Enhancing Research on Cancer Survivors

John Z. Ayanian and Paul B. Jacobsen

ABSTRACT

The United States devotes substantial resources to understanding the etiologies of cancer and improving treatments, but much less research has focused on the needs of cancer survivors after they have completed active treatment. This article augments findings from the Institute of Medicine about cancer survivorship research and ways to enhance quality of life and quality of care. Studies of cancer survivors should focus on mechanisms and risk factors for impaired quality of life and evaluate interventions to improve this domain. Research to improve quality of care should concentrate on survivorship care plans, surveillance tests, respective roles of primary and specialty care, and performance measures related to survivorship care. Opportunities to expand research on cancer survivors include clinical trials, large cohort studies, cancer registries, and national surveys. Research to understand the needs of cancer survivors will provide a foundation for effective programs to meet these needs.

J Clin Oncol 24:5149-5153. © 2006 by American Society of Clinical Oncology

INTRODUCTION

More than 10 million people alive today in the United States have been diagnosed with cancer. Most of them have completed active cancer treatments, and nearly two thirds of cancer survivors have survived more than 5 years since they were initially diagnosed with cancer. Although the United States devotes enormous research resources to understanding the etiologies of cancer and improving cancer treatments, much less research has focused on the needs and care of cancer survivors after they have completed active treatment.

The Institute of Medicine recently issued a major report, From Cancer Patient to Cancer Survivor: Lost In Transition. This report provided a comprehensive assessment of the health needs of cancer survivors and the currently fragmented approaches to serving them. The report also included 10 recommendations to improve the quality of life and quality of care for cancer survivors. As the capstone of the report, the 10th recommendation emphasized that federal and private organizations “should increase their support of survivorship research and expand mechanisms for its conduct. New research initiatives focused on cancer patient follow-up are urgently needed to guide effective survivorship care.”

The Institute of Medicine has specified four essential components of survivorship care that are important targets for greater research: prevention of recurrent or new cancers and the late effects of prior cancer and its treatment; surveillance for recurrent or new cancers that can be treated more effectively if detected early; interventions to alleviate physical and psychological symptoms that persist or occur beyond active cancer treatment and to improve quality of life; and coordination of primary and specialty care to address multiple conditions and needs.

The purpose of this article is to feature and expand on the findings from the Institute of Medicine about the current state of cancer survivorship research and ways to enhance it. Researchers who study cancer patients and clinicians who care for cancer patients can play a leading role in refining the priorities of this research agenda and moving it forward. By highlighting survivorship research priorities and opportunities for the oncology community to contribute to this effort, our goal is to stimulate greater attention and action to improve the care of the vast numbers of Americans who are cancer survivors.

IMPROVING QUALITY OF LIFE FOR CANCER SURVIVORS

In recent years, research on quality of life in cancer survivors has increased steadily. Using Medline as a metric, 40 articles published in 1994 were indexed under the combination of “quality of life,” “neoplasms,” and “survivors”; in 2004, this number had increased to 126 publications. The growing number of publications is consistent with the increasing recognition that end points other than survival and disease-free survival are important to consider when evaluating the effectiveness of cancer treatments. Research on quality of life addresses the question of how well patients are surviving. Key outcomes include patients’ self-reports of their health-related quality of life and symptoms, as well as standardized
measures of functioning, such as performance tests of attention and memory to assess cognitive functioning. Consistent with the aim of improving the quality of life of cancer survivors and with recent reports on cancer survivorship from the Institute of Medicine and the President’s Cancer Panel, the following topics are priorities for research: identifying common and important quality-of-life problems faced by survivors; identifying mechanisms and risk factors underlying these problems; and developing and evaluating strategies to prevent and treat these problems.

