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Utilization of Autologous Hematopoietic Cell Transplantation Over Time in Multiple Myeloma: A Population-Based Study

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Abstract

Purpose: Autologous hematopoietic cell transplantation (autoHCT) is associated with survival benefits in multiple myeloma (MM), but utilization remains low and differs by sociodemographic factors. Prior population-based studies have not fully captured autoHCT utilization or examined relationships between sociodemographic factors and autoHCT trends over time.

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Authorship Contributions:

TK, NE, and AB designed the research

AB primarily performed statistical methods and analysis.

NSE, TK, ASR, and AB analyzed the data.

NSE, TK, and AB primarily wrote the manuscript.

NSE, AB, ASR, SJS, BV, RA, JJPC, CLM, JJA, LLM, LM, TW, and THK each contributed significantly to the writing of the manuscript.

Patients and Methods: We used a novel data linkage between the California Cancer Registry, Center for International Blood and Marrow Transplant Research, and hospitalizations to capture autoHCT in a population-based MM cohort (n=29,109; 1991–2016). Due to interactions by treatment era, stratified multivariable Cox proportional hazards regression models determined factors associated with autoHCT.

Results: The frequency of MM patients who received autoHCT increased from 5.7% (1991–1995) to 27.4% (2011–2016). In models by treatment era, patients with public/no (vs private) health insurance were less likely to receive autoHCT (2011–2016 Medicare Hazard Ratio (HR) 0.70, 95% Confidence Interval (CI) 0.63 – 0.78; Medicaid HR 0.81, CI 0.72 – 0.91; no insurance HR 0.56, CI 0.32–0.99). In each treatment era, Black/African American (vs non-Hispanic White) patients were less likely to receive autoHCT (2011–2016 HR 0.83, CI 0.72 – 0.95). Hispanic patients were less likely to undergo autoHCT, most prominently in the earliest treatment era (1991–1995 HR 0.58, 95%CI: 0.37 – 0.90; 2011–2016 HR 1.07, CI: 0.96–1.19). Patients in lower socioeconomic status neighborhoods were less likely to utilize autoHCT, but differences decreased over time.

Conclusions: Despite increases in autoHCT utilization, sociodemographic disparities remain. Identifying and mitigating barriers to autoHCT is essential to ensuring more equitable access to this highly effective therapy.

MicroAbstract:

Autologous hematopoietic cell transplantation (autoHCT) is associated with survival benefits in multiple myeloma, but utilization remains low. Prior population-based studies have not examined relationships between sociodemographic factors and autoHCT utilization trends over time. We found that Black/African American patients and those with Medicaid, Medicare, or no health insurance were less likely to receive autoHCT in each treatment era.

Keywords

hematopoietic cell; transplant; transplantation; multiple myeloma; autologous; adult

Introduction

Consolidative autologous hematopoietic cell transplant (autoHCT) is the standard of care for transplant-eligible patients with multiple myeloma (MM) who achieve at least a partial response to induction therapy. Although MM remains incurable, autoHCT is associated with delayed disease progression and low treatment-related mortality for patients with MM [1–6]. Several large studies have demonstrated progression-free survival (PFS) and overall survival (OS) benefits of autoHCT in patients with MM compared to continuance of maintenance therapy without autoHCT [1–6]. The findings of these trials lead to consolidative autoHCT becoming the standard of care in this patient population. AutoHCT can be used as a front-line consolidative treatment or delayed until disease recurrence.

Despite survival benefits and some improvement in autoHCT utilization over time, overall utilization remains low, at approximately 10–40% [7–9]. The decision to proceed to autoHCT is complex, with disease characteristics and comorbidities affecting transplant

utilization. For instance, a higher comorbidity index score has been associated with inferior survival [10]. In addition, sociodemographic factors have been associated with autoHCT use, with lower rates of autoHCT among those residing in lower socioeconomic status neighborhoods (nSES) and those insured by Medicare or Medicaid in comparison to patients with private health insurance [11, 12]. Despite the higher incidence and younger age at diagnosis of MM among Black/African Americans, they are more likely to be referred for autoHCT later in their disease course compared to non-Hispanic White patients [13,14]. Prior population-based studies have not fully captured autoHCT utilization and did not examine trends over time regarding disparities in the utilization of autoHCT [12,14].

To address this gap, we used a novel data linkage between the California Cancer Registry (CCR), the Center for International Blood and Marrow Transplant Research (CIBMTR), and the California Patient Discharge Database (PDD) [15] to describe autoHCT utilization in a population-based cohort of patients diagnosed with MM. We evaluated sociodemographic characteristics associated with autoHCT utilization in different treatment eras to inform efforts to mitigate treatment disparities.

Methods

Database and Patients

This was a retrospective cohort study utilizing a data linkage between the CCR, CIBMTR, and hospitalization data from the California PDD [15]. The CCR is California's population-based cancer surveillance system, collecting cancer incidence on >99% of new cancer cases since 1988 [15]. Within the CCR, patients eligible for linkage were diagnosed with a hematologic malignancy between 1991 and 2016. Since 2007, participating CIBMTR institutions have been required to report data from all consecutive allogeneic HCT procedures and most centers voluntarily report autoHCT procedures using the same standardized forms. Within the CIBMTR, patients eligible for linkage were those with any HCT for a hematologic malignancy diagnosed during 1991–2016 who had a California residential zip code or, if zip code was missing, were transplanted at a California HCT center. Since 1991, the California Department of Health Care Access and Information has mandated reporting of diagnostic and procedure codes on all inpatient hospitalization admissions in California from nonfederal hospitals across the state through the PDD. The process for the linkage used a combination of probabilistic and deterministic methodology using 9 different linkage identifiers, as described previously [15]. This analysis was limited to MM patients in the CCR between the ages 18 to 79 at diagnosis due to rarity of autoHCT in patients ≥80 years; MM patients were excluded if they did not have a valid social security number for linking to the PDD, autoHCT date or follow-up dates were unknown, survival time was zero, their first HCT was allogenic, or if nSES or race/ethnicity was unknown (Figure 1).

