Assessing Quality of Life in Research and Clinical Practice

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There is a growing recognition in oncology of the importance of maintaining or improving patients’ quality of life (QOL) throughout the disease course. With this goal in mind, many clinical trials in oncology now seek to evaluate QOL end points.

In recent years, there has been a growing acceptance of the view that the goals of cancer treatment should include concerns about quality of life (QOL) as well as length of life. Patients with cancer experience a variety of symptoms due to their disease and its treatment, such as pain, fatigue, and nausea, that can have a significant negative impact on their well-being and functioning. The development of multidimensional self-report QOL instruments has allowed investigators to measure the adverse impact of disease and its treatment on well-being and functioning and evaluate the efficacy of interventions designed to prevent or treat these adverse effects. Findings from QOL research suggest that routine use of QOL instruments as part of clinical practice has the potential to improve the quality of care that patients receive as well as their health status. However, in addition to its many benefits, there are also many challenges to assessing quality of life in research and clinical practice.

Measurement of QOL End Points

Two features characterize most forms of QOL assessment currently used in oncology. First, it is generally recognized that quality of life is a multidimensional construct and is best measured using instruments that tap multiple domains of functioning and well-being.[1-3] Consistent with this view, most QOL instruments measure physical, social, and emotional aspects of functioning, as well as common symptoms of cancer and its treatment. Second, there is general agreement that quality of life is a subjective phenomenon and that patients are the best judges of their own quality of life.[1,2] Indeed, studies have shown that considerable disparities exist between concurrent ratings of quality of life made by patients and their physicians.[4,5] Accordingly, assessment of quality of life in oncology trials is typically performed using patient self-report questionnaires.

Two of the most widely used multidimensional QOL instruments in oncology are the General Version of the Functional Assessment of Cancer Therapy (FACT-G) [6] and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQC30).[7] (For a comprehensive list of these and other QOL scales discussed in this article, see the Appendix at the end of this supplement.)

The FACT-G (version 4) is a 27-item measure. For each item, respondents indicate on a 5-point rating scale (0 = not at all; 4 = very much) how true each statement (for example, "I have a lack of energy") has been for them during the past 7 days. The FACT-G yields a total score for overall quality of life as well as subscale scores for physical well-being, social/family well-being, emotional well-being, and functional well-being.

The EORTC QLQ-C30 is a 30-item measure. For each item, respondents indicate the rating that best applies to them. Seven items are rated yes or no for an unspecified time frame (eg, "Do you have any trouble taking a long walk?"); 21 items are rated on a 4-point scale (1 = not at all; 4 = very much) for the past week (eg, "Were you tired?"); and 2 items are rated on the 7-point scale (1 = very poor; 7 = excellent) for the past week (eg, "How would you rate your overall quality of life?"). The EORTC QLQ-C30 yields scores for five functional scales (physical, role cognitive, social, and emotional), three symptom scales (nausea, pain, and fatigue), and a global health and QOL scale. The measure also yields single-item ratings of additional symptoms commonly reported by cancer patients (dyspnea, appetite loss, sleep disturbance, constipation, and diarrhea) as well as the perceived financial impact of disease and its treatment.
Both the FACT-G and the EORTC QLQ-C30 have been shown to have adequate validity and reliability and to be able to distinguish patients according to their performance status.\(^6,7\) A number of disease-specific modules (eg, breast, lung, and prostate) have been developed to supplement each of these core measures. These modules assess additional symptoms and QOL issues that are relatively specific to certain forms of cancer.

Linear Analogue Self-Assessment (LASA) scales are also widely used in QOL research in oncology.\(^8\) A LASA scale consists of a 100-millimeter line with descriptors at each end. Respondents mark their current status somewhere along the line, and then the distance in millimeters from the lower end point (0 point) is measured to obtain their scores. LASA scales have been developed to measure a variety of symptoms (eg, pain) and aspects of functioning (eg, physical activity), as well as overall quality of life.

These measures are popular, in part, because they are relatively easy and quick to administer. Moreover, there is evidence to suggest that many LASA scales compare favorably with more established QOL measures in terms of both validity and ability to detect changes over time.\(^9\) Although the use of LASA scales is appealing, caution is advised. Investigators need to determine whether the specific set of LASA scales to be administered has been validated for its intended use. In the absence of existing validity data, LASA scales should be used in combination with the more established FACT-G and EORTC-QLQ-C30 measures. (For a discussion of the use of these and other instruments in the assessment of anemia and anemia therapy, see Dr. David Cella’s article in this supplement.)

