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

# Achieving Diversity, Inclusion, Equity In Clinical Research

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# Disclaimer

*The views and findings expressed in this document are those of the authors and do not imply endorsement or reflect the views or policies of the U.S. Food and Drug Administration or the affiliated organization or entity of any member who contributed to this work. Individuals have served in their individual capacity.*

The MRCT Center is supported by voluntary contributions (www.MRCTCenter.org) and grants.

# 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.

**DEVELOP STANDARDS**

**ESTABLISH BEST PRACTICES**

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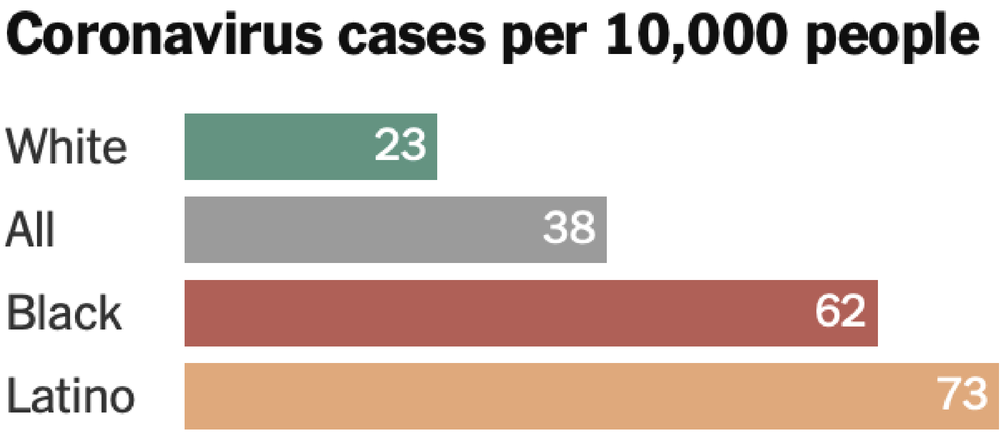
**IDENTIFY OPPORTUNITIES FOR IMPROVEMENT**

**IMPROVE TRANSPARENCY**

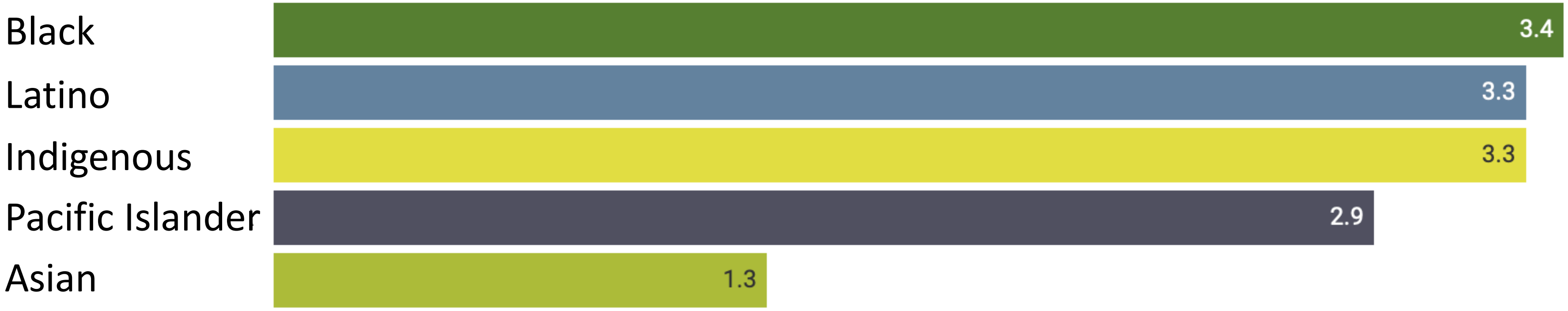
# Health disparities by race and ethnicity in the COVID-19 pandemic



The New York Times
July 5, 2020

https://www.nytimes.com/interactive/2020/07/05/us/coronavirus-latinos-african-americans-cdc-data.htm l