Autologous HCT

AutoHCT utilization was captured from all three data sources independently. As most autoHCT data were in multiple sources (Figure 2), we used information from the CIBMTR where available, then the PDD using specific International Classification of Diseases (ICD)

ICD-9/ICD-10 codes and CCR using reported treatment fields for the initial course of treatment.

Covariates

Patient sociodemographic and clinical characteristics were obtained from the CCR. Race/ethnicity was classified as non-Hispanic White, non-Hispanic Black/African American, Hispanic, Asian/Pacific Islander, American Indian, and other/unknown. Neighborhood socioeconomic status (nSES) is a composite measure comprising Census and American Community Survey education, occupation, unemployment, household income, poverty, rent, and house values at the block group level [16], and grouped into quintiles based on the distribution of SES across all census block groups in California. nSES was divided into low (1st, 2nd quintiles), middle (3rd quintile), and high (4th or 5th quintiles).

Type of health insurance at cancer diagnosis or initial treatment was categorized as private/military (health maintenance organizations, preferred provider organizations, managed care not otherwise specified, military care), Medicaid or other government, Medicare, no insurance/self-pay or unknown. Insurance information was not available in CCR before 1996. Initial treatment included a combination of chemotherapy and immunotherapy collected from CCR (either chemotherapy or immunotherapy, both chemotherapy and immunotherapy, neither chemotherapy or immunotherapy, or unknown). Comorbidities were identified using the Elixhauser Comorbidity Index and were captured up to two years prior to the date of cancer diagnosis. [17] Comorbidities were classified based on admissions in PDD as no admission (and thus no information), or 0, 1–2, or ≥3 comorbidities.

Statistical Analysis

Descriptive statistics and univariate analysis were used to evaluate differences in the distribution of covariates by receipt of autoHCT. Median follow-up time was estimated using the reverse Kaplan-Meier method [18]. The cumulative incidence and 95% confidence intervals (CI) of autoHCT utilization were determined from initial cancer diagnosis to autoHCT date, death date, last known date of contact, or study cutoff (12/31/18), whichever occurred first, accounting for the competing risk of death. Cumulative incidence was stratified by MM treatment era. Multivariable Cox proportional hazards regression models were performed to evaluate characteristics associated with autoHCT utilization, using the methods of Fine and Gray to account for the competing risk of death [19]. Interactions between autoHCT and treatment era were included in the multivariable Cox proportional hazards regression models to evaluate changes over time. As there were significant interactions (p-value for interaction <0.001) between year of diagnosis and race/ethnicity and year of diagnosis and nSES, the models were stratified by treatment era. Proportional hazard assumptions for all Cox models were evaluated using the Schoenfeld Residuals Test [20]. Variables violating proportional hazards assumptions [chemotherapy/immunotherapy, age at diagnosis (1991–1995), and comorbidities (1991–1995; 2006–2010) were included as stratification variables.

All p-values were two-sided; a p-value of <0.05 was considered statistically significant. All analyses were performed using SAS 9.4 (SAS, Cary, NC). This study was approved by the

Institutional Review Boards of the University of California Davis, the California Committee for the Protection of Human Subjects, and the National Marrow Donor Program and was determined to not be human subjects research by the National Cancer Institute.

Results

Our study identified 29,109 patients diagnosed with MM between 1991 and 2016. The median follow-up time from diagnosis was 10.2 years (95% CI 10.0 – 10.4 years). Overall, using all three data sources, 18.9% of patients (n=5500) underwent an autoHCT. The CIBMTR captured 70.8% of autoHCTs (17.8% of all three sources, 36.7% CIBMTR and PDD, 10.2% CIBMTR and CCR, and 6.1% CIBMTR only). The remaining autoHCTs were captured from PDD only (19.0%), CCR only (4.7%), or PDD and CCR (5.5%) (Figure 2). The median time from diagnosis to transplant was 9.7 months (interquartile range: 6.9–16.2).

Overall, patients of non-Hispanic White, Black/African American, Hispanic, and Asian/Pacific Islander race/ethnicity comprised 57%, 14%, 20%, and 9% of the cohort, respectively (Table 1). A lower proportion of Black/African American patients (15.8%) received an autoHCT than other racial/ethnic groups. The utilization of autoHCT was higher among patients residing in higher SES neighborhoods (15.2% low, 18.5% intermediate, and 22.0% high nSES). The frequency of MM patients who received autoHCT increased in each treatment era, from 5.7% during 1991–1995 to 27.4% during 2011–2016. The proportion of patients receiving an autoHCT was higher among those with private/military health insurance (28.4%) than other types of health insurance. There was no significant difference between male versus female sex and receipt of autoHCT throughout the study period. Patients with no or fewer comorbidities were also more likely to receive autoHCT. Among those with 0 comorbidites, 20.8% underwent autoHCT versus 17.9% among those with 1–2 comorbidites and 10.9% for those with 3 or more comorbidities. Older age at diagnosis was also associated with lower overall autoHCT utilization. Patients aged <40, 40–49, 50–59, 60–69, and 70–79 had autoHCT rates of 37.3%, 39.9%, 33.8%, 19.3% and 2.1%, respectively. Residing in a rural versus urban address had no statistically significant association with autoHCT utilization overall and in each time era. The cumulative incidence of autoHCT at 12 months increased over time, from 2.9% in 1991–1995, to 7.2% in 1996–2000, 11.9% in 2001–2005, 12.2% in 2006–2010, and 18.9% in 2011–2016 (Figure 3).

