Assessing Cancer-Related Quality of Life Across a Spectrum of Applications

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Health-related quality of life (HRQOL) is increasingly assessed to understand the effects of cancer and cancer-related interventions. At the macro level, monitoring HRQOL in the population and in cancer survivors may be important to track progress against cancer and evaluate the outcome of policies and programs. At the meso level, where most research, to date, has been focused, HRQOL data may be used in descriptive and analytic studies to understand the impact of cancer, patterns of care, and effects of interventions for cancer prevention, treatment, and continuing care. At the micro level, HRQOL data can inform individual patient and clinician decision making. Current data show that validated and commonly used HRQOL questionnaires are not interchangeable. Consequently, in determining which HRQOL measures are most appropriate for a given application, it is especially important to carefully consider both the study hypotheses and patient population. Future progress at all levels requires better understanding of the meaning and interpretation of HRQOL scores. [J Natl Cancer Inst Monogr 2004; 33:126–33]

Over the past decade, increasing numbers of researchers have assessed health-related quality of life (HRQOL) in cancer patients to gain important information about the impact of the disease and its therapies. Cancer differs in a number of ways from other acute and chronic diseases. A recent survey shows that it continues to be the top health concern of Americans, and nearly half believe that cancer is highly unlikely or impossible to prevent (*1*). Despite increasing cancer survival rates, due to earlier diagnoses and better treatments, almost half of all persons diagnosed with cancer will succumb to their disease. In addition, cancer is often associated with symptoms, such as high levels of pain, that distinguish it from other diseases. Further, the therapies used to treat cancer confer their own side effects. Surgery permanently removes a body part, whereas radiation therapy may create nausea at the time of treatment and long-term fatigue. Chemotherapy may also be associated with a wide range of concurrent effects (e.g., hair loss, vomiting, decreased resistance to infection), as well as long-lasting decrements in HRQOL *(2)*. All of these factors—the societal perceptions regarding cancer *(3)* and the direct effects of the disease and its therapies—provide a compelling justification for the importance and usefulness of measurement strategies that are sensitive to the specific effects of cancer on quality of life in patients and survivors.

The organizational framework for this article is based on the Lipscomb–Donaldson–Hiatt *(4)* adaptation of Erickson's general Health Outcomes Framework *(5)*. Consequently, the article examines the cancer literature at the macro, meso, and micro levels to identify examples that illustrate current approaches to HRQOL measurement, as well as strengths and weaknesses of the current state of the field. Research using economic assessments is addressed by Fryback *(6)* and, therefore, is not discussed further here.

Macro Level: Population Surveillance

There are a number of reasons why monitoring HRQOL in the population, including patients and survivors, may be important. As identified in the IOM report and in the National Cancer Institute's (NCI) Cancer Surveillance Research Implementation Plan *(7)*, population monitoring may allow measurement of changes in health status over time and identification of regions with better or worse indicators, so that targeted areas of intervention could be implemented. HRQOL data could be included as part of the national "Report Card," a tool proposed for regular monitoring and reporting of national progress toward conquering cancer, identifying opportunities to reduce the cancer burden, and disseminating information to the public and researcher *(7)*.

Example

Ostenso, et al. *(8)* reported on Wisconsin's efforts to track outcomes in lung cancer. These investigators studied changes in lung cancer mortality over a 20-year period on a countywide basis, in comparison to national figures. Results indicated that, as a whole, Wisconsin has not made as much progress in decreasing mortality as the rest of the United States. However, certain counties had much more positive outcomes than others, suggesting that some regions were able to develop more effective tobacco control activities that might be considered for wider dissemination.

