BRCA2

The *BRCA2* gene is a tumor suppressor gene. Tumor suppressor genes slow down cell division, repair DNA mistakes, or tell cells when to die. When they don't work properly, cells can grow out of control, which can lead to cancer. The primary role of *BRCA2* is repairing damaged DNA before a cell divides to make more copies of itself. *BRCA2* works together with other genes, such as *BRCA1*, *PALB2*, and the *RAD51* gene complex to direct the repair of the damage.

Like most genes, each person has two copies of the *BRCA2* gene: one inherited from each parent. A mutation in a single *BRCA2* gene inherited from either parent is known to increase risk of specific cancers (breast, ovarian, prostate, pancreatic, melanoma) over a lifetime.

In very rare cases, a person can inherit two *BRCA2* mutations, one from each parent. This causes a blood condition called Fanconi anemia, which is associated with bone marrow failure, physical disabilities, and childhood cancers.

How common are mutations in the *BRCA2* gene?

Mutations in the *BRCA2* gene are rare—found in approximately 1 in 1100 individuals in the general population and 1 in 40 Ashkenazi Jewish individuals.[1,2]

How mutations in this gene impact risk

Women

If a woman has a mutation in the *BRCA2* gene, her chances of developing breast, ovarian, melanoma, and pancreatic cancer are greater than that of the average US woman. This does not mean that she has a diagnosis of cancer or that she will definitely develop cancer in her lifetime.

Cancer by age 70	Average US woman[3]	With *BRCA2* mutation
Breast	7.1%	74%[4]
Ovarian	<1%	12%[4]

[1] Prevalence and penetrance of BRCA1 and BRCA2 mutations in a population-based series of breast cancer cases. Anglian Breast Cancer Study Group. Br J Cancer. 2000;83(10):1301-8.
[2] Moyer VA on behalf of the US Preventive Services Task Force. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: US Preventive Services Task Force recommendation statement. *Ann Intern Med.* February 2014;160(4):271-81.
[3] Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute. 2010-2012. DevCan software (http://surveillance.cancer.gov/devcan) V 6.7.0, Accessed June 2015.
[4] King MC, Marks JH, Mandell JB, New York Breast Cancer Study Group. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. *Science.* October 2003;302(5645):643-6.

Melanoma	<1%	Elevated (1-5%)[5]
Pancreatic	<1%	Elevated (2-3%)[6]

Elevated: Risk is increased, but further research may clarify the exact risk figure.

Men

If a man has a mutation in the *BRCA2* gene, his chances of developing male breast, prostate, pancreatic cancer and melanoma are greater than that of the average US man. This does not mean that he has a diagnosis of cancer or that he will definitely develop cancer in his lifetime.

Cancer by age 70	Average US man	With *BRCA2* mutation
Male breast	<1%	Elevated (3-12%)[7]
Prostate	7.2%	Elevated (7-16%)[8,9]
Pancreatic	<1%	Elevated (3-5%)[6]
Melanoma	1.2%	Elevated (2-6%)[5]

Elevated: Risk is increased, but further research may clarify the exact risk figure.

Screening guidelines

Below is a summary of screening guidelines from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) established by experts at the National Comprehensive Cancer Network (NCCN).[10] They are for individuals who have a mutation in the *BRCA2* gene. If you have a mutation in this gene, your healthcare provider may use these NCCN Guidelines® to help create a customized screening plan for you.

[5] Cancer risks in BRCA2 mutation carriers. Journal of the National Cancer Institute, 1999. *Journal of the National Cancer Institute.* August 1999; 91(15):1310-6.
[6] Mocci E, Milne RL, Mendez-Villamil EY, et al. Risk of pancreatic cancer in breast cancer families from the breast cancer family registry. *Cancer Epidemiology Biomarkers Prev.* May 2013;22(5)803-11.
[7] Tai YC, Domchek S, Parmigiani G, Chen S. Breast cancer risk among male BRCA1 and BRCA2 mutation carriers. *J Natl Cancer Inst.* December 2007; 99(23):1811-4.
[8] Liede A, Karlan BY, Narod SA. Cancer risks for male carriers of germline mutations in BRCA1 or BRCA2: a review of the literature. *J Clin Oncol.* February 2004; 22(4):735-42.
[9] van Asperen CJ, Brohet RM, Meijers-Heijboer EJ, et al. Cancer risks in BRCA2 families: estimates for sites other than breast and ovary. *J Med Genet.* September 2005; 42(9):711-9.
[10] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast and Ovarian V.1.2017. © National Comprehensive Cancer Network, Inc 2016. All rights reserved. Accessed September 20, 2016. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

