Current Value Frameworks—What's New?

Moderator: Richard J. Willke, PhD; Panelists: Richard H. Chapman, MS, PhD, Joshua J. Seidman, MHS, PhD, Lowell E. Schnipper, MD, Patrick P. Gleason, PharmD

Introduction

The first plenary session reviewed some of the current leading value frameworks and how they inform healthcare pricing decisions. While other sessions discussed future trends and novel approaches to value frameworks, this session reviewed the current state of value frameworks. Presenters discussed recent developments in value assessment, such as incorporating patient and societal perspectives into a broader value framework, the challenges in valuing potential cures and treatments for rare disorders, applications within cancer therapy assessments, and value-based contracting.

Institute for Clinical and Economic Research

The ICER value framework states that it was developed to help ensure that all patients have access to high-value healthcare. This value framework considers both long-term value for money and short-term affordability. In measuring long-term value for money, the ICER framework incorporates 4 factors: (1) comparative clinical effectiveness (comparing new interventions with the existing standard of care), (2) incremental cost-effectiveness over the long-term, (3) relevant contextual considerations, and (4) other benefits or disadvantages, recognizing that what matters to patients is not limited to measured “clinical” outcomes. Short-term affordability, in contrast, is based on the potential budget impact of treatments over their first 5 years on the market.

The ICER recently modified its evaluation approach to better capture the relative value of treatments indicated for ultrarare diseases (URDs). It defines URD therapies as those interventions designed to treat fewer than 10,000 patients and which have no ongoing or planned clinical trials for populations of more than 10,000. After a call for public input and a literature review, the ICER published its modified value framework for URDs in November 2017.

The ICER notes that modifications to its value framework did not call for using a different standard of evidence for judgments of comparative clinical effectiveness. Its value-based price benchmark remains $100,000 to $150,000 per quality-adjusted life-year (QALY). Nevertheless, their reports on URDs include cost-effectiveness thresholds from $50,000 to $500,000/QALY and note that decision makers may accept higher thresholds for treatments for URDs than for other conditions.

In addition, ICER’s modified framework recognizes that assessments of URD therapies might require a broader basis to recognize the substantial benefits and costs experienced by families, school, and communities, especially when no treatment had previously been available. These therapies may also benefit the clinical community as practitioners develop a deeper understanding of the URD and its treatment and new screening programs for the URD are established. Therefore, in cases in which indirect costs are large relative to healthcare costs, the framework incorporates the societal perspective.

Additional contextual considerations include whether the URD is a high-severity condition, whether the URD results in a high lifetime burden of illness, and whether the intervention represents the first therapy for this condition. And finally, the ICER considers whether there is significant uncertainty around a treatment’s long-term risk of serious side effects, or magnitude or long-term durability of benefit.

Since the unveiling of the modified framework for URDs, the ICER has evaluated treatments for several URDs, including hemophilia A, cystic fibrosis, and most recently spinal muscular atrophy. One policy recommendation that has come out of this work is that all stakeholders should realize that the financial sustainability of the healthcare system may be challenged if the growing stream of treatments for rare and ultrarare disorders continues to be priced at levels far above traditional cost-effectiveness thresholds. In other cases, new treatments may appear to be cost-saving, even at a high price, if they displace existing
treatments with high costs. In such cases, reasonable value-based pricing may require consideration of a new paradigm to consider how these savings achieved through cost offsets could be shared between innovators and society.

The ICER is currently considering whether modifications to our value framework are required for potentially curative therapies. Questions persist regarding how best to implement value-based pricing for these therapies, given their potential to produce enormous lifetime health gains and cost offsets far beyond those generated by traditional therapies. How should prices reflect the uncertainty around the inclusion of additional elements of value that may be important for potential cures, but which are not part of standard cost-effectiveness methods? And are there additional social values that need to be considered in some value decisions related to treatments for specific conditions (eg, rapidly fatal conditions, pediatric conditions, or those with a high lifetime burden of illness)? The potentially large magnitude of lifetime health gains and cost offsets from curative treatments may make full pricing at standard cost-effectiveness thresholds unsustainable for healthcare budgets over the long-term. This and other concerns have led some to suggest other options, such as using a “fair profit” approach, capping the price at the level associated with the health gain without considering cost offsets, or examining the feasibility of “shared savings” between innovators and society.

As the ICER considers future modifications, it invites feedback from stakeholders.

