August, 2015

Stakeholder Feedback to Proposed Genetic Testing Policy

Robin Fennimore, MD, FACOG

I am one of the faculty physicians at St. Joseph's Ob-Gyn Residency clinic in Denver. I understand that Medicaid is proposing to change their guidelines for coverage of multi-gene hereditary cancer testing, myRisk, which would not be available to our Colorado Medicaid members.

According to the National Comprehensive Cancer Network (NCCN) and Society of Gynecological Oncologists (SGO) guidelines, panel testing may be more efficient and/or cost effective. Particularly, for those cases where there is an overlap of cancers within a patient's personal or family history of cancer. This comprehensive understanding of an individual's cancer risk allows us to tailor management more accurately and deliver optimal medical recommendations.

Part of our mission statement is to continually improve the health and quality of life of people in the community we serve. This includes identifying patients at risk for hereditary cancers, stratifying their risk, and offering appropriate recommendations. We have recently implemented a protocol within our Seton Women's Care clinic, which includes hereditary panel testing with myRisk. This technology has allowed us to detect known cancer-causing gene mutations so that we can offer risk-reducing strategies to our patients who our affected. As a teaching institution, it's essential that we offer our residents and faculty the most up-to-date diagnostic tools available to us. As obstetrician-gynecologists, we are responsible for identifying at-risk patients and catering our care to help them avoid life-threatening diseases.

Currently, we are caring for a 35 year old pregnant patient who has a family history remarkable for breast, ovarian, colon, and pancreatic cancers. Rather than making a guess at which syndrome to test for (BRCA or Lynch syndrome), we ordered myRisk and uncovered her MLH1 mutation (Lynch syndrome). This information has significant implications toward her management and what we are now able to offer her. If we would have selected BRCA testing based on family history, we would have missed her 80+% colon, 70+% uterine and 12% ovarian cancer risk. The guidelines for this patient, once she is done child bearing are to remove her uterus and ovaries, and she is already 10 years behind her screening colonoscopy. If we miss these opportunities of panel testing, the implications for her future health are significant. Her family history had overlapping cancers, which is right in line with the indication of panel testing.

Up to 40% of our patient population is Medicaid, so a proposed change would greatly impact our patients. I would stress that Medicaid continue coverage of myRisk, particulary in our teaching setting. We are a progressive program that practices standard of care. All of our patients, including Medicaid patients, deserve access to myRisk testing.

August, 2015

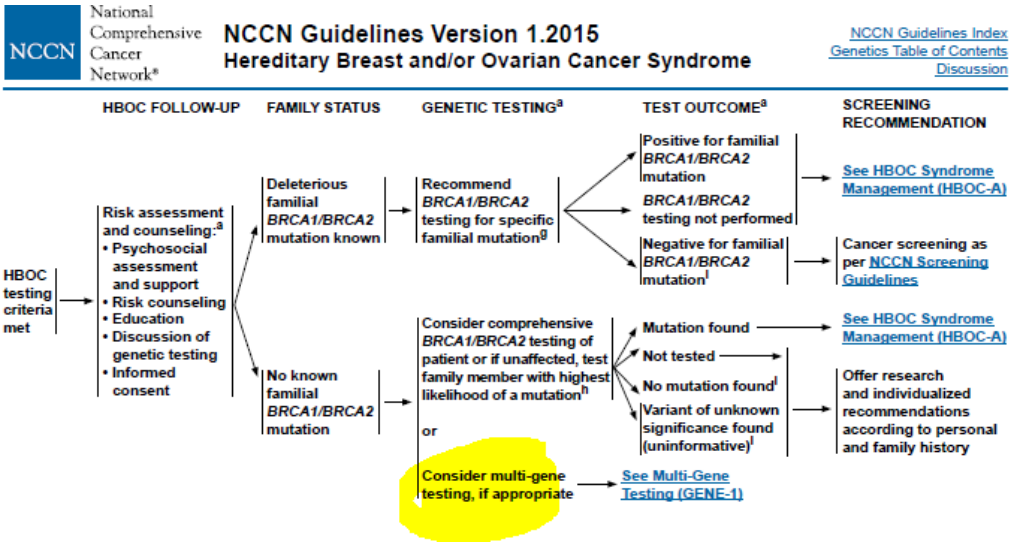
Kelli Swan, MS, MA, CGC

Thank you for taking time to review coverage of genetic testing within the state of Colorado. I am very pleased to see increased coverage for Lynch Syndrome testing. Thank you for making this positive change.

