



**MULTI-REGIONAL
CLINICAL TRIALS**

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

Achieving Diversity, Inclusion, Equity In Clinical Research

Monday, October 19, 2020

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Faculty Director, MRCT Center of BWH & Harvard

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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.



Today's Agenda

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



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.



Addressing the pressing issues of MRCTs



GLOBAL
REGULATORY
ENGAGEMENT



ETHICS,
CONDUCT, AND
OVERSIGHT



TRANSPARENCY



CAPACITY
BUILDING

Recognizing the need to focus on and with the participant



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

Join us:



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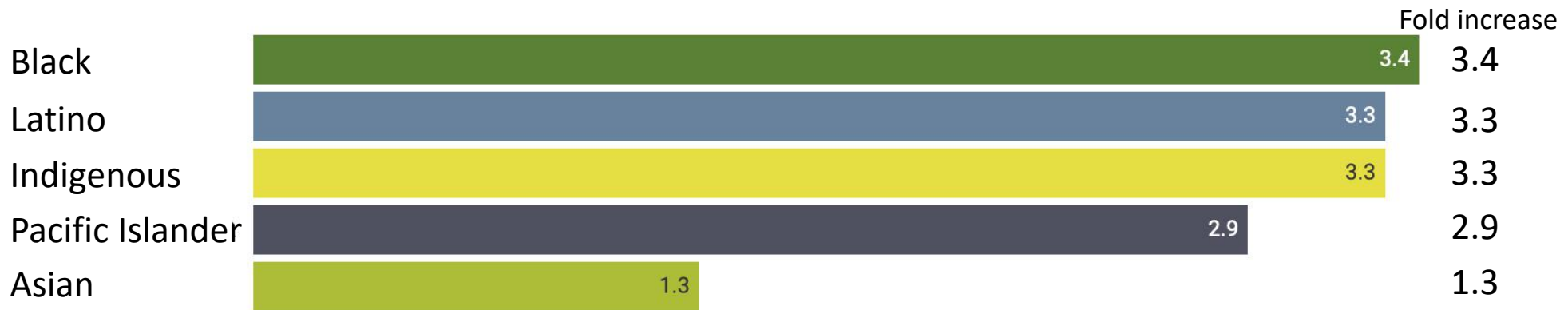


MRCTcenter.org



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

News & Analysis



Perspective
AUGUST 27, 2020

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>

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

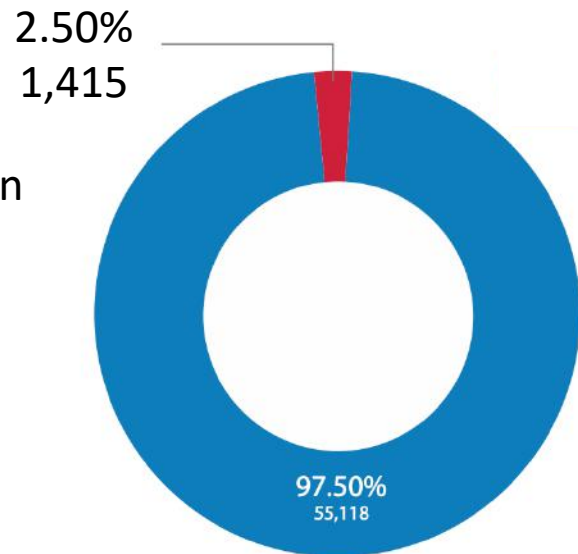


Drug Trial Snapshots: Summaries

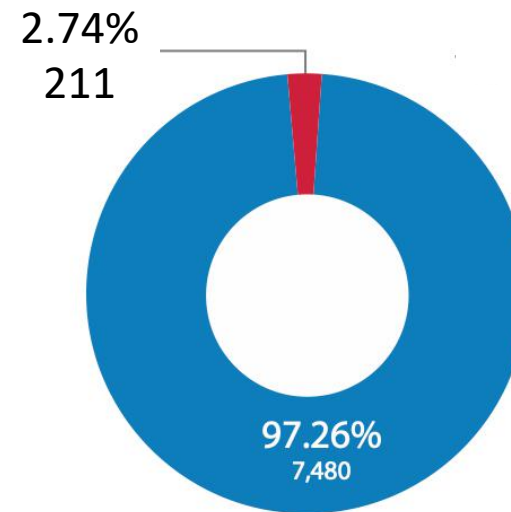


Participation of Black or African American individuals in clinical trials for oncology, cardiology, and psychiatry

