National Comprehensive Cancer Network®

2026

NCCN Guidelines for Patients®

Cancer care recommendations from leading experts at the National Comprehensive Cancer Network® (NCCN®)

Genetic Testing for Hereditary Breast, Ovarian, Pancreatic, and Prostate Cancers



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Available online at NCCN.org/patientguidelines



NCCN Guidelines for Patients®

The essential guide for people facing cancer.

Based on care recommendations from leading cancer experts.

Explains high-quality cancer care provided at state-of-the-art cancer centers.

Reviewed and revised every year.

Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).

Because cancer care is always evolving, NCCN develops and frequently updates evidence-based cancer care recommendations used by health care providers worldwide. These recommendations are known as the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).

The NCCN Guidelines for Patients plainly explain these expert recommendations, so you can talk with your care team about the best care for you.

These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate, Version 3.2026 — February 19, 2026.

View the NCCN Guidelines for Patients free online: NCCN.org/patientguidelines

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Contents

4 Chapter 1
About genetic testing

8 Chapter 2
The genetic testing process

17 Chapter 3
Testing criteria and results-based care

46 Chapter 4
Other resources

50 Words to know

52 NCCN Contributors

53 NCCN Cancer Centers

54 Index

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NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

National Comprehensive Cancer Network (NCCN) and NCCN Foundation
3025 Chemical Road, Suite 100, Plymouth Meeting, PA 19462 USA

1
About genetic testing

5 Which hereditary cancers are discussed in this guide?

6 What causes hereditary cancers?

7 How can I get the best care?

If you've been diagnosed with cancer, genetic testing can help your oncologist make the most informed recommendations for your care. If you don't have cancer but it runs in your family, genetic testing can help you understand your chance of developing it and take steps to lower your risk.

Which hereditary cancers are discussed in this guide?

This resource addresses testing for inherited gene variants (differences) associated with the following cancers and cancer syndromes:

- Breast cancer
- Ovarian cancer
- Pancreatic cancer
- Prostate cancer
- Li-Fraumeni syndrome (LFS)
- Cowden syndrome/PTEN hamartoma tumor syndrome

For information on genetic testing for other hereditary cancers and syndromes, health care providers are encouraged to refer to *NCCN Clinical Practice Guidelines in Oncology for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, Esophageal, and Gastric.*

Hereditary cancers aren't very different from non-hereditary cancers. It's more the pattern of how they occur in your family that makes them different. Hereditary cancers often develop earlier and affect multiple relatives on the same side of the family.



What causes hereditary cancers?

Hereditary cancers are caused by inherited variants (differences) in specific genes. Together, these genes are called cancer predisposition, or cancer susceptibility, genes.

Gene variants you're born with are called germline. They are part of the DNA of every cell in your body. In addition to your unique DNA, your risk of cancer is based on your personal and family health history.

What is penetrance?

In someone with a gene variant that increases the risk of a health problem, penetrance describes how likely they are to develop symptoms or features of the problem. For example, 100% penetrance means everyone with that variant will develop the problem if they live long enough. This is very rare.

Cancer predisposition genes are described as low-, moderate-, or high-penetrance. Cancer-causing variants in high-penetrance genes are generally more likely to result in a cancer diagnosis than variants in low- or moderate-penetrance genes. But other factors also affect how likely you are to develop cancer, including your age, family history, environment, and lifestyle.

How this guide can help you

Making decisions about cancer care is stressful. There's a lot to learn, and you don't know what the future holds.

Use this guide to get the information and support you need.

Patients, doctors, and other health care professionals trust the NCCN Guidelines for Patients. This guide uses clear, everyday language to explain current cancer care recommendations made by respected experts in the field. Their recommendations are based on the latest research and practices at leading cancer centers.

Your health is unique to you, so your cancer care should be, too. As you read this guide, you'll learn which treatments are likely to provide the best results for you. And you'll be better prepared to talk with your care team.

How can I get the best care?

Advocate for yourself. You have an important role to play in your care. Many people feel more satisfied when they actively take part in planning their cancer care.

The NCCN Guidelines for Patients will help you play a larger role in your care. Discuss the recommendations in this guide with your care team. Ask questions about your options and share your goals and concerns.

Don’t know what to ask? You’re not alone. That’s why we include suggested questions to ask at the end of chapters. Keep reading to find the best care for you.



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2
The genetic testing process

9 Pre-test counseling

11 Choosing the best test(s) for you

12 If results are positive

15 Other possible results

16 Key points

16 Questions to ask

This chapter describes what's involved in determining if you meet the criteria for genetic testing, and what to expect after a positive result.

Determining your risk for hereditary cancer and learning about genetic testing involves 3 steps:

- Counseling before any testing is ordered
- Choosing the best test(s) for you
- Counseling when your results are ready

Ideally, a health care professional trained in cancer genetics will be involved at each stage. This might be a genetic counselor, clinical geneticist, oncologist, oncology nurse, or other health care provider.

Pre-test counseling

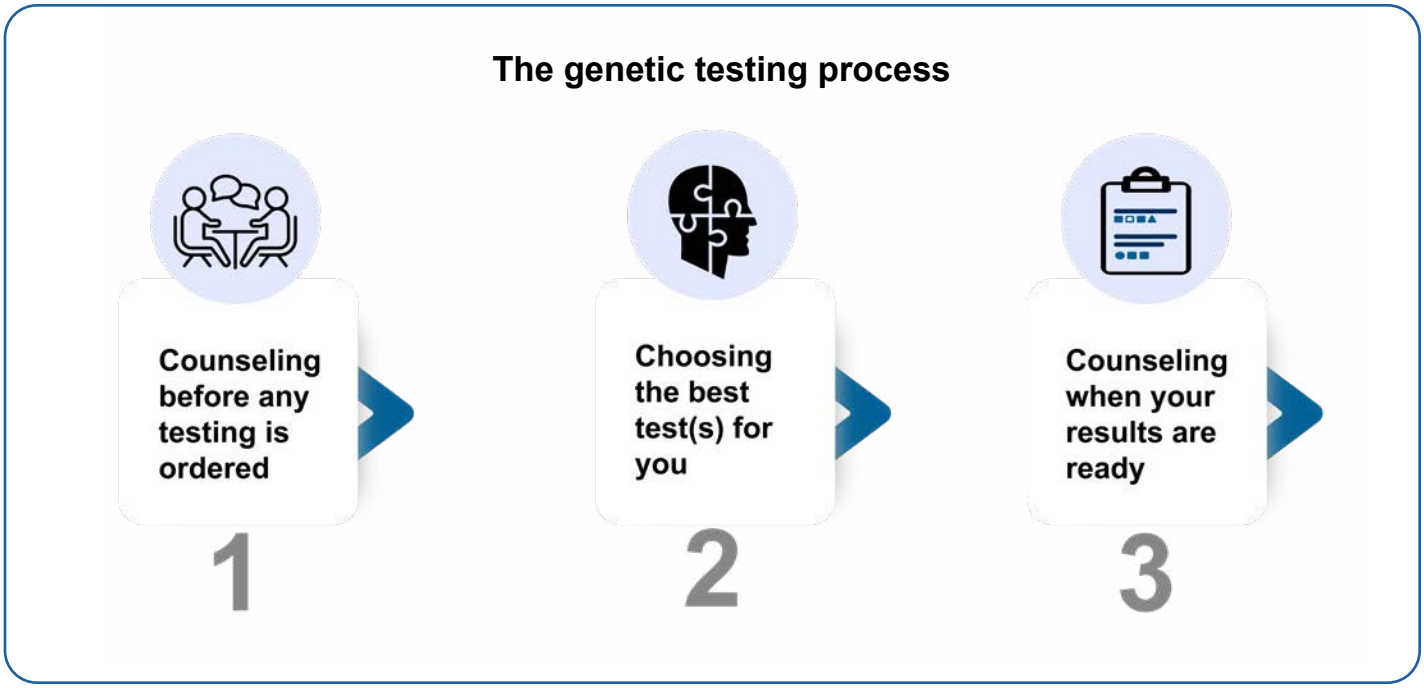
Before any testing is ordered, it's important to learn what the results could mean for you and your family. A genetics professional or other provider will explain the benefits, risks, and limitations of genetic testing for cancer risk.

Your health history

Your past and current health is a key factor in determining your risk of hereditary cancer. If you've been diagnosed with any cancers, your genetics provider will ask about:

- The type(s) of cancer
- Your age at diagnosis
- What cancer treatments you had (some can cause late side effects)

Whether you've had any surgeries to lower your risk of developing cancer is also important to share. Examples include risk-reducing



salpingo-oophorectomy (RRSO) and risk-reducing mastectomy (RRM). RRSO (also called bilateral salpingo-oophorectomy, or BSO) removes both ovaries and fallopian tubes. RRM removes both breasts.

Your provider is also likely to ask about hormonal factors that may affect your risk, such as:

- Your pregnancy history
- Whether you've used birth control pills or other hormonal birth control
- Whether you've received menopausal hormone therapy

Your family health history

Your testing provider will collect detailed information about the health of your family members.

Whether you have any close relatives with cancer is especially important. Close blood relatives include first-, second-, and third-degree relatives on both sides of your family. See the chart on the next page for details.

The type(s) of cancer your relatives were diagnosed with and their age at diagnosis is also important.

Your testing provider will also ask about your ethnicity. Founder variants are cancer-causing variants found in a specific group of people that can be traced back to common ancestors. People of Ashkenazi Jewish ancestry and other groups are at increased risk of founder variants, including *BRCA1* and *BRCA2* variants.

Prior hematopoietic cell transplant

If you've had an allogeneic hematopoietic cell transplant (HCT) to treat blood cancer, your genetic testing results could reflect the DNA of the **stem cell donor** when blood, saliva, or a cheek swab is used. To make sure your DNA (and not your donor's) is extracted, your provider may remove a small piece of your skin or other tissue for testing.

