CD summary
June 28, 2016 | Volume 65, Number 6
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Using Genomics for Cancer Prevention

Cancer is the leading cause of death in Oregon — in 2014, 4,117 men, and 3,745 women died of cancer. One in every two men, and one in every three women will develop an invasive cancer at some point in their lifetime. The risk of developing cancer depends on a number factors, including age (being older), risk behaviors (e.g. smoking), infectious agents (e.g. human papilloma virus), environmental exposures (e.g. sun, radiation), and genetics.

An estimated 5%–10% of all cancers are due to hereditary genetic mutations. Individuals with inherited mutations are at higher risk of cancer than the general population, they are also at higher risk of developing cancer at a younger age and of developing multiple primary cancers. These higher risk individuals must be identified early in order to implement prevention, early detection and treatment strategies. By definition, hereditary mutations run in families. Therefore, identifying a significant mutation in an affected individual can lead to identifying the mutation in other family members prior to disease onset. Knowing that a person carries a hereditary mutation leads to different screening and treatment options.

The Centers for Disease Control and Prevention, Office of Public Health Genomics ranks genomic tests and family health history applications by levels of evidence.[1] "Tier 1" genetic tests are recommended for implementation in practice based on systematic review of clinical practice guidelines and are covered by the Centers for Medicare and Medicaid Services (CMS). Hereditary breast and ovarian cancer (HBOC) and Lynch Syndrome are two hereditary cancer syndromes covered under Tier 1 genomic testing applications. Proper identification and referral of patients with HBOC and Lynch Syndrome has the potential to save many lives, since breast, ovarian and colorectal cancer consistently rank in the top ten leading causes of cancer incidence and cancer mortality. This *CD Summary* presents information for healthcare providers on how to identify these individuals, when to refer patients for genetic testing based on family health history, and resources for more information.

Hereditary breast and ovarian cancer

Heredity Breast and Ovarian Cancer (HBOC) is primarily caused by mutations to tumor suppressor genes, aka *BRCA1* or *BRCA2*. About 1 in every 500 women in the U.S. has a

BRCA gene mutation. Individuals with *BRCA* mutations have a much greater likelihood of developing breast and ovarian cancer by age 70 than the general population: 65% vs. 12% for breast cancer and 39% vs. 1% for ovarian cancer.[2,3] Mutations to these genes are also associated with increased risk of other cancers, such as prostate and pancreatic cancer. Family health history is the key component in assessing patient risk for HBOC. Appropriate family health history collection is described in detail in our previous *CD Summary.**

Once increased-risk individuals have been identified based on family history, they should be referred to a genetic counselor to receive further evaluation and testing, if appropriate. If a mutation is identified, other family members can be tested for the mutation. Treatment options for those with HBOC may include: risk-reducing medications (such as tamoxifen), risk-based mammography (earlier and/or increased screening), bilateral mastectomy, or bilateral salpingo-oophorectomy (Table).

Table. Summary of Tier 1 Cancer Genomic Screening Recommendations

Condition	Recommendation	Risk mitigation options
Hereditary breast and ovarian cancer	*Screen for high-risk family history associated with HBOC *If positive, refer patient for genetic counseling *If indicated after counseling, patient receives genetic testing	Risk-reducing medications (e.g. tamoxifen), risk-based mammography, bilateral mastectomy, bilateral salpino-oophroectomy
Lynch Syndrome	*Genetic testing among newly diagnosed colorectal cancer cases to identify LS *Cascade testing of close relatives to identify other LS cases	Colonoscopy age 25 or earlier Screen based only on colonoscopy

Lynch syndrome

Lynch Syndrome, also known as Hereditary Non-Polyposis Colorectal Cancer Syndrome, is another Tier 1 cancer genomics application. Individuals with Lynch Syndrome have a much higher likelihood of developing colorectal cancer by age 70 than the general population: 40% vs. 4%.[4] Lynch Syndrome is also associated with increased risk for other cancers, such as endometrial, ovarian, and stomach. The population incidence of Lynch Syndrome is estimated to be 1 in 370.[5]

One Tier 1 strategy for identifying Lynch Syndrome individuals is Universal Tumor Screening. Universal tumor screening is currently recommended for all colorectal cancer tissue samples to identify those that are Lynch Syndrome. Once a Lynch Syndrome case has been identified, asymptomatic family members of that patient can be contacted and tested – a process called "cascade testing" – because the first degree relatives of those affected with Lynch Syndrome have 50% chance of having the condition.

* See December 3, 2013 *CD Summary*, "Beyond Angelina Jolie: Inherited Breast and Ovarian Cancer", https://public.health.oregon.gov/DiseasesConditions/CommunicableDisease/CDSummaryNewsletter/Documents/2013/ohd6225.pdf.

Any asymptomatic family members who are found to have Lynch Syndrome can then begin enhanced surveillance protocols, such as earlier or more frequent colorectal cancer screenings (Table).

According to CDC's Office of Public Health Genomics, genetic counseling and testing for Lynch Syndrome is recommended for individuals who:

- Were diagnosed with colorectal cancer in the past
- Were diagnosed with endometrial cancer (especially if it was under age 50)
- Have multiple family members with colorectal cancer or other Lynch Syndrome -associated cancers
- Have a first-degree relative with Lynch Syndrome (parent, sibling, child).