**Methodologic Issues in the Evaluation of QOL End Points**

Perhaps the most important methodologic issue to consider in evaluating QOL end points in an oncology clinical trial is the selection of appropriate outcome measures. In most instances, the use of a well-validated multidimensional self-report QOL instrument (eg, FACT-G, EORTC QLQ-C30) will meet this requirement. Depending on the nature of the trial, it may be necessary to supplement these core measures with additional measures that provide more information about those symptoms that are most relevant to the patient population under study. For example, the lung subscale for Functional Assessment of Cancer Therapy (FACT-L)\(^1\) includes several items assessing respiratory difficulties. Likewise, in trials where relief of pain is a primary goal, it may be useful to collect additional information about the subjective experience of pain using a LASA scale or a measure such as the Brief Pain Inventory.\(^10\)

**Number and Timing of Assessments**

A second important issue to consider is the number and timing of QOL assessments. The desire to collect self-reported information at relatively brief intervals in order to increase the likelihood of detecting changes over time must be weighed against concerns about the burden to patients and the financial cost of conducting frequent assessments. Osoba\(^11\) has proposed a set of guidelines that may be useful in determining the timing of QOL assessments in oncology clinical trials. A baseline QOL assessment carried out before the initiation of treatment can be considered necessary for two reasons:

- First, in randomized trials, the baseline assessment will indicate whether there are preexisting differences in quality of life between patients in the various treatment arms; if present, these differences would need to be adjusted for statistically in order to accurately determine treatment effects.

- Second, the baseline assessment conducted prior to intervention provides an essential point of reference for identifying changes over time that may be attributable to the treatment under investigation.
In most instances, one or more on-treatment assessments are also necessary. As noted by Osoba,[11] the frequency and timing of these assessments will depend on the research question(s) being asked. If, for example, the goal is to determine whether chemotherapy improves quality of life in patients experiencing disease-related symptoms (eg, pain), on-treatment assessments should be conducted just before the start of subsequent chemotherapy cycles to reduce the likelihood that results will reflect short-term treatment side effects. In instances where multiple chemotherapy cycles are being administered, the nature of the research question being asked and the financial costs of data collection will determine whether on-treatment assessments are conducted after each cycle or at less frequent intervals.

Finally, there is the issue of off-treatment assessments—those conducted following the completion or cessation of treatment. Once again, the nature of the research question and issues of cost will be the primary factors determining the number and timing of these assessments. In studies of patients with advanced disease (and a poor prognosis for survival), it may be both desirable and feasible to follow patients until disease progression occurs or even until death.[11] Data collected during the off-treatment period would indicate if and for how long any of the observed on-treatment benefits to quality of life may have persisted.

**Handling Missing Data**

A third important methodologic issue to consider is the handling of missing data. This issue is of particular relevance to studies of quality of life end points. As Moinpour[12] has noted, "In the very setting where quality of life questions are most compelling, they are the most difficult to evaluate because the missing data mechanism is often dependent on the very outcome being assessed—the health status and quality of life of the patient." That is, patients who are experiencing negative health outcomes, such as treatment toxicity or progressive disease, are also most likely to have missing QOL data. Under these circumstances, analyses based only on available (nonmissing) data may lead to erroneous conclusions. For example, if QOL data are missing on a consistent basis due to treatment toxicity, the analysis of only nonmissing data is likely to lead to an overestimate of the actual QOL benefits of the agent under study.

At present, there is no consensus on the optimal method for dealing with nonrandom missing QOL data in clinical trials. As a general strategy, Fairclough and colleagues[13] suggest that two questions be considered in attempting to evaluate the impact of missing data. First, why are the data missing? If data are missing for reasons related to treatment toxicity or disease progression, then the missing data mechanism is "nonignorable" and statistical models appropriate for this situation should be explored. Second, how sensitive are the study results to different assumptions about the missing data mechanism? In the absence of a consensus on the "best" approach, sensitivity analyses are recommended to examine the effects of several different methods of handling missing data. Readers interested in learning about these methods may wish to consult a special issue of Statistics in Medicine (volume 17, numbers 5-7, 1998) devoted specifically to the topic of missing QOL data in oncology clinical trials.

