Principles

Background:

The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center) convened a multi-stakeholder working group to develop comprehensive resources aimed to clarify the importance of, advance the goals of, and provide practical and applicable ways to improve diverse representation of participants in clinical research. This work included a set of fundamental principles that help to frame considerations of diverse representation in clinical trials, found here.

While we recognize that a case-based analysis will be required for each clinical research question, we also believe that these principles will help guide those analyses. The accompanying MRCT Center Guidance Document and Toolkit can be found at www.mrctcenter.org/diversity-in-clinical-trials/

Principles:

3.1 Efforts to ensure diversity and inclusion in clinical research endeavor to be responsive to the ethical principle of justice by promoting greater fairness in the distribution of the benefits and risks of the research[1].

The clinical research enterprise—and healthcare – should endeavor to distribute the risks, burdens, and benefits of research fairly and responsibly. The health needs, and responses to interventions, of populations and individuals can only be identified, considered, and managed if those populations and individuals are represented and studied.

3.2 Race, ethnicity, sex, gender, age, and geographic ancestry do not define distinct genetic or biological groups; yet along with social, cultural, and economic factors, these factors can be associated with important differences in disease susceptibility and manifestation, treatment response, and rates of inclusion in clinical research.

Efforts to understand biologic variability and the complex contributions of social determinants of health, disease burden and progression, access to clinical trials, and treatment outcome require careful and diligent study. Approaches for determining and collecting relevant variables for a given disease, condition, diagnostic or therapeutic product, or intervention are necessary.

1 United States. National Commission for the Protection of Human Subjects of Biomedical, Behavioral Research. The Belmont report: ethical principles and guidelines for the protection of human subjects of research. Department of Health, Education, and Welfare, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research; 1978.

Principles

3.3 Enhancing diversity and inclusion in the clinical research enterprise serves to advance biomedical science and healthcare and may help reduce health disparities.

Diversity and inclusion in clinical research aims to identify subpopulation variability in diagnosis, treatment, and prevention. Diversity and inclusion also serve to broaden the knowledge base and may identify important group-specific efficacy and safety signals prior to approval of investigational products. Clinical research in which participants reflect the diversity of the intended population for treatment or intervention is better positioned to develop effective treatments for those most likely to use them. A greater understanding of the barriers that negatively impact diversity and inclusion in research is needed so that data supporting future medical innovation better reflect the intended populations of the intervention.

3.4 Appropriate inclusion of diverse populations requires action by, and should become the expectation of, all relevant stakeholders across the continuum of drug development and clinical research involving human participants.

Efforts to achieve enhanced and representative diversity require consideration of complex scientific, organizational, social, and cultural factors, and intrinsic biases. Progress requires engagement, commitment, and accountability by all stakeholders, including sponsors, research institutions, investigators, patients and their advocates, regulatory agencies, oversight bodies and others.

3.5 Refinement in methodology and data analytic tools is necessary to achieve the aims of increased diversity and inclusion.

Development and adoption of common standards, methodologies, and successful strategies will require global collaboration across stakeholders and scientific disciplines and are necessary to advance medicine and public health.

3.6 Advanced and innovative approaches, including use of real world data, may more readily detect differences across groups than can be achieved by individual clinical trials alone.

The size, time, and resource requirements of clinical trials typically preclude their use to detect small but potentially significant differences across all populations of interest. New research paradigms using real world data, curated data sources, machine learning, bioinformatics, and robust analytics are necessary.