Discussion

The example illustrates challenges in incorporating HRQOL data in the context of population surveillance. Although the assumption that fewer cases of lung cancer result in better HRQOL for the population seems reasonable, direct patient reports were not included in this project. However, relevant information is available from ongoing population-based surveillance activities such as the National Center for Health Statistics-sponsored National Health Interview Survey (NHIS) and the Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance System (BRFSS). Such data monitoring systems have the advantage of being up-to-date and large scale (e.g., the NHIS included 48 000 respondents in the year 2000, and the BRFSS about 90 000 in 50 states). In addition, the data from the surveys can be obtained for specific locations, including states, allowing possible geographical differences to be investigated. These

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large-scale surveys were not designed for HRQOL assessment, although a few items (such as asking individuals to rate their overall health status) are directly relevant to HRQOL. Most questions on these surveys relate to risk factors and health-related behaviors, which may be useful, depending on the goals of a particular HRQOL study. In addition, supplemental data are collected both nationally and in some states, including supplemental HRQOL questions on the NHIS in 1998. These items will provide useful information for HRQOL researchers. Linkage of information from these databases to information on cancer rates, coupled with other data such as health care expenditures, use of health care, and patterns of care, may contribute to more complete report cards and better population monitoring for progress against cancer in the future.

Meso Level: Descriptive and Analytic Studies To Understand the Impact of Cancer, Patterns of Care, and Effects of Interventions

To date, the majority of research on HRQOL in cancer patients falls into this category, in that it attempts to understand the effects of cancer on patients, or the impact of cancer-related interventions. Here we describe research that has attempted to understand end results of interventions; document the impact of cancer; understand variations in cancer care; and assess efficacy of interventions related to prevention, treatment, and continuing care of cancer patients. In each of these areas, we provide one or more research examples and discuss application-specific measurement issues.

Understanding End Results of Interventions

Even when cancer-related interventions have been demonstrated to be efficacious in clinical trials and controlled settings, their dissemination in the broader health care arena may require that barriers to their acceptance and adoption are identified and addressed.

Example

Tamoxifen has been shown to prevent breast cancer in high-risk women *(9).* Port and colleagues *(10)* identified 43 women eligible to take tamoxifen for breast cancer prevention on the basis of their risk status. After receiving educational materials about the risks and benefits of tamoxifen, the women were asked if they wanted to begin taking the drug. Only two agreed. The women who declined were more concerned about possible negative impacts of tamoxifen on their HRQOL (e.g., menopausal symptoms) and health status (e.g., the increased possibility for endometrial cancer) than about the potential for breast cancer prevention. This study illustrates that HRQOL concerns are important influences on individual decision-making for preventive agents and suggests how educational materials might be tailored to respond to primary concerns.

Discussion

Relatively few studies have investigated end results of interventions. However, there is need for considerable research to investigate how well interventions work in clinical practice and public health settings outside clinical trials. Such studies can inform the development of guidelines and policies for optimal care and implementation of innovations as part of standard care, as well as reimbursement policies.

Documenting the Impact of Cancer

Cancer outcomes, including HRQOL, are important for monitoring across the disease trajectory. Such monitoring can help identify sequelae of cancer and its treatment, including chronic health conditions and late effects.

Example

HRQOL outcome assessment can be incorporated within the framework of ongoing data collection efforts that focus on other outcomes. The largest and best-established cancer surveillance system in the United States is the Surveillance, Epidemiology, and End Results (SEER)[1] program. The SEER program currently collects data from 11 population-based registries and two supplemental registries representing about 14% of the U.S. population. Data routinely collected by the SEER program include patient demographics, primary tumor site, morphology, stage at diagnosis, first treatment course, and follow-up for vital status. The SEER registries do not include HRQOL assessment as part of their standard dataset; however, studies have used individual registries or groups of registries to identify patients in whom HRQOL is measured *(11,12).*

The largest SEER-based HRQOL study to date is the Prostate Cancer Outcomes Study *(13).* This research is being directed by the NCI in cooperation with six SEER registries. A random sample of about 2700 men recently diagnosed with prostate cancer completed mailed questionnaires 6 months and/or 12 and 24 months after their diagnosis. The questionnaire was developed for this study, although it was based on other surveys that had been used previously with cancer patients. The questionnaire included disease-specific HRQOL questions, with a focus on problem areas of particular concern to prostate cancer patients. Specifically, questions focused on incontinence, bowel problems, and sexual problems, and patients were asked about their function in each of these areas, as well as the degree to which they felt their levels of functioning were problems.

