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# Genetic counseling for hereditary cancer

## A primer for NPs

***Abstract: Many patients have concerns regarding their family's cancer history and may be appropriate for referral to genetic counseling. This article examines indications for referral for genetic counseling for hereditary cancer, the process of genetic counseling and testing, and ways for NPs to collaborate with genetics providers.***

**By Kate McReynolds, MSc, MSN, APRN, ANP-BC, AGN-BC and Sara Lewis, MS, LCGC**

Most hereditary cancer syndromes significantly increase the risk of multiple types of cancer, and many patients are concerned that cancer may be "running in the family." Identifying patients when there is concern for a hereditary cancer syndrome and providing ongoing support for these individuals are key tasks for NPs. It has been 20 years since the first commercial test for hereditary breast and ovarian cancer syndrome (HBOC) was offered, which sequenced the BRCA1 and BRCA2 genes using a blood sample. Since the first commercial test was developed, there have been many advances in testing for hereditary cancer susceptibility.

This article provides information to help NPs identify individuals who may benefit from a referral for genetic cancer counseling, review what happens during a genetic counseling appointment, and discuss how NPs can collaborate with genetics providers.

### What is genetic counseling?

The National Society of Genetic Counselors (NSGC) defines genetic counseling as:

> *…the process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease. This process integrates: the interpretation of family and medical history to assess the chance of disease occurrence or recurrence, education about inheritance, testing, management, prevention, resources, and research, and counseling to promote informed choices and adaptation to the risk or condition.*[1]

It is estimated that on average, approximately 5% to 10% of all cancers are caused by an inherited genetic mutation. Mutations may also be referred to as pathogenic variants or likely pathogenic variants. Family history collection is the key to identifying patients who should be referred for genetic counseling for cancer susceptibility.[2,3] Numerous organizations endorse collection of family health histories, including the CDC, the American Society of Clinical Oncology (ASCO), and the U.S. Preventive Services Task Force (USPSTF).[4-6]

The USPSTF recommends that primary care clinicians screen women with a family history of breast, ovarian, tubal, or peritoneal cancer for referral for genetic counseling and testing for HBOC.[6] It is also important to recognize individuals at risk for other hereditary cancer syndromes such as Lynch syndrome, which is often underrecognized.[7]

Families with a hereditary cancer predisposition often demonstrate certain features.[2,3,8-10] Patients with one or more

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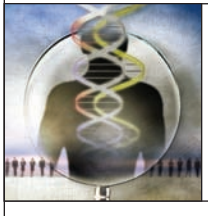
of the following features in their family may be appropriate for referral to a genetic specialist for further discussion of their family history:[3,8]

- Cancer diagnosed before age 50
- Multiple primary cancers or bilateral cancers in one individual
- Cancers that may be related in a syndrome and cancers in multiple generations
- Rare or unusual cancers or tumors in the family (adrenal cortical cancer, pheochromocytoma, male breast cancer)
- Certain benign tumors or lesions such as desmoid tumors, multiple adenomatous colon polyps, or certain skin findings (fibrofolliculoma)
- Certain ethnic backgrounds such as Eastern European Jewish ancestry.

When taking a family history, NPs should ask about cancer history in close blood relatives, which typically includes parents, siblings, children, nieces/nephews, aunts/uncles, grandparents, first cousins, and great aunts/uncles.[8] Hereditary cancer susceptibility will be most strongly suspected in a family when the cancers are all clustering on the same side of the family, although some families will have features of a hereditary cancer predisposition on both sides of the family. Both maternal and paternal family history is important to collect, as hereditary cancer susceptibility can be inherited from a mother or father.[8]



***It is best to begin the genetic risk assessment and testing process with an individual in the family who has a cancer diagnosis.***

Family history collection should not be a one-time event, as family histories are dynamic. Referral, or rereferral, to a genetics specialist is appropriate if there has been a significant change in personal and/or family history because this may change the genes in the differential diagnosis within a family. Additionally, new genes associated with hereditary cancer risk are rapidly being identified, resulting in the availability of new genetic testing options over time. It is possible that patients who previously tested negative could have a heritable mutation in a gene that was not previously tested.[11]

The Surgeon General's Family Health History Initiative website (www.hhs.gov/programs/prevention-and-wellness/family-health-history/index.html) has a family history tool that enables patients to collect their family health history. NPs may refer patients to this tool as a resource to help gather information and start the conversation about a possible hereditary cancer syndrome with their family.[12]

## Which family member should be tested first?

Whenever possible, it is best to begin the genetic risk assessment and testing process with an individual in the family who has a cancer diagnosis.[3] This individual will have the highest likelihood of having a germline mutation in a hereditary cancer susceptibility gene that could be detected with current technology. Testing results may influence whether genetic testing is appropriate for other relatives and clarify cancer risk for themselves and other family members. Unfortunately for many cancer families, testing an affected relative is not possible. In these situations, it is best to begin the testing process with a family member closest in bloodline to the affected individual, such as a child or a sibling.

