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Association of Primary Care Shortage Areas with Adverse Outcomes After Pediatric Liver Transplant

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Abstract

Objective—To characterize associations between living in primary care shortage areas and graft failure/death for children after liver transplantation.

Study design—Observational study of all pediatric patients (<19 years) who received a liver transplant between 1/1/2005-12/31/2015 in the U.S., with follow up through January 2019 (N=4964). Patients (N=195) were excluded if their home ZIP code could not be matched to primary care shortage area status. The primary outcome was a composite endpoint of graft failure or death. We used Cox proportional hazards to model the associations between health professional shortage area (HPSAs) and graft failure/death.

Results—Children living in HPSAs compared with those not in HPSAs had lower estimated graft survival rates at 10 years (76% vs. 80%, p<0.001). In univariable analysis, residence in an HPSA was associated with a 22% (hazard ratio [HR]: 1.22; 95% confidence interval [CI]: 1.09, 1.36, p<0.001) increased hazard of graft failure/death. Black children from HPSAs had a 67% increased hazard of graft failure/death compared with those not in HPSAs (HR: 1.67; 95%CI:

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CONFLICT OF INTEREST DISCLOSURES:
The authors declare no conflicts of interest.

PRIOR PRESENTATION:
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DISCLAIMER:
The data reported here have been supplied by the Hennepin Healthcare Research Institute (HHRI) as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government.

1.29, 2.16; p=0.006). For White children, the effect of HPSA status was less pronounced (HR: 1.11; 95%CI: 0.98, 1.27, p=0.10).

Conclusion—Children living in primary care shortage areas are at increased risk of graft failure and death after liver transplant, and this risk is particularly salient for Black children. Future work to understand how living in these regions contributes to adverse outcomes may enable teams to mitigate this risk for all children with chronic illness.

Keywords

Liver transplant; primary care availability; pediatric chronic disease; structural racism

Short-term outcomes have improved for children after liver transplant, yet long-term outcomes remain suboptimal.(1-4) After children recover from surgery, the goals of care shift towards chronic disease management, with a focus on maintaining graft health and minimizing immunosuppression-related comorbidities.(1, 5) Such care must be managed collaboratively between primary care providers (PCP) and hepatologists, and children/families may be increasingly reliant on their PCP for health maintenance.(5)

The home environment is an important contributor to chronic disease outcomes.(4, 6-10) We previously found that children from socioeconomically deprived neighborhoods have increased risk of medication nonadherence, graft failure, and death post-transplant.(4, 11, 12) Although deprivation indices contextualize the economic milieu of a neighborhood,(4, 13) such measures do not include data on local primary care availability. access to primary care may affect their ability of the child to receive consistent follow-up care. Indeed, in adults with chronic illness, there are lower rates of preventable hospital admissions in patients with greater access to primary care.(14) In adults with autoimmune hepatitis, greater access to primary care was also associated with increased likelihood of transplant-free survival.(15) Finally, in children with routine pediatric illness (e.g., dehydration, pneumonia), communication with a PCP in the preceding year was associated with lower rates of preventable hospital admissions.(16)

Children who have received liver transplants face many of the same challenges to sustained health as those with other chronic illnesses.(17) Furthermore, the United Network for Organ Sharing (UNOS) tracks all patients after transplantation, providing a robust dataset with reliable and objective health outcomes.(18)

The Health Resources and Services Administration (HRSA) seeks to increase access to high-quality primary care for people who are geographically, medically, or economically vulnerable.(19) HRSA maintains a database of primary care health professional shortage areas (HPSA) to prioritize national programmatic efforts to assist people in these areas.(19, 20) In this study, we examined the association between residing in an HPSA and long-term graft/patient survival among pediatric liver transplant recipients in the U.S. We hypothesized that residence in an HPSA would be associated with increased risk of graft failure/death. Additionally, because of historical and ongoing segregation that affects healthcare access, (21) we examined the effect of living in an HPSA on adverse outcomes among different races.

METHODS

Data Source

This study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors.

Study Population

We identified pediatric patients (<19 years) who received a liver transplant between 01/01/2005—12/31/2015 in the U.S. (N=5,964). Patients (N=195) were excluded if their home ZIP code could not be matched to HPSA status. Excluded patient characteristics are listed in Table I (available at www.jpeds.com).

Primary Exposures

Our primary exposure was residence in a primary care HPSA. A geographic area is defined as an HPSA if the population to provider ratio is >3,500:1 (or >3,000:1 in areas with "unusually high needs" [not further defined by HRSA]).(22) HPSA data are available at the census tract-level.(23) Because the SRTR database only includes patient home ZIP codes, we used the census tract at the centroid of each ZIP code to determine HPSA status. We used home ZIP code at the time of transplant as listed in SRTR. HPSA designations were analyzed as a dichotomous measure (HPSA or non-HPSA).

Primary Outcomes

Our primary outcome was a composite endpoint of graft failure and death (henceforth referred to as graft failure). This measure was defined as time from liver transplant to graft failure or death from any cause, whichever occurred first.(12, 24) For patients without documented graft failure, graft survival was censored at the last date of follow-up. We applied administrative censoring at 10 years posttransplant for patients followed longer than 10 years.

