



ARTICLE

# A Patient-First Approach to Achieving Diversity in Clinical Trials

Approximately 60% of the adult population, 154 million Americans, have at least one chronic health condition; 40% or 100 million have two or more conditions.<sup>1</sup> Hypertension, hyperlipidemia, and diabetes are exceedingly common:

- 45% of adults (113 million Americans) have hypertension (defined as having blood pressure >130/80 mm Hg or taking medication); of those, 21% or 53 million do not have the condition under control<sup>2</sup>
- 12% of adults (30 million Americans) have high cholesterol; another 25% or 63 million have borderline to moderately elevated cholesterol (200-239 mg/dl)<sup>3</sup>
- 14% of adults (34 million Americans) have diabetes; another 35% or 87 million have pre-diabetes, with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG)<sup>4</sup>

Among the general population, Black Americans develop hypertension at a younger age, have higher rates of hypertension, and are more likely to develop complications such as stroke, kidney, and heart disease.<sup>5</sup> As a percentage of the population, slightly fewer Blacks have elevated total cholesterol as compared to the white population.<sup>6</sup> The risk of diabetes is 77% higher in Black Americans than white Americans;<sup>7</sup> complications of diabetes include heart and kidney disease, neuropathy, retinopathy, and other conditions, and Blacks are 30% more likely to die of heart disease.<sup>8</sup>

<sup>1</sup> National Center for Chronic Disease Prevention and Health Promotion <https://www.cdc.gov/chronicdisease/about/index.htm>

<sup>2</sup> CDC Facts about hypertension. [https://www.cdc.gov/bloodpressure/facts.htm#:~:text=A%20greater%20percent%20of%20men,pressure%20than%20women%20\(43%25\).&text=High%20blood%20pressure%20is%20more,or%20Hispanic%20adults%20\(36%25\)](https://www.cdc.gov/bloodpressure/facts.htm#:~:text=A%20greater%20percent%20of%20men,pressure%20than%20women%20(43%25).&text=High%20blood%20pressure%20is%20more,or%20Hispanic%20adults%20(36%25))

<sup>3</sup> CDC High cholesterol facts. <https://www.cdc.gov/cholesterol/facts.htm>

<sup>4</sup> CDC National Diabetes Statistics Report, 2020 <https://www.cdc.gov/diabetes/data/statistics-report/index.html>

<sup>5</sup> High Blood Pressure in African-Americans. WebMD; September 6, 2019 <https://www.webmd.com/hypertension-high-blood-pressure/guide/hypertension-in-african-americans#:~:text=Environmental%20factors.&text=In%20the%20U.S.%2C%20however%2C%20the,compared%20to%2027%25%20of%20whites>

<sup>6</sup> Cholesterol, Heart Disease and African Americans. Verywell Health; November 18, 2020 <https://www.verywellhealth.com/cholesterol-heart-disease-and-african-americans-3571756>

<sup>7</sup> The Disparate Impact of Diabetes on Racial/Ethnic Minority Populations. *Clinical Diabetes*; July 2012 <https://clinical.diabetesjournals.org/content/30/3/130#:~:text=4.9%20million%20African%2DAmerican%20adults,among%20non%2DHispanic%20white%20Americans>

<sup>8</sup> U.S. Department of Health and Human Services Office of Minority Health: Heart Disease and African Americans. <https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=19>

### Outcome Disparities

MEASURE	RATE FOR COMPARISON GROUP (BLACK)	RATE FOR REFERENCE GROUP (WHITE)	RELATIVE DIFFERENCE
Breast cancer diagnosed at an advanced stage per 100,000 women age 40 and over	102.5	84.3	21.6
Adults age >40 with diagnosed diabetes with blood pressure less than 130/80 mm Hg	39.1	53.1	29.9
Colorectal cancer deaths per 100,000 population per year	18.0	13.5	33.3
Breast cancer deaths per 100,000 population per year	26.9	19.4	38.7
Hospital admissions for heart failure per 100,000 population	828.8	436.7	89.8
Hospital admissions for long-term complications of diabetes per 100,000 population	210.3	96.8	117.3
Hospital admissions for (diabetes) lower extremity amputations per 100,000 population	60.9	26.8	127.2
Adjusted incident rates of end stage renal disease due to diabetes per million population	366.2	138.4	164.6
Hospital admissions for hypertension per 100,000 population	200.0	44.4	350.5

2019 AHRQ Healthcare Quality and Disparities Report

Hispanics, despite lower incomes and limited access to healthcare, have lower death rates from heart disease (128.7 vs. 172.7 per 100,000) and cancer (122.2 vs. 169.7 per 100,000) than white Americans.<sup>9</sup> Hispanics do, however, have higher rates of obesity and develop diabetes at a far higher rate (17%) than non-Hispanic whites (8%). Hispanics have a 50% chance of developing diabetes during their lifetime, with higher rates of kidney complications and visual impairment.<sup>10</sup> Ethnicity and site of origin affect these data.

