Published in final edited form as:

J Pediatr Hematol Oncol. 2016 August ; 38(6): 423–428. doi:10.1097/MPH.0000000000000548.

Early post-therapy hospitalizations among survivors of childhood leukemia and lymphoma

Andrew B. Smitherman[1,2,†], **Tania M. Wilkins**[3], **Julie Blatt**[1,2], and **Stacie B. Dusetzina**[2,3,4]

[1]The Division of Pediatric Hematology & Oncology, University of North Carolina, Chapel Hill, NC

[2]UNC Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC

[3]UNC Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC

[4]The UNC Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC

Abstract

Long-term survivors of childhood cancers are at increased risk for hospitalization. To test the hypothesis that many treatment-related morbidities are identifiable in the early post-therapy period, we determined the rates and causes for hospitalization among survivors of leukemia and lymphoma during the first three years post-therapy. Using a health plan claims database, we identified patients aged 0-21 years-old treated for leukemia or lymphoma from 2000-2010. Survivors were matched 10:1 with similar children without a history of cancer. Hospitalization rates over three years were compared using Cox proportional hazards regression and risks of cause-specific hospitalization were compared using log-binomial models. Nineteen percent of childhood leukemia and lymphoma survivors were hospitalized in the first three years off therapy. Leukemia survivors (N=529) experienced over six times (HR: 6.3, 95%CI: 4.9-8.0) and lymphoma survivors (N=454) over three times the hospitalization rate of controls (HR: 3.2, 95%CI: 2.5-4.2). Compared with children without a cancer history, survivors were at increased risk for hospitalization due to infectious causes (leukemia RR: 60.0, 95%CI: 23.4-154.0; lymphoma RR: 10.0, 95%CI: 4.4-22.9). Additionally, lymphoma survivors were at increased risk for cardiovascular-(RR: 15.0, 95%CI: 5.4-42.0) and pulmonary-(RR: 8.1, 95%CI: 3.9-16.8) related hospitalizations. These findings highlight the morbidity experienced by survivors and suggest that treatment-associated complications may be emerging soon after therapy completion.

Keywords

childhood cancer survivor; leukemia; lymphoma; hospitalization; administrative data

Introduction

With increased survival for childhood cancers, there is a growing population of childhood cancer survivors estimated to be nearly 380,000 individuals in the United States in 2010.[1]

[†]Correspondence to Andrew B. Smitherman, Division of Pediatric Hematology & Oncology, 170 Manning Drive, 1185A Physicians' Office Building, CB#7236, Chapel Hill, NC 27599-7236; andrew_smitherman@med.unc.edu; 919-966-1178 (phone); 919-966-7629 (fax).

While the incidence of childhood cancers is relatively low compared to that in adults, more than 80% of childhood cancer patients will become long-term survivors.[2] Approximately two-thirds of survivors will have at least one major medical problem related to their prior therapy, and one-third will experience a complication that is severe or life-threatening.[3] In 2005 the Institute of Medicine recommended lifelong risk-based medical care for all survivors of cancer as many medical conditions in this population can be avoided or limited by screening and early detection.[4]

Studies have suggested that survivors are not receiving the risk-based follow-up care necessary to identify and prevent cancer-related comorbidities.[5-7] Comorbidities associated with prior treatment may lead to increased rates of high-acuity health care encounters such as hospitalizations. Prior studies have found an increased risk for hospitalization and longer lengths of stay among long-term survivors of childhood cancer.[8-12] The patterns of hospitalizations among childhood cancer survivors in the immediate period following completion of therapy have not been reported. Hospitalizations provide an indicator for the level of medical morbidities experienced by a population. A better understanding of early hospitalizations may allow for the identification of treatment-related morbidities that already are developing soon after completion of therapy.

