

Introduction to *Outcomes Assessment in Cancer*

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Understanding how a disease and its associated health care interventions affect the lives of individuals is important whatever the medical condition, but especially so for diseases that are chronic or incurable and for which treatments often have toxic and long-lasting consequences. For this reason, cancer provides an exceptionally compelling model for examining the impact of disease on individual well-being. It is the second leading cause of death in the US, with one out of every four deaths in 2004 (over 560 000 in total) projected to be attributable to cancer. Many more individuals (an estimated 9.6 million in 2000) will be undergoing cancer treatment, coping with progressive disease, or living cancer-free in the aftermath of diagnosis and treatment.¹

The principal means of treating cancer – surgery, chemotherapy, and radiation – are powerful and toxic. All of these treatments, and additional ones like hormonal therapy, have side effects, which may be short-term or time-limited, or chronic and persistent, or else generate late effects emerging only after treatment is completed and sometimes not evident until many years later. Efforts to prevent, screen for, and treat cancer are all aimed at maximizing the chances for a healthy life while, at the same time, minimizing the associated side effects. In addition to its mortality and morbidity impact, cancer inflicts an enormous economic burden on society. Total direct medical care costs attributable to cancer in the US in 2003 were projected to be \$64.2 billion (or 4.5% of all direct medical costs), while the total economic burden (measured as direct costs plus the indirect costs associated with cancer-attributable

morbidity and premature mortality) for 2003 was projected at nearly \$190 billion (or 8.4% of all disease-generated costs).¹ Consequently, documenting how cancer and cancer-related interventions affect the individual becomes crucial for determining whether these interventions are tolerable and acceptable, provide significant clinical benefits, and are economically viable.

“Outcomes research” may be defined generally as the scientific field devoted to measuring and interpreting the impact of medical conditions and health care on individuals and populations. According to the Agency for Healthcare Research and Quality, “outcomes research seeks to understand the end results of particular health care practices and interventions. . . . End results include effects that people experience and care about, such as change in the ability to function . . . and include quality of life as well as mortality.”² The Outcomes Research Branch of the US National Cancer Institute (NCI) (within the National Institutes of Health) states that “outcomes research describes, interprets, and predicts the impact of various influences, especially (but not exclusively) interventions on ‘final’ endpoints that matter to decision makers: patients, providers, private payers, government agencies, accrediting organizations, and society at large.”³ Such final endpoints, according to NCI, may include survival or disease-free survival (with or without an adjustment for variations in quality of life); health-related quality of life (HRQOL), as captured through either generic (non-disease specific), general cancer, or cancer site-specific measures; perceptions about

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and satisfaction with health care; and economic burden, as felt by patients, caregivers, payers (public and private), or society at large.

Consequently, the central task of outcomes assessment in cancer is to enhance our understanding about the impact of interventions (and possibly other factors) on these final endpoints from a variety of potential decision perspectives. Elsewhere, NCI has proposed a three-part categorization of these decision perspectives that, together, comprise the arenas of application for cancer outcomes research. These arenas have been defined as macro (population surveillance of progress against the cancer burden); meso (descriptive and analytical studies to understand the impact of cancer, patterns of service use, and the effects of interventions on outcomes); and micro (use of outcomes measurement and clinical decision modeling to facilitate patient-provider choice making).⁴

However, before outcomes research can be used in these arenas, it is essential to know that cancer outcomes can be measured in a scientifically sound manner. Some outcomes, such as survival and disease-free survival, are relatively straightforward to assess. Other measures commonly used in health care may involve more interpretation and calibration but be no less useful – for example, measurement of blood pressure. This assessment has a long and successful history in health care. There are standard, well-calibrated instruments yielding numerical values that have, over time, taken on comparatively clear meaning for purposes of diagnosing hypertension and identifying (through clinical research) effective interventions that reduce, delay, or eliminate serious target organ damage. Although there is much intra-individual variation in blood pressure readings (posing a threat to reliability), there is enough accumulated research and observational experience to conclude confidently that (for example) a sustained change in diastolic from 105 mmHg to 85 mmHg for a given individual is both a “clinically meaningful” and “clinically important” difference. Moreover, knowledge of the 105 mmHG reading undoubtedly would bring “added value” to the clinical deliberations lead-

ing the provider to prescribe and the patient to accept the medication and behavioral health changes generating such an improvement.

