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Utilization of allogeneic hematopoietic stem cell transplantation among patients with newly diagnosed acute myeloid leukemia in California: a population-based linked dataset study

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Supplemental Appendix: 1 Table, 1 Figure

Short Title: Utilization of Allogeneic Transplant Among Patients with AML in California

Key Words: Acute myeloid leukemia, hematopoietic cell transplant, access, age barriers, social determinants of health

Key Points:

- HCT utilization among patients newly diagnosed with AML in California increased in all age cohorts over time yet remained under-utilized for older adults.

- Factors associated with HCT utilization differed by age group and included: sex, age, neighborhood socioeconomic status, insurance type, marital status, race and ethnicity, year of diagnosis, number of comorbidities, and distance to the nearest transplant center.
- Collaborations with stakeholders are necessary to further understand, diminish and eliminate barriers to HCT.

Conflict of interest: Jeff Auletta: Advisory Boards, Ascella Health, Takeda
Lori Muffly: Advisory Boards/consulting, Kite, Autolus, Vor, Astellas, Cargo

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C.L.M, L.M., T.H.M.K, conceptualized and designed the study.
C.L.M primarily performed the analysis.
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ABSTRACT:

Acute myeloid leukemia (AML) often requires allogeneic hematopoietic cell transplantation (alloHCT) for cure, but historically alloHCT has been strikingly underutilized. Reasons for this remain uncertain at the population level. We examined alloHCT utilization over time and explored associations between demographic/healthcare factors and use of alloHCT by age group (AYA 15-39y, adult 40-64y, older adult 65-79y) using a linked dataset merging the Center for International Blood and Marrow Transplant Research, California Cancer Registry, and California Patient Discharge Database. Eligibility included patients newly diagnosed with AML in California between 2001-2016 who received induction therapy and had no prior HCT. Multivariable Fine-Gray regression analyses were fitted separately across age groups. Among 7,925 patients with AML, alloHCT utilization increased over time across all age groups; however, in the most recent time period studied (2011-2016), utilization within 2 years of diagnosis remained lowest in older adults (13%) relative to adults (41%) and AYAs (49%). Factors statistically significantly associated with lower alloHCT utilization: (1) AYAs: female sex, lower neighborhood socioeconomic status (nSES), uninsured or Indian Health Services (IHS) coverage; (2) adults: older age, male sex, non-Hispanic Black or Asian race and ethnicity, unmarried, lower nSES, uninsured or covered by Medicaid, Medicare, or IHS, higher comorbidity, and living 100+ miles from a transplant center; and (3) older adults: older age, Asian race, and unmarried. In conclusion, using a population-based linked dataset, we demonstrate that utilization of alloHCT among older patients newly diagnosed with AML remains low in California, and factors associated with utilization vary by age group.

INTRODUCTION

Approximately 20,000 people in the United States are diagnosed with acute myeloid leukemia (AML) each year, with fewer than 10% of new diagnoses occurring in children and adolescent/young adults (AYA), one-third in adults ages 40-64 years, and a majority occurring at ages 65 years and older.[1,2] Therapeutic strategies for AML are guided by patient fitness and cytogenetic/molecular genetic risk stratification. Whereas induction/consolidation therapy alone may be sufficient for many patients with favorable-risk AML, patients with intermediate and adverse-risk features commonly require allogeneic hematopoietic cell transplantation (alloHCT) to achieve leukemia cure.[3] Importantly, the proportion of patients with adverse-risk AML increases with age.[4]

Although AML represents the most common disease indication for alloHCT,[5] studies suggest that alloHCT is strikingly under-utilized in AML, particularly among older adults.[6–9] Previous investigations

defined factors associated with receipt of alloHCT, including age, race and ethnicity, and insurance type, but have been limited to cancer registry analyses that do not fully capture receipt of alloHCT or claims-based analyses of selected populations.[7,10,11] Other studies have used HCT registries to identify common variables within populations of transplanted patients, but lack the broader population of patients with transplant-eligible diagnoses who never undergo alloHCT.[12–15]

To address the limitations of each of these approaches, we used a novel linkage of population-based data from the California Cancer Registry (CCR), the California Patient Discharge Database (PDD), and the Center for International Blood and Marrow Transplant Research (CIBMTR)[16] to perform in depth analyses of alloHCT utilization among newly diagnosed patients with AML over time, with a secondary aim of identifying factors associated with receipt of alloHCT within 3 distinct age groups. We hypothesized that there would be variations in factors affecting utilization of alloHCT by age group; however, based on prior research, we expected that certain barriers such as race and ethnicity, insurance type, and socioeconomic status would be present across all age groups.

METHODS

Data Sources and Study Cohort

Details describing the CCR, PDD, CIBMTR, and linking methodology have been previously published.[16] Briefly, the CCR has served as California's population-based cancer surveillance system since 1988, collects cancer incidence on greater than 99% of new cancer cases, and harmonizes data from the regional cancer registries within the state.[17] The PDD includes diagnostic and procedure codes on all inpatient admissions from over 400 non-federal hospitals across the state of California, and has done so since 1991 when the California Department of Health Care Access and Information initially mandated such reporting.[18] The CIBMTR is a research collaboration between the NMDP and the Medical College of Wisconsin. It comprises a voluntary working group of approximately 420 centers worldwide contributing detailed data on allogeneic and autologous HCT and cellular therapies.

