Article from

Health Watch

February 2018
Issue 85

Genomic Testing: Cost-Saving or Cost-Inflating for Payers?

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Private payers are gradually adopting genomic testing to guide decision making in treatment pathways for selected disorders. Cancer mutations are a primary target for these tests, but can the early adoption of tailored, personalized approaches to care prove financially sound to payers? A deep dive into the return on investment (ROI) for these tests helps untangle some of the key risks.

Personalized medicine is gaining ground fast. At the very least, the idea that treatment pathways can be tailored to target the specific needs of patients based on predicted outcomes appeals to many. A corollary is the potential for reducing waste and other unnecessary procedures in the system. In breast cancer management, where genomic testing is more widely used to guide decisions regarding treatment, it is believed that the use of chemotherapy could decline in groups with selected genomic markers. But are these potential future savings actually worth the extra investments from a purely financial perspective? Although there is still some uncertainty regarding the future uptake of genomic testing and the levels of sophistication of new tests, we discuss in this article some relevant considerations that can support a greater appreciation of the risks and gains to payers involved in funding these tests now.

Many business areas rely on an ROI framework to help evaluate the financial implications of competing investment strategies. In health care particularly, ROI models have been employed to measure the impact of disease management programs or even determine the value of health risk assessments. Similarly, with genomic testing, an ROI analysis can provide a solid framework for determining whether payers should continue (or start) to allocate funding toward testing and for identifying key metrics.

GENOMIC TESTING OR GENETIC TESTING: WHAT'S THE DIFFERENCE?

The terms *genomic testing* and *genetic testing* are sometimes used interchangeably in the literature, yet the two tests have unique characteristics that differentiate them. The descriptions that follow should help clarify any misconceptions.

Genetic testing is more frequently quoted in the media, and it refers to a type of medical test that looks at the hereditary profiles of patients. It aims to determine the risk of developing genetic disorders in the future by identifying cells in humans carrying a particular mutation. These tests, which require DNA samples, are now commercialized in the United States and abroad and generally can be performed at home without any medical supervision. Results may prompt some individuals to alter their lifestyle decisions and, in some cases, operate or start treatment on a preventive basis.

Genomic testing helps to understand the activity and interactions of certain genes in the body once a gene mutation has occurred. It normally provides information on the likelihood of a tumor to spread and grow (aggressiveness), but it also sometimes indicates the likely benefit of a given intervention (responsiveness). Genomic testing can therefore offer guidance into the preferred course of treatment and is provided by health care professionals only.

ROI AND GENOMIC TESTING

We consider in this section three different approaches for calculating ROI for genomic testing, discussing advantages and drawbacks of each method.

Observational Study

Through an observational study, we can assess the financial impact to payers of genomic testing on health care resource use between comparable populations that have and have not undergone testing. This financial analysis would therefore look at the up-front cost of testing in relation to its impact on future utilization of services and disease recurrence. For instance:

- We can look at real-world data from two distinct population groups with similar risk profiles before and after a particular genomic test becomes available. Under this approach, we would use the year a specific test was introduced by payers as a marker and select populations as close to the marker as possible to reduce potential bias and externalities (i.e., new technologies uptake).

- We would follow patients for a predefined duration, yet the observation period for the two groups would differ. Ultimately, this approach requires looking at two distinct population cohorts.

- While in theory it is possible to control for health status in a similar way to other demographic factors, in practice risk adjustment mechanisms for health status are not perfect and are unlikely to capture all differences between the populations. Ultimately this may also add a level of complexity to the modeling.

Modeling "Theoretical" Approach

An alternate study design could focus on a single population group that fits the clinical or eligibility criteria for testing.

- Using a control population as baseline, we can develop a theoretical treatment group by applying assumptions regarding the expected impact of a given genomic test on health care resource utilization. Depending on the data available, this impact would vary by service categories.

- The use of peer-reviewed literature and other external sources may be necessary to supplement findings from real-world data and help provide additional input into the potential financial impact of testing on overall health care utilization and cost by disease area.

- This approach has the advantage of reducing the level of bias and potential confounding factors associated with using multiple populations, as the analysis is performed using a single cohort of patients over a single time period. However, this study design corresponds to a modeling exercise rather than being a true observational study.

Ultimately, both of the preceding approaches will compare two patient populations, with and without genomic testing.

Retrospective Analysis

A third option enables payers to blend the real-world evidence component of the observational study with the single population group focus of the theoretical approach. All participants in this analysis undergo genomic testing.

- Under a retrospective analysis, the initial treatment decisions for patients with a given condition are recorded using the conventional clinical approach. Then we perform genomic testing on the same population, and results are discussed between medical professionals and patients. The ultimate treatment decision is then documented (Figure 1).

- Looking at both the initial and final treatment choices, we can retrospectively identify patients whose treatment pathways were influenced by genomic testing and similarly determine the proportion of patients for whom genomic testing only confirmed the initial treatment choice and thus was redundant.