The purpose of this study was to determine the hospitalization rates for childhood leukemia and lymphoma survivors in the first three years post-therapy as compared with a cohort of matched children without a history of cancer. We hypothesize that, despite having completed active cancer treatment, survivors continue to require more high-acuity medical care than children without a history of cancer due to morbidities arising in the early post-therapy period. Secondarily, we sought to describe the causes for hospitalizations in order to improve our understanding of the particular types of morbidities developing during this time period.

Materials and Methods

Patient Cohort

Using the Truven Health Marketscan® Commercial Claims and Encounters database,[13] we identified pediatric and young adult patients (21 years-old and younger) treated for leukemia or lymphoma from January 1, 2000 to December 31, 2010. This data source includes de-identified inpatient, outpatient and pharmacy insurance claims data for over 50 million individuals and their dependents who are insured by commercial health plans in the United States. We identified children with leukemia (acute lymphoblastic and acute myeloid leukemias) and lymphoma (Hodgkin and non-Hodgkin lymphomas) using the AHRQ Clinical Classifications Software (CCS)[14] matched to International Classification of Diseases, ninth revision (ICD-9) codes for leukemia and lymphoma (CCS codes 37-38 for lymphomas and 39 for leukemia). Due to small sample sizes, patients were not stratified beyond the groupings of leukemia and lymphoma. We further restricted our cohort to those patients with Healthcare Common Procedure Coding System (HCPCS) codes or Current Procedural Terminology (CPT) codes and outpatient prescription drug claims for appropriate chemotherapy or radiation therapy (Supplemental Table). End of treatment (EOT) was defined at the last observed chemotherapy or radiation therapy date. This included the date

of last inpatient or outpatient claim use of chemotherapy or radiation therapy or the last fill date for oral chemotherapy. Patients were required to have three years of continuous health plan enrollment from the EOT in order to capture post-therapy hospitalizations. Patients who relapsed during the study period and underwent subsequent therapy were not included due to our defining the end of therapy based on the cessation of billing codes for treatment. Persons having ICD-9 codes for both leukemia and lymphoma were excluded. Individuals with procedural billing codes associated with hematopoietic stem cell transplant were excluded from the analysis population. After all exclusions there were 983 children included in our cancer cohort.

We selected a comparison cohort of children in the database without claims for a cancer diagnosis matched for three year continuous enrollment profile, age, sex and geographic region. Separate comparison cohorts were created for the leukemia and lymphoma cohorts. Controls were randomly sampled 10:1 from the MarketScan database.

The study design was reviewed by the UNC IRB and determined to qualify for a waiver as Not Human Subjects Research (NHSR).

Measures—The primary study outcome was hospitalization. Hospitalizations per person and time to first hospitalization were determined during the three years post-therapy. Hospitalization incidence rates were determined for the total three year period (reported as events per 100 patient-years) as well as for 6 month increments in order to determine trends following the end of treatment. Because hospitalization rates may be affected by recently completed therapy or by continued use of oral medications beyond the assigned EOT, we excluded hospitalizations occurring in the first month following the EOT. Length of stay per hospitalization was also determined for each admission. The diagnoses associated with each hospitalization were classified using the major diagnostic criteria (MDC) from the MarketScan inpatient database. This standardized method of admission categorization is based on both primary diagnosis classification and procedure coding.

Statistical Analysis—Demographic variables were compared between cancer and control cohorts using chi-square and student t-tests as appropriate. The median number of hospitalizations per person and length of stay were calculated. Cox proportional hazards models were used to estimate the risk for hospitalization over the three years post-therapy for survivors and matched controls. Log-binomial models were used to assess the risk for cause-specific hospitalization between survivors and matched cohorts. Statistical analyses were performed using SAS® Version 9.4 software (SAS Institute, Inc., Cary, NC).

Sensitivity Analyses—A sensitivity analysis sampling at a 25:1 ratio was performed to confirm observed hospitalization rates among the controls. Observed rates were comparable for both sampling populations and were consistent with previously published rates for children and adolescents.[15] For this reason, we proceeded with 10:1 sampling.

