Laboratory Stewardship for Genetic Tests

According to the Utilization Review Accreditation Commission (URAC), utilization management is, "the evaluation of the medical necessity, appropriateness, and efficiency of the use of health care services, procedures and facilities under the provisions of the applicable health benefits plan, sometimes called 'utilization review'." Such reviews can take place prior to the onset of the service (prospective review) or after services have been rendered (retrospective review).

Laboratory stewardship is synonymous with the term utilization management and highlights the collaborative approach to assessing the appropriateness of a requested genetic test. Three guiding principles are generally applied in laboratory stewardship: Right test, right patient, right time. These guiding principles are outlined below and may also be helpful for informing genetic testing practices for ordering providers. Involving a genetic counselor in pre-test counseling and test selection can also be particularly helpful for navigating this decision making process.

Is it the right test?

Often the first step in review for genetic testing is determining if the selected test is the most appropriate test for the patient. There are several aspects that health plans consider when assessing the medical necessity of a test:

- **Analytical validity:** How well does a test predict the presence or absence of a particular genetic change or mutation?
- **Clinical validity:** How well does the genetic change being analyzed predict the presence, absence, or risk of a specific disease?
- **Clinical utility:** How well does the test provide information about the diagnosis, treatment, management, and/or prevention of a disease that will be helpful to the patient?
- **Test methodology:** Does the test utilize the most appropriate technology for this patient and this disorder? For example, if the most common genetic etiology for the suspected condition involves large gene deletions or duplications, sequence analysis may not be the best first-tier test. Also, a broad panel approach is less likely to be reimbursed by a payer if there is a targeted test that is available and more appropriate for that patient (see ***Multi-Gene Panels*** on page 8 for additional information about testing strategy.

Is it the right patient?

Compared to many other medical disciplines, genetics presents the unique challenge of having to evaluate the patient in the context of their family history. Many times, family history must be considered when it comes to utilization review of genetic testing. Healthcare providers, when faced with an unaffected patient, may be surprised to learn that their patient's affected relative is the most appropriate person to test **first** for a genetic condition. This is because the affected relative is more likely to have a causative, pathogenic mutation identified on genetic testing, allowing the patient and other unaffected relatives to receive known familial mutation analysis

(targeted testing for the presence or absence of the specific mutation that was found in the affected relative). This provides the following potential benefits:

- **More complete reassurance with a negative test result.** If an unaffected patient receives full gene analysis and the causative mutation in their family has not been previously identified, a negative test result fails to be a "true negative." While it is possible that the patient simply did not inherit the condition, it is also possible that the familial mutation is not detectable with that test (for example, it is in a different gene, or in a region of the gene that was not effectively evaluated). This means that the patient cannot be completely reassured about the risk to develop symptoms of the condition. Alternatively, if the mutation in the family is known, and the patient is not found to have the mutation, both the patient and their healthcare providers can be more confident in the result and its implications for medical management.
- **Lower risk of uncertain results.** Targeted testing for a known familial variant will typically provide clear results; either the patient has the variant or they do not. When doing broader analysis, such as full gene analysis or a multi-gene panel, there is a greater risk that variants of uncertain significance (VUSs) will be found. These are genetic variations for which there are insufficient data to classify them as definitively pathogenic or benign. A VUS is often a confusing outcome that may increase patient distress and could lead the patient to undergo unnecessary diagnostic and preventative measures that are costly and risky in nature.
- **Decreased costs.** In general, targeted testing for a known familial mutation is more cost-effective than full gene analysis or panel testing. Such cost savings not only benefits the health plan but may also benefit the patient and their medical institution, who may have to absorb the additional cost of broader test methods.

Is it the right time?

Ensuring that a genetic test is ordered at the appropriate time in a patient's diagnostic journey is also an important part of utilization review. Consider whether there are other preliminary studies that should be completed prior to genetic testing. For example, biochemical screening tests (plasma amino acids, acylcarnitine profile, and/or urine organic acids, etc.) may be valuable first-tier tests for many metabolic disorders. The results could help narrow the focus of the test to a single gene or subset of genes that are more likely to be related to the patient's condition, and in some cases may allow more costly genetic testing to be bypassed altogether.

The age of the patient is another important factor to consider for the timing of genetic testing. It is important to exercise caution when it comes to testing asymptomatic minors for adult-onset genetic conditions. While parents may be eager to learn the genetic status of their at-risk child, testing an asymptomatic minor for adult-onset conditions (such as hereditary breast and ovarian cancer syndrome) or for their carrier status raises several concerns, and may not be approved by the patient's health plan.

One concern is the ethical ramifications of testing a child before the age of consent, and not allowing them to decide if or when they wish to obtain information about their genetic status. Also, it may be difficult to establish the medical necessity of such testing if it is requested many years before it would be used to inform medical management or reproductive decision making.