

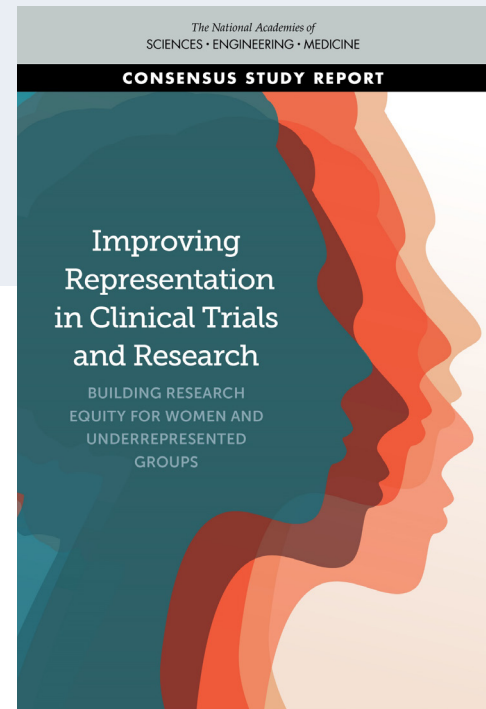
# Improving Representation in Clinical Trials and Research

## Building Research Equity for Women and Underrepresented Groups

The United States has long made substantial investments in clinical research with the goal of improving the health and well-being of our nation. There is no doubt that these investments have contributed significantly to treating and preventing disease and extending human life. Nevertheless, clinical research faces a critical shortcoming. Currently, large swaths of the U.S. population, and those that often face the greatest health challenges, are less able to benefit from these discoveries because they are not adequately represented in clinical research studies. While progress has been made with representation of white women in clinical trials and clinical research, there has been little progress in the last three decades to increase participation of racial and ethnic minority population groups. This underrepresentation is compounding health disparities, with serious consequences for underrepresented groups and for the nation.

At the request of Congress, the National Academies appointed the Committee on Improving the Representation of Women and Underrepresented Minorities in Clinical Trials and Research for the purpose making recommendations for improving representation of underrepresented and excluded populations in clinical trials and clinical research and creating lasting change. The committee's report, *Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups*,<sup>1</sup> identifies policies, procedures, programs, or projects aimed at increasing the inclusion of these groups in clinical research and the specific strategies used by those conducting clinical trials and clinical and translational research to improve diversity and inclusion. The report models the potential economic benefits of full inclusion of men, women, and racial and ethnic groups in clinical research, as well as highlights new programs and interventions in medical centers and other clinical settings designed to increase participation.

<sup>1</sup> To view the full report, visit: <https://nap.nationalacademies.org/catalog/26479/improving-representation-in-clinical-trials-and-research-building-research-equity>.



## DIVERSE REPRESENTATION IN CLINICAL RESEARCH MATTERS

By failing to achieve a more diverse clinical trial and clinical research enterprise, the nation suffers serious costs and consequences, including the following:

- Lack of representation compromises generalizability of clinical research findings to the U.S. population.
- Lack of representation costs hundreds of billions of dollars.<sup>2</sup>
- Lack of representation may hinder innovation.
- Lack of representation may compound low accrual that causes many trials to fail.
- Lack of representation may lead to lack of access to effective medical interventions.
- Lack of representation may undermine trust.
- Lack of representation compounds health disparities in the populations currently underrepresented in clinical trials and clinical research.

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<sup>2</sup> The committee used the Future Elderly Model to value how chronic conditions differentially affect the lives of older Americans.

### BARRIERS TO REPRESENTATION OF UNDERREPRESENTED AND EXCLUDED POPULATIONS

**INDIVIDUAL AND COMMUNITY FACTORS** These factors are often cited as reasons for lack of participation in clinical trials, but the evidence is clear: Asian, Black, Latinx Americans, and American Indian/Alaskan Native individuals are no less likely, and in some cases are more likely, to participate in research if asked. Distrust and mistrust exist but they are not shown to be associated with willingness to participate in medical research. The evidence suggests these concerns misrepresent barriers to participation in research or are surmountable with effort from research teams, funders, and policymakers.

**INDIVIDUAL RESEARCH STUDIES** Factors leading to the underrepresentation and exclusion of certain populations in clinical trials and research begin with and follow the life cycle of a project. This requires examining practices at every level of the research process, including: the development of research questions; the composition, training, and attitudes of the research team; research site selection; participant selection,

including sampling and recruitment methods and inclusion and exclusion criteria.

