Zanteris

DIVERSITY PLANS TO IMPROVE ENROLLMENT OF PARTICIPANTS

FROM UNDERREPRESENTED RACIAL AND ETHNIC POPULATIONS IN CLINICAL TRIALS

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Our wellbeing is a combination of mental and physical health that affects our environment, biology, social policies, behavior, and significantly our lived experiences. The personal experiences of citizens in the United States differ based on their ethnicity and race, geographic location, socioeconomic status, gender identity, sexual orientation, and other socio-demographic features.

Sex, age, race, and ethnicity can all impact how different communities respond to the same vaccine or medicine. This is why diversity amongst clinical trial participants is a crucial factor. The more diverse a community of clinical trial participants is, the more we can understand about the effectiveness, efficiency, and safety of a possible vaccine or medicine for citizens now and in the years to come.

BASICS ON
CLINICAL TRIALS

The Food and Drug Administration (FDA) emphasizes the importance of clinical trials as they are vital in assessing the safety, efficacy, and value of clinical treatments and devices, including diets, surgeries, drugs, behavioral approaches, and lifestyle interventions seeking to boost people's wellbeing [1]. To account for the various experiences and exposures of different communities, clinical trials should be suitably inclusive of racial and ethnic minority communities and other groups experiencing personal disparities, which include gender, sexual minority, or socioeconomic status.

THE IMPORTANCE
OF CLINICAL TRIALS

A clinical trial is vital to generate evidence for the safety and efficacy of new interventions or treatments. Some groups of patients might react differently to specific treatment; for instance, women might respond another way than men, and members from one ethnic or racial group may react differently than those of another. Therefore, a diverse group of clinical research participants is required to help ensure that the trial population is representative of those patients who will utilize the treatment while also ensuring that the outcomes are generalizable.

Clinical trials can:

- Determine if a new intervention or treatment is safe, functional, and/or has fewer side effects than the current treatment
- Assess ways to identify an illness earlier on rather than when it is potentially treatable
- Evaluate the ideal avenue for boosting overall quality of life for those with a disease or serious medical condition
- Take account of behavioral, environmental, social, and structural interventions [1]

THE SIGNIFICANCE OF DIVERSITY &

INCLUSION IN CLINICAL TRIALS

People might experience similar illnesses differently. It is crucial that clinical trials consider the combination of living conditions and personal experiences of a community, as well as factors such as ethnicity and race, gender, age, and sexual orientation so that all individuals benefit from advances made in science.
Factors that can affect the risk and chance of developing an illness, long-term health results, and reactions to treatment include the following:

- Age
- Pregnancy status
- Biological sex
- Life experiences (negatives such as lack of basic resources and psychosocial pressure, or positives such as employment and educational opportunities)
- Unhealthy behaviors including substance abuse, overeating, a sedentary lifestyle, and risky sexual activity
- Behaviors that promote well-being such as adequate sleep, receiving recommended preventive services, a healthy diet, and physical activity
- Environmental conditions such as access to health care, nutritious foods, pollution, and neighborhood segregation
- Geographic ancestry and genetic variation
- Underlying medical issues or the presence of additional conditions or comorbidities.

Clinical trials do not always recruit those participants that represent a community heavily affected by a specific medical condition, behavior, or disease. On a general basis, these clinical trials rely heavily on white male or female participants. This lack of diversity and inclusion has created gaps in the understanding of conditions and diseases, preventive factors, and the effectiveness of treatment across groups of individuals.

These gaps in information can obstruct the quality of decision-making in health care, the capability to counsel on methods for lessening risk, optimal treatment reactions, and the creation of an efficient medication.

Researchers and clinicians must carefully consider the addition or removal of criteria from their clinical trials. For instance, a clinical study excluding participants experiencing high blood pressure or other health conditions can result in ostracizing individuals older than 65 years old, who suffer from these medical issues. The clinical test could then underrepresent a specific group of individuals and cause the outcome to become less applicable to groups who could benefit from the findings.

HISTORICAL
UNDERREPRESENTATION

Based on the article published by Pew Research Center, African Americans account for almost 13% of the U.S. population but only constitute 5% of clinical research participants. Latinos and Hispanics comprise almost 19% of the U.S. population, though make up only 1% of clinical research participants [2].

Human rights violations and historic mistreatment in worldwide research have led to modifications in the regulations to ensure that clinical research is performed ethnically where the rights of participants come first. At this point, all clinical research should follow Good Clinical Practice (GCP), a global ethical and scientific quality standard for planning and conducting clinical trials.

As part of the GCP, Institutional Review Boards (IRB) or independent Ethics Committees (EC) oversee clinical research with a focus on securing the rights, health, and wellbeing of participants. An EC or IRB is an independent assembly that:

- Considers laypeople, scientists, and doctors
- Reviews the clinical research plan, along with its design, updates, and any data given to participants
- Has the right and ability to approve, ask for modifications, or not support a clinical trial or research study
- Has foundational knowledge of the diversity of minority presented in studies

We published a pointer in addition to the years of demonstration analysis of the racial, ethnic, age, and gender disparity in our clinical research. This study acts as a vital industry guide and benchmark, as well as a baseline from which to measure progress in the coming years to further advance wellbeing equity.

