Practical Approaches to Improving Diversity in Clinical Trials

Wednesdays
11AM - 12noon ET

LEANING IN: A WEBINAR SERIES
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Practical Approaches to Improving Diversity in Clinical Trials

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Recording available
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November 18, 2020
December 9, 2020
January 13, 2021
January 27, 2021
February 10, 2021

Community Awareness, Access, Knowledge
Workforce Development
Study Design, Eligibility, Site Selection & Feasibility
Study Conduct (Recruitment, Retention)
Data Standards and Analysis
Stakeholder Roles and Responsibilities
Role of Data in Diversity: Genetics & Real World Data
Today’s topic

Study Design, Eligibility, Site Selection & Feasibility

November 18, 2020
11AM -12noon ET

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Practical Approaches to improving Diversity in Clinical Trials

mrctcenter.org/diversity-in-clinical-trials
The Multi-Regional Clinical Trials Center (MRCT Center)

**Our Vision**

Improve the integrity, safety, and rigor of global clinical trials.

**Our Mission**

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.
Achieving Diversity, Inclusion, and Equity in Clinical Research

Guidance and Toolkit

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And the invaluable contributions of >50 workgroup members, representing:

• Patients, Patient Advocates
• Academia
• Pharmaceutical companies
• CROs
• Non-profit organizations
• Trade associations
• Government agencies
• Research institutes

Each serving in their individual capacity.
• Multi-stakeholder contributions and consensus
• Practical and actionable recommendations
• Accountability section considers how each stakeholder can change the paradigm
• Toolkit provides adaptable resources not easily found elsewhere

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Today’s agenda

Study Question
Social and scientific value
Resonance with affected population
Representing the impacted populations
Interrelatedness of topics

Study Design
Fit for purpose
Inclusive of impacted populations
Optimize design through considerations of conduct

Eligibility Criteria
Homogeneity (no “noise”) vs HTE
Scientifically or ethically justified

Feasibility Assessments
Product / study recruitment plan
Aggregate population
Informs site selection

Site Selection
Capacity for diverse enrollment
Metrics and performance tracking

18 November 2020
Leaning In Webinar Series

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Study Question

• In advance of a trial, the study question must address:
  • Diversity of the population affected by the question
  • Potential subgroup differences in safety, efficacy, and/or effectiveness in affected population.

• Is the question important to the population of interest?
  • Prioritize questions that matter to the intended population.
  • Select outcome measures that matter to the intended population.
### Study Design

- **Must be fit for purpose**
- **Interdependency between study design and study conduct**
- **Pragmatic trials, platform trials and decentralizing trials**

<table>
<thead>
<tr>
<th>Design</th>
<th>Conduct</th>
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<tr>
<td>Pragmatic, simple studies and cluster randomized designs</td>
<td>Decentralized studies</td>
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<td>Platform, master, adaptive, designs</td>
<td>Hybrid studies</td>
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<td>Randomized studies</td>
<td>Traditional in-person studies</td>
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<td>Cohort and registration studies</td>
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<td>Case control and observational studies</td>
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“Over the past few decades, FDA has promoted enrollment practices that would lead to clinical trials that better reflect the population most likely to use the drug if the drug is approved, primarily through broadening eligibility criteria.”
Eligibility criteria impacts diverse representation in research
Eligibility criteria impacts diverse representation in research

REVIEW

Systematic Review and Meta-Analysis of the Magnitude of Structural, Clinical, and Physician and Patient Barriers to Cancer Clinical Trial Participation

Joseph M. Unger, Riha Vaidya, Dawn L. Hershman, Lori M. Minasian, Mark E. Fleury

For 55.6% of patients overall, no trial was available for the patient’s cancer type and stage. When a trial was available, a further 21.5% of patients were ineligible due to structural or clinical barriers.
Eligibility Criteria

- Narrow eligibility criteria = greater *similarity*
  - Optimizes results consistency
  - Reduces “noise”

- Permissive eligibility criteria = greater *diversity*
  - Increases heterogeneity of results, but
  - Potentially reveals differential effects on outcomes, thus increasing generalizability of results
Eligibility Criteria

• Understand the population affected by the study question.

• As restrictive as necessary (generally, for safety reasons) and as permissive as possible.

• Maximize inclusivity through documentation of scientific rationale for all restrictions/limitations to eligibility.

“Homogeneity Review Board

“The important thing is that we only enroll the people who will FIT IN!”
Feasibility Assessments

- Feasibility assessments help sponsors, CROs, and investigators evaluate the possibility of conducting a particular trial with the objective for optimal project completion in terms of timeliness, targets, outcomes and cost.