Results

Five hundred and twenty-nine survivors of leukemia and 454 survivors of lymphoma were identified. As expected, patients with lymphoma were older than those with leukemia (mean age 15.6 years and 8.7 years, respectively). Fifty-five percent of leukemia survivors and 59% of lymphoma survivors were male. More patients were from the South than from any other region of the US due to health plan participation with the MarketScan database. Most patients were enrolled in a preferred provider organization (PPO) health plan. The number of patients reaching the EOT per year increased by over 10-fold during the study period which is a reflection of the growing number of enrollees within health plans included in MarketScan between 2000 and 2010. Controls were well-matched to the study cohorts (Table 1).

Approximately 20% of leukemia survivors and 18% of lymphoma survivors were hospitalized during the first three years post-therapy. Among leukemia survivors, the incidence rate of hospitalizations was 16.7 versus 1.7 per 100 patient-years for controls. Among lymphoma survivors, the rate of hospitalizations was 11.1 versus 2.7 per 100 patient-years for controls. More hospitalizations (34% among leukemia survivors and 28% among lymphoma survivors) occurred within the first six months following therapy completion than in any other time period. However, a sustained increased rate over the three years of observation was noted among both survivors of leukemia and lymphoma when compared to matched controls (Figure 1).

In adjusted hazard models, survivors of leukemia experienced over six times the rate of hospitalization of controls (HR: 6.3, 95%CI: 4.9-8.0, P<0.0001) and survivors of lymphoma over three times the rate of controls (HR: 3.2, 95%CI: 2.5-4.2, P<0.0001). Survivors and controls who were ever hospitalized tended to be hospitalized once over the three years with median lengths of stay of 3 days for survivors and 2 days for controls (Table 2).

Leukemia and lymphoma survivors also demonstrated increased risk for cause-specific hospitalizations compared to controls (Figure 2). Leukemia survivors were at increased risk of hospitalization for many conditions including infectious (RR: 60.0, 95%CI: 23.4-154.0), blood (RR: 36.0, 95%CI: 13.4-96.6), endocrine (RR: 14.3, 95%CI: 5.5-37.4) and pulmonary (RR: 8.9, 95%CI: 5.2-15.3) disorders. Lymphoma survivors were at increased risk for infections (RR: 10.0, 95%CI: 4.4-22.9), cardiovascular disorders (RR: 15.0, 95%CI: 5.4-42.0) and disorders of the pulmonary system (RR: 8.1, 95%CI: 3.9-16.8). Neither leukemia nor lymphoma survivors were at increased risk for hospitalization due to substance abuse or psychiatric-related conditions.

Discussion

Our findings demonstrate that survivors of childhood leukemia and lymphoma are at a markedly increased risk for hospitalization in the first three years following the completion of therapy with nearly one-fifth of all survivors having at least one hospitalization during this period. We observed that survivors of leukemia experience over six times, and survivors of lymphoma over three times, the hospitalization rate of controls. Once active therapy for

these patients is complete, survivors continue to face a significant health care burden necessitating ongoing high-acuity encounters during the early post-therapy period. Long-term sequelae of cancer treatment (20 to 30 years after treatment) have been well described. Our results suggest that medical complications may arise soon after therapy is completed for some survivors.

Many of the hospitalizations among survivors occurred in the first six months off therapy. Increased hospitalization rates during this time are not surprising as survivors are recovering from the acute effects of treatment. Such hospitalizations may not be indicative of developing long-term morbidities, but rather, of temporary therapy-related complications. However, while the hospitalization rates were highest among survivors in the first six months following therapy completion, the increased rate compared to controls persisted throughout the three-year study period. As patients are recovering from the immunosuppressive and myelosuppressive effects of active therapy, they are clearly at the highest risk for hospitalization in the early post-therapy, but the increased risk remains among survivors.

