NATIONAL ACADEMIES Sciences Engineering Medicine

Improving Representation in Clinical Trials and Research

Building Research Equity for Women and Underrepresented Groups

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Study Statement of Task

An ad hoc committee under the auspices of the Committee on Women in Science, Engineering, and Medicine will undertake a study examining the long-term medical and economic impacts of the lack of inclusion of women and underrepresented minority groups in clinical research and subsequent translational work. The study will:

- Review the existing research on the long-term health and economic benefits of increasing the participation of women and racial and ethnic minorities in clinical trials and research, including existing research on the fiscal implications of inclusion on the nation's overall health care costs.
- Review the existing literature on the factors that affect inclusion, including building equity into research designs and methods, unique inclusion-related challenges of specific medical or behavioral health conditions, and community-driven approaches to research including women and other underrepresented groups.
- Examine new programs and experimental initiatives in medical centers that are currently working to increase participation of women and members of racial and ethnic minority groups.
- Highlight programs that are positively addressing issues of underrepresentation in clinical trials, including models to address trust from a patient perspective, and analyze whether and how those programs are replicable and scalable.
- Identify more inclusive institutional and informational policies and procedures to increase the likelihood of improved health outcomes for women and racial and ethnic minorities, including health referral forms, continuing education classes for practitioners, and more.

Why Diverse Representation in Clinical Research Matters

Lack of representation:

1. **Compromises generalizability** of clinical research findings to the U.S. population.
2. **Costs hundreds of billions of dollars.**
3. May **hinder innovation**.
4. May **compound low accrual** that causes many trials to fail.
5. May lead to **lack of access to effective medical interventions**.
6. May **undermine trust**.
7. **Compounds health disparities** in the populations currently underrepresented in clinical trials and clinical research

Future Elderly Model

- •Lack of equal representation in clinical trials has consequences for health outcomes and contributes to persistent health disparities – what are the costs of this?
- Used the Future Elderly Model to value how chronic conditions differentially affect the lives of older Americans
- Looked at: non-Hispanic Black females and males, Hispanic females and males, and non-Hispanic females
- Estimated life expectancy, disability-free life expectancy, and working years gained if disparities were eliminated for diabetes, heart disease, and hypertension

DIABETES

Nearly 1 Year

Increase in life expectancy

1+ Year

Increase in disability-free life years

1/2 Year

Increase in years in the workforce

HEART DISEASE

1+ Year

Increase in life expectancy

1.5 Years

Increase in disability-free life years

1/3 Year

Increase in years in the workforce

HYPERTENSION

Nearly 1 Year

Increase in life expectancy

1.5 Years

Increase in disability-free life years

3/10 Year

Increase in years in the workforce

Economic Cost of Health Disparities

If all disability adjusted life expectancy disparities were eliminated for the 3 conditions, the value is approximately

$19.5 trillion

Value for even a modest reduction in health disparities due to better representation in clinical trials would be worth **billions of dollars.**

For example, if 1% of health disparities were alleviated by better representation in clinical research, it would result in more than **$40 billion** in gains for diabetes and **$60 billion** for heart disease alone.

Current Status of Clinical Trial Participation in the United States

	2013 (%)	2014 (%)	2016 (%)	2017 (%)	2018 (%)
Female	44.3	47.2	54.1	47.9	52.4
American Indian	2.1	1.3	0.8	0.7	1.0
Asian	15.1	17.2	8.4	26.4	7.8
Black/African American	12.2	14.3	10.0	10.8	13.5
Native Hawaiian/Pacific Islander	0.3	0.3	0.6	0.1	0.2
White	52.9	49.5	49.6	49.9	60.0
More than 1 race	1.1	1.1	2.0	1.9	2.3
Unknown race	1.1	1.1	2.0	1.9	2.3
Hispanic	9.8	8.1	10.8	6.7	8.5
Non-Hispanic	86.1	89.6	62.6	81.8	76.2
Unknown ethnicity	4.1	2.3	22.4	9.8	12.0
Sum of all races	84.7	84.8	73.5%	91.8	87.2
Sum of all ethnicities	100.0	100.0	95.8	98.3	96.7

- Data reporting practices are insufficient
- Women now represent over 50 percent of clinical trial participants in the U.S.
- Pregnant and lactating people, SGM populations, and racial and ethnic subgroups of women remain underrepresented
- Racial and ethnic diversity of clinical trials in largely stagnant

Barriers to Representation of Underrepresented and Excluded Populations in Clinical Research
Individual and Community Factors

- Frequently cited as the problem
- Underrepresented populations are no less likely to participate in clinical research if asked
- Distrust and mistrust matter, but are not insurmountable barriers

Barriers to Representation of Underrepresented and Excluded Populations in Clinical Research

