



Ending Racial Disparities in Clinical Trials

How BioPharma & Health Centers Can Come Together to Improve Health Equity

Abstract



The American population is increasingly racially and ethnically diverse: the 2010 US Census reported four “minority-majority” states, including Texas, California, Hawaii, and New Mexico. However, clinical trials have struggled to reflect the diversity of our nation. This truth has concerning downstream implications: First, clinical research suffers. Second, the healthcare community falls short of its collective goal to achieve health equity.

Health centers, which serve a higher percentage of racially diverse populations, may be the “missing link” in making sure new drugs and vaccines are both safe and effective for the entire US population. A workable solution, however, must align with the the health center mission, respect the population’s unique concerns and require minimal change to existing operations.

This white paper explores several main ideas:

- The downstream effects of a lack of socioeconomic, racial, and cultural diversity in clinical trials
- The socioeconomic and racial diversity of health center patient populations
- How health centers can assert a role in clinical research that helps achieve health equity for their patients

In discussing each of these areas, par80 sets the foundation for the par80 Research Network (PRN), a groundbreaking endeavor to improve disparity in healthcare treatment options accessible by the nation’s health center patients.

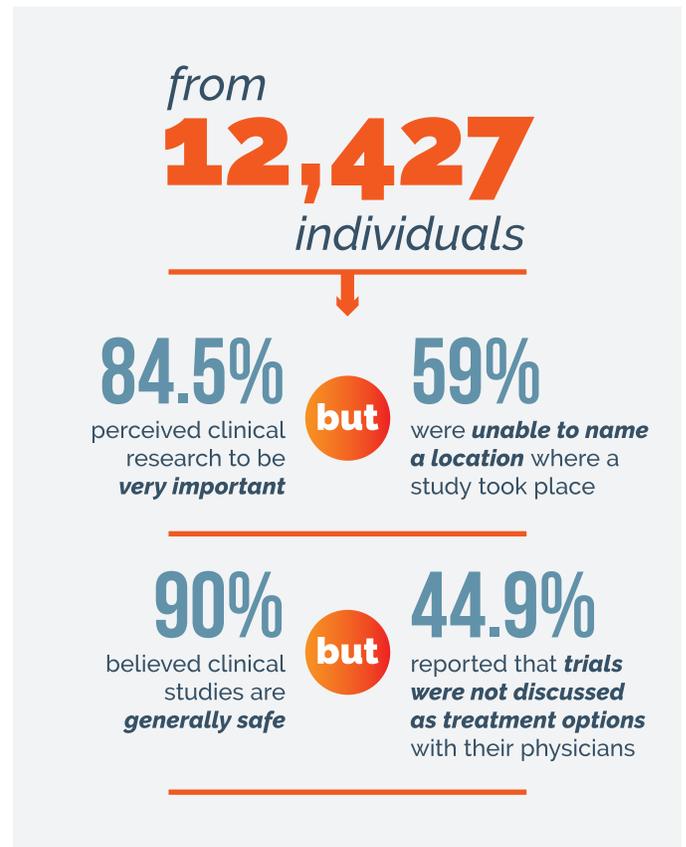
Importance of Clinical Research

It is generally accepted and understood that clinical research is vital to the advancement of medicine. Clinical trials represent the pathway that new treatments must pass through. Their results, which can differ dramatically among different patient populations, will also define the accuracy of predicted outcomes.

"Clinical research brings together all of the other aspects of medical research," a position paper by the Ochsner Clinic Foundation states. "The end product is the knowledge that allows us to understand disease processes and the prevention and treatment of these diseases. Clinical research is vital to achieving our ultimate goal of promoting health."

The broader population agrees: A 2017 study by *The Center for Information and Study on Clinical Research Participation* identified that out of 12,427 individuals, 84.5% perceived clinical research to be "very important" to discovering new medicines. However, 59% were unable to name a location where a study took place. While 90% believed clinical studies are "generally safe," 44.9% reported that trials were not discussed as treatment options with their physicians². This finding illustrates challenges both in awareness and education on behalf of both patients and treating physicians.

