Genomic Testing in Oncology to Improve Clinical Outcomes While Optimizing Utilization: the Evolution of Diagnostic Testing

David C. Collymore, MD, MBA; Shaunna L. Kobilis, RN, BSN, OCN; Thomas G. Lundquist, MD, MMM, FAAP, FACPE; William T. McGivney, PhD; Edmund J. Pezalla, MD, MPH; Wendy Poage, MHA

This article summarizes proceedings from a roundtable meeting conducted to explore the barriers to addressing unmet needs in cancer care and the potential for genomic testing to help meet those needs.

Cancer care accounted for $88.7 billion in direct medical costs in the United States in 2011. Half the cost was for outpatient or office visits, 35% for inpatient stays, and 11% for prescription medications.[1] Costs related to chemotherapy alone are high: as of 2009, the average cost for a chemotherapy-related visit to the emergency department was $800, and the average cost for a chemotherapy-related hospitalization was $22,000. The cost of medical care for chemotherapy patients was 4 times the cost of care for cancer patients who did not have chemotherapy.[2]

The cost of care is driven by supportive services, not just the chemotherapy itself. Supportive care services, such as chemotherapy-related hospitalizations, emergency department visits, and adverse-effect management, account for most of the costs for chemotherapy patients.[2,3] To illustrate, Table 1[3] shows how utilization (ie, hospitalization) for breast cancer patients is higher for those treated with chemotherapy than for those not treated with chemotherapy.[3]

Patients with cancer need appropriate treatment that will give them the best possible outcome, not a one-size-fits-all approach that can result in poor survival rates, overtreatment, and higher costs. A roundtable meeting and discussions were held September 26, 2015, to explore the barriers to addressing unmet needs in cancer care and the potential of genomic testing to help meet those needs. Sponsored by Genomic Health, the roundtable featured physicians from a large national health plan, a regional health plan, and an accountable care organization, along with representatives from an advocacy group and a healthcare contracting entity. The consensus was that genomic

Abstract

Cancer care is costly, particularly when chemotherapy and its supportive costs are considered. Yet, chemotherapy is not the right course for every patient. Patients with cancer need appropriate treatment that will give them the best possible outcome. Personalized medicine has become an important area of oncology. In addition to genetic testing, genomic testing has become a useful tool in diagnostics. For genomic assays to be viable, they must have clinical validity, analytic validity, and clinical utility. Stakeholders are willing to provide coverage for such testing through medical policy when there is strong evidence the tests are effective. Genomic testing can be used in decision making to rule out chemotherapy or other treatment options that would not be effective for the care of an individual patient. The use of genomic testing to help eliminate ineffective or possible harmful treatment options and determine appropriate care will benefit the patient while reducing healthcare utilization and costs.

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tests that can help determine important clinical information, such as whether a patient needs chemotherapy or not, could be beneficial for patient outcomes and could help optimize healthcare resource utilization.

Genomic testing can have an impact on a patient in regard to decision making, treatment options, and quality of life. Over the course of 10 years, Genomic Health has used its Oncotype DX assays for more than 500,000 patients, including more than 10,000 patients in clinical studies. Based on the company's experiences with its invasive breast cancer assay, approximately 30% of patients have seen a change in treatment decisions as a result of genomic testing.

Table 1. Hospitalization of Breast Cancer Patients Treated or Not Treated With Chemotherapy in the United States[3,a]

	Chemotherapy-Treated Patients	Patients Not Treated With Chemotherapy
Hospitalization rate	60%	40%
Unique hospital visits per 100 patients	84	50
Average LOS (days)	5.0	3.8
Total LOS per 100 patients (days)	420	190

LOS indicates length of stay.
[a]For 100 chemotherapy cancer patients: 60% hospitalized = 60 patients; 1.4 hospital visits/patient (60 patients x 1.4 visits/patient = 84 unique hospital visits per 100 patients); 5.0-day average length of stay (84 visits x 5 days/visit = 420 days per 100 patients). For 100 non-chemotherapy cancer patients: 40% hospitalized = 40 patients; 1.25 hospital visits/patient (40 patients x 1.25 visits/patient = 50 unique hospital visits per 100 patients); 3.8-day average length of stay (50 visits x 3.8 days/visit = 190 days per 100 patients).

The Role of Genetic Versus Genomic Testing and Companion Diagnostics in Oncology

For genomic assays to be a viable tool, they must be accurate and clinically meaningful. As Table 2[4-7] shows, genomic assays need to have analytic validity, clinical validity, and clinical utility. The analytic validity is the test's ability to accurately and reliably measure the genotype (or analyte) of interest in the clinical laboratory and in specimens representative of the population of interest. Regarding clinical validation, a major goal is to identify and quantify potential sources of biologic variation in the analysis of a given sample. Clinical utility is a test's ability to benefit patients by improving treatment decisions.[4-7]

Genomic Versus Genetic Testing

Personalized medicine has become important as a means to help patients receive the best possible outcomes while reducing adverse effects and high direct medical costs if a treatment will not benefit the patient.