### Identifying Important Quality-of-Life Issues

Identifying common and important quality-of-life issues faced by survivors can inform larger efforts to direct resources to yield the greatest benefits. From a practical perspective, it makes sense to focus efforts on problems that affect the greatest number of survivors. This consideration must be balanced against the relative importance of the problems. Addressing a problem or symptom that is relatively uncommon but has a profoundly negative impact on quality of life among survivors may be just as valuable as addressing a problem or symptom that has only a moderately negative impact on quality of life, but is common among survivors.

Data currently available to inform these decisions consist primarily of surveys of patients with single diseases at single institutions. To ensure greater generalizability of the findings, it will be important to conduct research that includes population-based sampling or large cohorts of survivors assembled from multiple treatment settings. Examples of such efforts include a population-based survey of quality of life among men with prostate cancer, a registry-based survey of the long-term quality of life among hematopoietic stem-cell transplant recipients seen at 40 different treatment centers, and the Cancer Care Outcomes Research and Surveillance Consortium that is studying patients with colorectal cancer or lung cancer from multiple regions and health care systems in the United States.

As common and important quality-of-life issues are identified, research then needs to focus on identifying the mechanisms and risk factors underlying these issues. Elucidating mechanisms is critical, thereby allowing empirical evidence to guide the development of interventions. When coupled with identifying risk factors, strategies can be developed to ameliorate problems in their early stages or even prevent them from developing. To date, efforts to identify risk factors have focused primarily on demographic and treatment variables. This line of research has shown, for example, that female sex predicts greater psychological distress among cancer patients. In moving forward, the field will be better served by considering a broader range of risk factors. One way to broaden the search is to evaluate modifiable risk factors—these factors can serve as targets for prevention efforts. A growing body of evidence suggests, for example, that avoidant forms of coping during treatment are a risk factor for post-treatment distress, and these approaches to coping may represent a modifiable risk factor. A second way to broaden the search is to consider biologic factors that may confer high-risk status. Preliminary research suggests that cancer patients who possess the e4 allele of the APOE gene are at greater risk for post-treatment cognitive problems, and this finding may represent a promising example of a biologic risk factor with clinical relevance to improving quality of life.

### Improving Quality of Care for Cancer Survivors

A second major priority for new research is to improve the quality of care for cancer survivors. Because of the multifaceted nature of cancer treatment and surveillance involving numerous physicians for most patients, cancer survivors’ perceptions of the overall quality of their care are strongly associated with their views about the coordination of their care. The Institute of Medicine has strongly recommended the widespread adoption of explicit survivorship care plans to overcome the fragmented care that cancer survivors often receive after they complete their primary course of cancer treatment. The President’s Cancer Panel similarly has recommended that patients receive a treatment summary form when they complete their primary cancer treatment, as well as a survivorship care plan based on this treatment summary. These treatment summaries and comprehensive written survivorship care plans would be developed for each patient by an oncology provider who coordinated his or her care. In addition to summarizing the clinical details of a patient’s primary cancer treatment, the care plan would provide recommendations for follow-up care, surveillance testing, potential preventive measures, and psychosocial support services.

Research on survivorship care plans could play a major role in defining how these patient-specific plans are developed, implemented, and refined. In either randomized or observational studies,

### Developing and Evaluating Prevention and Treatment Strategies

Systematic reviews and meta-analyses of randomized clinical trials have identified a number of interventions that effectively address quality-of-life issues faced by cancer survivors. Although some interventions have been effective, their impact on clinical care has been limited due to two common features of this research. First, much of the research has not included eligibility criteria with regard to the severity and sometimes even the presence of a targeted problem. This approach is inconsistent with the delivery of clinical care, which typically focuses on intervention with patients who present with problems of moderate to high severity. Much of the research on treatment of psychological distress in cancer patients, for example, has been based on cohorts in which the average level of distress was mild. A more promising strategy would be to demonstrate the effectiveness of interventions with patients who are experiencing problems of moderate to severe intensity, a group more typical of those for whom the interventions will be used clinically. Once efficacy has been demonstrated in this context, research would logically proceed to testing interventions to prevent problems from occurring or progressing to greater severity.

