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## Moving Beyond Patient-Level Drivers of Racial/Ethnic Disparities in Childhood Cancer

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### Abstract

Racial/ethnic disparities in childhood cancer survival persist despite advances in cancer biology and treatment. Survival rates are consistently lower among non-Hispanic Black and Hispanic children as compared with non-Hispanic White children across a range of hematologic cancers and solid tumors. We provide a framework for considering complex systems and social determinants of health in research examining the drivers of racial/ethnic disparities in childhood cancer survival, given that pediatric patients' interactions with the healthcare system are filtered through their caregiver, family, and societal structure. Dismantling the multi-level (patient, family, healthcare system, and structural) barriers into modifiable drivers is critical to developing policies and interventions toward equitable health outcomes. This commentary highlights areas at the family, healthcare system, and society levels that merit closer examination and proposes actions and interventions to support improvements across these levels.

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Hispanic and non-Hispanic Black (NHB) children have lower rates of survival compared with non-Hispanic White (NHW) children (1). In children with acute lymphoblastic leukemia (ALL), for example, the 5-year survival rates increased from 72.8% (1992–2000) to 82.1% (2001–2007) among NHB patients and from 85.9% to 89.0% among NHW patients; survival rates remain significantly lower among Black children than their White

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counterparts ( $P < 0.01$ ; ref. 2). Inequitable social conditions limit the reach and potency of medical advances (3), and thus, addressing drivers rooted in social structure is essential to close the racial/ethnic gap in childhood cancer survival.

Zhao and colleagues (4) quantified the role of health insurance coverage and social deprivation in mediating survival differences among children (<18 years) with newly diagnosed cancer. Their analysis of the National Cancer Database (NCDB) revealed reduced overall survival rates among NHB and Hispanic children compared with NHW children across a range of cancers (4). Although adjusting for differences in insurance coverage and zip-code level indicators of social deprivation attenuated disparities between groups, together these factors accounted for only 25.2% and 62.1% of the differences in survival rates between NHB and NHW children and between Hispanic and NHW children, respectively (4).

Zhao and colleagues' research on socioeconomic drivers of health at the patient-level set the foundation for further research considering other modifiable, multi-level drivers of childhood cancer survival. We propose that for children with cancer, patient-level drivers are nested within family-level determinants, which in turn are nested within a healthcare system informed by discriminatory policies shaped by a history of racism and segregation (Fig. 1). Although there are numerous possible drivers at each level, we focus on key modifiable drivers in the areas of caregiver capacity and health literacy, delivery of quality care, structural racism, and public policy. A multi-level approach is needed to raise awareness and identify solutions targeting modifiable drivers that can reduce racial/ethnic differences in childhood cancer survival (Table 1).

### **Family Level: Caregiver Capacity and Health Literacy**

Healthcare for children with cancer depends on their caregiver and family resources and functioning. Families endure demanding healthcare stressors spanning many years, with significant disruption in routines and in their social, occupational, and family roles (5). Care-givers are often required to manage complicated treatment regimens, including multiple medications with different dosing schedules, weekly or twice weekly outpatient appointments, acute care visits for treatment, off-treatment follow-up care, and specialty services and procedures (6). For example, patients with ALL have about 3 to 7 admissions with 24 to 55 hospital days in the first 6 months of therapy alone (7). Overall, 25% to 33% of children and their families acknowledge considerable challenges adapting to life with cancer (8). Complex, at-home, day-to-day disease management over 2 to 3 years further requires caregiver capacity and health literacy. The demands associated with having a chronically ill child and with navigating cancer care can have negative financial implications impacting work performance, absenteeism, and insurance access, particularly germane to families starting with limited resources. Research suggests that Hispanic ethnicity and living in a single mother household were associated with nonadherence to oral chemotherapy, with decreasing adherence correlated with a progressive increase in relapse (9). Higher caregiver burden is associated with lower survival for pediatric and adult patients (10). Thus, inequities in caregiver burden may be a key contributor to racial/ethnic disparities in childhood cancer survival. However, caregiver burden is difficult to

measure and intervene upon, given wide variability across treatment centers and in the type and amount of psychosocial care offered to families. Furthermore, despite evidence suggesting lower health literacy among NHB and Hispanic parents compared with NHW parents (11) and lower parent literacy linked to inferior child health (12), the role of health literacy in racial/ethnic disparities in childhood cancer remains understudied. Health literacy is a potentially modifiable driver that may improve caregiver engagement, adaptation, and treatment adherence, an area that merits future exploration (12).