As there were significant interactions between year of diagnosis with race/ethnicity and nSES, the models were stratified by treatment era. In multivariable models, we identified that Hispanic patients were less likely than non-Hispanic White patients to have an autoHCT in 1991–1995 (HR 0.58, CI: 0.37 – 0.90), but this difference was less pronounced in later years (HR 1.07, CI: 0.96–1.19 for 2011–2016) (Table 2). Black/African American patients had lower utilization throughout the study period, particularly after 2005 (HR 0.66, CI 0.55 – 0.79 in 2006–2010; HR 0.83, CI 0.72 – 0.95 in 2011–2016).

Increasing age at diagnosis was also associated with decreased utilization of autoHCTs throughout the study and in each time era. Patients over the age of 50 were less likely to undergo autoHCT overall in comparison to patients < 50 years of age (ages 50–59 HR

0.71, CI 0.67 – 0.71; age 60–69 HR 0.40, CI 0.37 – 0.43; age 70–79 HR 0.05, CI 0.04 – 0.05). The differences for patients residing in the lowest versus highest nSES became less pronounced over time, with the strongest association observed in 1991–1995 (HR 0.35, CI: 0.24 – 0.52). Compared with private insurance, patients with Medicare were less likely to undergo autoHCTs, but only after 2006 (HR 0.79, CI 0.65 – 0.97, 2006–2010; HR 0.70, CI 0.63 – 0.78, 2011–2016). Those with Medicaid were less likely to undergo autoHCTs over the entire study period, (HR 0.81, CI 0.72 – 0.91, 2011–2016). Patients who were never married or previously married were also less likely to undergo autoHCTs compared to married patients after 1996 (HR 0.71, CI 0.63–0.80, 2011–2016). Lastly, compared to patients with no comorbidities, patients with 1–2 comorbidities were less likely to have autoHCT during the treatment era from 1996 to 2000 (HR 0.74, CI 0.55–1.00) but not during other time periods, whereas those with ≥3 comorbidities were less likely to have autoHCT throughout the study (HR 0.71, CI 0.56–0.92, 2011–2016).

Discussion

In this population-based study, we examined sociodemographic disparities in the utilization of autoHCT among patients diagnosed with MM across treatment eras. To improve the precision of autoHCT ascertainment during 1991–2016, we linked three high-quality data sources (CCR, CIBMTR, and PDD), allowing for a more comprehensive analysis of autoHCT usage across patient subgroups. AutoHCT increased steadily over time, but utilization remained low in 2011–2016 with a cumulative incidence of 18.9% within one year of diagnosis. We found sociodemographic disparities in utilization decreased over time for specific subgroups, including patients of Hispanic race/ethnicity and those residing in lower SES neighborhoods. In contrast, Black/African American patients were less likely to have autoHCT throughout each treatment era and this difference increased after 2005. Further, MM patients with Medicaid or Medicare health insurance or no health insurance were also less likely to receive autoHCT in each treatment era. Whereas married or previously married patients and patients < 50 years were more likely to undergo autoHCT in each time era from 1996 onward, we did not identify differences in autoHCT utilization in other demographic categories, including sex or rural/urban residence. Despite some improvements over time, our findings highlight persistent disparities in autoHCT utilization among MM patients in California.

In our study, CIBMTR and the PDD each captured the majority (≥70%) of transplants, but each source also identified HCTs not captured by the others. Prior studies assessing autoHCT utilization have relied on SEER/Medicare databases, which is limited to those >65 years, and the CIBMTR, which does not include the non-HCT population or capture all autoHCTs due to voluntary reporting [21]. Studies utilizing a cancer registry [15] or the National Cancer Database only capture upfront autoHCT, likely resulting in an under-ascertainment of overall utilization. More fully capturing autoHCT utilization in a population-based cohort of MM patients allows us to identify patterns of autoHCT utilization more accurately. In addition, our study encompasses a longer follow-up time compared to prior studies [8, 9, 11, 12, 14, 22, 23], informing trends over time and changes in disparities in autoHCT utilization.

While we observed increases in autoHCT utilization in more recent treatment eras, utilization was observed among only 18.9% of patients within 12 months of MM diagnosis. Results of studies demonstrating PFS and OS benefits of autoHCT in MM patients [1–6] likely led to more patients being referred and considered for autoHCT. Our findings are similar to other population-based studies, including our prior work observing autoHCT utilization in 23.9% of MM patients between 1998 and 2012 using CCR and PDD data [7]. Al-Hamadani et al. [11] showed a similar increase in upfront autoHCT from 5.2% to 12.1% in the National Cancer Database from 1998 to 2010, although autoHCT estimates were lower than observed in our study. Differences in autoHCT utilization over time also have been observed by race/ethnicity. Schriber et al. reported increased utilization across all racial/ethnic groups over time in CIBMTR data. However, this increase was lowest among Hispanic and Black/African American patients [9]. A SEER-Medicare analysis by Ailwadhi et al. also showed increase in autoHCT utilization between 2007 and 2009 for all racial/ethnic groups, except Black/African American patients [8], consistent with our findings.

We found that Black/African American patients were less likely than non-Hispanic White patients to receive autoHCT throughout each treatment era, a difference more pronounced after 2005. Contrary to prior studies, Hispanic patients were less likely to undergo autoHCT only in the earliest era [8, 9, 11, 14]. Schriber et al. showed that Hispanic patients had a lower comorbidity score and achieved better treatment response before autoHCT compared to non-Hispanic White and Black/African American patients [9]. One study also showed that once patients were evaluated at a transplant center, there were no differences in who proceeded to autoHCT based on ethnicity [22]. Thus, access to transplant centers rather than disease characteristics, such as high-risk cytogenetic features, response to treatment, and clinical comorbidities, may be impacting disparities seen among race/ethnicity for autoHCT in MM [24]. Other factors such as physician bias, referral bias, social factors, and cultural beliefs regarding transplantation should be investigated further [25]. Exploring these factors will lead to better understanding of the potential causes of racial/ethnic disparities in autoHCT utilization, with the goal of increasing autoHCT referrals/evaluations and ultimately receipt of transplant.

