

# TeamScience@SWOG *Field Guide*

Improving Diversity and Representativeness of Clinical Trial Participants



**SWOG**

CANCER  
RESEARCH  
NETWORK

**W**e have to be willing to say that we are not doing enough to understand the racial barriers to clinical trials and remove those barriers. Barriers may be financial, or due to trust, language, or other issues. We have to think about them early in the process of developing new research – and not as an after-thought.

We must believe, and act on the belief, that recruitment of different patient populations is not only important in terms of health equity – but that it's scientifically important. From a research standpoint, we need to bring people of color to the table when we design our trials, right from the start. And that includes bringing scientists and physicians of color to the table. We need more patients of color in cancer trials; however, the disparities are also at the researcher and leadership level. We need SWOG leaders and members who are people of color to advance the science and help generate solutions to health inequity as well.

In light of our roles as researchers, advocates, and cancer survivors, now is the time for our actions to speak loudly in response to the current racial unrest by increasing diversity and inclusion in SWOG at every level.

While this work is not progressing fast enough, we can begin doing the difficult work of looking at our research, admitting it is not representative, and exploring new ways of working that allow trial access to more diverse populations. Though this work will never be complete, we have begun.



**Allison Caban-Holt**

*Chair, SWOG Recruitment and Retention Committee*

## ***Overview: TeamScience@SWOG Modules***

**T**he first five modules of the TeamScience@SWOG series and the associated *Field Guide* provide guidance and practical advice about how to support patient advocate engagement across the full life cycle of a research study. The modules include brief first person video vignettes from researchers and stakeholders, sharing their personal experiences with patient advocate.

**Module 6 and this associated *Field Guide* provide guidance about improving the diversity and representativeness of clinical trial participants.**

**SWOG members** can access Modules 1–6 through the SWOG Learning Management System. Check [www.SWOG.org](http://www.SWOG.org) or with the SWOG training manager for details.

**The general public** can access Modules 1–6 here: <https://www.pcori.org/research-results/2017/framework-patient-engagement-cancer-network-group-studies>

### **Module 1:** *For Leaders: Enabling, Reinforcing, and Rewarding Patient Advocate Engagement*

Orients executive officers and leadership, committee chairs, and study chairs to a vision for the engagement of patient advocates in every stage of research

### **Module 2:** *TeamScience@SWOG*

Provides strategies and downloadable tools to support patient advocate engagement in each stage

### **Module 3:** *Engaging Patient Advocates in the Define, Review, Design Stages*

Explains the specific tasks within the Implement Stage, and how patient advocates contribute

### **Module 4:** *Engaging Patient Advocates in the Implement Stage*

Explains the specific tasks within the Share Stage, and how patient advocates contribute

### **Module 5:** *Engaging Patient Advocates in the Share Stage*

Explains the specific tasks within the Share Stage, and how Patient Advocates contribute

### **Module 6:** *Improving Diversity and Representativeness of Clinical Trial Participants*

Provides practices and strategies across the clinical trial life cycle to align the patients who are accrued to the trial with the study population for the trial

