

Problem Solving to Enhance Clinical Trial Participation Utilizing a Framework-Driven Approach

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Abstract: Health professionals agree that increasing diversity in clinical trial participants is an important way to improve cancer care and address disparities in outcomes. However, trial participation among minority populations has been low historically and continues to be low. Underrepresentation has resulted in majority groups reaping greater benefit from research findings, thus widening cancer health disparities. Addressing these disparities effectively has proven to be challenging. To maximize diversity among participants, it is necessary to understand the steps patients take to enroll in trials; the barriers patients face at each step; and the needs and preferences of the patient population overall and subgroups specified by age, race, ethnicity, or sex, in order to develop interventions to address barriers to participation. To improve clinical trial participation, and most importantly to eliminate disparities, cancer centers should examine reasons patients fail to enroll in trials and develop interventions designed to meet their patients' needs and preferences.

Introduction

The Revitalization Act of 1993 mandates the inclusion of women and minorities in clinical research. Researchers who receive funding from the National Institutes of Health (NIH) must strive to achieve equitable representation among study participants of underrepresented subpopulations, such as people of advanced age, female sex, non-white race, or Hispanic ethnicity.¹ Further, in addition to leading the nation's efforts to identify new cancer treatments, National Cancer Institute (NCI)-designated comprehensive cancer centers are required to undertake outreach activities and research to identify the needs of underrepresented populations and address cancer care disparities, including the lack of participation in clinical trials.²

Keywords

Barriers, cancer center, cancer clinical trial, clinical trial enrollment, neoplasms, patient selection

Table 1. Accrual Rates for Patients at SKCCC^a

	Patient Population		Women		Minorities	
	Overall No.	No. Accrued (Percentage)	Overall No. (Percentage)	No. Accrued (Percentage)	Overall No. (Percentage)	No. Accrued (Percentage)
2016	4190	964 (23.0%)	2012 (48.0%)	415 (43.0%)	1255 (29.9%)	284 (29.4%)
			Disparity: 5.0%		Disparity: 0.5%	
2017	4163	1205 (28.9%)	1968 (47.3%)	452 (37.5%)	1214 (23.6%)	319 (26.4%)
			Disparity: 9.8%		Disparity: 0%	
2018	5134	1101 (21.4%)	2037 (39.7%)	466 (42.3%)	1485 (28.9%)	322 (29.2%)
			Disparity: 0%		Disparity: 0%	
2019	4073	866 (21.3%)	1930 (47.4%)	379 (43.8%)	1174 (28.8%)	255 (29.4%)
			Disparity: 3.6%		Disparity: 0%	

^aPatients are Maryland residents who have been newly diagnosed or treated at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins (SKCCC).

Although the Revitalization Act was passed more than 25 years ago, overall adult participation in cancer clinical trials nationwide remains low, and underrepresented groups make up a smaller fraction than expected based on the population of all cancer cases.³

The NCI evaluates disparities in participation by comparing the percentage of women and minorities among trial participants with the percentage they represent among the center's total patient population. At the Sidney Kimmel Comprehensive Cancer Center (SKCCC) at Johns Hopkins, 21.3% to 28.9% of patients residing in the state of Maryland, which is the SKCCC's catchment area, participated in an interventional trial between 2016 and 2019. This participation rate does not apply to all groups.^{4,5} At the end of 2019, 29.0% of interventional trial participants were minorities—the same percentage they represent among the SKCCC's overall number of patients. Only 43.8% of interventional trial participants were women, yet women accounted for 47.4% of patients overall. As a result, the SKCCC is working to address the 3.6% disparity in participation noted among women (Table 1).

Although overall trial participation at the SKCCC is high, achieving equitable trial representation among SKCCC patients has been challenging. To maximize diversity among participants, it is necessary to understand the steps patients take to enroll in trials; the barriers patients face at each step; and the needs and preferences of the patient population overall and demographic subgroups. In this way, researchers can develop effective interventions to address barriers to participation.

