ovarian cancer action

I have a BRCA1/2 gene mutation

Everything you need to know about BRCA1/2 gene mutations

(NHS England only)

What having a BRCA1/2 gene mutation means

Receiving a positive test result for a BRCA1/2 gene mutation can be frightening but there are steps you can take to make it less daunting. This guide aims to help you feel armed with all the information you need. A positive test means that your chance of developing certain cancers will be higher than someone who does not have a genetic mutation in these genes.

This table explains how your risk increases according to whether you have a BRCA1 or a BRCA2 gene mutation.

Estimated Cancer Risk by Age 70			
Type of Cancer	**Normal risk**	**BRCA1 Risk**	**BRCA2 Risk**
Ovarian cancer	2%	40-60%	10-20%
Breast cancer in women	11%	60-85%	45-60%
Breast Cancer in men	0.1%	Up to 3%	Up to 12%
Prostate cancer	12%	Elevated risk (% unknown)	35-40%
Pancreatic cancer	1.3%	3-4%	7%

Chance of passing mutations on

Whether you're a mother or a father, if you have a mutation in either BRCA1/2 gene then there is a 50% chance of passing the mutation on to your children.

There are a few possible outcomes if both parents carry a BRCA1/2 gene mutation:

- There is a 1 in 2 chance that your child will inherit a single BRCA1/2 gene mutation and a 1 in 4 chance that your child will not inherit any BRCA1/2 gene mutation at all. There is also a 1 in 4 chance that they will inherit both of the mutations.
- If one parent has a mutation in their BRCA1 gene and the other in their BRCA2 gene and the child inherits both, then their risk of developing breast or ovarian cancer is that of a BRCA1 carrier.
- If a child inherits the BRCA2 gene mutation from both sides, then they will have something called fanconi anaemia (also known as fanconi syndrome). This disorder can lead to shorter growth, a smaller head and underdeveloped thumbs. Fanconi anaemia also puts the child at higher risk of early childhood cancers, leukaemia and wilms tumours in the kidneys.

What action can I take?

Lifestyle

While these won't stop you from developing ovarian cancer, there are a number of lifestyle related factors that can help lower your risk. These include:

- Using the oral contraceptive pill
- Breast feeding, if you have the option
- Maintaining a healthy weight
- Eating a healthy, balanced diet
- Exercising regularly
- Not smoking

Screening

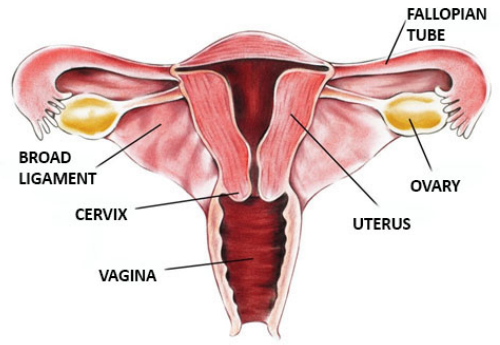
The National Breast Screening Programme offers 50-70 year old women mammograms every three years on the NHS. There is currently no national screening programme for ovarian cancer.

Surveillance

Women with a BRCA1/2 gene mutation are offered yearly MRI scans, from the age of 30, to check for breast cancer. Surveillance isn't routinely offered for ovarian cancer but it may be possible to have regular CA125 blood tests and pelvic ultrasound scans. Talk to your GP to find out what is available locally.

Surgery

You may have the option of having surgery to remove your ovaries and fallopian tubes, which will reduce the risk of cancer developing. As well as reducing your risk of developing breast cancer by 50%, having your ovaries and fallopian tubes removed (bilateral salpingo-oophorectomy) will reduce your risk of developing ovarian cancer to 5%.



