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# Sociodemographic disparities in the occurrence of medical conditions among adolescent and young adult Hodgkin lymphoma survivors

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## Abstract

**Purpose:** Hodgkin lymphoma (HL) survivors experience high risks of second cancers and cardiovascular disease, but no studies have considered whether the occurrence of these and other medical conditions differ by sociodemographic factors in adolescent and young adult (AYA) survivors.

**Methods:** Data for 5,085 patients aged 15–39 when diagnosed with HL during 1996–2012 and surviving ≥2 years were obtained from the California Cancer Registry and linked to hospitalization data. We examined the impact of race/ethnicity, neighborhood socioeconomic status (SES), and health insurance on the occurrence of medical conditions (≥2 years after diagnosis) and the impact of medical conditions on survival using multivariable Cox proportional hazards regression.

**Results:** Twenty-six percent of AYAs experienced at least one medical condition and 15% had ≥2 medical conditions after treatment for HL. In multivariable analyses, Black HL survivors had a higher likelihood (versus non-Hispanic Whites) of endocrine (hazard ratio (HR)=1.37, 95% confidence interval (CI): 1.05–1.78) and circulatory system diseases (HR=1.58, CI:1.17–2.14); Hispanics had a higher likelihood of endocrine diseases (HR=1.24 (1.04–1.48). AYAs with public

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Conflict of interest:
The authors declare that they have no conflict of interest.

**Ethical approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

or no insurance (versus private/military) had higher likelihood of circulatory system diseases, respiratory system diseases, chronic kidney disease/renal failure, liver disease and endocrine diseases. AYAs residing in low SES neighborhoods (versus high) had higher likelihood of respiratory system and endocrine diseases. AYAs with these medical conditions or second cancers had an over two-fold increased risk of death.

**Conclusion:** Strategies to improve health care utilization for surveillance and secondary prevention among AYA HL survivors at increased risk of medical conditions may improve outcomes.

### Keywords

Hodgkin lymphoma; insurance; adolescent; young adult; race/ethnicity; second cancer; circulatory system; respiratory system; endocrine system

## Introduction

Adolescents and young adult (AYA) cancer survivors have an elevated risk of health problems as a result of their curative intent cancer therapy [1], including a higher prevalence of asthma/chronic obstructive pulmonary disorder, stroke and diabetes [2,3], and an over-two fold increased rate of cardiovascular disease [4], compared to AYAs without cancer. For one of the most common cancers among AYAs (15 to 39 years of age), Hodgkin lymphoma (HL) [5], outcomes have improved substantially over time, but striking sociodemographic disparities in survival persist [6]. In particular, survival is worse among AYAs who are Black or Hispanic (versus non-Hispanic White), of lower neighborhood socioeconomic status (SES) or have no or public insurance (versus private insurance) [6].

HL survivors also experience higher risks of second cancers and cardiovascular disease [7–13], but population-based data describing these outcomes in AYAs are limited [14,15,2]. Among 442 5-year HL survivors diagnosed at 15–24 years of age from the British Columbia Cancer Registry, excess risks of late morbidity resulting in hospitalization, mortality and second malignancies were observed compared to a matched comparison cohort [14]. Another study comparing 1,768 5-year AYA HL survivors from the Danish Patient Register to age- and gender-matched controls found AYA HL survivors to have among the highest risk of hospitalizations, particularly for new malignancies and circulatory and respiratory system diseases, compared to AYA survivors with other cancers [15]. However, no population-based studies have addressed whether these outcomes differ by race/ethnicity, neighborhood SES or health insurance, which may contribute to disparities in these outcomes for AYAs in the U.S..

Determining whether the occurrence of medical conditions among AYA cancer survivors differ by sociodemographic factors will allow us to identify those patients at increased risk of medical conditions and inform strategies to enhance long-term surveillance and care. Therefore, we determined associations between sociodemographic characteristics (race/ethnicity, neighborhood SES and health insurance) and medical conditions among 2-year HL survivors utilizing population-based California Cancer Registry (CCR) data linked to

hospital data from the California Office of Statewide Health Planning and Development (OSHPD).

## Materials and Methods

### Patients

Patients eligible for the study were all persons age 15–39 years who resided in California when diagnosed with classical HL (International Classification of Diseases—Oncology, 3rd edition [16] morphology codes 9650–9655, 9663–9667) during the period January 1, 1996 through December 31, 2012, were reported to the CCR from all non-Veterans Administration facilities, and survived ≥2 years after diagnosis. For each patient, we obtained CCR information routinely recorded in the medical record at diagnosis on age, sex, race/ethnicity, summary stage [localized (Ann Arbor stage I), regional (stage II), advanced (stage III/IV)], B-symptoms, and census-block group of residence. In addition, we obtained registry data on initial treatment modality (radiation and chemotherapy), from which we created a combined modality measure; subsequent primary cancer(s) reported during the study period; follow-up time and vital status (routinely determined by the CCR through hospital follow-up and linkages to state and national vital status and other databases) as of December 2014.

Using a deterministic strategy based on social security number and gender, OSHPD staff linked the CCR data to OSHPD hospital discharge records. The OSHPD hospital data contain detailed information for each discharge from any non-Federal (e.g., not military or Veterans Administration) hospitals in California. Clinical variables recorded include a principal diagnosis and up to 24 other diagnoses and a principal procedure and up to 20 other procedures, including corresponding procedure dates. All diagnoses and procedures were coded using the International Classification of Diseases, 9th Revision, Clinical Modifications (ICD-9-CM). Serial records for an individual patient were identified using a record linkage number. Bone marrow or hematopoietic stem cell transplant was ascertained from the CCR and OSHPD data.

