Genetic Testing for Hereditary Cancer Risk: Family Insights

Not all cancer runs in families, but having a hereditary cancer syndrome can **significantly increase** your patients' cancer risk.

Identifying who should be tested is a crucial step to guide interventions for the best outcomes, from screening to catch cancer early, to risk reduction to avoid it altogether.

Approximately 25% of people[1] meet the criteria for genetic testing for hereditary cancer syndromes.

Clues about hereditary breast and ovarian cancer (HBOC) and Lynch syndrome risk

Use the following list to determine if your patient is at risk of having HBOC or Lynch syndrome, two of the most common hereditary cancer syndromes.

HBOC

HBOC is caused by a variation in the Breast Cancer 1 and 2 (BRCA1 and BRCA2) genes. **The lifetime risk of developing breast cancer for a woman* affected by HBOC is 44-80%.**[2,3] Ovarian cancer risk associated with HBOC is between 13 and 65%.[2,3]

Ashkenazi Jewish ancestry[4]

People with Ashkenazi Jewish ancestry are **10 times as likely** as the general population to carry a variant in the BRCA1 and BRCA2 genes.[5]

Immediate family history:

When gathering your patient's family history, consider genetic testing if there are first-degree relatives—parents, siblings, and children—who have had pancreatic cancer or metastatic prostate cancer.

- Pancreatic Cancer[4]

About **15% of pancreatic cancer** develops in patients with an inherited genetic variant.[6] The NCCN **recommends universal testing for all patients** with a family or personal history.[4]

- Metastatic prostate cancer.[4]

Rates of related genetic variants in men with metastatic prostate cancer are **significantly higher** than in men with localized prostate cancer (11.8% vs 4.6%).[7]

Extended family history:

Next, include second-degree relatives: aunts, uncles, nieces, nephews, and grandparents. Ask about the rare types of breast cancer, and ovarian cancer:

- Breast cancer before age 50[4]

Women with a family member who developed early-onset breast cancer—before age 50—are **significantly more likely** to carry a genetic variant associated with HBOC.[4]

- Recurring breast cancer[4]

Women with HBOC have a 20-40% risk of recurrent breast cancer.[2] A genetic link may be the cause when breast cancer comes back, whether in the same breast or the opposite one.

- Triple-negative breast cancer[4]

Triple negative breast cancer (without ER, PR, and HER2 receptors on the cells) is the most aggressive breast cancer. Among BRCA1 variant carriers, **70% of breast cancer cases are triple negative**.[8]

- Ovarian cancer[4]

Ovarian cancer accounts for less than 4% of female cancers but is **the leading cause of death from gynecologic cancer.** About 23% of cases are associated with genetic variations, particularly HBOC.[9]

- Male** breast cancer[4]

Up to **40% of breast cancer diagnoses in men** are caused by a genetic variant.[10] Men with a variant in BRCA2 are **ten times as likely** as men in the general population to be affected by breast cancer.[10,4]

Lynch syndrome: The most common form of hereditary colorectal cancer.

Lynch syndrome is associated with a **change in any of several genes**, including a group called the DNA mismatch repair genes (MLH1, MLH2, MSH6, and PMS2), and the epithelial cellular adhesion molecule gene (EPCAM).

Patients who have Lynch syndrome have a lifetime **risk of colorectal cancer ranging from 10 to 56%**.[11]

Colorectal cancer is the most common type of cancer associated with Lynch syndrome, but it also increases your patient's risk of endometrial, stomach, pancreatic, kidney, and other cancers[11 above]

Personal history:

Ask about cancers your patient has been affected by. Depending on what type, and what age they were diagnosed, they could point to Lynch syndrome. Think about genetic testing for patients who have:

- **One** Lynch syndrome-related cancer **before age 50**.[12]

Early-onset cancer is a classic marker of genetic cancers, including those related to Lynch-syndrome. **Up to a third of cases** of colorectal cancer under age 40 are reported to be linked to hereditary causes.