Patient Perspective Value Framework

The PPVF was developed by Avalere and FasterCures to ensure that patients’ perspectives of value were better considered in value assessments. The framework uses patient preferences (needs, values, expectations, and financial trade-offs) as its lens through which patient value is understood. From there, the model considers benefits—patient-centered outcomes (eg, effectiveness, efficacy, side effects, complications, quality of life, and complexity of regimen). Costs considered in the PPVF reflect patient and family financial obligations (out-of-pocket medical costs and nonmedical costs) rather than systemwide costs. Quality and applicability of existing evidence, including the extent to which data exist on the heterogeneity of effects, address the individual-level question “What does the available evidence mean for someone like me?” And finally, usability and transparency form the foundation upon which the model rests.

The PPVF has completed the first 2 phases of its development process. In phase 1, a condition-agnostic framework for patient-centered value assessment was developed through broad public input. Phase 2 focused on testing and refining the framework, quantifying a scoring methodology, and developing a prototype for a preparation for shared decision-making tool. Phase 3 (launched in June 2018 and scheduled for completion in May 2019) involves the application of the PPVF scoring methodology to other value assessment methods (eg, ASCO and the National Comprehensive Cancer Network [NCCN]) and validation of the upstream shared decision-making tool developed in phase 2.

The PPVF scoring methodology combines evidence from different study designs, such as randomized clinical trials (RCTs), including meta-analyses of RCTs, as well as several types of real-world data studies. The scoring methodology uses weights on the basis of the rigor of the study design and adjusts for various biases known to occur in these studies, such as confounding biases in real-world evidence studies and performance bias in RCTs. (A technical appendix on the scoring methodology is available at http://avalere-health-production.s3.amazonaws.com/uploads/pdfs/1527784663_PPVF_Scoring_Methodology_Report_Final.pdf.)

The PPVF requires strong patient-centered data—a need potentially filled by real-world evidence. Possibilities include patient registries, patient associations, real-world data sources, or health system data. The PPVF team is considering how to incorporate different kinds of data sources into value assessment to better support the model.

The PPVF team has been working with other organizations looking at how specific PPVF criteria and measures can be applied to their value frameworks, as well as exploring possible data sources to support that process. Eventually, the team intends to publish a set of technical recommendations around what we can do now as well as in the future.

A final aspect of this work is the PPVF shared decision-making tool. Development of this tool evolved from primary qualitative research with patients with cancer and quantitative research conducted by CancerCare. Both types of research found that patients often did not feel like active participants in the development of their care plans, that they often felt overwhelmed by the process and did not know what questions to ask. Patients needed a roadmap for their care journey. In response, the team developed the PPVF shared decision-making tool to support conversations between patients and providers at the point of care. The PPVF shared decision-making tool differs from traditional decision aids in that it prepares patients to engage in shared decision making. Working with focus groups of patients with advanced breast cancer, family, and practitioners, Avalere used a human-centered design process to develop a prototype, which has since gone through a formal validation process with an independent group of 30 patients (Avalere Health, unpublished data, 2019).

American Society for Clinical Oncology

Value frameworks have gained broader use in the field of oncology where the benefits of new and promising therapies are not necessarily uniformly distributed. With some new therapies, the evidence demonstrates improved results. With others, there may be only marginal gains. An article recently published in JAMA showed no strong relationship between drug effectiveness and price (annual price-per-year vs survival). For oncologists choosing a cancer treatment—especially when that treatment could financially imperil a patient—a cancer-specific value framework has become critically important. This environment of increasing costs of drugs and healthcare services (and increased patient cost-sharing) versus inconsistent benefits propelled ASCO to develop its cancer-focused value framework.

ASCO’s framework differs from other value frameworks (eg, ICER’s) not only in its cancer focus but also in its application to physician-patient decision making. It joins 2 other cancer-specific value frameworks, for example, NCCN and the European Society for Medical Oncology (ESMO), although NCCN is a more subjective tool for physician-patient decision making, and ESMO aids policy decisions at the Ministry of Health level. In fact, the parameters included in the ESMO framework so sufficiently resemble those included in the ASCO framework that it was deemed important to assess whether these 2 frameworks were measuring the same thing. Related questions include when should these different frameworks be used, and should there be a common threshold for defining value ($/QALY, net health benefit/$) to allow comparisons.

