Breast (BC) <input type="checkbox"/> Ovarian (OC) <input type="checkbox"/> Other (specify)..... Age at diagnosis.....years Criteria Met for Testing (tick all that apply): 1 <input type="checkbox"/> Non-mucinous OC, any age 2 <input type="checkbox"/> BC <40 years 3 <input type="checkbox"/> Bilateral BC, both <60 years 4 <input type="checkbox"/> Triple-negative BC, any age 5 <input type="checkbox"/> BC + OC, any age 6 <input type="checkbox"/> Male BC, any age 7 <input type="checkbox"/> Any BC patient in whom gene testing would impact current cancer management. MUST specify reason: 8 <input type="checkbox"/> Other (PP only) Please specify reason..... |
| NHS: | <input type="checkbox"/> | | | | | |
| PRIVATE: | <input type="checkbox"/> | | | | | |
| REQUESTING CLINICIAN: Name: Tel: <small>(Contact details above required in case of sample query. Results will be returned to Requesting Consultant)</small> | | SAMPLE COLLECTION <input type="checkbox"/> Blood : EDTA tubes ONLY (2x 9ml) Sample taken by: Date: Time: PLEASE ENSURE NAME AND AT LEAST ONE OTHER IDENTIFIER IS ON TUBE | | | | |
| REQUESTING CONSULTANT: Name: Hospital / Unit: | | FOR LABORATORY USE ONLY TGL FAMILY NUMBER: TGL LAB BARCODE: LOGGED IN BY: DATE RECEIVED: TIME RECEIVED: | | | | |
| PLEASE NOTE: On receipt of this sample, the laboratory staff assume the appropriate consent has been obtained. MCG F2 TGL_F_43_Mainstream_BRCA_Request_form BRCA Gene Test REQUEST FORM v4 – 06/02/2015 | | | | | | |

BRCA1 and BRCA2 gene testing

Frequently asked questions for breast and gynae units

MCG FAQ1 - last updated 23/04/2015

Q: Which patients can have BRCA testing through oncology?

Non-geneticists can only undertake BRCA testing (i.e. to look in blood for mutations in the BRCA1 and BRCA2 genes) in breast cancer (BC) or ovarian cancer (OC) patients that fulfill one or more of the following criteria (see Protocol MCG P1 and Protocol MCG P2).

NHS RM patient with

- Non-mucinous OC diagnosed at any age
- BC <40 years
- Bilateral BC, both <60 years
- Triple-negative BC, any age
- BC + OC, any age
- Male BC, any age
- Any BC patient in whom gene testing would impact current cancer management

Other patients, such as those with a family history of cancer who do not fulfill any of the above criteria may be eligible for testing, either through NHS or through research, but will need to be referred to Genetics by email and/or letter (not by EPR) for this to be evaluated and performed if appropriate. Referrals and queries about whether or not patients are eligible should be directed to cancergenetics@rmh.nhs.uk.

Q: Which non-geneticists can perform BRCA testing in eligible patients?

Only non-geneticists that have completed the 30 min online training can perform BRCA testing. Instructions for completing the training process are available at www.mcgprogramme.com/brcatesting. Contact mcg@icr.ac.uk if you have any queries.

Q: How were the eligibility criteria for ovarian cancer patients decided?

For ovarian cancer the eligibility criteria are in line with the NICE recommendations www.nice.org.uk/guidance/cg164 which state that any patient with $\geq 10\%$ chance of having a BRCA mutation should be tested. Several studies, and our own RM data, have shown that any non-mucinous ovarian cancer patient meets this threshold.

Q: How were the eligibility criteria for breast cancer patients decided?

When we introduced the mainstreaming programme for breast cancer patients we used eligibility criteria we believed would be at $\sim 10\%$ mutation detection threshold, however the mutation detection rate after the first year was 20%. Moreover the economic modelling for the NICE guidelines indicated that testing was cost-effective at 5% threshold but this was not formally recommended because of limited Clinical Genetic capacity. We therefore decided to change the criteria to increase testing access. The current testing eligibility criteria are being evaluated as part of a two year study funded by the NIHR RM/ICR Specialist BRC.

Q: Who is leading the Mainstreaming Cancer Genetics BRCA initiative?