We also observed that patients residing in the lowest nSES neighborhoods were less likely to utilize autoHCT. This is similar to findings in prior studies that showed decreased use of autoHCT in those with lower annual household income or who resided in lower nSES areas [8, 11, 14]. Consideration to several factors should be given, including access to a transplant center, referral for autoHCT evaluation, financial burden to the patient and/or their family, and social barriers to transplant such as caregiver support and availability of transportation to a transplant center. The importance of these social barriers are highlighted by our finding that married and previously married patients were more likely to undergo autoHCT, as supported by prior studies showing higher autoHCT utilization [7] and improved OS in married patients with MM [26]. Unlike prior studies [8, 11, 14], our results showed differences by nSES decreased over more recent treatment eras. As such, further investigation into what factors changed over time may aid in determining how factors contributing to lower autoHCT utilization among disadvantaged subgroups can be further mitigated.

Consistent with prior studies [11, 23], MM patients with Medicare and Medicaid insurance or no health insurance were less likely to undergo autoHCT. Notably, we are the first to report no improvements over time in the likelihood of autoHCT with Medicare or Medicaid compared to private insurance, emphasizing the need to identify the barriers to transplant for these patients. Our findings warrant further evaluation of how Medicare and Medicaid insurance coverage impacts pre-transplant evaluation, access to a transplant center, time/frequency of referral to a transplant facility, and financial burden to the patient and their family.

This study has several limitations. The CCR lacks information on performance status, molecular data, disease stage and risk stratification, systemic therapy, or treatment responses, which inform autoHCT eligibility. In addition, we were unable to determine whether patients were referred to a transplant center, and thus cannot differentiate between barriers to autoHCT at the initial provider level and those identified at the transplant center and any changes over time. The strengths of our study include a novel linkage of three datasets, which better captured autoHCT in a population-based cohort; a large number of MM patients, which allowed for adequate power to compare between subgroups within treatment eras; a long median follow-up time, allowing for the capture of later autoHCT utilization after MM diagnosis; and comprehensive data on sociodemographic factors, permitting us to identify relevant disparities in autoHCT utilization.

Conclusions

Through our novel data linkage and 26-year study period, we identified areas in which improvements have been made in autoHCT utilization, and where disparities persisted over time. While progress has been made in the overall utilization of autoHCT over time, barriers to autoHCT utilization remain, particularly in Black/African American patients and those with public or no health insurance. Notably, disparities between Black/African American and non-Hispanic White patients undergoing autoHCT widened in more recent time periods. In addition, we did not observe an improvement over time in the likelihood of autoHCT among patients with Medicare or Medicaid insurance compared to those with private insurance. Further studies should seek to more comprehensively understand the underlying factors contributing to these observed sociodemographic disparities by including additional disease characteristics, such as stage and molecular features, specific treatment regimens prescribed, and response to treatment in the MM population. Mitigating barriers to autoHCT access is essential to ensure more equitable use of this highly effective therapy.

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Clinical Practice Points:

AutoHCT is associated with delayed disease progression and survival benefit in transplant-eligible patients with multiple myeloma who achieve at least a partial response to induction therapy; however, utilization remains low. Prior studies have found associations between sociodemographic factors and autoHCT utilization; however, they have not fully captured autoHCT utilization or trends in such disparities over time.

We used a novel data linkage between the California Cancer Registry, Center for International Blood and Marrow Transplant Research, and hospitalizations to capture autoHCT in a population-based multiple myeloma cohort and examined trends in utilization over time. We found that Black/African American patients were less likely to have autoHCT throughout each treatment era and this disparity increased after 2005. Patients with Medicaid, Medicare, or no health insurance were also less likely to receive autoHCT throughout each treatment era. In multivariable models, Hispanic patients were less likely than non-Hispanic White patients to receive autoHCT, but this difference became less prominent in more recent treatment eras.

This study brings to attention the persistence of sociodemographic disparities associated with autoHCT utilization over time in patients with multiple myeloma. Further investigation into these disparities is warranted, to elucidate the causal factors and how they may be addressed and rectified. This will bring attention to these disparities and identify potential barriers to autoHCT, with the goal of more equitable access for all transplant-eligible patients with multiple myeloma.