Covariables

We used a causal inference approach and created a directed acyclic graph to identify the set of covariables necessary to quantify the direct effect of HPSA on graft failure (Figure 1). We conceptualize race as a social construct (i.e., effects resulting from structural racism, segregation), rather than a biological construct.(25-27) Therefore, we included race in our multivariable models as a proxy for these social effects. We classified race as "White," "Black," or "other." To adjust for area-level economic conditions that may confound the relationship between HPSA and graft failure, we measured fraction of the population below the federal poverty level (%<FPL) at the ZIP code level using data from the U.S. Census Bureau's 2015 American Community Survey and modeled this as a continuous variable.(12, 13, 28) We included insurance status in our models as an indicator of access

to healthcare services. We used the Rural-Urban Commuting Area (RUCA) codes from the U.S. Department of Agriculture to classify patients as rural/urban to better understand the interaction between rurality and HPSA status. Laboratory Model for End Stage Liver Disease (MELD)/Pediatric End Stage Liver Disease (PELD) and allocation MELD/PELD were used as measures of disease severity.

Statistical Analyses

Descriptive statistics were reported for patient demographic, allocation, and transplant characteristics. Patient characteristics were compared between those residing in an HPSA and non-HPSA using Wilcoxon rank-sum tests for continuous variables and chi-square tests categorical variables. We followed patients from time of transplant until 10 years post-transplant. We chose 10 years because we hypothesized that PCP access would be more relevant to long-term post-transplant outcomes. The associations between HPSA status and graft survival were visualized using Kaplan-Meier curves and evaluated using Coxs proportional hazards models. Given that morbidity and mortality in the first year post-transplant are primarily due to technical complications, rather than social factors, we conducted a landmark analysis(29) and excluded patients who had graft failure in the first year. To better understand the consequences of ongoing structural racism and segregation, we assessed for an interaction between race and HPSA on graft survival and performed subgroup analyses for Black and White children. To assess whether children in urban areas were less susceptible to the effects of HPSAs, we assessed for an interaction between rurality and HPSA on graft survival. Statistical significance was defined as $p<0.05$. Statistical analyses were performed in R (Version 4.1.0, The R Project for Statistical Computing).

This study was deemed exempt from review by the UCSF Institutional Review Boards.

RESULTS

Study Population

A total of 5,769 children were included in our analyses. Baseline characteristics are shown in Table II. Almost half (47.3%) of our cohort resided in an HPSA. Children from HPSAs were more likely to have public insurance, be of Black race, and live in a rural and high-poverty area. They were less likely to receive a living donor transplant.

Death-Free Graft Survival

The overall 1-, 5-, and 10-year graft survival in our cohort was 87%, 81%, and 78%, respectively. Patients from HPSAs compared with those in non-HPSAs had lower estimated graft survival rates at 1 year (86% vs. 88%, $p=0.01$), 5 years (79% vs. 82%, $p<0.001$), and 10 years (76% vs. 80%, $p<0.001$). In univariable analysis, residence in an HPSA was associated with a 22% (hazard ratio [HR]: 1.22; 95% confidence interval [CI]: 1.09, 1.36; $p<0.001$) increased hazard of graft failure (Table III; available at www.jpeds.com). Black children had a 29% increased hazard of graft failure (HR: 1.29; 95%CI: 1.13, 1.48; $p<0.001$) compared with White children, and for every 10% increase in %<FPL there was a 13% (HR: 1.13; 95%CI: 1.07, 1.19; $p<0.001$) increased hazard of graft failure. Public

insurance was associated with a 38% (HR: 1.38; 95%CI: 1.24, 1.55; p<0.001) increased hazard of graft failure compared with private insurance. In multivariable analysis adjusting for race, children in HPSAs had a 19% (HR: 1.19; 95%CI: 1.07, 1.33; p=0.002) increased hazard of graft failure compared with non-HPSAs (Table II). When adjusting for race and insurance status, children in HPSAs had a 13% (HR: 1.13; 95%CI: 1.01, 1.26, p=0.03) increased hazard of graft failure. When adjusting for race, insurance, and %<FPL, the effect size of HPSA status decreased (HR: 1.11; 95%CI: 0.98, 1.25; p=0.10). Rurality was not significantly associated with graft failure (HR: 1.12; 95%CI: 0.97, 1.30; p=0.12), and the effect of HPSA status on graft failure did not vary across rural and urban areas (interaction term p=0.33).

Subgroup Analyses by Race and Ethnicity

Figure 2 displays Kaplan-Meier curves of 10-year graft survival by HPSA status in Black and White children. The 10-year graft survival rate for White children in HPSAs was 75.8% versus 77.3% in non-HPSAs (p=0.11). The 10-year graft survival rate for Black children in HPSAs was 61.8% compared with 77.5% in non-HPSAs (p<0.001). The effect of HPSA status on graft failure varied by race (interaction term p<0.001). Black children in HPSAs compared with Black children in non-HPSAs had a 67% increased hazard of graft failure (HR: 1.67; 95%CI: 1.29, 2.16; p=0.006). For White children in HPSAs vs. those not, the association was less pronounced (HR: 1.11; 95%CI: 0.98, 1.27, p=0.10). Black children in HPSAs compared with White children in HPSAs had a 48% increased hazard of graft failure (HR 1.48; 95%CI: 1.24, 1.75; p<0.001), and a 64% increased hazard of graft failure (HR: 1.64; 95%CI: 1.39, 1.95; p<0.001) compared with White children in non-HPSAs. In Hispanic children of all races, there were no differences in outcomes by HPSA status (p=0.2), but there was a trend for children living in HPSAs to have worse outcomes (data not depicted).

Landmark Analysis at 1-Year Post-Transplant

A total of 788 children experienced graft failure/death or were lost to follow-up within the first-year post-transplant. In a landmark analysis excluding these patients, children from HPSAs had a 23% increased hazard of graft failure (HR: 1.23; 95%CI: 1.03, 1.46; p=0.02) compared with children from non-HPSAs (Table V; available at www.jpeds.com). In multivariable analysis adjusting for race, the effect size of HPSA decreased (HR: 1.16; 95%CI: 0.98, 1.38; p=0.09), but the effect size of race increased (HR: 1.93; 95%CI: 1.59, 2.34; p<0.001) compared with the above analyses including all patients. In multivariable analysis adjusting for HPSA, race, insurance, and %<FPL, HPSA status did not have a significant effect on graft survival (HR: 1.05; 95%CI: 0.87, 1.27; p=0.59), but Black children still had a 76% increased hazard of graft failure (HR: 1.75; 95%CI: 1.44, 2.16; p<0.001) compared with White children.

