Statewide Longitudinal Hospital Use and Charges for Pediatric and Adolescent Patients With Cancer

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Abstract

Purpose: We investigated longitudinal hospitalization outcomes (total charges, hospital days and admissions) among pediatric and adolescent patients with cancer compared with individuals from the general population without cancer using a novel and efficient three-step regression procedure.

Methods: The statewide Utah Population Database, with linkages to the Utah Cancer Registry, was used to identify 1,651 patients who were diagnosed with cancer from 1996 to 2009 at ages 0 to 21 years. A comparison group of 4,953 same-sex and -age individuals was generated from birth certificates. Claims-based hospitalization data from 1996 to 2012 were retrieved from the Utah Department of Health. Using the regression method, we estimated survival (differences due to survival) and intensity (differences due to resource accumulation) effects of the cancer diagnosis on hospitalization outcomes within 10 years after diagnosis.

Results: At 10 years after diagnosis, on average, patients with cancer incurred \$51,723 (95% CI, \$48,100 to \$58,284) more in charges, spent 30 additional days (95% CI, 27.7 to 36.1 days) in the hospital, and had 5.7 (95% CI, 5.4 to 6.4) more admissions than the comparison group. Our analyses showed that the highest hospitalization burden occurred during the first 4 years of diagnosis. Patients with leukemia incurred the greatest hospitalization burden throughout the 10 years from diagnosis. Intensity effects explained the majority of differences in hospital outcomes.

Conclusion: Our results suggest that children and adolescents who were diagnosed with cancer in 2014 in the United States will incur over \$800 million more in hospital charges than individuals without cancer by 2024. Interventions to reduce this burden should be explored in conjunction with improving health and survival outcomes.

Introduction

Treatments for childhood and adolescent cancer, which is the leading disease-related cause of mortality among this age group, typically extend over years and place a large economic burden on patients, their families, and the health care system. Childhood cancer-related hospitalizations cost almost twice as much as other pediatric related hospitalizations in the United States (\$3,900 *v* \$2,300 mean daily hospital cost).¹ Patients require long-term follow-up care²⁻⁵ that can add substantially to the economic burden of the initial treatments. Examining this longitudinal burden is vital for understanding the impact of cancer and evaluating the cost benefit or cost effectiveness of treatments. Because public resources (eg, research dollars) are limited, understanding the burden of cancer relative to other conditions can help in prioritizing policy and research areas for resource allocation purposes. Yet, only a few studies have conducted economic evaluations of childhood and adolescent cancer,^{1,6-9} and to our knowledge, no study has investigated the longitudinal burden of these diseases.

Inpatient care accounts for the largest share of health care expenditures in the United States.¹⁰ However, pediatric and adolescent cancer studies have only evaluated the rate of hospitalization without exploring the economic impacts of these events.^{4,5} To begin to understand the short- and long-term economic burden, we used hospital discharge data in Utah to investigate longitudinal outcomes (ie, hospital charges, days, and admissions within 10 years after diagnosis) among pediatric and adolescent patients with

cancer compared with same-sex and -age individuals from the general population without a history of cancer. We used data from the Utah Population Database (UPDB), which includes linkages to the Utah Cancer Registry (UCR) and birth certificates, as well as statewide hospital discharge data.

Analyses of health care use and costs can be methodologically complex, because these data are inherently semicontinuous, skewed, and censored (as a result of deaths and loss to follow-up). Also, patients experience varying rates of resource use over time that result in periods of observations with no resource use.^{11,12} To address these issues, we use a novel three-step regression estimator, which is unbiased, efficient, and consistent for analyzing longitudinal data in the presence of heavy censoring.^{12,13} We report average adjusted hospitalization outcomes by cancer type relative to the comparison group at 10 years after diagnosis, and the trajectory of these incremental effects at different time periods within the 10 years. The outcomes of our study will aid in understanding the burden of childhood and adolescent cancer on patients and the health care system, and identifying areas for future interventions to improve health care delivery for these patients.