As done previously [15,17], we grouped discharge diagnoses into five main diagnostic groups: circulatory system diseases [15], respiratory system diseases [15], chronic kidney disease/renal failure [17], liver disease [17], and endocrine and related diseases (hereafter referred to as endocrine diseases) [15] (eTable 1). We considered hypothyroidism (ICD-9-CM 244) separately from endocrine and related diseases based on prior studies [18,9]. Second cancers were identified by the CCR. Only medical conditions present ≥2 years after diagnosis were considered as outcomes in this study. In order to examine the temporal relationship between HL diagnosis and medical conditions, we excluded medical conditions present before HL diagnosis as outcomes.

From CCR information on the primary source of payment at initial diagnosis and/or treatment (health insurance), we created insurance categories of public (Medicaid and other government-assisted programs), private/military (health maintenance organizations, preferred provider organizations, and managed care not otherwise specified), none (self-pay) and unknown.[19] Consistent with prior observations that the small percentage of uninsured

AYA cancer patients (3.8% in our study) may reflect retroactive enrollment in Medicaid at cancer diagnosis [20], we considered publicly insured and uninsured patients together in the analyses.

We used a multi-component index of neighborhood SES based on patients' residential census-block group at diagnosis as geocoded by the CCR. The index is derived from 2000 U.S. Census (for cases diagnosed in 1996–2005) and 2006–2010 American Community Survey (for cases diagnosed in 2006–2007) data on education, occupation, unemployment, household income, poverty, rent, and house values [21]. The index is grouped into quintiles, based on the distribution of SES across all census block groups in California, and then, as done previously [6], into two categories--lower SES (quintiles 1–3) and higher SES (quintiles 4, 5).

The final study population included 5,085 AYA HL patients after exclusion of those with an unknown/invalid record linkage number (n=980) or evidence of human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS) from the CCR, OSHPD or death certificate [22] (n=120), because of the historically poorer outcome of HIV/AIDs-associated HL [23]. All study protocols were overseen by the Institutional Review Board of the University of California, Davis and by the California Committee for the Protection of Human Subjects.

## Statistical analyses

The cumulative incidence and associated 95% confidence intervals (CIs) of developing a medical condition ≥2 years after diagnosis was calculated using nonparametric methods that account for death as a competing risk [24]. Person-years of observation were compiled from two years after HL diagnosis to date of first hospitalization with a medical condition, the date of last known contact, date of death or the study cut-off date (12/31/2014), whichever occurred first. Gray's K-sample test statistic was used to determine whether cumulative incidence of a medical condition differed by sociodemographic or clinical factors [25].

To evaluate sociodemographic and clinical characteristics associated with the occurrence of each medical condition ≥2 years after diagnosis, we used multivariable Cox proportional hazards regression to calculate adjusted hazard ratios (HR) and 95% CIs. We also used multivariable Cox proportional hazard regression to evaluate overall and HL-specific survival associated with medical conditions. Survival time was measured in days from 2 years after diagnosis to the date of death from any cause for overall survival and from HL for HL-specific survival. Patients who died from other causes were censored at the time of death in analyses of HL-specific survival and patients alive at the study end date (12/31/2014) were censored at this time or at the date of last known contact, whichever occurred first. Survival time was left-truncated at two years after diagnosis and medical conditions and stem cell transplant were considered as time-dependent variables. In all models, the proportional hazards assumption was assessed numerically based on cumulative sums of Martingale residuals and visually based on inspection of the survival curves [log (−log) of the survival distribution function by log (months)]; variables that violated this assumption (stage at diagnosis, initial treatment and B-symptoms) were included as stratifying variables to allow for differing baseline hazards associated with these variables,

as done previously [6]. Models also included gender, age, race/ethnicity and year of diagnosis. All analyses were conducted using SAS version 9.4 software (SAS institute Inc., Cary, NC, USA).

## Results

Among the 5,085 AYAs in this study, 78% had a hospital admission before or after diagnosis and 39% of AYAs had an admission ≥2 years after diagnosis. The median follow-up time was 9.5 years (range: 2.0–19.0 years). AYAs of Black race/ethnicity, residing in low SES neighborhoods and with public/no insurance were more likely to have an admission ≥2 years from diagnosis; the mean number of hospital visits were also higher among those residing in low SES neighborhoods and with public/no insurance (eTable 2).

Sociodemographic and clinical characteristics of AYA HL patients varied by race/ethnicity (Table 1). Black (41%) AYAs were more likely to be diagnosed at an advanced stage than AYAs of other race/ethnicities, and more than 80% of Blacks and Hispanics resided in low SES neighborhoods compared to fewer than 46% of non-Hispanic Whites (hereafter referred to as Whites) and Asian/Pacific Islanders (APIs). Blacks (37%) and Hispanics (34%) were much more likely to have public or no insurance than Whites (16%) or APIs (16%).

Twenty-six percent of AYAs experienced at least one medical condition and 15% had two or more medical conditions ≥2 years from HL diagnosis. The prevalence of medical conditions among AYA HL survivors varied by baseline characteristics and treatment (Table 2). Blacks HL survivors were more likely to experience circulatory system (17%) and endocrine (21%) diseases than AYAs of other race/ethnicities. AYAs with public or no insurance or who resided in lower SES neighborhoods were generally more likely to experience medical conditions. As might be expected, medical conditions occurred more frequently among AYAs who underwent stem cell transplantation. Circulatory system, respiratory system and hypothyroidism occurred more frequently among AYAs who received radiation therapy alone.

