Practical Approaches to Improving Diversity in Clinical Trials

Wednesdays
11AM –12noon ET

MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

LEANING IN: A WEBINAR SERIES

Disclaimer

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Recording available	Community Awareness, Access, Knowledge
Recording available	Workforce Development
November 18, 2020	Study Design, Eligibility, Site Selection & Feasibility
December 9, 2020	Study Conduct (Recruitment, Retention)
January 13, 2021	Data Standards and Analysis
January 27, 2021	Stakeholder Roles and Responsibilities
February 10, 2021	Role of Data in Diversity: Genetics & Real World Data

Today's topic

Study Design, Eligibility, Site Selection & Feasibility

November 18, 2020
11AM –12noon ET

Barbara Bierer, MD
Moderator
Faculty Director,
MRCT Center

Laura Meloney, MSc, MPH
Moderator
Program Manager,
MRCT Center

Rachael T. Fones
Guest Speaker
Director, Government
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Theresa Devins, DrPH
Guest Speaker
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Global Trial Optimization
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Practical Approaches to improving Diversity in Clinical Trials

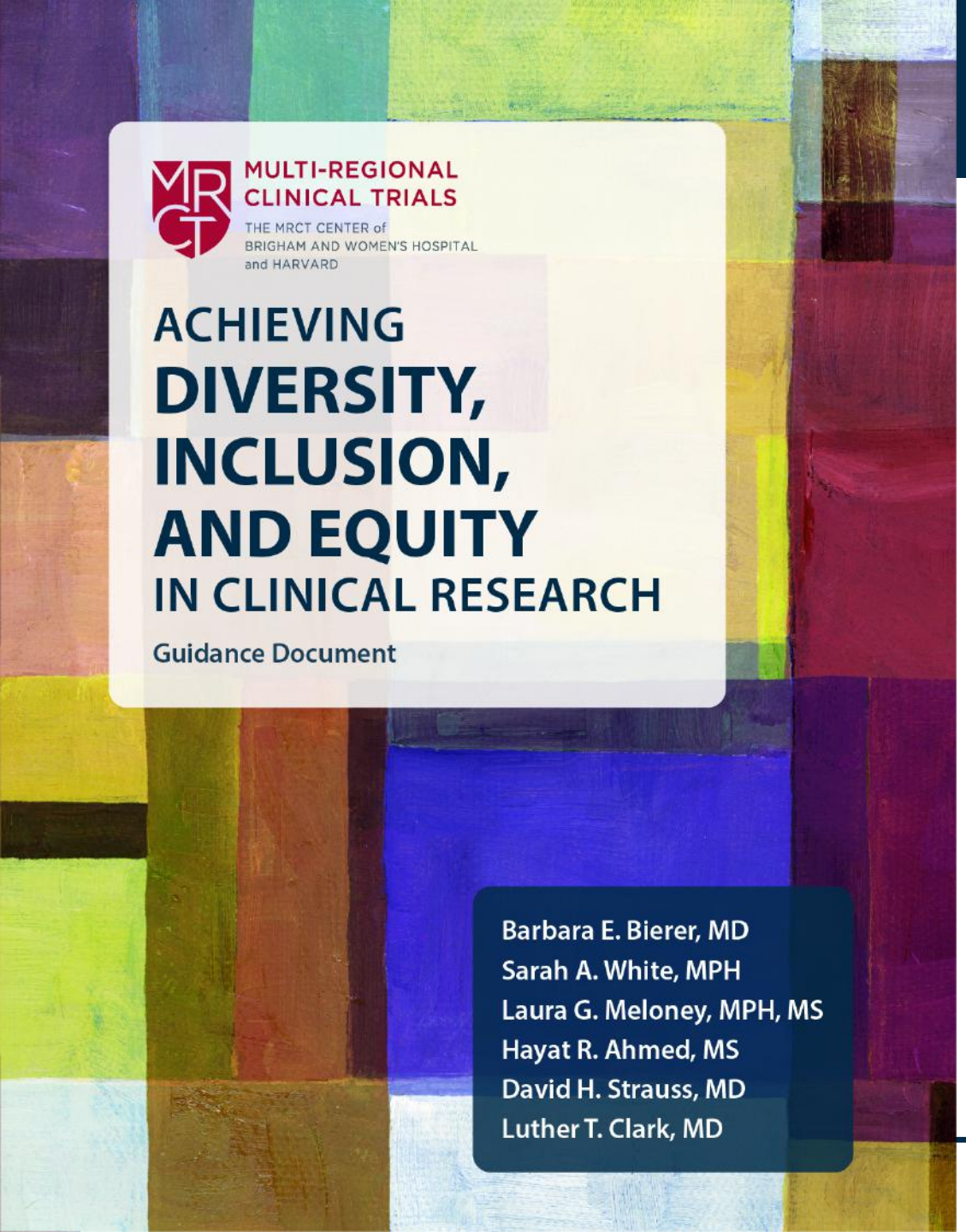
The Multi-Regional Clinical Trials Center (MRCT Center)

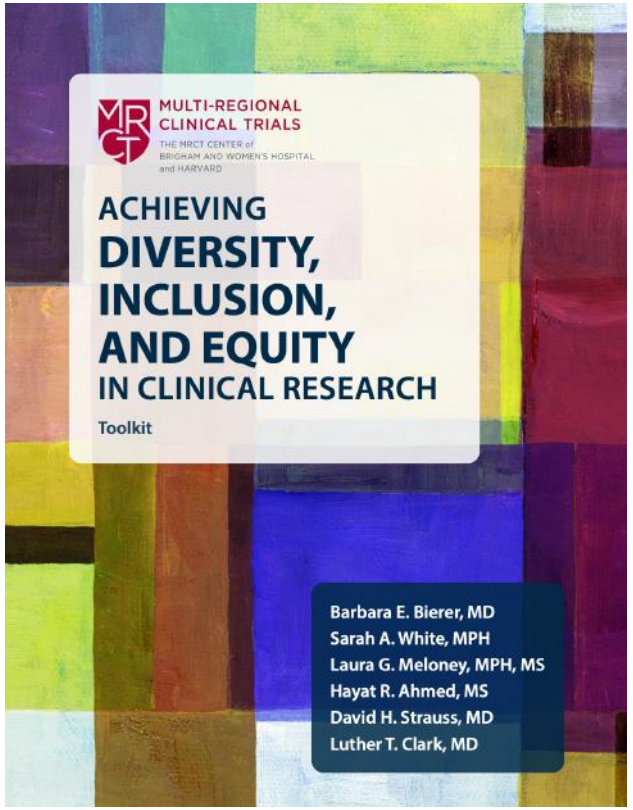
Our Vision

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, Equity In Clinical Research

Guidance and Toolkit

mrctcenter.org/diversity-in-clinical-trials

Released 6 August 2020

Leadership

- RADM Richardae Araojo, PharmD, MS, U.S. FDA
- Barbara E. Bierer, MD, MRCT Center
- Luther T. Clark, MD, Merck & Co., Inc.
- Milena Lolic, MD, U.S. FDA
- David H. Strauss, MD, Columbia University
- Sarah White, MPH, MRCT Center

MRCT Center staff:

- Carmen Aldinger, PhD, MPH
- Hayat Ahmed, MS
- Laura Meloney, MS, MPH
- Joshua Smith-Sreen, MPH

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.