How much does testing cost?

Ask your provider about the cost of genetic testing. Many insurance companies cover the cost if a health care provider confirms it's needed for your health care. The out-of-pocket cost for most people in the United States is $250 or less, depending on the number of genes tested and other factors.

Other things to discuss

You and your testing provider will also discuss:

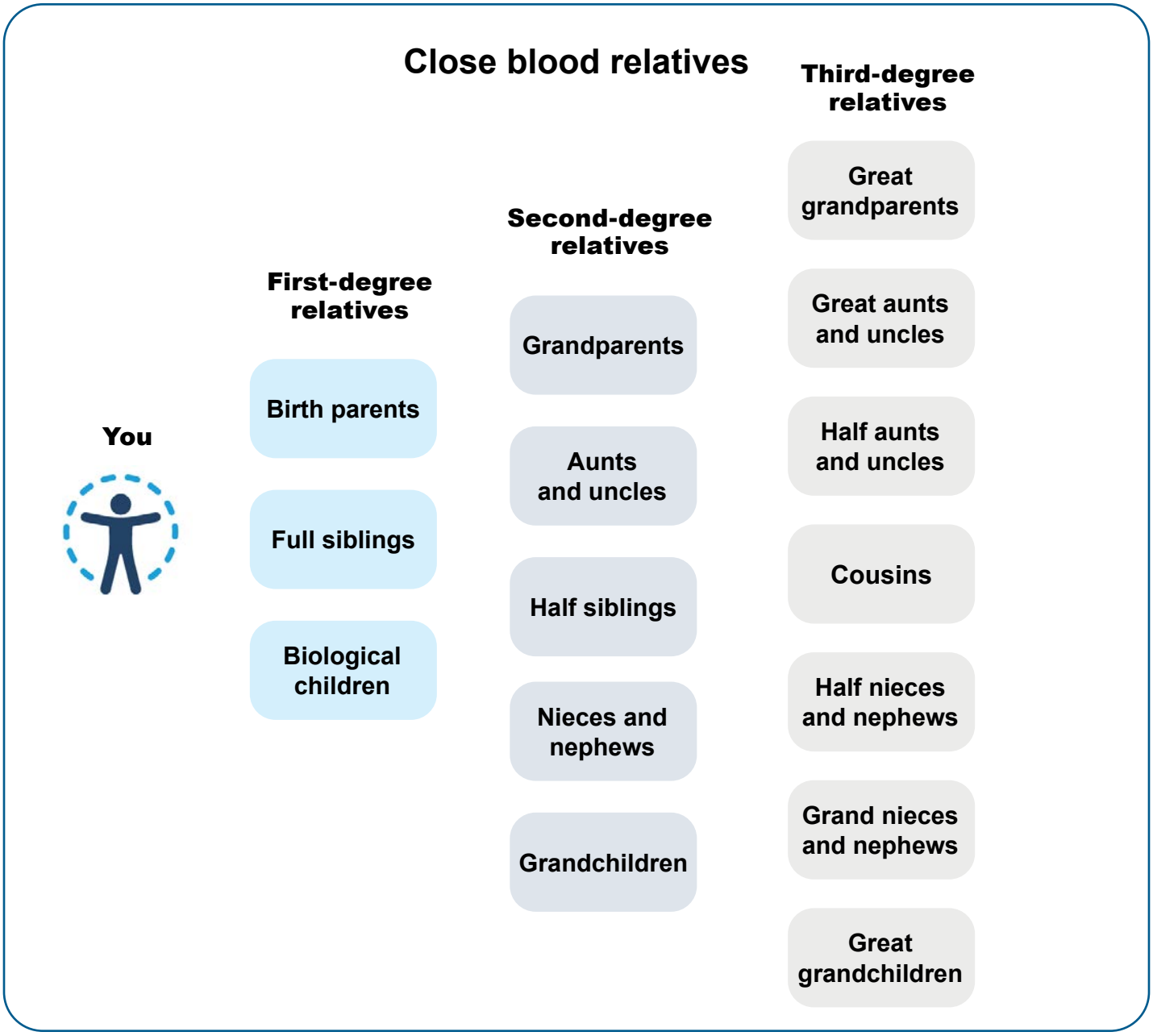
- Informed consent
- The privacy of your genetic information
- Current laws on genetic discrimination

Choosing the best test(s) for you

Genetic testing is often performed using next-generation sequencing (NGS). Also called a multi-gene panel, NGS analyzes entire sets of cancer predisposition genes at the same time. Multi-gene panels may include both moderate- and high-penetrance genes.

To be tested, you'll typically provide a sample of blood or saliva (spit). The sample is sent to a lab to check for gene variants that may cause hereditary cancers and syndromes.

Other types of samples may be used to obtain your DNA if needed. Testing can be performed on a sample of your cheek cells (buccal smear), skin, hair, or nails.



If results are positive

After testing, your genetics provider will explain your results and what they mean for your health and cancer risk.

A positive result means that a pathogenic (cancer-causing) or a likely pathogenic variant was found in 1 or more of the genes included in the testing panel. Seeing a genetics provider is recommended for positive results.

If you test positive and don't have a cancer diagnosis, the next step is discussing options for managing your cancer risk with your provider. This could involve more frequent screening, risk-reducing medicines, or risk-reducing surgery.

Some medical centers include specialized care and screening services for people with a positive genetic testing result. If available, your provider may refer you to these services. Ask your provider about cancer prevention clinics, hereditary cancer support or advocacy groups, and any available research studies.

If you are being treated for cancer, a positive result may affect your cancer care. It may also affect the clinical trials you're eligible for.

Sharing your results

Share your results with your biological family members to the extent possible. They may also be at increased risk and can benefit from risk assessment and possibly testing.

It's helpful to provide family members with a copy of your results so they can share them with their doctors and genetics professionals. Some providers offer easy-to-understand



At-home genetic tests

Genetic testing offered by companies that provide ancestry and health information, like 23andMe, is called recreational testing. Some downsides of these tests include:

- They only check for variants linked with a few cancers
- They don't consider your family history
- Results can be inaccurate

Discuss a positive recreational test result with a health care provider. You may need to do another genetic test to confirm the results before using them for your health care. Because of the limitations of recreational testing noted above, you should also discuss a negative result with a health care provider.

More comprehensive at-home tests are available through companies like Invitae. While these typically include the services of a genetic counselor, they often provide only limited opportunity to discuss and understand the significance of a genetic testing result.

materials and resources you can use to notify your family about your results and their risk.

Referral to a genetics provider

If your testing location doesn't have the resources for pre-test counseling or post-test care, ask to be referred to a genetics provider.

Seeing a genetics provider is also recommended for a positive result as well as for a complex result that needs expert interpretation and management.

Re-consultation about your risk

Over time, it may be helpful to have a follow-up visit with a genetics professional or other health care provider who is familiar with inherited cancer risk.

This visit allows you to check in with your provider about your cancer screening strategy. They may suggest changes based on the latest research, or if any new cancers have been diagnosed in your family. You can also discuss any newer options for genetic testing.

And if your life circumstances have changed, this is an opportunity to revisit earlier decisions about risk-reducing surgery and other screening and prevention options.

How often you should follow up with your provider depends on your age, reproductive planning, other health problems, risk-reducing surgeries, and other risk factors.

Family planning

If you are of reproductive age, your provider will explain what a positive genetic testing result could mean for starting or growing your family.

Some couples who have or carry genetic disorders choose to conceive naturally.

Pre-implantation genetic testing (PGT)

Embryos created through IVF can be tested for a hereditary cancer risk variant known to be carried by the egg or sperm donor. If desired, only embryos not carrying the variant can be transferred to the uterus.



Between the 10th and 14th weeks of pregnancy, the baby can be tested for cancer-causing variants using chorionic villus sampling (CVS). This is called prenatal diagnosis. Depending on the results, the parents may make difficult decisions regarding pregnancy management.

Another option for couples who have or carry genetic disorders is in vitro fertilization (IVF). In IVF, eggs are fertilized with sperm in a lab to create embryos. The embryos are implanted into the uterus or frozen for future use. Before being transferred to the uterus, the embryos can be tested for hereditary cancer-causing variants. This is called pre-implantation genetic testing (PGT). If desired, only embryos not carrying the variant(s) can be transferred to the uterus.

Couples can also choose to use eggs, sperm, or embryos from a donor for IVF.



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Other possible results

Other possible results of genetic testing are described next.

A negative result means you don't carry a pathogenic variant in the cancer-predisposing genes included in the testing panel. A negative result is either a true negative or an uninformative negative.

True negative results

If a cancer-causing variant runs in your family and you don't carry it, it's called a true negative. This is a reassuring result.

Keep in mind that you may still be at higher-than-average risk based on your personal and family history for any of the following reasons:

- You carry a variant in a tested gene that can't be detected using current technology
- You carry a variant in a gene that wasn't included in the testing panel
- You have several family members diagnosed with cancer, but none is linked to a known hereditary cancer gene

Uninformative negative results

If you test negative and your relatives with early-onset or suspicious cancers haven't been tested, it's called an uninformative negative.

It's uninformative because you still don't know whether they carry a variant that you didn't inherit, or whether their cancers can't be explained by known hereditary cancer genes.

Even though you tested negative, you may benefit from increased cancer screening and risk-reducing measures based on your family history. Some medical centers include specialized high-risk clinics that offer this type of family history-based screening.

Your family members may benefit from genetic testing, both to learn their own cancer risk and to contribute data about your family's overall cancer risk.

Over time, you may be a candidate for additional genetic testing due to new family history data and advances in testing.

Variant of uncertain significance

A variant of uncertain significance (VUS) is a genetic variant for which little information is available. VUS is a common result, especially when a large number of genes are tested at the same time. Because the significance is unclear, a VUS result isn't used to make care decisions.

