



Approaches to **Increasing Diversity** in Clinical Research and Addressing Health Inequities



AdvaMed

Advanced Medical Technology Association

Background and Goals

Starting in 2020, the global COVID-19 pandemic heightened the awareness of existing health disparities within the United States (US) healthcare system. Research has shown that people of color are less likely than white patients to have access to certain medical technologies, or undergo procedures that use medical technologies, than white patients.¹ People of color – especially Black people – are statistically more likely to suffer from a wide range of chronic and infectious diseases and other health conditions, including cardiovascular disease, stroke, diabetes, kidney disease, cancer, and chronic lower respiratory disease. These diseases are some of the leading causes of death and disability in the United States.²

The medtech industry, at its core, exists to ensure patients have access to safe, effective, and innovative medical technologies that save and improve patient lives. The medtech industry has an important role to play in ensuring health equity and mitigating health disparities as we make the technologies and tests that result in the accurate diagnosis of disease and in improved patient outcomes for all patients. The Advanced Medical Technology Association (AdvaMed) launched the Responding To Racial Disparities In Health initiative in 2020 and laid out a set of four [Principles on Health Equity](#) to promote inclusion and equity in healthcare and research in the medtech industry.

Generating evidence on medical technologies is critical for regulation, market access, and clinical adoption. AdvaMed partnered with Meharry Medical College on a workshop series convened in April, May, and June of 2021 that focused on increasing diversity in clinical trials. The workshops brought together a diverse group of interested stakeholders to discuss the need for and methods to achieve diversity in clinical research. Workshop topics included Ethics, Trust, & Engagement: Addressing the Challenges of Clinical Trial Diversity, Building Trusted Networks, and Addressing Diversity Through Patient Centered Trials. [Recordings and key takeaways from the 3-part series can be found at <https://events.advamed.org/diversity-in-clinical-trials>.]

Based on the insights from the workshops, this document is intended to outline some of the potential considerations and possible approaches to help research sponsors improve inclusion of under-represented groups in clinical research. It is our hope that it will empower individuals within our member companies to inspire and promote changes that will enable commitment to company missions with the goal of eliminating racial health disparities.



Principles for Responding To Racial Disparities In Health

- 1 Promoting Inclusion and Equity in Healthcare
- 2 Partnering in Education with Stakeholders
- 3 All Patients Deserve Access to Innovative Technology
- 4 Promoting Research Equity

The Benefits of Diversifying Participants in Clinical Research

Sponsor



With greater participant diversity, there is increased understanding of how your medical device will impact different types of patients within your target population.



Working with diverse investigators can lead to not only more diverse participants, but also may lead to innovative solutions that better meet the needs of the target population.



With a greater understanding of the target patient population, your internal product development teams will grow in their understanding of the needs of varied populations and will influence updates to existing product design that can further meet patient needs.



Lastly, marketing and medical team members will be able to better describe the impact of your medical device to healthcare decision makers based on data collected.

Patient



Early in development, this learning can impact final design, leading to potentially better outcomes for all patients impacted by the target condition and treatment.



Under-represented populations would be included in clinical trials and a larger segment of the population could benefit from and have awareness of these innovations.



Patients' needs will be addressed via updates to existing products.



Patients will benefit from using high quality medical devices.

Be Aware and Acknowledge the History of Abuse in Clinical Research

Trust in the research enterprise has been compromised due to past abuses in clinical research, especially as it applies to ethnic and racial minority populations. Efforts to increase participation in clinical research by diverse populations must address this history.

Despite efforts of the FDA and the Revitalization Act of 1993, (which required that NIH funded clinical trials include women and minority participants), diversity in clinical trials has stagnated. A large segment of the population still lacks information, access to care and the opportunity to participate in clinical research. In assessing this phenomenon, we must consider factors which contribute to the lack of diversity including historic distrust on the part of some populations due to racially biased treatment. Moving forward, study sponsors need to communicate with patients the various policies and safeguards in place today to protect study participants and to protect against repeating those behaviors.

As an initial step, research sponsors should evaluate their current clinical research portfolio, enrolled patients, study designs, site locations, and principal investigators to assess the diversity of the populations being included. A systematic assessment of the potential gaps in your current approach will help identify what needs to be addressed and will facilitate development of a more targeted plan.

Change External Expectations

The recent policy and regulatory focus on health equity is expected to drive lasting impacts for patients and their health outcomes. These changes will also necessitate changes by medtech innovators. Regulatory agencies such as FDA³ and CMS⁴ and research funders like NIH⁵ have prioritized health equity and have made known their goal of promoting equity via [strategic priorities](#) and [announced objectives](#).

Key factors to consider:

- **Understand the value of representative research.** Diversifying the participants in clinical research creates several benefits for both the patient and the sponsor.
- **Recognize the potential trade-offs** and take the time to find the right collaborators. Ideally, this should be part of a comprehensive company-wide diversity, equity, and inclusion plan.
- **Communicate internally, with clear intention, the need to change the system** and discuss impacts on all levels of the company (product development, clinical operations, IT infrastructure, finance, research, design, etc.).