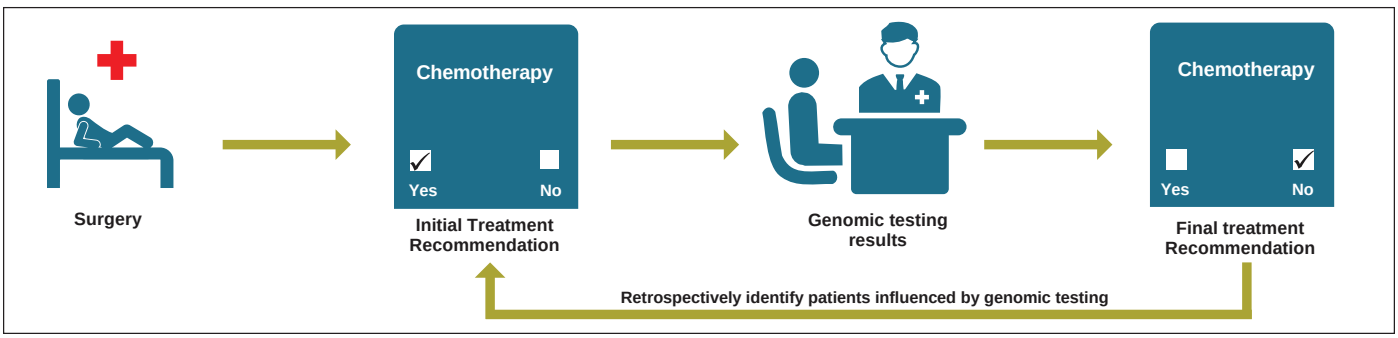
- Benefits of this approach are that the analysis is conducted on a single cohort of patients using real-world data, does not require risk adjustment and can be performed quickly due to the fast turnaround time for these tests. However, it relies on clinicians to keep track of both the initial and ultimate treatment decisions, which can increase the administrative burden.

These methodological approaches can apply to various disorders and disease areas to help measure the impact of testing at a population level. Yet often a proof-of-concept at a smaller scale can demonstrate what can and cannot be achieved given available data and time resources.

CASE STUDY: GENOMIC TESTING FOR EARLY BREAST CANCER MANAGEMENT

A current hot area for genomic testing is early breast cancer management. Traditionally, clinical markers would be used only to inform the use of chemotherapy alongside hormonal therapy (e.g., tamoxifen) after surgery. Prior prognosis tools would rely on information such as patient age, tumor size and grade and the number of positive nodes to evaluate the clinical risk of developing cancer recurrence and/or dying within 10 years. The resulting clinical risk score, broken out into low-, intermediate- and high-risk groups, would then be used to support decision making about adjuvant chemotherapy. While patients at high clinical risk would normally be recommended chemotherapy and patients at low risk be advised not to have it, patients in the intermediate-risk group would remain unclear about its potential benefits. This uncertainty is driving the need for additional tools to guide treatment pathways.

Figure 1
Patient Journey Following Surgery When Genomic Testing is Available



Similar to its use in existing clinical groupings, genomic testing for early breast cancer management allocates individuals to one of three genomic risk categories—low, moderate and high—based on their risks of recurrence. A high score, for instance, represents a high risk of developing recurrence, with benefits from chemotherapy likely to outweigh potential adverse effects. Using the prior example of patients assessed with intermediate risk of cancer recurrence based only on clinical factors, genomic testing can thus help narrow the number of patients undergoing chemotherapy by sparing its use on patients at low genomic risk and requiring its use on patients at high genomic risk. It is therefore the combination of clinical and genomic markers that can help inform better decision making, as shown in Figure 2.

Ultimately, patient segmentation by genomic risk factor and treatment recommendation (hormonal therapy alone versus hormonal therapy and chemotherapy) will likely influence ROI, alongside any future movement in this distribution, which is due to population dynamics. Already, real-world experience on survival and treatment outcomes at five years following genomic testing is emerging in the literature for patients with early breast cancer. This information could form the basis for an ROI analysis for these gene-profiling tests.

The two scenarios in Table 1 assume that all patients in the high clinical risk category would be recommended ET + CT and, similarly, that all patients in the low clinical risk group would adhere to ET only. A possible application of genomic risk testing could help reduce some of the uncertainty associated with the use of chemotherapy in patients in the intermediate clinical risk of cancer recurrence. However, we acknowledge that other external considerations are likely to influence the ultimate treatment recommendation and that a uniform rules-based approach may not be appropriate for all cancer cases.

Table 1
Example of Decision Making Regarding Chemotherapy, With and Without Genomic Testing

Clinical Risk Assessment Only			
	Low Clinical Risk	Moderate Clinical Risk	High Clinical Risk
Low genomic risk	ET	Uncertain	ET + CT
Moderate genomic risk	ET	Uncertain	ET + CT
High genomic risk	ET	Uncertain	ET + CT

Clinical Risk and Genomic Risk Assessments			
	Low Clinical Risk	Moderate Clinical Risk	High Clinical Risk
Low genomic risk	ET	ET	ET + CT
Moderate genomic risk	ET	Uncertain	ET + CT
High genomic risk	ET	ET + CT	ET + CT

Abbreviations: ET, endocrine therapy; ET + CT, endocrine therapy and adjuvant chemotherapy

KEY CONSIDERATIONS AND RISKS TO PAYERS

The example of early breast cancer frames the context for understanding some potential contributions of genomic testing in tailoring care to patients. In this section we discuss in greater length further key modeling considerations and financial risks to payers with testing, building on our current work in this area.