It is worth remembering that the first measurement of blood pressure occurred in 1733 (measured intra-arterially in a horse), and it took until 1905 for a technique to be developed that is similar to what is used today.⁵ Further, it was only in the 1960s that hypertension was recognized as a cardiac risk factor and medical interventions developed accordingly. The pathway to scientific consensus can be lengthy and serpentine, even for a comparatively “hard” endpoint like blood pressure. It should not be surprising, therefore, that we do not yet have definitively established, widely accepted, and extensively used measures for health-related quality of life, perceptions of and satisfaction with health care, and many aspects of economic burden. To be sure, there has been significant progress over the past two decades, as many chapters in this volume attest, with the result that certain HRQOL and satisfaction instruments are being used with increasing frequency and sophistication in clinical trials and observational studies. Still, there remains much that is not understood, and is currently under debate, about the scientific foundations, clinical utility, and overall decisional relevance of such patient-reported outcome measures. In blood pressure assessment, the relevant data are transmitted straight from the patient’s arm, as it were, into the sphygmomanometer. In HRQOL assessment, it is the patient who must perceive, interpret, and evaluate his or her own health-related circumstances at the moment and then map this assessment to a candidate survey item or some other form of evaluation (e.g., preference score). Thus, the measurement challenges here include not only obtaining an adequate physiological “pulse” about the health condition of interest, but also a cognitively meaningful sorting and evaluation of the data, so that a coherent assessment of something called “quality of life” emerges. Doing this successfully is arguably required for achieving the type of patient-centered health care long advocated by many public and private decision makers.⁶ Indeed, much of this volume is devoted to

the review and evaluation of where the field stands in developing and applying such patient-reported (and patient-centered) outcome measures.

As a review of publication trends in the peer-review literature indicates, there has been increasing attention to cancer-related outcomes in recent years. A MEDLINE search crossing the terms “cancer” with “quality of life” identified 2416 articles for the five-year period 1990–1994, 4683 articles over the 1995–99 period, and 5676 articles between 2000 and 2003. A similar trend was seen when “cancer” was crossed with “patient satisfaction,” with the number of citations across these three periods being 214, 666, and 970, respectively.

Despite this substantial and apparent growing interest in cancer outcomes measurement, there have been only limited efforts to review and synthesize the literature from a methodological perspective to understand what has been well-established, what remains unknown or equivocal, and what research is needed to accelerate progress. In fact, determining how best to address these issues became a first order of business for NCI’s Outcomes Research Branch after it was created in 1999. In the same year, NCI established a new research initiative (which continues today on a number of fronts) to improve the quality of cancer care. This has served to accentuate the potential policy import of cancer outcomes measurement. Specifically, this initiative has defined quality cancer care “as the provision of evidence-based, patient-centered services throughout the continuum of care in a timely and technically competent manner, with good communication, shared decision making, and cultural sensitivity. The ultimate aim is to improve a range of outcomes important to patients, families, and other decision makers, including patient survival and quality of life.”⁷ Consequently, it is centrally important to have scientifically sound, patient-centered outcome measures for assessing whether specific cancer interventions lead to the end results desired by decision makers.

For these measurement tools to be as useful as possible to NCI and other organizations that attempt to evaluate cancer care from a broad perspective, they

would ideally possess several characteristics. One is parsimony: for any given outcomes research application, there would be a small “core” set of measures available that meet rigorous scientific standards. Among other things, such a core would improve the comparability of outcome findings across studies, thus enhancing the quality and usefulness of meta-analyses by strengthening the statistical robustness and representativeness of conclusions about the impact of interventions. Another important characteristic is sensitivity: that is, that the outcome measure(s) in any given application are known to reflect what is important to patients. By the same token, it is also essential to know when such measures are detecting changes that are not in fact meaningful to the patient. Questions regarding what constitutes a “truly meaningful” change in a patient-reported outcome like HRQOL, and how to recognize and utilize such data, point to some thorny issues. There may be an unavoidable tradeoff between selecting measures that promote comparability across studies versus those that are sensitive to change within studies. On the other hand, might there be analytical approaches, either available now or in development, that would allow us to sidestep this tradeoff? More broadly, what are the methodological tools and research strategies for effectively tackling the broad range of challenges arising in outcomes measurement?

