
Genetic Services Policy Project

Genetic Technologies in the Management of Breast Cancer: A Vignette

Vignette 1: Patient perspective

Naomi Densmore is a 52-year-old, post-menopausal woman who was recently diagnosed with breast cancer through the National Breast and Cervical Cancer Early Detection Program. She did not previously have health insurance, but became eligible for Medicaid through the National Breast Cancer Treatment Program when she was diagnosed with cancer. After an abnormal clinical breast examination and mammogram, Naomi was referred to a radiologist for an ultrasound guided core needle biopsy of a suspicious lesion. The biopsy pathology revealed an invasive malignant tumor of moderate grade. Naomi was scheduled for a consultation with a breast surgeon. They discussed the surgical options of lumpectomy with radiation or mastectomy with or without immediate breast reconstruction. Naomi decided to pursue mastectomy with breast reconstruction. The surgeon first re-biopsied the tumor and confirmed the cancer diagnosis, then proceeded with the mastectomy and breast reconstruction. The axillary nodes were also removed to determine if the cancer had spread. Pathology demonstrated that the tumor was 2 cm in diameter, with grade 2 histology and positive estrogen receptors. HER2 testing and her lymph node biopsy were negative.

After her diagnosis, Naomi sees an oncologist for further evaluation and treatment. The oncologist recommends that Naomi begin tamoxifen treatment and possibly chemotherapy. For the past year, the oncologist has been using the Oncotype DX® prognostic test in similar patients as a method to determine who might be able to avoid chemotherapy. Even though the National Comprehensive Cancer Network clinical guidelines do not take a definitive position on the test, the oncologist feels it has helped determine a course of treatment in several situations. For the most part, private insurers have been covering the \$3,500 test. He knows that Medicaid has not covered this expensive test in the past, and there are significant administrative hassles involved in trying to get approval. On the other hand, Medicaid has covered chemotherapy costs, albeit at reduced rates. He decides to offer Naomi the Oncotype DX® test, but tells her that Medicaid may not cover it. He also indicates that, based on classic risk factors such as tumor pathology, she has an average risk of recurrence and that chemotherapy may or may not be of benefit.

Naomi is unsure about what course of treatment to take and turns to an online cancer support network for help. All the potential side effects of chemotherapy make her extremely nervous, but she also doesn't want to risk having the cancer to come back. She learns more about the Oncotype DX® test and how it has been useful for other cancer patients in deciding about chemotherapy. Several people online have written about a new clinical research trial using the test. She wonders why her oncologist didn't mention the trial, and if she should bring it up herself. Naomi also reads about the use of a genetic test called CYP2D6 that may predict how well she will respond to tamoxifen treatment. She wonders if this test would also be useful for her. She knows that she won't be able to afford either of these tests on her own, so she decides to ask her oncologist to petition Medicaid for coverage.

Vignette 2: Payer perspective

Marianne Parker is the medical director for Medicaid in her state. She is responsible for reviewing clinical cases and approving or disapproving coverage for certain non-routine or particularly expensive tests or procedures. The need to balance costs and benefits is particularly acute for her state Medicaid program, given state budget shortfalls and growing client volumes.

Recently, Marianne has had an increasing number of cases involving requests for genetic tests associated with breast cancer treatment. First, it was HER2 testing, then Oncotype DX®, and now the CYP2D6 drug metabolism test. Because HER2 testing and subsequent treatment with Herceptin™ in HER2 positive breast cancers has been found to be cost-effective and associated with increased survival, testing using approved protocols has been covered. Up until the last few months, Marianne has denied coverage for the Oncotype DX® test, given its investigational nature and lack of clinical outcome studies. However, she notes that emerging evidence suggests the test may actually be helpful in avoiding use of chemotherapy in individuals with low risk of cancer recurrence, and therefore may reduce costs of care. Evaluation of other health plan policies suggests that the test is becoming standard of care when used in appropriate candidates. Despite lack of Food and Drug Administration (FDA) approval, Medicare has issued a positive national coverage decision for Oncotype DX®, and many other plans have entered reimbursement agreements with Genomic Health, Inc., the company that developed and performs the test. Similar tests, such as the MammaPrint® test, which the FDA approved in February 2007, are also being evaluated in clinical studies but data are less clear on clinical usefulness. Choosing between various competing tests in the future may be a challenge. Marianne decides to bring up the topic with the Medicaid Advisory Board at the next monthly meeting, and possibly revise the coverage policy on the Oncotype DX® test.

The CYP2D6 test is another story. A recent request for coverage came from an oncologist who has begun to use the test to determine which patients to treat with tamoxifen and which to treat with alternatives such as aromatase inhibitors. Marianne explored the literature on cytochrome P450 drug metabolism and genetic testing. She found an October 2006 statement from FDA indicating that the CYP2D6 gene is a predictor of tamoxifen efficacy, that tamoxifen should be relabeled to indicate that CYP2D6 poor metabolizers have a higher risk of breast cancer recurrence, and that testing is available. However, clinical experience with the test is limited. Marianne denies the request, explaining that the test is investigational and not considered medically necessary. She is convinced this is only the beginning of an onslaught of requests for genetic tests, and she is concerned that her Medicaid program is not ready to address these issues.

