Multiple professional guidelines support genetic testing for HBOC syndrome.

Professional Community Support

Our representatives help clinical practices in their implementation of genetic testing.

Practice Support

in person.

Myriad offers medical support with a team of highly trained medical specialists, available via phone, email, and online.

Medical Support

implement BRAC Analysis® testing in your offices.

Our dedicated team of representatives and other staff can provide in-person and online assistance to help you.

Myriad Genetics support makes it easy

Assess HBOC risk with a proven 4-step protocol

1. SCREEN
- Screen every patient for personal and family history of cancers/diagnosis of HBOC
- Update information annually

2. CANDIDATE
- Assess for red flags
- Discuss BRACAnalysis® testing with appropriate patient

3. CONSENSUS
- Order BRACAnalysis® test using Myriad’s collection kit
- Interpret result and assign risk

4. MANAGEMENT
- Establish appropriate medical management plan according to clinical guidelines and recommendations

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### Technical information

BRACAnalysis® is a multianalyte diagnostic test for Hereditary Breast/Ovarian Cancer (HBOC) syndrome and cancers related to mutations in BRCA1 and BRCA2 genes. Genetic testing is performed by both full sequencing and large rearrangement methodologies.

**Sequencing:** The majority of mutations in the BRCA1 and BRCA2 genes are detected through sequencing technology which is considered the gold standard for molecular diagnostics. Myriad Genetics currently uses large sequencing technology.

- BRCA1 is located on chromosome 17 and is composed of 1498 base pairs in 42 coding exons. It is sequenced in the forward and reverse directions of all coding exons and 10 base pairs are in non-coding regions.
- BRCA2 is located on chromosome 13 and is composed of 14,580 base pairs in 55 coding exons. Non-coding regions are not analyzed. The wild-type BRCA1 gene encodes a protein of 1863 amino acids.
- BRCA2 is located on chromosome 13 and is composed of 14,580 base pairs in 55 coding exons. Non-coding regions are not analyzed. The wild-type BRCA2 gene encodes a protein of 2450 amino acids.

Large rearrangements: Approximately 10% of all mutations in high risk patient (10% risk for a deleterious mutation) and 1% of low risk patients (large rearrangements in the BRCA1 or BRCA2 gene). Large structural rearrangements (deletions, duplications, etc.) are generally not detectable through sequencing technology. Myriad Genetics utilizes Multiple Locus Linkage Analysis (MLPA) and/or a very robust and reliable technology for detecting large rearrangements. Mutations detected by MLPA are confirmed by multiple quantitative PCR sequencing or CGH-microarray.

**TEST OFFERINGS**

BRACAnalysis® sequencing and large rearrangement analysis of the BRCA1 and BRCA2 genes. This test is for people who do not have any known gene mutations in the family.

Single site BRACAnalysis®

This test is for individuals who already know about BRCA1 or BRCA2 gene mutation(s) in the family. A copy of the test results or the name of the gene member who has had prior testing will be required prior to testing.

Multisite BRACAnalysis®

This test examines the three most common (BRCA1 and BRCA2 gene mutations) in individuals of Ashkenazi Jewish (Central/Eastern European) ancestry. These three mutations (BRCA1: 187delAG, 538insC and BRCA2: 617delT) are present in up to 2.5% of individuals of Ashkenazi Jewish descent. If an individual of Ashkenazi Jewish ancestry has one of these mutations and has a significant family history, this test is recommended. If the test result is positive for a BRCA1/BRCA2 gene mutation, a referral to a genetic counselor is recommended.

### References


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A previously identified BRCA mutation in the family

**Pancreatic cancer with an HBOC-associated cancer**

**Triple negative breast cancer**

- Two individuals with breast cancer on the same side of the family
- Two primary breast cancers in the same individual
- Ovarian cancer

CHECK PERSONAL OR FAMILY HISTORY FOR THESE RED FLAGS*

† For reference and supporting data on risk factors and medical management visit www.myriadpro.com/references

The National Comprehensive Cancer Network and European Society for Medical Oncology (ESMO) are some of the many organizations with published medical management recommendations for these patients.

The testing and the surgeries were by far the best decision I ever made. I feel as though I had a chance to look through a crystal ball to see my possible future, and I was able to make choices while I was healthy. - Jodi V.

Myriad has the lowest VUS rate globally with a < 3% VUS rate for BRCA1 / BRCA2 mutations.

THE UNWANTED MEDICAL NEED

Only ~10% of BRCA mutations have been identified.†

DEFINING VUS

A genetic variant of uncertain significance is a variation in the DNA sequence that may or may not contribute to breast or ovarian cancer risk.