## Adjusted for age, race and ethnicity widens the gap in mortality compared to Whites



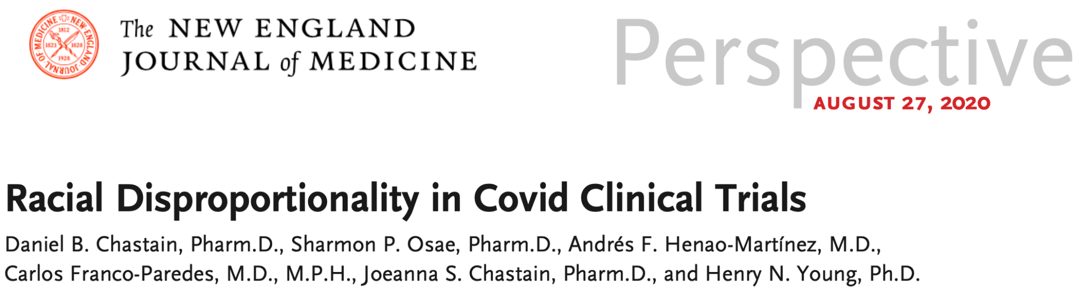
| | Fold increase |
|---|---|
| Black | 3.4 |
| Latino | 3.3 |
| Indigenous | 3.3 |
| Pacific Islander | 2.9 |
| Asian | 1.3 |

APM RESEARCH LAB

September 15, 2020

https://www.apmresearchlab.org/covid/deaths-by-race

# COVID-19 clinical trials



The NEW ENGLAND JOURNAL of MEDICINE

Perspective

AUGUST 27, 2020

**Racial Disproportionality in Covid Clinical Trials**

Daniel B. Chastain, Pharm.D., Sharmon P. Osae, Pharm.D., Andrés F. Henao-Martínez, M.D., Carlos Franco-Paredes, M.D., M.P.H., Joeanna S. Chastain, Pharm.D., and Henry N. Young, Ph.D.

THE READOUT LOUD

STAT

**Covid-19 clinical trials are failing to enroll diverse populations, despite awareness efforts**

*By* ADAM FEUERSTEIN @adamfeuerstein, DAMIAN GARDE @damiangarde, *and* REBECCA ROBBINS @rebeccadrobbins / AUGUST 14, 2020

**Researchers call out lack of diversity in COVID-19 clinical trials**

MedicalNewsToday

Contemporary Clinical Trials Communications 19 (2020) 100630

Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: http://www.elsevier.com/locate/conctc

ELSEVIER

COVID-19 disparities: An urgent call for race reporting and representation in clinical research

Hala T. Borno[a,*], Sylvia Zhang[a], Scarlett Gomez[b]

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**News & Analysis**

**Medical News & Perspectives**

**Researchers Strive to Recruit Hard-Hit Minorities Into COVID-19 Vaccine Trials**

**Mary Chris Jaklevic, MSJ**

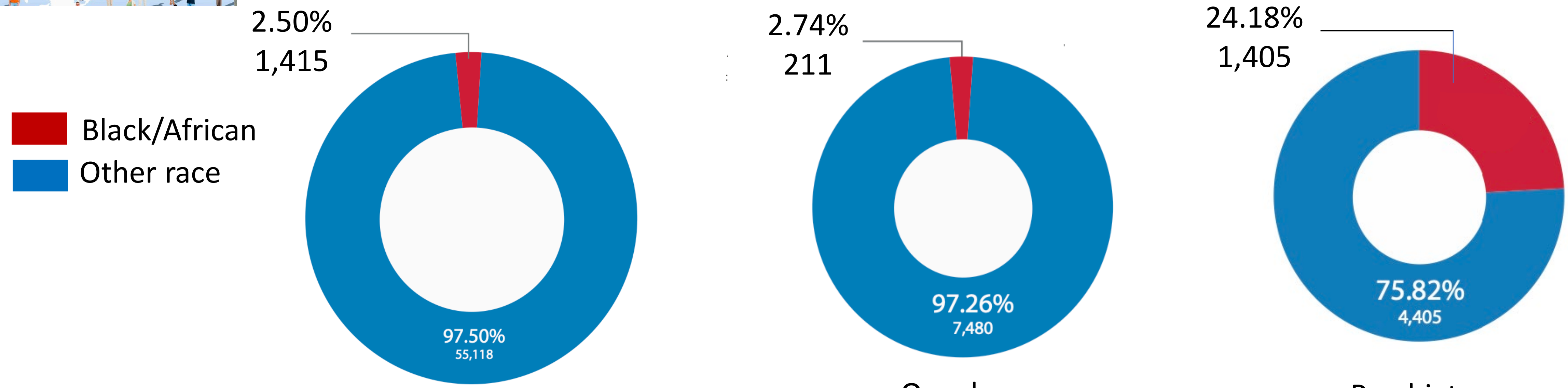
https://jamanetwork.com/journals/jama/fullarticle/2769611

