RESEARCH LETTER

blood advances

TO THE EDITOR:

Association between non-European ancestry, low socioeconomic status, and receipt of HLA-disparate allografts in adult BMT recipients

Warren B. Fingrut,[1] Stephanie Chinapen,[1] Jessica Flynn,[2] Angela Katrichis,[3] Melissa Stewart,[3] Eric Davis,[1] Brian C. Shaffer,[1,4] Gunjan L. Shah,[1,4] and Juliet N. Barker[1,4]

[1]Adult Bone Marrow Transplantation Service, Department of Medicine, [2]Epidemiology and Biostatistics, and [3]Department of Social Work, Memorial Sloan Kettering Cancer Center, New York, NY; and [4]Weill Cornell Medicine, New York, NY

Although ancestry[1-4] and socioeconomic status[5-7] (SES) both affect allogeneic transplant care delivery, the association between these variables and their interaction with stem cell donor type are not established. Given that patients from historically marginalized groups are more likely to have lower SES[8] and face financial hardship compared with other patients,[9,10] and because non-European ancestry patients are more likely to lack an 8/8 human leukocyte antigen (HLA)-matched unrelated donor (URD) compared with their European counterparts,[1,4] we hypothesized that low SES disproportionately affects non-European recipients of HLA-disparate grafts (cord blood [CB], haploidentical, or 4/8 to 7/8 mismatched URD [mmURD] grafts).

We examined SES in adults undergoing allogeneic transplantation consecutively between March 2020 and June 2022, stratified by the recipient ancestry and donor type. An analysis start date of March 2020 was selected because, at the onset of the pandemic, our center increased the amount of philanthropic support for patients. Because household income was not recorded for most patients, we evaluated 4 surrogates of low SES: (1) neighborhood poverty defined as area deprivation index (ADI) national percentile ≥60; (2) Medicaid as the primary insurance at bone marrow transplant referral; and/or receipt of financial support during treatment for (3) medical expenses, or (4) cost-of-living (ie, local accommodations, rent, utilities, transportation, and/or food) expenses within 6 months of the transplantation date, after a psychosocial assessment by a social worker at our center. We also assessed mean fold differences in the funding amount per patient receiving cost-of-living expense support. During the study period, in the absence of an HLA-identical sibling donor, an 8/8 HLA allele-matched URD was prioritized followed by either double unit CB or haploidentical grafts as previously described.[2] mmURDs have been used as an additional alternative more recently. Ancestry was classified as previously described[11] based on detailed kinship history performed by the transplant staff during the pretransplantation evaluation. This study was approved by the institutional review board of Memorial Sloan Kettering Cancer Center and conducted in accordance with the Declaration of Helsinki.

Of 425 patients (median age, 62 years; range, 19-81 years), 413 (97%) had hematologic malignancies. Nearly one-third (133; 31%) of the patients had non-European ancestry (38 non-Black Hispanic, 45 African, 37 Asian, 5 Middle Eastern, and 8 mixed non-European), whereas 292 (69%) had European origins. Overall, 58 (14%) received HLA-identical sibling, 220 (52%) 8/8 URD, 44 (10%) CB, 52 (12%) haploidentical, and 51 (12%) mmURD transplants. Compared with Europeans, more than

Submitted 10 February 2023; accepted 12 April 2023; prepublished online on *Blood Advances* First Edition 21 April 2023; final version published online 26 July 2023. https://doi.org/10.1182/bloodadvances.2023009955.

This work was presented as oral presentations at both the 64th annual meeting of the American Society of Hematology in New Orleans, Louisiana, USA (10-13 December 2022), and the 2023 Tandem Meetings (Transplantation & Cellular Therapy Meetings of American Society for Transplantation and Cellular Therapy and Center for International Blood and Marrow Transplant Research) in Orlando, Florida, USA (15-19 February 2023).

Data are available on request from the corresponding author, Juliet N. Barker (barkerj@mskcc.org).

