SPECIAL ARTICLE

Outcomes of Cancer Treatment for Technology Assessment and Cancer Treatment Guidelines

Adopted on July 24, 1995 by the American Society of Clinical Oncology*

In 1993, the Health Services Research Committee of the American Society of Clinical Oncology (ASCO) charged an Outcomes Working Group with defining the outcomes of adult and pediatric cancer treatment to be used for technology assessment and development of cancer treatment guidelines.

The Working Group defined by consensus outcomes for technology assessment and guideline development, focusing on cancer treatments. The Working Group considered a variety of perspectives on outcomes, including those of patients, physicians, clinical investigators, ASCO, and policy makers. Because ASCO's guidelines will define what constitutes the best treatment and not whether that treatment should be paid for, the Working Group gave higher priority to the clinical and clinical research perspectives than to the health policy perspective.

Survival is the most important outcome of cancer treatment. An improvement in at least disease-free survival is a prerequisite for recommending adjuvant therapy. In the case of metastatic cancer, treatment can be recommended even without an improvement in survival, if it improves quality of life.

Quality of life includes global quality of life, as well as its physical, psychologic, and social dimensions. To be an outcome of cancer treatment, quality-of-life measures must be sensitive to clinically meaningful changes produced by treatment; evaluations must control for placebo effects and determinants of quality of life not related to cancer or its treatment.

Toxicity, both short and long term, is vitally important, with the latter being particularly critical in children.

The value of cancer outcomes like tumor response (eg, complete or partial response) and biomarkers (eg, CA-125) for technology assessment and guideline development depends on their ability to predict patient outcomes (survival and quality of life) or to influence decisions about treatment. Complete response is an important outcome when it predicts survival. Progression is important because it signals the need to change or stop treatment.

Cost-effectiveness is an especially important outcome to consider when the benefits of treatment are modest or the costs are high.

Patient outcomes (eg, survival and quality of life) should receive higher priority than cancer outcomes (eg, response rate), but both types of outcomes are important in technology assessment and guideline development. Multiple outcomes should be considered because no single outcome adequately describes the results of cancer treatment. In general, there is no minimum benefit above which treatments are justified; rather, benefits should be balanced against toxicity and cost.


HEALTH SERVICES RESEARCH COMMITTEE

IN 1993, the American Society of Clinical Oncology (ASCO) formed a Health Services Research Committee to perform technology assessment and to develop guidelines for cancer treatment. The Committee was formed so that ASCO could address the value of emerging technologies and of new and established cancer treatment.

The Health Services Research Committee was formed in response to input from ASCO's members. As part of its recent long-range planning effort, ASCO surveyed its members about possible future directions of the Society. A significant majority indicated that ASCO should be more involved in areas of technology assessment and development of treatment guidelines.

The Health Services Research Committee is composed of clinical researchers and clinicians from academic centers and private practice (Appendix I). A number of Committee members are involved in health services research or quality improvement efforts.

The Health Services Research Committee will perform technology assessment after hearing from expert advisors. The Committee will not develop guidelines; instead, it will assemble expert panels to develop guidelines. Expert panels will be given direction by the Health Services Research Committee members and Outcomes Working Group.

See Appendixes for Health Service Committee members and Outcomes Working Group.

From the Outcomes Working Group, Health Services Research Committee, American Society of Clinical Oncology.

Submitted October 19, 1995; accepted October 19, 1995.

Address reprint requests to the American Society of Clinical Oncology, 225 Reinekers Lane, Suite 650, Alexandria, VA 22314.

*ASCO sincerely appreciates the contributions of the ASCO Health Services Research Outcomes Working Group, who devoted much time and effort to this project: Chair: John Fetting; and Panel Members: Paul Anderson, Harrison Ball, John Benear, Katy Benjammin, Charles Bennett, Susan Braun, Harman Breretton, John Burrows, Charles Cobau, Alfred Cohen, Leslie Ford, Michael Friedman, Patricia Ganz, Richard Gelber, Holcombe Grier, Gerald Hanks, Robert Justice, Patricia Legant, Mark Levine, Susan Parsons, Peter Raich, Sandra Schafer, Thomas Smith, Collier Smyth, A.T. van Oosterom, James Wade, Jane Weeks, Rodger Winn, and Janet Woodcock.

