MYRIAD myRisk®
Hereditary Cancer

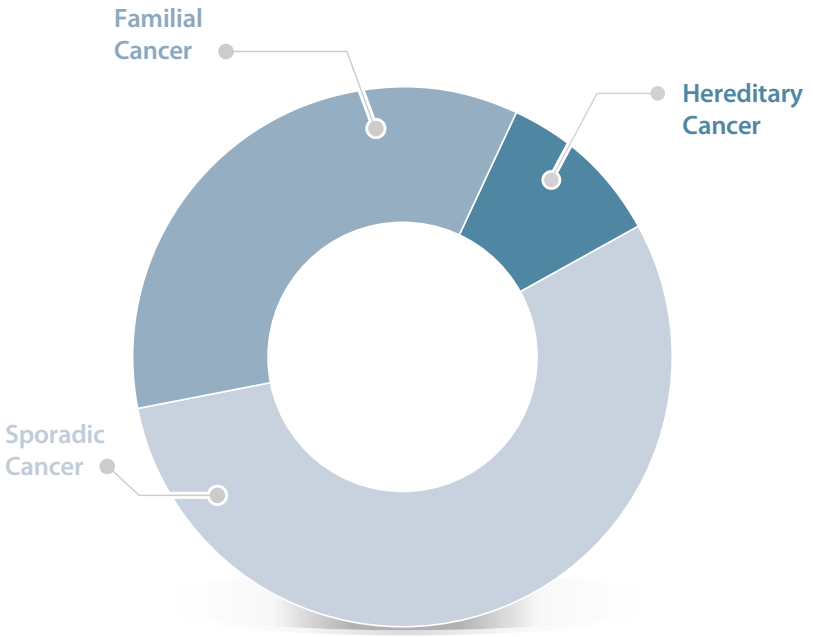
Genetic Testing for Hereditary Cancer

A Patient's Guide

myriad®
WHEN DECISIONS MATTER

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 pattern of related cancers can be categorized as either "familial cancer" 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 in 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 Family History Risk Factors

There are some risk factors that could indicate a hereditary cancer predisposition. Check all that apply in the list below and share this information with your healthcare professional.

HEREDITARY CANCER RED FLAGS

Personal and/or Family History Risk Factors (check all that apply):

Personal history of:

- O Breast cancer at any age
- O Ovarian cancer at any age
- O Metastatic prostate cancer at any age
- O Pancreatic cancer at any age
- O Colon, rectal or uterine/endometrial cancer under 65

Family history of:

- O Breast cancer under 50
- O Two breast cancers in one relative at any age
- O Three or more breast cancers in relatives on the same side of the family at any age
- O Ovarian, metastatic prostate, pancreatic cancer, or male breast cancer at any age
- O Colon, rectal, or uterine/endometrial cancer diagnosed under age 50
- O A gene mutation found in a family member

Hereditary Cancer Questionnaire

This is a screening tool for the common features of hereditary cancer syndromes. Please mark (Y) for those that apply to YOU and/or YOUR FAMILY. Next to each statement, please list the relationship(s) to you and age of diagnosis for each cancer in your family.

You and the following close blood relatives should be considered:
Parents, Brothers, Sisters, Sons, Daughters, Grandparents, Grandchildren, Aunts, Uncles, Nephews, Nieces, Half-Siblings, First-Cousins, Great-Grandparents and Great Grandchildren.

