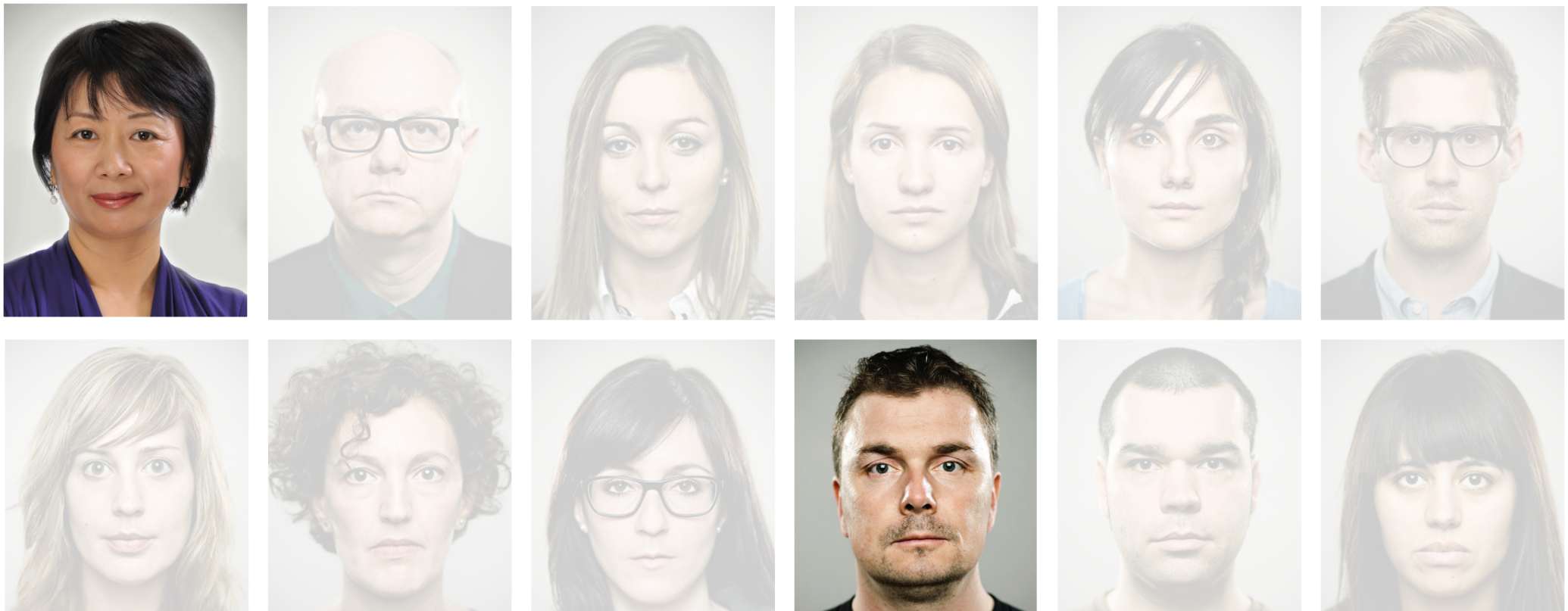
MYRIAD myRisk™ Hereditary Cancer

Incorporating Hereditary Cancer Risk Assessment into Your Practice



DISCLAIMER

This information is provided to help answer questions with respect to hereditary cancer risk assessment and hereditary cancer testing. It is general in nature and is not intended to provide a comprehensive, definitive analysis of specific risks. The information provided herein should be taken into consideration with other medical and research information regarding cancer risks, hereditary cancer risks and predispositional cancer testing and risk factors. This is not an accredited CME/CNE/CEU program.

Personal and Non-Commercial Use:
These slides are for your personal and non-commercial use. You may not modify, publish, reproduce, license, create derivative works from or sell any information obtained from these slides. Speaker receives honorarium from Myriad Genetic Laboratories, Inc.

Objectives

At the conclusion of this presentation, participants should understand the following concepts related to hereditary cancer risk assessment and patient management:

- How utilizing Cancer Family History (CFHx) can help you optimally manage all of your patients

- Why stratifying patients by risk categories will help you determine appropriate management and screening recommendations

- How to integrate a Hereditary Cancer Risk Assessment (HCRA) protocol into your practice

- How technology impacts patient care

Use of Cancer Family History

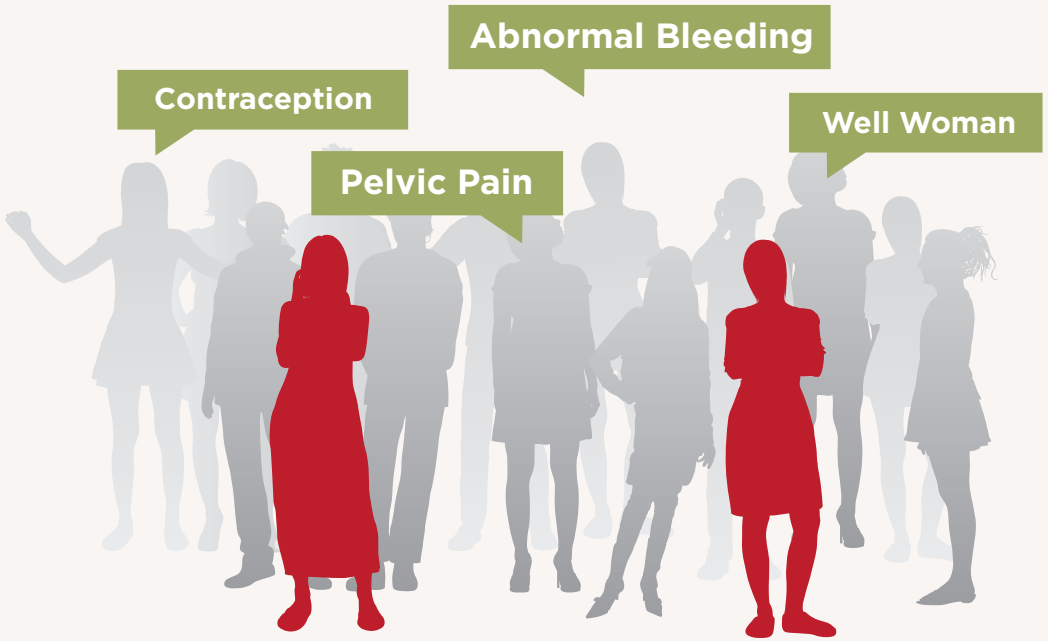
GATHER

CURRENTLY MOST PROVIDERS GATHER A CANCER FAMILY HISTORY FOR PATIENT CHARTS

UTILIZE

ACTIVELY UTILIZE CANCER FAMILY HISTORY FOR:

