Published OnlineFirst January 17, 2017; DOI: 10.1158/1055-9965.EPI-16-1023

Research Article

Cancer Epidemiology, Biomarkers & Prevention

# Trends in Radiation Therapy among Cancer Survivors in the United States, 2000–2030

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## Abstract

**Background:** Although the number of cancer survivors has increased substantially over the past several decades, the composition of survivors treated with radiotherapy is not well defined. Radiotherapy carries unique long-term toxicity risks for cancer survivors. This study describes the current estimates and future projections of the epidemiology of 5-year cancer survivors who receive radiation therapy.

**Methods:** We used cancer incidence and survival data from the Surveillance, Epidemiology, and End-Results (SEER) database linked to U.S. Census data to estimate the number of 5-year cancer survivors treated with radiation between 2000 and 2030. Future projections assumed continuing incidence and survival trends based on historical rates.

**Results:** In 2016, there were an estimated 3.05 million cancer survivors treated with radiation, accounting for 29% of all cancer survivors. The number of radiation-treated cancer survivors is projected to reach 3.38 million by 2020 and 4.17 million by 2030. In 2016, breast (40%) and prostate cancer (23%) composed the majority of radiation-treated survivors, followed by head and neck cancer (5.8%), lymphoma (5.6%), uterine (3.9%), and rectal cancer (3.8%). The percentage of 70 years or older radiation-treated survivors steadily increased between 2000 and 2030.

**Conclusions:** The next several years are projected to see a large increase in the number of cancer survivors treated with radiation.

**Impact:** This group of cancer survivors has unique needs given the long-term risks of radiation, and increased research and awareness are required to optimize health of this growing population. *Cancer Epidemiol Biomarkers Prev; 26(6); 963–70. ©2017 AACR.*

## Introduction

The number of cancer survivors in the United States has steadily increased over the past several decades, reaching an estimated 15.5 million individuals in 2016 (1). Of these, 10.3 million survivors (two thirds) were alive 5 years or more following their cancer diagnosis. The demographics of cancer survivors are also changing, with 63% of survivors projected to be 65 years or older by 2020 (2). These trends reflect improved cancer survival and underlying shifts in the age distribution of the U.S. population (1, 3). The expanding number and aging of cancer survivors are expected to increase national health expenditures due to a greater comorbidity burden compounded by the long-term demand for medical care associated with complications of cancer therapy (3).

Radiation therapy plays a central role in the management of cancer. Unlike other treatment modalities, the most burdensome toxicities of radiation often manifest years after treatment. Reducing the long-term late effects of radiation is a central research initiative within radiation oncology; however, the epidemiology of the cancer survivors who were treated with radiation is poorly defined. In this study, we use cancer registry and census data to describe and project trends in the population of radiation-treated, 5-year cancer survivors from 2000 projected through 2030.

## Materials and Methods

### Data sources

Cancer incidence data were obtained from the National Cancer Institute's (NCI's) Surveillance, Epidemiology, and End Results (SEER) database. SEER collects data from cancer registries across the United States and includes information about all incident cases of cancer within a defined population-based region. We studied the original 9 SEER registries (Utah, Hawaii, Iowa, Connecticut, New Mexico, and the greater areas of Detroit, San Francisco-Oakland, Atlanta, and Seattle-Puget Sound, representing about 9% of the population), as these contain data from the beginning of the SEER program in 1973 (3). We analyzed cases from 1975 (due to under-reporting in 1973 and 1974) through 2013 (the most recent year available). We categorized cases into the following 21 cancer sites: anus, bladder/kidney, bones and soft tissue, brain and other nervous system, breast, cervix, colon, esophagus, head and neck, leukemia, lung, lymphoma, myeloma, pancreas and hepatobiliary, prostate, rectum, skin excluding basal and squamous, stomach, uterus, testis, and other. We considered only the first diagnosed malignant tumor and excluded nonmalignant tumors. SEER records the delivery of radiation only when administered during the first course of treatment for an incident cancer. The definition of radiation in this study included either

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**Note:** Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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**doi:** 10.1158/1055-9965.EPI-16-1023

Published OnlineFirst January 17, 2017; DOI: 10.1158/1055-9965.EPI-16-1023



external beam radiation (any modality) or brachytherapy and excluded radioisotopes.

Population data were obtained from the U.S. Census intercensal population estimates for each calendar year, sex, and age (single-year), including projections to 2030. Population projections are calculated from the most recent decennial census (2010) and incorporate assumptions about future birth rates, death rates, and international migration patterns (4). All-cause mortality rates were obtained from the Social Security Administration.

**Prevalence calculations**

We used the Prevalence Incidence Approach Model (PIAMOD) to estimate prevalence using trends in cancer incidence, cancer survival, and all-cause mortality (3, 5). The PIAMOD approach uses incidence and relative cancer survival rates obtained from registry data to create projected estimates of incidence and survival beyond the range of known years. In this study, we used SEER data between 1975 and 2013 to calculate age-, sex-, and cancer site–specific incidence rates. We assumed that incidence rates from 2014 to 2030 would follow incidence trends from 2004 to 2013 (the 10 most recent years of data; ref. 3). For each age-, sex-, and site-specific group, we fit a linear equation to the yearly log-transformed incidence rates from SEER between 2004 and 2013 with the following equation

$$\ln(I_{\text{observed}}(y)) = \alpha + \beta y \tag{A}$$

where $I_{\text{observed}}(y)$ represents the observed incidence in year $y$ and $\alpha$ and $\beta$ are regression coefficients. We determined the predicted incidence for years 2014–2030 with the following equation

$$I_{\text{predicted}}(y) = I_{\text{average}} \times \exp(\beta(y - 2004)) \tag{B}$$

where $I_{\text{predicted}}(y)$ is the predicted incidence in year $y$, $I_{\text{average}}$ is the average incidence over the years 2011–2013, and $\beta$ is the regression coefficient from Equation (A). This approach to calculating predicted incidence has the advantage of incorporating historic incidence trends while using the most recent 3-year average incidence as an anchor point for the prediction.