Our results add to prior studies reporting increased rates of hospitalization among long-term survivors of pediatric cancers. Generally these studies have reported outcomes among survivors more than 10 years off therapy. Increased risks of 1.5 to nearly 5 times that of controls have been reported for all pediatric cancer survivors as well as for specific leukemia and lymphoma subgroups.[8-12] Additionally, survivors of young adult cancers (diagnosis 20-44 years-old) have been observed to have higher hospitalization rates than controls.[16] Comparable to our findings, this study also found that hospitalization rates for survivors decreased with time from diagnosis but remained higher than that among controls for all time periods. Our findings are distinct from these prior studies given our focus on the early post-therapy period. Further, we utilized data from a large population-based insured cohort allowing for deeper understanding of services used among privately-insured children. Our goal was to extend what is known regarding the increased risk for hospitalization among long-term survivors to those who have recently completed active therapy and to describe patterns that might lead to identification of developing post-therapy morbidities.

In addition to an increased overall risk for hospitalization, childhood cancer survivors also experience an increased risk for cause-specific hospitalization due to a wide range of diagnoses. Consistent with prior studies, we found that survivors of both cancer types were at increased risk for hospitalizations due to infectious causes.[10,11] Such a high burden of infectious complications is not surprising given the immunosuppression associated with treatment for leukemia and lymphoma and underscores the importance of limiting potential sources of infection as expeditiously as possible once therapy is complete. One such intervention may be to remove central venous catheters as quickly as possible when transitioning off therapy.

Survivors of leukemia were also at increased risk for hospitalizations due to hematologic disorders. After prolonged therapy, recovery of bone marrow function may take time leading to a susceptibility to cytopenias necessitating hospitalization. One could argue that the hospitalizations associated with infectious and hematologic causes are issues expected to

resolve with reconstitution of a patient's immune system and bone marrow function following completion of therapy. This is consistent with the decline in hospitalizations we noted after the first six months off therapy. However, long-term survivors continue to have a significantly increased risk for hospitalization well beyond three years post-therapy, and infectious and hematologic complications are common causes for hospitalizations even decades following therapy completion.[10,11]This suggests that these issues do not fully resolve with time off therapy and remain a significant contributor to ongoing survivor morbidity.

In addition to infections, we found high rates of cardiovascular, pulmonary, and endocrine complications among cancer survivors. Specifically, lymphoma survivors had significantly increased risk for hospitalizations due to cardiovascular and pulmonary causes – organ systems known to be at risk for ongoing treatment-related toxicities following therapy completion. These morbidities have been primarily reported among long-term survivors[17-22] and are associated with increased long-term hospitalization rates.[10] Our findings suggest that these complications may be developing earlier than previously anticipated among some survivors.

In our analysis, we observed a high rate of hospitalizations for mental health disorders among lymphoma survivors. An increased risk for mental health hospitalization has been previously reported among Danish survivors of childhood cancers.[23] However, when compared to the control group, the hospitalization rates for psychiatric causes we observed were no higher than those of the general pediatric population. Our findings are consistent with other studies that reported no increased risk of psychiatric hospitalization among pediatric cancer survivors[12] and that found an increased risk only among the subset of survivors of brain tumors.[24]

These findings should be interpreted in the context of several limitations. While our study examined hospitalizations among a nationally distributed cohort of survivors, only survivors continuously enrolled in private health care insurance plans were included. Our findings may not represent survivors with public health care insurance coverage or no coverage. A prior study reported that insured survivors and those with household incomes under $20,000 are at increased risk for hospitalization.[10] This suggests that those with public health care coverage may be at increased risk for hospitalization as compared to survivors covered by private health care plans. Consequently, our estimates among privately insured individuals may actually underestimate the true risk among all survivors. Additionally, we only considered survivors of childhood leukemia or lymphoma. We limited our study population for several reasons. Primarily these diagnoses are two of the most prevalent among pediatric patients, yielding suitably large study populations. Additionally, the multimodal treatment for these conditions provides ample opportunity to utilize procedural and treatment codes to confirm the diagnoses and to determine the end of treatment. Examination of hospitalization patterns in the early post-therapy period for survivors of all cancers is a potential future direction. Small sample sizes for certain cancer subtypes precluded further stratification of patients beyond the groupings of leukemia or lymphoma.