It is outside my scope to comment on anything outside of cancer genetics so I will leave those comments to medical providers who do specialize in those areas. Offering genetic testing to all appropriate patients who have a family history of cancer and meet current national testing guidelines is extremely important as it dictates appropriate cancer screening *and* prevention measures. These tests are cost effective to the health care system as cancer prevention is much cheaper than cancer treatment.

A few opportunities for improvement that I'd like to highlight include:

- Coverage of multi-gene panel next generation sequencing testing for hereditary cancers (myRisk testing).
  - Single syndrome testing has quickly become replaced by multi-gene panel testing as the new standard of care in cancer genetics. It is now known that multiple different genes can be associated with hereditary risk of cancer. By being limited to single syndrome tests, we will miss the opportunity to identify more mutation carriers and prevent more cancer. This will lead to cancer treatment costs that could have been prevented.
  - 2015 NCCN guidelines include multi gene panel testing as an option for first line testing for



  patients who meet Hereditary Breast and Ovarian Cancer testing criteria.
- In
- March of 2014, the Society of Gynecology Oncology published a practice statement which highlights the benefits of multi gene panel testing. Below is a summary of their practice statement. Benefits of panel testing include, cost-effectiveness and increased efficiency at obtaining a diagnosis.

SGO Clinical Practice Statement: Next Generation Cancer Gene Panels Versus Gene by Gene Testing, March 2014:

Knowledgeable health care providers and/or genetic counselors should discuss the limitations and advantages of NGS cancer gene panels with patients.

"Cancer panels allow testing of all genes in parallel without substantially increasing the cost, leading to a different clinical algorithm in which all known contributing genes can be assayed at first evaluation."

The main limitation of cancer gene panels is the potential complexity of results interpretation for medical management of the patient. The many advantages include:

- Increased cost-effectiveness
- Increased efficiency at obtaining a diagnosis, which reduces the number of patients who undergo a "diagnostic odyssey" that consists of several appointments and diagnostic tests over a period of time, to learn the underlying cause of the cancers in the family.
- Increased reassurance: "A negative genetic test is more reassuring at eliminating the likelihood of inherited risk when all known genes for that phenotype have been assayed."

BOTTOM LINE:

SGO states that "the advent of next generation sequencing has led to an era of inexpensive, high throughput DNA sequencing, which is having a major impact on both cancer research and clinical care."

References:
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2. Saam, J et al. (2014, March). Evaluating the personal and family history overlap between hereditary cancer syndromes. Presented at the National Comprehensive Cancer Network (NCCN), Hollywood, FL.
3. SGO Clinical Practice Statement: Next Generation Cancer Gene Panels Versus Gene by Gene Testing. Society of Gynecologic Oncology Web site. https://www.sgo.org/clinical-practice/guidelines/next-generation-cancer-genepanels-versus-gene-by-gene-testing/. Published March 2014. Accessed May 14, 2014.

Thank you for taking the time to consider this important aspects of coverage in helping to make sure Colorado Medicaid patients receive the same standard of care as all other Colorado patients.

Sarah Silver Payne, MD

I understand there is a proposal to guidelines indicating that multi-gene hereditary cancer testing would not be available to Colorado Medicaid members. I am an Obstetrician-Gynecologist in South metro Denver, and have extensive experience testing high-risk patients with the myRisk panel test. We have a fair amount of Medicaid patients.

Our practice follows ACOG, and the National Comprehensive Cancer Network (NCCN) guidelines to identify who is at increased risk for hereditary cancers. Specifically, breast, ovarian, uterine, colon and pancreatic cancers. My experience has been that several patient personal and family histories contain overlap of these cancers, so it's prudent that I am able to order a panel, rather than trying to tease out a single syndrome. Furthermore, selecting a single test could lead to false sense of security for me and my patients. It's my responsibility to guide and manage a patient's cancer risk when they present with a family history.

