

## Cancer Survivorship Research: A Review of the Literature and Summary of Current NCI-Designated Cancer Center Projects

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### Abstract

The number of cancer survivors and the amount of cancer survivorship research have grown substantially during the past three decades. This article provides a review of interventional and observational cancer survivorship research efforts as well as a summary of current cancer survivorship research projects being conducted by National Cancer Institute–designated cancer centers in an effort to identify areas that need further attention. *Cancer Epidemiol Biomarkers Prev*; 20(10); 2042–7. ©2011 AACR.

### Introduction

The number of cancer survivors in the United States has grown substantially during the past 3 decades. Recent estimates indicate nearly 12 million people—roughly 4% of the U.S. population—are cancer survivors, an increase from approximately 4 million people—or 1.8% of the U.S. population—in 1978 (1). As the number of cancer survivors has increased, the importance of understanding the needs of this unique population has also grown. The purpose of this article is to provide a review of interventional and observational cancer survivorship research efforts as well as a summary of current cancer survivorship research projects being conducted by National Cancer Institute–designated cancer centers (NCI CC) in an effort to identify areas that need further attention.

### Methods

Two methodologic procedures were taken to conduct this review. First, a review of the cancer survivorship literature was conducted to identify and summarize observational and interventional literature on cancer survivorship. We conducted a search of the cancer survivorship literature using the PubMed and MEDLINE databases in March 2011, limited to original research with human participants published in English. Reference lists of identified articles were also reviewed for relevant publications. We searched the PubMed database using the key words "cancer survivor" combined with each of

the following terms: "physiological interventions," "psychological interventions," "quality of life interventions," "late effects interventions," "long term effects interventions," and "functional status interventions." A separate PubMed search was conducted for the key words "cancer survivorship" in the title or abstract. We searched the MEDLINE database using the key words "cancer survivorship" in the title or abstract.

Second, a survey requesting information about current research efforts focused on cancer survivor populations was sent to 62 NCI CCs in April 2011. At the suggestion of multiple survey respondents, we also conducted a query using the NIH RePORTER tool to glean information about cancer survivorship research efforts that may have not been captured in survey responses. A search for currently funded projects in the United States using the key word "survivor" was conducted via the NIH RePORTER in June 2011.

Exclusion criteria were held constant throughout the literature review, the NCI CC survey, and NIH RePORTER query. Articles and research projects focusing on cost analysis, economic burden, utilization, nursing, curriculum, quality of care, caregivers, survivorship care plans, caregivers/family members of cancer survivors, basic or clinical research, education and/or program funding, training grants, pilot projects, dissemination research, and subcontracted projects were excluded mainly due to the predetermined scope of this article. Studies and projects focusing on both cancer survivors and caregivers/families were included.

The articles and ongoing research projects that met our inclusion criteria were categorized as quantitative or qualitative; observational, experimental, or descriptive; cross-sectional, case-control, cohort, or randomized controlled trials; and by tumor site. Those that addressed more than one cancer site or did not distinguish between cancer types were classified as "various."

Studies and projects were further categorized into 3 topic areas: late effects, quality of life, and prevention/early detection. Those pertaining to the sequelae of cancer treatments that emerge during or after treatment were

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categorized as late effects; those pertaining to the psychological effects of cancer were categorized as quality of life; and those addressing the screening of patients and prevention of second cancers and recurrences were categorized as prevention and early detection.

To gain a better understanding of how current research may be addressing holes in the previous literature, we counted the number of times a specific area of minor focus was addressed within each of the studies (see Table 3).

## Results

### Literature review

The primary PubMed search produced 900 citations, of which 263 met the inclusion criteria. The first published study that met our inclusion criteria was published in 1984. The secondary PubMed search for the key words "cancer survivorship" in the title or abstract resulted in 391 articles, 72 of which met the inclusion criteria and were not duplicated by the initial search. The MEDLINE search resulted in 719 articles. Of these, 170 articles met the inclusion criteria and were not duplicated by the initial searches. An additional 169 studies were identified in reference lists from articles that were identified in the searches conducted. The final result of the literature review was 674 articles.