The study population included all patients within the CCR who were diagnosed with an initial primary AML between 2001-2016 at ages 15-79 years old and received AML induction therapy based on reported receipt of chemotherapy collected in the CCR. Patients 80 years and older or patients who were not reported to have received chemotherapy for AML were excluded, given that these patients rarely receive HCT and/or generally had a poor prognosis precluding HCT.[19] Patients who underwent autologous HCT for AML were excluded. Additional cohort selection criteria are described in (**Supplemental Table 1)**. 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 NMDP and was determined to not be human subjects research by the National Cancer Institute.

Variables Considered in Multivariable Analyses

Individual patient characteristics were obtained from the CCR and included: age at diagnosis (by continuous measurement), sex, race and ethnicity, marital status, health insurance at diagnosis (categorized according to age group as defined below) and year of AML diagnosis. Elixhauser Comorbidity Index was calculated using admission data from the PDD.[20] A previously developed neighborhood socioeconomic status index (nSES) that incorporates information on education, poverty,

employment, rental/housing information, and household income of the patient's census block group was used to determine nSES.[21] ArcGIS (v 10.6, Redlands, CA, USA) was used to determine the distance in miles from the patient's residential ZIP code at diagnosis to the nearest transplant center. Rural and urban commuting area codes[22] were also included using the patient's ZIP code.

Statistical Analysis

Descriptive characteristics and modeling were performed separately across three age groups: adolescents and young adults (AYA, age 15-39 years), adults (age 40-64 years), and older adults (age 65-79 years). A sensitivity analysis of alloHCT utilization using different age groups (15-59, 60-69 versus ≥70 years) was also performed. Univariate and multivariable logistic regression analyses were conducted using Cox proportional hazards regression models, accounting for the competing risk of death using the methods of Fine and Gray.[23] Variables were tested for collinearity, and proportional hazard assumptions were evaluated for each model separately using the Schoenfeld Residuals Test.[24] Models were stratified on variables determined to be nonproportional. All variables described above were retained in the three models with the only difference being the categories used to analyze insurance coverage for older adults to account for the high percentage of Medicare coverage. A p-value of < 0.05 was used to determine statistical significance.

RESULTS

Baseline Patient Characteristics

A total of 7,925 patients newly diagnosed with AML met inclusion criteria; 1,432 (18%), 3,678 (46%), and 2,815 (36%) were categorized as AYAs, adults, and older adults, respectively (**Table 1**). Males outnumbered females in all age groups. The distribution by race and ethnicity differed across age groups with a greater proportion of Hispanic (41%) than non-Hispanic White (37%) patients among the AYAs, and the opposite pattern among older adults. Marital status also differed across age groups with 63% of AYAs classified as unmarried compared with 35% of adults and older adults. More comorbidity (Elixhauser score ≥3) was seen in adults (30%) and older adults (37%) than AYAs (18%). Over 94% of patients across all age groups lived in urban areas. However, more AYAs (48%) than adults (35%) or older adults (32%) lived in low SES neighborhoods. Insurance coverage was predominantly private (52%) or Medicaid (34%) in AYAs, private (65%) or Medicaid (20%) in adults, and various forms of Medicare (64%) in older adults. Distance to nearest transplant center was similar across age groups with approximately 25% of patients living >50 miles from a transplant center.

Utilization of AlloHCT Over Time

Over the time period studied, a total of 2,171 (27%) patients received an alloHCT: 668 (47%), 1,282 (35%), and 221 (8%) were AYAs, adults, and older adults respectively. The median time from AML diagnosis to alloHCT was 6 months, with 75% of alloHCTs occurring within 11 months of diagnosis and 90% within 21 months. Utilization of alloHCT was identified from all three data sources (**Figure 1)**: CIBMTR identified 85% of HCTs; PDD identified an additional 13%; and the CCR identified an additional 2%. The cumulative incidence of alloHCT utilization increased across all age groups over time; yet the incidence increase (measured at 2-years following diagnosis) from 2001-2005 to 2011-2016 was greatest among adults (24% to 41%) followed by AYAs (37% to 49%) and least among older adults (2%

to 13%) (**Figure 2**). The sensitivity analysis using different age group cut-offs revealed similar trends in alloHCT utilization over time (**Supplemental Figure 1**). However, this analysis revealed strikingly low utilization of alloHCT (5%) among patients aged 70-79 even in the most recent time period studied.

Factors Associated with Receipt of AlloHCT by Age Group

The results of each age-group multivariable analysis for alloHCT utilization are presented in **Table 2**.

In the AYA population, low or middle nSES relative to high nSES, and lacking insurance or coverage by Indian Health Services (IHS) or county public healthcare relative to private insurance were associated with reduced rate of alloHCT utilization. In contrast, male sex and a more recent year of diagnosis were associated with increased rate of alloHCT utilization. Medicaid and Medicare health insurance violated proportional hazards assumptions and were included as stratification variables in the models.

