Improving Diversity in Clinical Trial Participation

POLICY BRIEF

KEY TERMS

Clinical Trial – A research study in which one or more research participants are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Community-Engaged Research – a research model that seeks to involve a broad coalition of stakeholders throughout the planning, execution, and dissemination stages of clinical research. Specific applications include community-based participatory research, participative active research, and practice-based research networks.

Precision Medicine – Also known as personalized medicine, this refers to the tailoring of medical treatment to the individual characteristics of each patient, by classifying individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment.

Background

Clinical trials (CTs) are one of the final hurdles that candidate drugs must surmount before becoming available for approved clinical use. Assuming demonstration of both safety and efficacy in the trial (or trials), the Food and Drug Administration (FDA) will approve the drug for use in specific clinical indications. Following FDA approval, subsequent CTs may be performed to identify additional populations for which the drug may be beneficial. In recent decades, CTs have been critical to advancing cancer care, as treatments have become increasingly tailored to precise patient or tumor characteristics. Yet, there remains a population for whom current treatments are not effective. For these patients, CTs represent experimental options that have the potential to slow or stop the course of their disease, potentially providing them with additional months or even years of life.

With the notable exception of pediatric oncology, participation levels in cancer CTs has historically been far lower and less diverse than the actual demographics of patients living with cancer and the prevalence of the disease. Racial and ethnic minority populations, sexual and gender minorities, and older adults, are all dramatically underrepresented in CTs, often despite equal or higher cancer incidence rates compared to the general population.[1,2,3] Moreover, despite efforts by the National Cancer Institute (NCI) to improve minority representation, it is estimated that approximately 1% of

[1] Duma, Narjust, et al. "Representation of minorities and women in oncology clinical trials: review of the past 14 years." *Journal of oncology practice* 14.1 (2018): e1-e10.
[2] Murthy, Vivek H., Harlan M. Krumholz, and Cary P. Gross. "Participation in cancer clinical trials: race-, sex-, and age-based disparities." *Jama* 291.22 (2004): 2720-2726.
[3] Hutchins, Laura F., et al. "Underrepresentation of patients 65 years of age or older in cancer-treatment trials." *New England Journal of Medicine* 341.27 (1999): 2061-2067.

registered cancer CTs are primarily directed toward racial and ethnic minority populations, and only approximately 33% of all registered trials report race and ethnicity in trial results. It is important to note that underrepresentation results not only from failure to recruit adequately in CTs, but also from difficulty maintaining consistent retention rates across populations on study.

There are a variety of reasons for the lack of diversity in cancer clinical trials. These include issues with access and cost of care; failure of the health care system and clinical research enterprise to earn patient trust; inability of research centers to meet linguistic needs of patients, or literacy-related barriers; contextual factors such as family and community engagement; and stringent eligibility criteria (e.g., comorbidities, which are often more prevalent in underrepresented populations due to exposures to systemic discrimination) or other study design-related barriers. Provider-associated barriers have been reported as well, whether at the health system/organizational level (e.g. funding/staffing for clinical trial sites may be inadequate where underrepresented patients are likely to receive care), or individual providers failing to inform patients of CT availability. Physicians have many competing clinical priorities and payment systems often do not account for extra time necessary to identify appropriate trials and educate and enroll patients. The above obstacles are particularly problematic for patients from under-represented minority groups who may not independently seek to enroll on clinical trials.

Disentangling the effects of demographic characteristics and exposures to structural discrimination including factors such as age, socioeconomic status, geography, and race/ethnicity is difficult. However, studies consistently demonstrate that having a low income is an independent predictor of reduced CT participation, even after adjusting for comorbidity, education, and age older than 65 (i.e., with almost universal access to Medicare). Data suggest that this is due to the impact of the high cost of cancer care on patients. While the impact of costs related to CT participation on these trends requires further exploration, pilot studies are beginning to demonstrate the potential for financial assistance programs to significantly increase enrollment and retention of patients who would otherwise experience financial barriers to participation.