Here, we describe the SKCCC's experience to date, and review interventions instituted to address barriers to trial participation. We have structured our discussion around the steps to clinical trial enrollment using a

framework developed by Kanarek and colleagues.⁵ This framework builds on an early literature review by Ford and colleagues and was developed to find solutions to low clinical trial enrollment.⁶

This proposed framework highlights barriers by level of intervention (institutional, community, provider, or patient)⁷ and the steps toward enrollment. It outlines progression toward trial enrollment in 7 sequential steps⁵:

(1) *Trial availability*: Is the center's trial portfolio diverse enough to have available trials for the types of patients seen?

(2) *Patient eligibility*: Does the patient have the trial disease of focus, meet prior therapy requirements, and meet other broad eligibility specifications?

(3) *Physician triage*: Based on the physician's assessment, is the patient able to participate? Is the trial clinically appropriate based on the patient's current disease status and treatment plan?

(4) *Trial discussion*: Did the physician discuss the trial with the patient?

(5) *Patient interest*: Did the patient express interest in hearing more about the trial or enrolling?

(6) *Patient consent*: Did the patient sign the informed consent document? and

(7) *Patient enrollment*: Did the patient meet trial inclusion and exclusion criteria?

These steps effectively parse the often-aggregated reasons of "eligibility," "discussed and offered," and "enrolled." They provide clear terms for reported barriers to clinical trial participation and may offer better tools with which to solve problems.⁹ Evaluation of which patient subgroups are not completing the steps and where they fall off the path to enrollment can inform the development of interventions customized to a center's patient population.

Approach

In previously published work, Kanarek and colleagues proposed the sequential framework and demonstrated its utility for identifying the number, percentage, and demographics of patients who fall out at each step.⁵ Although this analysis is beyond the scope of this article, the steps to enrollment have fostered further examination. Their framework steps included: trial availability, patient eligibility, physician triage, trial discussion, patient interest, patient consent, and patient enrollment. Table 2 displays the enumerated factors influencing participation found in the literature.^{4-6,10-12}

We first presented barriers from the published review literature categorized by each framework step. Knowing the applicable barriers, we gathered pertinent information from SKCCC patients with whom oncologists completed clinical trial discussions, in order to pinpoint disparities in trial participation that might impede trial recruitment at a particular stage of enrollment. Then with SKCCC-specific data, we were informed about the need to and the context in which to address enrollment shortcomings. Finally, we designed an intervention that would improve particular outcomes. We were able to refine our remedies for low enrollment and move on to address other pressing barriers in a continuous quality improvement (CQI) manner.¹²⁻¹³ This analysis identified some CQI characteristics concerning environment and resources, quality improvement outputs, depth of implementation, implementation approach, and participation by the physician and other professionals.¹³

Results

Trial Availability

Funding is an important factor in the availability of institution-wide trials. Financial support for clinical trials comes from various outlets, including the cancer center itself, external funders such as the NIH, private companies, and investigator-driven support, such as career funding. No matter the source of funding, cancer centers require substantial research infrastructure—space, personnel, shared research resources, centralized oversight, and scientific and administrative management systems—to launch and complete clinical trials. NCI-designated cancer centers receive infrastructure funding to support research collaborations and core services,^{2,8} including support to implement clinical trials. However, content of the active trial portfolio is a center responsibility. The NCI recently summarized aspects of trial availability that might result in the most efficient and rational trial portfolios, including those that complement industry-funded research.¹⁴

At the SKCCC, disease-focused clinical research

groups determine their study portfolio based on patient population, scientific priorities, and available resources. Retrospective chart reviews of clinical trial participation, along with prospective participation assessments, were invaluable to assessing trial availability. We constructed a flow chart separating clinical trials according to disease characteristics and broad trial eligibility for each disease program by cancer site. From the framework flowchart, we ascertained whether a particular patient had an available trial in the SKCCC portfolio.¹⁵ In addition, collection of data regarding patients for whom no trials were available allowed us to provide feedback to study teams regarding gaps in their portfolio. This approach addresses the notion of “stratified medicine”¹⁶ and highlighted segments of the patient population for whom few or no trials were offered.