**INSTITUTIONAL STRUCTURES** Medical institutions of different types face structural barriers to inclusion in clinical trials. Although academic medical centers conduct most medical research funded by the federal government, engaging underrepresented populations in research and building relationships with communities does not align with traditional paradigms of promotion and tenure at these institutions. Many academic medical centers also struggle to recruit and retain diverse investigators and staff and often lack trust with their surrounding communities. Community Health Centers serve a more diverse population, but face challenges including with the electronic health record (EHR) infrastructure that can limit providers' ability to query the EHR using study inclusion and exclusion criteria.

**INSTITUTIONAL REVIEW BOARDS** IRBs can also present barriers to diverse participation in clinical trials by limiting the types and amount of compensation given to research participants to avoid the impression of coercion or undue influence. However, limiting incentives may ultimately compromise beneficence and justice, two of the ethical principles for research with human subjects detailed in the Belmont Report.

**RESEARCH FUNDERS** Research funders can influence the diversity of clinical trials in the following ways: setting funding priorities, deciding which projects ultimately get funded, providing adequate funding to recruit and retain participants, requiring transparent reporting, and evaluating research outputs. Industry trials often face pressure to gather data quickly and the selection of easy-to-recruit samples is often incentivized.

**MEDICAL JOURNALS** Peer-reviewed medical journals, which serve as the gatekeepers to scientific advancements in clinical practice and health, have responsibility for what is, and is not, published in their pages. Lack of representation on editorial boards and other journal leadership positions may contribute to biases in publication.

## FACILITATORS TO SUCCESSFUL INCLUSION IN RESEARCH

There is a dearth of critical qualitative data about facilitators of successful inclusion in clinical research. The study committee supplemented existing literature with commissioned research with 20 researchers who worked on trials that met criteria for diverse trial enrollment. The following eight major themes emerged from this research, they are actions that serve as key facilitators to inclusion.

- Starting with Intention and Agency to Achieve Representativeness
- Establishing a Foundation of Trust with Participants and the Community at Large
- Anticipating and Removing Barriers to Study Participation
- Adopting a Flexible Approach to Recruitment and Data Collection
- Building a Robust Network by Identifying All Relevant Stakeholders
- Navigating Scientific, Professional Peer, and Societal Expectations
- Optimizing the Study Team to Ensure Alignment with Research Goals
- Attaining Resources and Support to Achieve Representativeness

## STATUS OF CLINICAL TRIAL PARTICIPATION

The study committee commissioned an analysis to examine available data from the FDA and NIH, which found that women now represent more than 50 percent of clinical trial participants in the United States, particularly for white women. However, pregnant and lactating individuals, sexual- and gender-minority populations, and racial and ethnic subgroups of women remain underrepresented in clinical trials. The analysis also revealed that the racial and ethnic diversity of clinical trials is largely stagnant, with little changes in diversity over time.

## IMPROVING REPRESENTATION IN CLINICAL RESEARCH

### **1. IMPROVING REPRESENTATION IN CLINICAL RESEARCH IS URGENT**

Despite greater diversity in the United States today, deep disparities in health are persistent, pervasive, and costly. Failing to reach these growing communities will only prove more costly over time and prevent meaningful reductions in disparities in chronic diseases.

### **2. IMPROVING REPRESENTATION IN CLINICAL RESEARCH REQUIRES INVESTMENT**

In order to better address health disparities, our workforce should look more like our nation. Building trust with local communities cannot be episodic or transactional and pursued only to meet the goals of specific studies; it requires sustained presence, commitment, and investment.

### **3. IMPROVING REPRESENTATION REQUIRES TRANSPARENCY AND ACCOUNTABILITY**

Transparency and accountability throughout the entire research enterprise must be present at all points in the research lifecycle – from the questions being addressed, to ensuring the populations most affected by the health problems are engaged in the design of the study, to recruitment and retention of study participants, to analysis and reporting of results.

### **4. IMPROVING REPRESENTATION IN CLINICAL RESEARCH IS THE RESPONSIBILITY OF EVERYONE INVOLVED.**

The clinical research landscape involves multiple stakeholders— participants, communities, investigators, IRBs, industry sponsors, institutions, funders, regulators, journals, and policy-makers. The responsibility (and cost) will be borne to some extent by all stakeholders in the larger research ecosystem, acting in consort to improve representation.