The cumulative incidence of medical conditions at 10-years post diagnosis and by baseline characteristics is presented in Table 3. While the incidence of hypothyroidism was higher among AYA HL survivors with early-stage disease, the incidence of most other medical conditions was higher among those with late-stage disease. The incidence of circulatory system (18%), respiratory system (17%) and endocrine (22%) diseases was higher among Blacks compared to AYAs of other race/ethnicities (all p values <0.01). Circulatory system (13% vs 10%), respiratory system (18% vs 11%), chronic kidney disease/renal failure (5% vs 3%), liver disease (4% vs 2% ) and endocrine disease (21% vs 13%) incidence was higher among those with public or no insurance (vs private/military). Similarly, AYAs residing in low SES neighborhoods (vs high) had higher incidence of circulatory system (12% vs 9%), respiratory system (15% vs 10%) and endocrine (17% vs 12%) diseases.

In multivariable-adjusted models considering baseline characteristics associated with each medical condition (Table 4), Black HL survivors had a higher likelihood (vs Whites) of circulatory system (hazard ratio (HR)=1.58, 95% confidence interval (CI): 1.17–2.14) and

endocrine (HR=1.37, CI: 1.05–1.78) diseases; Hispanics had a higher likelihood of endocrine diseases (HR=1.24, CI: 1.04–1.48). AYAs who had public/no insurance (vs private/military) had greater likelihood of experiencing a number of medical conditions. AYAs residing in low SES neighborhoods (vs high) had higher likelihood of respiratory system (HR=1.28, 95% CI: 1.07–1.53) and endocrine diseases (HR=1.30, 95% CI: 1.10–1.53). The likelihood of experiencing medical conditions following HL did not appear to decrease over time.

In multivariable-adjusted models considering the associations of medical conditions with survival (Table 5), AYAs with respiratory system conditions experienced a markedly increased risk of death from all causes (HR=6.17, 95%CI: 4.50–8.46) and HL (HR=8.03 95% CI: 5.34–12.09), while those with circulatory system diseases, chronic kidney disease/renal failure, liver disease and endocrine disease had an over 2-fold increased risk of dying from any cause or HL. Subsequent cancers were associated with an increased risk of death from any cause.

## Discussion

Extending previous findings demonstrating an increased risk of hospitalizations in AYA HL survivors [15,14], we observed that sociodemographic factors are associated with an increased occurrence of medical conditions in AYA cancer survivors. AYAs who lacked or had public health insurance at initial diagnosis/treatment or resided in low SES neighborhoods at diagnosis were more likely to experience medical conditions ≥2 years after diagnosis. In addition, medical conditions varied by race/ethnicity. Black HL survivors were more likely than Whites to have circulatory system diseases, and Black and Hispanic HL survivors were more likely than Whites to have endocrine diseases. Each of these medical conditions was associated with increased risk of all-cause or HL-specific mortality in these cancer survivors. Clarifying and addressing these medical conditions will be critical for improving outcomes for HL survivors.

While it has been well-established that AYA cancer survivors are at increased risk for chronic health conditions and late effects of treatment compared to AYAs without cancer [2,15,4,3], this is the first U.S. population-based study of AYAs to examine the influence of race/ethnicity, neighborhood SES and health insurance on these outcomes. Long-term AYA HL survivors in Denmark were found to be at increased risk of hospitalization for the medical conditions considered in this study, including second cancers, circulatory system, respiratory system and endocrine diseases [15,26]. Prior studies have also noted increased risks among HL cancer survivors for second cancers, cardiovascular disease and hypothyroidism [7–12,14,18], conditions likely resulting from mediastinal radiation and anthracycline-based chemotherapy [1,8,18,9]. Furthermore, consistent with studies showing increased mortality from cardiovascular disease and subsequent cancers in long-term HL survivors [12,9,14], this study observed higher mortality among AYAs who experienced medical conditions.

Our study highlights the compounding effects for AYA cancer survivors who were uninsured or had public health insurance or lived in lower SES neighborhoods, with prior studies

demonstrating that these factors were associated with higher mortality among AYA HL patients [27,6]. Health insurance status and financial concerns among AYA cancer survivors impact health care utilization [2,28–30] and may place subgroups of AYA survivors at greater risk for medical conditions due to reduced access to preventive care and surveillance of medical conditions. AYAs have historically been among the most highly uninsured population [31,32] and health insurance rates have been found to decrease with time from cancer diagnosis [29,33]. Moreover, AYAs without insurance are less likely than AYA cancer survivors with insurance to receive cancer-related medical care [29] or undergo any doctor/clinic visits in the past year [30]. Even among those with health insurance, AYA cancer survivors are more likely to forgo medical care due to costs when compared with AYAs without cancer [2,28]. High health care expenditures or out-of-pocket burden have been noted among adult cancer survivors (18–64 year-olds), particularly the poor or those with public or no insurance, and this financial burden has been associated with delays in or an inability to obtain necessary medical care and lower breast cancer screening rates [34]. The implementation of the Patient Protection and Affordable Care Act (ACA) [35] may improve outcomes by increasing AYA cancer survivors' access to health insurance and reducing financial barriers to the receipt of recommended preventive care, and should be the focus of future research.

Previous research has shown racial/ethnic disparities in HL survival, with Blacks and Hispanics experiencing higher mortality than Whites [6,36]. In this study, Blacks were more likely than Whites to experience circulatory system diseases and Blacks and Hispanics were more likely to experience endocrine diseases. Our findings are consistent with reports of a higher mortality from coronary heart disease and stroke among Blacks [37] and a generally higher occurrence of endocrine disorders among Blacks and Hispanics [38] than other racial/ethnic groups in the U.S., and suggest that risk reduction strategies (e.g., health behavior change and management of risk factors) and early detection of medical conditions through screening [10,9] may reduce the adverse impact of medical conditions in these patients. Studies of interventions targeting these populations are warranted to address the poor outcomes.