<sup>9</sup> In Focus: Identifying and Addressing Health Disparities in Hispanics; December 27, 2018 <https://www.commonwealthfund.org/publications/2018/dec/focus-identifying-and-addressing-health-disparities-among-hispanics>

<sup>10</sup> Hispanic/Latino Americans and Type 2 Diabetes. CDC <https://www.cdc.gov/diabetes/library/features/hispanic-diabetes.html>

## Clinical trials for medical products need to be more inclusive of multiple populations

Clinical trial volunteers, also known as participants, “receive specific interventions according to the research plan or protocol created by the investigators.”<sup>11</sup> The intervention, a drug, a device, or a procedure, is compared to a standard, a placebo or no intervention. The research plan includes study objectives and endpoints; the study design (patient recruitment criteria for inclusion or exclusion, number of clinical sites, number of subjects and expected duration); the study procedure (timing of observations, lab tests, etc.); and data management and statistical analysis.<sup>12</sup> Patient recruitment is often the rate-limiting step to the completion of a clinical trial. Approximately 46.8 million Americans consider themselves Black, a figure that includes 3.7 million with a multiracial background and 2.4 million of Hispanic descent.<sup>13</sup> Although Blacks represent 14.1% of the U.S. population, they are often under-represented in clinical trials. This skewed enrollment can affect the generalizability of data findings.

In an overview study of participants in the clinical trials of 35 novel cardiometabolic drugs (24 cardiovascular and 11 diabetes drugs) approved by the FDA from 2008 to 2017, the median number of trial participants was 5,930 — yet Black participants represented only 4% of trial enrollees.<sup>14</sup> Consequently, the efficacy of these drugs in the Black population is unclear due to the significant underrepresentation in these studies.

As an example, the phase III clinical trial of Ninlaro, a cancer drug for multiple myeloma that the FDA approved in 2015, included a Black population of only 1.8% (n=722) — even though Blacks account for 20% of multiple myeloma patients. An analysis of cancer drugs approved since 2015 found less than 5% of the patients in 77.4% (24/31) of trials were Black.<sup>15</sup> Only 6.5% of the trials (2/31) reached 10% Black enrollment. Similar disparities were shown in immunotherapy trials.<sup>16</sup> Consequently, Black Americans are not gaining equal access to experimental cancer treatments. It also remains unclear how racial differences in immune status and incidence of tumor mutations affect outcomes.

Low enrollment of underrepresented populations may result from limited awareness of the trial, poor health literacy, financial (out-of-pocket costs) and logistical (distance from trial site) challenges, as well as mistrust — the last related to the Tuskegee Syphilis Study and forced sterilization in segregated hospitals.<sup>17,18</sup> Once enrolled, Black participants tend to drop out of trials at higher rates.<sup>19</sup>

## A Patient-centric Approach to Promote Diversity and Inclusion in Clinical Trials

A broader definition of patient diversity should be considered as a critical component of the clinical trial strategy. All stakeholders including sponsors, physicians, caregivers, and patient advocacy networks must work together to enable enrollment and retention of underrepresented patients. We’ve highlighted some key areas of focus and strategies that clinical trial sponsors should consider when planning their trials.

<sup>11</sup> Learn About Clinical Studies. Clinicaltrials.gov <https://www.clinicaltrials.gov/ct2/about-studies/learn#WhatIs>

<sup>12</sup> 6 High Level Components to Include in a Clinical Research Protocol. IMARC <https://www.imarcresearch.com/blog/6-high-level-components-to-include-in-a-clinical-research-protocol>

<sup>13</sup> The Growing Diversity of Black America. Pew Charitable Trust; March 25, 2021 <https://www.pewresearch.org/social-trends/2021/03/25/the-growing-diversity-of-black-america/>

<sup>14</sup> Ten-Year Trends in Enrollment of Women and Minorities in Pivotal Trials Supporting Recent US Food and Drug Administration Approval of Novel Cardiometabolic Drug. *Journal of the American Heart Association*; 19 May 2020 <https://www.ahajournals.org/doi/10.1161/JAHA.119.015594>

<sup>15</sup> Understanding the Impact of Racial Representation on Clinical Cancer Trials. OncoLive; August 25, 2020. <https://www.onclive.com/view/understanding-the-impact-of-racial-representation-on-clinical-cancer-trials>

<sup>16</sup> Ibid

<sup>17</sup> Tuskegee Syphilis Experiment <https://www.sciencedirect.com/topics/medicine-and-dentistry/tuskegee-syphilis-experiment>

<sup>18</sup> Forced sterilization policies in the US targeted minorities and those with disabilities – and lasted into the 21st century; September 23, 2020 <https://ihpi.umich.edu/news/forced-sterilization-policies-us-targeted-minorities-and-those-disabilities-and-lived-21st>

