EXPERT REVIEWS

Added value of health-related quality of life measurement in cancer clinical trials: the experience of the NCIC CTG

Expert Rev. Pharmacoeconomics Outcomes Res. 10(2), 119–128 (2010)

Heather-Jane Au†, Jolie Ringash, Michael Brundage, Michael Palmer, Harriet Richardson and Ralph M Meyer; on behalf of the NCIC CTG Quality of Life Committee

†Author for correspondence
Department of Medical Oncology, Cross Cancer Institute, University of Alberta, 11560 University Avenue, Edmonton, AB T6G 1Z2, Canada
Tel.: +1 780 432 8762
Fax: +1 780 432 8888
heather-jane.au@albertahealthservices.ca

Health-related quality-of-life (HRQoL) data are often included in Phase III clinical trials. We evaluate and classify the value added to Phase III trials by HRQoL outcomes, through a review of the National Cancer Institute of Canada Clinical Trials Group clinical trials experience within various cancer patient populations. HRQoL may add value in a variety of ways, including the provision of data that may contrast with or may support the primary study outcome; or that assess a unique perspective or subgroup, not addressed by the primary outcome. Thus, HRQoL data may change the study's interpretation. Even in situations where HRQoL measurement does not alter the clinical interpretation of a trial, important methodologic advances can be made. A classification of the added value of HRQoL information is provided, which may assist in choosing trials for which measurement of HRQoL outcomes will be beneficial.

Keywords: cancer • clinical trials • health-related quality of life • HRQoL • oncology • patient-reported outcomes • PRO • quality of life

Phase III clinical trials may be designed to evaluate efficacy, with emphasis placed on demonstrating causal relationships between interventions and outcomes; or effectiveness, seeking differences in outcomes between therapies that can inform clinical and health policy decision-making. Most trials test for superior efficacy of the experimental treatment; however, on occasion, noninferiority trials are conducted that require that competing arms have similar efficacy, but with a different advantage, such as reduced toxicity or cost, sought for the experimental treatment. The most common efficacy outcome end points evaluated in cancer clinical trials are measures of disease control, such as progression-free survival (PFS) or overall survival (OS). Effective palliation of symptoms is sometimes a primary study outcome. Evaluation of the balance of patient benefits and harms is typically addressed by survival, toxicity and economic outcomes; however, the measurement of health-related quality of life (HRQoL) is also now commonly integrated in Phase III cancer clinical trials [1–4].

The purpose of this review is to illustrate the added value of measuring HRQoL – and to propose a classification of these benefits – by drawing on examples from the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) Phase III trials experience. We will begin by briefly reviewing the nature of the NCIC CTG, the concept of patient-reported outcomes (PROs) in general and HRQoL outcomes specifically. Clearly, for HRQoL data to be useful, it must be acquired with appropriate instruments and methods. For the purposes of this review, we assume reliable, valid, responsive and interpretable HRQoL instruments are chosen, and administered accordingly with an adequate level of compliance. Additional information regarding these issues has been thoroughly addressed by others [5,6].

Assuming valid acquisition and interpretation of HRQoL data, we pose the following question: "Do HRQoL outcomes provide information that cannot be simply deduced by traditional biomedical measures?". We propose to address this question using an illustrative approach, rather than a systematic review. We draw on specific examples from the diverse NCIC CTG Phase III studies, conducted for patients with various stages and types of cancers.

 10.1586/ERP.10.15 ISSN 1473-7167

The NCIC CTG

The NCIC CTG is the only adult cancer clinical trials cooperative group based in Canada that has a national membership from all provinces and is committed to assessing all modalities of therapy across the spectrum of different cancer types. Between its inception in 1980 and 2009, the NCIC CTG has conducted or is conducting 262 trials within its Phase III program; these have included 59,000 patients. Within its Investigational New Drug Program, 176 Phase I or II studies have included more than 4150 patients. The NCIC CTG's scientific committees include eleven Disease Site Committees (DSCs), which represent the major disease sites of cancer including, for example, the Breast Committee and the Lung Committee, and are responsible for developing a disease-specific strategic agenda and specific trials that advance that agenda. These DSCs are further supported by three Scientific End Point Committees, which provide expertise in evaluating end points other than survival and include the Quality of Life (QoL) Committee, Correlative Sciences and Tumor Biology Committee, and the Working Group on Economic Analysis. A representative of each End Point Committee (e.g., a QoL liaison) sits on the executive committee of each DSC. The role of the QoL liaison includes the development of appropriate hypotheses, evaluation strategies and analysis plans that are included in trial protocols, such that studies are adequately powered for HRQoL end points. In these decisions, data management costs are assessed and considerations of patient burden are paramount.

With the European Organization for Research and Treatment of Cancer (EORTC), the NCIC CTG was among the pioneering groups to incorporate HRQoL into cancer clinical trials. A working group was established in 1986, and the QoL Committee became a standing committee of the NCIC CTG in 1989. The current QoL Committee consists of 16 members, including medical and radiation oncologists, a clinical research associate, a biostatistician and social scientists. The NCIC CTG requires by policy that HRQoL be evaluated in every Phase III trial, unless an explicit reason is stated in the protocol why this would be inappropriate [7]. Since January 1, 2004, 15 NCIC CTG-led Phase III trials have been activated and all (100.0%) of these collect HRQoL. Over the same time period the NCIC CTG has activated 38 Phase III trials led by others, and only four of these (10.5%) collect HRQoL. The inclusion of HRQoL outcomes in NCIC CTG-led studies is a testimonial to the perceived importance of HRQoL measurement among the leadership and DSCs of the NCIC CTG.

Moinpour suggested circumstances in which HRQoL information is likely to provide added value [8]. However, there is limited literature that formally examines the actual, rather than perceived, added value provided by HRQoL data in cancer clinical trials once trials have been completed and reported. The NCIC CTG QoL Committee sought to review our completed study findings for evidence that HRQoL assessments add appreciable benefit to cancer clinical trials, above and beyond what is obtained by other study end points.

Patient-reported outcomes

The US Institute of Medicine previously defined 'patient-centered' as one of the six aims of quality healthcare (the others being: safe, effective, timely, efficient and equitable) [9]. This perspective stresses the importance of the patient's preferences, values, beliefs, experiences and perceptions of healthcare delivery and health outcomes. To shift the paradigm away from an exclusively biomedical model requires the ability to measure health outcomes from a patient's perspective [10]. PROs are assessments of any aspect of health directly reported by the patient with no intervening interpretation by another observer or source [11,12]. In cases where individuals are unable to provide their own assessments, owing to influences such as cognitive factors associated with young age or disease (e.g., dementia), observer ratings of behaviors may also provide indicators of patient functioning that add to biomedical and clinical measures.

