

# BRCA2 gene

**Associated Syndrome Name:** *BRCA2*-associated hereditary breast and ovarian cancer syndrome

**BRCA2 Summary Cancer Risk Table**

CANCER	GENETIC CANCER RISK
Breast	High Risk
Male Breast	High Risk
Ovarian	High Risk
Pancreatic	High Risk
Prostate	High Risk
Skin	Elevated Risk

## BRCA2 gene Overview

*BRCA2*-associated hereditary breast and ovarian cancer syndrome <sup>1, 2</sup>

- Individuals with mutations in *BRCA2* have *BRCA2*-associated hereditary breast and ovarian cancer syndrome.
- Women with *BRCA2* mutations have a risk for breast cancer that is greatly increased over the 12.5% lifetime risk for women in the general population of the United States.
- Women with *BRCA2* mutations also have high risks for ovarian, fallopian tube, and primary peritoneal cancer.
- Men with *BRCA2* mutations have a high risk for breast cancer and prostate cancer. The increase in prostate cancer risk is most significant at younger ages. Additionally, men with a *BRCA2* mutation have a higher risk for an aggressive prostate cancer.
- Male and female patients with *BRCA2* mutations also have a high risk for exocrine pancreatic cancer. These are cancers developing in the enzyme-secreting cells of the pancreas.
- Male and female patients with *BRCA2* mutations also have an elevated risk for melanomas of both the skin and eyes.
- Although there are high cancer risks for patients with *BRCA2* mutations, there are interventions that have been shown to be effective at reducing many of these risks. Guidelines from the National Comprehensive Cancer Network (NCCN) for the medical management of patients with *BRCA2* mutations are listed below. It is recommended that patients with *BRCA2* mutations be managed by a multidisciplinary team with experience in the prevention and treatment of the cancers associated with *BRCA2* mutations.

**BRCA2 gene Cancer Risk Table**

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Female Breast	To age 50 <sup>3, 4, 5, 6, 7</sup>	17%-35%	2.1%
	To age 70 <sup>3, 4, 6, 7, 8</sup>	38%-84%	7.5%
	Second primary within 5 years of first breast cancer diagnosis <sup>5, 9, 10, 11</sup>	4%-9%	1.6%
Ovarian	To age 50 <sup>3, 6, 7, 8</sup>	0.4%-4%	0.2%
	To age 70 <sup>3, 5, 6, 7</sup>	15%-27%	0.6%
	Ovarian cancer within 10 years of a breast cancer diagnosis <sup>12, 13</sup>	6.8%	<1.0%

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Pancreatic	To age 80 <sup>7, 14, 15</sup>	7%, or higher if there is a family history of pancreatic cancer.	1.1%
Male Breast	To age 70 <sup>7, 16</sup>	6.8%	0.1%
Prostate	To age 70 <sup>7, 17, 18</sup>	20%	6.3%
Melanoma	To age 80 <sup>7, 19, 20</sup>	Elevated risk for melanomas of both the skin and eye	1.6%

## BRCA2 Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Female Breast	Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Periodic, consistent breast self-examination (BSE) may facilitate breast awareness. <sup>2</sup>	18 years	NA
	Clinical breast examination <sup>2</sup>	25 years	Every 6 to 12 months
	Breast MRI with contrast <sup>2</sup>	25 years, or individualized to a younger age if a relative has been diagnosed younger than age 30.	Annually
	Mammography <sup>2</sup>	30 years. If MRI unavailable, start at 25 years, or individualized to a younger age if a relative has been diagnosed younger than age 30.	Annually
	Consider risk-reducing mastectomy. <sup>2</sup>	Individualized	NA
	Consider options for breast cancer risk-reduction agents (i.e. tamoxifen). <sup>2</sup>	Individualized	NA
Ovarian	Bilateral salpingo-oophorectomy <sup>2</sup>	35 to 45 years, upon completion of childbearing	NA
	Consider options for ovarian cancer risk-reduction agents (i.e. oral contraceptives). <sup>2, 29</sup>	Individualized	NA

