NCCN® and ACOG Recognize the Importance of Testing for BRCA1 and BRCA2 Mutations

To learn more about our BRCAssure test offerings, please visit www.integratedgenetics.com or www.integratedoncology.com or call 800-345-GENE (4363).

BRCA1 and 2 Analysis

Integrated Genetics and Integrated Oncology are committed to providing comprehensive care to you and your patients.

Knowledge is a Powerful Tool

- Patients with BRCA1 or 2 mutations are at an increased risk for Hereditary Breast and Ovarian Cancer Syndrome.
- Avail yourself of the information needed to make informed surveillance and treatment strategies for your patients.

Experience You Can Trust

- Integrated Genetics: A leader in genetic testing and counseling services for more than 25 years
- Integrated Oncology: A leader in diagnostic, prognostic, and predictive testing services for breast cancer
- Together, we offer:
  - The largest national commercial genetic counseling team with unparalleled services
  - Extensive managed care contracts, helping patients maximize their benefits
  - Pre-authorization services to support you and your patients
  - A network of more than 1,700 patient service centers

BRCAssure®

Personal History
- Breast cancer, diagnosed of age 50 or younger
- Ovarian cancer
- Multiple primary breast cancers either in the same breast or opposite breast
- Both breast and ovarian cancer
- Male breast cancer
- Triple-negative (estrogen receptor negative, progesterone receptor negative, and HER2/neu (human epidermal growth factor receptor 2) negative) breast cancer
- Penetrance or aggressive prostate cancer with breast or ovarian cancer in the same individual or on the same side of the family

Family History
- A previously identified BRCA1 or BRCA2 mutation in the family
- Multiple breast cancer
- Two or more relatives with breast cancer, one under age 50
- Three or more relatives with breast cancer at any age

Other Considerations
- Comprehensive genetic testing includes full sequencing of BRCA1/BRCA2 and testing for large genomic rearrangements
- Once a specific mutation is identified in an affected individual, a single site test may be used for family members
- Results of unknown significance are considered uninformative and should not indicate testing or treatment of family members
- Genetic counseling is highly recommended when BRCA testing is offered and after results are provided

Notes:
- “Breast cancer” includes both invasive and ductal carcinoma in situ (DCIS). “Ovarian cancer” includes epithelial ovarian cancer, fallopian tube and primary peritoneal cancers.

Complete Guidelines may be found at www.nccn.org; www.ACOG.org
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If you are interested in genetic counseling services, please call 855-GC-CALLS or 855-422-2557.
Hereditary Breast and Ovarian Cancer

- Mutations in BRCA1 and BRCA2 account for the vast majority of families with Hereditary Breast and Ovarian Cancer Syndrome (HBOC).
- The estimated lifetime risk of breast cancer in women with BRCA1 mutations is 50-60% for BRCA2; the risk is 40-50%.
- The risk of ovarian cancer is 20-40% for a woman with BRCA1 and 10-15% with BRCA2.
- Both men and women with mutations in BRCA1/2 may also be at increased risk of other cancers, including pancreatic, prostate, melanomas, stomach, esophageal, and bile duct cancers.

> The overall prevalence of BRCA1 and BRCA2 mutations in the general population is estimated at 1 in 400 and varies with ethnicity. Approximately 1 in 40 Ashkenazi Jewish individuals carries one of three founder mutations.

### Table: Estimated Lifetime Cancer Risk for Individuals with BRCA1 and BRCA2 Mutations

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Range of Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>BRCA1: 50-60%, BRCA2: 40-50%</td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>BRCA1: 20-40%, BRCA2: 10-15%</td>
</tr>
<tr>
<td>Male Breast Cancer</td>
<td>BRCA1: 1-2%, BRCA2: 0.1%</td>
</tr>
<tr>
<td>Male Prostate Cancer</td>
<td>BRCA1: 18% African American, 15% N. European Origin</td>
</tr>
<tr>
<td>Female Breast Cancer</td>
<td>General Population Risk</td>
</tr>
<tr>
<td>Female Ovarian Cancer</td>
<td>2nd Primary Breast Cancer</td>
</tr>
<tr>
<td>Pancreatic Cancer</td>
<td>0.5%</td>
</tr>
<tr>
<td>Stomach Cancer</td>
<td>0.1%</td>
</tr>
<tr>
<td>Esophageal Cancer</td>
<td>0.1%</td>
</tr>
<tr>
<td>Bile Duct Cancer</td>
<td>0.1%</td>
</tr>
<tr>
<td>Melanoma Cancer</td>
<td>1-2%</td>
</tr>
<tr>
<td>Other Cancers</td>
<td>2%</td>
</tr>
</tbody>
</table>

### Suite of BRCAAssure tests to meet your patients’ needs

- **BRCAAssure Comprehensive BRCA1/2 Analysis**
  - Full sequencing of the BRCA1 and BRCA2 genes, plus deletion/duplication analysis. May be used to assess the risk of carrying a BRCA1/2 mutation when there is no known familial mutation.

- **BRCAAssure BRCA2 Targeted Analysis**
  - Targeted sequencing for specific familial or known mutations on the BRCA2 gene.