Guidance Document

- 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

mrctcenter.org/diversity-in-clinical-trials

Today's agenda

Study Question

Social and scientific value

Resonance with affected population

Representing the impacted populations

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

Interrelatedness of topics

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

Design

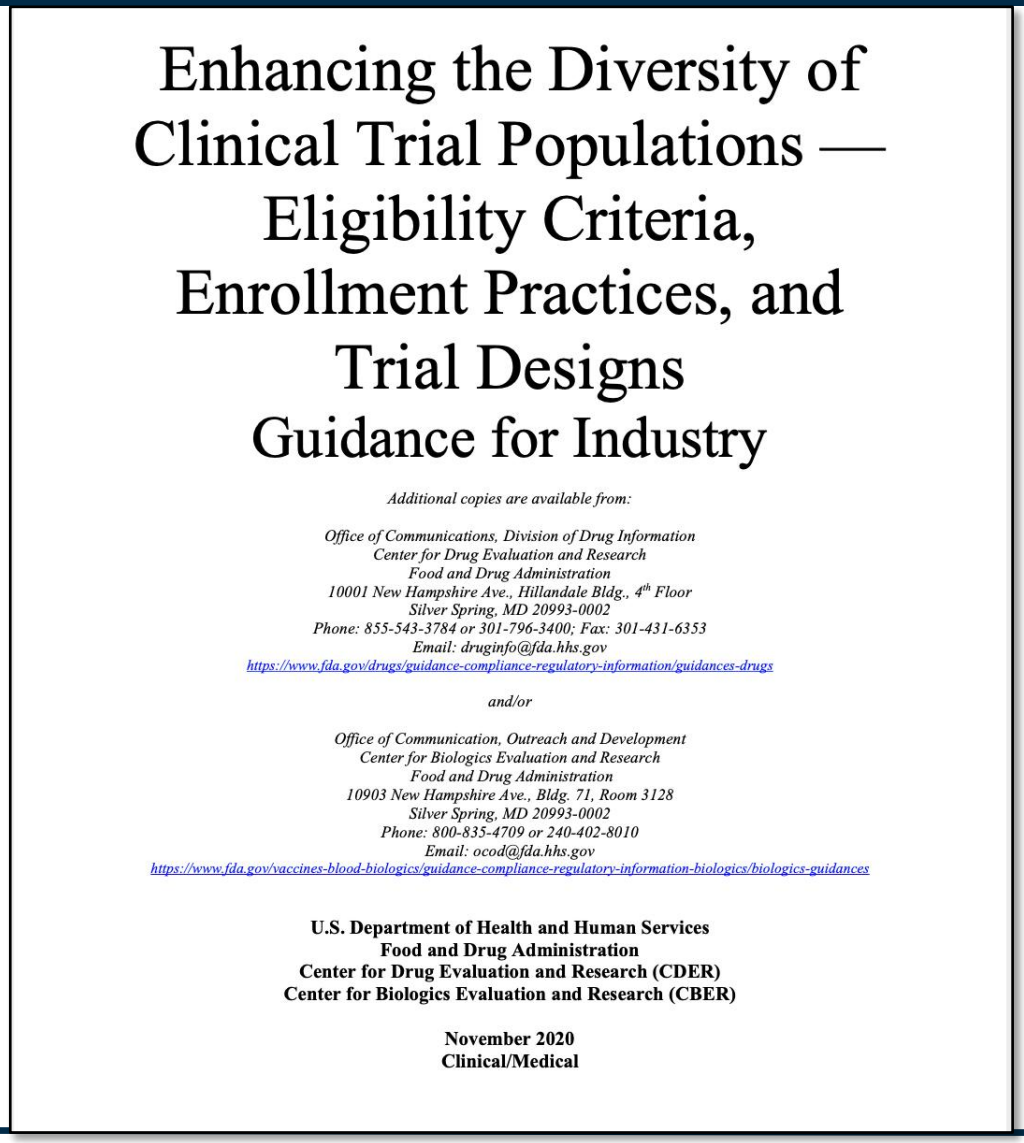
- Pragmatic, simple studies and cluster randomized designs
- Platform, master, adaptive, designs
- Randomized studies
- Cohort and registration studies
- Case control and observational studies

Conduct

- Decentralized studies
- Hybrid studies
- Traditional in-person studies

Eligibility Criteria

"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."



Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs

Guidance for Industry

Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

and/or

Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Room 3128
Silver Spring, MD 20993-0002
Phone: 800-835-4709 or 240-402-8010
Email: ocod@fda.hhs.gov
https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

November 2020
Clinical/Medical

Eligibility criteria impacts diverse representation in research

NEWS RELEASE 1-OCT-2020

Study details strategies to address barriers keeping older adults out of clinical trials

The study examined what has been done and chartered a roadmap to improve equitable access using the best-available scientific literature on barriers to older adult participation in cancer clinical trials

CITY OF HOPE

Research News

SHARE

DermatologyTimes®

Older adults underrepresented in atopic dermatitis research

October 20, 2020
John Jesitus

From the Blood Journals | News | Written in Blood

Are Strict Eligibility Criteria Keeping Patients From Clinical Trial Participation?