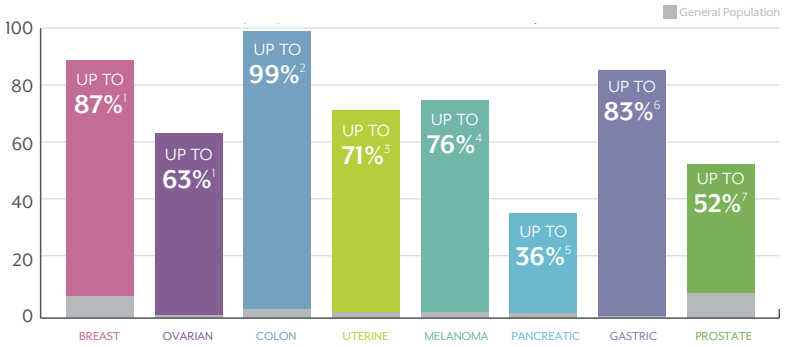
YOU and YOUR FAMILY'S Cancer History (Please be as thorough and accurate as possible)								
	CANCER	YOU Age of Diagnosis	PARENTS/SIBLINGS/ CHILDREN	Age of Diagnosis	RELATIVES on your MOTHER'S SIDE	Age of Diagnosis	RELATIVES on your FATHER'S SIDE	Age of Diagnosis
X O Y N	***Example: Breast Cancer***	***45***	----------	---	***Aunt Cousin***	***45 61***	***Grandmother***	***53***
O O Y N	Breast cancer (Female or Male)							
O O Y N	Ovarian cancer (Peritoneal/Fallopian tube)							
O O Y N	Endometrial (Uterine) cancer							
O O Y N	Colon/rectal cancer							
O O Y N	10 or more Lifetime Colon/ Rectal Polyps (Specify #)							
O O Y N	Pancreatic cancer							
O O Y N	Prostate cancer							
O O Y N	Other Cancer(s) (Specify cancer type)	Among others, consider the following cancers: Melanoma, Stomach (Gastric), Brain, Kidney, Bladder, Small bowel, Sarcoma, Thyroid						
O O Y N	Are you of Ashkenazi Jewish descent?							
O O Y N	Are you concerned about your personal and/or family history of cancer?							
O O Y N	Have your or anyone in your family had genetic testing for a hereditary cancer syndrome? (Please explain/include a copy of result if possible) If Yes, Who? _____ What gene(s)? _____ What was the result? _____							

Share this information with your healthcare professional to help determine your hereditary cancer risk.

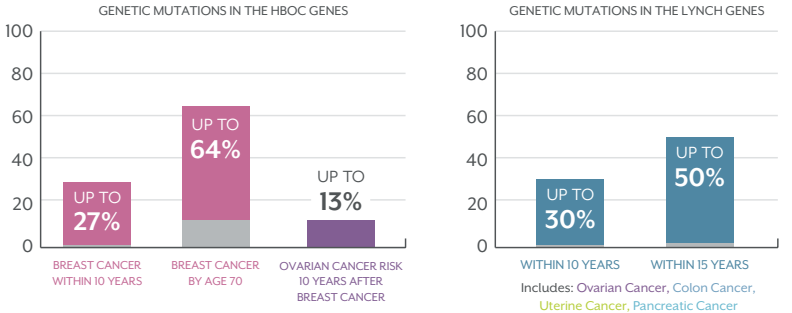
Hereditary Cancer Risk

Approximately 5% to 10% of all cancers develop because a person inherited a genetic mutation in a way that encourages the disease to grow. Individuals with these genetic mutations are far more likely to develop certain cancers, often at a much earlier age than the general population. In addition the risk of developing a second cancer is significantly increased.

*Lifetime cancer risk for people with an identified hereditary cancer risk**



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 is significantly increased:



**For the most up-to-date general population and gene-associated cancer risks, refer to the Gene Tables located at http://myriadmyrisk.com/products/myriad-myrisk/myrisk-gene-table*

About Myriad myRisk

What is Myriad myRisk?

Myriad myRisk is a multigene cancer panel test. Testing multiple genes helps avoid missing a possible cancer causing mutation.
Myriad myRisk is the only hereditary cancer test that combines your genetic information with the personal and family history you give your healthcare provider to generate guideline-based management options to help you lower your cancer risks.

What does the Myriad myRisk test tell you?

Myriad myRisk does not tell you whether you have cancer. It looks at multiple genes that impact inherited risks for eight important cancers. The result tells you if you have a mutation in one of these genes and how this affects your cancer risk.

What is the benefit of using Myriad myRisk?

Test result provides critical information for your healthcare provider to make optimal medical decisions and take action in building a personalized cancer risk-reduction plan.

Why Myriad myRisk?