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Clinical Trials and the Role of Primary Care

Presently, clinical research activities occur in a wide variety of settings, including academic medical centers (AMCs), hospitals, doctors' offices, community clinics, and more recently - virtually³⁴. Given the variety of opportunities to participate in a clinical trial, it stands to reason that the lack of participation must have more to do with the role trials play or do not play in most clinical workflows.

Primary care organizations are often the first part of a patient's care journey and coordinate subsequent downstream specialty care. Given this position, primary care clinics could play a crucial role in introducing clinical trials to patients. However, they are often understaffed and lack resources to introduce clinical trial opportunities to patients.

Primary care providers are also interested in championing clinical trials: when asked whether they would be interested in learning about cancer treatment options and referral to trials, 41.4% indicated a strong interest in learning more about their role in clinical trials, while 35.7% indicated a potential interest.

Primary care clinics could play a crucial role in introducing clinical trials to patients



Clinical Research Limitations: Enrollment & Diversity



The lack of knowledge and subsequent discussion of available clinical trials between providers and patients is further reinforced by the "failure" rate of clinical trials. Today, 37% of trials fail to meet enrollment targets, over 85% of trials are delayed, and hundreds of failed research sites cost sponsors ~\$50,000 per site⁶. These failures have significant scientific and financial costs⁷. Failing to recruit enough participants can jeopardize the results of a trial, which has been designed to answer a specific research question by recruiting a specific number of participants.

Trials also fail to reflect the diversity of our nation. The lack of racial, ethnic, socioeconomic, and gender diversity in clinical trials is apparent: Although 20 percent of cancer patients are eligible for treatment clinical trials, participation hovers around three to five percent. Moreover, patients from racial and ethnic minority groups and underserved populations remain underrepresented in clinical trials, even though these groups experience a higher cancer mortality rate than the population as a whole⁸.

The data speaks for itself:

- Nintelo, which treats blood cancer multiple myeloma, was approved by the Food and Drug Administration (FDA) when clinical trial results demonstrated an average of 6 months without cancer spreading. **20% of multiple myeloma patients are black, but only 1.8% - 13 people - of the 722 person Nintelo trial - were African American**⁹.
- 31 cancer drugs have been approved since 2015. **24 of the drug trials included fewer than 5% African Americans, despite blacks making up 13.4% of the US population**¹⁰.
- Asians account for about 6% of the US population but account for **only 1.7% of clinical trial participants**¹¹.
- Native Americans and Alaska Natives account for 2% of the US population but **were not represented at all** in two-thirds of drug trials conducted in the US¹².
- Albuterol, an asthma medication, **is less effective in African-American and Puerto Rican children** than European-American and Mexican children¹³.
- Plavix, a blood thinner, was found to be **less effective for patients of East Asian or Pacific Islander descent**¹⁴.
- Both Alunbrig and Alecensa trials, which treat non-small cell lung cancer, **had less than 2% black participants**, even though non-small cell lung cancer occurs in 56 of 100,000 black Americans versus 49 of 100,000 white Americans¹⁵.
- Prostate cancer affects 178 of 100,000 black Americans versus 106 of 100,000 white Americans, and Black Americans are twice as likely to die from prostate cancer. However, all seven prostate cancer trials conducted from 2009-2015 **had only 3% black participants**¹⁶.
- Erleada, a newer prostate cancer treatment, enrolled 66% white participants and **just 6% black**¹⁷.

The healthcare industry strives for equity amongst all patients; diversifying clinical trial recruitment efforts is an opportunity to further that professional goal.

Congress & the FDA Address Diversity in Clinical Trials

In 2012, Congress attempted to encourage and address inclusivity in clinical trials in Section 907 of the Food and Drug Administration Safety and Innovation Act. Section 907 directed the FDA to produce a report that examined the inclusion and analysis of demographic subgroups in biomedical research¹⁸. In the resulting "Action Plan to Enhance the Collection and Availability of Subgroup Data," the FDA detailed 27 actions divided into three priorities: improving subgroup data collection and reporting, identifying barriers to subgroup inclusion in clinical trials, and making demographic subgroup data more transparent¹⁹.