**Clinical Uses of QOL Findings**

Although QOL assessment in oncology research is a relatively new phenomenon, a number of clinical uses of QOL findings can be identified. First and foremost, QOL findings have permitted clinicians to understand the typical impact of specific forms of cancer treatment on patients’ functioning and well-being. This type of information can be used to communicate accurate expectations about likely limitations in function to patients about to begin treatment. For example, patients about to undergo blood and marrow transplantation can be advised as to the usual nature and duration of limitations in physical functioning or expected changes in emotional well-being. At the same time, this information can be used to identify the types of services most patients are likely to require to restore functioning or well-being. For example, QOL data have suggested that certain forms of cancer treatment can result in persistent fatigue that limits a patient’s ability to work or engage in social activities.[14] These findings have prompted efforts to develop interventions to prevent or reduce fatigue in the posttreatment period.[15]
Predicting Treatment Response

A second clinical use involves the potential for quality of life information to predict treatment response and survival time over and above standard clinical indicators such as disease stage and performance status. In other words, QOL data collected at the start of treatment may be helpful in identifying patients likely to have a poorer response to therapy or shorter survival. Along these lines, Coates and colleagues[16] demonstrated the predictive value of QOL information in a clinical trial that compared intermittent vs continuous chemotherapy in women with metastatic breast cancer. QOL scores at the start of treatment, and subsequent changes in those scores, were found to predict survival duration independent of treatment group, performance status, and treatment response.

Identifying Effective Palliative Care Interventions

Yet a third clinical use is to identify palliative care interventions that are effective in improving quality of life beyond pretreatment values. One of the most notable examples of this potential use of QOL data comes from a clinical trial that compared mitoxantrone (Novantrone) plus prednisone to prednisone alone in men with hormone-refractory prostate cancer.[17] Previous single-arm studies [18-21] had yielded preliminary evidence that prednisone, mitoxantrone, and mitoxantrone plus prednisone each produced some palliative benefit and had limited toxicity. Based on these findings, Tannock and colleagues designed a randomized trial to test the hypothesis that treatment with mitoxantrone plus prednisone would provide better palliation than prednisone alone. Results indicated that, although survival did not differ significantly between the two treatment arms, the primary criterion of a palliative response (ie, pain relief) was met by significantly more patients who received mitoxantrone plus prednisone than prednisone alone and that the duration of the palliative response also was longer in the combined therapy group.[17]

Additional analyses of quality of life data from this trial showed that, after 12 weeks of treatment, patients receiving prednisone alone did not exhibit any significant improvements relative to their baseline scores. In contrast, patients that received combined therapy exhibited significant improvements in physical, role, emotional, and social functioning and in global quality of life.[22] The results of this trial illustrate how inclusion of QOL end points in oncology clinical trials has the potential to improve palliation of patients with advanced cancer.

Applying QOL Results at the Individual Patient Level

The clinical uses of QOL findings described above represent ways in which the results of research studies incorporating QOL measures can improve the clinical care of patients in general. Can these findings also be applied to improve the care of an individual patient? At least four potential benefits of administering a QOL measure to an individual patient can be identified.

One obvious benefit is the potential for improving patient-provider communication. QOL measures can provide clear and unambiguous information about a patient’s current state of well-being and functioning. In addition, information obtained from patient self-report measures is not dependent upon the ability or willingness of a patient or provider to initiate a discussion of QOL concerns.

The potential also exists to identify frequently overlooked problems. By systematically prompting patients to respond to a standardized item set, QOL measures probe for problems that providers may be reluctant to inquire about and patients may be reluctant to complain about, such as problems with sexual functioning.

Administration of a QOL measure may also help in prioritizing problems. Since patients often present with multiple symptoms,[23] providers may be challenged in deciding where to focus their efforts in improving quality of life. By attaching numerical ratings to perceptions of symptom severity and problems in functioning, QOL measures can help both patients and providers identify those issues that are of more immediate concern.

Last but not least, QOL measures may help clinicians evaluate the impact of palliative care efforts. Direct comparison of scores obtained by administering the same QOL measures on multiple
occasions permits a determination of both the direction and magnitude of changes. This information can be quite helpful in deciding whether or not a patient is benefiting from a particular therapy or intervention.

