BRCA1/2 gene testing for ovarian cancer patients and their families

a policy report
Welcome

Over the last year, BRCA1/2 gene testing has come much more to the forefront of people’s minds as one of the ‘tools’ available to tackle cancer. At Ovarian Cancer Action we have long been advocates of this important test. This report, launched to coincide with Ovarian Cancer Awareness Month 2014, summarises our position on BRCA1/2 gene testing.

The report and our associated campaign shine a light on an area of public health that as yet hasn’t received the attention from the NHS, commissioners or the Government that it deserves. BRCA1/2 gene testing at the point of diagnosis in ovarian cancer patients offers them the opportunity for the best possible outcome for their treatment.

Women with the disease passionately want to know this information for themselves and their families. They have the right to this information and we believe that the NHS ought to provide it in the simplest and most cost effective way possible. Doing this will also help family members take action to prevent future cancer. This report identifies that path.

In this report, we make a number of recommendations about how the testing should be delivered, patient support and the commissioning of this service. We want this to now be made available across the country as is already the case in Scotland.

Gilda Witte
Chief Executive
Ovarian Cancer Action

Sequencing of the Human Genome is fast becoming a routine procedure. This will have an impact on every branch of medicine from identifying infections to targeting our medications.

The NHS is preparing to adapt but this will be a great challenge, comparable to introduction of antisepsis and anaesthetics. The key is to take steps which are substantial but achievable and which provide a demonstrable benefit.

People who carry spelling errors in the BRCA1 or 2 genes are at very high risk of cancers, particularly breast and ovarian. Traditionally, access to sequencing these genes has been highly selected using family history as the guide. We know this misses 3 people in 4 with the gene. As new drugs able to target these BRCA deficient cancers come close to being available, there is a need for a change of approach.

All women with ovarian cancer should be considered for this test at the time of diagnosis. It will change their management if they are found to have an underlying gene change and could save the lives of close relatives.

Sir John Burn MD FRCP FRCPE FRCPCH FRCOG FMedSci
Professor of Clinical Genetics, Newcastle University Genetics Chair, National Institute of Health Research Biomedicine West, Centre for Life, Newcastle
In the UK currently, one woman every two hours dies from ovarian cancer meaning our survival rates are amongst the poorest in Western Europe. Ovarian cancer is the fifth most common cancer amongst women, with approximately 7,000 new diagnoses each year. There is only a 46% survival rate five years after diagnosis.

In 2013 Ovarian Cancer Action launched a campaign for routine BRCA1/2 gene testing for all women newly diagnosed with ovarian cancer in England, Wales and Northern Ireland. All of us have BRCA1/2 genes but a mutation in these genes increases the risk of developing ovarian cancer from 1 in 54 to up to 1 in 2.

BRCA1/2 gene testing should be made routinely available at the point of diagnosis. Currently, testing is not available to patients consistently across the UK, despite the fact that NICE guidelines indicate that they qualify. Between 15 and 20% of patients with ovarian cancer have the BRCA1/2 gene mutation. This testing can ensure that women get the most relevant treatment quickly. It will also enable families to measure their own risk and take action to prevent future cancers. Children have a 50% chance of inheriting this gene mutation.

In Scotland testing for the BRCA1/2 gene mutation is standard for ovarian cancer patients. Trials at The Royal Marsden and other centres demonstrate that BRCA1/2 gene testing can be managed routinely as part of care in the oncology unit. This information is of vital importance to patients and their families.

This report is the outcome of Ovarian Cancer Action’s research, analysis and roundtable discussions with experts in the field. The consensus is that this testing is affordable, deliverable and beneficial to patients. It potentially prevents a significant number of future ovarian and breast cancer cases.

Our recommendations call on the Government and the NHS to ensure:

1. All women with non-mucinous epithelial ovarian cancer should be BRCA1/2 gene tested.
2. These women should be BRCA1/2 gene tested at the point of diagnosis.
3. Clarification is provided on where responsibility lies within the NHS for commissioning BRCA1/2 gene testing.