In the adult population, older age, male sex, and unmarried status were associated with a lower rate of alloHCT utilization. AlloHCT was also lower among non-Hispanic Black and Asian patients relative to White patients, those residing in low or middle nSES relative to high nSES, and those who were uninsured or covered by Medicaid, Medicare, or IHS relative to private insurance. Finally, the presence of comorbidities and living 100 miles or more from a transplant center were associated with a lower rate of alloHCT utilization.

In the older adult cohort, older age, unmarried status, and Asian race were associated with lower alloHCT utilization, while a more recent year of diagnosis was associated with a higher rate of utilization.

DISCUSSION

Using a novel population-based linked database encompassing >99% of patients newly diagnosed with AML in California, we found that alloHCT utilization increased in all age groups over time. However, as recently as 2016, only 13% of older adults who received initial AML therapy ultimately underwent alloHCT within 2 years of diagnosis. This is substantially lower than in AYAs or adults, where 53% and 44% of patients with AML underwent alloHCT, respectively. Despite numerous studies demonstrating that alloHCT is a viable curative option for older adults with AML,[8,25–27] these results suggest that transplantation remains markedly underutilized in this population. Unlike other studies investigating HCT utilization, our linkage of statewide cancer registry and hospitalization data with the CIBMTR provides what we believe to be the most complete capture of alloHCT in a large and diverse population-based cohort of U.S. patients with AML.

The finding that alloHCT remains relatively rare among adults ≥65 with AML is not new; yet it is concerning that in a population-based modern cohort such as ours, rates of alloHCT utilization in this age group remain far below expected. In this analysis, we limited the cohort to only patients with AML who received any type of induction therapy, thus reducing the potential of including older adults who received no treatment at all, which also remains an ongoing issue in AML.[19] Although we found that the use of alloHCT in this age group increased over time, more must be done to ensure that older adults are at least offered an opportunity to consider the risks and benefits of this therapy.

In our study, we were able to evaluate patient-related sociodemographic variables present in the cancer registry, which may influence whether a patient with AML receives an alloHCT. However, it is important to recognize that in the currently shifting landscape of AML therapy, a multitude of important variables

that we were unable to examine, including response to therapy, induction tolerance, and immortal time bias, may factor into whether a patient with AML undergoes transplantation. Among the numerous sociodemographic variables we were able to analyze, for older adults, we only found that being unmarried or Asian were associated with a lower rate of alloHCT. Previous studies have also suggested that older adults with strong social support are more likely to be offered alloHCT.[28–30] What our study was unable to uncover, which is important for understanding the reason for underutilization, is the proportion of older adults who were simply never referred or evaluated for alloHCT due to their age. We hypothesize that these are the major reasons for these patients not receiving potentially curative therapies. Specific nationwide interventions to educate and improve upon our findings may help in this regard. Further, with the recent shift towards more effective venetoclax-based induction regimens for older adults with newly diagnosed AML,[31–33] we hypothesize that the number of older patients who may benefit from consolidative alloHCT will continue to grow.

In addition to focusing on older adults, we identified sociodemographic characteristics associated with receipt of alloHCT by age group, demonstrating notable differences. For example, we found that both nSES and insurance coverage were particularly important in AYA and adult populations, but less so in older adults, where most patients with AML (>90%) were covered by either Medicare and/or private insurance. In California, very few patients with AML are listed as uninsured; however, one-third of AYAs and 20% of adult patients in our cohort were covered by Medicaid, which was associated with lower rates of alloHCT utilization. However, transplantation without insurance coverage at all is nearly impossible; thus, access to alloHCT may be more challenging in states that provide less expansive government funded health insurance.[34] Poverty is a known barrier to cancer care;[35,36] the intersection of poverty and under-insurance is a critical barrier to alloHCT and is the focus of a variety of ongoing policy and research efforts.[37]

Recent breakthroughs in the ability to safely transplant HLA mismatched donors led to a rise in haploidentical and HLA mismatched unrelated donor transplant.[38,39] This is particularly critical to ethnically diverse patients, where finding a suitable HLA-matched donor is substantially less common. Our study cohort resembled the racial and ethnic distribution of California residents, with 24%, 14%, and 5% of patients with AML identified through the registry as Hispanic, Asian, and Black, respectively. Our results demonstrate that Hispanic patients appear as likely as non-Hispanic White patients to receive alloHCT, which is reassuring, particularly given the large number of AYAs described as Hispanic and the shifting demographics of California. However, our results also demonstrate that Asian and Black adults and Asian older adults were less likely to receive alloHCT than White patients. The causes of racial and ethnic disparities in accessing HCT are more complex than solely HLA disparities. Cultural background and influences have been previously reported to play a role in patients desire and ability engage in shared decision making as well as their opinions about transplant.[13,28,40–42] These differences can range from lowered health literacy and language barriers, personal belief systems and variation in values when it comes to treatment and outcomes, trust in the health system and experiences with discrimination, and a patients desire to be involved in decision making.[42] In one study that looked at patients referred to HCT in the state of New York, European Americans were more likely to not receive HCT based on patient decision (20%) or stable disease (20%) compared to African Americans who were more likely to not receive an HCT due to physician decision or comorbidities (29%).[43] In the current era, where HLA is no longer a barrier to finding a suitable alloHCT donor, additional work is necessary to further understand patients experiences with shared decision making, ensure patients are receiving information about treatment options that matches their language and health literacy needs, and educate physicians on best

practices for providing culturally sensitive care to remove disparities in the uptake of alloHCT across different patient populations.

