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Dialogues on Diversifying Clinical Trials: Successful Strategies for Engaging Women and Minorities in Clinical Trials

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Abstract

There is mounting scientific evidence pointing to genetic or physiologic distinctions between genders and among racial and ethnic groups that influence disease risk and severity and response to treatment. The diverse enrollment of subjects engaged in clinical trials research is, thus, critical to developing safer and more effective drugs and medical devices. However, in the United States, there are striking disparities in clinical trial participation. To address this problem, the Food and Drug Administration (FDA) Office of Women's Health and the Society for Women's Health Research (SWHR) together convened the 2-day meeting, Dialogues on Diversifying Clinical Trials. The conference was held in Washington, DC, on September 22–23, 2011, and brought together a wide range of speakers from clinical research, industry, and regulatory agencies. Here, we present the major findings discussed at this meeting about female and minority patients and physicians and their willingness to participate in clinical trials and the barriers that sponsors face in recruiting a diverse trial population. We also discuss some recommendations for improving trial diversity through new technologies and greater efficiency in trial regulation and review.

Introduction

Since the early 1990s, the Food and Drug Administration (FDA) Office of Women's Health and the Society for Women's Health Research (SWHR) have worked toward the common goals of advancing women's health research through education, policy, and science. Together, these groups, with the support of the FDA Office of Minority Health, convened the meeting, Dialogues on Diversifying Clinical Trials, to address the need for greater representation of women and minority groups in the development of medical products. Invited speakers included representatives from the pharmaceutical and biotechnology industry, academic institutions, advocacy groups, government agencies, clinicians, and patients. Special interest brainstorming groups and a stakeholder roundtable session provided participants with an opportunity to provide reflections and new ideas.

The major themes surrounded new and novel methods for improving recruitment and retention of women and minorities, community-based approaches to clinical trial design, and federal perspectives on guidelines and regulations to improve diversity in government-funded and industry-funded research. The presentations stressed the disparate nature of clinical trial representation past and present and also highlighted successful means and methods for increasing women and minority enrollment.

Sex-Based and Race-Based Disparities in Healthcare and Clinical Trial Enrollment

Disparities in disease prevalence and risk

There are well-established differences in the incidence of disease between the sexes and among racial or ethnic groups. This meeting highlighted some of the more striking sex-based and race-based disparities in disease prevalence. The most important diseases that disproportionately affect ethnic minorities include type 2 diabetes, cardiovascular disease, stroke, infectious diseases (HIV/AIDS, sexually transmitted diseases [STDs]), and different types of cancer (colon, prostate, cervix, lung).

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Some of these variations result from genetic variants that are more common in certain subpopulations than others are; however, lifestyle and socioeconomic factors influence risk bias based on sex or race/ethnicity. For instance, women live longer and bear greater disease burden than men and require extra care for reproductive health and childbearing needs. Ethnic minority groups are disproportionately affected by poverty and low socioeconomic status (SES), which are linked to poorer health outcomes. Many racial health disparities stem from lack of access to quality healthcare and proper health awareness. Unfortunately this means that incidence of disease does not always match trial populations. For example, African Americans and Hispanics represent 12% of the U.S. population, respectively, but only 5% of clinical trial participants (P. Sanders, meeting presentation). (Classification of race and ethnicity varied throughout the conference, depending on the preference of the speaker. Unless otherwise noted, terms are interchangeable: Hispanic/Latino; African American/black; Native American/American Indian; Caucasian/white.) The numbers are even more disparate for the Hispanic population, which represent only 1% of trial participants but 16% of Americans (J. Tierney, meeting presentation). In cardiovascular device trials, sex distribution is 67% male.[1]

The Coalition to Eliminate Disparities and to Research Inclusion in Clinical Trials (CEDRICT) identified minority lack of disease education as a major barrier to recruitment. Other significant barriers to diversify enrollment, as reported by investigators and coordinators, are insurance status, patient inconvenience costs, availability of transportation, distance to the study site, and patient and family concerns about risk. However, race, age, and sex have been shown to play more significant roles in trial participation compared to proximity to trial location.[2]

There are also negative attitudes toward medical research that prevent patients from enrolling, but similar negativity is present in industry. From the sponsors' perspective, women and minority patients are more difficult to recruit, have less experience, and are relatively more costly to engage. In addition, minority patients with limited English proficiency can require costly translation services. National Institutes of Health (NIH)-funded studies have specific diversity requirements, but aside from FDA recommendations, there are no regulations currently in place that require industry sponsors to include women and minorities in their trials. Diversity is not a natural priority for industry, where decisions often are made by market attractiveness and potential for profit.

