ADVANCING EQUITY, DIVERSITY, AND INCLUSION IN CLINICAL RESEARCH

Every year on May 20th the Alberta Clinical Research Consortium (ACRC) joins in celebrating International Clinical Trials Day (ICTD) to help raise awareness of the value and importance of conducting clinical trials, with a spotlight on the benefits to Albertans. This year, we are focusing on a long-standing issue that was highlighted during the research and development of the COVID-19 vaccines - the need to enhance equity, diversity, and inclusion in clinical research. We want the research community to understand why this is important and what can be done to overcome the challenges associated with enrolling and retaining underrepresented racial and ethnic groups for clinical studies. We also share FDA's recent recommendations, as well as information on local organizations who can provide guidance and support to researchers.

Diversity in Clinical Research is an Imperative for Health Equity

Clinical research is necessary for generating evidence to prove the efficacy and safety of new therapies. In response to the pressing need to address healthcare disparities, there have been growing calls to the clinical health research community (including academic organizations, health system managers, researchers, clinicians, clinical research organizations, patient advocacy groups, community leaders) to enhance equity, diversity, and inclusion efforts - to allow for more well-rounded assessment of the impact of new therapies on different ethnic and racial groups. Undoubtedly, diversity in clinical research is necessary for advancing health equity, and this was aptly demonstrated and highlighted during the COVID-19 pandemic as racial and ethnic minorities were disproportionately affected across the world.[1]

Historically, clinical health research studies have often been criticized for enrolling homogeneous populations that do not accurately represent real-world communities. A 2020 report from the US Food & Drug Administration (FDA) about global participation in clinical trials[2] revealed a huge difference between enrolled participants and the global population. Out of 292,537 trial participants worldwide, 76% were White, 11% Asian and only 7% were Black; in comparison, to a global population of just over 7.8 billion people, where 60% are Asian, 16% are African, 10% are European and 8% are Latino (World Population Review). Similarly, review of the 379 clinical trials funded by the US National Institute of Mental Health and published between 1995 to 2004, it was revealed that all racial or ethnic groups except White and African American populations were under-represented.[3]

It is well established that study populations should mirror the characteristics of the population that will eventually use the intervention or approved therapy, to ensure that results are generalizable.

[1] Sharma, A., Palaniappan, L. (2021) Improving diversity in medical research. Nat Rev Dis Primers 7, 74

[2] Clinical study/trial: A type of clinical health research that is designed to assess the effect of a biomedical intervention (e.g., drug, device, cognitive-behavioral, process, diagnostic test, etc.). Clinical trials can take the form of a prospective cohort study, a prospective case-control study, or a randomized controlled trial. Clinical trials are incorporated into and an inextricable part of advanced clinical care (ACRC Glossary and Common Terminology Version 5.0).

[3] Mak, W. W. S. et al. (2007) Gender and ethnic diversity in NIMH-funded clinical trials: review of a decade of published research. Adm. Policy Ment. Health 34, 497–503.

Subgroups of patients may respond differently to interventions and therapies. Additionally, ethnicity, age, gender, genetic disposition, and lifestyle may affect how a treatment will work or how safe it will be to an individual. Differences in treatment outcomes and disease biology among subgroups, if they exist, can only be identified when those subgroups are present and are included as research participants. Without representation, the resulting treatment(s) may be less effective or less trusted in those groups despite their need for such a treatment. For example, 5-fluorouracil, a commonly used chemotherapeutic drug, was found to have adverse effects, like hematological toxicities, in some individuals.[4] These toxic effects occurred at higher rates in African Americans compared to White individuals. However, this was not observed in the preceding clinical trials, which had limited patient diversity, and this ultimately impacted the healthcare of some African Americans. Ethical obligations - particularly fairness in the distribution of the opportunities and potential benefits of health research, also drive the expectations for diverse participant inclusion in clinical research.

For these reasons, enhancing meaningful representation of diverse or under-represented populations in clinical research to overcome long-standing inequities in healthcare and patient outcomes requires the commitment of the research community.

Challenges to Racial and Ethnic Diversity in Clinical Research

There are a variety of reasons for the reduced participation in clinical trials among diverse racial and ethnic groups including: mistrust of the clinical research system due to historical abuses; transportation and participation conflicting with family or work responsibilities, frequency of study visits, time and resource constraints for participants, language or cultural barriers, health and research literacy challenges; religious beliefs, and stringent eligibility criteria (e.g., exclusion due to comorbidities, which are often more prevalent in underrepresented populations due to exposures to systemic discrimination). Provider-associated barriers have also been identified including: decreased funding and staffing levels for clinical trial sites where underrepresented patients are likely to receive care and staff failing to inform patients of clinical trial availability. Physicians have many competing clinical priorities and payment systems often do not account for the extra time necessary to identify appropriate trials and educate and enroll patients. The above obstacles are particularly problematic for patients from under-represented minority groups who may not independently seek to enroll in clinical trials.[5]

The FDA, and Others Provide Guidance on Enhancing Diversity in Clinical Research

Increasing clinical trial diversity in an effective and sustainable manner requires the joint efforts of stakeholders across the clinical research ecosystem. The FDA, in November 2020, issued a guidance document on Enhancing the Diversity of Clinical Trial Populations. The document provides a range of steps that sponsors, and research sites can take to facilitate the participation of the population most likely to use the drug if approved.