Observed survival was determined from the SEER-9 data, and expected survival was calculated from all-cause mortality data from the Social Security Administration. To allow for survival projections after 2013, we fit a mixture survival model to the existing data (5). The mixture survival model is a parametric model that assumes a fraction of the cancer cohort will be "cured" of cancer and experience the same risk of death as the non-cancer population. For the mixture survival model, we assumed that among those who die of cancer, their survival time would follow a Weibull distribution. The relative survival $S_{\text{relative}}(t,y)$ at time $t$ for patients diagnosed with cancer in year $y$ was defined as

$$S_{\text{relative}}(t, y) = P(y) + (1 - P(y)) \times S_{\text{cancer}}(t, y) \tag{C}$$

where $P(y)$ represents the fraction of cured patients in year $y$, represented by

$$P(y) = \frac{1}{(1 + a \times \exp(b(y - y_0)))} \tag{D}$$

and $S_{\text{cancer}}(t,y)$ represents cancer-specific survival at time $t$ in year $y$ per the Weibull distribution (3, 6)

$$S_{\text{cancer}}(t, y) = \exp(-(t \times c \times \exp(d(y - y_0)))^{e}) \tag{E}$$

In the above equations, $y_0$ represents an arbitrary reference year (1975) and parameters $a$, $b$, $c$, $d$, and $e$ represent regression parameters from the model. The above mixture survival model was fit for each disease site, sex, and age group (0–44, 45–54, 55–64, 65–74, and 75–84 years old; ref. 3). The above relative survival equations require closed age ranges; therefore, patients older than 85 years were assumed to have the same relative survival as the 75–84 age group.

Total and projected prevalence were determined by projecting the above age-, sex-, and site-specific incidence and relative survival estimates onto U.S. census data. Our primary analysis as presented focused on radiation-treated survivors alive a minimum of 5 years, although secondary analyses evaluated different lengths of minimum survivorship ranging from 1 to 10 years (Supplementary Table S1). Our projection of survivor numbers assume that incidence and survival trends would continue based on historical trends, per Equations (B) and (C). We tested 3 other scenarios in a sensitivity analysis where we assumed (i) constant incidence, (ii) constant relative survival, and (iii) both constant incidence and constant relative survival. In these sensitivity analyses, we assumed that the "constant incidence" scenario would use the average incidence from 2011 to 2013 [$I_{\text{average}}$ from Equation (A)] for years 2014 through 2030. In the "constant relative survival" scenario, we used the relative survival from the year 2013 (last known year) for years 2014 through 2030. The sensitivity analyses are presented in Supplementary Table S2. All data analysis was performed with SAS v9.4 (SAS Institute).

## Results

**Total numbers of radiation-treated cancer survivors**

In 2016, there were an estimated 10.5 million 5-year cancer survivors, of whom 3.05 million received radiation therapy (Fig. 1A). The number of radiation-treated survivors is projected to reach 3.38 million by 2020 and 4.17 million by 2030. In 2016, radiation-treated survivors constituted 29% of all cancer survivors (Fig. 1B). The fraction of all cancer survivors who received radiation increased from 24% in 2000 to a projected maximum of 29% in 2020. After 2020, the fraction of radiation-treated survivors is projected to slightly decline to 28% by 2030.

**By cancer site**

The absolute number of radiation-treated survivors increased from 2000 to 2030 for most cancer sites (Table 1, Fig. 2, and Supplementary Table S2) with the largest absolute increases coming from breast and prostate cancer. In 2016, there were an estimated 1.25 million radiation-treated breast cancer survivors and 713,000 radiation-treated prostate cancer survivors. The number of radiation-treated breast cancer survivors increased steadily from 2000, and by 2030, this number is projected to reach 2.01 million patients. The fraction of breast cancer survivors treated with radiation increased from 29% in 2000 to 54% in 2016, reaching 60% by 2030. The number of radiation-treated prostate cancer survivors increased from 266,000 in 2000 to a projected maximum of 721,000 in 2020, after which the number is projected to decline to 627,000 in 2030.

In lymphoma, cervical, and brain cancer, the absolute number of radiation-treated survivors is projected to increase but the

