

HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (HBOC) – *BRCA2*

PATIENT INFORMATION

What is Hereditary Breast and Ovarian Cancer syndrome?

People with *BRCA2* alterations have a genetic condition called Hereditary Breast and Ovarian Cancer syndrome (HBOC). HBOC is caused by an error (alteration) in the *BRCA1* or *BRCA2* gene. About 2% of women diagnosed with breast cancer have HBOC and about 10% of women with ovarian cancer have HBOC. Families with HBOC usually have several relatives who have developed breast cancer, ovarian cancer, prostate cancer, or pancreatic cancer.

Women with *BRCA2* alterations have higher risks of breast, ovarian, and pancreatic cancers. The breast cancers are often hormone receptor positive cancers. Some women with *BRCA2* alterations develop breast cancer in both breasts. Women with *BRCA2* alterations have a higher risk of developing ovarian cancer or other related cancers of the fallopian tube or peritoneum (lining of the abdomen).

Men with *BRCA2* alterations have higher risks of prostate, breast, and pancreatic cancers. Men with *BRCA2* alterations may be at risk for developing aggressive prostate cancer. Men with *BRCA2* alterations do have much lower risks of cancer than women with *BRCA2* alterations.

The two tables below show the risks of cancer for women and men with *BRCA2* alterations compared to people in the general population. These percentages are lifetime risks of cancer. This means that these are the risks of cancer totaled up over a lifetime.

Women:

Cancer	<i>BRCA2</i> Risk	General Population Risk
Breast	50-85%	12%
Second breast cancer	>50% depending on age	20%
Ovary	10-20%	1-2%
Pancreas	~3-5% or more	<1%

Men:

Cancer	<i>BRCA2</i> Risk	General Population Risk
Breast	~6-10%	0.1%
Prostate	increased	16%
Pancreas	~3-5% or more	<1%

<References: Moran et al., 2012; Antoniou et al, 2003; Chen et al., 2006>

What causes HBOC?

All of us have about 22,000 genes in almost every cell in our body. We have two copies of almost every gene (one copy from each parent). Each gene has a specific job in the body. Genes are made up of a series of four chemical letters (our DNA) in a set pattern. If there is an error (alteration) in the DNA pattern of a gene, then it will not be able to do its job. The *BRCA2* gene helps to fix DNA damage in our cells and keeps our cells growing normally.

People with HBOC are born with one altered *BRCA2* gene that does not work and one normal *BRCA2* gene that does work. As long as the one working *BRCA2* gene is doing its job, then cancer is unlikely to occur. This is why some people with *BRCA2* alterations never develop cancer. Over time, there is a chance that the working *BRCA2* gene will get damaged in a single cell. This happens because of chance or because of exposures to cancer-causing agents. Then the cell has no *BRCA2* gene to help protect its DNA. Cancer can eventually develop when this happens.

People with HBOC have one altered *BRCA2* gene in almost every cell of their body. But they are only at risk for developing certain types of cancer. This is because the *BRCA2* is most active in certain organs and cell types.

How is HBOC inherited?

BRCA2 alterations are passed on from parent to child, like other family traits. Hereditary Breast-Ovarian Cancer syndrome is an example of a “dominant” genetic condition. Dominant means that it takes only one altered copy of a gene in order to cause the condition. Hereditary Breast-Ovarian Cancer syndrome is caused by inheriting an altered *BRCA2* gene from one of your parents.

Both men and women can have *BRCA2* alterations and can pass it on to their children. *BRCA2* alterations do not skip generations. So if someone in your family does not have the altered gene, then their children cannot inherit it.

Here are the chances that your relatives might have the altered gene:

- **Your Children** – a 50% chance for each child. Both your daughters and your sons can inherit the altered gene.

Your Mother or Father – almost a 50% chance. In most cases, one of your parents will be found to have the altered gene. In rare cases, neither of your parents will have the altered gene.

- **Your Brothers and Sisters** – a 50% chance if one of your parents had the alteration. If neither of your parents had the alteration, then your siblings have a very low risk of having the alteration.
- **Your aunts, uncles, cousins, nieces and nephews** – their chances of having an altered gene depend on where they are in the family tree. Remember that only one side of your family will be at risk of having the altered gene.

Please ask us if you have any questions about the risks to your relatives or how best to share this news with your family

What are the recommendations for cancer screening and risk reduction?

Screening refers to medical tests that try to find cancer at an early stage of disease. Risk reduction strategies are used to try to prevent a specific type of cancer.

Screening:

For women:

- clinical breast exams every 6 months (beginning at age 25)
- breast MRIs every year (beginning at age 25)
- mammograms every year (beginning at age 25-30)

For men:

- clinical breast exams every year (beginning at age 35)
- prostate cancer screening every year (beginning at age 40)

For men and women:

- skin checks with a dermatologist every year for atypical moles and melanoma

For men and women with a family history of pancreatic cancer:

- pancreatic cancer screening

Risk Reduction:

- Preventive surgery to remove the ovaries and fallopian tubes – This surgery is called prophylactic salpingo-oophorectomy. This surgery reduces the risk of ovarian cancer by greater than 90%. Removing the ovaries and tubes before menopause also reduces the breast cancer risk by as much as 50%. It is recommended that women have this surgery after they are done having children. Ideally, surgery is performed between ages 35-40, but it can also be done at other ages. Some women choose to have a hysterectomy (removal of the uterus) at the same time. Issues to consider about salpingo-oophorectomy: the timing of the procedure, the type of surgery, the impact of becoming menopausal, and the benefits and risks of this surgery. We would be happy to refer you to a gynecological surgeon to talk more about these issues.
- Preventive surgery to remove breast tissue – This surgery is called prophylactic mastectomy. This surgery can reduce breast cancer risk by over 90%. Issues to consider about mastectomy: the timing of the procedure, the type of surgery, options for breast reconstruction, and the benefits and risks of this surgery. We would be happy to refer you to a breast surgeon and a plastic surgeon to talk more about these issues.
- Some medications can reduce the risk of breast and ovarian cancer in women with *BRCA2* alterations-
 - Taking a drug to reduce the risk of cancer is called chemoprevention. Drugs like tamoxifen, exemestane, and raloxifene may help reduce the risk of breast cancer in women with *BRCA2* alterations. Decisions about risk-reducing medications should be made after careful consideration with your doctor about the risks, benefits, and side effects. Our physicians are also happy to talk with you about this option.

- Oral contraceptives (birth control pills) reduce the risk of ovarian cancer. There has been concern about the use of birth control pills and increased breast cancer risk. There are risks and benefits of using birth control pills that should be considered with your doctor. Our physicians are also happy to talk with you about this option.

Where can I find more information?

Dana Farber Cancer Institute, Center for Cancer Genetics & Prevention
www.dana-farber.org/cancergenetics

Facing Our Risk of Cancer Empowered
<http://www.facingourrisk.org/>

Bright Pink
<http://www.brightpink.org/>

American Cancer Society
<http://www.cancer.org/>

National Cancer Institute
www.cancer.gov

References

- Antoniou et al. Am J Hum Genet. 2003 May;72(5):1117-30
- Chen et al. J of Clin Oncol. 2006 Feb 20;24(6):863-71
- Moran et al. Fam Cancer 2012 (11):235-242
- NCCN Guidelines Version 3.2013
- PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002-. Genetics of Breast and Ovarian Cancer (PDQ®): Health Professional Version. [Updated 2012 November 9]. Available at: <http://cancer.gov/cancertopics/pdq/genetics/breast-and-ovarian/HealthProfessional>.