Enforceable regulations were vague and limited to information about the trial subjects' demographics and lacked a mandate for participation minimums. FDA spokeswoman Gloria Sanchez-Contreareas stated that the organization did not have the regulatory authority to require specific minority representation in clinical trials²⁰. Ultimately, the challenge of ending disparities in clinical trials remains.

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Why Disparities In Clinical Research Trial Participation Continue to Exist

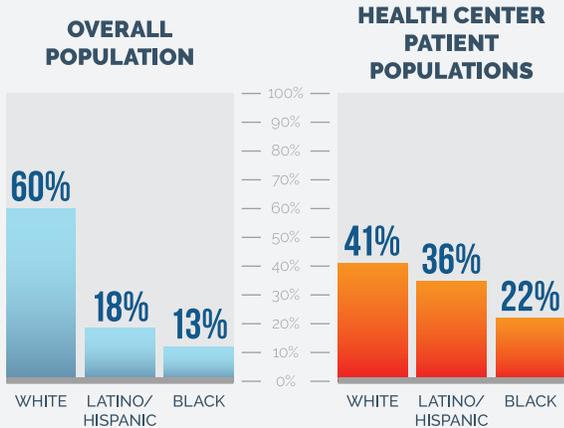
In a target enrollment failure analysis, *Cancer Control* identified several system-level barriers²¹. **First, enrollment barriers disproportionately affect minorities due to a higher likelihood of receiving care at under-resourced healthcare facilities, lack of insurance, and comorbidities that exclude them from trials. Second, healthcare providers play a critical role in discussing treatment options that may include clinical trials. Lastly, provider lack of awareness about available and appropriate trials was identified as a significant barrier to increased trial participation rates²².**

These systemic barriers, combined with a lack of enforceable regulation mandating the inclusion of socioeconomic minority groups in clinical trials, invite creative response to a national healthcare challenge. Proposed solutions generally suggest increasing awareness from a community and provider perspective and/or adjusting health center staffing to accommodate traditional operational and staffing needs required for clinical trial recruitment. Given that health centers face staffing and resource limitations, this type of solution is met with several concerns over financial, resourcing, and administrative burdens²³.

The Importance of Expanding Clinical Trial Awareness to Health Center Program Grantees



U.S. POPULATION



are uninsured or publically insured **82%** | **91%** are at or below 200% of the federal poverty level

Health Center Program Grantees, which include community health centers and federally qualified health centers, serve a racially and socioeconomically diverse population: while the US population is 60% White, 18% Hispanic/Latino and 13% Black, health center patient populations are 41% White, 36% Hispanic/Latino, and 22% Black. Further, 82% are uninsured or publically insured, and 91% are at or below 200% of the federal poverty level. Given the disparities identified in clinical trial access by minority groups, it stands to reason that if research initiatives could be optimized to include America's health centers, it would increase overall trial participation and the ratio of minority groups in clinical trials. A realistic solution, however, must have minimal operational and staffing requirements.

The Health Center Mission

Health centers were created in the 1960s as a part of President Lyndon B. Johnson's "War on Poverty." Modeled after community-based health care in South Africa, "Neighborhood Health Centers" combined federal funding with community resources in rural and urban America to provide affordable, high quality, comprehensive primary care to medically underserved populations, regardless of insurance status or ability to pay²⁴.

The program could largely be considered a success despite operating with minimal margin: In 2019, 1,362 federally funded health centers served 29 million Americans. Health centers also report better outcomes for treating patients with diabetes and hypertension than national benchmarks. Yet while demand and service needs continue to grow, 75% of health centers report funding gaps for needed expansions²⁵.

How Providing Access to Research Aligns with Health Center Missions

Ensuring patients have equal access to participate in clinical research is supported by the primary, original goal of health centers: to improve community health while narrowing healthcare disparities regardless of insurance status or ability to pay. In the short term, participating in research provides a health center with the opportunity to provide patients with access to innovative therapies. In the longer term, participating in research may also provide funding opportunities for the health center and give the health center the ability to provide additional or improved clinical services. Further, participation in research may be an employment incentive for some providers/staff and improve career satisfaction²⁶.

