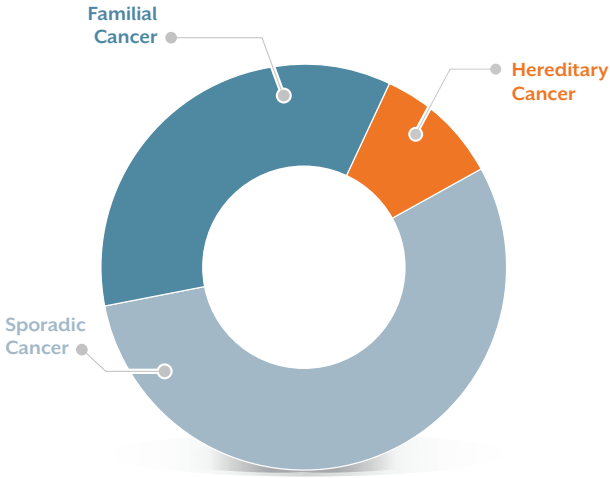
MYRIAD myRisk®
Hereditary Cancer

A Patient's Guide to Hereditary Cancer

Is Hereditary Cancer Testing Right for You?

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

Occurs when a gene 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 other related types of cancer. They may develop more than one cancer and their cancer often occurs at an earlier than average age.

FAMILIAL

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

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

Both men and women can inherit and pass down genetic mutations. Men with a family history of cancer, including breast and ovarian, should consider genetic testing.

Hereditary Prostate Cancer
ASSESSING YOUR RISK

About 1 in 9 American men receive a diagnosis of **prostate cancer** in their lifetime. It is the second leading cause of cancer deaths among men in the United States.[1] However, most prostate cancers are slow-growing and the majority of men with prostate cancer do not die from it.

What is Hereditary Prostate Cancer?

Some cancers are passed down through families. **Approximately 14% of all prostate cancer is hereditary.** Gene mutations can be inherited from the maternal or paternal side of the family. Individuals with hereditary cancer are more likely to have relatives with the same type or related types of cancer. They may develop more than one cancer. Many of these cancers can occur at earlier ages.

RED FLAGS FOR HEREDITARY PROSTATE CANCER

(CHECK ALL THAT APPLY IN YOU OR A FAMILY MEMBER)

- ☐ Metastatic prostate cancer
- ☐ Prostate cancer (Gleason score 7 or higher) AND relatives with breast, ovarian, prostate, or pancreatic cancers.
- ☐ Ovarian cancer diagnosed at any age
- ☐ Breast cancer diagnosed at age 50 or younger
- ☐ Male breast cancer diagnosed at any age
- ☐ Colon or endometrial cancer diagnosed before age 50 or any two Lynch syndrome-associated cancers* diagnosed at any age
- ☐ Ashkenazi-Jewish ancestry
- ☐ A previously identified mutation in the family

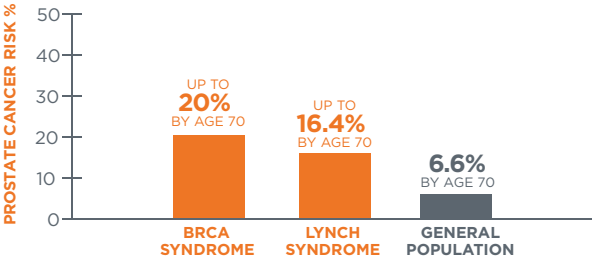
Who is at Risk?

If any of the red flags above apply to you or a family member, **you could have an inherited risk for prostate cancer** and may be appropriate for hereditary cancer testing. Please discuss these red flags with your healthcare provider.

*Lynch associated cancers include: colorectal, endometrial (uterine), gastric, ovarian, pancreas, ureter and renal pelvis, biliary tract, brain, and small intestinal cancers

What are the Risks?

All men have some risk of developing prostate cancer. The average man's risk of developing prostate cancer by age 70 is 6.6%. However, men with certain genetic mutations can have up to a 20% chance of developing prostate cancer by age 70. Men with hereditary prostate cancer are also at increased risk for developing a second cancer.



