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Barriers to Increased Participation of Minorities in Clinical Trials

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Clinical trials are at the heart of the process for bringing new medicines to patients. One of the most critical aspects to the conduct of any clinical trial is identifying the right group of people to include in the study. Unfortunately, many of the clinical trials conducted in the United States suffer from a lack of diversity, with minority populations being consistently underrepresented. In addition, there is often a lack of consideration of cultural and genetic factors which are particular to Asian, African-American, Hispanic, and other minorities that may influence results. This ethnic diversity gap can lead to less than ideal development of new medicines and can further exacerbate minority health issues.

In 2015, a study published in the journal of PLoS Medicine[1] concluded that biomedical research often does not reflect the American population. Sam Oh, an epidemiologist at the University of California, San Francisco Center for Genes, Environment and Health and researcher on the study recounts an example uncovered in the research. In a recent interview,[2] Oh states that “African-Americans and Puerto Ricans don’t respond as well to some of the most common asthma controller medications, and that’s really a tragedy since these two groups are the most affected by asthma in the United States.” Coming across disparities like the asthma example, Oh says, “you begin to wonder, ‘Well, why is this the case?’ And part of that reason might be because our biomedical studies in the past have not recruited as heavily in those populations.” Such findings are common across many therapeutic areas. For example, the study reports that, “Only 2% of cancer studies and less than 5% of pulmonary studies have studied enough minorities to provide useful information.”

In response to this issue, the Food & Drug Administration recently launched the first phase of a campaign to encourage minorities to participate in clinical trials. In a recent blog post, Jonca Bull, FDA’s Assistant Commissioner for Minority Health, Office of Minority Health, called for minorities to be “clinical trial champions,” and explained why it is critical to for the agency to encourage minority participation: “Clinical trials participants need to more closely mirror the patients who will ultimately use the medicine,” Bull writes. “This is especially important when considering health disparities - diseases that occur more frequently or appear differently in non-white populations. But most clinical trials participants are white and male... If we do not develop a more diverse pool of research participants, health disparities may persist because we will not know if a medical product is safe and effective in the actual population that will ultimately use it.”[3]

The Minority and Gender Gap in Clinical Trials

The National Institute of Health (NIH) Revitalization Act of 1993, passed by Congress and signed into law by President Bill Clinton, required that all NIH-funded medical research include women and minorities. Even though this act was passed 23 years ago, both gender and minority disparities remain in clinical trial participant populations. Minority groups include American Indian or Alaskan Native, Asian, Native Hawaiian or Pacific Islander, African American, and Hispanic. US 2015 census data shows that minorities currently make up around 40% of the US population.[4]

A 2013 NIH report, however, indicates that minorities only represent around 30% of those enrolled in domestic NIH clinical research. Broken down into individual minority groups, it is clear that there is still work to do in order to have clinical trials more closely match the population at large, particularly with regard to the Hispanic population.[5]

While the NIH appears to have made some progress in the inclusion of minorities in clinical trials, the picture outside the NIH is more bleak. One report found that Hispanic representation in industry-sponsored clinical trials may be as low as 3%.[6]

In addition, according to a 2011 report from the conference “Dialogues on Diversifying Clinical Trials,” sponsored by FDA’s Office of Women’ s Health and the Society for Women’s Health Research and supported by the Office of Minority Health (OMH):

- African Americans represent 12% of the U.S. population but only 5% of clinical trial participants
- Hispanics make up 16% of the population but only 1% of clinical trial participants[7]

According to John Lechleiter, Chairman, President and Chief Executive Officer of Eli Lilly and Company, the ethnic diversity gap is even worse when you look at clinical trials aimed at diseases disproportionately affecting minority communities. “African-American men are twice as likely as their white counterparts to die from prostate cancer. Yet they represent just 4% of prostate cancer clinical trial participants. Suicide is one of the top three causes of death among Asian-American women under 45 years of age; this cohort constitutes just 1% of trials for potential treatments for major depressive disorder. And while the prevalence of diabetes among Mexican-Americans and Puerto Ricans is more than double that of Caucasians, those groups combined represent just 4% of diabetes trial patients.

Table 1.

Minority Group	US Census Data (%)	% enrollment in domestic NIH clinical research (FY2012)
Hispanics	17.6	8.4
African Americans	13.3	11.1
Asians	5.6	6.9
American Indians	1.2	0.8
Pacific Islander	0.2	0.4

With regards to gender, the above-mentioned 2013 NIH report showed percent enrollment by gender in all NIH clinical studies, excluding male and female only studies, to be split evenly at 49% each in FY2012. Yet, there are some areas where a clinical trial gender gap remains. The 2011 FDA report mentioned above stated that men make up more than two-thirds of the participants in clinical tests of cardiovascular (heart and blood vessel) devices. In addition, a recent editorial in the British Journal of Sports Medicine, for example, cites a study from 2014, where researchers reviewed nearly 1,400 sports and exercise research studies involving six million people over three years. Those researchers found that only 39% of those study participants, just slightly more than a third, were women. The scientists who authored this editorial claimed that researchers have been excluding women from sports and exercise research studies due to “complexities of the menstrual cycle” and the consequent potential interference of fluctuating female hormones. Unfortunately, this kind of approach does not promote understanding of how real world hormonal fluctuations would affect trial outcomes.[8]