The first HRQOL results of this study are now available. In a report based on responses from men who had received radical prostatectomy, Stanford, et al. *(14)* found that sexual problems persisted for many men: 60% were impotent 18 months or more after their diagnosis, with impotence more frequent in men treated with non-nerve-sparing surgery and in older and Caucasian men. Long-term incontinence was a problem for 8% of the men, and it was also linked with older age. The authors were able to compare survey respondents to nonrespondents to understand some of the possible biases in their sample. This is a distinct strength of HRQOL research in the context of a population-based registry. In addition, these researchers plan to continue long-term follow-up of this cohort to document additional HRQOL changes over time.

Discussion

The choice of measures for various monitoring applications depends on the purposes of the study. For example, in studies of monitoring that seek to identify differences between cancer patients or survivors and healthy populations, it is important to focus on measuring aspects of HRQOL that are likely to differ between the populations. However, research on HRQOL changes over time within patient or survivor groups may focus instead on symptoms that are common in this population, even if they are not of major concern in the population at large. This was

the approach used in the study discussed above *(13)*. The primary measures focused on symptoms known to be important in prostate cancer patients and survivors in order for changes in levels of symptomatology to be tracked over time.

Interpreting HRQOL data in cancer populations for monitoring purposes requires comparison with other normative groups. These may include, for example, data based on healthy populations, general community populations, groups of individuals who have been treated for other medical conditions, and populations matched on various characteristics (e.g., sibling controls, friend controls). Comparative data may be collected in the course of a study (enabling matching on specified characteristics and data collection at the same time) or by comparison with previously collected data. In the example above, the discussion sections of the manuscripts cited data about the prevalence of incontinence and impotence in other samples, including other prostate cancer patient populations and the general population.

Further, certain instruments have been used widely and have ample comparative data available, allowing for age and gender matched comparisons. For example, the Medical Outcomes Study 36-Item Short Form Health Status Survey (SF-36) *(15)* has been administered in healthy populations, cancer patient and survivor populations, and in individuals with specified noncancer diagnoses. Thus, considerable information on age, gender, and health status-matched samples is available against which findings from a given sample may be compared. With respect to a cancer-specific questionnaire, the European Organisation for Research and Treatment of Cancer's Quality of Life-Cancer Questionnaire (the QLQ-C30) *(16)*, non-cancer population norms for age and gender-specific community samples have been reported *(17,18)*.

Understanding Variations in Cancer Care

Patient perspectives contribute a critical element to the evaluation of quality of cancer care. Both patient functioning and well-being, as reflected through HRQOL ratings, and patient levels of satisfaction with their cancer care, can provide information necessary to determine how good the care is and to suggest areas for improvement. The National Academy of Science's comprehensive report "Ensuring Quality Cancer Care" *(19)* specifically cites HRQOL and satisfaction as key outcomes of cancer care, along with relapse, complications, survival time, and death. However, to date, few studies have incorporated HRQOL measures as indicators of cancer care, although some questionnaires that do this are available. These include a three-item "Relationship with Doctor" subscale on the Functional Assessment of Cancer Therapy (FACT) *(20)*, 11 items about physician and nurse communication and control on the Cancer Rehabilitation Evaluation System (CARES) *(21)*, the Princess Margaret Hospital Satisfaction with Doctor Questionnaire *(22)*, a 29-item self-administered survey, and the Comprehensive Assessment of Satisfaction with Care *(23)*, a 61-item scale.

Example

Although there are few studies that directly use HRQOL data to evaluate quality of care, there is a provocative series of studies emerging in the prostate cancer literature with implications for prospective evaluation of prostate cancer care. A number of studies ask prostate cancer survivors who received a radical prostatectomy if they would make the same treatment choice again. Large percentages (>80%) of patients are asked this question within several years after surgery report that they would select the same treatment *(24–26)*. However, there is a suggestion that patient responses vary according to the side effects experienced. Kao, et al. *(27)* studied a large sample of radical prostatectomy patients at least 6 months after surgery (N = 1,069) and found that, although most men would choose surgery again, men who experienced incontinence, impotence, or stricture would be less willing to make the same treatment choice, compared with men who did not experience these sequelae (percentages of 74%, 80%, and 77% for men with each side effect, compared with 87%, 95%, and 83% for those who did not). Herr, et al. *(24)* asked prostate cancer survivors who were incontinent if they would choose surgery again; the percentage of survivors stating "yes" was 83% (N = 18) at 1–3 years after surgery, and only 53% (N = 17) after 5 years. The implications of these data (which need to be confirmed in additional research) are that the level of satisfaction with prostate cancer treatment may change over time; and that an intrusive and chronic side effect such as incontinence takes an increasing toll on HRQOL the longer a patient must live with it.