It became clear which subgroups of patients were coming to the SKCCC for care and were not being enrolled in trials. Consequently, SKCCC investigators developed trials tailored to these subgroups and their specific diseases. For example, in looking at the 2 main disease categories in the Head and Neck Program (human papillomavirus [HPV]-positive and squamous cell head and neck cancers), trial availability depended heavily on disease factors. Investigators increased the number of available trials, and intentionally designed trials for each of these groups to enable more patients to enroll.^{8,17} Another example is a randomized weight loss study called SPIRIT (Trial of Behavioral Weight Loss and Metformin Treatment to Lower Insulin Growth Factor in Cancer Survivors). This trial was designed to reach Baltimore City residents, who are often underenrolled, who had completed primary cancer therapy.¹⁸ The study was carried out in the community, making it more accessible to participants who were unable to travel or uninterested in traveling to the SKCCC main campus. Anwuri and colleagues at Washington University⁴ introduced a similar approach of monitoring minority participation, raising provider/study team awareness, and establishing a collaborative relationship with investigators as an effective means of increasing and broadening trial participation.⁴ As we have done at the SKCCC, these investigators met regularly with researchers to discuss study enrollment and take remedial action to resolve imbalances in recruitment-based study portfolios.

Patient Eligibility

According to prior literature, reported barriers affecting patient eligibility include study-specific eligibility criteria, time constraints, physician decisions regarding treatment, prior treatments, lack of communication methods, and comorbidities.^{5-6,10,19}

The goal of the American Society of Clinical Oncology (ASCO) and the Friends of Cancer Research in

Table 2. Barriers to Cancer Clinical Trial Participation by Framework Category

	Opportunity/Awareness of a Trial ⁶						
	Patient Trial Fit ⁵			Opportunity		Acceptance	
Steps	Trial Availability	Patient Eligibility	Physician Triage	Trial(s) Discussed	Patient Interest	Patient Consent	Patient Enrollment
Ethical Principle ⁵	Beneficence	Justice/ Beneficence	Beneficence	Respect for persons	Respect for persons	Respect for persons	Respect for persons
Level of Intervention							
Institutional⁶	Lack of protocols ⁵⁻⁶ Dissemination ⁶	Eligibility ⁵⁻⁶	Distance to tx ⁶	Distance to tx ⁶	Distance to tx ⁶	Distance to tx ⁶	Too understaffed to enroll ⁶
Community⁶			Distance to tx/ transportation ⁵	Distance to tx/ transportation ⁵	Distance to tx/ transportation ⁵⁻⁶ Community perceptions about clinical trials ¹⁰ Neighborhood violence, high-poverty zip code ¹⁰	Distance to tx/ transportation ⁵⁻⁶	
Provider⁶		Study design ⁶ Training ^{37,38}	Referral sources ⁶ Lack of provider referral ⁶ Job conflicts with participation ⁵	Provider characteristics ⁶ Provider attitudes ⁶ Provider-related ⁶ Awareness of patient hope ^{29,38}			
Patient⁶	Patient/tumor characteristics ⁶	Time urgency ⁵ Physician decision ⁵ Current/prior treatment ⁵ Comorbidities ^{6,10,35} No telephone ⁶	Legal status ¹² Low health literacy ⁶ Lack of education/information about clinical trials/cancer ^{6,12-13} with health literacy ⁶ Less use of Internet ¹⁰ Survival concerns ^{28,34}	Communication ^{7,13} Mistrust of research ⁶	Skeptical of benefit to oneself ¹¹ Stigmatizing, discriminating, or identifying ¹¹ Treatment preference ⁵⁻⁶ /open designs ³⁷ Negative about the research ¹¹ Comorbidities ⁶ Interest in health-related outcomes ³¹ Family ^{6,11} Social support ³¹ God reliance/fatalism ³¹ Provider support ³¹	Competing demands ^{6,12} Patient did not return ⁵ Loss of control; fear ^{6,10,12} Perceived harms ¹² Discomfort ^{6,12}	Costs in dollars, time, income ^{6,10,12} Lack of child care ^{10,12} Patient failed screening protocol ⁵ Comorbidities ⁶ Education about the clinical trial ¹⁰

tx, treatment.

