Hereditary Cancer Syndrome Recognition and Testing for the Primary Care Nurse Practitioner: Beyond BRCA

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Hereditary Cancer Syndrome Recognition and Testing for the
Primary Care Nurse Practitioner: Beyond BRCA

Hanford Blitch Shuman IV

A scholarly paper submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of

Master of Nursing

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ABSTRACT

Hereditary Cancer Syndrome Recognition and Testing for the Primary Care Nurse Practitioner: Beyond BRCA

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Hereditary cancer syndromes, resulting from mutations of tumor-suppressor genes, can significantly increase risk for breast cancer. While Hereditary Breast and Ovarian Cancer Syndrome caused by BRCA1/2 mutations is well known, less well-known hereditary cancer syndromes also exist. This clinical practice feature focuses on three other syndromes including, Li-Fraumeni, Cowden, and Peutz-Jeghers. This article will help prepare nurse practitioners to recognize key features of these syndromes and understand testing criteria. Additionally, this article discusses barriers to diagnosing hereditary cancer syndromes and the role of primary care nurse practitioners in ordering genetic tests and making genetic referrals for optimal patient care.

Keywords: Cowden hamartoma tumor syndrome, genetic testing, hereditary cancer syndrome, Li-Fraumeni syndrome, Peutz-Jeghers syndrome, primary care nurse practitioner
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Hereditary Cancer Syndrome Recognition and Testing for the
Primary Care Nurse Practitioner: Beyond BRCA

Introduction

More than 50 hereditary cancer syndromes (HCSs) have been identified and contribute to the development of 5-10% of all cancers. (PDQ Cancer Genetics Editorial Board, 2019) Most clinicians have a basic knowledge and awareness of \textit{BRCA1} and \textit{BRCA2} gene mutations as major causes of the HCS known as Hereditary Breast and Ovarian Cancer (HBOC) Syndrome. However, other gene mutations leading to other HCSs also increase risk for breast cancer. Examples of these syndromes include, Li-Fraumeni Syndrome (LFS); Cowden Hamartoma Tumor Syndrome, or Cowden Syndrome (CS); and Peutz-Jeghers Syndrome (PJS) (National Comprehensive Cancer Network, 2020) (see table 1). Although uncommon, each of these syndromes pose risks to individuals who inherit related mutations. Because they are uncommon, many patients may go undiagnosed for years, minimizing their ability to reduce risk.

Primary care providers (PCPs), including nurse practitioners (NPs) are gatekeepers in healthcare. Patients depend on PCPs’ expertise to guide them through the network of specialties and resources needed to treat and prevent diseases. Primary care NPs must be prepared to identify patients at risk for HCSs, encourage genetic testing when appropriate, and properly refer patients to genetic counselors.

Although patients rely on PCPs for guidance about genetic risk and testing, PCPs’ knowledge of HCSs may be limited because many are rare diseases only recently discovered and described. For example, in the years following the discovery of BRCA-related HBOC, PCPs have struggled to correctly identify, test, and refer these patients. (Bellcross et al., 2011; Bellcross, Leadbetter, Alford, & Peipins, 2013; Nair et al., 2017; Trivers et al., 2011) In contrast, many average-risk women, not meeting
criteria for genetic counseling or BRCA testing, have been offered counseling and/or testing. (Trivers et al., 2011) Although many PCPs are aware of BRCA testing, few have ordered it (Bellcross et al., 2011). Approximately, 90% of high-risk women meeting USPSTF criteria for counseling referral and testing have reported sharing their risk factors with their PCPs, yet only 20% were actually referred, and 8% were tested. (Bellcross et al., 2013) More recently, 44% of PCPs reported routinely referring patients for genetic counseling; most of them showed deficits in their understanding of HBOC. (Nair et al., 2017)

In spite of knowledge limitations, 81.5% of PCPs reported high interest in HBOC education. (Nair et al., 2017) Researchers have called for educational programs to “focus on narrowing the knowledge gap between basic genetics and clinical medicine, because identification of individuals at risk for HBOC [and other HCSs] is a critical first step to ensuring access to cancer genetics services and risk reducing interventions.” (Nair et al., 2017) The aim of this article is to inform primary care nurse practitioners about clinical characteristics and testing criteria, for three hereditary cancer syndromes associated with breast cancer and to encourage early recognition, appropriate genetic testing, and referral for genetic services.
Table 1
Comparison of Autosomal Dominant Hereditary Cancer Syndromes Associated with Breast Cancer