DISCUSSION

In this study, we sought to determine how living in an HPSA affects outcomes for children after liver transplantation. We found that children in HPSAs have an increased hazard of graft failure and death after transplant compared with children in non-HPSAs. This

finding persisted when we controlled for race and insurance but became less substantial when adjusting for %<FPL. Most children living in HPSAs are in high-poverty ZIP codes. This overlap, despite HPSA status and %<FPL measuring distinct constructs, suggests that economic deprivation may extend to medical deprivation. our study demonstrates that disparities in outcomes between HPSAs and non-HPSAs are primarily experienced by Black children, with Black children in HPSAs experiencing much worse outcomes than Black children in non-HPSAs and all White children in our cohort.For every 10 Black children living in an HPSA, almost 4 will experience an episode of graft failure within 10-years of transplantation—suggesting that HPSAs might be an important contributor to racial disparities after pediatric liver transplantation.(4, 30)

Primary care shortages pose a substantial challenge for many areas in the U.S., with over 80 million people living in areas designated as HPSAs.(31) One important marker of geographic vulnerability is rurality. Not surprisingly, children in HPSAs were more likely to live in rural areas than children in non-HPSAs. Despite this, the effect of living in an HPSA did not vary by rurality, suggesting that adverse effects of primary care shortages are prevalent across both urban and rural landscapes. In our sample, over 70% of children in HPSAs were also in areas with high poverty rates (%<FPL above sample median). This finding mirrors that of a previous study finding that the distribution of HPSAs has substantial overlap with other markers of medical, economic, and geographic vulnerability (e.g., low income, persistent poverty, lower education levels).(10) We conceptualized HPSA status and %<FPL as related but ultimately separate measures – that is, HPSA status specifically measures an aspect of health infrastructure (e.g., number of PCPs per capita) and %<FPL measures the proportion of the neighborhood living in poverty and characterizes underlying economic conditions of the area. Although the overlap between medical shortages and poverty is not surprising, it suggests that poverty may directly affect access to primary care by limiting the type, frequency, and quality of care these children receive. However, it remains unclear whether HPSA status fully captures factors such as primary care access, utilization, and quality, which may depend on other factors such as transportation, healthcare costs, discrimination, and poor working conditions leading to physician burnout.(21, 32-34) Children in HPSAs were also less likely to receive a living donor liver transplant; future studies should seek to understand the barriers to living donor transplantation in areas with primary care shortages.

As children live longer after transplantation, chronic disease management – including strong partnerships between transplant centers and primary care – will be essential to achieving optimal outcomes. Lifelong immunosuppression increases the risk of complications like posttransplant lymphoproliferative disorder (PTLD), chronic kidney disease, diabetes, and hypertension.(3, 35) Furthermore, medication adherence and allograft monitoring are necessary to ensure long-term graft health.(1, 3, 35) Although these complications are specific to liver transplantation, medication/symptom management and disease monitoring are part of the care for all children with chronic illnesses.(36, 37) Living in an HPSA may make it more difficult for patients to manage their care. This study lays the groundwork for future studies to uncover the underlying risk factors that lead to suboptimal outcomes for children living in HPSAs.

we found that race modifies the effect of HPSA status on graft/patient survival. It is well documented that Black and minority-race children have higher rates of graft failure and death after transplant,(4, 30) . Our subgroup analyses revealed that Black children in HPSAs are at the highest risk for such adverse outcomes. The hazard of graft failure for Black children (in both HPSAs and non-HPSAs) increased even further when excluding patients who experienced an adverse event within the first year post-transplant. Considering that episodes of death/graft failure in the first year are more likely driven by technical complications, excluding these patients may provide a more accurate depiction of the role social factors (e.g., physician shortages, racism, economic deprivation) play in disease outcomes for Black children. In our landmark analyses, other social factors became less significant and Black children had an almost 80% increased hazard of graft failure after adjusting for HPSA status, insurance, and %<FPL.

Here, we view race as a social construct that captures a range of social determinants not captured by other measures and include interpersonal and structural racism, segregation, bias, and cumulative exposure to adversity.(26, 27, 38) Structural racism encompasses the ways in which systems (e.g., housing, education, employment, healthcare, criminal justice, media) promote discrimination on the basis of race, and in turn reinforce discriminatory beliefs and resource distribution.(21, 39) Historical and continued residential segregation puts Black Americans at increased risk of poor birth outcomes, chronic disease, and decreased lifespan, and importantly, shapes the landscape of healthcare access and utilization.(21) In Black adolescents, race-related stress has been shown to be a significant predictor of chronic disease.(40, 41) Additionally, medical mistrust among Black patients, as a result of historical and ongoing mistreatment by the U.S. healthcare system,(25) might make it harder for families to seek care in neighboring communities.(42, 43) What is more, Black children were more likely than White children to live in HPSAs, compounding their risk for poor outcomes and creating another pathway for structural racism. The increased hazard of adverse outcomes, even when considering other important social factors, underscores the association between structural racism and poor health outcomes for Black children.