The number of survivorship studies overall has increased since 1984, with an observable increase around 1996, the year the Office of Cancer Survivorship was created (see Fig. 1). Of the 674 studies that met the inclusion criteria, 618 or 91.7% were quantitative. As depicted in Fig. 1, the use of descriptive and case-control studies has been relatively unchanged over time whereas the use of qualitative studies has fluctuated. Since 1996, randomized controlled trials and cross-sectional designs were used with increasing frequency, especially in the last decade.

Fifty-six articles (8.3%) used qualitative research designs. Forty-six or 82.1% of the qualitative studies

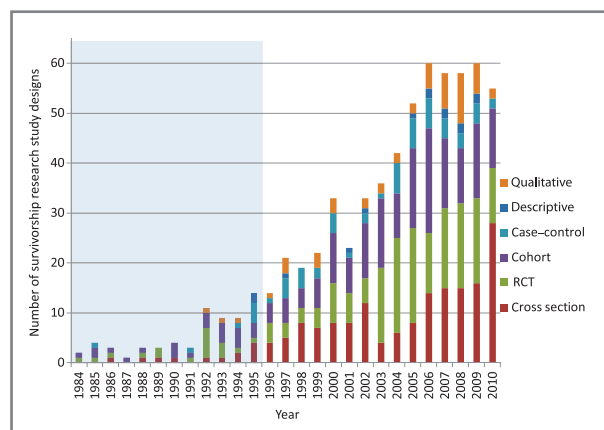


Figure 1. Survivorship study designs by year. Shaded area indicates time period before the creation of the Office of Cancer Survivorship. RCT, randomized controlled trial.

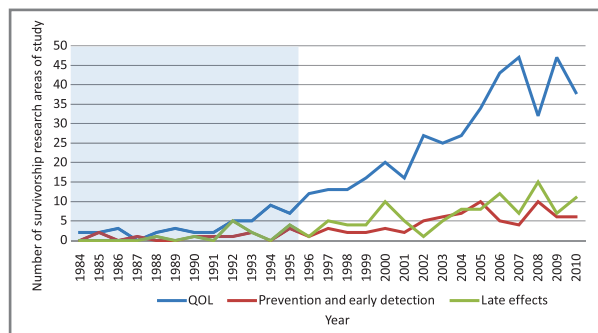


Figure 2. Survivorship areas of study by year. Shaded area indicates time period before the creation of the Office of Cancer Survivorship. QOL, quality of life.

addressed quality-of-life issues, and 31 articles or 55.4% of the qualitative studies focused on breast cancer survivors.

Quality-of-life studies have become the focus of survivorship research, increasing from 12 studies in 1996 to peaks of 47 studies in 2007 and 47 studies in 2009 (see Fig. 2).

Intermittent increases in late-effects research occurred in 2000, 2006, and 2008, though never to more than approximately a third of the total studies per year.

Prevention and early detection were the focus of between 0 and 11 survivorship studies per year, consistently the smallest area of focus.

In terms of tumor sites, the frequency of studies focusing on lung, bone, and head and neck cancers fluctuated, though each was fewer than 3 studies per year (see Fig. 3). There was a slight positive trend in the frequency of studies focusing on leukemia and lymphoma, gastrointestinal, prostate, pediatric, and "other" cancers, all with fewer than 10 published studies per year. Research focusing on "various" sites and gynecologic sites both show a moderately increasing trend. In contrast, the