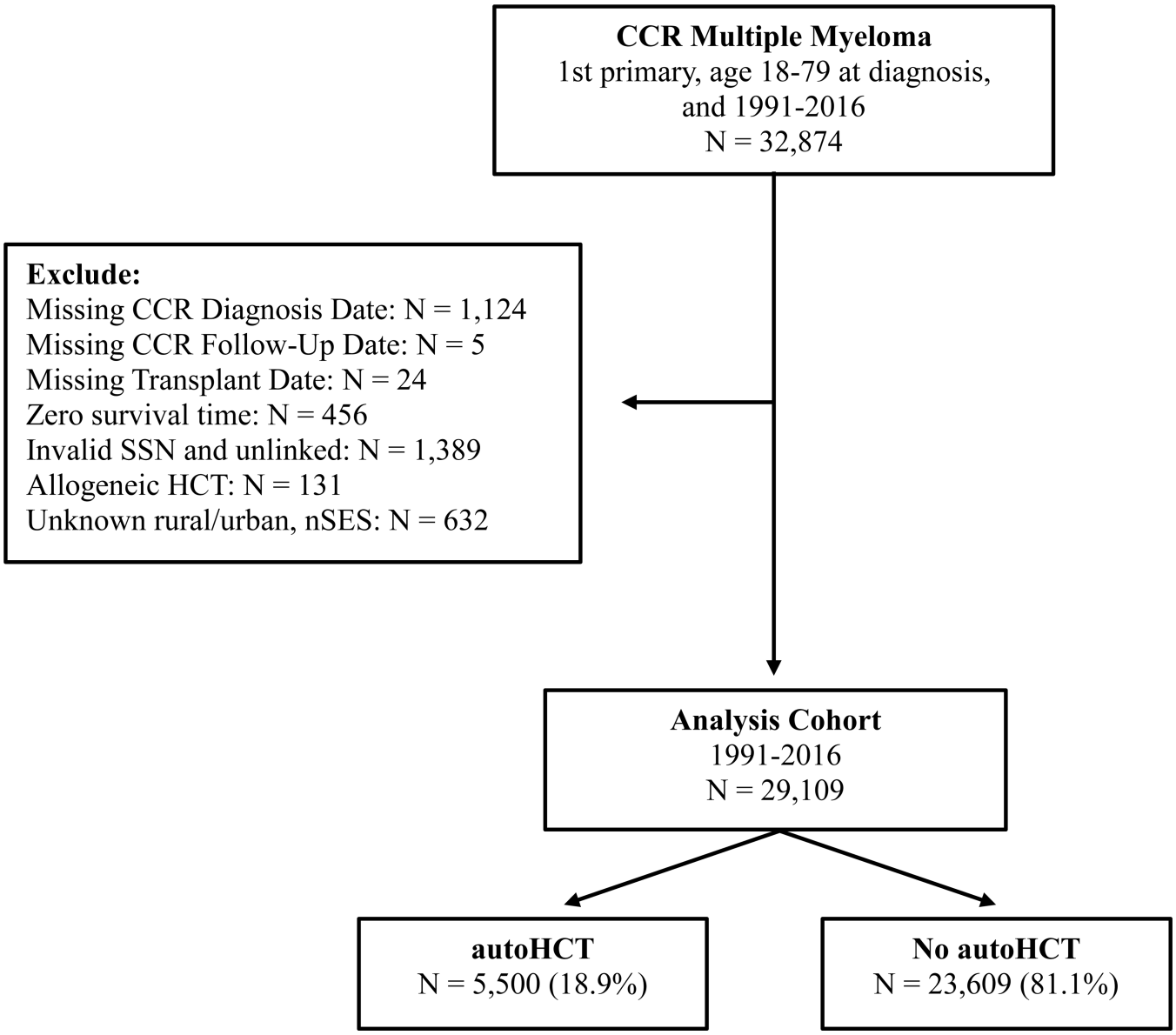

Figure 1: Selection of the California Cancer Registry multiple myeloma cohort by receipt of autologous hemopoietic cell transplant, 1991–2016.

CCR, California Cancer Registry; SSN, social security number; HCT, Hemopoietic Cell Transplant; autoHCT, Autologous Hemopoietic Cell Transplant (autoHCT); nSES, neighborhood socioeconomic status