Discussion

Future progress in this area of HRQOL research would be greatly facilitated by the development of systems to allow linkage of HRQOL outcomes (including patient satisfaction) and specific aspects of cancer care. Several databases include information about treatment, including SEER, the SEER-Medicare Database (which includes augmented treatment information for patients aged 65 years and older) and the American College of Surgeons' National Cancer Data Base (which includes detailed cancer treatment information from approximately 1,500 treatment centers nationwide). The addition of HRQOL data to these databases would permit an analysis of the relationship between distinct aspects of cancer care and patient perspectives on outcomes. In addition, the use of HRQOL scores as an indicator of quality of cancer care needs additional consideration; for example, is it possible to set an HRQOL score that indicates a break between acceptable and unacceptable quality of care?

Assessing Efficacy of Interventions Related to Prevention, Treatment, and Continuing Care of Cancer Patients

Considerable research has focused on HRQOL in cancer clinical trials. Depending on the purpose of the study, HRQOL data may be used to determine which treatment is preferable and/or to document patient perspectives on symptoms and other aspects of life that can be used to provide supportive care and to modify therapeutic regimens. Such information can also be used to inform future patients and recipients of preventive interventions about the side effects they are likely to experience. We discuss examples related to preventive, therapeutic, and supportive interventions.

Example: Cancer Prevention

The Breast Cancer Prevention Trial (BCPT), conducted by the National Surgical Adjuvant Breast and Bowel Project, was a randomized trial that demonstrated that tamoxifen prevented breast cancer in those women at increased risk of the disease *(9)*. The primary outcome of the study was invasive breast cancer, and HRQOL was a secondary outcome (along with other outcomes including heart disease and bone fractures). HRQOL

findings have been reported for baseline and over a 36-month period of follow-up in 11 064 women *(28)*. HRQOL was assessed through several questionnaires, including the Center for Epidemiologic Studies-Depression Scale (CES-D) *(29)*, the SF-36 *(15)*, and scales of sexual functioning and symptoms. The results indicated that there was no difference between the tamoxifen and placebo groups in depression or weight gain, two areas where possible adverse effects of tamoxifen had been suspected before the trial. The prevalence of a number of symptoms was equally high in both groups; for example, problems with bladder control (experienced by 48% of controls and 53% of tamoxifen takers). Several symptoms were more frequent in women who took tamoxifen, including vasomotor symptoms (i.e., cold and night sweats, hot flashes), vaginal discharge, and genital itching. However, even in the control group, prevalence of these symptoms was high; e.g., hot flashes were experienced by 65% of controls and 78% of women on tamoxifen, and symptom experience was associated with age in both groups. The use of HRQOL data in this study provided important information for counseling women who plan to take tamoxifen, so that they will be aware of side effects that they are likely to experience. This study also illustrates the importance of having information about HRQOL in healthy populations. Such information could be gleaned by a randomized trial including a placebo control group (such as this study), historical or concurrent control groups, or availability of population norms. Without information about baseline HRQOL and symptoms in the population, positive or negative HRQOL outcomes could be erroneously attributed to therapy.

Example: Cancer treatment

Increasing numbers of trials are beginning to report HRQOL data in the context of trials testing innovative cancer therapies. To date, the majority of such trials have assessed HRQOL using the QLQ-C30 *(16, 30–32)*, although other assessment methods have also been used in this context, such as the FACT *(20,33)* and linear analogue scales *(34)*.