Health-related quality of life

Health-related quality of life is a multidimensional construct that makes up a personal perception of well-being and functioning (physical, psychological, cognitive and social) as affected by wellness, illness, treatment, ability, infirmity, quality of, and satisfaction with, care. These may also be extended to include other issues of particular concern, such as sexual functioning, body image and spirituality [13]. Functioning and well-being may be considered at the level of each dimension as well as more globally. Multiple studies have shown that global HRQoL assessments comprise of more than the sum of identified component domains. HRQoL is a personal perspective and varies by patients' experiences, age, education and race [13–15]. By including HRQoL measurement in Phase III cancer trials, high-quality evidence regarding patients' perspectives on the impact of disease and its treatment can be determined.

Review methods

Annually, the NCIC CTG QoL Committee organizes workshops or symposia to advance the HRQoL field. In 2007, an internal workshop was held to assess the added value provided by HRQoL measurement in clinical trials. Committee members, all with expertise in HRQoL measurement, were asked to review completed NCIC CTG trials for which the HRQoL results had been analyzed and reported. Not every trial with a HRQoL component was reviewed in detail; rather, each DSC–QoL liaison selected up to two studies illustrating added value. Selected studies were analyzed using a template that included a summary of the hypothesis and overall outcomes, the HRQoL assessment and quality factors identified for HRQoL research [16,17]. A day-long workshop was subsequently conducted by the group with the added participation of an external reviewer from the EORTC QoL Group, Neil Aaronson. Through active discussion and group participation, we determined which studies indeed represented 'added value', and a classification system was proposed [18].

Subsequently, a symposium was held in spring 2008 for all members of the NCIC CTG. Through formal presentations, the proposed classification of added value was shared with all

participating investigators and NCIC CTG Central Office staff. The classification presented here builds on feedback and iterations from these two events.

Diversity of HRQoL added value exemplified by NCIC CTG Phase III trials

Our proposed classification of added value has two levels: first HRQoL added value is classified according to how the study results would be applied, and then within these categories, a second level details the specific nature of the findings. The first level includes three over-arching categories:

- Choosing the 'best' treatment
- Enriching the understanding of patient experiences (beyond treatment decision-making)
- Improving clinical trials methods

From these three main categories flow the eight subcategories of HRQoL added value observed in NCIC CTG cancer trials (Table 1). Of note, these categories are not mutually exclusive; several trials described below could be used as examples of more than one type of HRQoL added value.

Choosing the 'best' treatment

Health-related quality of life data can help patients and clinicians decide on the most appropriate therapy, by evaluating the balance of study outcomes. HRQoL information may support or counterbalance the primary outcome.

HRQoL as the primary outcome

Some randomized controlled trials are designed using a PRO as the primary study outcome, selecting PROs to best test the hypothesized benefit of the study intervention.

A Canadian randomized trial comparing prednisone with or without mitoxantrone as treatment for symptomatic hormone-resistant prostate cancer, demonstrated that mitoxantrone was associated with a sustained improvement in the study's primary outcome: patient-reported pain intensity (as measured by the McGill–Melzack Pain Questionnaire [19]) without an increase in analgesics [20]. The NCIC CTG provided independent external review of patient responses for this study. Patients allocated to receive mitoxantrone were also more likely to have improvements in multiple secondary HRQoL outcomes of the EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30) [21]: physical, emotional and social functioning; pain impact, pain relief; fatigue, insomnia, drowsiness; constipation; mood; and global HRQoL [20,22]. Although no difference in overall survival was detected between study arms, the experimental treatment was adopted on the basis of palliative benefit to patients. In contrast to PROs, neither imaging nor serum prostate-specific antigen were useful in determining 'responses'.

HRQoL outcomes that support the primary outcome

Several examples exist where HRQoL data provide supportive information that parallels other study outcomes, providing a more detailed illustration of the positive impact of treatment.

Cetuximab (a monoclonal antibody targeting the EGF receptor [EGFR]) was shown to prolong both OS and PFS, and to improve response and disease-control rates in patients with heavily pretreated advanced *KRAS*-wild-type colorectal cancer in the CO.17 study [23,24]. Not surprisingly, cetuximab did result in more grade 3–4 adverse events compared with the best supportive care control arm. However, as measured using the EORTC QLQ-C30, cetuximab was associated with less overall HRQoL deterioration, prolonged time to HRQoL deterioration, and improvements in pain, fatigue, nausea and dyspnea, thus confirming the palliative benefits of this therapy [25].

The tyrosine-kinase EGFR inhibitor erlotinib prolonged OS, 1-year survival and PFS, and also improved response rates, in patients with pretreated advanced non-small-cell lung cancer (NSCLC) in the placebo-controlled study BR.21 [26]. HRQoL was measured using the EORTC QLQ-C30 and QLQ-LC13 lung module [27]. Prolongation of time to worsening of cough, dyspnea and pain, as well as higher rates of improvement in physical functioning and in global HRQoL were observed with erlotinib therapy [28].

CE.3 provides a further illustration. This international Phase III study demonstrated a survival benefit for temozolomide added to radiotherapy for palliation of patients with glioblastoma [29]. As this is a population with a very poor prognosis even with treatment, there had been concern that more intensive therapy could result in impairment of well-being. As such, HRQoL was assessed using the EORTC QLQ-C30 and the EORTC BN-20

Table 1. Classification of added value of health-related quality-of-life outcomes.

Intended use	HRQoL outcomes
1. Choosing the 'best' treatment	1.1. Used as the primary outcome for comparing treatments 1.2. Support the primary trial outcome by improving understanding of treatment benefits or treatment risks 1.3. Counterbalance the primary trial outcome by improving understanding of treatment benefits or treatment risks
2. Enriching the understanding of patient experiences (for counseling beyond treatment decision-making)	2.1. Enhance understanding of treatment benefits or risks 2.2. Provide prognostic information for counseling purposes 2.3. Characterize under-evaluated populations
3. Improving clinical trials methods	3.1. Prognostic determinant (stratification) 3.2. Measurement advances in HRQoL research

HRQoL: Health-related quality of life.

brain cancer module [30]. Results revealed HRQoL was similar between treatment groups over time [31]. Reassuringly for patients and clinicians, it could be concluded that the survival benefit did not come at a substantial HRQoL cost.

