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Is There a Mathematical Resolution to the Cost-Versus-Value Debate?

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- Restricted clinical pathways
- Product tiering
- Step edits.

Proposed policy approaches to specialty drug cost control have included, but are not limited to:

- Empowering Medicare to negotiate drug prices (as the Veteran's Administration does)
- Allowing the importation of drugs for personal use
- Reforming the patent system to combat so-called pay-for-delay settlements between brand and generic drug makers.

Solutions proposed by patient advocates and physicians aim to control costs by providing standardized approaches to valuing new drug/treatments compared with 1 or several prevailing standards of care. Increasingly, the debate over cost is transitioning to a debate over value, but the value of cancer drugs—in what is often a complex multi-modality treatment of a terminal disease—is complicated to say the least.^{4,5}

VALUE CALCULATORS

Thus far 2 provider organizations, one a professional society and the other a cancer center, have developed a value-based cancer care model geared to the patient and the provider. These models were recently made available for peer and public review. A third was previewed with limited content restricted to 2 less-prevalent cancer diagnoses.

The American Society of Clinical Oncology (ASCO) announced its Value Framework in June 2015, which is designed to help physicians and patients assess specialty drug treatments based on their clinical benefit, side effects, and cost. ASCO's approach is thus far unique, released to the public and professional community using a peer-reviewed publication that included extensive background and content on methodology. Schnipper et al have detailed the nuances of the Value Framework, developed by ASCO's Value in Cancer Care Task Force, in the *Journal of Clinical Oncology*.⁶ The framework is expected to be applied by medical oncologists to assess the relative value of cancer therapies, in various clinical scenarios, as an element in the shared decision-making process with their patients.

In the same week, an interactive online tool developed by Peter B. Bach, MD, director of the Center for Health Policy and Outcomes at Memorial Sloan Kettering Cancer Center (MSKCC), was also made public. The DrugAbacus calcula-

tor attempts to place drug costs in line with their overall value (FIGURES 1 and 2). The calculator has primarily been developed as a tool for research and information only, but critics and supporters believe it “may be utilized by physicians to start a conversation discussing the value of chemotherapy agents with their patients.” However, the authors clearly state it is purely informational and should not be used to guide decision making.⁷

More recently, the National Comprehensive Cancer Network (NCCN) provided a preview of its Evidence Blocks via mainstream media and its website. The Evidence Blocks, for now, are limited to multiple myeloma (MM) and chronic myeloid leukemia (CML). The NCCN Evidence Blocks are published in a new version of the NCCN Guidelines and are intended as a visual representation of 5 key value measures: efficacy, expected associated toxicities, and the quality, quantity, and consistency of the evidence that provide important information about specific NCCN Guidelines recommendations (FIGURE 3).⁸

Other strategies aiming to gauge cancer-drug value are under development by the European Society of Medical Oncology and the Boston-based Institute for Clinical and Economic Review (ICER). ICER recently announced it had received a \$5.2 million grant from the Laura and John Arnold Foundation to produce 15 to 20 reports on the value of major new drugs approved by the FDA.⁹ Understanding the similarities, differences, and potential limitations of these approaches to calculate cancer-drug value will be critical to their adoption and appropriate use.

VALUE AND QUALITY

Interpreting value relative to cost, what is often also referred to as cost-effectiveness, is not a new concept in healthcare. For over 2 decades, cost-effectiveness analyses, particularly in the United States, have used a figure of \$50,000 per life-year or quality-adjusted life-year (QALY) gained as a threshold for affirming the cost-effectiveness of an intervention. The history of this practice is ill defined, although it has been linked to the end-stage renal disease kidney dialysis cost-effectiveness literature that dates back to 1968.¹⁰ The use of \$50,000 as a benchmark for assessing the cost-effectiveness of an intervention first emerged in 1992 and became widely used after 1996.¹¹ Critics have argued that this figure is arbitrary,

that its appeal lies more in the convenience of a round number rather than in the current value of renal dialysis or in stakeholder assessment.¹² Nonetheless, cost-effectiveness or value analyses of healthcare interventions have an extensive history.