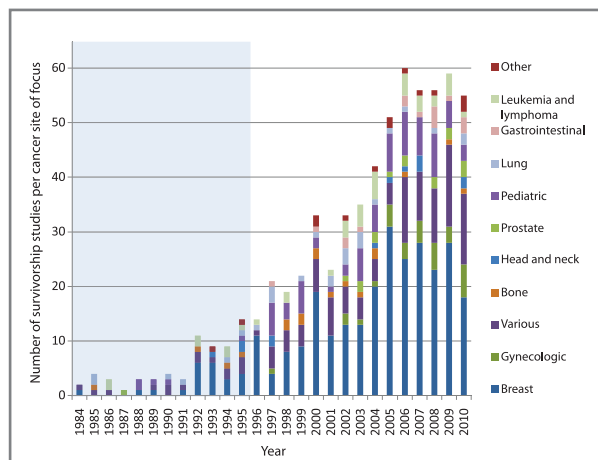


Figure 3. Survivorship study cancer sites of focus by year. Shaded area indicates time period before the creation of the Office of Cancer Survivorship.

number of survivorship studies aimed at breast cancer strongly increased by approximately 130% per year. In 1996, breast cancer was the most frequently studied cancer survivor site, and in 2010, it had more than 3 times the frequency of the second most commonly studied cancer site.

The rates of both interventional research and observational research have quadrupled since 1996. Interventional research increased from 5 studies in 1996 to 22 studies in 2009, and observational research increased from 9 studies in 1996 to 38 studies in 2009. Overall, there were 259 (38.4%) interventional and 415 (61.6%) observational studies since 1984. Studies focusing on breast cancer have by far been the focus of the overwhelming number of both intervention and observational studies (144 and 148, respectively). Although each type of research has increased with a comparable pace, there have been 5 to 10 more observational studies per year than interventional studies.

#### Current NCI CC research

Data were obtained for 50 of the 62 NCI CCs invited (80.6%); one center reported having no current survivorship studies. The survey responses of NCI CCs identified 96 cancer survivorship research projects that met the criteria previously outlined. The NIH RePORTER identified 367 projects with the keyword "survivor" in the project description. Of these 367 projects, 120 were excluded because they were not being conducted by NCI CCs. An additional 160 projects were excluded because they were either duplicate of the NCI CC survey responses or not focused on cancer survivorship as previously described. Because the search term used was simply "survivor," the query results were broadly representative of a variety of diseases. After these steps were completed, a total of 87 additional projects were identified from the NIH RePORTER query, for an overall total of 183 current projects (96 from the NCI CC surveys and 87 from the NIH RePORTER) that were focused on cancer survivorship research. Using 50 as the denominator, the average number of studies per NCI CC was 3.66.

Table 1 provides a breakdown of project counts and percentage of total by tumor site. Breast cancer was by far the most researched with 71 projects, which is just more than seven times the number of projects compared with the next highest single-volume site, prostate cancer, which had 10 projects. Roughly one fourth of the current research projects included more than one cancer type and are listed as "various" in Table 1. Projects focusing on pediatric cancer survivorship, which covered a variety of tumor sites, were grouped together and account for 10% of the total.

Although some projects focused on more than one area, each project's primary aim was used to determine the main focus area of the study. The majority of the projects, 114 or 62.3%, focused on quality of life. Prevention/early detection-oriented studies accounted for 35 projects (19.1%) and late effects made up 32 (17.5%) projects. Two

**Table 1.** Current cancer survivorship research by tumor site

Tumor site	Count	% of total
Breast	71	39
Various	47	26
Pediatric	19	10
Prostate	10	5
Colorectal	9	5
Hematologic	6	3
Brain/CNS	5	3
Head and neck	5	3
Gynecologic	4	2
Other	4	2
Lung	3	2
Total	183	100

Abbreviation: CNS, central nervous system.

projects did not have sufficient information available to make a determination as to which area it best fit.

In terms of study designs, the majority of current projects identified were randomized controlled trials (58 projects or 31.7%), followed by cohort studies (37 projects or 20.2%), case-control studies (19 projects or 10.4%), cross-sectional studies (13 projects or 7.1%), mixed-methods studies (13 projects or 7.1%), and descriptive studies (11 projects or 6%). Qualitative study designs accounted for 9 of the 183 studies or 4.9%. Twelve quantitative projects (6.6%) had unspecified or unclear study designs, and 11 projects (6%) had unspecified study designs. Seventy-two studies were interventional, whereas 111 were considered observational (the 11 projects with unspecified study designs were grouped into interventional and observational categories on the basis of project title information).

