Don’t Forget to Look Both Ways:

Driving Diversity and Inclusion in Clinical Research

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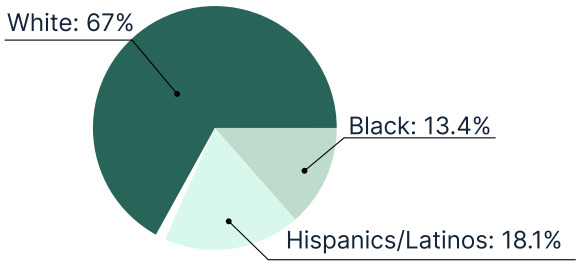
Table of Contents

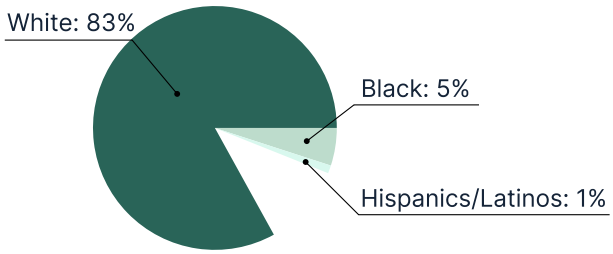
I. INTRODUCTION

Whether through socio-economic background, gender, race, ethnicity, religion, or political affiliation, diversity in clinical research is critical. It promotes greater health equity, ensures generalizability, and maintains scientific objectivity by reducing bias.

At an estimated USD$6.07 billion in 2022, the U.S. clinical trials market is projected to reach USD$8.07 billion by 2027.[1] Despite being the fastest growing market region, this market lacks speed in diversifying its participants and researchers. In 2018, White individuals accounted for 67% of the U.S. population and represented 83% of trial participants; in contrast, Black individuals accounted for 13.4% of the U.S. population yet represented only 5% of research participants, while Hispanics/Latinos made up 18.1% of the U.S. population, but represented only 1% of trial participants.[2]



U.S. Population (2018)



U.S. Trial Participants (2018)

The pandemic has disproportionately impacted people of color–with higher morbidity and lower survival rates–compared to White patients, making it a priority to address disparities in health care, particularly in clinical research.[3] Indeed, under-represented communities bear a high burden of both disease prevalence and the health inequities that drive this prevalence.[4] Lacking diversity in research participants arguably perpetuates a cycle of systemic health inequity, institutionalized racism, and exacerbates the pre-existent vulnerabilities of under-represented communities. Without adequate generalizability, clinical trials cannot reflect those most affected by the condition, and thus the real-world effectiveness and safety of clinical trial innovations and novel therapeutic treatments.

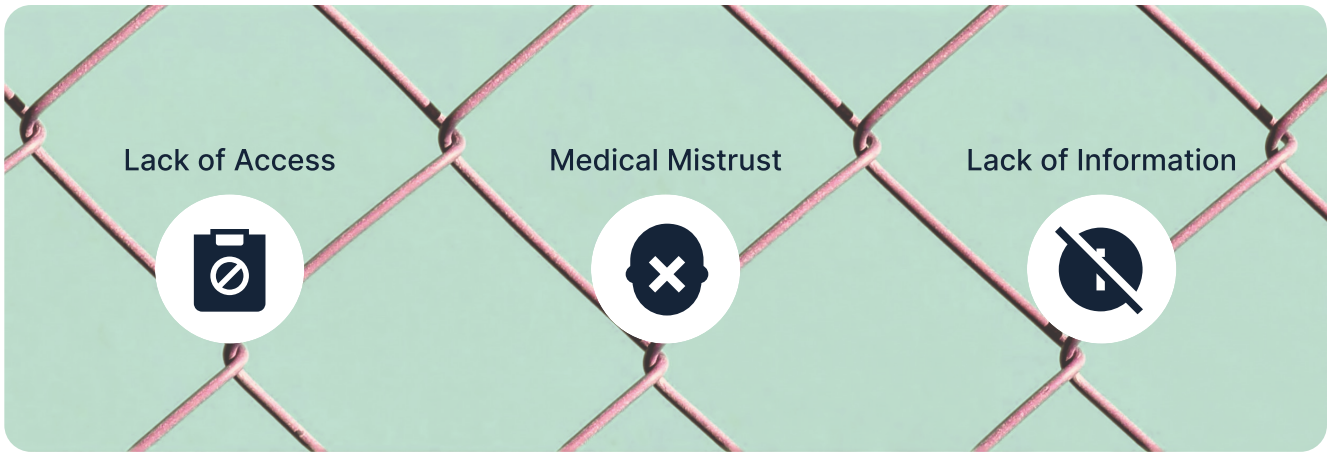
Enhancing clinical research diversity will likely be achieved when we start to acknowledge another major factor: the researcher. To both eliminate the traditional barriers of under-represented participation and increase health equity, we must start to look deeper - at both the research participants and researchers. Huge barriers to diversity and inclusivity in clinical research exists for both these populations, in the form of economic, social, cultural and technological barriers. The FDA guidelines for increasing diversity among clinical study populations convey the need to look at the relationship between these two populations more deeply, noting how researchers attuned and trained to meet to the needs of a diverse population could impact enrollment, retention and ultimately, the success of a study.[5] This white paper will explore how a lack of diversity among clinical researchers has ramifications for the clinical research ecosystem and its goals of promoting and conducting inclusive research.