This study demonstrates the relationship between living in an HPSA and pediatric chronic disease outcomes. Future studies are needed to better uncover the reasons for these disparities before efforts to narrow these disparities can be developed. One potential area of exploration that has emerged in the COVID-19 era is the use of telehealth technology to enable the healthcare system to mitigate the effect of HPSAs. Telehealth has the potential to increase access to providers in HPSAs and may better accommodate parents' schedules.(44) However, the implementation of telehealth may, itself, increase health disparities for vulnerable populations (i.e., those at risk for limited digital literacy/access).(45) Therefore, care should be taken to mitigate structural and individual barriers to telehealth(45) while exploring ways we might leverage telehealth for children with chronic disease in HPSAs. care.

We acknowledge the following limitations. First, although population-level data is helpful to characterize one's home environment, we recognize the risk of ecologic fallacy (i.e., extrapolating findings to individuals based on group-level findings).(46) Second, HPSA

status was matched at the ZIP code level. Even though ZIP codes are convenient to collect, they are created to increase mail delivery efficiency, and can encompass diverse neighborhood contexts. However, ZIP code level data were readily available in SRTR, and ZIP codes represent relatively granular geospatial units. Third, HPSAs can be designated, proposed for withdrawal, and withdrawn based on the percent of need for PCPs met. We included all areas that have ever been designated as an HPSA during or after the study period. Therefore, it is plausible that some ZIP codes were classified as an HPSA when indeed they were not. Such misclassification would bias our findings towards the null—that we still see a difference indicates that HPSA status is important for post-transplant outcomes. Fourth, we were unable to account for residential mobility, as these data are not available in SRTR. Reassuringly, there are data assessing how residential mobility impacts exposures such as deprivation indices and air pollution that demonstrate that, although a significant proportion of families move, these moves tend toward high exposure to low exposure (i.e., families are more likely to move from highly deprived neighborhoods to less deprived neighborhoods). Therefore, we would expect this to bias our findings towards the null.(47) Again, that we found an association between residence in HPSAs and transplant outcomes even with potential exposure misclassification, suggests that HPSA status is an important predictor of post-transplant outcomes. Fifth, we were unable to analyze the effects of HPSAs in the Indigenous community. Although important, there were only 45 patients (0.8%) who identified as Indigenous Americans in our dataset. Finally, there are limitations common to registry studies – such as data completeness and quality. However, the SRTR database is the most robust data source for transplant recipients and offers one of the most objective and well-maintained datasets for studying children with chronic illness in general.

Future work to understand how living in these regions contributes to adverse outcomes might enable medical teams to mitigate this risk and inform policies that further reduce the presence of HPSAs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS:

CI	confidence interval
HPSA	health professional shortage area
HR	hazard ratio
HRSA	Health Resources and Services Administration
MELD	Model for End Stage Liver Disease
OPTN	Organ Procurement and Transplantation Network
PCP	primary care provider
PELD	Pediatric End Stage Liver Disease
RUCA	Rural-Urban Commuting Area
SRTR	Scientific Registry of Transplant Recipients
UNOS	United Network for Organ Sharing
%<FPL	fraction of the population below the federal poverty level

REFERENCES

1. Rawal N, Yazigi N. Pediatric Liver Transplantation. Pediatr Clin North Am. 2017;64(3):677–84. [PubMed: 28502445]
2. Kamath BM, Olthoff KM. Liver transplantation in children: update 2010. Pediatr Clin North Am. 2010;57(2):401–14, table of contents. [PubMed: 20371044]
3. Ng VL, Alonso EM, Bucuvalas JC, Cohen G, Limbers CA, Varni JW, et al. Health Status of Children Alive 10 Years after Pediatric Liver Transplantation Performed in the US and Canada: Report of the Studies of Pediatric Liver Transplantation Experience. The Journal of Pediatrics. 2012;160(5):820–6.e3. [PubMed: 22192813]
4. Wadhwani SI, Beck AF, Bucuvalas J, Gottlieb L, Kotagal U, Lai JC. Neighborhood socioeconomic deprivation is associated with worse patient and graft survival following pediatric liver transplantation. American Journal of Transplantation. 2020;20(6):1597–605. [PubMed: 31958208]
5. Yazigi NA. Long Term Outcomes after Pediatric Liver Transplantation. Pediatr Gastroenterol Hepatol Nutr. 2013;16(4):207–18. [PubMed: 24511516]
6. Braveman P, Barclay C. Health disparities beginning in childhood: a life-course perspective. Pediatrics. 2009;124 Suppl 3:S163–75. [PubMed: 19861467]
7. Beck AF, Sandel MT, Ryan PH, Kahn RS. Mapping Neighborhood Health Geomarkers To Clinical Care Decisions To Promote Equity In Child Health. Health affairs (Project Hope). 2017;36(6):999–1005. [PubMed: 28583957]
8. Beck AF, Simmons JM, Huang B, Kahn RS. Geomedicine: area-based socioeconomic measures for assessing risk of hospital reutilization among children admitted for asthma. Am J Public Health. 2012;102(12):2308–14. [PubMed: 23078500]
9. Beck AF, Riley CL, Taylor SC, Brokamp C, Kahn RS. Pervasive Income-Based Disparities In Inpatient Bed-Day Rates Across Conditions And Subspecialties. Health affairs (Project Hope). 2018;37(4):551–9. [PubMed: 29608357]
10. Streeter RA, Snyder JE, Kepley H, Stahl AL, Li T, Washko MM. The geographic alignment of primary care Health Professional Shortage Areas with markers for social determinants of health. PloS one. 2020;15(4):e0231443–e. [PubMed: 32330143]