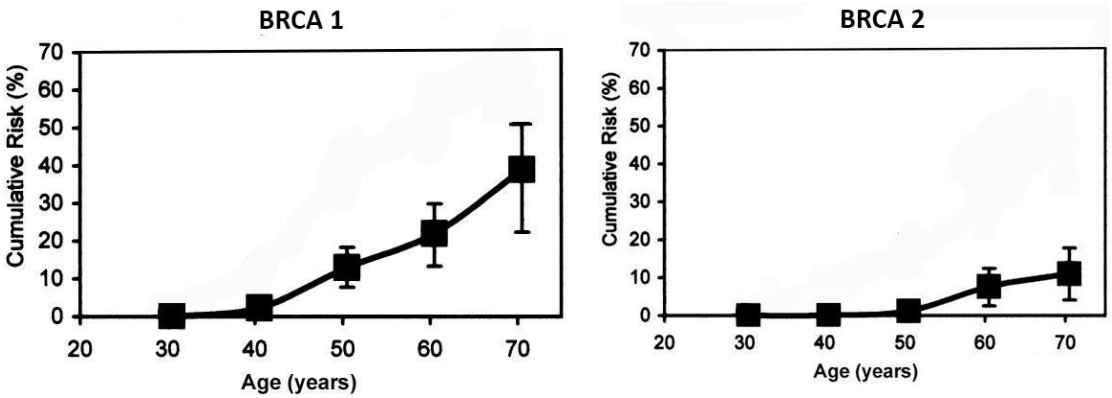
This surgery may be offered in addition to a risk-reducing mastectomy, which will reduce your breast cancer risk further; to 5-10%.

Another option you may be given is to have a risk-reducing salpingectomy (removing the fallopian tubes only); as evidence suggests that the majority of BRCA1/2-associated cancers start at the end of the fallopian tube.

However, while evidence from the general population suggests that removing tubes approximately halves risk of ovarian cancer, there is no current evidence of safety or efficacy of this approach in women with BRCA1/2 gene mutations. In fact, current research suggests that it offers less protection than removing the ovaries too.

When should I have surgery?

If you do decide to have surgery, you will need to consider when the best time is for you to do so. Age is the biggest factor and the below graphs look at how ovarian cancer risk changes with age in women with a BRCA1/2 gene mutation.



Graphs adapted from Antoniou et al. AJHG 2003

In both cases, the graphs show no significant increased risk of ovarian cancer until age 45. If you have a BRCA1 gene mutation, risk increases at age 45-49 and again at age 55-59. Therefore, surgery is advised by age 40. Risk increases later if you have a BRCA2 gene mutation, so surgery can be left until you are in your mid-40s.

You will also need to consider the age your relatives developed ovarian or breast cancer and, because risk reducing bilateral salpingo-oophorectomy will make you infertile, whether or not you've completed your family. You can discuss all of these factors with your genetics counsellor before making a final decision.

What will happen to me if I have surgery?

Medical menopause

The most significant side-effect of risk reducing bilateral salpingo-oophorectomy is the menopause; the time in a woman's life when she stops having periods.

The natural menopause is usually very gradual, giving a woman time to adjust to the changes that are happening to her body. But when the menopause occurs because the ovaries are surgically removed, symptoms can be quite severe due to the abrupt onset of hormonal changes.

Symptoms can include:

- Hot flushes
- Vaginal discomfort and dryness
- Needing to wee more frequently and urgently

Less common symptoms including brittle nails, thinning of the skin, hair loss and aches and pains

Besides the physical symptoms you may feel:

- Too young to be going through the menopause
- Worried about your options to have a baby
- Less feminine
- Worried about the future

There are many different ways to treat symptoms of a surgical menopause and you may like to discuss the options with your GP or consultant:

- Following a healthy lifestyle
- Hormone replacement therapy (HRT)
- Anti-depressants such as Citalopram, Paroxetine and Venlafaxine
- Cognitive behavioural therapy
- Counselling
- Herbal supplements
- Vaginal oestrogen

Starting a family

If you want to start a family, but are worried about passing on a genetic mutation, there are a few options you can explore. Besides adoption, these include:

Having your children as normal

A parent with a BRCA1/2 gene mutation has a 50% chance of passing it on to their child but you can, of course, have your children as normal. It's possible that there will be better screening and treatment of ovarian cancer over the next few decades and any child born today will not be at risk of cancer for many years.

Pre-implantation genetic diagnosis (PGD)

This is a procedure that aims to allow families to avoid passing on an inherited condition to their children. It is only available to parents who haven't already conceived naturally. For this procedure you will have to undergo in vitro fertilisation (IVF). This involves collecting your eggs and fertilising them with your partner's sperm in a laboratory. Cells from your fertilised eggs (embryos) are then tested for a gene mutation. An embryo that does not have the gene mutation is then transferred to your womb and then your pregnancy is allowed to continue as normal. Any remaining, non-mutated embryos can be frozen for use in future cycles. The success rate for PGD is around 20%.

