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## Racial and Socioeconomic Disparities in Long-Term Outcomes in 1 Year Allogeneic Hematopoietic Cell Transplantation Survivors: A CIBMTR Analysis

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## Abstract

**Introduction:** Racial/ethnic minorities have demonstrated a worse survival after allogeneic hematopoietic cell transplantation (HCT) compared to Whites. Whether the racial disparity in HCT outcomes persists in long-term survivors, and possibly may even be exacerbated in this population that frequently transitions back from the transplant center to their local healthcare providers, is unknown. In the current study we compared long-term outcomes among one-year allogeneic HCT survivors by race/ethnicity and socioeconomic status (SES).

**Methods:** The Center for International Blood and Marrow Transplant (CIBMTR) database was used to identify 5,473 patients with acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, or myelodysplastic syndromes who received first allogeneic HCT between 2007–2017 and were alive and in remission for at least 1 year after transplantation. Study was restricted to patients transplanted in the United States. SES was defined using patient neighborhood poverty level estimated from the recipient's ZIP code of residence; a ZIP code with 20% of persons below the federal poverty level was considered a high poverty area. The primary outcome was to evaluate the association of race/ethnicity and neighborhood poverty level with

overall survival (OS), relapse, and non-relapse mortality (NRM). Cox regression models were used to determine associations of ethnicity/race and SES with (OS), relapse, and (NRM). Standardized mortality ratios (SMR) were calculated to compare mortality rates of the study patients to their general population peers matched on race/ethnicity, age and sex.

**Results:** Patients were reported to be Non-Hispanic White (n=4,385), Non-Hispanic Black (n=338), Hispanic (n=516), and Asian (n=234). Overall, 729 (13%) patients resided in areas with high poverty level. We found that a significantly larger proportion of non-Hispanic Black (37%) and Hispanic (26%) patients lived in areas with higher poverty levels compared to Non-Hispanic Whites (10%) and Asians (10%) ( $p<0.01$ ). In multivariable analysis, we observed no significant association between OS, PFS, relapse, or NRM and race/ethnicity or poverty level when adjusted for patient-, disease- and transplant-related covariates.

**Conclusions:** Our retrospective cohort registry study highlights that among adult allogeneic HCT recipients who survived at least 1-year in remission, there was no observed association between race/ethnicity, neighborhood poverty level, and long-term outcomes.

## INTRODUCTION

It has been shown racial/ethnic minorities and recipients residing in areas with higher neighborhood poverty levels and poorer community health status have worse survival after allogeneic hematopoietic cell transplantation (HCT) compared to Whites and patients without socioeconomic adversity<sup>1-5</sup>. Factors such as race, socioeconomic status (SES), and healthcare insurance have been shown to influence decisions regarding stem cell transplantation.<sup>6</sup> There is limited information on access variations among different patient populations to HCT. Recent literature has tried to breakdown some disparities which may alter access to patients in need of HCT.<sup>2,7</sup> The identified barriers to access were age, gender, race, SES, and insurance status.<sup>8,9</sup> Even in the age of a growing geriatric oncology population, younger patients are still more likely to receive HCT.<sup>10</sup> With respect to sex, men are more likely to have HCT than females.<sup>11</sup> Studies have also shown uninsured status, Medicaid or Medicare insurance lowers likelihood of HCT.<sup>12</sup> In addition to these, race has also been identified as a significant factor affecting outcomes.<sup>10</sup>

Survivorship care focuses on the patient beyond treatment period and continues providing long term care after active treatment has ceased.<sup>13</sup> In HCT patients, unique complications and therapy related events can occur even years after HCT<sup>14,15</sup>. Many HCT patients are encouraged to maintain follow up with a transplant center for the duration of their lifetime.<sup>16</sup> This can pose a unique challenge for HCT survivors such as: monitoring for disease recurrence, presence of graft-versus-host disease, long term chemotherapy associated effects.<sup>17</sup> We chose the one-year landmark since this is the typical timeframe when care is transitioned from transplant center to community providers, especially those without significant graft versus host disease (GVHD). Outside of disease and treatment specific monitoring, survivorship can include assessments on quality of life, general health maintenance, and social and psychological adjustments after treatment.<sup>18</sup> Causes of death after transplantation can be attributed to secondary malignancies, recurrent disease, infections, chronic GVHD, respiratory diseases, cardiovascular diseases, all associated with transplantation.<sup>19</sup> Given racial minorities are more often from lower SES, these late

effects from HCT may be accentuated in this vulnerable population.<sup>20</sup> Without resources to integrate back into society after HCT, it is likely many of these patients are lost to follow up and do not follow the prescribed survivorship plan which may be a driver for worse outcomes.<sup>21</sup>

A previous large Center for International Blood and Marrow Transplant Research (CIBMTR) study investigated the association of race/ethnicity and SES with unrelated allogeneic HCT outcomes and showed that African American patients had worse overall survival (OS) after HCT compared to Whites.<sup>5</sup> African Americans and Hispanics were also shown to have higher cumulative incidence of non-relapse mortality (NRM).<sup>5</sup> Recipients from the lowest SES quartile had worse overall survival and higher NRM. Of note, the effects of race and SES on survival were independent of each other and it is important to note that the inferior outcomes among African Americans could not be explained by transplant-related factors or SES.<sup>22</sup> Survival was considered from the time of transplantation, and this study did not specifically focus on long-term HCT survivors who typically are no longer under the direct care of transplant centers and could be more prone to disparities in care and outcomes.

To address the gaps in literature, our study investigated racial and SES outcome disparities in long-term allogeneic HCT survivors. We selected a representative, multicenter cohort of survivors from the CIBMTR database who were in remission for at least 1 year after allogeneic transplantation. We sought to: 1) determine association of ethnicity/race and neighborhood poverty level on survival among adult allogeneic HCT survivors with hematologic malignancies, 2) investigate the cumulative incidence of NRM and relapse post-transplant by ethnicity/race and neighborhood poverty level in this patient population, and 3) compare standardized mortality ratios (SMR) between our cohort and that of their age- and gender-matched peers in the general population.