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Associated Tumor Suppressor Gene</th>
<th>Lifetime Risk for Breast Cancer with Syndrome</th>
<th>Other Malignancies/Conditions in Syndrome</th>
<th>De Novo Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary Breast and Ovarian Cancer Syndrome (HBOC)</td>
<td>BRCA1</td>
<td>46%-87% [Petrucelli, Daly, &amp; Feldman, 2010]</td>
<td>Ovarian</td>
<td>&lt;5% [Petrucelli et al., 2010]</td>
</tr>
<tr>
<td></td>
<td>BRCA2</td>
<td>38%-84% [Petrucelli et al., 2010]</td>
<td>Ovarian</td>
<td>&lt;5% [Petrucelli et al., 2010]</td>
</tr>
<tr>
<td>Li-Fraumeni Syndrome (LFS)</td>
<td>TP-53</td>
<td>85% [Mai et al., 2016]</td>
<td>Soft tissue sarcomas</td>
<td>7%-20% [Schneider K., 1999 Jan 19]</td>
</tr>
<tr>
<td></td>
<td>PTEN</td>
<td>85% [Eng, 2001 Nov 29]</td>
<td>Thyroid disease</td>
<td>10.7%-47.6% [Mester &amp; Eng, 2012]</td>
</tr>
<tr>
<td></td>
<td>STK11</td>
<td>45% [Hearle et al., 2006]</td>
<td>Gastrointestinal hamartomatous polyps</td>
<td>Unknown; approximately 45% of affected individuals have no family history of PJS [McGarrity, Amos, &amp; Baker, 2001 Feb 23]</td>
</tr>
</tbody>
</table>

**Li-Fraumeni Syndrome (LFS)**

Li-Fraumeni Syndrome (LFS) is a rare autosomal-dominant HCS associated with germline mutations in *TP53*, a cancer suppressor gene, which codes for the p53 tumor suppressor
protein. (Nandikolla, Venugopal, & Anampa, 2017) LFS was originally described by Li and Fraumeni in 1969 while analyzing families with childhood rhabdomysarcoma. TP53 mutations are highly penetrant, with a cumulative lifetime risk for developing some type of cancer at nearly 100% by age 70 years, and an 85% cumulative lifetime risk of developing breast cancer by age 60 years. (Mai et al., 2016; National Comprehensive Cancer Network, 2020)

LFS predisposes individuals to soft tissue sarcomas, osteosarcomas, breast cancer, colon cancer, gastric cancer, adrenocortical carcinoma, and brain tumors. Approximately 1% of all hereditary breast cancer cases are attributed to the presence of a TP53 gene mutation. (Sidransky et al., 1992) The syndrome is characterized by development of certain cancers at ages earlier than expected. For example, of all breast cancers and soft tissue sarcomas associated with LFS, 80% develop before the age of 45 years. (Vogel, 2017) Women appear to be more prone to any early cancer with a 50% chance by age 31 years and 90-100% by age 60 years. In comparison, men exhibit a 50% chance of any cancer development by age 46 years and 73% lifetime risk. (Mai et al., 2016)

In some cases, cancer onset occurs especially early. Frequently, children with LFS are found with soft tissue sarcomas, brain tumors, and adrenocortical carcinomas. (National Comprehensive Cancer Network, 2020) Studies have suggested a higher prevalence of individuals with germline TP53 mutations than previously thought, between 1 in 5,000 and 1 in 20,000. (Gonzalez et al., 2009; Laloo et al., 2003) It is suspected that there are other mutations that may also responsible for LFS characteristics.

**Identifying Patients for Li-Fraumeni Syndrome (LFS) Genetic Testing**

The National Comprehensive Cancer Network (NCCN) recommends using a combination of two sets of criteria to select patients for LFS testing, Classic LFS criteria and the Chompret criteria. (National Comprehensive Cancer Network, 2020) See table 2. Chompret criteria can be met
regardless of family history, allowing for detection of de novo \textit{TP53} germline variants that would be missed using Classic LFS criteria alone. (Chompret et al., 2001; Tinat et al., 2009) When both sets of criteria are used together, sensitivity increases to 95% from the estimated 40% that is seen with the use of Classic LFS criteria alone. (Gonzalez et al., 2009)

Testing may also be considered for patients that do not meet Classic LFS or Chompret criteria. \textit{TP53} germline mutations are commonly found in women with early-onset breast cancer; 3% to 8% of those with breast cancer before age 30 years with no family history have \textit{TP53} mutations. (Gonzalez et al., 2009) Thus, the NCCN recommends that women who develop breast cancer before age 30 years be considered for testing. (National Comprehensive Cancer Network, 2020) Cancer survivors should be tested because if they carry a harmful mutation, having this knowledge will qualify them for intensive cancer surveillance so that future cancers may be caught at earlier stages. Similarly, any person having a first-degree blood relative with a known \textit{TP53} mutation should consider testing.