11. Wadhwani SI, Bucuvalas JC, Brokamp C, Anand R, Gupta A, Taylor S, et al. Association Between Neighborhood-level Socioeconomic Deprivation and the Medication Level Variability Index for Children Following Liver Transplantation. Transplantation. 2020;104(11).
12. Wadhwani SI, Huang C-Y, Gottlieb L, Beck AF, Bucuvalas J, Kotagal U, et al. Center variation in long-term outcomes for socioeconomically deprived children. American Journal of Transplantation. 2021;n/a(n/a).
13. Brokamp C, Beck AF, Goyal NK, Ryan P, Greenberg JM, Hall ES. Material community deprivation and hospital utilization during the first year of life: an urban population-based cohort study. Ann Epidemiol. 2019;30:37–43. [PubMed: 30563729]
14. Bindman AB, Grumbach K, Osmond D, Komaromy M, Vranizan K, Lurie N, et al. Preventable Hospitalizations and Access to Health Care. JAMA. 1995;274(4):305–11. [PubMed: 7609259]
15. Kim D, Eshtiaghpour D, Alpern J, Datta A, Eysselein VE, Yee HF. Access to primary care is associated with better autoimmune hepatitis outcomes in an urban county hospital. BMC Gastroenterology. 2015;15(1):91. [PubMed: 26215250]
16. Zucco R, Pileggi C, Vancheri M, Papadopoli R, Nobile CGA, Pavia M. Preventable pediatric hospitalizations and access to primary health care in Italy. PLoS One. 2019;14(10):e0221852. [PubMed: 31644581]
17. Wagner EH. Chronic disease management: what will it take to improve care for chronic illness? Eff Clin Pract. 1998;1(1):2–4. [PubMed: 10345255]
18. UNOS. UNOS Data [Available from: https://unos.org/data/.
19. Health Resources and Services Administration. About HRSA 2021 [Available from: https://www.hrsa.gov/about/index.html.
20. Health Resources & Services Administration. Bureau of Primary Health Care 2019 [Available from: https://www.hrsa.gov/about/organization/bureaus/bphc/index.html.
21. Bailey ZD, Krieger N, Agénor M, Graves J, Linos N, Bassett MT. Structural racism and health inequities in the USA: evidence and interventions. Lancet. 2017;389(10077):1453–63. [PubMed: 28402827]
22. Health Resources & Services Administration. data.hrsa.gov 2021 [Available from: https://data.hrsa.gov/data/download?data=SHORT#SHORT.
23. United States Census Bureau. Glossary [Available from: https://www.census.gov/programs-surveys/geography/about/glossary.html#par_textimage_13.
24. Perito ER, Bucuvalas J, Lai JC. Functional status at listing predicts waitlist and posttransplant mortality in pediatric liver transplant candidates. American Journal of Transplantation. 2019;19(5):1388–96. [PubMed: 30506640]
25. Boyd EGL Rhea W., Weeks Lachelle D., McLemore Monica R.. Health Affairs Blog [Internet]2020.
26. Ford ME, Kelly PA. Conceptualizing and categorizing race and ethnicity in health services research. Health Serv Res. 2005;40(5 Pt 2):1658–75. [PubMed: 16179001]
27. Kaplan JB, Bennett T. Use of race and ethnicity in biomedical publication. Jama. 2003;289(20):2709–16. [PubMed: 12771118]
28. Wadhwani SI, Brokamp C, Rasnick E, Bucuvalas JC, Lai JC, Beck AF. Neighborhood socioeconomic deprivation, racial segregation, and organ donation across 5 states. Am J Transplant. 2021;21(3):1206–14. [PubMed: 32654392]
29. Morgan CJ. Landmark analysis: A primer. Journal of Nuclear Cardiology. 2019;26(2):391–3. [PubMed: 30719655]
30. Thammana RV, Knechtle SJ, Romero R, Heffron TG, Daniels CT, Patzer RE. Racial and socioeconomic disparities in pediatric and young adult liver transplant outcomes. Liver Transpl. 2014;20(1):100–15. [PubMed: 24136785]
31. Health Resources and Services Administration. Shortage Areas 2021 [Available from: https://data.hrsa.gov/topics/health-workforce/shortage-areas.
32. Glass DP, Kanter MH, Jacobsen SJ, Minardi PM. The impact of improving access to primary care. J Eval Clin Pract. 2017;23(6):1451–8. [PubMed: 28984018]