## **MATERIALS AND METHODS**

### **Data Source**

The CIBMTR is a voluntary working group composed of nearly 500 transplantation centers worldwide that contribute detailed HCT data to a statistical center at the Medical College of Wisconsin in Milwaukee and the National Marrow Donor Program (NMDP) in Minneapolis. Participating centers are required to report all transplants consecutively; compliance is monitored by onsite audits. Patients are followed longitudinally. Computerized checks for discrepancies, physician reviews of submitted data, and onsite audits of participating centers ensure data quality. Observational studies conducted by the CIBMTR are performed in compliance with all applicable federal regulations pertaining to the protection of human research participants and are under the guidance of the institutional review board of the NMDP.

### **Study Population**

The study population consisted of first allogeneic HCT recipients from 2007–2017, age >18 years at transplant who were alive and in remission 1 year from HCT with the diagnosis

of acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), chronic myeloid leukemia (CML), or myelodysplastic syndromes (MDS). The study was restricted to patients treated in the United States (US). All graft sources, donor sources, and conditioning regimens were considered. The CIBMTR database was used to identify 5,473 patients who met the study selection criteria and included 4,385 non-Hispanic White, 338 non-Hispanic Black, 516 Hispanic, and 234 Asian patients. Other race/ethnicity groups including American Indian/Alaskan Natives, Hawaiian/Pacific Islanders and mixed race were excluded because of the small number of patients in those categories to conduct meaningful analyses.

### Statistical Analysis

The primary objective was to evaluate the association of race/ethnicity (non-Hispanic White (referent) vs. non-Hispanic Black vs. Hispanic vs. Asian) and neighborhood poverty level with OS, relapse, and NRM. Neighborhood poverty exposure was used to describe SES in our study and was defined per the US Census definition as living in a high-poverty ZIP code, with high poverty level consisting of 20% of persons below 100% federal poverty level<sup>1</sup>. OS was defined as time from HCT to death from any cause. NRM was defined as time from HCT to death without relapse, with relapse being a competing event. Relapse was defined as time to recurrence of disease with NRM as a competing event. Patients were censored at date of last follow-up for all outcomes defined above. We also described the causes of death for our cohort.

Baseline characteristics were compared between racial and SES groups. OS was summarized using Kaplan-Meier method. Probabilities of NRM and relapse were calculated using cumulative incidence function. Cox proportional hazards regression model was used to evaluate the effect of the main variables of interest (race/ethnicity and neighborhood poverty level) on OS, NRM, and relapse after adjusting for demographic and disease variables. A significance level of 0.05 was used in our analyses.

The interaction between race/ethnicity and neighborhood poverty level was evaluated. Non-Hispanic White for race/ethnicity and low poverty level for SES were considered the referent groups for analyses. With these baseline groups, we had a sample size with the ability to detect a 10% difference in survival at 5 years among race/ethnicity groups, with an 80% power and hazard ratio of 0.65.

Variables considered for inclusion into the model: race/ethnicity and poverty (main effects which are always kept in the model), age at transplant, co-morbidity index (HCT-CI), insurance type, marital status, distance between residence and transplant center, location of residence (urban/rural), disease risk index at transplant (low/intermediate/high/very high), year of transplantation, conditioning regimen, donor/graft type, GVHD prophylaxis, development of acute GVHD by 1 year post HCT, chronic GVHD by 1 year post HCT. Center effect was accounted for via random effect with log-normal distribution.

We also conducted analyses to estimate the standardized mortality ratios (SMR) for non-Hispanic Whites, non-Hispanic Blacks, and Hispanics comparing the number of observed deaths in our cohort to expected number of deaths within their age- and sex-matched general population controls in the US. SMR could not be estimated for Asians since life tables for

this racial group are not available through the National Center for Health Statistics. The SMR analysis was performed according to methods described in prior CIBMTR studies.<sup>23–26</sup> Analyses were performed using SAS statistical software (SAS Institute, Cary, NC). All tests are two-sided, and 0.05 level of significance was used throughout the study.

## RESULTS

### Patient and Transplant Characteristics

The characteristics of the study population by race/ethnicity are presented in Table 1. Median follow up of survivors from 1-year post-HCT was 69 months for Non-Hispanic Whites, 50 months for Non-Hispanic Black, 59 months for Hispanics, and 57 months for Asians. There were significant differences in neighborhood poverty levels by race with a greater proportion of non-Hispanic Black (37%) and Hispanic (26%) recipients residing in high poverty areas compared to non-Hispanic Whites (10%) and Asians (10%) ( $P<0.01$ ). Significantly greater proportion of non-Hispanic White patients were privately insured compared to non-Hispanic Black and Hispanic patients who were more likely to be on Medicaid. Non-Hispanic Whites were also significantly more likely to be married, have a rural residence, and live at a greater distance from the transplant center. There were significant differences in the four race/ethnicity cohorts by age at transplantation, sex, Karnofsky score at HCT, HCT-CI score at HCT, diagnosis, disease risk index, donor type, graft type, conditioning regimen intensity, use of total body irradiation (TBI), GVHD prophylaxis, and year of transplantation.

Table 2 shows our cohorts characteristics by neighborhood poverty level. Median follow up of survivors for both low and high poverty areas was 62 months, respectively. As noted above, a significantly greater proportion of non-Hispanic Blacks and Hispanics live in high poverty neighborhoods. As expected, a greater number of recipients residing in low poverty neighborhoods were significantly more likely to have private health insurance, be married, have an urban residence, and lived closer to the transplant center. Among disease and transplant related characteristics, significant differences between the two cohorts were noted in age at transplantation, diagnosis, and donor type.

