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Increasing Minority Enrollment Onto Clinical Trials: Practical Strategies and Challenges Emerge From the NRG Oncology Accrual Workshop

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Abstract

Racial and ethnic diversity has historically been difficult to achieve in National Cancer Institute–sponsored clinical trials, even while as many as 80% of those trials have faced difficulty in meeting overall recruitment targets. In an attempt to address these issues, NRG Oncology recently convened a comprehensive workshop titled “Clinical Trials Enrollment: Challenges and Opportunities.” Discussants at the workshop included representatives of the three legacy groups of the NRG (ie, Gynecologic Oncology Group, National Surgical Adjuvant Breast and Bowel Program, and Radiation Therapy Oncology Group), a minority-based community clinical oncology program, a large integrated health care system, the leadership of the National Cancer Institute, and a large patient advocacy group. This article summarizes the concepts discussed at the workshop, which included: needs

assessments, infrastructural support, training of investigators and research staff, specific clinical trial recruitment strategies (both system and community based), and development and mentoring of young investigators. Many new, more specific tactics, including use of diverse cancer care settings, direct-to-consumer communication, and the need for centralized information technology such as the use of software to match trials to special populations, are presented. It was concluded that new, innovative trial designs and the realities of limited funding would require the adoption of effective and efficient recruiting strategies, specialized training, and stakeholder engagement. US clinical research programs must generate and embrace new ideas and pilot test novel recruitment strategies if they are to maintain their historic role as world leaders in cancer care innovation and delivery.

Introduction

Clinical trials supported by the National Cancer Institute (NCI) cooperative group clinical trials mechanism have been instrumental in advancing the most important paradigm-changing findings from randomized phase III trials. However, the reality of federal budget limitations, along with emerging concepts of personalized health care, prompted the Institute of Medicine (IOM) to evaluate the cost and sustainability of the cooperative group program. In 2009, the IOM made consensus recommendations designed to improve cancer clinical trials, which called for the merger and/or consolidation of the cooperative groups.¹ A subsequent workshop recommended implementation steps to increase the speed, volume, and diversity of patient accrual.²

The science of clinical trial accrual, particularly analysis of participant diversity, is an area of much-needed study.³⁻⁵ The IOM noted that despite programs such as minority-based community clinical oncology programs (MB-CCOPs) and patient navigator research programs, racial disparities in enrollment persist.⁶

In an effort to examine clinical trial accrual, and specifically to develop new ideas for improving the accrual of racial and ethnic minorities, the newly formed NRG Oncology (consoli-

dation of Gynecologic Oncology Group [GOG], National Surgical Adjuvant Breast and Bowel Program [NSABP], and Radiation Therapy Oncology Group [RTOG]) sponsored a workshop entitled “Clinical Trial Enrollment: Challenges and Opportunities” during the inaugural NRG semiannual meeting. Participants included representatives of three of the NCI legacy groups (ie, NSABP, RTOG, and GOG), an MB-CCOP, a large national health care system, patient advocacy leaders, and NCI Community Oncology Research Program (NCORP) leadership. This article explores barriers and opportunities to address clinical trial enrollment within the context of NRG Oncology.

Barriers to Clinical Trial Accrual Cooperative Groups Address Problem

GOG investigators presented findings from a recent study examining patient and physician factors associated with clinical trial accrual for women with gynecologic cancers. This prospective, observational study sought to identify modifiable factors related to availability, eligibility, and enrollment in GOG cervical and uterine cancer trials and included 150 physicians and 781 patients from 60 sites from across the United States.⁷ Fac-

tors associated with patient enrollment onto therapeutic trials included: belief that the trial might help, patients' concern about their care if they were not in a trial, and patients' perception of pressure from their provider to enroll onto a trial. Significant physician beliefs associated with enrollment were: believing patients would not do well with standard therapy and belief the trial would not be time consuming. Nonwhite patients and patients of black physicians (irrespective of race) had higher odds of enrolling onto clinical trials compared with other patients. The authors concluded that interventions designed to address the consent process, patient and physician understanding of beliefs, cultural factors, and trust could improve enrollment onto cancer clinical trials.