By making clinical trial discussion and awareness a part of routine healthcare, health centers are also more likely to retain patients that may be forced to seek treatment elsewhere if the patient is interested in research opportunities²⁷.

Current Approaches to Solving Awareness and Diversity Challenges

Barriers to trial awareness and access, together with a lack of enforceable regulation that mandates the inclusion of diverse groups in clinical trials, invites innovation. Some, such as the Automated Clinical Trial Eligibility Screener, endeavor to ease patient screening by parsing unstructured data into meaningful data to find information that may qualify (or disqualify) a trial candidate. Various approaches have been developed that attempt to address data, screening, recruitment, and retention challenges in the clinical research process. Further, the "All of Us" Research Program, which endeavors to facilitate minority inclusion in research, strives to support improvement through various national grant opportunities.

par8o, a SAAS health IT company based in Boston, became uniquely intimate with the operational and financial challenges that health centers confront on a daily basis when it entered the 340B software marketplace in 2017. Recognizing the challenges in this space and driven by a mission to continue to support community healthcare operations and increase inclusion in clinical research, par8o launched PRN - par8o Research Network - in 2020.

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par8o and the Nation's Health Centers

par8o was founded in 2012 by a group of physicians with a mission to match patients to healthcare resources at the most opportune time. The company's original offering was in the referral management space and is currently used by some of the country's largest health systems to help improve patient access and coordinate care between offices with disparate technical systems, such as EHRs.

par8o's 340B solution leverages the technical and operational expertise gained by innovating in the referral management space: par8o 340B Referral Capture assists health centers with capturing additional federal funding through HRSA's 340B program. Today, over 100 health centers that serve over 15 million Americans utilize par8o's 340B solution.

This position affords par8o a unique and detailed understanding of how essential it is to provide health centers with patient-centric solutions that do not require significant operational infrastructure or resources and can provide additional financial stability.

Automated, 'Concierge-Style' Trial Participant Identification

PRN - the par8o Research Network - offers a pathway for health centers to participate in clinical research without becoming trial sites nor risk losing patients to research-focused organizations.

PRN is a concierge service that identifies which patients can participate in clinical trials through intelligent, automated EHR data analysis. If PRN identifies a patient as a trial candidate, par8o works on behalf of the health center as a Business Associate to offer patient participation.

PRN requires no new software nor additional provider effort and empowers providers to offer patients cutting edge trials, monitor enrollment, and ensure patients return to their organization. In short, par8o aimed to create a way for organizations that do not typically participate in clinical research to provide their patients with the benefits of trials - which can dramatically improve quality of life - while limiting regulatory responsibility.

Once a health center joins PRN, par8o uses data feeds from its EMR to identify patients that could be candidates for local trials. When PRN identifies a potential trial candidate, the par8o team sources the information necessary to ensure that patients meet critical inclusion or exclusion criteria.

All subsequent research activities, including formal screening and informed consent, would occur at the actual research site, independent of the health center. This approach both minimizes the operational burden on health center staff and increases awareness of available trials. Additionally, health centers can receive compensation for their participation in PRN.



Health Center Population Special Consideration & Concerns

Health centers tend to have unique concerns when considering clinical trial participation. Special care must be taken to ensure that the approach is especially respectful of the racial and ethnic minority group populations they serve, considering the tragic history of minority exploitation in clinical research. par8o believes technology can help position providers so they can serve as advocates for their patients, keeping them informed of the possibilities and acting as true champions for their patients' health equity.

Legal and Regulatory Aspects Regarding Patient Privacy & Clinical Trial Recruitment

In order to understand how existing patient privacy laws apply to the proposed participant identification method, this section of the white paper will explore three aspects of current regulations: the Health Insurance Portability and Accountability Act (HIPAA); the HIPAA Privacy Rule, and under what circumstances a HIPAA Business Associate Agreement (BAA) allows a business associate to analyze patient data.