Table 2

\begin{tabular}{|l|l|l|}
\hline
\textit{Li-Fraumeni Syndrome (LFS) Testing Criteria} & \textit{Classic LFS Criteria} & \textit{Chompret Criteria} \textit{(Chompret et al., 2001; Tinat et al., 2009)} \textit{Additional NCCN Recommendations} \textit{(National Comprehensive Cancer Network, 2020)} \\
\hline
Any individual diagnosed with sarcoma under age 45 years with: & Any individual with multiple primary tumors under age 36 years, including at least 2 of the following & Any individual with breast cancer before age 30 years \textbf{Any individual with a blood relative diagnosed with \textit{P53} mutation} \\
- One 1\textsuperscript{st} degree relative diagnosed with cancer under age 45 years AND & - Sarcoma & \textbf{Any individual with breast cancer before age 30 years} \\
- One additional 1\textsuperscript{st} or 2\textsuperscript{nd} degree relative diagnosed with cancer under age 45 years or sarcoma at any age & - Breast cancer & \textbf{Any individual with a blood relative diagnosed with \textit{P53} mutation} \\
& - Adrenocortical carcinoma & \\
& - Brain tumor OR & \\
& Adrenocortical carcinoma at any age & \\
\hline
\end{tabular}
Cowden Syndrome (CS)

Cowden Syndrome (CS) is a disorder, inherited in an autosomal-dominant pattern that predisposes individuals to a number of conditions and cancers, including breast cancer, thyroid disease, thyroid cancer, macrocephaly, paired organ cancer, endometrial cancer, brain tumors, vascular malformations, and various mucocutaneous lesions. (National Comprehensive Cancer Network, 2020) Lloyd and Dennis (Lloyd & Dennis, 1963) were the first to identify CS based on unique clinical findings of a 20 year-old woman with the surname of Cowden.

The syndrome most often stems from a germline pathogenic mutation in the PTEN tumor suppressor gene (approximately 85% of the time), but other gene mutations are also suspected to cause CS. (PDQ Cancer Genetics Editorial Board, 2019) PTEN germline mutations do not always result in CS. Rather, CS is one of multiple syndromes associated with PTEN mutations, including; Bannayan-Riley-Ruvalcaba Syndrome, Proteus Syndrome, adult Lhermitte-Duclose Disease, and autism spectrum disorders with macrocephaly. However, these other syndromes are not typically associated with breast cancer. Collectively, this spectrum of disorders is known as the PTEN hamartoma tumor syndrome.

CS itself is understood to occur in about 1 in 200,000 people; however, considering the challenge of accurate clinical diagnosis, this figure is likely an underestimate. (National Comprehensive Cancer Network, 2020; Nelen et al., 1999) Penetrance is usually high at 80%. Multiple tumor-like hamartoma lesions with an associated increased risk for multiple cancers characterize CS. Breast cancer is the most frequently found malignancy in CS. (Nelen et al., 1999) Women with CS have an 85% lifetime risk of developing breast cancer, with an average age of 38 to 46 years at diagnosis. (Eng. 2001 Nov 29) Hamartomas form most frequently on the skin and mucous membranes. Other common sites include breast, thyroid, endometrium, and brain. (National Comprehensive Cancer Network, 2020)
Benign mucocutaneous lesions occur in an estimated 99% of individuals with CS, and most often manifest in patients’ twenties. (Pilarski & Eng, 2004) Gastrointestinal polyps occur in most patients. Patients with CS may present with a number of different lesions (see table 3); thyroid disorders like multinodular goiter, adenomatous nodules, and follicular adenomas are common, and lifetime risk for thyroid cancer is approximately 3% to 10%. (National Comprehensive Cancer Network, 2020) 

