Economics of cancer biomarkers

Cancer accounts for approximately 13% of all deaths worldwide, and in 2010 the estimated total cost of cancer in the USA was more than US$263 billion. Biomarker use for screening, monitoring, diagnosis and treatment optimization has the potential to improve patient outcomes and reduce costs associated with inappropriate (or suboptimal) therapeutic regimens. Since a new technology may have additional initial cost, a policy question arises regarding whether the improvement in outcomes is attained at a 'reasonable' additional cost compared with existing technology. This paper presents an overview of health economic issues surrounding biomarkers in general, with a focus on cancer care and treatment optimization in particular. While this article is not a systematic review of the literature, it includes relevant examples to provide a real-world perspective.

KEYWORDS: biomarkers ■ cancer ■ economics

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According to WHO estimates, 7.6 million people worldwide died from cancer in 2008, comprising nearly 13% of all deaths [101]. The overall costs of cancer care in the USA in 2010 amounted to US$263.8 billion ($102.8 billion in direct medical costs, $20.9 billion in indirect morbidity costs and $140.1 billion in indirect mortality costs) [102].

In the USA, total expenditures for healthcare increased from $7.14 billion in 1990 to $2.23 trillion in 2007. National health expenditure growth is expected to continue to outpace income growth, with total national health expenditure reaching $4.35 trillion by 2018, accounting for 20.3% of expected gross domestic product [103]. Studies have estimated that approximately half of the recent growth in health expenditures in the USA is attributable to advances in technology, including new pharmaceuticals, medical devices, imaging modalities, biomarkers and other *in vitro* diagnostics [1]. Within the context of unsustainable expenditure growth, a key question relates to whether improvement in outcomes associated with the use of a new technology is attained at a 'reasonable' additional cost. Recent political debates over the merits of 'comparative effectiveness research' (CER) as part of health reform initiatives suggest the rising importance of this approach to the efficient allocation of heath care resources [2].

This article's main objective is to provide an overview of the economic considerations of biomarkers associated with the use of biomarkers in oncology and, in particular, the use of biomarkers in treatment optimization for oncology patients.

Biomarkers in cancer & cost–effectiveness analysis

Biomarkers provide information about pathophysiological processes that can be objectively measured and evaluated in order to detect or define disease progression, or to predict treatment response. Traditional biomarker analysis consists of surrogate physiological measurements, individual protein molecules such as PSA and CEA, and imaging techniques. New and emerging molecular biomarker technologies that are used in cancer detection and treatment encompass SNP analysis, genomic and proteomic profiling, epigenetic profiling and gene expression profiling, which carry the promise of a greater level of individualized disease management. From a predictive stand point, a biomarker-based strategy may potentially help guide and target therapy towards those most likely to benefit, in addition to providing complex high-dimensional biological data that lead to better patient outcomes through more accurate diagnoses and optimal treatment routing [3]. As a prognostic tool, biomarkers can provide estimates of the chance of recovery or recurrence of a cancer, and as a predictive tool biomarkers can help determine whether a person's cancer will respond to a specific treatment [4].

The use of cancer biomarkers to guide treatment can confer both clinical and economic benefits. For example, predictive biomarker

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results may lead to better patient outcomes for patients likely to respond to a specific treatment, and reduced costs for likely nonresponders who do not receive the treatment [3]. Economic considerations include but are not limited to test and treatment costs, inpatient and outpatient resource utilization, insurance coverage and provider reimbursement.

The most appropriate tool for the quantitative assessment of biomarkers' health economic value is cost–effectiveness analysis (CEA) [5,6]. CEA has increasingly been used to assess the joint clinical and economic impact of medical and healthcare interventions and, when used correctly and judiciously, helps to ensure that scarce resources are allocated to the uses most likely to maximize clinical outcome and healthcare status [7]. CEA allows for the assessment of the comparative impact of two or more interventions. By providing a comprehensive estimate of both costs and outcomes, CEA illustrates the trade-offs involved in deciding among all the options under investigation [8].