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Pancreatic	For patients with a family history of pancreatic cancer, consider available options for pancreatic cancer screening, including the possibility of endoscopic ultrasonography (EUS) and MRI/magnetic resonance cholangiopancreatography (MRCP). It is recommended that patients who are candidates for pancreatic cancer screening be managed by a multidisciplinary team with experience in screening for pancreatic cancer, preferably within research protocols. <sup>15</sup>	Age 50, or 10 years younger than the earliest age of pancreatic cancer diagnosis in the family	Annually
	Provide education about ways to reduce pancreatic cancer risk, such as not smoking and losing weight. <sup>26</sup>	Individualized	Individualized
Male Breast	Breast self-examination <sup>2</sup>	35 years	Monthly
	Clinical breast examination <sup>2</sup>	35 years	Annually
	Consider mammography <sup>2</sup>	50 years, or 10 years earlier than the youngest male breast cancer diagnosis in the family	Annually
Prostate	Recommend prostate cancer screening. <sup>2, 28</sup>	40 years, or 10 years younger than the earliest prostate cancer diagnosis in the family	Annually, or adjusted based on results from first PSA screen
	Since mutation carriers are at an increased risk for more aggressive prostate cancer this information may be included as part of the risk and benefit discussion about prostate cancer screening. <sup>25, 28</sup>	NA	NA
	Since mutation carriers are at an increased risk for more aggressive prostate cancer this information may be considered when choosing management options for men with a diagnosis of prostate cancer. <sup>25</sup>	NA	NA
Melanoma	Whole-body skin and eye examinations, and education about minimizing exposure to UV radiation. <sup>2</sup>	Individualized	Annually
For Patients With A Cancer Diagnosis	For patients with a gene mutation and a diagnosis of cancer, targeted therapies may be available as a treatment option for certain tumor types (e.g., platinum chemotherapy, PARP-inhibitors) <sup>21, 22, 23, 24, 25, 26, 27</sup>	NA	NA

## Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the *BRCA2* gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

In rare instances, an individual may inherit mutations in both copies of the *BRCA2* gene, leading to the condition Fanconi anemia, complementation group D1 (FANCD1). This condition is rare and includes physical abnormalities, growth retardation, progressive bone marrow failure and a high risk for cancer. The children of this patient are at risk of inheriting FANCD1 only if the other parent is also a carrier of a *BRCA2* mutation. Screening the other biological parent of any children for *BRCA2* mutations may be appropriate.<sup>30</sup>

Parents who are concerned about the possibility of passing on a *BRCA2* mutation to a future child may want to discuss options for prenatal testing and assisted reproduction techniques, such as pre-implantation genetic diagnosis (PGD).<sup>2</sup>