Genetic services issues:

- Rapidly emerging role of genetic technology in disease management, adding to already complex treatment options
- Limited clinical outcome studies with new genetic tests
- Variable insurance coverage for genetic services
- Complex coverage decisions requiring evidence review
- Challenges for payers, especially public payers, in balancing costs and benefits of new tests and treatments with other population health needs
- Role of coverage decisions (or anticipated coverage decisions) in clinical care
- Role of clinical trials in determining the value of genetic services
- Competition between the industry players (multiple tests with similar functions emerging)
- Relationship of industry to payers (direct lobbying for tests and treatments, which tests and treatments to cover)
- Increasing involvement of FDA in providing guidance for genetic tests
- FDA approval of genetic tests does not assure clinical usefulness
- Educational needs of consumers, providers, and payers
- Role of virtual networks in providing consumer information and support

Case Issues for Discussion:

1. These vignettes highlight the rapidly emerging role of genetic technology in disease management, adding to already complex treatment decisions.
 - a. What education and/or resources are needed to assure health care providers are ready to incorporate these technologies into care?
2. Health care payers often rely on technology assessments in determining which tests and treatments to cover. These assessments use criteria to determine whether there is enough evidence to suggest that a technology is safe and effective. Emerging technologies, such as gene-based prognostic assays, may appear to have benefits but may have limited evidence in clinical studies.
 - a. How can payers address this issue?
3. Medicare has implemented a “Coverage with Evidence Development” program to address promising new technologies or treatments. This program allows Medicare to extend coverage to services that might otherwise be deemed experimental, increasing access as well as clinical experience with the technology or treatment.
 - a. Could this approach work for private payers as well?
 - b. What are the benefits and risks of this approach?
4. Each state Medicaid program is different. Some services are mandated for all Medicaid programs. Genetic tests are optional.
 - a. What is the impact of lack of standardization of Medicaid policies?

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- b. In developing coverage policies for genetic tests or other services, how is Medicaid different from private payers? How is it the same?
5. The Oncotype DX® test has been studied and validated using stored samples from patients with known health outcomes.
 - a. What are the potential problems with basing clinical recommendations on these studies? What are the potential benefits?
6. A new multi-center study, TAILORx, is currently recruiting patients to evaluate the Oncotype DX®, 21-gene assay, in the management of patients with intermediate risk of cancer recurrence.
 - a. How might this study impact payer coverage policies?
 - b. If the test demonstrates a clear lack of benefit from chemotherapy in specific groups, should payers be allowed to require the test to avoid paying for chemotherapy? Why or why not?
7. Currently, the Oncotype DX® test has the largest share of the market for gene-based prognostic assays for breast cancer; however, numerous companies have similar products in the pipeline. Exagen Diagnostics, Inc. has announced the development of a new fluorescence *in situ* hybridization (FISH) based breast cancer prognostic test called eXagenBC™, which it expects to cost \$700, significantly less than Oncotype DX®. The test, which will be sold as a kit, will have other advantages, including the ability to perform the test in multiple labs. As with Oncotype DX®, clinical experience with the test will be limited at first.
 - a. How might the entry of this product into the market impact Oncotype DX?
 - b. What are the implications for health care providers, who are still in the early phases of using Oncotype DX?
8. Genomic Health, Inc., the company that developed and performs the Oncotype DX® test, is working on the development of other genetic tests, although Oncotype DX® is their primary product. Despite the high cost of the test, the company does not generate enough revenue to offset costs and reports annual losses in the millions.
 - a. What implications, if any, does Genomic Health's experience have for the genetic testing industry?
9. Testing for the HER2/neu receptor gene has become a standard part of clinical care for breast cancer given the availability of targeted treatments for HER2+ cancers. Despite its high cost, Herceptin™, a monoclonal antibody directed to the HER2 receptor, is now routinely used for cancers that express the HER2 gene. The drug, which costs approximately \$50,000 per treatment course, has become a blockbuster for Genentech, the company that produces it. GlaxoSmithKline has recently announced the availability of Tykerb™, another targeted treatment for HER2+ breast cancers. Pricing is expected to be similar to Herceptin.
 - a. Is Herceptin's high price justifiable? Why or why not?
 - b. How does pricing affect access?

- c. Does industry have a moral obligation to ensure access to effective treatments?
 - d. How might competition influence pricing?
10. Tests for genetic variants that affect cytochrome P450 drug metabolism, including tests for CYP2D6, have recently become available. Cytochrome P450 enzymes are involved in the metabolism of numerous drugs, including tamoxifen, a mainstay in breast cancer treatment and prophylaxis.
- a. If testing for 2D6 genetic variants can show which individuals are likely to have a better or worse response to tamoxifen, is it ethical not to offer testing?
 - b. Is it reasonable to offer testing to people for whom there are no current options other than tamoxifen (e.g., pre-menopausal women)?