The vast majority of current research projects in cancer survivorship research, 121 of the 183 studies or 66.1%, were funded by the NIH. Of these NIH-funded projects, approximately half of the projects (85 projects or 46.4%) were funded by the NCI. The second largest area of funding was internal organizational funds not identified with any external funding source. Twenty-nine projects (15.8%) were funded by means of internal organizational resources.

Detailed information about funding amounts was available for 91 of the 183 projects. The total amount of annual funding for the most recently recorded fiscal year for these 91 projects was approximately \$29.1 million. The median amount of annual funding was \$279,863. Additional descriptive statistics about funding amounts are found in Table 2.

Minor areas of focus studied during the past 27 years are summarized in Table 3. For the bottom 10 focus areas, 6 areas [radiation effects, hot flashes, fertility, rural, complementary and alternative medicine (CAM), and dental

**Table 2.** Cancer survivorship research funding statistics

Number of studies with funding details	91
Total FY funding (all studies)	\$29,134,015
Mean FY funding (per study)	\$320,154
Median FY funding	\$279,863
Minimum FY funding amount (per study)	\$35,110
Maximum FY funding amount (per study)	\$1,231,396

Abbreviation: FY, fiscal year.

issues] have as much or more current research activity as there has been in nearly 3 decades combined. In addition, the focus on work and cancer survivorship has received much more attention by the current research vis-à-vis past efforts. The number of studies focused on age-related issues seems to have also increased relative to past efforts because 21 current projects have such a focus as opposed to 26 for the previously published literature. Some areas that seem to have declined somewhat include research focused on coping or adjustment, tobacco and/or alcohol use, and cognitive behavioral therapy.

## Discussion

The purpose of this article was to provide a review of published cancer survivorship research as well as a summary of current survivorship research being conducted by NCI CCs. The increase in cancer survivors, both in absolute and relative terms, has brought attention to the importance of understanding and addressing the needs of this unique population. This review has identified several important findings.

First, opportunities for cancer survivorship research received a significant boost by the creation of the Office of Cancer Survivorship by the NCI in 1996. Since that time, the annual amount of published cancer survivorship studies is approximately 5 times greater than it was the year the Office of Cancer Survivorship was created. The Office of Cancer Survivorship could have directly contributed to this increase by increasing the focus on survivorship research, lobbying for funding for survivorship research, and proposing a plan for survivorship research, including cosponsoring biannual survivorship conferences to highlight research and opportunities for research (2). Inversely, the Office of Cancer Survivorship may have been a response to the increased focus on survivorship studies during this time period. Although causality is not clear, it is evident that survivorship research enjoyed a boost during the mid 1990s and has continued to increase ever since, either in response to or causing the growth of corresponding institutions such as Office of Cancer Survivorship.

Second, though increases in survivorship research have been achieved, not all tumor sites are receiving equal attention from the cancer survivorship research commu-

