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Infection-related mortality in Hispanic and non-Hispanic children with cancer

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Abstract

Background: Hispanic children with cancer experience poorer survival than their White counterparts. Infection is a known cause of cancer-related mortality; however, little is known about the risk of infection-related death among Hispanic children with cancer. We examine the association of Hispanic ethnicity with infection-related mortality and life-threatening events among children with cancer.

Procedure: For a cohort of all pediatric cancer patients diagnosed from 1986 to 2012 and treated at a single tertiary care center, we obtained national death records to determine all-cause mortality and infection-related mortality, as well as intensive care unit (ICU) admissions as a surrogate for life-threatening events. Cox proportional hazard models assessed all-cause mortality and infection-related mortality using ethnicity as the main independent variable. ICU admission rates were modeled using a zero-inflated Poisson regression model. Models were adjusted for gender, diagnosis year, age, residential location, and diagnosis.

Results: Of 6,198 patients, 741 (12%) were Hispanic. Mean follow-up was 11 years (SD = 8.04). There were 1,205 deaths, with 193 attributable to infection. Differences in all-cause mortality between Hispanic and non-Hispanic patients did not reach significance (hazard ratio [HR] = 1.14, 95% confidence interval [CI]: 0.96–1.36). However, Hispanic patients were 68% (HR = 1.68, 95% CI: 1.16–2.43) more likely to have an infection-related cause of death. Hispanic ethnicity was statistically associated with a higher rate of ICU admissions (rate ratio = 1.32, 95% CI: 1.12–1.56).

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

Conclusion: Hispanic pediatric cancer patients were more likely to have an infection-related death and higher rates of ICU admissions than non-Hispanic patients. Infection may be an overlooked contributor to poorer outcomes among Hispanic patients.

Keywords

disparities; ethnicity; infection; intensive care unit; mortality; pediatric cancer; sepsis

1 | INTRODUCTION

Cancer is the leading cause of disease-related mortality among children and adolescents in the United States.^{1,2} Significant advancements over the last several decades have resulted in dramatic improvements in long-term outcomes in children with cancer.^{3,4} However, the majority of studies suggest poorer survival among children from racial and ethnic minority groups.⁵⁻¹⁰ Among the populations experiencing poorer outcomes are Hispanics, the fastest growing ethnic minority group in the United States.¹¹⁻¹⁵ Reports from the 1980s and 1990s demonstrate poorer survival among Hispanic patients with acute lymphoblastic leukemia (ALL) when compared with non-Hispanic White patients.¹⁶⁻²⁰ More recently, while pediatric ALL survival rates have improved for all children, the relative risk of death remains 1.5 times higher for Hispanic children compared with non-Hispanic Whites.³ Hispanic children with other common cancers, including acute myeloid leukemia, Wilms tumor,²¹ non-Hodgkin lymphoma,²² Ewing sarcoma,^{23,24} and noncentral nervous system cancer types,²⁵ also have poorer survival.²⁶

The cause of decreased survival rates among Hispanics remains unknown. Socioeconomic factors, including reduced access to care, have been implicated.²⁷⁻³⁶ However, the effect of such factors in pediatric cancers is unclear. Likewise, both host and tumor biologic factors have been proposed as possible contributors to cancer survival disparities. However, definitive evidence linking any biologic differences to survival is lacking.³⁶⁻³⁹

Infections during cancer therapy may be an underappreciated potential contributor to disparities in survival among pediatric cancer patients. Whether or not a child survives a life-threatening infection may depend on the type of pathogen, the state of the immune system, baseline organ function, and the time to appropriate therapy.⁴⁰ Sepsis in severely immune-compromised patients is an important cause of cancer-related mortality.⁴¹⁻⁴³ Differences in sepsis mortality rates, based on ethnicity, have been demonstrated among adult patients with a variety of underlying conditions.⁴⁴⁻⁴⁸ However, very little is known about the risk of life-threatening infection or sepsis among Hispanics and other minority children with cancer.

