Discrimination in Drug Development: Combating Gender and Racial Discrimination in Clinical Trials

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Discrimination in Clinical Trials

Clinical trial remain the method for determining human safety and efficacy of a new treatment or medicine. It an important part of the process of gaining better knowledge and understanding of human health and diseases as well as the development of new and effective therapies for treating theses diseases. It represents an essential component of evidence based medical research. Clinical trials are designed by groups of doctors, scientist, and other specialists.

Health care inequalities that disproportionately affect ethnic minority groups have been recognized for many decades. Congruently, the under-representation of ethnic minority groups in clinical research and trials has been, and continues to be, a major component of health care deficiencies in the United States. The underrepresentation of minorities occurs in all types of clinical research and all therapeutic areas, including those diseases that predominantly affect ethnic minorities, and the lack of diversity in drug development has become an important issue. Data from testing on patients reveals that efficacy and safety may differ among population subgroups depending on several factors, including sex, age, race/ethnicity, and genetic background (Clark et al., 2019).

Therefore, this thesis examines how social groups in the U.S have sought to combat gender and racial discrimination in clinical trials for the development of pharmaceuticals. It will address the stakeholders across the clinical trial ecosystem, including members of academia, government, patient advocacy, pharmaceutical companies, community leaders, health care providers, technology experts, and clinical research organizations (CROs) who are providing efforts to enhance or increase their diversity, equity, and inclusion (DE&I) around clinical trials and maintain open communication to overcome real and perceived barriers to clinical research participation.

Review of Research

According to the Food and Drug Administration (FDA), African Americans and Hispanics comprise 12 and 16 percent of the total US population respectively, but account for only 5 and 1 percent of clinical trial participants (FDA, 2017). In 1993 Congress passed the National Institute of Health (NIH) Revitalization Act requiring NIH-funded research to include minorities and women ("NIH Policy and Guidelines," 2017). Yet recruiting and retaining a diverse patient pool remains difficult. When clinical trial data are generated on diseases that particularly affect minority populations, the data are not necessarily applicable to all the key ethnic minorities who suffer a higher burden of these diseases. In many instances, diagnostic and therapeutic decisions that affect patients' well-being and health outcomes are based on data gathered in populations of patients not representative of the patients who will bear the consequences of these decisions.

Many studies have tried to understand the reasons why minorities are under-represented in clinical studies and there appear to be multiple barriers to participation. General agreement on the barriers to clinical trial participation, primarily include trust, access, and awareness. Surveys of racially and ethnically diverse community members suggests that the issue of trust is one of the most important and challenging barriers to overcome and is vital to clinical trial participation (Younossi et al., 2021).

This lack of trust is particularly important for African American patients as it's rooted in the legacy of the Tuskegee Syphilis studies conducted by the U.S. Public Health Service from 1932 to 1972 (McCallum et al., 2006). In those studies, nearly 400 patients with syphilis were deprived of appropriate therapy and were simply "observed" over a period of nearly 40 years to "better understand the natural history of the disease" (McCallum et al., 2006). Another example is the Henrietta Lacks' cells used for decades of research without consent. Besides that, lack of trust

is an issue with Hispanic patients who remember the oral contraceptive studies done with Hispanic women in the 1960s where researchers did not provide patients with the appropriate information about the study (Liao et al., 2012).

Strategies to diversify participation in Clinical Trials

Although research on diversity in clinical trials has revealed layers of barriers, researchers have recommended varied solutions. This report will discuss different strategies or approaches that have been adopted or implemented by the stakeholders to help combat discrimination in clinical trials and diversify participants. The main strategies that will be exploited as mentioned below with evidence found using primary sources.