According to the Foundation for the Accreditation of Cellular Therapy (FACT), at least 16 centers perform alloHCT across the state of California.[44] Few studies have evaluated how distance to a transplant facility may impact access. We found that adult patients with AML living >100 miles from a transplant center were significantly less likely to receive alloHCT. While these patients were a relatively small proportion of our overall study cohort (12%), the inability to reach the transplant center likely due to lack of referral or limited resources are both important issues that extend beyond California to patients living in HCT "deserts" across the country. The American Society for Transplantation and Cellular Therapy and the NMDP have recently partnered to launch the ACCESS Initiative, which focuses on improving awareness, SES, and racial/ethnic inequities related to HCT and cellular therapies.[37] Our data suggest that patients living in HCT/cellular therapy facility "deserts" should be considered a vulnerable population who are significantly less likely to access HCT.

While our population-based linkage approach has several strengths, we recognize limitations associated with using cancer registry and hospitalization data to answer these questions. The CCR captures data on nearly all newly diagnosed AML patients in California, but the registry lacks consistent data on cytogenetic/molecular features and thus, we were unable to precisely characterize risk categories. However, data suggests that approximately 30% of patients with AML fall into European Leukemia Net (ELN) "favorable" risk AML; with that proportion dropping in older adults to approximately 20%. Approximately 45% of patients have ELN "adverse" risk AML, rising to over 50% in older adults.[45] Given that alloHCT is indicated in first complete remission for adverse risk AML, for some patients with intermediate risk AML, and for previously un-transplanted patients in second complete remission regardless of risk category,[46] we would anticipate a large proportion of patients with AML across all of our studied age groups to have a disease indication for alloHCT. Similarly, we did not have detailed information from the CCR regarding AML induction and response in our analysis, but we excluded patients who received no initial therapy for AML, as these patients would not typically be considered for alloHCT. Interestingly, we found no significant association between baseline comorbidity and receipt of alloHCT in older adults—this was counter to our hypothesis and may be explained by a host of factors including the comorbidity index in this analysis representing comorbidity at AML diagnosis, not following initial treatment, when HCT referral decisions often occur. Additionally, we recognize that many of our sociodemographic characteristics are proxies for more complex factors- for example, we used marital status as a proxy for social support, but certainly recognize that social support comes in many forms. Finally, this analysis focused on patients diagnosed with AML in CA and may not be representative of other states.

In conclusion, despite observing an increase in alloHCT among patients with AML in California, transplant remains underutilized, particularly among older adults. As evidenced by the ACCESS Initiative and other endeavors, there is rising momentum to better understand, diminish, and ultimately eliminate barriers to accessing HCT and cellular therapies for patients with blood cancers and other diseases who may benefit from these therapies.[47] Systematically addressing these healthcare challenges across the transplant and cellular therapy ecosystem requires the concerted effort of key stakeholders.[48] Our data provide a benchmark of alloHCT utilization in the management of AML, and demonstrate the strength of linking datasets to uncover utilization rates of complex therapies.

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Table 1: Baseline Sociodemographic and Treatment Characteristics of Newly Diagnosed Acute Myeloid Leukemia Patients in California, Stratified by Age Group at Diagnosis, 2001-2016

Characteristics	**15-39 (n=1432)**	**40-64 (n=3678)**	**65-79 (n=2815)**
Age	n (%)	n (%)	n (%)
Median, years	29	55	71
Sex			
Male	742 (51.8)	2054 (55.8)	1655 (58.8)
Female	690 (48.2)	1624 (44.2)	1160 (41.2)
Race and Ethnicity			
Non-Hispanic White	535 (37.4)	2024 (55)	1874 (66.6)
Non-Hispanic Black	86 (6)	226 (6.1)	111 (3.9)
Hispanic	583 (40.7)	864 (23.5)	454 (16.1)
Asian	210 (14.7)	525 (14.3)	346 (12.3)
Other*	18 (1.3)	39 (1.1)	30 (1.1)
Marital Status			
Married**	500 (34.9)	2316 (63.0)	1778 (63.2)
Not Married	899 (62.8)	1287 (35.0)	974 (34.6)
Unknown	33 (2.3)	75 (2.0)	63 (2.2)
Rural Urban Commuting Area Codes			
Rural	63 (4.4)	166 (4.5)	159 (5.6)
Urban	1369 (95.6)	3512 (95.5)	2656 (94.4)
Neighborhood Socioeconomic Status			
Low	690 (48.2)	1289 (35)	914 (32.5)
Medium	274 (19.1)	781 (21.2)	564 (20)
High	468 (32.7)	1608 (43.7)	1337 (47.5)
Insurance category			
Self-pay, not insured	41 (2.9)	94 (2.6)	24 (0.9)
Private	747 (52.2)	2406 (65.4)	779 (27.7)
Medicaid	482 (33.7)	724 (19.7)	119 (4.2)
Medicare	34 (2.4)	257 (7.0)	1,804 (64.1)
Medicare with supplement (n)	6	80	777
Medicare without supplement (n)	11	90	591
Medicare Managed Care (n)	0	16	236
Medicare with Medicaid eligibility (n)	17	71	200
Military	31 (2.2)	86 (2.3)	42 (1.5)
Indian/Public Health Services/County, NOS	57 (4)	33 (0.9)	11 (0.4)
Unknown	40 (2.8)	78 (2.1)	36 (1.3)
Elixhauser Comorbidity Index			
0	210 (14.7)	387 (10.5)	155 (5.5)
1-2	394 (27.5)	991 (26.9)	569 (20.2)
≥3	260 (18.2)	1087 (29.6)	1050 (37.3)