The current study describes the association of Hispanic ethnicity with infection-related mortality and life-threatening events requiring intensive care unit (ICU) admission in children with cancer. Using an institutional clinical database for a large tertiary children's hospital, linked with the Center for Disease Control and Prevention's (CDC) National Death Index (NDI), we evaluated the hazard ratio (HR) of infection-related mortality among Hispanic and Non-Hispanic pediatric cancer patients. We hypothesized that Hispanic children with cancer would be more likely to die from infections compared with Non-Hispanic patients. Then, to better understand an association between Hispanic ethnicity and

infection-related mortality, we also explored whether Hispanic children were more likely to experience episodes of life-threatening sepsis or if differences in mortality could be explained by survivability of sepsis episodes. To that end, as most pediatric oncology patients with life-threatening conditions are admitted to the ICU, we evaluated rates of ICU admissions, as a surrogate for life-threatening events, including sepsis, to identify episodes of severe illness that may or may not have resulted in death.

2 | METHODS

2.1 | Study cohort

Intermountain Healthcare (IH) is a healthcare system consisting of more than 185 clinics and 22 hospitals, including Primary Children's Hospital (PCH), a state-of-the-art hospital, located in Salt Lake City, UT, that serves as the pediatric tertiary care center for much of Utah, Idaho, Wyoming, Montana, and Nevada. IH maintains a cancer registry containing patient, diagnosis, and treatment data for all oncology patients who received at least some portion of their treatment within the IH system, to report to the Utah Surveillance, Epidemiology, and End Results Program registry. Patients in this registry, aged 0–25, who were diagnosed with a cancer designated in the International Classification of Childhood Cancers between January 1, 1986 and December 31, 2012, were included in the study cohort (N = 6,198; Fig. 1).⁴⁹ In addition, we obtained data for ICU admissions (including admissions to pediatric intensive care units [PICU]) in the IH system that occurred within 3 years of diagnosis for all patients diagnosed after January 1, 2001 (n = 3,179) when the data became available.

All study methods and procedures were approved by the Institutional Review Boards of the University of Utah and the University of Utah's Resource for Genetic and Epidemiologic Research.^{50,51}

2.2 | Identification of deaths

For the full study cohort (n = 6,198), any patients that had a clinical visit in the IH system on, or after the last follow-up date, January 1, 2014, were presumed alive on January 1, 2014. This resulted in 4,135 individuals for which vital status was uncertain on January 1, 2014. NDI records were queried for death records in the years during and after the most recent IH clinic visit for each of these patients. The NDI, which is operated by the CDC and maintains death certificate information for deaths occurring within the United States, has been utilized by hundreds of studies to identify deaths and causes of death, including infectious causes.^{52–58} In accordance with NDI query standards, we sent eight individual identifiers per patient to increase the likelihood of exact matches and decrease the likelihood of false matches: first, middle, last name, month, day, and year of birth, gender, and state of birth. For patients with hyphenated last names, we sent three records that were identical except for the last name; the combined hyphenated name, and one for each of the hyphenated names alone, to ensure matching. Patients for whom no death record matched in the NDI query were presumed alive on January 1, 2014.

Each NDI record includes up to 20 listed causes of death as International Classification of Disease (ICD) codes. For purposes of analysis, deaths were defined both as “all-cause mortality” and as “infection-related mortality.” Infection-related death was assigned based on a previously validated list of infection ICD 9 and 10 codes.^{59,60}

2.3 | Demographic and clinical measures

Name, date of birth, and diagnosis were queried from the IH cancer registry. Rural versus urban residence at diagnosis was classified using Rural–Urban Commuting Area codes, a ZIP code-based geographic taxonomy system.^{61,62} Some patients had invalid or were missing ZIP codes.

Diagnosis type was separated into three categories: hematologic malignancies (leukemia or lymphoma), central nervous system (CNS) tumors, and non-CNS solid tumors.

2.4 | Ethnicity

Ethnicity (Hispanic or non-Hispanic) was assigned using a previously described combined method⁶³ utilizing both a surname matching algorithm and ethnicity data from the Utah Population Database, a unique database providing clinical, demographic, and genealogic data on more than 7 million individuals in Utah dating back several generations.

2.5 | Statistical methods

The main independent variable of interest was ethnicity. Chi-square tests were used to compare demographic variables by Hispanic or non-Hispanic.