Overview of Prostate Cancer Syndromes

BRCA-RELATED BREAST AND/OR OVARIAN CANCER SYNDROME. A majority of hereditary prostate cancers are caused by mutations in the *BRCA1* and *BRCA2* genes. Men with BRCA mutations have an increased risk for male breast cancer and prostate cancer. Women with BRCA have a greatly increased risk for both breast and ovarian cancer. Both men and women have an increased risk for pancreatic cancer and melanoma.

LYNCH SYNDROME. Hereditary Non-polyposis Colorectal Cancer (HNPCC) is also known as Lynch syndrome. It is the most common cause of hereditary colorectal cancer and also puts people at increased risk for developing other cancers including prostate, endometrial, ovarian, gastric, and many other types of cancer. Lynch syndrome is caused by a mutation in one of five genes: *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM*.

MUTATIONS IN OTHER GENES like *TP53*, *CHEK2*, *NBN*, and *HOXB13*[2] are also associated with hereditary prostate cancer.

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		●							
POLD1			●						
POLE			●						
GREM1			●						
HOXB13								●	
AXIN2			●						
MSH3			●						
NTHL1			●						
RNF43			●						
GALNT12			●						
RPS20			●						

Possible Myriad myRisk® Test Results for Men

POSITIVE

- A genetic mutation was found in 1 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

- 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

- 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

Managing Hereditary Cancer

Individuals with familial or hereditary cancer risk have a much greater chance of developing cancer during their lifetime. Knowing if you are at increased risk for cancer empowers you to make life-saving decisions. You and your physician can work together to create a personalized plan to prevent cancer, identify cancer at an earlier, more treatable stage or prevent secondary cancers. Your personalized prevention or treatment plan may include the following:

TREATMENT OPTIONS

If you have been diagnosed with cancer, your test results may help determine appropriate treatment options

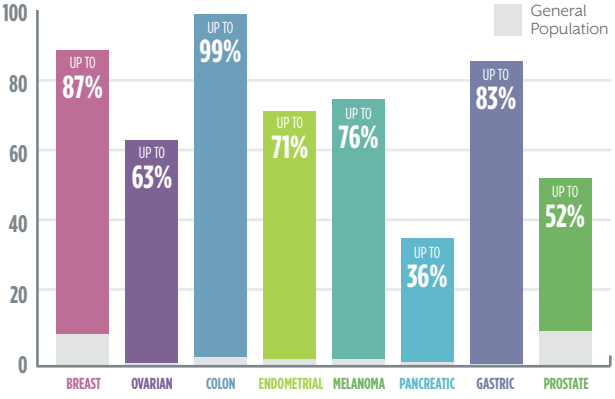
TARGETED THERAPY

If you have a gene mutation and a diagnosis of cancer, targeted therapies may be available for certain tumor types (e.g., platinum chemotherapy, PARP-inhibitors)

INCREASED SURVEILLANCE

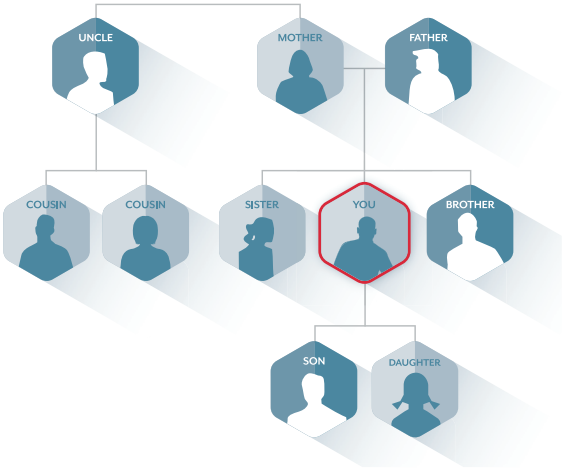
Increased surveillance may identify a cancer at its earliest, most treatable stage

Lifetime cancer risk for people with an identified hereditary cancer risk[2]



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.