Recognizing that race and ethnicity are not monolithic, empowering caregivers, and developing sustainable infrastructure supporting healthcare delivery approaches may be effective in ensuring equitable access and closing gaps in childhood cancer survival (13). Actions may include: routine screening and standardized measurement of social determinants of health and household material hardship (e.g., food, energy, and housing insecurity; ref. 14–16); expansion of financial support and psychosocial resources for caregivers; and provision of educational and culturally tailored interventions that help identify burden early on, augment caregiver capacity, and address patients'/families' unmet healthcare and social needs (see details in Table 1).

### **Healthcare System Level: Delivery of Quality Care**

Translation of advances in diagnostics, biology, and therapy also relies on the delivery of quality care. Differential enrollment in clinical trials and in dissemination and implementation of intensive therapies for Hispanic and NHB children may explain survival differences. Non-White patients are significantly underrepresented in clinical trials testing novel agents and new regimens (17). Differential enrollment may be partially explained by a distrust of healthcare institutions, providers, and research among minoritized populations due to a history of unethical medical research and care (18). Proposed strategies to improve the diversity, equity, and inclusion of clinical trials range from aligning family trust with provider bias and cultural competence to addressing regulatory and language barriers that may prevail in low-resource settings; this requires institutional policies and investment with metrics that need continued evaluation and corrective actions (Table 1; ref. 19–21).

Non-White children are also less likely to receive life-saving postrelapse treatment, such as hematopoietic stem cell transplantation (HSCT), potentially leading to inferior overall survival compared with NHW children (22). HSCT requires parental work absence and family support for at least 6 months. Access to HSCT services can be further impaired by the limited number of centers specializing in such procedures, with resulting limitations of the geographic distance from a family's home community. Strategies that incorporate families' social circumstances require consideration by pediatric oncology practices when tailoring and delivering patient-centered care (Table 1). Notably, information on cancer relapse and cause of death are missing in the NCDB, limiting Zhao and colleagues' evaluation of the overall survival rate. For pediatric lymphoma, overall survival was worse in non-White than NHW children, with lower postrelapse survival in non-White children driving the disparate overall survival (22). An in-depth understanding of the modifiable, multi-level drivers of racial/ethnic disparities in disease-specific survival, including postrelapse survival and noncancer mortality, will be an important future direction.

## Community and Society Level: Structural Racism

Reducing childhood cancer disparities requires confronting the structural racism defined by historic economic, public policies, and institutional practices that perpetuate social inequities across minoritized race/ethnic groups (23). Racial discrimination in hiring and employment practices contributes to the underrepresentation of NHB in jobs that offer health benefits (24). Policies that restrict job mobility for undocumented or recent immigrants curtail access to employer-sponsored health coverage among caregivers of Hispanic children (25). Parents' employment often dictates their child's access to private insurance coverage. The public insurance options for children, such as Medicaid, have not fully closed the race/ethnic gap in coverage in part due to the exclusion of vulnerable immigrants (26). Furthermore, state Medicaid programs require patients to provide income and other documentation to prove their eligibility at initial application and at intermittent renewal time points. These requirements can impose high burden on patients/families, in terms of time and paperwork to obtain and maintain Medicaid coverage, particularly while families balance the time commitments of managing a child with cancer. Together, discriminatory employment practices and immigration policies contribute to inconsistent health insurance coverage for racial/ethnic minoritized children, leading to disparate care access and cancer survival (27).

Racial residential segregation is another product of structural racism applied through legislative and judicial systems (23). Racial residential segregation creates inequitable neighborhood conditions (28), which directly influences educational and employment opportunities, determines timely and geographic access to care, and forms material hardship and physical environments (29). NHB children bear the greatest share of the adverse impact of segregation policies whose enduring legacies continue to stymie generations' achievements and outcomes in education, wealth, and health (23).