# ***Table of Contents***

## **Overview: TeamScience@SWOG Modules**

### Methodology to Improve Diversity and Representativeness of Clinical Trial Participants

#### Introduction

#### Build Team with Diversity and Representativeness Expertise

#### Advocate for Diversity and Representativeness

#### Develop Preliminary Forecast of Subpopulations

#### Discuss Subpopulation Barriers and Brainstorm Solutions

#### Build Funding to Bridge Gaps for Subpopulations

#### Review Inclusion and Exclusion Criteria

#### Develop Accrual Plan

#### Select and Solicit Sites Based on Subpopulations

#### Check Accrual Progress and Develop Countermeasures

#### Reach Out to Experts

#### Develop Audiences, Media, and Messaging for Sharing

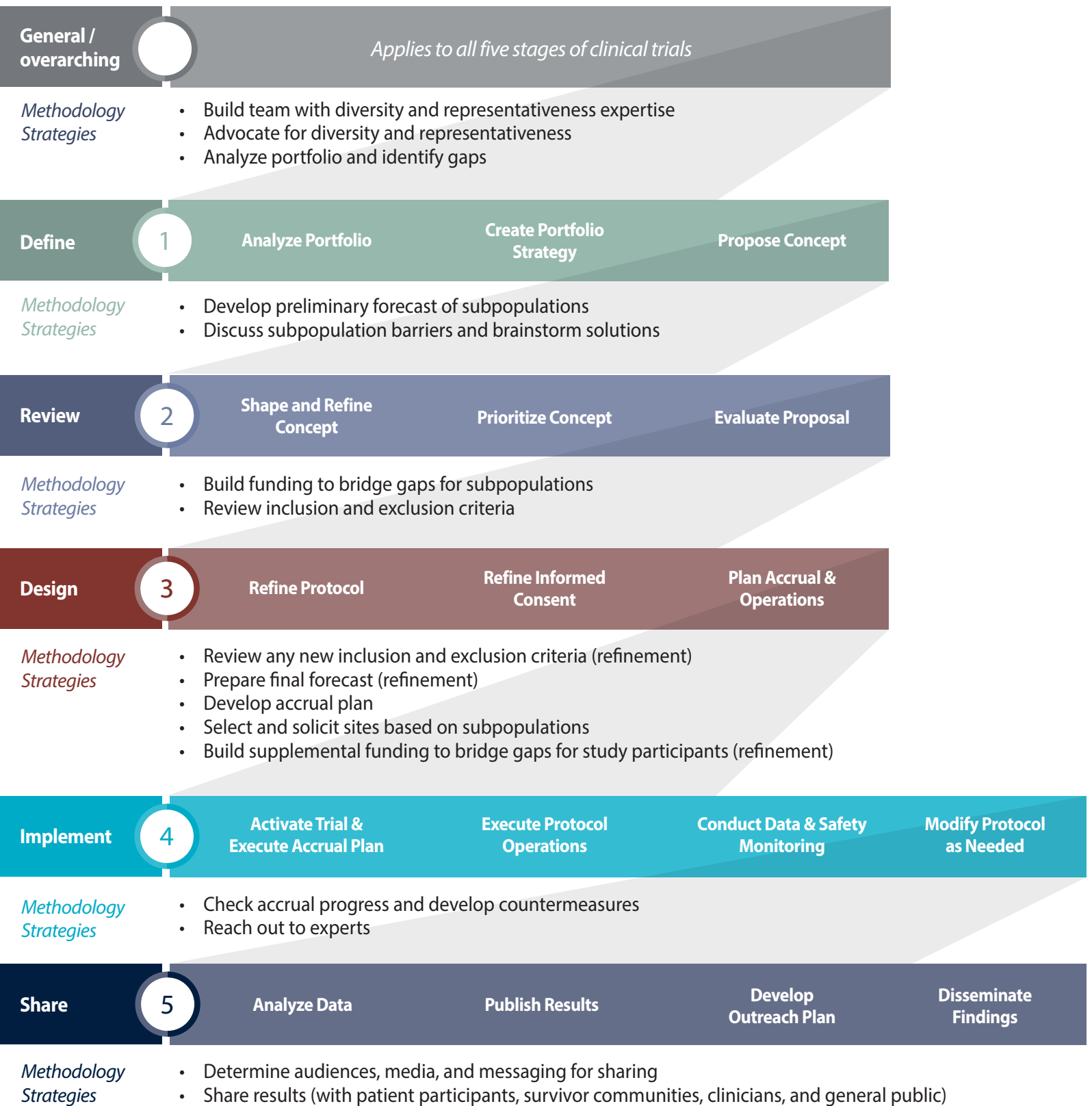
#### Share Results

#### APPENDIX 1 NCI/NIH Requirements for Forecasting

#### APPENDIX 2 Common Obstacles and Potential Solutions for Subpopulations

#### Acknowledgements

# Methodology to Improve Diversity and Representativeness in Clinical Trials



This training applies the methodology above for improving diversity and representativeness in clinical trials. This methodology should be calibrated to the specific trial both in terms of the activities being applied and the rigor to which each activity is taken.

## Introduction

**T**he *Field Guide* has been prepared for study chairs (a/k/a principal investigators or PI's), biostatisticians, patient advocates, other study team members, and leadership of clinical research organizations (executive officers, senior leaders, and committee chairs) to support improvement of diversity and representativeness of clinical trial participation.

The provided framework supports diversity and representativeness through inclusive team dynamics enabled by a methodology that reflects actions under the study team's control. This *Field Guide* is intended as a catalyst for the team and its leadership, providing guidance and opportunities that collectively define culture and values and stimulate continuous improvement.

The most critical takeaway from the training and the related *Field Guide* is clarity about strategies and tactics to improve diversity and representativeness of clinical trial participants across the research life cycle along with practical guidance on implementation.

A framework is meant to improve and shape, but not burden or constrain, a process – this methodology is no different. As you collectively put the *Field Guide* into practice, keep in mind:

- **Calibration** (the adjustment of expectations and activities based on the trial and the expertise and bandwidth of the study team) and role clarity are the cornerstones of TeamScience and high-performance teams. Without them, the team faces voids or collisions in work and lost opportunities.
- **Adapt the *Field Guide* to the circumstances** – one size does not fit all. Prioritize specific places to improve diversity and representativeness within the study or disease/committee context – you cannot do everything nor can you plan for all possibilities. Over time, opportunities will present themselves and needs during stages of the clinical trial life cycle are unique to the context.
- **Leaders will need to delegate as well as model team-oriented behaviors.** They cannot be everywhere, nor should they be. Their role is enabling, reinforcing, and rewarding diversity and representativeness.

## *Build Team with Diversity and Representativeness Expertise*

**T**he value of multi-disciplinary teams with the corresponding diversity in thought and experience is fully recognized in research. The ability to equitably engage the study population may require intentional inclusion of additional stakeholders to the team who represent the interests, values, and beliefs of those population(s).

These may include diversity, equity, and inclusion (DEI) experts (at SWOG, the SWOG recruitment and retention committee), community and research advocates, advocacy groups, and advocates. While internal resources can provide good insight into harnessing opportunities for engagement, it may be helpful to extend the membership of the study team beyond the network group to external parties who are asked or offer to provide specific input or help. External resources should be identified and invited early and added to a developing list of experts. Self-nominations should be vetted to ensure they complement the existing study team and provide a unique perspective.

### **BEST PRACTICE GUIDELINES**

- **Start early.** Begin thinking about the composition of the team as the Define stage is in process. Consider the subpopulations that will receive focus on the study and determine where emphasis and effort should be placed. Assess the capabilities of the existing team to meet established goals. If gaps are identified, bring in partners who can help. Building a diverse, representative, collegial, and cohesive team takes time and a strong network.
- **Calibrate and clarify roles.** Think about the backgrounds, prior experience working with populations of interest, and networks of the people you will have on the core study team and what additional help you may need. Engage others in this conversation to validate your assumptions. Sketch out the areas where the study would benefit from additional help and the expectations you and the study team will have for those roles. Know the role you want each person to play, the compensation (if any), the time commitment for meetings and independent work, and any recurring or one-time meetings. Confirm ability and availability to meet the study team's needs.

- **Plan ahead but remain flexible.** People who are successful at driving diversity and representativeness are in demand and managing many priorities. Review the diversity of the planned study team regarding reflecting the voice of the subpopulations and creating effective and efficient engagement of them. Consider adjustments to membership prior to announcing the final team and ensure that you are not just filling roles to meet requirements. Consider extending the team membership via study chairs at partner organizations (for example, NCTN counterparts), adding a specific DEI sub-team to assist the study team, or adding one or more subject matter experts (SME's) in DEI. Have a contingency plan.

*To build your team members' skills in building a team with diversity and representativeness expertise, use the "Try This" activities below.*

**Try This** | **As the study chair,** ask the patient advocate if they are aware of any advocacy groups or well-connected advocates who can guide the plans and implementation focused on one or more of the subpopulations of focus.

**Try This** | **As a member of the DEI team or a clinical trialist from a specific subpopulation of focus for a trial,** offer to assist the study team in outreach to subpopulations of focus.

**Try This** | **As the patient advocate,** ask the study chair to connect you with one of his or her colleagues who emphasizes a subpopulation of focus or authored an article regarding accrual barriers and related countermeasures for a subpopulation.

**Try This** | **As a study team,** conduct a landscape analysis to identify community and cultural leaders or influencers who have trusted relationships with the study population(s) of interest.

**Try This** | **As a community advocate invited by the study team to assist with outreach,** inquire about prior efforts by the research organization to engage the population(s) of interest — what worked well or didn't work well — and provide actionable recommendations for addressing identified barriers.



## *Advocate for Diversity and Representativeness*

**A**ll teams will experience differences of opinion. An important goal for every study team is to ensure that the diversity and representativeness perspective is one of several perspectives that members should be voicing, including scientific, logistical, ethical, patient, and other perspectives. A key distinction in how those differing opinions are shared is to aim for dialogue, rather than debate. Dialogue is collaborative, respectful, and thoughtful and works toward a common understanding. Debate is oppositional and aims to prove one side is right while the other is wrong. Follow these best practice guidelines to support productive and balanced dialogue.

