

HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (HBOC) – *BRCA1*

PATIENT INFORMATION

What is Hereditary Breast and Ovarian Cancer syndrome?

Hereditary Breast and Ovarian Cancer syndrome (HBOC) is the most common hereditary form of breast and ovarian cancer. About 2% of women diagnosed with breast cancer and about 10% of women with ovarian cancer have HBOC. Families with HBOC usually have several family members with breast or ovarian cancer. Other cancers may be seen, including male breast cancer, pancreatic cancer, prostate cancer and melanoma. Women with HBOC tend to develop cancers at an earlier age than the general population.

HBOC is due to problems in the way that our cells repair themselves and keep their genetic information healthy. All of us have about 22,000 genes in almost every cell in our body. Each of these genes is made up of a series of four chemical letters in a certain order (our DNA). Some of our genes, through the proteins that they make, act as caretakers to fix damage to our DNA and keep our cells growing normally. These caretaker genes include *BRCA1*.

Women with harmful *BRCA1* alterations (mutations) are more likely to develop hormone receptor negative, Her2/Neu negative (called “triple negative”) breast cancers. Below are the estimated lifetime risks of cancer in people with *BRCA1* gene alterations, as compared to the general population. The percentages cited may change as more research is done.

Women:

Cancer	<i>BRCA1</i> Risk	General Population Risk
Breast	50-85%	12%
Second breast cancer	>50%	20%
Ovary	20-40%	1-2%
Pancreas	~1-5% or more	<1%

Men:

Cancer	<i>BRCA1</i> Risk	General Population Risk
Breast	~1%	0.1%
Prostate	increased	16%
Pancreas	~1-5% or more	<1%

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

What causes HBOC?

HBOC is usually caused by alterations in the *BRCA1* and *BRCA2* genes. Up to 90% of families with a strong history of breast and ovarian cancer have alterations in the *BRCA1* and *BRCA2* genes. In contrast, up to 45% of families with a strong history of breast cancer (but not ovarian cancer) will

have *BRCA1* and *BRCA2* gene alterations. Alterations in other genes may contribute to the cancer history in other families.

A person who has an alteration in either of these genes is at risk for developing the cancers seen in HBOC. All of us have two copies of almost every gene (one from each parent), so even if one is altered, the other one can work normally. However, if the second copy of the gene is damaged by chance, the cell no longer has a working copy of the gene to help protect the DNA and keep the cell on track. Cancer can eventually develop when this happens.

How is HBOC inherited?

HBOC is inherited in an autosomal dominant manner. Autosomal means that both men and women can have HBOC and pass it on to their children (although the risks for men to develop cancer are much lower than for women). Dominant means that it takes only one altered copy of a gene in order to cause HBOC.

If you have an altered gene, here are the chances that other relatives might have inherited it:

- **Your Children** –50% risk for each child
- **Your Mother or Father** – almost a 50% risk. In most cases, you will have inherited the altered gene from either your mother or your father. In rare cases, neither of your parents will have the altered gene, because it has occurred as a new genetic event in you.
- **Your Brothers and Sisters** – 50% risk 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.
- More distant relatives like your **aunts, uncles, cousins, nieces, and nephews** may have inherited this gene alteration depending on where they are in the family tree. Please talk to your health care team about risks for specific relatives.

How is HBOC managed?

There are a number of medical recommendations to help manage the increased risks for cancer that should be considered. Although we do not currently have any perfect strategies for reducing cancer risks, we do know that by close monitoring, some cancers can be detected in their earliest stages when they are most treatable. Screening is testing that is done to try to find cancer early. Risk reduction strategies are used to try to prevent cancer.

Screening:

For women:

- self breast exams every month
- 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)

For men:

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

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

- consideration of pancreatic cancer screening

Risk Reduction:

- It is recommended that women undergo preventive removal of the ovaries and fallopian tubes (prophylactic bilateral salpingo-oophorectomies) after they have completed their families and are physically and emotionally ready (ideally between ages 35-40). This surgery reduces the lifetime risk of ovarian cancer by more than 90% regardless of the age at which it is performed. Removing the ovaries and fallopian tubes before menopause also reduces the breast cancer risk by as much as 50%. Removal of the uterus may also be considered.
- Women may wish to discuss the option of surgically removing breast tissue preventively (prophylactic mastectomies) to reduce the risk of breast cancer. Bilateral prophylactic mastectomies can reduce breast cancer risk by over 90%. For women who do choose this risk reduction strategy, we recommend a discussion of the timing, type of surgery, reconstruction options, benefits and risks with a breast surgeon or a plastic surgeon.
- Some medications can be effective in reducing the risk of breast and ovarian cancer in women with *BRCA1* alterations.
 - Drugs like tamoxifen, exemestane (a type of aromatase inhibitor), and raloxifene may help reduce the risk of breast cancer. Any decision about risk-reducing medications should be made after careful consideration with your doctor about the risks, benefits and side effects.
 - 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.

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 (FORCE)
<http://www.facingourrisk.org/>

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

American Cancer Society

National Cancer Institute

www.cancer.gov

References

- Antoniou et al. Am J Hum Genet. 2003 May;72(5):1117-30
- Chen et al., 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>.