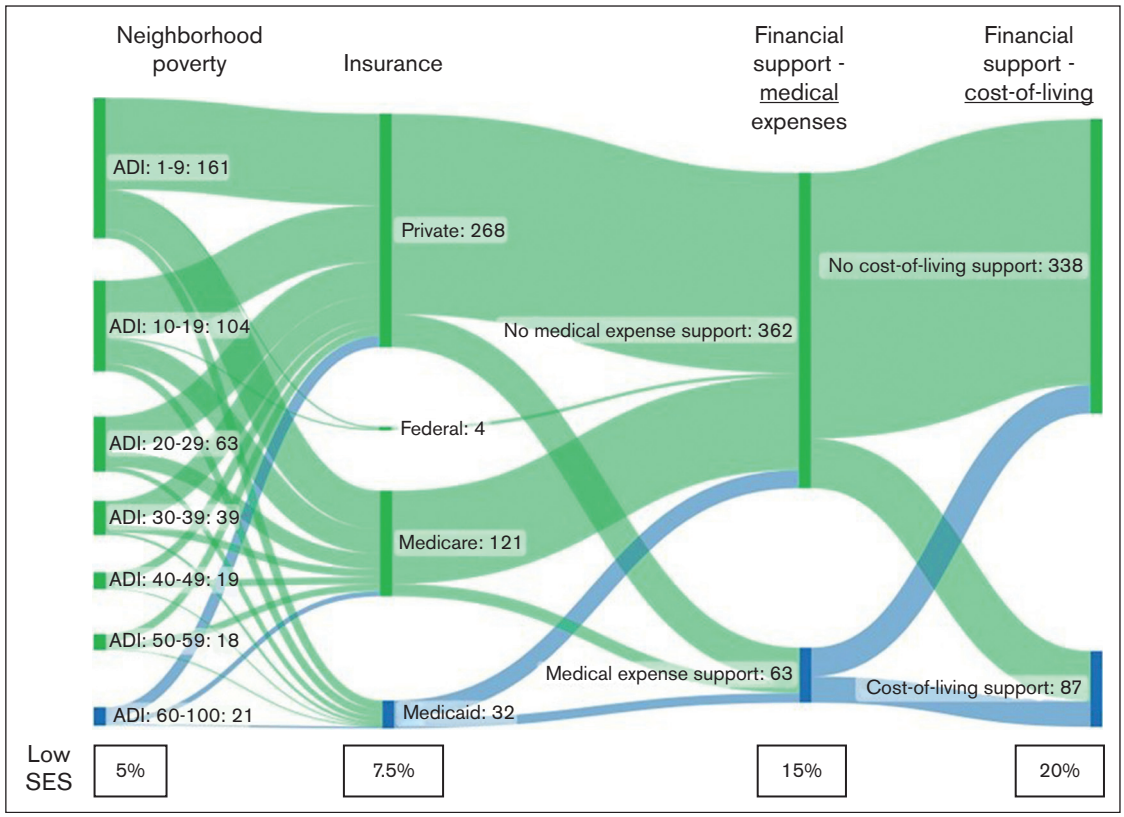

Figure 1. Sankey diagram comparing the classification of socioeconomic status (SES) of 425 allograft recipients based on 4 surrogates of low SES. These low SES surrogates were: (1) neighborhood poverty (Area Deprivation Index [ADI] national percentile ≥60); (2) Medicaid as the primary insurance at bone marrow transplant referral; and/or financial support for (3) medical expenses, or (4) cost-of-living (ie, local accommodations, rent, utilities, transportation, and/or food) expenses within 6 months of the transplant date. The percentage of patients with low SES based on each surrogate is shown across the bottom of the figure. Although 138 patients had low SES based on ≥1 of these measures, only 55 had low SES based on ≥2, 10 based on ≥3 and none based on 4 measures, demonstrating that different patient groups were classified as low SES based on each surrogate.

twice the proportion of non-Europeans received HLA-disparate grafts (71/292 [24%] vs 76/133 [57%]; $P < .001$).

The median ADI was 14 (range 1-100). Analysis of the distribution of each SES surrogate revealed 21/425 (5%) patients had low SES based on ADI ≥60; 32/425 (7.5%) based on Medicaid insurance; 63/425 (15%) based on a requirement for medical expense support; and 87/425 (20%) based on cost-of-living expense support. Notably, different patient subsets were classified as low SES based on each surrogate (Figure 1). Although 138/425 (32%) patients had low SES based on ≥1 of these measures, only 55/425 (13%) had low SES based on ≥2, only 10/425 (2%) based on ≥3, and none with 4 measures.