Sometimes it may be necessary to “advocate” for a change in process or meeting norms, to make space for advocating for a position. For example, if your team always ‘runs out of time’ before everyone gets a chance to speak, ask for a change so that the discussion leader asks halfway through the meeting if everyone has had a chance to speak. The discussion leader should encourage each person to speak at least once before allowing individuals who speak more to retain center stage. A discussion leader also needs to read the room and gauge what the appropriate level of engagement is to ensure robust and meaningful dialogue.

### **BEST PRACTICE GUIDELINES**

- **“I” statements**, such as “I think”, “I believe”
- **State your goal.** What is the outcome you are trying to achieve with this input?
- **Acknowledge pros and cons.** Promote your point of view while acknowledging downsides if you see them.
- **Encourage other perspectives.** How does your point of view strengthen or advance the study?
- **Contextualize.** Where is your point of view coming from? Your experience? Information from working in or being a member of underserved communities? From advocacy groups? Peer-reviewed journals? Other trials?
- **Provide evidence that clarifies your point of view** rather than just making your case.

***To build your team members' skills in advocating for diversity and representativeness, use the "Try This" activities below.***

**TryThis** | **As the study chair developing a concept, try out these questions to invite others to advocate for their perspective:**

- "The study population includes several subpopulations of focus, notably [list subpopulations of focus]? Who can we add to the team that can help us plan and countermeasure accrual from these segments? How can we build a relationship with that community?"
- "From your point of view, how important would the outcomes of this study be to the subpopulations of focus? What would make it more important? Who do you think would benefit the most from it?"
- "What do you think the biggest barriers to participating as a [subpopulation of focus] are?"
- "How do you think those barriers can be addressed?"
- "If you could change one thing about this concept for [subpopulations of focus], what would it be?"
- Given the target accrual for this trial, what accrual forecasts make sense from the subpopulations of focus?" [Note: a trial with less than 100 participants will be challenging.]

**TryThis** | **As a patient advocate asking for a change in a protocol, consent form, accrual plan or other issue, experiment with this format for your comments:**

- "If I think about this [protocol; exclusion criterion; consent form] from the point of view of a patient who is [from one of the racial/ethnic groups; LGBTQ; a survivor of advanced/metastatic cancer; female; male; a certain age], this is what jumps out at me:"
- "Let's look at this from the point of view of different patients. What concerns would older patients have with this trial? What about young patients? Hispanics? African-Americans? Other subpopulations?"

## *Develop Preliminary Forecast of Subpopulations*

**W**hile formal forecasts are not required by the NCI for all studies, establishing goals for subpopulations of focus and monitoring results against those goals will result in better diversity and representativeness. Once a trial is closed, it is too late to address inadequacies. Having goals and measuring progress is more likely to deliver the desired result by exposing issues while intervention is possible.

Forecast breakdowns should mirror subpopulations within the study population. These will vary with the context of the study. Generally, they will at least mirror the data provided to the NIH on qualifying studies for inclusion of women and minorities. Forecasts should be aggressive but achievable. Formal submission of the “forecast of women and minorities” template and inclusion with protocol submission is done where required. See Appendix 1 for more details.

**The forecast may vary by context of the study and the study population.** Smaller trials such as Phase 1 trials and some Phase 2 trials will probably not support a forecast with detailed granularity very well and this should be acknowledged.

### **BEST PRACTICE GUIDELINES**

- **This is an iterative process** and should start early in the development of the study. The Define stage of a concept, which is early in the clinical trial life cycle, is the time to begin thinking about subpopulations of focus within the studied population. Estimates prepared here will be very preliminary. Such forecasts should consider plans by the extended study team to include subpopulations of focus as study participants. Later, during the Design stage (after the sponsor/funding partner/collaborator (typically NCI) has approved and funded the trial), a more rigorous forecast is prepared.

- **Forecasts should reflect the study population as best they can, avoiding generic U.S. demographic data.** Data on cancer incidence by subpopulation is usually available. Multi-cancer studies can leverage blended data to derive the forecast where appropriate but may need to use U.S. demographic data. However, histology, variant, subtype, and biomarker incidence by subpopulation data may not be available within a cancer. In these cases, use a higher level of data for that disease condition, perhaps the data by subpopulation for the disease itself. For a pan-cancer study, U.S. demographics may be the best proxy. Use U.S. incidence rates sparingly, where no good alternatives exist. The biostatistician will have access to historical data in the context or can point you to resources who do.
  - **Potential data sources:** Publications or historical trials for this organization (e.g., NCTN such as SWOG) in this context
  - **Internal:** hospital tumor registries, planning and marketing departments, research support offices, and electronic health records teams
  - **External:** State cancer registries, state data centers, U.S. Census data, the Surveillance, Epidemiology, and End Results (SEER) program, American Cancer Society, the American College of Surgeons, and advocacy groups. These sources can all be accessed online.
- **Data on subpopulations is not always available.** Data on some subpopulations may not be collected in the study. For example, residence in “rural” populations is generally not collected directly in the study, though “rural” residence could be derived by the patient’s home address. Sexual orientation is not a data element collected in most cases. Confirm with the biostatistician which elements are available.
- **Representative will not mean statistically significant in most cases.** Our goal is to achieve results that can, to the best of our knowledge, be generalized to the study population and might pick up signal from subpopulations. Generally, that does not mean sufficient sample is collected for each subpopulation of focus to make statements about the study’s impact on any one subpopulation.
- **Formal, official forecasts should be viewed as a commitment, should reflect an underlying plan, and should be achievable.** Additional stretch goals can certainly be established and communicated internally, but forecasts released to the NCI or other sponsor/funding partner/collaborators should be reasonably aggressive in reflecting the study population. At the same time, they should acknowledge the realities of historical results, any underlying challenges, and proposed accrual plans.

*To build your team members' skills in developing forecasts for subpopulations, use the "Try This" activity below.*

**Try This** | As a study team, identify, review, and discuss the subpopulations of focus within the study population.

1. Collect data on incidence rates within the context of the study and historical data for this context and discuss their implications as a team.
2. With guidance from your biostatistician, generate the consensus official (published) target (this is the formal target provided to the sponsor/funding partner/collaborator such as the NCI and may or may not align with goals set internally for the study team), reflecting knowledge about the context, the history, and any plans to support or improve participation of the subpopulations.



## *Discuss Subpopulation Barriers and Brainstorm Solutions*

**F**or many patients, the path to enrolling in a clinical trial cannot be navigated due to barriers. Barriers can be a result of trial design, costs, logistics, frequency of visits, language, health literacy, trust, and other factors. To remove barriers, it is critical to understand the patient's perspective. This means putting aside what we think we “know” and speaking directly with patients, their families, and advocates to understand their lived experiences, needs, and preferences. Understanding is deeper than knowledge. While many people know us, not many understand us.