Methods

Data Sources

The data were drawn from the UPDB, which includes linkages to the UCR and statewide vital records for births and deaths,

driver licenses, and voter registration records. The UCR, a population-based registry for statewide cancer records, has been maintaining cancer records since 1966, is an active member of the SEER program of National Cancer Institute, and captures at least 98% of the cancer cases in Utah.¹⁴ The UPDB has linkages to the Utah Department of Health, which provides access to statewide hospitalization claims data. This study was approved by the University of Utah Institutional Review Board.

Study Sample

We used the UCR to identify pediatric and adolescent patients with cancer born in Utah. These patients were diagnosed with cancer between 0 and 21 years of age, from January 1, 1996, to December 31, 2009. We included patients with valid International Classification of Childhood Cancer codes,¹⁵ with the exceptions of nonmelanoma, in situ cancers, and unspecified diagnosis code. With these criteria, we had 1,651 eligible patients.

The Utah birth certificate data from the UPDB were used to identify a comparison group from the general population without a history of cancer. For each patient with cancer, we randomly selected three individuals with no history of cancer who were alive and living in Utah until the patient's diagnosis date. The comparison group individuals had to have the same birth date and sex as the corresponding patient. This resulted in a sample of 4,953 for the comparison group. We assigned the diagnosis date of the patient with cancer as an index date for each comparison group individual.

The current analyses focused on the claims-based hospitalization charges data provided to the UPDB from the Utah Department of Health between 1996 and 2012. Dependent variables were constructed from hospitalizations that occurred during the 10 years after the index date. Pregnancy, childbirth, and the puerperium-related hospitalizations were excluded. The charges data for our analyses were adjusted for inflation using the Gross Domestic Product deflator from the US Bureau of Economic Analysis with 2009 as the base year.¹⁶

In addition to sex and birth date, the UPDB provided information on other characteristics of patients with cancer and comparison group individuals such as race (white *v* others), county at birth (urban or rural), and last known follow-up date in Utah (populated using multiple statewide resources such as mother's driver license and Social Security). The urban and rural residential status at birth was based on the Office of Management and Budget metropolitan counties criteria. In addition, for each hospital encounter of patients and comparison group individuals, the Utah Department of Health provided the discharge-based International Classification of Diseases, ninth revision code (refer to the Data supplement, Appendix II, for a summary of commonly cited reasons for hospitalizations).

Statistical Analyses

The Basu and Manning (B&M) method was used to compare hospitalization outcomes between patients with cancer and individuals without cancer.¹² This method incorporates censor-

ing (ie, loss to follow-up for reasons other than death) and decomposes the overall effect of an independent variable (eg, cancer diagnosis) on the outcome variable into survival and intensity effects. The survival effect is the impact of an independent variable on the outcome due to differences in survival. Because the death rate among patients with cancer is higher than that of individuals without cancer, evaluating the survival effect is critical. The intensity effect estimates the impact of the independent variable on the outcome caused by differences in accumulation of resource for those who are alive. An important aspect of the B&M method is that it allows cost accumulation to vary over time. In this way, end-of-life costs can be measured. These costs, which can be substantial, would be incorporated in the intensity effect because they occur while a patient is still alive. However, the differences in costs between groups that occur because one group has a higher survival rate than the other (thereby experiencing more opportunities to incur costs) would be incorporated in the survival effect.

We investigated the impact of cancer diagnosis compared with no cancer diagnosis using two models for our three hospitalization outcomes (charges, hospital days, and admissions). In model 1, the key independent variable was a categorical variable capturing cancer diagnosis, with no cancer as the reference category. We used the International Classification of Childhood Cancer categorization to specify cancer diagnosis types: acute myeloid leukemia (AML), all leukemia except AML (non-AML leukemia hereafter), CNS tumors, lymphoma, and other solid tumors. In model 2, the key independent variable was a dichotomous indicator for cancer diagnosis (all cancer types aggregated into one category) versus no cancer diagnosis. The data set was constructed with one observation for each individual-period, where periods were defined as 2-year increments during the 10 years after the index date. Each individual in our data had, at most, five periods (0 to 2, 2 to 4, 4 to 6, 6 to 8, and 8 to 10 years after the index date). We used the hospital admission date to aggregate hospitalization outcomes at the individual-period level. If a patient was not lost to follow-up and had no hospitalization during a period, the outcomes in those periods were marked as zero.