To address these and many other related issues, the NCI established in 2001 the Cancer Outcomes Measurement Working Group (COMWG). Comprising 35 experts drawn from academia, government, industry, and the cancer patient and survivorship communities, the COMWG was charged with evaluating the state of the science in outcomes measurement and recommending approaches to improve the scientific quality and usefulness of measures. This volume reports the findings and recommendations of the COMWG members. In the remaining sections of this chapter, we describe the development and operation of the COMWG, suggest an organizational framework for analyzing cancer outcomes measurement, provide operational definitions for key terms

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used throughout the book, and finally present an overview of the book's organization and its individual chapters.

Development of the working group

With the state of the science in cancer outcomes measurement still evolving and diverse in its approaches and perspectives, NCI determined that the appropriate way forward was to establish a "working group" rather than a Federal advisory committee or some other mechanism geared to produce consensus recommendations to guide policy. As defined and formally chartered by NCI, a working group is not a decisional body. Rather, it is a group convened for the purpose of exchanging facts or information and reviewing data, with group members being expected to provide their "individual opinions on the information being reviewed."⁸ Consequently (and as the reader will readily discern), individual chapters addressing broadly similar topics may concur on some points, disagree on others, or even take varying perspectives on what the important issues are. An important question, further discussed in the book's concluding chapter, is whether there emerges from the COMWG analyses certain "natural pockets" of consensus that point the way to future consensus development.

The membership of the COMWG was carefully constituted to reflect a variety of perspectives on cancer outcomes measurement and to provide a broad range of clinical and methodological expertise. The working group members, with their affiliations, are listed at the beginning of this volume. They were selected on the basis of their contributions to the literature and to the conduct of clinical and outcomes research through major cancer-related organizations. The aim was to create a group whose skills, insights, and experiences would be complementary and sufficient, taken together, to address the many topics within the working group's purview. The majority of members were cancer researchers, many of whom were also clinicians representing medicine (with 9 of the 12 clinicians being oncologists),

nursing, psychology, and social work. There was expertise in economics, biostatistics, psychometrics, and health services research generally. The perspectives of the cancer patient and survivor were given particular focus through the appointment of two members nominated by the NCI Director's Consumer Liaison Group.

To chair the COMWG, NCI named Joseph Lipscomb, Ph.D., Chief of the Outcomes Research Branch (ORB), and Carolyn C. Gotay, Ph.D., a psychosocial oncology researcher at the University of Hawai'i. Claire Snyder, M.H.S., an ORB staff member with a background in health services research, served as the COMWG "initiator" (NCI's term for working group convenor) and provided both technical and scientific input throughout the process.

To obtain additional, complementary insight on particular topics in cancer outcome measures development and application, NCI commissioned the four invited chapters published in this volume.

Framework for COMWG cancer outcomes assessment

Evaluating the state of the science in cancer outcomes measurement is both a daunting task and potentially an ill-defined one, unless some additional structure is imposed. To focus the COMWG's work while striving to maintain adequate breadth of coverage, four key issues about content and scope were addressed early on, and their resolution effectively defined the framework for the working group's research.

1. Outcome measures of prime interest. Among outcome measures important for decision making in cancer, we believed those that pose the largest methodological challenges fall under the broad headings of health-related quality of life, patient perceptions of and satisfaction with care, and economic burden. Survival and disease-free survival are centrally important, but the challenge today lies with how to improve these outcomes, not how to measure them. Intermediate outcomes such as

time to tumor progression or time to recurrence were not a COMWG focus since they do not incorporate the patient's point of view or evaluation.

2. Disease focus. Cancer is not one disease but well over a hundred now, and our rapidly expanding understanding of the biological mechanisms of cancer will likely lead to ever more refined categorizations in years to come. As a practical matter, we elected to focus on a manageable number of cancer types that collectively account for a substantial portion of the total US cancer burden: breast (female), colorectal, lung, and prostate. In 2003, about 55% of all new cancer cases and just over 50% of all cancer deaths were attributable to these four diseases (with those proportions virtually the same, respectively, in men and women).¹ Moreover, the majority of cancer outcomes research studies published to date have examined one or more of these disease sites.
3. Continuum of care. The COMWG was charged with examining outcomes measurement across the entire cancer trajectory: prevention and screening, diagnosis and treatment, survivorship, and end of life. We believed that, especially for HRQOL, the appropriate choice of measure may vary along this continuum of cancer care. One could not assume, for example, that HRQOL measures designed to detect symptom relief and toxicity burdens during initial treatment would necessarily be appropriate for outcomes assessment in survivorship, or for evaluating the short-term impacts of preventive interventions.
4. Arenas of application. Cancer outcomes assessment can contribute to decision making at multiple levels in multiple ways. Consequently, the COMWG collectively was charged with examining progress across the three arenas of application (as defined above) – but with the implied proviso that the search was to be largely confined to the peer-review literature. As it turned out, that literature is dominated by meso-level papers with a clinical or health services research orientation: randomized trials, observational studies of interventions, investigations of cancer burden in particular populations, and economic