Some researchers have also stressed the need for congress to pass legislation requiring inclusion of minorities in clinical trials for FDA approval of drugs and empower an Office of Minority Health within the FDA (Younossi et al., 2021). Some have advice the FDA to adopt NIH guidelines on the inclusion of women and minority population. Others propose that the NIH and academic institutions should establish and maintain an infrastructure of minority physician and patient volunteers through training or mentorship programs for community-based physicians. Many studies also evaluate community-based participatory research in which "trusted community leaders can engage potential participants before they reach the doctor's office.

Furthermore, some recommend providing annual training in Good Clinical Research Practices and Cultural Competencies. These training aimed to increase better communication, including data transparency, standardized reports, and cultural sensitivity, to promote minority participation (Younossi et al., 2021). Wallerstein & Duran (2010) noted that sustained participation

through "long- term partnership commitments" improves engagement of diverse patients. Each stakeholder group approaches the problem from its own perspective, since each viewpoint is unique.

Overcoming Barriers and Achieving Diversity in Clinical Research

Recruitment of Minority Physician

Research has shown that minority patients seek physicians of their own race, therefore engaging these doctors into trials is critical. Physicians are considered as the gateways to the patient because minority physicians practicing in the communities and neighborhoods where ethnic minorities live rapidly gain the trust of these communities and easily "bond" with their patients, who tend to trust their doctors (Coakley et al., 2012).

In effort to increase diversity in clinical trials, researchers and physician groups are connecting to raise Primary care physician (PCP) awareness of clinical trials and offer ways to share information with minority patients. There has been collaboration across the clinical trial ecosystem to produce training packages and other materials or develop a shared platform accessible to stakeholders to help train physicians. Some organizations have focused extensively on creating training for anyone who interacts with a patient, including physicians and nonclinical staff such as security guards.

Enhancing Minority Participation in Clinical Trials (EMPACT), a consortium of researchers and universities, is working to facilitate physicians' engagement in clinical trials. EMPACT's online video training course offers strategies for researchers to increase trial awareness among PCPs ("Training Course," n.d). The consortium formed the Education Network

to Advance Cancer Clinical Trials and its Pilot Education Program, in which physician trainers coached other PCPs on "feasible clinical trial discussions with patient" (Getz, 2017). Morehouse School of Medicine has partnered with Clinical Research Pathways on its new program, "Training Minority Clinical Teams: Getting New Quality Medicines to All Americans" (Pemu, 2019). The goal of the program is to encourage more minority patients to participate in clinical trials by taking trials directly to minority patient populations (Pemu, 2019). It educates minority physicians through training videos and mentoring on discussion with patients (Pemu, 2019). However, physicians alone and training video cannot effect change.

Multisector Collaborations of Biopharmaceutical Companies

Many PhRMA member companies are collaborating to align goals and develop creative partnerships that facilitate recruitment and improve retention of underrepresented patients.

taking action to identify potential leading practices to increase clinical trial diversity. They are pursing strategies around partnerships, were many have engaged with patient advocacy groups, clinical research organizations, and academia. Others are pursing efforts in the future such as collecting racial and ethnic data from real-world data; developing and implementing standardized procedures for collecting diversity data; offering training to minority students and clinical trial staff in underserved communities.

Biopharmaceutical companies, such as Eli Lilly and Bristol Myers Squibb, are incorporating more African American in clinical trials. Eli Lilly recently partnered its African American Network with Tuskegee University's National Center for Bioethics in Research and Health Care "to help ensure the African American benefit equitably from advances in health

research" (Tonneslan, 2018). To increase diversity in clinical trials, Eli Lilly is recruiting minority investigators (Eli Lilly, n.d). Eli Lilly states, "people are more likely to volunteer for a trial if the investigator speaks their native language or is familiar with their culture" (Eli Lilly, n.d). According to Eli Lilly, there has already been some improvement in minority participation (Eli Lilly, n.d).