© 1996 by American Society of Clinical Oncology.

0732-183X/96/1402-0049$3.00/0


671

1 of 9

Celltrion, Inc., Exhibit 1023

Downloaded from ascopubs.org by 12.130.14.76 on December 20, 2016 from 012.130.014.076
Copyright © 2016 American Society of Clinical Oncology. All rights reserved.
Committee, one or more members of the Committee will serve on each panel, and the report of the expert panels will be approved by the Health Services Research Committee. Final approval of technology assessments and practice guidelines comes from the Board of Directors.

THE OUTCOMES WORKING GROUP

The Health Services Research Committee charged an Outcomes Working Group with defining the outcomes of cancer treatment that should be considered for technology assessment and cancer treatment guidelines. The Outcomes Working Group is composed of selected members of the Health Services Research Committee, representatives of organizations involved in the development and delivery of cancer treatment, and additional experts in health services research (Appendix II). A core group produced the preliminary drafts of this report for comment by the entire Working Group. This report of the Outcomes Working Group provides an introduction on the outcomes to be considered for technology assessment and guideline development, as well as evaluations of the effectiveness of cancer treatment in clinical practice.

WORKING GROUP DELIBERATIONS

The Working Group believed that ASCO should focus its initial efforts on therapies that produce tumor regression and related technologies, rather than other aspects of the care of cancer patients. Thus, a guideline for the treatment of metastatic lung cancer should focus on chemotherapy and radiation therapy and not on the more general issue of the care of patients with metastatic lung cancer. By focusing on therapies that produce tumor regression, ASCO will concentrate its available resources on an area that it is uniquely qualified to evaluate.\(^1\)

Patients, physicians, researchers, payors, and policy makers all have different ideas about which outcomes of cancer are most important. The Working Group recognized that broad acceptance of ASCO's technology assessments and guidelines would require that all of these perspectives be considered. However, the main purpose of ASCO's technology assessments and guidelines is to define what constitutes the best cancer treatment, not to inform policy development and payment decisions. The Working Group, therefore, considered outcomes primarily from the perspectives of the clinical investigators who produce evidence for the guidelines, the individual doctors and patients who make decisions about treatment, and the health services researchers who will evaluate the quality and cost of care produced by the guidelines. Because it recognized the health policy implications of ASCO's technology assessments and guidelines, the Working Group also took into consideration the outcomes that would convince health policy makers and payors that ASCO's technology assessment is sound and that its guidelines represent worthwhile cancer treatment.

Outcomes were defined by the Working Group as the products, both good and bad, of cancer treatment. The Working Group distinguished between cancer outcomes and patient outcomes. Cancer outcomes were defined as measures of the effect of treatment on cancer, eg, complete and partial response, response duration, time to progression, and tumor markers. Patient outcomes were defined as measures of the effect of treatment on the patient, eg, survival, toxicity, and quality of life.

The Working Group identified the most important outcomes of cancer treatment, but limited its consideration of their measurement to clinical trials and effectiveness research. It did not consider measurement of these outcomes as part of the day-to-day care of patients in clinical practice.

The Working Group did not attempt to define the universe of outcomes for clinical trials, because clinical trials are conducted for other reasons than to provide evidence for guidelines. For example, phase I and II trials are conducted to develop new and improved treatments. It is unnecessary to routinely collect quality-of-life and cost-effectiveness data until early trials demonstrate real promise. On the other hand, laboratory correlative studies are an important part of these trials, but are not important for technology assessment or guideline development.

The Working Group did not attempt to define the universe of outcomes for effectiveness research either. For example, patient satisfaction is increasingly used to evaluate the effectiveness of health care delivery, but it is not important in technology assessment and guideline development, which are shaped by evidence from clinical trials on the benefits and risks.\(^2\)

The Working Group also addressed how outcomes should be used to make guidelines. It considered the priority of outcomes including whether any one outcome (eg, survival) was ever so important that it overshadowed the others. The Working Group also considered the minimal amount of benefit that justified recommending treatment, since some cancer treatment produces so little benefit that it is not clear whether it should be administered at all. In the case of cancers for which treatment is more effective, the question is not whether treatment should be started, but when it should be stopped. For both types of cancer, the critical question is the same: Does the expected benefit justify recommending the treatment?