# Drug Trial Snapshots: Summaries

U.S. FOOD & DRUG ADMINISTRATION

2015 - 2016
GLOBAL PARTICIPATION IN CLINICAL TRIALS REPORT

## Participation of Black or African American individuals in clinical trials for oncology, cardiology, and psychiatry



Cardiovascular Disease
N = 92,329

Oncology
N = 7,691

Psychiatry
N = 5,810

2015-2016

https://www.fda.gov/media/106725/download

# Background

- Clinical trials are needed to develop new treatments and new vaccines.
- Participants in trials should reflect the population affected by the disease, or those intended to utilize the intervention.
- We should not assume that all individuals respond similarly to interventions.
- Underrepresentation in clinical trials of Black, Latinx, Asian, Native American, and other underserved populations—as well as women and individuals at either end of the age spectrum—is not new, and persists in both industry and academic trials, and across therapeutic areas.
- Race and ethnicity are not a biological determinants, but social determinants of health have a real impact on real biology.
- Diverse representation in clinical trials is not simply a matter of biology, but a matter of health equity, fairness, and public trust.

# 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, MBE

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.

# MRCT Diversity Workgroup

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Stacey Bledsoe* , Eli Lilly and Company
Shari Bodnoff* , Novartis
Racquel Bruton , Biogen
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Li Chen, Amgen
Patrick Cullinan, Takeda, currently BlueBird Bio
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Quita Highsmith, Genentech/ A Member of the Roche Group
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*involvement limited in time

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Paul Underwood, Boston Scientific
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Gerren Wilson*, Genentech/ A Member of the Roche Group
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Honghui Zhou*, Johnson & Johnson

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Guidance Document

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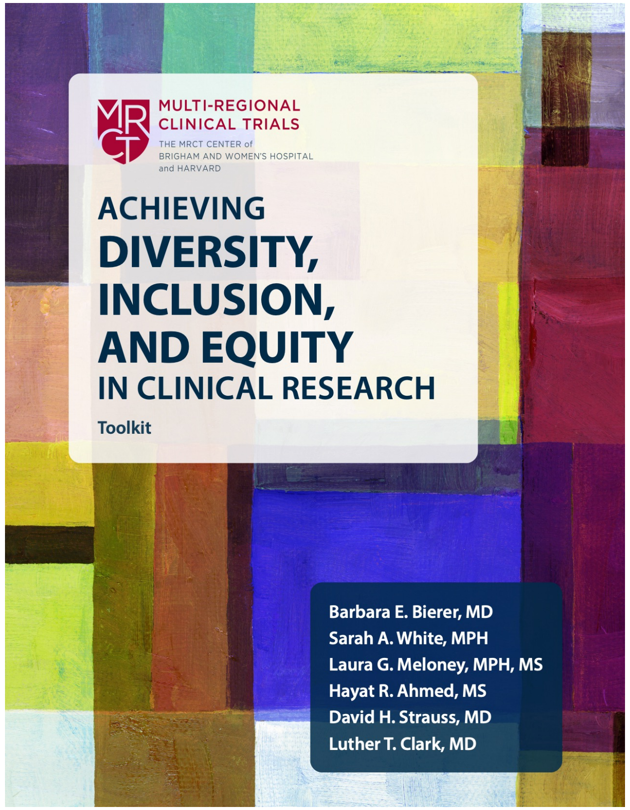

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ACHIEVING
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Toolkit

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Achieving Diversity, Inclusion, Equity In Clinical Research