Characteristics	15-39 (n=1432)	40-64 (n=3678)	65-79 (n=2815)
Unknown	568 (39.7)	1213 (33.0)	1041 (37.0)
Induction Therapy			
Therapy NOS	36 (2.5)	147 (4)	189 (6.7)
Single-agent therapy	83 (5.8)	362 (9.8)	944 (33.5)
Multi-agent therapy	1313 (91.7)	3169 (86.2)	1682 (59.8)
Diagnosis Year			
2001-2002	138 (9.6)	422 (11.5)	362 (12.9)
2003-2004	142 (9.9)	401 (10.9)	259 (9.2)
2005-2006	160 (11.2)	406 (11)	287 (10.2)
2007-2008	194 (13.5)	460 (12.5)	345 (12.3)
2009-2010	190 (13.3)	486 (13.2)	324 (11.5)
2011-2012	201 (14)	468 (12.7)	373 (13.3)
2013-2014	210 (14.7)	524 (14.2)	386 (13.7)
2015-2016	197 (13.8)	511 (13.9)	479 (17)
Distance to nearest transplant center (miles)			
<50	1107 (77.3)	2852 (77.5)	2076 (73.7)
50-99	149 (10.4)	405 (11.0)	400 (14.2)
≥100	176 (12.3)	421 (11.4)	339 (12)
Median distance (SE); IQR	22.2 (1.3); 31.3	23.3 (0.8); 32.2	24.3 (1.0); 40
Receipt of allogeneic transplant			
No	764 (53.4)	2396 (65.1)	2594 (92.1)
Yes	668 (46.6)	1282 (34.9)	221 (7.9)

Abbreviation: Standard Deviation (SD), Standard Error (SE), Interquartile Range (IQR), Acute Myeloid Leukemia (AML), Not otherwise specified (NOS)

*Other includes Native Hawaiian Pacific Islander, American Indian and Alaskan Native and Unknown race/ethnicity

**includes common law/unmarried domestic partner

Table 2: Multivariable Logistic Regression Analyses Demonstrating Characteristics Associated with Receipt of Allogeneic HCT Among Newly Diagnosed AML Patients in California, Stratified by Age Group

Characteristics	15 to 39 (n=1,432)		40 to 64 (n=3,678)		65 to 79 (n=2,815)	
	HR (95% CL)	**P-value**	**HR (95% CL)**	**P-value**	**HR (95% CL)**	**P-value**
Age at diagnosis (continuous)	1.00 (0.99, 1.01)	0.854	0.97 (0.96, 0.97)	**<0.001**	0.75 (0.71, 0.80)	**<.001**
Sex						
Female	Reference		Reference		Reference	
Male	1.17 (1.01, 1.37)	**0.041**	0.81 (0.72, 0.9)	**<0.001**	1.07 (0.68, 1.69)	0.763
Race & Ethnicity						
Non-Hispanic White	Reference		Reference		Reference	
Non-Hispanic Black	0.76 (0.51, 1.11)	0.150	0.55 (0.40, 0.75)	**<0.001**	0.79 (0.25, 2.47)	0.684
Hispanic	0.98 (0.81, 1.18)	0.813	0.92 (0.79, 1.07)	0.262	0.59 (0.30, 1.16)	0.123
Asian	1.18 (0.95, 1.48)	0.141	0.83 (0.71, 0.98)	**0.025**	0.47 (0.24, 0.94)	**0.033**
Other/Unknown*	1.28 (0.68, 2.41)	0.450	0.70 (0.36, 1.36)	0.293	0.6 (0.07, 5.26)	0.646
Marital Status						
Married**	Reference		Reference		Reference	
Not Married	0.92 (0.77, 1.11)	0.395	0.82 (0.72, 0.93)	**0.002**	0.55 (0.35, 0.88)	**0.013**
Unknown	0.57 (0.33, 0.98)	**0.042**	0.76 (0.50, 1.17)	0.215	0.20 (0.02, 1.71)	0.143
Rural/ Urban						
Urban	Reference		Reference		Reference	
Rural	1.24 (0.81, 1.9)	0.328	1.11 (0.80, 1.53)	0.538	1.03 (0.36, 2.95)	0.963
Neighborhood SES						
High	Reference		Reference		Reference	
Middle	0.74 (0.60, 0.92)	**0.006**	0.76 (0.65, 0.88)	**<0.001**	0.61 (0.35, 1.08)	0.092
Low	0.70 (0.58, 0.85)	**<0.001**	0.53 (0.46, 0.62)	**<0.001**	0.67 (0.41, 1.11)	0.118
Insurance Coverage: AYA/Adult						
Private/Military/Medicare with supplement	Reference		Reference		-	-
Self-pay, not insured	0.12 (0.04, 0.39)	**<0.001**	0.43 (0.24, 0.75)	**0.003**	-	-
Medicaid***			0.67 (0.57, 0.79)	**<.001**	-	-
Medicare****			0.73 (0.54, 0.99)	**0.040**	-	-
Other public*****	0.59 (0.37, 0.93)	**0.024**	0.33 (0.13, 0.81)	**0.016**	-	-
Unknown	0.85 (0.52, 1.39)	**0.522**	0.74 (0.49, 1.13)	**0.160**	-	-
Insurance Coverage: Older Adult						
Private	-	-	-	-	Reference	
Medicaid	-	-	-	-	0.45 (0.12, 1.72)	0.243
Medicare without supplement	-	-	-	-	1.02 (0.54, 1.93)	0.948
Medicare with supplement	-	-	-	-	1.44 (0.83, 2.49)	0.196
Medicare Managed Care	-	-	-	-	0.79 (0.37, 1.70)	0.549