HRQoL outcomes that counterbalance the primary outcome

There are times when HRQoL findings can illustrate outcomes that contrast with the primary study outcome, thus these findings alter treatment recommendations.

Such an example is found with the SR.2 study of pre- versus post-operative radiotherapy for adjuvant treatment of extremity soft-tissue sarcoma. This study's primary outcome, incidence of major wound complications, favored the postoperative approach with better acute wound healing [32,33]. However, longer term data revealed greater soft-tissue fibrosis in the patients who received postoperative radiotherapy. Patient-reported HRQoL assessments of difficulty experienced in activities of daily living (self-care, mobility and role functions) on the Toronto Extremity Salvage Score [34] revealed increased disability and a negative impact on long-term functioning with postoperative radiotherapy [35]. These findings changed the final interpretation and recommendations from this study, favoring preoperative radiotherapy.

Enriching the understanding of patient experiences

Health-related quality of life data can provide information regarding both positive and negative patient experiences that would not be available from traditional biomedical measurements alone. Although this HRQoL information might not always be used directly to choose the best treatment, it may better describe and quantify treatment benefits and toxicity. In addition, it may contribute to a fuller understanding of under-studied conditions or patient subgroups.

HRQoL enhances understanding of treatment benefits

Traditionally in clinical trials, 'response' refers to tumor shrinkage seen on imaging, by convention defined by Response Evaluation Criteria in Solid Tumors (RECIST) [36]. However, tumor response does not necessarily correlate with survival or other benefits that impact the patient [37]. PRO assessments may yield more clinically meaningful impressions of treatment response, particularly in the palliative setting.

MA.8 was a randomized trial of doxorubicin with or without vinorelbine for women with advanced breast cancer [38]. The relationship between objective tumor response and symptom improvement was evaluated using the EORTC QLQ-C30 and case report form (CRF) data. Improvements in the HRQoL outcomes cancer pain, dyspnea and abnormal mood were associated with objective responses [39]. This suggests that responding patients were actually receiving a meaningful palliative benefit, and provides information to patients that may be more useful for decision-making than an imaging report.

HRQoL enhances understanding of treatment toxicity

Health-related quality-of-life assessments of treatment toxicity can inform therapeutic decisions by more fully quantifying and qualifying treatment-related toxicity. This allows patients and clinicians to explicitly weigh the benefits of therapy against the trade-offs of toxicity.

For example, a Phase III study of adjuvant chemotherapy for early-stage NSCLC, JBR.10, revealed clinically and statistically improved survival with chemotherapy (hazard ratio: 0.69, and a 15% absolute improvement in 5-year survival) [40]. The study's HRQoL findings (as measured using the EORTC QLQ-C30 and a trial-specific checklist) were able to demonstrate that the expected negative impacts of chemotherapy were modest and temporary, with most patients returning to baseline functioning by 9 months [41]. A Quality-Adjusted Time Without Symptoms of Disease or Toxicity of Treatment (Q-TWiST) analysis was also performed, revealing adjuvant chemotherapy improved quality-adjusted survival despite treatment toxicity [42].

MA.17 was a placebo-controlled trial of letrozole following 5 years of tamoxifen as adjuvant therapy in postmenopausal women treated for early-stage breast cancer. Significant improvement in disease-free survival were found, leading to implementation of the *a priori* early stopping rule by an independent data monitoring committee [43]. HRQoL was measured using the SF-36 [44] and the MENQoL [45]. The HRQoL findings revealed no major impact of letrozole on overall well-being. However, it was found that a small proportion of patients did experience sustained worsening of HRQoL in some domains (physical function, bodily pain, vitality, vasomotor and sexual scales) [46]. These findings suggest that the majority of women tolerated the therapy well, but that a minority with problematic toxicity may require other supportive therapies or treatment discontinuation.

Measurement and reporting of toxicity, or adverse events, in clinical trials is conventionally performed by clinical and/or research staff. Through their assessment, an interpretation of the negative impact of the intervention on patients is determined. Despite the lack of formal validation for common scales, this has been a longstanding, familiar and accepted approach.

Adverse events and toxicity can also be collected as PROs, using single items or multidimensional questionnaires. This approach is clinically less familiar and may be perceived to require more complex analysis. However, there is evidence that PRO assessments yield different profiles of adverse events than those shown by traditional CRFs. Certain effects, such as pain and fatigue, are especially difficult for the outsider to rate. Furthermore, only PROs can provide the appropriate understanding of the impact of toxicity on patients' roles, functioning and degree of 'bother'. Several trials provide illustrations of the potential added value of HRQoL data in toxicity assessment.

We have previously discussed MA.8, the Phase III study of palliative chemotherapy for women with advanced breast cancer [38]. Savage *et al.* retrospectively analyzed the level of agreement between patients' and clinicians' evaluation of patients' symptoms on the study [47]. They found only fair to slight agreement at baseline, and the degree of agreement actually worsened over time for most symptoms. Overall, patients reported far more symptoms than did the clinicians, although clinicians reported more numbness in patients receiving vinorelbine.

The NCIC CTG participated in the Intergroup EORTC 55931/NCIC CTG OV.10 randomized study, which demonstrated that treatment of advanced ovarian cancer with cisplatin–paclitaxel resulted in superior survival compared with cisplatin–cyclophosphamide [48]. HRQoL information was collected, using the EORTC QLQ-C30, in 152 Canadian women participating in the study. This study revealed very weak to poor agreement between CRF reports of toxicity and HRQoL data for severe or moderate toxicity categories [49]. Patients were more likely to score a symptom as severe or moderate compared with the CRF data. HRQoL data from this study were also able to explain, at least in part, the impact of symptoms on patients' global well-being. We see by these examples that treatment toxicity is often under-reported by clinicians compared with patient self-evaluations. In their study, Savage *et al.* conclude that to obtain comprehensive information, an integrated system is needed, combining patient and clinician reporting of symptoms and toxicity [47].

HRQoL enhances understanding of under-evaluated populations

Health-related quality of life data can provide meaningful clinical information about cancer patients' experiences, beyond results that differentiate cancer treatments.