For the full cohort (N = 6,198), among patients who died, survival time was calculated from date of cancer diagnosis to the date of death (both all-cause and infection-related). For all other patients, survival was censored as of January 1, 2014. Cox proportional hazard models were then used to estimate the adjusted HRs and corresponding 95% confidence intervals (CIs) between ethnicity and all-cause mortality and infection-related mortality. The assumption of proportionality for the Cox models were tested on the basis of Schoenfeld residuals. Age at diagnosis was found to violate the assumption of proportionality in the Cox model for all-cause mortality. The model run with age at diagnosis stratified revealed similar HRs and CIs and, thus, we report the nonstratified model. Regression models were adjusted for gender, age at diagnosis, year of diagnosis, cancer diagnosis type (hematologic malignancy, CNS, or non-CNS solid tumor), and residential location.

For the subset of 3,179 patients diagnosed after 2001, for whom ICU admission data were available, Chi-square tests were used to compare demographic variables across the two ethnic groups. The rates of ICU admissions were modeled using zero-inflated Poisson (ZIP) regression models to account for the large number of patients with no admissions, using follow-up time as an offset. The ZIP regression model included ethnicity, gender, age at diagnosis, year of diagnosis, cancer diagnosis type, and residential location as covariates. All statistical analyses were performed using Stata, version 12.⁶⁴ All reported *P* values are two-sided and *P* less than 0.05 was considered statistically significant.

3 | RESULTS

3.1 | Demographic and clinical measures

After a mean follow-up of 10.97 years (SD = 8.04) for the full cohort, there were 1,205 deaths, with 193 of these attributable to infection. Table 1 shows the demographic and clinical characteristics of the full cohort. Of the 6,198 patients in our cohort, 741 (11.9%) were classified as Hispanic. Hispanic patients tended to be slightly younger at diagnosis, with an average age at diagnosis of 11.45 (SD = 8.29) compared with non-Hispanics (12.59, SD = 8.32; $t(6,196) = 3.67$, $P < 0.001$). Hispanics also tended to be diagnosed in more recent years, with average years since diagnosis of 11.2 (SD = 7.24) compared with non-Hispanics (13.66, SD = 7.67; $t(6,196) = 8.60$, $P < 0.001$) and were more likely to live in an urban county. The proportion of deaths as of the last follow-up did not differ between Hispanics and non-Hispanics (19.43 vs. 19.44%, respectively, $P = 0.99$; Table 1).

3.2 | All-cause and infection-related mortality

In Table 2, male patients, patients in earlier diagnosis years (1986–1990), and patients with CNS tumors were more likely to die from any cause than their respective comparison groups. However, Hispanic ethnicity was not related to all-cause mortality.

Hispanic patients were more likely to have an infection-related death compared with non-Hispanic patients (HR = 1.68, 95% CI: = 1.16–2.43, $P = 0.007$). Patients who were diagnosed in more recent years were less likely to die from an infection compared with those diagnosed from 1986 to 1990 (HR = 0.61, 95% CI: = 0.38–0.96, $P = 0.032$ for 2001–2005, and HR = 0.60, 95% CI: = 0.38–0.93, $P = 0.023$ for 2006–2012). Patients with CNS tumors and non-CNS solid tumors were less likely to die from an infection compared with patients with hematologic malignancies (HR = 0.38, 95% CI: = 0.24–0.59, $P < 0.001$ for CNS tumors; HR = 0.26, 95% CI: = 0.19–0.38, $P < 0.001$ for non-CNS solid tumors). Patients aged 15–19 at diagnosis were more likely to die from infection than those from other age groups (HR = 1.58, 95% CI: = 1.04–2.39, $P = 0.03$) despite having a similar overall mortality.

3.3 | ICU admissions

Among patients diagnosed after January 1, 2001, the pattern of demographic characteristics mirrored that of the overall sample with Hispanic patients being younger at diagnosis, more urban, diagnosed in more recent years, and more likely to have a hematologic malignancy. Table 3 shows the results for the rate of ICU admissions. Hispanic patients experienced 32% more admissions on average (rate ratio = 1.32, 95% CI: = 1.12–1.56, $P = 0.001$) than their non-Hispanic counterparts. Despite a higher rate of admissions, approximately the same proportion of Hispanics and non-Hispanics were admitted to an ICU at least once (33.71% of non-Hispanics vs. 34.41% Hispanics). No other factors were significantly associated with admission rate.

