The conduct of clinical trials is vital for developing new therapies for patients with cancer. It is sometimes forgotten that the entire clinical trial system hinges on the availability of patients who participate. Yet few adult patients with cancer participate in clinical treatment trials. Therefore, research that aims to improve understanding about barriers to trial participation and disparities in access to trials is critical.

A 2019 study by Unger et al delineated the structural, clinical, physician, and patient barrier domains that may prohibit trial participation for most patients. Structural barriers are underpinned by the institutional commitment and investment in resources that are required to conduct cancer clinical trials, which can be burdensome. For this reason, trials are much more commonly conducted at major academic centers, limiting access for many patients who do not live near such centers. Even if a trial is available, a patient may not be clinically eligible. And even if a patient is eligible for an available trial, there is no certainty that a treating physician will offer a patient the opportunity to participate. Indeed, in their role guiding patients’ care, physicians may prefer a specific treatment or may face practical considerations of reimbursement and the time and effort to conduct a trial.

Under this framework, patient agency in the trial decision-making process arrives only at the end of a very long pathway, ie, a trial must be available, the patient must be eligible, and the physician must offer the patient the opportunity to participate. Only then do patients have the opportunity to assess whether receiving care in a trial is the appropriate choice for them. In fact, structural and clinical barriers preclude trial participation for more than three-quarters of patients. Importantly, along this lengthy decision-making pathway, numerous disparate barriers may arise that result in reduced trial participation for patients of different demographic, socioeconomic, and geographic backgrounds.

Such disparities can have adverse consequences for the patients interested in trials for their cancer care. Seminal work had been done to examine enrollment disparities in federally sponsored trials conducted by National Cancer Institute (NCI) network groups. However, until recently, there had been little comprehensive examination that focused on representation in trials focused on US Food and Drug Administration (FDA) drug approvals, which are predominantly conducted by pharmaceutical companies. In 2019, a study by Loree et al reported that in a large sample of trials leading to FDA drug approvals, representation of Black and Hispanic patients was egregiously poor. Compared with the expected proportion among the US cancer population, Black patients represented only 22% of patients and Hispanic patients represented only 44% of patients in FDA pivotal trials. International recruitment to pharmaceutical company-sponsored trials explains some of this disparity; however, even accounting for this, the estimates would be very low. The importance of studying representation in trials predominantly conducted by pharmaceutical companies was cast in sharp relief in a follow up study from 2020 by the same study team: Black patient representation was 3-fold higher (9.0%) among federally sponsored network group trials compared with pharmaceutical company-sponsored trials (2.9%) conducted over the same time for a similar set of cancers. Given that NCI-sponsored trial programs include dedicated efforts to include recruitment from community, minority, and underserved sites, this latter observation highlights how prospectively planned outreach to the community can improve representation of patients to trials from different backgrounds.
A key limitation of studies that rely on published trial reports is that important demographic information pertinent to the examination of disparities is often missing. The 2019 study by Loree et al.\(^5\) found that fully 37% of trials did not report enrollment by race at all, and only 8% of trials documented enrollment by all 4 of the major racial and ethnic groups in the US (i.e., Asian, Black, Hispanic, and White). The absence of complete reporting suggests that aggregate representation estimates from available trials may be biased.

This study by Pittell et al.\(^7\) fills in a critical gap by evaluating racial and ethnic disparities in trial participation using data from electronic health records rather than trial reports, alleviating a major source of bias and providing a ground’s-eye view about trial access disparities. Based on a retrospective analysis of 50,411 patients from 280 US cancer clinics, Pittell et al.\(^7\) found that Black (4.2%) and Latinx (4.4%) patients were underrepresented in trials compared with White patients (7.2%). The findings were generally consistent among the 5 cancers that were studied. The approximately 45% relative reductions in trial participation for each racial and ethnic group represented less extreme underrepresentation compared with estimates from Loree et al.\(^5\). This is likely due in part to the fact that Pittell et al.\(^7\) examined enrollments to trials from any sponsor, whether industry, federal, or institutional. Therefore, their estimates of representation may be higher due to improved representation of underserved groups in nonindustrial trials.\(^6,7\)

Another important finding by Pittell et al.\(^7\) is the specification of the overall trial participation rate. Until recently, it has been routinely assumed that participation of adult patients with cancer in trials is approximately 2% to 3%. This estimate was noted in an influential report in 2010 by the Institute of Medicine, “A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program,”\(^8\) that reviewed the landscape of trial conduct based on federal support. As these estimates were derived from studies that focused on enrollments to federally sponsored studies alone, they did not account for the sizeable contributions of patient participation in industry sponsored trials, which has been increasing over time. More recent estimates suggest greater levels of participation in trials than has been assumed, between 6% and 8%.\(^5\) In the article by Pittell et al.,\(^7\) the weighted mean participation rate across racial and ethnic groups was 6.6%. This important aggregate result, based on a novel data source for estimating trial participation, provides further support to the idea that the contributions of adult patients with cancer to clinical trial research is greater than has been assumed.\(^7\)

As Pittell et al.\(^7\) note, the findings from their article are important to consider in light of the recent guidance from the FDA directing industry sponsors to proactively implement trial-specific plans for improving representation.\(^9\) Of note, the focus of the FDA guidance is about improving enrollment of participants from underrepresented racial and ethnic populations.\(^9\) The rationale is grounded in the observation that “the lack of representation of these populations in clinical research reflects, in part, a broader issue regarding differential access to health care.”\(^9\) Consistent with the observations from prior studies that industry-sponsored trials have poor outreach beyond large academic centers, the guidance suggests that sponsors consider in their diversity plans such measures as “partnering with community-based organizations to provide support to study or trial participants.”\(^9\) Furthermore, although the guidance emphasizes racial and ethnic disparities, it also encourages sponsors to “seek diversity in clinical trial enrollment beyond populations defined by race and ethnicity, including other underrepresented populations defined by demographics such as sex, gender identity, age, socioeconomic status, disability, pregnancy status, lactation status, and co-morbidity.”\(^9\)

As suggested by this passage, disparities in access to clinical trials span a broad spectrum of sociodemographic domains that likely, commonly, overlap. If so, positive steps to alleviate racial and ethnic enrollment disparities may have the salutary benefit of beginning to resolve disparities for other domains as well. Taken together, these actions could speed the evolution of clinical trial conduct in the US toward the ultimate goal of an inclusive system easily accessible to patients with cancer of any background.
ARTICLE INFORMATION

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