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Clinician Management Resource for *BRCA2*

This overview of clinical management guidelines is based on this patient's positive test result for a *BRCA2* gene mutation. Unless otherwise stated, medical management guidelines used here are limited to those issued by the National Comprehensive Cancer Network® (NCCN®)[1] in the U.S. Please consult the referenced guideline for complete details and further information.

Clinical correlation with the patient's past medical history, treatments, surgeries and family history may lead to changes in clinical management decisions; therefore, other management recommendations may be considered. Genetic testing results and medical society guidelines help inform medical management decisions but do not constitute formal recommendations. Discussions of medical management decisions and individualized treatment plans should be made in consultation between each patient and his or her healthcare provider, and may change over time.

SCREENING/SURGICAL CONSIDERATIONS[1]	AGE TO START	FREQUENCY
Female Breast Cancer		
Breast awareness* • Women should be familiar with their breasts and promptly report changes to their healthcare provider.	18 years old	Periodic and consistent
Clinical Breast Exam	25 years old	Every 6-12 months
Breast Screening** • Breast MRI with contrast • Mammography with consideration of tomosynthesis	25-29 years old	Individualized
	30-75 years old	Every 12 months
	>75 years old	Individualized
Consider options for risk reduction agents	Individualized	Individualized
Discuss option of risk-reducing mastectomy	Individualized	N/A
Ovarian Cancer		
Recommend risk-reducing salpingo-oophorectomy (RRSO)^	Typically 35 to 40 years old, and upon completion of child bearing	N/A
If RRSO not elected, transvaginal ultrasound combined with serum CA-125, although of uncertain benefit, may be considered	30-35 years old	Clinician's discretion
Consider options for risk reduction agents	Individualized	Individualized
Male Breast Cancer		
Breast self-exam training and education	35 years old	Periodic and consistent
Clinical breast exam	35 years old	Every 12 months
Consider mammogram screening in men with gynecomastia	50 years, or 10 years before the earliest known male breast cancer in the family (whichever comes first)	Every 12 months
Prostate Cancer		
Recommend prostate cancer screening	40 years old	Clinician's discretion

* Breast self exam (BSE) may facilitate breast self awareness. Premenopausal women may find BSE most informative when performed at the end of menses.
** Women treated for breast cancer, and have not undergone bilateral mastectomy: follow screening as described.
^ Ovarian cancer onset in patients with BRCA2 mutations is an average of 8-10 years later than in patients with BRCA1 mutations. Therefore, it is reasonable to delay RRSO for management of ovarian cancer risk until age 40-45y in patients with BRCA2 mutations , unless age at diagnosis in the family warrants earlier age for consideration of prophylactic surgery.

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. V2.2021. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed September 24, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way

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SCREENING/SURGICAL CONSIDERATIONS[1]	AGE TO START	FREQUENCY
Melanoma		
General risk management, such as annual full-body skin examination and minimizing UV exposure	Individualized	Annual, or shorter intervals if indicated
Pancreatic Cancer		
For individuals with exocrine pancreatic cancer in >1 first-or second-degree relative on the same side of the family as the identified pathogenic/likely pathogenic germline variant, consider pancreatic cancer screening.ˆ	50 years (or 10 years younger than the earliest exocrine pancreatic cancer diagnosis in the family)	Annually (with consideration of shorter intervals if worrisome abnormalities seen on screening)
Family Planning		
For individuals of reproductive age, advise about options for prenatal diagnosis and assisted reproduction including pre-implantation genetic diagnosis. Discussion should include known risks, limitations, and benefits of these technologies. Counsel for risk of autosomal recessive condition in offspring • If both parents have a *BRCA2* mutation, each of their children have a 25% chance to have a condition such as Fanconi anemia	Individualized	N/A
Other		
Consider investigational imaging and screening studies, when available (*eg*, novel imaging technologies, more frequent screening intervals) in the context of a clinical trial		

ˆ For individuals considering pancreatic cancer screening, the Guidelines recommends that screening be performed in experienced high-volume centers, ideally under research conditions. The Guidelines recommends that such screening only take place after an in-depth discussion about the potential limitations to screening, including cost, the high incidence of pancreatic abnormalities, and uncertainties about the potential benefits of pancreatic cancer screening.

The Guidelines recommends that screening be considered using annual contrast-enhanced MRI/MRCP and/or EUS, with consideration of shorter screening intervals for individuals found to have worrisome abnormalities on screening. The Guidelines emphasizes that most small cystic lesions found on screening will not warrant biopsy, surgical resection, or any other intervention. The panel does not currently recommend pancreatic cancer screening in the absence of a close family history of exocrine pancreatic cancer.