Diversity in Researchers

Diversity in Participants

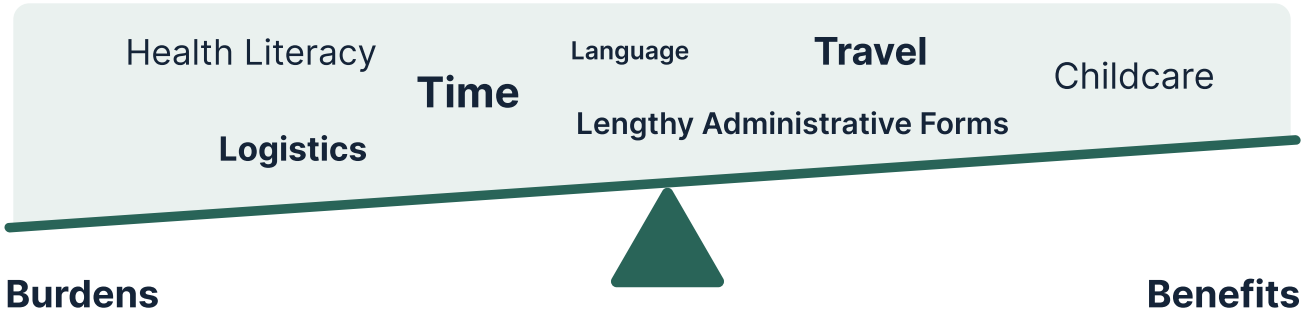
II. BARRIERS TO DIVERSITY IN CLINICAL RESEARCH PARTICIPANTS

For many patients of color, major factors prevent their participation in clinical trials, including lack of access, medical mistrust, and lack of information.[6,7]



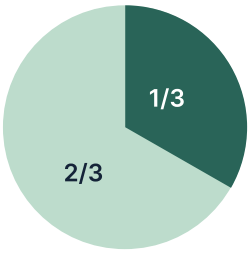
Lack of Access

The lack of both awareness and ease of access contribute to low diverse patient recruitment and retention.[6] Clinical trials are time-consuming, logistically difficult, and often expensive, which for minorities and low-income groups are reasons to avoid or drop out of trials. A 2020 qualitative evaluation of decisions by individuals diagnosed with lupus to participate in clinical trials found that major obstacles for minorities involved "lengthy administrative forms, childcare, travel, logistics, and time."[8] Informed consent, another major barrier impeding access, is especially difficult with language and health literacy gaps among participants.[9] Ultimately, for minority patients, the burdens of clinical trials may outweigh the benefits.