Concerns for ASCO Members & the Cancer Community

Diversifying CT participation will address multiple areas of concern: improving the overall conduct of clinical research, improving the evidence base for high-quality cancer care, and helping to resolve health equity concerns related to underrepresentation in CTs.

Inability of cancer CTs to recruit and retain all willing and eligible patients may contribute to slow enrollment and accrual, and ultimately delays completion and reporting of results. This can delay the availability of cancer medicine to patients who need it. Additionally, a clinical research enterprise that does not recruit representative study populations may be unable to ascertain potential differences in drug efficacy or tolerability between subpopulations. As cancer care becomes increasingly focused on the molecular characterization of specific tumor types (i.e. precision medicine), the impact of the failure to understand safety and efficacy in increasingly granular subpopulations will increase.

From a cancer health equity perspective, underrepresentation in CTs reduces access to potentially promising experimental medicines for advanced cancer. Patients who may wish to participate but are either not screened or are ruled ineligibile (e.g. due to overly stringent exclusion criteria) are essentially

denied access to the opportunity to participate in research. The desire to participate in a CT also stems from contextual factors including a patient's beliefs about CTs and support from family and community. Accounting for these context-sensitive patient perceptions, and employing responsive communication strategies (sometimes referred to as community-engaged research), is critical to improving CT participation but generally remains underprioritized.

Where ASCO Stands on Improving Clinical Trial Diversity

ASCO believes improving the diversity of CT participants will benefit all cancer care stakeholders, and should be prioritized. Addressing disparities in cancer care, including in CT enrollment, has long been a priority for ASCO. To that end we have been engaged on issues that include insurance coverage for CT participation, including for phase I trials; refining coverage and prior authorization policies that may impede CT enrollment; addressing CT-related patient out of pocket costs (through removing impediments to targeted financial support); and improving the fragmented Medicaid policies related to CTs. A recent joint statement by multiple organizations, including ASCO, specifically cites ongoing efforts to improve the diversity of the cancer care workforce (including physicians, nurses, and research staff), and suggests that this impact could extend to improving diversity in research participation.

ASCO's Cancer Research Committee published a statement devoted to making clinical trials more representative through refining eligibility criteria, and continues to work with FDA and other stakeholders to refine these recommendations. A statement in 2015 made recommendations to improve the care of older adults, which included a call for increased CT recruitment. Another recently published ASCO guideline on patient-physician communication explicitly calls for discussion of clinical trial options (where appropriate), and suggests methods for integrating such discussions into clinic visits.

ASCO has also made it a goal to prioritize the passage of legislation that would require Medicaid coverage of the routine costs of clinical trials, bringing Medicaid in line with existing Medicare and commercial coverage requirements. This is particularly important to the goal of diversifying clinical trial populations, given the overlap between the Medicaid beneficiary population and the historically underrepresented CT subpopulations.

ASCO is currently partnering with the Association of Community Cancer Centers on a set of joint recommendations and practical strategies to increase participation of racial and ethnic minority populations in cancer treatment trials.

For More Information

Cancer Disparities and Health Equity: A Policy Statement From the American Society of Clinical Oncology

Press Release: ASCO & ACCC Join Forces to Increase Participation of Racial and Ethnic Minority Populations in Cancer Treatment Trials

Addressing Financial Barriers to Patient Participation in Clinical Trials: ASCO Policy Statement

Broadening Eligibility Criteria to Make Clinical Trials More Representative: American Society of Clinical Oncology and Friends of Cancer Research Joint Research Statement

Charting the Future of Cancer Health Disparities Research: A Position Statement From the American Association for Cancer Research, the American Cancer Society, the American Society of Clinical Oncology, and the National Cancer Institute

Improving the Evidence Base for Treating Older Adults With Cancer: American Society of Clinical Oncology Statement

American Society of Clinical Oncology Policy Statement Update: The Critical Role of Phase I Trials in Cancer Research and Treatment

Patient-Clinician Communication: American Society of Clinical Oncology Consensus Guideline