FRIDAY, JUNE 29, 2018

FDA Broadens Eligibility Criteria for Pediatric Clinical Trial Participants

BRIELLE BENYON
Monday, July 13, 2020

The FDA recently released guidelines expanding clinical trial eligibility for investigational cancer drugs

Chicago Tribune

COMMENTARY | OPINION

Commentary: Clinical trials for a COVID-19 vaccine must include more Black, Latino and Indigenous people

There are also barriers that include lack of knowledge of trials in general, lack of opportunities to participate in trials, exclusion criteria that have systematically excluded diverse participation (including non-English speaking populations), and excessive out-of-pocket expenses in trial participation. There are also citizenship concerns with respect to eligibility and identification of data or lack of transparency with respect to confidentiality and human subject protection in research

Eligibility criteria impacts diverse representation in research

OXFORD

First published online February 19, 2019
Review

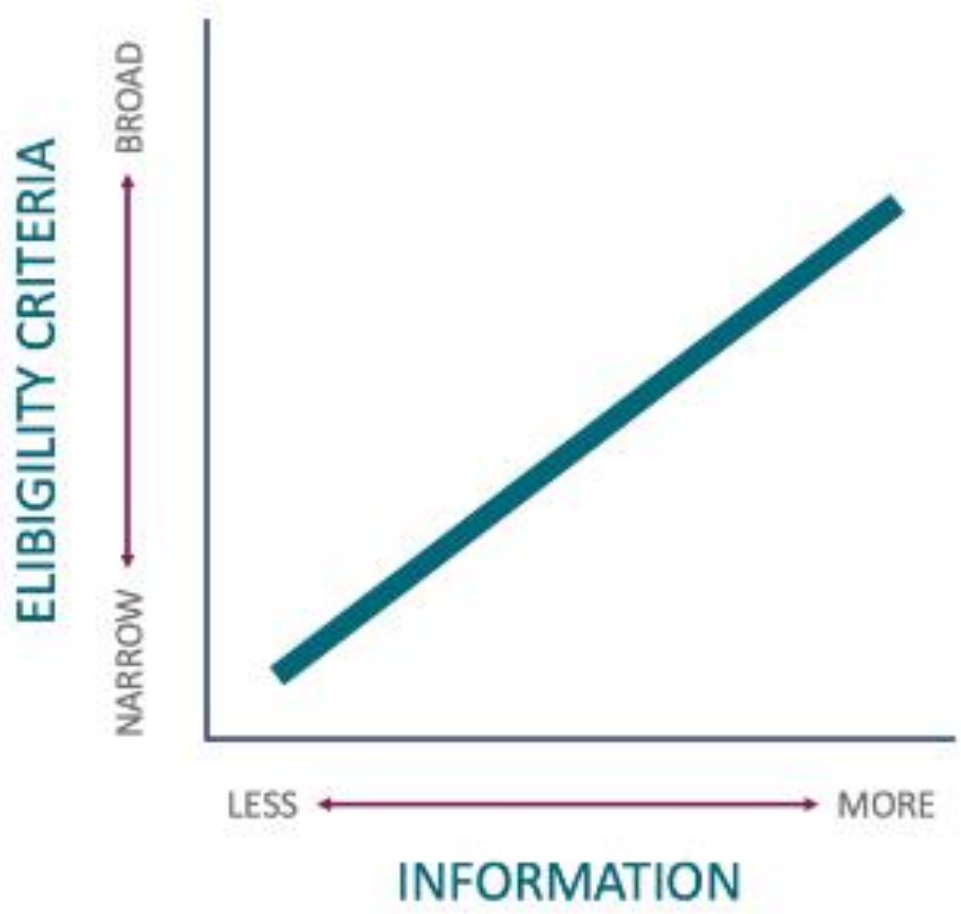
REVIEW

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

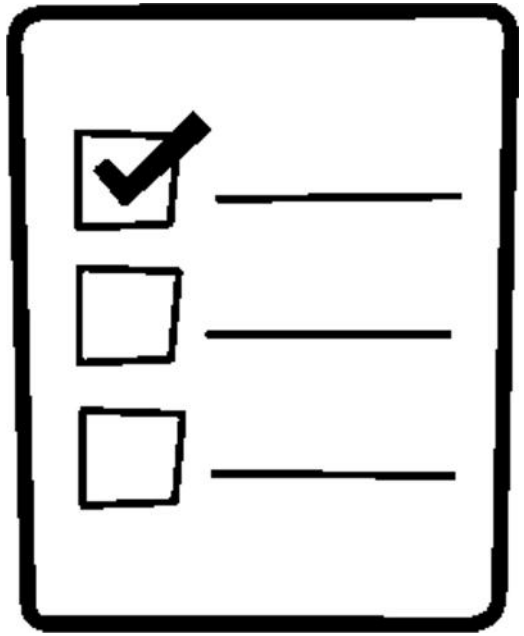
- Understand the population affected by the study question.
- As restrictive as necessary (generally, for safety reasons) and as permissive as possible.
- Maximize inclusivity through documentation of scientific rationale for all restrictions/limitations to eligibility.

Feasibility Assessments

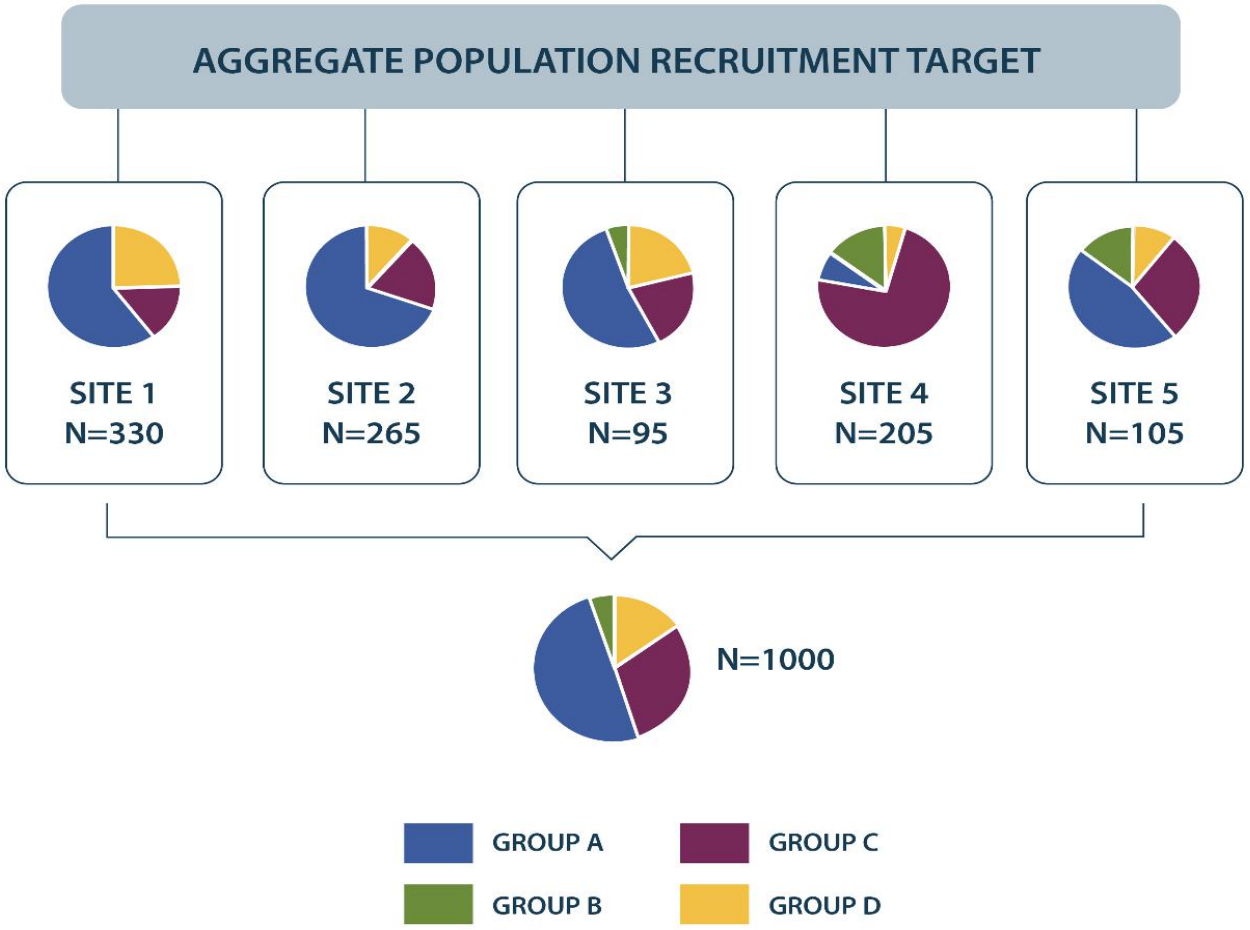
- Feasibility assessments help sponsors, CROs, and investigators evaluate the possibility of conducting a particular trial with the objective for optimal project completion in terms of timeliness, targets, outcomes and cost.

