MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

The Roles and Responsibilities of the IRB in Addressing Diversity in Clinical Research

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SACHRP presentation

Disclaimer

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Agenda

- MRCT Center introduction
- Introduction to Achieving Diversity, Inclusion, Equity In Clinical Research Project
- Role of the IRB as presented in the Guidance and Toolkit

The Multi-Regional Clinical Trials Center (MRCT Center)

Our Vision

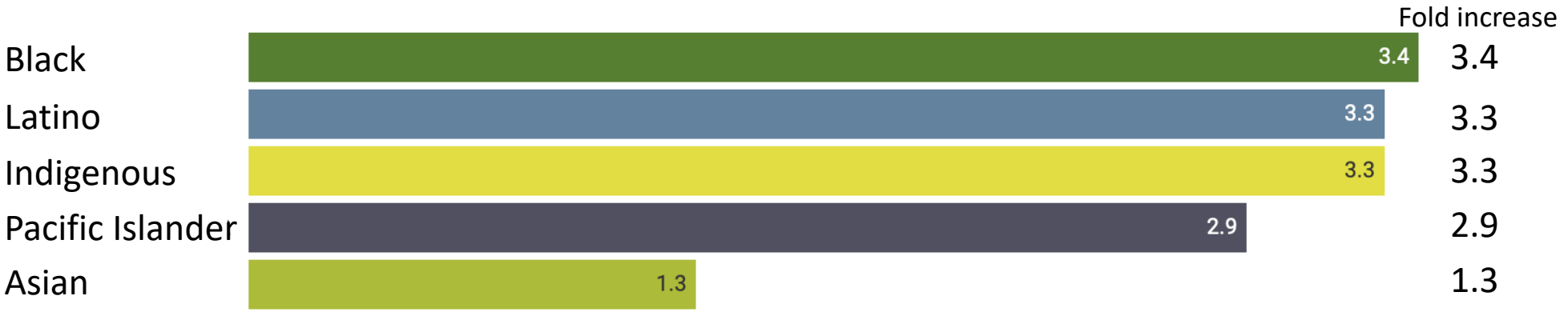
Improve the integrity, safety, and rigor of global clinical trials.

Our Mission

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.

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

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



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

But are underrepresented in research

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.