The confusion inherent to the casual interchangeable use of terms like quality, value, and cost-effectiveness was clarified in a seminal report published in 2002 by the Institute of Medicine (IOM), *Crossing the Quality Chasm*.¹³ This influential work framed all future discussions of quality healthcare. In the report, IOM outlined 6 specific aims that a healthcare system must fulfill to deliver quality care:

1. **Safe:** care should be as safe for patients in healthcare facilities as in their homes.
2. **Effective:** the science and evidence behind healthcare should be applied and serve as the standard in the delivery of care.
3. **Efficient:** care and service should be cost-effective and waste should be removed from the system.
4. **Timely:** patients should not experience waits or delays in receiving care and service.
5. **Patient-centered:** the system of care should revolve around the patient, respect patient preferences, and put the patient in control.
6. **Equitable:** unequal treatment should be a fact of the past; disparities in care should be eradicated.

Although the focus of the IOM report was not the medical intervention itself, but the healthcare system delivering it, its conclusions broadened value concepts for interventions beyond safety and efficacy. Cancer-care value assessments, which historically have focused on efficacy and toxicity, have been informed by this seminal work. Patient-centered aspects of treatment value like route, frequency, and site of administration are now routinely considered. The IOM's report on quality and the legacy of research using QALYs serve as a foundation on which these new value tools can be evaluated.

METHODOLOGY USED BY THE VALUE CALCULATORS

The authors of the ASCO Value Framework have attempted to define value in terms of 3 of the 6 IOM elements of quality healthcare delivery: efficacy (clinical benefit), safety (toxicity), and efficiency (cost). They have chosen to use “net health benefit” (NHB), which is the dif-

The projections for the rising cost of cancer care have spurred robust dialogue from every sector of the healthcare economy.¹ Among the many targets for cost control are the rising cost of cancer specialty drugs—drugs distinguished by their route of administration, synthesis or bioengineering, mechanism of action, cost, etc.² Although there are examples of market forces and competition emerging to tamp down prices to more acceptable levels (eg, pharmacy benefit manager negotiations for hepatitis C drugs), stakeholders seem impatient for these market-based solutions.³

Payer approaches to specialty drug cost control have included, but are not limited to:

- Bundled reimbursement
- Episode-of-care reimbursement

FIGURE 1. Actual and DrugAbacus-Calculated Medicare Monthly Drug Price of Oncology Agents

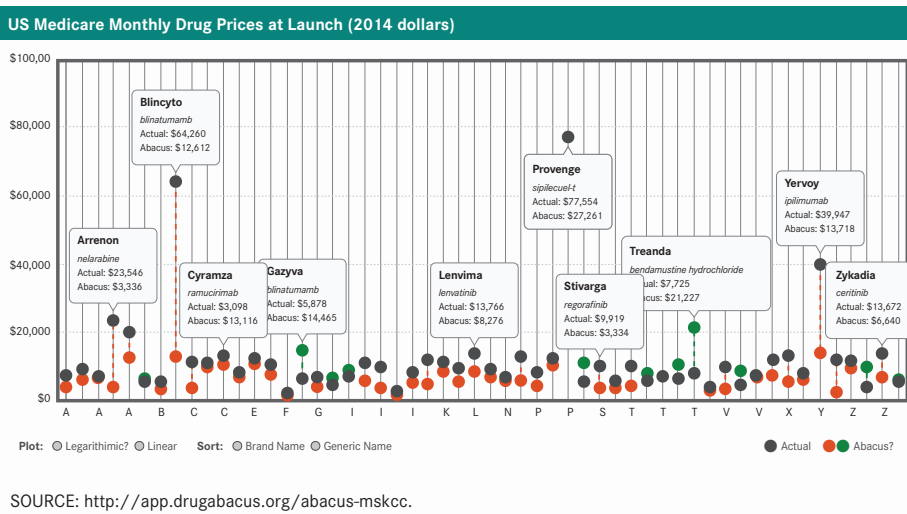
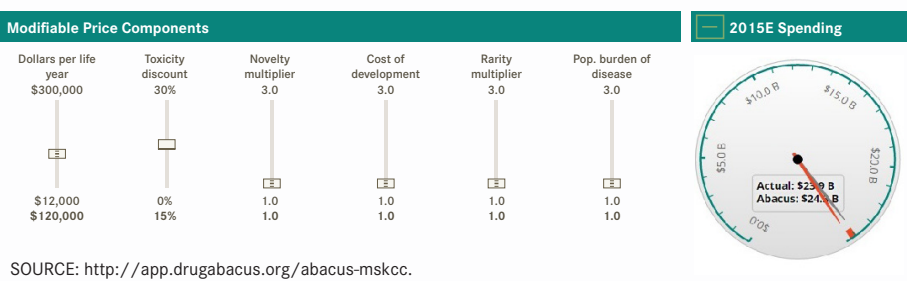