### Analysis by Race/Ethnicity

Table 3 highlights outcomes from the 1-year post-transplant time point. There was a significant difference in OS at 5 years with highest survival in Asian recipients (74%), followed by Hispanic (70%), and non-Hispanic White (65%) and non-Hispanic Black (65%) patients ( $P=0.003$ ). There was no difference in the cumulative incidence of relapse, although the cumulative incidence of NRM mirrored that of OS with lowest rates in Asians (13%), followed by Hispanics (16%), and non-Hispanic Blacks (20%) and non-Hispanic Whites (21%) ( $P=0.002$ ). However, in multivariable analyses adjusting for transplant, disease, and transplant related characteristics, there was no difference in OS or NRM between the four race/ethnicity groups (Table 4). Of note, there was a significant association noted between urban/rural place of residence and insurance status and OS and NRM. Recipients with rural residence have higher risks of overall mortality (hazard ratio [HR] 1.22 vs. urban residence, 95% CI 1.08–1.38;  $P=0.002$ ) and NRM (HR 1.33, 95% CI 1.13–1.57;  $P=0.0005$ ).



Compared to patients with private health insurance, higher risk of overall mortality was seen in patients on Medicaid (HR 1.17, 95% CI 1.01–1.35; P=0.033) and on Medicare (HR 1.22, 95% CI 1.07–1.39, P=0.0029), although this association was only observed in Medicare recipients for NRM (HR 1.25, 95% CI 1.06–1.48; P=0.008). There was no association between residence location and insurance status with risks of relapse. The causes of death were similar in all four groups, with disease relapse being the most common cause followed by GVHD, infections, and organ failure.

### Analysis by Neighborhood Poverty Level

Tables 3 and 4 also show results for univariate and multivariable analysis by neighborhood poverty level. In univariate analysis, there was no difference in 5-year OS, relapse, or NRM between patients coming from low and high poverty neighborhoods. This was confirmed in multivariable analyses, which again did not show any significant differences in risks of OS, relapse, or NRM among the two groups. As noted above, residence location and insurance status were associated with OS and NRM.

### Mortality Rates Compared to General Population

The analysis comparing observed versus expected mortality for non-Hispanic White, non-Hispanic Black, and Hispanic recipients is shown in Table 5. Our cohort of 1-year HCT survivors had mortality rates that were approximately 10-times higher than their age- and sex-matched controls from the general population. We also observed differences by race/ethnicity, with Hispanic recipients having higher mortality rates (SMR 19.2) than non-Hispanic Whites (SMR 10.0) and non-Hispanic Blacks (SMR 11.2).

## DISCUSSION

In our study of adult allogeneic HCT recipients with hematologic malignancies who had survived in remission for 1 year, we observed no differences in OS, relapse, or NRM either by race/ethnicity or by neighborhood poverty levels. Previous CIBMTR studies that have considered HCT recipients from the time of transplantation have demonstrated significant differences in survival by race/ethnicity, neighborhood poverty levels, and community health status<sup>1,3,5</sup>. We had hypothesized that these disparities would persist or even be accentuated in long-term survivors since many patients frequently transition back to their local healthcare ecosystem after the first 3–6 months following transplantation, where the systemic racial and socioeconomic disparity factors may be prevalent in their communities. Previously recognized disparity in the outcomes of allogeneic HCT is once again evidenced by the differences in overall survival and non-relapse mortality seen in this study. However, these differences in OS and NRM among various racial/ethnic groups become less pronounced when adjusted for other risk factors. These findings may suggest that those differences are occurring due to the variability in certain patient and treatment characteristics of different racial/ethnic groups.

We postulate several hypotheses for our observed lack of association between race/ethnicity, neighborhood poverty level, and outcomes in long-term HCT survivors seen after accounting for other risk factors and sociodemographic characteristics. First, patients from minority

groups who are able to receive allogeneic transplantation are not representative of the universe of racial/ethnic and socioeconomically disadvantaged populations. For example, HCT recipients have been reported to have higher literacy levels, education status, and SES than the general population<sup>8,27,28</sup>. Hence, HCT survivors who transition back to their communities may have different and better healthcare access and experience than their peers in the general population. Second, a substantial portion of mortality occurs in the first year following allogeneic transplantation, where the impact of healthcare disparities may be the most significant. Also, a larger proportion of racial minority patients lived closer to their transplant center and may have had the advantage of closer follow up by their treating institution. For example, among non-Hispanic Whites, 53% lived within 50 miles of the transplant center and 15% reported a rural place of residence. In contrast, a greater proportion of racial/ethnic minority recipients lived close to the transplant center (65% non-Hispanic Blacks, 66% Hispanics, 66% Asians lived within 50 miles) or in an urban area (7%, 3%, and 3%, respectively, reported rural residence). It is also important to note that our study cohort consisted of patients transplanted in the contemporary era where there is emphasis on providing systematic post-transplant survivorship care, routine utilization of social workers to assess and provide psychosocial support to patients and their families, and increased availability of financial and other support services from patient advocacy organizations. These factors may have mitigated the adverse effect of healthcare disparity factors in long-term HCT survivors. Additionally, the use of newer GVHD prevention strategies such as post-transplant cyclophosphamide may have contributed, as evidenced by comparable rates of acute and chronic GVHD among the four race groups despite the greater use of donors other than HLA-identical siblings or matched unrelated donors in racial minorities.

In a related single center study of allogeneic and autologous HCT 1 year survivors, Joo et al also did not find any association between post-transplant survival and community health status – a measure that was previously reported to significantly influence 1-year survival<sup>3,29</sup>. It is well recognized that healthcare disparities is a complex construct, and as supported by our analysis, other related factors such as insurance status and neighborhood poverty level may be the mechanism for adverse outcomes previously reported among minority HCT recipients.