While many new technologies, such as biomarker-guided strategies and new testing technologies, offer the potential to better target therapy towards patients most likely to benefit and thereby potentially improve clinical outcomes, there may be a perception that overall healthcare expenditures will increase owing to rising costs associated with the relevant tests. However, this is dependent upon the cost of the biomarker test (and associated costs) in relation to the cost of the events and interventions avoided. Thus, the economic aspects of these new technologies have become increasingly subject to scrutiny by reimbursement and regulatory authorities worldwide. The focus of the economic aspects surrounding biomarkers should not just address the cost of the test, but should also examine the infrastructure and additional resources required for the test, as well as the potential costs saved from interventions avoided and outcomes improved.

Many countries have a strong government focus on healthcare costs and are implementing health technology assessments (HTAs). For example, in the UK the National Health Service (NHS) bases payment policy decisions for new technologies in part on recommendations from NICE. Recommendations from NICE are substantially influenced by the results of CEAs, which yield an estimated additional 'cost per quality-adjusted life-year (QALY) gained' from use of the new technology. Currently, NICE generally considers technologies offering improved outcomes at a cost less than GB£20,00–30,000 per QALY gained (or approximately $33,000–50,000) acceptable, although exceptions are common [8]. In 2006, NICE did not approve the use of two targeted therapies, bevacizumab and cetuximab, for colorectal cancer (although certain advanced patients may achieve extended life expectancy) since the average cost per QALY was higher than the £30,000 threshold. Still, in the same year NICE approved the use of imatinib to target specific types of leukemia and gastrointestinal tumors, at a cost of as much as £35,000 per QALY [9], indicating a potential place for targeted therapies and biomarkers within reimbursement decisions. NICE is currently reviewing the use of bevacizumab and cetuximab for use in second-line metastatic cancer, although the results of the initial appraisal consultation document are not yet known [104].

In the USA, large third-party payers are establishing internal technology assessment organizations that evaluate economic implications of health technology, including CEAs to assist with their formulary recommendations, policy decisions and care pathways [105]. In addition, within the private healthcare insurer market there is increasing reliance upon HTA-type analyses to evaluate the use of biomarkers to select targeted therapies [10]. Although CEA does not currently play a prominent role in US public payment policy, the pressures created by rising expenditures are likely to lead to greater scrutiny of the value of new technology [11,12]. The ability to compare clinical outcomes of health technologies (comparative effectiveness), however, is an important tenet of US healthcare reform. Under the 2010 Patient Protection and Affordable Care Act, the US Congress created the Patient-Centered Outcomes Research Institute (PCORI). The PCORI is an independent, nonprofit organization that is charged with providing evidence on the effectiveness, benefits and harms of different treatment options for different patients with an emphasis on patient perspective. The PCORI website notes that the Institute "investigates (or may investigate) optimizing outcomes while addressing burden to individuals, resources, and other stakeholder perspectives" [105,106]. Therefore, both CER and the PCORI need long-term evidence of the benefits of using biomarkers in cancer therapy, which is linked to health outcomes in a 'real-world' setting [13].

Health economic considerations, such as the potentially high costs of screening in large populations as opposed to targeted screening, may depend on the specific use of a cancer biomarker. Other biomarker applications such as diagnosis,

monitoring of effects during treatment and surveillance of patients during or following treatment (referred to as 'monitoring' throughout this document), as well as treatment optimization, derive economic value from guiding cancer treatment approaches via selection of the most appropriate treatment among potential alternatives and minimizing the likelihood and cost of adverse events.

In the context of biomarker uses and economic considerations specified in TABLE 1, the following sections further examine cancer screening, diagnosis, monitoring and treatment optimization. Where available, illustrations utilize economic analyses and systematic reviews from the Center for Reviews and Dissemination and the Cochrane Library.

Cancer biomarkers used in screening, diagnosis, monitoring & treatment optimization

Screening

While screening has the potential to save resources through earlier identification and management, there are instances where the costs of screening a large population is greater than the treatment costs of a group patients with the disease. There is also a lack of a broad consensus on the economics of population-based cancer screening of asymptomatic individuals [14].