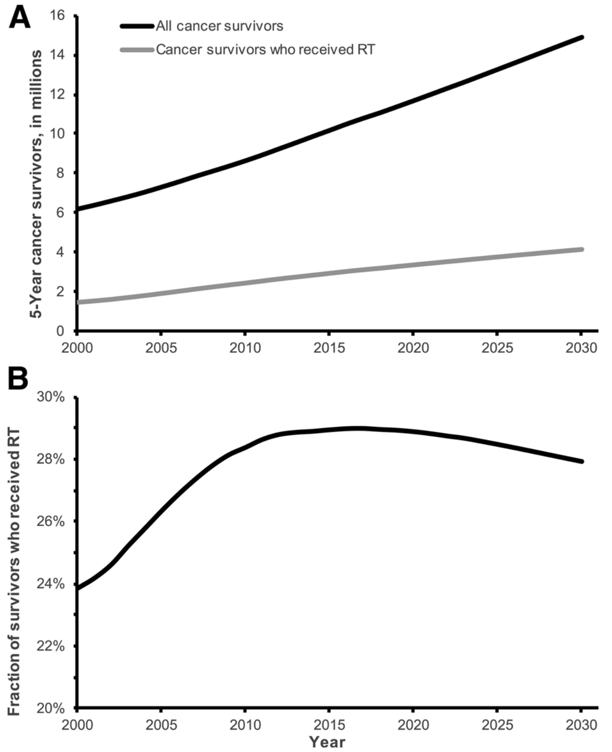


**Figure 1.**
Number and percentage of 5-year cancer survivors between 2000 and 2030. **A,** Total number of 5-year cancer survivors and the number who received radiation therapy. **B,** Proportion of all cancer survivors who received radiation therapy (RT).

fraction of cancer survivors treated with radiation is projected to decrease. For example, in 2000, there were 135,000 radiation-treated lymphoma survivors which constituted 42% of all lymphoma survivors. By 2030, the number of radiation-treated lymphoma survivors is projected to reach 234,000, but the fraction of survivors treated with radiation will decrease to 25%. With head and neck, rectal, and lung cancer, the absolute number and fraction of cancer survivors treated with radiation are both projected to increase. In head and neck cancer, there were 105,000 radiation-treated survivors (47% of all head and neck cancer survivors) in 2000, and by 2030, this increases to 242,000 and 56%.

### By age group

The age distribution of radiation-treated cancer survivors has shifted steadily toward older ages (Table 2 and Fig. 3). In 2016, an estimated 1.59 million radiation-treated survivors were older than 70 years, representing 52% of all radiation-treated survivors. This number increases to 2.70 million by 2030, constituting 65% of all radiation-treated survivors. The absolute number of radiation-treated survivors younger than 70 years is projected to remain relatively stable over the study period (Fig. 3A), although the fraction is projected to decrease substantially (Fig. 3B). Similarly, the relative number of pediatric and young adult radiation-treated survivors (those younger than 40 years) is projected to decrease from 2.8% of all radiation-treated survivors in 2016 to 2.3% in 2030.

### By sex

The projected sex distribution of radiation-treated cancer survivors shifts toward females for all age groups (Table 2). The total number of female radiation-treated survivors is projected to increase from 1.78 million in 2016 to 2.75 million in 2030. Between 2000 and 2016, the fraction of female radiation-treated survivors remained stable at 58% and then is projected to increase to 66% in 2030.

## Discussion

The purpose of this study was to describe the landscape of 5-year cancer survivors treated with radiation therapy. The number and composition of cancer survivors who receive radiation has

**Table 1.** Number of cancer survivors who received radiation, by cancer site

| | Radiation-treated cancer survivors in thousands (% of all site-specific cancer survivors) | | | | |
|---|---|---|---|---|---|
| **Site** | **2000** | **2010** | **2016** | **2020** | **2030** |
| All sites | 1,477 (24) | 2,454.5 (28) | 3,045.1 (29) | 3,378.4 (29) | 4,166 (28) |
| Breast | 396.9 (29) | 933.9 (48) | 1,247.1 (54) | 1,465.5 (57) | 2,011 (60) |
| Prostate | 265.9 (31) | 568.5 (36) | 712.5 (35) | 720.5 (33) | 627.2 (27) |
| Head and neck | 104.6 (47) | 129.6 (53) | 157.5 (55) | 179.8 (56) | 241.8 (56) |
| Lymphoma | 135.3 (42) | 176.3 (37) | 199.5 (33) | 211.9 (31) | 233.7 (25) |
| Uterus | 150.1 (35) | 115.9 (27) | 115.2 (24) | 123.3 (23) | 163.6 (21) |
| Rectal | 41.2 (23) | 76.1 (32) | 101.2 (37) | 118.2 (39) | 160 (42) |
| Other | 96.1 (16) | 95 (12) | 96.7 (10) | 99.7 (9) | 115.1 (7) |
| Lung | 26.5 (16) | 38.7 (18) | 48.6 (21) | 57.2 (23) | 89.3 (31) |
| Cervix | 61.1 (30) | 56.9 (28) | 57.8 (28) | 60 (29) | 70.7 (32) |
| Bones and soft tissues | 22.9 (27) | 33.9 (29) | 42.1 (31) | 48.6 (32) | 69.1 (35) |
| Brain and other nervous system | 39.9 (59) | 46.6 (48) | 51.5 (43) | 55.4 (41) | 68.5 (37) |
| Testis | 53.8 (45) | 75.7 (43) | 81.3 (39) | 79.2 (34) | 67.4 (23) |
| Anus | 8.2 (63) | 16 (76) | 23.8 (79) | 30.8 (81) | 49 (76) |
| Leukemia | 26.5 (23) | 28.5 (15) | 30 (12) | 31.1 (10) | 36.2 (8) |
| Bladder and kidney | 20.7 (5) | 17.4 (3) | 17.5 (3) | 19.1 (2) | 29.4 (3) |
| Myeloma | 4.5 (25) | 8.4 (27) | 12.2 (26) | 15.8 (26) | 28.3 (24) |
| Stomach | 2.9 (8) | 7.4 (16) | 12 (21) | 15.7 (24) | 28.3 (30) |
| Esophagus | 3.4 (51) | 7.1 (53) | 10.6 (53) | 13.9 (55) | 27.4 (61) |
| Pancreas and hepatobiliary | 3 (6) | 5.7 (8) | 8.6 (8) | 11.2 (8) | 21.8 (9) |
| Skin excluding basal and squamous | 3.6 (1) | 6.3 (1) | 9.1 (1) | 11.3 (1) | 18.4 (2) |
| Colon | 10 (2) | 10.7 (2) | 10.4 (2) | 10.2 (2) | 9.7 (1) |