RTOG investigators also conducted a study to assess attitudes, beliefs, and practices of principal investigators and clinical research associates that might influence clinical trial accrual at 267 member institutions.⁸ Specific barriers included large time commitments for the participants, insurance coverage, lack of family support, fear of toxicity, and preference for a particular type of therapy. Nearly one third of the staff indicated there was no formal mechanism for screening patients for eligibility for a trial and that translated consents were needed for non-English speakers. Analysis of the data led to the following recommendations: development of scripts to reduce the potential for bias, creation of training modules for principal investigators and clinical research assistants, and expansion of patient navigator programs.

The RTOG team used these findings to create a cultural competency training program that recognizes the importance of cultural diversity, awareness, sensitivity, and competence among health care providers and investigators.⁹ Guided by this model, investigators created a four-module 3.5-hour training program that focused on barriers, myths, beliefs, and norms regarding clinical trials within Latino and African American cultures.¹⁰ The modules contain role-playing examples of patient discussions. Assessment of this program is ongoing.¹¹

NSABP representatives reported on the Diversity Strategic Planning Working Group (DSPWG), designed to enhance minority participation through education of investigators, research staff, and community groups, and the establishment of relationships with minority organizations. The DSPWG provided culturally sensitive input during the development phase of protocols and made recommendations regarding the need for targeting certain populations for accrual. The DSPWG additionally created a resource list of culturally appropriate educational information about clinical trials and conducted special educational sessions on cultural competency at NSABP group meetings.

Recognizing that a diverse research workforce is pivotal to a holistic strategy for recruitment of underserved populations, the DSPWG developed a junior minority investigator travel award to encourage young investigators and a minority mentoring program to facilitate collaboration of junior minority investigators with senior investigators. Incorporation of these best practices is currently being explored by the NRG Health Disparities Committee.

Large Health Care System Addresses Problem

Kaiser Permanente of Northern California (KPNC) recently examined structural features that facilitate clinical trial accrual in general and among minority and underserved populations. This large, integrated health care delivery system has 3.5 million members, which represents approximately 35% of the northern California health care market and 1% of the US cancer burden. Furthermore, the insured membership of KPNC reflects the insured population in the geographic area it serves in terms of age, race/ethnicity, and socioeconomic status.¹²

Of great importance, members with cancer receive virtually all of their care in a coordinated fashion from KPNC physicians at community medical centers, where the workforce reflects the diversity of their locations.¹³ The provision of coordinated care, along with the use of a system-wide comprehensive electronic medical record and associated research databases and a widely disseminated clinical trials program, has reduced disparate clinical trial enrollment by race/ethnicity. This is consistent with other research that has shown that integration of care serves to reduce racial/ethnic disparities in cancer outcomes.¹⁴

KPNC recently completed "CHOICES: Understanding Clinical Trials As a Treatment Option" to evaluate barriers to trials among oncologists and patients as part of this effort. Patients who participated in CHOICES (N = 905) were eligible for a breast, colorectal, or lung NCI cooperative group trial being conducted at KPNC. A survey, which assessed KPNC oncologists' (N = 88) attitudes, demographics, and trial experience, revealed that oncologists' awareness of open trials, their willingness to discuss trials with eligible patients, and their perception of the organizational value of clinical trial activity were strong predictors of their subsequent trial accrual.¹⁵

MB-CCOP Addresses Problem

In 1983, the NCI created the MB-CCOP to address minority recruitment to clinical trials, serving as a laboratory for testing enrollment strategies.¹⁶ Leadership from the MB-CCOP based at Tulane University in Louisiana indicated the most consistently successful strategies included: use of culturally sensitive investigators and coordinators, incorporation of a community advisory board, and partnership with local churches, community groups, and language-based media outlets on an ongoing basis (Table 1).