MRCT Center
Guidance and Toolkit
Released 6 August 2020

mrctcenter.org/diversity-in-clinical-trials

# Diversity exists across many dimensions

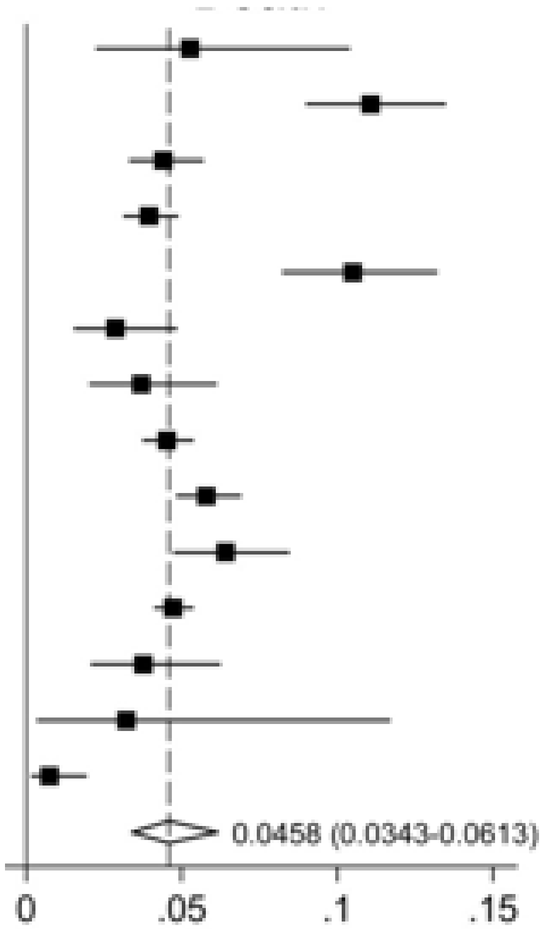
## A broad definition of diversity

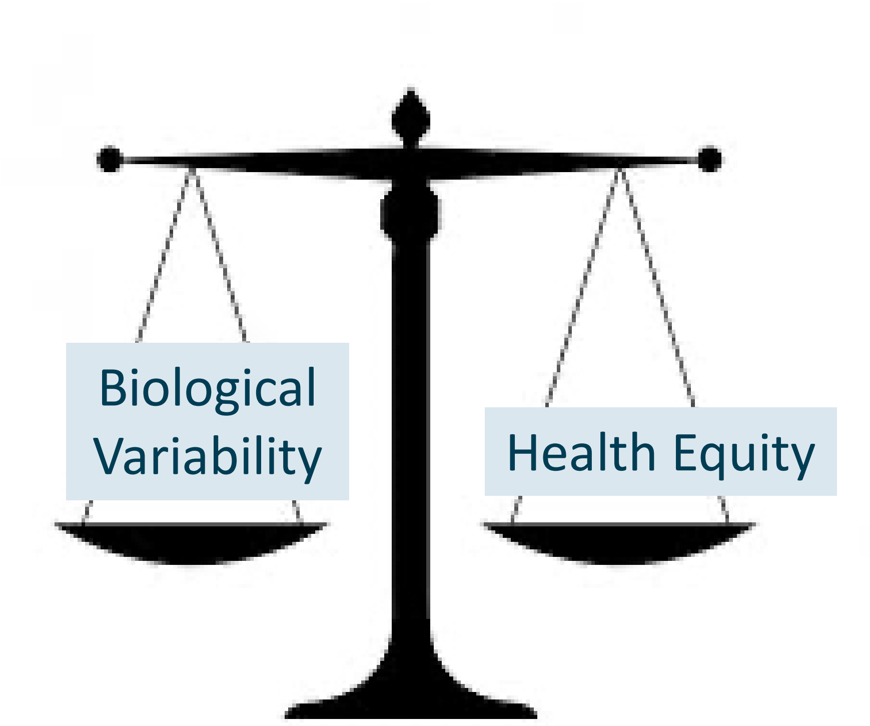
- Race
- Ethnicity
- Sex
- Gender
- Ancestry
- Age
- Social Determinants of Health
- Environmental factors
- Genetics
- Co-morbidities
- Concurrent medications
- Other