Understand Diverse Health Care Needs and Patient Populations

As an industry, we acknowledge that the most important part of our work is to create technology that improves patient health outcomes. This involves the development of innovative technologies as well as understanding the needs of all the patients the products will treat.

- **Compare current study population to real-world populations:** Are the patients that are most likely to have the condition included in your current study populations?
- **Use real-world data (RWD) to help shape your study design and better understand patient populations:** Identifying and using real-world datasets that are diverse can help identify potential health disparities and promote health equity.
- **Understand how the diversity of your clinical investigators and institutions influence the diversity of your studies:** Building diverse research networks may require sponsors to create partnerships with new investigators and health care organizations committed to serving diverse populations—a key consideration in addressing patient access, trust, enrollment, and retention barriers.

Establish the Current Baseline and Set a New Benchmark

- **Identifying the current industry baseline:** Various sources such as clinicaltrials.gov can be used as a resource to understand the trials within a therapeutic area, the current industry baseline, create benchmarks for improvement, and identify possible research sites with more diversity.
- **Examine the limitations of the current data sources:** Data sources also reflect some of the health inequities within the current healthcare system. Evaluate limitations of the dataset you are using to inform your strategy. For example: What is the source of the data? Are there regional limitations? Is race/ethnicity coded? What is the age distribution? Are there unexpected gender differences? Consider identifying datasets that incorporate measures of social determinants of health (SDOH)⁶, which can help further your understanding of the patient population that you are trying to serve and address the needs of those communities.
- **Start collecting data and evaluate ongoing clinical trials:** Don't wait to start collecting information. Don't let the perfect be the enemy of good and delay action. Collecting information on trials currently underway can be used to identify strengths and areas for improvement. If discrepancies are observed, the first thing to do is to identify if the current trial can be adjusted. Use this information to shape future studies.
- **Set internal goals:** Establishing internal benchmarks, informed by evidence, can drive discussions about the need for more representative clinical trial populations. This information, in combination with the more granular subpopulations (subject to any regulatory requirements), can help sponsors identify potential enrollment targets for studies.



Plan for Diversity in New Clinical Trials

Current research, development strategies and the way in which they are implemented have long histories for many companies—including relationships with clinicians, facilities, and researchers. Examining current practices may identify gaps that undermine efforts to capture more representative patient populations in your studies. **Sponsors should consider:**

- **Working with their current sites to improve the diversity of enrollment.** This is likely to require more direct and clear communications about the importance of diversity for the study with the principal investigators (PIs).
- **Helping current sites and PIs support changes in their research programs.** Researchers may benefit from additional support including the development of cultural and linguistically appropriate outreach and study information/materials.
- **Thinking about the best method for attracting the range of patients needed.** This may mean considering additional and alternative sites, if current sites are not best suited to recruit and/or retain diverse participants.
- **Identify areas where the study design is inadvertently reducing diversity.** Aspects of your study design (e.g., inclusion/exclusion criteria, follow-up visits requirements) may undermine efforts to increase diversity in enrollment. Consider using tools like RWD to shape inclusion and exclusion criteria to ensure they are targeting the array of patients impacted by the medical device (e.g., data from the Centers for Medicare & Medicaid Services (CMS)). Logistical challenges like limited office hours and locations may lead to loss of patients for follow-up.

Strategies for Recruitment of Diverse Populations

Accomplishing successful recruitment not only requires us to potentially modify and rethink our research partnerships to include sites that serve diverse patient communities, but it also requires sponsors to be more proactive in efforts to engage with patients to communicate the value of research. Recruitment information should be readily accessible by patients and easily understood. It should be culturally sensitive and available in several languages and dialects depending upon the diversity of the area and the diversity of patient population. Establishing longstanding mutually respectful patient-clinician relationships is important for establishing trust in diverse communities. Patient outreach and trust building opportunities between clinicians and communities before clinical trials start is vital for successful enrollment.

The following considerations for recruitment strategies have been identified:

Address diversity through patient-centered trials by:

- Relocating trial sites to academic institutions closer to minority patient communities.
- Selecting or creating pathways for trial sites that are trusted care facilities or where established patient and provider relationships exist.

Be prepared to go to the patient

- Use nurses as a trusted source in reaching community members; additionally, involve the community in the trial design process for authentic patient representation.
- Reduce logistic barriers such as transportation to ensure that once enrolled, patients stay in the study and are engaged.
- Expand the catchment area to include areas typically underserved whether it be urban, rural, or suburban.
- Go to where the patients are for recruitment. Include non-traditional sites (e.g., barber shops, salons, faith-based groups, partner with local physicians, community centers, health fairs).
- Improve awareness of enrollees so they understand what the trial is, how it's run, benefits to themselves and their communities, and the commitment needed.