Genetic and genomic tests each have a place in personalized medicine. Genetic tests typically focus on a single, known gene, while genomic tests focus on expression and interaction of groups of genes. Genetic tests concentrate on the presence or absence of mutations, or overexpression, of individual genes, while genomic tests provide gene signature profiles based on expression levels of specific component genes. Examples of genetic tests include BRCA-1 and -2 in breast cancer, EGFR in non-small cell lung cancer, and BRAF in melanoma. Examples of genomic tests include the Oncotype DX assays in breast, colon, and prostate cancers, and the 70-gene assay in breast cancer.

Determining the Clinical Value Proposition

In addition to analytic validity, clinical validity, and clinical utility, a series of questions has been proposed to consider when evaluating new diagnostic tests. The questions are designed to more completely determine a test's clinical value proposition (Table 3[8]).[8]

"Will we act on the information provided by the test?" is the first question. In response to it, David C. Collymore, MD, MBA, asked another question: "Will it change the way in which we manage that patient? If it does, then it's worth it to do the test." But "if it's not going to affect the treatment or the care of that patient, if it's not going to affect the overall outcome, then I don't think we can have expectation that the payer will be willing to cover the cost of that test."

Edmund J. Pezalla, MD, MPH, agreed that a test is worthwhile "if it gives you knowledge that you didn't have before so that you can make a different clinical decision." Another reason for testing is "if you actually have data to show that the use of the test changes patient outcomes."

In response to the question on whether a test is affordable, Thomas G. Lundquist, MD, MMM, FACPE, said, "I would actually add a secondary question to that: can we afford *not* to do it?" He noted that just because you can afford to do something doesn't mean you should. Another question to ask, he said, is, "What is the value to the patient? It may not have clinical efficacy or impact outcome and, therefore, maybe shouldn't be paid for by

Table 2. Evidence Requirements for Genomic Assays[4-7]

Analytic validity	Ability to accurately and reproducibly measure analyte (or genotype)
Clinical validity	Ability to accurately and reliably predict phenotype, clinical disease, or predisposition to disease
Clinical utility	Evidence that guides patient management and affects decision making, resulting in added value and improved outcomes

the payer and the manager of the healthcare resource dollars. But it still may have value to the patient."

Acceptable Evidence

In evaluating new products overall, Dr Pezalla stressed the importance of published data. "If there are published economic data, that's good," he said. "Randomized controlled trials are gold standards, but we don't require the gold standard for absolutely everything that comes through the door."

The panel agreed that peer-reviewed studies are best. Dr Pezalla added, "We want to see the whole study eventually, not just the abstract," although there can be exceptions "in the short term until we see better data, because what else are these patients going to do?"

Dr Lundquist said, "If we're going down a path and we're going to either approve a test or procedure, or not approve it, and the data is inconsistent to make a clear determination in support or not, we'll also see what the marketplace is doing, what is being done on a regional or national level in terms of clinical best practice," because "that's a bar we're going to get measured against." And, he said, you don't want to have a worst-case scenario where "a bad outcome occurs because you didn't approve a particular test that would have helped decision making," or conversely, because you *did* approve a test or procedure, prematurely, ahead of evidence-based support, and it created an adverse set of events leading to harming the patient.

When asked about what other types of evidence insurers look at, Dr Pezalla said, "We look at a lot of things. We actually look outside the United States quite a lot," such as to pharmaceutical groups in Australia. He said that although US health plans don't operate exactly the way the other countries' health systems do, "we look at what they chose to look at, why they chose to look at it that way, how they developed the evidence. And that can inform some of the things we do."

Cost and Value Factors

Dr Pezalla also suggested the use of a condition analysis group, which performs economic analysis to see whether a health plan would have overall medical cost savings if they promoted a particular test. The "promotion" could be adding a test as a criteria for prior authorization of another intervention, or encouraging a particular health element that could lead to overall cost savings. He said the condition analysis group would get involved if a test were not only a "good idea" but had a positive return on investment (ROI) or a positive impact on a quality or outcome measure that a health plan was applying in a particular area.

Dr Collymore said that patient care is the top priority to providers, not cost. However, as providers get involved in more risk-based agreements or shared savings plans, cost will become more of a priority, he said.

Insurers on the panel said diagnostics should be performed only if they have the potential to change the way a patient's care is managed, not just to confirm information that will have no effect on care. And the insurers said they want to limit use of a test or procedure to practitioners who know how to use or interpret the information gained.

