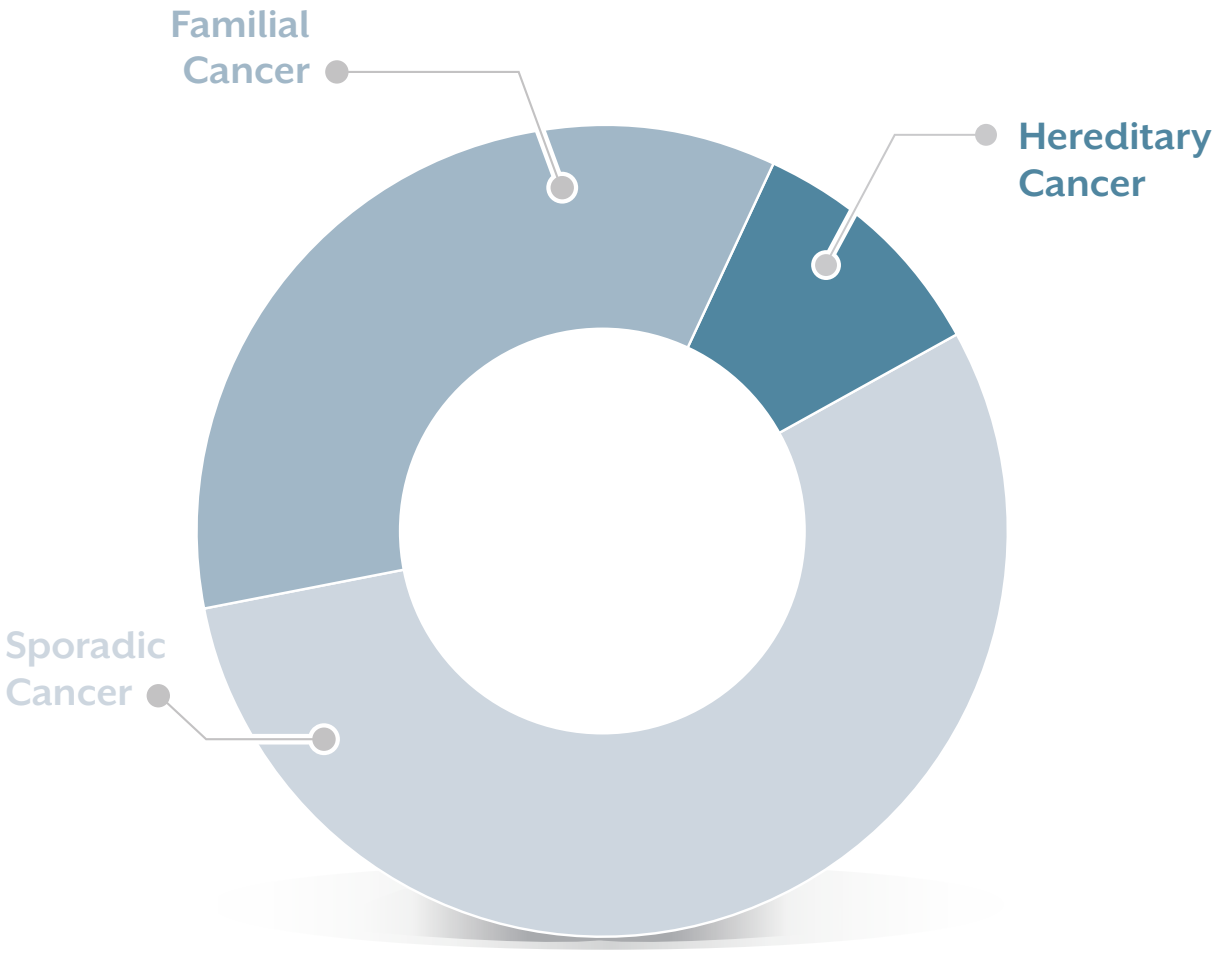
MYRIAD myRisk®
Hereditary Cancer

A Patient's Guide to Hereditary Cancer

Is Hereditary Cancer Testing Right for You?

What is Hereditary Cancer?