According to NHS England's clinical commissioning policy '*Pre-implantation Genetic Diagnosis*' up to three cycles are available on the NHS in the UK, but only one unaffected child will be funded. Referrals for PGD will need to go through the genetics service so, if you would like to consider this procedure, speak to your genetics specialist. For more information, see www.geneticalliance.org.uk/aboutpgd.htm

Pre-natal testing

Early on in a pregnancy it is possible to test for inherited genetic mutations. You will then have a choice whether to carry on with the pregnancy or terminate it early. This is an invasive procedure with a slight risk of miscarriage. For more information about pre-natal testing and the options available to you, you can speak to your genetics specialist, gynaecologist or GP.

Egg or sperm donation

Depending on whether it's the future mother or father that has the mutation then egg or sperm donation can be considered to avoid passing on the genetic mutation. If the mother is the carrier of the mutation, eggs can be donated and if the father is the carrier, sperm can be donated. Once donated, IVF can be carried out.

Telling your family

Telling your family that you have a BRCA1/2 gene mutation may seem daunting. Just remember that you do have options, and there is support available.

Telling your children

1. You can delay telling your children until you feel they are old enough. The benefit of this is that it doesn't cause them any distress at an age when you may feel it is too much for them to handle or understand.

2. You can tell them at a young age. The benefit of this is that they have time to come to terms with their possible risk and you can start having discussions early on about some of the difficult decisions they may have to make.

There is no right or wrong time to tell your children. You'll want to discuss this with someone close to you, and with your genetics team, to help you to decide which would be the best option for your family.

Given that the cancers attributed to the BRCA1/2 gene mutations don't usually arise until people are in their 20s or 30s (or later), the testing of young children is not usually available, as action can't be taken until they are over 18. It is also generally better if children can be involved in discussions about their own genetic testing, and this is not possible for very young children. Teenagers may benefit from a discussion with a genetics team, even if testing is not carried out until they are 18.

Telling your extended family

Your genetics team will help you identify which of your extended family may also have inherited the mutation. This will depend on what side of the family – your father's or mother's – the gene was passed down from.

Once this is established, your brothers, sisters, aunts, uncles and cousins on that side of the family will be known to be at risk of having inherited the mutation. While it is recommended that they are informed, there are currently no official procedures to assist with this and the responsibility and decision to tell them lies with you.

If you don't feel comfortable having this discussion with your family members, your genetics clinic can help with this. For example, they may be able to give you information to pass on.

This will explain that a family member has an inherited genetic mutation and will describe what this might mean to them and how they can obtain a referral to their nearest genetics clinic for genetic counselling and testing.

The real impact of BRCA1/2 testing: The patient view

Angela Walker found out she had a BRCA1/2 gene mutation after her ovarian cancer diagnosis.
"Knowing I had the BRCA2 gene mutation helped me greatly because my children were little. It means we know what to look for in my daughter and she can be monitored in the future."

Annie Chillingworth says that knowing her BRCA1/2 status was useful for her whole family.
"My siblings and cousins are all taking measures to protect themselves. It puts them in a strog position of control. My daughter does not have the mutation so she's able to move on from the anxiety of not knowing."

Niki Orchard has a BRCA1/2 mutation and had preventative surgery after losing her mother to cancer.
"Knowledge is power and each individual person can choose what to do with that knowledge."

Caroline Presho is BRCA2 positive and has opted for risk reducing surgery.
"I felt vulnerable not knowing my BRCA status, given my family history of cancer, and I couldn't live with the worry and anxiety. After the surgery I felt happy and relieved that I have taken away another risk for breast and ovarian cancer."

References & resources

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Clinical Commissioning Policy: Genetic Testing for BRCA1 and BRCA2 Mutations, NHS England, 2015

Ovarian cancer: recognition and initial management, NICE, 2011
Familial breast cancer: classification, care and managing breast cancer related risks in people with a family history of breast cancer, NICE, 2013

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NHS England Clinical Commissioning Policy: Pre-implantation Genetic Diagnosis (PGD), April 2013. https://www.england.nhs.uk/wp-content/uploads/2013/04/e01-p-a.pdf

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