Our study was subject to some limitations. Because we ascertained medical conditions from hospitalization data, we failed to capture diagnoses occurring only during clinic visits and potentially underestimated these medical conditions in our study population. We also may have underestimated medical conditions occurring in HL survivors who left California after diagnosis; however, our findings were similar when we excluded patients who were censored due to reasons other than death more than one year prior to the study end date or limited our analyses to AYAs with at least one admission ≥ 2 years after diagnosis (data not shown). Excluding medical conditions present before HL diagnosis as outcomes also could have underestimated medical conditions in our study population. While available data allowed us to consider initial combined modality therapy, our study lacked details (e.g., dosing) on chemotherapy, radiation and other treatment received after this period, resulting in the potential for treatment under-ascertainment [39,40] and limiting our ability to detect associations. Studies with more complete treatment information are needed before more definite conclusions can be drawn.

Our study also lacked information on changes to health insurance after initial treatment, treatment adherence or quality of care--factors that can influence subsequent care and outcomes. Yet, findings from our study and those of others [30,29,33] indicate that the percentage of survivors who are uninsured or publicly insured increases over time, suggesting that our findings may underestimate the impact of health insurance on medical conditions. In particular, among a subset of survivors (n=1979) with insurance information after two years, we found that 32% had public or no insurance, somewhat higher than the 26% at diagnosis or initial treatment. Further, 2008–2012 data showed that 5-year AYA cancer survivors were more likely to have public insurance than AYAs without cancer (18% vs 9%) and 16% were uninsured [30]. Lastly, our study lacked individual-level measures of SES, although our multifaceted neighborhood measure incorporated several domains of education, income, employment, and cost of living that capture elements of the socioeconomic environment. Despite these limitations, the generalizability of our findings was enhanced by our use of population-based data and inclusion of a large, diverse population of AYA HL cancer survivors who received care across all types of institutions.

This study found that AYA HL cancer survivors of Black or Hispanic race/ethnicity, who were uninsured or publicly insured, or who resided in lower SES neighborhoods were at higher risk for medical conditions and mortality ≥2 years after diagnosis. Inadequate health insurance and lower SES may lead AYA HL survivors to delay or forego medical care that can negatively affect their outcomes. Given the markedly increased mortality among survivors who are likely cured of their cancer and develop these medical conditions, it is important to develop strategies that overcome sociodemographic disparities in survival [6] and improve health-related quality of life [41] and patient outcomes by addressing primary and secondary prevention of medical conditions among these young, high-risk cancer survivors. Additional population-based and targeted intervention studies can help define the optimal approaches for AYA cancer survivors.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1.**

Characteristics of 2-year survivors of adolescent and young adult Hodgkin lymphoma (HL) (N=5,085) by race/ethnicity, California, 1996–2012

| | Race/ethnicity | | | | | |
|---|---|---|---|---|---|---|
| | Overall[a] | NH White | NH Black | Hispanic | NH Asian/Pacific Islandern | |
| | N = 5085 | N = 3021 | N = 346 | N = 1251 | N = 399 | |
| Characteristics | No. (%) | No. (%) | No. (%) | No. (%) | No. (%) | p-value[b] |
| Sex | | | | | | |
| Female | 2714 (53.37) | 1586 (52.50) | 194 (56.07) | 693 (55.40) | 206 (51.63) | |
| Male | 2371 (46.63) | 1435 (47.50) | 152 (43.93) | 558 (44.60) | 193 (48.37) | 0.33 |
| Year of diagnosis | | | | | | |
| 1996–2000 | 1372 (26.98) | 889 (29.43) | 82 (23.70) | 309 (24.70) | 72 (18.05) | |
| 2001–2004 | 1167 (22.95) | 729 (24.13) | 71 (20.52) | 263 (21.02) | 93 (23.31) | |
| 2005–2008 | 1377 (27.08) | 777 (25.72) | 116 (33.53) | 340 (27.18) | 124 (31.08) | |
| 2009–2012 | 1169 (22.99) | 626 (20.72) | 77 (22.25) | 339 (27.10) | 110 (27.57) | <.001 |
| Stage at diagnosis | | | | | | |
| I/II – localized/regional | 3181 (62.56) | 1960 (64.88) | 192 (55.49) | 743 (59.39) | 249 (62.41) | |
| III/IV – advanced | 1650 (32.45) | 908 (30.06) | 141 (40.75) | 440 (35.17) | 139 (34.84) | |
| Unknown | 254 (5.00) | 153 (5.06) | 13 (3.76) | 68 (5.44) | 11 (2.76) | <.001 |
| Initial treatment | | | | | | |
| Chemotherapy and radiation | 2066 (40.63) | 1317 (43.59) | 101 (29.19) | 444 (35.49) | 185 (46.37) | |
| Chemotherapy only | 2353 (46.27) | 1305 (43.20) | 197 (56.94) | 639 (51.08) | 181 (45.36) | |
| Radiation only | 185 (3.64) | 126 (4.17) | 14 (4.05) | 34 (2.72) | 9 (2.26) | |
| None/unknown | 481 (9.46) | 273 (9.04) | 34 (9.83) | 134 (10.71) | 24 (6.02) | <.001 |
| Stem cell transplant | | | | | | |
| Yes | 749 (14.73) | 394 (13.04) | 65 (18.79) | 214 (17.11) | 68 (17.04) | |
| No | 4336 (85.27) | 2627 (86.96) | 281 (81.21) | 1037 (82.89) | 331 (82.96) | <.001 |
| Neighborhood socioeconomic status (SES) | | | | | | |
| Low SES (quintiles 1–3) | 2829 (55.63) | 1375 (45.51) | 276 (79.77) | 961 (76.82) | 175 (43.86) | |
| High SES (quintiles 4,5) | 2256 (44.37) | 1646 (54.49) | 70 (20.23) | 290 (23.18) | 224 (56.14) | <.001 |
| Health insurance | | | | | | |
| Private/military | 3639 (71.56) | 2324 (76.93) | 201 (58.09) | 760 (60.75) | 315 (78.95) | |