Most cancers occur in people who do not have a strong family history of that cancer. This is often called "sporadic cancer". In some families, we see more of the same kind, or related kinds, of cancer than we would expect to see when compared to the general population. This is often called "familial" or "hereditary cancer". In those families with hereditary cancer, that cancer risk is passed down through generations by inheriting altered genes (in other words, genes with mutations) which increase the risk to develop cancer. Determining which of these families have cancer related to an inherited gene mutation is important, as the cancer risks in hereditary cancer families are much higher than the general population.



Hereditary Cancer:

Occurs when an altered gene (gene with a mutation) is passed down in the family from parent to child. People with hereditary cancer are more likely to have relatives with the same type or related type of cancer. They may develop more than one cancer and their cancer often occurs at an earlier than average age.

Familial Cancer:

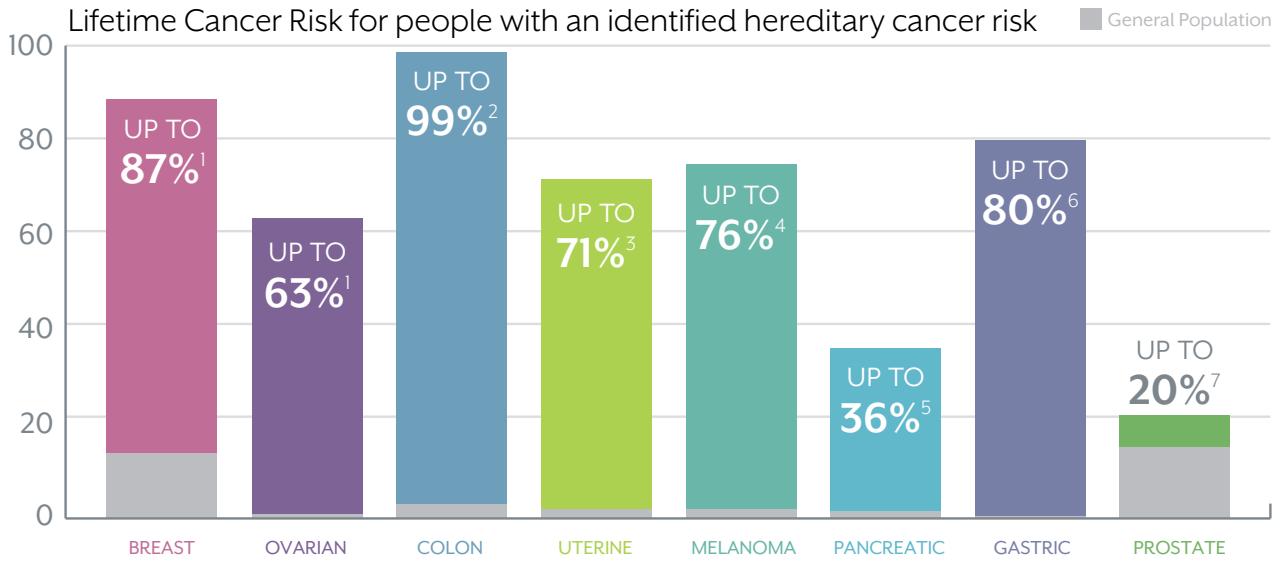
Likely caused by a combination of genetic and environmental factors. People with familial cancer may have one or more relatives with the same type of cancer; however, there does not appear to be a specific pattern of inheritance (e.g., the cancer risk is not clearly passed from parent to child).

Sporadic Cancer:

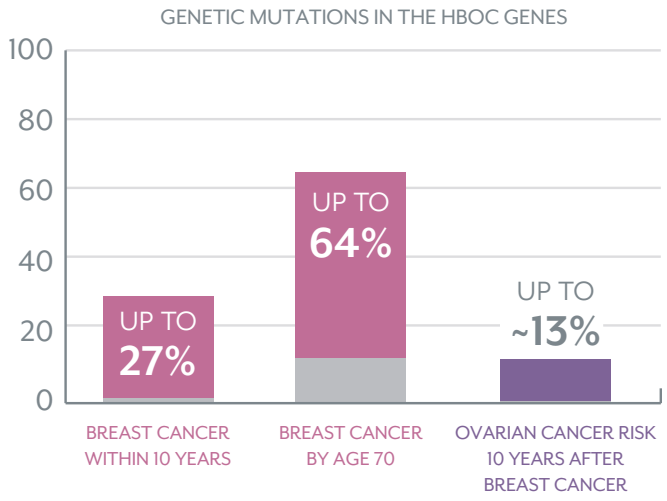
Occurs by chance. People with sporadic cancer typically do not have relatives with the same type of cancer.