FIGURE 2. Modifiable Inputs That Determine Drug Cost Using DrugAbacus



ference in mean effectiveness of a new treatment compared with a standard, as the aggregated metric for a value assessment in this tool. NHB is composed of 3 elements: clinical benefit (max 80% contribution), toxicity (+/- 20% contribution), and bonus points (maximum, 30). Clinical benefit is assigned a score between 1 and 5 based on the fractional improvement in overall survival (OS) or if not available, progression-free survival (PFS) based on a specific clinical scenario comparator. The clinical benefit score is then multiplied by a weighting factor (16 for OS and 11 for PFS). Toxicity is also assigned a categorical value ranging between -20 and +20 based on fractional decrease or increase in grade 3 to grade 5 toxicities of the comparator. Finally, bonus points can be awarded for differential symptom palliation or treatment-free interval.

The task force has decided to display NHB as a separate calculation without the cost factored in so that physicians and patients can view the clinical information independent of the cost. Although this methodology deviates significantly from formal economic analysis, it may feel more realistic to both the physician and the patient who are focused on a very specific clinical scenario.

The DrugAbacus uses 4 of the 6 parameters outlined by the IOM for quality healthcare delivery: efficacy (clinical benefit), safety (tolerability), efficiency (cost), and equity (rarity and population burden). Only timeliness and patient centeredness are not considered.

The 6 specific attributes that DrugAbacus does consider in value determina-

tion, include: efficacy, toxicity, novelty, development cost, disease rarity, and population burden—all at the individual drug level. In this tool, as in the ASCO framework, efficacy is measured in terms of OS; if OS is not available, then PFS or response rate are used as a surrogate, but modified by a level of evidence grade into an estimated OS benefit. Toxicity scoring has 2 components: differential proportion of grade 3 to 4 adverse events (AE) and differential probability of drug discontinuation due to AE. The user determines the weight of each of the components. For example, the user must determine the value of efficacy in order to output a price, and can also manipulate the weight of the other factors. The output is dependent solely on how the user values each of those 6 attributes.

The NCCN Evidence Blocks are in development, but from the information currently available, value determination is regimen-based, rather than drug-based, and comprises the following:

- Efficacy of regimens
- Safety of regimens
- Quality and quantity of evidence for regimens
- Consistency of evidence for regimens
- Affordability of regimens

Each of the attributes is graded 1 to 5 and presented to the user in a visual 5 x 5 grid of 25 squares, with the X axis having 5 columns, 1 for each attribute, and the Y axis having 5 rows for low to high assessment. The higher the value, the more opaque the grid. The affordability measurement represents an estimate of

overall total cost of a therapy, including, but not limited to, acquisition, administration, in-patient versus out-patient care, supportive care, infusions, toxicity monitoring, anti-emetics and growth factors, and hospitalization. Although a detailed methodology that explains the process used to assign grade is not yet available on the NCCN website, a list of the criteria used by the panel members to score the measures is elaborated, suggesting that as per the historical guidelines, the Evidence Block grading system will be by subjective consensus among panel members.

EFFICACY

In regard to efficacy determinations, the tools use significantly different approaches, as evidenced by their use to assess systemic treatment value in stage IV, or metastatic, non-small cell lung cancer. The Value Framework presents 4 different clinical scenarios, 2 comparators at a time, which may include as many as 5 drugs incorporated into treatment cocktails or regimens.

In the DrugAbacus, the comparison is made at the single-drug level even when the drug is only administered as one component of a regimen. Although DrugAbacus currently has information pre-populated for 54 different chemotherapeutic agents, all information is based on the drug's first approved indication and monotherapy, neither of which may apply to the specific clinical scenario of interest.