As implied in Zhao and colleagues' research, the structural sources of racial/ethnic discrimination are particularly consequential for children with cancer, and investigations targeting the structural drivers of racial/ethnic inequities in cancer survival are warranted. Particularly, medical and health services research must engage community stakeholders and incorporate widely available geographic data on area-level deprivation that are orthogonal to patient/family characteristics. Area-level deprivation—including neighborhood access to employment, education, food/nutrition, healthcare, transportation, and environmental pollutants—can impact child health by itself, regardless of characteristics at the patient and family levels. Furthermore, directing research funding towards designing and implementing interventions that address the modifiable and unjust structural drivers of gaps in childhood cancer survival is essential.

## Community and Society Level: Public Policy

Public policies to enhance insurance coverage and care access may attenuate racial/ethnic health disparities. The Affordable Care Act (ACA) contains multiple provisions designed to improve insurance coverage relevant for racial/ethnic minoritized children (30). Under the ACA, participating states expanded Medicaid eligibility to all parents with income 138% of the federal poverty level (30); these coverage gains can increase the proportion of

Medicaid-insured children and decrease the uninsured rate among children (31). Other ACA provisions that benefit disadvantaged children include: enhanced funding for Children's Health Insurance Program (CHIP); outreach to increase enrollment of eligible but previously uninsured children into Medicaid/CHIP; and subsidized private coverage options (30). We recently demonstrated that ACA insurance expansions were associated with a narrowing of racial/ethnic disparities in coverage and cancer stage at diagnosis in a young cohort (32, 33). Future research that demonstrates the impact of ACA provisions on disparities in childhood cancer survival is needed to inform policies designed to ensure universal and seamless healthcare coverage to improve access for children experiencing cancer survival disparities.

## Conclusion

Identification of modifiable and unjust drivers of racial/ethnic disparities in childhood cancer is critically important to inform evidence-based policies and to develop interventions toward a sustained reduction in disparities. Zhao and colleagues' research underscores health insurance and neighborhood social deprivation as two measurable and modifiable drivers. We highlight a combination of supports and interventions targeting modifiable drivers across multiple levels—including families, the healthcare system, and community and society—are imperative for future research and quality initiatives (Table 1), to facilitate meaningful changes towards decreasing structural racism, improving equitable care delivery and access, and reducing survival differences for children with cancer.

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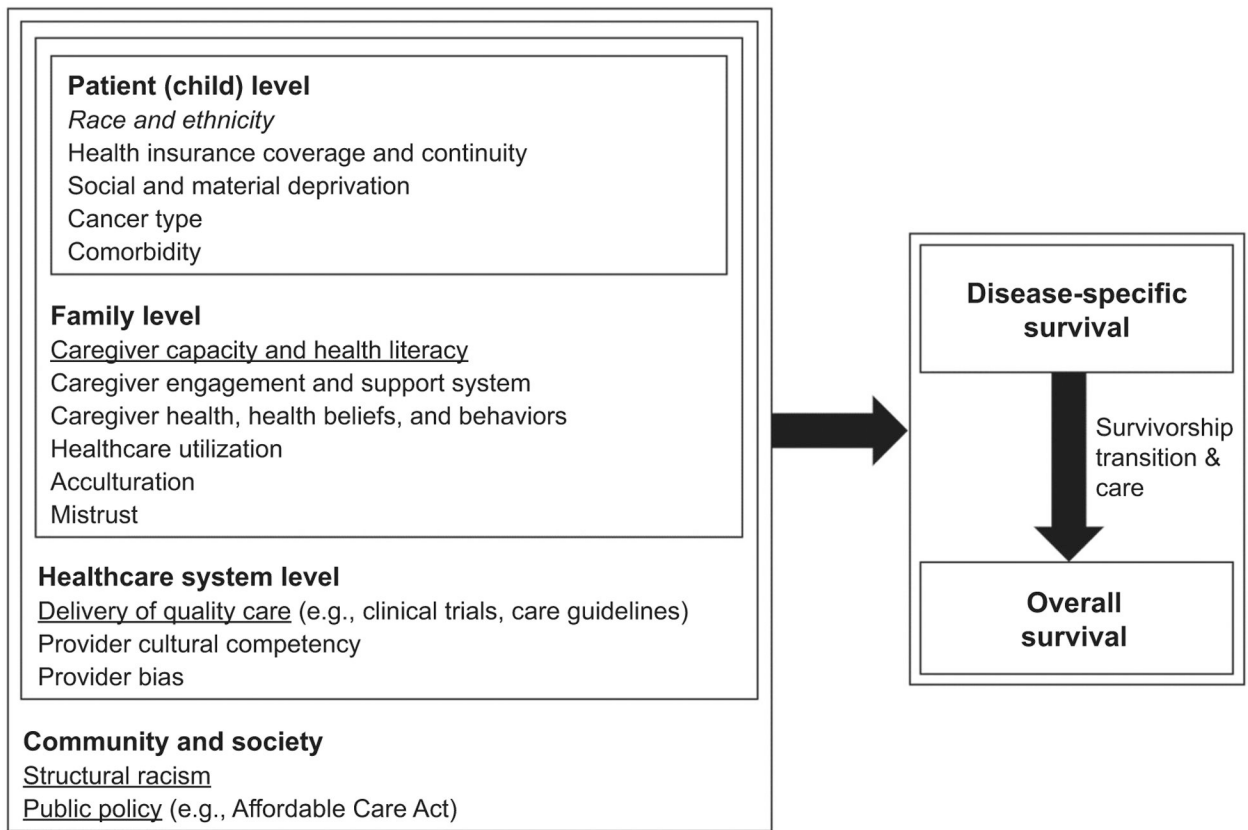
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**Figure 1.**