When analyzing by recipient ancestry (Table 1A), compared with Europeans, more than twice as many non-Europeans had low SES based on ≥1 or ≥2 measures. Specifically, although non-Europeans had a similar ADI distribution, more than quadruple of the proportion had Medicaid insurance, and twice as many received financial support for medical or cost-of-living expenses. Moreover, those receiving cost-of-living support were granted a mean of 40% more funds than Europeans. African and non-Black Hispanic ancestry patients had the highest proportions with ≥1 (30/45 [67%] African and 19/38 [50%] non-Black Hispanic), or ≥2 (12/45 [27%] African and 11/38 [29%] non-Black Hispanic) measures of low SES. Additionally, these groups had the highest proportions on Medicaid (8/45 [18%] African and 6/38 [16%] non-Black Hispanic), receiving financial support for medical (12/45 [27%] African and 13/38 [34%] non-Black Hispanic) or cost-of-living (20/45 [44%] African and 9/38 [24%] non-Black Hispanic) expenses, and the highest level of cost-of-living support (58% more support in African and 21% more in non-Black Hispanic ancestry patients) relative to Europeans.

When stratifying by recipient ancestry and graft source (Table 1), because very few European recipients of HLA-disparate grafts had low SES, all European ancestry patients were combined. Relative to Europeans, the 76 non-European ancestry patients who received HLA-disparate grafts (25 CB, 30 haploidentical, and 21 mmURD) had more than double the proportion with ≥1 low SES surrogates and triple the proportion with ≥2. Specifically, non-Europeans recipients of HLA-disparate grafts had over quadruple the proportion on Medicaid, nearly triple the proportion requiring medical expenses support, and more than twice the proportion receiving cost-of-living expense support (with these patients receiving a mean of 50% more funds relative to Europeans).

African and non-Black Hispanic patients who received HLA-disparate grafts had the highest proportions of low SES with ≥1 (23/36 [64%] African and 12/19 [6%] non-Black Hispanic) or ≥2

Table 1. Intersectionality of recipient ancestral group and surrogates of low SES on the donor type

Associations between recipient ancestral group and low SES surrogates				
		European ancestry* (n = 292), %	Non-European ancestry (n = 133), %	*P* value†
Low SES surrogates	≥1	7/292, 24%	67/133, 50%	**< .001**
	>2	25/292, 9%	30/133, 23%	**< .001**
Neighborhood poverty‖		14/292, 5%	7/133, 5%	.80
Medicaid insurance		11/292, 4%	21/133, 16%	**< .001**
Financial support	Medical	29/292, 10%	34/133, 26%	**< .001**
	Cost-of-living	47/292, 16%	40/133, 30%	**< .001**
Mean fold difference in funds/patient supported		Reference	140%	–

Associations between recipient ancestral group, low SES surrogates, and donor type					
			Non-European ancestry		
		European ancestry* (n = 292), %	HLA-matched (n = 57), %	HLA-disparate (n = 76), %‡,§	*P* value†
Low SES surrogates	≥1	71/292, 24%	24/57, 42%	43/76, 57%	**< .001**
	≥2	25/292, 9%	9/57, 16%	21/76, 28%	**< .001**
Neighborhood poverty‖		14/292, 5%	2/57, 4%	5/76, 7%	.80
Medicaid insurance		11/292, 4%	8/57, 14%	13/76, 17%	**< .001**
Financial support	Medical	29/292, 10%	12/57, 21%	22/76, 29%	**< .001**
	Cost-of-living	47/292, 16%	13/57, 23%	27/76, 36%	**< .001**
Mean fold difference in funds/patient supported		Reference	117%	150%	–

*Because very few European HLA-disparate graft recipients had low SES, all European recipients' data were combined.
†*P* values were generated via Pearson χ^2 tests or Fisher exact tests. Significant *P* values are shown in bold.
‡Includes 19 non-Black Hispanic, 36 African, 20 Asian, and 1 mixed non-European ancestry patients.
§25 patients received CB, 30 haploidentical, and 21 mmURD grafts.
‖ADI national percentile ≥60.

(11/36 [31%] African and 8/19 [42%] non-Black Hispanic) measures. These groups had the highest proportions of patients using Medicaid as a primary insurance (8/36 [22%] African and 3/19 [16%] non-Black Hispanic) and receiving financial support for medical (8/36 [22%] African and 10/19 [53%] non Black Hispanic) or cost-of-living expenses (17/36 [47%] African and 6/19 [32%] non Black Hispanic) with the highest mean fold increase in support (75% more in African and 30% more in non-Black Hispanic patients) relative to Europeans.

We demonstrate intersectionality between ancestry and SES, and an association with donor type, with the most vulnerable patients (non-Europeans with low SES, especially African and non-Black Hispanic patients) receiving the most specialized (ie, HLA-disparate) transplants. Such transplants are more likely to require higher levels of medical care. Our analysis, therefore, suggests that successful extension of transplant access to non-European patients will be contingent on addressing financial hardship encountered by many patients, especially those from historically marginalized groups.