evaluations including cost-effectiveness analyses. With respect to macro-level studies on the cancer burden using the outcome measures of interest here, there are many government reports, but comparatively few papers in the peer-review literature. While there is increasing discussion of the role cancer outcome measures can, or should, play in patient-provider decision making and clinical care, the scientific literature on these micro-level applications is small (though growing), as the recent analysis by Donaldson confirms.⁹

In sum, the COMWG was asked to examine current practices, and identify best practices, for assessing the three outcomes of interest in the four selected cancers across the continuum of care, with attention also to likely decision-making applications. As will be seen, some chapters in this volume evaluated the published literature at various points of intersection implied by these four factors (e.g., assessment of HRQOL in initial treatment of breast cancer, with implications for clinical decision making). Other chapters focused on the methodological underpinnings of outcomes assessment (e.g., defining and modeling HRQOL, patient satisfaction, or economic burden; psychometric advances to improve HRQOL measurement generally; or statistical considerations in evaluating the impact of interventions on outcomes).

However, the work of the COMWG, and the book that flows from it, was never intended to address all of the questions and needs of the cancer outcomes researcher. Additional cancer disease sites await evaluation. We do not provide here a detailed guide or tutorial for how to develop, test, or actually use outcome measures; nor how to carry out psychometric analyses step-by-step; nor how to conduct statistical evaluations of outcomes data. For lucid discussions on such matters, the reader is referred to such texts as Fayers and Machin¹⁰ and Spilker.¹¹ We note also that the chapters in this volume reviewing and evaluating the outcomes measurement instruments employed to date for a particular purpose generally do not “pick a winner.” Rather, they attempt to provide an objective, side-by-side comparison of the

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strengths and limitations of competing instruments to provide a basis for choosing among instruments for a particular application. It will be clear in many cases that certain measures and instruments are the strongest and most promising, but these conclusions emerge from the analysis and discussion, rather than from directives to make recommendations for particular approaches to measurement.

Operations of the working group

COMWG members were asked to review and evaluate specific aspects of cancer outcomes measurement, to meet periodically as a group to discuss their findings, and to prepare written reports for submission to the NCI. These reports, collectively, constitute the basis for Chapters 2–27 of this book.

Given the outcomes assessment framework noted above, we developed “question sets” that were assigned to COMWG members, either individually or in pairs. The question sets were intended to encompass the major issues arising from consideration of the four dimensions defining the framework, as well as cross-cutting methodological topics. For example, members addressing the performance of a particular type of outcome measure (e.g., HRQOL) at a specific point along the cancer continuum (e.g., treatment) for a specified cancer type (e.g., lung) were asked to assess the psychometric properties of the commonly used instruments, their overall strengths and weaknesses, their value-added compared with biomedical outcome measures, and the additional research now needed. To the extent appropriate, we attempted to standardize the question sets so that inquiries about the same broad topic (e.g., HRQOL) were as comparably phrased as possible. As the working group proceeded, we also developed common definitions for key terms and standardized approaches to data abstraction, and table construction, as discussed below.

The process of report generation and chapter preparation was an iterative one: research, initial manuscript drafts, group discussions, electronic communication between editors and authors,

revision and re-revision, and final editing. The three working group meetings (February 2001, December 2001, and December 2002) provided important opportunities for presentations, panel discussions, and small-group sessions. In addition, each COMWG member was assigned to an “affinity group” consisting of COMWG members with allied methods or application interests, in order to promote interdisciplinary peer review and discussion.

Throughout the period from early 2001 until the final assigned chapter was completed in 2004, the editors had both the responsibility and the remarkable opportunity to work closely with the other 32 members of the COMWG in a number of respects. Beyond the initial designation of topic areas, this involved tailoring question sets in response to author suggestions, reviewing chapter drafts, and working interactively through the multi-step review and editing process that led to the chapters found here.