This line of research is illustrated by several studies comparing the effects of novel chemotherapeutic regimens compared with standard chemotherapy for advanced breast cancer. For example, Nabholtz, et al. *(30)* compared docetaxel versus mitomycin plus vinblastine in patients with metastatic breast cancer and found that the docetaxel arm experienced better response rates, times to progression, and overall survival, whereas the HRQOL (measured by the QLQ-C30) did not differ between arms. Global HRQOL and physical functioning were specified as primary HRQOL measures. Similarly, Bishop, et al. *(34)* investigated the role of paclitaxel versus combination chemotherapy for previously untreated metastatic breast cancer and found that paclitaxel led to better overall survival with no significant HRQOL differences between arms. Linear analogue scales were used to measure HRQOL, and included assessments of physical well-being, mood, pain, nausea and vomiting, appetite, and overall HRQOL. Similarly, Kaufmann et al. *(31)* compared exemestane, an oral aromatase inactivator, with megestrol acetate in women with progressive, advanced breast cancer. Results indicated that exemestane was superior in response rate, time to progression, and overall survival; this agent was also better in a number of aspects of HRQOL (i.e., physical functioning, role functioning, global HRQOL, fatigue, dyspnea, constipation), whereas megestrol acetate was superior in other areas (i.e., emotional functioning, appetite, pain, insomnia). Several other aspects of HRQOL (measured by the QLQ-C30) did not differ between groups. These studies illustrate the complexity of relationships between biomedical endpoints (e.g., survival) and HRQOL, and among the different domains of HRQOL.

Example: Cancer rehabilitation and continuing care

Randomized trials addressing management of cancer-related symptoms frequently include measures of HRQOL. Other aspects of continuing care have also been explored, such as trials of psychosocial support *(35)*, comprehensive menopausal assessment *(36)*, and varying follow-up schedules *(37)*. Such trials generally include HRQOL assessment, as well as focused measurement of particular domains of interest. For example, Segal and colleagues *(38)* explored the effects of a structured exercise program on physical functioning in women with stage I or II breast cancer (N = 123). Their interventions included self-directed or supervised exercise programs, which were compared with a usual care control group. Outcomes included HRQOL (measured by the SF-36 and the FACT), as well as physiological measures (aerobic capacity and body weight). They found strong positive effects for the exercise programs, particularly the self-directed approach, in the physical functioning scale of the SF-36, whereas other measures of HRQOL and the physiological indicators did not differ across groups.

Discussion

At the present time, a number of tools have been reasonably well validated to measure overall cancer-related HRQOL in intervention studies (e.g., QLQ-C30, FACT, CARES) and HRQOL in specific diagnoses [(e.g., disease-specific modules for QLQ *(39)* and FACT *(40)*, Breast Cancer Questionnaire *(41)*, UCLA Prostate Cancer Index *(42)*, Lung Cancer Symptom Scale *(43)*]. In addition, there are questionnaires that have been developed specific to special populations such as children [e.g., Pediatric Quality of Life Inventory *(44)*] and patients with advanced disease *(45)*]. Finally, questionnaires are available to assess specific aspects of cancer-related HRQOL [e.g., Rotterdam Symptom Checklist *(46)*, Brief Pain Inventory *(47)*].

As a rule, the development of these questionnaires has followed accepted psychometric procedures *(48)*, such as assessing internal consistency, construct validity (e.g., discriminant validity, predictive validity, concurrent validity), and external validity (to some extent). Many papers using these questionnaires report psychometric information about their performance in the study sample in recognition of the principle that questionnaire validation is a continuing process. As surveys are used in new populations and over time, their scientific properties need to be examined on an ongoing basis.

Even if investigators determine that they want to assess HRQOL using a cancer-specific measure in a specific study, they still face the choice of selecting a questionnaire from an array of choices. For example, three frequently used cancer-specific HRQOL measures—the QLQ-C30, the FACT, and the CARES—all purport to provide a multidimensional measure of HRQOL. These questionnaires were developed for use in cancer patient populations, and have been validated and used in a variety of cancer patient populations. To select among these questionnaires, an investigator might consider their length: the CARES contains 132 questions (not all of which will pertain to

every patient) and the CARES short-form contains 59 questions *(49)*, whereas the FACT has 34 items and the QLQ-C30, 30 items.