Initial steps for the study team:

- Ask advocates and members of the patient communities to give feedback on the protocol content. What challenges do they see with joining or staying on the study? What changes can they suggest that would make it easier to join or stay on study? What ideas do they have about how to talk to patients about the study?
- Assess the study's eligibility criteria. Are they too narrow? Are the criteria essential to answer the study question, or are they present due to habit and history? Are there any hidden biases against any patient populations due to inclusion/exclusion criteria?

Making it as easy as possible for patients to say yes requires removing obstacles and implementing solutions. A list of common obstacles is provided in Appendix 2 but should not be considered comprehensive nor authoritative.

### **BEST PRACTICE GUIDELINE**

**Subpopulations are not monochromatic.** Understanding differences within any subpopulation is extremely important in developing communications and programs. What works for one part of a subpopulation may not work for another. And what works in one geography or at one institution may not work in another. Calibration to the context is critical to successfully meeting diverse needs.

*To build your team members' skills in discussing obstacles and countermeasures for subpopulations, use the "Try This" activities below.*

**Try This** | **As the study chair or patient advocate**, lead a discussion with the core study team and any external partners including community members to identify potential obstacles which may be significant for the subpopulations of focus on the trial. Once completed, brainstorm potential countermeasures.

**Try This** | **As the study chair**, work with patient advocates, site resources, and DEI experts to further refine potential solutions. Work to compile a list of helpful external/internal resources to share with patients from subpopulations to address identified obstacles.



## *Build Funding to Bridge Gaps for Subpopulations*

**I**n some cases, supplemental funding will be necessary to deliver representativeness. Ideally, those needs are identified at the beginning of the study, well before funding has been approved. Such funding may include helping to bridge gaps for participants. More than one grant mechanism or funder may be needed.

### **Funding may be needed to offset costs such as:**

- Grant writing or grant administration
- Inclusion of external resources
- Consulting costs or costs to secure subject matter experts (including their travel)
- Compensation to sites for enrolling representative patients
- Culturally calibrating patient materials
- Creative, photography, videography, and graphics design costs
- Translating materials (including awareness, education, accrual and retention, consent, and sharing results with clinicians and patient communities)
- Testing materials
- Printing materials
- Distributing materials
- Outreach to and continued engagement of community clinicians or organizations
- Hosted events (in person, virtual, or a combination)
- Payments to patients
- Transportation
- Parking
- Meals
- Lodging
- Costs of medical co-pays and deductibles
- Administrative costs of issuing payments to patients including any indirect costs (IDC's)

*NOTE: Patient payments will require IRB approval.*



Philanthropic organizations should be investigated as potential funders. Donors who have provided funds historically to the network group or to other studies are potential candidates (at SWOG, The Hope Foundation for Cancer Research would be a good starting point). Check also with members of the study team, colleagues and counterparts, and advocacy groups. Seek out opportunities to partner or connect with existing community-based collaboratives that have received funding in the past.

## BEST PRACTICE GUIDELINES

- **Plan ahead.** Funding should be estimated, requested, approved, and granted well in advance of need. Grants may require significant work and the timing of funding must align with the needs of the study. Collect input and lessons learned from similar contexts.
- **Estimate as accurately as possible.** Some calibration of estimates is always preferred. Leverage budget actuals and forecasts from similar studies with similar emphasis on subpopulations of focus.
- **Look internally and externally for funding.** Funding may not be available from the primary sponsor/funding partner/collaborator. Philanthropic partners may be needed and exist outside the boundaries of the sponsor/funding partner/collaborator.
- **Make plans to monitor and share results of funded components.** Good stewardship of funds requires careful oversight and, as feasible, an assessment of which components of the accrual plan were effective and how effective they were. Follow guidance provided in the grant application or by the funder.

*To build your team members' skills in building funding to bridge gaps for subpopulations, use the "Try This" activities below.*

**Try This** | **As the study team,** take the bulleted list of costs that may need to be offset and create a prioritized checklist of costs. Once completed, brainstorm sources for potential funding and consult internal and external networks.

**Try This** | **As a patient advocate,** work with the team to identify the barriers that are most consequential for patients in this context to inform prioritization of costs.

## *Review Inclusion and Exclusion Criteria*

**I**nclusion criteria define specific characteristics of the studied population required for any patient to participate in the trial. Exclusion criteria define specific characteristics that will exclude a person from being considered. They may include underlying conditions, prior cancers, language spoken, age, and other criteria. They are sometimes necessary to ensure that conditions are not made worse or drugs do not interact (safety considerations). However, exclusion of participants can sometimes have unexpected and undesirable consequences on the diversity and representativeness of the accrued patients.

The balance between intervention results that are representative and adverse events (from conditions not directly being treated or from drug interactions) is one that must be carefully managed. Efforts are now focused on making trial participants reflect “real world” patient populations while maintaining patient safety. One example is the ASCO-Friends of Cancer Research joint guidelines manuscript on broadening eligibility criteria in JCO 2017 (<https://ascopubs.org/doi/full/10.1200/JCO.2017.73.7916>).

### **BEST PRACTICE GUIDELINES**

- **Ask for the logic behind inclusion and exclusion criteria.** The study chair (PI) may need to engage the pharmaceutical company for explanations.
- **Challenge inclusion and exclusion criteria that are known to limit participation of subpopulations.** For example, a requirement for the patient to read English will limit the participation of people who speak Spanish or other languages. Many institutions have bilingual staff on site and family members of the patient can also assist. While not ideal, this is better than restricting to English speaking participants. Note that some survey instruments, however, are not validated in other languages nor cultures.

- **Know the common exclusions** which negatively impact diversity and representativeness.
  - African-Americans have higher incidence of some cancers (such cancers may or may not be the specific focus of the trial), hypertension, diabetes.
  - Asian-Pacific Islanders tend to have lower hematocrits.
  - Seniors have lower creatinine clearances and more co-morbidities.
  - Younger patients are more likely to have fertility concerns or need to employ contraception.
  - Positive HIV status has a higher incidence with gay men, African-Americans, and Hispanics.

*To build your team members' skills in reviewing inclusion and exclusion criteria, use the "Try This" activities below.*

**Try This** | **As the study chair developing a concept, ask the pharmaceutical company for the biologic rationale for inclusions and exclusions:**

- "The study population includes several subpopulations of focus, notably [list subpopulations of focus]? The exclusion for [specify the inclusion] will likely reduce participation in this trial and could negatively impact the generalizability of results. What is the logic for it? Can we remove this exclusion?"

**Try This** | **As the study chair developing a concept, ask the patient advocate for insights on inclusions and exclusions:**

- "From your point of view, do you believe any of the inclusions and exclusions will negatively impact the diversity and representativeness of the outcomes of this study?"