HN.2 was a multicenter, randomized, double-blind controlled trial of an oral antimicrobial versus placebo to prevent and treat mucositis for head and neck cancer patients undergoing radiation therapy. This was a negative trial, demonstrating no mucositis reduction with the antibiotic lozenge [50]. However, little HRQoL data from large multicenter randomized trials was previously available in the literature regarding head and neck cancer patients. Using the EORTC QLQ-C30 and a trial-specific checklist, this study demonstrated a high rate of oral pain, persistent and severe dry mouth, fatigue, and functional impairment in this small, but important, cancer patient population.

Improving clinical trials methods

Health-related quality of life data may be used to improve the methodology of clinical trials in general, and to advance the science of HRQoL evaluation for future studies. Recent recognition that HRQoL may be a strong prognostic indicator suggests its use as a stratification or inclusion factor in defining trial populations. Other results may improve future trials by informing the method of administration or analysis of HRQoL instruments.

HRQoL as a prognostic determinant

As mentioned previously, OV.10 was a trial of palliative chemotherapy for women with advanced ovarian cancer [48]. Further analyses from this study revealed that baseline global HRQoL was an independent predictor of both PFS and OS in this population. Baseline cognitive functioning, treatment and performance status (PS) were also independent predictors of OS [51].

Similarly, Dancey *et al.* performed a prognostic analysis of 474 patients with various cancers pooled from two NCIC CTG supportive care Phase III studies, SC.8 [52] and SC.9 [53]. Both studies were designed to evaluate antiemetic control with chemotherapy. The pooled analysis examined the association between HRQoL scores and survival in this heterogenous population [54]. Stage of disease, diagnosis of lung or ovarian cancer, PS and two elements of the baseline EORTC QLQ-C30 (global HRQoL and emotional functioning) were all independent predictors of survival.

These results support a growing body of literature revealing HRQoL as an independent predictor for survival in various cancer settings [51,55–58], although there are a few studies (particularly in early breast cancer) that have not confirmed this relationship [51,55,57–61]. Poorer HRQoL probably reflects the impact of greater disease burden and/or comorbidity in advanced cancer populations and in many studies has been a stronger predictor than PS alone. In populations where this relationship has been confirmed, HRQoL could, theoretically, be used as a stratification variable in clinical trials. Of course, the prognostic information provided by HRQoL may have further value over and above its contribution to clinical trial methodology; it may also be of value for patients and clinicians for shared decision-making, when prognosis may impact treatment preferences.

HRQoL advances in measurement methods

We provide an illustration here of the opportunity within clinical trials to advance HRQoL research methodology.

SC.11 was a Phase III supportive care study of antiemetics for control of chemotherapy-induced nausea and vomiting [62]. A substudy within this trial included an evaluation of the impact of the reference time frame of HRQoL questions and of the timing of administration of the questionnaires themselves [63]. The findings revealed that in situations where the impact of treatment being evaluated is not constant, careful attention needs to be paid to the scheduling and to the time frame of HRQoL questionnaires.

Expert commentary

Health-related quality of life findings provide important information for patients and clinicians. HRQoL information can enhance decision-making by providing a better understanding of the potential impact on a patient of both disease and treatment. The available literature has provided useful information to advance the science and reporting of HRQoL measurement in cancer clinical trials [5,6,16,17]. However, little guidance has previously been available to evaluate and classify its added value.

Recently, Efficace *et al.* reported a systematic review of the reporting of HRQoL in randomized controlled trials of leukemia patients [64]. This publication discusses the paucity of HRQoL research in patients with hematologic malignancies, but also presents examples where HRQoL study data provided unique information regarding the patient's perspective on the burden of the disease and treatment-related effects. However, the paper was mainly intended as a methodologic critique of the published leukemia Phase III HRQoL studies and it did not provide a classification of the added value of HRQoL in cancer studies.

Osoba proposed a taxonomy of the uses of HRQoL instruments as they relate to three levels of decision-making: macro (aimed at population policy making), meso (aimed at group

or institutional levels) and micro (aimed at the individual patient) [65], and also described potential applications of HRQoL in clinical practice [66]. This was intended to provide guidance when choosing the type of instrument most appropriate for each of these settings, but was not meant as a formal evaluation of types of added benefit.

Schwarz *et al.* outlined four areas where HRQoL research has contributed to high-quality cancer care [13]. These were:

- To assess treatment outcome and to qualify survival
- To assess late problems
- To predict mortality
- To support transfer of information

The US National Cancer Institute's Cancer Outcomes Measurement Working Group (COMWG) have defined HRQoL outcomes as providing added value when they are actionable by being "instrumental in interpreting a study's findings and would be expected to influence clinical recommendations" [67]. This is a helpful definition when evaluating the direct impact of HRQoL outcomes on patient care. However, we have also provided illustrations of the added value of HRQoL where clinical decisions were not altered, but, for instance, patients and clinicians had a more complete picture of the expected impact of disease and treatment as experienced by patients. The COMWG definition does not explicitly address such situations, nor those where clinical trials methodology is advanced.

Our review did not include preference-based measures. These instruments provide added value to health economic analyses by providing a quality weighting to survival, a utility score [68]. Furthermore, as our stated focus was on Phase III cancer studies, we have not presented illustrations where HRQoL information in Phase II trials may be of added value. However, such examples certainly exist. For instance, HRQoL results from Phase II studies may provide variance estimates for power calculations regarding HRQoL outcomes in Phase III studies, especially where this is planned as the primary outcome. HRQoL data could even help in selecting 'the winner' to take forward to Phase III in a randomized Phase II study of two or more experimental therapies.

Our review of added benefits of HRQoL does not provide an assessment of limitations in HRQoL data collection, analysis or interpretation. We refer the reader to discussions provided in the literature with regards to issues of instrument reliability, validity, responsiveness and translation; interpretation of HRQoL changes; burden of HRQoL collection; and missing HRQoL data [1–6,69–71]. However, as our examples have illustrated, the previous and ongoing research regarding these potential limitations continue to move the field forward such that added benefit of HRQoL assessment is realized.

The development of this classification was based on expert opinion and conducted in a qualitative fashion, through interactive discussion and evaluation of selected examples. In the future, we plan to use our classification system of the added value of HRQoL outcomes in Phase III cancer trials to perform a more quantitative, fully inclusive systematic review of such studies. We further hope that our classification will be of use to other researchers as the science of HRQoL assessment in clinical trials continues to evolve.