The ASCO framework first considers net health benefit and the cost of administering a particular medical regimen to both health...
system and patient. The framework determination, on the basis of consensus among framework developers, is weighted most heavily by clinical benefit, with overall survival being the most important (derived from the hazard ratio in a comparative study); progression-free survival is less important (not a universally reliable surrogate for survival, therefore not as valuable), and response rate is the least valuable because it does not necessarily correlate with ultimate survival. The framework includes bonus points for extended survival to reflect “tail of the curve” survival for those therapies that benefit only a meaningful minority, but that help those few patients tremendously. Toxicity is included as a liability all therapies face, detracting from clinical benefit. And finally, the patient’s out-of-pocket costs are included, which, given the expense of cancer therapies, are extremely important to patients and a cause of “financial toxicity.”

The ESMO and ASCO frameworks are similar in that they both base their judgments on hazard ratios, they both consider toxicity, and they both differentiate their recommendations in curative versus noncurative (adjuvant or metastatic) settings. And neither uses cross-tail comparisons, and thus the importance of the control. Yet there is an important difference—ESMO does not address cost because this organization informs 28 European nations, all of which face very different economic situations.

Despite these similarities, the ASCO and ESMO value frameworks can lead to differing determinations of clinical benefit and, thus, different treatment recommendations. As presented in Table 1, a recent study comparing the 2 frameworks’ scoring of the clinical benefit of thyroid cancer treatment found stark differences, resulting in contrary treatment recommendations; use of the ASCO framework supported this treatment choice, whereas ESMO rejected it.

The ASCO team investigated further, hoping to better understand the differences between these frameworks. Using the ASCO framework, the team rescored 103 assessments previously conducted by ESMO. They found a correlation coefficient of 0.71 for those trials in which overall survival was the primary endpoint and 0.67 when progression-free survival was the primary endpoint.

These differences could stem from multiple model differences. For instance, ASCO values progression-free survival more highly than does ESMO. ASCO also applies a more complex formula for assessing toxicity; a reconciled approach to toxicities has been suggested given how important toxicity is to patients.

An important cause of score divergence stems from ASCO scoring relative benefit without considering absolute gain, whereas ESMO does consider absolute gain. This may be especially important from the patient perspective given that in some cancers (eg, pancreatic cancer) a few months of additional survival can be very meaningful to these patients, whereas in other diseases such a small amount of additional survival may carry less importance.

In brief, multiple value frameworks may still be beneficial given that different frameworks can address different purposes. If a framework is needed to assist physician-patient shared decision making, frameworks must capture patient preferences (eg, toxicity avoidance, convenience, and quality of life vs length of life). But with more uniform measurements of clinical benefits and toxicity, thereby facilitating convergent validity, these frameworks could be used more widely in policy formation. With these considerations in mind, the ASCO framework is undergoing further refinement.

**Payer Perspective**

The perspective of Prime Therapeutics, a US payer, provides some useful insights into how payers use value frameworks in their coverage decisions. Prime Therapeutics, a pharmacy benefits manager covering 20 million enrollees, currently uses a form of the ICER model to inform coverage decisions and pricing negotiations with a goal of sustaining access to high-value care for all enrollees.

Prime Therapeutics considers 2 primary factors in determining access to a given treatment—the treatment’s long-term value for money and its short-term pharmacy spend. Long-term value for money weighs (1) clinical outcomes, (2) comparative effectiveness, (3) total cost of care, and (4) persistence and/or adherence. Short-term pharmacy spend addresses potential budgetary impact, which incorporates forecasting the new drug therapy utilization and financial impact on both pharmacy benefit and medical benefit.

Forecasting, supported by medical and pharmacy claims data analyses, helps payers set premiums sufficient to absorb the costs many new drugs bring to the market. In addition, value-based contracts can help mitigate costs, especially for new drug/gene therapy with substantial durability and safety uncertainty. These contracts may be outcomes-based or financial-based contracts (summarized in Figure 1). But this type of contracting varies depending on whether therapy is curative or is a chronic/lifetime treatment.

- Curative therapies tend to have a very high per-patient cost burden, often with uncertain durability of the treatment effect. Effectiveness and safety may be tracked using registry data. Payers are strongly motivated to find ways to spread the cost over time rather than incur a massive charge in the very short term.
- Chronic lifetime therapies typically impact far larger populations. The slower disease progression provides a longer time

