THE IMPORTANCE OF DIVERSITY, EQUITY, AND INCLUSION IN CLINICAL TRIALS

WHAT IS DEI?

Diversity, Equity, and Inclusion (DEI) encompass vital concepts that can be applied in healthcare and clinical research aimed at ensuring that individuals from various backgrounds have equitable access to medical advancements and opportunities to participate in research.

- Diversity refers to the range of unique attributes and characteristics that individuals possess, which include visible traits such as race and gender, as well as invisible attributes like beliefs, experiences, and socioeconomic status.
- Equity involves recognizing that individuals have different circumstances and allocating resources and opportunities to achieve equal outcomes.
- Inequity denotes unequal outcomes that arise from biased or unfair practices and policies, leading to disparities in health and well-being.
- Inclusion is defined by the extent to which individuals feel valued and encouraged to fully participate in their communities.

Understanding how to integrate principles of diversity, equity, and inclusion is essential for addressing systemic barriers in healthcare and ensuring that clinical trials yield results that can be applied to individuals of all backgrounds.

Lack of Inclusion in Medical Research

ADDRESSING HISTORICAL CONTEXTS

The significance of incorporating DEI in medical research extends beyond the ethical need to ensure all patients are treated fairly; it also addresses a history of systemic discrimination and inequity in healthcare. Historically marginalized communities, including racial and ethnic minorities, have often been excluded from clinical research. This exclusion has led to significant gaps in medicine's ability to treat people from all backgrounds, with treatments being designed for and tested primarily on populations that do not reflect the diversity of the general population. Not only is developing medicine in this way not inclusive, it fails to fully treat the diseases doctors and researchers seek to alleviate.

Furthermore, there has been significant harm done by the medical field to Black (and Indigenous) Americans, which needs to be rectified in order to effectively build trust and inclusion in medical research. To overcome this deep mistrust stemming from unethical medical practices, such as the Tuskegee Syphilis Experiment, the field of medicine must implement long-term, community-centered approaches that prioritize transparency, inclusivity, and ethical integrity. Community-based participatory research (CBPR), where communities are co-creators in the research process, can help foster mutual trust by valuing the lived experiences and health concerns of participants, allowing for more culturally sensitive research and treatment approaches (Wallerstein & Duran, 2018). Increasing the representation of Black healthcare providers and researchers can further mitigate mistrust, as patients are more likely to feel understood and respected when treated by professionals who reflect their own communities (Laurencin & Walker, 2020). Additionally, enhancing informed consent practices and emphasizing transparent communication regarding potential risks and benefits can reassure participants of their rights and safety in medical research (Scharff et al., 2010). Addressing historical and ongoing inequities in healthcare thus involves not only improving research and clinical protocols but also committing to structural reforms that ensure equity, respect, and accountability within medical institutions.

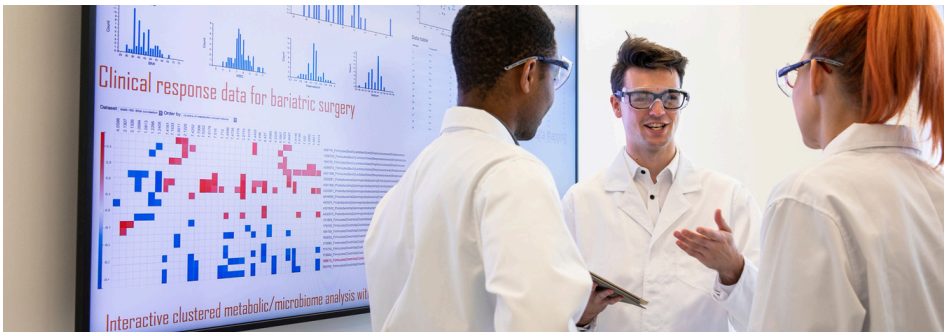
THE CASE FOR INCLUSION

Diversity, equity, and inclusion in clinical trials are essential to achieving equitable healthcare outcomes, as they ensure that new advances in medicine can benefit everyone regardless of identity. However, historically, clinical trials participants have been restricted in terms of race and gender, which limits the generalizability of study results to all demographic groups. This lack of diversity can lead to health disparities by resulting in treatments that may not be as effective or safe for underrepresented populations, such as women, racial and ethnic minorities, and older adults (Oh et al., 2015). Including diverse populations in trials allows for a better understanding of genetic, biological, and environmental differences that impact drug metabolism, side effects, and efficacy, which are crucial to creating safe, personalized medical treatments. Moreover, enhancing DEI in trials fosters trust within marginalized communities, which have historically been

"lack of diversity can lead to health disparities by resulting in treatments that may not be as effective or safe for underrepresented populations"

underserved and underrepresented in research, and increases their access to potentially life-saving therapies and cutting-edge treatments. Overall, DEI in clinical trials is vital for developing healthcare solutions that serve all individuals equitably, enhancing the reliability of study outcomes, and promoting public trust in medical research.