## What happens during a genetic consult?

Several organizations, including ASCO and NSGC, recommend genetic risk assessment and counseling prior to completion of genetic testing.[2,13] These organizations have identified several elements to be discussed as part of the informed-consent process in a pretest setting. NSGC has also developed guidelines for posttest counseling. These include (but are not limited to) the following:

*Collection of the patient's medical history and collection of a three- to four-generation family pedigree.* The pedigree should include affected relatives who have been diagnosed with cancer as well as unaffected relatives. An individual's current age or age at death, his or her cancer type(s), and age(s) at diagnosis are recorded. Any surgical procedures that may have been completed that would reduce the cancer risk, such as risk-reducing bilateral mastectomies or total hysterectomy/bilateral salpingo-oophorectomy, are also noted.[2,5] Certain family characteristics such as small family size, a dominant gender, or an adoption are noted, as these characteristics can mask the presence of a hereditary cancer predisposition.[14]

*Discussion of the testing options for genes in the differential diagnosis.* There may be multiple genes that could explain the clustering of cancers in a family. Patients will be informed about the genes in the differential diagnosis and why those genes are under consideration. The discussion will also include information about how knowledge of a mutation in a particular gene may impact medical management.[2] In some families, testing may be specific for certain genes (or even specific mutations). In other families, multiple genes may be considered, and completion of a next-generation sequencing, multigene panel will allow for testing of all genes in the differential diagnosis simultaneously.

*Education regarding inheritance.* Most cancer susceptibility genes are inherited in an autosomal dominant manner,

where one copy of the mutation confers an increased risk for the cancers in the syndrome.[10] All first-degree relatives of a carrier would have a 50% chance of also having inherited the same mutation. Extended family members also may be at risk for having the identified mutation. While rare, some cancer predisposition genes may cause a different genetic syndrome if inherited in a recessive manner.[10] Education about the genetics of cancer is not mandated for informed consent but is often discussed during the initial visit.[2]

*Discussion of possible genetic testing results.* Results may be positive, negative, true negative, or a variant of uncertain significance (VUS).[2,13] A positive result (mutation found) means the patient is at increased risk of associated cancers, and the result will be used to assist in determining appropriate screening/risk reducing options. Genetic counseling and testing should be offered to other at-risk family members.

A negative result (when not testing for a mutation identified in another family member) means there is no detectable mutation in any of the genes tested. However, there may be a mutation in a different gene that was not tested or a mutation in the genes tested that was not detectable with the technology utilized. It is also possible that there may be a mutation in the family that the patient did not inherit. Genetic counseling and testing may still be warranted for other family members. The patient's cancer risk and screening plan will be based upon personal and/or family history.

A true negative result occurs when the patient tests negative for a known pathogenic mutation that was previously identified in a family member. In this case, the patient is not at significantly elevated genetic risk of cancer development. However, his or her risk of cancer development is not zero.

A VUS is a change in the DNA sequence of a gene that may or may not affect the function of the gene. It is possible that this change could be a pathogenic variant that elevates cancer risk. It also may be a benign variant that does not increase risk. This result is a common finding when testing with a panel of multiple genes and the presence of a VUS in multiple genes is not unexpected.[15]

Testing unaffected family members for a VUS is not recommended, as the presence or absence of this variant will not clarify their risk of cancer development. However, some labs offer testing for affected family members for a VUS in order to determine if this variant is tracking with the cancer diagnoses in the family.

## Social concerns

Many patients express concerns about how a health insurance company can use their genetic testing results. In the United States, the Genetic Information Nondiscrimination Act of 2008 is a federal law that protects most individuals from discrimination by health insurance companies and employers.[16] Cost of the counseling and testing is a frequent concern and barrier for patients.[17]

There may be two separate costs to patients: the cost of the counseling consult and the cost of genetic testing. Patients should be encouraged to determine if there is a charge for the consult and should contact their insurance company to determine if this is a covered expense. The cost of testing and the billing process are typically discussed during the genetic consult once appropriate testing options have been established.[2,13]