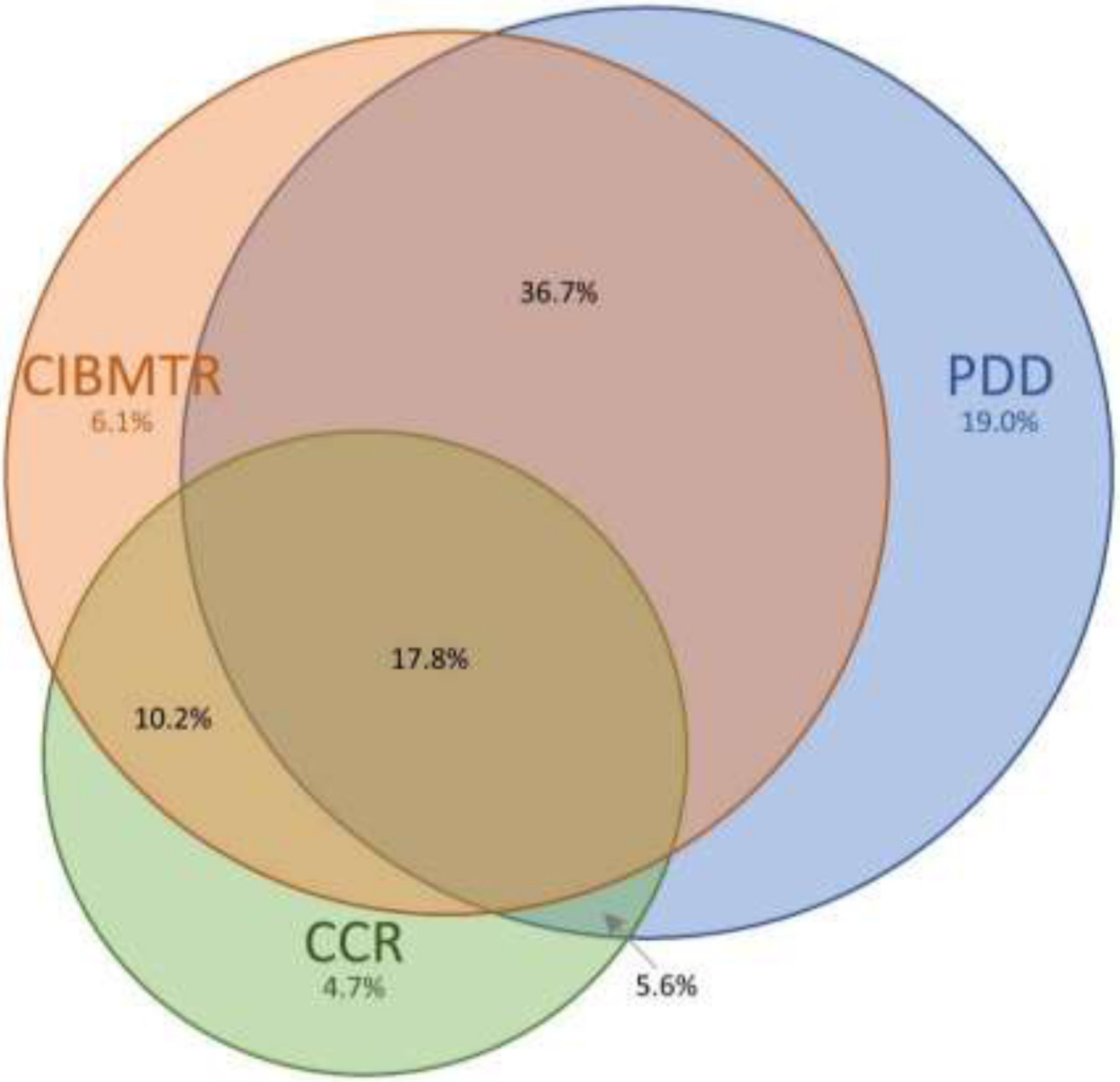

Figure 2: Venn diagram describing the overlap of autologous hemopoietic cell transplant data in the CIBMTR, PDD and CCR among California patients with multiple myeloma, 1991–2016.
CCR, California Cancer Registry; PDD, Patient Discharge Database; CIBMTR, Center for International Blood and Marrow Transplant Research

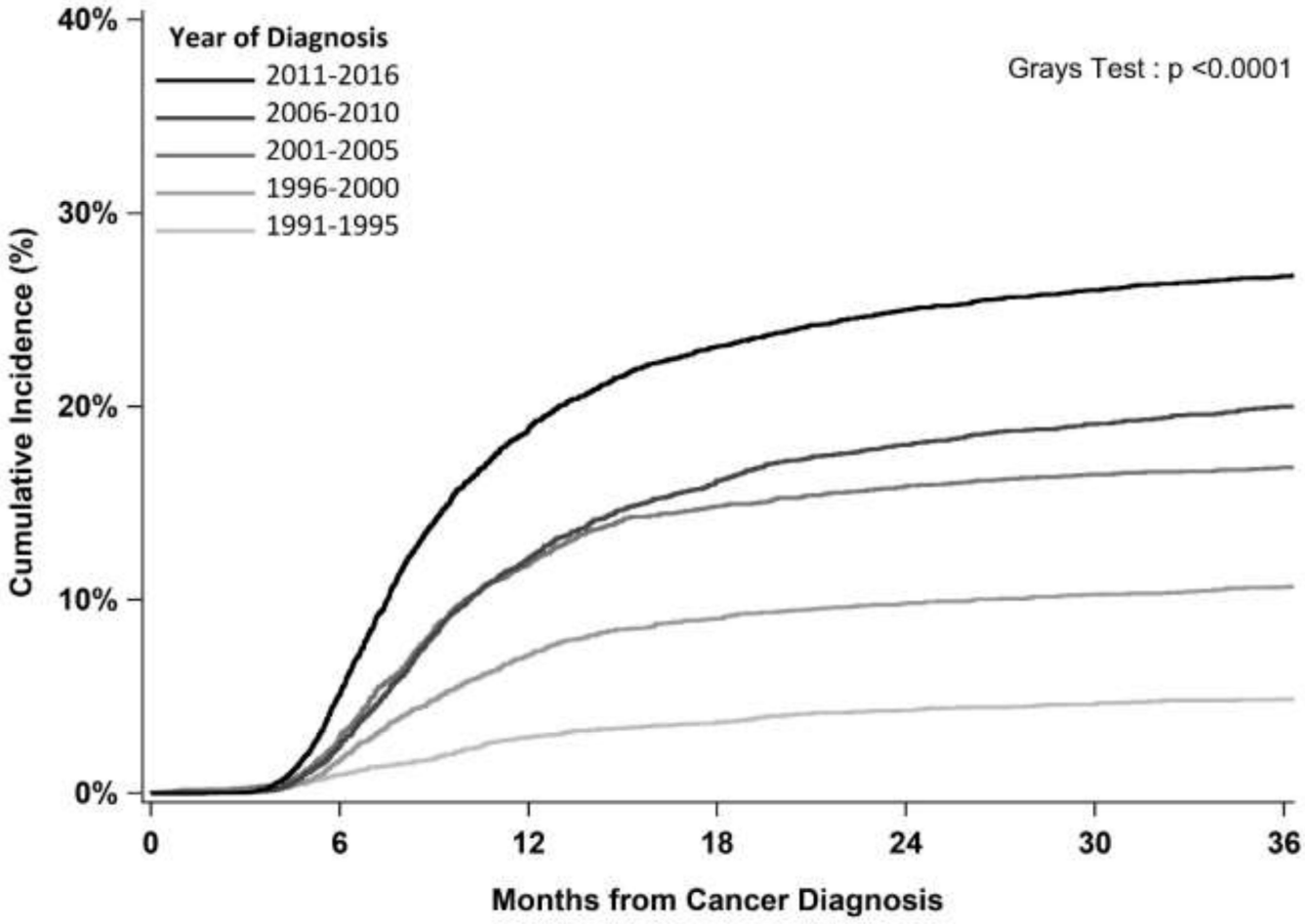

Figure 3.