MYTHS AND MISCONCEPTIONS ABOUT DEI IN MEDICAL RESEARCH



If DEI is so beneficial in medicine, then why do practitioners face so much backlash when trying to make progress in these areas? One reason is that there are a lot of myths surrounding DEI, who it serves, and what the goals are. Because of this misinformation, many shy away from the critical work of making medical research more inclusive for fear that it will isolate others or that it does not truly address the root of disease.

Below are several common myths that impede greater diversity, equity, and inclusion in medical research:

DEI is Only About Race: While race is a critical component, DEI encompasses a broader range of identities, including gender, socioeconomic status, age, sexual orientation, and disabilities. Intersectionality highlights how these identities interact and influence health outcomes, suggesting that focusing solely on race oversimplifies the complexities of inequality.

Underrepresented Groups Are Not Interested in Participation: There is a misconception that marginalized communities are uninterested in clinical trials. However, many individuals from these groups are eager to participate, but face systemic barriers and mistrust stemming from historical injustices in medical research.

Diverse Participants Complicate Research: Some believe that including diverse populations adds unnecessary complexity to studies. However, diversity enhances the validity and applicability of research findings, as different populations may respond differently to treatments, leading to more comprehensive and effective healthcare solutions.

Eligibility Criteria Are Neutral: It is often assumed that eligibility criteria for trial participation are unbiased and purely scientific. In reality, these criteria can disproportionately exclude individuals from underrepresented groups, particularly those with comorbidities or atypical health profiles, thereby perpetuating health inequities.

All People Have Equal Access to Trials: Many believe that once trials are publicly advertised, all interested individuals have equal access to participate. However, barriers such as healthcare

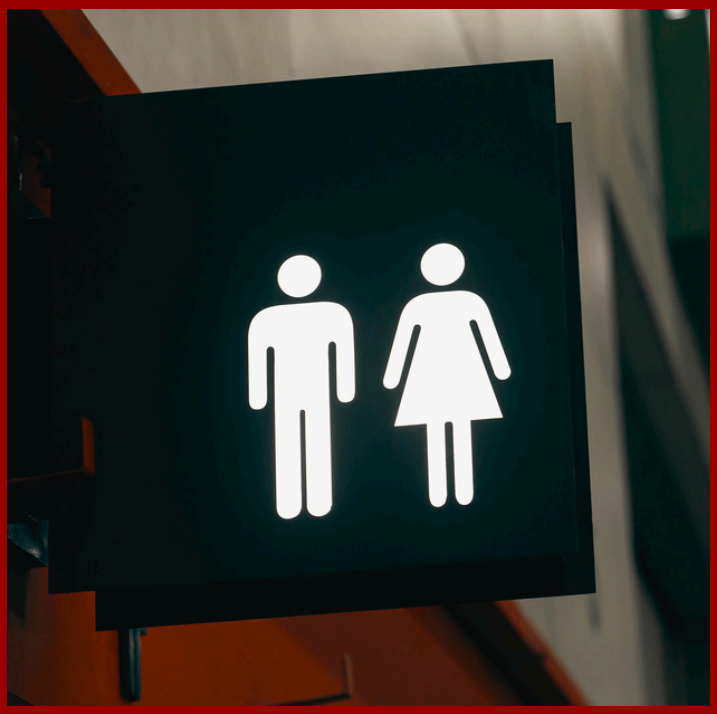
access, transportation, and socioeconomic status can significantly impact who can actually enroll in a trial (Thakur et al, 2021).

DEI Efforts Are Just a Trend: Some view DEI initiatives as temporary or merely performative. In reality, fostering diversity, equity, and inclusion is essential for ethical medical research and is increasingly recognized as crucial for improving health outcomes across populations.