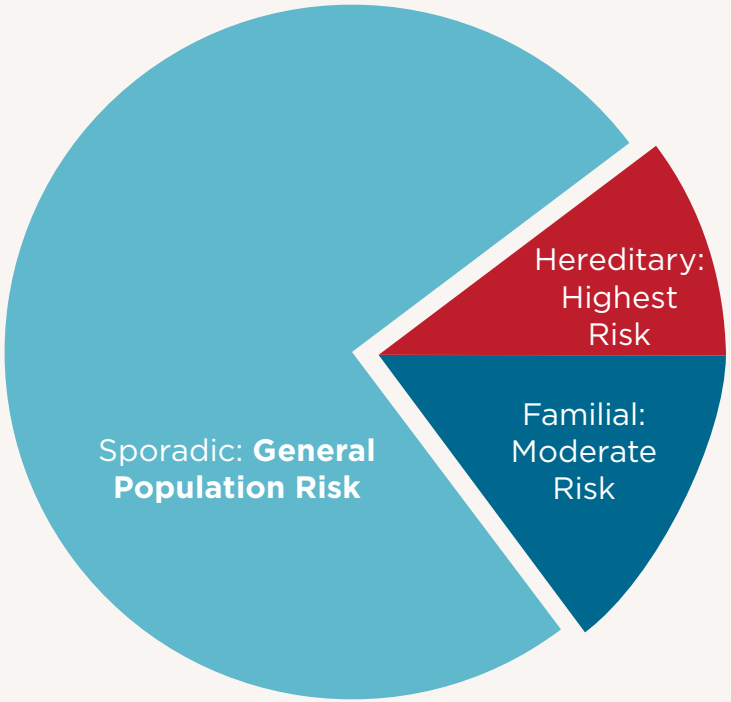
- All visits including well-woman exams
- Identifying patients with significant risk
- Optimal management for all patients



MYRIAD myRisk™ Hereditary Cancer

Risk Stratification

- **Cancer family history alone can help you optimize management.**
- **If your patient is positive for a syndrome, management will be different. Even a negative result will impact medical management.**

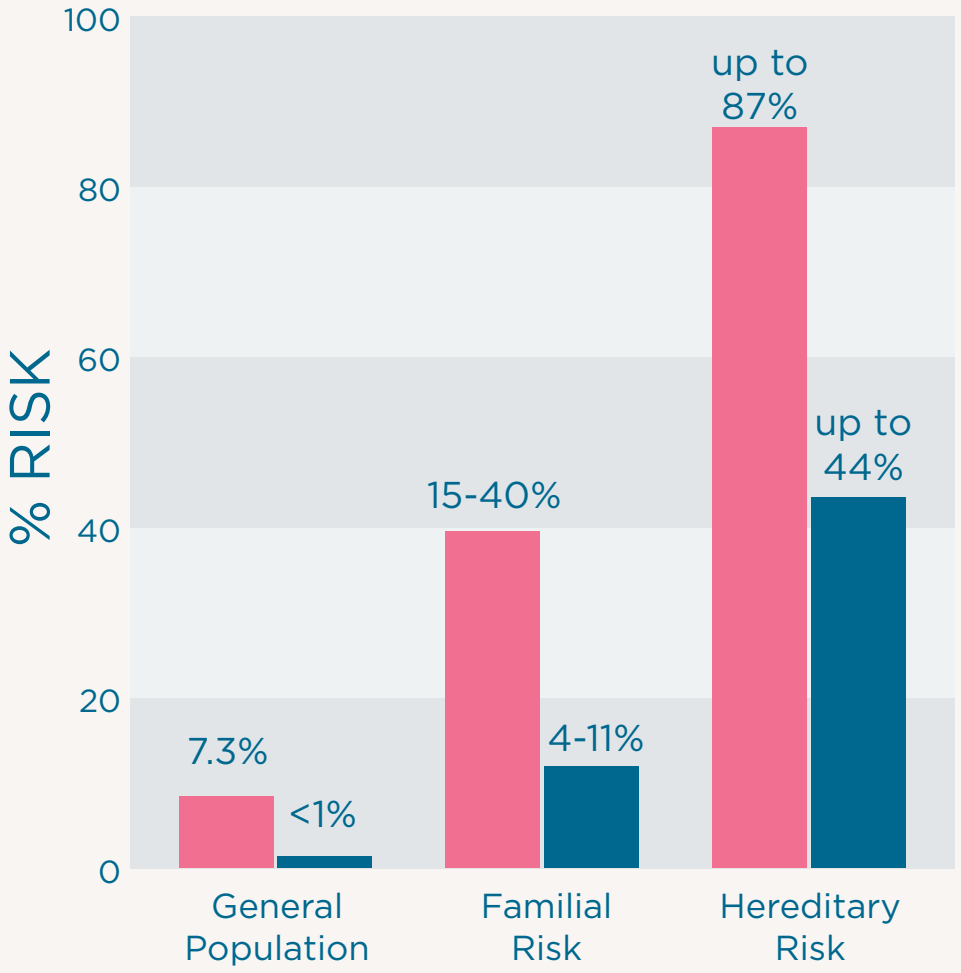


Genetic testing is the only way to stratify risk between these two groups and find those at highest risk for cancer

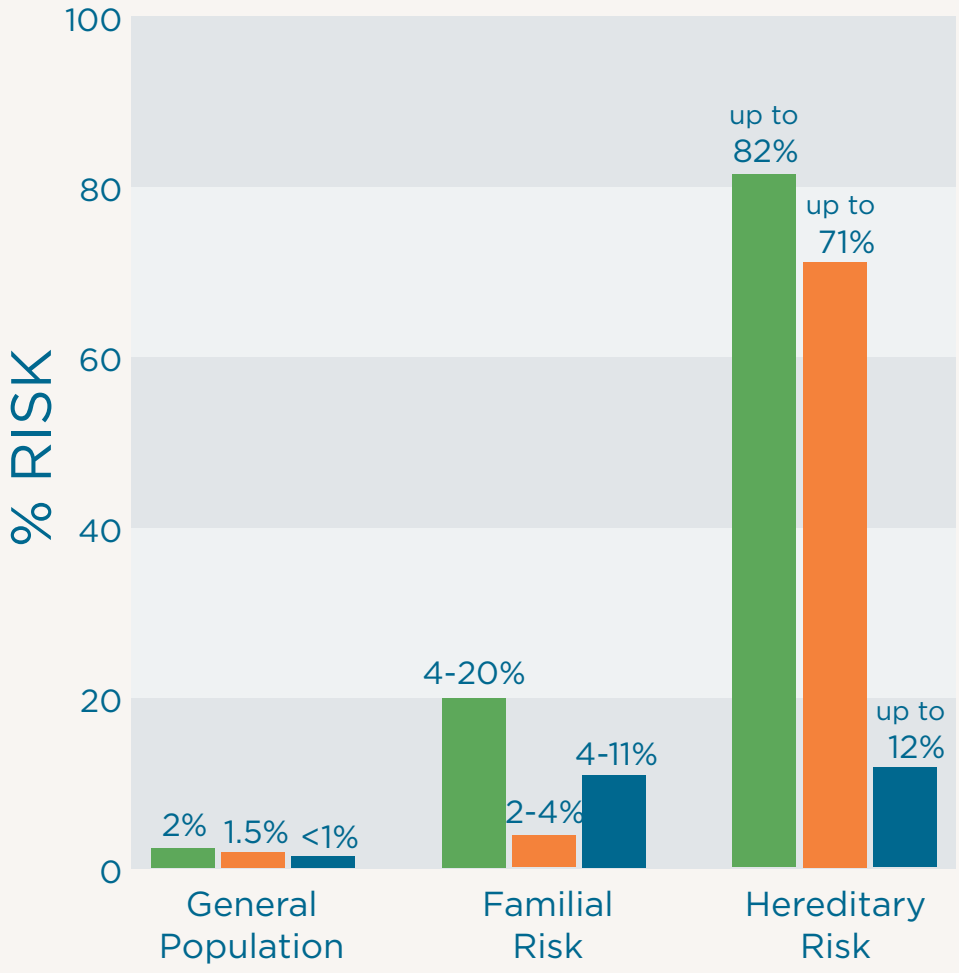
MYRIAD myRisk™ Hereditary Cancer

Hereditary Cancer Syndromes

Hereditary Breast & Ovarian Cancer (HBOC)