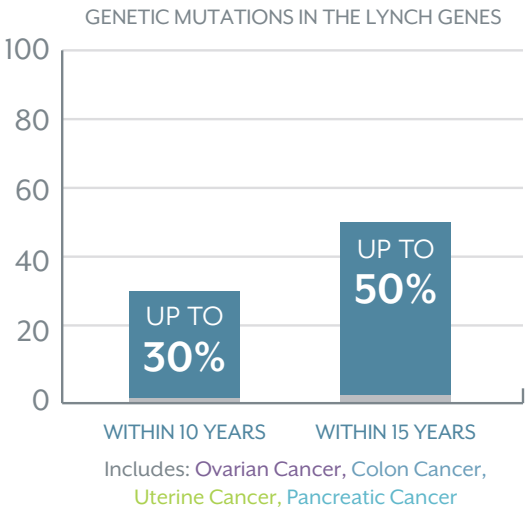
Personal and/or Family History Risk Factors

MULTIPLE A combination of cancers on the same side of the family	› **2 or more:** breast / ovarian / prostate / pancreatic cancer **OR** › **2 or more:** colorectal / uterine / ovarian / stomach / pancreatic / other cancers (i.e., ureter/renal pelvis, biliary tract, small bowel, brain, sebaceous adenomas) **OR** › **2 or more:** melanoma / pancreatic cancer
YOUNG Any 1 of the following cancers at age 50 or younger	› Breast cancer › Colorectal cancer › Uterine cancer
RARE Any 1 of these rare presentations at any age	› Ovarian cancer › Breast: male breast cancer or triple-negative breast cancer › Colorectal cancer with abnormal MSI/IHC, MSI- associated histology › Uterine cancer with abnormal MSI/IHC › 10 or more gastrointestinal polyps