Implications of lack of diversity in clinical trials

Sex differences are observed in response to many drugs.[3] Females have a 1.5–1.7-fold greater risk of developing an adverse drug reaction, and several drugs have been withdrawn from the market over the last two decades because of sex-based adverse events.[4] Medical devices are particularly subject to gender bias, based on the significant physical differences between men and women. With regard to race and ethnicity, a number of studies have found variations in drug metabolism and toxicity in chemotherapy,[5] antiretroviral agents,[6] immunosuppressant drugs,[7] and cardiovascular medications.[8]

Successful Strategies for Diversity

Recruit female and minority physicians

The first step in engaging women and minorities in clinical trials is finding them. Research has shown that minority patients seek physicians of their own race, so bringing these doctors into trials is critical. Physicians are the gateway to the patient. There are a number of organizations dedicated to training female and minority investigators to increase their participation, including the National Clinical Trials Network, National Minority AIDS Council, Project Increase Minority Participation and Awareness of Clinical Trials (IMPACT, initiated by the National Medical Association), and the National Hispanic Research Network. Some pharmaceutical companies are also taking their own initiatives.

Build trust through communication

Many racial and ethnic groups have been exploited in medical research in the past, so they are often hesitant to participate. Investigators must make a concerted effort to overcome this history of distrust. The National Bioethics Research Initiative, Building Trust Between Minorities and Researchers, is working to assess the experiences and attitudes of African Americans and Hispanics toward medical research.

Throughout the meeting, many speakers stressed the need for transparent communication. Sponsors must demonstrate the importance of the trial and the potential benefits for the patient and his or her community. All patients, not just minorities, want to feel that they are valued and appreciated. Most importantly, the dialogue must take place on a level the patient can relate to, without condescension. Cultural sensitivity is also important when engaging minority communities. This is particularly critical in the American Indian and Alaska Native (AI/AN) communities, who often have cultural traditions or religious beliefs that conflict with modern research methods.

Educate to raise awareness

Lack of health awareness and disease education in underserved populations means they often do not (1) recognize the signs and symptoms of disease, (2) recognize the importance of treatment, (3) readily seek or comply with treatment, and (4) know or understand their treatment options or the possibility for clinical trial enrollment. Patients must be empowered to demand quality healthcare and have all the information needed to make their own decisions about their treatment.

Physicians need to be educated as well. They not only must be made aware of trials but also must fully recognize sex-based or race/ethnicity-based differences in disease prevalence or symptoms. For example, a study found that only 17% of cardiologists correctly identified women as having greater risk for heart disease than men.[9] Project IMPACT uses education to increase awareness, knowledge, and participation for both minority patients and physicians to overcome the barriers to minority enrollment. They also train investigators on trial ethics and regulation and the business aspect of clinical trials participation.

Involve communities

One particularly successful means for building trust, educating patients, and raising awareness is through

community-based participatory research (CBPR). Trial sponsors and investigators are developing new paths to diversity by eliciting the support of trusted community leaders. In this way, they can engage potential participants before they reach the doctor's office. A number of studies targeted African American participants through black churches, barbeques, community events, barbershops, and beauty salons. Eli Lilly is engaging community support through a Latino Advisory Board to help in their recruitment efforts, and CBPR approaches in AI/AN communities have sought approval from tribal leaders to legitimize their efforts. Other success stories include the Gender, Race, and Clinical Experience (GRACE) study, SisterTalk Hartford, the Healthy Black Family Project, Project IMPACT's Alliance for Clinical Trial Trustworthiness in Our Neighborhoods (ACTTION) plan, and the Stop Atherosclerosis in Native Diabetics (SANDS) trial.

Recommendations

Investigators and sponsors can learn from the effective recruitment efforts of the groups represented at this meeting. Many of the strategies are applicable across a wide range of studies, and each success story has provided some insight into the critical aspects surrounding women and ethnic/racial minority enrollment. Beyond these examples, there are broad changes to be made that have the potential to radically transform the face of clinical trial research beyond simple changes in recruitment methods.