A systematic review, conducted by Cohen *et al.*, analyzed the contents of the Tufts-New England Medical Center Cost–effectiveness Analysis Registry, collecting published studies (up to 2005) that addressed the cost–effectiveness of preventive care (279 studies on preventive care and 1221 studies on treatment) [15]. The authors found that the cost–effectiveness ratios (cost per QALY) were surprisingly similar between prevention and treatment, and that these similarities generally remained constant through the range of cost–effectiveness ratios. The review found that "opportunities for efficient investment in healthcare programs are roughly equal for prevention and treatment" [15].

There are several other important factors that affect the economic value of screening. First, the sensitivity and specificity of the biomarker directly contribute to the number of false positives and false negatives that result from screening. Inappropriate secondary testing and intangible costs arising out of false-positive screenings can be very costly at the population level. Second, the economic value of screening is dependent on the prevalence of disease in the target population. Disease prevalence will also affect the predictive value (both positive and negative) of the test. In general, more false-negative results occur if the disease is relatively common, and more false positives occur if the disease if relatively uncommon [16]. Third, and potentially most importantly, is the clinical utility of the test. If the results of the test do not alter treatment practice or lead to improved patient outcomes, then the biomarker cannot be considered cost-effective. Finally, average costs per screening are very important at the population level; screening methods that are inexpensive at the margin can be very expensive when aggregated across an entire subpopulation (e.g., women age ≥50). Thus, the comparatively low cost of biomarkers (compared with, for example, colonoscopies or mammograms) has the potential to lower aggregate screening costs, which may in turn alter the economic properties of screenings that in the past have relied on more costly diagnostic approaches [17].

Table 1. Use and potential economic value of cancer biomarkers in patient care.

Biomarker use	Clinical objective	Economic considerations
Screening	Detect and treat early-stage cancers among the asymptomatic	Potential savings if total costs of treatment for patients diagnosed with early-stage cancer are less than costs for those diagnosed in later stages
Diagnosis	Accurately and quickly establish the presence of cancer	Potential savings from optimizing treatment approach† and timing
Monitoring	Determine whether treatment is having the intended effect; enable timely detection of post-treatment recurrence	Potential savings from optimizing treatment approach† and facilitating timely second-line treatment
Treatment optimization	Predict outcomes; determine aggressiveness of treatment; predict response to particular treatments ('stratified' medicine‡)	Potential savings from optimizing treatment approach† leading to improved outcomes, and minimizing costs of adverse events

†'Optimize treatment approach' refers to selecting the most appropriate treatment and treatment venue with the best possible outcome given a patient's biomarker levels and other relevant characteristics.
‡See [27].
Adapted with permission from [9].

A biomarker commonly used for screening large populations is the Papanicolaou's cervical smear (Pap) test. Studies of the cost–effectiveness of cervical cancer screening have reached different conclusions, with the majority of studies showing that Pap tests and subsequent treatment result in lower mortality and are more cost-effective than alternative screening modalities. The total cost per use of a Pap test is relatively low ($56), and the 74% reduction in death rates for cervical cancer between 1955 and 1992 is largely attributable to the introduction of the Pap test [18]. Still, the cost–effectiveness of Pap tests is not entirely clear, mainly owing to substantial variance in age-related cervical cancer, whereas the screening of women age 60 years or greater is associated with a relatively low cost per life year gained ($11,000). The annual screening of younger women (e.g., beginning at age 20 years) has been shown to cost as much as $1.5 million per life year gained. In addition, the cost–effectiveness of Pap tests has also been shown to depend upon on how frequently the test is performed and the intervals between successive tests [19].

Biomarker use for the purpose of ovarian cancer screening has also been evaluated for cost–effectiveness. Similar to the Pap test, results were found to be dependent upon screening intervals, test characteristics, and costs of testing and treatment. A CEA by Havrilesky *et al.* [20] did not evaluate specific tests, but considered markers in general based on test sensitivity and specificity. Results suggested that annual screening from age 50–85 years was associated with a reduction in ovarian cancer mortality of 43% and 0.0080 life-years gained at an additional cost of $589 per person. The incremental cost–effectiveness ratio was $73,469 per year of life saved compared with no screening, and $36,025 for women at high risk. The study results also estimated mortality reduction improvements of approximately 1% for every 5% increase in test sensitivity.