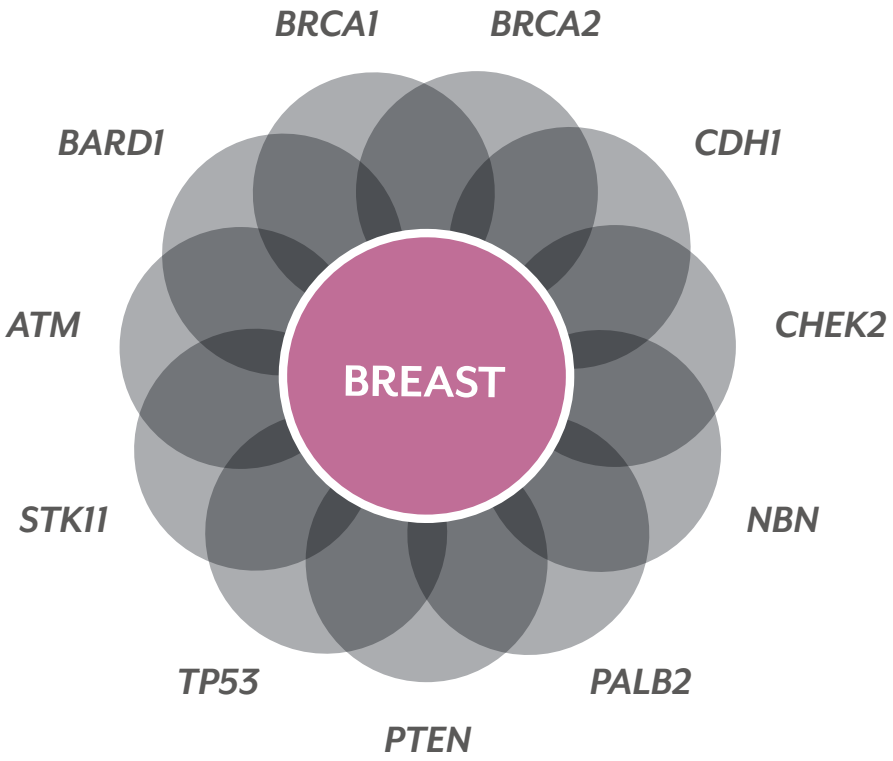


If you have a genetic mutation in the HBOC genes (*BRCA1/2*) or Lynch Genes (*MLH1, MSH2, MSH6, EPCAM, PMS2*) your risk of developing a second cancer are significantly increased:

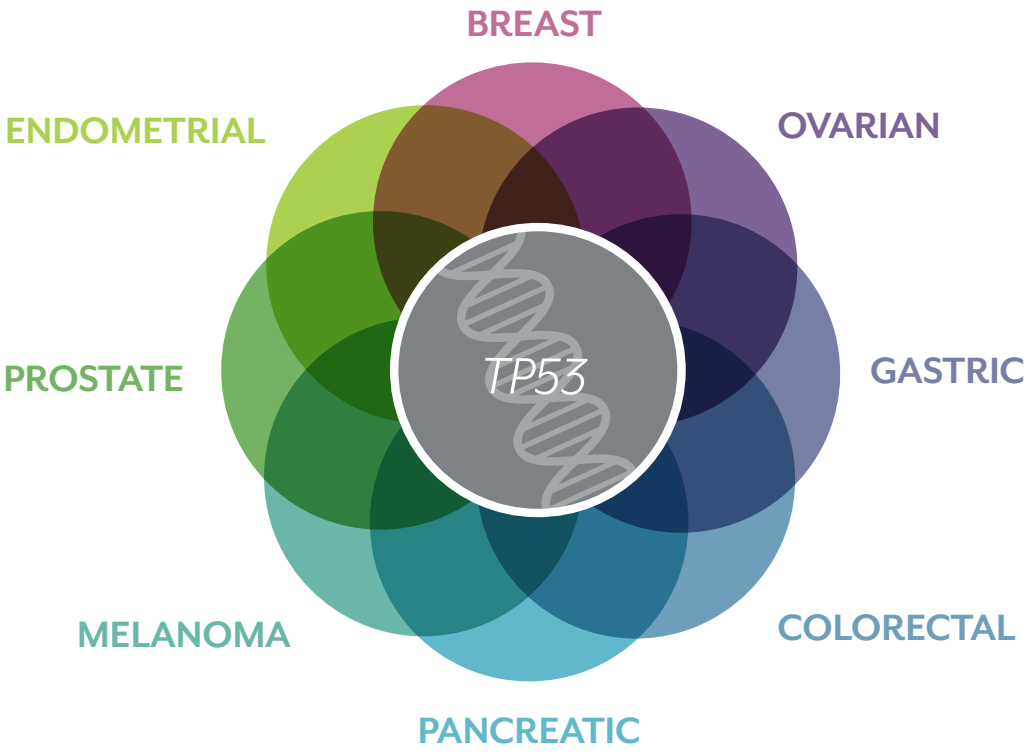




Multiple genes can be associated with a single cancer



Multiple cancers can be associated with a single gene



28 Genes Across 8 Important Cancer Types

Syndrome/Genes	Breast	Ovarian	Colorectal	Uterine	Melanoma	Pancreatic	Stomach	Prostate	Other
Hereditary Breast and Ovarian Cancer Syndrome- *BRCA1 / BRCA2*	●	●				●		●	
	●	●			●	●		●	
Lynch Syndrome- *MLH1 / MSH2 / MSH6 PMS2 / EPCAM*		●	●	●		●	●		●
		●	●	●		●	●		●
		●	●	●		●	●		●
		●	●	●		●	●		●
		●	●	●		●	●		●
Familial Adenomatous Polyposis- *APC*			●			●	●		●
MUTYH Biallelic			●						●
MUTYH Monoallelic			●						
CDKN2A (p16INK4a)					●	●			
CDKN2A (p14ARF)					●	●			
CDK4					●	●			
TP53	●	●	●	●	●	●	●	●	●
PTEN	●		●	●	●				●
STK11	●	●	●	●		●	●		●
CDH1	●		●				●		
BMPR1A			●			●	●		●
SMAD4			●			●	●		●
PALB2	●					●			
CHEK2	●		●					●	
ATM	●					●			
NBN	●							●	
BARD1	●								
BRIP1		●							
RAD51C		●							
RAD51D		●							
POLD1			●						
POLE			●						
GREM1			●						