Over time, the lab that did your testing may have updated information on the meaning of certain VUS. Ideally, they will automatically share any new information with you. If they don't, contact your testing provider every 3 to 5 years to confirm that you have up-to-date results.

Mosaic results

When someone has two or more sets of cells that differ genetically from one another, the results are called mosaic. This is thought to be caused by an error in mitosis (cell division) in a growing baby during pregnancy.

Mosaicism can lead to many kinds of disorders. Referral to a genetics provider is recommended for mosaic results.

Key points

- Determining your risk of hereditary cancer involves counseling before testing, choosing the best gene(s) to test, and counseling when your results are ready.
- Your health and cancer history, and that of your biological family members, are key factors in determining your risk of hereditary cancer.
- Genetic testing is often performed using next-generation sequencing (NGS). To be tested, you'll typically provide a sample of blood or saliva.
- If a cancer-causing variant is found (a positive result), share your results with your biological family members. They may also be at increased risk and can benefit from risk assessment and possibly testing.
- Family planning options for couples who have or carry genetic disorders include prenatal diagnosis after natural conception, and in vitro fertilization (IVF) with pre-implantation genetic testing (PGT).
- Other possible results include true negative, uninformative negative, variant of uncertain significance (VUS), and mosaicism. If results are negative, you may still be at higher-than-average risk based on your family history.
- Over time, check in with your genetics provider about your cancer screening and prevention strategy. Tell them about any new cancers diagnosed in your family and learn about any newer options for testing.

Questions to ask

- What are the advantages and disadvantages of genetic testing?
- How long does it take to get the results?
- Can my health or life insurance company increase my rates if I test positive?
- I don't think I can handle the emotional impact of a positive result. What do I do?
- What can I do to lower my risk if I test positive?

3

Testing criteria and results-based care

18 General recommendations

19 Hereditary breast cancer

24 Hereditary ovarian cancer

27 Hereditary pancreatic cancer

29 Hereditary prostate cancer

31 Li-Fraumeni syndrome

34 Cowden syndrome/PHTS

38 Gene-specific care

45 Key points

45 Questions to ask

This chapter describes the criteria used to determine whether genetic testing would be helpful for you, as well as recommended care for a positive result.

General recommendations

Testing is generally recommended in the situations described next. If you have a personal or family history of any of the following cancers or syndromes, more specific guidance is provided later in this chapter.

- Li-Fraumeni syndrome (LFS)
- Cowden syndrome or other *PTEN* hamartoma condition
- Breast cancer
- Ovarian cancer
- Pancreatic cancer
- Prostate cancer

For information on genetic testing for other hereditary cancers and syndromes, health care providers are encouraged to refer to *NCCN Clinical Practice Guidelines in Oncology for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, Esophageal, and Gastric.*

Relative(s) with a known cancer-causing variant

If you have any blood relatives with a confirmed cancer-causing gene variant, genetic testing is recommended.

To make informed cancer care decisions

If you have cancer, genetic testing can help your provider make decisions about chemotherapy and other forms of systemic therapy—specifically, whether platinum chemotherapy and PARP inhibitors would be helpful for certain cancers. Some variants can also affect decisions about surgery or radiation therapy.

If you're at risk of breast or ovarian cancer, genetic testing can help you decide, together with your care team, whether to have risk-reducing surgery.

The tumor has a feature that may also be inherited

If you have cancer, your tumor tissue may have been tested for unique features, called biomarkers. Many biomarkers are mutations (changes) in the tumor's DNA. Changes in the tumor or cancer itself are described as somatic or acquired.

Sometimes, a mutation found in the tumor may be inherited. In these situations, your health care provider may recommend genetic testing to learn if the mutation was inherited and, if so, what this means for you and your family.

And, for some hereditary cancers, choosing the best treatment(s) depends on whether a tumor mutation is inherited.

Who else might benefit from testing?

People of Ashkenazi Jewish ancestry are at higher-than-average risk of carrying certain cancer-causing gene variants. Testing may be considered if you are of Ashkenazi Jewish

ancestry, even if you don't have any other risk factors.

Genetic testing may also be considered for people diagnosed with serous endometrial cancer, a rare type of uterine cancer that may be linked with *BRCA* variants.

Testing may also be appropriate for certain rare tumors and in other situations not directly addressed in this guide.

Hereditary breast cancer

Breast cancer starts in the cells of the breast. Anyone can develop breast cancer, including those assigned male at birth.

Almost all breast cancers are carcinomas. Carcinomas start in the cells that line the inner or outer surfaces of the body. The most common type of breast cancer, ductal carcinoma, starts in the cells that line the milk ducts. Lobular carcinoma starts in the lobules (milk glands) of the breast.

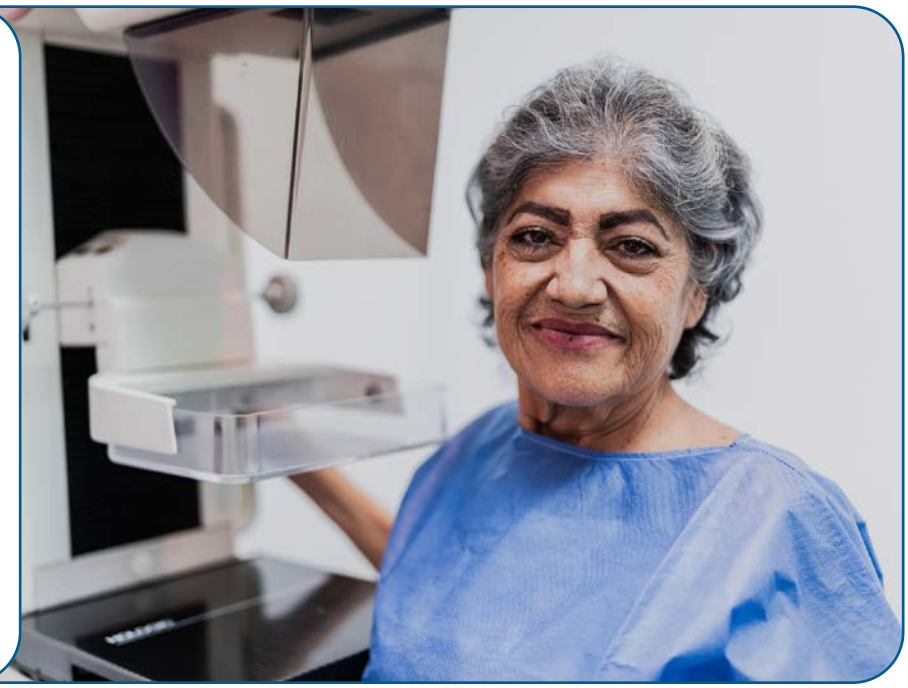
In this patient guide, the term breast cancer includes invasive ductal carcinoma (IDC) and ductal carcinoma in situ (DCIS).

About 1 in 10 breast cancers has a hereditary cause. Breast cancer susceptibility genes include *ATM, BARD1, BRCA1, BRCA2, CDH1, CHEK2, NF1, PALB2, PTEN, RAD51C, RAD51D, STK11,* and *TP53.*

If you meet the testing criteria described next, personalized risk assessment and genetic counseling are recommended. Genetic testing is often part of the process.

Managing your risk

For people at increased risk of hereditary breast cancer, screening with mammograms, breast MRIs, or both is often recommended to detect cancer growth early.



Testing in people with breast cancer

If you've been diagnosed with breast cancer and any of the following apply to you, genetic testing is recommended.

Age – You were diagnosed with breast cancer at or before age 50

Ancestry – You are of Ashkenazi Jewish ancestry

Cancer type – You've been diagnosed with any of the following:

- Male breast cancer
- Triple-negative breast cancer
- More than 1 type of breast cancer
- Lobular breast cancer with a personal or family history of diffuse gastric cancer

Family history – You have 1 or more close blood relatives with any of the following:

- Breast cancer diagnosed at age 50 or earlier
- Male breast cancer
- Ovarian cancer
- Pancreatic cancer
- Metastatic or high-risk prostate cancer

Testing is also recommended if you have 3 relatives (including you) on the same side of your family who have breast or prostate cancer.

To guide your care – In people with metastatic breast cancer, genetic testing is recommended to help decide whether PARP inhibitor therapy should be considered.

In those with high-risk, HER2-negative breast cancer, testing is recommended to help decide if PARP inhibitor therapy would be helpful after primary treatment. Ask your oncologist if the cancer is high risk.

If you're receiving treatment for any type of cancer, a positive result may affect the clinical trials you're eligible for.

If you don't meet the criteria described above

If you haven't been diagnosed with breast cancer, or you have but don't meet the criteria described above, testing is recommended in the following situations:

- You have a first- or second-degree blood relative that meets the criteria described above.
- You have a 5% or higher risk of a *BRCA1/2* variant based on a risk calculator, like BRCAPro or CanRisk.

Genetic testing may also be considered if any of the following apply to you:

- You were diagnosed with breast cancer between age 51 and age 65.
- You were diagnosed with breast cancer (at any age) and have 1 or more close blood relatives with certain types of prostate cancer.
- You have a history of malignant phyllodes tumors.

Testing may also be an option for people with a 2.5% to 5% risk of a *BRCA1/2* variant

according to a risk calculator. In this case, when deciding whether to include genes other than *BRCA1/2,* your provider will consider your preferences, your insurance coverage, and the speed of results. The more genes tested, the more likely you are to get a variant of uncertain significance (VUS).

Who isn't likely to benefit from testing?

In people who don't have close relatives with breast, ovarian, pancreatic, or prostate cancer, testing is unlikely to find high-risk variants in the following groups:

- Those assigned female at birth diagnosed with breast cancer after age 65
- Men diagnosed with localized prostate cancer who have a Gleason Score below 7. The Gleason score usually ranges from 6 to 10. The lower the score, the slower the cancer cells are expected to grow and spread.

