The Imperative for Diversity and Inclusion in Clinical Trials and Health Research Participation

For 3 decades, inclusion of women and underrepresented racial and ethnic groups in clinical trials and clinical research has been a stated federal policy priority. A new report from the National Academies of Sciences, Engineering, and Medicine finds that the US has fallen short of achieving this goal, with substantial costs to the communities excluded from participation, to science, and to society as a whole.1

From 2013-2018, progress toward equitable representation in clinical trials largely stalled, with American Indian or Alaska Native, Asian, Black, and Hispanic populations underrepresented compared with their proportional share of the US population. Trends vary widely across the 27 institutes and centers comprising the National Institutes of Health. For example, the National Institute of Allergy and Infectious Diseases reported that the proportion of Black individuals among the participants in clinical trials was greater than 25% in all years, whereas the National Cancer Institute reported participation rates for Black individuals of just 10.5% at most, in any year;6 falling short of population representation as well as the disparate burden of common cancers in the US Black population. Progress has been made in the inclusion of women, minority women, and other groups, but participation varies markedly by therapeutic area. Pregnant and lactating individuals and sexual and gender minority populations remain underrepresented.7

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who now represent more than 50% of US clinical trial participants, but participation varies markedly by therapeutic area. Pregnant and lactating individuals and sexual and gender minority populations remain underrepresented. However, data on trial participation is not readily or uniformly available across federal agencies, underscoring the lack of transparency and mechanisms for accountability that have plagued this area over the last 30 years.

Everyone bears the cost of the absence of diversity and inclusion in clinical trials. Scientific integrity is adversely affected because diversity is critical for new discoveries, because results of these studies may not generalize to all the communities for whom they are purportedly intended, and because the lack of inclusion may be a factor hampering clinical trial accrual. Populations underrepresented and excluded from research bear the greatest cost because they may not reap the benefit from the nation’s substantial investment in scientific advancement and may specifically be deprived of access to novel treatments only available in clinical trials. Moreover, the gap between the stated commitment to inclusion in clinical research and the lack of progress in this area may engender or reinforce mistrust in scientific and medical establishment.

Society as a whole shoulders the toll of the extraordinary disparities in the US in health outcomes. The economic analysis in the National Academies’ report estimates the economic “value” of the disparate disability-adjusted life-years lost for Black and Hispanic populations (compared with White populations) for diabetes, hypertension, and heart disease alone at nearly $20 trillion over 30 years.8 Although most of the roots of disparities in health are not directly addressed by representation in research, some are. If improvements in scientific discovery for those historically excluded from trials alleviated just 1% of these disparities, the results would be an estimated $40 billion in gains from diabetes and an estimated $60 billion from heart disease.

A repeated trope is that poorly represented communities are unwilling to participate in research. However, the evidence on this issue is both clear and contrary. American Indian or Alaska Native, Asian, Black, and Hispanic individuals are no less likely, and in some cases more likely, to participate in research when asked. Many studies have found that distrust and mistrust exist but are not necessarily associated with willingness to participate in medical research. Barriers to fully inclusive trials do exist but are surmountable with investment and focused, sustained, community-partnered effort. The National Academies report provides case studies from investigative teams that have successfully conducted inclusive trials to better elucidate barriers, facilitators, and best practices.

In view of the decades-long lack of progress and the evidence that barriers to trial participation may be overcome, the committee focused its conclusions and recommendations on urgent and actionable systemic changes that would improve representation. Inclusive clinical research will require committed and accountable action on the part of all stakeholders of the research enterprise. Funders, researchers, industry, and regulators, community leaders, patient interest groups, and journals that publish clinical research—all have an important role. Unsurprisingly, these will require investments of time, money, commitment, and effort. Building trust with local communities requires a sustained commitment and presence, with financial investment in research infrastructure and systems and technologies to reduce barriers to participation. Inclusive clinical research will require transparency and accountability. This begins with community-centered engagement and prioritization across the research life cycle, from the

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substance and design of questions being asked, to culturally cognizant recruitment and retention of study participants, to analysis and reporting of results, and to monitoring and reporting across the research ecosystem to ensure that the goals of inclusion are met.

The 17 recommendations included in the report cluster across several central themes, including the following:

- **Federal Leadership and Coordination.** The federal government has a pivotal role in ensuring diverse and inclusive research. It occupies a uniquely powerful position as funder, regulator, and gatekeeper to commercialization of novel discovery, as well as a purchaser of new drugs. The report’s recommendations call for high-level coordination across agencies within the US Department of Health and Human Services (HHS), active and real-time reporting and transparency on progress toward goals, and accountability for achieving these goals. Explicit recommendations are directed at the US Food and Drug Administration (FDA) review of new drug applications, the NIH grant review process, institutional review board regulation of trials, and reimbursement coverage for new drugs by the Centers for Medicare & Medicaid Services (CMS).

- **Increased Accountability.** When investigating new drugs and devices intended for the general public or a targeted population, industry has a responsibility to ensure that the individuals enrolled in those clinical trials are actually reflective of the population. The report recommends that FDA enforce regulations to ensure representative studies are preplanned and appropriately executed, and that Congress empowers FDA to refuse to allow new drug and device applications that do not adequately represent the product’s target population. The report also supports exploration of positive inducements, including tax incentives, market exclusivity, and fast-track criteria for applications that ensure representative trials, as well as recommends that CMS expedite coverage decisions for drugs approved on the basis of inclusive trials.

- **Equitable Investments.** Participating in research is costly in terms of time, financial implications, and expenditure of personal energy. Participation may pose greater hardship or burdens for historically underrepresented groups. Investments should be made to ensure equitable compensation to participants and their caregivers. New guidance should encourage and permit differential compensation to research participants and their caregivers according to the time and financial burdens of their participation. Differential compensation may include additional reimbursement for lost wages for those with lower socioeconomic status, transportation costs, per diem payment, dependent care, and housing or lodging when applicable. HHS should make substantial investments in community research infrastructure designed to improve representation in clinical trials and research, particularly in community health centers and safety-net hospitals.

The National Academies report presents a transformative vision for equitable clinical research. To construct a more equitable future, the epilogue challenges the field, writ large, to embrace a true and major shift that moves the balance of power to determine what research is conducted and with whom, away from institutions. It then places the priorities, interests, and voices of the communities meant to be served at the center of all of these decisions.

Most important, the report calls for immediate and urgent action. Ensuring diverse and inclusive clinical research is an existential imperative. Throughout history, biomedical research has contributed enormously to progress in treating and preventing disease and overall life expectancy. The imperative of scientific integrity, fairness, and equity in the investment in the US scientific enterprise, and the critical need to address the enormous and consequential costs of health disparities, make swift and sustained advances in the inclusion of underrepresented and excluded populations in health research an undeniable priority.

**ARTICLE INFORMATION**

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**REFERENCE**