reconsidering eligibility criteria was motivated by 3 factors: to increase access to clinical trials, to assure a more representative population in clinical trials, and to generally broaden access to new treatments while protecting individuals from harm.¹⁹ In 2017, the US Food and Drug Administration (FDA) created an internal department called the Oncology Center of Excellence in order to accelerate technologies and methodologies for oncology clinical trials.²⁰⁻²¹ Through this FDA initiative, traditional phase 1 and phase 2 studies may include a hybrid evaluation of safety and efficacy in the same patient, either simultaneously or in close sequence. Furthermore, the FDA has implemented changes in trial planning to focus on safety and consent parameters to expand the inclusion of children and women.^{19,22,23,26} In this instance, investigators consider whether a child might benefit from a treatment that is ordinarily reserved for adults.

Comorbidities also have relevance to final eligibility criteria within specific trial designs or interventions.^{19,22,24-26} Comorbidities have emerged as a relatively common exclusion criteria, and recently there has been an increased willingness to expand the pool of individuals eligible for participation. In the SKCCC clinical trial data from 2014 to 2017, comorbidities were an influential factor for exclusion from clinical trial enrollment in working-age adults. The most common comorbidities were tobacco exposure, heart disease, diabetes, and lung disease. Less common factors included HIV and renal disease.²⁶

The SKCCC's Clinical Research Review Committee is responsible for the review of studies for scientific merit and for whether the protocol will support execution of the trial to achieve the study's objectives. The Clinical Research Review Committee has updated its review process to encourage investigators to broaden eligibility. Similarly, investigators may consult with the center's Assistant Director of Diversity and Inclusion in Clinical Research (ADDICR) if they believe that the cancer type, the study's design, or participation requirements might pose challenges to recruiting a diverse patient population. Consultation is not mandatory; however, a review takes place 1 year after institutional review board (IRB) approval. If enrollment at that point is below the projected target or there is a disparity among participants by race, sex, or across the age continuum, the ADDICR reviews the study to identify gaps to reconsider and offers the study team assistance to develop an action plan. This plan may include input from community advisory groups regarding recruitment.

Physician Triage

During the physician triage step of the framework, the treating healthcare provider makes a decision about

whether an available trial provides a clinically appropriate treatment option and whether the potentially eligible patient is able to fully participate in the trial.⁵ In this step, the patient could lose the opportunity to enroll according to the physician's presumptions about his or her ability and/or willingness to participate.⁶ Later in the enrollment process, the IRB requires physicians to document whether they believe the patient can make an informed decision; however, the consideration for participation in a clinical trial initially occurs at this stage. Physician triage is not the final determination for patient enrollment; rather, it is an early point when, based on broad factors such as stage of disease, prior therapy, and the patient's performance status and ability to participate, the physician will determine whether to discuss a trial with the patient. At this step, physician bias may lead to unfounded assumptions that the patient may have difficulties with adherence or stamina, or lack a general understanding of the trial itself; this bias can lead to racial or other disparities in study populations.^{27,28} Among the patient barriers inhibiting triage are low education, poor health literacy, and difficulty in understanding clinical trials.^{5-6,8}

A member of our group (D. L.) conducted one-on-one interviews with 20 physicians and research nurses about recruiting patients to clinical trials in an attempt to shed light on minority recruitment. Staff did not report conscious biases about enrollment based on patients' cultural, racial, or ethnic backgrounds. Nevertheless, the physician is the gatekeeper as to whether a discussion is initiated, and is ultimately responsible for assessment of the patient's ability to understand the risks and benefits of a study. This survey led to a best-practice mandate¹¹ consisting of a center-wide policy requiring broad-based cultural sensitivity training for oncology physicians and research staff. This mandate was an important step toward raising awareness of the importance of diversity and inclusion in trial participation, and also highlighted the seriousness with which we aim to meet the needs of the SKCCC's diverse patient population. To individual practitioners, physician triage may be the most nuanced step of the enrollment process.