## Posttest discussion

*Results disclosure and patient medical management.* Patients will be informed of their results (positive, negative, true negative, VUS) and, if positive or a VUS, which gene(s) has this finding. A positive result will often direct appropriate risk management options, such as increased cancer screenings or consideration of risk-reducing surgery. The National Comprehensive Cancer Network and the American Cancer Society have established management guidelines for several cancer susceptibility genes.[8,18,19]

In situations where management guidelines are not available, cancer screenings should be based upon the patient's personal and/or family history. A VUS should not be used to make decisions related to medical management, as its impact on cancer risk is unknown. Instead, patient cancer risk should be based upon personal and family history.[8,18]

A negative result when not testing for a mutation previously identified in another family member should be interpreted carefully, as patients can construe a negative result in this scenario to mean they are not at increased risk of cancer development. Patients still may be at elevated risk of cancer development based upon their family history, and enhanced cancer screenings/surveillance may be warranted.

*Risk reassessment.* Cancer risk in patients positive for a hereditary cancer mutation will be determined based upon available data specific to the genetic mutation identified. For patients with a VUS or a negative result, personal and/or family history factors will be taken into consideration. Risk assessment models, if available, will be used to determine risk. Most of these models are for specific cancers, such as breast and colon. Examples of risk models that may be used include the Claus, Tyrer-Cuzick, or Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm models for breast cancer risk assessment or the National Cancer Institute's Colon Cancer Risk Assessment tool.[20-23]

*Implications for other family members.* The appropriateness of genetic testing for other family members will be readdressed. If there is a pathogenic mutation, testing will be recommended for first-degree relatives and may be considered for other family members. Testing is usually offered

to adults at risk for inheriting a mutation; testing children may be appropriate if the cancers in a syndrome occur in childhood.[24] If patients test negative, it may be helpful to test other family members, as a mutation could still be present in the family. A cancer risk assessment for other family members, such as children or siblings, may be completed to determine the best screening options.

*Psychosocial impact.* Patients may experience many different feelings related to their testing results. The emotional reaction to the test results will be assessed, and support will be provided.[2] In addition, coping strategies may be discussed. Information regarding patient support groups/resources will be provided to the patient if available.

## Who should provide genetic counseling and testing?

Ideally, genetic counseling is done by a provider who has undergone specific education and training to support individuals and families at increased risk of hereditary cancer. Historically, genetic counselors and clinical geneticists have been the main providers for those undergoing testing for hereditary cancer susceptibility. Genetic counselors are master's-prepared providers with specific education and board certification from the American Board of Genetic Counseling who provide education and support for those undergoing genetic testing.

There are currently about 4,000 genetic counselors in the United States shared among various disciplines, including cancer genetics, reproductive genetics, pediatrics genetics, and other specialties.[25] Clinical or medical geneticists are physicians, typically with a background in pediatrics or internal medicine, who have completed an accredited clinical genetics residency and are boarded by the American Board of Medical Genetics and Genomics.[26]

Patients with hereditary cancer risk may be seen by other physicians, such as surgeons, oncologists, gynecologists, and primary care providers who have undergone specific genetics education. In addition, nurses may provide hereditary cancer risk services. The American Nurses Association (ANA) in conjunction with the International Society of Nurses in Genetics (ISONG) have established multiple core competencies for nurses providing counseling in genetics and genomics.[27] However, it is recognized that there is currently a shortage of trained genetics providers in the United States (see *Locating a genetics provider*).[28]

In 2015, the American Nurses Credentialing Center began offering board certification in Advanced Genetics Nursing (AGN-BC) for master's-prepared nurses who specialize in genetics.[29] While there are currently few nurses certified in genetics, this new nursing specialty offers hope for increased access to patients and cutting-edge career opportunities for nurses.

### Locating a genetics provider

**Genetic Counseling Services**
www.geneticcounselingservices.com

**Informed DNA**
www.informeddna.com

**National Cancer Institute Cancer Genetics Services Directory**
www.cancer.gov/about-cancer/causes-prevention/genetics/directory

**National Society of Genetic Counselors Find a Genetic Counselor**
www.nsgc.org/p/cm/ld/fid=164

## How NPs can collaborate with genetics providers?

It is important to note that genomic competencies have been identified for all healthcare professionals, including NPs. Together, the ANA, ISONG, and the National Coalition for Health Professional Education in Genetics have established the "Essential Genetic and Genomic Competencies for Nurses with Graduate degrees."[30] NPs should familiarize themselves with these guidelines. To help support patients through the cancer genetic testing process, NPs should consider the following:

*Identify patients for referral.* NPs play a vital role in ensuring that patients with features concerning for a hereditary cancer syndrome are identified and appropriately referred for genetic counseling. Conversely, NPs can reassure those who are not at increased risk for cancer based on family history, thereby avoiding inappropriate referrals.