At Zanteris, we are dedicated to progressing change for good by maintaining our part in creating a more inclusive future for clinical trials and by developing a foundation of trust amongst various groups and communities [3]. Ensuring diversity in clinical studies is a matter of fairness and impartiality. We are committed to designing clinical studies where enrollment can mirror the ethnic and racial diversity of the geographic locations where we where we perform clinical studies and the epidemiology of the illnesses we plan to prevent or treat. We are dedicated to addressing practical and informational obstructions in clinical study participation. That is why we are taking the following steps to meet this objective:

Embedding the significance of variation in clinical studies into the culture of our organization

Developing how we work with clinical studies sites by choosing those locations in communities which represent a diverse group of participants

Collaborating with patient support institutions to raise awareness, develop trust, and work towards eliminating obstructions to diversity in clinical trials

Offering convenience for patients to obtain essential information regarding clinical trials by offering cultural and linguistically suitable materials in several languages

Embracing state-of-the-art tools to decrease the load on volunteers by providing flexibility within a clinical trial plan, design, and state of participation [3].

ELEVEN IMPORTANT AND USEFUL TECHNIQUES THAT CAN HELP IN ENHANCING

DIVERSITY IN CLINICAL STUDIES

Increasing ethnic and racial diversity of clinical study participants is both an ethical and scientific imperative emerging from disparities in presentation, disease causality, development, access to health care, and efficiency and safety of the treatment in diverse communities or populations.

Released along with the rising, long overdue industry scientific and moral imperative for more varied clinical trial participation, the proposed plan of the FDA has the potential to be a vital propellant for more inclusive clinical research. Meaningful and sustainable transformation should be obligatory and achievable in this context of a transformed focus on equity, diversity, and inclusion. For the first time, the guidance provided by the FDA is prescriptive in telling pharmaceutical and biotech companies to construct a clinical trial plan [4].

We highlight various opportunities to boost the existing recommendations integrated into the FDA's draft control and regulation in order to optimize the improvement of clinical studies - which are as varied and inclusive as possible, and as a result,

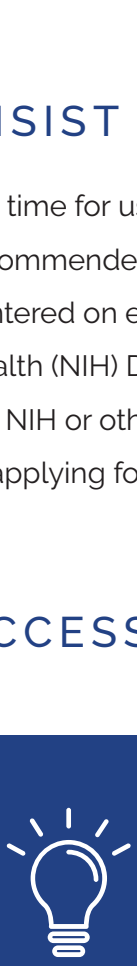
can boost patient outcomes.

The strategies below outline the parameters for shoring up more robust engagement in individuals to boost clinical research diversity. Additionally, these strategies are key to developing trust in ensuring that clinical trials better mirror patient populations.

INSIST ON RESPONSIBILITY

It is time for us to move from it is time for us to move from we should to we must. Instead of being recommended, we believe the FDA insists on the development and execution of enrollment designs centered on enhancing diversity for all Stage II through Stage IV clinical trials. The National Institute of Health (NIH) Diverse Trials Act of 2022 states that any person seeking public backing or support through the NIH or other organizations should be provided with a necessary clinical diversity plan when asking for or applying for approval [5].

ACCESS DISPARITIES AND ADDRESS HEALTH CARE



Require sponsors to give insight into how their understandings of disparity (access to genetic screening, prior treatment) have been included in the proposed plans.

CHARACTERIZE THE REAL MEANING OF A DIVERSE POPULATION

Recent guidance by the FDA shows that a diverse population is inclusive of all populations as characterized by demographic factors such as ethnicity, race, gender identity, sex, lactation status, pregnancy status, age, and the presence of specific clinical features like multiple medical conditions [6]. Given this broad meaning, including nonclinical considerations such as socioeconomic status, geographical location, language, disability, and greater specificity associated with clinical factors like genetic profiles, concomitant treatments, and organ dysfunction, stakeholders require knowledge around the safety and efficacy of medical items or medicines in natural world environments.

SET ENROLLMENT OBJECTIVES

The recent FDA guidance suggests that sponsors should identify enrollment objectives for underrepresented ethnic and racial participants as early as possible in clinical expansion for a given indication [6]. At Zanteris, we believe that it is vital to take this a step further. Enrollment objectives should be accompanied by an explanation of how enrollment objects were determined, which considers quantitative as well as qualitative assessments that assist in connecting enrollment objectives to illness epidemiology.

CLINICAL TRIAL SITES IN UNDERSERVED GROUPS

Establishing research sites where participants presently receive medical attention, considering non-traditional locations such as community health centers and pharmacies, can also assist in improving diversity in a clinical trial.

CREATE A DIFFERENT POOL OF STAFF AND INVESTIGATORS

Ethnically and racially supportive staff and investigators who represent the group or community in which they serve are key ambassadors for clinical studies. They can assist in ensuring trials are ethnically competent and mindful of implicit and unconscious bias.

