

Achieving diversity in drug development programs for obesity

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Understanding the importance of diversity in clinical trials

In an ideal world, the participants in a clinical trial would reflect the race and ethnicity of those who will use the medication in the real world. Reaching a broad study population helps understand how a medical product affects people of different races and ethnicities, yet the past and even current disparities in clinical trial populations are well known.

Consider the example of the inclusion of Black and Hispanic Americans in obesity trials. They represent 13% and 18% of the population, respectively. However, obesity prevalence is higher in these two groups, and they are disproportionately affected by the associated comorbidities.¹ Nevertheless, these populations are grossly underrepresented as participants in clinical trials. Sex differences in studies also differ, with females being significantly overrepresented as participants in weight-loss studies. The paucity of sex and racial/ethnic diversity in clinical research can lead to research findings that are not generalizable to the entire population.²

Lack of proper representation is due to a variety of reasons. Some barriers are related to the clinical trial itself, such as the design, eligibility, sites and long enrollment periods. Other factors are directly related to patients and the health system. Of relevance is the limited access to healthcare that is prevalent in this population as well as the lack of incentive for participating hospitals.

While the FDA has previously encouraged sponsors to include traditionally underrepresented demographic subgroups, the U.S. FDA's Omnibus Reform Act of 2022 (FDORA) was enacted in December 2022 and included provisions to promote diversity and inclusion in clinical trials.

To help sponsors reach their diversity goals throughout the regulatory process and trial execution, this white paper discusses the FDA's requirement for a Diversity Action Plan (DAP). Learn what to expect and how you can best support your Phase III or pivotal study equivalent clinical trials of new drugs or devices with registrational intent.

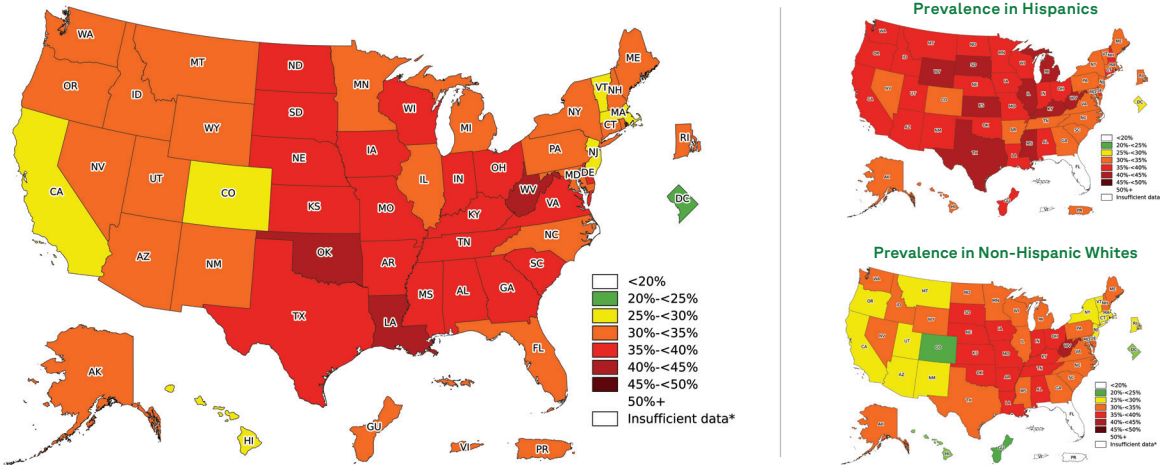
Obesity prevalence and trends in obesity-related mortality and racial disparities

Worldwide adult obesity prevalence has more than doubled since 1990, and adolescent obesity has quadrupled. From 1990 to 2022, the age-standardized prevalence of underweight among adults decreased in 129 countries (65%) for women and 149 (75%) for men. Age-standardized prevalence of obesity in adults increased from 1990 to 2022 in 188 countries (94%) for women and in all except one country for men.³ The rise in obesity is surpassing the decline in underweight individuals.⁴ There is a clear transition from underweight to obesity dominance in most low- and mid-income countries.

In the U.S., overall obesity prevalence in adults is 41.9%. However, significant disparities in the prevalence, complications, and treatment outcomes of obesity among Blacks and other racial or ethnic groups in the United States have been well-documented over time. Black and Latinos have the highest obesity rates (49.9% and 45.6%, respectively, in adults). Obesity rates are also increasing among children and adolescents and have tripled among this population since the mid-1970s. Black and Latino youth have higher rates than their white peers. There is also a steady increase in Asian and Pacific Islander people and people who identify as multiracial in the U.S. Single-race Asian groups had lower odds of obesity compared with White individuals when using standard BMI cutoffs. However, when applying Asian-specific BMI cutoffs, the prevalence of obesity among single-race Asian groups is similar to that among White individuals. Furthermore, obesity prevalence is higher among Pacific Islander groups compared with Asian groups and White individuals.⁵

Figure 1: Overall obesity prevalence in the U.S.

Source: [Adult Obesity Prevalence Maps](#). U.S. Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion, Division of Nutrition, Physical Activity, and Obesity. (Sept. 21, 2023).