A second factor limiting clinical applicability is that many interventions studied in randomized clinical trials require commitments of patient and professional time so considerable that they may be difficult to disseminate even if found to be efficacious. Designing and evaluating interventions with regard to how well they can be disseminated is one means of improving the translation of research into practice.
patients who received survivorship care plans could be compared with patients receiving usual care without these plans regarding their satisfaction with care, coordination of care, and communication with health care providers about symptoms, surveillance testing, and psychosocial concerns. In the decentralized US health care system, the primary goal of written survivorship care plans would be to improve communication and coordination of care among patients, cancer specialists, and primary-care physicians.

Another focus for improving the quality of care should be to assess the value of current and proposed surveillance tests. The goal of this research is to provide better evidence about whether surveillance tests improve patients’ outcomes by identifying early cancer recurrences or second primary cancers while they can be alleviated or cured. Research on survivorship care provided by cancer specialists and primary-care physicians should then be conducted to assess adherence to evidence-based guidelines regarding surveillance testing. To optimize the allocation of health care resources, quality-of-care research can evaluate underuse of appropriate tests, such as annual mammography for breast cancer survivors or colonoscopy for colorectal cancer survivors, as well as overuse of inappropriate tests such as routine chest radiographs or bone scans in asymptomatic breast cancer survivors.

In addition to conducting better research on surveillance tests, studies are needed to assess how survivorship care is delivered by primary-care physicians, oncologists, or collaborative care that is shared by these two groups. Randomized studies in the United Kingdom and Canada have found that breast cancer survivors received effective survivorship care from primary-care physicians who were well informed about cancer survivors’ symptoms and needs as defined by evidence-based guidelines. In recent observational research in the United States, elderly breast cancer survivors were most likely to receive appropriate surveillance mammography when observed by cancer specialists or by both cancer specialists and generalist physicians. Among elderly cancer survivors with other noncancer conditions such as congestive heart failure or diabetes, necessary services not related to cancer were most likely provided when patients were observed by both primary-care physicians and medical oncologists, least likely provided when observed by only oncologists, and intermediate in likelihood when observed by only primary-care physicians.

Finally, better evidence is needed to define performance measures that can be used to monitor and improve the quality of cancer survivors’ care. Most current efforts to define and test performance measures are focused on the initial treatment of newly diagnosed patients with cancer, such as the Quality Oncology Practice Initiative of the American Society of Clinical Oncology. Performance indicators related to survivorship care could include technical measures, such as the use of surveillance tests for cancer recurrence and standardized assessment tools for important symptoms and late effects of treatment, as well as interpersonal measures related to coordination of care and psychosocial support. Public and private organizations that can help to promote the implementation of such performance measures include the federal Center for Medicare and Medicaid Services, American Society of Clinical Oncology, National Quality Forum (www.qualityforum.org), and National Committee for Quality Assurance (www.ncqa.org).

The Institute of Medicine has identified four major approaches to expand cancer survivorship research. First, greater follow-up of participants is needed in randomized clinical trials with a focus on health-related quality of life and survivorship care. Second, greater follow-up of participants is needed in large observational cohort studies. Third, population-based cancer registries should have an increased role. Fourth, greater focus should be placed on cancer survivors in federal health surveys.

Patients in clinical trials represent an underused resource for assessing the long-term effects of cancer and its treatments on quality of life, and assessing ways that survivorship care can be improved. These patients have demonstrated their willingness to participate in research on the acute treatments for cancer, and many of them would be willing to participate in subsequent survivorship studies if such opportunities were offered to them. Incorporating long-term assessments of quality of life into randomized clinical trials of chemotherapeutic agents, for example, would make it possible to determine whether differences in quality of life evident between treatment arms during active treatment are sustained after treatment is completed. A specific challenge is to convince sponsors and investigators of clinical trials to build long-term follow-up assessments of quality of life into the design of their studies. Essential elements of such studies include prospective data collection on health-related quality of life at enrollment and at appropriate intervals after treatment is completed; additional resources are required to maintain contact with cancer survivors and analyze more comprehensive data beyond overall survival and disease-free survival.