An important finding from our study that has immediate application in clinical practice is the observation of mortality risks that are ~10 times higher for non-Hispanic Whites and non-Hispanic Blacks and ~20 times higher for Hispanics. This is consistent with other studies that have shown higher rates of mortality in allogeneic HCT survivors than what may be expected in the general population till at least 10–15 years post-transplantation<sup>24,30–32</sup>. Our study did show worse mortality for the Hispanic population, we postulate this is due to health-related factors associated with decreased survival other than the primary malignancy. More work is needed to understand why this minority community continues to show worsening mortality. Our findings underscore the importance of continued lifelong vigilance for late complications of transplantation with screening, prevention, and prompt management according to published guidelines<sup>14,15,17</sup>. There is additionally a need to develop care models and infrastructure such as survivorship care plans, telemedicine, web

based self-management applications, that can facilitate the care of long-term survivors who may not be under the direct care of their transplant centers<sup>27,33–35</sup>.

Some limitations of our study have to be considered. First, our study is limited due to its retrospective registry-based design. As noted earlier, we cannot address the totality of healthcare disparities in transplantation given that our study population consisted of patients who were able to get to an allogeneic HCT and we have no mechanism of ascertaining patients who needed a transplant but could not receive one. It is also possible that we are underestimating the true representation of long-term care for HCT survivors. Although we had a very robust median follow up it is still possible that longer follow up may be needed to reveal differences in late effects that manifest much later post-transplant. Our findings are only applicable to the US and are not generalizable to other countries.

In summary, we found that among adult allogeneic HCT recipients who survived for at least 1 year in remission, there were no significant differences in OS, relapse, or NRM based on race/ethnicity or neighborhood poverty level. HCT survivors have significantly higher risks of mortality compared to the general population and require long-term monitoring and prevention of late effects irrespective of race/ethnicity or SES.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

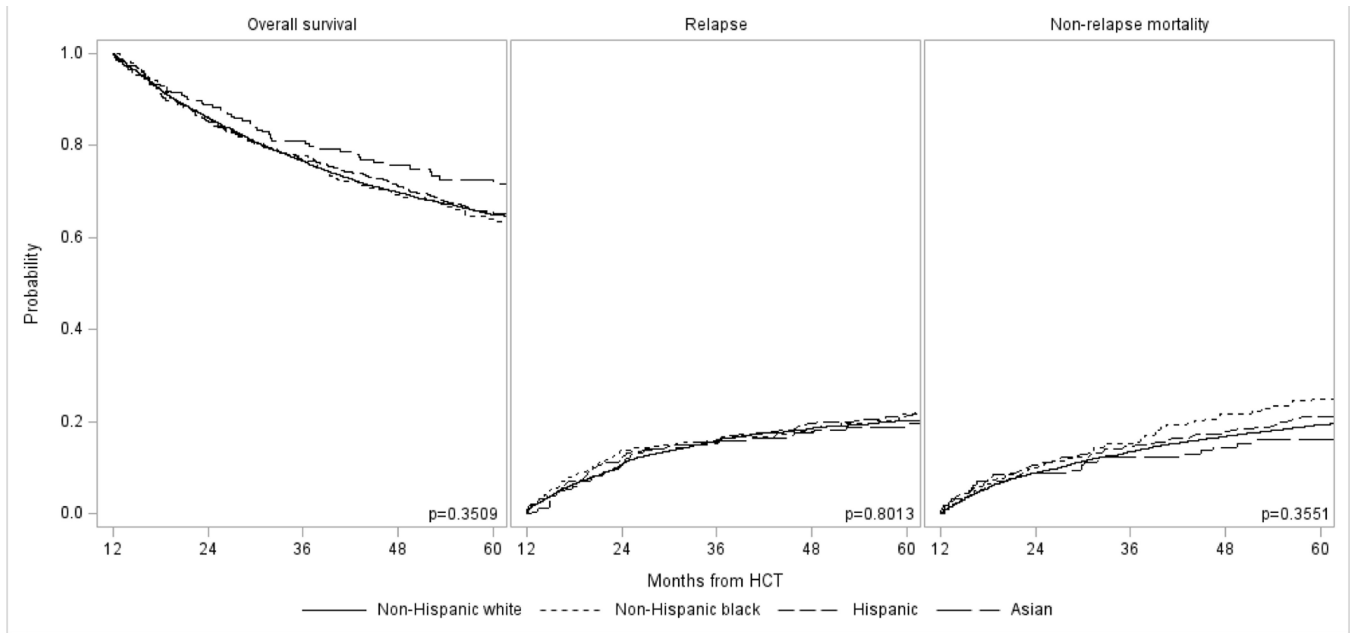
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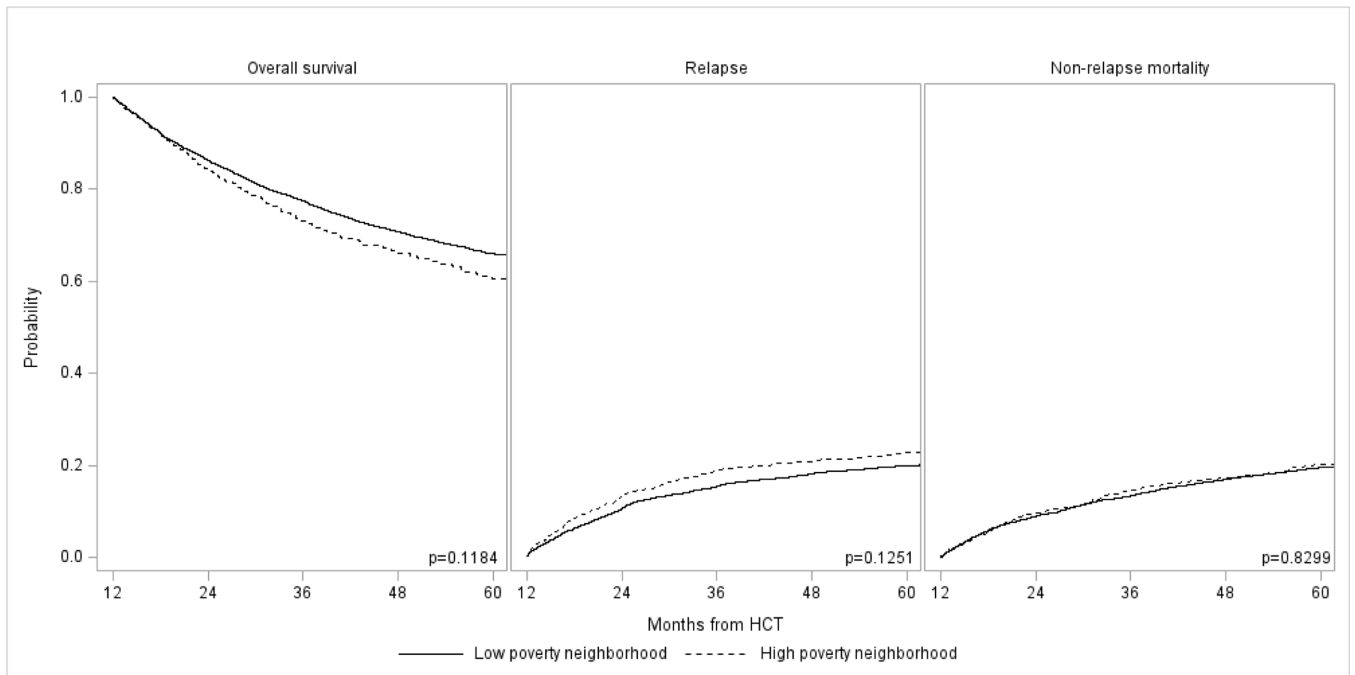
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**Figure 1:**  
Long-term outcomes in adult allogeneic HCT survivors with AML, ALL, CML, and MDS who had survived in remission 1 year in remission by race/ethnicity: (A) Overall survival, (B) Relapse, and (C) Non-relapse mortality