The content of the questionnaires might also guide selection. Both the FACT and the QLQ-C30 have numerous modules available to provide additional HRQOL information specific to particular cancer sites or treatments. The CARES is the only scale to include subscales on sexual and marital functioning, and the QLQ-C30 does not include a measure of interaction with medical personnel, as the other scales do. None of the scales includes a subscale of positive well-being (although several FACT items are worded positively) nor of spiritual well-being. All three scales assess global HRQOL, as well as provide profiles of scores in different HRQOL areas. The CARES also provides a single summary score. None of these questionnaires (nor any cancer-specific HRQOL questionnaires of which we are aware) provides a global HRQOL index that weights various aspects of HRQOL according to patients' perspectives about their importance in overall functioning. An early version of the FACT included this type of measurement, but it has been omitted from current versions of the instrument.

Only a few studies have compared these questionnaires head-to-head by administering more than one to the same individuals and examining the concordance or lack thereof. Sharp, et al. *(50)* administered both the FACT and QLQ-C30 to 110 mostly low income, African American patients with metastatic prostate cancer (N = 110) and compared results across questionnaires on subscales purporting to measure the same HRQOL domain. The QLQ-C30 and FACT subscales for emotional, physical, and role/emotional functioning were reasonably well correlated (correlation coefficients between .54 and .72), but social functioning was not (correlation coefficient of .12). Kemmler, et al. *(51)* also administered the QLQ-C30 and FACT (244 patients). Their results were consistent: considerable convergence on the physical functioning domain (correlation coefficient of .66), but significant differences in other areas such as social functioning (correlation coefficient of .14). Except for physical functioning, subscale scores on the FACT did not explain the large variance in the corresponding subscale of the QLQ-C30. These authors identified a number of differences in the content of the two questionnaires and the wording of specific items that may account for the varying data they obtained. Their conclusion that "neither of the two HRQOL instruments can be replaced by the other, and ...a direct comparison of study results obtained with the two instruments is not possible" (p. 2937) is an appropriate cautionary note to researchers.

Micro-Level: Patient–Clinician Decision Making

Given time constraints on clinicians, standardized approaches to HRQOL assessment that could be efficiently applied in clinical practice hold considerable promise. Patient perspectives on their HRQOL may be important to develop more effective therapy or supportive care. Meeting patient needs may enhance adherence to treatment regimens and lead to more positive biomedical outcomes as well as increased patient satisfaction. Research indicates that patient perceptions of their HRQOL are significant predictors of prognosis, providing independent information that goes beyond biological indicators *(52,53)*. In addition, HRQOL data could assist clinicians in identifying individuals with high levels of need or who are at risk for developing problems. Thus, HRQOL information could be useful to clinicians for a number of purposes.

Examples

Several groups have investigated the effects of patient completion of a self-administered HRQOL questionnaire on patient–oncologist interaction and decision-making, with varying results. Detmar and Aaronson *(54)* employed a pretest–post-test design. The first outpatient appointment provided baseline measures of patient–oncologist interaction (abstracted from chart data) and patient evaluations of how well-informed their physician was about the patient's health. At the next two visits, the patients completed the QLQ-C30, with summary information provided to the oncologist. The findings indicated that although the length of office visits did not change over the course of the study, physicians were significantly more likely to initiate discussion of patient HRQOL issues by the third visit. Most patients and all oncologists believed that routine HRQOL assessment could facilitate doctor–patient communication. Taenzer, et al. *(55)* conducted a randomized trial in a lung cancer outpatient clinic to assess whether providing computerized HRQOL data would affect patient satisfaction and the likelihood that HRQOL issues would be raised during the oncologist consultation. This study also demonstrated that providing the HRQOL information significantly increased discussion of HRQOL issues.

However, McLachlan, et al. *(56)* compared the effects of providing computerized HRQOL feedback to oncologists (versus standard care) in a study of 450 cancer patients with a variety of diagnoses. Before consultation with the patient, physicians received their responses on the QLQ-C30, a patient needs inventory, and a measure of depression (the Beck Depression Inventory). The study found that the feedback did not affect patient needs, satisfaction with care, or HRQOL. However, a subset analysis of patients with moderate to severe depression indicated that these patients experienced benefits from the HRQOL condition.