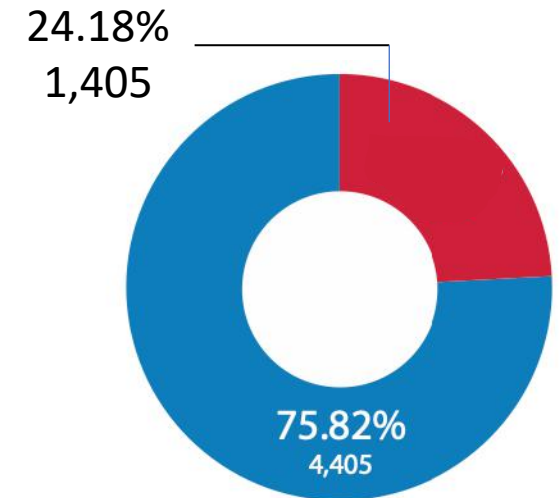
Black/African
Other race



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; 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 Hosseinzadeh ,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

*involvement limited in time

Jianchang Lin*, Takeda
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
Bryant (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 Skirboll, 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





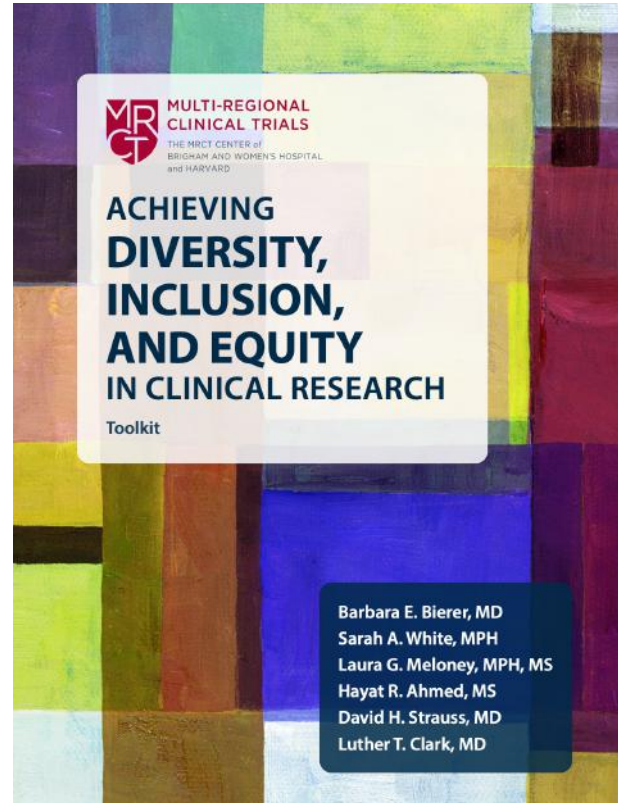
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ACHIEVING DIVERSITY, INCLUSION, AND EQUITY IN CLINICAL RESEARCH

Guidance Document

Barbara E. Bierer, MD
Sarah A. White, MPH
Laura G. Meloney, MPH, MS
Hayat R. Ahmed, MS
David H. Strauss, MD
Luther T. Clark, MD



Achieving Diversity, Inclusion,
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