The initiative is part of the Mainstreaming Cancer Genetics (MCG) programme. Professor Nazneen Rahman is Programme Director and Drs Helen Hanson, Zoe Kemp and Angela George are on the Programme board. All are also Consultant Cancer Geneticists at the Royal Marsden. You can read more about the initiative at www.mcgprogramme.com.

Q: Why is there a testing category for BC patients in whom testing would impact cancer management?

Traditionally eligibility for BRCA testing was decided by estimating the chance that a mutation would be detected. However, over the last 5 years it has become apparent that BRCA testing can impact on treatment options and increasingly patients and cancer doctors have been requesting testing to help with management decisions. Through the study we wish to evaluate the reasons why BRCA testing is requested, the mutation detection rates in groups tested for treatment decisions, and the impact of the testing for the patient.

Q: Which BC patients should I offer BRCA testing to on the basis that it would impact current cancer management?

For the first six months of the pilot we are operating an open-door policy such that you can use your own judgement and offer testing to anyone that you feel it would be helpful. We only ask that you document the reason so that we can perform evaluations and determine the mutation detection rate in different scenarios. After six months we will review the data and may stipulate specific cancer management criteria for testing.

Q: Where do I record the reason for carrying out BRCA testing for BC patients tested because it would impact current cancer management?

Please document the reason on the lab referral form (MCG F2) in the space provided.

Q: What is the testing eligibility for private patients?

Any Royal Marsden private patient with breast or ovarian cancer can have BRCA testing. A specific process for this has been set-up and is available in Private Care, or from rahmanRMPC@icr.ac.uk.

Q: What about one-off second opinions?

Patients that are seen as one-off second opinions are currently excluded from BRCA testing through the RM breast and gynae units because the processes for return of results, follow-up and reimbursement are not in place. We are looking into how we might address the needs of these patients.

Q: How strict are the age cut-offs for testing?

These are strictly applied. For example, a woman with bilateral breast cancer diagnosed at 58 years and 60 years (and no family history) would not be eligible for testing, but if she were diagnosed at 58 years and 59 years she would be eligible. It is recognised, and inevitable, that individuals close to a threshold may have similar likelihoods of carrying a mutation but different eligibility. We are working hard to make eligibility generally more permissive, but in the meantime it is important for clinicians and patients to have confidence that criteria are being consistently applied.

Q: How is triple-negative breast cancer defined?

For the purpose of eligibility for genetic testing a triple-negative breast cancer is defined as a tumour with an Allred score of 0, 1 or 2 for ER and PR receptors and HER2 negativity by IHC or FISH.

Q: Should *in situ* breast cancer be included?

In situ cancer, such as DCIS (ductal carcinoma in situ) and LCIS (lobular carcinoma in situ), should be included in the same way as invasive breast cancer in assessing eligibility for BRCA testing.

Q: How should multiple metachronous ipsilateral breast cancers be assessed?

Two (or more) separate, ipsilateral breast cancers which have occurred 5 or more years apart should be considered as separate cancers (i.e. counted as a bilateral breast cancer) when assessing eligibility for BRCA testing, unless it is clear that the second cancer is a

recurrence. This is a pragmatic approach as it is not possible to robustly identify which are separate cancers and which recurrence.

Q: How should multiple synchronous ipsilateral breast cancers be assessed?

Simultaneous ipsilateral breast cancers, whether termed synchronous, multicentric or multifocal, should be counted as a single breast cancer for assessing eligibility for BRCA testing.

Q: What is the BRCA testing eligibility for Ashkenazi Jewish patients?

Exactly the same eligibility criteria apply for Ashkenazi Jewish patients, who will have full gene testing, not just testing for the three Ashkenazi founder mutations.

Q: When should discussion of BRCA testing be undertaken?

This should be at the discretion of the clinician. BRCA testing can be discussed and undertaken at the time of diagnosis, during active cancer management or during follow up. However, please be aware that the result takes ~4 weeks from receipt of sample, so if the result is required for management decisions, timing of testing must be planned accordingly.

Q: What information should I give to the patient prior to obtaining consent?

The information sheet 'BRCA1 and BRCA2 gene testing - Information sheet for patients with cancer' (MCG IS1) should be given to the patient. Patients should be informed that BRCA mutations are a cause of cancer and knowing whether or not a BRCA mutation is involved in causing their cancer can be helpful for their current and future management. The clinician may like to describe the specific relevance of the test for the specific patient. The patient should also be aware that the result can provide information of relevance to the wider family. However, it is important to remember that most tests are normal and therefore detailed discussions regarding risk management for patient and relatives, prior to testing, are not required. If a patient has questions that require either more time or more expertise than you are able to provide, the patient should be referred to Genetics. E-learning modules 1 (MCG ELM1) and 2 (MCG ELM2) provide further information about BRCA testing.