Medical Mistrust

The historical mistrust of minorities towards pharmaceutical and research companies also drives low research participation. With abuse present in the history of U.S. clinical research, their valid skepticism and fear towards research groups is not unfounded. For example, in the 1932 US Public Health Service Tuskegee Syphilis Experiment, researchers failed to provide effective care to African-American patients with syphilis, leading to painful and often fatal health issues. In fact, recent research from Genentech demonstrated that nearly "52% of medically disenfranchised patients believe that the healthcare industry is rigged against them," and 1 in 3 individuals categorized as medically disenfranchised avoid participating in clinical trials because of their distrust in the healthcare system.[10] Further, research organizations often fail to understand that it is not only race and ethnicity that can drive mistrust among potential participants, but also culture, context and surroundings as well.[11]



1 in 3 individuals categorized as medically disenfranchised avoid participating in clinical trials because of their distrust in the healthcare system

"52% of medically disenfranchised patients believe that the healthcare industry is rigged against them."

Lack of Information

Finally, limited information and understanding of the value of clinical research form a barrier to diverse participation. With little to no priority given by researchers to increase the distribution of trial information and participation resources among marginalized communities, White patients represent the majority of clinical trial populations.[12] Even when successfully recruited, patients consistently receive little to no communication or follow-up from researchers during and after the trial, which leads to higher drop-out rates among these populations. Engaging patients and meeting their needs throughout the clinical trial, from recruitment to trial follow-up is essential to reduce patient burden and include diverse population samples. These participation barriers perpetuate systemic racism and reinforce the social and structural determinants of health, which are underlying symptoms of low diversity in clinical trials.

III. THE BENEFITS OF DIVERSITY IN THE CLINICAL RESEARCHER WORKFORCE

Despite comprising 40% of the U.S. population today, minority and racial/ethnic groups are under-represented in clinical trials. In 2020, 75% of the 32,000 clinical trial participants investigating 53 new drugs approved by the FDA were White.[13]

Often, clinical trial populations do not reflect the real-world populations affected by the condition. For example, nearly 4-12% of pancreatic cancer diagnoses in the U.S. are among Black individuals, but they only account for 2-8% of participants in pancreatic clinical trials.13 Similarly, little genetic research–which is essential for data on disease predispositions and carrier status–exists among American Indian and Alaska Natives (AI/ANs), despite being one of the populations with the greatest health disparities in multiple diseases.[14]

Diverse research teams increase trust among participants. More trust in pharmaceutical and research companies, clinical investigators, and individual researchers enhances minority representation in patient recruitment and retention and improves trial population generalizability.[15-18] A 2021 report assessing the research workforce found that diverse research teams "maintain social justice, patient advocacy, scientific objectivity, as well as trust in science".[19]

Building patient trust in individual researchers also is critical in an ecosystem marred by implicit biases, particularly racially-motivated assumptions, which influence trial referral practices. For example, research found that compared to minority physicians, White clinicians are more likely to believe falsely that Black patients have low intelligence and compliance with medical treatment, resulting in fewer clinical trial recommendations.[20] Similarly, in the cancer workforce, a 2021 DEI study found that only 2.3% of practicing oncologists are Black or African American, and only 5.8% of practicing oncologists are Hispanic which negatively impacts trial referrals and patient trust.[21]

Additionally, diverse research teams ensure various conditions and populations are accurately represented and studied, which close gaps in diversity data. A Northwestern Medicine cross-sectional study of 20,020 U.S. clinical trials between 2000-2020 found that women are severely under-represented in studies of neurological, immunological, hematological, oncologic and cardiac diseases–the two latter conditions being most concerning as they are the leading causes of death among American women.[22] In contrast, clinical trials lack male-participants in "musculoskeletal disease, trauma, psychiatry, and preventive medicine."[22] Sex bias worsens patient disease burdens; however, enhancing diversity among researchers ensures a better understanding of diseases, lending to improved treatment interventions and prevention through new innovative medicines and medical products.[23]

- Neurological
- Immunological
- Hematological
- Oncologic
- Cardiac

Women are under-presented in studies of above fields.

- Musculoskeletal disease
- Trauma
- Psychiatry
- Preventive medicine

Men are under-presented in studies of above fields.