Addressing these myths is vital for creating a more inclusive and equitable landscape in medical research, ultimately leading to better health outcomes for all populations.

Debunking Race-Based Medicine and the Role of Social Constructs

Understanding Social Constructs



Social constructs are categories or concepts that are created and maintained through social agreement. They differ from natural constructs or facts, which exist independently of human beliefs or behaviors. Money is a social construct that most people generally agree upon, whereas gender is a social construct that is highly personal and can be expressed in unique ways. However, both concepts of money and gender can change over time, be represented differently, and depend on the culture in which it exsists. Many social constructs were thrust upon others by those in power and maintained by the status quo. Other common examples of social constructs include time, race, and socioeconomic status.

Social constructs significantly influence inclusion by shaping perceptions, beliefs, and behaviors toward various identity groups based on harmful stereotypes. In general, biases derived based on socially constructed identities can marginalize certain populations, often leading to their exclusion from critical dialogues and opportunities. In medical research, these constructs manifest through biases that affect recruitment strategies and eligibility criteria for clinical trials, often resulting in underrepresentation of marginalized communities. By recognizing and addressing these social constructs, researchers can create more inclusive environments that foster diverse participation, ultimately enhancing the validity and applicability of medical findings across all demographics.

Race as a Social Construct

Using race as a proxy for environmental factors in medical research creates challenges because it overgeneralizes complex social determinants of health and may reinforce racial biases in clinical practice.

Race is often used as a social construct rather than a biological or genetic determinant of illness, and relying on it as a substitute for factors like socioeconomic status, exposure to environmental toxins, food access, and stress can conceal the actual causes of health disparities. In fact, research has shown that environmental factors, not race itself, account for many of the differences in disease prevalence and health outcomes observed across racial and ethnic groups. For example, African Americans are more likely to live in areas with limited access to healthcare and higher exposure to environmental pollution, factors that are not inherently tied to race but rather structural inequities like income gaps and housing segregation. When race is used as a proxy for these factors, it conflates the real issues reinforcing the misconception that certain biological differences lead to health disparities, potentially resulting in underdiagnoses and inaccurate treatment. Utilizing more precise variables — such as socioeconomic access, geographic factors, and environmental exposures — can improve the accuracy of medical research and promote more equitable healthcare by addressing the root causes of health inequities rather than attributing them to race.

Clinical Trials and Health Equity

<u>What are Clinical Trials?</u>

Clinical trials are conducted to evaluate the safety and efficacy of new medical interventions. They serve multiple purposes, including:

- Assessing the efficacy of a new drug or treatement.
- Identifying potential side effects.
- Determining ideal dosages.
- Establishing the safety of new drugs or therapies.

Who Typically Participates in Clinical Trials?

Historically, clinical trial participants have primarily been white, male, and of higher socioeconomic status. We also typically see participation from those with higher educational backgrounds, those who have access to health insurance, those from less rural communities, and those who do not experience multiple disabilities (which typically disqualify disabled participants due to the exclusion criteria in some trails). Understanding who is left out of medical research helps us to draw direct inferences about who experiences the most medical disparities, which demographics have the most desperate outcomes, and why.

<u>Systemic Barriers to Clinical Trial Participation</u>

Systemic barriers and environmental factors significantly impact participation in clinical trials, particularly among underrepresented groups. Key barriers include:

Historical Mistrust: Historical injustices in medical research, such as unethical experimentation on marginalized populations, have created a deep-seated mistrust of clinical trials within these communities and can deter individuals from participating.

Access to Healthcare: Many underrepresented groups face systemic barriers to healthcare access, including lack of insurance, inadequate healthcare facilities, and limited availability of culturally competent care, which can restrict participation.

Socioeconomic Status: Socioeconomic disparities, such as lower income and education levels, can affect participation by creating logistical challenges with things like transportation, time off work, or childcare (CDC, 2023).

Cultural and Linguistic Barriers: Lack of culturally relevant information and language barriers can hinder understanding and awareness of clinical trials. Recruitment materials that

do not consider cultural contexts may also fail to engage potential participants effectively.

Eligibility Criteria: Strict eligibility criteria often exclude individuals with pre-existing conditions or those who may not fit traditional demographic profiles. This can disproportionately affect marginalized populations who may have unique health profiles or comorbidities.