Work with new sites and investigators

- Provide or liaise peer mentorship for sites not experienced in conducting clinical trials.
- Resist the tendency to be transactional in setting up trials.

Innovations in Clinical Study Design and Execution

Changing how clinical research is designed to reduce patient burden and improve engagement can help support more representative results and advance innovation. A number of innovative trial approaches such as decentralized clinical trial (DCT) models are a step in the right direction towards taking the research to the patients that need it. Sponsors should weigh the use of new digital technologies and solutions such as remote patient monitoring and telemedicine for follow-up care.

By embracing new digital technologies, sponsors could both reduce the burden to patients and also to trial sites. In place of time-consuming office visits, telemedicine appointments can replace and/or supplement patient follow-up when appropriate. Directly capturing RWD such as patient-generated health data (PGHD) through apps and wearables can give you more information about daily activities and can ease the challenges of long-term follow-up for patient-reported outcomes.

While some of these technologies may address some of the barriers for participation, they are not a perfect solution. Sponsors should consider patient aversions, access limitations, and sensitivities regarding these technologies.



KEY RECOMMENDATIONS

- Be aware of historical biases that exist in clinical research and potential mistrust of the healthcare system by underrepresented populations.
- Have intentional conversations with company leadership and various stakeholders to highlight the potential impact of the lack of diversity in current trials. Develop goals to broaden evidence generation efforts to include a more diverse patient population in clinical research and measure your progress.
- Use a variety of available tools to adequately define the targeted patient population, including leveraging RWD sources.
- Create a sustainable community of researchers. Partner with more community-based clinicians. Coordinate with clinical investigators to inform other local clinicians of study opportunities to support diverse enrollment.
- Be prepared to go to the patient by broadening the types and locations of the trial sites and diversity of investigators.
- Understand the importance of building trust in recruiting diverse participants: between patients and clinicians, companies and clinical investigators/sites, and companies and communities.























References

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- 2. CDC website:** Leading Causes of Death. U.S. Centers for Disease Control and Prevention. Published December 2, 2020. Accessed January 24, 2021. (<https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm>)
- 3. FDA resources:**
 - [2020 guidance Enhancing the Diversity of Clinical Trial Populations](#)
 - [2018 FDA's Action Plan for FDASIA](#)
 - [2016 guidance Collection of Race and Ethnicity Data in Clinical Trials guidance](#)
 - [FDA brochure for patients](#)
- 4. CMS resources:**
 - [Advance Equity](#) – CMS definition of health equity and applicability to the Agency's work and programs
 - [Expand Access](#) – enrollment data and access to health coverage
- 5. NIH resources:**
 - [Diversity & Inclusion in Clinical Trials website](#)
 - [Guidelines for the Review of Inclusion on the Basis of Sex/Gender, Race, Ethnicity, and Age in Clinical Research](#) (Updated 2019)
- 6. Centers for Disease Control and Prevention.** 2021. "Social Determinants of Health: Know What Affects Health." September 30, 2021. (<https://www.cdc.gov/socialdeterminants/>)
- 7. Ziemssen, Tjalf, Jan Hillert, and Helmut Butzkueven.** 2016. "The Importance of Collecting Structured Clinical Information on Multiple Sclerosis." BMC Medicine 14 (1): 81. <https://doi.org/10.1186/s12916-016-0627-1>.

Appendix: The Landscape of Clinical Evidence

There are multiple types of data that can be collected to support the clinical and economic value of technology. Ensuring diversity of patients (based on your target population) is important, whether prospectively collecting data from patients participating in clinical trials and/or observational studies or retrospectively analyzing data collected in real-world data sources such as administrative databases, electronic health records, or registries. While we include evidence from other research types, the focus of this document is on improving the representativeness of clinical trials.

Figure 1: Different types of evidence – randomized clinical trials versus real-world evidence studies (Figure adapted from Ziemssen et al., Fig. 1)⁷

Randomized Controlled Trials	Real-world Evidence Studies
 Experimental/interventional trial	 Observational/non-interventional trial
 Protocol-driven, compliance with Good Clinical Practice (GCP) mandatory	 Usually care-driven, results derived from clinical practice
 Efficacy and safety primary outcomes	 Primary outcomes are long-term efficacy and safety, effectiveness and economic assessments
 Narrow and restricted patient population with extensive inclusion and exclusion criteria	 Wide and unrestricted patient population with few exclusions including co-morbidities
 Gold standard or placebo comparators used	 No comparators used or compared to standard clinical practice
 Patients are randomized and blinded to treatment	 No randomization or blinding
 High cost per patient	 Low cost per patient (due to large number of patients)
 Internal validity	 Relevant to clinical practice
 Valuable to regulators	 Valuable to payers
 Key advantages are the randomized and controlled design and the use of gold-standard comparisons	 Key advantages are the broad patient population producing more generalizable data and collection of wide variety of real-world outcomes
 Key limitations are the restricted patient population resulting in limited generalizability of the data, high cost and short timeframe	 Key limitations are the non-randomized design leading to bias