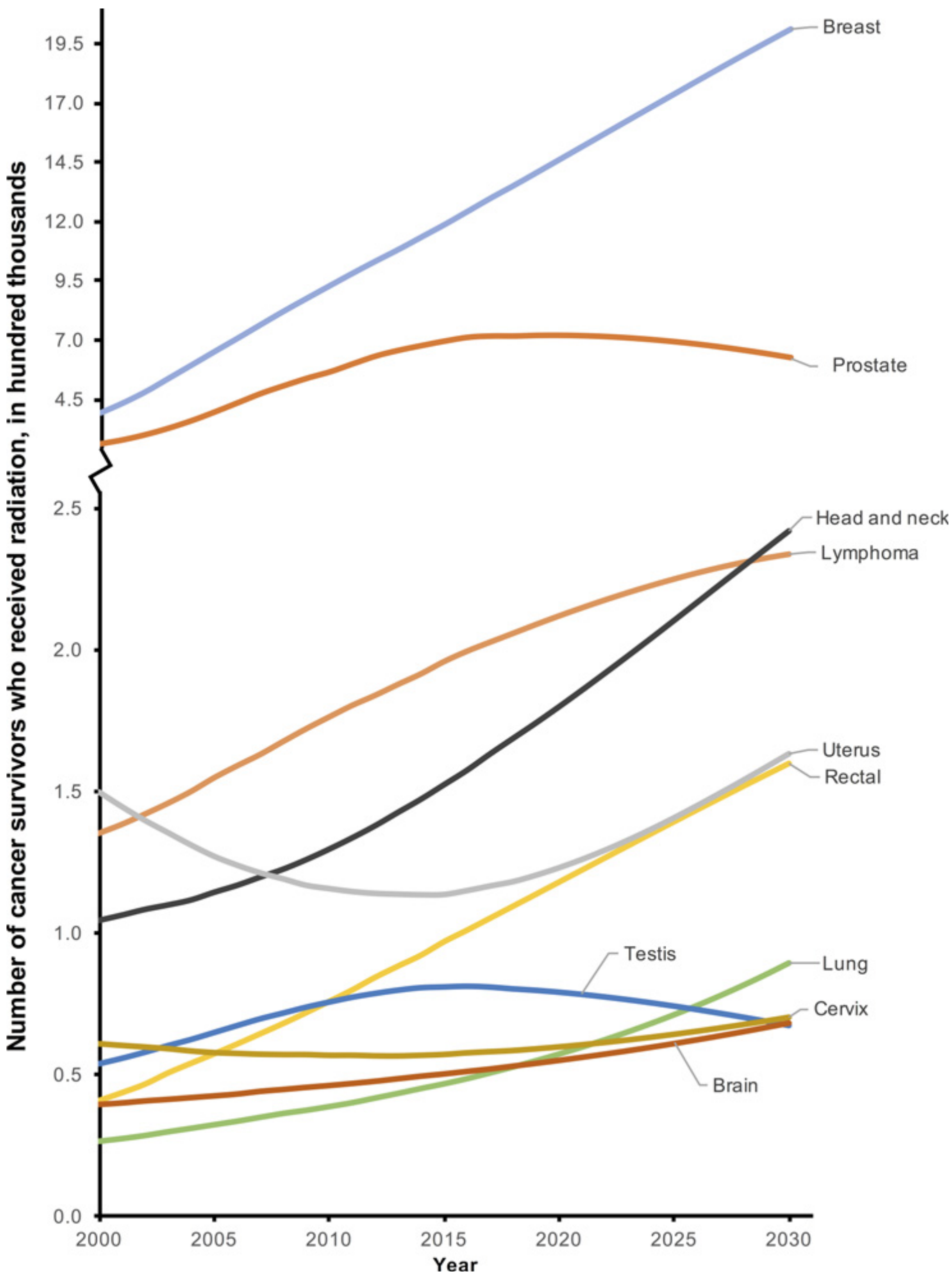


**Figure 2.**
Cancer site–specific distribution of 5-year cancer survivors treated with radiation. This plot presents the absolute number of radiation-treated cancer survivors from 2000–2030 for the 10 most prevalent cancer sites. Note that the *y*-axis changes scale to allow visualization of breast and prostate cancer survivors (top half of plot) as well as trends for cancers with an overall lower prevalence (bottom half of plot).

changed over the past several decades and this will continue in years to come. In 2016, an estimated 3.05 million 5-year cancer survivors received radiation, which we project will increase to 4.17 million survivors by 2030. The wide array of radiation-treated survivors across multiple disease sites emphasizes the broad use of radiation in cancer therapeutics.

Breast cancer accounted for the greatest number of radiation-treated cancer survivors, with 1.25 million survivors in 2016 and a projected steady increase to 2.01 million by 2030. Pivotal trials reported in the 1980s and 1990s established the role of adjuvant radiotherapy after lumpectomy in early-stage breast cancer (7–9), and additional trials demonstrated the benefits of radiation in select subsets of women after mastectomy (10, 11). In our study, the large number of breast cancer survivors arose from the frequent use of radiation in breast cancer coupled to the high incidence and effective treatment for this disease (12). Breast cancer also drove the increased relative proportion of female radiation-treated survivors from 58% in 2000 to 66% in 2030. Our sensitivity analysis demonstrated relative stability in future projections of the number of breast cancer radiation survivors; however, unforeseen changes in breast cancer treatment in the future could influence these estimates.