“We told my daughter clearly about the gene mutation and what it might mean for her. We explained that if you knew you had the mutation there were things you could do to take control and prevent yourself getting cancer. This had not been an option for my mother or me. She was aware that knowing would put her in a position of control emotionally and physically.” – Annie Chillingworth, who has the BRCA1 gene mutation.
About Ovarian Cancer Action

Ovarian Cancer Action strives to stop women dying from ovarian cancer. We fund a broad range of research to achieve accurate and early detection of ovarian cancer, more effective treatments to combat the disease and improved quality of life after diagnosis. Ovarian Cancer Action campaigns to ensure women and GPs know risk factors, symptoms and treatment options to enable informed and rapid action. Fundamentally we demand that every woman in the UK should have the best treatment available.

History of our BRCA1/2 gene testing campaign

Throughout 2013 Ovarian Cancer Action has campaigned to raise awareness of familial cancer and the BRCA1/2 gene mutation. We were concerned by the surprising lack of awareness about BRCA1/2 and gene testing amongst the public and, perhaps more remarkably, amongst some GPs.

In September 2013 we hosted a roundtable discussion about the implications of BRCA1/2 gene testing for women with ovarian cancer, their families and the NHS. The roundtable brought together eminent geneticists, clinicians and psychologists including Professor Sir John Burn, Professor Paul Pharoah and Professor Anneke Lucassen as well as Professor Charlie Gourley who has implemented the testing across Scotland. The discussion demonstrated a clear consensus that BRCA1/2 gene testing is a necessary part of the treatment path for women with ovarian cancer and that the result is of critical importance for their families.

Building on the outcomes from the expert discussion panel (Appendix 1) we launched an initial positioning statement on BRCA1/2 gene testing. This report builds on that document.
Our recommendations for change

Ovarian Cancer Action is calling for:

1. **All women with non-mucinous epithelial ovarian cancer should be BRCA1/2 tested.**

2. These women should be offered *BRCA1/2* gene testing **at the point of diagnosis**.

3. This needs to be part of a patient’s standard of care. Who commissions and pays for *BRCA1/2* gene testing must be urgently clarified.

What are *BRCA1/2* genes?

- All of us have *BRCA1/2* genes, but a mutation in these genes increases the risk of developing ovarian cancer from 1 in 54 women to up to 1 in 2.\(^3\)
- This was famously brought to public attention in 2013 with Angelina Jolie’s announcement that she carried this mutation and is therefore on a path of risk-reducing surgery.
- The gene was only discovered 20 years ago and our understanding of it and how it works is always progressing.
- Currently women are alerted to the condition through a family history of breast and/or ovarian cancer.
- Women with non-mucinous ovarian cancer have a 15-20% of carrying the *BRCA1/2* gene mutation.\(^4\) Studies have indicated that around 50% of them will have no family history of the disease.\(^5\)
- Women with breast cancer have a 5% likelihood of carrying the *BRCA1/2* gene mutation.\(^6\)
- Currently in order to qualify for *BRCA1/2* testing NICE recommends a likelihood of having inherited the genetic mutation of 10% or over. This is determined through family history.

**Ovarian Cancer Action** is campaigning for routine *BRCA1/2* gene testing for newly diagnosed women in England, Wales and Northern Ireland, as is the case in Scotland. This testing should be extended to their families where appropriate. Trials at The Royal Marsden demonstrate that this can be done in an affordable and scalable way.
Cost benefit analysis for the NHS
Investing for the future

Expanding BRCA1/2 gene testing will have a cost impact for the NHS. This is not, however, the sole consideration. We need to look at down-stream costs and the value of offering the testing.

A BRCA1/2 gene test for someone already diagnosed with ovarian cancer costs between £600 to £850.7 Associated counselling can cost between £250 to £500. Together this can amount to approximately £1,000 per patient. Around 15-20% of those tested are likely to receive a result that shows they have the gene mutation.

