

Advocating for Minority Inclusion in Clinical Trials: A Call for Representation and Justice

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Off-label prescribing of medications has been a long-standing practice in pediatric medicine because, in the types of studies regarding safety, efficacy, and pharmacokinetics needed for labeling, researchers often only enroll adult subjects.¹ The Best Pharmaceuticals for Children Act (BPCA) and Pediatric Research Equity Act have significantly increased the number of pediatric trials submitted to the US Food and Drug Administration for drug labeling in the past 10 years.^{1,2} Prioritizing minority enrollment in BPCA-funded clinical trials will increase the generalizability of scientific findings within the broader pediatric population.³

In this issue of *Pediatrics*, Abdel-Rahman et al⁴ present new findings on the representation of racial and ethnic minorities participating in federally BPCA-funded pediatric studies. Pediatric enrollment in BPCA-funded studies remained comparable to or higher than expected in all minority groups, except Asian Americans. Despite observing some racial and ethnic differences in enrollment on the basis of geography, study type, and degree of study burden, in the findings from this report, it is suggested that overall, in BPCA-sponsored pediatric studies, there are no racial or ethnic biases or disparities in subject enrollment. However, as the authors note, we suspect that these studies were likely not sufficiently powered to reveal such differences between racial and ethnic groups, especially given the

inherent incomplete capture of information on race and ethnicity. Although race and ethnicity are social constructs and crude proxies to account for the substantial heterogeneity of mixed ancestry, in their continued use in clinical trials, researchers have attempted to create standard terminology, and, in many historical studies, researchers have found clinically significant differences in pharmacokinetics and pharmacodynamics on the basis of these measures.⁵

Historically, Black and Hispanic subjects are underrepresented in clinical trials.⁶ Lack of representation hinders our ability to discern factors that may influence a drug's performance on the basis genetic ancestry and excludes the presence of particular racial and ethnic groups from inclusion within the full scientific body of evidence.⁷ Well-known barriers to subject enrollment in clinical trials include language preference, health literacy, geography, transportation, cost, and resources.⁸ In addition, the willingness of racial and ethnic minorities to participate in clinical trials has been significantly compromised by mistrust, historical abuses, and religious or cultural differences.⁹ Both concepts are further challenged in the pediatric population because of the ethical, clinical, and logistic considerations unique to children.¹⁰

Although the current findings on BPCA-sponsored studies are encouraging,

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equitable demographic distribution of subjects enrolled in clinical trials should reflect our minimum standards of scientific rigor.¹¹ In the adult literature, researchers discuss how stark underrepresentation of racial and ethnic minorities has limited access to potentially life-sustaining cancer drug treatments for eligible subjects at an increased risk for disease.¹² In addition, drug therapies for adults with cardiac failure have been shown to perform differently on the basis of race and ethnicity.¹³ Therefore, the inclusion of racial and ethnic minorities in clinical trials should be free of bias and remains an issue of equity and justice.¹⁴ We suspect that there may be similar racial and ethnic differences in the performance of certain medications in pediatric populations; however, current trials may be underpowered to detect these differences. On the basis of findings from adult trials, developing strategies to increase and maintain minority inclusion in pediatric clinical trials remains imperative.

Consideration of minority inclusion and subject enrollment should be tackled at the onset of clinical trial design and should include ensuring diversified BPCA site selection. Equitable demographic distribution of participants should be prioritized in such a way that a study is powered to reveal racial and ethnic differences. Furthermore, underscoring diversity and representation within the local study personnel is critical for both patient-oriented design and outreach. Finally, emphasizing the need for diversity and inclusion through community outreach and engagement regarding clinical trial participation is a key component to robust enrollment.

The lack of racial and ethnic bias in patient enrollment in BPCA-funded sites is a positive sign, but historical evidence beckons caution. The call for diversity, equity, and inclusion remains vital to ensure that such findings are continuously sustained and integrated into the fabric of our scientific process.

ABBREVIATION

BPCA: Best Pharmaceuticals for Children Act

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