There is limited economic evidence that would definitively prove or disprove screening as a cost-effective strategy; however, it is evident that targeted screening can only be deemed cost-effective if the tests are clinically effective. Clinical effectiveness can only be evaluated through large clinical trials and epidemiological studies. The more 'orphan' a disease, the less likely, at present, that robust clinical-effectiveness data would be available to screen patients. Furthermore, the cost–effectiveness of a screening test will be dependent upon the costs of the future events avoided as well as the cost of resources and infrastructure required to set up the test within a healthcare setting.

Diagnosis

The use of biomarkers with higher sensitivity and specificity than standard diagnostic methods has the potential to save scarce resources by optimizing the therapeutic approach and treatment timing; however, no systematic reviews with a focus on the economics of this element of biomarkers were found.

However, a recent cost–effectiveness study of a biomarker-based diagnosis, Risk of Ovarian Malignancy Algorithm (ROMA™), provides an example of the potential for cancer biomarkers to direct patients to appropriate specialists and treatment venues [Schneider JE, Depriest PD, Udeh B, Gillis K, Unpublished Data]. The authors conducted a CEA of ROMA versus CA125 alone using a combination of data from ongoing HE4 trials and published literature. The ROMA strategy was found to be less expensive and was associated with slightly better outcomes. Among premenopausal women, the ROMA strategy was associated with incremental savings of $696 and a small gain in life years of 0.12. The incremental savings associated with the ROMA strategy among postmenopausal women is approximately 50% higher, resulting in an incremental cost savings of $935 and a small gain of 0.08 life years. Based on the population of postmenopausal women presenting with a pelvic mass, approximately $187 million could be saved by relying exclusively on the ROMA test strategy. Although the incremental cost difference is relatively small ($696 and $935 for pre- and postmenopausal women, respectively), aggregate costs would be substantial when summed over the larger population of women with ovarian tumors. The principal source of savings lies in the circumvention of 'suboptimal' treatment that is more likely to lead to additional procedures and services and is associated with slightly lower levels of life years gained.

Likewise, the capability of biomarkers in their role of investigating diagnoses and monitoring is demonstrated in esophageal adenocarcinoma. Rubenstein *et al.* conducted a literature-based cost–effectiveness Markov model of 50-year-old men with gastroesophageal reflux monitored until patients reached age 80 years [21]. Strategies of surveillance were examined and compared against each other to determine their respective effectiveness as tools to identify esophageal adenocarcinoma: observation only, current practice (dysplasia-guided surveillance), surveillance

every 3 months for patients with a positive biomarker (biomarker-guided surveillance) and esophagectomy immediately for a positive biomarker (biomarker-guided esophagectomy). Results suggested that the biomarker-guided esophagectomy method of surveillance would be more effective and less costly than the current practice in the USA (dysplasia-guided surveillance), with average lifetime cost per patient at $104 for observation alone, $2444 with dysplasia-guided surveillance, $2356 with biomarker-guided surveillance and $2291 for biomarker-guided esophagectomy. Biomarker-guided surveillance was found to be cost-effective in comparison with dysplasia-guided surveillance under an assumption of a unit cost of $100 per biomarker, with sensitivity and specificity of at least 80% [21].

Similar to the economics of biomarkers mentioned in regards to screening, the cost–effectiveness of biomarkers in diagnosis is heavily dependent upon the sensitivity and specificity of the test, which can only be validated through larger population based trials. In addition, evidence from payer research reveals that the cost of the test is not as important as the impact that the test has on the longer-term health outcomes [22]. It can be deduced, therefore, that this, along with a growing focus on CER, indicates that the applicability of biomarkers within a 'real-world' setting requires large observational studies that can link the outcome of the biomarker to a longer-term health outcome, and are able to show a cost benefit.