There is also a cost impact for the numbers of relatives who may then wish to access testing. For every woman diagnosed with ovarian cancer and the BRCA1/2 gene mutation it is possible that one to three relatives could be tested. Half of these relatives are likely to receive a positive test result. The costs for testing and counselling relatives are lower (from £140 to £340 for testing and £125 to £375 for counselling) than for those already diagnosed with ovarian cancer. The costs for testing relatives can therefore amount to £300 to £800 per person.

When testing is carried out in the oncology department, as is currently done at The Royal Marsden, there are efficiencies. No additional appointments need be made as the patient is being tested as part of her overall treatment path.

Specialist genetic services therefore only see women who are found to have the BRCA1/2 gene mutation. This is efficient for both the patient and the NHS.

For the NHS, expanding BRCA1/2 gene testing will have associated costs. It could lead to more preventative surgery and increased surveillance amongst relatives of women known to have the BRCA1/2 gene mutation. The extent of the costs rests on individuals’ take up of testing, counselling, surveillance and surgery.

Research tells us that BRCA1/2 gene testing is cost effective in other countries. We also know that modelling conducted to support NICE guidelines on familial testing suggested that BRCA1/2 gene testing versus no BRCA1/2 gene testing was cost effective in women aged 35 to 55.8

As a result of finding out BRCA1/2 status we can significantly reduce the risk of a woman developing breast and ovarian cancer. Since the cost of cancer to the NHS is in the region of £13,000 to £18,000 there are potential savings for the NHS.

Expanding testing is not just a pure cost driver. It could help the NHS save on treating cancer in the future.

“All non-mucinous epithelial ovarian cancer patients should be BRCA1/2 tested at diagnosis. This is what currently happens in Scotland (not in England). These families then benefit from genetic counselling, screening and risk reduction surgery for breast and ovarian cancer.” – Professor Charlie Gourley, Professor of Medical Oncology at the University of Edinburgh.

“After being diagnosed with ovarian cancer, being genetically tested was my way of understanding and protecting my child’s future. My family is precious. It made sense to utilise the information in a positive way. Encouraging genetic testing for my daughter, sisters and their children will, hopefully, prevent them from developing cancer.” – Della Lamden, who has the BRCA1 gene mutation.
At present there is no routine testing for women with ovarian cancer. Women with ovarian cancer have an up to one in five chance (20%) of carrying the mutation and therefore exceed the NICE requirement of 10% probability. It is for their and society’s benefit that they should be tested because:

1. Knowledge of a patient’s genetic makeup can have a direct impact on that patient’s treatment path, their responsiveness to certain types of drugs and their potential for accessing clinical trials.
2. If a patient’s BRCA1/2 status is known, their family members can be informed of the potential risk to themselves. These families can be offered prevention or early detection advice as soon as possible, reducing future cancer cases in the UK.
3. Ovarian cancer is a highly complex disease that can only be combatted through progressive research. The scientific community needs robust population based data that demonstrates the significance of patients’ hereditary links for developing ovarian cancer.

Up to as many as 5,000 women in England, Wales and Northern Ireland annually are diagnosed with non-mucinous epithelial ovarian cancer. If this population group were tested for the BRCA1/2 gene mutation as a matter of routine, potentially 750 - 1,000 BRCA1/2 gene mutations would be identified. This would enable all of their families to be offered preventative and early detection advice, contributing to the Department of Health’s target of preventing 500 ovarian cancer deaths a year. In addition a large number of breast cancer diagnoses could also be prevented. The Department of Health’s Strategy for Cancer recognises the importance of information for patients so that they can make the right choices about their health, treatment and potential to reduce the risk of developing cancer.

In Scotland BRCA1/2 gene testing is routinely offered to all women with non-mucinous epithelial ovarian cancer. This standard of care has recently been written into SIGN guideline. Similarly, in British Columbia and Australia women with non-mucinous epithelial ovarian cancer are routinely tested for the BRCA1/2 gene mutation. Major studies have shown that up to 20% of these women have the BRCA1/2 gene mutation. More than half of this group had no family history of cancer.

