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Addressing Health Disparities through Clinical Trial Diversity: Advancing Medicine for Historically Marginalized Communities

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Executive Summary

Clinical trials are critical components in healthcare and improve the lives of millions. Despite federal regulatory policies, clinical trials continue to lack representation of ethnic and racial minority populations. Many pharmaceutical medications originated as clinical trials. However, lack of representation in these clinical trials will continue to widen health disparities among underrepresented populations. Clinical trials advance medicine, and everyone needs to be part of the advancement. Without diversity, knowledge gained from research is less applicable to certain populations and results in complications after drug approval. With today's shift towards precision medicine and understanding the needs of different approaches for different populations in achieving healthier lives, inclusion and diversity in clinical trials is imperative.

Background

What are Clinical Trials and How do They Work?

Pharmaceutical medications are prescribed to treat many medical conditions. The Food and Drug

Administration (FDA) is the primary regulator for medications that come to the U.S. market. The FDA reviews evidence of the medication to ensure it is safe and effective for public use. Before a medication is approved, medications first undergo clinical trials.¹ Clinical trials are a type of research studying the effects of these medications on humans. People can volunteer to participate in clinical trials. Clinical trials are often led by a principal investigator, usually also a medical doctor, who works with a research team.² The FDA defined four phases of a clinical trial (see Figure 1). After a drug leaves preclinical research in animal models, it enters phase one to study the safety, side effects, and metabolism of the drug in less than one hundred people. Phase two is larger, made up of hundreds of participants to study drug effectiveness. Phase three is the largest phase with thousands of participants to study the efficacy of the drug with different dosages and in combination with other drugs. The FDA then approves a drug and enters phase four. This phase is called the post-marketing monitoring stage. Here the drug is available on the market but

maintains monitoring for any adverse events.³

The Issue of Lack of Diversity in Clinical Trials

Ethnic and racial minorities are repeatedly excluded from medical research.⁴ Approximately over 80% of non-Hispanic White people make up today's clinical trials.⁵ When ethnic and racial minority groups are underrepresented in clinical trials, the medical knowledge gained from this research is less applicable to these populations. For example, cancer is the second most common cause of death in the U.S. Of the 1.7 million cancer cases diagnosed in 2019, about 606,880 of those Americans died.⁶ However, cancer disparities disproportionately burden racial and ethnic minorities. The African American community has a 22% higher death rate than all major racial and ethnic groups.⁷ In the Latino community, cancer is the leading cause of death, accounting for almost a quarter (21%) of deaths.⁸ In cancer studies that lead to FDA drug approvals, Latinos represented only 6.1% and African Americans 3.1% of trial participants.⁹ Ensuring diversity in clinical trials leads to an overall

Although close to 133 million Americans will suffer from at least one chronic condition, these diseases disproportionately burden minorities, often more severely, and with higher rates of mortality.¹⁵

healthier country while also specifically addressing health disparities among racial and ethnic minority groups. With today's shift towards precision medicine and understanding the needs of different approaches for various populations in achieving healthier lives, inclusion and diversity in clinical trials is imperative.

Current U.S. Regulatory Processes

The lack of diversity in clinical trials is nothing new. In fact, in 1994 the government acknowledged this issue and passed the National Institutes of Health (NIH) Revitalization Act of 1993 (further referred to as Revitalization Act). This law requires NIH-funded researchers to enroll more women, and ethnic and racial minorities in their clinical trials. However, more than 25 years after enactment, minorities remain underrepresented.¹⁰ According to the most recent U.S. Census data, Latinos make up 18.5% and African Americans 13.4% of the overall U.S. population.¹¹ Still, Latinos make up only 1% and African Americans 5% of clinical trial participants.¹² The U.S. has one of the largest pharmaceutical markets in the world, alongside China, Japan, Germany and France who are also acknowledging the importance of this issue and taking steps to address it.¹³ For example, Japan requires a sufficient number of Japanese patients to have participated in international medical trials to demonstrate safety and efficacy before marketing the medicine within their country.¹⁴