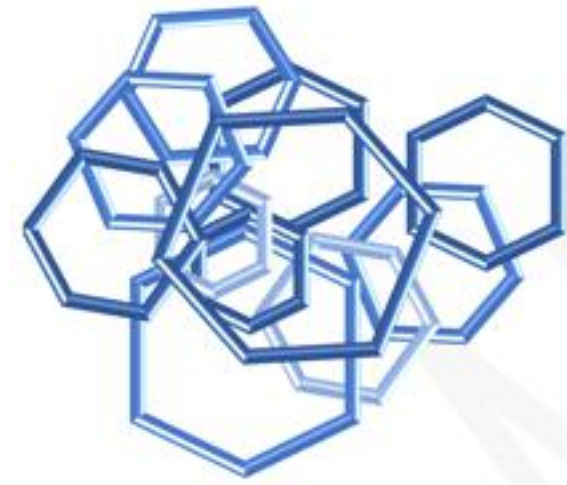
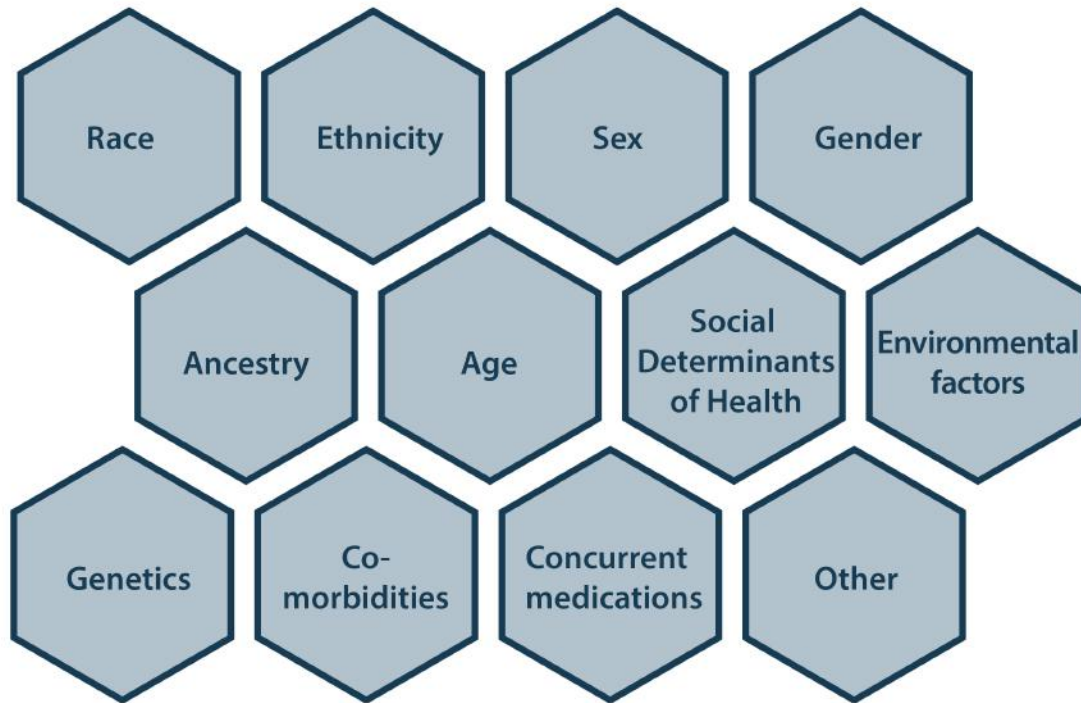
- Preface
- Part A – Building the Case
- Part B – Background, Ethical Principles, and Regulatory Directives
- Part C – Broadening Engagement
- Part D – Data Standards and Analysis
- Part E – Study Design, Conduct, and Implementation
- Part F – Stakeholder Commitments and the Future
- Part G – Appendix