Multi-level drivers that affect the association between race/ethnicity and survival among children diagnosed with cancer. Notes: The multi-level drivers do not refer to a linear relationship, rather nesting relationships; patient-level drivers are nested within families, and patient-and family-level drivers are nested within the healthcare system, which are all nested within community and society.



**Table 1.**

Call for actions in key areas across multi-level drivers of disparate childhood cancer survival.

| Level                         | Proposed action or intervention  |
|-------------------------------|--|
| <i>Family:</i>                |  |
| Caregiver capacity            | <ul style="list-style-type: none"> <li>Standardize measures of household material hardship<sup>a</sup></li> </ul>  |
| Caregiver health literacy     | <ul style="list-style-type: none"> <li>Standardize measures of key social determinants of health</li> <li>Develop community programs to address patient/family social and material hardship</li> <li>Increase psychosocial resources (social workers, financial navigators) for caregivers</li> <li>Provide educational and culturally tailored interventions to improve caregiver health literacy</li> <li>Increase access to care after hours and on weekends</li> </ul>   |
| <i>Healthcare system:</i>     |  |
| Delivery of quality care      | <ul style="list-style-type: none"> <li>Improve DEI in childhood cancer clinical trials:                             <ul style="list-style-type: none"> <li>Align family trust with provider cultural competence to engage patients/families</li> <li>Address regulatory and language barriers</li> <li>Include bilingual and culturally competent study team members to enhance engagement with minoritized patients/families</li> <li>Invest in language translation and use simplified, accessible language in consents</li> <li>Implement institutional approaches and metrics to overcome mistrust rooted in the history of unethical research including minoritized patients</li> <li>Capture reasons for refusal and ineligibility in trials</li> </ul> </li> <li>Incorporate patients'/families' social circumstances when tailoring and delivering patient-centered care</li> <li>Collect institutional data beyond 5-year survival: disease-specific survival; postrelapse survival; early and late noncancer mortality</li> <li>Invest in transition to postcancer care</li> </ul> |
| <i>Community and society:</i> |  |
| Structural racism             | <ul style="list-style-type: none"> <li>Utilize available data on geographic concentration of deprivation in medical and health services research</li> <li>Call for RFAs to study and inform policies to eliminate modifiable and unjust drivers of structural racism</li> </ul>  |
| Public policy                 | <ul style="list-style-type: none"> <li>Evaluate the impact of the ACA provisions and insurance products on childhood cancer survival</li> <li>Enhance research to inform evidence-based policies toward universal and seamless insurance coverage</li> </ul>   |

Abbreviations: DEI, Diversity, Equity, and Inclusion; RFA, Research Funding Announcement.

<sup>a</sup>Evaluate at cancer diagnosis and through cancer survivorship.