Discussing Results With Your Family

It's important to discuss your results with your family. Knowing whether or not they carry a gene mutation can allow family members to make more informed decisions on their cancer prevention strategies. For those who test negative, the results can bring peace of mind.[3-9]

Privacy

HIPAA created federal privacy protections that apply to all health information created or maintained by healthcare providers and insurance plans. Myriad Genetic Laboratories complies with HIPAA practices. For more information on specific privacy practices, please visit: **www.myriad.com.**

Who is Myriad?

Myriad is the established leader in the field of hereditary cancer genetic testing with over 25 years of experience and over 2.5 million people tested. Our passion for patients drives everything we do. We are committed to providing healthcare professionals and patients with affordable and accurate information they can rely upon when decisions matter most.

Can my health insurance coverage be impacted by the results?

The Genetic Information Non-discrimination Act (GINA) and laws in most states prohibit discrimination regarding employment eligibility, health benefits, or health insurance premiums solely on the basis of genetic information. For information about Myriad's privacy policy, visit www.myriad.com/patients-families/the-myriad-difference/your-privacy.

Will my health insurance pay for my testing?

- 97% of private insurance companies have coverage for hereditary cancer testing
- 3 out of 4 patients pay $0
- Average patient out-of-pocket cost is $54

What if I have a high deductible plan or co-insurance?

If you have a high deductible or co-insurance, you may qualify for the Myriad Financial Assistance Program (MFAP) for a reduced out-of-pocket cost of no more than $295.†

† Patients who are recipients of U.S. government-funded programs such as Medicaid, Medicare, Medicare-Advantage and Tricare may not be eligible.

*How do I apply for Myriad's Financial Assistance Program?**

1. Include your income and number of family members in your household on the Test Request Form (TRF) your healthcare provider asks you to sign.
2. Provide your correct email address and phone number on the TRF so Myriad can contact you with further details.
3. Provide income verification (from your most recent tax return) and complete a 1-page application.

What is the difference between an Explanation of Benefits (EOB) and a bill?

Your insurance carrier will process our claim and then send you an Explanation of Benefits (EOB)—THIS IS NOT A BILL. Most patients do not receive a bill, and you will NOT be responsible for any balance unless you receive a bill directly from Myriad, even if you receive a denial letter from your insurance company. If you have concerns about your EOB please contact Myriad at (844) 697-4239 or billinghelp@myriad.com.

* For uninsured patients please go to www.MyriadPro.com/mfap for application information

Myriad Promise™

BECAUSE PATIENTS and their families use test results to make life saving medical decisions, Myriad promises to provide affordable access to testing, a lifetime commitment to accurate results, and comprehensive support for ALL appropriate patients and their families.

If you encounter ANY financial hardship associated with your genetic test, Myriad will work with you toward your complete satisfaction. Myriad provides payment plans without interest, where you can pay as little as $15/month if you have a bill.

For more information visit **myriadpromise.com**

NOTES:

MYRIAD myRisk®
Hereditary Cancer

See back of brochure for next steps.

REFERENCES

1. American Cancer Society: http://www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-key-statistics
2. For the most up-to-date general population and syndrome associated cancer risks, please refer to the Gene Table at https://www.MyriadPro.com/myRisk
3. Ford D, et al. Risks of cancer in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. Lancet. 1994 343:692-5.
4. 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/
5. Baglietto L, et al. Risks of Lynch syndrome cancers for MSH6 mutation carriers. J Natl Cancer Inst. 2010 102:193-201.
6. 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.
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8. 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.
9. Beebe-Dimmer, et al: Cancer Epidemiol Biomarkers Prev. 2015 Sep;24(9):1366-72.

Notice and Statement Concerning Nondiscrimination and Accessibility

Discrimination is Against the Law

Myriad Genetic Laboratories, Inc. (Myriad) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Myriad does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

Aids and Services

Myriad provides free aids and services to people with disabilities to communicate effectively with us, such as TTY/TDD calls or written information in suitable formats. Myriad will also provide free language services to people whose primary language is not English through qualified interpreters.