Possible Genetic Test Results

Positive Result
A mutation has been identified

Increased Cancer Risk
Medical management based on recommendations for the specific gene mutation(s)

Negative Result

A gene mutation has been previously identified in the family (Single Site Analysis)

No Increased Risk
Medical management based on general population cancer screening recommendations

No gene mutation has been previously identified in the family (Comprehensive Analysis)

Risk Not Fully Defined
Medical management based on personal and family history of cancer

Uncertain Variant
A change has been identified in the DNA, but it is not currently known if the change will cause disease.

Risk Not Fully Defined
Medical management based on personal and family history of cancer

Myriad has a lifetime commitment to patients. When an uncertain variant is reclassified, whether it is tomorrow or years from now, Myriad will contact your provider to alert them to reclassifications.

Managing Hereditary Cancer Risk

Increased Surveillance
Close and continuous observation and testing

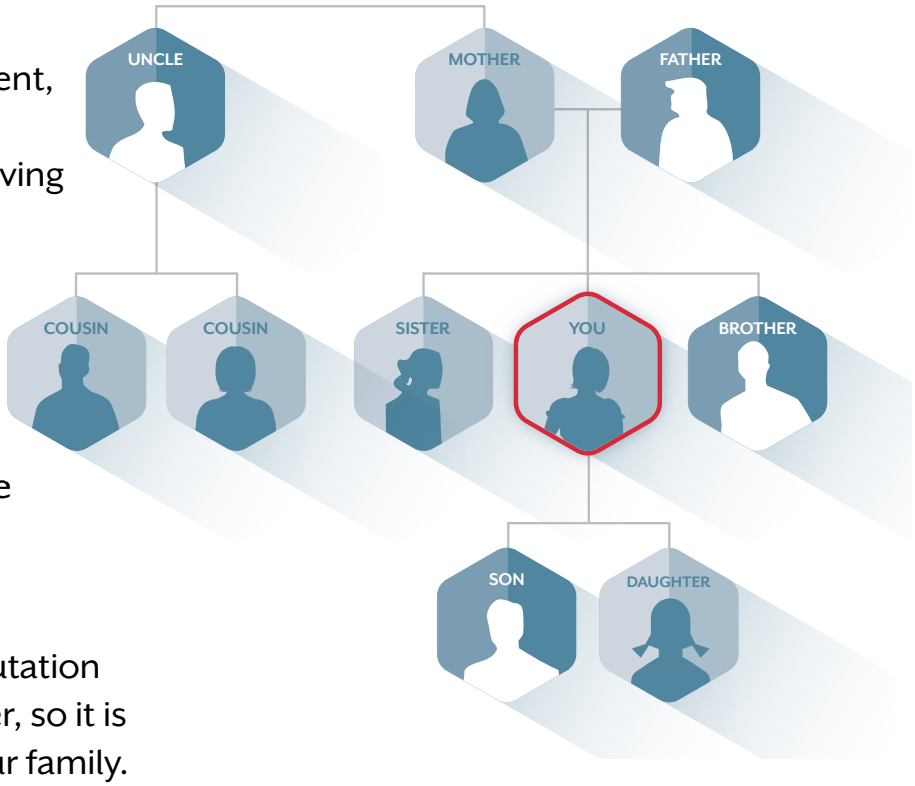
For Example:
- Breast MRI in addition to mammogram
- Annual colonoscopy

Chemoprevention
The use of drugs to prevent the development of cancer.