Perceived Risks and Benefits: Concerns about potential risks and a lack of perceived benefits from participation can lead to reluctance to participate. Many individuals may feel that the trial does not address their specific health needs or may not trust that they will receive adequate care during the study.

Addressing Systemic Barriers

To foster inclusivity, clinical trials must address the systemic causes of participation disparities. Addressing these barriers requires a multifaceted approach that involves building trust, improving healthcare access, and ensuring that clinical trials are designed with the needs and perspectives of diverse communities in mind.

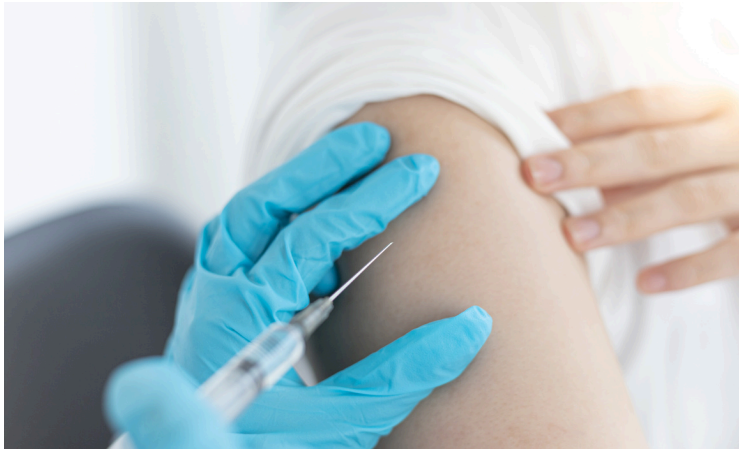
"Another strategy includes diversifying the research workforce to improve representation, as participants may feel more comfortable enrolling in studies when research teams share similar backgrounds or understand their cultural contexts (Oh et al., 2015). "

Overcoming systemic barriers to equitable participation in medical research requires targeted strategies that address issues of access, trust, and representation. One effective approach is to increase accessibility by conducting research within diverse communities, reducing the logistical challenges related to transportation, time off work, and childcare that often prevent underserved populations from participating (Yancey et al., 2006). Additionally, improving informed consent practices and sharing information in digestable formats helps manage perceived risks. Another strategy includes examining exclusion criteria to ensure it is not unintentionally impacting the applicability of research findings to certain populations. By implementing these strategies, researchers can make strides towards more inclusive studies that enhance the validity of research findings and ensure that scientific advancements benefit all populations equitably.

Who Typically Benefits from Clinical Trials?

While clinical trials are designed to advance medical knowledge and improve patient care, the benefits are often unequally distributed. Historically, those most involved in clinical trials tend to be individuals already privileged in terms of access to healthcare. Therefore, Individuals from marginalized communities often do not experience the same level of benefit from medical advancements due to their historical exclusion from research. This delays discovery of differential impact of new medicines and inability to test for potential risks in a controlled, trial environment. Instead, marginalized communities are only offered access to many therapies post-trials, and are left to deal with any complications or side effects outside of the protections of the clinical trial process.

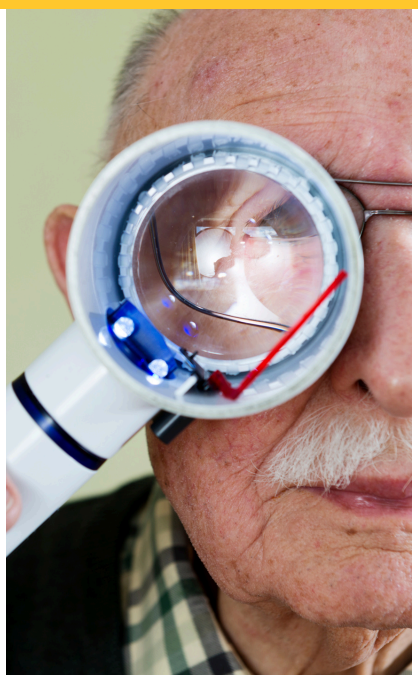
For example, limiting COVID-19 vaccine testing to certain countries and populations had potential negative effects on vaccine efficacy, public trust, and health equity globally. When early clinical trials primarily included participants from high-income countries with specific demographic profiles, they overlooked the unique health factors, environmental conditions, and genetic diversity present in other regions, and among minoritized populations within the country, leading to gaps in understanding vaccine performance across diverse populations (Flores & Frontera, 2021). This underrepresentation of diverse groups led to challenges in assessing potential side effects for people in underrepresented groups, such as immunocompromised individuals, racial minorities, and those in low- and middle-income countries with different public health conditions. Beyond undermining global confidence in the vaccine, these limitations also intensified existing health disparities by delaying equitable vaccine access and targeted vaccination strategies for the most vulnerable populations worldwide.