Prostate cancer comprised the second largest group of radiation-treated cancer survivors in 2016. Unlike in breast cancer, the projected number of radiation-treated prostate cancer survivors is projected to peak in 2020 at 721,000 and decrease thereafter. This decline likely comes from the decreasing

Published OnlineFirst January 17, 2017; DOI: 10.1158/1055-9965.EPI-16-1023



**Table 2.** Number of 5-year radiation-treated cancer survivors by age and sex

| | | Radiation-treated survivors by age and sex, in thousands (% total) | | | | |
|---|---|---|---|---|---|---|
| **Age group, years** | **Sex** | **2000** | **2010** | **2016** | **2020** | **2030** |
| 0–19 | Total | 8.5 | 9 | 9.9 | 10.5 | 14.7 |
| | Male | 4.2 (49) | 4.8 (54) | 5.6 (56) | 5.8 (55) | 8 (55) |
| | Female | 4.3 (51) | 4.1 (46) | 4.3 (44) | 4.7 (45) | 6.6 (45) |
| 20–39 | Total | 81.2 | 72.9 | 74.1 | 72 | 79.2 |
| | Male | 41.7 (51) | 36.3 (50) | 37.3 (50) | 35.5 (49) | 36.4 (46) |
| | Female | 39.5 (49) | 36.6 (50) | 36.7 (50) | 36.6 (51) | 42.8 (54) |
| 40–49 | Total | 133.4 | 160.4 | 146.6 | 142.2 | 147.3 |
| | Male | 57 (43) | 60 (37) | 51.7 (35) | 48.2 (34) | 44.9 (30) |
| | Female | 76.4 (57) | 100.4 (63) | 94.9 (65) | 94.1 (66) | 102.5 (70) |
| 50–59 | Total | 213.9 | 382.9 | 430.4 | 419.1 | 374.9 |
| | Male | 70.5 (33) | 120.3 (31) | 132 (31) | 122.4 (29) | 103.2 (28) |
| | Female | 143.4 (67) | 262.6 (69) | 298.4 (69) | 296.7 (71) | 271.7 (72) |
| 60–69 | Total | 270.2 | 594.1 | 794.5 | 847.2 | 850.7 |
| | Male | 98.8 (37) | 220.6 (37) | 293.1 (37) | 292.5 (35) | 260.4 (31) |
| | Female | 171.4 (63) | 373.5 (63) | 501.4 (63) | 554.7 (65) | 590.4 (69) |
| 70–79 | Total | 427.1 | 639.9 | 858.7 | 1,061 | 1,405.9 |
| | Male | 198.3 (46) | 309.8 (48) | 394 (46) | 447 (42) | 469 (33) |
| | Female | 228.9 (54) | 330.1 (52) | 464.7 (54) | 614 (58) | 936.8 (67) |
| 80+ | Total | 342.7 | 595.4 | 730.9 | 826.2 | 1,293.2 |
| | Male | 144.7 (42) | 281.3 (47) | 351 (48) | 382.9 (46) | 492.3 (38) |
| | Female | 198 (58) | 314.1 (53) | 379.8 (52) | 443.3 (54) | 800.9 (62) |
| All ages | Total | 1,477 | 2,454.5 | 3,045.1 | 3,378.4 | 4,166 |
| | Male | 615.2 (42) | 1,033.1 (42) | 1,264.8 (42) | 1,334.3 (39) | 1,414.2 (34) |
| | Female | 861.8 (58) | 1,421.4 (58) | 1,780.4 (58) | 2,044.1 (61) | 2,751.7 (66) |

NOTE: Age group estimates are based on age at cancer diagnosis.

incidence of prostate cancer, which mostly reflects changes in prostate-specific antigen (PSA) screening (13, 14). In addition, changes in patterns of treatment including more men choosing active surveillance may reduce the number of men undergoing radiation therapy (15, 16). The landscape of prostate cancer survivorship may continue to evolve with the recently published PROTECT study that found similar cancer-specific survival among active surveillance, surgery, and radiation in early-stage prostate cancer (17, 18).

While breast and prostate cancer together account for the majority of all long-term radiation-treated survivors, other disease sites deserve discussion. Head and neck cancer represents a steadily increasing survivor population, and by 2030, it will represent the third most common group of radiation-treated cancer survivors. The shifting epidemiology in head and neck cancer with increasing numbers of human papilloma virus–related cancers will likely alter the demographics of this survivorship population in the years to come (19, 20).

From a survivorship perspective, one must consider the potential for long-term or delayed toxicity from radiation therapy. Breast cancer historically carried a nontrivial risk of cardiovascular mortality from radiation to the heart, but in recent years, this risk has decreased because of improved efforts to spare the heart from radiation (21, 22). However, sparing the heart is often difficult in other thoracic cancers including Hodgkin disease, lung cancer, and esophageal cancer, and these survivors have an increased risk of cardiovascular mortality (23–25). Radiation directed at the pelvis in prostate, rectal, anal, and gynecologic cancers carries risks of long-term rectal and bladder toxicity, as well as risks of sexual dysfunction (26–29). Radiation therapy to the head and neck may be curative for many patients, but radiation in this region bears a risk of toxicities that have the potential to decrease quality and length of life, including salivary dysfunction, radiation fibrosis, dental disease, taste alterations, and osteoradionecrosis (30). Finally, radiation treatment in any part of the body carries a small but real lifetime risk of a secondary radiation–induced malignancy (31, 32).