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

- Accurate, triangulated data sources



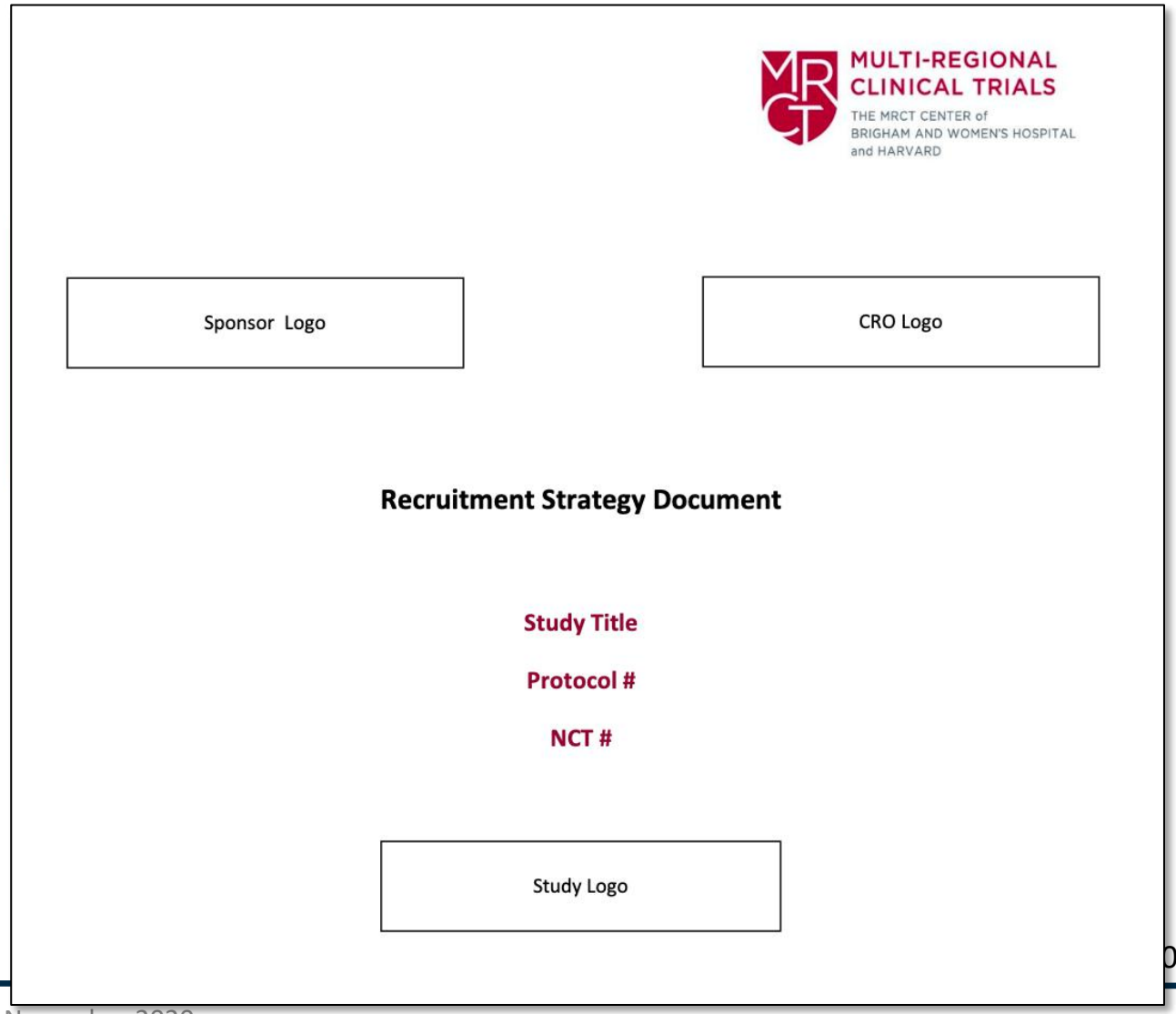
Feasibility Assessments



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

Bierer BE, et al. (2020) From: https://mrctcenter.org/diversity-in-clinical-trials/

Feasibility Assessments



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Sponsor Logo

CRO Logo

Recruitment Strategy Document

Study Title

Protocol #

NCT #

Study Logo

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0) From: https://mrctcenter.org/diversity-in-clinical-trials/

Feasibility Decision Tree & Site Selection

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Feasibility Decision Tree

A tool to prioritize the recruitment of a representative population during 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.[1]