| | Race/ethnicity | | | | | |
|---|---|---|---|---|---|---|
| | Overall[a] | NH White | NH Black | Hispanic | NH Asian/Pacific Islandern | |
| | N = 5085 | N = 3021 | N = 346 | N = 1251 | N = 399 | |
| **Characteristics** | **No. (%)** | **No. (%)** | **No. (%)** | **No. (%)** | **No. (%)** | **p-value[b]** |
| Public/none | 1121 (22.05) | 489 (16.19) | 129 (37.28) | 424 (33.89) | 65 (16.29) | |
| Unknown | 325 (6.39) | 208 (6.89) | 16 (4.62) | 67 (5.36) | 19 (4.76) | <.001 |
| B symptoms | | | | | | |
| Yes | 2130 (41.89) | 1209 (40.02) | 163 (47.11) | 559 (44.68) | 166 (41.60) | |
| No | 2295 (45.13) | 1398 (46.28) | 143 (41.33) | 549 (43.88) | 185 (46.37) | |
| Unknown | 660 (12.98) | 414 (13.70) | 40 (11.56) | 143 (11.43) | 48 (12.03) | 0.004 |
| Vital status | | | | | | |
| Alive | 4678 (92.00) | 2791 (92.39) | 311 (89.88) | 1146 (91.61) | 367 (91.98) | |
| Death from HL | 232 (4.56) | 124 (4.10) | 22 (6.36) | 65 (5.20) | 17 (4.26) | |
| Death from NHL | 37 (0.73) | 19 (0.63) | 5 (1.45) | 9 (0.72) | 3 (0.75) | |
| Death from other cancer | 33 (0.65) | 20 (0.66) | 4 (1.16) | 6 (0.48) | 3 (0.75) | |
| Death from heart/cerebrovascular | 22 (0.43) | 13 (0.43) | 1 (0.29) | 7 (0.56) | 1 (0.25) | |
| Death from other cause | 60 (1.18) | 42 (1.39) | 2 (0.58) | 11 (0.88) | 5 (1.25) | |
| Death from unknown cause | 23 (0.45) | 12 (0.40) | 1 (0.29) | 7 (0.56) | 3 (0.75) | 0.79 |

NH=Non-Hispanic; NHL=Non-Hodgkin lymphoma

[a]Includes 68 patients with other/unknown race/ethnicity.

[b]Chi-squared test assessing whether the distribution of selected characteristics differ by race/ethnicity.

**Table 2.**

Prevalence of medical conditions[a] among 2-year adolescent and young adult Hodgkin lymphoma survivors (n=5,085), California, 1996–2012

| Characteristics | Medical conditions | | | | | | |
|---|---|---|---|---|---|---|---|
| | Diseases of circulatory system No. (%) | Diseases of respiratory system No. (%) | Chronic kidney disease and renal failure No. (%) | Liver disease No. (%) | Endocrine and related diseases No. (%) | Hypothyroidism No. (%) | Subsequent cancers No. (%) |
| Race/ethnicity | | | | | | | |
| NH White | 310 (10.26) | 346 (11.45) | 106 (3.51) | 77 (2.55) | 403 (13.34) | 209 (6.92) | 115 (3.81) |
| Black | 58 (16.76) | 53 (15.32) | 21 (6.07) | 6 (1.73) | 74 (21.39) | 17 (4.91) | 7 (2.02) |
| Hispanic | 136 (10.87) | 174 (13.91) | 45 (3.60) | 42 (3.36) | 226 (18.07) | 79 (6.31) | 36 (2.88) |
| Asian | 48 (12.03) | 46 (11.53) | 13 (3.26) | 10 (2.51) | 63 (15.79) | 26 (6.52) | 13 (3.26) |
| P-value | 0.002 | 0.06 | 0.19 | 0.24 | <.001 | 0.59 | 0.25 |
| Stage at diagnosis | | | | | | | |
| I/II – localized/regional | 332 (10.44) | 367 (11.54) | 104 (3.27) | 70 (2.20) | 446 (14.02) | 254 (7.98) | 115 (3.62) |
| III/IV - advanced | 193 (11.70) | 223 (13.52) | 77 (4.67) | 59 (3.58) | 285 (17.27) | 62 (3.76) | 43 (2.61) |
| Unknown | 30 (11.81) | 35 (13.78) | 6 (2.36) | 6 (2.36) | 45 (17.72) | 18 (7.09) | 14 (5.51) |
| P-value | 0.37 | 0.11 | 0.03 | 0.03 | 0.006 | <.001 | 0.03 |
| Health insurance | | | | | | | |
| Private/military | 361 (9.92) | 389 (10.69) | 107 (2.94) | 85 (2.34) | 490 (13.47) | 221 (6.07) | 127 (3.49) |
| Public/none | 164 (14.63) | 197 (17.57) | 67 (5.98) | 42 (3.75) | 237 (21.14) | 75 (6.69) | 30 (2.68) |
| Unknown | 30 (9.23) | 39 (12.00) | 13 (4.00) | 8 (2.46) | 49 (15.08) | 38 (11.69) | 15 (4.62) |
| P-value | <.001 | <.001 | <.001 | 0.04 | <.001 | <.001 | 0.18 |
| Neighborhood socioeconomic status (SES) | | | | | | | |
| Low SES | 335 (11.84) | 398 (14.07) | 123 (4.35) | 82 (2.90) | 501 (17.71) | 173 (6.12) | 87 (3.08) |
| High SES | 220 (9.75) | 227 (10.06) | 64 (2.84) | 53 (2.35) | 275 (12.19) | 161 (7.14) | 85 (3.77) |
| P-value | 0.02 | <.001 | 0.005 | 0.23 | <.001 | 0.14 | 0.17 |
| Initial treatment | | | | | | | |
| Chemotherapy and radiation | 204 (9.87) | 247 (11.96) | 65 (3.15) | 46 (2.23) | 290 (14.04) | 194 (9.39) | 88 (4.26) |
| Chemotherapy only | 278 (11.81) | 306 (13.00) | 104 (4.42) | 67 (2.85) | 396 (16.83) | 77 (3.27) | 60 (2.55) |
| Radiation only | 30 (16.22) | 32 (17.30) | 8 (4.32) | 7 (3.78) | 34 (18.38) | 36 (19.46) | 7 (3.78) |
| None/unknown | 43 (8.94%) | 40 (8.32) | 10 (2.08) | 15 (3.12) | 56 (11.64) | 27 (5.61) | 17 (3.53) |