Monitoring

Monitoring refers to the monitoring of effects during treatment and the surveillance of patients during or following treatment. The economic value of monitoring includes effects from each of the biomarker uses that have been described throughout this document. Monitoring has the potential to save resources if the costs of side effects or inefficacy of treatment are minimized by means of early avoidance and appropriate monitoring, respectively. However, no systematic reviews of the cost–effectiveness of monitoring have been found. Beachy and Repasky stress that detectable and easily accessible biomarkers of tumor cell death are necessary to evaluate early therapeutic efficacy of immunotherapy and chemotherapy, which can inform decisions concerning the continuation of a given therapeutic strategy [23]. Currently, image-based tests such as CT and MRI scans are used to visualize changes in tumor size and characteristics. However, the high cost of computed tomography/MRI imaging results in relatively long periods of time between scans. Biomarkers such as CEA and PSA are commonly used to monitor tumor status during therapy and between image evaluations; however, the levels of these proteins do not consistently correlate with the actual tumor response [23]. Laboratory studies have shown that tumor cells undergoing apoptosis can release cellular components into cell culture media such as cytochrome c, nucleosomes, cleaved cytokeratin-18 and E-cadherin. Studies have found that these and other macromolecules can be found in circulation during cancer therapy, providing a potential source of clinical indicators for monitoring treatment efficacy.

Returning to the example of ovarian cancer, Helleman *et al.* investigated biomarkers used for monitoring disease progression during and after chemotherapy [24]. SELDI TOF mass spectrometry was used to create serum protein profiles of ovarian cancer patients before chemotherapy or at progression and were compared with those of healthy individuals. In addition, sera profiles from ovarian cancer patients after chemotherapy were compared with those of ovarian cancer patients at progression. Eight primary (sensitivity: 94%; specificity: 97%; $p < 0.0001$) and seven progression tumor (sensitivity: 91; specificity: 97%; $p < 0.0001$) biomarkers were identified. In addition, the authors discovered eight potential progression monitoring biomarkers (sensitivity: 75; specificity: 83%; $p = 0.0008$), of which one, a biomarker of 11.7 kD, was further identified as serum amyloid A1. Independent validation exhibited an elevated expression of amyloid A1 at relapse in four of seven ovarian cancer patients tested. Combining the eight biomarkers with CA125 resulted in an increase in sensitivity (91–100%). This study suggests both a potential disease-monitoring and a screening role for the ovarian cancer biomarker assay. There may be further clinical evidence for the use of certain cancer biomarkers in the use of monitoring, especially if these have also been used in a screening paradigm, leading to future resource savings.

Treatment optimization

Biomarkers have shown potential value in matching patients to the most appropriate therapies [9]. Treatment optimization is becoming center-stage in many healthcare cost discussions, especially in oncology. Referred to variously as 'personalized,' 'stratified' or 'individualized' medicine [25,26], this clinical application of biomarkers is

defined by the ability of biomarkers to provide a "reliable, predictive correlation to differential patient responses" [27]. In their model of stratified medicine, Trusheim *et al.* identify several factors that support patient differentiation, including: underlying disease variability; indistinguishable clinical presentations; differential absorption, distribution, metabolism and excretion (ADME) characteristics, toxicity or tolerability of the therapeutic regimen(s); and the existence of multiple treatment options with heterogeneous responses [28].

A systematic review of the cost–effectiveness of pharmacogenomics, by Wong *et al.*, found 34 economic studies published through October 2009, of which seven studies were oncology based [28]. The review found that all identified biomarkers were clinically valid, with only one biomarker (HER-2; Herceptin®) also having clinical utility, where clinical validity is defined as consistently and accurately detection or prediction of intermediate or final outcomes of interest, and clinical utility is defined as how likely the test is to improve patient outcomes. Although HER-2 was identified as a test regularly implemented in clinical practice and considered to be successful in improving patient care, the cost–effectiveness study reported HER-2 to be over the $55,000 QALY-gained threshold. However, the study in question was published in 2004; therefore, it is possible that the cost–effectiveness has since changed due to several potential time-related variations in the underlying clinical and economic parameters used to assess the cost–effectiveness ratios.