Projection Time Frame

Choosing the right time horizon for the ROI analysis is important as it will allow us to consider external changes that are likely to impact the future financial landscape of genomic testing. A longer time frame—for example, 10 to 15 years—could allow quantification of any forgone medical costs from a reduction in the use of a particular treatment or a decrease in disease recurrence. Moreover, it could also include the additional cost of care and surveillance for those populations where genomic testing failed to predict the right course of care.

A longer time frame may be more appropriate to payers or governmental organizations with longer time horizon and wider societal views of the benefits accrued, yet we note any improvements in treatment outcomes that are due to genomic testing may bear other financial consequences, for example, because of an increase in survival rates.

A shorter, one-year time frame by comparison could be more suitable to private payers, as it replicates the typical duration of most health insurance policies. This may also be more appropriate for medical conditions or disease likely to be diagnosed and treated within a one-year period. However, it will fail to capture any disease recurrence or persistence outside of the experience period. Given the potential impact on price of demographic shifts on incidence and, similarly, technology uptake, several ROI analyses can be conducted at several points in time—for instance at five, 10 or 15 years—to understand the financial implications from changes in key model inputs.

Population Segmentation

As mentioned earlier, genomic testing has the potential to guide decision making for particular therapies based on likelihood of treatment response. Therefore, risk stratifying your population of interest to home in on patient groups likely to benefit from testing can have a large impact on the overall level of return and can make the difference between an intervention being cost-saving or cost-inflating. The hypothetical example in Table 2 illustrates how selecting 100 patients at random for genomic testing versus carefully identifying 100 patients with given

Table 2
Example of Potential Savings Linked to Genomic Testing

Description	Scenario 1 Population at Random	Scenario 2 Population Segmentation
Cost of genomic test	$3,000	$3,000
Cost of treatment	$15,000	$15,000
Number of patients at risk of treatment nonresponsiveness	5 in 100	30 in 100
Potential treatment cost avoided due to genomic testing	5 • $15,000 = $75,000	30 • $15,000 = $450,000
Total cost of genomic testing (100 patients)	100 • $3,000 = $300,000	100 • $3,000 = $300,000
Overall financial outcome due to testing	$75,000 – $300,000 = ($225,000)	$450,000 – $300,000 = $150,000

clinical markers and other criteria may produce very different financial outcomes to payers.

Moreover, stratifying experience by medical service categories can help pinpoint the differences in utilization and costs between a control group (no genomic testing) and a treatment group (genomic testing), ultimately laying the foundation to derive ROI for a given intervention and support benchmarking over time.

Perspective Matters

Moving away from the more traditional considerations of ROI, too often it is assumed that the oncologist's or medical professional's view will prevail regarding the choice of treatment for patients. While the well-understood concept of information asymmetry between clinicians and patients may support this belief, multiple other factors can motivate patients to go against clinical guidance sometimes. Considerations related to patient age, degree of risk aversion to potential adverse events and availability of other, less invasive treatments can influence patients' ultimate decisions for treatment. For the purposes of deriving ROI for genomic testing, choosing between the perspectives of the oncologist and that of the patient can yield very different ROI metrics, thus prompting payers to consider including both views in their analyses.

Uses of Genomic Testing

As a final consideration, we note the scope of genomic testing can be twofold. We mentioned previously that genomic testing for cancer could lead, for instance, to a decrease in the use of chemotherapy in populations initially identified as candidates for treatment. This reduction could benefit payers while sparing the unnecessary use of chemotherapy in patients likely to derive little to no benefit. Yet genomic testing can also identify patients initially spared a given therapy under the conventional approach to decision making, but later recommended treatment due to the presence of certain genomic markers. This scenario will of course increase the use of therapy, and costs associated with treating those patients, but likely will improve patient outcomes. Therefore, recognizing the conditions and scope under which genomic testing can be used will have a strong influence on the overall ROI to payers.

The process for evaluating financial implications of genomic testing includes several other uncertainties, notably the future cost and uptake of testing, levels of sophistication of new tests and future costs of standard and alternative treatments, including costs of adverse events. From a cost-benefit standpoint, additional considerations linked to poor handling of genomic samples, low sample size and the randomness and heterogeneity of the cancer mutations can reduce the ability to generate findings, while generating further expenses to payers. Scenario analysis can therefore provide the degree of sensitivity of ROI to changes in these assumptions. The future direction of personalized medicine will inevitably influence the outcome of ROI and ultimately determine whether new interventions such as genomic testing are cost-saving or cost-inflating for payers. ■

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