Achieving Diversity, Inclusion, Equity In Clinical Research

Monday, October 19, 2020

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

• MRCT Center introduction
• Introduction to Achieving Diversity, Inclusion, Equity In Clinical Research Guidance Document
• Presentations by:
  o Paul Underwood, M.D., FACC, FSCAI
  o Eldrin Lewis, M.D., MPH
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.
The MRCT Center’s work

Addressing the pressing issues of MRCTs

Recognizing the need to focus on and with the participant

- Post trial access to medicines
- Return of Results
- Health Literacy
- Diversity, Inclusion, Equity

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mrcctcenter.org/diversity-in-clinical-trials
Join us:

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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

<table>
<thead>
<tr>
<th>Race/Culture</th>
<th>Fold Increase</th>
</tr>
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<tbody>
<tr>
<td>Black</td>
<td>3.4</td>
</tr>
<tr>
<td>Latino</td>
<td>3.3</td>
</tr>
<tr>
<td>Indigenous</td>
<td>3.3</td>
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<tr>
<td>Pacific Islander</td>
<td>2.9</td>
</tr>
<tr>
<td>Asian</td>
<td>1.3</td>
</tr>
</tbody>
</table>

But are underrepresented in research

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., Joëanna S. Chastain, Pharm.D., and Henry N. Young, Ph.D.

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

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

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

2015-2016

Cardiovascular Disease
N = 92,329

- Black/African: 2.50% (1,415)
- Other race: 97.50% (55,118)

Oncology
N = 7,691

- Black/African: 2.74% (211)
- Other race: 97.26% (7,480)

Psychiatry
N = 5,810

- Black/African: 24.18% (1,405)
- Other race: 75.82% (4,405)

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; and social determinants of health have a real impact on 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

Maria Apostolaros, PhRMA
Abhijit Bapat *, Novartis
Stacey Bledsoe*, Eli Lilly and Company
Shari Bodnoff*, Novartis
Racquel Bruton, Biogen
Elizabeth Cahn, Cancer Connection
Li Chen, Amgen
Patrick Cullinan, Takeda, currently BlueBird Bio
Liza Dawson*, National Institutes of Health (NIH)
Maria De Leon*, Parkinson’s Foundation
Theresa Devins, Boehringer Ingelheim, currently Regeneron Pharmaceuticals
Anthony Edmonds, Takeda
Rhona Facile, Clinical Data Interchange Standards Consortium (CDISC)
Rachael Fones, IQVIA
Laura Gordon*, Institute for Advanced Clinical Trials for Children (iACT)
Anya Harry, GlaxoSmithKline (GSK)
Melissa Heidelberg, Genentech/ A Member of the Roche Group
Quita Highsmith, Genentech/ A Member of the Roche Group
Sharareh Hosseinizadeh, Novartis
Lloryn Hubbard*, Genentech/ A Member of the Roche Group
Anne Marie Inglis*, GlaxoSmithKline (GSK), currently Mallinckrodt Pharmaceuticals
Aarthi B. Iyer*, Kinetiq, now Advarra
Becky Johnson*, IQVIA
Tesheia Johnson, Yale School of Medicine
Jonathan Jackson*, Massachusetts General Hospital
Marcia Levenstein, Vivli
Roberto Lewis, Columbia University
Eldrin Lewis, Brigham and Women’s Hospital, currently Stanford University

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Erin Muhlbradt, National Cancer Institute (NCI)
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Latha Palaniappan, Stanford University
Claude Petit, Boehringer Ingelheim
Claire Pigula*, Biogen
Melissa Poindexter*, Advances in Health
Nicole Richie, Genentech/ A Member of the Roche Group
Bryan (Abel) Riera*, Population Council
Suzanne M. Rivera, Case Western Reserve University
Frank W. Rockhold, Duke University
Ricardo Rojo*, Pfizer
Rosanne Rotondo*, Novartis
Fabian Sandoval, Emerson Clinical Research Institute
Richard Sax*, IQVIA
Hollie Schmidt, Accelerated Cure Project for Multiple Sclerosis
Karlin Schroeder, Parkinson’s Foundation
Mary Scroggins*, Pinkie Hugs
Jessica Scott*, Takeda
Lana Skiboll, Sanofi
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Stacey Springs*, Harvard Medical School
Sara Tadesse-Bell, Genentech/ A Member of the Roche Group
Ann Taylor*, Columbia University
Paul Underwood, Boston Scientific
Junyang Wang, Food and Drug Administration (FDA)
Robert Winn*, University of Illinois
Gerren Wilson*, Genentech/ A Member of the Roche Group
Crispin Woolston, Sanofi
Honghui Zhou*, Johnson & Johnson

*involvement limited in time
Achieving Diversity, Inclusion, and Equity in Clinical Research

Guidance and Toolkit
Released 6 August 2020

mrctcenter.org/diversity-in-clinical-trials
It starts with evidence, information, and trust

- Data must include those populations affected.
- It starts with public and community engagement.
- Clinical trials should:
  - address questions of importance to the community
  - be designed with study outcomes that people care about
  - use language and words that people understand
  - be conducted in ways that decrease burden for the participants, and
  - communicate results to the communities affected.
- We should hold each other accountable at every stage.
Sections of the 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
Diversity exists across many dimensions

A broad definition of diversity

Intersectionality:
• Dimensions of diversity are not independent variables
Barriers: Every stakeholder has responsibility

Sponsors/Institutions/Sites/Regulators
- Lack of engagement
- Lack of diverse workforce
- Trial time and cost
- Variable regulatory expectations

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

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

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
Individuals must be invited

"Who me!? I thought you'd never ask."
The patient and community to be in key leadership roles, as advisors, and as consultants.