The increasing age of radiation-treated cancer survivors reflects the increasing age of overall cancer survivors and the aging of the U.S. population (2). The elderly cancer survivor population stands apart with respect to their healthcare needs. Elderly cancer survivors have more functional physical limitations, higher levels of lost productivity, and poorer overall health outcomes (33–35). This population also has higher healthcare costs compared with individuals without cancer (3).

While the number of elderly cancer survivors treated with radiation is projected to increase, the fraction of young adults and pediatric cancer survivors treated with radiation is projected to decrease, consistent with long-term declines in radiation therapy utilization for many pediatric cancers (36). However, with U.S. population growth and improved survival among pediatric patients with cancer, the absolute number of radiation-treated pediatric cancer survivors is expected to increase through 2030. This indicates a continuing need to manage the long-term effects of radiation therapy in pediatric cancer survivors, including increased risks of secondary malignancy, growth deficiency, and neurocognitive deficits (37). As a result, this growing population will continue with special healthcare needs extending into the foreseeable future (38–40).

Our methodology has several limitations. First, while PIAMOD is a standard method to estimate complete cancer prevalence, it requires estimation of incidence and mortality beyond the interval for which data are available (2, 3). In our sensitivity analyses (presented in the Supplementary Material), we found that survivorship predictions for certain disease sites—particularly prostate cancer—depended on assumptions about continuing future incidence and survival trends. While our method relied on projections from historic trends, any future variability in cancer incidence or survival will impact the projected numbers of radiation-treated

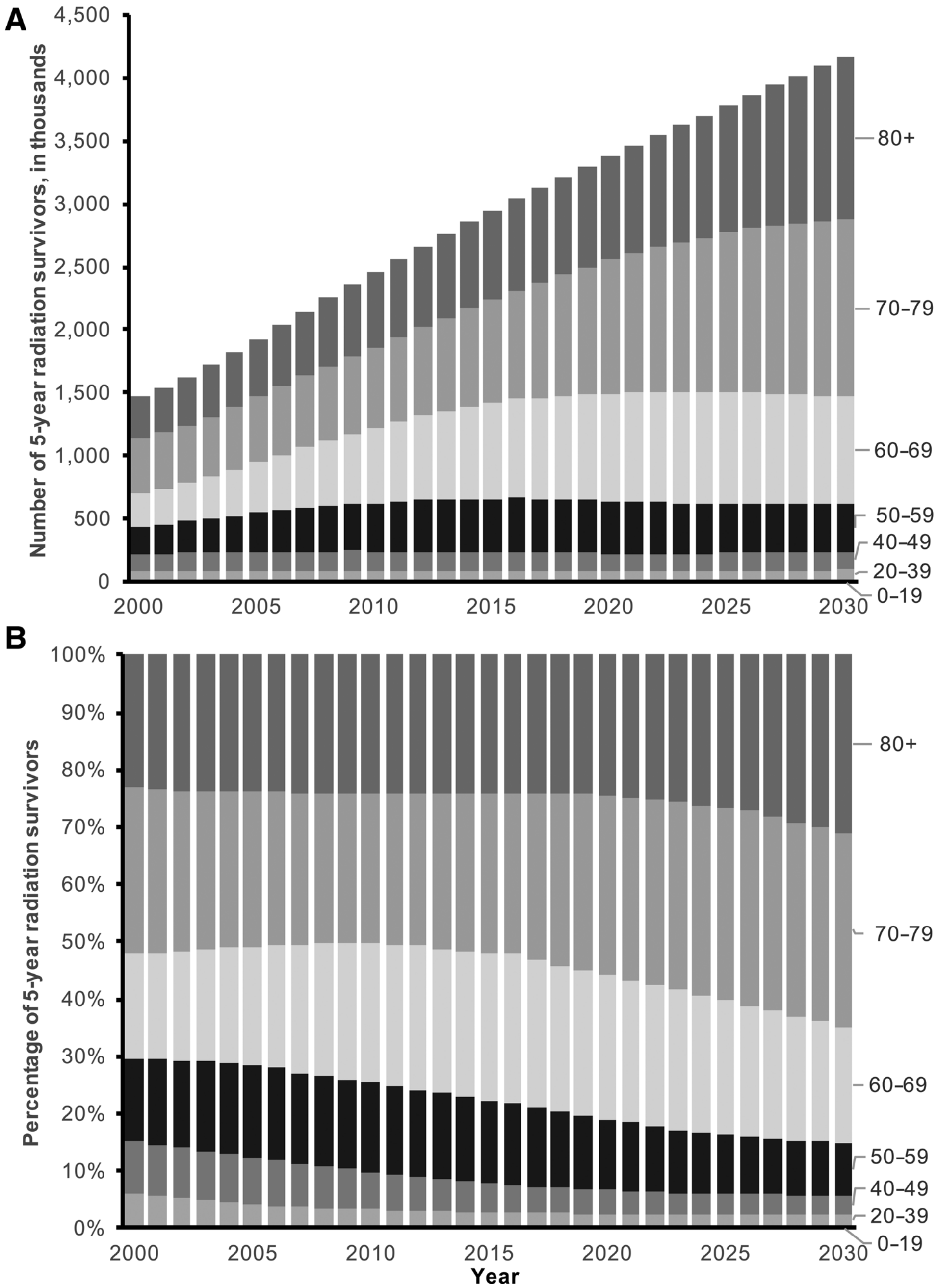


**Figure 3.**
Age distribution of 5-year cancer survivors treated with radiation. This figure shows the absolute number (**A**) and relative proportion (**B**) of 5-year cancer survivors who received radiation therapy between 2000 and 2030 in the United States.