Five-year view

The future is bright regarding the use of HRQoL and other PROs in randomized clinical trials, in other research methods and in direct clinical care. Changes are anticipated in the field regarding the nature of PROs and how these measures are obtained; for example, computer adaptive testing (CAT) is a promising administrative method associated with methodologic implications [12,72,73]. The clinical application of PROs going forward may include both communication of trial results and, potentially, the day-to-day use of PROs in individual patient care [74]. Future research challenges will include better development of strategies for summarizing and communicating PRO data in a way that is understandable and useful for clinicians and patients.

Nature of PROs

The recognition of the importance of PROs is reflected in several major initiatives of the American National Cancer Institute (NCI), including the work of the COMWG [67] and the Patient-Reported Outcomes Assessment in Cancer Trials (PROACT) [75]. In addition, the Patient-Reported Outcomes Measurement Information System (PROMIS) initiative [76,77] of the NCI has been developed to address three major objectives:

- To develop and test item banks of standardized PRO items
- To create a CAT system that would facilitate robust evaluation of PROs in clinical research
- To create a repository of PROs for use by clinical researchers

These objectives are intended to make both the measurement of, and analysis of PROS standardized across a wide spectrum of clinical conditions, including oncology. Web-based or other electronic data capture, linked to the standardized CAT approach, will further facilitate the efficient collection of robust data with less patient burden and fewer missing assessments.

Application of PROs

Standardized approaches to collection and analysis open further opportunities to employ PROS in and out of clinical trials. For example, a plenary session at the 16th Annual Meeting of the International Society for Quality of Life Research in 2009 was devoted to exploring the use of PROs for measuring treatment-related toxicity and adverse event reporting, and to exploring the possibility of new drug labeling claims based on improved PRO profiles of new drugs. Expanded use of PROs in Phase II trials is also anticipated.

Beyond clinical trials, increased use of PROs in routine clinical practice may be helpful for a variety of reasons, including screening for symptom status change, evaluating patients' progress on treatment regimens, comparing outcomes in practice to clinical trial results and improving clinician–patient communication [78–80].

Research into these applications will require ongoing attention to enhance our understanding of clinically meaningful changes in PRO outcomes, the influence of response-shift on longitudinal data and the impact of missing data on the interpretation of PRO findings [81].

Communication of PRO results

The increased standardization of PROs and the increased application both in research and practice, will both require and facilitate communication of these results to clinicians and patients. Increased standardization of the items will facilitate clinicians' familiarity with the instruments and their application, whereas using PROs more frequently will facilitate physicians' comfort with PRO data. Both, however, will require that effective knowledge transfer and communication strategies are developed, particularly for reporting clinical trial results for the purposes outlined herein.

Acknowledgements

The authors thank Neil Aaronson, EORTC Quality of Life Group, for his insightful contributions to our workshop, Anne Leis for her comments on an earlier draft of the manuscript, and Dina McMahon for her clerical support.

Financial & competing interests disclosure

The National Cancer Institute of Canada Clinical Trials Group is a cancer clinical trials cooperative group that independently conducts clinical trials research with funds provided by the Canadian Cancer Society. Additional funds are also received from other sources, which include the US National Cancer Institute/Cancer Therapy Evaluation Program, other peer-review agencies and industry contracts. Many of the trials described within this manuscript included funding support from the pharmaceutical industry. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Key issues

- Conventional Phase III study outcomes are poor surrogates for health-related quality-of-life (HRQoL) information.
- HRQoL data provide unique information, from patients' perspectives.
- In Phase III studies, several types of circumstance exist where HRQoL data are important to the interpretation of, and/or the advancement of the science of Phase III studies.
- The information provided by HRQoL studies of cancer therapies can assist patients and clinicians with medical decision-making.
- HRQoL outcomes are and will continue to be key clinical trial outcomes, across many types and stages of cancer.

References

Papers of special note have been highlighted as:
• of interest
•• of considerable interest

1 Brundage M, Osoba D, Bezjak A, Tu D, Palmer M, Pater J. Lessons learned in the assessment of health-related quality of life: selected examples from the National Cancer Institute of Canada Clinical Trials Group. *J. Clin. Oncol.* 25(32), 5078–5081 (2007).

2 Bottomley A, Aaronson NK. International perspective on health-related quality-of-life research in cancer clinical trials: the European Organisation for Research and Treatment of Cancer experience. *J. Clin. Oncol.* 25(32), 5082–5086 (2007).

3 Bruner DW. Outcomes research in cancer symptom management trials: the Radiation Therapy Oncology Group (RTOG) conceptual model. *J. Natl Cancer Inst. Monogr.* 37, 12–15 (2007).

4 Buchanan DR, O'Mara AM, Kelaghan JW, Minasian LM. Quality-of-life assessment in the symptom management trials of the National Cancer Institute-supported Community Clinical Oncology Program. *J. Clin. Oncol.* 23(3), 591–598 (2005).

5 Sloan JA, Frost MH, Berzon R *et al*. The clinical significance of quality of life assessments in oncology: a summary for clinicians. *Support Care Cancer* 14, 988–998 (2006).

•• **Review summarizing the six-manuscript series within the Mayo Clinic Proceedings resulting from the 2000 Clinical Significance Consensus Meeting Group and subsequent work.**

6 Osoba D, Bezjak A, Brundage M, Zee B, Tu D, Pater J. Analysis and interpretation of health-related quality-of-life data from clinical trials: basic approach of The National Cancer Institute of Canada Clinical Trials Group. *Eur. J. Cancer* 41(2), 280–287 (2005).

•• **Summary of the National Cancer Institute of Canada Clinical Trials Group standard approach to analyzing and interpreting health-related quality-of-life (HRQoL) data, emphasizing the clinical meaning of results.**

7 Osoba D. The Quality of Life Committee of the Clinical Trials Group of the National Cancer Institute of Canada: organization and functions. *Qual. Life Res.* 1(3), 211–218 (1992).

8 Moinpour CV, Donaldson GW, Redman MW. Do general dimensions of quality of life add clinical value to symptom data? *J. Natl Cancer Inst. Monogr.* 37, 31–38 (2007).

9 Committee on Quality of Health Care in America. Crossing the quality chasm: a new health system for the 21st Century. *Washington: National Academy Press* (2001).