Sources of data

The primary source of data for the majority of findings reported in this book is the peer-review literature. Some authors performed re-analysis of existing data bases (see the chapters by Hambleton,¹² Reise,¹³ and Wilson¹⁴), and one relied heavily on websites and government reports (Gotay and Lipscomb¹⁵).

Early on, some COMWG members noted the paucity of data on certain topics. In response, we organized a series of focus groups under NCI sponsorship during the summer of 2001. A professional focus group facilitator (Ellen Tobin) led the effort, working with COMWG members to define the eligibility criteria for group participation, develop discussion guides, and analyze and report the results.

A total of 92 cancer patients and survivors each participated in one of 12 focus groups conducted at a facility designed for such research in suburban Washington, DC. These groups included diverse participation with respect to gender, site of disease, and time since diagnosis.

In addition, a focus group comprising 11 national experts in outcomes data development, linkage, and analysis was convened, by electronic video-conference, in the summer of 2001 in support of the COMWG chapter on data for cancer outcomes research.¹⁵

Establishing a common approach

Standardized definitions of key terms and procedures for data abstraction and reporting were developed in the course of the working group, are used throughout this book, and are briefly described below.

Defining health-related quality of life

We were aware that an entire chapter of this volume (Ferrans¹⁶) would be devoted to identifying and evaluating alternative definitions and conceptual models of HRQOL, so we imposed no fixed definition of HRQOL on the COMWG at the start. However, it became evident over time that varying definitions were being used in the literature and by different working group members, and that some consistency was needed. In this book, a key defining feature of a HRQOL measure is that it must be patient-reported and thus involve the patient's (or, more generally, the individual respondent's) subjective assessment or evaluation. The potential usefulness of the patient-reported outcome concept for cancer outcomes assessment has been noted by both the US Food and Drug Administration (FDA)¹⁷ and the pharmaceutical industry.¹⁸

In the guidelines we developed with the COMWG members analyzing HRQOL, we defined patient-reported measures of HRQOL to include symptoms, functional status, and/or global well-being. Symptom measures include patient reports on the frequency, severity, bother, or impact of symptoms (both disease-related and treatment-related). Toxicities are distinct from patient-reported symptoms, in that they involve the clinician's evaluation and recording; the clinician's evaluation may result from

discussion with the patient or in other ways (e.g., laboratory test values). Functional status measures include patient reports on the impact of cancer and its treatment on everyday life and overall well-being. Functional status measures may be multi-dimensional and thus include more than one domain of HRQOL and/or symptoms (e.g., the FACT-G or the EORTC QLQ-C30), or unidimensional and focus on a single domain of HRQOL (e.g., a measure of pain or fatigue). Global rating measures capture the individual's overall assessment of personal well-being. These can be preference-based (involving utility scores) or non-preference based (involving an overall rating or summary score on a unidimensional psychometric scale).

Identifying the desirable properties of outcome measurement instruments

The comprehensive instrument review criteria assembled by the Medical Outcomes Trust (MOT)¹⁹ were adopted as the basis for evaluating the psychometric properties of the patient-reported outcome measures analyzed by the COMWG. As constructed, the MOT criteria are to be applied in assessing the adequacy of an instrument on the following eight attributes: conceptual and measurement model, reliability, validity, responsiveness, interpretability, burden of administration, alternative forms (modes of administration), and cultural and language adaptations. The MOT attributes and criteria were distributed to all COMWG members in the early months of the project.

Categorizing HRQOL measures by breadth of application

For the purposes of this book, *generic* measures of HRQOL are not specific to cancer but can be applied to healthy and ill individuals, or populations, regardless of health state. Examples include the SF-36, the Sickness Impact Profile, and the Brief Pain Inventory. *General cancer* measures are designed to assess HRQOL in cancer regardless of disease site.

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Examples include the FACT-G and the EORTC QLQ-C30. *Cancer site-specific* measures assess HRQOL in a particular type (disease site) of cancer. For example, the general FACT and the core of the EORTC can be supplemented with questionnaires developed for patients with particular cancers; for example, the FACT-B and EORTC-LC13 are cancer site-specific measures for breast and lung cancer, respectively.