Figure 1. Proportional Contribution of the Social Determinants of Health

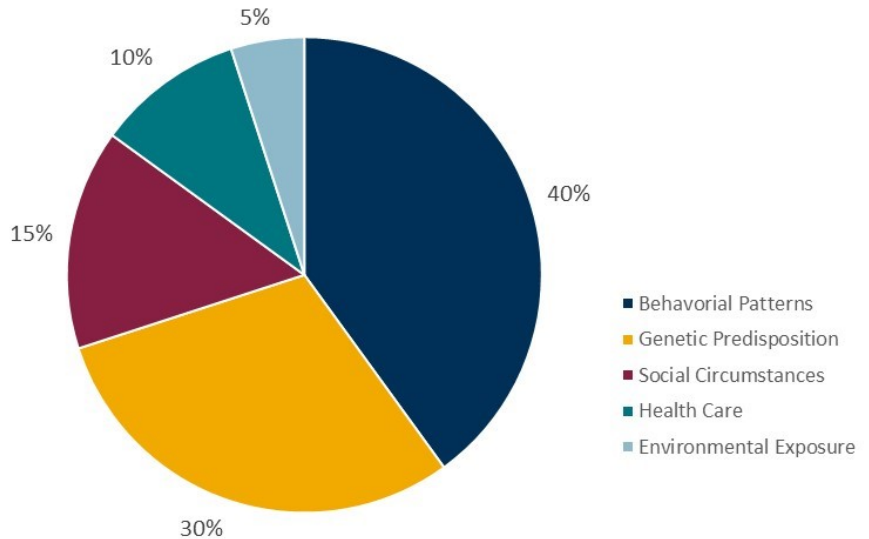


Figure 1. Breakdown of determinant factors that affect health. Source: J. Michael McGinnis, et al., "The Case for More Active Policy Attention to Health Promotion," *Health Affairs*, (2002): 78-93.

Policy Problem

The issue of lack of diversity in clinical trials is especially concerning when it comes to researching diseases that disproportionately affect ethnic and racial minorities. Even though non-Hispanic Whites make up the majority of clinical trials, ethnic and racial minorities are ultimately the patients who will take these drugs. Although close to 133 million Americans will suffer from at least one chronic condition, these diseases disproportionately burden minorities, often more severely, and with higher rates of mortality.¹⁵ Numerous factors influence health, especially among ethnic and racial minorities, such as behavioral patterns and cultural beliefs, genetic predispositions, social and living circumstances, lack of access to

quality health care, and environmental exposures (Figure 2).¹⁶

Social Determinants of Health

Social determinants of health (SDOH) are the circumstances, conditions, and environments in which people live that impact their health. SDOH are often grouped into five domains: economic stability, education, quality health care access, neighborhood and built environment, and social and community context.¹⁷ These SDOH contribute to a person's overall health, wellbeing, and quality of life. For example, a person born in a neighborhood where food deserts, unpaved roads, and poorer water infrastructure commonly exist, is likely to be exposed to unhealthy food, endure long drives to find a nearby clinic, and lack clean water for basic hygienic

Asthma in children in the Bronx exceeds state and national rates of asthma, with Puerto Ricans having the highest rates among all ethnic and racial minorities.

needs. These families face higher risk of disease than a more affluent family from a different area. It is these determinants that give rise to a person or population's socioeconomic status and class in society. This essentially unveils the inequities that privilege and power dynamics define.¹⁸ Because of these SDOH, ethnic and racial minorities disproportionately experience lower socioeconomic status and higher rates of health disparities in comparison to other populations.¹⁹

For example, high rates of asthma and cardiovascular disease among ethnic and racial minorities are often associated with social determinants of health. The Bronx, New York is one of the poorest counties in the U.S. with a high prevalence of poverty and minority status.²⁰ In the Bronx, the poverty rate is 29.1% and Latinos make up 32.4% and African Americans 28.9% of the population.²¹ Asthma in children in the Bronx exceeds state and national rates of asthma, with Puerto Ricans having the highest rates among all ethnic and racial minorities. These children are twice as likely to be hospitalized and die from asthma than any other children in the U.S.²² This disease is associated with higher environmental exposures like allergens, poorer housing conditions with higher presence of mold and irritant nitrogen dioxide, and high psychological stress among the family.²³ In another example, just in the U.S alone, nearly 29% of all deaths were due to cardiovascular disease.²⁴ However, African Americans have the highest cardiovascular

disease mortality rate of all ethnic and racial minority groups²⁵ and are 20% more likely to die.²⁶ Researchers found that lower socioeconomic status (like education, unemployment and income), poorer living conditions, high stress levels from racial discrimination, and societal standing is associated with these poorer cardiovascular health outcomes.^{27,28}

Genetic Predisposition

People of racial and ethnic minority backgrounds have an increased risk or genetic predisposition towards certain diseases. A genetic predisposition is an increased likelihood of developing a particular disease because of a person's genetic makeup.²⁹ When commonly shared ancestral genes contain a disease-causing mutation, certain ethnic and racial minority groups are more likely to suffer from a particular genetic disorder.³⁰ Two of the most prominent examples of genetic diseases among ethnic and racial minorities are sickle cell disease and diabetes.