Cumulative incidence of autologous hemopoietic cell transplant utilization, accounting for the competing risk of death, among California patients with multiple myeloma by time period, 1991–2016

Table 1:

Baseline characteristics of California patients with multiple myeloma by receipt of autologous hemopoietic cell transplant, 1991–2016

Characteristics	All N (%)	autoHCT N (%)	No autoHCT N (%)	P-value
All	29,109 (100.0)	5,500 (18.9)	23,609 (81.1)	
Sex				
Male	16,567 (56.9)	3,266 (19.7)	13,301 (80.3)	0.0002
Female	12,537 (43.1)	2,233 (17.8)	10,304 (82.2)	
Race/Ethnicity				
non-Hispanic White	16,667 (57.3)	3,109 (18.7)	13,558 (81.3)	<.0001
Black/African American	3,946 (13.6)	622 (15.8)	3,324 (84.2)	
Hispanic	5,721 (19.7)	1,207 (21.1)	4,514 (78.9)	
Asian/Pacific Islander	2,501 (8.6)	529 (21.2)	1,972 (78.8)	
Other/Unknown	274 (0.9)	33 (12.0)	241 (88.0)	
Age at Diagnosis				
Age < 40	619 (2.1)	231 (37.3)	388 (62.7)	<.0001
40–49	2,577 (8.9)	1,029 (39.9)	1,548 (60.1)	
50–59	6,493 (22.3)	2,197 (33.8)	4,296 (66.2)	
60–69	9,525 (32.7)	1,837 (19.3)	7,688 (80.7)	
70–79	9,895 (34.0)	206 (2.1)	9,689 (97.9)	
Year of Diagnosis				
1991–1995	4,390 (15.1)	249 (5.7)	4,141 (94.3)	<.0001
1996–2000	4,960 (17.0)	600 (12.1)	4,360 (87.9)	
2001–2005	5,487 (18.8)	1,027 (18.7)	4,460 (81.3)	
2006–2010	5,938 (20.4)	1,347 (22.7)	4,591 (77.3)	
2011–2016	8,311 (28.6)	2,276 (27.4)	6,035 (72.6)	
Elixhauser Comorbidities (≤ 2 years prior to diagnosis)				
Unknown/No admissions	14,547 (50.0)	3,352 (23.0)	11,195 (77.0)	<.0001
0 Comorbidities	1,895 (6.5)	394 (20.8)	1,501 (79.2)	
1–2 Comorbidities	5,379 (18.5)	963 (17.9)	4,416 (82.1)	
≥3 Comorbidities	7,288 (25.0)	791 (10.9)	6,497 (89.1)	
Initial Treatment				
Combination Chemotherapy or Immunotherapy				
Yes	20,197 (69.4)	5,078 (25.1)	15,119 (74.9)	<.0001
No	8,840 (30.4)	421 (4.8)	8,419 (95.2)	
Unknown	72 (0.2)	1 (1.4)	71 (98.6)	
Radiation				
Yes	7,453 (25.6)	1,613 (21.6)	5,840 (78.4)	<.0001
No	21,620 (74.3)	3,886 (18.0)	17,734 (82.0)	
Unknown	36 (0.1)	1 (2.8)	35 (97.2)	
Neighborhood Socioeconomic Status				
Low	10,160 (34.9)	1,542 (15.2)	8,618 (84.8)	<.0001

Characteristics	All N (%)	autoHCT N (%)	No autoHCT N (%)	P-value
Intermediate	6,077 (20.9)	1,123 (18.5)	4,954 (81.5)	
High	12,872 (44.2)	2,835 (22.0)	10,037 (78.0)	
Residence at Diagnosis				
Urban	27,739 (95.3)	5,301 (19.1)	22,438 (80.9)	<.0001
Rural	1,370 (4.7)	199 (14.5)	1,171 (85.5)	
Health Insurance				
No insurance/Self Pay	376 (1.3)	37 (9.8)	339 (90.2)	<.0001
Private/Military Insurance	12,039 (41.4)	3,414 (28.4)	8,625 (71.6)	
Medicaid/Public Government	2,199 (7.6)	559 (25.4)	1,640 (74.6)	
Medicare	9,087 (31.2)	1,140 (12.5)	7,947 (87.5)	
NA-prior 1996	4,413 (15.2)	250 (5.7)	4,163 (94.3)	
Unknown Insurance	991 (3.4)	99 (10.0)	892 (90.0)	
Marital Status				
Never Married	3,952 (13.6)	754 (19.1)	3,198 (80.9)	<.0001
Married/Domestic Partner	17,836 (61.3)	3,840 (21.5)	13,996 (78.5)	
Previously Married	5,923 (20.3)	712 (12.0)	5,211 (88.0)	
Unknown Marital Status	1,398 (4.8)	194 (13.9)	1,204 (86.1)	

autoHCT, autologous hemopoietic cell transplant

Table 2.

Characteristics associated with autologous hemopoietic cell transplant utilization among California patients with multiple myeloma overall and stratified by time period, 1991–2016