Risk Reducing Surgery
Based on individual considerations, the following surgical considerations may be recommended:
- Removal of the breasts
- Removal of the uterus
- Removal of the ovaries and fallopian tubes
- Removal of the colon

It's a Family Affair

- If you have a gene mutation, your parent, your children and your brothers and sisters could have a 50% chance of having the same gene mutation.
- Other relatives such as aunts, uncles and cousins may also be at risk to carry the same gene mutation.
- Testing is the only way to identify gene mutations which could impact your medical management.
- Remember, you can inherit a gene mutation from either your mother or your father, so it is important to look at both sides of your family.



Myriad Promise™

The vast majority of patients pay $0 out-of-pocket.

The Myriad Promise is a program for patients who encounter any financial hardship associated with their bill. Myriad will work directly with you, the patient, towards your complete satisfaction, **GUARANTEED**.

Privacy

The Health Insurance Portability and Accountability Act (HIPAA) of 1996 created federal privacy protections that apply to all health information created or maintained by healthcare providers, health plans, and healthcare clearinghouses. Myriad Genetic Laboratories complies with HIPPA practices.

For more information on specific privacy practices, please visit: myriad.com/patients-families/the-myriad-difference/your-privacy.

References:

1. Ford D, et al. Risks of cancer in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. Lancet. 1994 343:692-5.
2. Brand R, et al. MUTYH-Associated Polyposis. 2012 Oct 04. In: Pagon RA, et al., editors. GeneReviews® [Internet]. Available from http://www.ncbi.nlm.nih.gov/books/NBK107219/
3. Baglietto L, et al. Risks of Lynch syndrome cancers for MSH6 mutation carriers. J Natl Cancer Inst. 2010 102:193-201.
4. Begg CB, et al. Genes Environment and Melanoma Study Group. Lifetime risk of melanoma in CDKN2A mutation carriers in a population-based sample. J Natl Cancer Inst. 2005 97:1507-15.
5. Provenzale D, et al. NCCN Clinical Practice Guidelines in Oncology® Genetic/Familial High-Risk Assessment: Colorectal. V 2.2014. May 19. Available at http://www.nccn.org.
6. Pharoah PD, et al. International Stomach Cancer Linkage Consortium. Incidence of stomach cancer and breast cancer in CDH1 (E-cadherin) mutation carriers from hereditary diffuse stomach cancer families. Gastroenterology. 2001 121:1348-53.
7. Tai YC, et al. Breast cancer risk among male BRCA1 and BRCA2 mutation carriers. J Natl Cancer Inst. 2007 99:1811-4. PMID:18042939..

Next Steps:

☐ Pursue Testing by giving blood or saliva sample

☐ Decline Testing-
Medical management based on personal and family history of cancer

☐ Undecided / Talk to Family

Who to Contact with questions: _____

Provider Testing Options to be discussed with your physician or genetic counselor.

☐ Integrated BRAC*Analysis*® with Myriad myRisk® Hereditary Cancer Update Test

- ☐ Multisite 3 BRAC*Analysis*
  - ☐ **REFLEX** to Integrated BRAC*Analysis* with Myriad myRisk Hereditary Cancer Update Test if the Multisite 3 is negative.
  - ☐ **Check here** if a family member has tested positive for one of the above 3 mutations.

☐ COLARIS® PLUS with Myriad myRisk Hereditary Cancer Update Test

☐ COLARIS *AP*® PLUS with Myriad myRisk Hereditary Cancer Update Test

☐ Single Site Testing (for family of known mutation carriers) **Specify Gene:** _____ **and Mutation:** _____

Relationship: My patient is the _____ (e.g. maternal aunt) of the known mutation carrier.
Required: Include a copy of the known mutation carrier's report.

☐ Myriad myRisk Update Test

☐ Other: _____

Resources:

Your healthcare provider is always your number one resource. You are also invited to visit www.MySupport360.com, the Myriad program offering information and support for patients. You will find valuable information that will help you better understand your test result, and you will join a community of people who are on the same hereditary cancer testing journey as you.

You may also contact Myriad's Medical Services team at 1-800-469-7423 ext. 3850.

myriad® WHEN DECISIONS MATTER

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