The incremental effects of cancer diagnosis versus no cancer diagnosis on hospitalization outcomes were estimated for both models 1 and 2 (detailed explanation of the B&M method is provided in Appendix I). Several other independent variables were included in these models. We present the B&M overall, intensity and survival effects in the results. CIs (95%) for these effects were estimated via nonparametric bootstrapping ($N = 1,000$ bootstraps) with clusters at the individual level. See the Data Supplement for intermediate regression results (Appendix III) and survival estimates (Appendix IV).

We also examined the univariable distribution of the independent variables and calculated unadjusted average hospital charges, number of hospital days, and number of admissions for patients with cancer and individuals without cancer. Statistical analyses were conducted in Stata (Stata, College Station, TX) and R (2013 R Foundation for Statistical Computing). Two-sided statistical significance was set at $\alpha = .05$.

Results

The characteristics of the patients with cancer were similar to those of the individuals without cancer (Table 1). The overall sample was 53.8% male, and almost 90% of individuals were born in an urban county. Over 34% of patients with cancer were less than 5 years old, at the index date, and 33.4% were between 16 to 21 years old. Close to half (45.1%) of the patients were diagnosed with solid tumors, 19.8% with CNS, 18.7% with non-AML leukemia, 11.9% with lymphoma, and 4.5% with AML. The average follow-up time for cancer and comparison group individuals was 10.0 ($SD = 4.3$) and 8.4 ($SD = 5.0$) years, respectively (not reported in table).

The overall cumulative incremental effect at 10 years after diagnosis for total charges (Table 2) was highest for patients with AML (\$64,782; 95% CI, \$51,058 to \$91,073) and non-AML (\$65,080; 95% CI, \$56,670 to \$75,169). On average, charges for patients with CNS tumors, other solid tumors, and lymphoma were \$49,861 (95% CI, \$63,988 to \$42,835), \$48,289 (95% CI, \$42,644 to \$56,514), and \$42,857 (95% CI, \$34,136 to \$52,384) higher, respectively, than those for the comparison group. Model 2 for aggregate cancer group demonstrates that, on average, hospital charges for patients with cancer were \$51,723 (95% CI, \$48,100 to \$58,284) more than those for the comparison group. The majority of the overall effects were explained by the intensity effects in both models 1 and 2 for *all* hospital outcomes, and survival effects were mostly small.

At 10 years after diagnosis, patients with AML spent over 100 more days in the hospital on average (102.2 days; 95% CI, 81.3 to 140.9 days) compared with comparison group individuals, followed by patients with non-AML leukemia (37.8 days; 95% CI, 31.8 to 45.1 days). Patients with CNS, lymphoma, and other solid tumors were hospitalized for 27.7 (95% CI, 23.0 to 38.2 days), 25.2 (95% CI, 19.6 to 31.5 days), and 23.4 (95% CI, 20.4 to 28.7 days) additional days, respectively, compared with individuals in the comparison group. On average, all patients with cancer (model 2) spent 30.1 (95% CI, 27.7 to 36.1 days) days longer in the hospital than comparison group participants.

With respect to the number of hospital admissions, on average, patients with AML, non-AML leukemia, and CNS tumors had seven, seven, and five, respectively, more hospitalizations than individuals in the comparison group. Patients with other solid tumors and lymphoma had six and four more hospitalizations, respectively, than comparison group participants. Model 2 results for number of hospitalizations were similar. On average, individuals with cancer had approximately six more hospitalizations than individuals without cancer, and the majority of this effect was explained by the intensity effect.