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

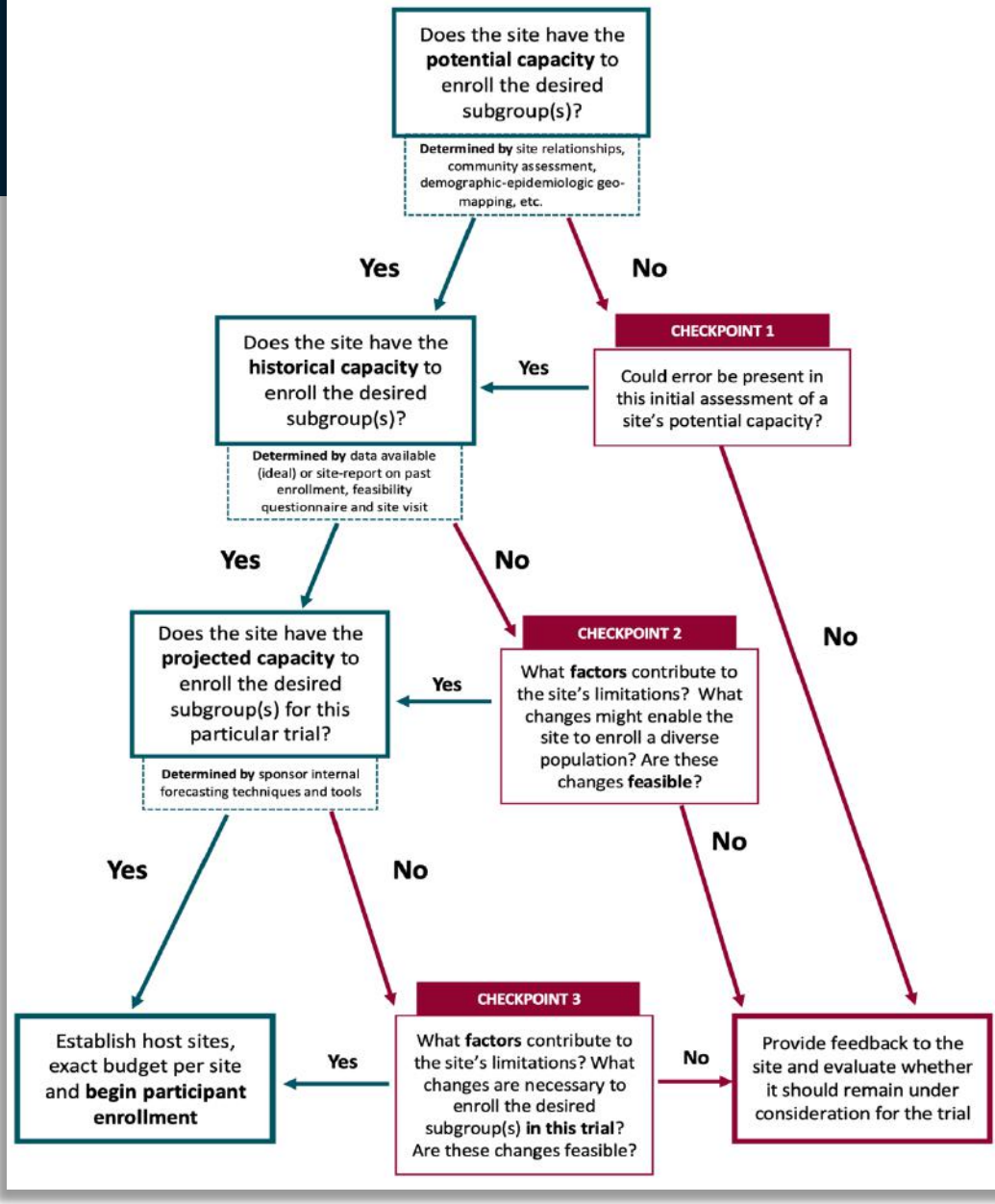
This tool aims to be

- **Supplementary** user should em
- **Multi-regional** clinical trials co
- **Capacity-buildi** enroll diverse p can objectively **is possible.**

Background

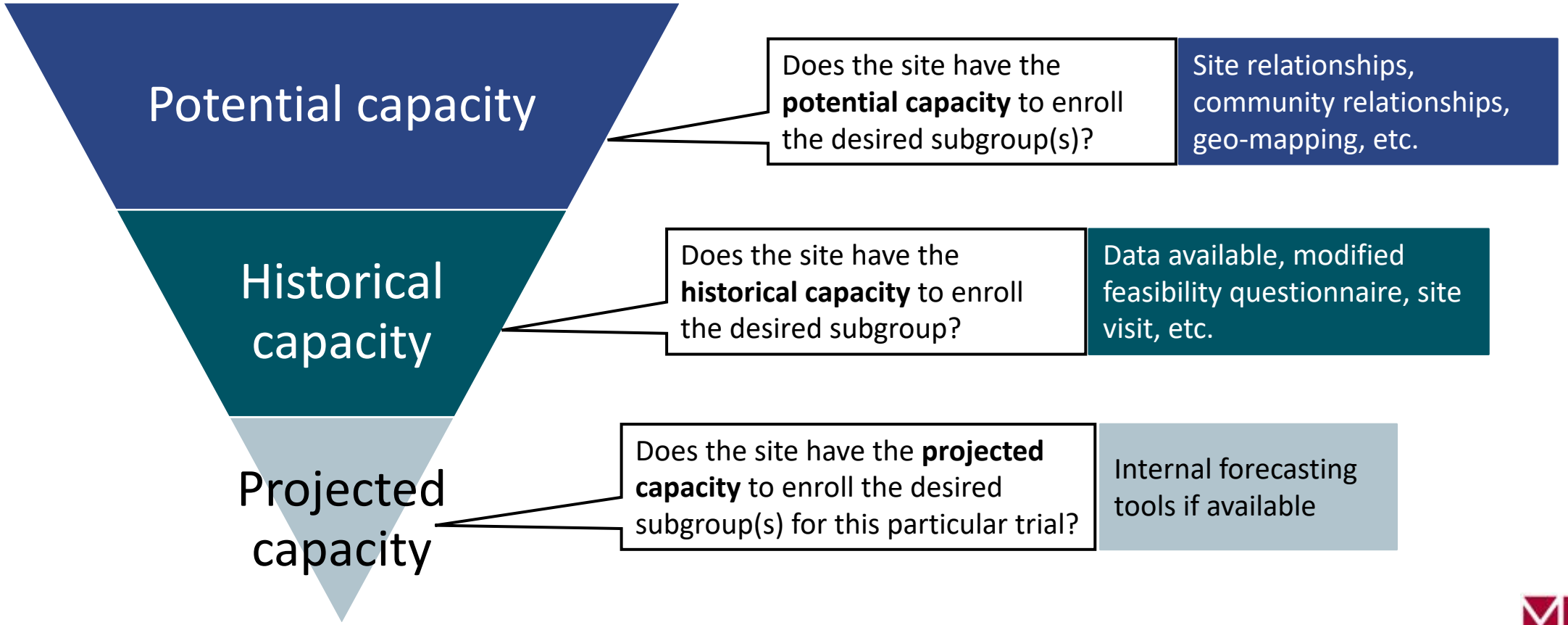
Despite the proliferati clinical trials in recent

Checkpoint	Capacity Tier	Purpose
Checkpoint 1	Potential Capacity	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).
Checkpoint 2	Historical Capacity	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.
Checkpoint 3	Projected Capacity	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.