**Barriers to Assessing Quality of Life in Routine Clinical Practice**

Given the many potential benefits of routine clinical assessment of quality of life, why is the practice not more widespread? Three broad categories of barriers to routine assessment of quality of life in clinical practice can be identified. These are provider inexperience with quality of life assessment, methodologic concerns about reliability and validity, and logistic barriers that inhibit feasibility of clinical implementation and integration. Nine specific barriers falling under these three broad categories are summarized in Table 1 and discussed briefly below.

**Provider Inexperience With QOL Assessment**

Lack of provider experience conducting formal QOL assessments is one of the most important barriers to routine use in clinical practice.[24,25] Because providers are the information gatekeepers in the health-care setting, their support in the use of QOL data to inform and guide clinical practice is essential.

Presently, there is a large discrepancy between the number of providers who report that QOL assessments are useful and those who actually use an instrument to assess quality of life.[24] Surveys of providers reveal that the knowledge base about assessment is limited but that with greater experience and exposure to available instruments, providers may be willing to use them on a routine basis.[26] Understanding the role that provider inexperience with QOL measures plays and determining ways to increase health-care professionals’ exposure to QOL measures are critical for any attempt at integrating these data into routine clinical practice.

An implication of provider inexperience with QOL assessment is the potential for limited patient-provider communication. Although some physicians have expressed concerns that QOL data will be used as a substitute for direct communication rather than as an adjunct to care,[27] the opposite appears to be true. Recent studies have reported that patients and staff find QOL assessments helpful for identifying patient concerns and improving communication.[28,29]

**Methodologic Concerns About Reliability and Validity**

A second category of barriers relates to methodologic problems and several specific concerns have been identified within this category. Historically, physicians have been skeptical about the sensitivity and specificity of QOL instruments.[24,30] In spite of significant efforts to define quality of life and improve measures, doubts about the methodologic development of instruments persist.

At present, clinicians doubt the ability of available instruments to measure subtle individual changes. This is of particular concern for cancer patients who may present from one week to the next with slight clinical changes that represent significant QOL changes according to the patients themselves and/or family members. To date, there are not enough data available for most instruments to determine the meaning of change scores with respect to their clinical significance. The more the instruments are used, however, the greater the amount of information available to determine clinically meaningful change scores over time.

A final methodologic concern is the limited ability to compare scores across different instruments. Technology such as computer adaptive testing (CAT) can address this and other methodologic concerns.[31,32]

**Feasibility and Logistical Problems**

A third category of barriers pertains to feasibility and logistic problems associated with data collection and recording. These barriers apply to both providers and patients. Assessments need to be understandable, user-friendly, and short.[25] If not, health-care providers are less likely to use the
assessments.[25] Additionally, results must be ready in "real-time," at the visit when the data are gathered. Concern about the timeliness of results was the most common problem cited by oncologists in a study of QOL assessment with advanced non-small-cell lung cancer.[33]

Oncologists also stated that more frequent assessments were necessary to help guide treatment planning and decision-making. Routine assessment (at each visit) of quality of life will require a major commitment of resources from both clinical and administrative areas.

Scoring and interpretation of data for clinical usefulness constitutes another barrier. Scores must be clinically meaningful to both providers and patients. Results must be presented in a format that is easy to read, provides useful information, and facilitates direct discussion about topics such as treatment options and general and specific aspects of quality of life.[25,29]

Factors Critical to Success in Assessing Quality of Life in Clinical Practice

Several factors are likely to be critical to the success of efforts to increase the use of QOL assessment in routine clinical practice. As with barriers, these can be grouped into three broad categories of nine specific factors. The categories are an acceptable set of core measures, clinical relevance and ease of use, and "buy-in" from providers and patients. Each of the three categories and their associated factors are summarized in Table 2 and discussed briefly below.

An Acceptable Set of Core Measures

A core set of QOL measures needs to be accepted and endorsed by health-care providers. Having a variety of standardized measurements from which clinicians can choose may increase the use of routine assessment. This set would include an array of tools with adequate validity and reliability that are good estimates of longer instruments. The establishment of a core set of measures would allow clinicians to tailor the use of assessments to meet their needs and those of their patients.