Approach to tables

For reporting on the development of commonly used HRQOL instruments and their psychometric properties, a standardized table shell, modeled after similar reports in other studies,²⁰ was constructed and distributed to COMWG members early in the project. In addition, we worked closely with the authors of the disease-specific chapters (breast, colorectal, lung, and prostate) to develop table shells for abstracting data from the literature to identify the most commonly used measures of HRQOL and biomedical outcomes, and to facilitate an assessment of the added value of HRQOL outcomes compared with biomedical outcomes. For purposes of the COMWG's deliberations, and this book, we defined HRQOL ratings as providing "added value" when they were instrumental in interpreting the study's conclusions and therefore would be expected to influence recommendations about appropriate intervention(s). Consequently, a given study needed to include both HRQOL and biomedical outcomes (e.g., survival, disease-free survival, toxicities) to facilitate a direct determination of whether HRQOL data did provide added value. That said, we acknowledge that HRQOL data may provide added value in other ways and encourage the reader to keep in mind the specific way the term is being used here.

Organization of the book

This book evaluates the state of the science in cancer outcomes assessment and offers perspectives on what is required to advance the field. The chapters

collectively cover a diverse set of topics, which are examined in a sequence suggested by the broad section headings below. Developed as stand-alone documents, the chapters can be read in any order. Cross-citations to other relevant chapters are provided throughout. Each chapter presents a number of findings and recommendations, and the previews below provide only a flavor of the full range of results.

HRQOL in cancer: general concepts and generic measures

Carol Ferrans¹⁶ discusses alternative definitions and conceptual models for HRQOL, emphasizing the distinction between measuring the patient's perceived health state descriptively and obtaining also the patient's evaluation of the state. She urges further work on causal models to understand better the determinants of HRQOL and also the possibility that patient perceptions and evaluations of health may shift over time. The chapter's recommendations are directed towards developing a common understanding of the meaning of HRQOL.

Pennifer Erickson²¹ analyzes the use of the most common generic and general cancer HRQOL measures in cancer outcomes research. The chapter reviews the development and psychometric properties of these measures, and assesses their relative strengths and weaknesses and their application to specific cancers and across the continuum of care. It discusses the merits of new measurement systems that would combine generic or general cancer measures with modules of additional items tailored to specific applications.

David Feeny²² reviews the foundations of health state preference measurement, its importance in cancer outcomes assessment, and the major available preference measurement systems currently available to researchers. Preference-based measures are already employed in most economic evaluations and many clinical decision analysis studies of cancer care. He discusses how, and why, such measures should also be used routinely in cancer clinical

trials and observational studies of the effectiveness of interventions.

Assessing HRQOL during treatment

By far, the most extensive application of HRQOL in cancer to date has occurred in randomized clinical trials of biomedical or psychosocial therapies. Across tumor types, the greatest number of applications are found in breast cancer.

Patricia Ganz and Pamela Goodwin²³ examine the relative performance of HRQOL and biomedical outcome measures across a wide range of breast cancer trials. They recommend that the decision about whether to measure HRQOL in any given study, as well as the choice of specific measure(s), should be driven by the study's specific aims and hypotheses. They conclude that, based on the studies reviewed, HRQOL has contributed greater value added to psychosocial trials than to biomedical trials in breast cancer, and that routine use of HRQOL measures in breast cancer biomedical trials is not supported by the existing evidence. But they also note that future studies using breast cancer-specific measures of HRQOL will provide additional empirical insight about value added.

In their analysis of HRQOL applications in prostate cancer, Mark Litwin and James Talcott²⁴ discuss the importance of and challenges in measuring the impact of alternative therapies on disease symptoms (sexual, urinary, and bowel dysfunction). They conclude that the role of quality-of-life considerations in treatment choice is highly personal and find that prostate cancer-specific measures of HRQOL are often more useful than global measures in detecting important changes for prostate cancer patients.

Craig Earle and Jane Weeks²⁵ compare the most commonly used lung cancer-specific HRQOL measures, and note that the choice among them in a given application will depend on the purpose of the trial (biomedical versus psychosocial therapy) and the saliency of respondent burden; rapid patient deterioration is a major problem in lung cancer studies. They discuss the potential value added of HRQOL

measurement in describing the balance between symptomatic improvement with treatment and its toxicity.

In their assessment of HRQOL applications to colorectal cancer treatment trials, Carol Moinpour and Dawn Provenzale²⁶ find that many studies to date have suffered from small sample sizes or missing data, hampering one's ability to draw clear conclusions about the value added of HRQOL. They make important recommendations about improving the content validity of HRQOL measures for colorectal cancer application.