<sup>19</sup> Retention and Attrition Among African Americans in the STAR\*D Study: What Causes Research Volunteers to Stay or Stray? *Depression and Anxiety*; November 2013 [https://www.researchgate.net/publication/236977617\\_Retention\\_and\\_Attrition\\_Among\\_African\\_Americans\\_in\\_the\\_STAR\\_D\\_Study\\_What\\_Causes\\_Research\\_Volunteers\\_to\\_Stay\\_or\\_Stray](https://www.researchgate.net/publication/236977617_Retention_and_Attrition_Among_African_Americans_in_the_STAR_D_Study_What_Causes_Research_Volunteers_to_Stay_or_Stray)

### Diversity and Inclusion in Clinical Trials – A Patient-centric approach



### Key Considerations and Partnerships for Clinical Trial Implementation

Trial Planning and Startup	Trial Conduct			Publications/ Analysis & Reporting
 <b>Diversity in Design</b>	 <b>Hospital/Provider Partnerships</b>	 <b>Community Outreach</b>	 <b>Patient Engagement</b>	 <b>Scientific Advancement</b>
<ul style="list-style-type: none"> <li>– Define Diversity</li> <li>– Incorporate diversity in Clinical Trial Strategy</li> <li>– Set diversity targets</li> <li>– Define data collection requirements</li> <li>– Tailored messaging targeting key demographics</li> <li>– Cultural competency training for research team</li> <li>– Data-driven approach to diverse PI and Site selection</li> </ul>	<ul style="list-style-type: none"> <li>– Partner on strategy and method to achieve diverse patient enrollment</li> <li>– Support and listen to feedback from local/community organizations (i.e. churches, charities, etc.) and advocacy groups</li> </ul>	<ul style="list-style-type: none"> <li>– Outreach to national organizations focused on ethnic minority and health equity</li> <li>– Provide culturally concordant education on clinical research through attainable channels (i.e. Chinese Newspapers, etc.)</li> </ul>	<ul style="list-style-type: none"> <li>– Work with patients on financial incentives, transportation and/or childcare needs</li> </ul>	<ul style="list-style-type: none"> <li>– Improved and targeted health outcomes serving a diverse patient community</li> <li>– Diverse patient clinical impact success stories</li> </ul>

#### ROI Opportunities

The return on investment for implementing a diverse clinical program can take years to realize. However, value and success can be aligned to:

- Better outcomes for patients
- Value-based care
- Long-term sustainable impact
- Rebuilding trust with select minority groups
- Potential faster enrollment
- Societal and scientific contributions

- Broaden eligibility criteria in trial designs and definespecific diversity recruitment targets
- Recruit patients with diverse demographic characteristics (e.g., sex, race, ethnicity, age, etc.) and non-demographic characteristics (e.g., comorbid conditions, disabilities, and populations with diseases or conditions with low prevalence)
- Collaborate with patient advocacy groups and patients to incorporate theirperspectives of into the main trial design, including value-based care
- Engage the target community with “culturally concordant staff” in discussions around the recruitment plan<sup>20</sup>
- Establish clinical trial sites at clinics and medical centers located in areas with significant underrepresented populations
- Include approaches in trial design to reduce visit frequency and provide for flexibility in visit schedules
- Leverage the use of electronic communications and digital health technologies to replace site visits and provide investigators with real-time data
- Use AI and predictive analytics tools to identify patients who will most likely stop taking medication and suggest methods of intervention
- Engage physicians of the same racial and ethnic backgrounds at trial sites to attract participants
- Provide incremental financial assistance to subsidize out-of-pocket costs
- Increase the use of electronic medical records with secure online messaging as an approach to recruitment<sup>21</sup>

The National Institutes of Health (NIH) has shown it is possible to increase minority representation in clinical trials. NIH-defined phase III clinical trials are now required to report outcomes stratified according to sex or gender and by race and ethnicity.<sup>22</sup> Black recruitment in NIH-funded trials increased from 11.9% in 2015 to 16.0% in 2018.<sup>23</sup>

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*FTI Consulting, Inc., including its subsidiaries and affiliates, is a consulting firm and is not a certified public accounting firm or a law firm.*

<sup>20</sup> Black Patients Miss Out on Promising Cancer Drugs. Propublica; September 19, 2018, <https://www.propublica.org/article/black-patients-miss-out-on-promising-cancer-drugs>

<sup>21</sup> Study Reveals Racial Disparities in Clinical Trial Recruitment and Points to Strategies to Achieve More Inclusive Clinical Research. Beth Israel Deaconess; September 21, 2020 <https://www.bidmc.org/about-bidmc/news/2020/09/racial-disparities-in-clinical-trial-recruitment>

<sup>22</sup> Racial Disproportionality in Covid Clinical Trials. *New England Journal of Medicine*; August 11, 2020 <https://www.nejm.org/doi/full/10.1056/NEJMp2021971>

<sup>23</sup> Presentation: IPPCR 2019 Women and minorities as Participants in NIH Clinical Research <https://www.youtube.com/watch?v=VTsLA8zNqcY&t=490s>

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