HIPAA and the Privacy Rule

HIPAA was originally introduced in 1996 with several goals related to improving the efficiency and effectiveness of the healthcare system. The law's Administrative Simplification provisions include regulations related to electronic healthcare transactions. Congress recognized that an increased use of electronic technology could "erode the privacy of health information" and subsequently mandated the adoption of personal health information (PHI) protections, which became known as the Standards for Privacy of Individually Identifiable Health Information, or "Privacy Rule" in 2000²⁸.

The Privacy Rule addresses the use and disclosure of individuals' PHI, by organizations subject to the Privacy Rule — described as "covered entities"²⁹. Congress's goal in mandating information privacy is to "[strike] a balance that permits important uses of information, while protecting the privacy of people who seek care and healing."

The Privacy Rule permits covered entities, or organizations such as health centers, to disclose PHI to their business associates as long as a Business Associate Agreement (BAA) that outlines how the information is to be used is in place³⁰. Business Associates, such as par8o, are persons or entities that perform certain functions or services on behalf of a covered entity.

If formal arrangement and a BAA is not in place, the Privacy Rule permits researchers to access, use, or disclose PHI in the following scenarios:

- If the subject of the PHI has granted permission in writing via a valid HIPAA Authorization Form.
- If an IRB or Privacy Board has granted a waiver or alteration of the standard authorization process for the study.
- If the PHI is contained in a Limited Data Set governed by a Data Use Agreement between the Researcher and the Covered Entity that is going to disclose the PHI.
- If the Informed Consent document includes the Authorization language in full or modified with IRB/Privacy Board approval.
- If PHI is de-identified³¹.

The Preparatory to Research Provision

The Privacy Rule also includes a "Preparatory to Research Provision" that allows for the analysis of patient data to aid in study recruitment³². However, the provision makes a distinction between accessing PHI for analysis purposes and for contacting trial candidates.

The Research Provision states the candidate may be contacted to assess interest in trial opportunities and obtain Authorization to release PHI to the trial site in the following scenarios:

- If a researcher is an employee of the covered entity, or an independent researcher if the researcher provides documentation of an IRB partial or complete Authorization waiver to the covered entity
- By a healthcare provider when the provider is employed by the covered entity
- By a business associate of the covered entity³³

The par8o Research Network's Approach to Regulatory Compliance

par8o holds compliance and ethics at the forefront of each of its offerings. PRN's novel approach to patient recruitment has been submitted for approval to a leading centralized IRB (sometimes called an "ethics committee") to ensure that the appropriate patient protections are in place. Further, par8o plans to obtain a waiver for the standard authorization process required for the health center to disclose PHI by the IRB.

More generally, par8o becomes a HIPAA Business Associate of the health center in order to access and analyze PHI; to contact patients; and to assist the health center with identifying trial candidates. Upon identification, par8o contacts the candidate on behalf of the health center to inform the candidate about the trial, assess interest and ask the candidate high-level inclusion/exclusion criteria questions. par8o then obtains a HIPAA-compliant patient authorization to allow for their information to be shared with the trial site.

In summary, PRN is a HIPAA compliant way for health centers to provide patients with access to clinical research. The BAA between par8o and a health center allows par8o to work on behalf of the health center to identify clinical research candidates, qualify candidates based on preliminary inclusion/exclusion criteria, and facilitate connection to trial sites.

IRB approval of the PRN methodology and IRB-waiver of the standard patient authorization to disclose PHI from the covered entity or health center to par8o will be in place as additional safeguards.



PRN: Empowering Health Centers to Champion Health Equity Through Clinical Trials



The disparities in clinical trial access and resulting implications are well known, well documented, and well understood. The fact that this disparity still exists indicates that the challenge is multifaceted with technological, cultural, and operational challenges to overcome.

If health centers were empowered to offer clinical research opportunities to patients in a way that considers their unique operational needs, diversity inclusion in trials would improve and clinical research would better meet its goals. Further, racial and socioeconomic minority groups would have access to therapies in development that may significantly improve quality of life.

With their patient-centric focus, mission-driven culture, and patient demographics, health centers are uniquely positioned to participate in a solution that respects their operational and funding challenges. The right solution needs to be highly automated to avoid implementation burden, offer patient benefits that align with their mission, and ideally also offers some level of financial benefit.

par8o's answer is PRN.

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