The cumulative incremental effects of cancer types (in reference to comparison group) on charges for each period are shown in Figure 1A. The incremental intensity effects were highest in the first 4 years of diagnosis for all cancer types. Beginning at 6 years after diagnosis, the incremental intensity effects were relatively flat. Survival effects were negligible compared with the intensity effects at any time within 10 years after

Table 1. Characteristics of Individuals in Cancer Group and Comparison Group

Characteristic	Cancer Group (n = 1,651)		Comparison Group (n = 4,953)	
	No.	%	No.	%
Sex				
Female	763	46.2	2,289	46.2
Male	888	53.8	2,664	53.8
Race				
White	1,596	96.7	3,904	78.8
Others	55	3.3	1,049	21.2
County at birth				
Urban	1,469	89.0	4,392	88.7
Rural	182	11.0	561	11.3
Index years				
1996-2000	513	31.1	1,539	31.1
2001-2005	602	36.5	1,806	36.5
2006-2009	536	32.5	1,608	32.5
Age at index date, years				
0-5	575	34.8	1,725	34.8
6-10	241	14.6	723	14.6
11-15	284	17.2	852	17.2
16-21	551	33.4	1,653	33.4
Cancer diagnosis				
AML	75	4.5	—	—
Non-AML	309	18.7	—	—
CNS	326	19.8	—	—
Lymphoma	197	11.9	—	—
Other solid tumor	744	45.1	—	—

NOTE. Dashes indicate that cancer diagnosis is not applicable to comparison group individuals.

Abbreviation: AML, acute myeloid leukemia.

diagnosis. The same trend is seen for aggregate cancer group (not reported). Similar trends were seen for days in the hospital (Figure 1B) and hospital admissions (Figure 1C), with patients with AML spending significantly longer days in the hospital in the first 4 years of cancer diagnosis.

Discussion

This is the first study to our knowledge to examine longitudinal hospital use and charges incurred by pediatric and adolescent patients with cancer in comparison to individuals from the general population without a history of cancer. Using data from a unique statewide resource in Utah, we found that cumulative hospital charges, hospital days, and hospital admissions among pediatric and adolescent patients with cancer, as compared to individuals without cancer, were much higher within the first 10 years after diagnosis. On average, patients with childhood and adolescent cancers incurred \$51,723 more in charges compared with individuals without cancer during the first 10 years after cancer diagnosis. In the United States, an estimated 16,000 children and adolescents under the age of 19 are diagnosed with cancer every year.¹⁷ Projecting our estimate to chil-

Table 2. Cumulative Incremental Effects of Cancer Type on Hospitalization Outcomes Versus Comparison Group Within 10 Years After Diagnosis