Managing your breast cancer risk after a positive result

A positive result means that a germline pathogenic or likely pathogenic variant was found in the susceptibility genes included in the testing panel.

Based on your results, your provider may recommend some of the strategies described next to reduce your risk of breast cancer.

Recommendations for lowering risk are guided by the penetrance of the specific gene variant(s) identified. See pages 38-44 for complete guidance according to gene.

Breast awareness

Breast awareness involves becoming familiar with your breasts and reporting any changes to your health care provider. Doing breast self exams on a regular basis may help you notice changes. If you are premenopausal, doing the exams when your period is almost over may be most helpful.

Screening mammogram

A screening mammogram uses low-dose x-rays to take pictures of your breast in 4 different positions. A radiologist reviews the images and decides if you need additional imaging. If you do, you will likely have a diagnostic mammogram.

This type of mammogram usually involves taking more detailed x-rays of the breast from different angles to check the suspicious area more closely.

Clinical breast exam

A clinical breast exam (CBE) is a physical exam of the bare breast performed by a health care provider to check for lumps or

other changes. While you're seated or lying down, your provider will palpate (feel) the entire breast, including the armpit. A nurse or assistant might also be in the room during the exam.

Breast MRI

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of areas inside the body. It doesn't use radiation.

Your provider may recommend breast MRI in addition to mammography. They will consider your age, family history, breast density, and preferences to determine whether to use both methods.

For a breast MRI, a gadolinium-based contrast agent (GBCA)—a rare, heavy metal—is used to enhance the quality of the MRI. There are no known harmful effects from GBCA, but it may linger in the body for months to years afterward. Talk to your provider if you have any concerns. The MRI should be done with and without contrast.

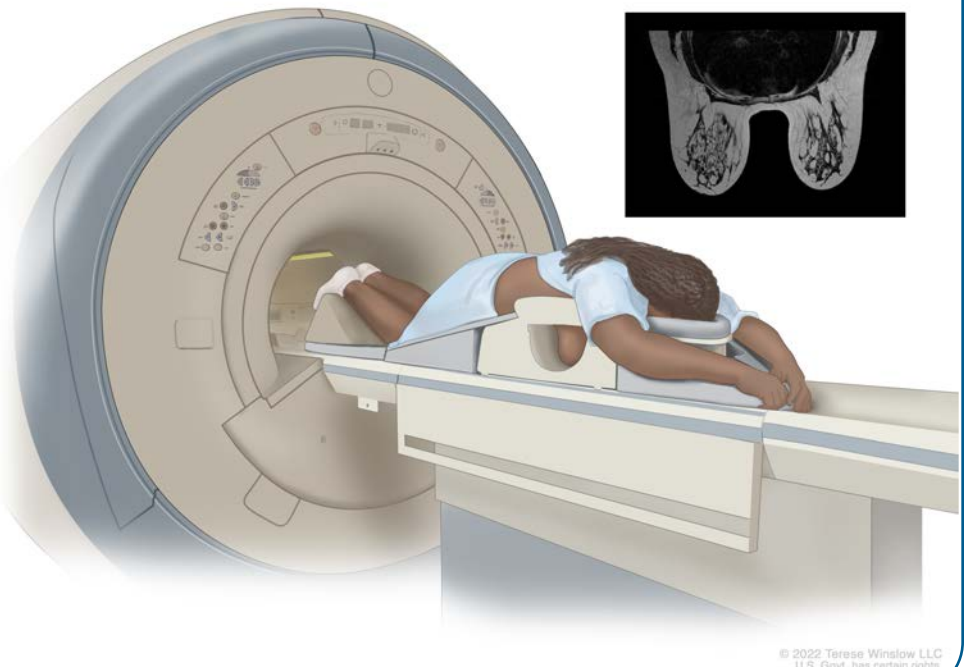
Risk-reducing mastectomy

Having surgery to remove the breasts lowers the risk of developing breast cancer. Surgery to remove both breasts for this purpose is called risk-reducing bilateral mastectomy.

Risk-reducing mastectomy is an option to consider for people with germline variants in certain breast cancer susceptibility genes, including *BRCA1/2, CDH1, PALB2, PTEN* (associated with Cowden syndrome), *STK11,* and *TP53* (associated with Li-Fraumeni syndrome). Information on care for Li-Fraumeni syndrome and Cowden syndrome is provided later in this chapter.

Breast MRI

For people at increased risk of breast cancer, breast MRI may be recommended in addition to mammography. Your provider will consider your specific gene variant(s), age, family history, breast density, and preferences to determine whether to use both methods.



Your provider will explain the risks of this surgery, the extent of its cancer protection, and your potential options for breast reconstruction. If you have a strong family history of breast cancer, take this into consideration when making decisions about risk-reducing mastectomy.

Having your breasts removed can have a major impact on your emotional well-being and quality of life. Ask your provider about resources and information available to you.

Risk-reducing drugs

Certain medicines can help lower the risk of developing breast cancer in people at high risk.

In **premenopausal** people, tamoxifen is most commonly used. This selective estrogen receptor modulator (SERM) reduces the amount of estrogen in the body. Tamoxifen is typically prescribed as a 20-mg pill for 5 years. Sometimes it's prescribed for fewer years at a lower dose.

In **postmenopausal** people, either raloxifene or an aromatase inhibitor is typically recommended. Raloxifene is an estrogen blocker like tamoxifen. For breast cancer prevention, raloxifene is typically prescribed at a dose of 60 mg per day for 5 years.

Anastrozole and exemestane are examples of aromatase inhibitors. These drugs lower estrogen levels by stopping aromatase (an enzyme in fat tissue) from converting other hormones in the body into estrogen.

Hereditary ovarian cancer

Most ovarian cancers actually start in the fallopian tubes. The cancer forms in the surface layer of tissue, called the epithelium. There are more than 5 types of epithelial ovarian cancer. The most common forms are:

- High-grade serous carcinoma (HGSC)
- High-grade endometrioid carcinoma

Ovarian cancer susceptibility genes include *ATM*, *BRCA1*, *BRCA2*, *BRIP1*, *PALB2*, *RAD51C*, *RAD51D*, and the Lynch syndrome genes (*MLH1*, *MSH2*, *MSH6*, *EPCAM*).

Based on your specific results, your provider may recommend taking steps to reduce your risk of ovarian cancer, such as risk-reducing surgery.

Who should be tested?

If you've ever been diagnosed with epithelial ovarian cancer (including fallopian tube and peritoneal cancer), genetic testing is recommended.

Testing is also recommended for people diagnosed with certain types of non-epithelial ovarian cancer, such as small cell carcinoma of the ovary or sex-cord tumors with annular tubules.

If you've never been diagnosed with ovarian cancer, testing is recommended if:

- You have a first- or second-degree blood relative diagnosed with epithelial ovarian cancer (including fallopian tube cancer or peritoneal cancer) at any age.
- You don't meet the criteria above but have a probability above 5% of a *BRCA1/2* variant based on a risk calculator, like *BRCA*Pro or CanRisk.

Surgical menopause

In premenopausal people, surgically removing the ovaries can cause symptoms of menopause, including sleeping problems. Consulting with a menopause specialist is recommended.



Who might be tested?

Genetic testing can be helpful if you've ever been diagnosed with serous tubal intraepithelial carcinoma (STIC). People with STIC may be more likely to have a germline *BRCA1/2* variant.

Risk-reducing salpingo-oophorectomy

Surgery to remove the ovaries and fallopian tubes to lower the risk of cancer is called risk-reducing salpingo-oophorectomy (RRSO).

RRSO **is recommended** for people with germline cancer-causing variants in the following genes addressed in this guide:

- *BRCA1/2*
- *BRIP1*
- *RAD51C*
- *RAD51D*

RRSO is **an option** for those with a cancer-causing variant in the *PALB2* gene.

While not addressed in this guide, RRSO may be recommended for other hereditary cancers and syndromes.

RRSO can impact your health, emotional well-being, and quality of life. If you will be premenopausal when RRSO is performed, consider meeting with a menopause specialist beforehand. More information on surgical menopause is provided next.

Option of hysterectomy at time of RRSO

Some people with cancer-causing germline variants may consider hysterectomy at the time of RRSO. The decision depends on several factors, including the specific gene involved, your personal and family history, other uterine conditions, and your preferences. Discuss the risks and benefits with your provider.

Surgical menopause

If you are premenopausal, surgically removing the ovaries results in a sudden drop in estrogen in the body. This drop can cause symptoms of menopause, including:

- Hot flashes
- Sleeping problems
- Night sweats
- Changes in mood
- Thinning, drying, and irritation of the vaginal lining
- Cognitive changes
- Weight gain

If you have symptoms, your provider may suggest menopausal hormone therapy (MHT). If you don't have breast cancer, consider MHT to help lessen side effects.

There are also long-term risks of having a low estrogen level, including heart disease and weak bones (osteoporosis).

If your **uterus is left in place** at the time of RRSO, MHT with estrogen alone may increase your risk of endometrial cancer. For this reason, options typically include:

- A levonorgestrel intrauterine device (IUD) and an estrogen pill or patch
- Combination estrogen with a selective estrogen receptor modulator (SERM, such as bazedoxifene)

- Combination oral contraceptive pills
- Other combinations of estrogen and progestin

If you **opt for hysterectomy** during RRSO, you will be a candidate for estrogen-only MHT. Using estrogen alone is linked with a lower risk of breast cancer than use of both estrogen and progestin.

Risk-reducing salpingectomy

Surgery to remove the fallopian tubes is called salpingectomy. If you're premenopausal and don't want to lose your ovaries, removing the fallopian tubes first and the ovaries later may be an option. But this approach is **not** the standard of care for people at high risk of ovarian cancer.