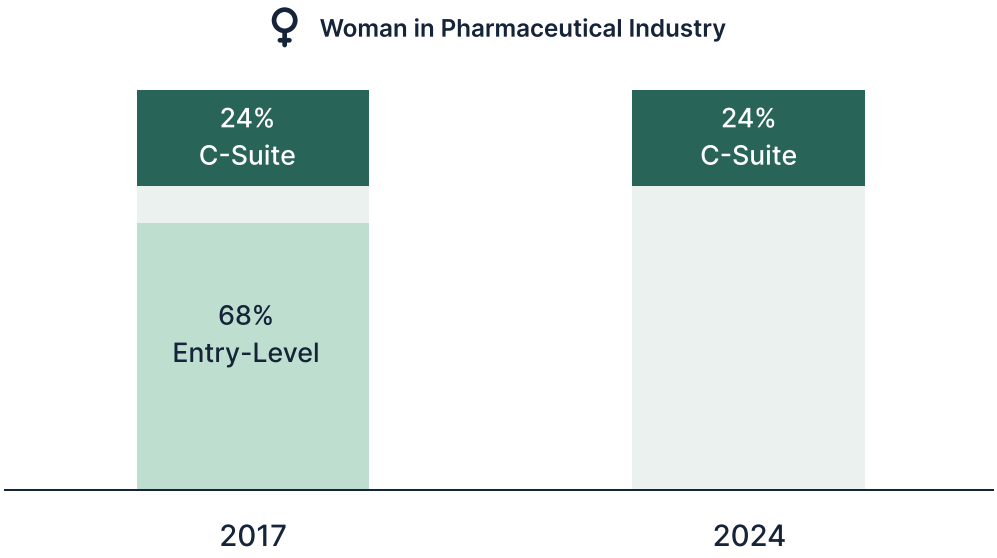
Finally, enhanced researcher diversity improves power dynamics and increases patient engagement. In fact, the cultural, socioeconomic, religious, racial/ethnic, and political background of researchers "[influence] the way that research is funded, conducted, and applied."19 Under-represented researchers may be more culturally competent at maintaining provider-patient communications and addressing health disparities compared to White researchers.[24] With improved participant-researcher communication, patients are more compliant with medication management and feel more engaged in their medical decision-making, which improves real-world data collection and accuracy.[25]

On a policy scale, diversity in the research community affects public health decisions. The pandemic shed light on the "biopolitics of care," as MIT professor and medical anthropologist Dr. Erica Caple James describes it, policymakers are making health decisions -- that increase the disease burdens of POC -- which serve to ask "Whose lives are deemed disposable?"[26]

IV. THE CURRENT RESEARCHER WORKFORCE

Like clinical trial participant-populations, the researcher community is lacking diversity in various healthcare fields.

In the pharmaceutical industry, only 37% of workers are female compared to 67% male professionals.27 Of this professional community, White researchers account for 58.7% while 26.8% are Asian, 8.7% are Hispanic or Latino, 5.5% are Black, and 0.3% AI/ANs. These discrepancies are also visible when looking at gender diversity and leadership. A 2017 McKinsey study revealed that only 24% of women in the pharmaceutical industry belong to the C-Suite compared to 68% working at entry-level.[27] As of 2022, the needle hasn't moved, and women still occupy a meager 24% of C-Suite roles.[28]In the biopharmaceutical industry, while representation of women has improved since 2017, gender representation for non-binary, transgender, and other identities is nearly non-existent.