Finally, disparities in obesity care disproportionately impact racial and ethnic minorities mainly in Black individuals with obesity. Obesity-related conditions such as hypertension and pancreatic cancer and treatments for obesity-related diseases such as sleep apnea disproportionately affect racial/ethnic minorities. These disparities are most significant for Black Americans. Studies have found that while Black women have the highest rates of obesity, Black men have the highest mortality rates from obesity-related illnesses. Such disparities highlight the need to address the existing inequities in access and quality of obesity care.⁶

Following the progression of U.S. legislation leading to Diversity Action Plans

The FDA first published draft guidance in April 2022, which recommended that sponsors develop Diversity Action Plans (DAPs).⁷ On December 29, 2022, legislation was passed, which contained several provisions to promote diversity in clinical trials and support the FDA's evaluation of safety and efficacy. This included requirements for the FDA to finalize guidance on clinical trial DAPs.

Per the Consolidated Appropriations Act of 2023 (sections 3601 and 3602), the FDA is mandated to finalize the guidance on DAPs, and 180 days after its publication, an FDA-approved DAP will be required for enrollment of Phase III, or any pivotal study in the U.S., of new drugs or medical devices and diagnostics that use the 510(k), premarket approval (PMA, *de novo* and investigational device exemption [IDE]).

In November 2023, the FDA published information about clinical trial participation that highlights the importance of including a diverse population in clinical trials and provides resources to potential participants.⁸

Aligning with the FDA's current request for data on underrepresented populations

Since 2022, the FDA has asked sponsors to discuss their plans to ensure diversity and inclusion of underrepresented populations in pivotal clinical trials. Even though ongoing Phase III studies and those starting in 2023 have been grandfathered in, sponsors have been preparing DAPs and submitting them to the FDA. They are actively gathering the agency's feedback to better prepare for studies that will start once approval of a DAP is mandated.

As mentioned earlier, a DAP for all Phase III/registration studies applies to any investigational drug/biologic or medical device studies that will support a marketing application. This requirement applies to pediatric and rare diseases, but not to expanded access programs.

The DAP should be submitted to the FDA before the protocol is submitted for a Phase III or other registrational study and can be modified after submission. The FDA *may* consider one DAP for an indication covering multiple studies. Finally, if the inclusion of a certain population is impractical or unreasonable, the sponsor can submit an official waiver request and the FDA will review it within 60 days.

Based on the prevalence/incidence of the disease condition, a DAP's overall aim is to ensure that the clinical trial population reflects the medicine's target population in the real world. The DAP's structure follows the FDA's recommendations providing specific target enrollment of underrepresented ethnic populations and operational measures to ensure enrollment and retention of these populations. In addition, the DAP should also describe the progress against enrollment targets, actions to meet targets and post-marketing data collection, if goals cannot be met.



Our role in promoting diversity in clinical trials

At Fortrea, we're committed to helping sponsors increase the diverse representation of populations in their clinical trials. Our Diversity in Clinical Trials Multifunctional Workstream and Advisory Board oversee a complete and integrated solution across our Consulting and Clinical Operations services that provides the appropriate framework for success under an Integrated Research Organization (IRO) strategy.

From protocol development to study close, we offer an innovative and comprehensive diversity solution that encompasses:

- DAP: Write, submit and engage with regulators and support the final report writing and submission
- Incorporate the Voice of Patient to understand patients' needs, support protocol optimization and capture feedback at the close of the study to continually improve the DAP design
- Assess the impact and track progress toward study enrollment goals (and potentially identify safety signals) with a real-time dashboard
- Perform corrective actions and adjust enrollment and retention strategies based on findings presented in the dashboard

Additionally, a comprehensive, multi-faceted, strategic operational approach is needed to ensure diversity targets are met in obesity trials. This approach may include (but is not limited to) the following:

- **Pre-identification of a population:** Due to the rapid enrollment of obesity studies, pre-identification of a diverse patient population is needed to ensure diversity while maintaining fast enrollment
- **Strategic site selection:** Appropriate site selection can ensure sites have dietitians that can meet the needs of the patient populations being recruited
- **Investigator selection:** Including obesity investigators from underrepresented populations, as it has been demonstrated that underrepresented participants are more likely to enter clinical trials where the investigators are from similar racial and/or ethnic backgrounds
- **Targeted training:** Through training, trial teams should understand the importance and rationale of participation from diverse groups in clinical trials and explore barriers, which may require mitigation, at the site and investigator level
- **Feasibility outreach questions:** The importance of diversity at the site level can be highlighted through specific feasibility outreach questions, such as: "Does your institution have a process or initiative to increase patient diversity in the clinical trials in which you participate?" and "Does your institution track recruitment of diverse patient populations?"
- **Patient advocacy group outreach:** Engage patient advocacy groups to promote awareness to specific populations in a format most likely to be successful for those patients
- **Targeted patient communications:** Develop targeted multimedia approaches to reach specific populations in a way that speaks directly to each group

Together with our sponsors, learn how we're advancing our shared goals to bring clinical research closer to all.

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