While salpingectomy has been shown to lower ovarian cancer risk in the general population, it hasn't been proven to lower risk in people at high risk. In those at high risk, removing the ovaries and fallopian tubes is recommended. This is called a risk-reducing salpingo-oophorectomy (RRSO).

If only the fallopian tubes are removed, consider continuing your combination birth control pills or hormonal IUD. This may keep your ovarian cancer risk low while you still have your ovaries.

Salpingectomy is an option for people assigned female at birth who also want tubal ligation. This form of surgical sterilization prevents pregnancy by stopping the sperm and egg from meeting.

If you freeze eggs or embryos, to become pregnant later you'll need your uterus but not your ovaries or fallopian tubes.

Hereditary pancreatic cancer

Pancreatic cancer starts in a digestive gland called the pancreas. The pancreas makes enzymes that break down proteins, fats, sugars, and starches. It also makes hormones called insulin and glucagon that control blood sugar levels.

There are 2 main types of pancreatic cancer. The more common type (exocrine) forms in cells that make and move digestive enzymes. About 1 in 10 exocrine pancreatic cancers has a hereditary cause.

Pancreatic cancer susceptibility genes include *ATM*, *BRCA1*, *BRCA2*, *CDKN2A*, *PALB2*, *STK11*, *TP53*, and Lynch syndrome genes (*MLH1*, *MSH2*, *MSH6*, *EPCAM*).

Who should be tested?

Genetic testing is recommended for everyone diagnosed with exocrine pancreatic cancer, including those with a rare form called acinar cell carcinoma.

If you have hereditary pancreatitis

Hereditary pancreatitis is a genetic condition that typically causes lifelong issues with inflammation of the pancreas. It can be caused by variants in *PRSS1*, *SPINK1*, and related genes.

People with hereditary pancreatitis are more likely to develop pancreatic cancer at some point than those without. While these individuals are at increased risk, testing for variants in these genes is only recommended if you also have a personal or family history of exocrine pancreatic cancer.

If results are positive

If genetic testing finds cancer-causing variants in certain susceptibility genes, your provider may recommend yearly screening for pancreatic cancer once you reach a certain age.

The benefit of screening for pancreatic cancer is less clear than for other hereditary cancers. Current screening methods find abnormalities that are harmless, or that may never become cancer. It's also unclear whether finding pancreatic cancer early changes any important outcomes, like how long you live.

Before you make a decision, it's important to discuss the possible benefits and drawbacks of screening with your doctor or care team. They can provide additional information to help guide your decision.

If surveillance is planned, the age at which you'll start screening depends on the affected gene(s). See **Guide 1.**

Screening method

If pancreatic surveillance is planned, recommended methods include contrast-enhanced magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS).

MRCP is a type of MRI that makes clear pictures of the pancreas and bile ducts.

A substance called contrast is used to help identify small tumors.

EUS is similar to an upper endoscopy, except that the endoscope also has an ultrasound probe that makes images of the pancreas and nearby structures.

Guide 1
Suggested screening approach for exocrine pancreatic cancer

Cancer susceptibility gene with a cancer-causing variant	Age surveillance will start, if planned
STK11	Age 30 to 35*
CDKN2A	Age 40*
ATM* or *BRCA2	Age 50*
BRCA1*, *MLH1*, *MSH2*, *MSH6*, *EPCAM*, *PALB2*, or *TP53	If you have a cancer-causing variant in one of these genes, pancreatic screening is most helpful if **you also have** a close family history of exocrine pancreatic cancer. If planned, surveillance starts at age 50* for people with at least 1 first- or second-degree relative diagnosed with exocrine pancreatic cancer on the same side of the family (or assumed to be).
Hereditary pancreatitis genes including *PRSS1* and *SPINK1*	If you have a cancer-causing variant in one of these genes, pancreatic screening is most helpful if you have a clinical diagnosis of hereditary pancreatitis **and** a personal or family history of pancreatic cancer. If planned, surveillance starts at age 40, or 20 years after the onset of pancreatitis (whichever is earlier).

*Or 10 years before the earliest exocrine pancreatic cancer diagnosis in your family, whichever is earlier.

Hereditary prostate cancer

The prostate is a gland located deep inside the pelvis. In the United States, prostate cancer is the second most common cancer in people assigned male at birth.

Prostate cancer susceptibility genes include *ATM*, *BRCA1*, *BRCA2*, *CHEK2*, *HOXB13*, *PALB2*, and *TP53*.

Who should be tested?

In people diagnosed with prostate cancer, genetic testing is recommended for those who meet the criteria in **Guide 2.**

If you don't have prostate cancer, or you do but don't meet these criteria, testing is recommended if you have a first- or second-degree blood relative who does meet the criteria.

Guide 2
Testing criteria for people diagnosed with prostate cancer (at any age)

Ancestry	Genetic testing is recommended for people of Ashkenazi Jewish ancestry.
Cancer features	Genetic testing is recommended for people with: • Metastatic prostate cancer (stage 4B) • Prostate cancer that has spread to lymph nodes (stage 4A) • Very high-risk or high-risk prostate cancer

Family history	Genetic testing is recommended in the following situations:
	• You have 1 or more close blood relatives with any of the following:
	  • Breast cancer diagnosed at age 50 or earlier
	  • Male breast cancer
	  • Ovarian cancer
	  • Pancreatic cancer
	  • Prostate cancer that is high-risk, very high-risk, has spread to lymph nodes, or is metastatic
	• You have 3 or more close relatives (including you) with prostate cancer or breast cancer on the same side of the family.

Who else might benefit from testing?

Testing may also be appropriate if:

- You were diagnosed with prostate cancer at or before age 55 and don't meet testing criteria
- You were diagnosed with intermediate-risk prostate cancer with intraductal/cribriform histology at any age

If results are positive

Based on your specific results, your provider may recommend screening for prostate cancer by checking your prostate specific antigen (PSA) level. More information on PSA is provided below.

In the past, screening for prostate cancer involved getting a digital rectal exam (DRE). Now, DRE is generally only performed if needed.

For people who test positive for a germline *BRCA1/2* variant, screening may also include a multiparametric MRI (mpMRI) by age 50 (or earlier, depending on your family history). This specialized type of MRI shows the prostate gland in greater detail than a standard MRI.

PSA

PSA is a protein made inside the prostate gland. Its job is to help semen transport sperm. All prostate cells, both normal and cancer cells, make PSA.

If there's something wrong with the prostate—like prostate cancer—it may make more PSA. While most PSA goes into semen, a little bit ends up in the bloodstream, too. An unusually high amount of PSA in the blood may be a sign of prostate cancer.

However, age and other factors—such as an enlarged prostate or a urinary tract infection—can also cause high levels of PSA.

Li-Fraumeni syndrome

Li-Fraumeni syndrome (LFS) is caused by a pathogenic variant in the *TP53* gene. This gene helps control repair or survival of damaged cells.

Families with Li-Fraumeni syndrome have a high risk of developing a range of cancers. The 5 most common, or core, LFS cancers include:

- Sarcomas
- Leukemias
- Brain cancers
- Breast cancers
- Adrenocortical tumors

Who should be tested?

Genetic testing is recommended in the following situations:

- A germline *TP53* variant runs in your family
- You meet the classic criteria or the Chompret criteria (see **Guide 3**)
- You or someone in your family has been diagnosed with pediatric hypodiploid leukemia
- You have a first- or second-degree relative who was never tested and is no longer alive, but who meets any of the other testing criteria

Who might be tested?

It's common for someone born without a germline *TP53* variant to have a tumor with a somatic *TP53* mutation. For example, unlike other types of sarcoma, germline

Guide 3
Criteria for diagnosing LFS

Classic criteria
You were diagnosed with sarcoma before age 45
and
You have a first-degree relative diagnosed with cancer before age 45
and
You have a first- or second-degree relative in the same line diagnosed with cancer by age 45 or with a sarcoma at any age
Chompret criteria
You were diagnosed with a tumor in the LFS spectrum before age 46, and you have at least 1 first- or second-degree relative diagnosed with a cancer in the LFS spectrum before age 56, or with multiple primary cancers at any age
or
You've had more than 1 type of cancer, 2 of them are in the LFS spectrum, and the first was found before age 46
or
You were diagnosed with 1 of several rare cancers
or
You were diagnosed with breast cancer before age 31

TP53 variants are rare in people with Ewing sarcoma, gastrointestinal stromal tumors (GISTs), desmoid tumors, or angiosarcoma.

If you don't meet the testing criteria but the cancer has a *TP53* mutation, genetic testing might be ordered. Your personal and family history will be reviewed to determine if genetic testing is worthwhile.

Testing is typically ordered for people diagnosed with any cancer before age 30, or if your provider feels that it's appropriate.

Managing cancer risk in adults

Li-Fraumeni syndrome is rare. Referral to a specialized team or center with expertise in this syndrome is recommended.

People with LFS are at high risk of developing more than one type of cancer. Unfortunately, there isn't a good screening method for all of them.

See **Guide 4** on the next page for cancer screening recommendations in adults. More frequent screening may be appropriate based on your health and family history.

Whole-body MRI

Screening with whole-body MRI can find cancer early in families with Li-Fraumeni syndrome. But it can also flag things as cancer that aren't (false-positive results).

If whole-body MRI isn't available to you, ask your provider about clinical trials you may be able to join. Also ask about other advanced imaging methods that may be an option.

LFS and radiation therapy

Radiation increases the risk of developing a sarcoma. If you're receiving treatment for cancer, radiation therapy is typically avoided if you have other good treatment options.

But sometimes radiation therapy is needed. In this case, make an informed decision by fully discussing the benefits of radiation compared to the risk of second cancers caused by radiation.