Next, we defined end of treatment based on the last observed claim for infused or oral chemotherapy or radiotherapy. Some patients may continue to use oral therapies following the assigned EOT date which may lead to misclassification. In order to limit the inclusion of hospitalizations while patients were undergoing active therapy, we excluded hospitalizations during the first month following the identified end of treatment date.

The secondary analysis of administrative claims data also presents certain limitations. Patient classification and outcomes of interest are dependent on appropriate coding. We have attempted to minimize misclassification by requiring patients to meet multiple criteria for inclusion as survivors – requiring evidence of both diagnoses and procedures for leukemia and lymphoma and their treatment. Due to limitations of the data we are unable to distinguish between primary and secondary cancers, so individuals with relapsed or secondary cancers who completed therapy during our assessment period would be classified similarly to those completing treatment for their initial diagnosis. Although hospitalizations are likely to be accurately identified, reasons for hospitalizations may be less consistently captured. The major diagnosis categories (MDC) provide objective and reproducible indicators for the reasons underlying hospitalizations, but they only offer a general understanding for the cause of the hospitalization at an organ system level and may lack some specificity. For instance, a condition such as pneumonia may be classified as a pulmonary instead of an infectious diagnosis. While this is correct, one may argue that a condition such as pneumonia is primarily secondary to an infectious cause and not a disorder of the lung itself. Finally hospitalizations provide an incomplete picture of medical complications as survivors may develop medical morbidities not severe enough to warrant inpatient hospitalization. Future studies should investigate treatment for less severe morbidites through investigation of patterns of outpatient and prescription drug use.

In conclusion, our findings suggest that pediatric leukemia and lymphoma survivors are at high risk for hospitalization following therapy completion, with the highest risk occurring immediately after the end of treatment but persisting over the first three years post-therapy. Often the focus for patient follow-up encounters during this time is surveillance for disease recurrence. Our findings suggest that attention should also be given to the detection and prevention of treatment-associated morbidities during the early off-therapy period. This could include implementing infection control measures, such as early central catheter removal, and more targeted surveillance with careful attention to obtaining the recommended risk-based screening for treatment-related morbidities even in the early post-therapy period.

Acknowledgments

Dr. Smitherman is a St. Baldrick’s Foundation Fellow and the recipient of a NC Children’s Promise Grant. Dr. Dusetzina is supported by the NIH Building Interdisciplinary Research Careers in Women’s Health (BIRCWH) K12 Program and the North Carolina Translational and Clinical Sciences Institute (UL1TR001111).

References

1. American Cancer Society. Cancer Facts & Figures, 2014: Special Section: Cancer in Children and Adolescents. American Cancer Society; Atlanta: 2014.