Macrocephaly, defined as having a head circumference in the 97th percentile, or 58 cm for females, 60 cm for males, is an especially common manifestation in CS, occurring in 80% to 100% of patients. (Pilarski et al., 2013; Roche, Mukherjee, Guo, & Moore, 1987) Strong associations have been found between CS and Lhermitte-Duclose Disease and autism spectrum disorder characterized by macrocephaly. (Zhou et al., 2003) Patients with CS exhibit some risk of developing endometrial cancer, brain tumors, vascular malformations, and colon cancer. (National Comprehensive Cancer Network, 2020) Cumulative risk for developing any cancer and/or Lhermitte-Duclose Disease by age 60 years is estimated to be 56% for men and 87% for women. (Nieuwenhuis et al., 2014)

**Identifying Patients for Cowden Syndrome (CS) Genetic Testing**

The NCCN (National Comprehensive Cancer Network, 2020) suggests the use of three sets of criteria, and various combinations of each, to evaluate the need for genetic testing for CS. See table 3. The first criteria set includes individuals meeting diagnostic criteria for CS with a history of certain diagnoses or a family history positive for a known PTEN mutation. The second and third criteria sets include identified “major” and “minor” features of CS. (National Comprehensive Cancer Network, 2020) Patients may meet different combinations of these categorized criteria, and are considered to meet threshold criteria if they meet any of the conditions in table 2. Testing may also be considered for those not meeting criteria with symptoms of concern, suggestive personal cancer histories, or suggestive family histories. (National Comprehensive Cancer Network, 2020)
Table 3
Cowden Syndrome (CS) Testing Criteria

Individuals meeting any of the following warrant testing:

- Meets at least one stand-alone criteria
- 2 or more major criteria, with one being macrocephaly
- 3 or more major criteria, without one being macrocephaly
- 1 major criterion and 3 or more minor criteria. If 2 or more major criteria are met without one being macrocephaly, then 1 may be counted as 1 of the 3 minor criteria in this case.
- 1 or more major criteria or 2 or more minor criteria, AND a relative diagnosed with Cowden Syndrome/PHTS or Bannayan-Riley-Ruvalcaba Syndrome.

<table>
<thead>
<tr>
<th>Stand-alone Criteria</th>
<th>Major Criteria</th>
<th>Minor Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meets diagnostic criteria for Cowden Syndrome</td>
<td>Breast cancer</td>
<td>Autism Spectrum Disorder without macrocephaly</td>
</tr>
<tr>
<td>History of Bannayan-Riley-Ruvalcaba Syndrome</td>
<td>Macrocephaly</td>
<td>Colon cancer</td>
</tr>
<tr>
<td>History of adult Lhermitte-Duclose Disease</td>
<td>Endometrial cancer</td>
<td>Esophageal glycogenic acanthosis, 3 or more</td>
</tr>
<tr>
<td>Autism Spectrum Disorder with macrocephaly</td>
<td>Follicular thyroid cancer</td>
<td>Lipomas</td>
</tr>
<tr>
<td>2 or more biopsy-proven trichilemommas</td>
<td>Multiple gastrointestinal hamartomas or ganglioneuromas</td>
<td>Intellectual disability</td>
</tr>
<tr>
<td>Family history with a known PTEN mutation</td>
<td>Macular pigmentation of glans penis</td>
<td>Papillary thyroid cancer, papillary or follicular variant</td>
</tr>
<tr>
<td></td>
<td>Mucocutaneous lesions (Trichilemommas, palmoplantar keratoses, oral mucosal papillomatoses, cutaneous facial papules)</td>
<td>Other thyroid structural lesions; adenoma, nodules, goiter, etc.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Renal cell carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>One gastrointestinal hamartoma or ganglioneuroma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Testicular lipomatosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vascular anomalies</td>
</tr>
</tbody>
</table>

Individuals not meeting testing criteria should be followed according to his/her personal cancer history and family history. (National Comprehensive Cancer Network, 2020)

Peutz-Jeghers Syndrome (PJS)

Peutz-Jeghers Syndrome (PJS) is an autosomal dominant HCS most often caused by a mutation in the STK11 tumor suppressor gene. Few cases characteristic of PJS have been identified without this mutation. Gastrointestinal hamartomatous polyps, most frequently in the stomach and intestines, are characteristic of PJS. In children, darkly-pigmented spots can often
be found on the oral mucosa, and around the eyes, nostrils, and anus. These spots often fade with age. When asked, young adults may recall the presence of these spots during childhood.