Managing cancer risk in children

Tell your pediatrician if LFS runs in your family. In families with LFS, the following screening measures are recommended to help detect cancer early in children:

- Complete physical exam, including a neurological exam, every 3 to 4 months starting in infancy
- Complete blood count with differential every 3 to 4 months in children who have received chemotherapy or radiation therapy
- Yearly MRI of the brain and whole body starting in infancy
- For adrenocortical carcinoma, ultrasound every 3 to 4 months starting in infancy (a blood test panel can be used if ultrasound is unhelpful)
- Yearly whole-body skin exam

Guide 4
Cancer screening in adults with a germline *TP53* variant (associated with LFS)

Screening for breast cancer in those assigned female at birth	**Breast awareness:** Start becoming familiar with your breasts at an early age and report any changes to your health care provider. Doing breast self exams on a regular basis may help you notice changes. If you are premenopausal, doing the exams when your period is almost over may be most helpful. **Starting at age 20:** Clinical breast exam every 6 to 12 months (or, if someone in your family was diagnosed before age 20, start at that age). **Age 20 to 29:** Yearly breast MRI (or, if someone in your family was diagnosed before age 20, start at that age). **Age 30 to 75:** Yearly breast MRI (with and without contrast) and mammogram. **Risk-reducing mastectomy** is an option for people with germline TP53 variants. Your provider will explain the risks of surgery, the extent of cancer protection it provides, possible quality-of-life effects, and your options for breast reconstruction.
Screening for other cancers	**General recommendations** • Complete physical exam, including neurological exam, every 6 to 12 months for cancer survivors. Your provider will look closely for any signs or symptoms of rare and second cancers. • Complete blood count with differential every 3 to 4 months in people who have received chemotherapy or radiation therapy. • Yearly whole-body and brain MRI. **Skin cancer** Yearly whole-body skin exam. **Colon and stomach cancers** Colonoscopy and upper endoscopy every 2 to 5 years starting at age 25, or 5 years before the earliest colorectal or gastric cancer in the family. If your abdomen or whole body was treated with radiation therapy, colonoscopy is recommended starting 5 years after treatment. **Prostate cancer** Yearly screening with prostate-specific antigen (PSA) starting at age 40.

Cowden syndrome/PHTS

Germline variants in the *PTEN* gene can cause a spectrum of disorders called *PTEN* hamartoma tumor syndrome (PHTS). PHTS includes the following disorders:

- Cowden syndrome (CS)
- Bannayan-Riley-Ruvalcaba syndrome (BRRS)
- Adult L'hermitte-Duclos disease (LDD)
- Proteus-like syndrome
- Autism spectrum disorders with macrocephaly

PHTS syndromes cause benign (harmless) tumors called hamartomas to form in or on the body. In addition to benign tumors, people with Cowden syndrome are at increased risk of developing malignant (cancerous) tumors or lesions, often in the following areas:

- Skin
- Mucous membranes
- Breasts
- Thyroid
- Endometrium (lining of the uterus)
- Brain

Cowden syndrome can be diagnosed based on signs, symptoms, and health history. This is called a **clinical diagnosis.** A clinical diagnosis is made if you have certain combinations of the health conditions listed in **Guide 5**.

Guide 5 **Cowden syndrome features**
Autism spectrum disorder
Breast cancer
Colon cancer
Endometrial cancer
Esophageal glycogenic acanthoses (thickened, raised areas on the inner lining of the esophagus)
Gastrointestinal hamartomas (benign tumors with a distorted structure made of an abnormal mixture of cells and tissue found in that area)
Gastrointestinal ganglioneuromas (benign nerve cell tumors)
Hyperpigmentation (darkening of the skin) on the glans penis
Intellectual disability
Kidney cancer (renal cell carcinoma)
L'hermitte-Duclos disease
Lipomas (benign fatty tumors)
Macrocephaly (enlarged head)
Thyroid cancer (papillary or follicular)
Thyroid problems (nodules, goiter)
Testicular lipomatosis (benign lesions in the testicles)
Trichilemmomas (benign tumors that form in hair follicles)
Vascular problems

Who should be tested for germline *PTEN* variants?

Testing for germline *PTEN* variants is recommended in the following situations:

- You meet the criteria for a clinical diagnosis of Cowden syndrome or a different *PTEN* syndrome
- A *PTEN* variant runs in your family
- You have Bannayan-Riley-Ruvalcaba syndrome
- You don't meet the criteria for a clinical diagnosis but have certain combinations of other features in **Guide 5**
- Tumor biomarker testing found a somatic *PTEN* variant
- You have a first- or second-degree relative who was never tested and is no longer alive, but who meets any of the above testing criteria

If results are positive

If available to you, seek care from a specialized team or center with expertise in this rare syndrome. Your cancer care provider will explain the possible signs and symptoms of *PTEN*-related cancers. If you develop any symptoms, tell your care team promptly.

Annual physical exams

A yearly, comprehensive physical exam, including a thorough check of your thyroid gland, is recommended for everyone with Cowden syndrome. Yearly exams should start at age 18, or 5 years before the youngest diagnosis of a *PTEN*-related cancer in your family (whichever comes first).

Cancer-specific screening

About 1 in 2 people assigned female at birth with Cowden syndrome will develop breast cancer, usually by age 50. Recommendations for managing breast cancer risk are provided on the next page in **Guide 6.**

Guidance on managing your risk of endometrial, colorectal, and other cancers is provided in **Guide 7.**

Guide 6
Managing breast cancer risk in adults with a germline *PTEN* variant

Increased risk of	Recommended steps to lower your risk
Breast awareness	Start becoming familiar with your breasts at an early age and report any changes to your health care provider. Doing breast self exams on a regular basis may help you notice changes.
Cancer screening	• A clinical breast exam is recommended every 6 to 12 months starting at age 25, or 5 to 10 years before the earliest breast cancer diagnosis in your family (whichever comes first). • A mammogram and breast MRI are recommended every year starting at age 30, or 10 years before the earliest breast cancer diagnosis in your family (whichever comes first). • If you've been treated for breast cancer but didn't have a double mastectomy, you will continue screening as described above. • Screening and management are individualized for people above age 75.
Risk-reducing mastectomy	Risk-reducing mastectomy is an option for people with a germline *PTEN* variant. Your provider will explain the risks of surgery, the extent of cancer protection it provides, the possible effects on your quality of life effects, and your options for breast reconstruction.

Guide 7
Managing risk of other cancers in adults with a germline *PTEN* variant

Increased risk of	Recommended steps to lower your risk
Endometrial cancer	• Report possible symptoms, including bleeding between cycles or after menopause, to your care team promptly. Tracking changes in your menstrual cycle on a calendar can be helpful. • While there is a good way to detect endometrial cancer (endometrial biopsy), routine screening isn't typically recommended for people with Cowden syndrome. Some patients and providers decide together to do an endometrial biopsy every 1 to 2 years, starting by age 35. • Talk to your provider about the option of hysterectomy after childbearing. The ovaries and fallopian tubes are typically left intact.
Colorectal cancer	• If you don't have any signs or symptoms of colorectal cancer, colonoscopy is recommended every 5 years starting at age 35. • If a close relative was diagnosed with colorectal cancer before age 40, start screening 5 to 10 years before they were diagnosed.
Kidney cancer	Talk to your provider about having a kidney ultrasound every 1 to 2 years, starting at age 40.
Skin cancer	A yearly dermatology exam is recommended.
Thyroid cancer	A yearly thyroid ultrasound is recommended starting at age 12.

Gene-specific care

The charts that follow provide recommendations for lowering your cancer risk based on your genetic testing results.

The recommendations are presented alphabetically by gene.

ATM

Increased risk of	Recommended steps to lower your risk
Breast cancer	Get a yearly mammogram starting at age 40. Your provider may recommend breast MRI starting at age 30 or 35, based on your age, family history, breast density, and preferences.
Epithelial ovarian cancer	There isn't enough evidence to recommend risk-reducing salpingo-oophorectomy (RRSO). Care is guided by your family history.
Pancreatic cancer	See pages 27-28 for information on pancreatic cancer screening.
Prostate cancer	There is growing evidence of a link between the *ATM* gene and prostate cancer. Your provider may check your PSA level yearly, starting at age 40.
Other cancer risks	People with this variant are at increased risk of colorectal cancer. Speak with your provider about screening recommendations and other care.

BARD1

Increased risk of	Recommended steps to lower your risk
Breast cancer	Get a yearly mammogram starting at age 40. Your provider may recommend breast MRI (in addition to mammography), also starting at age 40, based on your age, family history, breast density, and preferences.

BRCA1 and *BRCA2* (continued on next page)

Increased risk of	Recommended steps to lower your risk
Breast cancer (in people assigned female at birth)	**Breast awareness:** Start becoming familiar with your breasts at an early age and report any changes to your doctor. Self exams can help. **Age 25 to 75:** Clinical breast exams are recommended every 6 to 12 months. **Age 25 to 29:** Breast MRI is recommended yearly (if a family member was diagnosed with breast cancer before age 30, you and your doctor will decide together when to start screening with MRI) **Age 30 to 75:** A yearly mammogram **and** breast MRI are recommended. **Risk-reducing mastectomy** is an option. Your provider will explain the risks of surgery, the extent of cancer protection it provides, the possible effects on your quality of life, and your options for breast reconstruction. After mastectomy you should continue receiving clinical breast exams, but don't need routine screening with mammogram and breast MRI. **Risk-reducing agents (medicines)** are an option your doctor will consider to help lower your risk.
Breast cancer (in people assigned male at birth)	Starting at age 35: • Breast self-exam training and education • Clinical breast exam every 12 months Your provider may recommend a yearly mammogram, starting at age 50 or 10 years before the earliest male breast cancer in the family (whichever comes first).
Melanoma	There aren't specific recommendations for screening for melanoma. Steps you can take to reduce your risk include limiting your exposure to ultraviolet (UV) rays from sunlight, avoiding UV-based tanning beds, and receiving yearly full-body skin exams.