Feasibility & Site Selection

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



Site Selection: Metrics, indicators, and tracking progress

Site Selection – Potential Key Performance Indicators (KPIs)

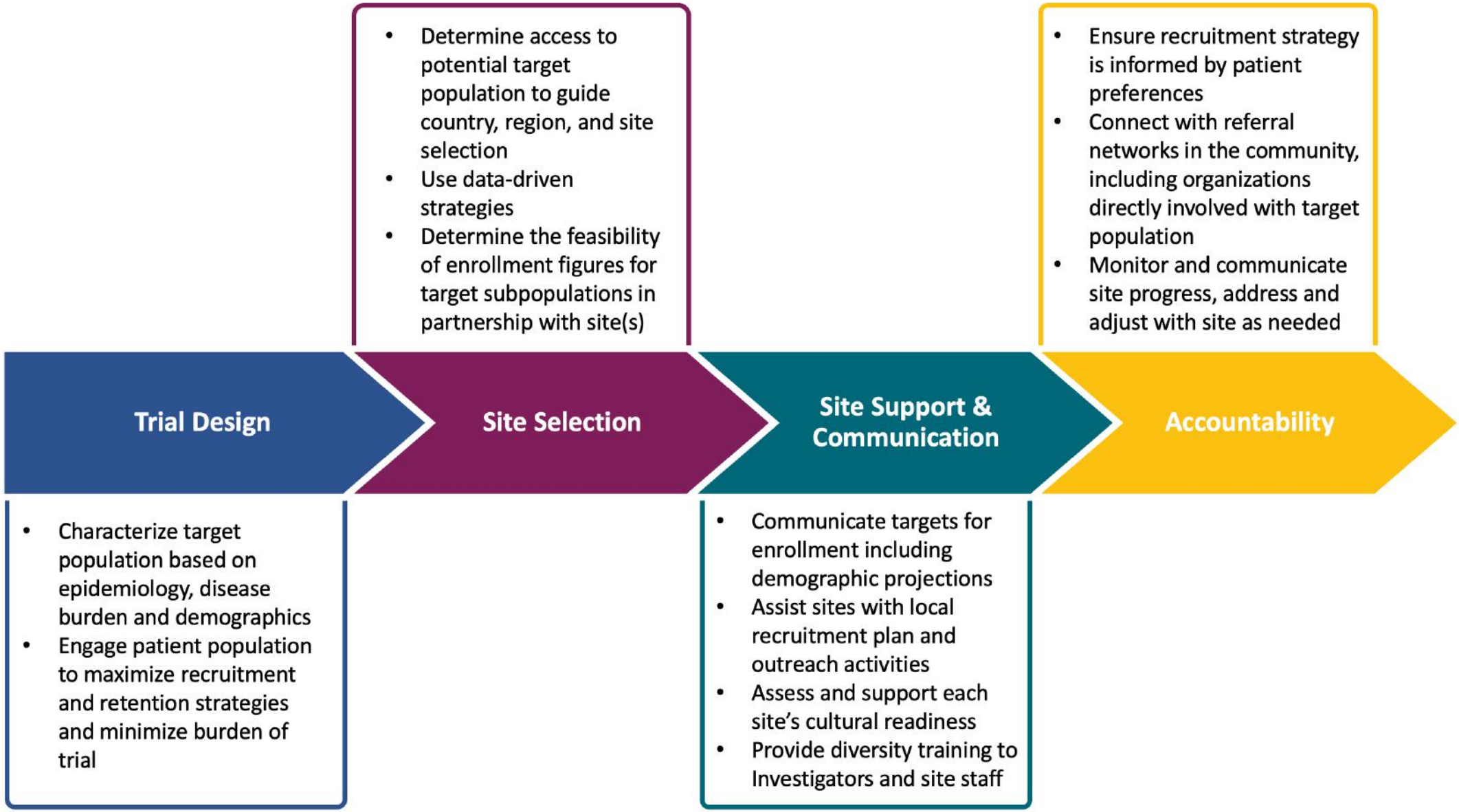
Output indicators

- ☐ 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



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:

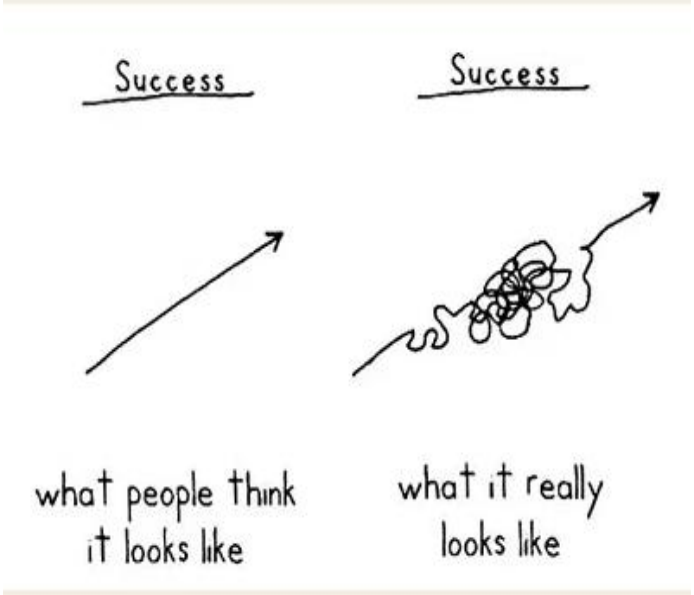
- Consider sites that may be new to the sponsor and/or new to research
- Explore new options for study placement including inner city sites and institutions
- Increase more ethnically and culturally diverse investigators
- Develop and support sites that have demonstrated the ability to recruit diverse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

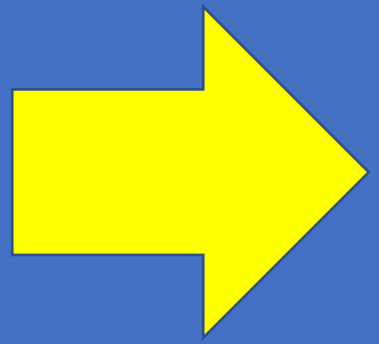
The pandemic has driven change in unexpected ways:

- 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



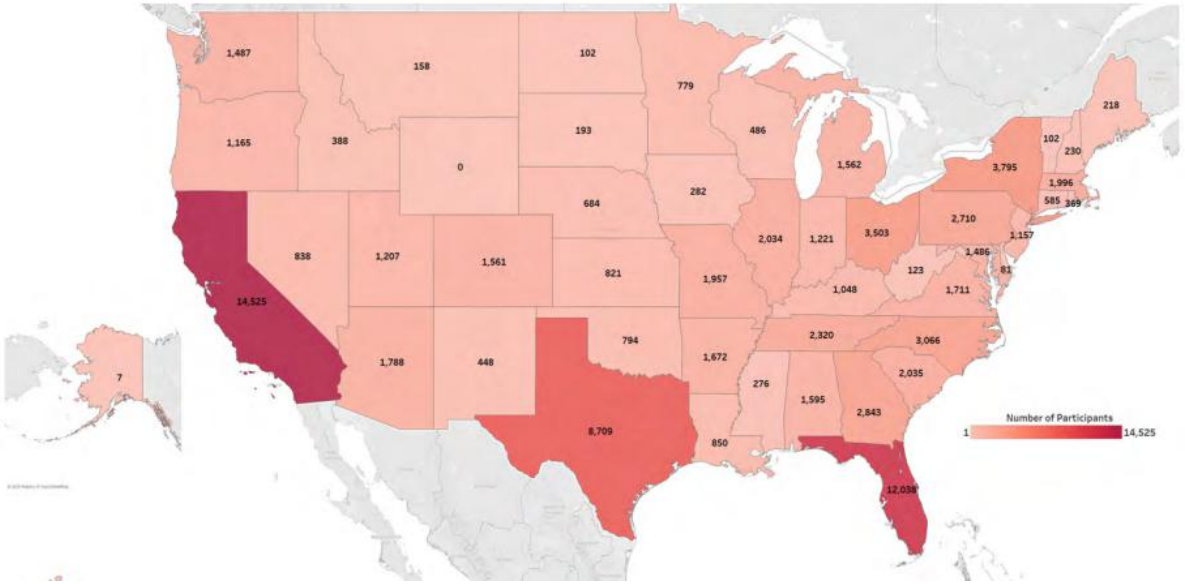
New options for participation:

- Home healthcare
- Mobile devices (e.g. ePRO)
- Telemedicine
- Home delivery of investigational product
- Patient apps and portals
- Unlimited access without geographic restrictions