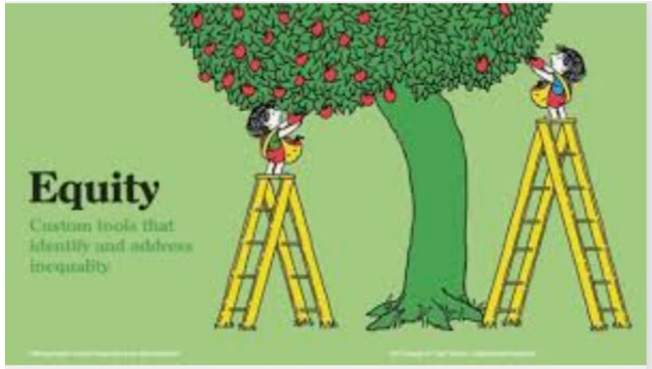
Intersectionality:

- Dimensions of diversity are not independent variables

# Science and Justice







In the end, an individual is being treated

# Sections of the MRCT Center Guidance Document

- Preface
- Part A – Building the Case
- Part B – Background, Ethical Principles, and Regulatory Directives
- Part C – Broadening Engagement
- Part D – Data Standards and Analysis
- Part E – Study Design, Conduct, and Implementation
- Part F – Stakeholder Commitments and the Future
- Part G – Appendix

Toolkit

# Features of the MRCT Center 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

# Barriers : Every stakeholder has responsibility

## Sponsors/Institutions/Sites/Regulators

- Lack of engagement
- Lack of diverse workforce
- Trial time and cost
- Variable regulatory expectations

## Data Collection/Data Analysis

- Lack of data standards
- Data collection and reporting variable
- Analyses inconsistent

## Investigators/Referring Physicians/ Staff

- Uncertain scientific utility of inclusion
- Eligibility criteria limiting
- Site feasibility inaccurate
- Inadequate staffing and time constraints
- Recruitment and retention challenges
- Lack of cultural competence and diverse staff

## Patients/Advocates/Communities

- Lack of awareness
- Lack of access
- Study design and research procedures burdensome
- Outcomes of uncertain value
- Logistics of trial conduct
- Payment and other concerns
- Mistrust

# Patient and community engagement support diverse participation

Forming Relationships

The patient and community to be in key leadership roles, as advisors, and as consultants