**Table 3.** Past and current cancer survivorship research by specific focus area

Research focus area	Completed research, <sup>a</sup> n (%)	Ongoing research, <sup>a</sup> n (%)
Psychologic/QOL	157 (23.3)	25 (13.7)
Exercise/physical activity	121 (17.9)	25 (13.7)
Psychosocial	69 (10.2)	17 (9.3)
Coping/adjustment	49 (7.3)	4 (2.2)
Depression/anxiety	47 (7.0)	6 (3.3)
Recurrence/secondary cancers/prevention	47 (7.0)	13 (7.1)
Function (i.e., cognitive, motor)	45 (6.7)	12 (6.6)
Fatigue/sleep	32 (4.7)	14 (7.7)
HRQOL	32 (4.7)	13 (7.1)
Tobacco/alcohol	27 (4.0)	2 (1.1)
Minority/ethnicity	26 (3.9)	13 (7.1)
Energy/diet	26 (3.9)	6 (3.3)
Undefined late effects, comorbidities	26 (3.9)	12 (6.6)
Age-focused (young, elderly survivors)	26 (3.9)	21 (11.5)
CBT	24 (3.6)	2 (1.1)
Obesity, weight, BMI	23 (3.4)	5 (2.7)
Stress/relaxation	20 (3.0)	5 (2.7)
Lymphedema	17 (2.5)	5 (2.7)
Sexual QOL	15 (2.2)	3 (1.6)
Menopause	14 (2.1)	2 (1.1)
Immunity	14 (2.1)	2 (1.1)
Cardiovascular risk	12 (1.8)	5 (2.7)
Communication	12 (1.8)	3 (1.6)
Pain	9 (1.3)	4 (2.2)
Bone density	9 (1.3)	1 (0.5)
Spirituality/meaning	8 (1.2)	1 (0.5)
Radiation effects	7 (1.0)	7 (3.8)
Hot flashes	7 (1.0)	7 (3.8)
Fertility	6 (0.9)	9 (4.9)
Work	6 (0.9)	5 (2.7)
Gender-focused	5 (0.7)	1 (0.5)
Rural	4 (0.6)	5 (2.7)
CAM	2 (0.3)	8 (4.4)
Follow-up care	2 (0.3)	1 (0.5)
Dental	1 (0.1)	2 (1.1)

Abbreviations: BMI, body mass index; CBT, cognitive behavioral therapy; HRQOL, health-related quality of life; QOL, quality of life.

<sup>a</sup>Because each study could be categorized into more than one research focus area, percentage totals do not add up to 100%. The total number of studies (675 for completed research and 183 for ongoing research) was used as the denominator.

nity. For example, prostate cancer survivors make up 20% of the total cancer survivorship population, yet only 5% of current research projects focus specifically on prostate

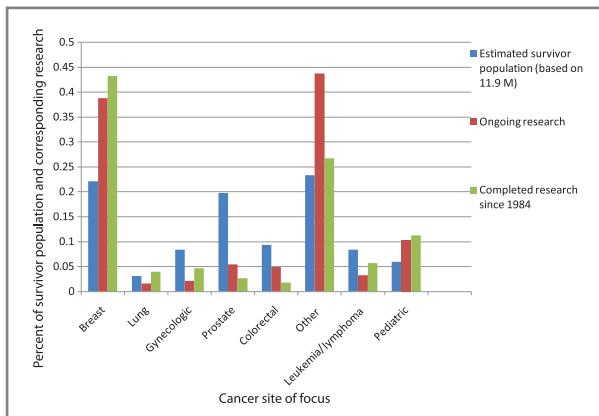


Figure 4. Survivor population versus research focus percentages by site.

cancer survivors and even less prior work has been done in this area (see Fig. 4). Colorectal, gynecologic, and hematologic cancers are also underrepresented in current cancer survivorship research but by a narrower margin. Colorectal cancer seems to be gaining ground as depicted in Fig. 4—a greater percentage of current studies are focused on colorectal cancer than in the previous literature.

In contrast, breast cancer is disproportionately overrepresented in current cancer survivorship research efforts. Although female breast cancer survivors represent 22% of cancer survivors in the United States, 40% of the current research projects are focused on breast cancer survivors. In addition, there seem to be a fair number of studies conducted among pediatric cancer survivors, based on our reviews. This could be due to the structure of the cooperative groups in adults versus pediatric cancer where there are many adult groups but only one pediatric group. Thus, efforts to study issues affecting pediatric survivors are centralized and well coordinated. Furthermore, because pediatric patients are young and have a longer potential of years ahead, the impact of survivorship research may be perceived to be greater and of more importance. Regardless of the reason, this area has indeed flourished and may serve as a model for adult survivorship research.