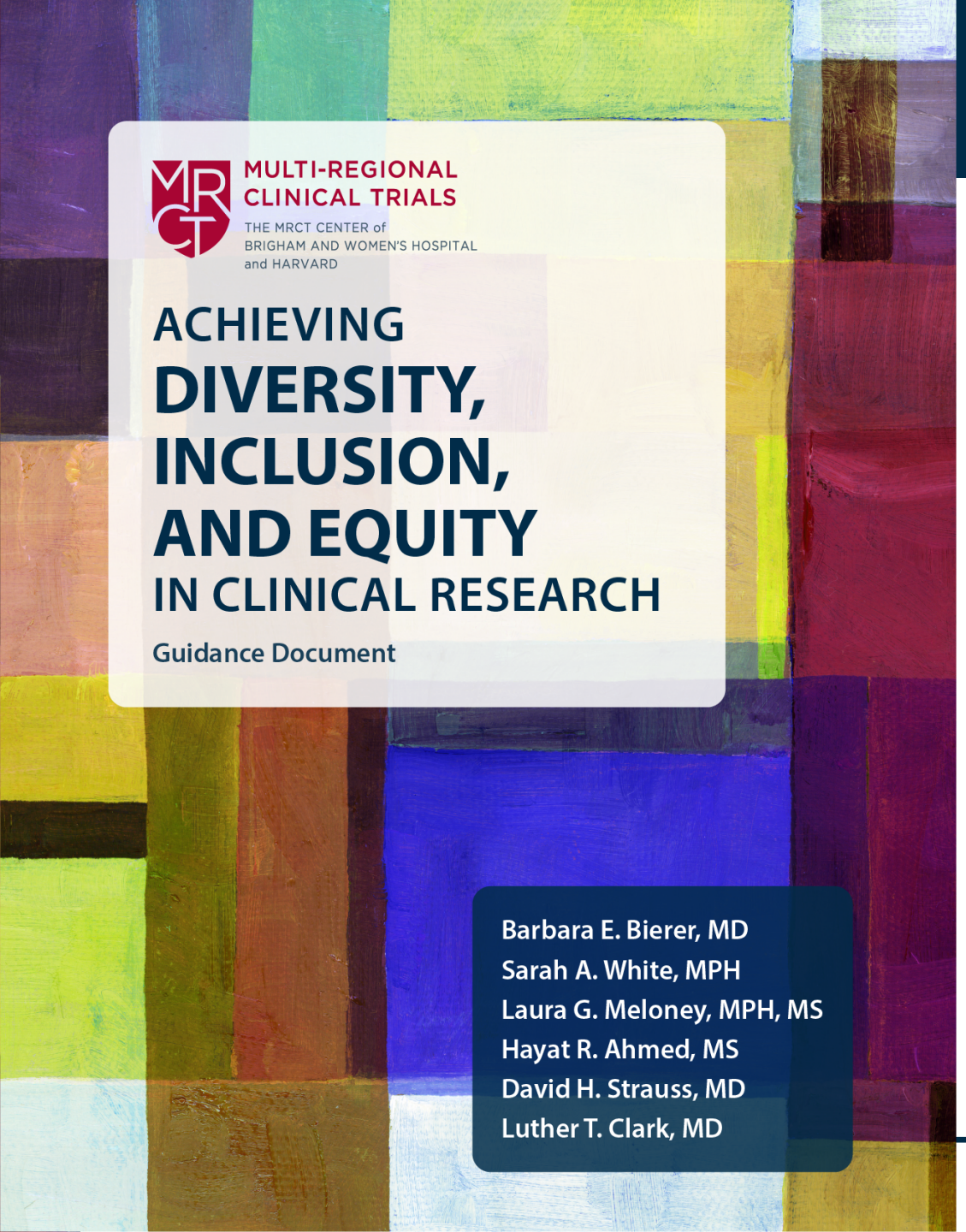
News & Analysis

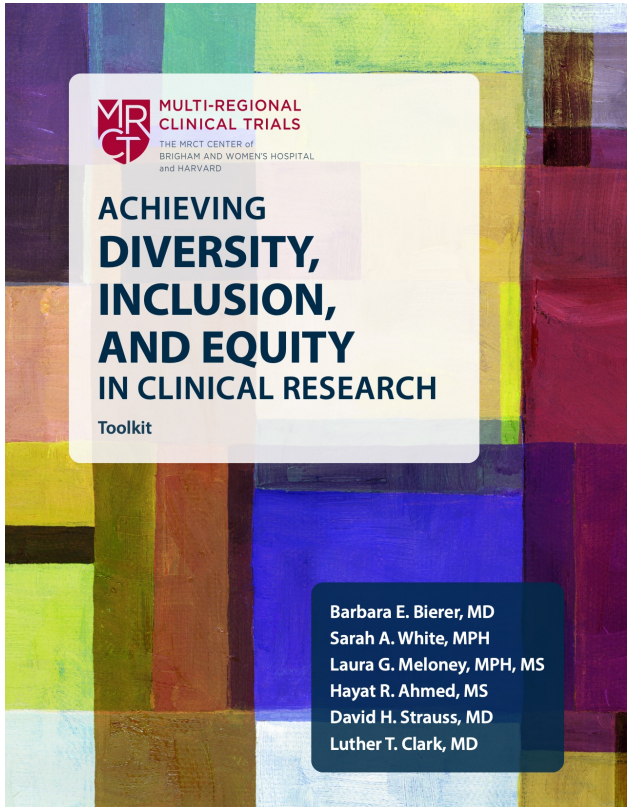
Medical News & Perspectives

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

Mary Chris Jaklevic, MSJ

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





Achieving Diversity, Inclusion, Equity In Clinical Research

Guidance and Toolkit

mrctcenter.org/diversity-in-clinical-trials

Released 6 August 2020

Leadership

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- 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, MRCT Center

MRCT Center staff:

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- 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.