Discussion

To include HRQOL assessment routinely in clinical care, providers need a tool and approach that is consistent with clinical practice. Many of the current questionnaires may be too lengthy and hard to score, and use of standardized HRQOL assessment in clinical practice is uncommon *(57)*. However, the studies cited above found that the QLQ-C30 could be completed in the waiting room, was quickly scored by the computer with results easily readable, and provided information that could be used by both patient and physician. Thus, as patient computer use in medical offices increases, integration of HRQOL assessments may be feasible. In fact, as Velikova, et al. *(58)* suggest, widespread use of the Internet may facilitate ongoing patient HRQOL monitoring even outside the office setting. Although not all cancer patients are likely to be familiar or comfortable with computers, several investigators have assessed computers that input data through a "touch-screen" for assessing HRQOL in cancer patients and found this approach well-accepted and easily used *(59,60,56)*. The very act of completing a standardized HRQOL assessment may have a positive impact on clinical care by conveying provider caring. The opportunity to complete an HRQOL questionnaire and share it with one's physician may provide patients with a nonthreatening method of communicat-

ing concerns without seeming to complain, bothering the busy doctor, or otherwise violating "good patient" behavior.

Current HRQOL questionnaires provide only a part of the information a provider needs to make recommendations for appropriate therapy and supportive care. For a given patient, the clinician must be attentive to multiple perceptual, motivational, and external factors that may intervene between an experience related to cancer and/or its therapy (such as a symptom or a change in functioning) and its evaluation by the patient as a problem or effect on HRQOL. In elderly persons, in whom the majority of cancer cases are diagnosed, other pre-existing and concurrent chronic diseases and health problems often complicate interpretation of HRQOL responses. For example, many HRQOL questionnaires ask the patient to distinguish between pain that is caused by cancer or by other conditions, such as arthritis. This may be difficult for many patients. When they devise treatment plans for individual patients, clinicians need to consider the patients in the context of their lives as whole, including the relative weight that patients attribute to cancer-related concerns in the context of other aspects of life quality, such as crime, poverty, and availability of social support. A recent study by Detmar, et al. *(61)* found that HRQOL considerations were not an important factor in treatment decisions about chemotherapy for palliative care patients. Although tumor progression and severe toxicity resulted in a change in therapy, serious HRQOL decrements did not. The investigators discuss a number of explanations for their findings and conclude that "additional efforts should be directed toward incorporating HRQL factors, both formally and informally, in patient–physician communication and in clinical decision making" [*(61)*, p. 1061].

Overall Discussion

This article illustrates the contributions that HRQOL assessment can make to understanding the impact of cancer in different kinds of research applications. Although the majority of research to date has focused on "meso" applications that use HRQOL measures to document the effects of interventions, there has been some attention to how HRQOL can be used to understand the impact of cancer in the broader context and also at the patient–clinician interface. Below, questions that emerge across studies are discussed: how to choose among assessment tools and how to interpret HRQOL data.

Choosing Among Assessment Tools

The dilemma of how to select an appropriate HRQOL measurement remains a recurrent issue. To a large extent, the choice of assessment approach must be made in the context of the specific study population and research questions. For example, in randomized clinical trials including treatment comparisons, the assessment tool must be sensitive and focused enough to detect small differences against a background of considerable similarity in patients and, frequently, treatment regimens. In addition, treatments may be very unlikely to have differential effects on certain domains (e.g., spiritual concerns and family functioning). At the same time, however, the treatments may have profoundly different effects on aspects of patient well-being that are usually measured in only a cursory way on most cancer-specific HRQOL inventories (e.g., sleep patterns, fatigue). For such research questions, the use of TRQOL (trial-related quality of life) questionnaires may be appropriate. For novel therapies, it may not be known which areas of HRQOL are likely to be affected by the treatment. In such cases, adoption of a narrowly focused approach to HRQOL assessment may miss important impacts of treatment. In general, the safest approach is to include trial specific questions along with a cancer-specific assessment tool. Most of the clinical trials described above included both global HRQOL assessment and measurement of morbidities likely to be associated with the treatments under study.

For research that aims to describe the wide-ranging impact of cancer and its treatment in defined populations, HRQOL assessment that includes multiple aspects of well-being is likely to be most appropriate. Either cancer-specific questionnaires or tools developed for measuring HRQOL in the general population may be suitable choices for measuring HRQOL domains in cancer patient or survivor populations. For example, a study of fatigue *(62)* in a large sample of breast cancer survivors (N = 1957) included a wide variety of assessments, some generic (e.g., SF-36, CES-D) and some specific to areas of concern in this population (e.g., symptom checklist). These measures enabled the investigators to examine differences between the breast cancer survivors and the general population (based on comparison with normative data), as well as to identify a subgroup of survivors at high risk of fatigue. Supportive or preventive interventions could be directed at this group.