cancer survivors. Second, our projections assume no change in current patterns of radiation therapy utilization that might substantially change our projections. For example, our breast cancer projections assume that radiation therapy will play the same role in local control as it does in current practice. Third, recent studies in breast cancer suggest that SEER may underestimate the true rates of radiation delivery (41, 42). In addition, SEER only records radiation during a patient's first course of treatment, which implies that patients receiving radiation for recurrent or metastatic disease beyond their first course of treatment would not be included. However, patients receiving radiation beyond their first treatment course likely have recurrent or metastatic disease and therefore would be less likely to survive for 5 years or more. Finally, our study included only invasive malignant disease; therefore, patients with noninvasive histologies such as breast ductal carcinoma *in situ* or benign central nervous system tumors would not be included in our survivorship estimates. Together, these limitations suggest that our radiation-treated survivorship estimates may be low compared with the true number of radiation-treated cancer survivors in the United States.

Despite these limitations, this study provides a description of current and future trends in the population of cancer survivors who received radiation. From a survivorship perspective, radiation represents a unique challenge in that long-term side effects may take years to manifest. Increased research and awareness of survivorship issues are needed to care for this growing segment of the population.

## Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

## Authors' Contributions

**Conception and design:** A.K. Bryant, J.D. Murphy
**Development of methodology:** A.K. Bryant, J.D. Murphy
**Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.):** A.K. Bryant, J.D. Murphy
**Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis):** A.K. Bryant, L.K. Mell, J.D. Murphy
**Writing, review, and/or revision of the manuscript:** A.K. Bryant, M. Banegas, M.E. Martinez, L.K. Mell, J.D. Murphy
**Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases):** A.K. Bryant, L.K. Mell, J.D. Murphy
**Study supervision:** J.D. Murphy

## Grant Support

This study was supported by NIHTL1TR00098 (A.K. Bryant).

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Received December 14, 2016; revised January 9, 2017; accepted January 10, 2017; published OnlineFirst January 17, 2017.