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

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

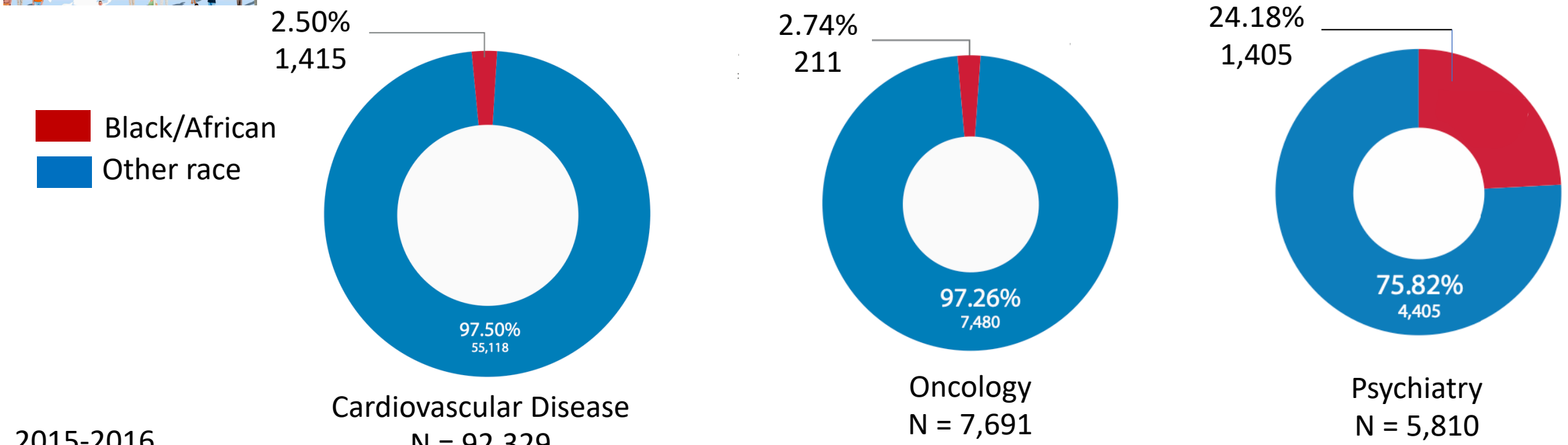
mrctcenter.org/diversity-in-clinical-trials

Diversity and Inclusion in Clinical Research: a role for the IRB

- Beyond COVID-19, is there a problem to solve?
- Is a role for the IRB justified?
- What practical steps can be taken?

Drug Trial Snapshots: Summaries

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



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

Background

- To develop new diagnostics, treatments, and vaccines, we need clinical trials.
- Participants in trials should reflect the population affected by the disease, or those intended to use or utilize the intervention.
- We should not assume that all individuals will respond similarly to interventions. Affirmative evidence of safety and efficacy is not the same as lack of evidence of a difference (particularly when the assumption is homogeneity).
- Underrepresentation in clinical trials of Black, Latinx, Asian, Native American, women, and individuals at either end of the age spectrum, and other underserved populations is not new, persists in both industry and academic trials, and across therapeutic areas.
- Biology is intricately intertwined with social determinants of health.
- Representation is not simply a matter of understanding biological heterogeneity; it is a matter of health equity, fairness, and public trust.
- It is also fundamental to reliable and generalizable research.

Application of the Belmont Principles

- Ethics and protection from research risk
- Ethics and access to the direct benefits of novel/investigational therapies
- Ethics, inclusion, and access to the benefits of scientific knowledge
- The objective to contribute to generalizable knowledge is foundational to the definition and justification of clinical research

The importance of *inclusion*

- Analyses of group differences in safety and efficacy among diverse populations can promote identification of both underlying biological factors and socially relevant factors that affect health, the "social determinants of health" (Beneficence)
- Fairness in the distribution of the benefits of research (Justice)
- Builds public trust

Belmont Report

- Justice:
  - "Justice is relevant to the selection of subjects of research at two levels: the social and the individual."
  - "Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society."
  - "An injustice occurs when some benefit to which a person is entitled is denied without good reason…"
  - Notion of distributive justice introduced

Belmont Report

- Justice:
  - "Who ought to receive the benefits of research and bear its burdens?"
  - "…moral requirements that there be fair procedures and outcomes in the selection of research subjects."