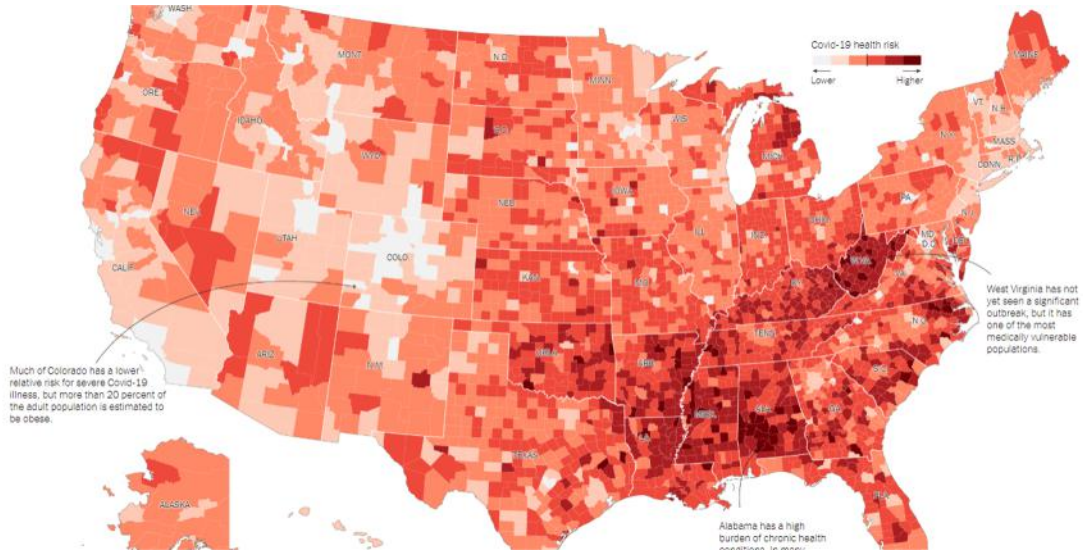
Building on Pandemic Learnings

- 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

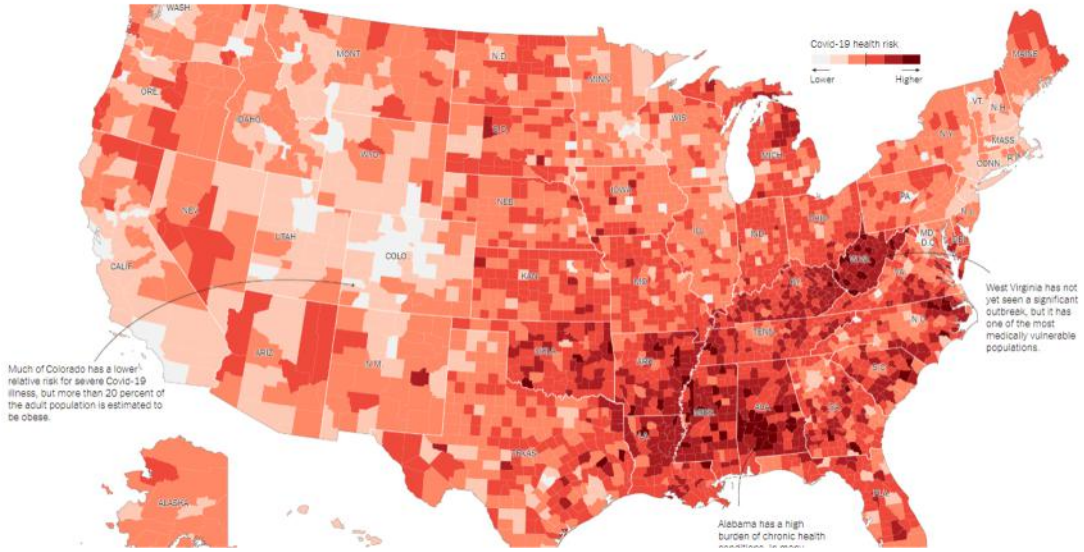


Clinical Trial Participation 2015-2019

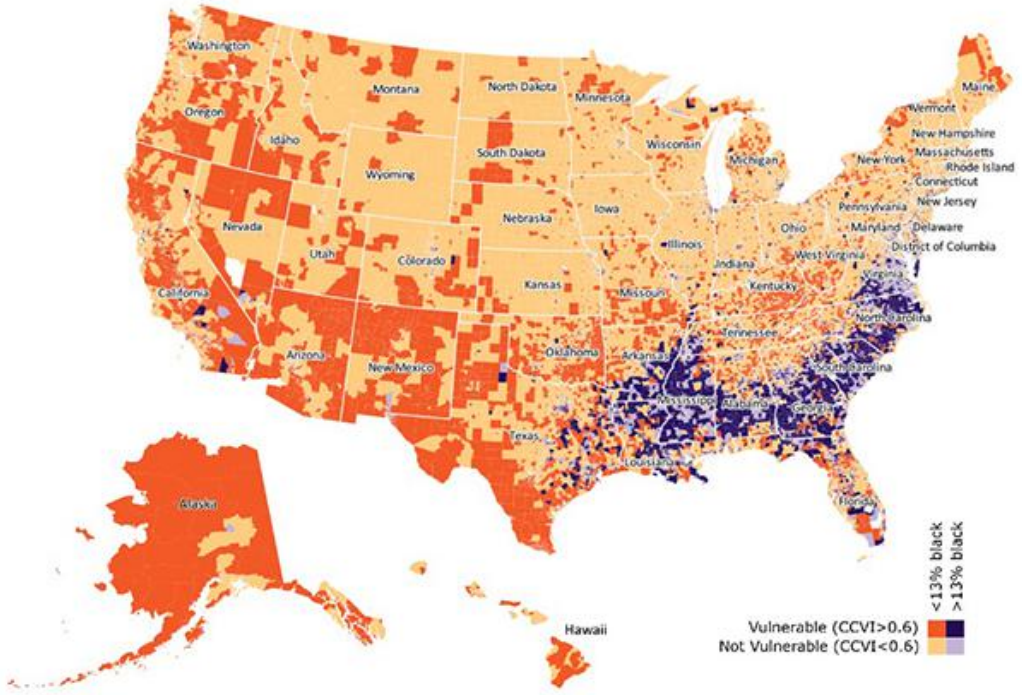


COVID 19 Cases 2020

The Evolution of Change – COVID 19

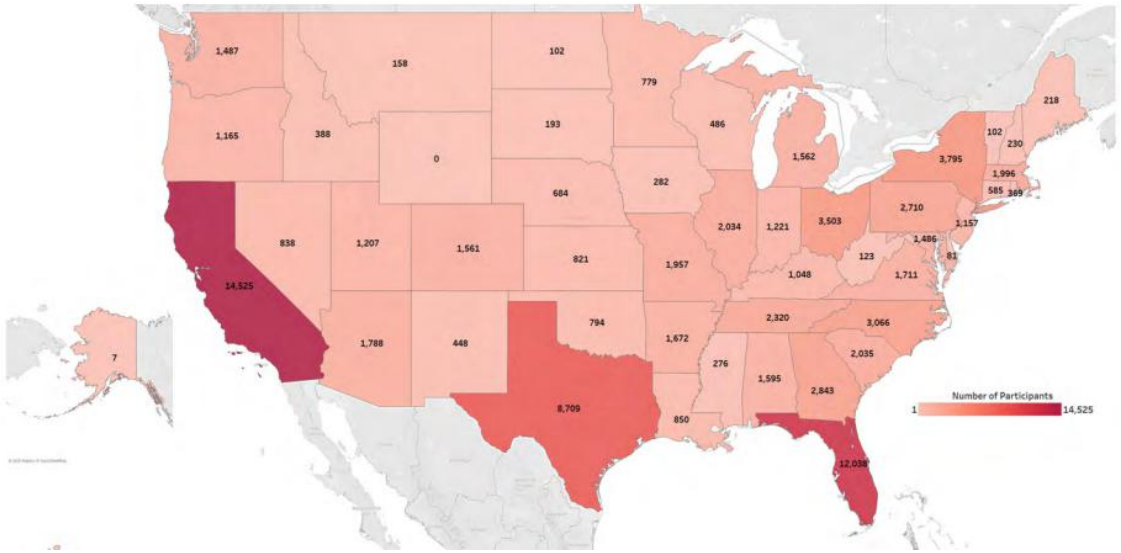


COVID 19 Cases 2020

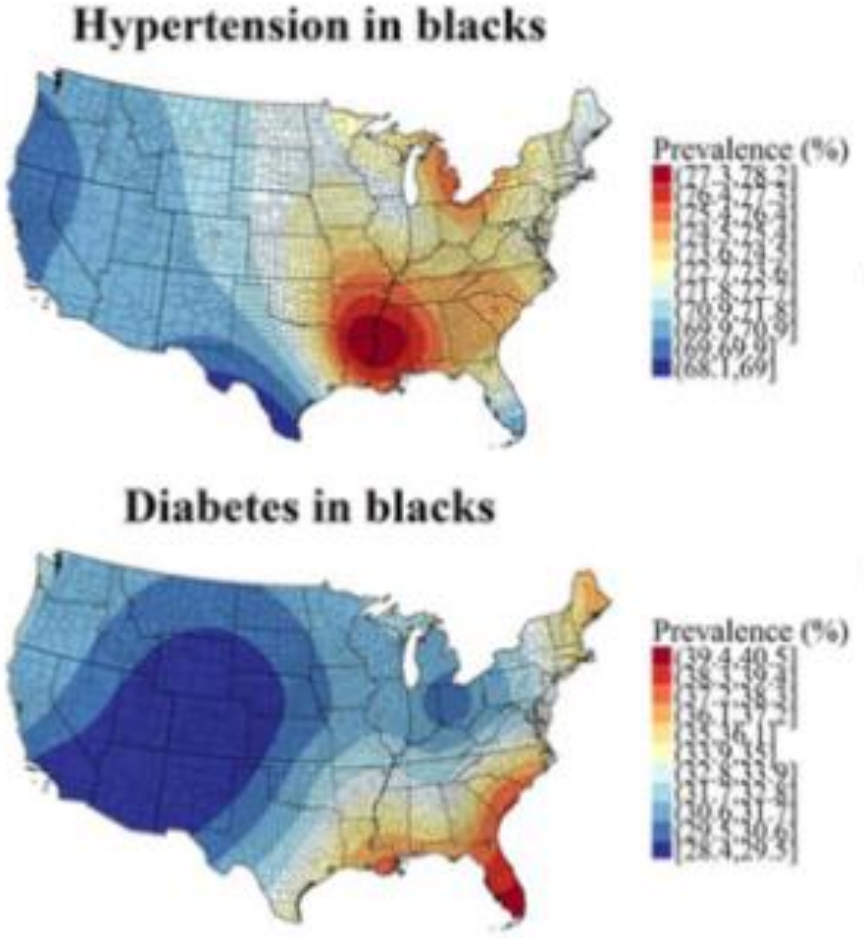


Census tracts with higher-than-average percentages of Black Americans are often more vulnerable to COVID-19.

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.

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Discussion and Questions


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