BRCA1 and *BRCA2* (continued)

Increased risk of	Recommended steps to lower your risk
Ovarian cancer	• If desired, speak with a fertility specialist to discuss family planning. • Nonsurgical options to lower risk include birth control pills (with both estrogen and progestin) and levonorgestrel IUDs. • For *BRCA1* carriers, RRSO is recommended between age 35 and 40. For *BRCA2* carriers, it may be delayed until age 40 to 45. • Option of hysterectomy at time of RRSO. • Menopausal hormone therapy can help with menopause symptoms. • Removing the fallopian tubes first (and the ovaries later) may be an option if you're not ready to lose your ovaries and want tubal ligation.
Pancreatic cancer	See page 27 for information on pancreatic cancer screening.
Prostate cancer	Starting at age 40, yearly screening with PSA is recommended for *BRCA2* carriers and **may be** recommended for *BRCA1* carriers. Screening may also include a baseline multiparametric MRI by age 50, or a different age depending on your family history.

BRIP1

Increased risk of	Recommended steps to lower your risk
Epithelial ovarian cancer	Risk-reducing salpingo-oophorectomy is recommended around age 45 to 50.

CDH1

Increased risk of	Recommended steps to lower your risk
Breast cancer	• Get a yearly mammogram starting at age 30. • Your provider may recommend breast MRI in addition to mammograms. • Risk-reducing mastectomy is an option.
Other cancer risks	People with this variant are at increased risk of hereditary diffuse gastric cancer (HDGC). Ask your provider what this means for your care.

CDKN2A

Increased risk of	Recommended steps to lower your risk
Melanoma	A whole-body skin exam by a dermatologist, including total body photography and dermoscopy, is recommended every 6 months.
Pancreatic cancer	See page 27 for information on pancreatic cancer screening.
Other cancer risks	Nerve sheath tumors, sarcomas, and other cancers are also possible. Your provider may suggest surveillance beyond screening for pancreatic cancer and melanoma. This might include yearly full-body and brain MRI.

CHEK2

Increased risk of	Recommended steps to lower your risk
Breast cancer	• Get a yearly mammogram starting at age 40. • Considering your age, family history, breast density, and preferences, your provider may recommend breast MRI starting at age 30 to 35.
Prostate cancer	There is growing evidence of a link between the *CHEK2* gene and prostate cancer. Your provider may recommend yearly screening with PSA starting at age 40.

HOXB13

Increased risk of	Recommended steps to lower your risk
Prostate cancer	Your provider may recommend yearly screening with PSA starting at age 40.

MSH2, MLH1, MSH6, PMS2, EPCAM (associated with Lynch syndrome)

Lynch syndrome is the most common cause of hereditary colon and endometrial (uterine) cancers. Families with Lynch syndrome are also at increased risk of urothelial, brain, gastrointestinal, ovarian, breast, pancreatic, biliary, and other cancers.

The criteria for testing for Lynch syndrome and care for a positive result is beyond the scope of this guide. For more information, health care providers are encouraged to refer to the *NCCN Clinical Practice Guidelines in Oncology for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric*.

NF1

Increased risk of	Recommended steps to lower your risk
Breast cancer	• Start having yearly mammograms at age 30. • Your provider may also recommend breast MRI from age 30 to 50.
Other cancer risks	You may be at increased risk of malignant peripheral nerve sheath tumors, gastrointestinal stromal tumors (GIST), and others. Seeing an *NF1* specialist is recommended.

PALB2

Increased risk of	Recommended steps to lower your risk
Breast cancer	• Start having yearly mammograms and breast MRI at age 30 • Discuss the option of risk-reducing mastectomy with your provider. • For those assigned male at birth, your provider may recommend the same breast cancer screening strategy recommended for *BRCA* carriers.
Epithelial ovarian cancer	Talk to your provider about the option of RRSO around age 45 or 50.
Pancreatic cancer	See page 27 for information on pancreatic cancer screening.

PTEN (associated with Cowden syndrome)

People with germline PTEN variants are at increased risk of breast, thyroid, colorectal, endometrial, and kidney cancer. See pages 34-5 for information on Cowden syndrome/PTEN hamartoma tumor syndrome (PHTS).

RAD51C and *RAD51D*

Increased risk of	Recommended steps to lower your risk
Breast cancer	• Start having yearly mammograms at age 40 • Your provider may recommend breast MRI in addition to mammography (also starting at age 40). Other care is guided by your family history.
Epithelial ovarian cancer	RRSO is recommended around age 45 or 50.

STK11 (associated with Peutz-Jeghers syndrome)

Peutz-Jeghers syndrome (PJS) is a hereditary cancer syndrome that causes benign tumors to grow in the gastrointestinal tract and dark spots to form on the skin. People with PJS have a high risk of developing cancers of the **breast, colon, stomach, ovaries, small intestine, pancreas, cervix, uterus, lungs, and testes**. Most people with PJS have a cancer-causing germline variant in the *STK11* gene.

Genetic testing for PJS and care for a positive result are beyond the scope of this guide. For more information, health care providers are encouraged to refer to the *NCCN Clinical Practice Guidelines in Oncology for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric*. See below for information on managing breast and pancreatic cancer risk in people with this variant.

Breast cancer	• Get a yearly mammogram and breast MRI starting at age 30. • Discuss the option of risk-reducing mastectomy with your provider.
Pancreatic cancer	See page 27 for information on pancreatic cancer screening.

TP53 (associated with Li-Fraumeni syndrome)

Li-Fraumeni syndrome (LFS) is caused by a pathogenic variant in the *TP53* gene. Families with LFS have a high risk of developing a range of cancers, especially **sarcomas, leukemias, brain cancers, breast cancers, and adrenocortical tumors**.

Many other cancers have been linked with LFS, including melanoma, colorectal, gastric, malignant phyllodes, and prostate cancers. See pages 31-32 for information on Li-Fraumeni syndrome.

Key points

- In people diagnosed with breast cancer, genetic testing decisions are based on age, ancestry, family history, cancer type, and cancer features. If results are positive, your provider may recommend managing your risk with clinical breast exams, mammograms, breast MRIs, risk-reducing mastectomy, or risk-reducing drugs.
- Genetic testing is recommended for everyone diagnosed with epithelial ovarian cancer (at any age) and for their first- and second-degree blood relatives. If results are positive, risk-reducing salpingo-oophorectomy may be recommended to lower your risk. Menopausal hormone therapy (MHT) may be an option to relieve symptoms of surgical menopause.
- Genetic testing is recommended for everyone diagnosed with exocrine pancreatic cancer. If results are positive, your provider may recommend yearly screening with magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound (EUS) once you reach a certain age.
- In people diagnosed with prostate cancer, genetic testing decisions are based on ancestry, family history, cancer stage, and cancer risk level. If results are positive, your provider may recommend yearly blood tests to check your prostate specific antigen (PSA) level.
- Genetic testing for Li-Fraumeni syndrome is recommended if you meet specific criteria, if a germline TP53 variant runs in your family, and in some other situations. In adults with a positive result, frequent physical exams and yearly MRIs (whole-body and brain) are recommended. Mammograms and breast MRIs are recommended to manage breast cancer risk. Risk-reducing mastectomy is also an option.
- Genetic testing is recommended for people with a clinical diagnosis of Cowden syndrome/PTEN hamartoma tumor syndrome and in some other situations. If results are positive, care to manage your risk involves having yearly physical exams; staying alert for signs of endometrial cancer; and screening for breast, colorectal, kidney, skin, and thyroid cancers. Risk-reducing mastectomy is an option to lower breast cancer risk.

Questions to ask

- Based on my results, am I at risk for any cancers? If so, which one(s)?
- Does having risk-reducing surgery to prevent ovarian or breast cancer mean that I'll never develop those cancers?
- Is risk-reducing mastectomy something I need to consider? If so, who can help me decide?

4
Other resources

16 Questions to ask

47 What else to know

47 What else to do

47 Where to get help

48 Questions to ask

Want to learn more? Here's how you can get additional help.

What else to know

This guide helps you know your options so you can make informed decisions and improve your cancer care. But it's not the only resource that you have.

Ask for as much information and help as you need. Many people are interested in learning more about:

- Managing side effects
- Genetic testing
- Building a support system
- Lifestyle changes after cancer
- Coping with other health problems

What else to do

Your health care center can help you with next steps. It often has on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself.

Where to get help

Look through the list below and visit the provided websites to learn more about these organizations.

Breastcancer.org
breastcancer.org

Breast Cancer Alliance
breastcanceralliance.org

CanCare, Inc.
cancare.org

Cancer*Care*
cancercare.org

Cancer Hope Network
cancerhopenetwork.org

DiepC Foundation
diepcfoundation.org

FORCE: Facing Hereditary Cancer Empowered
facingourrisk.org

GPAC Global Patient Advocacy Coalition
gpacunited.org

GRACE
cancergrace.org

HIS Breast Cancer Awareness
hisbreastcancer.org

Imerman Angels
imermanangels.org

Lustgarten Foundation
lustgarten.org

My Faulty Gene
myfaultygene.org

National Ovarian Cancer Coalition
ovarian.org

Ovarcome
ovarcome.org

Ovarian Cancer Research Alliance
ocrahope.org

Sharsheret
sharsheret.org

Triage Cancer
triagecancer.org

Questions to ask

- Who can I talk to about help with housing, food, and other basic needs?
- What help is available for transportation, childcare, and home care?
- Are there other services available to me and my caregivers?