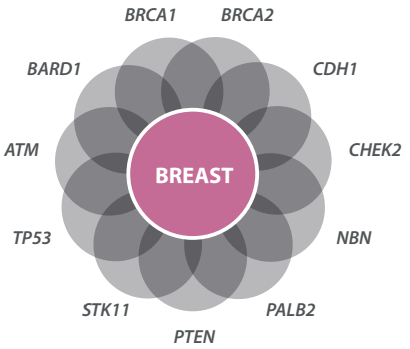
Myriad myRisk incorporates your family history and genetic results to help optimize your medical management. Myriad myRisk is the gold standard in accuracy and offers fast turnaround time for panel testing.

Myriad myRisk evaluates clinically significant genes associated with 8 cancer sites

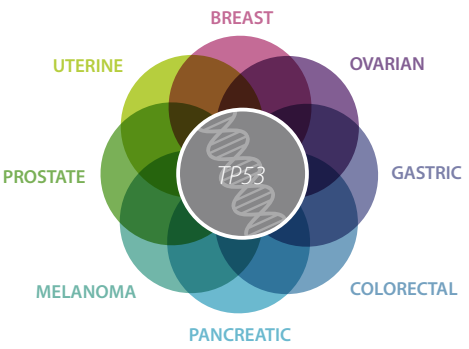
Multiple Genes Across 8 Important Cancer Types

Gene	Breast	Ovarian	Colorectal	Endometrial	Melanoma	Pancreatic	Gastric	Prostate	Other Cancers
BRCA1	●	●				●		●	
BRCA2	●	●			●	●		●	
MLH1		●	●	●		●	●	●	●
MSH2		●	●	●		●	●	●	●
MSH6			●	●		●	●	●	●
PMS2			●	●		●	●	●	●
EPCAM		●	●	●		●	●	●	●
APC			●			●	●		●
MUTYH (2 copies)			●						●
MUTYH (1 copy)			●						
CDKN2A (p16INK4a)					●	●			
CDKN2A (p14ARF)					●	●			
CDK4					●	●			
TP53	●	●	●	●	●	●	●	●	●
PTEN	●		●	●	●				●
STK11	●	●	●	●		●	●		●
CDH1	●		●				●		
BMPR1A			●			●	●		●
SMAD4			●			●	●		●
PALB2	●					●			
CHEK2	●		●						
ATM	●					●			
NBN	●							●	
BARD1	●								
BRIP1, RAD51C, RAD51D		●							
HOXB13								●	
POLD1, POLE, GREM1, AXIN2, GALNT12, MSH3 NTHL1, RPS20, RNF43			●						

Multiple genes can be associated with a single cancer



Multiple cancers can be associated with a single gene



Possible Myriad myRisk Test Results

Positive Result A mutation has been identified	• A genetic mutation was found in one or more of the genes tested • You are at increased risk for cancer • A summary of medical management guidelines will be provided specific to your gene mutation(s)
Elevated Result	• No genetic mutation was found in the genes tested • You are at elevated risk for cancer based on an analysis of additional genetic markers, personal clinical risk factors, and/or your family's history of cancer • A summary of medical management guidelines will be provided based on your elevated risk
Negative Result	• No genetic mutation was found in the genes tested • The common causes of hereditary cancer have been ruled out, but depending on family history of cancer, increased risks could still remain • Depending on your family history, medical management is usually based on general population screening guidelines; however, you should talk with your healthcare provider to determine if there are any changes in medical management that are right for you
Variant of Uncertain Significance	• A change in a gene has been identified • It is not yet known if the change is associated with increased cancer risk • Medical management based on personal and family history of cancer until more is understood about this specific change

If you are a woman*, you may also receive a riskScore® result and/or a Tyrer-Cuzick breast cancer risk estimate.

riskScore® is a breast cancer risk prediction result that provides women, who are unaffected by breast cancer, with a personalized calculation of their future breast cancer risk. riskScore result uses a combination of genetic markers and clinical factors in its calculation.

Tyrer-Cuzick is a breast cancer risk model used to predict a woman's risk of developing breast cancer. The Tyrer-Cuzick model takes into consideration family history of cancer and other personal clinical risk factors.

If your remaining lifetime breast cancer risk is calculated to be 20% or greater with Tyrer-Cuzick or riskScore, a summary of medical management guidelines will be provided.