**Current developments**

There are several pilot programmes in progress in centres across England which test ovarian cancer patients for the BRCA1/2 gene mutation. These centres include The Christie in Manchester, The University of Cambridge and The Royal Marsden. These studies indicate that the prevailing trend is to test ovarian cancer patients for BRCA1/2 gene mutations as a necessary part of their diagnosis.

“Our BRCA testing is critical for the successful delivery of personalised therapy of women with ovarian cancer. The Royal Marsden offers women the opportunity to have a BRCA test through a new pathway for gene testing which takes place in oncology clinics. Women found to have BRCA mutation also see a geneticist. The feedback has been overwhelmingly positive from patients, clinicians and geneticists. The whole new ‘oncogenetic pathway’ is very efficient. The BRCA results have already made a difference to treatment for individual patients.” – Dr Susana Banerjee, Consultant Medical Oncologist at The Royal Marsden.
Our recommendations

All women with non-mucinous epithelial ovarian cancer should be BRCA1/2 tested at the point of diagnosis.

For those diagnosed with ovarian cancer, chemotherapy is usually part of their treatment. Women with the BRCA1/2 gene mutation respond well to platinum chemotherapy. We believe it is crucial to a patient’s recovery to ensure that BRCA1/2 gene testing of patients is offered at the point of diagnosis of ovarian cancer.

By testing women for the BRCA1/2 gene mutation immediately, their clinicians are able to make informed decisions about subsequent treatment strategies, in particular in the event of relapse. Furthermore, it can help a patient understand how she got the disease and give her confidence that her disease is fully understood by her clinical team and that she has the most appropriate care.

BRCA1/2 gene testing can be included as part of a patient’s routine tests and appointments at the point of diagnosis and could therefore be most time and cost effectively managed for both the patient and the NHS.

Trials at The Royal Marsden Hospital demonstrate this can be effectively performed in the supportive environment of the oncology clinic by the consultants, doctors and nurses with whom the patient develops a close relationship during the treatment of their disease. Their family members, for whom the information has a critical bearing, would be referred to a UK genetics resource centre. Training has been effectively developed to manage pre-screening consent and negative results, freeing the time of the geneticists to focus on the patients who have the BRCA1/2 gene mutation.

Anticipating future demand

We predict that there will be an increase in demand for BRCA1/2 gene testing at the point of diagnosis. Oncology services need to be ready to meet this increased need, which will come as a result of:

- Developments in treatment paths for women with ovarian cancer. At the point where treatments that specifically benefit women with the BRCA1/2 gene mutation are licensed there will be significantly increased take up.
- Growth in understanding of importance of BRCA1/2 gene testing in the medical community.
- Growth in awareness amongst the general public as a consequence of campaigning by charities and high-profile cases such as Angelina Jolie’s.

“I frequently work with women who are going through treatment for ovarian cancer. My colleagues and I are ‘genetically literate’ but those of us working in oncology need consistent guidelines on when to test and how to counsel. With training the nurses can do the counselling, as this type of support is part of our daily interaction with patients.” – Dr Tracie Miles, President, National Forum Gynaecological Oncology Nurses.

“At the Christie in Manchester genetic counselling is being embedded into the clinics where ovarian and breast cancers are treated. We need to be ready before an explosion in demand as a result of product licensing. Testing needs to be quicker and counselling managed through the clinics.” – Professor Gareth Evans, Honorary Professor of Medical Genetics and Cancer Epidemiology at The University of Manchester.
Our recommendations
This needs to be part of a patient’s standard of care. Who commissions and pays for BRCA1/2 gene testing must be urgently clarified.

Exactly who commissions and pays for BRCA1/2 gene testing is confused. We believe that NHS England is responsible for commissioning medical genetics including BRCA1/2 gene testing. That contrasts to the NICE clinical guideline published earlier in 2013 that suggests that Clinical Commissioning Groups (CCGs) commission and pay for BRCA1/2 testing. Clinicians we have spoken to are unclear, and that is hindering access for patients. This lack of clarity results in barriers to women with ovarian cancer and their families accessing potentially lifesaving information.