§46.111 Criteria for IRB approval of research.

(3) Selection of subjects is equitable.

Belmont Report

- Beneficence
  - "In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the **maximization of benefits**… "
  - "In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result…"

Belmont Report

- Respect for Persons
  - Obligations to treat individuals as autonomous agents
  - Obligations to protect those with diminished autonomy

Focusing on the role of the IRB in advancing diversity

- Initial Review:
  - Study Aims and Subject Selection
    - Do the demographics of the proposed sample reflect that of the population affected by the condition or for whom the intervention is intended?
      - When it does not, is the deviation adequately justified?
      - Is planned under- or over- representation by age, race, ethnicity, or gender in the sample scientifically justified?
      - Is there a statistical plan for examining heterogeneity in outcome or across subgroups?

Focusing on Role of the IRB in advancing diversity

- Criteria for Inclusion and Exclusion
  - Will inclusion and exclusion criteria inadvertently or unnecessarily result in under- or over-representation of understudied subgroups?
  - Have alternative approaches to minimizing risk that do not rely on exclusion been considered?
- Recruitment
  - Have recruitment procedures considered specific approaches to engage underserved populations?

Focusing on Role of the IRB in advancing diversity

- Study Conduct
  - Are study procedures flexibly organized to accommodate the needs of under-represented groups?
  - Do all participant-facing materials conform to health literacy principles?
  - Are participant materials translated? If not, why not?
- Payment
  - Is payment sufficient to cover costs of participation?
- Return of results
  - Are study results intended to be returned in a manner that meets the needs of populations studied?

Focusing on Role of the IRB in advancing diversity

- Continuing review:
  - Has the study fulfilled its recruitment/accrual goals?
  - Is demographic distribution on track to approximate the study goals?
  - If not, are adequate corrective actions described, sufficient, and likely to be successful?

The role of the IRB

- Ensuring ethical research
- Creating expectations, promoting dialogue
- Establishing accountability
- Fostering competence, education, and the development of infrastructure

- Institutional support for the role and responsibility of the IRB
  - (and note Title VI of the Civil Rights Act of 1964, 42 U.S.C. 2000d et seq.)
- Responsibilities of HRPP in addition to IRB

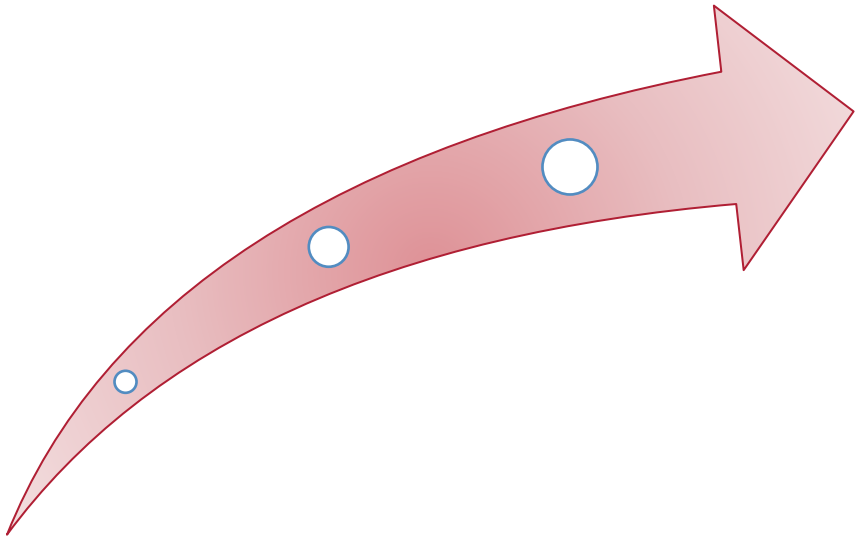
Ask the question.

Key Performance Indicators

The importance of:

- Metrics
- Transparency
- Accountability

Progress takes time



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

Join us:

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