- **BRCAAssure BRCA1 Targeted Analysis**
  - Targeted sequencing for specific familial or known mutations on the BRCA1 gene.

- **BRCAAssure BRCA2 Deletion/Duplication Analysis**
  - May be used to detect the presence of a deletion or duplication in the BRCA2 genes. After previous sequencing tests were negative and deletion/duplication analysis was not offered.

### Specimen Requirement
Whole blood in one full lavender tube, minimum of 3 mL tube to be used.

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**Cancers diagnosed in individuals with BRCA1 and BRCA2 mutations**

- 50% to 60% of breast cancers in women with BRCA1 mutation are triple negative.
- 80% of the breast cancers in women with a BRCA2 mutation are estrogen receptor positive, progesterone receptor positive, and HER2 negative.

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**REFERENCES**

7. www.integratedgenetics.com
8. www.oncology.com
Hereditary Breast and Ovarian Cancer

Patients with BRCA1 and BRCA2 mutations are at increased risk for breast, ovarian, and other cancers. Approximately 1 in 40 Ashkenazi Jewish individuals carries one of three founder mutations.2

The overall prevalence of BRCA1 and BRCA2 mutations in the general population is estimated to be 1 in 400 and varies with ethnicity. Mutations in BRCA1 account for the vast majority of families with Hereditary Breast and Ovarian Cancer Syndrome (HBOC).1

The estimated lifetime risk of breast cancer in women with BRCA1 mutations is 50-60%, for BRCA2 the risk is 40-50%.1

The risk of ovarian cancer is 20-40% for a woman with BRCA1 and 15-18% with BRCA2.1

Both men and women with mutations in BRCA1/2 may also be at increased risk of other cancers, including pancreatic, prostate, melanomas, stomach, esophageal, and bile duct cancers.1

BRCA1/2

Estimated lifetime cancer risk for individuals with BRCA1 and BRCA2 mutations1:

- Breast Cancer:
  - 80% to 90% of breast cancers in women with a BRCA1 mutation are estrogen receptor positive, and HER2 negative.5
  - 60% to 90% of breast cancers in women with a BRCA2 mutation are estrogen receptor positive, and HER2 negative.5
  - 80% of breast cancers in women with a BRCA1 mutation are progesterone receptor positive, and HER2 negative.5

- Ovarian Cancer:
  - 5% or more by age 70.5

- Pancreatic Cancer:
  - 4% or more by age 60.5

- Prostate Cancer:
  - 1-2% by age 60.5

- Male Breast Cancer:
  - 12% by age 70.5

- Second Primary Breast Cancer:
  - 4% by age 60.5

- Male Breast Cancer:
  - 1-2% by age 60.5

- Ovarian Cancer:
  - 2% by age 60.5

- Other Cancers:
  - Pancreatic, prostate, melanoma, stomach, esophageal, and bile duct cancers.

- Risk reduction strategies include, but are not limited to:
  - Surveillance strategies include, but are not limited to:
    - Annual mammography and breast magnetic resonance imaging (MRI), starting at age 25 or individualized by family history
    - Transvaginal ultrasonography
    - CA-125 biomarker screening
    - Annual prostate cancer screening
    - Risk reduction strategies include, but are not limited to:
      - Prophylactic mastectomy, oophorectomy
      - Chemoprevention

- BRCA1 and BRCA2 Alternative Test Codes

- Exploring the analysis of the founder mutations found within the Ashkenazi Jewish population. May be used as a first line test for individuals of Ashkenazi Jewish descent. If negative the option to run a Comprehensive BRCA1/2 Analysis is available.

- Targeted sequencing for specific familial or known mutations on the BRCA1 gene.

- Targeted sequencing for specific familial or known mutations on the BRCA2 gene.

- May be used to detect the presence of a deletion or duplication in the BRCA2 genes after previous sequencing tests were negative and deletion/duplication analysis was not offered.

- Whole blood in one full lavender tube, minimum of 3 mL tube to be used

Test Code | Test Name | Test Description
--- | --- | ---
252911 | BRCA1/2 Analysis | Full sequencing of the BRCA1/2 genes, plus deleterion/duplication analysis. May be used to assess the risk of carrying a BRCA1/2 mutation when there is no known familial mutation
252910 | BRCA1/2 Analysis | Targeted analysis of the founder mutations found within the Ashkenazi Jewish population. May be used as a first line test for individuals of Ashkenazi Jewish descent. If negative the option to run a Comprehensive BRCA1/2 Analysis is available.
252235 | BRCA1/2 Analysis | Targeted sequencing for specific familial or known mutations on the BRCA2 gene.
252230 | BRCA1/2 Analysis | Targeted sequencing for specific familial or known mutations on the BRCA1 gene.
25288 | BRCA1/2 Analysis | May be used to detect the presence of a deletion or duplication in the BRCA2 genes after previous sequencing tests were negative and deletion/duplication analysis was not offered.

To learn more about our comprehensive genetic testing services and how they can help inform healthcare decisions, call us at 855-GC-CALLS or 855-422-2557.