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



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

Individuals must be invited



Patient and community engagement support diverse participation

Forming Relationships

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

Sustained partnerships

Training and Support

Patient perspective to influence research priorities and questions

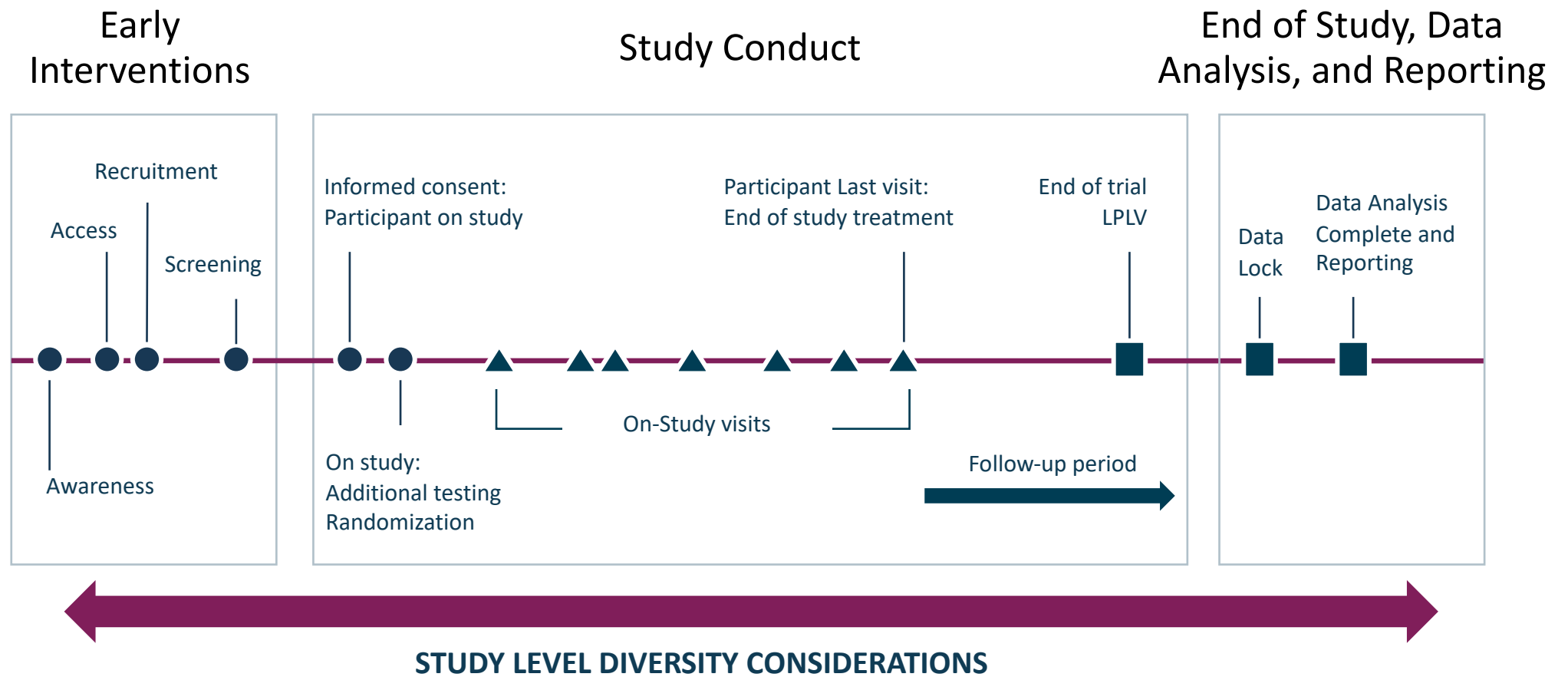
Shared Goals

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

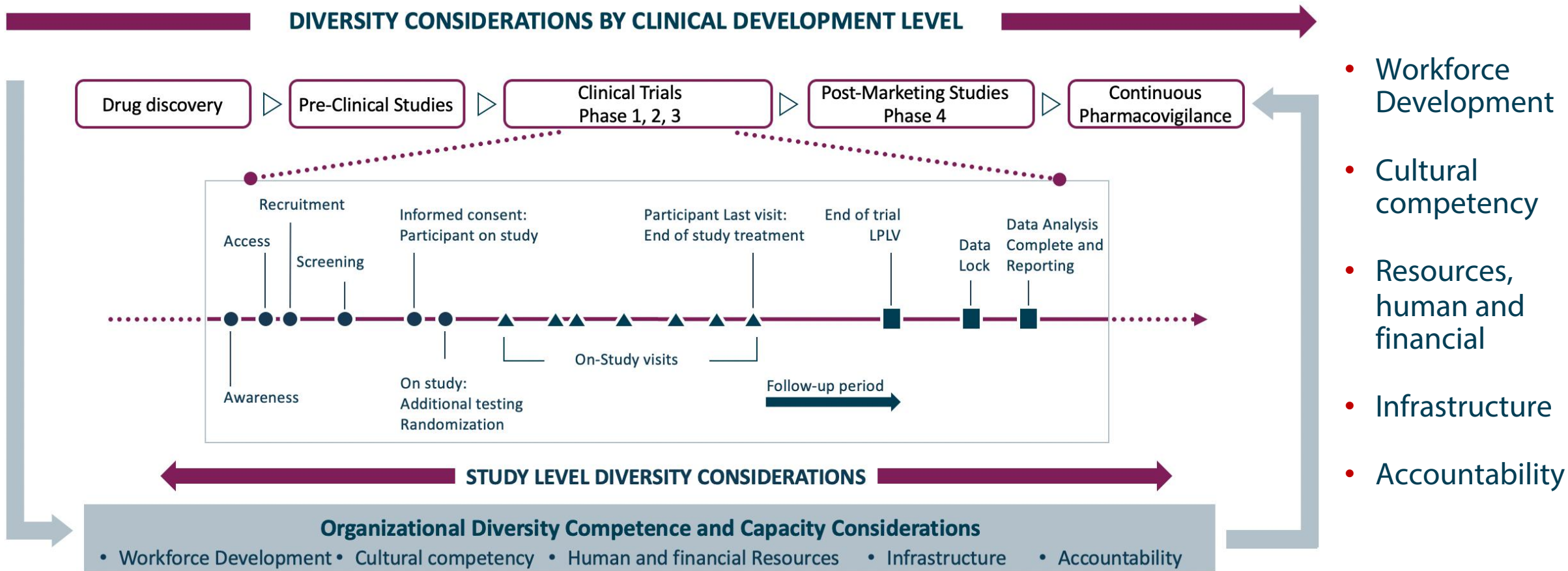


Build Trust

Participant's Clinical Trial Journey



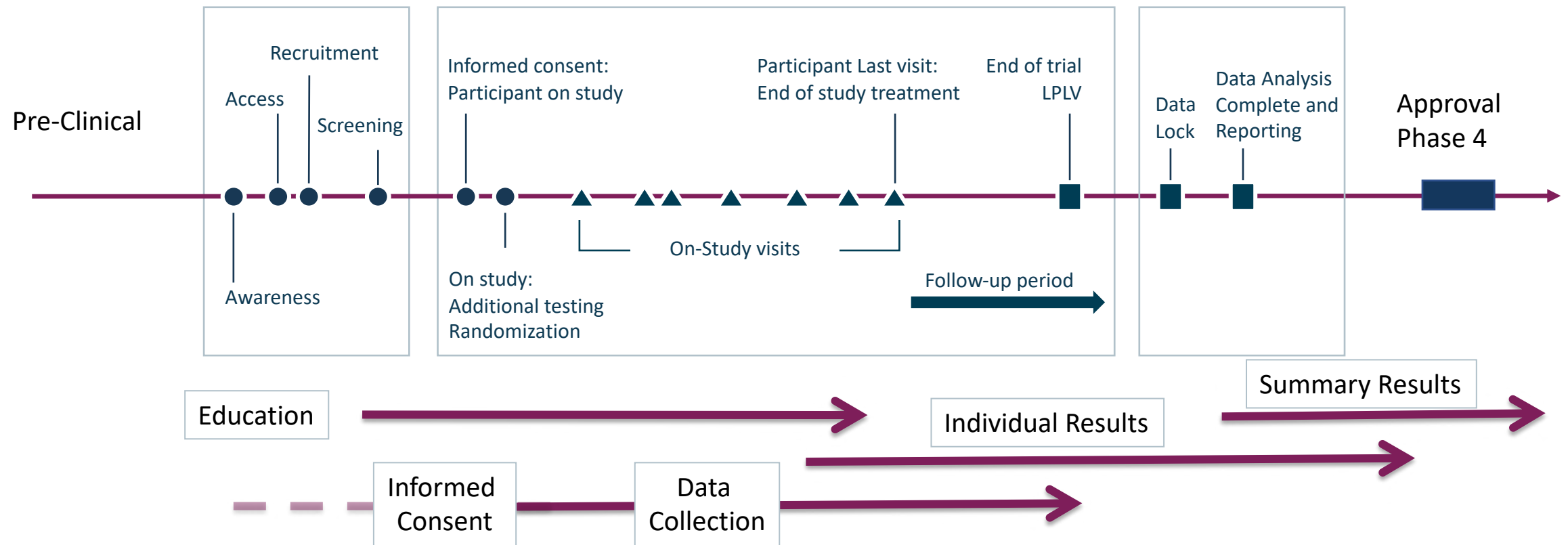
Product Development Pathway



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



Clear communications throughout the product development program

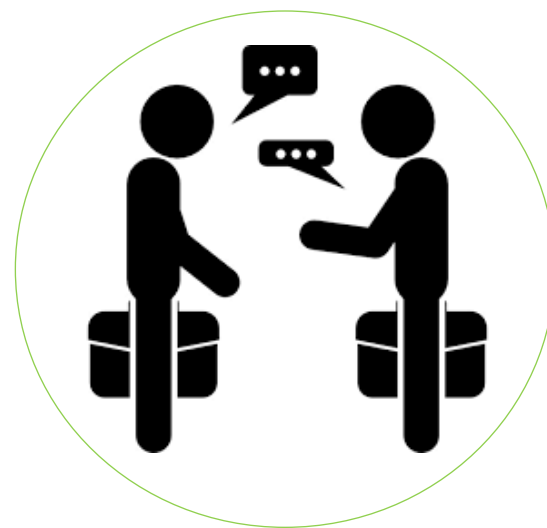


Clear communication is a shared responsibility



- 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

Tools and Resources

Information on techniques that are key to successful research communications.



www.mrctcenter.org/health-literacy



“Should I join?”

Resources for the public


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

I AM HEALTHY: Should I Join a COVID-19 Research Study?

People who do not have COVID-19 can help researchers learn more about the disease.

A research study:

- collects new information about health and disease.
- tries to answer new questions that researchers have.
- needs volunteers to sign up.



Why are there research studies about COVID-19 right now?

COVID-19 is a new disease, so it is important to understand more about:


- How the virus spreads.
- Why some people get very sick, and some people do not.
- Which treatments work best, and if they work for everyone.
- How to prevent new infections.

Being in a COVID-19 research study is your choice.

More can be learned about COVID-19 if you join a research study.


What should I ask the research team before joining a COVID-19 research study?

<ul style="list-style-type: none"> ✓ Why is the study being done? ✓ What will happen if I agree to join? ✓ Could the study help me? Could it help others? ✓ Could the study cause risks to me? ✓ Do I have to pay money to be in the study? ✓ Will I be paid to be in the study? 	<ul style="list-style-type: none"> ✓ How will my personal information be protected? ✓ How long will the study last? ✓ Can I leave the study at any time? ✓ What will happen if I get hurt in the study? ✓ Who should I call with questions about the study? ✓ Will I get to see the study results?
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What else should I know about being in a COVID-19 research study?

- You can talk to people you trust about whether to join the study.
- You can change your mind at any time.



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Thank you for thinking about joining a COVID-19 research study for healthy volunteers. Please ask the research team ANY questions you have.



HARVARD CATALYST
Harvard Clinical & Translational Science Center

En Español


¿Debería unirme?

SOY UN ADULTO SANO: ¿Debería participar en un estudio de investigación de COVID-19?

Las personas no infectadas por COVID-19 pueden ayudar a los investigadores a conocer más sobre esta enfermedad.