Sickle cell disease is a genetic disorder in which red blood cells take a "sickle" shape rather than a normal disk shape, limiting blood and/or oxygen flow. It is caused when a baby inherits the sickle cell trait, a mutated gene, from both parents.³¹ Alone, the single sickle cell trait does not usually cause any symptoms but can still be passed down to children. Researchers believe that this mutation probably originated in Africa as a protective factor against malaria. The sickle cell shape triggers the spleen to

recognize infected cells caused by the malaria parasite, and eliminate them.³² This disorder can lead to a multitude of complications like stroke, pulmonary hypertension, organ damage, blindness, gallstones and pregnancy problems.³³ In the U.S., African Americans are the most common ethnic and racial group to be impacted by sickle cell disease.³⁴ Another example of genetic predisposition among ethnic and racial minorities is the diabetes type 2 among the Pima Indians. The Pima Indians have the highest rates of diabetes in the world.³⁵ Researchers believe that Pima Indians carry diabetes and obesity susceptibility genes.³⁶

Conclusion and Recommendation

Barriers to Diversity in Clinical Trials

The reasons for lack of diversity in clinical trials are many. Some stem from structural and recruitment barriers while some are due to mistrust of the system. Building trust within the medical system with ethnic and racial minorities is one of the most necessary steps. Below are some further recommendations to some of the most common barriers including insurance and accessibility, federal regulations, and recruitment efforts.

Insurance and Accessibility

- The Affordable Care Act (ACA) ensures that private insurers cannot deter patients from participating in federally funded trials, limit or deny routine

costs, or increase costs because of trial participation. This coverage needs to be expanded to allow for Medicaid to cover clinical trial expenses, likely supporting participants from low-income backgrounds.

Federal Interventions

- FDA and NIH regulators need to more strictly mandate the inclusion of minorities in recruitment and clinical trial processes like insisting on a detailed plan enforcing representative sample or subgroup analyses.
- Federal regulation should incentivize and encourage research and development in the pharmaceutical space to emphasize this issue and pursue studies that address issues among ethnic and racial minorities.
- Ensure safeguards for minorities who have been historically mistreated in research to ensure they will be protected. Many minorities distrust clinical studies because of previous unethical experiments done on racial minorities such as the Tuskegee Syphilis Study.³⁷

Recruitment Efforts

- **Inclusive Site Selection.** Clinical trials are very time consuming and expensive. To perform well and maintain funding, participants must be enrolled within a certain timeline. Site selection must shift away from choosing familiar sites that typically perform well, to sites that can reflect the population impacted by the disease being studied. Inclusive site selection must also consider the accessibility needs of different communities with various socioeconomic statuses.

- **Eligibility & Criteria.** Eligibility criteria often list comorbidities as an exclusion.³⁸ Researchers must first understand the demographics of the disease they are studying and ensure a representative sample of participants in the trial. Researchers may opt to exclude participants with comorbidities for safety precautions, but 45.4% of Americans live with a comorbidity.³⁹ Understanding the dynamics of the disease and who are most impacted will help list relevant eligibility criteria to those who suffer from the disease being studied.

- **Workforce Diversity.** Providers are heavily involved in the clinical trial process, often acting as primary investigators. Beyond language barriers, a diverse healthcare workforce is likely to provide more competent care to various cultural and socioeconomic backgrounds. Patients are more likely to trust their providers, adhere to medical plans, and experience improved health outcomes when their providers are from similar backgrounds. A diverse workforce brings a variety of perspectives and awareness to clinical research and improves patient outcomes and patient-provider trust.

- **Community Outreach and Relations.** To better share clinical trial information and opportunities among ethnic and racial minority communities, sponsors must form partnerships and alliances with trusted community organizations and community health workers (CHW). It is these organizations and CHW who can supply resources and deliver appropriate information to increase awareness

and garner trust around clinical trials.

Although the U.S. has acknowledged the need to address diversity in clinical trials, further work remains to be done. If the role of clinical trials is to ensure safety and efficacy for patients, exclusion of ethnic and racial minorities cannot be ignored. Clinical trials advance medicine, and everyone needs to be part of the advancement.

Endnotes

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