**Try This** | **As a patient advocate, ask for a change in inclusions and exclusions:**

- "I have some concern about [exclusion criterion] and note that the ASCO-Friends of Cancer Research joint guidelines manuscript might address when discussing with the pharmaceutical company/NCI/ other entity."
- "I have heard from my network or seen some research that suggested that [inclusion or exclusion criteria] will limit participation of patients who are [Hispanic; LGBTQ; a survivor of advanced/metastatic cancer; female; male; a certain age; a survivor of another cancer; etc.]. Can we confirm this before locking that criterion down?"

## *Develop Accrual Plan*

**T**he accrual plan is a collection of future actions to be taken to ensure that a clinical trial reflects the disease burden and mortality of subpopulations and recognizes the challenges of historical accrual. These actions should collectively deliver the forecast prepared for the study. Accrual plans may be tailored to individual sites or to the mix of planned or actual sites which agree to open a trial.

### **BEST PRACTICE GUIDELINES**

- **Accrual plans should identify and mitigate barriers to all impacted subpopulations.** Barriers to trial participation will vary by subpopulation and may vary geographically as well. The study team should discuss barriers and develop mitigation strategies to reduce them. Common barriers include: insurance and other financial support; availability of transportation; transportation, parking, and lodging costs; time away from job and family; mistrust; language; failure to ask subpopulations to consider a trial; and poor awareness of site and clinical trials.
- **Site mix is part of the accrual plan and should be reviewed and discussed from the beginning, typically starting with the Review stage.** Recalibration may be necessary after the trial is accruing if the results do not align with the forecast. Outreach to new sites with demographics that align with gaps in accrual may be necessary.
- **Patient outreach and related materials must reflect the needs and values of subpopulations to be effective.** Cultural competence and humility are critical as promotional, recruitment, and retention materials and methods are developed. These materials should reflect subpopulations of the local communities within the catchment areas..
- **Accrual results will trigger modifications to accrual plans.** Accrual plans should be flexible and modified as needed to meet accrual goals. They should reflect historical successes and lessons learned along with best, good, and emerging practices at the time they are created. However, once accrual data start coming in, the study team needs to be responsive and adaptive. Modifications should be developed by a broad group of people including members of study teams, external experts, sites, and sponsor/funding partner/collaborators.

*To build your team members' skills in developing an accrual plan, use the "Try This" activities below.*

**Try This** | **As the study chair or member of the study team, develop a thoughtful accrual plan using one or more of the available accrual plan templates:**

- NCI Accrual Core Team Protocol Accrual Planning Checklist
- NCI Accrual Core Team Promotional Tactics for NCTN Protocol Teams

Then, discuss and refine as a group.

**Try This** | **As the study chair,** invite an internal expert (at SWOG, someone from the recruitment and retention committee or a SWOG research or community advocate), a relevant advocacy group, or other external expert, to join a team discussion on study barriers and assist with developing strategies.



## *Select and Solicit Sites Based on Subpopulations*

**T**he mix of patients who accrue to any trial reflects the underlying demographics of the trial's activated sites. It is critical that the study team carefully plan and continually review sites for their ability to deliver the targeted subpopulations at either a statistically significant or representative level.

The mix of activated and accruing sites is a consolidation of many "catchment areas." The catchment area is much like the trading area for a store and reflects the population served generally by a site. The geographic boundaries of each catchment area may vary, sometimes corresponding to a state or to one or more counties and sometimes to a collection of cities, towns or zip codes. The catchment area can be further broken down by age, sex, race, and ethnicity. Based on demographics, local characteristics, and other factors, the incidence of people with cancer and the types of cancers catchment areas have will vary.

The study team should consider historical data for similar trials and ask if there were any accrual patterns or trends, assuming the participating sites will be similar. For example:

- Was it harder to retain older patients?
- Were women more likely to decline therapeutic trials?
- Were African-Americans under-represented?

Historical data is a good reference point for understanding the feasibility of accruing representative populations for the trial. Given that approximately 20 percent of new drugs approved in the past six years demonstrated differences in exposure and/or response across racial/ethnic groups and resulted in population-specific prescribing recommendations in some cases, the importance of managing site mix is clear<sup>1</sup>.

Site PI's may be helpful in calibrating the mix of sites participating in the trial, though each site clearly makes its own decisions on participating.

<sup>1</sup> <https://pubmed.ncbi.nlm.nih.gov/11798060/>

## BEST PRACTICE GUIDELINES

- **Plan site mix early.** Once the subpopulation forecasts have been developed, a review of historical accrual in similar trials should begin.
- **Recalibrate site mix after activations have begun.** The mix of sites at the beginning of implementation may not fully deliver representativeness. Monitor accrual and consider adding sites that might help with over-sampling.
- **Communicate additional compensation, if any, for subpopulations.** If there is additional compensation to sites for effectively recruiting representative subpopulations, make sure that has been clearly communicated.

*To build your team members' skills in selecting and soliciting sites based on subpopulations, use the "Try This" activities below.*

**TryThis** | **As the study chair,** ask if there are sites with catchment area populations that over-represent the desired subpopulations. Compare the historical results by subpopulations for similar trials with your proposed forecast. Review the activated sites and explore with your colleagues the addition of new sites.

**TryThis** | **As the patient advocate,** review historical results and identify facilitators and constraints that impacted site enrollment and retention of subpopulations in catchment areas. Consider these factors when evaluating current capacity/resources and developing site recommendations.

## *Check Accrual Progress and Develop Countermeasures*

**R**eporting for some subpopulations is typically part of ongoing trial status provided to the study chair, study team, the data safety and monitoring committee/board, and the group. Ideally, the reporting would be available on demand, be broken down into every subpopulation of focus, and would compare against informal study team targets or formal, official commitments, both of which have been standardized for incidence within the study population. In practice, the reporting is typically provided on a predetermined schedule, will reflect many, but not all, subpopulations of focus, and does not provide comparison against formal or informal targets.

At SWOG, the “Report of Studies” is prepared in advance of each semi-annual meeting at the trial, committee, and group levels. This report can be used to assess progress against informal or formal forecasts to determine what, if any, countermeasures need to be taken.

Actions to countermeasure shortfalls can be undertaken by the study team and the extended study team which includes external parties with expertise in diversity and representativeness or people or groups who can engage the specific communities that are underrepresented. See Appendix 2 for a list of some potential solutions to shortfalls, but challenges and solutions should always be tailored to the context.

### **BEST PRACTICE GUIDELINES**

- **Monitor and countermeasure early.** Do not wait until the trial is fully accrued or almost fully accrued to assess accrual by subpopulations or the need for additional sites. Monitoring and reviewing results twice a year is likely sufficient to get a handle on results that need countermeasures. Interim reporting between standard output dates may be helpful but could require a special request.
- **Plan ahead.** Influencing accrual results is difficult as it requires actions at the site level or modifying the site mix, neither of which are easy. Carefully consider the timing and the funding in advance of changes.



