The Value of Addressing Patient Preferences

Jeff D. Allen, PhD*, Mark D. Stewart, PhD, Samantha A. Roberts, PhD, Ellen V. Sigal, PhD
Friends of Cancer Research, Washington, DC, USA

ABSTRACT

Recent scientific progress is, in some cases, leading to transformative new medicines for diseases that previously had marginal or even no treatment options. This offers great promise for people affected by these diseases, but it has also placed stress on the health care system in terms of the growing cost associated with some new interventions. Effort has been taken to create tools to help patients and health care providers assess the value of new medical innovations. These tools may also provide the basis for assessing the price associated with new medical products. Given the growing expenditures in health care, value frameworks present an opportunity to evaluate new therapeutic options in the context of other treatments and potentially lead to a more economically sustainable health care system. In summary, the contribution to meaningful improvements in health outcomes is the primary focus of any assessment of the value of a new intervention. A component of such evaluations, however, should factor in timely access to new products that address an unmet medical need, as well as the magnitude of that beneficial impact. To achieve these goals, value assessment tools should allow for flexibility in clinical end points and trial designs, incorporate patient preferences, and continually evolve as new evidence, practice patterns, and medical progress advance.

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postmarket studies are conducted to confirm clinical benefit, as opposed to requiring significantly longer and more limited access to premarket studies to demonstrate an effect on overall survival before the treatment becomes available to patients.

In some proposed value frameworks, a drug would be determined to be more valuable, and consequently would likely command a higher price, if it showed a significant effect on overall survival. Although this seems logical, it may penalize some of the more effective drugs currently available to cancer patients (e.g., precision medicine or targeted therapies), many of which have demonstrated unprecedented effects on response rates and disease control rates in the premarket setting such that a randomized trial to assess survival might not be acceptable to patients.

Tools that overemphasize overall survival while underemphasizing other outcomes that also matter to patients, such as reduction of tumor or symptom burden or reduction in hospital admissions, may inadvertently create an incentive structure that prioritizes the development of long-term clinical benefit data in the premarket setting at the expense of providing patients timely access to potentially beneficial treatments. When interventions are approved based on surrogate end points, it does create some uncertainty as to whether the surrogate end point will reflect improvements in overall survival.

There are instances where surrogate end points do not always equate to improvements in overall survival when analyzed in later, postmarket confirmatory trials. Value frameworks, however, should ensure patients are able to designate the level of uncertainty they are willing to accept as they use these frameworks to potentially guide their therapy decisions. Importantly, when these confirmatory data are available, value frameworks should quickly incorporate this information so patients have the most up-to-date information.

When options have been exhausted, patients want access to experimental therapies provided through innovative clinical trial designs. In addition to end point selection, the experimental design of a clinical research trial plays a role in balancing the optimal evaluation of a new intervention with patient access. Patients who had been treated with the standard of care might be allowed access to the investigational intervention once the primary end point has been met in some clinical trials. This approach, referred to as crossover, allows more of the study participants to have access to the intervention under study and is an example of how a patient-centric approach can positively influence clinical trial designs.

Crossover, however, can also result in loss of information about the clinical impact of any new interventions when compared with a more rigid clinical trial design in which crossover would not be allowed [9,10]. If a value assessment is made by comparing the relative improvement in survival yielded by a new intervention to that of another, sponsors may inadvertently be driven to rely solely on premarket overall survival data; patients then may be denied the opportunity to crossover to make the intervention be perceived as more valuable in value assessment frameworks. Precluding crossover may result in a more clearly defined assessment of magnitude of benefit, but patients may also be less likely to participate in studies that prohibit crossover.

These examples are not intended to suggest that clinical end points, such as overall survival, should not be included as important components of value-based assessments of medical technologies. Understanding the long-term implications of providing and paying for new treatment options is necessary to improve health care for patients and ensure that it is accessible and affordable for society and for individuals. These scenarios demonstrate, however, that value framework metrics should be constructed in a flexible manner that ranks appropriate timely access as a component of value to encourage the development of treatments that address unmet medical needs and patient needs. To accomplish this goal, value frameworks should appraise the full spectrum of available evidence and employ appropriate methods to ensure they fairly capture the benefits of each therapy. The long-term value of an effective intervention also needs to reflect nonfinancial end points, such as impact on family and community, route of administration, and other functional elements, which may not easily be quantifiable in standard, short-term pecuniary terms. They should also evaluate the therapy’s impact on the overall cost of care (e.g., physician visits, hospital care, surgery).

Some value frameworks do incorporate the use of the quality-adjusted life-years, which have become standard in economic evaluations that attempt to identify what is optimal for society. Quality-adjusted life-years may not, however, adequately capture what is important for individual decision making. Therefore, value frameworks directed toward patients should work to provide a tailored output based on the needs of the individual end user. Value frameworks could serve to promote the inclusion of these important patient-focused metrics in future trials to better accomplish this goal.

Until patient-reported outcomes are routinely captured in clinical trials, framework developers should consider other methods to collect this information. Methods could include less formalized, postmarket data collection to better understand if an intervention is having a positive impact on aspects of patients’ lives that are not frequently collected in premarket clinical trials. The involvement of patients and their caregivers in identifying aspects of daily life that were undesirably interrupted by an illness could also help inform future value assessments of different interventions. For example, patients often note that a desired outcome of treatment is the ability to continue to work [11]. An intervention that consistently allows patients to return to work more quickly than an alternative may be more valuable to some patients and may positively inform their treatment decisions.

Frameworks should also be flexible in incorporating evolving information regarding the context of use, such as the future availability of additional treatments for the same condition, as well as in assessing the value associated with different uses of the product, such as in a different line of treatment, population subset, or indication [12]. Because the body of evidence on medical products continues to evolve after approval, the value of a treatment should not be a static measure that is assigned at a single time point but rather should be a dynamic measurement that incorporates new evidence collected in the postmarket setting through additional clinical trials or real-world use in clinical practice.

The incorporation of real-world evidence into value frameworks will facilitate the inclusion of long-term safety and effectiveness data and provide information as to how different products perform in patient populations that are typically excluded from clinical trials. Real-world evidence may also yield important insight into the tolerability of different products based on treatment adherence or dose modification patterns, information that is not always reflected on drug labels. Overall, real-world evidence can help ensure that value frameworks do not solely rely on the best average treatment effect by recognizing the heterogeneity that is associated with cancer. Conducting postmarket trials has challenges and limitations, but efforts are underway with the goal of uncovering long-term, longitudinal information that will help inform and optimize the use of new products [13,14].

As these value frameworks undergo improvements, developers should consider including patient input early and throughout the development process; incorporating molecular diagnostics into these frameworks to better integrate the concept of precision medicine; defining value and making it explicitly known to end
users; developing methodology to incorporate new data as they are rapidly produced in oncology drug development; and ensuring that frameworks align with improved understanding and reliability of surrogate end points and innovative trial designs.

In addition, these frameworks may ultimately help improve the dialogue between the drug industry and society as they continue to be refined and utilized. We recognize the complexity of assessing the value of new therapies, particularly in a rapidly evolving field like oncology, but it should not come at the cost of blocking patient access to potentially life-saving therapies or undermining their current treatments.

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REFERENCES