Words to know

***BRCA1 and BRCA2* genes**
Related genes everyone is born with. When working properly, they perform helpful jobs, including cell repair. When damaged, they increase the risk of developing breast, ovarian, prostate, pancreatic, colorectal, and other cancers.

cancer predisposition genes
Genes that—if altered in specific ways—increase your risk of developing certain types of cancer. Also called cancer susceptibility genes.

clinical breast exam (CBE)
A physical exam of the breast performed by a health care provider to check for lumps or other changes.

close blood relatives
Close blood relatives include first-, second-, and third-degree relatives on the same side of the family.

epithelial ovarian cancer
The most common type of ovarian cancer. Starts in the surface layer of tissue surrounding the fallopian tubes and ovaries.

fallopian tube
A thin tube through which an egg travels from the ovary to the uterus. Where most ovarian cancers start.

founder variant
A disease-causing variant that occurs frequently in distinct groups of people whose shared ancestor(s) carried the variant.

genetic counseling
A discussion with a health expert about the risk for a disease caused by changes in genes.

genetic testing
Testing of the blood, saliva, or other samples for germline (inherited) variants that cause cancer.

germline variant
A gene difference passed from a parent to their biological child(ren).

Li-Fraumeni syndrome (LFS)
A hereditary cancer syndrome caused by a cancer-causing variant in the TP53 gene. Families with LFS have a high risk of developing sarcomas, leukemias, brain cancers, breast cancers, and adrenocortical tumors.

mammogram
A picture of the inside of the breast made using x-rays.

menopausal hormone therapy (MHT)
The use of hormones to lessen side effects of menopause. This approach used to be called hormone replacement therapy (HRT).

next-generation sequencing (NGS)
Testing a sample for many gene variants at one time. Also called a multigene panel.

pathogenic/likely pathogenic (P/LP) variant
A variant (difference) in a gene that increases your risk of developing 1 or more cancers.

penetrance
Describes how likely someone with an inherited cancer-causing variant is to develop signs and symptoms of the cancer. Not everyone who has the variant will develop the cancer.

Peutz-Jeghers syndrome (PJS)
A hereditary cancer syndrome in which many polyps form in the lining of the gastrointestinal (GI) tract and dark spots appear on the skin. Increases the risk of developing cancers of the GI tract, breast, pancreas, ovary, lung, and cervix. PJS is usually caused by differences in the STK11 gene.

risk-reducing mastectomy (RRM)
Surgery that removes the whole breast to lower the risk of developing breast cancer.

risk-reducing salpingo-oophorectomy (RRSO)
Surgery that removes the ovaries and fallopian tubes to lower the risk of ovarian cancer, fallopian tube cancer, and primary peritoneal cancers in people at high risk.

screening mammogram
X-rays of the breasts taken to look for cancer in someone without signs or symptoms of breast cancer.

somatic mutation
A non-hereditary change in your DNA that occurred sometime after you were conceived. Also called acquired mutation or tumor mutation.

surgical menopause
The forced start of menopause caused by surgery to remove the ovaries. Results from the sudden drop in estrogen in your body.

variant
A difference in a gene that may be helpful, harmful, or have no (known) effect on your health. Variants you are born with are called germline variants.



Take our survey and help make the NCCN Guidelines for Patients better for everyone!

NCCN.org/patients/comments

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate, Version 3.2026. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS
Assistant Vice President
Patient Information

Erin Vidic, MA
Senior Medical Writer, Patient Information

Susan Kidney
Senior Graphic Design Specialist

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate, Version 3.2026, were developed by the following NCCN Panel Members:

Mary B. Daly, MD, PhD/Chair
Fox Chase Cancer Center

Tuya Pal, MD/Vice-Chair
Vanderbilt-Ingram Cancer Center

Zahraa AlHilli, MD
Case Comprehensive Cancer Center/ University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

Banu Arun, MD
The University of Texas MD Anderson Cancer Center

Heather H. Cheng, MD, PhD
Fred Hutchinson Cancer Center

Jane Churpek, MD, MS
University of Wisconsin Carbone Cancer Center

Sarah Colonna, MD, MSCI
Huntsman Cancer Institute at the University of Utah

Susan M. Domchek, MD
Abramson Cancer Center at the University of Pennsylvania

Mauricio R. Escobar, MD
O'Neal Comprehensive Cancer Center at UAB

Laura Fejerman, PhD, MSc
UC Davis Comprehensive Cancer Center

*Susan Friedman, DVM
FORCE: Facing Our Risk of Cancer Empowered

Veda N. Giri, MD
Yale Cancer Center/Smilow Cancer Hospital

Michael Goggins, MD
Johns Hopkins Kimmel Cancer Center

Andrea Hagemann, MD, MSCI
Siteman Cancer Center at Barnes- Jewish Hospital and WashU Medicine

Ashley Hendrix, MD, MBA
St. Jude Children's Research Hospital/ The University of Tennessee Health Science Center

Dezheng Huo, PhD
The UChicago Medicine Comprehensive Cancer Center

Mollie L. Hutton, MS, CGC
Roswell Park Comprehensive Cancer Center

Beth Y. Karlan, MD
UCLA Jonsson Comprehensive Cancer Center

Nawal Kassem, MD, MS
Indiana University Melvin and Bren Simon Comprehensive Cancer Center

Seema Khan, MD
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Katia Khoury, MD
O'Neal Comprehensive Cancer Center at UAB

Allison W. Kurian, MD, MSc
Stanford Cancer Institute

Christine Laronga, MD
Moffitt Cancer Center

Julie S. Mak, MS, MSc, CGC
UCSF Helen Diller Family Comprehensive Cancer Center

Kara N. Maxwell, MD, PhD
Abramson Cancer Center at the University of Pennsylvania

Kevin McDonnell, MD, PhD
City of Hope National Medical Center

Carolyn S. Menendez, MD
Duke Cancer Institute

Sofia D. Merajver, MD, PhD
University of Michigan Rogel Cancer Center

Jacqueline Mersch, MS, CGC
UT Southwestern Simmons Comprehensive Cancer Center

Barbara S. Norquist, MD
Fred Hutchinson Cancer Center

Kenneth Offit, MD, MPH
Memorial Sloan Kettering Cancer Center

*Jennifer Plichta, MD, MS
Duke Cancer Institute

Dominique Rash, MD
UC San Diego Moores Cancer Center

Gwen Reiser, MS, CGC
Fred & Pamela Buffett Cancer Center

Leigha Senter-Jamieson, MS, CGC
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

*Kristen Mahoney Shannon, MS, CGC
Mass General Cancer Center

Jeanna Welborn, MD
UC Davis Comprehensive Cancer Center

Myra J. Wick, MD, PhD
Mayo Clinic Comprehensive Cancer Center

Marie Wood, MD
University of Colorado Cancer Center

Matthew B. Yurgelun, MD
Dana-Farber/Brigham and Women's Cancer Center

NCCN

Susan Darlow, PhD
Associate Director, Guidelines Digitization

Zeenat Diwan, MS, PhD
Associate Scientist/Medical Writer

Mary Dwyer, MS
Senior Director, Guidelines Operations

* Reviewed this patient guide. For disclosures, visit NCCN.org/disclosures.

NCCN Cancer Centers

For contact information, visit NCCN.org/cancercenters.

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio

City of Hope National Medical Center
Duarte, California

Dana-Farber Cancer Institute
Boston, Massachusetts

Duke Cancer Institute
Durham, North Carolina

Fox Chase Cancer Center
Philadelphia, Pennsylvania

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska

Fred Hutchinson Cancer Center
Seattle, Washington

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah

Indiana University Melvin and Bren Simon
Comprehensive Cancer Center
Indianapolis, Indiana

Johns Hopkins Kimmel Cancer Center
Baltimore, Maryland

Mass General Brigham Cancer Institute
Boston, Massachusetts

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota

Memorial Sloan Kettering Cancer Center
New York, New York

Moffitt Cancer Center
Tampa, Florida

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama

Robert H. Lurie Comprehensive Cancer Center
of Northwestern University
Chicago, Illinois

Roswell Park Comprehensive Cancer Center
Buffalo, New York

Siteman Cancer Center at Barnes-Jewish Hospital
and WashU Medicine
St. Louis, Missouri

St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center
Memphis, Tennessee

Stanford Cancer Institute
Stanford, California

The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute
Columbus, Ohio

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois

The University of Texas MD Anderson Cancer Center
Houston, Texas

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Los Angeles, California

UCSF Helen Diller Family Comprehensive Cancer Center
San Francisco, California

University of Colorado Cancer Center
Aurora, Colorado

University of Michigan Rogel Cancer Center
Ann Arbor, Michigan

University of Wisconsin Carbone Cancer Center
Madison, Wisconsin

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee

Yale Cancer Center/Smilow Cancer Hospital
New Haven, Connecticut

Index

aromatase inhibitors 23

Ashkenazi Jewish ancestry 10, 18–19

Cowden syndrome 5, 18, 22, 34–37

family planning 13–14, 40

in vitro fertilization (IVF) 13–14

levonorgestrel intrauterine device (IUD) 25–26, 40

Li-Fraumeni syndrome (LFS) 18, 22, 31–32

magnetic resonance cholangiopancreatography (MRCP) 28

mammogram 19, 21, 33, 36, 38–39, 41–44

menopausal hormone therapy 25–26, 40

mosaic results 15

penetrance 6

pre-implantation genetic testing (PGT) 13–14

prenatal diagnosis 14

PSA test 30, 33, 38, 40–42

recreational genetic testing 12

risk-reducing mastectomy (RRM) 39, 41, 43–44

risk-reducing salpingo-oophorectomy (RRSO) 10, 24–26, 40, 43

tamoxifen 23

thyroid cancer 34–37

tubal ligation 26, 40

variant of uncertain significance (VUS) 14



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Genetic Testing for Hereditary Breast, Ovarian, Pancreatic, and Prostate Cancers



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3025 Chemical Road, Suite 100
Plymouth Meeting, PA 19462
215.690.0300

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PAT-N-1983-1026