NCCN's approach to MM and CML suggests that an efficacy grade of 1 to 5 will be assigned based on panel consensus for each regimen and comparator. Although all tools limit comparisons to prospective published peer-reviewed study data comparing the new agent or specific regimen of interest with known comparator(s) of interest, NCCN offers some redress by addressing quality, quantity, and consistency of evidence.

TOXICITY

In regard to redress of toxicities, the approaches are again different. ASCO's Value Framework limits AE inclusion to those grade 3 to 5 only and treats all of them equally. The DrugAbacus also limits to higher grade (3 and 4) AE, then augments that number by determining

their influence on value by including toxicities that impact discontinuation rates or impact resource utilization. NCCN takes a more inclusive approach grading toxicity from 1 (not meaningful) to 5 (severe, life threatening). Despite such thoughtful and varied approaches to the impact of safety/toxicity on value, AE burden remains incredibly subjective for most patients.

Despite such thoughtful and varied approaches to the impact of safety or toxicity on value, AE burden remains incredibly subjective for most patients. Alopecia is unlikely to result in treatment discontinuation or acute care intervention cost, but it is a deciding factor in some patients' treatment selection. Severe neutropenia has a real mortality risk yet can be effectively prevented, but only at a potentially significant cost. Intermediate grade neuropathy may neither incur acute care intervention cost nor impact treatment intensity, but physicians are all too aware it may become a lifelong disability.

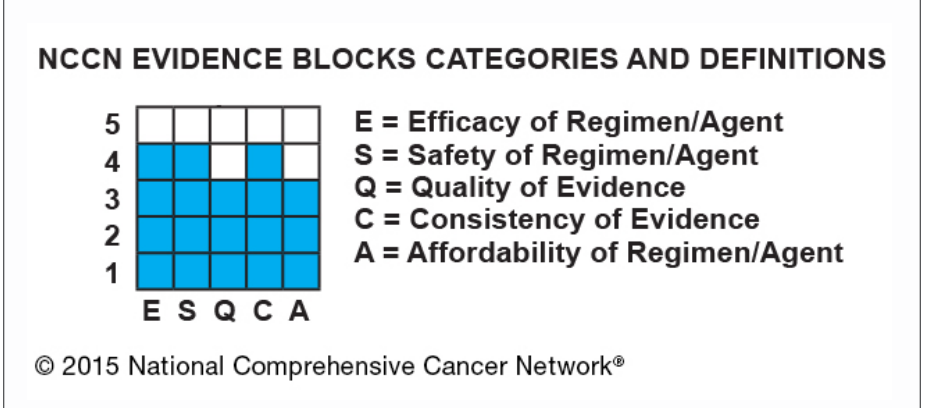
EFFICIENCY

These approaches have their greatest differentiation in the assessment of their cost-effectiveness. The Value Framework separates the clinical assessment from the economic, asking the user to determine value. The DrugAbacus incorporates cost based on Medicare reimbursement, but provides significant latitude for user discretion through the use of price (or value) modifiers. NCCN uses a 1-to-5 grading system incorporated into the visual Evidence Block, but we currently lack insight into their approach to affordability grading (whether it uses absolute dollar thresholds of cost or relative to comparators). Regardless of approach, the inclusion of cost represents a sea change from prior approaches to cancer treatment valuation and selection.

CONCLUSIONS

The ASCO Value Framework, DrugAbacus, and NCCN Evidence Blocks provide opportunities for discussions about the financial costs and associated value gained from the various treatments of oncology patients. By the authors' own accounts, the ASCO tool is designed as

FIGURE 3. NCCN Evidence Blocks



a patient decision-support tool, DrugAbacus is research-focused and informational, and the stated goals of the NCCN are to provide the healthcare provider and patient information to make informed choices.

These tools are not completely intuitive, suggesting providers and patients will need experience or training to optimize them. ASCO clearly states their vision is to preload comparisons into user-friendly software. The DrugAbacus has default values if modifiers are not specified. NCCN's panel consensus may suffer for subjectivity. Critical evaluations of these approaches to value assessment provide a telescopic view into the existing gaps in evidence and literature, and provide additional opportunities for research.

The complexity of cancer treatment and the related design of clinical trials further complicate tool design. Use of drugs in combination rather than as monotherapy, mandatory or reflexive use of supportive care drugs, crossover trial design, prevailing therapeutic, or best supportive care comparator, are but

a sampling of the intricacies of oncologic research that may bedevil any approach to value calculation. Traditional clinical research may itself be problematic in value determination, as declining single-digit participation of adult oncology patients who are often younger and healthier and less diverse than their real-world counterparts may be less than representative of the target population.