Exposure	Total Charges (\$)				Days in Hospital				No. of Hospitalizations			
	Incremental Effects*				Incremental Effects*				Incremental Effects*			
	Mean Unadj.†	Overall	Survival	Intensity	Mean Unadj.†	Overall	Survival	Intensity	Mean Unadj.†	Overall	Survival	Intensity
Model 1												
Comparison group	1,149		Reference		0.6		Reference		0.1		Reference	
AML	68,360	64,782	1,331	63,451	109.0	102.2	4.4	97.7	7.4	7.1	0.1	7.0
95% CI		51,058 to 91,073	298 to 24,569	48,637 to 77,778		81.3 to 140.9	2.5 to 27.2	75.1 to 124.9		5.7 to 10.7	0.1 to 3.4	5.4 to 9.0
Non-AML leukemia	71,532	65,080	941	64,139	43.3	37.8	1.6	36.2	7.8	7.4	0.2	7.2
95% CI		56,670 to 75,169	476 to 6,145	54,584 to 72,414		31.8 to 45.1	0.9 to 7.2	29.2 to 41.4		6.2 to 8.3	0.1 to 0.8	5.9 to 7.9
GNS	49,951	49,861	1,502	48,359	25.6	27.7	3.1	24.7	5.4	5.6	0.2	5.4
95% CI		63,988 to 42,835	767 to 13,115	39,661 to 55,949		23.0 to 38.2	1.7 to 15.5	19.0 to 29.5		4.8 to 7.3	0.1 to 1.8	4.4 to 6.3
Lymphoma	40,102	42,857	608	42,250	25.5	25.2	1.0	24.2	4.4	4.6	0.1	4.5
95% CI		34,136 to 52,384	189 to 3,809	33,016 to 51,339		19.6 to 31.5	0.4 to 4.5	17.9 to 29.8		3.7 to 5.6	0.03 to 0.6	3.6 to 5.5
Other solid	53,965	48,289	894	47,395	26.2	23.4	1.7	21.6	6.0	5.4	0.1	5.3
95% CI		42,644 to 56,514	497 to 7,359	40,260 to 53,119		20.4 to 28.7	1.0 to 8.3	17.7 to 24.5		4.8 to 6.4	0.1 to 1.0	4.5 to 6.0
Model 2												
Comparison group	1,149		Reference		0.6		Reference		0.1		Reference	
Cancer group	55,460	51,723	975	50,748	32.9	30.1	2.0	28.1	6.1	5.7	0.1	5.6
95% CI		48,100 to 58,284	616 to 8,781	46,143 to 54,379		27.7 to 36.1	1.1 to 9.0	24.8 to 30.5		5.4 to 6.4	0.1 to 1.0	5.2 to 6.1

Abbreviation: AML, acute myeloid leukemia; Unadj., unadjusted.

* Cumulative incremental effects within 10 years from diagnosis were estimated using the Basu and Manning method (B&M) three-step regression procedure. The comparison group is the reference category for interpreting the incremental effects. Other covariates that were included in the B&M regressions were sex, race (white v others), urban or rural county residence at birth, age at index date, index year category, period, and interaction between period and cancer exposure variable. Results are not reported here. 95% CIs were estimated via nonparametric bootstrapping using 1000 samples with replacement and individuals as clusters.

† The first set of columns for total charges, days in hospital, and No. of hospitalizations present the unadjusted (Unadj.) means for comparison group and cancer types.

Figure 1. Cumulative incremental effects of cancer type on hospital outcomes: (A) Total charges, (B) number of days in hospital, and (C) number of hospital admissions. Incremental effects for hospital charges, days, and admissions were estimated using Basu and Manning's three-step regression estimator. These figures plot the cumulative incremental effects (survival and intensity) of cancer types (in reference to the comparison group) from date of diagnosis (index date) to 10 years after diagnosis. In the first 2 years of cancer diagnosis, patients with leukemia on average incurred over \$40,000 more in charges in comparison to individuals from the general population (A). Within the first 4 years of diagnosis, the cumulative impact of cancer diagnosis on charges is approximately \$60,000 higher, which means that from year 2 to year 4, on average, approximately \$20,000 per year was added to total charges. AML, acute myeloid leukemia.

dren and adolescents who were diagnosed in 2014 in the United States demonstrates that hospital charges for these cancers will account for over \$840 million more than hospital charges for individuals without cancer within the next 10 years.

We applied a novel method to estimate adjusted hospitalization outcomes that considers censoring and deaths, which are known sources of bias in health care data analyses.^{12,13} Using the B&M methodology, we disaggregated the impact of cancer diagnosis type on hospitalization outcomes into survival (ie, differences due to survival) and intensity (ie, differences due to resource accumulation) effects. The average survival effects on total charges, days in hospital and hospital admissions at 10 years after diagnosis were small in comparison to the intensity effects. These findings suggest that the biggest costs are borne by the intensity of resource use by patients with cancer, which has been found in other studies that have implemented the B&M method.^{12,13}