Training and Support

Patient perspective to influence research priorities and questions

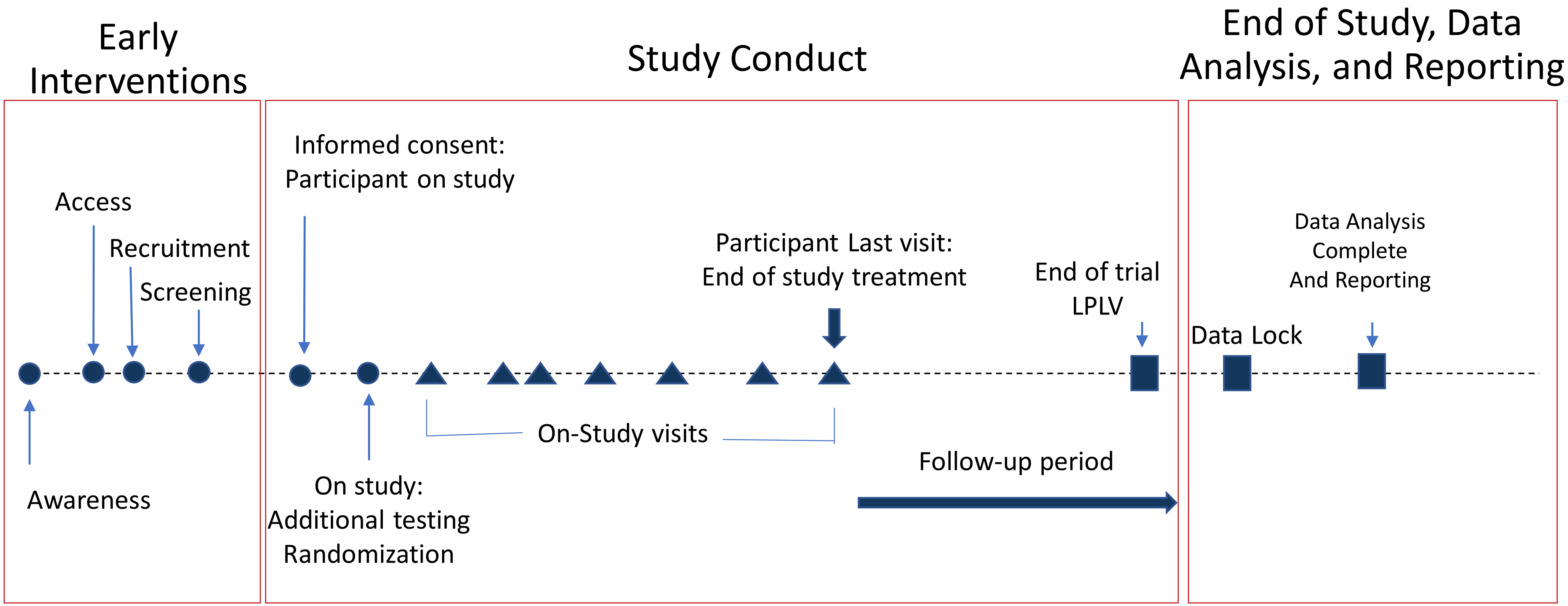
Shared Goals

Seek input to tailor study design and conduct to improve access, enrollment, and retention

Sustained partnerships

Build Trust

# Participant’s Clinical Trial Journey



## Early Interventions

Access

Recruitment

Screening

Awareness

## Study Conduct

Informed consent:
Participant on study

On study:
Additional testing
Randomization

On-Study visits

Participant Last visit:
End of study treatment

End of trial
LPLV

Follow-up period

## End of Study, Data Analysis, and Reporting

Data Lock

Data Analysis
Complete
And Reporting

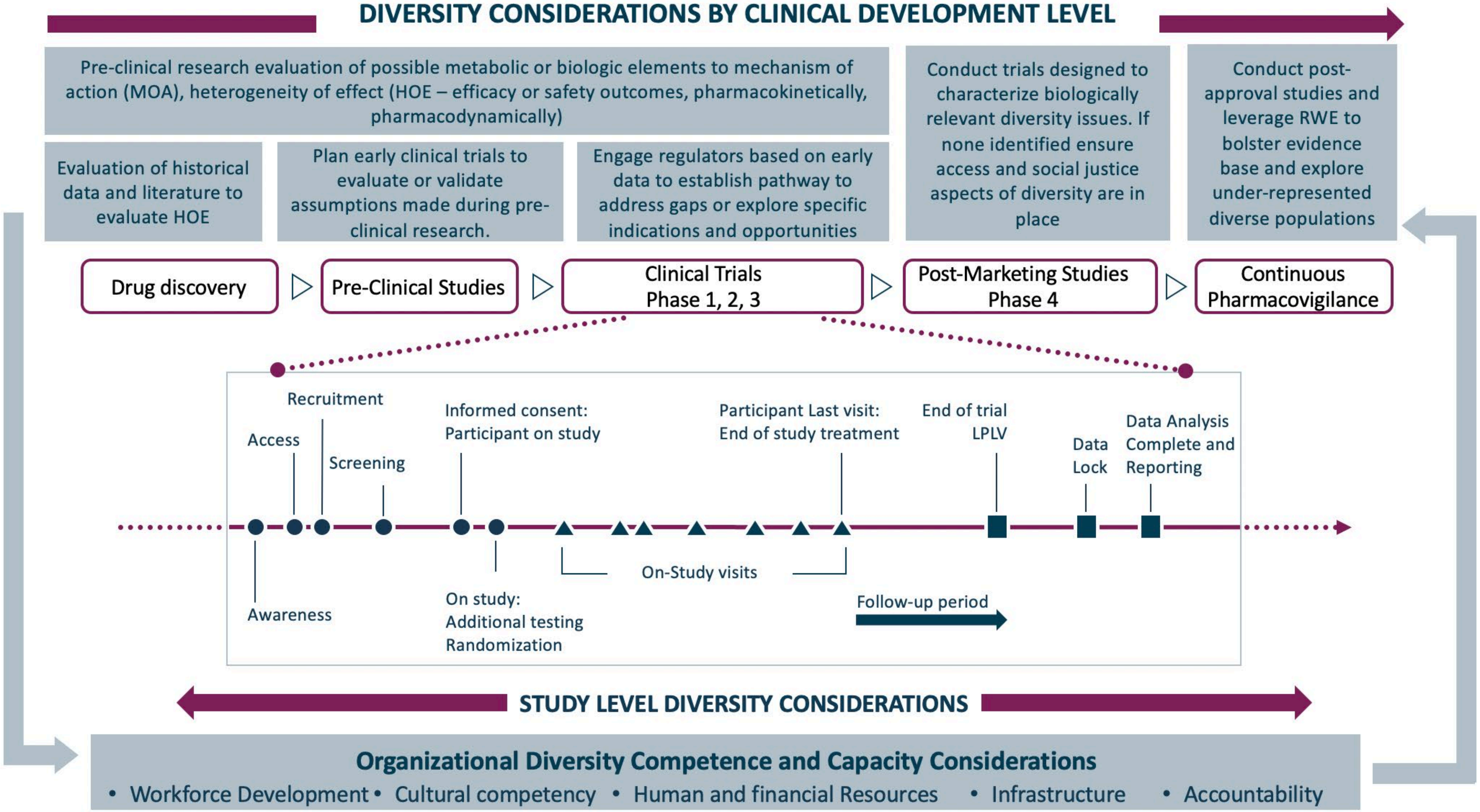
Patient and
Community Engagement
Education & Health Literacy
Feasibility Assessment
Eligibility Criteria