33. Tawfik DS, Profit J, Morgenthaler TI, Satele DV, Sinsky CA, Dyrbye LN, et al. Physician Burnout, Well-being, and Work Unit Safety Grades in Relationship to Reported Medical Errors. Mayo Clin Proc. 2018;93(11):1571–80. [PubMed: 30001832]
34. Davy C, Harfield S, McArthur A, Munn Z, Brown A. Access to primary health care services for Indigenous peoples: A framework synthesis. Int J Equity Health. 2016;15(1):163. [PubMed: 27716235]
35. Feng S, Bucuvalas J. Tolerance after liver transplantation: Where are we? Liver Transpl. 2017;23(12):1601–14. [PubMed: 28834221]
36. Williams-Reade JM, Tapanes D, Distelberg BJ, Montgomery S. Pediatric Chronic Illness Management: A Qualitative Dyadic Analysis of Adolescent Patient and Parent Illness Narratives. J Marital Fam Ther. 2020;46(1):135–48. [PubMed: 30725488]
37. Drotar D, Bonner MS. Influences on adherence to pediatric asthma treatment: a review of correlates and predictors. J Dev Behav Pediatr. 2009;30(6):574–82. [PubMed: 19996903]
38. Williams DR, Priest N, Anderson NB. Understanding associations among race, socioeconomic status, and health: Patterns and prospects. Health Psychol. 2016;35(4):407–11. [PubMed: 27018733]
39. Krieger N. Discrimination and health inequities. Int J Health Serv. 2014;44(4):643–710. [PubMed: 25626224]
40. Brody GH, Lei MK, Chae DH, Yu T, Kogan SM, Beach SRH. Perceived discrimination among African American adolescents and allostatic load: a longitudinal analysis with buffering effects. Child Dev. 2014;85(3):989–1002. [PubMed: 24673162]
41. Bonnie CS Richard J., and Breiner Heather, Editors; Committee, on Improving the Health S, and Well-Being of Young Adults,; Board on, Children Y, and Families; Institute of Medicine,; National Research, Council. Investing in the Health and Well-Being of Young Adults 01/27/2005.
42. Brandon DT, Isaac LA, LaVeist TA. The legacy of Tuskegee and trust in medical care: is Tuskegee responsible for race differences in mistrust of medical care? J Natl Med Assoc. 2005;97(7):951–6. [PubMed: 16080664]
43. Tekeste M, Hull S, Dovidio JF, Safon CB, Blackstock O, Taggart T, et al. Differences in Medical Mistrust Between Black and White Women: Implications for Patient-Provider Communication About PrEP. AIDS Behav. 2019;23(7):1737–48. [PubMed: 30264207]
44. Utidjian L, Abramson E. Pediatric Telehealth: Opportunities and Challenges. Pediatr Clin North Am. 2016;63(2):367–78. [PubMed: 27017042]
45. Nouri S, Khoong EC, Lyles CR, Karliner L. Addressing equity in telemedicine for chronic disease management during the Covid-19 pandemic. NEJM Catalyst Innovations in Care Delivery. 2020;1(3).
46. Cottrell EK, Hendricks M, Dambrun K, Cowburn S, Pantell M, Gold R, et al. Comparison of Community-Level and Patient-Level Social Risk Data in a Network of Community Health Centers. JAMA Network Open. 2020;3(10):e2016852–e. [PubMed: 33119102]
47. Brokamp C, LeMasters GK, Ryan PH. Residential mobility impacts exposure assessment and community socioeconomic characteristics in longitudinal epidemiology studies. J Expo Sci Environ Epidemiol. 2016;26(4):428–34. [PubMed: 26956935]

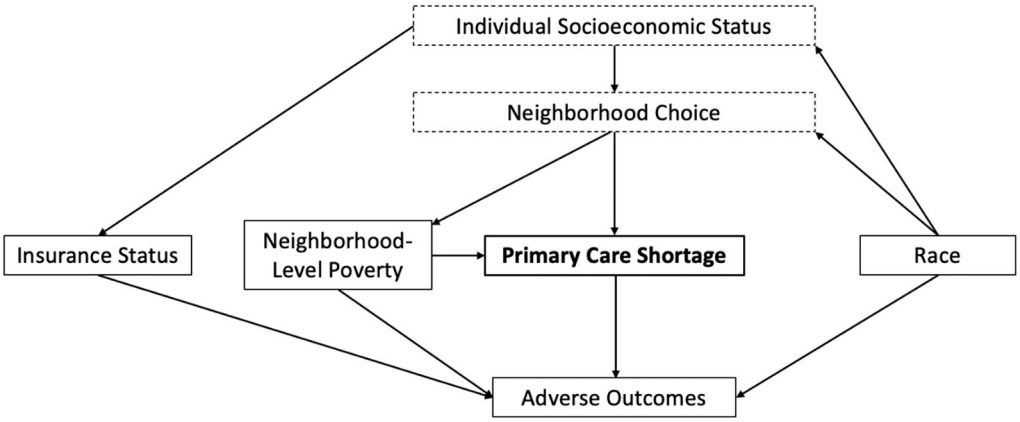

Figure 1. Directed acyclic graph of hypothesized causal pathway.

The solid boxes indicate measurable variables while the dotted boxes indicate unmeasurable variables within the Scientific Registry for Transplant Recipient data system. This diagram is the theoretical model of the hypothesized causal pathway for the impact of residence in an area with a primary care shortage on outcomes for children following liver transplantation.