Women

Breast and ovarian cancer[11]

- Starting at age 18: Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Performing regular breast self exams may help increase breast awareness, especially when checked at the end of the menstrual cycle.
- Starting at age 25: Breast exam by your provider every 6-12 months.
- Between ages 25-29 or individualized based on family history: Breast MRI screening with contrast (preferred) every year or mammogram if MRI is unavailable.
- Between ages 30-75: Mammogram and breast MRI screening with contrast every year. Your provider may wish to alternate between these two screenings every 6 months.
- Between ages 35-40, or after you are finished having children: NCCN recommends a risk-reducing salpingo-oophorectomy (the surgical removal of the ovaries and fallopian tubes) to lower the risk of developing breast and ovarian cancer. If you have had a risk-reducing bilateral mastectomy (the surgical removal of both breasts), NCCN states that it is reasonable to delay salpingo-oophorectomy until age 40-45.
- After age 75: Your provider may discuss an individualized management plan with you.
- Your provider may discuss the option of having a risk-reducing bilateral mastectomy (the surgical removal of both breasts).
- Your provider may discuss the use of medications that might reduce the risk of developing breast or ovarian cancer.
- While there may be circumstances where ovarian cancer screening with transvaginal ultrasound and a blood test for a protein called CA-125 are helpful, these techniques have not been shown to be effective in detecting early ovarian cancer.

Melanoma[11,12]

- Your healthcare provider may discuss skin exams and eye exams for melanoma screening.
- To reduce the chance of developing melanoma, the American Cancer Society recommends limiting exposure to UV light by avoiding excess sun exposure, wearing a hat, sunglasses and long protective clothing, applying sunscreen with SPF of 30 or higher and avoiding tanning beds and sun lamps.

Pancreatic cancer[11,13]

- Currently, there are no pancreatic cancer screening guidelines from the NCCN specific to *BRCA2* mutation carriers. Please discuss your risk of pancreatic cancer with your healthcare provider.

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[11] National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian. *NCCN Guidelines Version 1.2017.* Available at www.nccn.org. Published September 2016.

[12] Skin Cancer Prevention and Early Detection. The American Cancer Society. Available at www.cancer.org. Updated 3/20/2015. Accessed April 2015.

[13] Canto MI, Harinck F, Hruban RH, et al. International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. *Gut*. 2013;62(3):339-47.

Men

Male breast cancer[11]

- Starting at age 35: Breast self-exam training and education. Breast exam by your provider every year.

Prostate cancer[11]

- Starting at age 45: NCCN recommends prostate cancer screening.

Melanoma[11,12]

- Your healthcare provider may discuss skin exams and eye exams for melanoma screening.
- To reduce the chance of developing melanoma, the American Cancer Society recommends limiting exposure to UV light by avoiding excess sun exposure, wearing a hat, sunglasses and long protective clothing, applying sunscreen with SPF of 30 or higher and avoiding tanning beds and sun lamps.
- Any new, unusual, or changing moles should be reported to your provider or dermatologist.

Pancreatic cancer[11,13]

- Currently, there are no pancreatic cancer screening guidelines from the NCCN specific to *BRCA2* mutation carriers. Please discuss your risk of pancreatic cancer with your healthcare provider.

Useful resources

FORCE

Providing support, education, research, and resources for survivors and people at increased risk of cancer due to an inherited mutation or family history of cancer.
www.facingourrisk.org

Bright Pink

Focused on the prevention and early detection of breast and ovarian cancer in young women, while providing support for high-risk individuals.
www.brightpink.org

Susan G. Komen

Dedicated to reducing deaths from breast cancer by funding breast cancer research, ensuring access to care through community programs worldwide and supporting public health policies that help people facing breast cancer.
www.komen.org/

His Breast Cancer
Information about male breast cancer. Here to inform, educate, bring awareness, and teach prevention regarding breast cancer in men.
www.hisbreastcancer.org

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