If you need these services, contact Ms. Sara Greene:
Sara Greene
Compliance Specialist
320 Wakara Way
Salt Lake City, UT 84108
Telephone: (801) 584-3600
Fax: (801) 883-3472
Email: compliance@myriad.com

Grievances

If you believe that Myriad has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance by mail, telephone, fax, or email. If you need help filing a grievance, Ms. Greene is available to help you (see contact information above).

Grievance Procedure

1. Any person who believes someone has been subjected to discrimination by Myriad on the basis of race, color, national origin, sex, age or disability may file a grievance with Myriad. It is against the law for Myriad to retaliate against anyone who opposes discrimination, files a grievance, or participates in the investigation of a grievance.

2. Grievances must be submitted within 60 days of the date the person filing the grievance becomes aware of the alleged discriminatory action.

3. The complaint must be in writing, containing the name and address of the person filing it. The complaint must state the problem or action alleged to be discriminatory and the remedy or relief sought.

4. Myriad will conduct an investigation of the complaint. This investigation may be informal, but it will be thorough, affording all interested persons an opportunity to submit evidence relevant to the complaint. Myriad will maintain the files and records relating to such grievances. To the extent possible, and in accordance with applicable law, Myriad will take appropriate steps to preserve the confidentiality of files and records relating to grievances and will share them only with those who have a need to know.

5. Myriad will issue a written decision on the grievance, based on a preponderance of the evidence, no later than 30 days after its filing, including a notice to the complainant of their right to pursue further administrative or legal remedies.

6. The person filing the grievance may appeal Myriad's decision in writing to the President of Myriad Genetic Laboratories, Inc. within 15 days of receiving Myriad's initial decision. The President will issue a written decision in response to the appeal no later than 30 days after its filing.

7. Individuals seeking access to Section 1557 and its implementing regulations may be facilitated by contacting Ms. Greene (see contact information above).

8. The availability and use of this grievance procedure does not prevent a person from pursuing other legal or administrative remedies, including filing a complaint of discrimination on the basis of race, color, national origin, sex, age or disability in court or with the U.S. Department of Health and Human Services, Office for Civil Rights. A person can file a complaint of discrimination electronically through the Office for Civil Rights Complaint Portal, which is available at: https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201

9. Complaint forms are available at: http://www.hhs.gov/ocr/office/file/index.html. Such complaints must be filed within 180 days of the date of the alleged discrimination. Myriad will make appropriate arrangements to ensure that individuals with disabilities and individuals with limited English proficiency are provided auxiliary aids and services or language assistance services, respectively, if needed to participate in this grievance process. Ms. Greene will be responsible for such arrangements.

gratuitos de asistencia lingüística. Llame al 1-801-584-3600.

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Myriad Genetic Laboratories, Inc. 遵守適用的聯邦民權法律規定，不因種族、膚色、民族血統、年齡、殘障或性別而歧視任何人。注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 1−801−584−3600.

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Myriad Genetic Laboratories, Inc. tuân thủ luật dân quyền hiện hành của Liên bang và không phân biệt đối xử dựa trên chủng tộc, màu da, nguồn gốc quốc gia, độ tuổi, khuyết tật, hoặc giới tính. CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-801-584-3600.

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ملحوظة: إذا كنت تتحدث اذكر اللغة، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم 1-801-584-3600

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فارسی (Farsi)
توجه: اگر به زبان فارسی گفتگو می کنید، تسهیلات زبانی بصورت رایگان برای شما فراهم می باشد. با 1-801-584-3600. تماس بگیرید.

NEXT STEPS:

- ❑ Pursue Testing by giving a 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: _____

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 Myriad myRisk if Multisite 3 is negative
    - ❑ **Check here** if a family member has tested positive for one of these 3 mutations
- ❑ Single Site Testing (For family of known mutation carriers)
  Specify Gene: _____ and
  Mutation: _____
  Relationship: I am the _____
  (e.g. paternal uncle) of the known mutation carrier. Required: Include a copy of the known mutation carriers report.
- ❑ 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.

MYSUPPORT360