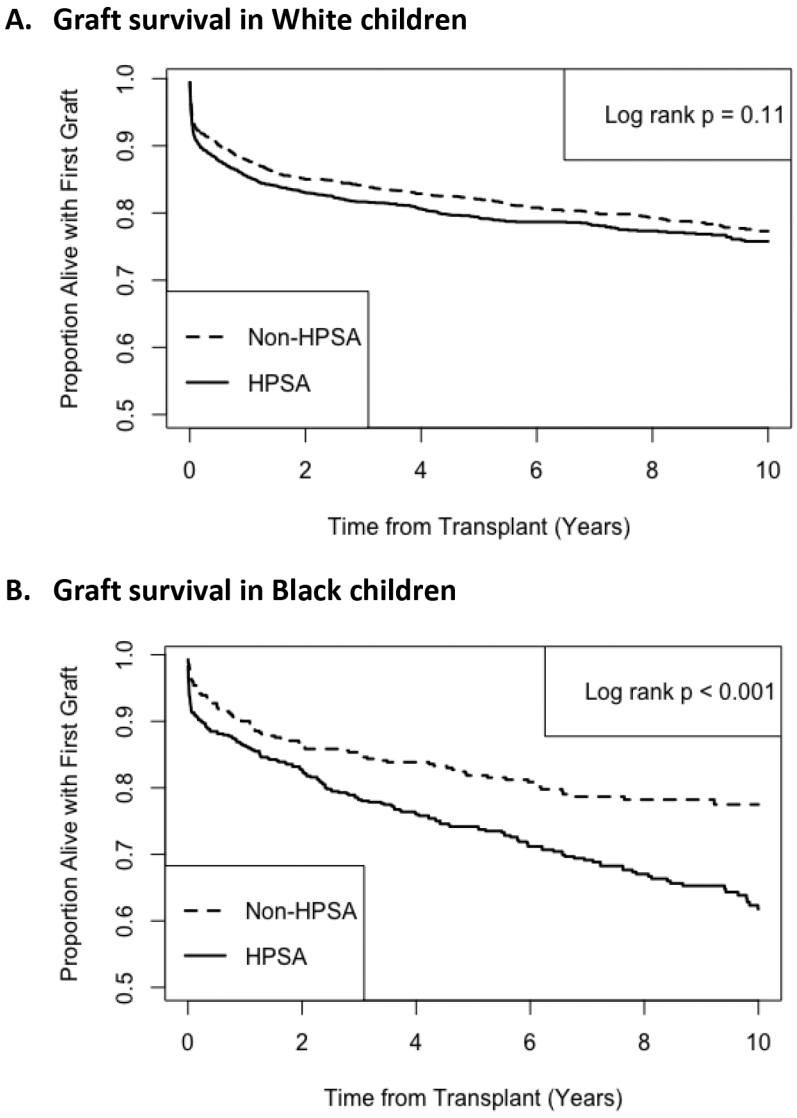

Figure 2. Subgroup analyses for race stratified by HPSA status.

Graft survival by HPSA status in (A) White children, (B) Black children. Abbreviations: HPSA, health professional shortage area

Table 1.
Demographic characteristics of included and excluded patients.

Values are represented as N (%) or median (IQR). Empty cells in p-value column represent comparison across all categories of a variable.

Abbreviations: IQR, interquartile range; MELD, Model for End-Stage Liver Disease; PELD, pediatric end-stage liver disease.

	Included	Excluded	p-value
	N = 5769	**N = 195**	
Age at Transplant (yrs.)	2.3 (0.8, 9.8)	3.2 (1.0, 10.2)	0.29
Female	2895 (50.2)	101 (51.8)	0.71
Hispanic	1338 (23.2)	36 (18.5)	0.15
Race			
White	4290 (74.4)	152 (77.9)	0.52
Black	984 (17.1)	29 (14.9)	
Other	495 (8.6)	14 (7.2)	
Primary Insurance			
Public	2594 (45.0)	43 (22.1)	<0.001
Private	3056 (53.0)	58 (29.7)	
Other	119 (2.1)	94 (48.2)	
Recipient Diagnosis			
Biliary Atresia	1768 (30.6)	35 (17.9)	<0.001
Other cholestatic	1146 (19.9)	58 (29.7)	
Acute Liver Failure	640 (11.1)	17 (8.7)	
Metabolic	545 (9.4)	36 (18.5)	
Tumor	467 (8.1)	14 (7.2)	
Autoimmune Hepatitis	250 (4.3)	9 (4.6)	
Other	945 (16.4)	26 (13.3)	
Laboratory MELD/PELD at Transplant	16 (5, 25)	17 (4, 26)	0.97
Actual MELD/PELD at Transplant	25 (16, 32)	28 (18.5, 34.5)	0.11
Status 1a/1b	1600 (27.7)	47 (24.1)	0.34
Donor Age at Transplant	11 (2, 21)	6 (1, 20)	0.06
Transplant type			
Living Donor Transplant	600 (10.4)	18 (9.2)	0.68
Deceased Donor Transplant	5169 (89.6)	177 (90.8)	
Cold Ischemia Time	6.7 (5.0, 8.4)	6.5 (5.0, 8.1)	0.61

Table 2.

Baseline characteristics by HPSA status.

Values are represented as median (IQR) or number (%). Empty cells in p-value column are because p-value represents comparison across all categories of a variable. An HPSA was classified as an area with >3,500 individuals to 1 primary care provider or 3000:1 in areas with unusually high needs.

Abbreviations: HPSA, health professional shortage area; IQR, interquartile range; %<FPL, fraction of the population below the federal poverty line; MELD, Model for End-Stage Liver Disease; PELD, pediatric end-stage liver disease.

Characteristic	Overall	HPSA	Non-HPSA	p-value
N	5769	2726	3043	
Age at transplant, yrs.	2.3 (0.8, 9.8)	2.3 (0.8, 9.3)	2.5 (0.9, 10.3)	0.11
Sex				
Female	2895 (50.2)	1385 (50.8)	1510 (49.6)	0.38
Ethnicity				
Hispanic	1338 (23.2)	705 (25.9)	633 (20.8)	<0.001
Race				
White	4290 (74.4)	1969 (72.2)	2321 (76.3)	<0.001
Black	984 (17.1)	573 (21.0)	411 (13.5)	
Other	495 (8.6)	184 (6.7)	311 (10.2)	
Primary Insurance				
Private	2594 (45.0)	922 (33.8)	1672 (54.9)	<0.001
Public	3056 (53.0)	1756 (64.4)	1300 (42.7)	
Other	119 (2.1)	48 (1.8)	71 (2.3)	
%<FPL	0.15 (0.09, 0.22)	0.19 (0.14, 0.27)	0.11 (0.07, 0.16)	<0.001
Rurality				
Urban	4750 (82.3)	1974 (72.4)	2776 (91.2)	<0.001
Rural	912 (15.8)	700 (25.7)	212 (7.0)	
Recipient Diagnosis				
Biliary Atresia	1768 (30.6)	861 (31.6)	907 (29.8)	<0.001
Other Cholestatic	1146 (19.9)	538 (19.7)	608 (20.0)	
Acute Liver Failure	640 (11.1)	327 (12.0)	313 (10.3)	
Metabolic	545 (9.4)	211 (7.7)	334 (11.0)	
Tumor	467 (8.1)	206 (7.6)	261 (8.6)	
Autoimmune Hepatitis	250 (4.3)	114 (4.2)	136 (4.5)	
Other	945 (16.4)	464 (17.0)	481 (15.8)	
Laboratory MELD/PELD at transplant	16 (5, 25)	16 (6, 26)	15 (4, 25)	0.02
Allocation MELD/PELD at transplant	25 (16, 32)	25 (16, 32)	26 (17, 32.3)	0.07
Status 1a/1b	1600 (27.7)	737 (27.0)	863 (28.4)	0.28
Donor Age at Transplant, yrs.	11 (2, 21)	10 (2, 20)	12 (2, 22)	<0.001
Living Donor Transplant	600 (10.4)	240 (8.8)	360 (11.8)	<0.001

Characteristic	Overall	HPSA	Non-HPSA	p-value
Cold Ischemia Time, hrs.	6.7 (5.0, 8.4)	7 (5.0, 8.6)	6.5 (4.9, 8.1)	<0.001

Table 3.