- Individual research studies
  - Requires careful examination of research process
- Institutional Structures
  - Engaging underrepresented populations is not aligned with academic institutional incentives
  - Community health centers face challenges
- IRBs
- Research Funders
  - Setting funding priorities, evaluating projects for funding, providing adequate support to recruit and retain participants, requiring transparent reporting, and evaluating research output
- Medical Journals

Facilitators of Successful Inclusion in Research
Systemic Approach Needed

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

Committee Conclusions

01

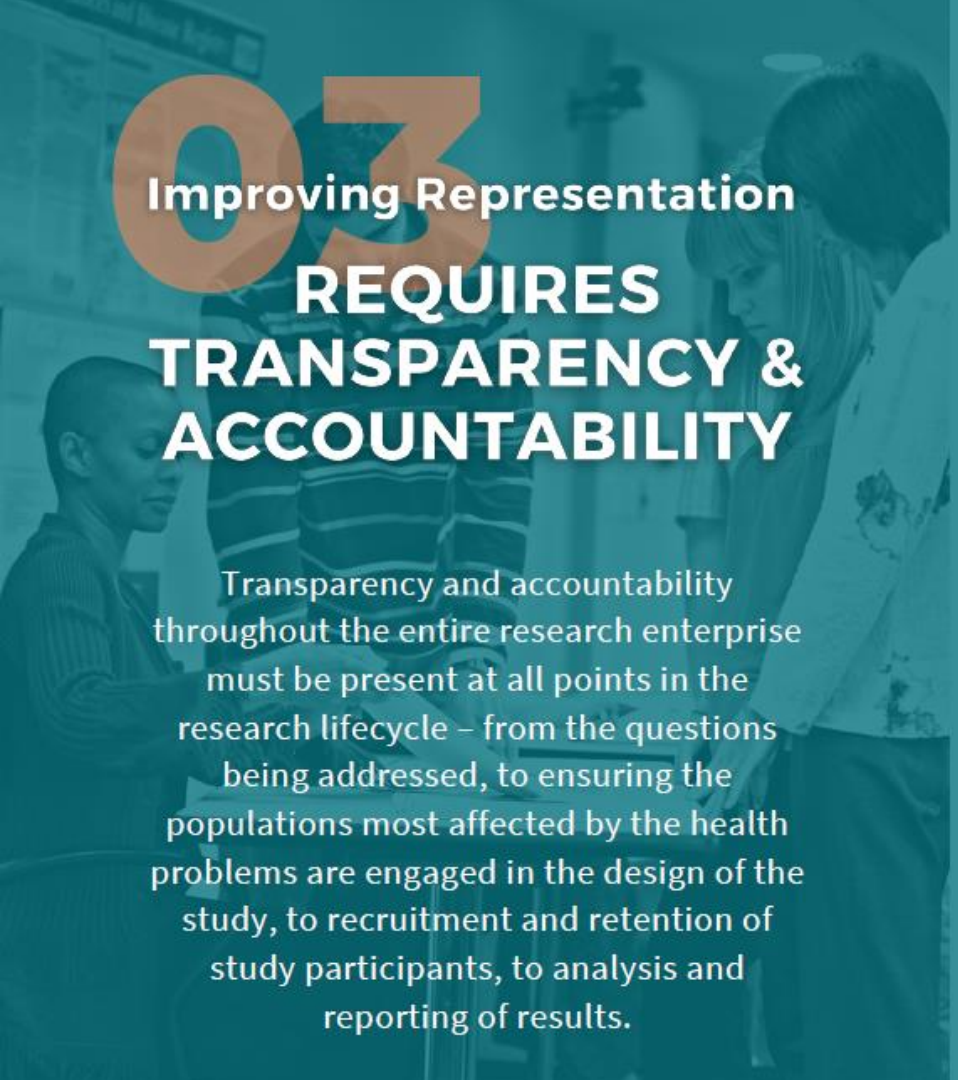
Improving Representation IS URGENT

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.

02

Improving Representation 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.



03

Improving Representation

REQUIRES TRANSPARENCY & 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.

04

Improving Representation

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.

05

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.

Committee Recommendations

Recommendations
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, particularly relative to the affected population**

Recommendations
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**
- **The CMS should amend its guidance for coverage with evidence development (CED) to require that study protocols include the following:**

    a. A plan for recruiting and retaining participants who are representative of the affected beneficiary population in age, race, ethnicity, sex, and gender

    b. A plan for monitoring achievement of representativeness as described above, and a process for remediation if CED studies are not meeting goals for representativeness

Recommendations
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 Centers for Medicare and Medicaid Services (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.**

Recommendations
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.**

Recommendations
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.**

- **HHS should substantially invest in community research infrastructure that will improve representation in clinical trials and clinical research.**

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improve-representation