Lynch Syndrome



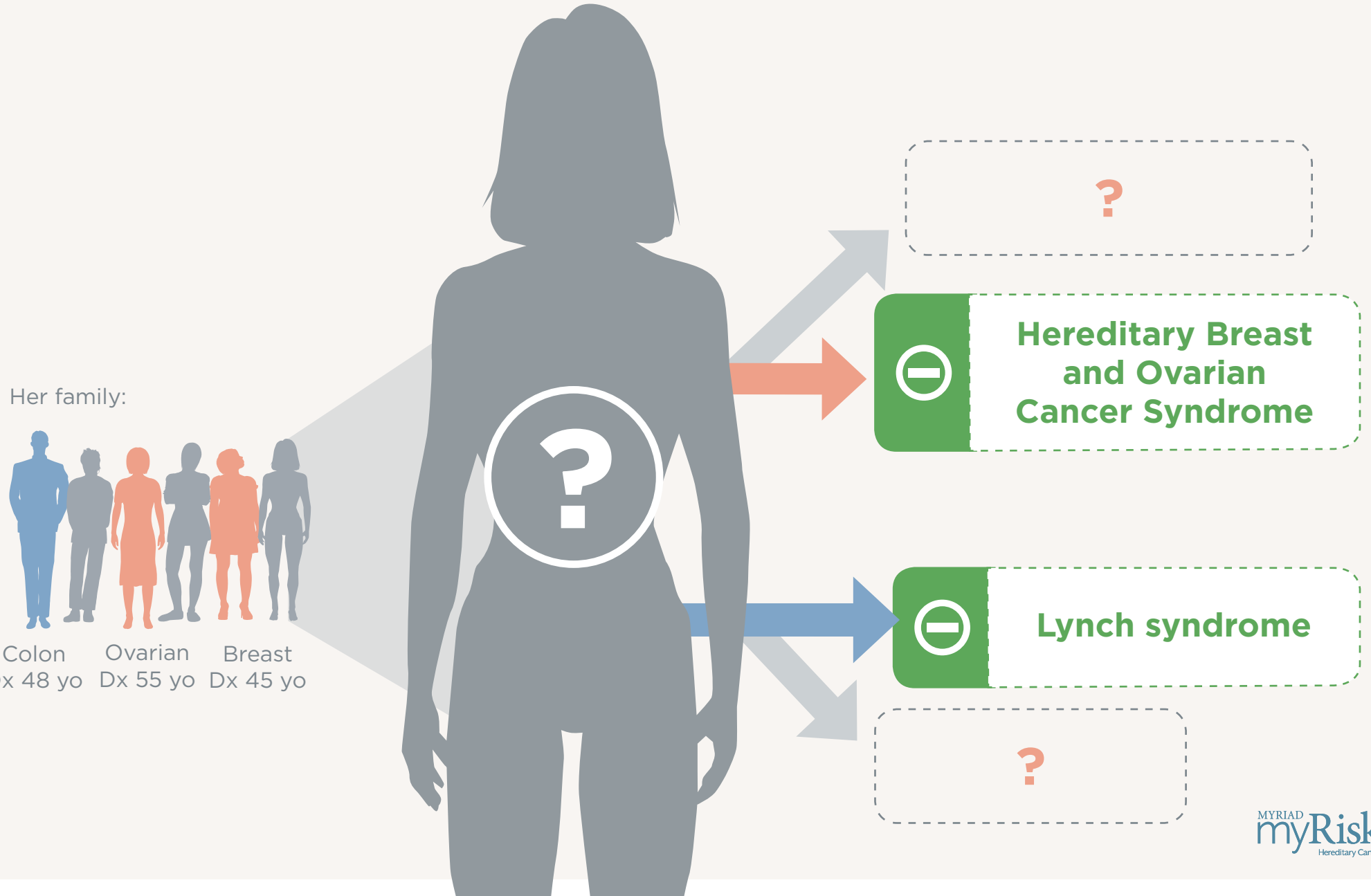
Breast Cancer by Age 70 | **Colon Cancer by Age 70** | **Endometrial Cancer by Age 70** | **Ovarian Cancer by Age 70**

HBOC REFERENCES: 1. Domchek SM, et al. Br Ca Res Treat. 2010 Jan;119(2):409-14. 2. Ford D, et al. Lancet. 1994;343:692-5. 3. Struewing JP, et al. NEJM. 1997;336:1401-8. 4. Antoniou A, et al. AJHG. 2003;72:1117-30. 5. The Breast Cancer Linkage Consortium.JNCI. 1999;15:1310-6. 6. Easton DF, et al. AJHG. 1995;56:265- 71. 7. King MC, et al. Science. Oct 24 2003:643-6. 8. Narod SA, Offit K. JCO. 2005 Mar 10;23(8):1656-63. 9. DevCan: Probability of Developing or Dying of Cancer Software, Version 6.0. Statistical Research and Applications Branch, National Cancer Institute, 2005. http:// srab.cancer. gov/devcan. Assessed Jan 2010. 10. Metcalfe KA, et al. Br J Cancer. 2009 Jan 27;100(2):421-5.Epub 2008 Dec 16. 11. Kauff ND, et al. JNCI. 2005;97(18):1382-4. 12. Pharoah Paul PD and Ponder BA. Best Practice & Research Clinical Obstetrics and Gynecology. Vol 16. No.4. 449- 68. 2002. 13. Sutcliffe, et al. Int J Cancer. 2000 Jul 1;(87)1:110-7. 14. Whittemore AS, et al. AJHG. 1997;60:496-504. 15. Ford D, et al. AJHG. 1998;62:676-89.

LYNCH REFERENCES: 1. Vasen HFA, et al. Gastroenterology. 1996;110-1020-7. 2. Aarnio M, et al. Int J Cancer. 1999;81:214-8. 3. Vasen HF, et al. J Clin Oncol. 2001 Oct 15;19(20);4074-80. 4. Hampel H, et al. Gastroenterology. 2005 Aug; 129(2):415-21. 5. Hendriks YM, et al. Gastroenterology. 2004;127:17-25. 6. Stoffel E, et al. Gastroenterology. 2009;137(5):1621-7. 7. Surveillance Epidemiology End Result (SEER), National Cancer Institute 2007. http://SEER.cancer.gov/faststats. 8. Jasperson KW, et al. Gastroenterology. 2010;138:2044-58. 9. Taylor DP, et al. Gastroenterology. 2010;138:877-885. 10. Grady, WM, et al. Gastroenterology. 2003;124:1574-94. 11. Burt RW. Gastroenterology 2000; 119:837-853. 12. Butterworth AS, et al. European Journal of Cancer. 2006;42:216-217. 13. Pharoah Paul PD and Ponder BA. Best Practice & Research Clinical Obstetrics and Gynaecology. Vol 16. No.4. 449- 68. 2002.