Patients with leukemia, on average, incurred the highest hospitalization charges and were most frequently hospitalized as compared with the comparison group individuals. Therapy for leukemia may extend over years and is characterized by multiple cycles of outpatient and inpatient chemotherapy that can potentially increase admissions for these patients. Patients with AML spent over 100 more days in hospital as compared with individuals without cancer at 10 years after diagnosis. AML therapy is intensive and requires longer hospitalization for recovery after each cycle of chemotherapy than other cancers. Thus, patients with AML may face prolonged hospitalizations in the initial phases of diagnosis. Also, patients with AML report ongoing late effects such as cardiomyopathy and organ dysfunction that can also increase their length of hospital stay in comparison with other patients with cancer.¹⁸

Despite having the highest average number of days spent in the hospital, the average charges for patients with AML were not significantly different from those incurred by other patients, who spent 39 days on average in the hospital. Existing research shows that overall hospitalization costs are driven more by the number of admissions than by the length of stay for those admissions,¹⁹ and the costs may also be affected by the treatment intensity or the presence of complex health conditions that are difficult to treat.

We find that the largest hospitalization burden occurs within the first 4 to 6 years from diagnosis. Although our estimates of the incremental differences in hospital outcomes did not change substantially beyond 6 years after diagnosis, this does not mean that the burden of late effects was nonexistent in our study sample. First, the potential of developing late effects in 6 to 10 years after diagnosis may be marginal. Existing studies show that the likelihood of developing late effects among childhood cancer survivors continues to increase 20 to 30 years after diagnosis.^{3,20} Second, we examined hospitalization data only, and it is unknown how much health care costs for late effects may be borne in outpatient/ambulatory visits.

We recommend that strategies for reducing costs should be considered in conjunction with recognizing the typical reasons for admissions for pediatric and adolescent patients with cancer. Patients with cancer are most commonly hospitalized for che-

motherapy administration, or as a result of fever and neutropenia, infections, pain, or nausea. Existing evidence indicates that diverting care from inpatient to outpatient settings can result in substantial cost savings.²¹⁻²³ Low-risk patients with cancer could be attended in outpatient clinics for managing fever and neutropenia and administering chemotherapies.^{24,25} Future studies should investigate cost effectiveness and comparative effectiveness of these interventions.

Our study has certain limitations. Our analyses were conducted using data on individuals from one state, raising the possibility that the results would not be generalizable to other states. We used hospital charges data, which may not fully represent the cost incurred by individuals and the health care system.²⁶ It is difficult to predict the bias in cost differences using charge data because charges are typically constructed using a margin on cost, which may differ across time or health facilities. Although health care costs and reimbursements give the most accurate assessment of financial burden, these data were not readily available for our cohort. Other costs (eg, outpatient costs, travel costs and opportunity costs of loss in productivity) were not included in our analyses. Examining hospital-related burden is critical as it accounts for the largest share of health care spending in the United States,¹⁰ yet incorporating other direct costs (eg, outpatient) would provide more robust estimates of the burden.

Information on health status and/or comorbidities was not available, leaving us unable to account for other conditions that may influence hospitalizations. Sample size restrictions precluded estimating separate effects for more refined cancer types, which means that we were unable to evaluate differences in subtypes to account for treatment heterogeneity (eg, for different brain tumors). Future studies should examine short- and long-term (extending to 20 or 30 years from diagnosis) direct (hospital and outpatient) and indirect financial burden with more refined childhood cancer categorization.

Our results are compelling in light of the growing need to address cancer-related costs in the United States that are expected to increase in the coming decade.²⁷ Our study results provide input parameters for future cost-benefit and cost-effectiveness analyses, and for identifying strategies and interventions for reducing the burden of cancer. Because health care resources are limited, examination of the financial burden of high-cost conditions such as childhood and adolescent cancers can help in prioritizing policy and research areas. Finally, identifying charges, costs and utilization can help in devising more effective models for capitation.

In summary, this study estimated the statewide longitudinal burden of hospitalization for childhood and adolescent cancer patients in comparison to individuals from the general popula-

tion without cancer. Future studies should investigate other costs of health care for cancer patients and identify interventions to reduce the health care burden among these patients while improving health/survival outcomes.

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Authors' Disclosures of Potential Conflicts of Interest

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