10 Oliver A, Greenberg CC. Measuring outcomes in oncology treatment: the importance of patient-centered outcomes. *Surg. Clin. N. Am.* 89(1), 17–25 (2009).

11 Avery KNL, Gurjal S, Blazeby JM. Patient-reported outcomes to evaluate surgery. *Expert Rev. Pharmacoeconomics Outcomes Res.* 8(1), 43–50 (2008).

12 Lipscomb J, Gotay CC, Snyder CF. Patient-reported outcomes in cancer: a review of recent research and policy initiatives. *CA Cancer J. Clin.* 57(5), 278–300 (2007).

•• **Review of patient-reported outcome (PRO) definition, measurement, use in cancer research and role in cancer therapy approval, evaluation of cancer care, patient-provider decision-making and population assessments.**

13 Schwartz CE, Sprangers MAG. An introduction to quality of life assessment in oncology: the value of measuring patient-reported outcomes. *Am. J. Manag. Care* 8(18 Suppl.), S550–S559 (2002).

•• **Review of the uses, benefits and challenges of HRQoL research in cancer trials and cancer care.**

14 Krause NM, Jay GM. What do global self-rated health items measure? *Medical Care* 32(9), 930–942 (1994).

15 Warnecke RB, Ferrans CE, Johnson TP *et al*. Measuring quality of life in culturally diverse populations. *J. Natl Cancer Inst. Mongr*. 20, 29–38 (1996).

16 Efficace F, Osoba D, Gotay C, Sprangers M, Coens C, Bottomley A. Has the quality of health-related quality of life reporting in cancer clinical trials improved over time? Towards bridging the gap with clinical decision-making. *Ann. Oncol.* 18(4), 775–781 (2007).

•• **Systematic review to assess the HRQoL reporting in cancer clinical trials based on minimum predefined criteria.**

17 Efficace F, Bottomley A, Osoba D *et al*. Beyond the development of health-related quality of life (HRQOL) measures. A checklist for evaluating HRQOL outcomes in cancer clinical trials – does HRQOL evaluation in prostate cancer research inform clinical decision-making? *J. Clin. Oncol.* 21(18), 3502–3511 (2003).

• **Prior paper determining the minimum predefined criteria for HRQoL reporting in cancer clinical trials.**

18 Au HJ, Brundage M, Ringash J *et al*. Added value of health-related quality of life (QoL) outcomes in NCIC CTG clinical trials: results from QoL Committee Workshop. *Qual. Life Res. Suppl.* A-71 (2007).

19 Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. *Pain* 1(3), 277–299 (1975).

20 Tannock IF, Osoba D, Stockler MR *et al*. Chemotherapy with mitoxantrone plus prednisone or prednisone alone for symptomatic hormone-resistant prostate cancer: a Canadian randomized trial with palliative end points. *J. Clin. Oncol.* 14(6), 1756–1764 (1996).

21 Aaronson NK, Ahmedzai S, Bergman B *et al*. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J. Natl Cancer Inst.* 85, 365–376 (1993).

22 Osoba D, Tannock IF, Ernst D, Neville AJ. Health-related quality of life in men with metastatic prostate cancer treated with prednisone alone or mitoxantrone and prenisone. *J. Clin. Oncol*. 17(6), 1654–1663 (1999).

23 Jonker DJ, O'Callaghan CJ, Karapetis CS. Cetuximab for the treatment of colorectal cancer. *N. Engl. J. Med*. 357(20), 2040–2048 (2007).

24 Karapetis CS, Khambata-Ford S, Jonker DJ. K-ras mutations and benefit from cetuximab in advanced colorectal cancer. *N. Engl. J. Med*. 359(17), 1757–1765 (2008).

25 Au HJ, Karapetis CS, O'Callaghan CJ *et al*. Health-related quality of life in patients with advanced colorectal cancer treated with cetuximab: overall and KRAS-specific results of the NCIC CTG and AGITG CO.17 trial. *J. Clin. Oncol.* 27(11), 1822–1828 (2009).

26 Shepherd F, Pereira J, Ciuleanu T *et al*. Erlotinib in previously treated non-small-cell lung cancer. *N. Engl. J. Med*. 353(2), 123–132 (2005).

27 Bergman B, Aaronson NK, Ahmedzai S *et al*. The EORTC QLQ-LC13: a modular supplement to the EORTC Core Quality of Life Questionnaire (QLQ-C30) for use in lung cancer clinical trials. *Eur. J. Cancer* 30A, 635–642 (1994).

28 Bezjak A, Tu D, Seymour L *et al*. Symptom improvement in lung cancer patients treated with erolotinib: quality of life analysis of the National Cancer Institute of Canada Clinical Trials Group study BR.21. *J. Clin. Oncol.* 24(24), 3831–3837 (2006).

29 Stupp R, Mason WP, van den Bent MJ *et al*. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N. Engl. J. Med*. 352(10), 987–996 (2005).

30 Osoba D, Aaronson NK, Muller M *et al*. The development and psychometric validation of a brain cancer quality-of-life questionnaire for use in combination with general cancer-specific questionnaires. *Qual. Life Res.* 5(1), 139–150 (1996).

31 Taphoorn MJB, Stupp R, Coens C *et al*. Health-related quality of life in patients with glioblastoma: a randomised controlled trial. *Lancet Oncol*. 6(12), 937–944 (2005).

32 O'Sullivan B, Davis AM, Turcotte R *et al*. Preoperative versus postoperative radiotherapy in soft tissue sarcoma of the limbs: a randomized trial. *Lancet* 359(9325), 2235–2241 (2002).

33 Davis AM, O'Sullivan B, Bell RS *et al*. Function and health status outcomes in a randomized trial comparing preoperative and postoperative radiotherapy in extremity soft tissue sarcoma. *J. Clin. Oncol.* 20(22), 4472–4477 (2002).

34 Davis AM, Wright JG, Williams JI, Bombardier C, Griffin A, Bell RS. Development of a measure of physical function for patients with bone and soft tissue sarcoma. *Qual. Life Res*. 5(5), 508–516 (1996).

35 Davis AM, O'Sullivan B, Turcotte R *et al*. Late radiation morbidity following randomization to preoperative versus postoperative radiotherapy in extremity soft tissue sarcoma. *Radiother Oncol.* 75(1), 48–53 (2005).

36 Eisenhauer EA, Therasse P, Bogaerts J *et al*. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur. J. Cancer* 45(2), 228–247 (2009).