- **Seek directional convergence toward the forecast, not 100% compliance.** This is both art AND science, and accrual will reflect some randomness in results. The critical point is eventual convergence toward the forecast goal and actively managing significant shortfalls. This will be easiest with larger trials and difficult with small ones. The biostatistician may provide helpful perspective on interim results and convergence.
- **Accrual data by subpopulations is not always available.** Data on some subpopulations may not be collected in the study. For example, residence in “rural” populations is generally not collected directly in the study, though “rural” residence could be derived by the patient’s home address. Sexual orientation is not a data element collected in most cases. The biostatistician can help here.
- **Get to the root cause.** Countermeasures need to first identify the real problem for missing the forecast. The root cause may be at the site, trial, or patient level or some combination thereof. Data from clinicians, sites, and patients is extremely helpful, and should be solicited. Hypotheses should be generated and explored. Countermeasures against the wrong root cause may not provide the desired outcomes.
- **Results reflect the mix of activated sites.** That mix evolves over time. Early mix may be different from the later mix. As the mix changes, so do the underlying catchment areas. In cases where deficits are revealed, it may make sense to reach out to sites with catchment areas that could compensate. Such sites may not have activated the trial and could be willing to participate with a personal appeal or nudge from the study chair, the patient advocate, a member of the leadership team, sponsoring study chairs from other groups, or a colleague or friend from the committee.
- **Accrual is a result of the protocol and consent form.** Inclusions and exclusions, language requirements, consent language, and other factors should all be thought about as potential barriers when accrual for subpopulations is not on target. Tweaks via amendments may need to be considered.
- **Consider closing accrual to subpopulations that have met accrual goals for that group.** This will enable representative accrual by the other subpopulations and ensure knowledge gained is generalizable to all populations.

***To build your team members' skills in checking accrual progress and developing countermeasures, use the "Try This" activities below.***

**Try This | As the study chair, ask these questions when reviewing shortfalls:**

- "We are missing our targeted accrual for African-Americans. Are there any sites with greater representation of African-Americans in their catchment areas which have activated the trial but are not accruing? Any new sites that we should specifically ask to open the trial?"
- "The study population is missing several subpopulations of focus, notably [list subpopulations of focus]? Who can we add to the team that can help us countermeasure accrual from these segments?"
- "Accrual is inadequate for a [subpopulation of focus]. Does anyone on the study team have a strong network with that community?"

**Try This | As a patient advocate, try out these questions when reviewing results:**

- "I am concerned about the gender mix from an accrual perspective. This cancer skews 3:1 to males, yet we have over 90 percent males accrued so far. We should be closer to 75 percent. What could be done to correct this?"
- "Does anyone know if one of the other groups in the network has sites which deliver patients in this subpopulation or has people with expertise with this subpopulation?"

## *Reach Out to Experts*

**R**eaching out for help during **Implementation stage** and throughout the study can ensure that the trial meets its goals for representativeness. Experts may assist by:

- Analyzing accrual data to identify specific subpopulations where additional outreach is needed
- Providing advice such as helping the team decide where and how to engage specific subpopulations and determine appropriate recruitment methods
- Counseling the team on how to approach the study's diverse recruitment need and determine which populations need outreach. The expert may help create a process for targeted recruitment and retention
- Coaching the team and enhancing their skills to increase success with recruitment outreach

*As was true when starting up the original team, such help can be found internally or externally. The focus of this help may be identifying reasons why accrual is not representative which may include potential trust issues that had not been discussed previously and lack of awareness among relevant communities.*

*Once root causes/factors contributing to recruitment gaps have been identified, the team should work to identify and apply countermeasures to course correct, which may include:*

- *Further tailoring patient materials*
- *Getting input from site clinical trial staff on reported barriers/needs at the patient and clinic levels (factors impeding feasibility and/or adherence such as insufficient capacity, resources, time, buy-in, etc.)*
- *Expanding sites*
- *Expanding criteria*
- *Making the protocol more flexible*
- *Expanding the use of technology for virtual/remote interaction*

*NOTE: any outreach must be aligned with privacy and confidentiality considerations.*

*To build your team members' skills in reaching out to experts, use the "Try This" activities below.*

**Try This** | **As the study chair,** reach out to diversity, equity, and inclusion experts such as the SWOG recruitment and retention committee or a similar group along with research and community advocates for expert guidance or advice when the study team does not have such expertise, if the challenges are perceived to be significant, or if the study team does not have sufficient capacity to navigate and handle the barriers.

**Try This** | **As a member of the study team,** examine barriers at both site level and patient/community level and ask whether expertise at both of those levels is represented on the team/being consulted.

**Try This** | **As the patient advocate,** ask advocates or advocacy groups to brainstorm problems or solutions.

## *Develop Audiences, Media, and Messaging for Sharing*

**A**t the completion of a trial, results are published in medical journals and shared with the medical community. Sharing results with the public and with subpopulations has been limited. This leads to poor awareness of clinical research. Improving awareness of clinical research and willingness of subpopulations to participate in clinical trials will require engagement of these populations by the research community, including sharing results.

To share results, the study team must start by deciding three things:

1. **Who** should receive it (audience)
2. **Where** should they find it (media)
3. **What** should it say (message)

The “who” (audience) includes the subpopulations previously identified in the forecast. Audiences should be defined early and stakeholders representing those audiences in dissemination planning should be convened early as well.

Plans for “where” to share (media) should include resources to engage the subpopulations and may require budget and customization to the subpopulation. The study team should consider where the subpopulation audiences seek information that they find interesting and credible. Social media, advocacy groups, research advocates, and local media should be considered.

The “what” (message) content of the sharing should recognize relevant motivators for participating in research: help advance science, seek better medical therapy and better access to quality medical care, convenient site locations, help self/others, understand risks and benefits, and recommendation of doctor/family member. It is helpful to include information about knowledge gained from the study such as efficacy, outcomes, adverse events, side effects, and differences by subgroups (where statistically significant).