### Table 1. Clinical benefits of anticancer agents approved by the FDA in 2015-2016.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>ESMO grade*</th>
<th>ASCO score</th>
<th>Monthly cost ($)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lenvatinib</td>
<td>Thyroid cancer</td>
<td>2</td>
<td>43</td>
<td>24,105</td>
</tr>
<tr>
<td>Panobinostat</td>
<td>Multiple myeloma</td>
<td>3</td>
<td>29</td>
<td>11,733</td>
</tr>
<tr>
<td>Triludirine/ tipiracil</td>
<td>Colorectal cancer</td>
<td>2</td>
<td>29</td>
<td>14,293</td>
</tr>
<tr>
<td>Trabectedin</td>
<td>Soft-tissue sarcoma</td>
<td>3</td>
<td>27</td>
<td>11,599</td>
</tr>
<tr>
<td>Cobimetinib</td>
<td>Melanoma</td>
<td>3</td>
<td>29</td>
<td>7,856</td>
</tr>
<tr>
<td>Ixazomib</td>
<td>Multiple myeloma</td>
<td>3</td>
<td>20</td>
<td>10,821</td>
</tr>
<tr>
<td>Necitumumab</td>
<td>Non-small cell lung carcinoma</td>
<td>1</td>
<td>14</td>
<td>13,056</td>
</tr>
<tr>
<td>Elotuzumab</td>
<td>Multiple myeloma</td>
<td>3</td>
<td>22</td>
<td>10,094</td>
</tr>
<tr>
<td>Palbociclib</td>
<td>Metastatic breast cancer</td>
<td>3</td>
<td>25</td>
<td>13,155</td>
</tr>
<tr>
<td>Olaratumab</td>
<td>Soft-tissue sarcoma</td>
<td>4</td>
<td>44</td>
<td>15,859</td>
</tr>
</tbody>
</table>

ASCO indicates American Society of Clinical Oncology; ESMO, European Society for Medical Oncology; FDA, Food and Drug Administration.

*Calculation of ESMO grades requires statistically significant results on toxicities; nevertheless, P values are often omitted from tables in reports of clinical trials, and thus have not been incorporated into scoring shown herein.

†Drug costs according to the current lowest average wholesale price calculated for treatments with 1.79 kg/m² body surface area or 70 kg body weight and averaged over a 28-d period.

‡Price of 2 doses per 28-d cycle.

Source: Adapted from Booth and Del Paggio.
Value-based contracting (and the cost-of-value drug pricing it supports) may be critical in eliminating controversial drug rebate programs—a step that many stakeholders support.

An example (see Figure 2) helps illustrate how payers use value framework results in helping to close the gap between drug prices and their value points for all drugs and healthcare technologies.
payers identify as having a price to value gap. Identifying a price to value gap is frequently informed by an ICER report. In this example, Prime Therapeutics took ICER’s 2017 report and calculated an average annual actual cost for all self-administered multiple sclerosis disease-modifying drugs (MS DMDs). The calculated 2017 average annual cost using the ICER reported wholesale acquisition cost was $80,073. Prime Therapeutics averaged the ICER report value-based price at the $150,000/QALY threshold of $30,379. This resulted in a difference of roughly $50,000 between the actual drug price and its value price. Given that manufacturers offered cost discounts of $28,015 (split between the manufacturer’s coupon and rebates), a cost gap of $21,679 remained. Value-based contracts may help to close such gaps. Prime Therapeutics and Biogen (the manufacturer of MS DMDs dimethyl fumarate [Tecfidera®], natalizumab [Tysabri®], interferon beta 1a [Avonex®], and peginterferon beta 1a [Plegridy®]) have entered into a value-based contract that places accountability on Biogen to deliver safety, efficacy, and value for the patients who receive these life-impacting therapies and for the payers who finance them. Although value-based contracting for MS DMDs improves the value-to-price ratio, the large gap can lead payers to prioritize clinical program development to other conditions in which there is more healthcare improvement for the investment.

Conclusions

Although current value frameworks have much to offer to decision makers, there is clearly much room for improvement, both in terms of how value is measured and how those measures are used. Oncology provides some illustrative examples of these opportunities. A common endpoint in oncology trials is progression-free survival, but its use in regulatory and payer decision making has been controversial because of its imprecise correlation with overall survival. An improvement would be to routinely measure and report patient quality of life directly during the progression-free survival period in oncology trials for incorporation into value assessments. Although quality of life is more commonly measured in oncology and other disease trials than it used to be, significant gaps in capturing the patient experience during treatment remain. With respect to use of value measures, the gaps are even more obvious. Changes in the pricing of products in recent years probably do not reflect changes in value, even adjusting for the effects of discounting on net prices. And although many products have multiple indications, few allow for prices to be adjusted when different indications have different values.

The subsequent sessions of this summit will explore these and other gaps in more detail and will suggest some specific approaches for making improvements.

REFERENCES