**Figure 2:**  
Long-term outcomes in adult allogeneic HCT survivors with AML, ALL, CML, and MDS who had survived in remission 1 year in remission by neighborhood poverty level: (A) Overall survival, (B) Relapse, and (C) Non-relapse mortality

**Table 1.**

Characteristics of adult patients receiving first allogeneic HCT for AML, ALL, CML, or MDS between 2007–2017 in the United States, by race/ethnicity

Characteristic	Non-Hispanic white	Non-Hispanic black	Hispanic	Asian	P-Value <sup>a</sup>
No. of patients	4385	338	516	234	
No. of centers	140	83	94	68	
Age at HCT					<.01
Median (min-max)	55 (18–83)	47 (18–75)	41 (18–76)	47 (18–74)	
18–29	467 (11)	45 (13)	154 (30)	42 (18)	
30–39	469 (11)	62 (18)	92 (18)	44 (19)	
40–49	716 (16)	88 (26)	102 (20)	44 (19)	
50–59	1243 (28)	71 (21)	91 (18)	48 (21)	
60–69	1271 (29)	67 (20)	68 (13)	45 (19)	
70	219 (5)	5 (1)	9 (2)	11 (5)	
Recipient sex					<.01
Male	2530 (58)	148 (44)	283 (55)	118 (50)	
Female	1855 (42)	190 (56)	233 (45)	116 (50)	
Neighborhood poverty level *					<.01
Low	3937 (90)	214 (63)	383 (74)	210 (90)	
High	448 (10)	124 (37)	133 (26)	24 (10)	
Health insurance type					<.01
Disability insurance +/-others	103 (2)	10 (3)	8 (2)	6 (3)	
Private health insurance +/- others	2889 (66)	181 (54)	251 (49)	144 (62)	
Medicaid +/-others	420 (10)	85 (25)	171 (33)	40 (17)	
Medicare +/-others	810 (18)	40 (12)	58 (11)	28 (12)	
Other	120 (3)	17 (5)	19 (4)	8 (3)	
Missing	43 (1)	5 (1)	9 (2)	8 (3)	
Highest level of education completed					<.01
No primary	1 (0)	0 (0)	1 (0)	1 (0)	
Less than primary	2 (0)	1 (0)	4 (1)	1 (0)	
Primary	4 (0)	0 (0)	22 (4)	1 (0)	
Lower secondary	74 (2)	11 (3)	35 (7)	4 (2)	
Upper secondary	1015 (23)	110 (33)	164 (32)	37 (16)	
Post-secondary (vocational)	358 (8)	37 (11)	47 (9)	11 (5)	
Tertiary (4-year degree)	1094 (25)	65 (19)	50 (10)	56 (24)	
Tertiary (2-year degree)	235 (5)	18 (5)	26 (5)	14 (6)	
Advanced research degree	212 (5)	13 (4)	15 (3)	25 (11)	
Missing	1390 (32)	83 (25)	152 (29)	84 (36)	
Marital status					<.01
Single, never married	626 (14)	96 (28)	161 (31)	41 (18)	
Married	3163 (72)	179 (53)	286 (55)	152 (65)	