In addition to longer-term follow-up of participants in clinical trials, survivorship research should be expanded in large observational cohort studies. The Childhood Cancer Survivor Study is a well-established model for such research, enrolling more than 14,000 participants who have survived at least 5 years after treatment for a childhood cancer. Through the Cancer Care Outcomes Research and Surveillance Consortium and the Cancer Research Network, the National Cancer Institute has already made substantial investments in assembling research cohorts of adults with newly diagnosed cancer identified from population-based registries and large health care systems. The infrastructure developed for these projects provides promising platforms for expanded research on cancer survivors.

Cancer registries represent another mechanism for new research on large, representative cohorts of cancer survivors. Since 1973, the National Cancer Institute has funded the Survival, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) to monitor cancer incidence, staging, primary treatment (within 4 months of diagnosis), and overall survival in multiple regions representing more than one fourth of the U.S. population. During the last decade, the National Program of Cancer Registries (NPCR) funded by the Centers for Disease Control and Prevention (www.cdc.gov/cancer/npcr) has supported substantial improvements in data collection at 45 state cancer registries. In addition, the National Cancer Data Base sponsored by the American College of Surgeons Commission on Cancer (www.facs.org/cancer/ncdb/index.html) has collected data on about three fourths of newly diagnosed patients in the United States through voluntary participation of hospital-based registries.

The registry data systems that comprise SEER, NPCR, and National Cancer Data Base provide a framework that could be used more actively for identifying and contacting cancer survivors to participate in research studies related to their quality of life and quality of care.
Each of these major data resources could play a substantially greater role in cancer survivorship research if participating registries were funded to collect data on cancer recurrences from cancer providers or through linkages with Medicare claims or electronic records of health care delivery systems. The SEER database has been linked to Medicare claims for patients diagnosed through 2002 (www.health-services.cancer.gov/seermedicare), providing another source of data on surveillance tests and cancer recurrences.

The fourth approach to expanding research on cancer survivors would be to collect more detailed data on cancer survivors in federal surveys. The National Health Interview Survey has included periodic supplements devoted to cancer control in 1987, 1992, 2000, and 2005. These supplements have provided useful information on cancer survivors in the general population, and with increased funding they could be conducted more frequently and in greater depth to assess the quality of life and health care experiences of cancer survivors. Similarly, the Medical Expenditure Panel Survey, which is the main federal survey on the costs and uses of health care, could sample cancer survivors in larger numbers to provide greater statistical power for analyses of their care. The National Ambulatory Medical Care Survey, which collects data annually on a nationally representative sample of office visits to physicians, is adding a separate stratum for sampling medical oncologists in 2006, providing opportunities for more extensive comparisons of survivorship care provided by primary-care physicians and oncologists.

In conclusion, research is essential to improve the quality of life and quality of care of cancer survivors. The research agenda that we have outlined to achieve these goals would also advance multiple clinical and policy recommendations of the Institute of Medicine related to cancer survivorship. New funding can help to expand the existing infrastructure for clinical and health services research to promote a greater focus on cancer survivors. An expanded emphasis on long-term follow-up in clinical trials, large cohort studies, cancer registries, and national surveys will enhance our understanding of the needs of cancer survivors and provide a stronger foundation for effective programs to meet these needs.

REFERENCES

Enhancing Research on Cancer Survivors

Authors’ Disclosures of Potential Conflicts of Interest
The authors indicated no potential conflicts of interest.

Author Contributions

| Conception and design: John Z. Ayanian, Paul B. Jacobsen |
| Manuscript writing: John Z. Ayanian, Paul B. Jacobsen |
| Final approval of manuscript: John Z. Ayanian, Paul B. Jacobsen |