The Decision-Making Process in Determining Policy for Review of Genomic Testing Products

Coverage Decisions

Insurers on the panel said they tend to be willing to cover tests related to personalized care if the tests have proven clinical utility and are incorporated into leading guidelines. Evidence is crucial for making coverage decisions, they said. Although they named published data as the best source of evidence, they are willing to consider information such as provider input. Some insurers said provider support can be a factor in deciding on whether to cover a new product in cases where data are limited. This can be particularly true for diagnostic products because diagnostics have a higher level of uncertainty than drugs, which go through a more stringent FDA approval process.

There are several approaches to covering cancer-related procedures and services by health plans. Services such as drugs, procedures, and diagnostic tests typically need to be addressed by coverage policies. Another approach is value-based contracting with providers in which health plans work with oncology groups and other cancer care providers to develop comprehensive approaches, including bundled care and compensation based on clinical pathways. Rather than being dictated by health plans,

the pathways can "come from the providers," said Dr Pezalla. As long as the pathways are consistent with the National Comprehensive Cancer Network (NCCN) and the health plan's clinical policies, he said, the providers can make the decisions. Health plans must also consider large self-insured employers, as these groups can be concerned with particular conditions and treatments that drive up their overall costs. To address those concerns, insurers are working to get patients the right kind of care, often by provider groups who have enough patient volume to take on risk.

Acceptance of New Testing Technologies

A diagnostic product must be recognized by the patient and provider as adding value in order to be accepted in clinical practice. Providers need to understand how to incorporate the new diagnostic into their practice, and patients need to understand the importance of the test to their health. Cost to the patient is also an important factor. Wendy Poage, MHA, said her organization recently surveyed patients on genomic testing and how valuable they consider it to be. The survey asked patients about specific dollar figures for tests. "The results showed that as the cost to the patient increased, the patient's willingness to pay decreased," she said. "Nearly all of the survey respondents were willing to pay $500 for a test that provided information to help with deciding between treatment options and whether treatment was needed," she said, but if a test cost the patient more than $500, fewer patients were willing to pay.

Ms Poage applauded genomic testing, saying she knows of many patients for whom it has been effective. "I work with many patients who have had the opportunity to use genomic tests in their decision-making process, and that information has been beneficial for both the patients and the physician," she said. "I've seen genomic tests change the treatment choices for patients and improve the patient's outcome and quality of life."

Precertification

Health plans are still using precertification as a means of managing many new products. However, as risk-based contracting and clinical pathways become more common, precertification could be phased out. Some self-insured clients are already opting out of certain precertification programs, Dr Pezalla said. Precertification is still the norm for individual providers, but groups such as accountable care organizations and patient-centered medical homes may have certain precertification requirements waived if they are taking on risk or if they can document they are providing high-quality care. With the growth of organizations such as clinically integrated networks, health plans will have more transparency with providers and will have access to the clinical data in which they are interested without needing precertification.

One of the reasons for requiring precertification is to ensure tests are being used for the proper reasons—that patients who really need the tests will get them, and that those who do not have the need do not receive coverage for the test.

Dr Collymore said that as providers become more aware of the total cost of care and more involved with the health plan, the issue of over-utilization of testing will subside. He said that shared savings agreements can be an "incentive to the provider to make sure that they understand the value of the tests, the evidence behind the tests, and the need for the tests when you're treating a patient."

Contracting With Vendors

Health plans will contract with vendors if the ROI is right. They don't like a portfolio approach, based on their experience with drugs, but they are willing to consider it if all elements are of high quality and the vendor offers added value, such as clinical information. New technologies such as diagnostic testing are the perfect situation for value-based contracting "if the evidence shows it works and it looks like it should have some return on investment," Dr Lundquist said. A new test could be put under a pilot program with a risk-based contract to help

Table 3. A Framework for Evaluating Diagnostic Tests[8]

A proposed template contains the following 6 questions:
1. Who should be tested and under what circumstances?
2. What does the test tell us that we did not know without it?
3. Can we act on information provided by the test?
4. Does the outcome change in a way in which we find value, relative to the outcome without the test?
5. Will we act on the information provided by the test?
6. Can we afford it?

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get to a critical mass of patients. Provider acceptance is crucial: "If the providers aren't going to use it, then it's not worth either of our time," he said.

For an outcomes-based contract, Dr Pezalla said, "The most important reason for doing it is because you're trying to overcome a level of uncertainty." He said there is more uncertainty with tests than with drugs, noting the differences in the FDA approval processes. As such, a vendor may be willing to guarantee an outcome such as reduced use of surgery or chemotherapy in order to help a payer become more comfortable with coverage.

Genetic Counseling

Shaunna L. Kobilis, RN, BSN, OCN, a contracting consultant, emphasized the importance of genetic counseling as a factor in personalized medicine. She said genetic counseling should be involved more often to ensure appropriate utilization. Experts in the field are becoming an increasingly important part of overall decision making regarding personalized care, she said, noting she has seen increased adoption of genetic counselors in the marketplace. She encouraged insurers to find ways to promote genetic counseling as a means of providing value in the long run.