2. Howlader, N.; Noone, AM.; Krapcho, M., et al. SEER Cancer Statistics Review, 1975-2012. National Cancer Institute; Bethesda, MD: http://seer.cancer.gov/csr/1975_2012, based on November 2014 SEER data submission, posted to the SEER web site, April 2015. Accessed June 29, 2015
3. Oeffinger KC, Mertens AC, Sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med. 2006; 355(15):1572–1582. [PubMed: 17035650]
4. Hewitt, M.; Greenfield, S.; Stovall, E. From Cancer Patient to Cancer Survivor: Lost in Translation. National Academies Press; Washington, DC: 2006.
5. Shaw AK, Pogany L, Specchley KN, Maunsell E, Barrera M, Mery LS. Use of health care services by survivors of childhood and adolescent cancer in Canada. Cancer. 2006; 106(8):1829–1837. [PubMed: 16541445]
6. Nathan PC, Greenberg ML, Ness KK, et al. Medical care in long-term survivors of childhood cancer: a report from the childhood cancer survivor study. J Clin Oncol. 2008; 26(27):4401–4409. [PubMed: 18802152]
7. Kirchhoff AC, Lyles CR, Fluchel M, Wright J, Leisenring W. Limitations in health care access and utilization among long-term survivors of adolescent and young adult cancer. Cancer. 2012; 118(23): 5964–5972. [PubMed: 23007632]
8. Kirchhoff AC, Fluchel MN, Wright J, et al. Risk of hospitalization for survivors of childhood and adolescent cancer. Cancer Epidemiol Biomarkers Prev. 2014; 23(7):1280–1289. [PubMed: 24925676]
9. Brewster DH, Clark D, Hopkins L, et al. Subsequent hospitalization experience of 5-year survivors of childhood, adolescent, and young adult cancer in Scotland: a population based, retrospective cohort study. Br J Cancer. 2014; 110(5):1342–1350. [PubMed: 24366296]
10. Kurt BA, Nolan VG, Ness KK, et al. Hospitalization rates among survivors of childhood cancer in the childhood cancer survivor study cohort. Pediatr Blood Cancer. 2012; 59(1):126–132. [PubMed: 22180128]
11. Lorenzi MF, Xie L, Rogers PC, Pritchard S, Goddard K, McBride ML. Hospital-related morbidity among childhood cancer survivors in British Columbia, Canada: report of the childhood, adolescent, young adult cancer survivors (CAYACS) program. Int J Cancer. 2011; 128:1624–1631. [PubMed: 21280033]
12. Bradley NME, Lorenzi MF, Abanto Z, et al. Hospitalisations 1998-2000 in a British Columbia population-based cohort of young cancer survivors: report of the childhood/adolescent/young adult cancer survivors (CAYACS) research program. Eur J Cancer. 2010; 46(13):2441–2448. [PubMed: 20732288]
13. Truven Health Analytics: Databases and Online Tools. http://truvenhealth.com/your-health care-focus/life-sciences/data-databases-and-online-tools. Accessed July 30, 2015
14. Elixhauser, A.; Steiner, CA.; Whittington, C., et al. Health care Cost and Utilization Project, HCUP-3 Research Note. Agency for Health Care Policy and Research; Rockville, MD: 1998. Clinical classifications for health policy research: Hospital inpatient statistics, 1995; p. 98-0049.AHCPR Pub. No
15. Yu, H.; Wier, LM.; Elixhauser, A. HCUP Statistical Brief #118. Agency for Health care Research and Quality; Rockville, MD: Aug. 2011 Hospital Stays for Children, 2009. http://www.hcup-us.ahrq.gov/reports/statbriefs/sb118.pdf. Accessed June 29, 2015
16. Richardson DP, Daly C, Sutradhar R, et al. Hospitalization rates among survivors of young adult malignancies. J Clin Oncol. 2015; 33(24):2655–2659. [PubMed: 26169617]
17. Galper SL, Yu JB, Mauch PM, et al. Clinically significant cardiac disease in patients with Hodgkin lymphoma treated with mediastinal irradiation. Blood. 2011; 117(2):412–418. [PubMed: 20858859]
18. Hancock SL, Donaldson SS, Hoppe RT. Cardiac disease following treatment of Hodgkin's disease in children and adolescents. J Clin Oncol. 1993; 11(7):1208–1215. [PubMed: 8315419]
19. Aleman BMP, van den Belt-Dusebout AW, De Bruin ML, et al. Blood. 2007; 109(5):1878–1886. [PubMed: 17119114]
20. van Nimwegen FA, Schaapveld M, Janus CP, et al. Cardiovascular disease after Hodgkin lymphoma treatment: 40-year disease risk. JAMA Intern Med. 2015; 175(6):1007–1017. [PubMed: 25915855]