[4] McCollum, A. D. et al. (2002) Outcomes and toxicity in African American and Caucasian patients in a randomized adjuvant chemotherapy trial for colon cancer. J. Natl Cancer Inst. 94, 1160–1167

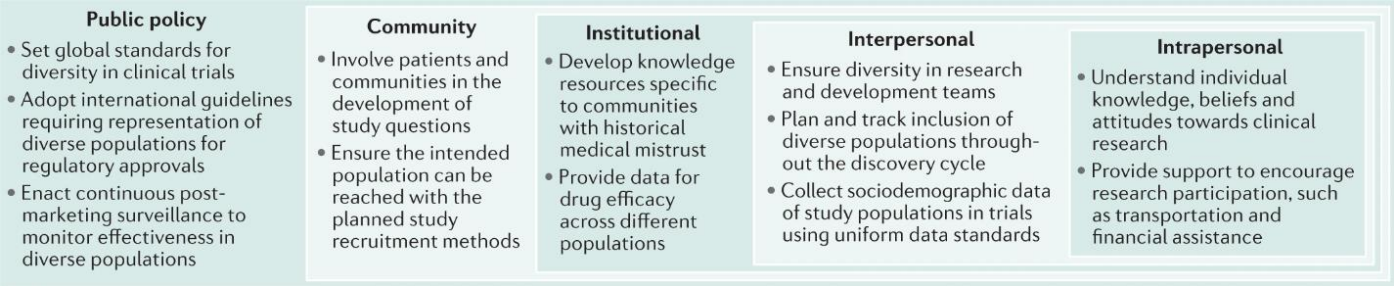
[5] Improving Diversity in Clinical Trial Participation Policy Brief 2020 (asco.org)

Recommendations include broadening eligibility criteria to increase diversity, adopting enrollment practices that enhance inclusiveness, and considering trial designs that make participation less burdensome.

A follow-up guidance from the FDA in April 2022 specifically provides recommendations to sponsors developing medical products on how to submit a "Race and Ethnicity Diversity Plan" to enroll and retain adequate numbers of participants in clinical trials from underrepresented racial and ethnic populations. The FDA encourages submission of the plan as early as possible during the investigational new drug (IND) stage, and before launching pivotal Phase III studies.

A framework for enhancing diversity in clinical research was also presented in 2021 by researchers from Stanford University School of Medicine.[6] The authors described how changes to public policy, community, institutional, interpersonal, and intrapersonal domains can be used to increase diversity in clinical research (Figure 1). For instance, at the public policy level, strict requirements for representation of diverse populations can be set as a necessity for the approval of new drugs or devices. At the institutional level, knowledge resources must be developed specifically for communities with historical clinical research system mistrust.

Figure 1: A framework for improving diversity in clinical research[6]



More Information, Guidance and Support for Researchers

The Alberta SPOR SUPPORT Unit (AbSPORU) collaborates closely and purposefully with patients from diverse communities and with its network of healthcare partners to improve health outcomes for all Albertans. AbSPORU's Patient Engagement Team builds community partnerships and research collaborations to enhance health research opportunities and improve health outcomes in the province. With their partners, they combine efforts to better hear and include diverse Albertan voices in the health research that matters to them. Their partners include, Alberta Health Services (AHS), Strategic Clinical Networks (SCNs), community organizations, rural networks, patient groups, post-secondary research institutions, among others across the province.

[6] Sharma, A., Palaniappan, L. (2021) Improving diversity in medical research. Nat Rev Dis Primers 7, 74 https://doi.org/10.1038/s41572-021-00316-8

Researchers can connect with the AbSPORU's Patient Engagement Team to learn more about how you can enhance the participant diversity in your clinical health research projects.

Be The Cure is another provincial initiative where patients can search for current opportunities to participate in research studies and clinical trials being conducted in Alberta, based on the searched disease/disease area. Physicians can share this initiative with their patients, and review opportunities for underrepresented minority groups who may not seek to enroll in clinical trials independently.

The Alberta Clinical Research Consortium (ACRC) co-created with our Patient Partner Advisory group this guidance document, which also lists a variety of local, national and international resources on how patients can find opportunities to participate in clinical health research.