Reexamine trial design and ethics

Improving trial diversity must begin at the design stages. Studies with single-sex cohorts, such as the Women's Health Initiative (WHI) and the Women's Ischemia Syndrome Evaluations study (WISE) have been successful. The Zip Code Analysis Project revealed that 80% of minorities reside in 20% of U.S. Zip codes.[10] Sponsors can use this information to carefully select trial sites based on geographic distribution of ethnic/racial minority patients and physicians, keeping in mind the prevalence of the disease in that region.

The Eliminating Disparities in Clinical Trials (EDICT) Publications Working Group identified the possibility to influence trial design and diversity through more stringent requirements for population diversity in scientific publications. If journal editors and reviewers begin to demand change, the research establishment will follow.

Ethics must adapt in time with technologic advances. Current ethical standards for informing patients and gaining consent are not adequate in communities with limited English proficiency or that have cultural traditions that conflict with certain scientific methods. Genomics, in particular, will undoubtedly present difficulties and not just for ethnic/racial minorities. Community-driven strategies that emphasize collaborative efforts throughout the community and with investigators will ensure that both parties fully understand ethical and regulatory guidelines.

Foster multisector collaborations

Biopharma industry leaders, such as Eli Lilly and Johnson & Johnson (J&J), are already making strides in collaborating across sectors. They are both working with the National Medical Association and National Hispanic Medical Association, among others. J&J is making its TranSMART software and data-sharing consortia available in open-source format to allow for expansion of the network. EDICT is working to improve diversity policy changes, which they are acting on based on their discussion with the key stakeholders in medical product research and regulation.

Incorporate new technology

Technology offers many tools, and scientists need to think outside the box and use everything at their disposal. Collaborations with the IT industry will be critical in facilitating collection, storage, access, analysis, and security of patient information and trial data. This is especially true if the data are to be used effectively in analysis of the effects of race/ethnicity or sex/gender on clinical outcomes. The implementation of data standards across research bodies, industry, and regulatory agencies will increase speed and efficiency and facilitate data interpretation across platforms.

There is massive potential for web-based direct-to-participant (D2P) venues to revolutionize clinical trial research. Giving patients access to trials within the convenience of their own homes reduces overhead costs and eliminates geographical barriers, transportation costs, and scheduling difficulties. The National Clinical Trials Network Database of disease maps and physician information will help sponsors to advertise their trial, locate investigators, and pinpoint locations for trial sites in order to target populations most affected by the disease.

Adapt to the changing face of medicine

The changing face of medical research and development, from a blockbuster drug model to stratified medicine, could put the economic health of innovative biotechnology and the medical product industry at risk. Clinical trials are failing in greater numbers than ever, and the lack of return on investment could break the cycle of financial investment in drug research. Future research grants are also influenced by outcome trends. For instance, immunologic therapies and codevelopment of drugs and diagnostics are becoming more popular based on the successes of Herceptin® and Gleevec®.

As the field of genomics rapidly progresses, gene-gene interactions and subtle variations among racial groups could play a significant role in selecting treatment options with the most potential for success. Although the movement toward personalized medicine is an exciting prospect, there are warnings against overestimating the value of genetics, as the information is not fully valuable until it is compared against phenotypic data and outcomes. Clinical trials will have to analyze the data accordingly for greatest success.

Increase efficiency in regulation and review

FDA has recently released a strategic plan to advance regulatory science, which it believes is critical in creating a more cost-effective design for drug development.[11] FDA is working with industry to see how it can help American businesses confront challenges in the global market and stay in the United States. FDA can work on cross-training and educating small business leaders while still maintaining the necessary firewalls for being a regulator and protecting public health. Institutional Review Boards were accused of

sometimes stepping beyond the scope of their purpose and creating redundant paperwork and review standards.

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. Ideally, industry as a whole will catch on to the value of diverse trial enrollment without the need for new regulatory guidelines. Eli Lilly and others are already making efforts to stratify data by subpopulation.

There is much to consider in diversifying clinical trial enrollment, but the outlook is promising. The changing face of medical product research and development and technological advancement, coupled with a rapidly evolving population, means exciting times are ahead. The entire field will have to anticipate change and adapt accordingly. Access to clinical trials can mean the difference between life and death, and equal access to healthcare and quality of treatment will benefit all.

Disclosure Statement

The authors have no conflicts of interest to report.

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