## References

1. Giri VN, et al. Implementation of Germline Testing for Prostate Cancer: Philadelphia Prostate Cancer Consensus Conference 2019. *J Clin Oncol*. 2020 38:2798-2811. PMID: 32516092.
2. Daly M et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast, Ovarian and Pancreatic. V 3.2023. Feb 13. Available at <https://www.nccn.org>.
3. Ford D, et al. Genetic heterogeneity and penetrance analysis of the *BRCA1* and *BRCA2* genes in breast cancer families. The Breast Cancer Linkage Consortium. *Am J Hum Genet*. 1998 62:676-89. PMID: 9497246.
4. Breast Cancer Association Consortium, et al. Breast Cancer Risk Genes - Association Analysis in More than 113,000 Women. *N Engl J Med*. 2021 384:428-439. PMID: 33471991.
5. Kuchenbaecker KB, et al. Risks of Breast, Ovarian, and Contralateral Breast Cancer for *BRCA1* and *BRCA2* Mutation Carriers. *JAMA*. 2017 317:2402-2416. PMID: 28632866.
6. Chen S, et al. Characterization of *BRCA1* and *BRCA2* mutations in a large United States sample. *J Clin Oncol*. 2006 24:863-71. PMID: 16484695.
7. SEER\*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2023 Mar 24]. Available from <https://seer.cancer.gov/explorer/>.
8. Mavaddat N, et al. Cancer risks for *BRCA1* and *BRCA2* mutation carriers: results from prospective analysis of EMBRACE. *J Natl Cancer Inst*. 2013 105:812-22. PMID: 23628597.
9. Yadav S, et al. Contralateral Breast Cancer Risk Among Carriers of Germline Pathogenic Variants in *ATM*, *BRCA1*, *BRCA2*, *CHEK2*, and *PALB2*. *J Clin Oncol*. 2023 Mar 20;41(9):1703-1713. PMID: 36623243.
10. Engel C, et al. Breast cancer risk in *BRCA1/2* mutation carriers and noncarriers under prospective intensified surveillance. *Int J Cancer*. 2020 146:999-1009. PMID: 31081934.
11. Giannakeas V, et al. The risk of contralateral breast cancer: a SEER-based analysis. *Br J Cancer*. 2021 Aug;125(4):601-610. PMID: 34040177.
12. Metcalfe KA, et al. The risk of ovarian cancer after breast cancer in *BRCA1* and *BRCA2* carriers. *Gynecol Oncol*. 2005 96:222-6. PMID: 15589605.
13. Curtis RE, et al. New Malignancies Following Breast Cancer. 2006 In: Curtis RE, et al., editors. *New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000*. National Cancer Institute. NIH Publ. No. 05-5302.
14. van Asperen CJ, et al. Netherlands Collaborative Group on Hereditary Breast Cancer (HEBON) . Cancer risks in *BRCA2* families: estimates for sites other than breast and ovary. *J Med Genet*. 2005 42:711-9. PMID: 16141007.
15. Goggins M, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. *Gut*. 2020 69:7-17. PMID: 31672839.
16. Tai YC, et al. Breast cancer risk among male *BRCA1* and *BRCA2* mutation carriers. *J Natl Cancer Inst*. 2007 99:1811-4. PMID: 18042939.
17. Struwing JP, et al. The risk of cancer associated with specific mutations of *BRCA1* and *BRCA2* among Ashkenazi Jews. *N Engl J Med*. 1997 336:1401-8. PMID: 9145676.
18. Liede A, et al. Cancer risks for male carriers of germline mutations in *BRCA1* or *BRCA2*: a review of the literature. *J Clin Oncol*. 2004 22:735-42. PMID: 14966099.
19. Moran A, et al. Risk of cancer other than breast or ovarian in individuals with *BRCA1* and *BRCA2* mutations. *Fam Cancer*. 2012 11:235-42. PMID: 22187320.
20. Gumaste PV, et al. Skin cancer risk in *BRCA1/2* mutation carriers. *Br J Dermatol*. 2015 172:1498-506. PMID: 25524463.
21. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/209115s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/209115s000lbl.pdf)
22. Tempero MA, et al. NCCN Clinical Practice Guidelines in Oncology®: Ampullary Adenocarcinoma. V 2.2022. Dec 6. Available at <https://www.nccn.org>.
23. Gradishar WJ et al. NCCN Clinical Practice Guidelines in Oncology®: Breast Cancer. V 4.2023. Mar 23. Available at <https://www.nccn.org>.

24. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2018/208558s002lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208558s002lbl.pdf)
25. Schaeffer E, et al. NCCN Clinical Practice Guidelines in Oncology®: Prostate Cancer. V 1.2023. Sep 16. Available at <https://www.nccn.org>.
26. Tempero MA, et al. NCCN Clinical Practice Guidelines in Oncology®: Pancreatic Adenocarcinoma. V 2.2022. Dec 6. Available at <https://www.nccn.org>.
27. Armstrong DK, et al. NCCN Clinical Practice Guidelines in Oncology®: Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. V 1.2023. Dec 22. Available at <https://www.nccn.org>.
28. Moses KA, et al. NCCN Clinical Practice Guidelines in Oncology®: Prostate Cancer Early Detection. V 1.2023. Jan 9. Available at <https://www.nccn.org>.
29. Gupta S, et al. NCCN Clinical Practice Guidelines in Oncology® Genetic/Familial High-Risk Assessment: Colorectal. V 1.2023. May 30. Available at <https://www.nccn.org>.
30. Mehta PA, Tolar J. Fanconi Anemia. 2021 Jun 3. In: Pagon RA, et al., editors. GeneReviews® [Internet]. PMID: 20301575.

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