Trial Discussion

Trial discussion is an important step because it offers the patient the opportunity to learn about, and subsequently participate in, clinical trials suitable for his or her condition. Moreover, this step advances communication and conveys the physician's support for clinical trial participation.²⁹ Two review papers on barriers to treatment^{6,12} addressed provider-related characteristics, attitudes, and other factors,⁶ highlighting potential barriers at this step. George and colleagues highlighted that communication styles are also important at this step.¹² Addressing miscon-

ceptions and answering questions are important aspects of discussions about clinical trials.²⁹⁻³⁰ In fact, it is necessary to address any patient concerns prior to enrollment in a clinical trial. The clinical trial discussion is critical to successful recruitment and participation.

The SKCCC implemented a prescreening pilot study and collected data on trial candidates to understand why available trials are not discussed with some SKCCC patients, and why others do not enroll after a discussion. The study screened new patients for available trials prior to their physician visit and physicians were told of the screening result. After the visit, physicians were asked whether a discussion of the identified, available trial took place. If the trial was not discussed, physicians were asked to indicate the reason: trial not clinically appropriate, patient ineligibility, or other reasons. For example, the trial may not have been clinically appropriate at that point in the patient's care owing to a decline in physical condition or a change in disease status that was not noted in the medical records available during prescreening. If a trial discussion took place and the patient was deemed a candidate and referred to the trial's research nurse, research teams were then asked to document whether enrollment occurred and, if not, to record the reason in the SKCCC Clinical Research Management System (CRMS).

During our retrospective review of 4 cancer disease sites, we found that 89% of our patients had a clinical trial discussion documented in the medical record.¹⁵ Rates of documented trial discussions were lowest among lung cancer physicians and staff, and highest among members of the prostate cancer program. These 2 programs pointed to differences among their patient populations at the time of doctor visits to discuss clinical trials. Physicians in the lung cancer program noted occasions when they identified available trials in the program's portfolio, but upon meeting the patient, found a decline in performance status since the last recorded visit and realized the patient would not be eligible. As a result, trials were not discussed. Physicians triaged these cases away from clinical trial participation unless there was another available trial for which the patient was then eligible. Conversely, in the prostate cancer program, clinical trials were a standard part of discussions with every new patient even when no trial was immediately available. This could be an anticipatory guidance message that could encourage proactivity among all SKCCC programs.³¹ This evidence also highlights the unique factors specific to the cancer and the patient that influence whether a physician discusses a specific trial and whether the patient considers enrollment. These factors include the cancer's intricacies of survival and associated quality of life, as well as the patient's fitness level. The wishes of the patient and his or her family are also important contributing factors. As a result, SKCCC

members committed to review their program portfolio and to document discussions in the medical record.

Patient Interest

From the literature, community-level factors affecting patient interest in clinical trial participation include distance to treatment and transportation^{5,6}; community perceptions about clinical trials¹⁰; neighborhood violence¹⁰; high poverty; and skepticism about trial benefits. In addition, patient-level factors around interest in a clinical trial include fear that the experience will be stigmatizing, discriminating, or identifying; patients feeling negatively toward research^{10,12}; patients worried about treatment preferences^{5,10} and open research designs; and patient decisions influenced by family,^{6,10} friends,¹⁰ and belief in God.¹⁰ At times, the patient's health took priority, whether it concerned comorbidities or health-related outcomes from the clinical trial.³² Furthermore, fatalism¹⁰ about their disease sometimes influenced participation decisions.

In a retrospective chart review, we found that health insurance was a barrier to participation for our patients from Pennsylvania, where a mandate for cancer clinical trial coverage was lacking. Lack of insurance coverage did not correlate to the traditionally under-represented groups by sex, age, race, or ethnicity. In the health insurance review, we were able to ascertain patient demographics, insurance carrier/plan, and time to approval through pre-enrollment insurance clearances completed by our Access Services group. Before enrollment, standard-of-care treatment costs and clinical trial expenses are enumerated so that the insurer and the patient understand the clinical trial expenditures. At the time of this retrospective review (2003-2007), 20 states, including Maryland, had mandates requiring the coverage of standard-of-care treatment costs associated with clinical trial participation.³² In 2013, the Affordable Care Act (ACA) mandated that all health insurance carriers cover these costs for qualified participants.³³