37 Huff CA, Matsui W, Smith BD, Jones RJ. The paradox of response and survival in cancer therapeutics. *Blood* 107(2), 431–434 (2006).

38 Norris B, Pritchard K, James K *et al*. A Phase III comparative study of vinorelbine (VNB) combined with doxorubicin (DOX) versus doxorubicin alone in metastatic/recurrent breast cancer (MBC): a National Cancer Institute of Canada (NCIC CTG) study. *Proc. Am. Soc. Clin. Oncol.* 15, 98a (1996) (Abstract 59).

39 Geels P, Eisenhauer E, Bezjak A, Zee B, Day A. Palliative effect of chemotherapy: objective tumor response is associated with symptom improvement in patients with metastatic breast cancer. *J. Clin. Oncol.* 18(12), 2395–2405 (2000).

40 Winton T, Livingston R, Johnson D *et al*. Vinorelbine plus cisplatin vs observation in resected non-small-cell lung cancer. *N. Engl. J. Med*. 352(25), 2589–2597 (2005).

41 Bezjak A, Lee CW, Ding K *et al*. Quality-of-life outcomes for adjuvant chemotherapy in early-stage non-small-cell lung cancer: results from a randomized trial, JBR.10. *J. Clin. Oncol.* 26(31), 5052–5059 (2008).

42 Jang RW, Le Maître A, Ding K *et al*. Quality-adjusted time without symptoms or toxicity analysis of adjuvant chemotherapy in non-small-cell lung cancer: an analysis of the National Cancer Institute of Canada Clinical Trials Group JBR.10 trial. *J. Clin. Oncol*. 27(26), 4268–4273 (2009).

43 Goss PE, Ingle JN, Martino S *et al*. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. *N. Engl. J. Med*. 349, 1793–1802 (2003).

44 Ware JE, Snow KK, Kosinksi M *et al*. SF-36 Health Survey Manual and Interpretation Guide. The Health Institute, MA, USA (1993).

45 Hilditch JR, Lewis J, Peter A *et al.* A menopause-specific quality of life questionnaire: development and psychometric properties. *Maturitas* 24, 161–175 (1996).

46 Whelan TJ, Goss PE, Ingle JN *et al.* Assessment of quality of life in MA.17: a randomized, placebo-controlled trial of letrozole after 5 years of tamoxifen in postmenopausal women. *J. Clin. Oncol.* 23(28), 6931–6940 (2005).

47 Savage C, Pater J, Tu D, Norris B. He said/she said: how much agreement is there on symptoms between common toxicity criteria and quality of life? *Proc. Am. Soc. Clin. Oncol*. 21(Part 1), 386a (2002).

48 Piccart MJ, Bertelsen K, James K *et al.* Randomized intergroup trial of cisplatin–paclitaxel versus cisplatin–cyclophosphamide in women with advanced ovarian cancer. *J. Natl Cancer Inst.* 92(9), 699–708 (2000).

49 Butler L, Bacon M, Carey M, Zee B, Tu D, Bezjak A. Determining the relationship between toxicity and quality of life in an ovarian cancer chemotherapy clinical trial. *J. Clin. Oncol*. 22(12), 2461–2468 (2004).

50 Duncan GG, Epstein JB, Tu D *et al*. Quality of life, mucositis, and xerostomia from radiotherapy for head and neck cancers: a report from the NCIC CTG HN2 randomized trial of an antimicrobial lozenge to prevent mucositis. *Head Neck* 27(5), 421–428 (2005).

51 Carey MS, Bacon M, Tu D, Butler L, Bezjak A, Stuart GC. The prognostic effects of performance status and quality of life scores on progression-free survival and overall survival in advanced ovarian cancer. *Gynecol. Oncol.* 108(1), 100–105 (2008).

52 Latreille J, Stewart D, Laberge F *et al*. Dexamethasone improves the efficacy of granisetron in the first 24 h following high-dose cisplatin chemotherapy. *Support Care Cancer* 3(5), 307–312 (1995).

53 Kaizer L, Warr D, Hoskins P *et al*. Effect of schedule and maintenance on the antiemetic efficacy of ondansetron combined with dexamethasone in acute and delayed nausea and emesis in patients receiving moderately emetogenic chemotherapy: a Phase III trial by the National Cancer Institute of Canada Clinical Trials Group. *J. Clin. Oncol.* 12(5), 1050–1057 (1994).

54 Dancey J, Zee B, Osoba D *et al*. Quality of life scores: an independent prognostic variable in a general population of cancer patients receiving chemotherapy. *Qual. Life Res.* 6(2), 151–158 (1997).

55 Gotay CC, Kawamoto CT, Bottomley A, Efficace F. The prognostic significance of patient-reported outcomes in cancer clinical trials. *J. Clin. Oncol*. 26(8), 1355–1363 (2008).

- **Systematic review of the impact of PROs on prognosis for survival in cancer clinical trials.**

56 Curran D, Giralt J,Harari PM *et al*. Quality of life in head and neck cancer patients after treatment with high-dose radiotherapy alone or in combination with cetuximab. *J. Clin. Oncol*. 25(16), 2191–2197 (2007).

57 Quinten C, Coens C, Mauer M *et al*. Baseline quality of life as a prognostic indicator of survival: a meta-analysis of individual patient data from EORTC clinical trials. *Lancet Oncol.* 10, 865–871 (2009).

58 Montazeri A. Quality of life data as prognostic indicators of survival in cancer patients: an overview of the literature from 1982 to 2008. *Health Qual. Life Outcomes* 7, 102 (2009).

59 Coates AS, Hurny C, Peterson HF *et al*. Quality-of-life scores predict outcome in metastatic but not early breast cancer: International Breast Cancer Study Group. *J. Clin. Oncol.* 18(22), 3768–3885 (2004).

60 Efficace F, Therasse P, Piccart MJ *et al*. Health-related quality of life parameters as prognostic factors in a nonmetastatic breast cancer population: an international multicenter study. *J. Clin. Oncol.* 22(16), 3381–3388 (2004).

61 Tross S, Herndon J 2nd, Korzun A *et al*. Psychological symptoms and disease-free and overall survival in women with stage II breast cancer: Cancer and Leukemia Group B. *J. Natl Cancer Inst.* 88(10), 661–667 (1996).