Biomarkers have also shown promise when stratifying patients according to likely treatment response. In colorectal cancer, for example, the expression of DPD has been shown to be predictive of outcomes associated with combination treatment of capecitabine plus irinotecan. Koopman *et al.* studied 556 advanced colorectal cancer patients who were randomized between sequential treatment and combination treatment [29]. DPD expression showed a statistically significant predictive value for the combination treatment with low versus high values, resulting in an improved median progression-free survival and median overall survival of 8.9 versus 7.2 months, and 21.5 months versus 16.9 months, respectively.

Breast cancer biomarker use in selecting trastuzumab therapy for HER-2-positive tumors has demonstrated clinical effectiveness [30], while results (clinical and cost–effectiveness) for some gene-expression-based assays is inconclusive [31]. As an example of patient stratification in breast cancer, Hornberger *et al.* conducted an evaluation of a 21-gene assay (used with other data to calculate a recurrence score; RS) that predicts distant recurrence-free survival in lymph-node-negative, estrogen-receptor-positive patients with early-stage breast cancer receiving tamoxifen [32]. Among a hypothetical cohort of 100 patients, treatment based on RS reclassification was predicted, on average, to increase quality-adjusted survival by 8.6 years and reduce overall costs by $202,828. This stratification was cost saving in more than two-thirds of probabilistic simulations, with cost–effectiveness most influenced by the propensity to administer chemotherapy based on RS results.

The use of personalized medicine strategies is growing in popularity, especially within the oncology space; however, the effectiveness and thus the cost–effectiveness of biomarkers in this field will become more definitive as clinical evidence in a real-world setting emerges. The positive and negative predictive value data available for biomarkers will likewise improve as more real-world evidence is collected, particularly through large observational studies. The effectiveness of the biomarker may guide the direction of whether a biomarker works, but the cost element will illustrate its value to payers. It is not just the cost of the test, but the total costs and outcomes as a result of a biomarker-based strategy, including the cost of administration, resources to follow-up, patients' counseling and the infrastructure required, which will impact the cost–effectiveness and hence the value of the biomarker and the overall strategy and treatment pathway that it is eventually incorporated into.

Conclusion

The use of cancer biomarkers in patient care is not new, but recent technological developments in genomics, proteomics and metabolomics have increased the scope, breadth and thus the potential number and applicability of biomarkers available to clinicians. Improvements in biomarker sensitivity and specificity may also contribute to earlier and more accurate disease detection and enhanced treatment efficacy for stratified groups of patients [9]. Properly targeted cancer therapies may improve patient outcomes and economic efficiency owing to increased probability that those most likely to benefit are exposed to the intervention, and decreased probability that those who will not benefit would be subject to costly and potentially risky interventions.

The lack of cost–effectiveness or comparative-effectiveness data highlights the demands from

payers and policy-makers alike for better evidence regarding economic impact; literature suggest that private payers are beginning to use HTAs for personalized medicine coverage decisions [10]. Costs of biomarker tests are high; however, they are beginning to be viewed by many as medical advances with potential to add value, and payers require evidence to make value-based decisions regarding coverage [13]. A survey carried out by Cohen *et al.* [22] found that payers, for example, believed they should be allowed to limit reimbursement to certain drugs based upon test results. Key determining factors in these reimbursement limits include the likely impact the test could have on events avoided, and costs avoided for therapy that would not have

Executive summary

Background

- 7.6 million people worldwide died from cancer in 2008.
- Costs of cancer care in the USA in 2010 were US$263.8 billion, of which $102.8 billion were for direct medical care.
- Approximately half of the recent growth in health expenditures in the USA is attributable to advances in technology, including: new pharmaceuticals; medical devices; imaging modalities; biomarkers; and other *in vitro* diagnostics.

Biomarkers in cancer & cost–effectiveness analysis

- Use of cancer biomarkers to guide treatment can lead to improved clinical and economic benefits.
- Cost–effectiveness analyses provide a comprehensive comparison of both costs and outcomes among alternative scenarios, and can be used to assess the economic value of biomarkers. Costs may include (but are not limited to): cost of the test; associated costs (i.e. infrastructure and resources); and cost of events avoided.