**Based on research at time of product launch, riskScore® is only calculated for women of solely European ancestry under the age of 85 and without a personal history of breast cancer, LCIS, hyperplasia, atypical hyperplasia, or a breast biopsy of unknown results. riskScore® is not calculated if a woman or a blood relative is known to carry a mutation in a breast cancer risk gene.*

Managing Hereditary Cancer Risk

Myriad myRisk blends genetic test status AND personal/family cancer history into clinically actionable risk assessment and follow-up.

The result gives your healthcare provider information about your personal risk and also guideline-based recommendations for further prevention and/or therapy.

Possible options are:

Increased Surveillance

Close and continuous observation and testing, for example:

- Breast MRI in addition to mammogram
- Annual colonoscopy

Risk Reducing Medication

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 breast
- Removal of the uterus
- Removal of the ovaries and fallopian tubes

Other Questions You Might be Asking

Who is Myriad?

With over 25 years of experience and more than two million people tested, Myriad is the established leader in the field of hereditary genetic testing. Myriad's genetic tests are known for quality and accuracy. The extensive knowledge base, a highly specialized professional staff and the commitment to support healthcare providers, make Myriad the unquestioned leader in genetic testing for hereditary cancer.

What is Myriad's lifetime commitment?

Myriad performs ongoing investigations and research on all findings. Your healthcare provider will be contacted if new genetic information affects your medical management. Patients who were previously tested by Myriad are eligible for affordable Myriad myRisk Update Testing to update their personal cancer risk-reduction plan.

Will my health insurance pay for my testing?

Health care reimbursement and coverage for genetic testing varies greatly throughout the world. Please check with your physician, insurance, Myriad affiliate or distribution partner in your country for additional information.

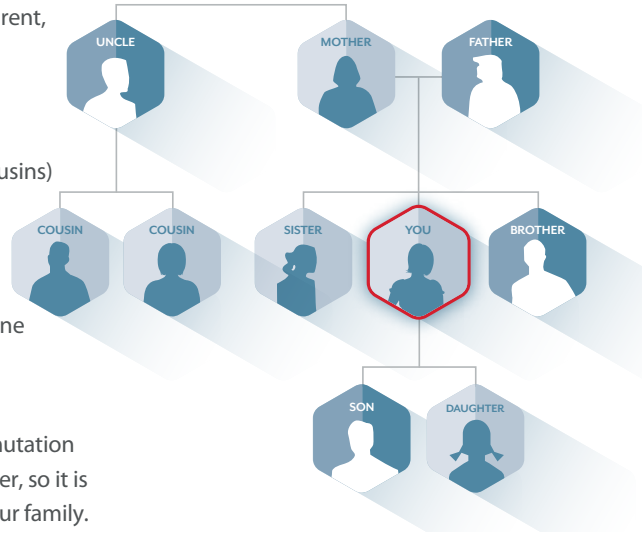
Will my results remain confidential?

Myriad is dedicated to offering high-quality laboratory services and is committed to securing your privacy through full compliance with international regulations. Myriad has an active privacy program. Myriad discloses test results only to the requesting healthcare provider/ designee, and not to anyone else (including insurance carriers) without your written permission. Additionally, Myriad does not disclose results to patients directly, but only to their designated healthcare provider.
Myriad Genetic Laboratories complies with HIPAA and GDPR practices.

It's a Family Affair

Cancer-relevant gene mutations can be passed on in a family:

- If you have a gene mutation, your parent, your children and your brothers and sisters could have a 50% chance of having the same genetic mutation.
- Other relatives (aunts, uncles and cousins) on the same side of the family are at risk of carrying the same genetic 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.



Notes:

Myriad myRisk® Hereditary Cancer Panel:

- Evaluates a broad number of hereditary cancer syndromes
- Blends genetic test status with personal/family cancer history for clear and actionable follow-up
- Focuses on eight clinically significant cancer sites, including breast, colorectal, gastric, ovarian, endometrial, pancreatic, prostate, and melanoma.

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. Beebe-Dimmer, et al: Cancer Epidemiol Biomarkers Prev. 2015 Sep;24(9):1366-72.

ADDITIONAL RESOURCES

Myriad Genetics GmbH

E-mail Medical Services with questions about testing:

helpmed@myriadgenetics.eu

MYRIAD myRisk® Hereditary Cancer

A diagnostic test that detects gene mutations associated with eight major cancers.

myriad® WHEN DECISIONS MATTER

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