Characteristic	Non-Hispanic white	Non-Hispanic black	Hispanic	Asian	P-Value <sup>a</sup>
Separated	47 (1)	8 (2)	12 (2)	4 (2)	
Divorced	356 (8)	32 (9)	35 (7)	12 (5)	
Widowed	105 (2)	7 (2)	8 (2)	8 (3)	
Missing	88 (2)	16 (5)	14 (3)	17 (7)	
Urban/rural residence					<.01
Urban	3733 (85)	316 (93)	498 (97)	228 (97)	
Rural	652 (15)	22 (7)	18 (3)	6 (3)	
Distance between residence and transplant center (miles)					<.01
< 20	1281 (29)	168 (50)	238 (46)	116 (50)	
20–50	1045 (24)	52 (15)	106 (21)	60 (26)	
50–150	1247 (28)	72 (21)	82 (16)	26 (11)	
> 150	812 (19)	46 (14)	90 (17)	32 (14)	
Karnofsky score at HCT					<.01
<90	1569 (36)	133 (39)	140 (27)	75 (32)	
90	2738 (62)	201 (59)	370 (72)	155 (66)	
Missing	78 (2)	4 (1)	6 (1)	4 (2)	
HCT-CI score at HCT					<.01
0	1078 (25)	74 (22)	196 (38)	82 (35)	
1–2	1145 (26)	105 (31)	128 (25)	58 (25)	
3	1719 (39)	140 (41)	157 (30)	85 (36)	
Missing	443 (10)	19 (6)	35 (7)	9 (4)	
Disease					<.01
AML	2225 (51)	172 (51)	222 (43)	125 (53)	
ALL	544 (12)	75 (22)	180 (35)	44 (19)	
CML	167 (4)	21 (6)	34 (7)	7 (3)	
MDS	1449 (33)	70 (21)	80 (16)	58 (25)	
Refined disease risk index					<.01
Low	307 (7)	27 (8)	56 (11)	21 (9)	
Intermediate	2347 (54)	204 (60)	286 (55)	151 (65)	
High	977 (22)	68 (20)	101 (20)	43 (18)	
Very high	60 (1)	5 (1)	11 (2)	1 (0)	
N/A - year of transplant <2008	457 (10)	18 (5)	41 (8)	8 (3)	
Missing	237 (5)	16 (5)	21 (4)	10 (4)	
Donor type					<.01
HLA-identical sibling	1368 (31)	101 (30)	189 (37)	92 (39)	
Other related	357 (8)	99 (29)	84 (16)	31 (13)	
Well-matched unrelated (8/8)	1972 (45)	40 (12)	93 (18)	46 (20)	
Partially-matched unrelated (7/8)	317 (7)	34 (10)	56 (11)	18 (8)	
Mis-matched unrelated ( 6/8)	16 (0)	1 (0)	3 (1)	3 (1)	
Cord blood	355 (8)	63 (19)	91 (18)	44 (19)	

Characteristic	Non-Hispanic white	Non-Hispanic black	Hispanic	Asian	P-Value <sup>a</sup>
Graft type					<.01
Bone marrow	631 (14)	49 (14)	73 (14)	29 (12)	
Peripheral blood	3399 (78)	226 (67)	352 (68)	161 (69)	
Cord blood	355 (8)	63 (19)	91 (18)	44 (19)	
Conditioning intensity					<.01
MAC	2636 (60)	232 (69)	373 (72)	158 (68)	
RIC/NMA	1737 (40)	105 (31)	140 (27)	76 (32)	
Missing	12 (0)	1 (0)	3 (1)	0 (0)	
TBI usage					<.01
No	2791 (64)	158 (47)	248 (48)	114 (49)	
Yes	1582 (36)	179 (53)	265 (51)	120 (51)	
Missing	12 (0)	1 (0)	3 (1)	0 (0)	
GVHD prophylaxis					<.01
Post-CY + other(s)	307 (7)	86 (25)	71 (14)	32 (14)	
Post-CY alone	12 (0)	0 (0)	1 (0)	0 (0)	
TAC + MMF +- other(s) (except post-CY)	817 (19)	64 (19)	68 (13)	20 (9)	
TAC + MTX +- other(s) (except MMF, post-CY)	2149 (49)	115 (34)	228 (44)	101 (43)	
TAC + other(s) (except MMF, MTX, post-CY)	312 (7)	13 (4)	55 (11)	25 (11)	
TAC alone	110 (3)	12 (4)	13 (3)	6 (3)	
CSA + MMF +- other(s) (except post-CY)	368 (8)	31 (9)	55 (11)	38 (16)	
CSA + MTX +- other(s) (except MMF, post-CY)	211 (5)	10 (3)	17 (3)	9 (4)	
CSA + other(s) (except MMF, MTX, post-CY)	20 (0)	1 (0)	2 (0)	0 (0)	
CSA alone	16 (0)	1 (0)	4 (1)	1 (0)	
Other(s)	42 (1)	1 (0)	1 (0)	1 (0)	
Missing	21 (0)	4 (1)	1 (0)	1 (0)	
Year of HCT					<.01
2007	457 (10)	18 (5)	41 (8)	8 (3)	
2008	592 (14)	36 (11)	64 (12)	17 (7)	
2009	578 (13)	30 (9)	61 (12)	25 (11)	
2010	449 (10)	39 (12)	53 (10)	26 (11)	
2011	311 (7)	17 (5)	38 (7)	19 (8)	
2012	324 (7)	19 (6)	44 (9)	15 (6)	
2013	486 (11)	29 (9)	56 (11)	30 (13)	
2014	420 (10)	27 (8)	42 (8)	17 (7)	
2015	324 (7)	44 (13)	47 (9)	26 (11)	
2016	244 (6)	45 (13)	40 (8)	29 (12)	
2017	200 (5)	34 (10)	30 (6)	22 (9)	
Acute GVHD (grade II-IV)					0.44
No	2521 (57)	214 (63)	290 (56)	142 (61)	
Yes	1837 (42)	122 (36)	223 (43)	91 (39)	
Missing	27 (1)	2 (1)	3 (1)	1 (0)	

Characteristic	Non-Hispanic white	Non-Hispanic black	Hispanic	Asian	P-Value <sup>a</sup>
Chronic GVHD before 1 year					0.76
No	1904 (43)	144 (43)	219 (42)	102 (44)	
Yes	2447 (56)	193 (57)	290 (56)	130 (56)	
Missing	34 (1)	1 (0)	7 (1)	2 (1)	
Follow-up of survivors from 1 year post-HCT (months) - median (range)	69 (0–138)	50 (0–133)	59 (0–133)	57 (0–130)	

HCT – hematopoietic cell transplantation; HCT-CI – hematopoietic cell transplantation comorbidity index; AML – acute myeloid leukemia; ALL – acute lymphoblastic leukemia; CML – chronic myeloid leukemia; MDS – myelodysplastic syndrome; MAC – myeloablative conditioning; RIC/NMA – reduced intensity/non-myeloablative conditioning; TBI – total body irradiation; Cy – cyclophosphamide; MMF – mycophenolate mofetil; TAC – tacrolimus; CSA – cyclosporine; MTX – methotrexate; GVHD – graft-versus-host disease