Ovarian Cancer Action seeks to clarify the commissioning and funding of BRCA1/2 gene testing so that patients across the UK are able to access the same care and treatment. A high quality of service needs to be provided in every area. At present women’s access to BRCA1/2 gene testing is dependent on which centre they are treated at. During our roundtable discussion, Professor Sir John Burn, Institute of Genetic Medicine, commented, ‘It’s important to tell the truth and critical we tell the same story.’ This recognises the need for patients and family members in all areas to have access to consistent information about their genetic status and options to protect their health.

In order to ensure gold standard treatment across the UK, the BRCA1/2 gene testing pathway needs to be written into the standard of care. This can include testing protocols, waiting times, and the funding channel. The funding structure therefore requires clarification.
Conclusion

Ovarian Cancer Action is calling for improved access to genetic testing for women with ovarian cancer and their families. The need is there now and we anticipate that it will grow. We want the NHS to be ready to meet this demand in an efficient and cost effective way. These are the changes that need to be made:

1. All women with non-mucinous epithelial ovarian cancer should be BRCA1/2 gene tested.
2. These women should be BRCA1/2 gene tested at the point of diagnosis.
3. This needs to be part of a patient’s standard of care. Who commissions and pays for BRCA1/2 gene testing must be urgently clarified.

Expanding BRCA1/2 gene testing will represent an additional cost to the NHS. However, it is important to look at the value of this spending, in terms of how it can provide valuable information for patients and their relatives and choices that they can make about their future health. When considering BRCA1/2 gene testing the NHS must not only focus on the upfront costs but also consider the potential for savings when avoiding cases of cancer in the future. Lives can be saved and patients can be spared the trauma of diagnosis and treatment for a disease that has poor survival rates.

Facts about ovarian cancer

- One woman every two hours dies from the disease in the UK.
- It is the fifth most common cancer amongst women, with approximately 7,000 new UK diagnoses each year. The UK survival rates are amongst the poorest in Western Europe. It is the UK’s most deadly gynaecological disease.
- There is currently no proven screening tool and symptoms awareness amongst healthcare providers and women can be poor.
- Around 30% of ovarian cancer patients in the UK are diagnosed each year through emergency admissions.
- Early diagnosis has an important effect on outcomes. If diagnosed in the early stages up to 90% of women will survive for more than five years. This is the message of the current regional ‘Be Clear on Cancer’ campaign.
- Most women are not diagnosed until it has already spread, resulting in poor survival rates. More widespread availability of BRCA1/2 gene testing can change survival rates, as women are able to opt for risk-reducing surgery.
- Many GPs lack the necessary education about BRCA1/2 to be able to spot significant family histories of cancer and refer for genetic testing appropriately.

“Before my BRCA1 gene mutation test I’d considered the choices a positive result would offer me. With my family complete my main priority was doing all I could to be around for my children. Having seen the operations and treatments my mother endured for breast and ovarian cancer I felt that prevention was definitely better than cure.” – Niki Orchard, who was tested and found to have the BRCA1 gene mutation.

“We need to give young women information and advice about how to time risk-reducing surgery. Without this they cannot make informed choices about reducing their risk of developing ovarian cancer.” – Dr Adam Rosenthal, Consultant Gynaecological Oncologist.
Appendix 1

Overview of the discussion
A very lively and positive discussion about the complexities of BRCA1/2 gene testing followed by a question and answer session. The event was well attended by both clinicians and patients and their families.

The panel
- Robin Lustig, Journalist and radio broadcaster (Chair)
- Professor Sir John Burn, Professor of Clinical Genetics, Newcastle University
- Professor Paul Pharoah, Professor of Cancer Epidemiology / Department of Oncology, University of Cambridge
- Professor Anneke Lucassen, Professor of Clinical Genetics, Southampton University
- Vicki Kiesel, Registered Genetic Counsellor
- Dr Sue Gessler, Consultant Clinical Psychologist, UCLH
- Dr Mark Sheehan, Oxford BRC Ethics Fellow / The Ethox Centre
- Professor Charlie Gourley, Medical Oncologist, Honorary Consultant in Medical Oncology, University of Edinburgh