Cancer biomarkers used in screening, diagnosis, monitoring & treatment optimization

- In addition to cost considerations, the economic value of biomarker testing is affected by: sensitivity and specificity of the biomarker; prevalence of the disease in the target population; and clinical utility of the test, such as the likelihood of the change in practice or improvement in patient outcomes from treatment based on the use of a biomarker.

Screening

- Comparatively low cost of biomarkers (compared with, for example, colonoscopies or mammograms) have the potential to lower aggregate screening costs, which may in turn alter the economic properties of screenings that in the past have relied on more costly diagnostic approaches.

Diagnosis

- The use of biomarkers with higher sensitivity and specificity than standard diagnostic methods has the potential to save scarce resources by optimizing the therapeutic approach and treatment timing.

Monitoring

- Monitoring has the potential to save resources if the costs of side effects or inefficacy of treatment are minimized by means of early avoidance and appropriate monitoring, respectively.

Treatment optimization

- Biomarkers have shown promise in stratifying patients according to likely treatment response and matching patients to the most appropriate therapies.

Conclusion

- Properly targeted cancer therapy may improve patient outcomes and economic efficiency due to increased probability that those most likely to benefit are exposed to the intervention and the decreased probability that those who will not benefit would be subject to costly and potentially risky interventions.
- Recent technological developments and improvements in biomarker sensitivity and specificity may contribute to earlier and more accurate disease detection and enhanced treatment efficacy for stratified groups of patients.
- Newer biomarkers may have a higher initial cost due to more advanced and specialized techniques; it is vital to assess their incremental and full economic impact including costs and outcomes of the downstream decisions that ensue.
- There is a lack of data assessing the economic impact of biomarkers. However, this evidence is needed as payers and policy-makers make value-based decisions to ensure that scarce healthcare resources are put to their most efficient use.

Future perspective

- There will be a need to develop additional cancer biomarkers; for example, to identify which treatments are most likely to succeed for a specific patient, and which treatments are unlikely to succeed.
- To better understand the health economic value of targeted cancer therapy, cost–effectiveness analyses will more frequently take a comprehensive view across the spectrum of screening, diagnosis, monitoring and treatment.
- Additional real-world research correlating long-term patient outcomes with the use of biomarker results will provide a foundation for future cost–effectiveness analyses and payer decisions.

been effective for the patient. The cost of the biomarker test was not necessarily a determining factor in its reimbursement, but payers required strong evidence of the link between the test and the outcomes.

In addition to the benefits to patients, there is clearly potential benefit in developing robust biomarkers, especially for oncology, for the healthcare industry. Developing a new drug is costly, with substantial risk of failure [33] as the product progresses from Phase I–III. During these phases, a growing number of patients are needed; this is particularly evident in oncology products where many Phase II/III trials are conducted in late-stage patients. As the HER-2 example shows, there is a potential for the targeted development of cancer drugs that would otherwise fail in the general nontargeted cancer population [33] and thus cause financial loss to the pharmaceutical company as well as discontinuing the production of a therapy that could otherwise offer a significant treatment option to many patients.

In the climate of cost containment and heightened scrutiny over healthcare expenditures, clinicians and decision-makers must understand the economic ramifications of any new approach to disease management. Since newer biomarkers may have higher initial costs as a result of more advanced and specialized techniques, it is vital to assess their incremental and full economic impact, including the costs and outcomes of the downstream decisions that ensue, to ensure that scarce healthcare resources are put to their most efficient use.

Future perspective

Compelling clinical evidence continues to mount for new cancer therapies, but these advances may come at an increased cost to the health system. Policy and reimbursement decisions help payers allocate limited funds, and consideration is also increasingly given to new technologies, such as biomarkers, that may contribute to overall cost containment.

There will be a need to develop additional cancer biomarkers, for example to identify which treatments are most likely to succeed for a specific patient, and which are unlikely to succeed. To better understand the health economic value of targeted cancer therapy, CEAs will more frequently take a comprehensive view across the spectrum of screening, diagnosis, monitoring and treatment. Additional real-world research correlating long-term patient outcomes with the use of biomarker results will provide a foundation for future CEAs and payer decisions.

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