OUTCOMES FOR TECHNOLOGY ASSESSMENTS AND GUIDELINE DEVELOPMENT

Survival

Survival, whether measured overall, disease-free, progression-free, or event-free, is the most important out-
come in cancer treatment. Nevertheless, survival alone is not sufficient; the quality of survival and cost of maintaining or improving it must also be assessed. Disease-free survival is especially important in the adjuvant setting, as is progression-free survival in metastatic disease. Event-free survival has been used to denote survival free of any bad outcome, including failure to attain a complete remission, relapse, or death due to toxicity. Although an improvement in overall survival is desired, an improvement in disease-free, progression-free, or event-free survival can also justify recommending treatment, as long as the quality of that survival is good and the cost of producing it compares favorably to the cost of no treatment or of alternative treatment.

Survival outcomes can be represented in several ways, including percent surviving at a particular time, median survival, and percent reduction in the odds of death over a time interval or at a particular point in time. Representing survival benefits in more than one way permits physicians and patients to evaluate thoroughly the value of treatment; for example, although chemotherapy for non–small-cell lung cancer has minimal long-term effect on survival (seven of 100 treated patients alive at 1 year), and a modest effect on mean or median survival times (6 to 8 weeks), the short-term risk reduction (20 of 100 patients alive at 6 months due to chemotherapy) may be important.

The choice between alternative treatment approaches often involves a trade-off between length and quality of life; survival alone may not answer the question of whether gains in survival justify the toxicity. Quality-adjusted survival adjusts the absolute length of life to reflect the patient’s quality of life. Quality-adjusted survival provides a framework within which trade-offs that influence treatment choices can be explicitly defined, as in decision and cost-effectiveness analyses, to assess the effectiveness of alternative therapies. The quality-adjusted time without symptoms of disease and toxicity (Q-TWIST) methodology is one example of a quality-adjusted survival calculated from observed survival in randomized clinical trials. Practical methods for estimating the appropriate utility weights, or value given to time in a healthy state, are still experimental. In particular, estimation of utility weights in children is a particularly formidable conceptual and methodologic challenge, and relatively little has been done to address this problem.

Quality of Life

Cancer-related quality of life has been defined as a multidimensional concept that considers the impact of cancer and its treatment on the physical, psychologic, and social components of patients’ lives. Even in the absence of consensus regarding the definition and measurement of this complex concept, the Working Group was in agreement that quality of life is an important outcome of cancer treatment because it reflects how patients feel. The Working Group viewed cancer-related quality of life as a family of outcomes (including the global quality of life, as well as its physical, psychologic, and social dimensions), each one of which is a potentially separate outcome (Table 1).

Because of its subjective nature, assessment of quality of life should generally include an evaluation by the patient. In pediatrics, an evaluation by the patient is often problematic because of the developmental limitations of the child. Other observers (e.g., parents) can contribute to the evaluation, but it is important to note that their evaluation is likely to differ from that of the patient.

Little research has been conducted to determine which dimensions of cancer-related quality of life are most important to patients. The research that has been done suggests that patients believe that the effects of cancer and its treatment on all three dimensions of quality of life are important. Quality-of-life measures should have basic types of reliability and validity. They should be relatively brief, easy to read, and easy to complete; when used to evaluate cancer treatment, they should be administered before, during, and after treatment. Some quality-of-life measures are listed in Table 2. Measures used in pediatric patients should be developmentally appropriate.

Quality-of-life measures must also be responsive (e.g., sensitive to change). The more specific a quality-of-life measure is to a particular treatment situation, the more responsive it generally is. Several approaches can be used to enhance specificity. One is to develop an entire quality-of-life measure for a particular treatment situation. Another approach is to develop a module for a particular disease or treatment situation that augments the information obtained by a more general measure. Yet another approach is to measure only the dimension of quality of life that is most likely to change with treatment, eg, the
Physical dimension by using the physical symptom and physical functioning subscales of a quality-of-life measure or by using a symptom checklist. The limitation of this selective approach is that it fails to capture the effects of treatment on the other dimensions of quality of life.