4 | DISCUSSION

Our data demonstrate a higher risk of infection-related death among Hispanics when compared with non-Hispanics in a cohort of pediatric oncology patients from a single institution. While all-cause mortality did not differ, remarkably Hispanic patients were 67% more likely to have an infection-related death than non-Hispanic patients. In addition, we found rates of ICU admissions, which we examined as a surrogate measure of life-threatening events such as infections, to be approximately one-third higher among Hispanic patients compared with non-Hispanic patients. To our knowledge, this is the first study specifically demonstrating these phenomena. Our findings that Hispanic patients had higher rates of infection-related mortality and greater rates of ICU admissions point to a potentially underappreciated contributor to cancer mortality in this minority population.

While previous studies have consistently demonstrated survival disparities for Hispanic cancer patients,²⁷⁻²⁹ the exact cause of such disparities, and how this relates to the risk of infection-related mortality, remains unclear. The higher rate of infection-related mortality and ICU admissions among Hispanic patients in our sample may be due to some combination of biologic, genetic, cultural, or socioeconomic differences between non-Hispanic and Hispanic patients.

Hispanic families, compared with non-Hispanic Whites, are more likely to be socioeconomically vulnerable, have limited English proficiency, and encounter challenges to accessing quality health care.³⁰⁻³² While poor healthcare access has been associated with a delay in time to cancer diagnosis and more advanced cancer stage at diagnosis in a variety of adult cancers,³³⁻³⁵ the effect of reduced healthcare access is less clear in pediatric cancer.³⁶

Timely delivery of antibiotics has been shown to vastly improve survival of septic children.^{40,65-73} Barriers in communication are well documented and have been shown to impact clinical understanding in a variety of healthcare settings.^{12,29,74-76} Such barriers could cause delays in antibiotic administration. Of note, delays in seeking emergency care and barriers to high-quality health care, including intensive care, have been demonstrated in this population.⁷⁷⁻⁸⁰ A prospective study documenting the average time between the onset of fever and antibiotic administration may help to explore the concept of “delay of care” as a potential reason for an increased risk of infection-related death in Hispanics. Of note, one study has documented a decrease in PICU mortality among Latino children using a multilevel healthcare delivery intervention.⁸⁰ Similar interventions may prove beneficial for Hispanic pediatric oncology patients as well.

Biologic factors may also impact the overall survival and infection risk. Hispanic children with ALL may have adverse prognostic features or high-risk genomic alterations more often than non-Hispanic Whites, which may require more intensive therapy. Also, genetic differences in chemotherapy metabolism, based on ethnicity, have been demonstrated,³⁶⁻³⁹ which may lead to more therapy-related toxicity and more prolonged periods of immunosuppression. Another potential biologic factor would be a higher risk for developing certain types of life-threatening infections among Hispanics, just as susceptibility to specific infectious agents has been demonstrated in other ethnic groups.⁸¹⁻⁸⁶ Further research should

determine if the distribution of pathogens is similar between ethnic groups and could investigate potential differences in the severity and length of time of neutropenia. It should be noted that Hispanic children were more likely to have a hematologic cancer, which was associated with infection-related mortality. However, our model adjusted for diagnosis to minimize possible confounding.

Another notable finding of our study was that patients diagnosed more recently were not only less likely to die from any cause but also less likely to die from an infection-related death. This is likely due to improvements in both prevention of treatment complications and supportive care for septic patients.⁸⁷ It is important to note that although Hispanic children were disproportionately diagnosed in more recent years in our sample, and thus, likely should have benefited from these improvements in infection prevention and supportive care, they were still more likely to experience an infection-related death.

Although patients diagnosed with CNS tumors were more likely to die due to any cause, compared with hematologic malignancies, they were less likely to have an infection-related death. The higher rate of all-cause mortality among CNS patients points to the worse prognosis for these patients due to the severity of the disease.⁸⁸ Also, therapy for some brain tumors may rely less on cytotoxic and immunosuppressive chemotherapy in favor of more local control measures that may be less likely to put patients at risk for systemic infection (e.g., surgery and/or radiation). Patients with non-CNS solid tumor were also less likely to die from an infection compared with patients with a hematologic malignancy. While patients with non-CNS solid tumors are often treated with immunosuppressive chemotherapy, the time of immunosuppression for each cycle is typically shorter than that for most hematologic malignancies. In addition, patients with leukemia are particularly prone to infection early in therapy when underlying leukemia-related immunosuppression may factor into infection risk.