Patient perspective to influence research priorities and questions

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

Forming Relationships

Training and Support

Shared Goals

Sustained partnerships

Build Trust
Participant’s Clinical Trial Journey

Early Interventions
- Recruitment
- Access
- Screening
- Awareness

Study Conduct
- Informed consent: Participant on study
- On study: Additional testing Randomization
- On-Study visits
- Participant Last visit: End of study treatment
- Follow-up period

End of Study, Data Analysis, and Reporting
- End of trial LPLV
- Data Analysis Complete and Reporting

STUDY LEVEL DIVERSITY CONSIDERATIONS

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Product Development Pathway

DIVERSITY CONSIDERATIONS BY CLINICAL DEVELOPMENT LEVEL

- Drug discovery
  - Recruitment
  - Access
  - Screening
  - Awareness
- Pre-Clinical Studies
  - Informed consent: Participant on study
  - On study: Additional testing Randomization
- Clinical Trials Phase 1, 2, 3
  - Participant Last visit: End of study treatment
  - On-Study visits
- Post-Marketing Studies Phase 4
  - End of trial LPLV
- Continuous Pharmacovigilance
  - Data Analysis Complete and Reporting

STUDY LEVEL DIVERSITY CONSIDERATIONS

Organizational Diversity Competence and Capacity Considerations

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

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Clear communications throughout the product development program

Pre-Clinical

- Awareness
- Recruitment
  - Access
  - Screening
- Informed consent: Participant on study
- On study: Additional testing Randomization
- Participant Last visit: End of study treatment
- End of trial LPLV
- Follow-up period
- Data Lock
- Data Analysis Complete and Reporting

Education

- Informed Consent
- Data Collection

Individual Results

Summary Results

Approval

Phase 4

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Clear communication is a shared responsibility

- It is not that the listener has “poor literacy.”
- The communicator is responsible for sharing information that is understandable to the listener.
- The listener should be comfortable communicating any lack of understanding.

- Plain language
- Numeracy
- Visualization
- Clear design
- Cultural considerations
- Interactive techniques
- Teach-back

Written Materials
Verbal Communications
The MRCT Center launched a “Health Literacy in Clinical Research” website.

In a language understandable to the participant

www.mrctcenter.org/health-literacy
COVID-19 Research Flyers

“Should I join?”

Resources for the public

https://mrctcenter.org/blog/resources/covid-19-clinical-research-flyers/

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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
Solve for logistical challenges

- Easy and quick reimbursement processes
- Consider compensation for missed work or caregiver support
- Flexible, extended site hours (after work hours and weekends)
- Flexible appointments
- On-site childcare and eldercare
- Provide transportation or assist with arrangements
- Health literate study information in the correct language
- Culturally competent and linguistically-capable staff
Key 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...”
Practical Approaches to Improving Diversity in Clinical Trials

Wednesdays
11AM – 12noon ET

LEANING IN: A WEBINAR SERIES

October 14, 2020  Community Awareness, Access, Knowledge
October 28, 2020  Workforce Development
November 11, 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
No slides, Please listen to the [webinar](#)

Paul Underwood, M.D., FACC, FScai
Medical Director, Close the Gap and Interventional Cardiology
Boston Scientific
Today’s speakers

Eldrin Lewis, M.D., MPH
Professor of Medicine,
Stanford Medicine
Achieving Diversity, Inclusion, and Equity in Clinical Research

Eldrin Lewis, MD, MPH, FAHA, FACC
Professor of Medicine
Chief, Cardiovascular Medicine
Stanford University

October 19, 2020
Faculty Disclosures

- Novartis (Consulting, Institutional research support)
- NHLBI (Institutional research support)
- Sanofi (Institutional research support)
- Merck (Consulting, Institutional research support)
- DalCor (Consulting)
Outline

• Brief history/intro, entry into current work
• Perspective as an investigator for site activities to increase diversity
• Experience in workforce development for diversity and inclusion
• Any relevant success stories or lessons learned
My Journey: Training and Education
My Journey: Training and Education and Practice

- CV Clerkship director
- Recruitment
- STARS program
Scientific Interest and Mission

**Research Mission:** To improve outcomes in patients with heart failure and at risk for CVD

- Diabetes mellitus
- Chronic kidney disease
- Sleep apnea
- Hypertension

- Heart failure
- CAD
- Myocardial infarction
- Sleep apnea

- CV morbidity
- Mortality
- Quality of life

**Quality of life**

**Randomized Clinical Trials**

**Management strategies**

**Disparities and Health Equity**
Outline

• Brief history/intro, entry into current work
• Perspective as an investigator for site activities to increase diversity
• Experience in workforce development for diversity and inclusion
• Any relevant success stories or lessons learned
Perspective as an Investigator for Site Activities to Increase Diversity

- Develop strategies
- Evaluate commitments
- Recruitment materials
- Patient and community groups

- CRAs
- Partner with faculty
- Organizations

- National examples
- One size does not fit all
- Recruitment teams

- Set expectations

- Expectations
  - “Can mentality”
Outline

• Brief history/intro, entry into current work
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Pillars of Workforce Development in Research and Medicine
Pillars of Workforce Development in Research and Medicine

Academic Medicine

- Diversity and Inclusion
- Pipeline Development
- Patient care and access
- Training
- Leadership Training

Diversity, Equity, and Inclusion
Pillars of Workforce Development in Research and Medicine

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Diversity, Equity, and Inclusion
Outline

• Brief history/intro, entry into current work
• Perspective as an investigator for site activities to increase diversity
• Experience in workforce development for diversity and inclusion
• Any relevant success stories or lessons learned
Conclusions

• Diverse workforce can enrich clinical research enterprise
• Need extended pipelines and training
• Diversity training and leadership training paramount
• Involving community groups can allow shared vision for enrolling patients into clinical studies
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