## References

1. American Cancer Society. Cancer treatment & survivorship facts & figures, 2016–2017. Atlanta, GA: American Cancer Society; 2016.
2. Parry C, Kent EE, Mariotto AB, Alfano CM, Rowland JH. Cancer survivors : a booming population. Cancer Epidemiol Biomarkers Prev 2011;20:1996–2005.
3. Mariotto AB, Robin Yabroff K, Shao Y, Feuer EJ, Brown ML. Projections of the cost of cancer care in the United States: 2010–2020. J Natl Cancer Inst 2011;103:117–28.
4. US Census Bureau. Methodology, assumptions, and inputs for the 2014 National Projections [Internet]. December 2014. Accessed July 1, 2016. Available from: http://www.census.gov/population/projections/files/methodology/methodstatement14.pdf.
5. Verdecchia A, De Angelis G, Capocaccia R. Estimation and projections of cancer prevalence from cancer registry data. Stat Med 2002; 21:3511–26.
6. Weibull W. A statistical distribution function of wide applicability. J Appl Mech 1951;18:293–7.
7. Fisher B, Anderson S, Redmond CK, Wolmark N, Wickerham DL, Cronin WM. Reanalysis and results after 12 years of follow-up in a randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer. N Engl J Med 1995;333:1456–61.
8. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002;347:1233–41.
9. Bernard F, Carol R, Roger P, Richard M, Norman W, Lawrence W, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. N Engl J Med 1989;320:822–8.
10. Bernard F, Madeline B, Richard M, Roger P, Yosef P, Carol R, et al. Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. N Engl J Med 1985;312:665–73.
11. Group EBCTC. Effects of radiotherapy and surgery in early breast cancer — an overview of the randomized trials. N Engl J Med 1995;333: 1444–56.
12. National Cancer Institute. SEER cancer statistics factsheets: female breast cancer. 2016. Accessed August 1, 2016. Available from: https://seer.cancer.gov/statfacts/html/breast.html.
13. Sammon JD, Abdollah F, Choueiri TK, Kantoff PW, Nguyen PL, Menon M, et al. Prostate-specific antigen screening after 2012 US Preventive Services Task Force Recommendations. JAMA 2015;314:2077.
14. Jemal A, Fedewa SA, Ma J, Siegel R, Lin CC, Brawley O, et al. Prostate cancer incidence and PSA testing patterns in relation to USPSTF screening recommendations. JAMA 2015;314:2054–61.
15. Cooperberg MR, Carroll PR. Trends in management for patients with localized prostate cancer, 1990–2013. JAMA 2015;314:80–2.
16. Ingimarsson JP, Celaya MO, Laviolette M, Rees JR, Hyams ES. Trends in initial management of prostate cancer in New Hampshire. Cancer Causes Control 2015;26:923–9.
17. Hamdy FC, Donovan JL, Lane JA, Mason M, Metcalfe C, Holding P, et al. 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. N Engl J Med 2016;375:1415–24.
18. Donovan JL, Hamdy FC, Lane JA, Mason M, Metcalfe C, Walsh E, et al. Patient-reported outcomes after monitoring, surgery, or radiotherapy for prostate cancer. N Engl J Med 2016;375:1425–37.
19. Young D, Xiao CC, Murphy B, Moore M, Fakhry C, Day TA. Increase in head and neck cancer in younger patients due to human papillomavirus (HPV). Oral Oncol 2015;51:727–30.
20. Deschler DG, Richmon JD, Khariwala SS, Ferris RL, Wang MB. The "New" head and neck cancer patient-young, nonsmoker, nondrinker, and HPV positive: evaluation. Otolaryngol Head Neck Surg 2014;151:12–7.
21. Giordano SH, Kuo Y-F, Freeman JL, Buchholz TA, Hortobagyi GN, Goodwin JS. Risk of cardiac death after adjuvant radiotherapy for breast cancer. J Natl Cancer Inst 2005;97:419–24.
22. Darby SC, Ewertz M, McGale P, Bennet AM, Blom-Goldman U, Brønnum D, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer supplementary information. N Engl J Med 2013;368:987–98.
23. Tucker SL, Liu A, Gomez D, Tang LL, Allen P, Yang J, et al. Impact of heart and lung dose on early survival in patients with non-small cell lung cancer treated with chemoradiation. Radiother Oncol 2016;119:495–500.
24. Aleman BMP, van den Belt-Dusebout AW, De Bruin ML, van 't Veer MB, Baaijens MHA, de Boer JP, et al. Late cardiotoxicity after treatment for Hodgkin lymphoma. Blood 2007;109:1878–86.
25. Frandsen J, Boothe D, Gaffney DK, Wilson BD, Lloyd S. Increased risk of death due to heart disease after radiotherapy for esophageal cancer. J Gastrointest Oncol 2015;6:516–23.
26. Kao M-S. Intestinal complications of radiotherapy in gynecologic malignancy — clinical presentation and management. Int J Gynecol Obstet 1995;49:S69–75.
27. Coia LR, Myerson RJ, Tepper JE. Late effects of radiation therapy on the gastrointestinal tract. Int J Radiat Oncol 1995;31:1213–36.
28. Mitchell SE, Mendenhall WM, Zlotecki RA, Carroll RR. Squamous cell carcinoma of the anal canal. Int J Radiat Oncol 2001;49:1007–13.
29. Viswanathan AN, Lee LJ, Eswara JR, Horowitz NS, Konstantinopoulos PA, Mirabeau-Beale KL, et al. Complications of pelvic radiation in patients treated for gynecologic malignancies. Cancer 2014;120:3870–83.
30. Cooper JS, Fu K, Marks J, Silverman S. Late effects of radiation therapy in the head and neck region. Int J Radiat Oncol 1995;31:1141–64.
31. Wallis CJD, Mahar AL, Choo R, Herschorn S, Kodama RT, Shah PS, et al. Second malignancies after radiotherapy for prostate cancer: systematic review and meta-analysis. BMJ 2016;352:i851.
32. Kumar S. Second malignant neoplasms following radiotherapy. Int J Environ Res Public Health 2012;9:4744–59.

33. Sweeney C, Schmitz KH, Lazovich D, Virnig BA, Wallace RB, Folsom AR. Functional limitations in elderly female cancer survivors. J Natl Cancer Inst 2006;98:521–9.
34. Yabroff KR, Lawrence WF, Clauser S, Davis WW, Brown ML. Burden of illness in cancer survivors: findings from a population-based national sample. J Natl Cancer Inst 2004;96:1322–30.
35. Keating NL, Nørredam M, Landrum MB, Huskamp HA, Meara E. Physical and mental health status of older long-term cancer survivors. J Am Geriatr Soc 2005;53:2145–52.
36. Jairam V, Roberts KB, Yu JB. Historical trends in the use of radiation for pediatric cancers: 1973–2008. Int J Radiat Oncol Biol Phys 2013;85:e151–5.
37. Armstrong GT, Stovall M, Robison LL. Long-term effects of radiation exposure among adult survivors of childhood cancer: results from the childhood cancer survivor study. Radiat Res 2010;174:840–50.
38. Oeffinger KC, Mertens AC, Hudson MM, Gurney JG, Casillas J, Chen H, et al. Health care of young adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. Ann Fam Med 2004;2:61–70.
39. Rebholz CE, Reulen RC, Toogood AA, Frobisher C, Lancashire ER, Winter DL, et al. Health care use of long-term survivors of childhood cancer: the British Childhood Cancer Survivor Study. J Clin Oncol 2011;29:4181–8.
40. Kimberg C, Klosky JL, Zhang N, Brinkman TM, Ness KK, Srivastava DK, et al. Predictors of healthcare utilization in adult survivors of childhood cancer exposed to CNS-directed therapy. Cancer 2015; 121:774–82.
41. Jagsi R, Abrahamse P, Hawley ST, Graff JJ, Hamilton AS, Katz SJ. Under-ascertainment of radiotherapy receipt in SEER registry data. Cancer 2012;118:333–41.
42. Walker GV. Muddy Water? Variation in reporting receipt of breast cancer radiation therapy by population-based tumor registries. Int J Radiat Oncol Biol Phys 2013;86:686–93.

Published OnlineFirst January 17, 2017; DOI: 10.1158/1055-9965.EPI-16-1023

Cancer Epidemiology, Biomarkers & Prevention



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*Cancer Epidemiol Biomarkers Prev* 2017;26:963-970. Published OnlineFirst January 17, 2017.