



the jill lamb foundation

Breast Cancer Risks – Inherited Genetic Mutations

Inherited genetic mutations have been found to be a cause of breast cancer; the most commonly known inherited mutations occur in the following genes: BRCA1, BRCA2, p53 and PTEN/MMAC1.

Although the known inherited mutations greatly increase the risk of developing breast cancer, they are very rare in the general population and account for only 5 to 10 percent of all breast cancers diagnosed in the U.S.¹.

BRCA1/BRCA2 and Breast Cancer

BRCA1 and BRCA2 (standing for BREast CANcer gene 1 and 2) are the most well-known genes of those linked with breast cancer. It is estimated that about 250,000 women in the United States carry a BRCA1 or BRCA2 mutation; these women have a much higher risk of breast cancer.

A woman only has about a 12 percent chance of developing breast cancer in her lifetime (assuming she lives until the age of 85) if she does not have a BRCA1 or BRCA2 mutation. However, the chances of a woman developing breast cancer if she has a BRCA1 or BRCA2 vary greatly. For women with the BRCA1 mutation, the chance of developing breast cancer in her lifetime is somewhere between 60 and 90 percent; for women with the BRCA2 mutation the chances are between 30 and 85 percent.²

¹ National Cancer Institute. Genetics of breast and ovarian cancer (PDQ).

http://www.nci.nih.gov/cancertopics/pdq/genetics/breast-and-ovarian/HealthProfessional/page1#Section_66, 2008.

² Struewing JP, Hartge P, Wacholder S, et al. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. *N Engl J Med.* 336: 1401-8, 1997.

Thorlacius S, Struewing JP, Hartge P, et al. Population-based study of risk of breast cancer in carriers of BRCA2 mutation. *Lancet.* 352: 1337-9, 1998. cohort study in Ontario, Canada. *J Natl Cancer Inst.* 98(23):1694-706, 2006.

Antoniou A, Pharoah PDP, Narod S, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case Series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet.* 72(5):1117-30, 2003.

Together, mutations in the BRCA1 and BRCA2 genes are thought to explain a large portion of hereditary breast cancer cases³. However, most breast cancers are not hereditary or genetic. Up to 40 percent of women with a BRCA1 mutation will never have breast cancer. It is likely that a combination of factors determines who will develop breast cancer. In fact, recent research suggests that certain lifestyle factors, including breastfeeding and being physically active during adolescence, may help reduce breast cancer risk in women with BRCA mutations⁴.

BRCA Mutations & Risk of a Second Primary Breast Cancer

BRCA mutations can increase the risk of a second primary breast cancer (a second breast tumor that is unrelated to the first one) among women who have already had breast cancer. The chance of developing a second primary cancer ten years after diagnosis of the first cancer is about 30 percent for breast cancer survivors with a BRCA mutation (32 percent for BRCA1 mutation and 25 percent for BRCA2 mutation), compared to about 10 percent for survivors without mutations⁵. In young women with a BRCA mutation, the lifetime chance of a second primary tumor in the opposite breast may be as high as 60 percent⁶.

BRCA Mutations & Risk of Ovarian Cancer

In addition to increasing the risk of breast cancer, BRCA mutations increase a woman's risk of ovarian cancer. A woman's chance of developing ovarian cancer by age 70 is about 1 to 2

Risch HA, McLaughlin JR, Cole DEC, et al. Population BRCA1 and BRCA2 mutation frequencies and cancer penetrances: a kin-cohort study in Ontario, Canada. *J Natl Cancer Inst.* 98(23):1694-706, 2006.

King MC, Marks JH and Mandell JB. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. *Science.* 302: 643-6, 2003.

³ National Cancer Institute. Genetics of breast and ovarian cancer (PDQ). http://www.nci.nih.gov/cancertopics/pdq/genetics/breast-and-ovarian/HealthProfessional/page1#Section_66, 2008.

⁴ King MC, Marks JH and Mandell JB. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. *Science.* 302: 643-6, 2003.

Jernstrom H, Lubinski J, Lynch HT, et al. Breast-feeding and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. *J Natl Cancer Inst.* 96: 1094-8, 2004.

⁵ Metcalfe K, Lynch HT, Ghadirian P, et al. Contralateral breast cancer in BRCA1 and BRCA2 mutation carriers. *J Clin Oncol.* 22(12):2328-35, 2004.

⁶ Domchek SM and Weber BL. Chapter 17: Inherited Genetic Factors and Breast Cancer, in Harris JR, Lippman ME, Morrow M, Osborne CK. *Diseases of the Breast*, 3rd edition. Lippincott Williams and Wilkins, 2004.

percent if she does not have a BRCA1 or BRCA2 mutation⁷, 39 to 63 percent if she has a BRCA1 mutation and 11 to 27 percent if she has a BRCA2 mutation⁸. Women with a BRCA mutation can reduce their risk of ovarian cancer by having prophylactic oophorectomy (surgical removal of the ovaries).

⁷ Ries LAG, Melbert D, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2005, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2005/, based on November 2007 SEER data submission, posted to the SEER web site, 2008.

⁸ Isaacs CJD, Peshkin BN, Schwartz M. Chapter 19: Evaluation and Management of Women with a Strong Family History, in Harris JR, Lippman ME, Morrow M, Osborne CK. Diseases of the Breast, 3rd edition. Lippincott Williams and Wilkins, 2004.