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.

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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
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.
Hereditary Breast & Ovarian Cancer (HBOC)

- General Population:Breast Cancer by Age 70: 7.3%<1% Colon Cancer by Age 70: 15-40% Endometrial Cancer by Age 70: 4-11% Ovarian Cancer by Age 70: up to 87%
- Familial Risk:Breast Cancer by Age 70: 4-11% Colon Cancer by Age 70: up to 44% Endometrial Cancer by Age 70: up to 82% Ovarian Cancer by Age 70: up to 87%
- Hereditary Risk:Breast Cancer by Age 70: up to 87% Colon Cancer by Age 70: up to 87% Endometrial Cancer by Age 70: up to 82% Ovarian Cancer by Age 70: up to 87%

Lynch Syndrome

- General Population:Breast Cancer by Age 70: 2% Colon Cancer by Age 70: 4-20% Endometrial Cancer by Age 70: 2-4% Ovarian Cancer by Age 70: up to 71%
- Familial Risk:Breast Cancer by Age 70: 1.5% Colon Cancer by Age 70: 4-20% Endometrial Cancer by Age 70: 2-4% Ovarian Cancer by Age 70: up to 71%
- Hereditary Risk:Breast Cancer by Age 70: up to 71% Colon Cancer by Age 70: up to 71% Endometrial Cancer by Age 70: up to 71% Ovarian Cancer by Age 70: up to 71%

Hereditary Cancer Syndromes


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

Her family:
- Hereditary Breast and Ovarian Cancer Syndrome
- Lynch syndrome

Colon Dx 48 yo  Ovarian Dx 55 yo  Breast Dx 45 yo
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
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**

<table>
<thead>
<tr>
<th>Relative</th>
<th>Cancer Site</th>
<th>Age Dx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Aunt</td>
<td>Breast</td>
<td>65</td>
</tr>
<tr>
<td>Maternal Aunt</td>
<td>Breast</td>
<td>45</td>
</tr>
</tbody>
</table>

**Hereditary cancer risk assessment impacts medical decisions**
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

**FEMALE BREAST**

<table>
<thead>
<tr>
<th>PROCEDURE</th>
<th>AGE TO BEGIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical breast examination every 6 to 12 months</td>
<td>30 years</td>
</tr>
<tr>
<td>Consider breast MRI in addition to mammography</td>
<td>30 years</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>FAMILY HISTORY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Mother</td>
</tr>
<tr>
<td>Maternal Aunt</td>
</tr>
</tbody>
</table>

*Hereditary cancer risk assessment impacts medical decisions*
myRisk Case Study: **Contraception Consult**

**Family History**
- Breast Ca lifetime risk: >20%

**Expected Single Syndrome Result**
- HBOC

**Actual Result**
- MLH1 (Lynch)
- **RESULT:** Positive

**Management Now**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Age to Begin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COLORECTAL</strong></td>
<td></td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>20 to 25 years, or individualized to a younger age based on the earliest diagnosis in family</td>
</tr>
<tr>
<td><strong>ENDOMETRIAL AND OVARIAN</strong></td>
<td></td>
</tr>
<tr>
<td>Consider hysterectomy and bilateral salpingo-oophorectomy</td>
<td>After completion of childbearing</td>
</tr>
</tbody>
</table>

Assessment that is too narrow can create a false sense of security and patient mismanagement
A significant number of patients meet criteria for multiple syndromes.

- ~1 in 10 HBOC patients meet criteria for Lynch.
- ~3 in 10 Lynch patients meet criteria for HBOC.

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

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.

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?

Moving Forward
Avoid a false sense of security and mismanagement of patients you see today.

Cancer Family History Impacts Every Patient Visit
The Society of Gynecologic Oncology (SGO) and the National Comprehensive Cancer Network (NCCN) recognize the benefits of hereditary cancer panels\(^1\),\(^2\)

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

Myriad myRisk™ Hereditary Cancer Panel

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

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2. NCCN Guidelines version 1.2015: Genetic/Familial High-Risk Assessment: Breast and Ovarian
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
A protocol should be used to efficiently stratify your patient’s risk for a hereditary cancer.

“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
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
Provide medical management for POSITIVE and NEGATIVE results based on leading societal guidelines

Identifies 104.5% more mutations in clinically actionable genes

Powered by Myriad’s myVision™ Variant Classification Program

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
- Powered by Myriad’s myVision™ Variant Classification Program

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

Your lab needs to be accountable for 3 things:

1. Find DNA Changes
2. Determine if DNA Changes Cause Cancer
3. Report Updated Data

Medical societies highlight the importance of 1 accurate results, 2 transparent variant classification and 3 amended reports

**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**
- **BRCA1**
  - c.xxxxdel (p.xxxxfs*)

**HIGH RISK: Female Breast, Ovarian**

**ELEVATED RISK: Pancreatic**

**PERSONAL/FAMILY HISTORY SUMMARY AND MANAGEMENT INFORMATION**

- **Patient**: None
- **Mother**: Breast, Invasive 49
- **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**

**MODIFIED MEDICAL MANAGEMENT MAY BE APPROPRIATE**

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