Furthermore, when racial and ethnic minorities have been included in medical research, their communities have still been kept away from the scalable benefits of those subsequent medical advances. Henrietta Lacks and the HeLa cells highlights a significant ethical failure in medical research that deprived Lacks and the Black community of both recognition and the potential benefits derived from her biological contributions. Henrietta Lacks was an African American woman whose cancer cells were taken without her consent in 1951 at Johns Hopkins Hospital, one of the few institutions that offered medical care to Black patients at the time (Skloot, 2010). Her cells, labeled "HeLa," were the first human cells to be successfully replicated indefinitely in lab settings, which contributed immensely to advancements in vaccines, cancer treatments, and genetics. However, Lacks' family was not informed about the use of her cells until decades later and received no financial benefit from the billions generated by research using HeLa cells (Skloot, 2010). This lack of consent, transparency, and compensation reveals systemic inequities that have historically disadvantaged Black individuals in medical research. Addressing these injustices required ethical reforms in biomedical research to prioritize informed consent, compensation, and equitable distribution of benefits for all research participants, particularly those from historically marginalized communities.

The Work of the USC Race and Equity Center in Clinical Trials

Currently, the USC Race and Equity Center is working on Phase 2b of clinical trails for a new retinal implant designed to slow and reverse blindness from age-related macular degeneration. This work is being done in partnership with Regenerative Patch Technologies, Keck Medicine of USC, the Clinical Trials Research Group, and funded by the California Institute for Regenerative Medicine with the USC Race and Equity Center leading the DEI aspect of the work. Specifically, we are supporting with inclusive patient recruitment, outreach, and messaging as well as with surgeon and trails staff DEI training, and research that assess the impacts of integrating DEI frameworks into clinical trial facilitation.



The importance of diversity, equity, and inclusion in the Phase 2b clinical trial for the retinal implant cannot be overstated, especially given the significant health disparities associated with age-related macular degeneration (AMD).

By ensuring diverse representation in this trial, researchers can better understand how the implant impacts different populations, which may respond uniquely to the treatment due to genetic, environmental, and socio-economic factors. This inclusivity not only enhances the robustness of the trial results but also supports health equity by ensuring that the benefits of innovative treatments, like the stem cell-based implant, are accessible to all individuals, regardless of their background. Ultimately, this approach can lead to more effective, personalized interventions that improve outcomes for patients suffering from geographic atrophy and contribute to the overall advancement of ocular health.

Conclusion

Diversity, equity, and inclusion are not just ethical imperatives in clinical trials; they are critical for advancing medical science and ensuring equitable healthcare access. Addressing systemic barriers that hinder diverse participations is crucial for improving health outcomes and making clinical trials more representative of the populations they serve. By embracing DEI principles, the medical research community can enhance the quality and applicability of findings, ultimately leading to better health for all, and can help rectify the historical wrongdoings that have plagued medical research historically.

About the USC Race and Equity Center

The University of Southern California is home to a dynamic research, professional learning, and organizational improvement center that serves educational institutions, corporations, government agencies, and other organizations that span a multitude of industries across the United States and in other countries. We actualize our mission through rigorous interdisciplinary research, high-quality professional learning experiences, the production and wide dissemination of useful tools, trustworthy consultations and strategy advising, and substantive partnerships. While race and ethnicity are at the epicenter of our work, we also value their intersectionality with other identities, and therefore aim to advance equity for all persons experiencing marginalization. Our rigorous approach is built on research, scalable and adaptable models of success, and continuous feedback from partners and clients.

We acknowledge that our center is on the traditional land of the Gabrielino-Tongva peoples. We also recognize the Chumash, Tataviam, Serrano, Cahuilla, Juaneño, and Luiseño People for the land that USC occupies around Southern California. We honor their past and present.

Our mission is to **ILLUMINATE**, **DISRUPT**, and **DISMANTLE** racism in all its forms.

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