As detailed earlier, family history collection is a prerequisite for identifying individuals at increased genetic risk for cancer. Although there are significant time constraints and lack of widely acceptable tools to collect family history in the primary care setting, several promising family history tools have been developed that provide hope for the future.[31]

*Preparing patients.* It is important for NPs to have a basic understanding of what happens during a genetic counseling appointment and help patients understand why they are being referred. All too often, patients arrive for a genetic counseling appointment with a very limited understanding of the indication of why they are there. Providers also may explain the potential benefits of attending their appointment, which may include the possibility of finding out why a cancer has occurred, potential access to increased cancer screening in the future, and the opportunity to gain information that will help their wider family.

Patients should be encouraged to find out as much as possible about their family cancer history prior to their genetic counseling appointment. The goal of counseling is to assist patients in making an informed decision as to

whether testing is an appropriate option for them. They can also learn more about the benefits, risks, and limitations of testing before deciding to test. Genetic counseling for hereditary cancer syndromes involves a cancer risk assessment for patients and their families, and this does not always result in a recommendation for genetic testing. Concerns about genetic discrimination and cost should also be addressed.

*Management and emotional support.* Providing care following testing requires an understanding of patients' test results and its implications. If a mutation is identified (a positive result), the NP should become familiar with the major cancer risks for the syndrome and surveillance guidelines.[32] It is important to note that ordering cancer screening tests is out of the scope of practice for the genetic counselor.[1] Therefore, genetic counselors may require the ongoing assistance of the NP to ensure patients are getting necessary cancer screenings. For example, the NP may order breast magnetic resonance imaging for a patient who is positive for a mutation in a gene conferring a high risk of breast cancer, or order a colonoscopy for a patient with a mutation in a gene associated with significantly increased risk for colon cancer.

An ongoing challenge for patients and their providers is that testing with panels may reveal mutations in genes where cancer risks are not well defined and there is a lack of clinical management guidelines. In these situations, the NP may benefit from talking with a genetic specialist about the identified mutation and management considerations.

Finding a mutation in an individual or family member can cause anxiety and stress.[33] Although a positive gene test result may provide a helpful explanation for cancer in the family, it could indicate that the individual is at significantly increased risk for an initial cancer (if unaffected) or additional cancer (if already affected). The patient may have feelings of guilt about passing on a mutation to children and grandchildren and have anxiety about other loved ones' cancer risks if they also test positive. Sometimes, other family members choose not to be tested. This can cause worry and distress to individuals who have a mutation, as the untested relative may be missing out on early cancer screening/risk reducing measures if he or she were known to carry the familial mutation.

The degree of distress caused by a positive gene test result may be affected by the experience of loved ones with cancer. For example, the psychological impact on the individual may be stronger if the patient has lost a close family member to cancer.[34] Spouses and partners of mutation carriers also may experience stress when worrying about their significant others and children.[35]

It is also important to understand the psychological impact on family members who test negative for a known familial mutation. Although there is relief if they do not carry the mutation, many have feelings of survivor guilt, and some feel anger at the appropriate reduction of screening with a meaningful negative result.[32] Prior to genetic testing for a familial mutation, many family members have enhanced cancer surveillance based on the family history. This enhanced surveillance is no longer necessary if an individual is negative for a familial mutation and is not considered at increased genetic risk for cancer. Despite the negative result, it can be difficult to give up the safety net of additional screening when returning to surveillance- or population-based screening guidelines.[32]

The NP may provide support by referring some patients who experience distress going through the process of genetic counseling and testing to psychological counseling and/or prescribe antidepressants/anxiolytics (even if just short term).

## The NP's role

Identification of patients at risk for hereditary cancer is important to ensure patients obtain appropriate cancer screenings and risk-reducing measures based on their personalized level of risk. Genetic counseling for patients considering hereditary cancer testing is recommended by many organizations so patients are educated about the benefits and limitations of testing for themselves. Ideally, counseling and testing are offered by a provider with training and expertise in genetics. NPs can assist patients considering hereditary cancer testing in a variety of ways, including identifying those appropriate for referral, preparing them for the visit, and providing clinical management after testing results become available. NP

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Kate McReynolds is a genetic NP associate in medicine at the Division of Genetic Medicine, Clinical and Translational Hereditary Cancer Program, Vanderbilt University Medical Center, Nashville, Tenn.

Sara Lewis is a genetic counselor assistant in medicine at the Division of Genetic Medicine, Clinical and Translational Hereditary Cancer Program, Vanderbilt University Medical Center, Nashville, Tenn.

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