We acknowledge that our surrogates of SES are imperfect, and our findings warrant multicenter investigation including centers and regions with varying patient demographics. However, our analysis does highlight that relying solely on a single surrogate of low SES will not capture many patients who are at-risk for financial hardship.[9] This concept has been highlighted recently in JAMA Oncology[12] and Journal of the National Cancer Institute[13] editorials that emphasize there is no single validated measure of the social determinants of health or social vulnerability in patients with cancers or who are transplant and cell therapy candidates or recipients. Furthermore, Auletta et al.[14] recently highlighted that transplant centers lack an understanding of the sociodemographic composition in their region, which can contribute to inequities in care. This fact, along with our findings and those of others, underscore the importance of including patient ancestry and socioeconomic status (and considering their intersectionality) along with more standard outcome determinants in posttransplant survival analyses.

Overall, given that different SES surrogates confer different SES assignments, interventions to advance equity will require better SES classifications as well as detailed prospective[15] recordings of patient SES, including household income and/or net worth, patient debt,[16] and poor quality health insurance (as evidenced by difficulty obtaining coverage for essential high-cost posttransplant medications[17]) alongside patient area-based measures (eg, ADI and community health status[18]) and other key demographic data including patient race/ ethnicity/ ancestry,[19] language barriers,[20] and health literacy. A potential additional low SES surrogate could include patient[9,21] or caregiver[22] self-reported financial hardship (vs that evaluated by providers). Collection of these data is critical to guide efforts to address inequities in care delivery in the increasingly diverse US population,[23] especially given recent findings showing that structural racism (the ways in which our society fosters interrelated and mutually reinforcing discriminatory systems, institutions, and laws) is a primary mediator of disparities in therapy

for patients with acute myeloid leukemia.[24] Prospective[25] interventions are also warranted to mitigate financial toxicity, improve clinical outcomes, and ensure equity across populations.

Acknowledgment: This work was supported, in part, by the National Cancer Institute P30 CA008748.

Contribution: W.B.F., G.L.S., and J.N.B. designed and performed the research; W.B.F., J.F., G.L.S., and J.N.B. analyzed the data; W.B.F., G.L.S., and J.N.B. wrote the paper; and all authors interpreted the data, reviewed and edited the manuscript, and approved the submitted version of the manuscript.

Conflict-of-interest disclosure: B.C.S. has received consultancy payments from Gamida Cell and Hansa Biopharma, and research funding from Gamida Cell. J.N.B. has received consultancy payments from Gamida Cell and the New York Blood Center and a research funding from Merck. G.L.S. has research funding to the institution from Janssen, Amgen, Beyond Spring, and Bristol Myers Squibb and participates in a data and safety monitoring board for Arcellx. The remaining authors declare no competing financial interests.

ORCID profiles: W.B.F., 0000-0002-5017-1583; S.C., 0000-0001-6308-9346; J.F., 0000-0001-8310-6684; A.K., 0009-0000-4557-4997; M.S., 0000-0002-9317-7758; E.D., 0000-0001-9197-2523; G.L.S., 0000-0002-9977-0456.

Correspondence: Juliet N. Barker, Adult Bone Marrow Transplantation Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, 530 E 74th St, New York, NY 10021; email: barkerj@mskcc.org.