MYRIAD myRisk™ Hereditary Cancer

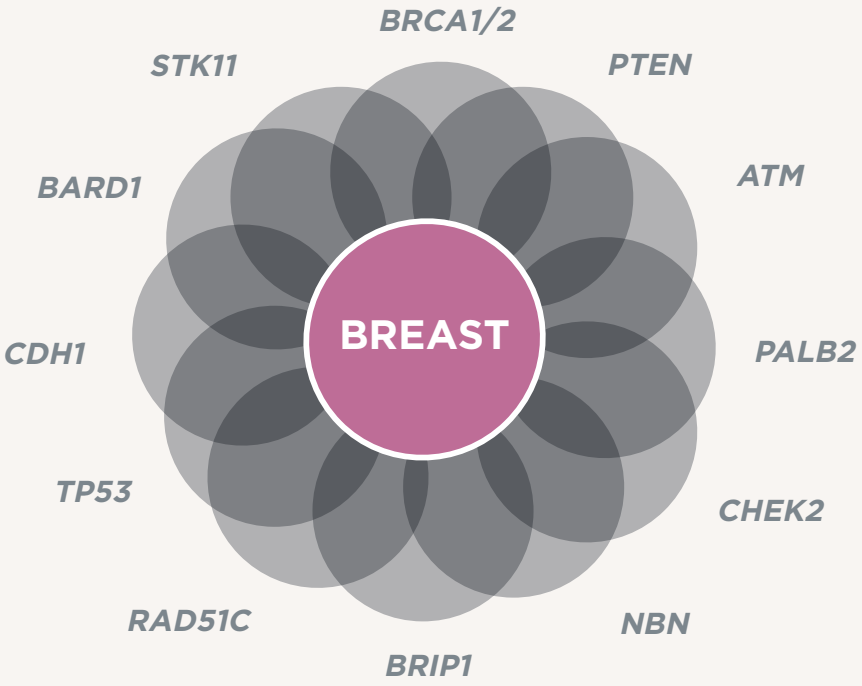
However, evaluating cancer family history based on single syndromes is **too NARROW and can lead to a false sense of security and patient mismanagement**



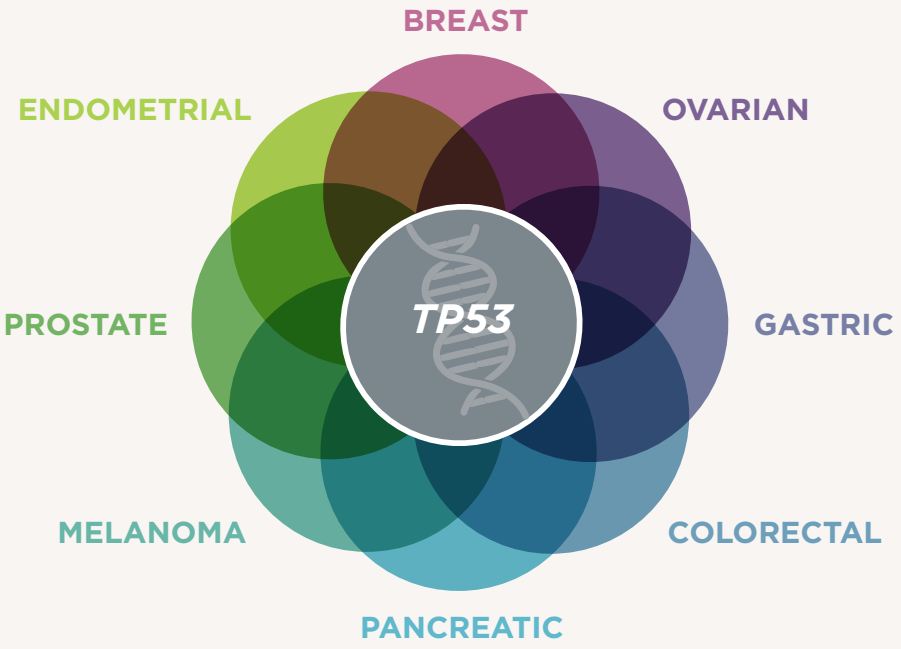
MYRIAD myRisk™ Hereditary Cancer

The Clinical Dilemma

Multiple genes can be associated with increased risk of a single cancer



Multiple cancer risks can be associated with a single gene



Assessment that is too narrow can lead to a false sense of security and patient mismanagement

MYRIAD myRisk™ Hereditary Cancer

myRisk Case Study: **Well Woman Exam**

Patient Information

- 40-year-old
- G2 P2
- Childbearing complete

Visit Type

- Well Woman Exam

Visit Notes

- First mammogram scheduled next week
- Discuss breast screening plan

FAMILY HISTORY		
Relative	**Cancer Site**	**Age Dx**
Maternal Aunt	Breast	65
Maternal Aunt	Breast	45

Hereditary cancer risk assessment impacts medical decisions

MYRIAD myRisk™ Hereditary Cancer

myRisk Case Study: **Well Woman Exam**

Family History

Breast Ca
lifetime risk:
<20%*

Management

- ***General population breast screening***

Expected Single Syndrome Result

HBOC

Management

- ***Early and frequent MRI / mammograms***
- ***Other increased cancer risks***
- ***BSO***

Actual Result

PALB2

RESULT:
Positive

Management Now

PROCEDURE	AGE TO BEGIN
FEMALE BREAST	
Clinical breast examination every 6 to 12 months	30 years
Consider breast MRI in addition to mammography	30 years
PANCREATIC	
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 the screening for pancreatic cancer, preferably within research protocols.	Individualized

In addition to other genetic, personal and/or family history based management considerations

*Tyrer-Cuzick http://www.ems-trials.org/riskevaluator/

BRCA1/2 testing in 2012

RESULT: ***Negative***

Assessment that is too narrow can create a
false sense of security and patient mismanagement