	1996–2016		1991–1995		1996–2000		2001–2005		2006–2010		2011–2016	
Characteristics	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Sex												
Male	0.99 (0.93, 1.04)	0.634	1.04 (0.80, 1.37)	0.753	0.96 (0.81, 1.13)	0.626	1.00 (0.88, 1.13)	0.982	0.91 (0.81, 1.01)	0.085	1.00 (0.92, 1.09)	0.954
Female	Reference		Reference		Reference		Reference		Reference		Reference	
Race/Ethnicity												
non-Hispanic White	Reference		Reference		Reference		Reference		Reference		Reference	
African American	0.78 (0.71, 0.85)	**<0.001**	0.78 (0.52, 1.17)	0.225	0.81 (0.62, 1.05	0.111	0.82 (0.67, 1.01)	0.058	0.66 (0.55, 0.79)	**<0.001**	0.83 (0.72, 0.95)	**0.008**
Hispanic	0.94 (0.88, 1.01)	0.109	0.58 (0.37, 0.90)	**0.015**	0.82 (0.64, 1.05)	0.118	0.93 (0.79, 1.10)	0.410	0.86 (0.74, 0.99)	**0.040**	1.07 (0.96, 1.19)	0.214
Asian/Pacific Islander	0.97 (0.89, 1.07)	0.567	0.57 (0.31, 1.04)	0.068	0.78 (0.56, 1.08)	0.135	1.03 (0.83, 1.28)	0.758	0.87 (0.73, 1.05)	0.145	1.10 (0.96, 1.26)	0.180
Age at Diagnosis												
< 50	Reference		Reference		Reference		Reference		Reference		Reference	
50–59	0.71 (0.67, 0.77)	**<0.001**	PH Stratification Variable		0.74 (0.61, 0.89)	**0.001**	0.74 (0.63, 0.86)	**<.001**	0.73 (0.64, 0.84)	**<.001**	0.79 (0.70, 0.89)	**<.001**
60–69	0.40 (0.37, 0.43)	**<.001**			0.25 (0.20, 0.32	**<.001**	0.41 (0.34, 0.48)	**<.001**	0.42 (0.36, 0.49)	**<.001**	0.56 (0.49, 0.64)	**<.001**
70–79	0.05 (0.04, 0.05)	**<.001**			0.01 (0.00, 0.02)	**<.001**	0.04 (0.02, 0.05)	**<.001**	0.03 (0.02, 0.05)	**<.001**	0.09 (0.08, 0.12)	**<.001**
Year of Diagnosis												
1991–1995		Reference		–		–		–		–		–
1996–2000	2.59 (2.24, 3.00)	**<.001**	–		–		–		–		–	
2001–2005	4.35 (3.79, 5.00)	**<.001**	–		–		–		–		–	
2006–2010	5.30 (4.63, 6.06)	**<.001**	–		–		–		–		–	
2011–2016	7.46 (6.54, 8.51)	**<.001**	–		–		–		–		–	
Comorbidities												

Characteristics	1996–2016		1991–1995		1996–2000		2001–2005		2006–2010		2011–2016	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Unknown/No Admissions	1.04 (0.93, 1.16)	0.458			1.13 (0.87, 1.45)	0.362	1.06 (0.87, 1.29)	0.591			1.11 (0.87, 1.40)	0.403
None	Reference				Reference		Reference				Reference	
1–2	0.86 (0.76, 0.97)	**0.013**	PH Stratification Variable		0.74 (0.55, 1.00)	**0.050**	0.95 (0.75, 1.19)	0.638	PH Stratification Variable		0.97 (0.76, 1.25)	0.833
≥3	0.56 (0.49, 0.63)	**<.001**			0.33 (0.22, 0.51)	**<.001**	0.42 (0.32, 0.56)	**<.001**			0.71 (0.56, 0.92)	**0.008**
Neighborhood Socioeconomic Status												
Low	0.75 (0.70, 0.80)	**<.001**	0.35 (0.24, 0.52)	**<.001**			0.75 (0.64, 0.88)	**<.001**	0.77 (0.68, 0.88)	**<.001**	0.81 (0.73, 0.90)	**<.001**
Intermediate	0.85 (0.79, 0.91)	**<.001**	0.67 (0.48, 0.92)	**0.014**			0.90 (0.77, 1.06)	0.200	0.80 (0.69, 0.92)	**0.002**	0.91 (0.82, 1.02)	0.106
High	Reference		Reference				Reference		Reference		Reference	
Residence at Diagnosis												
Rural	0.96 (0.83, 1.11)	0.607	1.20 (0.63, 2.32)	0.578	0.90 (0.63, 1.27)	0.532	1.19 (0.92, 1.52)	0.179	0.83 (0.55, 1.27)	0.402	0.90 (0.69, 1.16)	0.399
Urban	Reference		Reference		Reference		Reference		Reference		Reference	
Health Insurance												
No insurance	0.42 (0.31, 0.59)	**<.001**			0.40 (0.18, 0.92)	**0.030**	0.29 (0.14, 0.62)	**0.001**	0.43 (0.23, 0.79)	**0.007**	0.56 (0.32, 0.99)	**0.046**
Private/Military	Reference				Reference		Reference		Reference		Reference	
Medicaid/ Government	0.79 (0.72, 0.87)	**<.001**			0.68 (0.48, 0.96	**0.029**	0.84 (0.67, 1.06)	0.140	0.79 (0.65, 0.97)	**0.021**	0.81 (0.72, 0.91)	**0.001**
Medicare	0.86 (0.80, 0.92)	**<.001**			1.06 (0.85, 1.33)	0.599	1.05 (0.89, 1.22)	0.573	0.85 (0.74, 0.97)	**0.019**	0.70 (0.63, 0.78)	**<001**
Marital Status												
Married	Reference		Reference		Reference		Reference		Reference		Reference	
Never Married	0.72 (0.66, 0.78)	**<.001**	0.75 (0.48, 1.17)	0.207	0.66 (0.49, 0.87)	**0.004**	0.76 (0.63, 0.93)	**0.007**	0.74 (0.63, 0.86)	**<.001**	0.71 (0.63, 0.80)	**<001**
Previously Married	0.77 (0.71, 0.84)	**<.001**	0.79 (0.54, 1.17)	0.242	0.76 (0.60, 0.96)	**0.020**	0.79 (0.65, 0.95)	**0.015**	0.80 (0.68, 0.95)	**0.009**	0.74 (0.65, 0.84)	**<001**

autoHCT, autologous hemopoietic cell transplant; PH, proportional hazards

Multivariable Cox proportional hazard regression, accounting for the competing risk of death; significant individual interactions for time period by race/ethnicity ($p < 0.001$), and neighborhood socioeconomic status ($p < 0.001$). Treatment violated proportional hazard assumption for all models and therefore stratified by treatment and other models that violated proportional hazard assumption.

Unknown race/ethnicity, health insurance and marital status are not presented.