Q: What are the insurance implications for cancer patients?

If a cancer patient applies for life cover, critical illness or income protection cover after the gene test is performed then it will need to be disclosed, along with the other information about their cancer diagnosis. This is unlikely to have impact on the cover/terms they are offered over and above the impact of their cancer diagnosis. If the gene test was performed after an insurance policy was set-up the result does NOT need to be disclosed.

Q: Are there insurance implications for the cancer patients relatives?

Relatives would need to tell the insurance company about the cancer diagnosis and if a gene mutation has been found when asked about their family history (if they are aware of it). If the test is normal some insurance companies may take this into consideration to mitigate the unfavourable impact of the family history on the policy. Unaffected individuals do not have to disclose the results of predictive gene testing to insurance companies but may choose to do so, particularly if the test is negative.

Q: Which consent form should I use?

You should use the 'Consent for Genetic Testing' form (MCG F1) which is available on EPR. The form is also available online at www.mcgprogramme.com/BRCAtesting. E-learning module 4 (MCG ELM4) explains how to take consent. Once completed, the form should be scanned onto EPR and a copy given to the patient. It should NOT be sent to the lab.

Q: Which lab form should I use?

There is a specific lab form 'BRCA gene test request form' (MCG F2). The form will be available in clinics and online at www.mcgprogramme.com/BRCAtesting. Please send the form to the TGL clinical lab in BLB in ICR, together with the sample (2x9ml EDTA).

Q: How long does it take to get a BRCA result?

The results of full analysis of the BRCA1 and BRCA2 genes typically take about 4 weeks, but may take up to 6 weeks. If there is a known mutation in the family the result takes 2-4 weeks.

Q: How is the BRCA testing being done?

We are using a next-generation sequencing panel called the TruSight Cancer panel, which has undergone extensive validation. All mutations are further confirmed by Sanger sequencing and/or MLPA as appropriate. Further details of the panel are available at www.mcgprogramme.com.

Q: Will we receive results of only the BRCA genes?

Yes. At the current time we are reporting just the results of the BRCA1 and BRCA2 genes. We will be extending to additional genes that cause breast and/or ovarian cancer in the near future.

Q: What if a patient meets the criteria but chooses not to have a test?

The test is optional. A patient may decline to be tested, ask to have longer to think about testing or be referred to Genetics if they want, or need, more detailed discussions.

Q: What if a patient does not meet the testing criteria but wants a test?

Patients who do not meet the mainstreaming testing criteria may be eligible for a test on account of their family history. If this seems possible they should be referred to Genetics. Please note, acceptance of the referral by Genetics does not indicate that testing will definitely be performed. Queries about whether or not patients are eligible should be directed to cancergenetics@rmh.nhs.uk. Alternatively they could choose to have the test privately.

Q: What if a family member has already had BRCA testing?

If a member of the family has already had a BRCA test, please contact the Genetics unit on cancergenetics@rmh.nhs.uk and note this on the lab form. It may influence the testing that is performed.

Q: Who will give the patient the result of the BRCA test?

The Genetics team will write to the patient with the result and will send an information sheet with additional information. The referring clinician and GP will also be notified. The result will be uploaded to the Germline Genetics tab on EPR together with an EPR annotation of the result.

Q: What happens if no mutation is identified?

The Genetics team will inform the patient of the result in writing and will send the patient a copy of the report and the information sheet 'Receiving a normal BRCA1 and BRCA2 test result' (MCG IS2). You should use the result as appropriate for their cancer management, but usually no further input is required from Genetics. If the patient has additional questions about the result please ask the Genetics team to send an appointment. Please note, patients and their relatives may still be eligible for enhanced mammographic surveillance on account of their family history. Relatives can seek advice about enhanced screening at their local Regional Genetics centre, via a GP referral.

Q: What happens if a mutation is identified?