Michael Barry and Janet Dancey²⁷ examine treatment-specific measures of HRQOL that cut across cancer types. They find only a very limited number of measures available that assess the morbidity and side effects attributable to specific treatments (e.g., radiation, chemotherapy). While they conclude it is premature to recommend a definitive measurement strategy, they suggest exploration of treatment-specific modules that could be linked to general cancer or cancer site-specific instruments.

Assessing HRQOL across the cancer continuum

Jeanne Mandelblatt and Joe Selby²⁸ propose a framework for assessing the short-term HRQOL outcomes associated with cancer prevention and screening, review the small literature to date on how measures have been applied in particular areas (e.g., chemoprevention), and consider specific recommendations for improvement. For example, they suggest that many generic HRQOL measures may not be sufficiently sensitive, and recommend further research to examine whether preference-based measures might perform well in capturing the net impact of such effects as relief, anxiety, reassurance, and discomfort.

Brad Zebrack and David Cella²⁹ evaluate the HRQOL measures commonly used in survivorship studies, comparing generic and general cancer measures with those developed specifically for survivorship populations. They find that while the

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generic and general cancer measures have generally performed adequately, they tend not to encompass such survivor-specific issues as fear of disease recurrence, chronic physical compromise, and post-traumatic growth.

Betty Ferrell³⁰ discusses how HRQOL assessment can play a vital role in end-of-life care, helping to evaluate and improve the quality of care. Measuring HRQOL at end of life, and appropriately interpreting the findings, poses challenges because one should take into account not only the patient's disease status, but a variety of personal, family, and environmental circumstances. At present, there are several viable HRQOL instruments appropriate to this point on the cancer continuum.

Measuring the experience and needs of cancer patients and caregivers

James Williams³¹ discusses how HRQOL information can be helpful to patients and families, as well as some of the barriers that presently prevent wider use of such data. His remarks have particular credence since he himself is a prostate cancer survivor.

Charles Darby³² examines the emerging literature on measuring the patient's perspectives on cancer care, including both descriptive reports and ratings of the care received (or not received). He proposes the development of new instrumentation that would include a core set of items for application across all cancer disease sites and the continuum of care, supplemented by additional items tailored to the application at hand.

David Gustafson³³ reviews current methods for assessing patient needs and proposes innovative new approaches (such as conjoint analysis) that would apply modern statistical techniques to survey data to create tighter links between perceived needs and constructive strategies for meeting them. He also probes the complex interconnections among patient needs, satisfaction with care, and HRQOL.

Claire Snyder³⁴ examines caregiver impact. She seeks to identify the positive and negative impacts that caring for a loved one with cancer can have on the informal caregiver, evaluates the most commonly

used measures, and proposes additional research on instruments designed to assess these effects.

Methodological considerations in applications to cancer outcomes research

Diane Fairclough³⁵ looks at a host of practical considerations in planning and executing a cancer outcomes research study. These include identifying the appropriate role of HRQOL assessment (and noting this may vary in drug evaluations depending on the phase of development), the mode and medium of questionnaire administration, and approaches to the problem of missing data. While there are sophisticated statistical techniques for coping with a variety of missing data dilemmas, she emphasizes that the best policy is prevention – through careful study design and conscientious execution.

Jeff Sloan³⁶ provides a brief yet relatively comprehensive overview of statistical modeling and analysis techniques relevant to cancer outcomes research. To promote thoughtful and transparent analysis, he recommends simple, robust analytical models; careful attention to subtle patterns of variations in the underlying data; and methods of presentation (such as graphical approaches) that provide a more descriptive picture of findings than summary statistics alone.

David Osoba³⁷ assays the various potential ways that HRQOL information can be useful to clinical decision making in oncology. He urges that HRQOL data be analyzed for both statistical and clinical significance (using both distribution-based and anchor-based approaches), and points to recent convergent evidence on what *may* constitute a perceptible and clinically meaningful difference in HRQOL scores.

Neil Aaronson³⁸ reviews the need for and challenges in adapting HRQOL instruments for use across different populations and cultures. He concludes there are several available instruments meeting minimum psychometric requirements, with the choice among these depending on the study at hand. There should be greater attention to standardization and quality monitoring in the instrument translation