Another important finding of our review is that cancer survivorship research is not being actively pursued by all NCI CCs. The centers that did not respond to our survey might have had additional studies that would have added valuable information to our review. Although only one center acknowledged that it had no active studies in survivorship, our search on the NIH RePORTER did not yield funded projects that fell into our search criteria for the remaining centers. The limitations of our query and survey methods may contribute to some underreporting of current cancer survivorship research efforts. However, it is apparent that there is noticeable variability in the number of cancer survivorship studies being presently conducted by NCI CCs.

Both interventional research and observational research have experienced great growth in the last decade,

each quadrupling in the number of studies per year since the general increase in cancer survivorship research after 1996. There are 72 ongoing interventional studies and 111 ongoing observational studies, which would seem to indicate that the similarly increasing trend will continue for both study types, despite the anomaly of a decrease in interventional research during the past 2 years. A closer look at study design and focus reveals that a decrease in cohort studies, case-control studies, and randomized controlled trials corresponds with the decrease in interventional studies in the last 2 years. Similarly, there was a spike in cross-sectional studies corresponding to the increase in observational research. Much of the interventional research of the last decade focused on exercise and physical activity interventions. In the last few years, however, much of that research seems to have shifted to an observational approach, as researchers are assessing the natural exercise and physical activity behavior of the survivor population, either to reassess for future interventional research or to address the sustainability of such interventions among survivors. Thus, there is a need for more interventional studies.

Looking over the research being conducted in the major areas of focus, it is apparent that many studies have been conducted related to quality of life whereas fewer studies have been conducted in terms of prevention/early detection and late effects. In terms of the minor focus areas explored over the last 27 years, several topical areas emerged as historically understudied and these gaps have in some cases persisted in ongoing research (Table 3). For example, radiation effects, hot flashes, fertility, rural populations, CAM use, and dental issues are the areas with the fewest studies conducted, although these may be of great importance to survivors (3–6). Research on coping and tobacco/alcohol use has declined. These problems have not been eliminated (7) among survivors, and interventions to address them are not widely implemented, as yet, in clinical settings as part of usual care (8,9). However, considering the previous research was conducted over 27 years, the volume of current research efforts in these areas may not be a true departure from previous efforts but rather a continuation of previous levels of research in these areas.

A major strength of our article is the dual nature in which the literature review was combined with a thoroughly conducted review of current cancer survivorship research efforts. This approach, it is hoped, provides the reader with a sense of not only historical accomplishments in this field but also the present and near-future state of cancer survivorship research. Limitations to our article include exclusively focusing on NCI CCs when compiling current research projects in cancer survivorship while excluding efforts being conducted by other institutions. In addition, a limitation may potentially be the use of search terms and phrases in our PubMed and MEDLINE literature review searches and NIH RePORTER query that unintentionally excluded some of the relevant literature and current research projects being conducted in cancer

survivorship research. Furthermore, contribution of this study to understanding the needs of the cancer survivorship population is also constrained by the intentional exclusion of economic and dissemination studies from this review. Although this allowed the review to focus on content areas affecting the health and quality of lives of survivors, it limited the scope of this review in regard to the implementation of such survivorship research.

In summary, survivorship research has grown over the past 3 decades, as has the population of survivors. The establishment of the Office of Cancer Survivorship has contributed greatly to the expansion of research in this area. There are many opportunities to explore the myriad of issues survivors of all cancers experience, and more NCI CCs should include these types of research studies in their portfolios. All cancers—not just breast cancer—need attention. Research needs to expand in 2 of major areas of research focus—prevention/early detection and late effects—as more survivors are living longer and face the risk of late effects, recurrence, and

second cancers. Qualitative studies have an important place in cancer survivorship research, as they help identify the issues survivors face as well as how to intervene on problems or encourage healthier lifestyles. In addition, intervention studies, although more costly, need to be initiated to change the prevalence of late effects and improve healthy lifestyles. As the population of cancer survivors continues to grow, this area of research will need to grow to keep up with the needs of this population.

#### Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were reported.

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# BLOOD CANCER DISCOVERY

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