In our efforts to reduce barriers, we have explored patient interest in research. Patients were telling our nurse coordinator that they had come to the SKCCC for cancer care, and not for research. In addition, family members had concerns about trial participation given that caregiver time is finite. Furthermore, patients felt they did not know enough about clinical trials. For example, they did not always know how the standard of care fit with the experimental therapy, or about the necessity of randomization and blinding of treatment. Researchers told us they wanted to convey hope and anticipation, yet patients may perceive this as valuing research over patient care.³⁰ To address this concern, we developed *Power in Choices*, a series of 3 videos about clinical trials. The first video,

Clinical Trials: Words & Phrases, defines the language of clinical trials. The second video, *Clinical Trials: Hope and Anticipation*, concerns the science behind developing clinical trials. The third video, *Clinical Trials: Expectations, Realities & Challenges*, highlights patient and caregiver perspectives regarding the decision to participate. These award-winning videos are found on YouTube (<https://www.youtube.com/user/JohnsHopkinsKimmel/featured>), and thus are widely accessible to a broad audience of cancer patients.

Patient Consent

Consent to a clinical trial is a required step for participation that presumes a person is completely aware of the study demands, benefits, and risks. Informed consent is a cornerstone of ethical research. It is often the step when barriers such as logistics, transportation, fears, loss of control, perceived harms, and discomforts arise and influence whether the patient provides consent for a specific clinical trial.^{6,10,12} Langford and colleagues examined clinical trial enrollment and also found that consent hinged on consent page length and readability.³⁴

Presentation of the consent form for review is typically the point at which patients and their families begin formulating questions, expressing concerns regarding participation, and considering logistics required for participation in offered trials. In a retrospective chart review of prostate cancer patients, most patients who dropped out at this step had decided not to return for care at the SKCCC and to continue their care elsewhere. Some did not return to provide consent owing to the distance between their residence and the cancer center.¹⁵ In unpublished findings, SKCCC patients living in Baltimore, the center's immediate neighborhood, were under-enrolled in clinical trials, regardless of race. We believe that other factors besides race may play a part in under-enrollment, including social and cultural factors, competition among 6 nearby hospitals, and public transportation challenges for travel between cities. In some instances, however, those patients traveling a greater distance, such as those residing in West Baltimore or Prince George's County, had a higher likelihood of enrolling in a clinical trial than those residing in East Baltimore, where the SKCCC is located.

In addition to supplying additional information about specific clinical trials and consenting patients, research nurses often learn about patients' potential barriers to enrollment. In 2013, the SKCCC mandated that research teams collect the reasons why trial candidates with whom trials were discussed did not agree to participate. Research nurses were tasked with entering these reasons into our CRMS for the ADDICR (D. L.) to review. Reasons patients did not consent included

physician decision, decline in performance status, preference for standard of care, concerns about randomization, lack of interest in research, financial/logistic constraints, too many visits required, and distance from home. We are currently working on a data analysis of 4760 candidate entries from 2015 to 2019, and our findings will be published separately.

An initial look at the data noted that the underlying reasons of financial/logistical constraints, too many visits, and distance from home were broadly categorized as related to transportation difficulty, which is a barrier to enrollment that is well documented in the literature.⁶⁻⁷ These reasons formed the basis for our institutional remedy, a cancer center-funded transportation, IRB-approved study, "Enhancing clinical trial participation: assistance for parking and transportation for patients participating in therapeutic oncology trials," to investigate the influence of the provision of transportation on the decision to enroll. The study covers the cost of parking for visits associated with therapeutic clinical trials that do not provide parking/transportation, beginning when a patient is identified as a candidate and extending up to 1 year after enrollment. Further, patients residing in Baltimore may choose taxi transportation in lieu of paid parking. Enrollment is ongoing, with 650 patients enrolled to date. Results regarding whether transportation/parking support influenced the decision to participate, or if the patient felt the provision made participation easier, are pending.