- **More than one** Lynch syndrome-related cancer.[12,12]

If multiple types of cancer affect a patient, suspect a genetic component. **Many genetic syndromes** can lead to multiple cancers. Consider consulting with a genetic counselor to navigate the right tests for these patients.

Family history:

Having certain Lynch-syndrome related cancers in a family are evidence that testing should be pursued. Ask about:

- Colorectal or endometrial cancer before age 50.[12]

Endometrial and colorectal cancer are the most common types of cancer related to Lynch syndrome. Family members affected an early age are a significant factor in guiding testing.

- Pancreatic cancer.[12]

Lynch syndrome leads to **9 times higher risk** of developing pancreatic cancer than the general population, making it another clue.[13]

Next steps

Family history provides key insights into your patient's cancer risk profile. With genetic testing, you can identify syndromes where proactive measures can **lower cancer risk and find developing cancer at its earliest stages**.

The (****) analyzes 84 genes, including 23 linked to breast cancer, and the variants associated with HBOC and Lynch syndrome.

Did you know you can consult with a qualified genetic counselor from (***) for targeted testing guidance, or for help on a specific patient case? Learn more, get support, and find clinical practice resources on the (****) website.

Read real stories from patients who got **better outcomes** through management **guided by genetic insights** here.

**Assigned female at birth: applies to gender related language through document.*
***Assigned male at birth: applies to gender related language through document.*

1 DeFrancesco MS, Waldman RN, Pearlstone MM, et al. Hereditary Cancer Risk Assessment and Genetic Testing in the Community-Practice Setting. Obstet Gynecol. 2018;132(5):1121-1129. doi:10.1097/AOG.0000000000002916

2 American Society of Clinical Oncology. Hereditary Breast and Ovarian Cancer. Published June 25, 2012. Accessed September 2, 2023. https://www.cancer.net/cancer-types/hereditary-breast-and-ovarian-cancer

3 Chen J, Bae E, Zhang L, et al. Penetrance of breast and ovarian cancer in women who carry a BRCA1/2 mutation and do not use risk-reducing Salpingo-oophorectomy: An updated meta-analysis. *JNCI Cancer Spectr*. 2020;4(4):kaa029. doi:10.1093/jncics/pkaa029

4 NCCN Clinical Practice Guidelines® for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic V.1.2024. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed September 2, 2023..

5 BRCA1 and BRCA2 (PDQ®) - NCI. Accessed September 2, 2023. https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-genes-hp-pdq#_589,

6 Crowley F, Gandhi S, Rudshteyn M, Sehmbhi M, Cohen DJ. Adherence to NCCN genetic testing Guidelines in pancreatic cancer and impact on treatment. *Oncologist*. 2023;28(6):486-493. doi:10.1093/oncolo/oyad044

7 Pritchard CC, Mateo J, Walsh MF, et al. Inherited DNA-repair gene mutations in men with metastatic prostate cancer. *N Engl J Med*. 2016;375(5):443-453. doi:10.1056/nejmoa1603144

8 Stevens KN, Vachon CM, Couch FJ. Genetic susceptibility to Triple-negative breast cancer. *Cancer Res*. 2013;73(7):2025-2030. doi:10.1158/0008-5472.can-12-1699

9 Toss A, Tomasello C, Razzaboni E, et al. Hereditary ovarian cancer: not only BRCA 1 and 2 genes. *Biomed Res Int*. 2015;2015:341723. doi:10.1155/2015/341723

10 Campos FAB, Rouleau E, Torrezan GT, et al. Genetic landscape of male breast cancer. *Cancers (Basel)*. 2021;13(14):3535. doi:10.3390/cancers13143535

11 Genetics of colorectal cancer (PDQ®). National Cancer Institute. Published August 4, 2023. Accessed September 5, 2023. https://www.cancer.gov/types/colorectal/hp/colorectal-genetics-pdq

12 NCCN Clinical Practice Guidelines® for Genetic/Familial High-Risk Assessment: Colorectal V.1.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed September 5, 2023

13 Kastrinos F. Risk of pancreatic cancer in families with lynch syndrome. *JAMA*. 2009;302(16):1790. doi:10.1001/jama.2009.1529