## BEST PRACTICE GUIDELINES

- **Messages should be relevant to the subpopulation**, particularly where incidence is higher than in the general population or when outcomes are worse. Prioritization of audiences beyond the research community is helpful when leveraging limited resources. Patients, subpopulations, advocates, and advocacy groups with a vested interest in the findings are likely to have highest priority. Best practice is to have a member of the subpopulation deliver the message. To increase interest, communications should recognize literacy, language, gender, cultural beliefs, faith and values, and other factors relevant to each audience. Discuss with the community and related organizations how best to communicate messages.
- **Budget may be needed but do not overlook low cost options.** Early in the development of the study concept, budget considerations should include reducing barriers, outreach, and dissemination of study results. Consider low cost, effective methods of sharing; for example, use of social media by the trial sponsor/funding partner/collaborator, PI and colleagues at other groups, research advocates, community advocates, and advocacy groups and posting on the NCTN or sponsor site. Webinars are relatively low cost. Advocacy groups and individuals with large networks may be effective partners for outreach.
- **Plan messaging in advance and get sponsor/funding partner/collaborator approval.** The content of any communications must meet the specifications of the sponsor/funding partner/collaborator and major stakeholders. Work with the appropriate communications person or team to ensure that messages align with those requirements.

*To build your team members' skills in developing audiences, media, and messages for sharing, use the "Try This" activities below.*

**Try This** | **As the study chair**, work with community advocates, specialists in diversity, equity, and inclusion and subpopulations (at SWOG, the recruitment and retention committee), advocacy groups for specific cancer subpopulations, and other experts to prioritize audiences, identify media, and craft messages.

**Try This** | **As the patient advocate**, work with the study team to populate plain language templates to build awareness of trials or share results.

**Try This** | **As the study chair, patient advocate or member of the study team**, answer questions posed in templates like SWOG's Accrual Tactics menu to choose appropriate strategies.

**Try This** | **As the member of the study team designated to prepare collateral materials or do outreach to subpopulations**, prepare materials for use by patients, communities, and advocacy groups. Review ideas presented in SWOG's social media toolkit and choose elements that will work within the budget, time, and resources available.

**Try This** | **As a community advocate**, reach out to local organizations and support groups at specific sites which are likely to have large numbers of the subpopulations of focus. National or regional groups within the study team's network may have contacts or insights.

**S**haring study results with patient participants and survivor communities is an ethical practice and builds awareness of trial activities, encourages future participation, and acknowledges the contribution of individuals and subpopulations to research. Having previously identified the audience, media, and message, sharing is executing plans and monitoring related results.

### **BEST PRACTICE GUIDELINES**

- **Monitor results and collect feedback from sharing activities**, particularly where incidence is higher or outcomes are worse than in the general population.
- **Include outreach to patient participants in the trial.** These individuals are ambassadors in the community and influence awareness and interest of others in future trials. Thank patients, acknowledge their important efforts, and keep them informed of study progress, results, and next steps. Let them know how this research has accelerated cancer research and how it benefits their community.
- **Dissemination of results should be timely, though bundling may be helpful.** Share results as quickly as possible. Synergy can be created by providing a current state of the disease or context with any new knowledge about onset, incidence, treatment, or outcomes. This may have greater interest than the results of one study. Consider including results from partner network groups or industry trials to complete the current state. Timing the communications to align with cancer awareness months, subpopulation and advocacy events, or campaigns (for example, clinical trials awareness) can be an effective strategy.



*To build your team members' skills in sharing results, use the "Try This" activities below.*

**TryThis** | **Begin each of these activities as a full team; delegate development of materials; and review all of them as a team.**

- Brainstorm audiences the study team wants to reach
- Identify relevant dissemination channels for the study audiences, including community newsletters, direct dissemination to participants, use of a study web page, and/or articles or press releases
- Develop a plan for generating messages and delivering them through identified channels
- Develop a base presentation that can be customized to the audience

**TryThis** | **As a member of the study team,** offer communities an opportunity to participate in Q and A and collect their input. Document lessons learned and share with the group.



## APPENDIX 1 NCI/NIH Requirements for Forecasting

The NCI/NIH required language and table for documenting specific subpopulations is provided below.

This study was designed to include women and minorities but was not designed to measure differences of intervention effects. The anticipated accrual in the ethnicity/race and sex categories is shown in the table below.

### DOMESTIC Planned Enrollment Report

Racial Categories	Ethnic Categories				TOTAL
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native					
Asian					
Native Hawaiian or Other Pacific Islander					
Black or African American					
White					
More Than One Race					
<b>TOTAL</b>					

## INTERNATIONAL (including Canadian participants) Planned Enrollment Report

Racial Categories	Ethnic Categories				TOTAL
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native					
Asian					
Native Hawaiian or Other Pacific Islander					
Black or African American					
White					
More Than One Race					
<b>TOTAL</b>					

## **Determining requirements for formal (official) forecasts**

General guidance on the need for government forecasting (confirm with biostatisticians or operations staff):

1. If previous studies support that there are significant differences in intervention effect based on gender or racial/ethnic comparisons, then the trial must include sufficient patients to be able to answer the intervention question in each of the relevant sub-categories. NOTE: this is unusual.
2. If previous studies support that there are no significant differences in intervention effect based on gender or racial/ethnic comparisons, then gender or racial/ethnic characteristics are not required as a subject selection criterion.
3. If previous studies neither support nor negate significant differences in intervention effect based on gender or racial/ethnic comparisons, then the trial must include appropriate entry of participants so that analyses may be performed in sub-categories but high statistical power is not required.

Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources.

For Phase 3 trials, “evidence must be reviewed to show whether or not clinically important sex/gender and race/ethnicity differences in the intervention effect are to be expected” per NIH Policy and Guidelines on The Inclusion of Women and Minorities as Subjects in Clinical Research. If so, the required forecast is developed and submitted to NCI as sponsor of the trial.

Government requirements may be a subset of the subpopulations on which the study team should focus.

### **From Section II.A of the NIH Policy:**

*The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design or contract proposal appropriate to the scientific objectives of the study/contract. The research plan/proposal should describe the composition of the proposed study population in terms of sex/gender and racial/ethnic group and provide a rationale for selection of such subjects. Such a plan/proposal should contain a description of the proposed outreach programs for recruiting women and minorities as participants.*

## On Race and Hispanic Ethnicity

Race and Hispanic origin are two separate concepts in the federal statistical system.

- People who are Hispanic may be of any race.
- People in each race group may be either Hispanic or Not Hispanic.
- Each person has two attributes, their race (or races) and whether they are Hispanic.
- Overlap of race and Hispanic origin is the main comparability issue.
  - For example, Black Hispanics (Hispanic Blacks) are included in both the number of Blacks and in the number of Hispanics.
- “More than one race” option increases possible numbers and overlapping groups.
- Hispanics

Census data shows that Hispanic respondents disproportionately choose “some other race.” Nationwide, more than 25% of Hispanics choose “some other race” compared to a fraction of a percent of non-Hispanics. To reduce large numbers of responses in the “some other race”, or “unknown race” category, the Census allows the collection of Hispanic as a race equivalent (Table B03002). Thus, many state cancer registries present data this way:

- Non-Hispanic White
- Non-Hispanic Black
- Non-Hispanic Asian-Pacific Islander
- Non-Hispanic American Indian-Alaskan Native
- Hispanic (of any race)

This stratification may increase studies’ power regarding to generalize results for Hispanics and people of color.

