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Diverse populations and enrollment in pediatric cancer clinical trials: Challenges and opportunities

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1 | RACIAL/ETHNIC SURVIVAL DISPARITIES AND CLINICAL TRIAL ENROLLMENT INEQUITY IN CHILDREN WITH CANCER

Survival rates for pediatric cancer have improved significantly over the past five decades,¹ mainly due to clinical trial (CT) participation.² Hispanic children have a significantly higher incidence of leukemia and lymphoma; however, Hispanics and African Americans have poorer 5-year overall survival rates than their non-Hispanic White (NHW) counterparts.^{3–5} Lower survival rates are at least partially attributable to lower enrollment in CTs.⁶

The National Institutes of Health Revitalization Act of 1993 mandated the inclusion of women and minorities in CTs.⁷ However, to date, only 2% of approximately 10 000 National Cancer Institute (NCI) CTs have sufficient minority participants.⁸ Despite the NCI's efforts to include minorities in research, Hispanics and African Americans are severely underrepresented compared to NHWs (1–7% and 15% vs 67%, respectively).⁸ Enrollment rates in cancer CTs are even lower at 0.4–2.2% for Hispanics and 5.4% for African Americans, even at NCI-designated cancer centers.⁸ Our work demonstrated that Hispanics are underrepresented in pediatric cancer research.⁹ Consequently, cancer outcomes data are primarily based on data from NHWs, providing inadequate information to adequately assess treatment benefits for minorities.

According to U.S. Census Bureau projections, more than half of the U.S. population is expected to be other than NHW by 2045.¹⁰ Without proactive CT planning and effective interventions, the disparity between the CTs population and the changing population of patients with cancer is likely to expand.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

2 | BARRIERS TO ENROLLMENT IN PEDIATRIC CANCER CLINICAL TRIALS

Minority racial/ethnic patients in the United States have a similar level of willingness to enroll in cancer CTs, compared to NHWs,¹¹ but there are multilevel barriers that prevent patients from enrolling in CTs. These include structural, clinical, and attitudinal/sociodemographic (at physician level and patient level) barriers.

Structural barriers include availability and complexity of CTs, time constraints for proper informed consent and CT paperwork, and lack of dedicated CT staff to serve minority populations.¹² The complexity of protocol designs often presents a general barrier to CTs enrollment, especially in populations with lower literacy and/or limited English proficiency.

Clinical barriers are related to patient ineligibility due to CTs with narrow eligibility criteria, limiting access to patients, and generalizability of results. Disparities in enrollment also vary depending on the source of funding. Most adult cancer CTs—and an emerging number of pediatric cancer CTs—are now sponsored by the pharmaceutical industry. This creates the dual problem of seeking a homogeneous CT population to minimize confounding patient-related factors while also attempting to open CTs at high-enrolling sites, which tend not to be minority-serving institutions.¹³

At the physician level, physician preference has been described as the primary reason for nonenrollment in patients for whom a protocol was available and the patient was eligible.¹² Physicians play a pivotal role in CT enrollment, since patients may only be aware of CTs and consider enrollment if recommended by their physician. Physicians may not offer a CT if they think it may interfere with the physician-patient relationship. Moreover, unconscious bias may lead to the perception that minority patients are less likely to follow up with the often complex requirements of a CT and not being offered participation. Lastly, patient-level factors include negative connotation or lack of awareness of CTs; fear of side effects, experimental procedures, and randomization; culture and language barriers; transportation barriers; travel costs; access to insurance; and availability of child care.¹⁴ Mistrust of the healthcare and CTs systems has been cited by minority patients as a common reason for nonenrollment, particularly by African Americans.¹⁵

Recently, Russo et al published in this journal that major barriers to CTs enrollment for minority patients at St. Jude Affiliate Clinics included language discordance, travel difficulties, and complex CT designs.¹⁶ Major facilitators included building trust with parents and education about the merits of CTs. The role of mistrust in pediatric CTs has not been well studied. Russo et al provide new insights from providers regarding minority enrollment to cancer CTs,¹⁶ which adds to existing literature that describes the perspectives of potential participants. Thus, recognizing and managing mistrust may play a role in increasing minority CT enrollment.

3 | OPPORTUNITIES TO INCREASE ENROLLMENT OF MINORITY POPULATIONS IN PEDIATRIC CANCER CLINICAL TRIALS

It is imperative that the demographics of pediatric patients enrolled in CTs of novel cancer therapeutics be comparable to that of the current U.S. population. By 2060, Hispanic children will make up 33% of the childhood population in the United States and 50% in California;¹⁰ therefore, we need to prepare to provide adequate care to this growing population. Efforts to improve enrollment of minority patients are clearly needed. Barriers existing in academic and nonacademic settings may differ, and therefore approaches to optimizing CTs enrollment should be tailored to specific practice environments.

Strategies to improve minority enrollment should address structural barriers related to study design and conduct, including informed consent processes, and interventions at physician and patient levels. Strategies at the clinical level should aim at reducing the rigidity of inclusion/exclusion criteria to ensure that the CT population is a better reflection of patients who are most likely to receive those therapies. As described by Russo et al, regional partnerships between large academic cancer centers and satellite sites in underserved communities can be established to increase enrollment.¹⁶ Moreover, the role of telehealth in improving CTs enrollment in pediatrics is yet to be investigated. Additionally, programs at the NCI, such as the Center to Reduce Cancer Health Disparities,¹⁷ facilitate the creation of effective partnerships between minority-serving institutions and NCI-designated cancer centers and the training of cancer scientists from diverse backgrounds.

To address provider-level barriers, culturally appropriate tools and training can facilitate minority enrollment, including training in patient-provider communication and the use of medical interpreters. At the patient level, promoting awareness of CTs for minority patients with anticipatory guidance and multimedia presentations to improve visibility may increase enrollment. Strategies to address socioeconomic barriers may have a beneficial impact on minority enrollment. Funds used to provide additional staff time for minority enrollment and reimbursement for food and/or transportation costs can increase enrollment and retention.¹⁴

4 | CONCLUSIONS

There is a positive relationship between CT enrollment and improvement in survival outcomes. Racial/ethnic minority populations have a high burden of cancer incidence but low enrollment in CTs. Although CTs have rapidly become a key element for cancer treatment, there is limited understanding of the impact of race/ethnicity on the efficacy of new discoveries and treatments because of the dramatically low number of racial/ethnic minority patients enrolled in CTs. Interventions to increase enrollment in cancer CTs have focused on adults and communities rather than individuals, with scant information on improving patient-provider communication during enrollment for pediatric cancer CTs. It is, therefore, imperative that concerted efforts should be carried out to address disparities in minority enrollment in pediatric cancer CTs. At the national level, regulatory interventions and policy enactments driven by advocacy groups will be required to achieve improved access of pediatric minority patients to CTs. With the evolving changes in racial/ethnic distribution of children in the United States, assessing the health needs to equitably serve

racial/ethnic minority patients will both remove a social justice impediment and will improve the generalizability of discoveries and treatments to mitigate disparities in clinical outcomes.

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Abbreviations:

CT	clinical trial
NCI	National Cancer Institute
NHW	non-Hispanic White

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