\* High poverty neighborhood defined as ≥20% of persons living below 100% federal poverty level; low-poverty neighborhood defined as <20% of persons below 100% federal poverty level Hypothesis testing:

<sup>a</sup>Pearson chi-square test

**Table 2.**

Characteristics of adult patients receiving first allogeneic HCT for AML, ALL, CML, MDS between 2007–2017 in the United States, by neighborhood poverty level\*

Characteristic	Low poverty	High poverty	P Value <sup>a</sup>
No. of patients	4744	729	
No. of centers	142	106	
Age at HCT			<.01
Median (min-max)	54 (18–83)	50 (18–76)	
18–29	585 (12)	123 (17)	
30–39	562 (12)	105 (14)	
40–49	808 (17)	142 (19)	
50–59	1285 (27)	168 (23)	
60–69	1281 (27)	170 (23)	
70	223 (5)	21 (3)	
Recipient sex			0.15
Male	2687 (57)	392 (54)	
Female	2057 (43)	337 (46)	
Race			<.01
Non-Hispanic white	3937 (83)	448 (61)	
Non-Hispanic black	214 (5)	124 (17)	
Hispanic	383 (8)	133 (18)	
Asian	210 (4)	24 (3)	
Health insurance type			<.01
Disability insurance +/-others	114 (2)	13 (2)	
Private health insurance +/- others	3076 (65)	389 (53)	
Medicaid +/-others	533 (11)	183 (25)	
Medicare +/-others	820 (17)	116 (16)	
Other	139 (3)	25 (3)	
Missing	62 (1)	3 (0)	
Highest level of education completed			<.01
No primary	3 (0)	0 (0)	
Less than primary	6 (0)	2 (0)	
Primary	17 (0)	10 (1)	
Lower secondary	95 (2)	29 (4)	
Upper secondary	1122 (24)	204 (28)	
Post-secondary (vocational)	391 (8)	62 (9)	
Tertiary (4-year degree)	1138 (24)	127 (17)	
Tertiary (2-year degree)	258 (5)	35 (5)	
Advanced research degree	234 (5)	31 (4)	
Missing	1480 (31)	229 (31)	
Marital status			<.01

Characteristic	Low poverty	High poverty P	Value <sup>a</sup>
Single, never married	752 (16)	172 (24)	
Married	3347 (71)	433 (59)	
Separated	50 (1)	21 (3)	
Divorced	368 (8)	67 (9)	
Widowed	106 (2)	22 (3)	
Missing	121 (3)	14 (2)	
Urban/rural residence			<.01
Urban	4190 (88)	585 (80)	
Rural	554 (12)	144 (20)	
Distance between residence and transplant center (miles)			<.01
< 20	1574 (33)	229 (31)	
20–50	1181 (25)	82 (11)	
50–150	1187 (25)	240 (33)	
>150	802 (17)	178 (24)	
Karnofsky score			0.92
<90	1666 (35)	251 (34)	
90	2999 (63)	465 (64)	
Missing	79 (2)	13 (2)	
HCT-CI			0.34
0	1232 (26)	198 (27)	
1–2	1263 (27)	173 (24)	
3	1818 (38)	283 (39)	
Missing	431 (9)	75 (10)	
Disease			<.01
AML	2371 (50)	373 (51)	
ALL	700 (15)	143 (20)	
CML	192 (4)	37 (5)	
MDS	1481 (31)	176 (24)	
Refined disease risk index			0.54
Low	358 (8)	53 (7)	
Intermediate	2582 (54)	406 (56)	
High	1043 (22)	146 (20)	
Very high	68 (1)	9 (1)	
N/A - year of transplant <2008	443 (9)	81 (11)	
Missing	250 (5)	34 (5)	
Donor type			<.01
HLA-identical sibling	1515 (32)	235 (32)	
Other related	482 (10)	89 (12)	
Well-matched unrelated (8/8)	1913 (40)	238 (33)	
Partially-matched unrelated (7/8)	350 (7)	75 (10)	
Mis-matched unrelated ( 6/8)	19 (0)	4 (1)	

Characteristic	Low poverty	High poverty P	Value <sup>a</sup>
Cord blood	465 (10)	88 (12)	
Graft type			0.10
Bone marrow	671 (14)	111 (15)	
Peripheral blood	3608 (76)	530 (73)	
Cord blood	465 (10)	88 (12)	
Conditioning intensity			0.75
MAC	2937 (62)	462 (63)	
RIC/NMA	1793 (38)	265 (36)	
Missing	14 (0)	2 (0)	
TBI usage			0.80
No	2878 (61)	433 (59)	
Yes	1852 (39)	294 (40)	
Missing	14 (0)	2 (0)	
GVHD prophylaxis			0.83
Post-CY + other(s)	417 (9)	79 (11)	
Post-CY alone	12 (0)	1 (0)	
TAC + MMF +- other(s) (except post-CY)	827 (17)	142 (19)	
TAC + MTX +- other(s) (except MMF, post-CY)	2261 (48)	332 (46)	
TAC + other(s) (except MMF, MTX, post-CY)	354 (7)	51 (7)	
TAC alone	124 (3)	17 (2)	
CSA + MMF +- other(s) (except post-CY)	433 (9)	59 (8)	
CSA + MTX +- other(s) (except MMF, post-CY)	214 (5)	33 (5)	
CSA + other(s) (except MMF, MTX, post-CY)	20 (0)	3 (0)	
CSA alone	19 (0)	3 (0)	
Other(s)	39 (1)	6 (1)	
Missing	24 (1)	3 (0)	
Year of HCT			0.25 <sup>a</sup>
2007	443 (9)	81 (11)	
2008	600 (13)	109 (15)	
2009	617 (13)	77 (11)	
2010	496 (10)	71 (10)	
2011	340 (7)	45 (6)	
2012	350 (7)	52 (7)	
2013	529 (11)	72 (10)	
2014	440 (9)	66 (9)	
2015	372 (8)	69 (9)	
2016	313 (7)	45 (6)	
2017	244 (5)	42 (6)	
Acute GVHD (grade II-IV)			0.19 <sup>a</sup>
No	2727 (57)	440 (60)	
Yes	1986 (42)	287 (39)	