- Purpose and impact on diversity in clinical research
  - Top-down: data driven
  - Bottom-up: experience led

- Accurate, triangulated data sources
Feasibility Assessments

- No single site needs to be diverse
- It’s the aggregate that needs to be representative, and ideally diverse
Feasibility Assessments

- No single site needs to be diverse
- It’s the aggregate that needs to be representative, and ideally diverse

Recruitment Strategy Document

- Study Title
- Protocol #
- NCT #
- Study Logo
# Feasibility Decision Tree & Site Selection

## Purpose

This tool provides a high-level decision-making framework that can be used by industry or academic sponsors and/or CROs during the feasibility assessment and site selection process in order to select sites that can best fulfill the trial’s target representative population.2

The overall objective of a feasibility assessment is to select sites for “optimum project completion in terms of timelines, targets and cost.” Rajadhyaksha, 2010

## Background

Despite the proliferation of clinical trials in recent years, they are still constrained by the need for the appropriate level of patient diversity. This tool aims to help sponsors and CROs identify sites that can effectively address this need.

## Checkpoints

<table>
<thead>
<tr>
<th>Checkpoint</th>
<th>Capacity Tier</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Checkpoint 1</td>
<td>Potential Capacity</td>
<td>Assessment of methods used to determine a site’s lack of “potential capacity” for enrollment of desired subgroup(s). If bias/inaccuracy is detected in these methods, the site remains eligible for consideration in site selection for enrollment of that subgroup(s).</td>
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<tr>
<td>Checkpoint 2</td>
<td>Historical Capacity</td>
<td>Identification and assessment of factors that contribute to a site’s lack of “historical capacity” for diverse enrollment; the changes needed in order to build that capacity in the future, and whether supportive measures might be feasible for the sponsor/CRO to provide. If changes are deemed feasible to make, the site remains eligible for consideration in site selection for diverse enrollment.</td>
</tr>
<tr>
<td>Checkpoint 3</td>
<td>Projected Capacity</td>
<td>Similar to that of “historical capacity,” identification and assessment of those factors limiting a site’s “projected capacity” for diverse enrollment in the trial at hand, according to whatever diversity goal and target population established by the sponsor. If identified changes are feasible to make, the site should be included in the study at hand.</td>
</tr>
</tbody>
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## Checkpoints Diagram

- **Checkpoint 1**: Does the site have the potential capacity to enroll the desired subgroup(s)?
  - Yes: Could error be present in this initial assessment of a site’s potential capacity?
  - No: What factors contribute to the site’s limitations? What changes might enable the site to enroll a diverse population? Are these changes feasible?

- **Checkpoint 2**: Does the site have the historical capacity to enroll the desired subgroup(s) for this particular trial?
  - Yes: What factors contribute to the site’s limitations? What changes are necessary to enroll the desired subgroup(s) in this trial? Are these changes feasible?
  - No: Provide feedback to the site and evaluate whether it should remain under consideration for the trial.

- **Checkpoint 3**: Establish host sites, exact budget per site and begin participant enrollment.
  - Yes: Overall objective of feasibility assessment is to select sites for optimum project completion in terms of timelines, targets and cost.
  - No: What factors contribute to the site’s limitations? What changes might enable the site to enroll a diverse population? Are these changes feasible?
Feasibility & Site Selection

Feasibility Assessment tool - ensuring study sites have capacity to enroll a diverse population

- Potential capacity
  - Does the site have the potential capacity to enroll the desired subgroup(s)?
  - Site relationships, community relationships, geo-mapping, etc.

- Historical capacity
  - Does the site have the historical capacity to enroll the desired subgroup?
  - Data available, modified feasibility questionnaire, site visit, etc.

- Projected capacity
  - Does the site have the projected capacity to enroll the desired subgroup(s) for this particular trial?
  - Internal forecasting tools if available

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### Site Selection – Potential Key Performance Indicators (KPIs)

#### Output indicators
- Data available on potential capacity of sites to enroll target subpopulation
- Modified feasibility assessment available for target subpopulation
- Modified feasibility assessment conducted at each site with potential capacity
- Data available on projected capacity of sites to enroll target subpopulation
- List of potential site supports to enroll target subpopulation available

#### Outcome indicators
- Each site selected has an estimate for its capacity to enroll target subpopulation(s)
- Each capacity estimate is derived from more than one data source
- Each site selected has a justification including reference to their capacity to enroll target subpopulation(s)
Recommendations for Stakeholders

Trial Design
- Characterize target population based on epidemiology, disease burden and demographics
- Engage patient population to maximize recruitment and retention strategies and minimize burden of trial