MYRIAD myRisk™ Hereditary Cancer

myRisk Case Study: **Contraception Consult**

Patient Information
- 36-year-old
- G2 P2
- Childbearing complete

Visit Type
- Contraception consult

Visit Notes
- Patient desires permanent sterilization

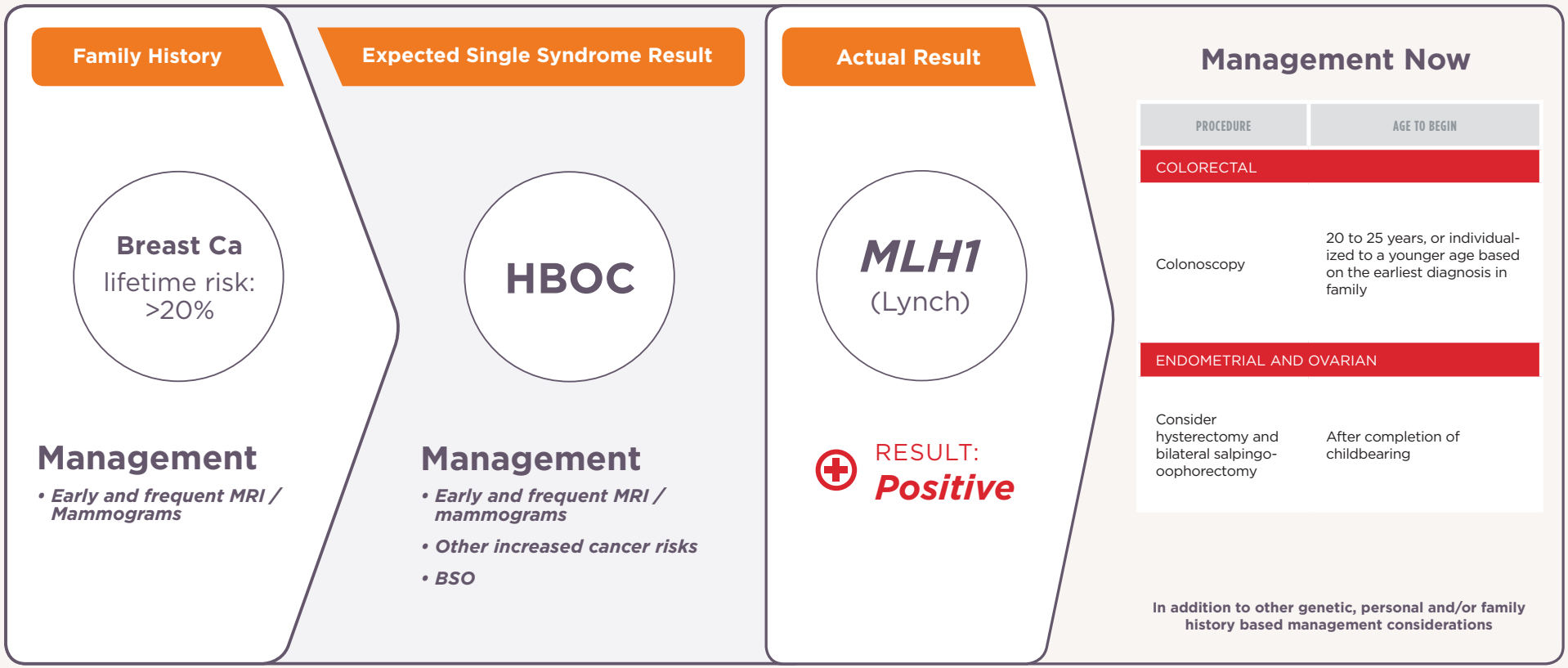
Recommended Management
- Common recommendations may include:
  - Tubal ligation or bilateral salpingectomy
  - Tubal occlusion
  - Vasectomy (for partner)

FAMILY HISTORY		
Relative	**Cancer Site**	**Age Dx**
Mother	Breast	65
Maternal Aunt	Ovarian	55

Hereditary cancer risk assessment impacts medical decisions

MYRIAD myRisk™ Hereditary Cancer

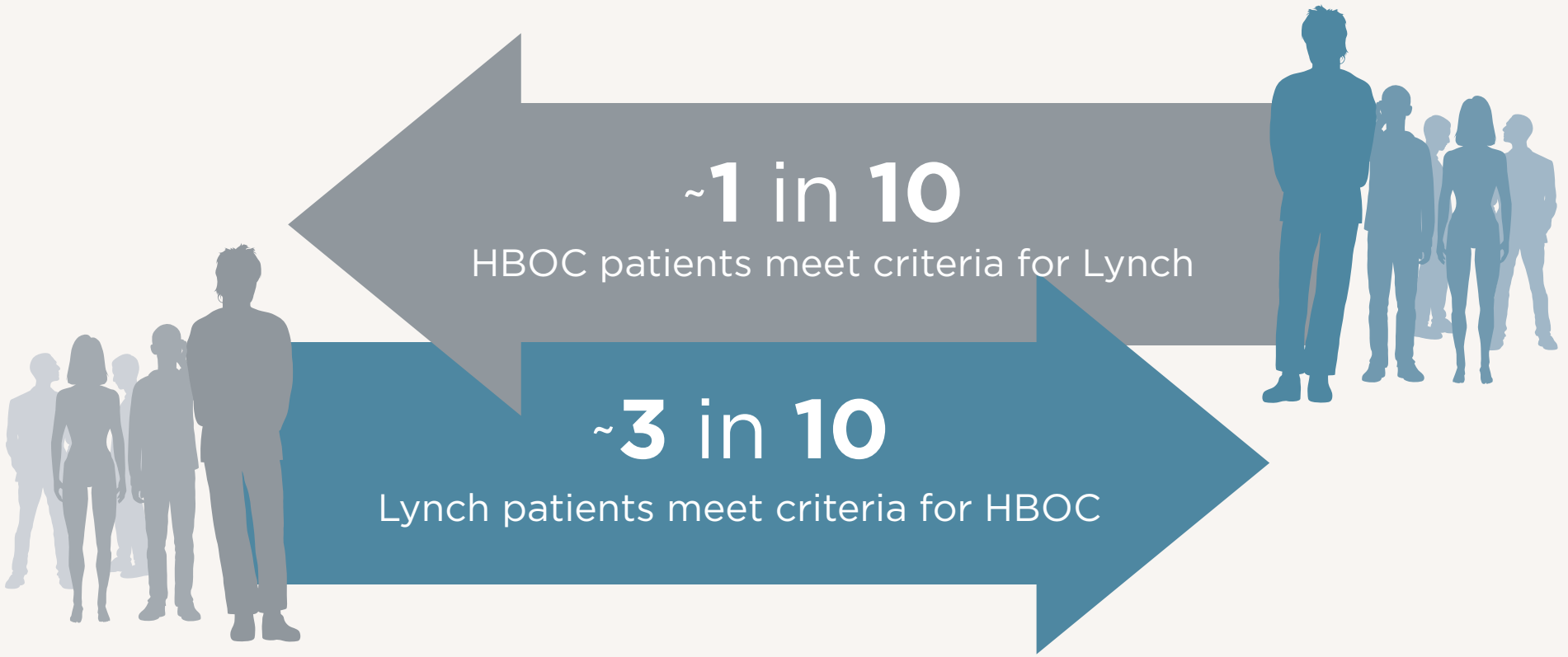
myRisk Case Study: **Contraception Consult**



Assessment that is too narrow can create a
false sense of security and patient mismanagement

MYRIAD myRisk™ Hereditary Cancer

A significant number of patients meet criteria for multiple syndromes



Assessment that is too narrow can lead to a false sense of security and patient mismanagement

Saam, J., et al. (2014, March). Overlap between Lynch syndrome and hereditary breast and ovarian cancer syndrome among family histories in patients tested for hereditary cancer syndromes. Presented at the NCCN, Hollywood, FL.

MYRIAD myRisk™ Hereditary Cancer

Panel Testing Increases the Number of Diagnosed High-Risk Hereditary Cancer Mutations

Panels may increase the likelihood of capturing hereditary cancer gene mutations in those patients who tested negative for HBOC or Lynch syndrome

1. Sharma, L., et al. (2014, December) Spectrum of Mutations Identified in a 25-gene Hereditary Cancer Panel for Patients with Breast Cancer. Presented at SABCS, San Antonio, TX. **2.** Yurgelun, MB., et al., Identification of a Variety of Mutations in Cancer Predisposition Genes in Patients with Suspected Lynch Syndrome, *Gastroenterology*, (2015, May). **3.** Allen, B., et al. (2014, March) Prevalence of gene mutations among hereditary breast and ovarian cancer patients using a 25 gene panel. Presented at the ACMG, Nashville, TN

MYRIAD myRisk™ Hereditary Cancer

A broader risk assessment will impact the outcome of patients you see **today**, have tested in the **past**, and will see **tomorrow**

Past Negatives

Do you have patients that are **over or undermanaged**?