Un estudio de investigación:

- Obtiene nueva información sobre salud y sobre enfermedad.
- Trata de responder nuevas preguntas que los investigadores tienen.
- Necesita voluntarios para que participen en el estudio.



¿Por qué hay estudios de investigación sobre COVID-19 ahora?

COVID-19 es una enfermedad nueva, así que es importante entender más sobre:


- Como se disemina el virus.
- Porque algunas personas se enferman gravemente y otras no.
- Cuales tratamientos funcionan mejor y si estos funcionan con todas las personas.
- Como prevenir nuevas infecciones.

Unirse a un estudio de investigación sobre COVID-19 es su decision.

Se puede aprender más sobre la COVID-19 si participa en un estudio de investigación.


¿Qué preguntas debo hacerle al equipo de investigación antes de participar en un estudio de investigación sobre COVID-19?

<ul style="list-style-type: none"> ✓ ¿Por qué se está realizando el estudio? ✓ ¿Que pasará si acepto participar? ✓ ¿El estudio puede ayudarme de alguna forma? ¿Puede ayudar a otros? ✓ ¿El estudio puede causarme algún riesgo? ✓ ¿Debo pagar para estar en el estudio? ✓ ¿Me pagarán para estar en el estudio? 	<ul style="list-style-type: none"> ✓ ¿Por cuánto tiempo se protegerá mi información personal? ✓ ¿Cuánto tiempo durará el estudio? ✓ ¿Puedo retirarme del estudio en cualquier momento? ✓ ¿Qué pasará si resulto lesionado en el estudio? ✓ ¿A quién puedo llamar si tengo preguntas sobre el estudio? ✓ ¿Recibiré los resultados del estudio?
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¿Qué más debo saber sobre participar en un estudio sobre COVID-19?