Adolescents, aged 15–19 at diagnosis, experienced a higher rate of infection-related death compared with other age groups. Teenage cancer patients differ from both younger children and adults with respect to a variety of physiological, social, and psychological issues.^{89,90} Adolescents with cancer have demonstrated more toxicity than younger children receiving similar treatments,⁹¹ often receive more intensive therapy than older adults,⁹² and have a higher risk of death than other age groups.⁹³ Indeed, prior studies have shown poorer compliance with cancer treatment regimens among adolescents.^{94,95} Lack of compliance and poorer outcomes of infections may, in part, be due to the fact that, while parents tend to direct cancer care for younger patients, teenage patients more often coordinate their own care. Self-directed care may lead to decreased recognition and delays in therapy for serious infections.

The lack of differences in all-cause mortality in our cohort, despite differences in the risk of infection-related deaths, may be due to certain study limitations. First, our study is from a single institution with a limited sample size. Several prior studies from single institutions and with small sample sizes also report no mortality disparities,^{7,9,10,96} where larger studies have demonstrated significant differences in mortality rates.²⁵ The proportion of Hispanic patients has risen dramatically over the last two decades, meaning that, on average, Hispanic

patients were diagnosed and treated more recently. As treatment and overall survival rates have improved dramatically over time,^{3,4} a higher proportion of Hispanics would have been treated with more contemporary therapy, which is associated with higher survival rates. However, a subanalysis of patients in our cohort diagnosed after 2001 revealed no significant differences in the overall mortality. Also, relying on an NDI query for death records may disproportionately impact the ability to capture death records for Hispanics given a higher rate of hyphenated surnames and potentially higher rates of emigration. Indeed, national databases have traditionally overestimated overall mortality for non-Hispanic Whites while underestimating the overall mortality in minorities.⁹⁷

Of note, while we utilized a validated method of classifying patients as Hispanic versus non-Hispanic, making such distinctions has traditionally been difficult and may introduce error. While the NDI is a very powerful tool for evaluating mortality for those dying in the United States, it does not capture those who may have died outside the United States. Therefore, our query may underestimate the overall mortality for segments of patients who are more likely to emigrate. In addition, NDI queries rely on accurate and specific patient identifiers, which may not be equally reliable between our two main cohorts of interest. In addition, with the exception of our Hispanic cohort, given our regional demographics, we were unable to evaluate the risk of infection-related mortality in other ethnic minorities. Lastly, due to the relatively small number of ICU admissions, and diversity of diagnoses, we were unable to systematically evaluate diagnosis codes associated with those admissions. Future research should evaluate causes of admission across ethnicities.

In conclusion, we found that Hispanic children with cancer were more likely to experience an infection-related death and experienced a higher rate of ICU admissions in comparison with a cohort of non-Hispanic pediatric oncology patients. While we were unable to demonstrate a difference in the overall mortality between the two groups in this single-institution study, these data introduce infectious complications as potential contributors to survival disparities among Hispanic cancer patients. Further research will explore the etiology and clinical course of infection in Hispanic patients and identify interventions to improve outcomes.

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Abbreviations:

ALL	acute lymphoblastic leukemia
CDC	Center for Disease Control and Prevention
CNS	central nervous system

HR	hazard ratio
ICD	International Classification of Disease
IH	Intermountain Healthcare
NDI	National Death Index
P/ICU	pediatric/intensive care unit
ZIP	zero-inflated Poisson

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FIGURE 1.
Patient population of the study

TABLE 1

Characteristics of the cohort of pediatric cancer patients diagnosed 1986–2012, by ethnicity (N = 6,198)

	Non-Hispanic N (%)	Hispanic N (%)	P value
Total	5,457 (88.04)	741 (11.95)	
Gender			
Female	2,700 (49.4)	382 (51.6)	0.289
Male	2,757 (50.5)	359 (48.5)	
Age at Diagnosis			
0–4	1,411 (25.9)	230 (31.0)	0.008
5–9	739 (13.5)	113 (15.3)	
10–14	841 (15.4)	101 (13.6)	
15–19	931 (17.1)	119 (16.1)	
20–25	1,535 (28.1)	178 (24.0)	
Diagnosis year			
1986–1990	839 (15.4)	62 (8.4)	<0.001
1991–1995	923 (16.9)	100 (13.5)	
1996–2000	981 (18.0)	114 (15.4)	
2001–2005	1,146 (21.0)	163 (22.0)	
2006–2012	1,568 (28.7)	302 (40.8)	
County of residence			
Urban	4,196 (87.7)	588 (12.3)	<0.001
Rural	1,150 (90.9)	115 (9.1)	
International/missing	111 (75.5)	38 (25.5)	
Diagnosis			
Hematologic malignancy	1813 (33.2)	309 (41.7)	<0.001
CNS	986 (18.1)	115 (15.5)	
Non-CNS solid tumor	2,658 (48.7)	317 (42.8)	
Vital status as of January 1, 2014			
Alive	4,396 (80.6)	597 (80.6)	0.995
Dead	1,061 (19.4)	144 (19.4)	
Infection-related death			
No	5,299 (97.1)	706 (95.3)	0.007
Yes	158 (2.9)	35 (4.7)	