REFERENCES:
2. Panetta JF et al. ABCG1 and BRCA2 Nonsense-Bound Ovarian Cancer. Clinical Cancer Research. December; Available at: http://clincancerres.aacrjournals.org/content/17/22/6297.
Hereditary Breast and Ovarian Cancer

Patients with BRCA1 and BRCA2 mutations are at increased risk for breast, ovarian, and other cancers. The overall prevalence of BRCA1 and BRCA2 mutations in the general population is estimated at 1 in 400 and varies with ethnicity. Approximately 1 in 40 Ashkenazi Jewish individuals carries one of three founder mutations.1

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Estimated Lifetime Risk (1%/2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Breast Cancer</td>
<td>1-2%</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>15%</td>
</tr>
<tr>
<td>Female Breast Cancer</td>
<td>80-90% (African American)</td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>24-40%</td>
</tr>
<tr>
<td>Second Primary Breast Cancer</td>
<td>12%</td>
</tr>
<tr>
<td>Pancreatic Cancer</td>
<td>18%</td>
</tr>
<tr>
<td>Male Breast Cancer</td>
<td>0.1%</td>
</tr>
<tr>
<td>Male Ovarian Cancer</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

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<table>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>252911</td>
<td>BRCA1/2 Analysis</td>
<td>Full sequencing of the BRCA1/2 genes, plus deletion/duplication analysis. May be used to assess the risk of carrying a BRCA1/2 mutation when there is no known familial mutation.</td>
</tr>
<tr>
<td>252910</td>
<td>BRCA1/2 Genotyping</td>
<td>Targeted analysis of the founder mutations found within the Ashkenazi Jewish population. May be used as a first line test for individuals of Ashkenazi Jewish descent if negative the option to run a Comprehensive BRCA1/2 Analysis is available.</td>
</tr>
<tr>
<td>252235</td>
<td>BRCA1/2 Targeted Analysis</td>
<td>Targeted sequencing for specific familial or known mutations on the BRCA1 gene.</td>
</tr>
<tr>
<td>252250</td>
<td>BRCA1/2 Targeted Analysis</td>
<td>Targeted sequencing for specific familial or known mutations on the BRCA2 gene.</td>
</tr>
<tr>
<td>253884</td>
<td>BRCA1/2 Deletion/Duplication Analysis</td>
<td>May be used to detect the presence of a deletion or duplication in the BRCA1/2 genes after previous sequencing tests were negative and deletion/duplication analysis was not offered.</td>
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</table>

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BRCA1 and BRCA2 are genes that play a role in the development of breast and ovarian cancers. People who carry mutations in these genes are at increased risk for developing these cancers. BRCA1 and BRCA2 mutations are more common in individuals of Ashkenazi Jewish descent, but can also occur in individuals of other ethnic backgrounds.

Comprehensive Services

Suites of BRCA analysis tests to meet your patients’ needs.

Because Knowledge is a Powerful Tool

Surveillance strategies include, but are not limited to:
- Annual mammography and breast magnetic resonance imaging (MRI)
- Annual colonoscopy
- Annual Pap smear
- Annual prostate cancer screening

Risk reduction strategies include, but are not limited to:
- Prophylactic mastectomy, oophorectomy
- Chemoprevention

Cancers diagnosed in individuals with BRCA1 mutations often have specific characteristics.

BRCA1 and BRCA2 mutations are known to increase the risk of breast, ovarian, and other cancers. Genetic testing can help identify individuals who may benefit from increased surveillance and risk reduction strategies.

The largest national commercial genetic counseling team is available to help patients make informed healthcare decisions.

Call us at 855-GC-CALLS or 855-422-5257.

References:
NCCN® and ACOG Recognize the Importance of Testing for BRCA1 and BRCA2 Mutations

Personal History
- Breast cancer diagnosed at age 50 or younger
- Ovarian cancer
- Multiple primary breast cancers within the same breast or opposite breast
- Multiple breast and ovarian cancer
- Male breast cancer
- Triple-negative (estrogen receptor negative, progesterone receptor negative, and HER2 negative) breast cancer
- Familial or aggressive prostate cancer with breast or ovarian cancer in the same individual or on the same side of the family

Family History
- A previously identified BRCA1 or BRCA2 mutation in the family
- Breast cancer before age 40
- Two or more relatives with breast cancer, one under age 50
- Three or more relatives with breast cancer at any age

Other Considerations
- Comprehensive genetic testing includes full sequencing of BRCA1/BRCA2 and testing for large genomic rearrangements
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Notes: "BrCa cancer" includes both invasive and ductal carcinoma in situ (DCIS). "Ovarian cancer" includes epithelial ovarian cancer, fallopian tube and primary peritoneal cancer

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NCCN® and ACOG Recognize the Importance of Testing for BRCA1 and BRCA2 Mutations

The following testing criteria is based on clinical practice guidelines:

**Personal History**

- Breast cancer diagnosed at age 50 or younger
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- Multiple primary breast cancers either in the same breast or opposite breast
- Both breast and ovarian cancer
- Male breast cancer
- Triple-negative (estrogen receptor negative, progesterone receptor negative, and HER2/neu [human epidermal growth factor receptor 2] negative) breast cancer
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