Quality-of-life outcomes are affected by more than cancer and its treatment, eg, the physical dimension of cancer-related quality of life is affected by comorbid conditions and their treatments, and improvement in quality of life with treatment can reflect the placebo effect. Optimal control of these factors is found in randomized (ie, phase III) clinical trials. Quality-of-life outcomes can also be measured in nonrandomized (phase I and II) trials, as well as in descriptive studies of clinical practice (ie, medical effectiveness research), but appropriate controls (eg, evaluation of comorbidity, measures of cancer response, and toxicity assessments) are required before inferences can be drawn about the relationship between cancer treatment and quality-of-life outcomes.

Currently available quality-of-life measures have been used primarily for research and their suitability for day-to-day patient care in clinical settings has not been established. There is a pressing need to develop quality-of-life measures for clinical practice.

Toxicity

Treatment toxicity is an important outcome for technology assessment and guideline development because it reduces the quality of life and can be life-threatening. Many toxic effects can be minimized or avoided if treatment toxicity is carefully evaluated. Management of treatment toxicity also raises the cost of treatment and can reduce its cost-effectiveness.

Both the short-term and long-term toxicity of all treatment modalities deserve careful consideration. The latter is particularly important in pediatric patients because of the effects of treatment on growth and development. Three toxicity dimensions need to be evaluated: frequency, severity, and duration. For instance, when anthracycline cardiotoxicity is being evaluated, the assessment should distinguish the various cardiac toxicity syndromes (ie, acute toxicity should be distinguished from the late effects that may develop long after anthracyclines are administered). The frequency of each syndrome should also be determined, including the frequencies observed at different doses. In addition, the degree of cardiac dysfunction and the duration of each type of cardiotoxicity should be assessed.

Toxicities are subjective, objective, or both. Subjective toxicities are symptoms (eg, nausea) that are often not associated with overt signs or laboratory abnormalities; evaluation of these toxicities rests with the patient’s report. The evaluation of a subjective toxicity is begun by asking the patient whether the toxicity occurred. Just because the patient does not report toxic symptoms voluntarily does not mean that they did not occur. If the toxicity has occurred, patients should next be asked to describe the severity and duration of the toxicity. Subjective toxicities can be evaluated by patient interview or a reliable, valid patient-completed questionnaire.

Quality-of-life instruments typically evaluate some symptoms of common toxicities, but these instruments do not evaluate all of the potentially important subjective toxicities or evaluate any thoroughly enough to substitute for a formal evaluation of toxicity.

Objective toxicities are measured by physical examination or laboratory tests. The reliability and validity of laboratory tests commonly used to evaluate treatment toxicity have generally been well established; the physical examination has been less rigorously evaluated.

The common toxicity criteria (CTC), a system for categorizing toxicities of cancer treatment according to their severity, are widely used in cooperative group trials. For some toxicities (eg, WBC count and liver function tests), the CTC do not specify the methods of toxicity evaluation, but only how to categorize the data. In these cases, the reliability and validity of the toxicity data depend on the method of toxicity evaluation. For other toxicities (eg, nausea and vomiting, and mucositis), the CTC actually suggest the form in which the data should be collected. The reliability and validity of toxicity data collected in these ways have not been established.

Measures of Cancer Response

Measures of cancer response have long been used as outcomes of cancer treatment. These include measures of tumor response (ie, complete response, partial response, response duration, and time to progression), biomarkers (eg, CA-125), and cancer-induced abnormalities in common blood tests (eg, alkaline phosphatase). The usefulness of cancer response measures for technology assessment and guideline development depends on their ability to predict patient outcomes (eg, survival and quality of life) and to assist clinicians in making decisions.