References

1. Fingrut W, Gyurkocza B, Davis E, et al. Racial disparities in access to alternative donor allografts persist in the era of "donors for all". *Blood Adv*. 2022;6(20):5625-5629.
2. Fingrut WB, Gyurkocza B, Flynn J, et al. Analysis of disparities in time to allogeneic transplantation in adults with acute myelogenous leukemia. *Blood Adv*. 2023;7(15):3824-3833.
3. Kosuri S, Wolff T, Devlin SM, et al. Prospective evaluation of unrelated donor cord blood and haploidentical donor access reveals graft availability varies by patient ancestry: practical implications for donor selection. *Biol Blood Marrow Transplant*. 2017;23(6):965-970.
4. Barker JN, Boughan K, Dahi PB, et al. Racial disparities in access to HLA-matched unrelated donor transplants: a prospective 1312-patient analysis. *Blood Adv*. 2019;3(7):939-944.
5. Bona K, Brazauskas R, He N, et al. Neighborhood poverty and pediatric allogeneic hematopoietic cell transplantation outcomes: a CIBMTR analysis. *Blood*. 2021;137(4):556-568.
6. Paulson K, Brazauskas R, Khera N, et al. Inferior access to allogeneic transplant in disadvantaged populations: a center for international blood and marrow transplant research analysis. *Biol Blood Marrow Transplant*. 2019;25(10):2086-2090.
7. Brewer B, Sharma P, Gakhar N, et al. Quality of life following cord blood versus matched sibling donor transplantation: pre-transplantation psychiatric and socioeconomic factors significantly impact outcomes. *Bone Marrow Transplant*. 2022;57(8):1344-1346.
8. Guzman G. Household income by race and Hispanic origin: 2005-2009 and 2015-2019. US census bureau American community survey brief ACSBR-7. Accessed 15 January 2023 from. 2020. www.census.gov/content/dam/Census/library/publications/2020/acs/acsbr19-07.pdf
9. Voleti S, Warsame R, Mead-Harvey C, et al. Assessing patient-reported financial hardship in patients with cancer in routine clinical care. *JCO Oncol Pract*. 2022;18(11):e1839-e1853.
10. Panzone J, Welch C, Pinkhasov R, et al. The influence of race on financial toxicity among cancer patients. *J Clin Oncol*. 2021;39(suppl 15):1525.
11. Fingrut W, Davis E, Chinapen S, et al. Inaccuracies in assignment of patient race/ ethnicity: implications for unrelated donor searches and healthcare delivery. *Blood Adv*. 2022;7(10):1996-1999.
12. Mullangi S, Aviki E, Hershman D. Reexamining social determinants of health data collection in the COVID-19 era. *JAMA Oncol*. 2022;8(12):1736-1738.
13. Bona K, Keating N. Addressing social determinants of health: now is the time. *J Natl Cancer Inst*. 2022;114(12):1561-1563.
14. Auletta J, Sandmaier B, Jensen E, et al. The ASTCT-NMDP ACCESS initiative: a collaboration to address and sustain equal outcomes for all across the hematopoietic cell transplantation and cellular therapy ecosystem. *Transplant Cell Ther*. 2022;28(12):802-809.
15. Zheng DJ, Shyr D, Ma C, Muriel AC, Wolfe J, Bona K. Feasibility of systematic poverty screening in a pediatric oncology referral center. *Pediatr Blood Cancer*. 2018;65(12):e27380.
16. Shankaran V, Li L, Fedorenko C, et al. Risk of adverse financial events in patients with cancer: evidence from a novel linkage between cancer registry and credit records. *J Clin Oncol*. 2022;40(8):884-891.
17. Eng S, Vadakkel G, Fingrut W, et al. Insurance barriers to high-cost anti-infective medications post allogeneic hematopoietic cell transplant. *Transplant Cell Ther*. 2023;29(2):S349-S350.
18. Joo J, Hong S, Rybicki LA, Hamilton BK, Majhail NS. Community health status and long-term outcomes in 1-year survivors of autologous and allogeneic hematopoietic cell transplantation. *Bone Marrow Transplant*. 2022;57(4):671-673.
19. Shapiro A, Meyer D, Riley L, Kurtz B, Barchi D. Building the foundations for equitable care. *NEJM Catal*. 2021:1-9.
20. Mukherjee A, Gooley T, Mielcarek M, et al. Outcomes after hematopoietic cell transplantation among non-English- compared to English-speaking recipients. *Bone Marrow Transplant*. 2022;57(3):440-444.
21. de Souza JA, Yap BJ, Wroblewski K, et al. Measuring financial toxicity as a clinically relevant patient-reported outcome: the validation of the comprehensive score for financial toxicity (COST). *Cancer*. 2017;123(3):476-484.
22. Meehan K, Meehan J, Hill J, et al. Caregivers' out-of-pocket expenses and time commitment following hematopoietic stem cell transplantation at a rural cancer center. *Biol Blood Marrow Transplant*. 2020;26(9):e227-e231.
23. National population by characteristics: 2010-2019. United States census bureau. Accessed 15 January 2023 from. 2020. https://www.census.gov/data/tables/time-series/demo/popest/2010s-national-detail.html
24. Abraham I, Rauscher G, Patel A, et al. Structural racism is a mediator of disparities in acute myeloid leukemia outcomes. *Blood*. 2022;139(14):2212-2226.
25. Knight T, Aguiar M, Robinson M, et al. Financial toxicity intervention improves outcomes in patients with hematologic malignancy. *JCO Oncol Pract*. 2022;18(9):e1494-e1504.