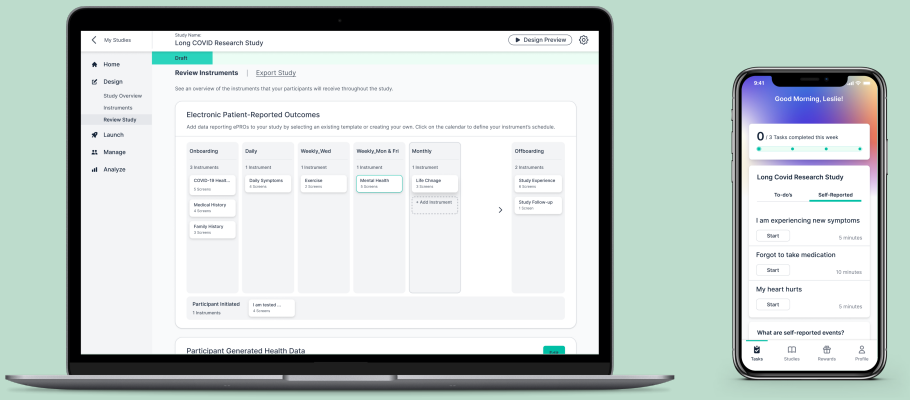


In the U.S. infectious disease workforce, compelling evidence shows that this underrepresentation is due to significant barriers, including "gaps in physician salaries based on gender and race, [...] implicit race, gender bias, and social and professional networks," among others.[29] In the biomedical workforce, underrepresented groups also face social, cultural, and financial barriers that reduce their participation in the workforce. For example, minorities may experience "cost of living, limited parental leave, and insecure extramural funding" as well as unique obstacles involving "limited exposure to science at a young age, absence of role models and mentors from [similar] underrepresented backgrounds, and social norms."[30] Because of these factors, diversity remains low in the researcher workforce.

Finally, clinical trials continue to prioritize research in specific regions and conditions, creating a mismatch between the burden of a disease and clinical research efforts for that disease.

In 2020, Asia-Pacific was the largest segment for the clinical trials market, and North America was the fastest growing region in the clinical trials market. However, Africa accounts for nearly 25% of the global disease burden, yet only 2.5% of clinical trials take place in this ethnically and racially rich continent.[31] For example, nearly 80-90% of the global burden of diabetes is in low and middle income countries ("LMIC"), yet only 3% of clinical research is conducted in LMIC.[32] In 2020, the oncology segment dominated the clinical trials market, accounting for 31.6% of its revenue. In fact, the U.S FDA spent more than USD $38 billion towards the development of oncology therapy products. Increasing diversity among conditions and populations studied is essential to reduce health disparities.

V. DEMOCRATIZING CLINICAL RESEARCH



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As an industry, we must think more deeply about the multi-faceted nature of diversity in clinical research. Tremendous work has already begun across life sciences in the improvement of participant diversity; initiatives such as the NIH's All of Us Research Program have shown promise.[33] As this work continues and more diverse participants are brought into the world of clinical research, we must now work to lower the barriers to conducting high quality research. For researchers, however, the barriers to entry into this industry still remain too high, from a technological, economic and social perspective. If we want to meaningfully impact diversity in clinical research, and hopefully, the healthcare system, then we have to lower the barriers to conducting high quality, rigorous clinical research from anywhere in the world.

In the wake of Covid-19, we have a small window of opportunity to capitalize on the interest in the intersection of intuitive technologies and clinical research. We must build tools that enable any and all types of clinical research to conduct high quality studies, and collect the type of rich real-world evidence in pilot and feasibility studies that can lay the foundation of the next generation of therapeutics. Researchers, both within and outside of "Big Pharma," are so often priced out of the use of sophisticated technologies for clinical trials, often resorting to free or makeshift tools that were not made for them.

We must borrow from the software industries around us that have leaned into enfranchising their end users – try before you buy, freemiums, no-code environments, Stripe integrations, license-based versus deliverable-based pricing, comprehensive end-to-end platforms, transparency and control over individual data - these are all approaches that have delivered enormous value to highly regulated industries from finance to insurance to utility industries. We must accept that clinical researchers today are coming to the field from myriad places – from patient-led research communities, from health policy, from nutraceutical industries, from app developers–and we must build tools that give them equal opportunity and equal clinical rigor.

The time has come to fearlessly seek to democratize the tools that have been accessible only within academia and life sciences for too long. When we consider the lack of diversity among clinical researchers in the field–from a socioeconomic, demographic and even disciplinary perspective–the missed opportunity for innovation in this category itself is striking. It is that unbridled, unencumbered innovation that we must encourage through partnership, cross-pollination with other industries, and investments in technology if we are to continue to make dents in reducing health inequities.

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