Table 2. Some Quality-of-Life Measures

<table>
<thead>
<tr>
<th>Eponym</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLIC</td>
<td>Functional Living Index, Cancer</td>
</tr>
<tr>
<td>FACT</td>
<td>Functional Assessment of Cancer Treatment</td>
</tr>
<tr>
<td>EORTC QLQ-C30</td>
<td>European Organization on Research and Treatment of Cancer Quality-of-Life Questionnaire</td>
</tr>
<tr>
<td>SF-36</td>
<td>Medical Outcomes Survey Short Form 36</td>
</tr>
<tr>
<td>QLI</td>
<td>Spitzer Quality of Life Index</td>
</tr>
</tbody>
</table>

Copyright © 2016 American Society of Clinical Oncology. All rights reserved.
about whether to continue treatment. Only some of these measures will be useful for technology assessment and guideline development. The complete response rate is an important intermediate outcome because it often predicts the potential of a drug or regimen to effect a significant improvement in survival or even a cure; lesser degrees of response do not.\(^{3,30,31}\)

Some studies have demonstrated a positive relationship between response rate and quality of life; others have not.\(^{32-35}\) Whether a responding patient experiences improvement in quality of life is probably dependent on the extent to which that patient was symptomatic before treatment, the completeness of response of the cancer, and the toxicity of the treatment. The tumor response is likely to be positively correlated with improvement in quality of life when a patient is symptomatic from the cancer before treatment, the complete response rate of the tumor is relatively high, and the treatment toxicity is modest.

It is important to distinguish between the use of cancer response rates for technology assessment and guidelines, on the one hand, and drug development, on the other. While lesser degrees of response (e.g., partial response and minimal response) are unlikely to be important for the former, they are often important indicators of promising treatment activity in the latter.

Cancer progression is an important negative outcome because it indicates that a treatment has stopped working, even if the patient has not declined symptomatically. Therefore, recommendations on how to monitor cancer progression are an important part of guidelines on cancer treatment. Freedom from progression, on the other hand, may not be a convincing indication of the benefits of treatment if it does not predict significantly improved survival or cure. By itself, freedom from progression is not an adequate measure of quality of life.

Much of the evidence available for technology assessment and guideline development will be related to tumor response. Expert panels must bear in mind the limitations of tumor response as an outcome measure and remember that tumor response is not always easy to measure reliably.\(^{36,37}\)

Because they lack adequate sensitivity and specificity, biomarkers are not likely to be among the outcome-related evidence to be considered in the development of guidelines. Biomarkers have not been established as good predictors of survival, and there have been virtually no studies of the relationship between biomarkers and quality of life. Biomarkers might be incorporated into guidelines as measures of disease progression. The more sensitive and specific the biomarkers and the more effective the treatment available after progression, the more useful the biomarkers will be. For example, biomarkers are very useful in stage I testis cancer when alpha-fetoprotein and beta-human chorionic gonadotropin can be used to monitor for disease recurrence after surgery.\(^{38}\) Less useful, but still potentially valuable, are some markers for common epithelial cancers (e.g., prostate-specific antigen, CA-125, and CA 15-3).\(^{39-42}\)

**Cost-Effectiveness**

Cost per se is not an outcome; it is what we expend to produce an outcome. Cost-effectiveness, on the other hand, is an increasingly important outcome.\(^{1}\) Cost-effectiveness is often reported in terms of cost per year of life saved (LY) or cost per quality-adjusted year of life saved (QALY). Cost-effectiveness is a way to evaluate cancer treatment and also to compare the benefits of cancer treatment with the benefits of other kinds of medical treatment (e.g., dialysis) that are competing for the same health-care dollar. Because interest in this outcome is recent, there have been relatively few evaluations of the cost-effectiveness of cancer technologies and treatments.\(^{1}\)

How do cost-effectiveness studies add to the evaluation of cancer treatment? In some cases, not much. In the case of first-line chemotherapy for germ cell cancer, survival benefits are large and long-term toxicity is modest; cost-effectiveness adds relatively little to the treatment evaluation. On the other hand, cost-effectiveness analysis can provide an important perspective when treatment costs are high and benefits are small (e.g., in high-dose chemotherapy for cisplatin-refractory germ cell cancer), or when treatment benefits are modest (e.g., in adjuvant chemotherapy for breast or colon cancer).