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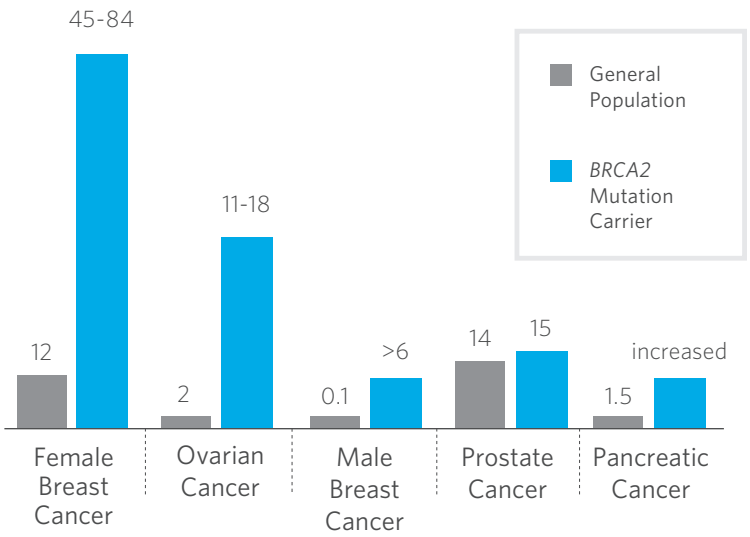
Understanding Your Positive *BRCA2* Genetic Test Result

INFORMATION FOR PATIENTS WITH A **PATHOGENIC MUTATION** OR **VARIANT, LIKELY PATHOGENIC**

5 Things To Know

1	*BRCA2* mutation	Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the *BRCA2* gene.
2	Hereditary breast and ovarian cancer (HBOC)	People with *BRCA2* mutations have hereditary breast and ovarian cancer (HBOC).
3	Cancer risks	You have an increased chance to develop female or male breast cancer, ovarian cancer, pancreatic cancer, prostate cancer, and possibly other types of cancer.
4	What you can do	There are risk management options to detect cancer early or lower the risk to develop cancer. It is important to discuss these options with your doctor, and decide on a plan that best manages cancer risks.
5	Family	Family members may also be at risk – they can be tested for the *BRCA2* mutation that was identified in you.

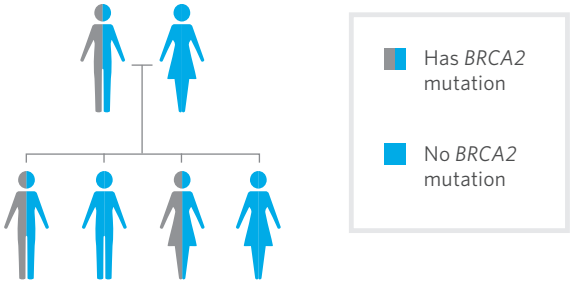
BRCA2 Mutation Lifetime Cancer Risks (%)*



**The above cancer risks represent the typical range for individuals with a mutation in this gene. If available, cancer risks specific to the mutation found in you will be provided in your results report.*

BRCA2 Mutations in the Family

There is a 50/50 random chance to pass on a *BRCA2* mutation to your sons and daughters. The image below shows that both men and women can carry and pass on these mutations.



Understanding Your Positive *BRCA2* Genetic Test Result

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Result	**MUTATION**	Your testing shows that you have a pathogenic mutation (a disease-causing change in the gene, like a spelling mistake) or a variant that is likely pathogenic in the *BRCA2* gene. Both of these results should be considered positive.
Gene	***BRCA2***	Everyone has two copies of the *BRCA2* gene, which we randomly inherit from each of our parents. Mutations in one copy of the *BRCA2* gene can increase the chance for you to develop certain types of cancer in your lifetime.
Condition	**HBOC**	People with *BRCA2* mutations have hereditary breast ovarian cancer (HBOC).
Cancer Risks	**INCREASED**	You have an increased chance to develop female or male breast cancer, ovarian, fallopian tube, or primary peritoneal cancer, pancreatic cancer, prostate cancer, and possibly other types of cancer.
Other Medical Concerns	**MAY BE PRESENT**	Individuals with *BRCA2* mutations may have an increased risk to have a child with Fanconi anemia, but only if their partner also carries a mutation in the *BRCA2* gene. Fanconi anemia is a rare condition that can cause specific physical characteristics, bone marrow failure, and an increased risk of certain cancers.
Management Options	**FOR WOMEN**	Options for early detection and prevention for women may include: breast exam, mammogram, breast MRI, transvaginal ultrasound, a blood test called CA-125, preventive medications, and options for preventive surgery. Talk to your doctor about what options may be right for you.
Management Options	**FOR MEN**	Options for screening and early detection for men may include: breast exam, mammogram, and increased prostate screening. Talk to your doctor about what options may be right for you.
Risk Management	**VARIES**	Risk management decisions are very personal, and the best option depends on many factors. Screening typically begins earlier than the general population and is often more frequently performed. It is important to discuss these options with your doctor.
Family Members	**50/50 CHANCE**	Your close relatives (like your parents, brothers, sisters, children) have a 50/50 random chance of inheriting the *BRCA2* mutation that you carry, and other family members (like your aunts, uncles, cousins) may also inherit it. Your relatives can be tested for this same mutation. Depending on the family history, those who DO NOT have it may not have an increased chance (above the general population) to develop cancer.
Next Steps	**DISCUSS**	It is recommended that you share this information with family members so they can learn more and discuss this with their healthcare providers.
Reach Out	**RESOURCES**	• Ambry's Hereditary Cancer Site for Families patients.ambrygen.com/cancer • Bright Pink brightpink.org • FORCE facingourrisk.org • Sharsheret sharsheret.org • Susan G. Komen Foundation komen.org • Genetic Information Nondiscrimination Act (GINA) ginahelp.org • National Society of Genetic Counselors nsgc.org • Canadian Society of Genetic Counsellors cagc-accg.ca

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *BRCA2* result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.

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