In addition, investigators from this large, inner-city MB-CCOP reported a recent study of factors affecting enrollment of women with cervical cancer onto clinical trials. The most important factor was patients' perception of the degree of commitment of the primary oncologist to the trial.¹⁷

Patient Advocate/Consumer Addresses Problem

A cancer survivor with extensive experience in leading patient advocacy work presented concerns regarding clinical trial accrual drawn from her constituency. Noting that an increasing number of trials target specific molecular characteristics of individual cancers, the patient advocate noted that such targeted therapy studies may compete with larger, more accessible trials

Table 1. Partnerships to Address Minority Recruitment to Clinical Trials

Partner	Target Audience	Description
Helping Hands Across the Divide churches	African American	Health promotion–related collaboration and clinical trial education
Vietnamese–US Representative Louisiana Department of Wildlife and Fisheries field offices	Vietnamese	Health promotion
Spanish language news, television, and radio	Hispanic/Latino populations, largely Honduran	Clinical trial information

with wider eligibility. Patients or their physicians may not be aware of or have access to the more targeted studies, which may then affect enrollment onto those studies.

An example would include poly (ADP-ribose) polymerase inhibitor studies that focus on individuals with *BRCA* mutations, which account for approximately 7% and 15% of all women with breast and ovarian malignancies, respectively. These studies have the potential to compete directly with more numerous breast and ovarian cancer trials.

To further illustrate, a recent search of ClinicalTrials.gov for treatment studies of advanced breast cancer revealed 181 studies open to women with advanced breast cancer: 36 studies for advanced estrogen receptor– and progesterone receptor–positive breast cancer (common in women with *BRCA2* mutations) and 29 studies for women with advanced triple-negative breast cancer (common in women with *BRCA1* mutations). The five studies open specifically for women with advanced *BRCA*-associated breast cancer were thus competing with all of these other studies. The prospect of being unable to complete *BRCA*-specific clinical trials jeopardizes progress in treating these cancers. Furthermore, it could seriously threaten the viability of targeted therapy research. A more comprehensive approach (and less confusing for patients) would include both physician/investigator-based and patient/consumer-based strategies. Physicians and investigators would benefit from prioritization of studies focused on limited population groups and financial or other encouragement to refer patients to targeted therapy trials. Approaches that are patient (or consumer) friendly would include direct education, clinical trial matching services, and use of advocacy groups, such as FORCE (Facing Our Risk of Cancer Empowered), which currently sponsors several such programs.¹⁸

NCI Leadership Addresses Problem

From the perspective of the NCI, it is vitally important that participation in clinical trials is sufficient to support novel trial designs and inclusive enough to translate scientific advances to the general population. Figure 1 demonstrates that although there has been some increase in enrollment of minority populations onto clinical trials over the past decade, there remains substantial opportunity for improvement.

In August 2014, the NCI launched a new community-based research program that expanded the scope of clinical trials to include cancer care delivery research. This provides an opportunity to explore the multilevel influences of providers and organizations on the enrollment of minority and underserved patients onto clinical trials.

The structure of this new program—the NCI Community Oncology Research Program (NCORP)—encourages trial-based recruitment networks for large clinical trials (eg, phase III chemoprevention and screening trials) and perhaps most importantly includes additional funding, including supplements for navigators or other specifically needed local personnel. To further enhance accessibility of trials, the NCI is also currently seeking ways to support research bases in translating consents for the multitude of languages spoken within the NCI National Clinical Trials Network.

Strategies for Enhancing Clinical Trial Enrollment and Plans for the Future

The concepts presented and discussed at this workshop covered diverse aspects of poor enrollment and disparity in accrual to clinical trials. A number of common themes emerged.

First, novel trial designs using targeted agents with biomarker end points will become standard. These designs will naturally create subgroups from larger disease populations. Targeted recruitment and emphasis on the personalized nature of such trials may facilitate accrual to these specialized studies. Inclusion of diverse subgroups should be considered during the trial design phase. Review of protocols in development using a disparity lens will lessen the potential for future problems.