PJS greatly increases an individual’s risk for gastrointestinal, pancreatic, cervical, ovarian, and breast cancers. Prevalence of PJS is estimated to be between 1 in 25,000 and 1 in 300,000 (U. S. National Library of Medicine, 2013). Penetrance in affected individuals is high. Risk for developing any first cancer has been shown to be 2% by age 20 years and increase gradually with age to reach 85% by age 70 years (Hearle et al., 2006). In addition, women with PJS have an increased risk for developing breast cancer, with 8% by age 40 years, increasing to 45% by age 70 years (Hearle et al., 2006).

**Identifying Patients for Peutz-Jeghers Syndrome (PJS) Genetic Testing**

PJS should be suspected in individuals presenting with two or more PJS-type intestinal polyps, mucocutaneous macules, gynecomastia in males as a result of estrogen-producing Sertoli cell testicular tumors, or a history of intussusception (especially in a child or young adult) (McGarrity et al., 2001 Feb 23). Testing for PJS is recommended when an individual meets any one of four conditions in table 4. Additionally, testing may be considered when patients present with other concerning symptoms or histories under circumstances in which these criteria are not met.

**Table 4**

*Peutz-Jeghers Syndrome (PJS) Testing Criteria*

<table>
<thead>
<tr>
<th>Individuals meeting any one of these criteria should be tested (Beggs et al., 2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• More than 2 histologically confirmed PJS-type hamartomatous gastrointestinal polyps</td>
</tr>
<tr>
<td>• Any number of PJS-type polyps with a family history of PJS in close relatives</td>
</tr>
<tr>
<td>• Characteristic mucocutaneous pigmentation, with a family history of PJS in close relatives</td>
</tr>
<tr>
<td>• Any number of PJS-type polyps, along with characteristic mucocutaneous pigmentation</td>
</tr>
</tbody>
</table>
Barriers to Identification of Hereditary Cancer Syndromes (HCS)

Beyond the need for further PCP education, other barriers to HCS patient detection and counseling exist. These include incomplete collection and assessment of family histories, time constraints, patient perceptions and beliefs, limited patient knowledge, and financial concerns. While most providers collect family histories with all patients, family histories are often incomplete and not routinely assessed for genetic risk factors. It is important to recognize that family history collection should not be a one-time event, as family histories are ever changing. (McReynolds & Lewis, 2017) Time constraints and other pressures may limit complete collection and assessment. Even with electronic family history-taking tools that allow patients to electronically enter their own family history information and give providers organized pedigree and risk information, providers have been found to only refer 54% of those for whom a genetic counseling referral is recommended. (Buchanan et al., 2015)

While providers experience barriers to making genetic referrals, patients also experience barriers to receiving genetic counseling and testing after being referred by a PCP. Only 8% of women identified by family history as high-risk for hereditary breast cancer went to a genetic counseling appointment within one year of receiving a referral. (Kne et al., 2017) Among women who did not go through with a genetic counseling appointment, three main barriers were identified. First, patient-held perceptions may prevent follow through with referrals. For example, patients might not perceive urgency or benefit to undergoing counseling; patients may not believe they are at risk or believe that breast cancer in their families was due to genetic causes. Second, women lacked knowledge about genetic counseling and its purpose. Women worried about the complexity of genetic services and feared the possibility of a positive test. Third, women worried about financial challenges. They feared genetic counseling would bring high costs of
testing and management, cause challenges dealing with insurance companies, and result in insurance discrimination. (Kne et al., 2017) Many women of this study also discussed the fact that their PCP, when presented with a letter identifying high risk based on family history taken during screening mammograms, were often dismissive of the letter or ignored it completely and did not recommend genetic counseling. (Kne et al., 2017)

Although patients experience multiple barriers, certain factors have proven to motivate and facilitate in their decision to seek genetic counseling and testing. Most importantly, more verbal discussion with PCPs, along with more written information and a strong recommendation for counseling encourage the uptake of counseling and testing. (Kne et al., 2017) Thus, PCPs play an important role in helping high-risk women receive genetic counseling services and testing. They must be thorough in collecting and assessing family histories, well-versed in basic genetics, ready to educate and provide information, and highly encouraging genetic counseling services.

**PCP-NP Role in Genetic Testing**

Genetic counselors are experts in reviewing pedigrees, selecting genetic tests, and providing pre- and post-test counseling. However, relying exclusively on genetic counselors to recommend genetic testing presents a dilemma. Currently in the United States, there are only 4,000 genetic counselors, less than one counselor per 80,000 people living in the U.S. (Bookman, 2016 Apr 21) Because of challenges finding a counselor and wait times for visits, individuals needing services may opt not to follow through with referrals. If they decide to be seen, they may wait for months for an appointment. Another option is for PCPs to provide appropriate pre-test counseling and order genetic testing for high-risk individuals before meeting with genetic counselors. Patients with positive findings could then attend genetic counseling appointment
with results in-hand, allowing for much faster adoption of risk-reducing and screening interventions.