Characteristic	Low poverty	High poverty P	Value <sup>a</sup>
Missing	31 (1)	2 (0)	
Chronic GVHD before 1 year			0.74
No	2044 (43)	325 (45)	
Yes	2662 (56)	398 (55)	
Missing	38 (1)	6 (1)	
Follow-up of survivors from 1 year post-HCT (months)- median (range)	62 (0–138)	62 (0–134)	

HCT – hematopoietic cell transplantation; HCT-CI – hematopoietic cell transplantation comorbidity index; AML – acute myeloid leukemia; ALL – acute lymphoblastic leukemia; CML – chronic myeloid leukemia; MDS – myelodysplastic syndrome; MAC – myeloablative conditioning; RIC/NMA – reduced intensity/non-myeloablative conditioning; TBI – total body irradiation; Cy – cyclophosphamide; MMF – mycophenolate mofetil; TAC – tacrolimus; CSA – cyclosporine; MTX – methotrexate; GVHD – graft-versus-host disease

\* High poverty neighborhood defined as ≥20% of persons living below 100% federal poverty level; low-poverty neighborhood defined as <20% of persons below 100% federal poverty level

Hypothesis testing:

<sup>a</sup>Pearson chi-square test

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**Table 3.**

Univariate analysis for 5-year outcomes, by race/ethnicity and neighborhood poverty level

Outcomes <sup>#</sup>	N	Overall survival		Relapse		Non-relapse mortality	
		Probability (95% CI)	P-value	Probability (95% CI)	P-value	Probability (95% CI)	P-value
Race/Ethnicity							
Non-Hispanic White	4385	65 (64–66)%	0.003	20 (19–21)%	0.218	21 (19–22)%	0.002
Non-Hispanic Black	338	65 (59–70)%		23 (19–28)%		20 (15–25)%	
Hispanic	516	70 (65–74)%		21 (17–25)%		16 (13–20)%	
Asian	234	74 (67–80)%		19 (14–25)%		13 (9–18)%	
Neighborhood poverty level <sup>*</sup>							
Low	4744	66 (65–68)%	0.156	20 (18–21)%	0.108	20 (19–21)%	0.653
High	729	62 (58–66)%		23 (20–26)%		20 (17–23)%	

CI – confidence intervals

<sup>#</sup> Outcome estimates are from 1-year post-transplant<sup>\*</sup> High poverty neighborhood defined as ≥20% of persons living below 100% federal poverty level; low-poverty neighborhood defined as <20% of persons below 100% federal poverty level



**Table 4.**

## Results of multivariable analysis

Outcomes	Overall survival <sup>a</sup>			Relapse <sup>b</sup>			Non-relapse mortality <sup>c</sup>		
	N	Hazard ratio (95% CI)	P-value	N	Hazard ratio (95% CI)	P-value	N	Hazard ratio (95% CI)	P-value
Race/Ethnicity									
Non-Hispanic White	4385	1.00	0.3509	4385	1.00	0.8013	4373	1.00	0.3551
Non-Hispanic Black	338	1.16 (0.95–1.41)	0.1433	338	1.10 (0.86–1.41)	0.4418	338	1.24 (0.95–1.62)	0.1226
Hispanic	516	1.01 (0.84–1.20)	0.9500	516	1.05 (0.85–1.30)	0.6601	515	1.04 (0.82–1.32)	0.7570
Asian	234	0.89 (0.69–1.15)	0.3636	234	0.94 (0.69–1.27)	0.6818	234	0.87 (0.61–1.25)	0.4488
Neighborhood poverty level <sup>*</sup>									
Low	4744	1.00	0.1184	4744	1.00	0.1251	4732	1.00	0.8299
High	729	1.11 (0.97–1.26)		729	1.14 (0.96–1.36)		728	1.02 (0.86–1.21)	

CI – confidence intervals

<sup>\*</sup> High poverty neighborhood defined as ≥20% of persons living below 100% federal poverty level; low-poverty neighborhood defined as <20% of persons below 100% federal poverty level

<sup>a</sup> Other variables significantly associated with overall survival included age at HCT, sex, acute graft-versus-host disease, chronic graft-versus-host disease by 1-year post-transplant, conditioning regimen intensity, donor type, disease risk index, HCT comorbidity index score, insurance type, rural/urban residence, and year of HCT

<sup>b</sup> Other variables significantly associated with relapse included acute graft-versus-host disease, chronic graft-versus-host disease by 1-year post-transplant, conditioning regimen intensity, donor type, disease risk index, and year of HCT

<sup>c</sup> Other variables significantly associated with non-relapse mortality included age at HCT, sex, acute graft-versus-host disease, chronic graft-versus-host disease by 1-year post-transplant, donor type, graft type, HCT comorbidity index score, graft-versus-host disease prophylaxis, insurance type, rural/urban residence, and year of HCT (13 patients who had received post-transplant cyclophosphamide as graft-versus-host disease prophylaxis were excluded from the multivariable analysis for non-relapse mortality since they did not have any events)

**Table 5.**

Standardized mortality ratios for non-Hispanic White, non-Hispanic Black, and Hispanic patients compared to their age- and sex-matched general population controls

Population	N	Person years	Observed	Expected	SMR (95% CI)	P-value
All patients	5239	23346	2074	198.6	10.4 (10.0–10.9)	<0.0001
Non-Hispanic White	4385	19950	1791	179.2	10.0 (9.5–10.5)	<0.0001
Non-Hispanic Black	338	1254	124	11.1	11.2 (9.3–13.3)	<0.0001
Hispanic	516	2142	159	8.3	19.2 (16.4–22.5)	<0.0001

CI – confidence intervals

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