Broader use of more modern item response theory (IRT) models in the development of instruments should be considered. IRT measurement models may allow ways to compare scores across instruments as well as estimate how patients would score on a given instrument based on their responses to another instrument.[34] Computer adaptive tests are one way these types of measurements could be developed and used while preserving other critical factors. This practice could result in more precise assessments of an individual's ability, while simultaneously decreasing the number of questions that need to be administered.

Ease of Use

Ease of use is one of the most important factors necessary for assessing quality of life as part of routine clinical practice. Computer-based testing (CBT) is one way that more frequent assessments can be conducted with minimal burden on patients and providers. CBT eliminates the need for a test administrator, as needed for traditional paper and pencil formats. Rather, the patient administers the instrument to him/her self. This gives patients a sense of control that is particularly important for cancer patients who often feel that the cancer diagnosis severely limits their control in life.

CBT also decreases the burden on clinic staff, while providing immediate "real-time" feedback. Information from assessments can be displayed in graphic reports as visual aids that help guide discussions about treatment options and care planning. Patients have reported that these types of discussions improve communication between themselves and providers.[28] Additionally, discussions help patients feel understood both physically and emotionally.[28] These positive feelings experienced by patients can impact "buy-in" and encourage clinicians to use QOL assessments on a regular basis.

‘Buy-in’ From Providers and Patients

The more providers are educated about quality of life and the benefits to clinical practice, the greater the likelihood that they will use these data. This is supported by results from a study by
Bezjak and colleagues,[25] who reported that the majority (82%) of oncologists surveyed felt that their knowledge about quality of life was limited. These same oncologists said they believed in the benefit of QOL assessment for patient care and that they would likely increase their use of QOL information in the future.

This "buy-in" from key staff is critical to a successful program.[24,25,27,28,34-39] If an introduction to QOL assessment was incorporated into general medical education, it might eventually become a routine component of patient care.[35] Education needs to focus on information about quality of life conceptually, interpretation of specific measures, and uses of QOL data in clinical practice. Organizational requirements for inclusion of QOL end points in clinical trials, as have been mandated by the National Cancer Institute of Canada,[40] may also increase exposure, knowledge, and use of QOL assessments by clinicians.

"Buy-in" from patients, including the desire for and willingness to undergo routine assessments, is equally important. Support can be attained by presenting QOL assessments as a standard part of patient care to highlight unstated patient concerns or issues typically only indirectly assessed by health-care professionals. Providers can explain that assessments at regular intervals are a way to facilitate patient-provider communication. Detmar and Aaronson[28] reported that most patients felt that after multiple assessments, physicians were more informed and aware of the physical and psychosocial impact of treatment on their daily life activities.

**Summary**

Patients with cancer suffer from a variety of symptoms that can adversely affect their well-being and functioning. In recent years, there has been a growing recognition that maintaining or improving the quality of life for cancer patients is an important treatment goal. Accordingly, many clinical oncology trials now seek to evaluate QOL end points.

There is general agreement that quality of life is a complex construct best measured by using instruments which assess multiple aspects of functioning and well-being as viewed from the patients’ perspective. Reliable and valid multidimensional self-report QOL measures have been developed that are sensitive to changes in patients' health status. In seeking to use these measures as research tools, there are a number of important methodologic issues to consider. These issues include selecting instruments that measure QOL outcomes pertinent to the patient population under study, determining the optimal number and timing of QOL assessments to include in the study, and resolving the handling of data missing due to toxicity, morbidity, and mortality.

There have been several clinical uses of findings from QOL research. These include the ability to provide clinicians and patients with accurate expectations about the likely impact of treatments on well-being and functioning, the ability to identify common problems that will need to be addressed, and the ability to identify therapies and interventions effective in addressing these problems. In addition, findings suggest that QOL data may improve clinicians’ ability to predict treatment response and survival time in certain contexts.

The clinical uses of QOL measures may extend beyond the application of research findings. Routine assessment of quality of life as part of clinical practice has the potential to improve communication between patients and providers, identify frequently overlooked problems, prioritize problems, and evaluate the impact of therapeutic efforts at the individual patient level. There are, however, a number of barriers to the routine use of QOL measures in clinical practice. Provider inexperience with QOL assessment, unresolved methodologic issues in QOL assessment, and questions about the feasibility and logistics of integrating QOL assessment into routine clinical care are among the more commonly identified barriers. These barriers are not insurmountable if factors that can contribute to successful implementation and use of QOL data in routine clinical practice are carefully considered.

**References:**


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