Both Eli Lilly and Bristol Myers Squibb have collaborated with the National Medical Association and National Hispanic Medical Association to increase enrollment of racially and ethnically diverse volunteers in U.S clinical trials, and to educate physicians and patients about the importance of diversity. In 2020, Bristol Myers Squibb committed expanding health equity and clinical trial inclusion (McGrail, 2021). Acknowledging that social determinants of health perpetuate health disparities and inequities, the company has announced that it has allocated $50 million in grants over the next five years to promote disease awareness and education in underserved patient populations (McGrail, 2021).

Many pharmaceutical companies such Johnson and Johnson (J &J) and Merck, are partnering with HBCUs to offer internships to undergraduates and opportunities to graduate students from underrepresented population to conduct clinical research and learn about clinical trials (Younossi et al., 2021). These efforts to improve the future pipeline of investigators take time but are important for improving diversity in clinical trials (Younossi et al., 2021). J&J is making its TranSMART software and data-sharing consortia available in open-source format to allow for expansion of the network (Coakley et al., 2012). TranSMART enables analysis of integrated data for the purposes of hypothesis validation, and cohort discovery in translational research (Scheufele et al., 2014). TranSMART bridges "the prolific world of basic science and clinical practice data at the point of care by merging multiple types of data from disparate sources

into a common environment" (Scheufele et al., 2014). Based on discussion with key stakeholders in medical product research and regulation, EDICT (Eliminating Disparities in Clinical Trials) is working to improve diversity policy changes surrounding clinical trials.

The EDICT named unreliable transportation as a major barrier to both participation and retention in clinical trials. Continuum Clinical is indirectly involved in clinical trials. It helps clients overcome the challenges associated with conducting multinational patient recruitment campaigns (Continuum Clinical, n.d.). Continuum partnered with Lyft to provide free transportation to patients' drug trials (Continuum Clinical, n.d). For participants who cannot afford to get to the appointment, Lyft recently partnered with Axovant Sciences to provide transportation. They have served elderly women enrolled in an Alzheimer's clinical trial in California (Resendez, 2016). This novel partnership model may be adapted to serve other marginalized communities.

Government Agencies

The FDA recently released a strategic plan to advance regulatory science, aimed to increase the diversity of clinical trial participants. The agency is encouraging drug and biologics sponsors to broaden enrollment criteria and to avoid unnecessarily excluding participants (Schneider, 2020). The agency stated, "Unnecessary exclusion of participants such women and minorities may lead to a failure to discover important safety information about the drug after approval" (Schneider, 2020). In 2016, the FDA launched the Diverse Women in Clinical Trials initiative in partnership with the National Institute of Health (NIH) office of Research on Women's Health to promote clinical trial participation from women from all ages and ethnicities (FDA, 2018). The initiative includes a Partner Social Media Toolkit (FDA, 2018) that helps women, policymakers, and

researchers encourage participation in trials by women of all ages and ethnicities (FDA, 2018). For example, with the toolkit, a consumer tweeted, "Help yourself and women like you. Learn why it's important for #Hispanic women to join #clinicaltrials" to bring awareness to Hispanic women (FDA, 2018).

Since the FDA approves and regulates all drugs, its policies carry weight. In 2015, Congress initiated the Minority Inclusion in Clinical Trials Bill directing the National Institute on Minority Health and Health Disparities to implement a plan to include underrepresented subgroups in clinical trials ("H.R.2468," 2015). This bill also directs the Department of Health and Human Services (HHS) to award grants for expanding existing opportunities for scientists and researchers, and for promoting the inclusion of underrepresented minorities in the health professions ("H.R.2468," 2015). The bill is still in a House subcommittee for review ("H.R.2468," 2015). Other current regulatory policy pertaining to the mandatory inclusion of women and minorities in clinical trials applies only to NIH-funded research. There may be room to impose more regulatory action, but this could create more problems than it solves (Coakley et al., 2012).

Past exploitation of racial and ethnic groups in medical research has left a legacy of distrust, which can deter participation in clinical trials. Investigators are making a concerted effort to overcome this history of distrust. The National Bioethics Research Initiative (NBRI) has developed a project called Building Trust. Through training and educational programs, it strives to increase the participation of minorities in public health and biomedical research (University of Maryland).