A process intervention study assessing the integration of routine hereditary cancer risk assessment, counseling, and genetic testing in OB/GYN practices found it is feasible to incorporate hereditary cancer risk assessment, education, and testing into community obstetrics and gynecology practices. (DeFrancesco et al., 2018) In this study, OB/GYN providers were appropriately trained and acted competently in assessing risk and ordering tests. Both providers and patients reported high levels of confidence and satisfaction with the process, and the number of patients who underwent genetic testing increased eightfold over the previous year. (DeFrancesco et al., 2018) This finding implies that during the previous year many patients who would have qualified for genetic testing and would have accepted it did not receive that option. As PCPs develop knowledge and skills in assessing family pedigrees for genetic risk and ordering genetic tests with appropriate pre-test counseling, more patients will benefit from receiving personalized risk information.

**Multi-gene Panel Testing**

PCPs should consider the utility of ordering multigene panel testing as opposed to single gene testing. Previously, single gene testing has been standard practice. However, multigene panel testing can be more efficacious for several reasons. Primarily, less common HCS, such as the three discussed in this article, may go undetected for great lengths of time if PCPs order single gene tests. Multigene panel testing has the ability to identify significant cancer risks that otherwise would not be recognized, and it enables appropriate risk-reducing medical management decisions. (DeFrancesco et al., 2018) In studies of women already diagnosed with breast cancer, half of all pathogenic variants identified among individuals meeting HBOC criteria were
in genes other than *BRCA1/2*. In other words, panel testing revealed twice as many women with genetic risk for breast cancer than single gene testing for *BRCA1/2* would have. (Buys et al., 2017; Rosenthal, Bernhisel, Brown, Kidd, & Manley, 2017) Panel testing allows for quicker diagnosis of HCSs and thus greater opportunity for risk-reducing surveillance and potentially greater uptake of genetic counseling services.

**Conclusion**

Various HCSs beyond *BRCA*-related HBOC predispose many individuals to breast and other cancers. As gatekeepers of healthcare, primary care nurse practitioners must be prepared to identify patients at risk for HCSs and guide them through genetic testing, referral, and follow-up care. Multiple provider and patient factors act as barriers to the utilization of genetic resources. Among other barriers, limitations in provider knowledge and understanding of genetic disorders prove to be a prominent barrier, but most providers express high interest in learning more about genetic principles and HCSs. Due to barriers, many high-risk patients who have inherited a HCS may be currently undiagnosed, thus inhibiting the ability to initiate risk-reducing measures. In this article, three less common HCSs, their etiologies, and recommended testing criteria have been reviewed in an effort to inform provider practice. As genetic counselor availability is limited, PCPs have the opportunity to be a valuable genetics resource for many individuals. Primary care nurse practitioners should identify patients with presentations and family histories consistent with HCSs, and either offer pre-test counseling and order multi-gene panel testing or refer at-risk people to genetic counseling. Finally, all patients with positive findings should be referred for genetic counseling for support and recommendations on prevention and screening.
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Kne, A., Zierhut, H., Baldinger, S., Swenson, K. K., Mink, P., Veach, P. M., & Tsai, M. L. (2017). Why Is Cancer Genetic Counseling Underutilized by Women Identified as at Risk for


Hereditary Cancer Syndrome Recognition and Testing


Appendix

Definitions:

**Hereditary Cancer Syndrome (HCS)** – An inherited genetic mutation or variant that predisposes an individual to certain types of cancer.

**Autosomal dominant inheritance** – A pattern of inheritance in which an affected dominant autosomal gene is passed on to offspring. This results in a 50% chance that offspring will inherit at least one affected dominant gene and manifest the associated disorder.

**De novo mutation** – A genetic variation that occurs for the first time in an individual as the result of a mutation in a parental germ cell or in the fertilized egg.

**Germline mutation** – A variation in a reproductive cell, egg or sperm, that is passed to all subsequently developed cells in the offspring.

**Penetrance** – The likelihood that a disorder or disease will manifest itself in the presence of the corresponding genotype. Usually described by the individual’s age, sex, and organ site.

**Positive predictive value** – The likelihood that a positive test result corresponds with the true presence of the particular suspected disorder.