Characteristics	15 to 39 (n=1,432)		40 to 64 (n=3,678)		65 to 79 (n=2,815)	
	HR (95% CL)	**P-value**	**HR (95% CL)**	**P-value**	**HR (95% CL)**	**P-value**
Medicare Medicaid Eligibility	-	**-**	-	**-**	1.22 (0.51, 2.88)	0.658
Unknown/No insurance/Self-pay	-	**-**	-	**-**	0.22 (0.02, 2.71)	0.238
Elixhauser Comorbidity Index						
0	Reference		Reference		Reference	
1 – 2	1.01 (0.80, 1.29)	**0.908**	0.79 (0.65, 0.95)	**0.014**	0.86 (0.25, 2.94)	0.809
≥3	0.76 (0.57, 1.01)	**0.054**	0.59 (0.48, 0.72)	**<.001**	0.44 (0.13, 1.51)	0.191
Unknown	0.87 (0.69, 1.09)	**0.227**	0.8 (0.66, 0.96)	**0.018**	0.74 (0.22, 2.47)	0.629
Diagnosis Year (continuous)	1.03 (1.01, 1.05)	**0.001**	1.08 (1.07, 1.10)	**<.001**	1.21 (1.15, 1.28)	<.001
Distance to Nearest Transplant Center (miles)						
<50	Reference		Reference		Reference	
50-99	0.97 (0.75, 1.26)	**0.815**	0.98 (0.81, 1.19)	**0.845**	0.74 (0.38, 1.43)	0.370
≥100	0.78 (0.59, 1.02)	**0.070**	0.78 (0.64, 0.95)	**0.015**	0.56 (0.27, 1.14)	0.108

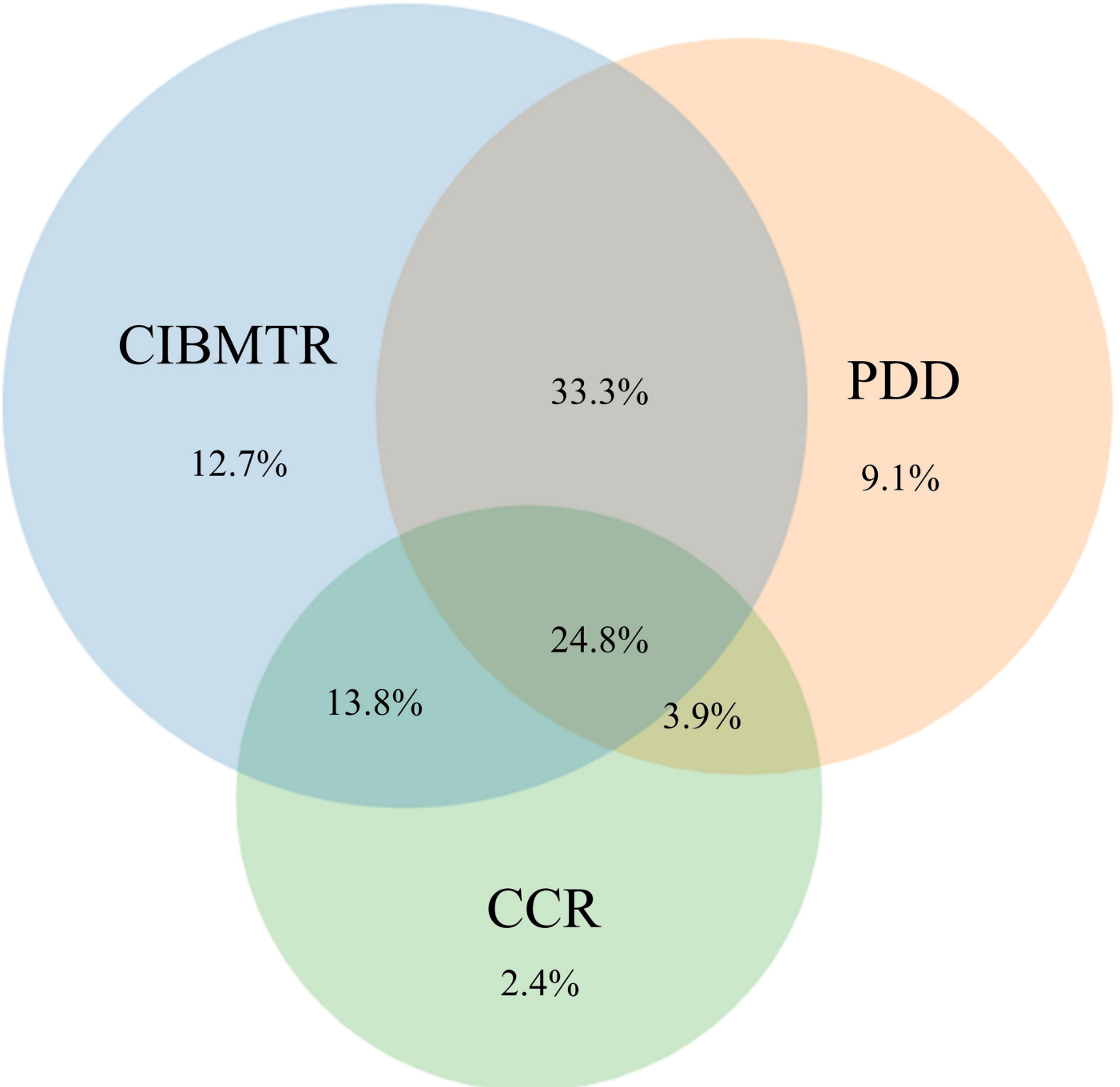
Abbreviation: HCT-Hematopoietic Cell Transplantation, AML-Acute Myeloid Leukemia, nSES-Neighborhood Socioeconomic Status, NOS- not otherwise specified