Conversations on costs and value at both the patient and population levels may provide insights into areas for improvement in medical education and training. Lastly, it behooves all stakeholders to give consideration whether this is a discussion best conducted at the patient, policy, or payer level as we move toward considering both value and costs in our medical decision processes. **EBO**

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Targeted Therapies

Will spending more in cancer bring value by improving survival? Read here <http://bit.ly/1XCU2A1>.

PROVIDER COMMENTARY

ABOUT THE AUTHOR



21st Century Oncology

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The venture discussed in this article is a successful collaboration of 21st Century Oncology with the Lee Memorial Health System.

The cancer care environment today is defined largely by medical innovations. No matter the setting, patients are exposed to physicians using pioneering treatments. As a result, health outcomes are better than ever and survival rates are rising for almost every form of the disease. The 5-year survival rate for all cancers has increased by 20% over the past 4 years.¹ Such positive statistics, which manifest themselves in the form of lives saved, suggest something quite vital: When it comes to cancer, we are finally getting the science and subsequent therapies right. And with each subsequent biomedical discovery, we put ourselves on a path towards solutions once thought impossible.

Maximizing Value of Freestanding and Outpatient Hospital Setting in Cancer Care Delivery

CONSTANTINE MANTZ, MD

Even as science races forward, breakthroughs still take time. Therefore, it is imperative that we supplement critical areas like biomedical innovation with equivalent advances in care delivery to reform the way physicians operate—anticipating powerful outcomes. Perhaps most importantly, changes to the efficiency of cancer care—unlike changes to the medicine or technology we use—can be implemented immediately. In the short run, structural and procedural changes are the most effective tools to improve health outcomes and could do the most to provide better value and low-cost cancer treatment.

Ultimately, there is a simple way to bolster the efficiency of cancer care: collaboration. Although this may seem obvious, collaboration in healthcare is no simple task. In most cases, oncologists, treating the same patient, operate across a myriad of specialties in disparate settings, resulting in minimal communication and lack of a unified vision for a patient's course of care. Additionally, there are consistent gaps in care coordination among cancer specialists, diagnostic radiologists, and pathologists. This system leads to obvious inefficiencies, such as repeated and unnecessary

tests. It also prevents patients from receiving the highest quality care following a cancer diagnosis.

Quite simply, collaboration would eliminate inefficiencies—saving critical time, improving patient outcomes, and cutting system costs. Therefore, over the past 4 years, we at 21st Century Oncology and Lee Memorial Health System have put ideas into action, working together to establish a multidisciplinary breast cancer clinic in Lee County, Florida.

Our goal was to eliminate the clutter of cancer care and create a single, unified breast cancer treatment center that combined the best parts of a freestanding oncology setting and the outpatient hospital environment. Just 2 short years after initiating the project, we were able to achieve a National Accreditation Program for Breast Centers certification. Our hope is that our experience can generate a replicable model of collaboration across all spectrums of cancer care.

IMPROVING QUALITY OF CARE THROUGH COLLABORATION

The process began with the creation of a multidisciplinary Breast Program Leadership Team Committee, composed of physicians (including radiation oncol-

gists), breast fellowship-trained surgeons, general surgeons, and radiologists. It also included a chief administrative officer, a medical director, 2 breast cancer navigators, and a cancer registrar. Following multiple rounds of deliberations, experts experienced with the local patient population drafted comprehensive plans for a new breast cancer clinic that would effectively integrate radiation oncology, surgery, and medical oncology.

Thus far, the results have been very encouraging and measurable in key areas. Since the establishment of the clinic, we have witnessed a significant reduction in the “screening to call back” average, which essentially measures the time patients wait for test results. Before oncology services were unified in the multidisciplinary clinic, patients were forced to wait an average of 12.5 days for screening results; subsequently, the average fell to 6.5 days. We witnessed an even more dramatic reduction in the “screening to diagnosis” average—9.55 days compared with a staggering 34 days prior to unification. In other words, even in its nascent stages, patients were reaping the rewards of integrated care.

In addition to strengthening quality
(continued on SP546)