Site Selection
- Determine access to potential target population to guide country, region, and site selection
- Use data-driven strategies
- Determine the feasibility of enrollment figures for target subpopulations in partnership with site(s)

Site Support & Communication
- Communicate targets for enrollment including demographic projections
- Assist sites with local recruitment plan and outreach activities
- Assess and support each site's cultural readiness
- Provide diversity training to Investigators and site staff

Accountability
- Ensure recruitment strategy is informed by patient preferences
- Connect with referral networks in the community, including organizations directly involved with target population
- Monitor and communicate site progress, address and adjust with site as needed
Today’s speaker

Theresa Devins, DrPH
Associate Director, Global Trial Optimization
Global Clinical Operations
REGENERON
As industry continues to pursue solutions to enrolling minority patients in clinical trials, the world has changed around us and the path forward offers new opportunities. MRCT has now provided the comprehensive guideline complementary toolkit to allow all stakeholders to build on the knowledge shared in these documents. Using this information as a foundation, and incorporating the rapidly changing environment precipitated by the pandemic, industry should:

- Consider sites that may be new to the sponsor and/or new to research
- Explore new options for study placement including inner city sites and institutions
- Increase more ethnically and culturally diverse investigators
- Develop and support sites that have demonstrated the ability to recruit diverse patients

Lessons from a Pandemic

- Sites in many inner cities have access to and engage diverse populations
- These sites welcome sponsored studies and have the infrastructure to be successful
- Search for patients who may be disproportionately impacted by the disease and identify the practices that are treating them
- Commit to rigorous testing across diverse populations
- Share the results in language that is understandable to the participants
- Provide access to the approved product
COVID 19 has changed how industry approaches site selection and have gained unprecedented access to minority patients

1. Identification of sites during the pandemic has shifted due to searches for large volume of new cases which by default, have been in many large inner cities.
2. Due to the treatment needs, many minority patients have accessed the healthcare system and have been offered participation in clinical trials, as effective treatment options are not yet available.
3. Decentralized approaches have been rapidly implemented to accommodate study participants across all indications.
4. Home healthcare, telemedicine, study drug shipment and dosing at home have been used to reduce the burden of study participation and to reduce risk of exposure to COVID 19.
5. Feasibility questionnaires include questions regarding experience with wearable devices and use of remote technologies.
6. Many minority patients have sought care in a system that they may have avoided for a variety of reasons.
7. Sponsors and site staff have offered clinical trial options to patients that were previously unknown to the healthcare ecosystem.
8. The opportunity to maintain engagement with these “new” patients is an imperative.
9. Sharing study results, especially by race and ethnicity, and ensuring access to approved treatments may be first steps towards building trust within the communities.
Success story: The Silver Lining of a Pandemic

The pandemic has driven change in unexpected ways:

• Site selection has focused on new sites in inner cities where case numbers are high
• There has been an increase in minority patients entering the healthcare system and out of necessity, they are being invited to participate in clinical trials
• Site selection has shifted to a rare disease-like model where patients are identified before sites are considered
• Stakeholders must commit to new approaches and opportunities made possible by the pandemic
Decentralizing Clinical Trials

Pre-Pandemic Barriers to Participation:
- Unknown to Study Site
- Inconvenient location
- Lack of childcare
- No paid time off
- Study visits during normal business hours
- Access restricted due to proximity to study site

New options for participation:
- Home healthcare
- Mobile devices (e.g. ePRO)
- Telemedicine
- Home delivery of investigational product
- Patient apps and portals
- Unlimited access without geographic restrictions
Building on Pandemic Learnings

- Approach study planning by beginning with patients who are disproportionately burdened by specific diseases such as hypertension and obesity
- Identify the areas of highest disease prevalence and develop sites serving those communities
- Treat the approach to diverse populations as diligently as the pursuit of patients with rare disease
- Think of innovative ways to accommodate patients’ needs and collaborate with sites that are treating these patients
- Commit to change and agree there is “No Going Back”
The Evolution of Change - COVID 19

Clinical Trial Participation 2015-2019

COVID 19 Cases 2020
The Evolution of Change – COVID 19

COVID 19 Cases 2020

Census tracts with higher-than-average percentages of Black Americans are often more vulnerable to COVID-19.
The Evolution of Change – Hypertension and Diabetes

Clinical Trial Participation 2015-2019

Locating high prevalence areas
Summary

Commit to the change → Select patients before sites

Reduce burden of participation → Explore new technologies

Invite new sites to participation → Support new investigators

Share results → Never Go Back
Today’s speaker

Rachael Fones
Director, Government & Public Affairs
IQVIA

Please view the webinar recording for Rachael’s presentation.
Discussion and Questions
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