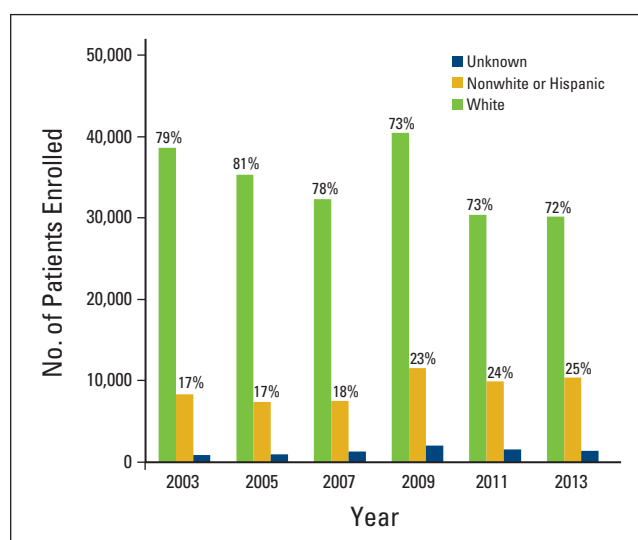


Figure 1. Minority enrollment onto National Cancer Institute–funded trials from 2003 to 2013. Minority indicates nonwhite race or Hispanic ethnicity; majority indicates white race and non-Hispanic ethnicity. Data adapted with permission.

Second, novel trial design using agents targeted at the molecular level could lessen the need to define a study population as homogenous based on traditional, less precise eligibility criteria. Rather, individuals will be defined by their personal molecular (genomic) structure, which will in turn determine their eligibility for a specific trial.

Third, the influence of local health care payers/insurers on the delivery of cancer care must be evaluated in much more detail than it has been to date. Cancer care delivery research must be made available at both the community and academic levels to best develop interventions designed to improve health outcomes. Organized study of these concepts will likely require modifications in process, including an examination of the consent process, to facilitate this research.

Fourth, the commitment of the physician/investigator is paramount. Investigators must be culturally sensitive and aware of the impact of appropriate communication and patient trust. Above all, they must believe in the importance of clinical research and be committed to enrollment and possess the ability to encourage diverse groups of patients to also believe and participate in clinical trials. The cooperative groups are well positioned to address this need by designing ongoing training programs for investigators, particularly junior investigators who are available to all groups and stakeholders involved in clinical trials participation.

Fifth, direct-to-patient (consumer) communication/advertising must become more widespread. Collaboration with key stakeholders such as community groups, survivor advocacy groups, churches, and other local institutions can include novel approaches to facilitate accrual of underrepresented populations. The NCORP places increased emphasis on cancer prevention trials and studies of chronic toxicities, both of which are particularly well served by direct-to-community messaging.

Sixth, local institutional commitment and adequate infrastructure including translation of consents, navigator programs, and research friendly electronic medical records provide examples of such support.

Seventh, expansion and standardization of demographic data collection and capture of real-time information about accruals relative to the burden of disease in special populations should also be priorities. The NRG Oncology Health Disparities Committee is currently evaluating this issue. In addition to standardized collection of race/ethnicity and sex, country of origin, sexual orientation, veteran status, and income data are being discussed.

Eighth, strengthened information technology infrastructure and direct interface with existing national and local databases should occur.

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Ninth, recruitment, training, and mentorship of young investigators interested in clinical research, particularly those of ethnic minority backgrounds and/or those with an interest in cancer disparities, must be more fully developed. Existing local educational programs may serve as models for larger efforts from the cooperative groups or directly from the NCI.

Tenth, underlying all of this is the need for continued and improved budgetary support for clinical cancer research within the NCI by Congress.

This workshop was the direct responsibility of the NRG Health Disparities Committee, which is charged with developing strategies to increase enrollment of minorities and the underserved onto clinical trials. The committee includes experienced investigators from a wide range of disciplines and backgrounds and is chaired by representatives of the three legacy groups (ie, GOG, RTOG, and NSABP). The committee plans to incorporate the best practices presented at this workshop through involvement in disease site committees, input into protocol development, analysis of educational workshops, development of mentoring programs, and dissemination of information and research.

The workshop described represents an initial step in this direction by combining the collective experience and potential of the new NRG Oncology Group and the NCI to enhance clinical trial accrual. Moving forward, input will be solicited from a wide array of stakeholders, including community investigators, the patient advocate community, and basic science researchers. This will be essential for these trials to ultimately improve the quality of cancer care.

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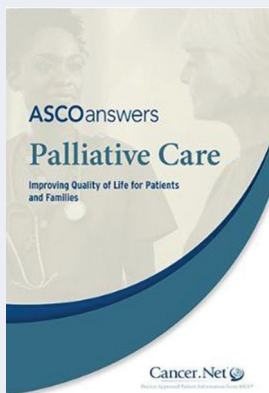
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