A recent example comes to mind where my unaffected patient presented with a maternal aunt with breast cancer under the age of 45, and I tested her with myRisk. She was done child-bearing, making a contraception choice, so it was critical I understood her breast and ovarian cancer risk, prior to making a recommendation. Her result was positive for a CHEK2 mutation (it gave me the information I needed for her ovaries), as well as, her breast cancer risk. She has up to a 48% lifetime risk of breast cancer, and an increased risk of colon cancer. If I tested her for the just the BRCA genes, we would have completely missed the opportunity to increase her

breast surveillance, including MRI, and referral to the breast surgeon. To me, this is exactly what the technology available to us through panel testing, offers. NCCN also has updates to their guidelines because it is now known that multiple different genes can be associated with hereditary risk of cancer. In my patient's case, this is precisely what occurred.

Let's move forward with the advanced technology panel testing offers our patients, and I urge Medicaid to continue covering a test, like myRisk. I would imagine the costs for a missed opportunity to prevent cancer, far outweighs coverage of a diagnostic test on the front end.

Karon Montgomery

In the wake of Medicaid's upcoming proposal to change their guidelines to make multi-gene hereditary cancer testing unavailable to Colorado Medicaid members, I wanted to stress the importance of these panels to being able to appropriately diagnosis and manage patients with hereditary cancer syndromes. The NCCN (National Comprehensive Cancer Network) guidelines recommend multi-gene panel testing and SGO (Society of Gynecological Oncologists) guidelines say that it is more cost effective and more effective in obtaining a complete diagnosis (see tables below). For example, for a patient with a personal or family history of breast cancer or ovarian cancer, only testing them for the BRCA1 and BRCA2 genes might miss a mutation in one of the other 11 breast cancer genes or 10 other ovarian cancer genes included in Myriad Genetics' myRisk hereditary cancer panel. We have had quite a few patients with strong family histories of breast cancer come back negative for a BRCA1 or BRCA2 mutation, only to test positive for an ATM, NBN or CHEK2 mutation. If we had not tested them using the multi-gene panel and only tested them for a BRCA1 or BRCA2 mutation, the mutations in these other genes would have been missed and their significantly increased risk for breast and other cancers would have gone undiagnosed. Because of the mutations found in these other genes, these patients are being managed appropriately to reduce their risk of developing cancer.

In my professional opinion, making multi-gene panels unavailable to Colorado Medicaid patients would be doing a great disservice to these patients by under-diagnosing many hereditary cancer syndromes and therefore taking away the opportunity to reduce the risk for cancer in this deserving patient population.

Karen Heller, MS, CGC, Medical Policy Specialist, Myriad Genetic Laboratories

Thank you for the ongoing work of the Department with the Genetic Testing Benefits Collaborative Process, and for the opportunity to provide input. We are grateful to see a broadening of coverage benefits in response to stakeholder comments to ensure beneficiaries receive the current standard of care and we support the Department's plan to review this policy on an annual basis.

We recognize that the Department has used the CDC Genomic Testing Tier system as the basis for the coverage policy. While the CDC Tier system is useful because it ranks tests based on the level of available evidence, practitioners generally reference practice guidelines to determine which patients are suitable to undergo each particular test, i.e. for the implementation of testing. The CDC system on its own does not readily translate to implementation for coverage. In order to provide more detailed information for healthcare providers, we encourage the use of NCCN guidelines.[1,2] Referring to NCCN guidelines for the tests you choose to cover based on evidence

in the CDC system will ensure that the most appropriate patients receive testing. Healthcare providers readily refer to NCCN guidelines to delineate which patients are appropriate candidates for testing for BRCA1/2 and for Lynch syndrome. NCCN guidelines are also the most well-recognized and widely utilized guidelines for testing and managing patients with hereditary cancer conditions. These guidelines are also regularly updated (at least annually), based on literature and consensus of the most experienced providers in the field at the world's leading cancer centers. It may be advisable for your coverage policy to reference the "current" NCCN guideline for each test that is chosen for coverage, so that the policy will always reflect the most current version and prevent additional workload of updating on the Department. Further, NCCN guidelines form the basis for test coverage criteria for Medicare, many Medicaid programs (including Oregon), as well as most private payors.