We note that in our clinical enrollment framework, the final stop is actual enrollment rather than consent.^{5,6}

Patient Enrollment

After providing informed consent, patients may be enrolled. This step depends on the results of patient screening using study-specific inclusion and exclusion criteria, and the availability of a study slot in a reasonable time so that treatment is not unnecessarily delayed. As with aforementioned candidate data, reasons for non-enrollment of consented SKCCC patients are also entered in the CRMS. Common reasons for non-enrollment include laboratory values that fall outside of protocol limits, a decline in patient performance status, inadequate study slot availability, changes in the treatment plan, and a decision by the patient to not enroll or receive care elsewhere. In addition, evolving comorbidities may render the patient ineligible for enrollment.^{5,6} Rivers and colleagues and George and colleagues described social support factors, such as lack of childcare, inadequate time, and monetary costs, that affect this stage in the proposed framework.^{10,12} At this point, however, most patients are able to proceed with enrollment because any barriers have been addressed at an earlier time.

Conclusions

Although just 3% of adult cancer patients overall¹⁰⁻¹² participate in a clinical trial, a SKCCC study found that 17% of patients at longstanding cancer centers enrolled.⁵ We have parsed why this percentage is significantly higher at cancer centers than at other types of treatment facilities, but still low, using a conceptual framework to understand how patients traverse several hierarchical steps, from trial availability to enrollment. A patient may face barriers to enrollment during any one of these steps. The final percentage of accruals is the aggregation of transitions from step to step. To increase clinical trial participation and improve diversity among participants, interventions³⁵⁻³⁷ may be more precisely developed in response to a cancer center's patient population based on the reasons they do fail to complete the steps to enrollment.

At the SKCCC, use of the framework, collection of data at each step, and the development of intervention(s) in response to reasons patients failed to enroll contributed to a decrease in disparities in interventional trial participation among women and minorities. During the 2016 NCI site visit, the SKCCC reported a decrease in the trial disparity from 2010 to 2015 for women, from 7.1% to 2.1%, and for African Americans, from 8.5% to 1.8%. The center's accrual and disparities for women and minorities since the site visit are noted in Table 1.

Our framework approach might be of help to other centers. It has allowed us to focus on exactly where patients fall off the path to enrollment, and more importantly, to identify who these patients are in terms of demographics, because certain barriers affect some populations more than others. This information was invaluable to developing interventions at the SKCCC. For example, our clinical trial education videos are designed to educate patients about trials, addressing knowledge gaps and informing the decision-making process. Another example is our IRB-approved study, "Enhancing clinical trial participation: assistance for parking and transportation for patients participating in therapeutic oncology trials," which provides parking or taxi transportation to address logistical and financial barriers. Although it is helpful to know which interventions have proven effective at other cancer centers, differences in patient populations could affect both the implementation and outcome of the same interventions at another center. Therefore, we encourage centers to make use of available literature regarding barriers to participation, while investing time and effort into identifying which barriers specifically affect their patient population.³⁸ This will allow centers to design tailored interventions, or modify those presented here.

Our recommendations include:

Prescreening. Review new patient medical records to

identify available trials in advance of a provider visit, and to collect contemporaneous documentation of clinical trial discussions and reasons patients do not consent or enroll.

Retrospective chart review. Review medical records with a focus on cancer type, specific patient demographics, or research team/disease program to identify if trials were available, discussed, and patients enrolled/not enrolled. Provide findings to research teams to evaluate their study portfolio and accrual to open studies.

Trial candidate discussions. Encourage documentation of all clinical trial discussions, including which trial was discussed and reasons why some patients did not consent to participate. Evaluate candidate data to identify trends in patient demographics or reasons for nonconsent to inform the design and implementation of interventions to improve enrollment and diversity among participants.

Cultural sensitivity. Institute cultural sensitivity and implicit bias training and education through online training modules and lectures.

Education. Develop education materials for clinical trials based on assessed knowledge gaps of patients being seen, or expressed reasons that some patients do not enroll.

New clinical trials. Develop new studies designed to enhance subgroup enrollment based on gaps in the study portfolio and the cancers of patients being seen.

Community engagement. Seek opportunities to engage community members in outreach efforts to educate about clinical trials, plan or improve trial enrollment, and disseminate study findings.

A systematic and interactive process of identifying specific recruitment problems; gathering and summarizing facts to be shared with research programs; matching intervention(s) with the needs of patients seen; and establishing a good fit between patients and clinical trials have merit in ongoing troubleshooting for thoughtful improvement of trial enrollment and diversity among participants.

Disclosures

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