The Genetics team will inform the patient in writing and will send the patient a copy of the report and the information sheet 'Receiving a BRCA1 and BRCA2 test result that identifies a mutation' (MCG IS3) and an appointment for the Genetics clinic. The Cancer team should use the information as appropriate for their cancer management. The Genetics team will discuss with the patient the implications for their future cancer risk and will also evaluate which relatives may be impacted. The processes for cascading the information to relatives will be explained.

Q: What if there is a variant requiring evaluation (VRE) identified?

Very occasionally (<1%), we identify a variant that does not fulfill the criteria for pathogenic mutations, but requires further evaluation. In such cases, an information sheet (MCG IS4) and an appointment with Genetics is sent to the patient. The result and further analyses required are discussed with the patient. Once the additional evaluation has been completed (typically 2-6 months) the patient and clinician are informed of the final management class. Variants are only classified as VREs if there is suggestive evidence of pathogenicity that can potentially be confirmed by additional analyses (e.g. a splicing assay).

Q: What if there is an equivocal result?

No equivocal reports are issued. Genetics / TGL review all the BRCA results, determine the pathogenicity of any identified sequence variants, and interpret their clinical relevance. We have a sophisticated clinical and bioinformatic interpretative system that allows us to do this. The reports thus include clear information about whether or not a pathogenic mutation was identified. Very occasionally (<1%), there are sequence variants that do not fulfill the criteria for pathogenic mutations, but merit further evaluation as described above.

Q: What if new evidence in the future shows a variant is pathogenic?

We keep all variants identified under review and if any are reclassified Genetics will automatically re-issue reports and clear, revised recommendations. It is important to remember that rare sequence variants in these genes are collectively common in the general population (present in about 10%), and the great majority are not pathogenic.

Q: If a mutation is identified who will follow-up the patient's relatives?

The Genetics team will give the patient a "To whom it may concern letter" to give to relatives. The letter will explain that a cancer predisposition gene mutation has been identified in the family and that relatives can ask their GP to refer them to the Royal Marsden Genetics team or their local genetics service to discuss the implications. This is standard practice in Genetics.

Q: If the patient does not have a BRCA mutation, are there additional genetic tests that should be performed?

Some patients may be eligible for further tests, particularly if they were diagnosed at a particularly young age, if they have multiple primary cancers or if there is an extensive family history of cancer. We recommend that such patients are referred to Genetics.

Q: Who should I contact if I have any questions?

Questions should be addressed to Angela George (Gynae) on angela.george@rmh.nhs.uk or Zoe Kemp (Breast) on zoe.kemp@rmh.nhs.uk.

Please contact cancergenetics@rmh.nhs.uk if you have suggestions for additional questions.

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e-learning module 1 (MCG ELM1)

**Background to Mainstreaming
Genetic Testing**

Duration: 6 minutes

MCG Mainstreaming
Cancer Genetics



Knowledge of genetic mutations in the person (germline) and those restricted to the cancer (somatic) are each important to personalised medicine.

MCG Mainstreaming
Cancer Genetics

Germline genetic information is helpful for cancer patients and their relatives.

- Provides clinically useful information about why and how an individual got cancer.
- Provides information to improve management of cancer patients e.g. second cancer risk.
- Provides information about efficacy of treatments.
- Provides information of potential impact to relatives.

MCG Mainstreaming
Cancer Genetics

MCG Mainstreaming
Cancer Genetics

'Cancer predisposition gene' is the term used to describe genes in which germline mutations confer increased risks of cancer.

In 2015, >100 cancer predisposition genes, involved in ~35 different cancers, recognised.

MCG Mainstreaming
Cancer Genetics

MCG Mainstreaming
Cancer Genetics

Cancer predisposition genes cause
~3% of cancers overall, but much
higher in certain cancers
e.g. ~15-20% ovarian,
40% pheochromocytoma.

MCG Mainstreaming
Cancer Genetics

Cancer predisposition gene testing is
currently very restricted.

We need to be able to test more
genes in more people.

MCG Mainstreaming
Cancer Genetics

Genetic testing in people with
cancer is similar to other medical
tests = **medical genetic testing**.
Genetic testing in unaffected people
is different to medical tests =
predictive genetic testing.

MCG Mainstreaming
Cancer Genetics

Doctors are comfortable with the
concept of medical genetic testing
and already do a lot more than they
realise!

MCG Mainstreaming
Cancer Genetics

We have implemented a new model
in which medical genetic testing can
be done by non-geneticists.