| Characteristics | Medical conditions | | | | | | |
|---|---|---|---|---|---|---|---|
| | Diseases of circulatory system No. (%) | Diseases of respiratory system No. (%) | Chronic kidney disease and renal failure No. (%) | Liver disease No. (%) | Endocrine and related diseases No. (%) | Hypothyroidism No. (%) | Subsequent cancers No. (%) |
| P-value | 0.009 | 0.005 | 0.03 | 0.37 | <.001 | <.001 | 0.02 |
| Stem cell transplant | | | | | | | |
| Yes | 179 (23.90) | 264 (35.25) | 82 (10.95) | 54 (7.21) | 309 (41.26) | 78 (10.41) | 51 (6.81) |
| No | 376 (8.67) | 361 (8.33) | 105 (2.42) | 81 (1.87) | 467 (10.77) | 256 (5.90) | 121 (2.79) |
| P-value | <.001 | <.001 | <.001 | <.001 | <.001 | <.001 | <.001 |

NH=Non-Hispanic

[a]Medical conditions obtained from hospital discharge records

[b]Data for patients with other/unknown race/ethnicity (n=68) not presented

[c]Chi-squared test assessing whether the distribution of medical conditions differs by baseline characteristics and treatment

**Table 3.**

Ten-year cumulative incidence (%, percentage) with 95% confidence intervals (95% CI) of medical conditions[a] among 2-year adolescent and young adult Hodgkin lymphoma survivors, California, 1996–2012

| Characteristics | Medical conditions | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Circulatory system diseases % (95% CI)** | **Respiratory system diseases % (95% CI)** | **Chronic kidney disease/renal failure % (95% CI)** | **Liver disease % (95% CI)** | **Endocrine and related diseases % (95% CI)** | **Hypothyroidism % (95% CI)** | **Subsequent cancers % (95% CI)** |
| Race/ethnicity[b] | | | | | | | |
| NH White | 9.29 (8.14, 10.52) | 11.17 (9.94, 12.48) | 3.10 (2.46, 3.86) | 2.42 (1.84, 3.12) | 12.24 (10.95, 13.60) | 6.00 (5.07, 7.04) | 3.03 (2.37, 3.81) |
| NH Black | 17.60 (13.11, 22.63) | 17.33 (12.90, 22.32) | 6.54 (3.96, 9.99) | 2.25 (0.91, 4.67) | 21.50 (16.73, 26.68) | 6.13 (3.60, 9.58) | 1.48 (0.38, 4.12) |
| Hispanic | 10.64 (8.72, 12.78) | 14.98 (12.76, 17.37) | 3.33 (2.28, 4.67) | 3.83 (2.67, 5.31) | 19.40 (16.89, 22.05) | 6.10 (4.61, 7.86) | 2.73 (1.74, 4.08) |
| NH API | 11.61 (8.19, 15.68) | 12.04 (8.70, 15.95) | 3.87 (1.99, 6.71) | 2.77 (1.29, 5.21) | 16.42 (12.37, 20.99) | 7.67 (4.88, 11.26) | 2.88 (1.33, 5.43) |
| P-value[c] | <.001 | 0.004 | 0.12 | 0.13 | <.001 | 0.70 | 0.47 |
| Stage at diagnosis | | | | | | | |
| I/II | 9.58 (8.44, 10.80) | 11.52 (10.29, 12.83) | 2.82 (2.21, 3.54) | 2.21 (1.66, 2.88) | 13.36 (12.03, 14.75) | 7.24 (6.23, 8.34) | 2.64 (2.02, 3.39) |
| III/IV | 12.03 (10.22, 13.99) | 14.67 (12.77, 16.71) | 5.13 (3.98, 6.49) | 3.80 (2.81, 5.02) | 18.26 (16.16, 20.47) | 3.61 (2.65, 4.79) | 2.84 (2.00, 3.90) |
| P-value[c] | 0.14 | 0.03 | 0.01 | <.001 | <.001 | <.001 | 0.04 |
| Health insurance | | | | | | | |
| Private/military | 9.52 (8.44, 10.68 ) | 10.96 (9.83, 12.15) | 2.97 (2.38, 3.66) | 2.33 (1.80, 2.97) | 13.18 (11.95, 14.48) | 5.56 (4.73, 6.47) | 3.08 (2.45, 3.82) |
| Public/none | 13.41 (11.16, 15.86) | 18.42 (15.81, 21.19) | 5.20 (3.79, 6.92) | 4.18 (2.89, 5.83) | 21.07 (18.34, 23.94) | 6.97 (5.27, 8.99) | 2.15 (1.31, 3.34) |
| P-value | <.001 | <.001 | <.001 | 0.01 | <.001 | 0.06 | 0.47 |
| Neighborhood SES | | | | | | | |
| High SES | 8.77 (7.48, 10.18) | 9.91 (8.57, 11.36) | 2.73 (2.03, 3.58) | 2.36 (1.71, 3.18) | 12.00 ( 10.52, 13.59) | 6.52 (5.38, 7.79) | 3.00 (2.25, 3.91) |
| Low SES | 11.50 (10.16, 12.92) | 14.74 (13.27, 16.29) | 4.05 (3.27, 4.96) | 3.03 (2.34, 3.86) | 17.29 ( 15.72, 18.92) | 5.83 (4.87, 6.91) | 2.63 (1.97, 3.43) |
| P-value[c] | 0.007 | <.001 | 0.003 | 0.20 | <.001 | 0.20 | 0.18 |
| Initial treatment | | | | | | | |
| Chemotherapy and radiation | 9.08 (7.75, 10.54 ) | 11.98 (10.45, 13.61) | 3.04 (2.27, 3.98) | 2.29 (1.62, 3.13) | 13.63 ( 12.03, 15.34) | 8.55 (7.23, 9.99) | 3.34 (2.51, 4.36) |
| Chemotherapy only | 11.50 (10.01, 13.10) | 13.47 (11.92, 15.12) | 4.59 (3.67, 5.66) | 3.04 (2.28, 3.97) | 17.42 ( 15.65, 19.27) | 2.99 (2.25, 3.90) | 2.22 (1.59, 3.03) |
| Radiation only | 9.70 (5.76, 14.85) | 14.14 (9.36, 19.89) | 0.71 (0.06, 3.56) | 2.63 (0.86, 6.17) | 11.08 ( 6.81, 16.51) | 12.96 (8.30, 18.68) | 1.96 (0.53, 5.22) |
| None/unknown | 10.02 (7.03, 13.62) | 9.95 (7.05, 13.42) | 1.18 ( 0.38, 2.89) | 3.24 (1.68, 5.61) | 10.34 ( 7.46, 13.77) | 6.39 (4.04, 9.47) | 3.07 (1.53, 5.46) |