TABLE 2
Multivariable HRs and 95% CIs for all-cause mortality and infection related mortality by ethnicity (N = 6,198)

	Counts	Person-years	All-cause mortality			Infection-related death		
			HR	95% CI	P value	HR	95% CI	P value
Ethnicity								
Non-Hispanic	5,457	61,198	1 (ref)			1 (ref)		
Hispanic	741	6,768	1.12	0.94–1.34	0.208	1.71	1.17–2.48	0.005
Sex								
Female	3,082	35,364	1 (ref)			1 (ref)		
Male	3,116	32,602	1.32	1.18–1.49	<0.001	1.12	0.84–1.49	0.439
Age at diagnosis								
0–4	1,641	16,780	1 (ref)			1 (ref)		
5–9	852	9,492	0.83	0.69–1.00	0.055	1.14	0.73–1.80	0.560
10–14	942	10,660	0.90	0.75–1.08	0.252	1.19	0.73–1.85	0.441
15–19	1,050	10,935	1.05	0.88–1.24	0.606	1.58	1.04–2.38	0.031
20–25	1,713	20,099	0.90	0.76–1.06	0.205	0.94	0.60–1.47	0.790
Diagnosis year								
1986–1990	901	17,403	1 (ref)			1 (ref)		
1991–1995	1,023	17,331	0.71	0.59–0.85	<0.001	0.64	0.40–1.02	0.061
1996–2000	1,095	13,746	0.82	0.69–0.98	0.028	0.79	0.51–1.23	0.300
2001–2005	1,309	12,008	0.61	0.51–0.73	<0.001	0.60	0.38–0.95	0.031
2006–2012	1,870	74,477	0.61	0.51–0.73	<0.001	0.59	0.37–0.92	0.019
Diagnosis								
Hematologic malignancy	2,122	22,843	1 (ref)			1 (ref)		
CNS	1,101	11,204	1.50	1.29–1.75	<0.001	0.37	0.24–0.58	<0.001
Non-CNS solid tumor	2,975	33,918	0.91	0.79–1.04	0.179	0.26	0.18–0.37	<0.001

*Model adjusted for county of residence.

TABLE 3
Multivariable rate ratios and 95% CIs for number of ICU admissions by ethnicity (N = 3,179)

	Counts	Mean (SD)	number admissions	Rate ratio	95% CI	P value
Ethnicity						
Non-Hispanic	2,714	0.49 (0.89)		1 (ref)		
Hispanic	465	0.55 (0.94)		1.33	1.13–1.57	0.001
Sex						
Female	1,530	0.45 (0.88)		1 (ref)		
Male	1,649	0.54 (0.90)		1.11	0.98–1.26	0.115
Age at diagnosis						
0–4	878	0.67 (0.91)		1 (ref)		
5–9	427	0.64 (0.92)		0.97	0.81–1.15	0.694
10–14	450	0.67 (1.21)		0.98	0.82–1.17	0.792
15–19	554	0.36 (0.73)		0.90	0.72–1.13	0.359
20–25	870	0.25 (0.66)		0.88	0.71–1.09	0.226
Diagnosis year						
2001–2004	1,050	0.47 (0.86)		1 (ref)		
2005–2008	1,035	0.53 (0.97)		1.03	0.88–1.20	0.702
2009–2012	1,094	0.49 (0.85)		1.13	0.97–1.32	0.122
Diagnosis						
Henatologic malignancy	1,094	0.39 (0.79)		1 (ref)		
CNS	594	1.02 (0.92)		1.10	0.90–1.35	0.332
Non-CNS solid tumor	1,491	0.36 (0.88)		1.09	0.87–1.36	0.471

* Model adjusted for county of residence.