Predictive genetic testing will
continue to be done by geneticists.

MCG Mainstreaming
Cancer Genetics

This system is more patient-centred,
flexible, affordable and has higher
capacity.

MCG Mainstreaming
Cancer Genetics

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e-learning module 2 (MCG ELM2)

BRCA1 and BRCA2 testing

Duration: 5 minutes

MCG Mainstreaming
Cancer Genetics



**A clinician's guide to BRCA1 and
BRCA2 testing**

MCG Mainstreaming
Cancer Genetics

**Hereditary (germline) mutations in
BRCA1 and BRCA2 predispose to
breast and ovarian cancer.**

MCG Mainstreaming
Cancer Genetics

**About 15% of ovarian cancer and 3%
of breast cancer are due to BRCA
mutations.**

MCG Mainstreaming
Cancer Genetics

The chance of finding a mutation is increased if:

- An individual has breast *and* ovarian cancer
- An individual has triple-negative breast cancer (BRCA1 only)
- There is a family history of ovarian and/or breast cancer

MCG Mainstreaming
Cancer Genetics

**A BRCA mutation carrier has a
lifetime risk of ~70% of developing
breast cancer.**

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Cancer Genetics

A BRCA mutation carrier who already has breast cancer has ~50% lifetime risk of a contralateral breast cancer.

MCG Mainstreaming
Cancer Genetics

BRCA mutation carriers can consider breast surveillance with MRI and mammography and/or risk-reducing mastectomy.

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Cancer Genetics

A BRCA1 mutation carrier has ~50% lifetime risk of ovarian cancer.

A BRCA2 mutation carrier has ~20% lifetime risk of ovarian cancer.

MCG Mainstreaming
Cancer Genetics

There is no effective form of ovarian surveillance. BRCA mutation carriers can consider bilateral salpingo-oophorectomy (usually in 40s).

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Cancer Genetics

Male BRCA2 mutation carriers have small increased risks of breast and prostate cancer. No surveillance is recommended.

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Cancer Genetics

Relatives of mutation carriers may or may not also carry the mutation. The risk of having the mutation is 50% for first-degree relatives.

MCG Mainstreaming
Cancer Genetics

If an unaffected relative wants to consider having a test to see if they have inherited the familial mutation, they should be referred to a Geneticist by their GP.

MCG Mainstreaming
Cancer Genetics

Testing for other genes that predispose to breast and/or ovarian cancer is increasingly becoming available.

MCG Mainstreaming
Cancer Genetics

Ovarian cancer BRCA testing checklist

After you have completed the training you will be asked to confirm the following, so please ensure that you are clear about these points as you go through the training.

Q1: What is your name and job title?

Q2: What is your email address?

Q3: Which hospital/NHS centre do you work for?

Q4: Have you:

Listened to the e-learning modules MCG ELM1, MCG ELM2, MCG ELM3b and MCG ELM4?

Read the Ovarian cancer BRCA testing protocol MCG P2?

Read the patient information sheets MCG IS1, MCG IS2, MCG IS3 and MCG IS4?

Read the consent form MCG F1 and lab referral form MCG F2?

Read the frequently asked questions document MCG FAQ1?

Q5: Do you feel confident that you understand the described processes and your role in them and do you feel ready to start offering genetic testing to appropriate patients?

Q6: Are you clear about which patients you can offer genetic testing to?

Q7: Are you aware that some patients that do not meet the direct testing criteria outlined in the Ovarian cancer BRCA testing protocol MCG P2 will still be eligible for genetic testing, but will need referral to genetics? Are you confident that you will be able to refer and/or contact the genetics team to discuss potential referral when appropriate?

Q8: Are you aware that the timing of testing is at the discretion of the clinician and patient and can be undertaken at any time in the cancer patient pathway?

Q9: Do you feel confident about discussing genetic testing with your patients and are you clear that you should refer the patient for a genetics appointment if there are any issues that emerge that you are not able to address, either because of knowledge or time constraints?

Q10: Are you clear about the different follow-up processes for tests in which a mutation is identified, tests in which no mutation is identified and tests in which a variant requiring evaluation (VRE) is identified?

Q11: We designed training to provide the required information in the most time-effective fashion, in response to the wishes of the people to be trained. How did you find it?

If there is anything that you would like further clarity about, please contact cancergenetics@rmh.nhs.uk