21. Bossi G, Cerveri I, Volpini E, et al. Long-term pulmonary sequelae after treatment of childhood Hodgkin's disease. Ann Oncol. 1997; 8(Suppl 1):19–24. [PubMed: 9187424]

22. Martin WG, Ristow KM, Habermann TM, Colgan JP, Witzig TE, Ansell SM. Bleomycin pulmonary toxicity has a negative impact on the outcome of patients with Hodgkin's lymphoma. J Clin Oncol. 2005; 23(30):7614–7620. [PubMed: 16186594]

23. Lund LW, Winther JF, Dalton SO, et al. Hospital contact for mental disorders in survivors of childhood cancer and their siblings in Denmark: a population-based cohort study. Lancet Oncol. 2013; 14(10):971–980. [PubMed: 23954078]

24. Ross L, Johansen C, Dalton SO, et al. Psychiatric hospitalizations among survivors of cancer in childhood or adolescence. N Engl J Med. 2003; 349(7):650–657. [PubMed: 12917301]

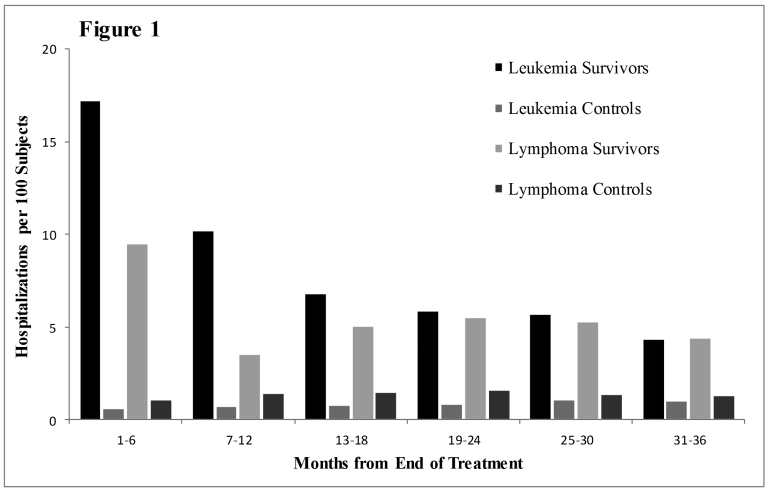

Figure 1.
Hospitalization incidence rate per 100 subjects over time from the end of treatment.

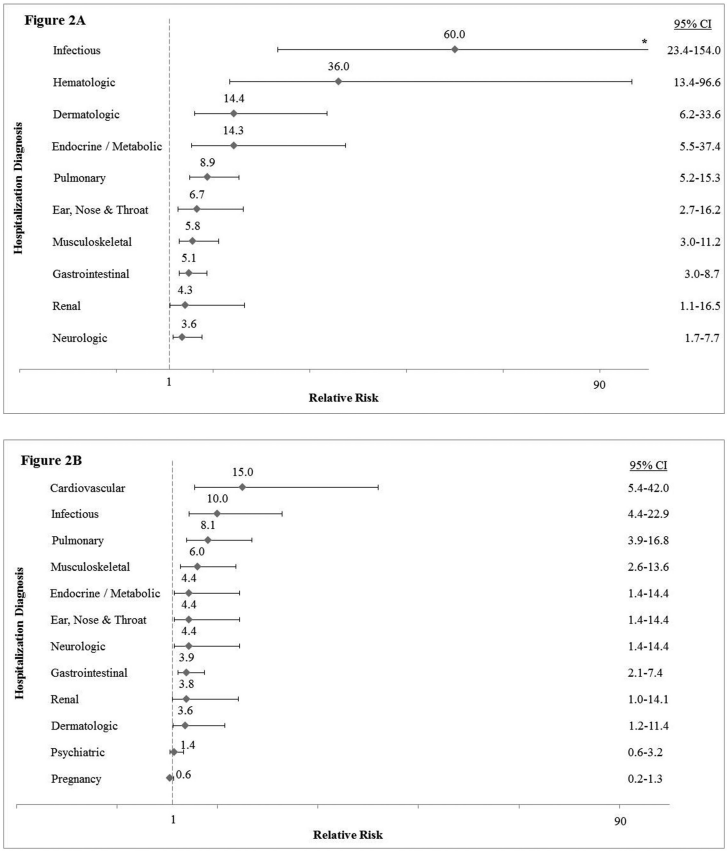

Figure 2.