CREATE LONG-TERM CONNECTIONS AND INVEST IN THE PEOPLE

Community-based clinical trial infrastructure stakeholders must prioritize sustainable and long-term community-building efforts, such as investing in health learning or building the next generation of health investigators and practitioners.

ENGAGE IN DISCUSSIONS

Sponsors must communicate and progress towards a collective understanding with individuals regarding the significance of volunteer participation in clinical trials. They should commit to clear engagement and transparency throughout the process from clinical trial design through the desired endpoints and outcomes of the clinical trial. Additionally, they should seek input regarding the design elements which may influence an individual's capability to join or participate in the trial.

SUSTAINABLE SUPPORT AND STANDARDIZED PLATFORMS

Developing a foundational data infrastructure that influences and controls factual world information could help facilitate health investigators in identifying and recruiting patients fit for clinical studies and should consider baseline measurements to boost data on ethnicity and race.

ENROLLMENT AND RETENTION TECHNIQUES

In a position to the suggested range of guidance, the FDA requests an explanation of special trial enrollment, as well as retention techniques. This is a realistic opportunity to make a connection to additional guidance previously published such as, "Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs," and Section VI of the FDA's Patient-Focused Drug Development Guidance series - which provides important considerations for recruiting individuals from diverse cultures or those with unique physical, sensory, intellectual, and communication capabilities.

SETTING MISTRUST IN A HISTORICAL CONTEXT

We entrust the recognition of the FDA of mistrust amongst the underrepresented population in the clinical study via this declaration: "In addition, distrust of the clinical trial system might come from past events, which unfavorably impacted racial as well as ethnic minorities, which takes account of the unprincipled Tuskegee experiments." On the other hand, we are concerned that a reference to Tuskegee alone could have a harmful and even reductionist influence by casing a long narration of unethical trial practices toward many underserved subpopulations, such as the Indigenous, Latinx or Hispanic communities through one egregious study. It is vital for today's research populations to understand the various historical origins which have generated distrust, in order to pave more diverse trails to inclusive clinical research.

Developing trust and improving opportunities for various individuals to participate in clinical studies are key steps in improving medical equity.

WHY LACK OF DIVERSITY MAY
LEAD TO CLINICAL FAILURE

Lack of diversity in clinical trials is a scientific, moral, ethical, and medical issue. A new report from the commission shines heavily on the "critical shortcomings" in clinical trial studies conducted in the U.S; therefore, a lack of representation in clinical studies. While diversity has become increasingly crucial in clinical trials, ethnic and racial minority populations continue to be left out. However, progression has been made in the scope of integrating a better balance of women to men ratio in clinical research.

The degree of (unknown) heterogeneity in the target patient population is one of the major

challenges with clinical development in rare diseases. In fact, it is a common case in many clinical trial development programs. Often, this becomes the root cause for why studies may fail, especially during the later stages, where a more general patient population tends to be enrolled to meet guidelines. In addition to the FDA's guidance for the industry, we underscored that understanding the target patient population in all its heterogeneity and being able to target populations living with the disease earlier may help de-risk late-stage clinical development studies.

We postulated that state-of-the-art artificial intelligence (AI) can be used to inform a better, more targeted selection of patient populations to consider in clinical development programs.

COULD AFRICA BE A POWERHOUSE
IN CLINICAL TRIALS?

At this point, the majority of the African geography is made up of more than 1.34 billion individuals, and it's expected to increase to 2 billion people by the year 2038. By the year 2050, the anticipated population will be 2.5 billion.

Consisting of more than 17% of the global population with a high range of diversity and extensive disease burden at approximately 25%, the African continent can provide unique conditions suitable to conduct clinical studies.

Notably, several illnesses – particularly those described as tropical and deserted – are widespread in the developing world, including Africa. Despite the clinical advantages, this continent adds to less than 2% of the total number of clinical studies

CHALLENGES OF CONDUCTING
CLINICAL STUDIES IN AFRICA

There is ongoing investment and development in the there is ongoing investment and development within the logistics segment of Africa that is actively supported by local influences. There are national healthcare organizations, extremely motivated, skilled, there are national healthcare organizations, extremely motivated and skilled investigators, and remarkable clinical trial facilities that can be held up as opposed to the best in class worldwide.

From a lab perspective, some clinical tests are conducted overseas in central laboratories when there is, in fact, the ability to complete lab work in a variety of local nations. Central laboratory hubs placed deliberately in Africa can assist scientific overall progress and improve the skill pool around understanding illnesses.

UNDOING UNDERREPRESENTATION
IN CLINICAL TRIALS

When participants choose to engage in a clinical trial, they are serving as representatives of the community in which they come from. The decision to join in clinical research is personal and must be made in discussion with a professional health provider and their internal support network.

Advancing inclusive clinical trials or research is multifaceted and involves genomic particulars, as well as the interconnected social drivers of wellbeing. Achieving a wider range diversity, equity, and inclusion in clinical trials needs nothing less than a worldwide commitment to varied, equitable, and inclusive research, which can result in enhanced medical intervention or treatments for various communities.

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