Hereditary Breast and/or Ovarian Cancer Susceptibility Panels

A hereditary breast and/or ovarian cancer susceptibility panel includes genes that are associated with an inherited susceptibility to breast cancer, ovarian cancer, or both.

I. Genetic testing using a hereditary breast and/or ovarian cancer susceptibility panel is considered **medically necessary** when:

A. The panel includes, at a minimum, the following genes: *BRCA1*, *BRCA2*, **AND**

B. The member has one of the following:

1. The member has a personal history of breast cancer ≤ age 65, **OR**
2. The member has a personal history of ovarian cancer (including fallopian tube cancer or peritoneal cancer), **OR**
3. The member has a personal history of breast cancer, **AND**

a) One of the following:

(1) Ashkenazi Jewish ancestry, **OR**

(2) Male (sex assigned at birth), **OR**

(3) Triple-negative breast cancer, **OR**

(4) Pancreatic or ampullary cancer, **OR**

(5) Metastatic prostate cancer, **OR**

(6) High- or very-high-risk group prostate cancer, **OR**

(7) Multiple primary breast cancers (diagnosed synchronously or metachronously), **OR**

(8) The member has a close relative with any one of the following:

(a) Breast cancer diagnosed ≤age 50, **OR**

(b) Male breast cancer, **OR**

(c) Ovarian cancer, **OR**

(d) Pancreatic cancer, **OR**

(e) Prostate cancer that is either metastatic, intermediate-risk or high- or very-high-risk group, **OR**

b) There are 3 or more total diagnoses of breast cancer and/or prostate cancer (any grade) on the same side of the family including the member with breast cancer, **OR**

4. The member has a personal history of lobular breast cancer, **AND**

   a) A personal or family history of diffuse gastric cancer, **OR**

5. The member is unaffected or the member does not have a personal history of breast cancer that meets the above criteria, **AND**

   a) The member has a first- or second-degree relative diagnosed with breast cancer at or before age 50 years, **OR**

   b) The member has a first- or second-degree relative meeting any of criteria I.B.2, I.B.3, or I.B.4, **OR**

   c) The member's probability of having a *BRCA1* or *BRCA2* pathogenic variant is greater than 2.5% based on prior probability models (e.g., Tyrer-Cuzick, BRCApro, CanRisk), **OR**

6. The member has a personal history of breast cancer, **AND**

   a) The member has recurrent unresectable or metastatic breast cancer and is being considered for systemic treatment using PARP inhibitors, **OR**

   b) The member has recurrent or metastatic breast cancer and is being considered for adjuvant treatment with olaparib therapy.

II. Genetic testing using a STAT hereditary breast cancer panel is considered **medically necessary** when:

A. The member meets any of the above criteria, **AND**

B. The member requires a rapid turn-around-time for decision making related to surgical interventions or treatment.

III. Genetic testing using a hereditary breast and/or ovarian cancer susceptibility panel is considered **investigational** for all other indications.

IV. *BRCA1/BRCA2* mRNA sequencing analysis in genes associated with breast and/or ovarian cancers for the interpretation of variants of unknown significance is considered **investigational** because it is typically either considered an existing component of the genetic testing process for quality assurance or follow up testing without proven utility.

RATIONALE AND REFERENCES

Hereditary Breast and/or Ovarian Cancer Susceptibility Panels

National Comprehensive Cancer Network (NCCN): Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate (1.2026)

This guideline outlines clinical criteria for germline genetic testing of high-penetrance breast cancer genes. Criteria include:

1) Personal history of breast cancer at 50 years of age or younger (p. CRIT-2).

2) Personal history of breast cancer at any age with specific features (p. CRIT-2):

- Treatment indications
  - To aid in systemic treatment decisions using PARP inhibitors for metastatic breast cancer
  - To aid in adjuvant treatment decisions with olaparib for high-risk, HER2-negative breast cancer, including triple-negative breast cancer
- Pathology/histology
  - Triple-negative breast cancer
  - Multiple primary breast cancers (synchronous or metachronous)
  - Male breast cancer
  - Lobular breast cancer if there is also a personal/family history of diffuse

gastric cancer
- Ashkenazi Jewish ancestry
- Family history of at least 1 close blood relative with:
    - Breast cancer at age 50 years or younger
    - Male breast cancer
    - Ovarian cancer
    - Pancreatic cancer
    - Prostate cancer with metastatic, or high- or very-high-risk group
    - 3 or more total diagnoses of breast cancer and/or prostate cancer in patient and/or close blood relatives on the same side of the family

3) Family history-based criteria (p. CRIT-2): Testing is also recommended in select unaffected individuals and those with a personal history that does not meet the above criteria. Qualifying scenarios include the presence of a first- or second-degree blood relative meeting any of the criteria listed above with the exception of relatives who meet criteria only for systemic therapy selection. If the affected relative has pancreatic cancer or prostate cancer, then only first-degree relatives should be offered testing unless indicated based on additional family history.