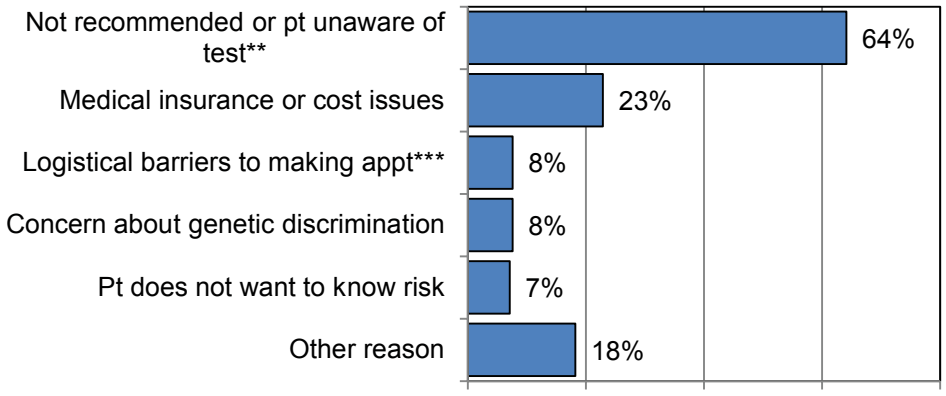
Some Oregon providers already provide Universal Tumor Screening and cascade screening to their patients. Three Oregon institutions are members of the Lynch Syndrome Screening Network www.lynchscreening.net), an organization promoting Universal Tumor Screening. Other providers who are not members may also be doing Universal Tumor Screening; however, many are not. A 2014 survey of Oregon and Washington gastroenterologists showed that only a third were doing Universal Tumor Screening.

Barriers

Data from several sources show that Oregon patients who should be referred for genetic counseling and testing are not getting appropriate care. According to the 2011 Oregon Behavior Risk Factor Surveillance System (BRFSS) survey, 63% of adult Oregon women with HBOC increased-risk family histories† that would make them appropriate candidates for genetic counseling and testing had never seen a genetic counselor and had never heard of the BRCA genetic test.

A more recent study conducted in 2013 and 2014 by the Oregon Genetics Program, in collaboration with the Oregon Cancer

Figure. Reasons for NOT receiving genetic counseling of testing services among Oregon cancer survivors*



*Data comes from an Oregon Genetics Program survey of Oregon high-risk breast and ovarian cancer survivors identified through collaboration with the Oregon Cancer Registry. Data as of 3/24/2014. NOTE: Categories are not mutually exclusive.
**This category includes patients whose doctor never told them about the test, patients whose doctor discouraged counseling or testing, and patients who never knew the test existed.
***Logistical barriers include transportation, distance, time, child care, or health issues.

† As defined by the United States Preventive Services Task Force (USPSTF) 2013 recommendation statement, "Risk Assessment, Genetic Counseling, and Genetic Testing for BRA-Related Cancer in Women", available at www.uspreventiveservicestaskforce.org/uspstf/uspsbrgen.htm.

Registry (OSCaR), surveyed cancer survivors with specific high-risk breast cancer types that would warrant referral to a genetic counselor. Among respondents who did not receive genetic counseling or testing, 64% indicated "no one ever recommended" genetic services to them, or their doctor "told them not to go" for genetic testing or counseling (Figure).

A 2012 national survey of primary care physicians showed a large degree of variability in physician familiarity with available genetic services, which could account for some of these patient-reported barriers.[6] Among those physicians who said they did have access to a genetics specialist, 72.5% indicated they used those services. Unfortunately, 53.4% of physicians indicated that they did not have access to genetics expertise. However, the study noted that this may have been lack of awareness of genetic services available. Improving physician awareness of available genetic counselors in the state may improve referral and testing rates.

Oregon resources

- **Genetic Specialists**. Oregon has several genetic specialists working in cancer genetics clinics across the state, in both on-site clinics as well as telemedicine locations. The Oregon Genetics Program has a list of all genetics programs, including cancer genetics clinics, and their contact information at https://public.health.oregon.gov/DiseasesConditions/GeneticConditions/Documents/Contacts_GeneticClinics.pdf.
- **Heredity Breast and Ovarian Cancer**: Several tools are available to physicians to help identify HBOC patients. A new educational program called "Hereditary Breast and Ovarian Cancer: Is Your Patient at High Risk?" is available on the National Coalition for Health Professional Education in Genetics (NCHPEG) website: http://www.nchpeg.org/hboc. The program is available for up to two Category 1 CME credits through Michigan University at no cost until October 19, 2016.
- **The Breast Cancer Genetics Referral Screening Tool**, or B-RST, recommended by the USPSTF, can be used to identify patients who should be referred for genetic counseling. It is available at: http://www.breastcancergenescreen.org/default.aspx.
- **Lynch Syndrome:** More information on Lynch Syndrome screening is available on the CDC website: http://www.cdc.gov/features/lynchsyndrome/.

For more information

- Contact the Oregon Genetics Program at 971-673-0273, Oregon.geneticsprogram@state.or.us
- CDC Public Health Genomics website. http://www.cdc.gov/genomics/
- CDC Public Health Genomics grand rounds, April 19, 2016: www.cdc.gov/

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OHA 8130 (06/2016)