| Characteristics | Medical conditions | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Circulatory system diseases % (95% CI)** | **Respiratory system diseases % (95% CI)** | **Chronic kidney disease/renal failure % (95% CI)** | **Liver disease % (95% CI)** | **Endocrine and related diseases % (95% CI)** | **Hypothyroidism % (95% CI)** | **Subsequent cancers % (95% CI)** |
| P-value[c] | 0.004 | 0.003 | 0.003 | 0.24 | <.001 | <.001 | 0.06 |
| Stem cell transplant | | | | | | | |
| Yes | 22.55 (19.38, 25.88) | 36.46 (32.64, 40.29) | 10.58 (8.31, 13.15) | 7.11 (5.26, 9.30) | 41.42 (37.57, 45.21) | 10.20 (7.96, 12.74) | 5.94 (4.24, 8.02) |
| No | 8.06 (7.13, 9.06) | 8.28 (7.36, 9.28) | 2.16 (1.69, 2.72) | 1.94 (1.48, 2.50) | 10.15 (9.12, 11.25) | 5.40 (4.63, 6.25) | 2.22 (1.73, 2.82) |
| P-value[c] | <.001 | <.001 | <.001 | <.001 | <.001 | <.001 | <.001 |

NH=Non-Hispanic, API=Asian/Pacific Islander, SES=Socioeconomic status

[a]Medical conditions obtained from hospital discharge records

[b]Data for patients with other/unknown race/ethnicity, unknown stage at diagnosis and unknown health insurance are not presented

[c]Gray's K-sample test statistic for the difference in cumulative incidence of late effects by baseline characteristics and treatment over entire study period

**Table 4.**

Multivariable adjusted hazard ratios(HR) and associated 95% confidence intervals (95% CI) of medical conditions[a] among 2-year adolescent and young adult Hodgkin lymphoma survivors (n=5,085), California, 1996–2012