We would like to make a few specific suggestions (see below) to incorporate for BRCA testing criteria and Lynch syndrome testing criteria, based on NCCN guidelines. Please let us know if any clarifications are needed. We are happy to provide additional supporting data at your request.

Regarding BRCA testing:

1) The draft states only that "BRCA mutation testing is covered for individuals with a known Family History of BRCA related cancers, as specified on Tier 1". The concept of testing individuals based on their family history is derived from the U. S. Preventive Services Task Force guideline, which, by definition, is a preventive guideline targeted specifically to women without a personal history of cancer. However, the most common indications for BRCA testing are women with breast cancer at a young age or ovarian cancer at any age (with or without family history). As currently drafted, these indications are excluded. The information about hereditary cancer is critical to the management of women with cancer, as the risk for additional cancers will directly inform the management of the current cancer, [3-5] and the choice of therapy may be determined by the underlying genetic basis of the cancer.[6] Given the proliferation of personalized medicine, genetic testing of individuals with cancer is becoming more and more important.

2) The BRCA testing criteria as stated in the draft may be too broad and vague for effective implementation in the preauthorization process. CDC Tier 1 only states "family health history of breast/ovarian or other types of BRCA-related cancer". Utilizing the list of criteria in the NCCN guideline will provide clear coverage criteria, simplify the preauthorization process, and be consistent with the current standard of care.

- We encourage the draft to reference the current NCCN testing criteria for BRCA testing, as those criteria are very clearly delineated for both individuals with and without cancer. Please see page HBOC-1 in the NCCN Hereditary Breast and/or Ovarian Cancer syndrome guideline.[1] (Screenshot included at bottom of this document.)

Regarding testing for Lynch syndrome:

1. The draft appears to list the NCCN criteria for Lynch syndrome testing as listed in the CDC Tier 2; however, the draft has omitted two criteria that are standard, Medicare-covered and well-recognized NCCN criteria which happen to be included on the same CDC Tier 2 list. These missing criteria are (1) "endometrial cancer in women under 50 years of age" and (2) "synchronous or metachronous colorectal or other Lynch syndrome-related tumors, at any

age". It has long been recognized that the lifetime risk of endometrial cancer is similar to the risk of colorectal cancer in women with Lynch syndrome,[7] and the chance of Lynch syndrome in a woman with endometrial cancer under the age of 50 is about 9%.[8] The management of a woman with endometrial cancer will depend on whether or not she has Lynch syndrome, with the additional significant risk for other cancers. With regard to the criterion of synchronous/metachronous Lynch-related cancers, the occurrence of more than one cancer in the Lynch syndrome spectrum in the same individual greatly increases the likelihood of Lynch syndrome in that individual, regardless of age or family history,[9] and this criterion is a part of the Revised Bethesda guidelines[10] that form the basis of criteria for Lynch syndrome in NCCN and other guidelines.

- We encourage the draft to include coverage for the following criteria for Lynch syndrome:
  - endometrial cancer under age 50
  - synchronous or metachronous colorectal or other Lynch syndrome-related tumors, at any age

2. Since many individuals with Lynch syndrome who develop cancer will unfortunately die from their cancer prior to undergoing genetic testing, the NCCN guidelines include a provision to consider testing of unaffected family members when no affected member is available. While the criterion for 5% risk of Lynch syndrome in the draft will cover some of these at-risk individuals, the risk models have limitations and may miss someone with a family history meeting NCCN guidelines for Lynch testing. Adding a provision for testing unaffected family members would also be consistent with the BRCA testing approach for those with a family history of BRCA-related cancers.
   - We encourage the draft to add the following Lynch syndrome criterion for coverage:
     - First- or second-degree relative meeting criteria for testing for Lynch syndrome.

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