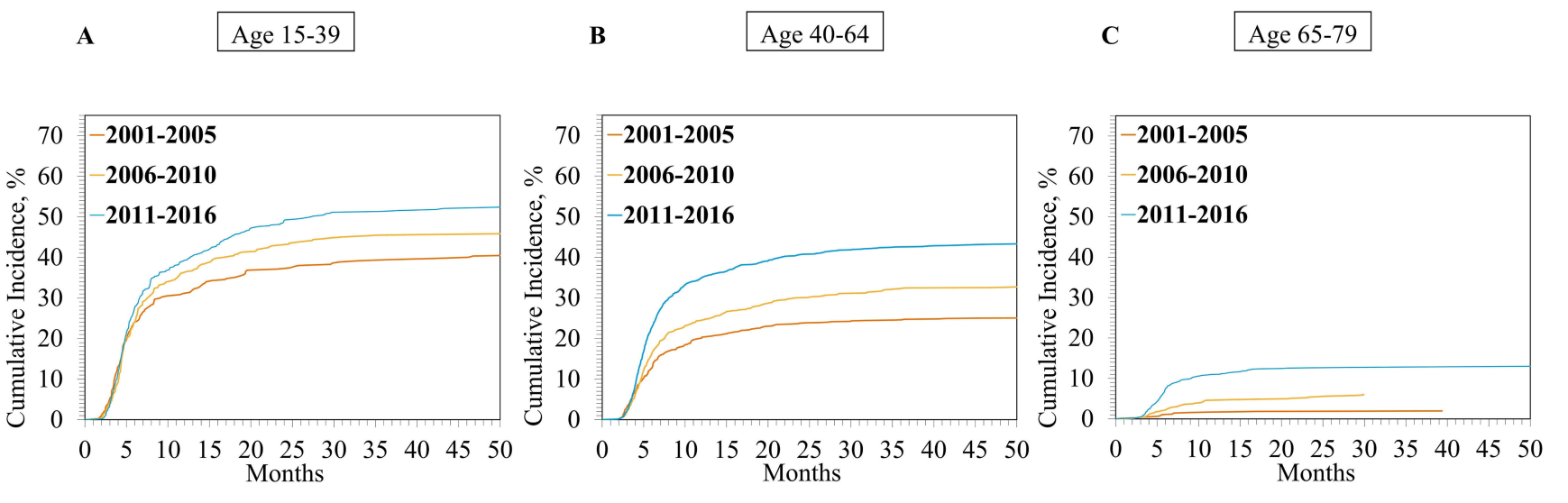
Note: Multivariable Cox proportional hazard regression, accounting for the competing risk of death; treatment
*Other includes: American Indian/Alaskan Native & Pacific Islander
**Married including common law/unmarried domestic partner
***Variable violated proportional hazard assumption and therefore stratified by Medicaid indicator
****Medicare without supplement, administered through managed care, with Medicaid eligibility. Variable violated proportional hazard assumption and therefore stratified by Medicare indicator
*****Indian/Public Health Service, county funded NOS

Figures Legend:

Figure 1. Registry source of allogeneic hematopoietic cell transplant data among newly diagnosed acute myeloid leukemia patients across California, 2001-2016. Three data sources, the California Cancer Registry (CCR), Center for International Blood and Marrow Transplant Research (CIBMTR), California Patient Discharge Database (PDD), were used to identify the occurrence of allogeneic hematopoietic cell transplants for the entire cohort. The Venn diagram shows the percentage of transplants that are identified in each dataset and the overlap between the three datasets.