All clinical practice guidelines, including ASCO’s, must be informed by cost-effectiveness considerations, or they risk being ignored. When the information is available, cost-effectiveness should be considered in technology assessment and in the development of cancer treatment guidelines. When cost-effectiveness analyses are not available, cost-consciousness should be a part of technology assessment and guideline development. For example, if two chemotherapy regimens produce the same patient outcomes but one costs more than the other, the less costly regimen should be preferred. However, a cost comparison is more than a simple comparison of the charges for the drugs and their administration. Costs associated with the ease or difficulty of administration, the treatment facility, concomitant medications, and adverse events must also be considered.\(^{1}\)

The Working Group recommends that cost-effectiveness be measured when appropriate and feasible and that it be considered as an outcome of cancer technology and treatment under these circumstances. If cost-effectiveness
data from clinical trials are to be generalizable to clinical practice, future trials will need to approximate clinical practice as closely as possible with less restrictive eligibility criteria, minimal monitoring costs, and outpatient rather than inpatient care. Of all clinical trial settings, phase III trials are the most appropriate for economic analysis, especially when the drugs or technologies that are being evaluated are well established and stable. Yet there is concern about the generalizability of economic data from phase III trials to clinical practice because of variations in practice patterns and economic outcomes among participating centers, and because trial participation affects physician practice patterns.43

SUGGESTIONS ON HOW TO USE OUTCOMES FOR TECHNOLOGY ASSESSMENTS AND GUIDELINE DEVELOPMENT

The Priority of Patient Outcomes

In the final analysis, patient outcomes are more important than cancer outcomes for technology assessment and development of cancer treatment guidelines. If a technology or cancer treatment is not ultimately shown to make patients live longer or feel better, its use cannot be justified. Although it gave priority to patient outcomes, the Working Group believed that selected cancer outcomes will also be important.

The Need to Use Multiple Outcomes

No single outcome, even survival, adequately represents the results of cancer treatment. Each outcome provides a unique perspective on treatment, but each also has its own conceptual and methodologic limitations. Therefore, multiple outcomes should be used for technology assessment and guideline preparation.

The Benefit Required to Justify Treatment

The amount of benefit required to justify treatment is different for patients, physicians, payors, and policy makers. Patients generally require less benefit than the other groups and a small fraction of patients requires almost no benefit at all.44 Payors and policy makers, on the other hand, require more substantial benefits. Which perspective(s) should expert panels adopt when performing technology assessment and developing guidelines? Panels should recall that the purpose of ASCO's technology assessment and guidelines is to make recommendations about what is the best medical care. The concept of best medical care takes into account the fact that the quality of life of some few patients is better maintained by trying a treatment with very little chance of benefit than by not trying it. However, the Working Group did not believe that treatments with very limited benefits should be routinely recommended just because they improve the quality of life of a minority of patients. Routine recommendation of such treatments ignores the fact that the majority of patients not only receive no benefit, but also suffer toxicity. Moreover, if treatments with marginal benefits are very toxic or very costly, it is not appropriate to recommend them, regardless of how strongly a patient may desire them.

The Working Group did not believe that there was any specific amount of benefit above which treatments should always be recommended and below which they should not. Rather, beneficial outcomes must be balanced against toxicity and cost. If the toxicity or cost of therapy is considerable, the benefit required to recommend therapy should be greater. The Working Group believed that the amount of benefit required to justify treatment varied with the value associated with the outcome. For example, cure is generally valued over symptom relief. Therefore, a small probability of cure with one treatment may justify its use, whereas the same probability of symptom relief might not justify the use of another treatment.

Even modest improvements in survival are potentially important. In the adjuvant setting, minimal improvement in survival in the case of common cancers (i.e., breast and colon) could translate into the saving of many thousands of lives. If adjuvant therapy does not at least improve disease-free survival, it should not be recommended. Improved survival, disease-free and overall, is the goal of adjuvant therapy and is its only justification. A question that frequently arises is whether early clinical trial results that demonstrate a significant improvement in disease-free survival, but not overall survival, justify recommending a treatment. The Working Group believed that they did. Improvements in disease-free survival have been shown to translate eventually into an overall survival benefit.545 In addition, some patients may wish to remain disease-free in the immediate future, even if treatment does not produce overall survival benefit, because of family or career reasons.

The Working Group further agreed that improvement in survival is not required to justify recommending treatment for metastatic cancer. Treatment could still be recommended when it would improve the quality of life. Modest improvements in survival may be an indicator of significant symptom relief. On the other hand, just because a treatment produces a modest improvement in survival does not mean that its use is justified. The survival benefit must be balanced against the toxicity and cost.