4) An affected or unaffected individual who otherwise does not meet the criteria above but has a probability of greater than 5% of a *BRCA1/2* pathogenic variant based on prior probability models (e.g., Tyrer-Cuzick, BRCAPro, CanRisk) (p. CRIT-2).

These guidelines also recommend consideration of testing for patients with a personal history of breast cancer diagnosed at or before age 65, patients diagnosed with breast cancer at any age with ≥1 close blood relative with intermediate-risk prostate cancer with intraductal/cribriform histology, and for patients affected or unaffected with breast cancer who otherwise do not meet any of the above criteria but with a 2.5%–5% probability of BRCA1/2 P/LP variant based on prior probability models (e.g., Tyrer-Cuzick, BRCAPro, CanRisk) (p. CRIT-3).

The NCCN guidelines further recommend that patients with epithelial ovarian cancer be offered germline genetic testing for genes including *ATM*, *BRCA1, BRCA2, BRIP1, MLH1, MSH2, MSH6, EPCAM, PALB2, RAD51,* and *RAD51D* (p. CRIT-4). The guideline goes on to list non-epithelial ovarian cancers with a known genetic association, including Peutz-Jeghers (*STK11*), *DICER1*-related disease, and *SMARCA4* (p. CRIT-4).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate 1.2026 https://www.nccn.org/professionals/physician_gls/pdf/genetics_bopp.pdf

National Comprehensive Cancer Network (NCCN): Breast Cancer (4.2025)

This guideline recommends germline *BRCA1, BRCA2,* and *PALB2* sequencing to determine eligibility for the FDA approved therapies olaparib and talazoparib in patients with "recurrent unresectable (local or regional) or stage IV (M1) disease" (p. BINV-Q 7 of 15).

The guideline also recommends germline *BRCA1* and *BRCA2* germline testing in patients with recurrent or metastatic breast cancer, regardless of HER2 status, to assess for PARPi eligibility (p. BINV-Q 2, 3, and 4 of 15).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer 4.2025 https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

American Society of Clinical Oncology (ASCO) and Society of Surgical Oncology (SSO)

Guidelines published by ASCO/SSO (2024) recommend BRCA1/2 testing to all newly diagnosed patients who are 65 years of age or younger at diagnosis (Type: Formal Consensus; Agreement 87.50%) (p. 590).

Bedrosian I, Somerfield MR, Achatz MI, et al. Germline testing in patients with breast cancer: ASCO-Society of Surgical Oncology Guideline. J Clin Oncol. 2024;42(5):584-604. doi:10.1200/JCO.23.02225

DEFINITIONS

1. **Adenomatous polyposis** are conditions that cause multiple adenomas (i.e., benign polyps) in the gastrointestinal tract.
2. **Breast cancer** is a term that applies to patients with invasive cancer or ductal carcinoma in situ (DCIS).
3. **Close relatives** include first, second, and third degree blood relatives:
    a. **First-degree relatives** are parents, siblings, and children
    b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings

c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

4. **Adjuvant treatment with olaparib therapy** may be indicated for cancer defined as

    a. Triple-negative breast cancer treated with either:

        i. Adjuvant chemotherapy with axillary node-positive disease or an invasive primary tumor greater than or equal to 2 cm on pathology analysis, **OR**

        ii. Neoadjuvant chemotherapy with residual invasive breast cancer in the breast or resected lymph nodes, **OR**

    b. Hormone receptor positive disease treated with either:

        i. Adjuvant chemotherapy with four or more positive pathologically confirmed lymph nodes, **OR**

        ii. Neoadjuvant chemotherapy which did not have a complete pathologic response, with a CPS+CG score [pre-treatment clinical (CS) and post-treatment pathological stage (PS), estrogen-receptor status (E) and grade (G)] of 3 or higher.

5. **High-risk prostate cancer** is defined by NCCN as an individual who has one or more of the following high-risk features, but does not meet criteria for very-high-risk features:
    a. cT3-cT4
    b. Grade Group 4 or 5
    a. PSA > 20ng/ml

6. **Juvenile polyps** are associated with Juvenile Polyposis Syndrome. These polyps are exophytic and eroded. They typically contain the following: marked edema and inflammation within the lamina propria, cystic glands filled with thick mucin, and some degree of smooth muscle proliferation.

7. **Lynch syndrome-related cancer** is defined as any of the following cancer types: colorectal, endometrial, gastric, ovarian, pancreatic, urothelial, brain (usually glioblastoma), biliary tract, small intestinal, sebaceous adenoma, sebaceous carcinoma, or keratoacanthoma.

8. **Maori ancestry** describes individuals who are of indigenous New Zealand ethnic background.

9. **Very-high-risk prostate cancer** is defined by NCCN as an individual who has at least two of the following:
    a. cT3-cT4
    b. PSA >40 ng/mL
    a. Grade Group 4 or 5