In clinical settings, there is not yet enough information available to know which questionnaires are likely to be the most useful. The QLQ-C30 has been used in several studies and appears to be feasible in the clinic setting, particularly with computerized support to facilitate administration and scoring. However, the impact of providing such information is not completely clear. Qualitative research would be useful to understand more about what oncologists and other providers, as well as patients, find helpful in standardized assessments; for example, what information provided in a QLQ-C30 profile is new, what confirms information they already discuss, and what is ambiguous or unhelpful? What else would they like to know if providing a care plan?

Interpreting HRQOL Scores

A potential limitation of using HRQOL data in clinical research is that the clinical significance of HRQOL ratings is often not clear. To what degree is a statistically significant difference also a clinical difference? Velikova and colleagues *(58)* contrast "distribution-based interpretations," in which HRQOL scores are compared in groups known to vary in clinical characteristics; and "anchor-based interpretations," in which HRQOL scores, and changes in those scores, are linked with particular clinical states. Both of these approaches give guidance about the meaning of a particular HRQOL score and have been used in this literature.

King *(63)* used a distribution-based approach in an examination of 14 studies using the QLQ-C30 in different cancer patient populations; data were analyzed to provide information about means, medians, ranges, and variability to guide future uses of this scale. In contrast, Osoba, et al. *(64)* used an approach closer to an anchor-based interpretation, in which patients completed the QLQ-C30 at two time points and also indicated their perception of how much their HRQOL had changed (for better or worse) since the last assessment. Results indicated that changes in mean scale scores between 5 and 10 represented a small change, between 10 and 20, a moderate change, and greater than

20, a large change. Similarly, Cella, et al. *(40)* found that a change of 5 units on the FACT was considered clinically significant. A recent study *(65)* used both simulated data and results of four studies of asthma and respiratory disease to assess the relationship between effect size (a distribution based estimate) and proportions of patients estimated to benefit from treatment (derived from anchor-based approaches). This study found that both approaches yielded equivalent information. As additional studies are conducted to examine the meaning of HRQOL scale scores in cancer research, interpretation will be facilitated. The clinical utility of using specific HRQOL scale scores, or changes, on an individual basis, as well as their use in population studies, depends on such research. For example, information supporting the predictive validity of scores, such as the likelihood that a patient with a particular response will deteriorate over a specified period of time, would be very useful to clinicians. In addition, understanding the meaning of HRQOL scores, or changes in score, is important in drug approval and developing policy. Taking results beyond the research context into broader, more "macro" applications requires concrete information about how to interpret HRQOL data.

Conclusions

An article such as this one could not have been written 15 years ago. Most of the literature cited has been published in the last decade, as HRQOL measures for use in cancer research have been developed and tested. It is only through additional such testing that measures can be further refined, with their contributions to various arenas of application made more apparent. It would be particularly helpful for research to investigate the use of selected instruments across various kinds of studies. For example, the SF-36 is one questionnaire that has been used in studies of cancer survivors and patients under treatment, as well as in the general population. The extent of its covariation with frequently used cancer-specific questionnaires such as the FACT and QLQ-C30 would be useful data. Additional information about normative data in varying populations would assist in the development of interpretation and in understanding the clinical meaningfulness of scores in different patient and population groups. When it comes to specific questionnaires for different applications, investigators are urged to examine the items in the questionnaires under consideration, as well as evidence indicating that the questionnaires have established psychometric properties. As the small group of studies that have made comparisons between questionnaires have demonstrated, questionnaires do not always yield equivalent information, even if subscales are given the same titles. In their (appropriate) desire to use tools that have been found to meet acceptable scientific criteria for questionnaire validity, researchers need to remember that their scientific hypotheses and knowledge of the patient or subject population are the principles that should guide their selection of outcome assessment measures.

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NOTE

[1]*Editor's note:* SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.