62 Lofters WS, Pater JL, Zee B *et al*. Phase III double-blind comparison of dolasetron mesylate and ondansetron and an evaluation of the additive role of dexamethasone in the prevention of acute and delayed nausea and vomiting due to moderately emetogenic chemotherapy. *J. Clin. Oncol.* 15(8), 2966–2973 (1997).

63 Pater J, Osoba D, Zee B. Effects of altering the time of administration and the time frame of quality of life assessments in clinical trials: an example using the EORTC QLQ-C30 in a large anti-emetic trial. *Qual. Life Res.* 7(3), 273–278 (1998).

64 Efficace F, Kemmler G, Vignetti M, Mandelli F, Molica S, Holzner B. Health-related quality of life assessment and reported outcomes in leukaemia randomised controlled trials – a systematic review to evaluate the added value in supporting clinical decision-making. *Eur. J. Cancer* 44(11), 1497–1506 (2008).

65 Osoba D. A taxonomy of the uses of health-related quality-of-life instruments in cancer care and the clinical meaningfulness of the results. *Med. Care* 40(Suppl.), III-31–III-38 (2002).

66 Osoba D. The clinical value and meaning of health-related quality of life outcomes in oncology. In: *Outcomes Assessment in Cancer: Measures, Methods, and Applications*. Lipscomb J, Gotay CC, Snyder D (Eds). Cambridge University Press, UK, 386–405 (2005).

67 Lipscomb J, Gotay CC, Snyder C. Introduction to outcomes assessment in cancer. In: *Outcomes Assessment in Cancer: Measures, Methods, and Applications*. Lipscomb J, Gotay CC, Snyder D (Eds). Cambridge University Press, UK, 1–14 (2005).

68 Shih YCT, Halpern MT. Economic evaluations of medical care interventions for cancer patients: how, why, and what does it mean? *CA Cancer J. Clin.* 58(4), 231–244 (2008).

69 Osoba D, Rodrigues, G, Myles J, Zee B, Pater J. Interpreting the significance of changes in health-related quality-of-life scores. *J. Clin. Oncol*. 16, 139–144 (1998).

70 Sadura A, Pater J, Osoba D, Levine M, Palmer M, Bennett K. Quality-of-life assessment: patient compliance with questionnaire completion. *J. Natl Cancer Inst.* 84(13), 1023–1026 (1992).

71 Osoba D, Bezjak A, Brundage M, Pater J; National Cancer Institute of Canada Clinical Trials Group. Evaluating health-related quality of life in cancer clinical trials: the National Cancer Institute of Canada Clinical Trials Group experience. *Value Health* 10(Suppl. 2), S138–S145 (2007).

72 Bush N, Donaldson G, Moinpour C *et al*. Development, feasibility and compliance of a web-based system for very frequent QOL and symptom home self-assessment after hematopoietic stem cell transplantation. *Qual. Life Res.* 14, 77–93 (2005).

73 Fayers P. Applying item response theory and computer adaptive testing: the challenges for health outcomes assessment. *Qual. Life Res.* 16, 187–194 (2007).

74 Osoba D. Translating the science of patient-reported outcomes assessment into clinical practice. *J. Natl Cancer Inst. Monogr.* 37, 5–11 (2007).

75 Clauser SB, Ganz PA, Lipscomb J, Reeve BB. Patient-reported outcomes assessment in cancer trials: evaluating and enhancing the payoff to decision-making. *J. Clin. Oncol.* 25(32), 5049–5050 (2007).

76 Cella D, Yount S, Rothrock N *et al.* The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap Cooperative Group during its first two years. *Medical Care* 45(5), S3–S11 (2007).

77 Revicki DA, Sloan J. Practical and philosophical issues surrounding a national item bank: if we build it will they come? *Qual. Life Res.* 16, 167–174 (2007).

78 Arora NK. Importance of patient-centred care in enhancing patient well-being: a cancer survivor's perspective. *Qual. Life Res.* 18, 1–4 (2009).

79 Greenhalgh J. The applications of PROs in clinical practice: what are they, do they work, and why? *Qual. Life Res.* 18, 115–123 (2009).

80 Lohr KN, Zebrack BJ. Using patient-reported outcomes in clinical practice: challenges and opportunities. *Qual. Life Res.* 18, 99–107 (2009).

81 Mandrekar S, Dueck A. Future direction in QOL research. *Curr. Probl. Cancer.* 29(6), 343–351 (2005).

Affiliations

- Heather-Jane Au, MD, MPH
Department of Medical Oncology, Cross Cancer Institute, 11560 University Avenue, Edmonton, AB T6G 1Z2, Canada
Tel.: +1 780 432 8762
Fax: +1 780 432 8888
heather-jane.au@albertahealthservices.ca
- Jolie Ringash, MD, MSc
Department of Radiation Oncology, The Princess Margaret Hospital, 610 University Avenue, 5th Floor, Department of Radiation Oncology, Toronto, ON M5G 2M9, Canada
Tel.: +1 416 946 4662
Fax: +1 416 946 2111
jolie.ringash@rmp.uhn.on.ca
- Michael D Brundage, MD, PhD
Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute, 10 Stuart St Level 2, Kingston, ON K7L 3N6, Canada
Tel.: +1 613 533 6895
Fax: +1 613 533 6794
michael.brundage@krcc.on.ca
- Michael Palmer, MSc
NCIC Clinical Trials Group, Cancer Research Institute, 10 Stuart St, Kingston, ON K7L 3N6, Canada
Tel.: +1 613 533 6430
Fax: +1 613 533 2941
mpalmer@ctg.queensu.ca
- Harriet Richardson, PhD
NCIC Clinical Trials Group, Cancer Research Institute, 10 Stuart St, Kingston, ON K7L 3N6, Canada
Tel.: +1 613 533 6430
Fax: +1 613 533 2941
hrichardson@ctg.queensu.ca
- Ralph M Meyer, MD
NCIC Clinical Trials Group, Cancer Research Institute, 10 Stuart St, Kingston, ON K7L 3N6, Canada
Tel.: +1 613 533 6430
Fax: +1 613 533 2941
rmeyer@ctg.queensu.ca

Members of the NCIC CTG Quality of Life Committee

- Andrea Bezjak, Lori Brotto, Allana Buhl, Aileen Davis, Carolyn Gotay, Nancy Johnson, Christopher Lee, Julie Lemieux, Elizabeth Maunsell, David Osoba, Jonathan Sussman and Dongsheng Tu