Today's Appointments

Moving Forward

Avoid a false **sense of security** and mismanagement of patients you see today

Cancer Family History Impacts Every Patient Visit

MYRIAD myRisk™ Hereditary Cancer

Technological advancement in hereditary cancer testing allows **greater assurance of optimal patient management**

The Society of Gynecologic Oncology (SGO) and the National Comprehensive Cancer Network (NCCN) recognize the benefits of hereditary cancer panels[1,2]

- Cost Effective Approach
- Improved Efficiency
- Greater Assurance in Test Results

Myriad myRisk™ Hereditary Cancer Panel

1. SGO Clinical Practice Statement: Next Generation Cancer Gene Panels Versus Gene by Gene Testing, March 2014
2. NCCN Guidelines version 1.2015: Genetic/Familial High-Risk Assessment: Breast and Ovarian

MYRIAD myRisk™ Hereditary Cancer

Solution

Hereditary Cancer Risk Assessment STANDARD OF CARE for every patient:

Education

Regional Medical Specialists (RMS) can help enhance your:

- Clinical knowledge
- Risk assessment based on society guidelines
- Informed consent discussions
- Test result interpretation and medical management plans

Process

Account Executives (AE) and Strategic Account Managers (SAM) can help:

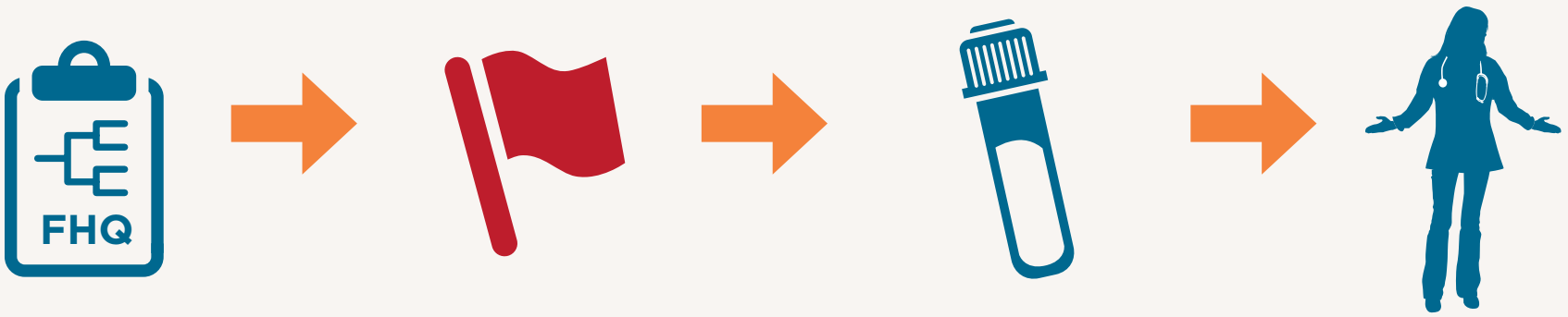
- Create a tailored protocol to efficiently assess the cancer risk of every patient
- Measure progress with quality metrics
- Continuously improve the protocol for Hereditary Cancer Risk Assessment

MYRIAD myRisk™ Hereditary Cancer

Hereditary & Familial Cancer: Establishing a Protocol

A protocol should be used to efficiently stratify your patient's risk for a hereditary cancer

SCREEN → **EVALUATE** → **DIAGNOSE** → **MANAGE**



"Protocols and checklists have been shown to improve patient safety through standardization and communication. Standardization of practice to improve quality outcomes is an important tool in achieving the shared vision of patients and their healthcare providers."

- ACOG No. 526, 2015: Standardization of Practice to Improve Outcomes

MYRIAD myRisk™ Hereditary Cancer

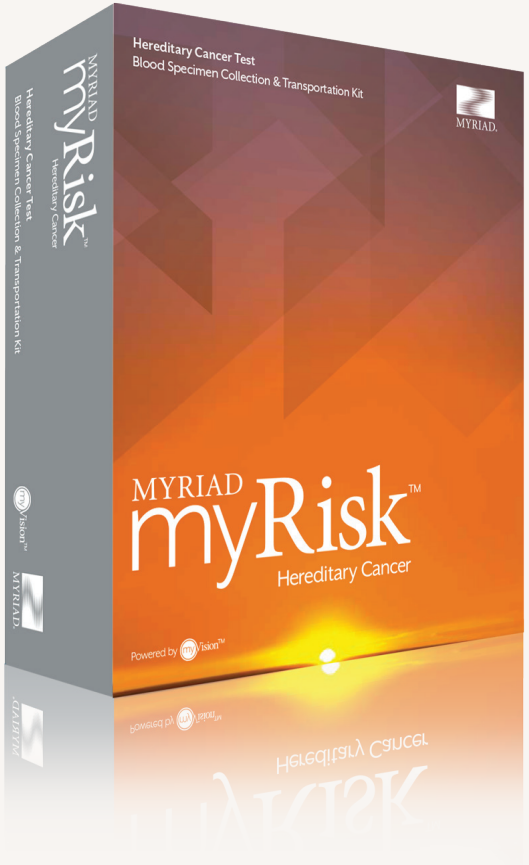
Informed Consent or Refusal

If patient meets testing criteria:

- Discuss testing with patients just as you do with other common diagnostic tests such as a colposcopy
- Emphasize the need for a diagnostic test result in order to manage the patient optimally
- Obtain and document patient's consent or refusal

Solution: **Myriad myRisk™ Hereditary Cancer Panel**

Evaluate risk for **8 important cancers** by analyzing multiple, clinically actionable genes



Accurate knowledge of cancer risks.
Actionable direction for patient management.