MANAGING THE PATIENT

Management will be based on patients’ personal and/or family history of cancer.

RECLASSIFYING A VARIANT

When data allows a previously uncertain variant to be reclassified as harmless or deleterious, Myriad Genetics provides on-assignment to healthcare professionals.

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Myriad has the lowest VUS rate globally with a < 3% VUS rate for BRCA1 / BRCA2 mutations.

Mammography 25 years

Pelvic exam 30 years in patients

PET and CA-125

TVUS and CA-125

Annual

Twice a year

Twice a year

Twice a year

No increased cancer risk

- NCCN guidelines suggest patients who do not elect RRBSO consider concurrent transvaginal ultrasound (TVUS) and cancer antigen-125 (CA-125) testing.
- The testing and the surgeries were by far the best decision I ever made. I feel as though I had a chance to look through a crystal ball to see my possible future, and I was able to make choices while I was healthy.

**Pancreatic cancer with an HBOC-associated cancer**

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** HBOC-associated cancers include breast, ovarian, and pancreatic cancer.

* Assessment criteria based on medical society guidelines. For these individual society guidelines, go to www.myriadpro.com/guidelines.

** A previously identified BRCA mutation in the family

• Ashkenazi Jewish ancestry with an HBOC-associated cancer

• Pancreatic cancer with an additional HBOC-associated cancer

• Triple negative breast cancer

• Male breast cancer

• Two primary breast cancers in the same individual

• Breast cancer diagnosed ≤50 years

• Ovarian cancer

CHECK PERSONAL OR FAMILY HISTORY FOR THESE RED FLAGS*

Mutations dramatically increase the risk of developing cancer

Comply with International societal guideline recommendations.1-5

FOR YOUR PRACTICE

- treatment decisions.
- to aid in their surgical decision making .6
- 76% of women chose to undergo BRCA mutation testing, and 79% of these women used genetic test results to aid in their surgical decision making .6

- 87% up to 2nd breast cancer by age 70
- 53%* up to ovarian cancer by age 70

- 50% up to breast cancer by age 70
- 64% up to 2nd breast cancer by age 70

- Risk-reducing surgeries• Preventive drug therapy

- NCCN guidelines suggest risk-reducing salpingo-oophorectomy (RRBSO), ideally between 35 and 40 years of age, and upon completion of child bearing or individualized based on earliest age of onset of ovarian cancer in the family.

- NCCN guidelines suggest patients who do not elect RRBSO consider concurrent transvaginal ultrasound (TVUS) and cancer antigen-125 (CA-125) blood testing every 6 months starting at age 30, or 5 to 10 years before the earliest age of first diagnosis of ovarian cancer in the family.

- According to NCCN relative contraindications for breast-conserving therapy requiring radiation therapy.*

- May have higher risk of bilateral recurrence or contralateral breast cancer in patients with breast-conserving therapy.

- prophylactic bilateral mastectomy for breast reduction should be considered prior to radiation therapy.

- NCCG guidelines, the American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO) make specific screening suggestions for BRCA positive patients. **

- 50% for a contralateral breast cancer.

- 4% for a contralateral breast cancer.

** In breast cancer prior to the BRCA-positive mutation, it took me fewer than 4 months to have all the prophylactic surgeries to try and prevent me from becoming a victim of cancer.4

** In breast cancer prior to the BRCA-positive mutation, it took me 7 years to be tested for the BRCA mutation, it took me 7 years to be tested for the BRCA mutation.
A previously identified BRCA mutation in the family
Ashkenazi Jewish ancestry with an HBOC-associated cancer
Pancreatic cancer with an additional HBOC-associated cancer
Triple negative breast cancer
Male breast cancer
Two individuals with breast cancer on the same side of the family
Two primary breast cancers in the same individual
Breast cancer diagnosed ≤50 years
Ovarian cancer

CHECK PERSONAL OR FAMILY HISTORY FOR THESE RED FLAGS*

INCREASED RISK FOR PRIMARY AND SECONDARY CANCER*

Mutations dramatically increase the risk of developing cancer

AMONG BREAST CANCER PATIENTS:†
56% of women diagnosed with breast cancer carried a BRCA 1 or 2 mutation, according to recent studies. 7-9
76% of women chose to undergo BRCA mutation testing, and 79% of these women used genetic test results to inform their treatment decisions. 6

THE UNMET MEDICAL NEED

• Risk reduction and prevention for BRCA-positive patients
• Accurate and timely identification of BRCA-positive patients
• Appropriate and timely management of BRCA-positive patients

FOR YOUR PATIENTS

BRACAnalysis® testing benefits

POWER OF A POSSIBLE TEST RESULTS

DIAGNOSIS OF HBOC SYNDROME INCREASE CANCER RISK
Evaluate medical management guidelines for mutation carriers