Caution was expressed by the Working Group with regard to the generalizability of benefits from clinical trial to practice. The amount of benefit produced by a technology or treatment in clinical practice may be sometimes less than that reported in clinical trials. This reduction in
benefit can occur if patients in clinical practice are sicker or older than those in clinical trials and therefore survive a shorter time or realize less improvement in quality of life. For example, adjuvant chemotherapy improves the survival of postmenopausal patients with node-negative, receptor-negative breast cancer, but may not be appropriate for elderly patients with comorbidities, because competing causes of death limit their survival benefit from chemotherapy. A reduction in benefit may also occur in going from trial to practice when the extent of the disease or the treatment history of a patient in practice is not like that of the patients in the trial. For example, a 25% response rate in chemotherapy-naive breast cancer patients will not mean a 25% response rate in patients who have failed to respond to multiple regimens. Expert panels should take potential reductions in benefit into account by making recommendations not only concerning the types of patients who should receive a treatment, but also on the types of patients who should not. Furthermore, they should make recommendations about the resources required to administer the treatment effectively.

In conclusion, patient outcomes (eg, survival, toxicity, and quality of life) should receive higher priority than cancer outcomes (eg, response rate and response duration) for guideline development and technology assessment. In general, there is no minimum benefit above which treatments are justified and below which they are not; rather, benefits should be balanced against toxicity and cost.

Survival is the most important outcome of cancer treatment. An improvement in disease-free survival is a prerequisite for recommending adjuvant therapy. In metastatic cancer, treatment can be recommended without an improvement in survival, if it improves quality of life.

Cancer-related quality of life is important because it is the patient's evaluation of how cancer and its treatment affect the physical, psychologic, and social aspects of his or her life. To evaluate the effects of cancer and its treatment on quality of life, reliable, valid measures must be used; there must also be controls for other factors, including the placebo effect, that affect quality of life.

The value of cancer outcomes (eg, response) for technology assessment and guideline development depends on their ability to predict patient outcomes (eg, survival and quality of life) or to influence treatment decisions. Complete response is an important outcome when it predicts survival; progression is important because it signals the need to change or stop treatment.

Cost-effectiveness is important to consider when the benefits of treatment are modest or the costs are high, and is best measured in phase III clinical trials. When formal cost-effectiveness data are unavailable, comparative costs among clinical strategies should be considered.

APPENDIX I
Health Services Research Committee Members

Rodger Winn, MD, Chair
Paul Anderson, MD
Joseph Bailes, MD, Clinical Practice Committee Liaison
Robert Bast, MD
Stacey Beckhard, MS
Robert Becker, JD, CAE
Colin Begg, MD
Gregory Curt, MD
Ross Donohower, MD
Gary Dosik, MD
Harmon Eyre, MD
John Fetting, MD
Patricia Ganz, MD, Patient Advocacy Committee Liaison
Gerald Hanks, MD
Charlotte Jacobs, MD, Board Liaison
Carl Kardinal, MD
Mark Levine, MD
Thomas Smith, MD
Glenn Steele, Jr, MD, PhD
Jane Weeks, MD
Jerome Yates, MD

APPENDIX II
ASCO Outcomes Working Group

Paul N. Anderson, MD*
Harrison Ball, MD
John B. Benear II, MD
Kary Benjamin
Charles Bennett, MD*
Susan G. Braun
Harman D. Breerton, MD
John H. Burrows, MD
Charles Coban, MD
Alfred M. Cohen, MD
John H. C. Fetting, MD, Chairman*
Leslie Ford, MD
Michael Friedman, MD
Patricia Ganz, MD*
Richard Gelber, PhD*
Holcombe Grier, MD
Gerald Hanks, MD
Robert L. Justice, MD
Patricia Legant, MD
Mark N. Levine, MD*
Susan Parsons, MD*
Peter Raich, MD
Sandra Schaefer
Thomas J. Smith, MD*
A. Collier Smyth, MD
Professor A.T. van Oosterom
James L. Wade III, MD
Jane Weeks, MD*
Rodger J. Winn, MD*
Janet Woodcock, MD

*Core Group.
REFERENCES


18. Skeel RT: Quality of life dimensions that are most important to cancer patients. Oncology 7:55-61, 1993