Consequences of the Minority and Gender Gap in Clinical Trials

This clinical trial diversity problem can have serious consequences, as effectiveness of a particular medication or medical device can vary depending on ethnicity and gender. Certain blood pressure drugs (beta blockers, angiotensive converting enzyme (ACE) inhibitors, and angiotensin II antagonists), for example, don’t work well for many African-Americans. If there are no African Americans in the clinical trials to approve these drugs, then these kind of efficacy exceptions will not be caught, and doctors won’t get the data they need to customize treatments for diseases disproportionately affecting minority populations. In addition, some studies have shown that women are twice as likely to suffer from adverse reactions to drugs, and 80 percent of drugs are withdrawn from the market due to unacceptable side effects in women.[9]

Increasing the participation of all minorities and women in clinical trials is critical for the production of knowledge about new therapies, because having diverse research participants can improve the generalizability of medicine. Additionally, minority participation in clinical trials is an important topic in public health discussions because this representation touches on issues of equality and the elimination of disparities, which are core values of the field.

The bottom line is that in order to clinical trial participants need to reflect the populations who suffer from the disease being investigated. It is therefore important to include in drug development an accurate representation of the broad range of patients who will eventually receive the drug, including people of both genders, representatives of major racial/ethnic groups, and patients with a wide range of disease severity, concomitant illnesses, and use of concomitant treatments.

Causes of the Minority Gap in Clinical Trials

Trust, or the lack of it, is one barrier to increased participation. Many minorities have had less than excellent cultural experiences which have made them distrustful of authority figures. Minorities are thus often wary of sharing the most intimate details of their health in a clinical trial setting. Many minorities simply haven't learned about the vital role these trials play in creating new treatments and cures.

There can be other concrete matters that hinder participant diversity. Sometimes trial materials haven't been translated into a minority's native language, or may be somewhat insensitive to their religious beliefs. Transportation to and from clinical sites can be prohibitively expensive or even unavailable for some potential participants, while others simply can't afford to miss work. In addition, sponsors repeatedly run trials in large city hospitals, not small community hospitals that can't support clinical trials, but where many minority patients seek treatment. Sometimes, doctors don't invite minorities, making assumptions based on institutional bias, that all minorities lack funds, compliance, transportation, and a desire to follow through.

Finally, studies show that minority patients are more comfortable selfreporting to minority, rather than non-minority, doctors. Yet, in 2010, out of 13,000 oncologists, only 3% were black and 7.5% Hispanic, according to the American Association of Clinical Oncology.

Solutions to the Minority Gap in Clinical Trials

In addition to the FDA, other groups are coming forward to close the minority gap in clinical trials. Eli Lilly and The Center for Drug Development and Clinical Trials at Roswell Park Cancer Institute in Buffalo, New York developed a program in 2013 to train minority doctors to become principle investigators, based on the notion that recruiting minority physicians to care for minority communities will increase cultural comfort with clinical trials. The partnership has resulted in an annual 3-day workshop, "Reducing Cancer Disparities Through the Training of Diverse Workforce," which trains minority oncologists in research and trial design for underserved populations in order to become principal investigators, with the intention to reduce cancer health inequalities among minorities. The program provides continued mentorship with the workshop faculty for participating physicians and, according to Vun-Sin Lim, M.D., research associate at Roswell Park, enhances collaboration among participants, who can pass their training on to other physicians. "The result," says Lim, "is better patient care."

The National Minority Quality Forum (NMQF) is also attempting to fill the diversity discrepancy. NMQF is a nonprofit research and educational organization focused on improving healthcare to high-risk ethnic populations by integrating data and expert initiatives to eliminate health disparities. "We have billions of patient records to

help us understand who and where populations are that have diseases, and rare diseases that hit Americans," says Gary Puckrein, Ph.D., president and chief executive officer. Between the years 2000-2014, NMQF collected data on how many people at specific ZIP codes had particular diseases, such as diabetes, HIV, and hepatitis C, and who treated them. Sponsors can now use this data to help facilitate trial recruitment. In addition, NMQF and the Pharmaceutical Research and Manufacturers of America (PhRMA) launched "I'm In," a national education program designed to engage underrepresented populations and communicate the value of clinical trials. This program also connects with prominent local figures and care providers to encourage minority patients to enroll.

Conclusion

The importance of diversity in clinical trial participants has been known for some time. Yet a minority, and sometimes a gender, gap still remains a major issue – a problem we can only expect to increase in magnitude as medicines become more precise and tailored to individual genomes. Increasing the participation of all minorities and women in clinical trials is vitally important in order to generate knowledge about new therapies and improve the generalizability of medicine. Increasing minority participation in clinical trials should be a top priority throughout the health care system.

Fortunately, steps are being taken by a variety of industry stakeholders in order to effectively close the diversity gap in clinical trials. But in order to close the diversity gap, we need more companies and public agencies to throw their weight behind initiatives like these. These steps will help the industry to more effectively develop medicines, to diminish minority health disparities and to achieve a stronger overall public health benefit.

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