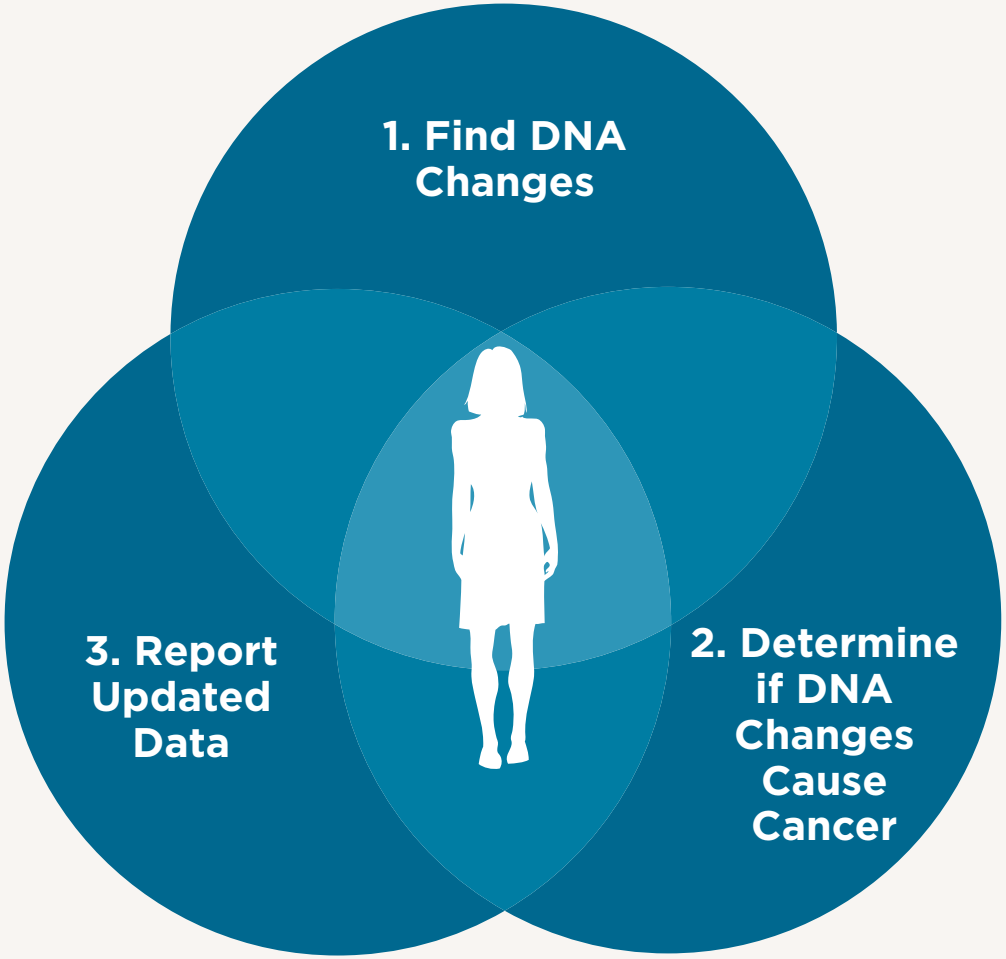
- Provides medical management for POSITIVE and NEGATIVE results based on leading societal guidelines
- Identifies 104.5% more mutations in clinically actionable genes[1,2,3]
- Powered by Myriad's myVision™ Variant Classification Program

1. Sharma, L., et al. (2014, December) Spectrum of Mutations Identitfied in a 25-gene Hereditary Cancer Panel for Patients with Breast Cancer. Presented at SABCS, San Antonio, TX. **2.** Yurgelun, MB., et al., Identification of a Variety of Mutations in Cancer Predisposition Genes in Patients with Suspected Lynch Syndrome, *Gastroenterology*, (2015, May). **3.** Tung, et al. (2014, March) Prevalence of gene mutations among hereditary breast and ovarian cancer patients using a 25 gene panel. Presented at the ACMG, Nashville, TN

MYRIAD myRisk™ Hereditary Cancer

The most important factor in hereditary cancer prevention is providing an accurate test result

Your lab needs to be accountable for 3 things:



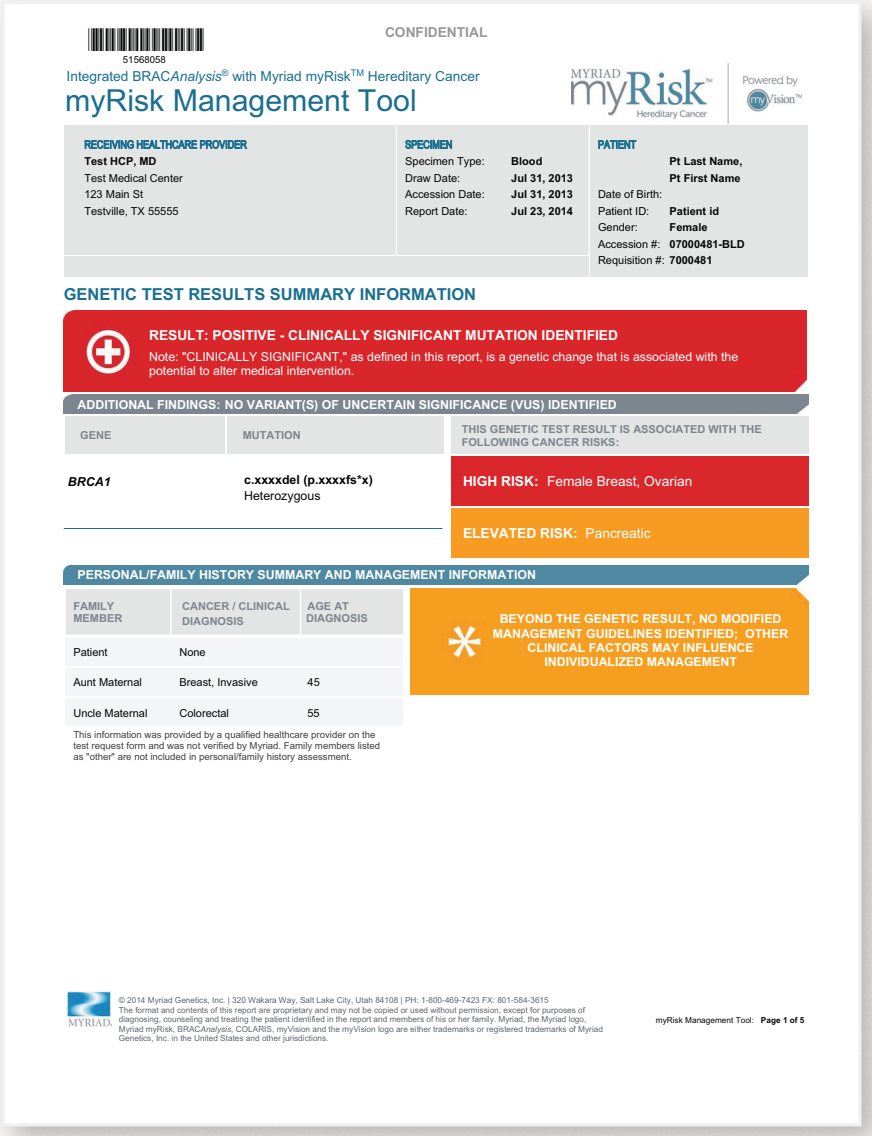
Medical societies highlight the importance of ❶ accurate results, ❷ transparent variant classification and ❸ amended reports[1]

MYRIAD myRisk™ Hereditary Cancer

1. NCCN Genetic/Familial High-Risk Assessment: Breast and Ovarian Cancer Guidelines (Version 1.2015).

Myriad myRisk™ Report

Medical management considerations based on leading medical guidelines for both POSITIVE and NEGATIVE results



51568058

CONFIDENTIAL

Integrated BRAC*Analysis*® with Myriad myRisk™ Hereditary Cancer

myRisk Management Tool

MYRIAD myRisk™ Hereditary Cancer | Powered by myVision™

RECEIVING HEALTHCARE PROVIDER
Test HCP, MD
Test Medical Center
123 Main St
Testville, TX 55555

SPECIMEN
Specimen Type: **Blood**
Draw Date: **Jul 31, 2013**
Accession Date: **Jul 31, 2013**
Report Date: **Jul 23, 2014**

PATIENT
Pt Last Name, Pt First Name
Date of Birth:
Patient ID: **Patient id**
Gender: **Female**
Accession #: **07000481-BLD**
Requisition #: **7000481**

GENETIC TEST RESULTS SUMMARY INFORMATION

RESULT: POSITIVE - CLINICALLY SIGNIFICANT MUTATION IDENTIFIED
Note: "CLINICALLY SIGNIFICANT," as defined in this report, is a genetic change that is associated with the potential to alter medical intervention.