Figure 2. Cumulative incidence of allogeneic hematopoietic cell transplant utilization among newly diagnosed acute myeloid leukemia patients in California, by diagnosis era. The cumulative incidence of allogeneic hematopoietic stem cell transplant was calculated accounting for the competing risk of death for each age group: Age 15-39 (A), Age 40-64 (B), Age 65-79 (C). The models were stratified by year of diagnosis grouped into 3 separate time periods (2001-2005, 2006-2010, 2011-2016). Time was calculated from month of acute myeloid leukemia diagnosis.

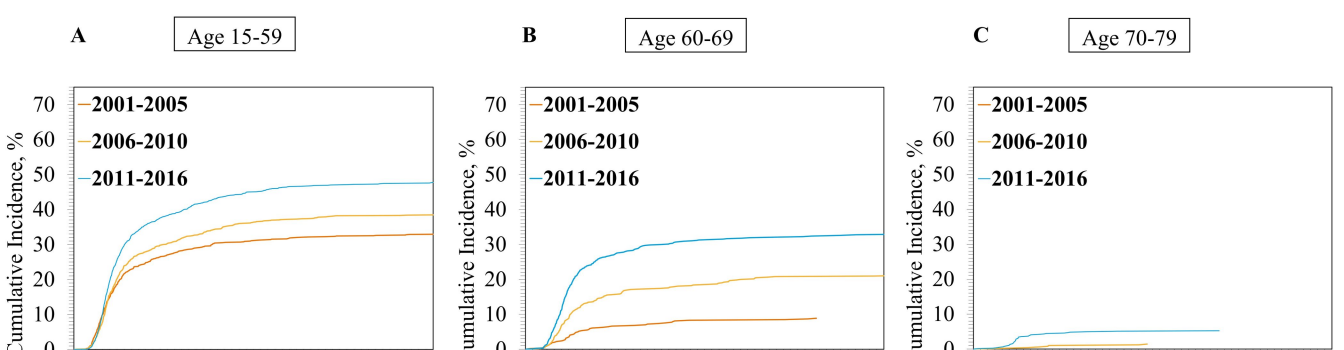

CIBMTR
12.7%
33.3%
PDD
9.1%
24.8%
13.8%
3.9%
CCR
2.4%


A
Age 15-39
B
Age 40-64
C
Age 65-79
2001-2005
2006-2010
2011-2016
Cumulative Incidence, %
0
10
20
30
40
50
60
70
0
5
10
15
20
25
30
35
40
45
50
Months

Supplemental Table 1. Selection criteria table

Selection Criteria	Excluded	Included
CCR Dataset		N =373,381
Acute myelogenous leukemia (AML) diagnosed between 2001-2016	N =351,908	N =21,473
Include where AML is the only, or first, neoplasm reported to CCR	N =5,966	N =15,507
Include where AML is the only, or first, neoplasm reported to CIBMTR	N =118	N =15,389
Exclude Histology Type ICD-O-3: 9898-Myeloid leukemia associated with Down Syndrome (n=27), 9920-Therapy-related myeloid neoplasms (n=23), 9930-Myeloid sarcoma (n=145), 9931-Acute panmyelosis with myelofibrosis (n=92), 9987-Therapy-related myelodysplastic syndrome, NOS (n=31)	N =318	N =15,071
Exclude cases where survival was not calculated due to diagnosis being reported on a death certificate or autopsy only	N =156	N =14,915
Exclude if socioeconomic status (SES) is missing	N =417	N =14,498
Exclude if patient sex is not male or female (n=<5) or distance to center is not able to be calculated (n=<40)	N =32	N =14,466
Exclude if missing diagnosis date (n=206), missing HCT date (n=7), date of transplant is prior to date of diagnosis (n=7), date of last follow is prior to diagnosis date in CCR (n=16)	N =140	N =14,326
Exclude if age <15 (n=863) or >80 (n=2,863)	N =3,726	N =10600
Exclude if patient did not receive induction therapy	N =2,264	N =8,336
Exclude if transplant type is autologous (n=402) or unknown (n=9)	N =411	N =7,925

CCR=California Cancer Registry, CIBMTR=Center for International Blood and Marrow Transplant Research, ICD-O-3=International Classification of Diseases for Oncology (3rd Edition), HCT= Hematopoietic Cell Transplantation, NOS=Not otherwise specified



Supplemental Figure 1. Sensitivity Analysis: Cumulative Incidence of Allogeneic Hematopoietic Cell Transplant Utilization Among Newly Diagnosed Acute Myeloid Leukemia Patients in California, by Diagnosis Era. The cumulative incidence of allogeneic hematopoietic stem cell transplant was calculated accounting for the competing risk of death for each age group: Age 15-59 (A), Age 60-69 (B), Age 70-79 (C). The models were stratified by year of diagnosis grouped into 3 separate time periods (2001-2005, 2006-2010, 2011-2016). Time was calculated from month of Acute Myeloid Leukemia diagnosis.