Univariable Cox proportional hazard models on composite outcome of graft failure/death (whichever occurred first) at 10 years posttransplant.

Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval; HPSA, health professional shortage area; %<FPL, fraction of the population below the federal poverty line; MELD, Model for End-Stage Liver Disease; PELD, pediatric end-stage liver disease.

*The fraction of the population below the federal poverty line was scaled so that the HR represents a 10% increase in %<FPL.

	Graft Failure or Death		
Characteristic	**HR**	**95% CI**	**p-value**
HPSA	1.22	1.09, 1.36	<0.001
Age at transplant, yrs.	1.00	1.00, 1.00	0.33
Sex			
Male	1.00	0.90, 1.12	1
Ethnicity			
Hispanic	0.99	0.87, 1.13	0.9
Race			
White	REF	REF	
Black	1.29	1.13, 1.48	<0.001
Indigenous American	1.17	0.64, 2.12	0.61
Other	0.92	0.75, 1.13	0.43
Primary Insurance			
Private	REF	REF	
Public	1.38	1.24, 1.55	<0.001
Other	0.90	0.58, 1.41	0.64
%<FPL*	1.13	1.07, 1.19	<0.001
Rurality			
Urban	REF	REF	
Rural	1.12	0.97, 1.30	0.12
Recipient Diagnosis			
Biliary Atresia	REF	REF	
Other Cholestatic	1.74	1.47, 2.05	<0.001
Acute Liver Failure	1.75	1.44, 2.12	<0.001
Metabolic	1.23	0.97, 1.54	0.08
Tumor	1.84	1.49, 2.28	<0.001
Autoimmune Hepatitis	1.96	1.51, 2.54	<0.001
Other	1.85	1.56, 2.20	<0.001
Laboratory MELD/PELD at transplant	1.01	1.01, 1.02	<0.001
Allocation MELD/PELD at transplant	1.00	1.00, 1.01	0.03
Status 1a/1b	1.35	1.20, 1.52	0.01

	Graft Failure or Death		
Characteristic	**HR**	**95% CI**	**p-value**
Donor Age at Transplant, yrs.	1.00	1.00, 1.01	0.23
Living Donor Transplant	0.64	0.51, 0.79	<0.001
Cold Ischemia Time, hrs.	1.02	1.00, 1.03	0.03

Table 4.

Multivariable Cox proportional hazard models on composite outcome of graft failure/ death (whichever occurred first) at 10-years posttransplant.

Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval; HPSA, health professional shortage area; %<FPL, fraction of the population below the federal poverty line.

*The fraction of the population below the federal poverty line was scaled so that the HR represents a 10% increase in %<FPL.

	HPSA + Race			HPSA + Race + Insurance			HPSA + Race + Insurance + %<FPL		
Variable	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
HPSA	1.19	1.07, 1.33	0.002	1.13	1.01, 1.26	0.03	1.11	0.98, 1.25	0.10
Race									
White	REF	REF	REF	REF	REF	REF	REF	REF	REF
Black	1.27	1.11, 1.45	<0.001	1.20	1.05, 1.38	0.009	1.17	1.02, 1.35	0.03
Other	0.93	0.76, 1.15	0.51	0.93	0.76, 1.15	0.52	0.94	0.76, 1.15	0.53
Insurance									
Private				REF	REF	REF	REF	REF	REF
Public				1.31	1.17, 1.48	<0.001	1.29	1.14, 1.46	<0.001
Other				0.89	0.57, 1.40	0.63	0.99	0.63, 1.55	0.95
%<FPL*							1.04	0.97, 1.11	0.25

Table 5.

Landmark analysis of multivariable Cox proportional hazard models excluding patients (N=788) with graft failure/death/loss to follow-up in the first year posttransplant (N=4981)

Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval; HPSA, health professional shortage area; %<FPL, fraction of the population below the federal poverty line.

*The fraction of the population below the federal poverty line was scaled so that the HR represents a 10% increase in %<FPL.

	HPSA + Race			HPSA + Race + Insurance			HPSA + Race + Insurance + %<FPL		
Variable	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
HPSA	1.16	0.98, 1.38	0.09	1.13	0.95, 1.35	0.18	1.05	0.87, 1.27	0.59
Race									
White	REF	REF	REF	REF	REF	REF	REF	REF	REF
Black	1.93	1.59, 2.34	<0.001	1.88	1.54, 2.28	<0.001	1.76	1.44, 2.16	<0.001
Other	1.02	0.73, 1.41	0.92	1.02	0.73, 1.42	0.91	1.01	0.73, 1.41	0.93
Insurance									
Private				REF	REF	REF	REF	REF	REF
Public				1.16	0.96, 1.39	<0.12	1.09	0.90, 1.32	0.37
Other				1.06	0.56, 1.99	0.87	1.1	0.58, 2.09	0.76
%<FPL*							1.12	1.01, 1.23	0.03