ADDITIONAL FINDINGS: NO VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED

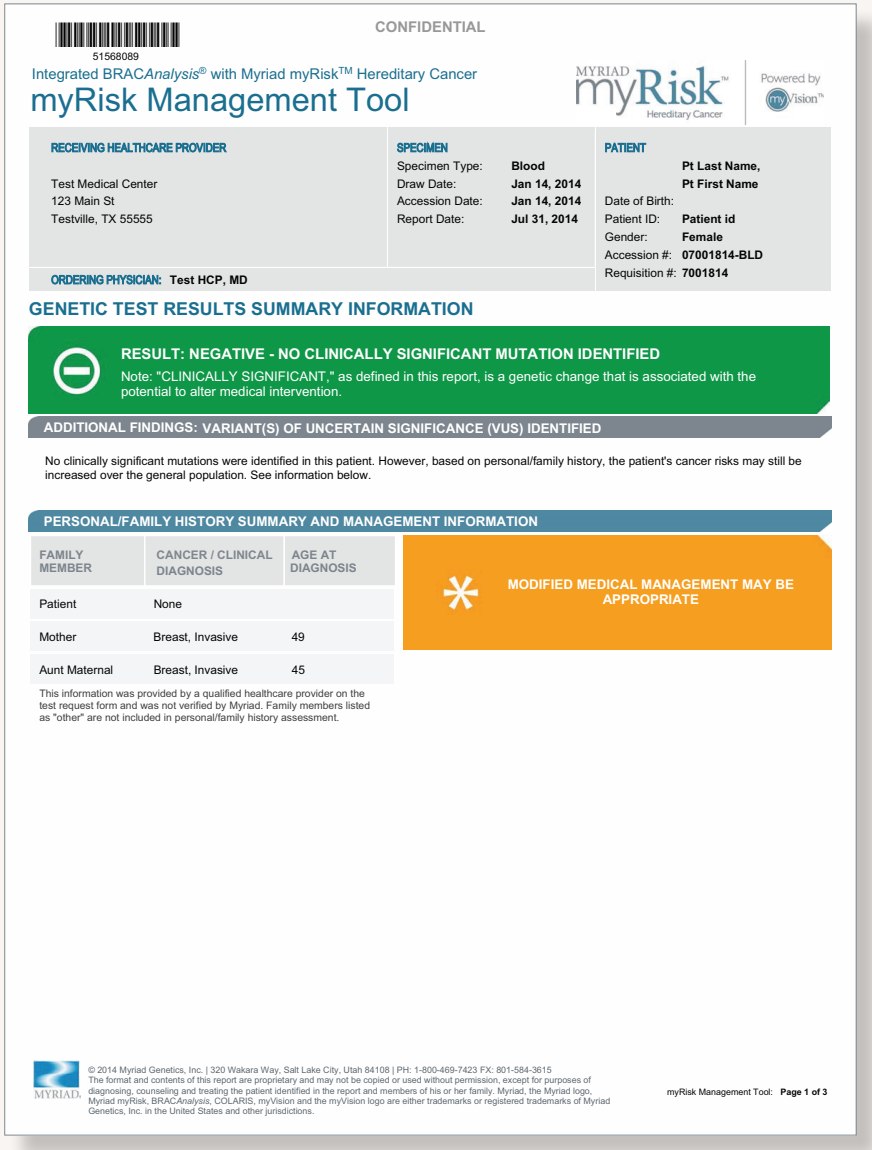
GENE	MUTATION	THIS GENETIC TEST RESULT IS ASSOCIATED WITH THE FOLLOWING CANCER RISKS:
BRCA1	**c.xxxxdel (p.xxxxfs*x)** Heterozygous	**HIGH RISK:** Female Breast, Ovarian
		ELEVATED RISK: Pancreatic

PERSONAL/FAMILY HISTORY SUMMARY AND MANAGEMENT INFORMATION

FAMILY MEMBER	CANCER / CLINICAL DIAGNOSIS	AGE AT DIAGNOSIS
Patient	None	
Aunt Maternal	Breast, Invasive	45
Uncle Maternal	Colorectal	55

This information was provided by a qualified healthcare provider on the test request form and was not verified by Myriad. Family members listed as "other" are not included in personal/family history assessment.

***** BEYOND THE GENETIC RESULT, NO MODIFIED MANAGEMENT GUIDELINES IDENTIFIED; OTHER CLINICAL FACTORS MAY INFLUENCE INDIVIDUALIZED MANAGEMENT



51568089

CONFIDENTIAL

Integrated BRAC*Analysis*® with Myriad myRisk™ Hereditary Cancer

myRisk Management Tool

MYRIAD myRisk™ Hereditary Cancer | Powered by myVision™

RECEIVING HEALTHCARE PROVIDER
Test Medical Center
123 Main St
Testville, TX 55555

SPECIMEN
Specimen Type: **Blood**
Draw Date: **Jan 14, 2014**
Accession Date: **Jan 14, 2014**
Report Date: **Jul 31, 2014**

PATIENT
Pt Last Name, Pt First Name
Date of Birth:
Patient ID: **Patient id**
Gender: **Female**
Accession #: **07001814-BLD**
Requisition #: **7001814**

ORDERING PHYSICIAN: **Test HCP, MD**

GENETIC TEST RESULTS SUMMARY INFORMATION

RESULT: NEGATIVE - NO CLINICALLY SIGNIFICANT MUTATION IDENTIFIED
Note: "CLINICALLY SIGNIFICANT," as defined in this report, is a genetic change that is associated with the potential to alter medical intervention.

ADDITIONAL FINDINGS: VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED

No clinically significant mutations were identified in this patient. However, based on personal/family history, the patient's cancer risks may still be increased over the general population. See information below.

PERSONAL/FAMILY HISTORY SUMMARY AND MANAGEMENT INFORMATION

FAMILY MEMBER	CANCER / CLINICAL DIAGNOSIS	AGE AT DIAGNOSIS
Patient	None	
Mother	Breast, Invasive	49
Aunt Maternal	Breast, Invasive	45

This information was provided by a qualified healthcare provider on the test request form and was not verified by Myriad. Family members listed as "other" are not included in personal/family history assessment.

***** MODIFIED MEDICAL MANAGEMENT MAY BE APPROPRIATE

MYRIAD myRisk™ Hereditary Cancer

Summary

Do you understand how the importance of the following concepts are related to hereditary cancer risk assessment and patient management?

- Utilizing a Cancer Family History (CFHx) to stratify risk with every patient at every visit
- Using consistent evaluation criteria (red flags) to identify appropriate patients for Hereditary Cancer Testing
- Implementing an HCRA protocol for consistent patient evaluation
- Knowing you have accurate results for patient management of patients with both POSITIVE and NEGATIVE results