The project's curricula serve minority communities, particularly those whose residents endure significant health disparities, and investigators, research staff, and health professional students (University of Maryland). The project stresses the need for transparent communication. Most importantly, the conversion must take place on a level the patient can relate to without

condescension. Going beyond a declaration and projects, the federal agencies have developed a variety of initiatives and materials to promote change which can mean the difference between life and death, and equal access to healthcare and quality of treatment (Coakley et al., 2012).

Building Trust Though Community Engagement

Stakeholders have emphasized the importance of building trust through meaningful relationships. There are several ways of building trust within a community. Community-Based Participatory Research (CBPR) is a successful means for rebuilding trust, educate patients, and raise awareness (De las Nueces, 2012). CBPR supports collaborative interventions that involve scientific researchers and community members to address diseases and conditions disproportionately affecting health disparity populations (De las Nueces, 2012).

Trial sponsors and investigators have also developed new paths to diversity by eliciting the support of trusted community leaders. One equity researcher noted that "the most effective community leader is not always the one who might be expected; it may be a church leader, a barber shop worker, and sometimes it may be a grandmother who knows everyone in the community" (Younossi et al., 2021). Several studies targeted African American participants through black churches, black community events, and beauty salons. In 2017, at the Healthy Churches National Conference of 400 people, the Association of Black Cardiologists (ABC), and Boston Scientific Corporation (BSC) raised awareness about the role churches can take to eliminate disparities and increase diversity in clinical trials (ABC, 2017). The theme of the event was, "Faith and Public Health: Leading Together to Find Solution!". Dr. Brewer of ABC promotes conversations at familiar venues, saying "when you're asked" to enroll in a clinical trial "by your pastor, or church

member, that's where the trust comes from" (ABC, 2017). Dr. Brewer also urges that they practice self-care and model healthy lifestyles, as they are influential

in their faith communities (ABC, 2017).

As noted above, community partnerships and collaborations play critical roles in the development and implementation of effective, sustainable solutions for overcoming barriers to participant diversity — particularly mistrust (Weinstein JN et al., 2017). The Yale Center of Clinical Investigation (YCCI) Cultural Ambassadors Program is one example of a highly regarded and effective community partnership. The YCCI Cultural Ambassadors Program is a partnership with Junta for Progressive Action and the African Methodist Episcopal Zion (AME Zion) Church that has resulted in broadened community participation in clinical research and increased participant diversity by linking clinical investigators directly to trusted community leaders (Weinstein JN et al., 2017). Minority participation in Yale clinical trial has gone from as low as 2% to an average of 22 to 67% (Tonneslan, 2018). Reverend Leroy Perry of AME Zion stated that the effort has not only informed and build trust with people, "it has empowered them to act" (Tonneslan, 2018).

As mentioned above, this effort demonstrates that appropriate and meaningful engagement between trusted community stakeholders (participants, patients, caregivers, patient advocacy organizations and leaders) and researchers (clinical trial sponsors, investigators, clinical research sites) can effectively address those issues (perspectives and priorities) that are important for patients, participants, patient groups, and communities — those who will be impacted by the research.

Conclusion

To combat gender and discrimination in clinical trials, research must include diverse patient pools. Improving clinical trial diversity can help improve health equity by increasing patient access to clinical trials, educate them about the potential benefits and risks associated with these studies, and improve the scientific bias and applicability of research. Although many stakeholders - FDA, pharmaceutical companies, academia, and others, have taken important steps to address the challenges of clinical trial diversity, discrimination in clinical trials is still ongoing.

Based on the strategies analyzed in this report, physicians, patient and community engagement, community partnerships, and collaborations can play crucial roles in overcoming barriers to clinical trials. As mentioned, previous disregard for individuality, and poor communication creates barriers. Building meaningful relationships is essential to effective teamwork.

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