Study Design
Informed consent simplification
Logistical issues
Decentralized trials
Payment, transportation, childcare, etc.

Standardized data collection
Post-trial access to medicines
Return of results
Referring physician engagement

Data standards
Data analysis
Results reporting
Community outreach

# Product Development Pathway



**DIVERSITY CONSIDERATIONS BY CLINICAL DEVELOPMENT LEVEL**

Pre-clinical research evaluation of possible metabolic or biologic elements to mechanism of action (MOA), heterogeneity of effect (HOE – efficacy or safety outcomes, pharmacokinetically, pharmacodynamically)

Evaluation of historical data and literature to evaluate HOE

Plan early clinical trials to evaluate or validate assumptions made during pre-clinical research.

Engage regulators based on early data to establish pathway to address gaps or explore specific indications and opportunities

Conduct trials designed to characterize biologically relevant diversity issues. If none identified ensure access and social justice aspects of diversity are in place

Conduct post-approval studies and leverage RWE to bolster evidence base and explore under-represented diverse populations

Drug discovery ▷ Pre-Clinical Studies ▷ Clinical Trials Phase 1, 2, 3 ▷ Post-Marketing Studies Phase 4 ▷ Continuous Pharmacovigilance

**STUDY LEVEL DIVERSITY CONSIDERATIONS**

**Organizational Diversity Competence and Capacity Considerations**

- Workforce Development
- Cultural competency
- Human and financial Resources
- Infrastructure
- Accountability

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- Workforce Development
- Cultural competency
- Resources, human and financial
- Infrastructure
- Accountability

# Opportunities: What can we do?

**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

# Key Sponsor Opportunities & Future Actions

- Patient and Community Awareness, Access, Engagement, and Participation; Trust, Trustworthiness
- Workforce Diversity
- Eligibility and Study Design
- Logistics and Flexibility
- Data Standards and Analyses
- Innovation
- Genetics
- Diversity in data sources and databases; RWE

> “*Is there anything that we should understand to make your participation easier?*”

# Accountability in Partnership

## Holding ourselves and one another accountable

- Metrics
- Transparency
- Dialogue

# The work ahead

- What can each of us do now?
  - One step at a time towards change
- Targeted recommendations for special populations
- Additional tools and resources
- Need for local, national, and international focus going forward
- Committing to inclusion is our first step.

> *“…the real work of change is done year by year, month by month, and day by day, by all of us, by each of us…”*

mrctcenter.org/diversity-in-clinical-trials

# Leaning in: *Practical Approaches to improving diversity in Clinical trials*

| Webinar Topic | Date |
|---|---|
| Community awareness, access, knowledge | October 14, 2020 |
| Workforce Development | October 28 , 2020 |
| Study Design, Eligibility, Site Selection & Feasibility | November 11, 2020 |
| Study Conduct (Recruitment, Retention) | December 9, 2020 |
| Data Standards and Analysis | January 13, 2021 |
| Stakeholder Roles and Responsibilities | January 27, 2021 |
| Role of Data in Diversity: Genetics & RWD | February 10, 2021 |

***Leaning in* webinars will be held Wednesdays 11 AM -12 noon ET**

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# Discussion and Questions