The National Comprehensive Cancer Network and European Society for Medical Oncology (ESMO) are some of the many organizations with published medical management recommendations for BRCA mutation carriers, which include:

• Increased surveillance initiated in the 20s, including breast MRI
• Intensive surveillance initiated in the 30s, including twice-yearly mammography
• Risk-reducing surgeries• Preventive drug therapy

DEFINING VUS
A genetic variant of uncertain significance is a variation in the DNA sequence that may or may not contribute to breast or ovarian cancer risk

GENETIC VARIANT OF UNCERTAIN SIGNIFICANCE (VUS)

DEFINING VUS
A genetic variant of uncertain significance is a variation in the DNA sequence that may or may not contribute to breast or ovarian cancer risk

MANAGING THE PATIENT
Management should be based on the patient's personal and/or family history of cancer

RECLASSIFYING A VARIANT
When data allows a previously identified BRCA mutation to be reclassified as deleterious, Myriad Genetics provides a consulting package for healthcare professionals

BY THE NUMBERS*%

Risk of cancer (%)

• Breast cancer

• Ovarian cancer

• Breast cancer by age 50

• Breast cancer by age 70

• 2nd breast cancer by age 70

• Ovarian cancer by age 70

44% 8% 11% ≤1% ≤1%

2% 52% 8% 64% 44%

Mammography

Clinical breast exam

Breast self-exam

Breast MRI

TVUS and CA-125

Prophylactic bilateral mastectomy

Prophylactic oophorectomy

Prophylactic salpingo-oophorectomy

Clinical breast exam

Mammography

Breast self-exam

Breast MRI

TVUS and CA-125

Ovarian cancer

Ovarian cancer

Ovarian cancer

Ovarian cancer

Ovarian cancer

12% 4% 9% 2% 2% 6% 3%

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Professional Community Support

6. **NCCN clinical practice guidelines in oncology (NCCN guidelines): breast cancer. Version 1.2012.** National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment: Breast and Ovarian. Myriad Genetics currently offers a four-step protocol for testing for HBOC syndrome. The purpose of the first step is to determine which patients are appropriate candidates for genetic testing. The fourth step is to interpret the result and assign risk. Myriad’s BRACAnalysis® test examines the three most common mutations in the BRCA1 and BRCA2 genes in individuals of Ashkenazi Jewish (Central/Eastern European) ancestry. These three mutations (617delT) are present in up to 2.5% of individuals of Ashkenazi Jewish ancestry. If an individual of Ashkenazi Jewish ancestry: 
- is symptomatic of HBOC, and 
- has a significant family history, 
reflex testing to full BRACAnalysis® is recommended. Myriad currently uses Sanger sequencing technology which is considered to be the gold standard for molecular diagnostics. Large structural rearrangements (deletions, duplications, etc.) are usually not detectable through sequencing technologies. Myriad Genetics utilizes Multiple Ligation-Dependent Probe Amplification (MLPA), a very robust and reliable technology for detecting large structural rearrangements. Mutations detected by MLPA are confirmed by multiple quantitative PCR sequencing or CGH-microarray. 

**BRACAnalysis® (Myriad Genetics, Inc., in the United States and other jurisdictions. ©2013, Myriad Genetic Laboratories, Inc.)**

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BIO Zürich
Switzerland
www.myriad.com

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Medical Support

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Practice Support

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Multiple professional guidelines support testing for HBOC syndromes.

<table>
<thead>
<tr>
<th>Professional Society</th>
<th>Website URL</th>
</tr>
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<tbody>
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<td>European Society for Medical Oncology (ESMO)</td>
<td><a href="http://www.esmo.org/content/esmo/screening/2010/breast/cancer/screening-bc-overview.html">http://www.esmo.org/content/esmo/screening/2010/breast/cancer/screening-bc-overview.html</a></td>
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Familial High-Risk Assessment: Breast and Ovarian 1

European Society for Medical Oncology (ESMO)2

European Society for Medical Oncology (ESMO)3

American Society of Clinical Oncology (ASCO)4,5 http://www.cancer.net/cancer-types/hereditary-

Primary breast cancer

Establish appropriate medical management plan according to clinical •

Interpret result and assign risk •

Order BRAC® Analysis® test using Myriad's collection kit •

Screen every patient for personal and family history of cancer/ages of diagnosis •

Update information annually •

DIAGNOSE

EVALUATE

SCREEN

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MANAGE

References


The The impact of hereditary breast and ovarian cancer (HBOC) syndrome testing on patient management and your practice Use BRAC® Analysis® as a guide in your medical and surgical management