Key points
- It was agreed by the panel that an individual had a right to know about the opportunity for and the subsequent outcome of genetic testing.
- It was agreed that testing should be offered at point of diagnosis.
- It was agreed that the current process of pre-testing counselling was making a wider roll out of BRCA1/2 gene testing prohibitively expensive.
- NICE guidelines are already advocating wider testing and support equality amongst those who should be tested.
- BRCA1/2 gene testing will help to reform thinking about ovarian cancer. This will encourage people to think of this as a treatable disease.
- Pathways to care/treatment following diagnosis of a BRCA1/2 gene mutation need to be agreed to ensure that regional variation doesn’t cause alarm amongst family members undergoing treatment.
- Ideally a couple of centres can do all the BRCA1/2 gene testing for ovarian cancer to produce consistency.
Appendix 2
Glossary

There are three main types of ovarian cancer:
- Epithelial ovarian cancer
- Germ cell ovarian cancer
- Sex-cord stromal ovarian cancer

In this policy report we have used the following terms:

**Epithelial ovarian cancer** – this develops in the cells that line the surface of the ovary. The main histological sub-types of epithelial ovarian cancer are:
- High grade serous
- Low grade serous
- Endometrioid
- Clear cell
- Mucinous
- Undifferentiated

**High grade serous ovarian cancer** – this is a type of cancer that is now felt to predominantly arise in the fallopian tube. High grade means it is an aggressive type of cancer that grows quickly. It is a type of invasive non-mucinous epithelial ovarian cancer.

**Non-mucinous epithelial ovarian cancers** – these are all types of epithelial cancers except mucinous cancers. This includes invasive non-mucinous epithelial cancer, meaning cancers that have started to spread or are capable of spreading outside of the ovary.

**BRCA gene mutations**
BRCA1 and BRCA2 are human genes that belong to a class of genes known as tumour suppressors. Mutation of these genes has been linked to hereditary breast and ovarian cancer.

**Chemotherapy and platinum chemotherapy**
Chemotherapy is a drug-based treatment used to fight a wide variety of cancers. Platinum chemotherapy uses platinum-based drugs to fight particular forms of cancer.

**Clinical Commissioning Groups** – Clinical Commissioning Groups are groups of GP Practices that are responsible for commissioning most health and care services for patients.

**Familial cancer**
Cancer that occurs in families more often than would be expected by chance. These cancers often occur at an early age, and may indicate the presence of a gene mutation that increases the risk of cancer.

**Genetic testing**
Analysing DNA to look for a genetic alteration that may indicate an increased risk for developing a specific disease or disorder.
Appendix 3

Bibliography


- NICE 2013b, Cambridge University Hospitals Undated.


1. NICE guidelines for familial breast cancer (CG164) reference BRCA1/2 gene testing relating to ovarian cancer. BRCA1/2 gene testing is not specifically referenced in NICE guidelines for ovarian cancer (CG122).

2. This includes women with high grade serous as well as clear cell endometrioid, undifferentiated and unclassified tumours to ensure that all possible BRCA1/2 gene mutation carriers are identified. This high-risk group is around 70% of all ovarian cancers.

3. Women who have a BRCA1 gene mutation have a 40%-60% lifetime risk of developing ovarian cancer. Women who have a BRCA2 gene mutation have a 10%-30% chance of developing ovarian cancer. A Beginner’s Guide to BRCA1 and BRCA2, The Royal Marsden NHS Foundation Trust, April 2013.


7. NICE 2013b, Cambridge University Hospitals Undated.


10. Figures were calculated based on the National Cancer Intelligence Network’s incidence by morphology group data. Overview of Ovarian Cancer in England: Incidence, Mortality and Survival, November 2012.


14. Women with non-invasive non-mucinous epithelial ovarian cancer may not require testing at the point of diagnosis.


For further information about BRCA1/2 gene testing and the other work undertaken by Ovarian Cancer Action, please do contact us at:

Ovarian Cancer Action  
8-12 Camden High Street  
London  
NW1 0JH  
info@ovarian.org.uk  
020 7380 1730