Relative risks and 95% confidence intervals for cause-specific hospitalizations among all survivors of leukemia (2a) and lymphoma (2b) compared to controls. Psychiatric: includes substance abuse and psychiatric-related admissions.

Table 1

Baseline Characteristics of Cancer Survivors and Matched Controls

	Leukemia (N = 529)	Controls (N = 5,290)	Lymphoma (N = 454)	Controls (N = 4,540)
Age [Mean (SD)]	8.7 (4.75)	8.7 (4.75)	15.6 (4.24)	15.6 (4.24)
Sex [N (%)]				
Female	239 (45)	2390 (45)	186 (41)	1860 (41)
Male	290 (55)	2900 (55)	268 (59)	2680 (59)
Region [N (%)][a]				
Northeast	80 (15)	662 (13)	59 (13)	517 (11)
North Central	142 (27)	1439 (27)	116 (26)	1172 (26)
South	191 (37)	2140 (41)	183 (40)	1180 (42)
West	109 (21)	1013 (19)	93 (21)	946 (21)
Plan Type [N (%)][a]				
Health Maintenance Organization	111 (21)	949 (18)	79 (18)	764 (17)
Preferred Provider Organization	317 (61)	3198 (62)	261 (58)	2772 (63)
Other	95 (18)	1026 (20)	108 (24)	886 (20)
Year of EOT [N (%)]				
2000	8 (2)	80 (2)	6 (1)	60 (1)
2001	10 (2)	100 (2)	6 (1)	60 (1)
2002	17 (3)	170 (3)	17 (4)	170 (4)
2003	33 (6)	330 (6)	29 (6)	290 (6)
2004	30 (6)	300 (6)	40 (9)	400 (9)
2005	33 (6)	330 (6)	31 (7)	310 (7)
2006	55 (10)	550 (10)	44 (10)	440 (10)
2007	69 (13)	690 (13)	52 (11)	520 (11)
2008	77 (15)	770 (15)	72 (16)	720 (16)
2009	84 (16)	840 (16)	72 (16)	720 (16)
2010	113 (21)	1130 (21)	85 (19)	850 (19)

[a]Unknown or missing data were excluded; SD: Standard Deviation; EOT: End of Treatment

Table 2

Comparisons of hospitalization rates, hospitalizations per child, and lengths of stay between cancer cohorts and controls.

	Hospitalizations				Hospitalizations per Child[c]		Length of Stay[c]	
	Rate[a]	HR[b]	95% CI	p-value	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Leukemia	16.7	6.3	4.9-8.0	<.0001	2.5 (2.9)	1 (1-3)	5.5 (9.4)	3 (2-5)
Controls	1.7	1	Referent		1.4 (1.0)	1 (1-1)	4.0 (5.2)	2 (1-4)
Lymphoma	11.1	3.2	2.5-4.2	<.0001	1.9 (2.0)	1 (1-2)	6.1 (7.9)	3 (2-6)
Controls	2.7	1	Referent		1.4 (0.9)	1 (1-1)	3.7 (4.6)	2 (1-4)

CI: confidence interval; SD: standard deviation; IQR: interquartile range

[a] Incidence rate for number of hospitalizations per 100 patient-years;

[b] Hazard ratio adjusted for age, sex, geographic region and year of treatment end using Cox proportional hazards model;

[c] Among patients with ≥ 1 hospitalization;