### **5. CREATING A MORE EQUITABLE FUTURE ENTAILS A PARADIGM SHIFT**

The clinical research field must embrace a paradigm shift that moves the balance of power from institutions and puts at the center the priorities, interests, and voices of the community. An ideal clinical trial and research enterprise pursues justice in the science of inclusion through scalable frameworks, expects transparency and accountability, invests more in people, institutions and communities to drive equity, and invests in the science of community engagement and empowerment.

## RECOMMENDATIONS

The Committee on Improving the Representation of Women and Underrepresented Minorities in Clinical Trials and Research developed 17 recommendations to improve the representation of underrepresented and excluded populations in clinical trials and clinical research and create lasting change. The committee focused on system-level recommendations to drive change on a broader scale. The recommendations focus on tangible actions that must urgently be taken within the context of the existing structures of the clinical research ecosystem to achieve the goals of representation and inclusion.

### REPORTING

- The Department of Health and Human Services (HHS) should establish an intradepartmental task force on research equity charged with coordinating data collection and developing better accrual tracking systems across federal agencies.
- The NIH should standardize the submission of demographic characteristics for trials to ClinicalTrials.gov beyond existing guidelines so that trial characteristics are labeled uniformly across the database and can be easily disaggregated, exported, and analyzed by the public.
- Journal editors, publishers, and the International Committee on Medical Journal Editors should require information on the representativeness of trials and studies for submissions to their journals.

### ACCOUNTABILITY

- The Food and Drug Administration should require study sponsors to submit a detailed recruitment plan no later than at the time of Investigational New Drug and Investigational Device Exemption application submission that explains how they will ensure that the trial population appropriately reflects the demographics of the disease or condition under study.
- In grant proposal review, the NIH should formally incorporate considerations of participant representativeness in the score-driving criteria that assess the scientific integrity and overall impact of a grant proposal.
- The Office of Human Research Protections (OHRP) and the FDA should direct local institutional review boards (IRBs) to

assess and report the representativeness of clinical trials as one measure of sound research design that it requires for the protection of human subjects.

- The CMS should amend its guidance for coverage with evidence development to require that study protocols include a plan for recruiting and retaining participants who are representative of the affected beneficiary population and a plan for monitoring achievement of representativeness and a process for remediation if CED studies are not meeting goals for representativeness.

### FEDERAL INCENTIVES

- Congress should direct the FDA to enforce existing accountability measures, as well as establish a taskforce to study new incentives for new drug and device for trials that achieve representative enrollment.
- The CMS should expedite coverage decisions for drugs and devices that have been approved based on clinical development programs that are representative of the populations most affected by the treatable condition.
- CMS should incentivize community providers to enroll and retain participants in clinical trials by reimbursing for the time and infrastructure that is required.
- The Government Accountability Office (GAO) should assess the impact of reimbursing routine care costs associated with clinical trial participation for both Medicare (enacted in 2000) and Medicaid (enacted in 2020).

### REMUNERATION

- Federal regulatory agencies, including OHRP, NIH, and

FDA, should develop explicit guidance to direct local IRBs on equitable compensation to research participants and their caregivers.

- All sponsors of clinical trials and clinical research (e.g., federal, foundation, private and/or industry) should ensure that trials provide adequate compensation for research participants.

#### **EDUCATION, WORKFORCE, AND PARTNERSHIPS**

- All entities involved in the conduct of clinical trials and clinical research should ensure a diverse and inclusive workforce, especially in leadership positions.
- Leaders and faculty of academic medical centers and large health systems should recognize research and professional efforts to advance community-engaged scholarship and other research to enhance the representativeness of clinical trials as areas of excellence for promotion or tenure.
- Leaders of academic medical centers and large health systems should provide training in community engagement and in principles of diversity, equity, and inclusion for all study investigators, research grants administration, and IRB staff as a part of the required training for any persons engaging in research involving human subjects.
- HHS should substantially invest in community research infrastructure that will improve representation in clinical trials and clinical research.

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This Consensus Study Report Highlights is prepared by the Committee on Women in Science, Engineering, and Medicine, based on the Consensus Study Report, *Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups*. (2022).

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For additional information, visit <https://nap.nationalacademies.org/catalog/26479>.

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