## Resources

The applicable NIH policy documents are located at: <https://grants.nih.gov/policy/inclusion/women-and-minorities.htm> (regarding grants), and at <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-014.html> (important revision to the policy) and at <https://grants.nih.gov/policy/inclusion/women-and-minorities/guidelines.htm> (full policy prior to the revision).

## APPENDIX 2

### Common Obstacles and Potential Solutions for Subpopulations

OBSTACLE	SOLUTIONS
<i>Costs of treatment</i>	Advocate for costs of study-related care being reimbursed or provided at no charge for participants. This would include out-of-pocket costs associated with the study, such as tests for eligibility or additional scans or procedures. Clarify costs and access after the trial as well. Ways to mitigate the impact of these costs on patients may include funding from sponsor/funding partner/collaborator or philanthropic organizations (national or local) or site development offices, patient financial assistance offices, social work offices. Budget accordingly.
<i>Transportation costs</i>	Providing compensation for gas mileage, cab vouchers, parking reimbursements, and food vouchers may ease patients' concerns about travel costs. Build these costs into your study.
<i>Transportation time</i>	Offer rideshares such as Uber and Lyft if the patient would have to travel for a significant time on public transportation or rely on family or friends.
<i>Logistical burden</i>	Make the study procedures as simple as possible for the participant by having the study procedures completed in the least number of visits; when possible, implement remote methods (phone, telehealth, computer).
<i>Time off from work or away from child, senior, special needs person</i>	Offer compensation for time off work, childcare, senior care, special needs care, Saturdays and non-working hours.
<i>Language</i>	Ensure that appropriately translated materials about the study, like consent, are available; ensure that there are translators available when the participant will be at the study site. Make it a goal to hire multi-lingual staff if you have many patients for whom English is a second language or not spoken. All study information should be written in plain language. People who are sick, ill, or distressed will often have impaired health literacy. They simply do not have the "bandwidth" to decipher all but the most critical information. Make it easy for patients to understand their treatment options. This is more challenging than it seems and the engagement of a professional in plain language is suggested.

*Trust or mistrust of clinical staff or clinical trials*

Being transparent with the participant about your actions and the study goals is vital to dispelling myths and building trust. Be mindful of the words you use. Build trust with a clear communication style, using plain language and minimal jargon. Recruit multi-lingual staff for the research team as needed. Studies on trust have shown that communication ease, more than race/ethnic concordance, impacts trust. If patients do not understand you, they will not trust you, and they are less likely to be open to participating in your study. Humility, respect, and transparency are also important considerations.

Allow patients time to consult with their families and arrive at a decision. Enlist the help of patient or research navigators if available. Other vital members of your team should include social workers, patient advocates, community health workers, and interpreters.

*Patient not asked to participate due to assumptions*

Provide information and training to physicians about the need to increase the referrals of underrepresented individuals and that a common reason for these groups not to participate is that they are not asked. Document which patients are assessed for eligibility, the outcome, and the patients' responses. If they said "no," document the reason. The best way to reduce unconscious bias is by systematically documenting the process to ensure that everyone was assessed and considered for participation.

*Lack of community referrals*

Partner with community physicians and make it easy for them to refer patients to the study. Provide one-page patient flyers, talking points about the study and its goals in plain language, and PI and staff contact information for quick response to questions. Make sure staff is responsive to answer questions (minimize or avoid voicemail).

Partner with advocacy and community organizations for opportunities to talk with communities about the research. Involve community leaders and patient advocates. Ask questions to understand community concerns, ideas, and suggestions.

Be sure to close the loop by providing interim and final results of the study. Failure to do so perpetuates distrust of research.



## ***Thank You's and Acknowledgements***

TeamScience@SWOG Module 6, including the *Field Guide*, includes the contributions of the following:

### **PROJECT TEAM**

**Project Lead and Co-Sponsor:** Rick Bangs, MBA, PMP, *SWOG Patient Advocate Committee Chair*

**Project Co-Sponsor:** Allison Caban-Holt, PhD, *SWOG Recruitment and Retention Committee Chair*

**Instructional Designer:** Sue Vargo, Psy.D., *American Institutes for Research*

### **CONTRIBUTORS**

Wendy Lawton, MA

Jennifer Maeser, MS

Dana Sparks, MAT

Tandrea Hilliard, PhD

Melyssa Foust, MSN, RN, OCN

Jeremy Kilburn, MD

Kamara Mertz-Rivera, MA, CCRC

Joe Unger, PhD

### **INTERVIEWEES**

Charles Blanke, MD

Colmar Figueroa-Moseley, PhD, MPH

Dina G. Lansey, MSN, RN

Michael LeBlanc, PhD

Worta McCaskill-Stevens, MD, MS

Lynne Nguyen, MPH

Edith Perez, MD

Veena Shankaran, MD, MS

Parminder Singh, MD

Ian Thompson, Jr., MD

Desiree A.H. Walker, BA

### **REVIEWERS**

Jack Aiello, MS

Lisa Barnstrom, MBA

Hildy Dillon, MPH

Marvella Ford, PhD

Eileen Fuentes, MA, CHHC

Lucy Gansauer, RN, MSN, CPSO,  
OCN

Julie Gralow, MD

Sam Guild, JD

Dawn Hershman, MD

Marcia Horn, JD

Cheryl Jernigan, CPA, FACHE

Judy Johnson, MBA

Florence Kurttila, MS

Jamie Myers, PhD, RN, AOCNS

Elektra Paskett, PhD

Cathy Rankin, MS

Barbara Segarra-Vasquez, PhD

Carole Siegel, MBA

Gail Sperling, MPH

Irene Tami-Maury, PhD

Rob Taylor

Peggy Zuckerman, MS

### **GRANT MANAGEMENT**

Jo Horn

Morgan Cox





## FUNDING

**This training was generously funded by Genentech with the exceptional support of The Hope Foundation for Cancer Research.**

TeamScience@SWOG (Modules 1-5) were funded through a Patient Centered Outcomes Research Institute© (PCORI©) Eugene Washington PCORI© Engagement Award (#6180-AIR) and developed by the American Institutes for Research (AIR).

## DISCLAIMER

The views and statements presented in this work are solely the responsibility of the authors and do not necessarily represent the views of the Patient-Centered Outcomes Research Institute© (PCORI©), its Board of Governors or Methodology Committee, AIR, or Genentech.

Modules 1-5 are publicly available here: <https://www.pcori.org/research-results/2017/framework-patient-engagement-cancer-network-group-studies>

