



Oncology Treatments, Health-Related Quality of Life, and Value Assessments

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New oncology treatments are intended to increase survival without compromising health-related quality of life (HRQL) due to adverse effects and disease progression. HRQL outcomes are important and relevant for patients and their clinicians in order to better understand the effects of treatment on functioning and well-being.¹ Survival benefits and decreases in disease progression of new chemotherapies often come at some cost in terms of toxicity and HRQL, and patients and their families need information on these effects to make more informed decisions about their cancer care.² For the past 35 years,^{1,3} clinical trials comparing oncology treatments have included measures of health-related quality of life outcomes to evaluate the impact of treatment on

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patient-reported functioning and well-being. Clinical trials comparing cancer treatments continue to incorporate symptom assessments and HRQL endpoints and provide information that is useful for understanding the overall effects of these interventions.

While there are exciting developments in the discovery and evaluation of new cancer therapies, some of these new treatments may be costly for the healthcare system. Increasingly, organizations are developing methods for the evaluation of treatment value for a healthcare system based on analyses of effectiveness, benefits and risks, and healthcare costs.⁴ Several of the existing treatment valuation approaches include some mention of HRQL.^{4,5} However, to date, it is uncertain how these HRQL data are being incorporated into the valuation process for new oncology treatments. In many cases, there is little formal evaluation of HRQL outcome data, and published clinical trial data may have limited reporting of HRQL endpoints.

Chandra and colleagues completed a recent review and comparison of valuation frameworks, with many of these frameworks mostly focusing on oncology products.⁴ Treatment effectiveness for these frameworks mostly focus on survival and progression-free survival and indicators of toxicity. How does data on health-related quality of life effects fit into the treatment valuation process? For some models, such as the European

Society for Medical Oncology (ESMO), the National Comprehensive Cancer network, and the Institute for Clinical and Economic Review (ICER), there is some mention of HRQL outcomes. For example, in the ESMO approach, HRQL effects are assumed based on survival or delayed disease progression, and although the ICER methods consider HRQL outcomes, it is unclear exactly how these data are taken into account when determining the value of the oncology treatment for the healthcare system. Even when clinical trials with symptom and HRQL assessments are included in the evidence base, many oncology clinical trials incompletely report these patient-reported outcomes.²

Given the range of cancer-specific HRQL measures incorporated into clinical trials comparing new oncology interventions, consideration of these HRQL outcomes may be problematic. For example, the Functional Assessment in Chronic Illness Therapy (FACIT) and the European Organization for Research and Treatment of Cancer (EORTC) families of instruments include generic cancer-specific HRQL instruments^{6,7} and a number of cancer-specific modules (see www.facit.org; www.eortc.org). These HRQL instrument scores are not measured on common metrics, making it difficult to synthesize results of HRQL analyses based on different instruments across clinical trials. These differences in score metrics make it challenging to evaluate the HRQL findings from clinical trials for a particular oncology treatment, and, if different HRQL measures are used, across different treatments for a specific cancer (e.g., non-small cell lung cancer). In addition, many registration clinical trials recruit samples of patients that may not necessarily be generalizable to the cancer population.

Many of the valuation frameworks for cancer treatments quantify effectiveness based on estimated quality-adjusted life years (QALYs). QALYs combine the impact of survival and HRQL, and may provide an acceptable indicator of treatment benefit. However, there are challenges associated with methods for estimating preferences for cancer-related health states, in the underlying assumptions for calculating QALYs, and there is continued debate as to whether patients or the general public should provide the preference valuations.

Methods other than quality-adjusted life years may be needed to evaluate treatments for cancers and other diseases so that effectiveness, adverse effects, and survival are incorporated. For example, quality-adjusted time without symptoms or toxicity (Q-TWiST) methods⁸⁻¹¹ may be effectively applied to evaluate the overall effectiveness of treatments for cancer, where apart from progression-free survival and overall survival, there may be treatment-related toxicity of varying severity that can

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also be evaluated. The Q-TWiST method involves the partitioning of survival duration into clinically relevant health states (e.g., treatment toxicity, disease progression, progression free), assigning preference weights (or utilities) to these health states, and calculating quality of life-adjusted weighted sums of the mean duration of each health state to create the overall Q-TWiST scores. The utilities for each health state may be generated by physicians, patients, or the clinical investigators, and range from 0 (representing dead) to 1.0 (representing complete health).

The Q-TWiST method, however, may not be applicable to the evaluation of all disease conditions and treatments. More comprehensive approaches to evaluating treatment effectiveness in oncology should be identified and assessed. All of the HRQL and other outcomes that are relevant to patients may not be included in the available evidence package at the time of the valuation assessment, but understanding which relevant (to patients and clinicians) outcomes are absent and their importance may provide for a more complete understanding of the limitations of the evaluation of the targeted treatment in comparison with alternative treatments. This will be most challenging for some cancer diagnoses where there are few approved, effective treatment options, and where only limited effectiveness evidence may be available.

In summary, patient-reported symptom and HRQL outcomes are critical for a more complete understanding of the effects of oncology treatments on patient functioning and well-being. The patient perspective is important in quantifying the risks and benefits of new cancer interventions. Increasingly, efforts are underway to increase patient engagement in identifying relevant effectiveness outcomes and in the objectives and design of clinical trials and comparative effectiveness studies.^{12,13} Improvements can and should be made in the methods for quantifying the benefits and harms of new oncology treatments, whether QALYs or other approaches are utilized. The incorporation of important and relevant effectiveness and toxicity indicators, from the patient's perspective, can only improve the valuation of new oncology treatments for the healthcare system.

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