Who Should Determine Appropriate Care?

The advisors were somewhat mixed about where overall decisions regarding cancer care management should come from. A consortium of national experts, such as NCCN, the American Society of Clinical Oncology, US Oncology, and other large physician groups, was suggested. NCCN was mentioned as a possible aggregator of various experts. Dr Pezalla said, "I think it's okay that it's done at a lot of different levels, as long as everybody is looking at the same evidence."

Practical Considerations for Medical Policy and Reimbursement for Personalized Care

Cost as a Barrier

The panel agreed that determining which patients need chemotherapy and which patients do not is at the top of the list of reasons for considering a new test in oncology. However, cost of testing is a primary consideration. "Any lab test over a few hundred dollars is going to raise an eyebrow," Dr Lundquist said, either if it's going to be a test with potential for high volume, or if it's a low-volume test but costs several thousand dollars. For the latter tests, factors that will be considered include whether the test really meets a need, whether it has proven efficacy, and whether it changes clinical outcomes. If so, he said, it's likely to get approved—but on the basis of how it fits into evidence-based guidelines. He said that health plans need to establish checks and balances to make sure the right patients are getting the right test, and that a test isn't going to be overused for patients where it will not add value.

"You can look at all of these things with an arrow going one way for clinical improvement and the other way for cost," said Dr Pezalla. "If you've got clinical improvement going up and you've got cost decreasing, so they're both in the positive direction, then that's a win. If you've got cost going the other way, then now you've got a problem because you have to figure out, is the clinical improvement worth the additional cost?" He said there isn't necessarily a set rule for determining acceptable costs for tests, "but if it's a reasonable amount, we're not going to worry about it. If it's a lot, then we're going to have to think about it."

Coverage Determinations

Dr Pezalla said that if a test isn't covered, it's not primarily because of cost, but rather "because we can't figure out if the test is worthwhile at all from a clinical point of view." He said health plans are undergoing increased internal scrutiny in regard to whether costs are justified. "More and more, there will be clinical policies, and if there's not a clinical policy, more and more there will be a cap on it." If someone bills over the cap for something, "it's not going to get paid."

The issue extends to laboratory quality. Dr Pezalla said that labs "have to meet a series of quality standards on every test they do for us," adding that health plans have "been known to move tests out of the national labs to other labs because of quality issues" if they have evidence that a test is not consistently accurate. If a lab can't demonstrate "a certain level of quality, then we'll move even just that one test out."

Involvement of Physician Groups

Dr Collymore emphasized the importance of the physician. "Even though it may be a test that's approved by the payer, if the clinicians are not convinced," they're not going to have the test done, he said. "At the end of the day, clinically, the test has to be superior to the competition" for the providers to use it. "Provider education is the key. You've got to get enough providers to adopt it for it to be the standard of care."

Dr Lundquist said, "If an oncology group takes on that willingness to look at total cost of care, then they,

with us, start making the decision around how these tests fit in." By avoiding chemotherapy for patients who won't benefit from it, the oncology group helps reduce total cost of care. "They're ahead because they helped save the total cost, and we've set up a program where we bring value back to them through shared savings," he said. "The challenge in oncology is that this is an area where a lot of payers get nervous about touching total cost of care. I think the oncologists have to be able to prove the quality and the clinical outcomes are there. The oncologists have an equally important role to help ensure cost-effectiveness, along with making sure that the patients still feel like they got the very best care."

Summary

Appropriate treatment is needed in cancer care to ensure the best possible outcome for patients. Cancer treatments are diverse and resource-intensive. Personalized medicine has emerged as a means to help identify the most appropriate options for care. With personalized medicine, it is possible to avoid the use of potentially harmful treatments, such as chemotherapy, by determining when those treatments are not appropriate for particular patients. Avoiding use of chemotherapy, when it is appropriate to do so, leads to reduced healthcare utilization and costs. Genomic tests are among the diagnostic products in personalized medicine that can lead to more appropriate treatment. If there is strong evidence that such tests are clinically effective, stakeholders are willing to provide coverage via medical policy.

In conclusion, genomic tests can be useful for providers and patients when deciding how best to manage cancer care, and the tests are beneficial for patient outcomes and efficient healthcare resource utilization.

Author affiliations: Acacia Network, New York, NY (DCC); Optima Health Plan of Sentara Health Plan, Virginia Beach, VA (TGL); McGivney Global Advisors, King of Prussia, PA (WTM); Aetna, Hartford, CT (EJP); Prostate and Men's Health Education Councils, Centennial, CO, and University of Colorado Medical Campus, Aurora, CO (WP).

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Address correspondence to: dcollymore@acacianetwork.org.

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Notes

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