| Characteristics | Medical conditions | | | | | | |
|---|---|---|---|---|---|---|---|
| | Circulatory system diseases[b] HR (95% CI) | Respiratory system diseases[b] HR (95% CI) | Chronic kidney disease/ renal failure[b] HR (95% CI) | Liver disease[c] HR (95% CI) | Endocrine and related diseases[b] HR (95% CI) | Hypothyroidism[b] HR (95% CI) | Subsequent cancers[c] HR (95% CI) |
| Race/ethnicity[d] | | | | | | | |
| NH White | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| NH Black | 1.58 ( 1.17, 2.14) | 1.12 ( 0.82, 1.52) | 1.31 ( 0.80, 2.15) | 0.56 ( 0.24, 1.32) | 1.37 ( 1.05, 1.78) | 0.82 ( 0.49, 1.38) | 0.58 ( 0.27, 1.27) |
| Hispanic | 1.01 ( 0.82, 1.25) | 1.08 ( 0.89, 1.31) | 0.84 ( 0.59, 1.21) | 1.22 ( 0.82, 1.81) | 1.24 ( 1.04, 1.48) | 1.05 ( 0.79, 1.39) | 0.88 ( 0.60, 1.29) |
| NH Asian/Pacific Islander | 1.33 ( 0.98, 1.80) | 1.05 ( 0.76, 1.45) | 0.94 ( 0.51, 1.71) | 1.06 ( 0.54, 2.05) | 1.29 ( 0.98, 1.69) | 1.16 ( 0.76, 1.76) | 1.05 ( 0.59, 1.84) |
| Health insurance | | | | | | | |
| Private/military | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Public/none | 1.41 ( 1.16, 1.73) | 1.57 ( 1.30, 1.89) | 1.76 ( 1.27, 2.46) | 1.52 ( 1.03, 2.24) | 1.51 ( 1.28, 1.79) | 1.29 ( 0.98, 1.72) | 0.89 ( 0.59, 1.35) |
| Unknown | 0.78 ( 0.53, 1.16) | 0.94 ( 0.68, 1.31) | 1.26 ( 0.69, 2.30) | 0.94 ( 0.44, 2.03) | 1.02 ( 0.75, 1.38) | 1.24 ( 0.88, 1.74) | 0.91 ( 0.53, 1.56) |
| Neighborhood socioeconomic status (SES) | | | | | | | |
| Low SES | 1.10 ( 0.91, 1.33) | 1.28 ( 1.07, 1.53) | 1.30 ( 0.93, 1.81) | 1.09 ( 0.76, 1.55) | 1.30 ( 1.10, 1.53) | 0.94 ( 0.74, 1.19) | 0.92 ( 0.67, 1.27) |
| High SES | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Stem cell transplant | | | | | | | |
| Yes | 2.04 ( 1.65, 2.52) | 3.39 ( 2.82, 4.08) | 3.31 ( 2.42, 4.54) | 2.93 ( 2.01, 4.27) | 2.58 ( 2.16, 3.07) | 1.70 ( 1.26, 2.31) | 2.07 ( 1.43, 3.02) |
| No | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Year of diagnosis | | | | | | | |
| 1996–2000 | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| 2001–2004 | 0.97 ( 0.78, 1.21) | 0.82 ( 0.67, 1.01) | 1.10 ( 0.75, 1.62) | 1.01 ( 0.66, 1.55) | 1.00 ( 0.82, 1.20) | 1.05 ( 0.81, 1.36) | 0.86 ( 0.57, 1.29) |
| 2005–2008 | 0.79 ( 0.62, 1.01) | 0.73 ( 0.58, 0.91) | 1.45 ( 0.98, 2.15) | 0.91 ( 0.55, 1.53) | 1.02 ( 0.84, 1.25) | 0.61 ( 0.43, 0.87) | 0.90 ( 0.56, 1.47) |
| 2009–2012 | 0.86 ( 0.61, 1.21) | 0.70 ( 0.51, 0.94) | 0.94 ( 0.51, 1.73) | 1.39 ( 0.73, 2.65) | 0.84 ( 0.63, 1.12) | 0.58 ( 0.32, 1.03) | 0.51 ( 0.20, 1.31) |

NH=Non-Hispanic

[a] Medical conditions obtained from hospital discharge records

[b] Stratified by stage at diagnosis, initial treatment and B-symptoms; adjusted for all variables in the table and sex and age at diagnosis

[c] Stratified by stage at diagnosis and initial treatment; adjusted for all variables in the table and sex, age at diagnosis, and B symptoms

[d] Data for patients with other/unknown race/ethnicity not presented

**Table 5.**

Multivariable[a] hazard ratios (HR) and 95% confidence interval (95% CI) estimates for death from all causes (overall survival) and death from Hodgkin lymphoma (HL-specific survival) among 2-year adolescent and young adult Hodgkin lymphoma survivors (n=5,085), California, 1996–2012.

| | Overall Survival | | HL-Specific Survival | |
|---|---|---|---|---|
| **Medical conditions[b]** | **Deaths** | **HR (95% CI)** | **Deaths** | **HR (95% CI)** |
| Circulatory system diseases | | | | |
| Yes | 201 | 2.08 (1.56, 2.77) | 123 | 2.18 (1.54, 3.09) |
| No | 176 | Reference | 109 | Reference |
| Respiratory system diseases | | | | |
| Yes | 140 | 6.17 (4.50, 8.46) | 75 | 8.03 (5.34, 12.09) |
| No | 237 | Reference | 157 | Reference |
| Chronic kidney disease/ renal failure | | | | |
| Yes | 277 | 2.88 (2.15, 3.87) | 171 | 2.44 (1.69, 3.51) |
| No | 100 | Reference | 61 | Reference |
| Liver disease | | | | |
| Yes | 319 | 3.08 (2.19, 4.34) | 199 | 2.61 (1.66, 4.09) |
| No | 58 | Reference | 33 | Reference |
| Endocrine and related diseases | | | | |
| Yes | 143 | 3.10 (2.24, 4.29) | 75 | 4.50 (2.95, 6.85) |
| No | 234 | Reference | 157 | Reference |
| Hypothyroidism | | | | |
| Yes | 317 | 1.37 (0.97, 1.93) | 201 | 1.52 (0.96, 2.42) |
| No | 60 | Reference | 31 | Reference |
| Subsequent cancers | | | | |
| Yes | 330 | 3.83 (2.60, 5.65) | 224 | 0.68 (0.30, 1.53) |
| No | 47 | Reference | 8 | Reference |

[a]Stratified by stage at diagnosis and initial treatment; adjusted for all variables in the table and race/ethnicity, neighborhood socioeconomic status, sex, age at diagnosis, year of diagnosis, stem cell transplant and B-symptoms

[b]Medical conditions obtained from hospital discharge records