- Puede hablar con personas de su confianza sobre su decisión de participar en el estudio o no.
- Puede cambiar de opinión en cualquier momento.



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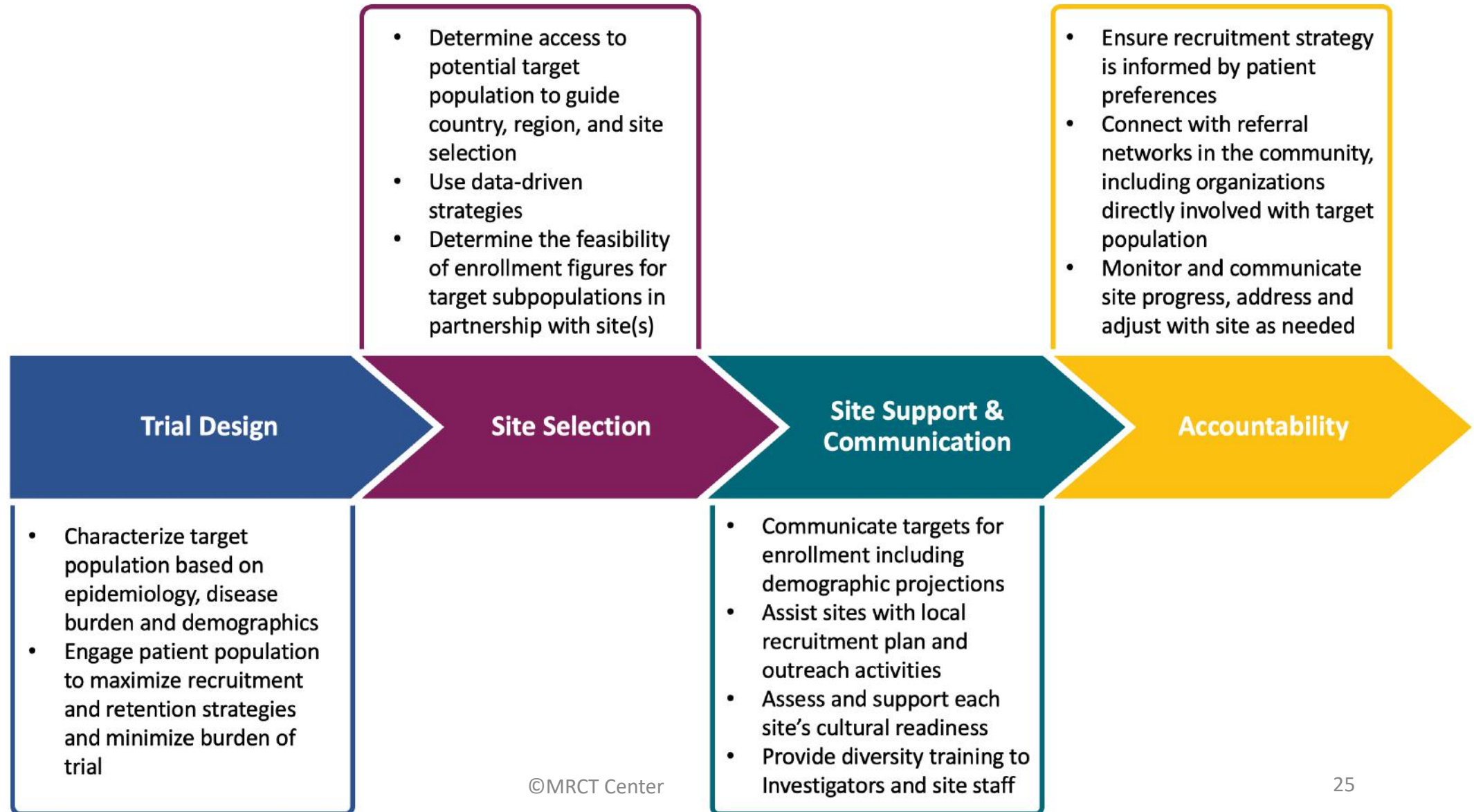
Gracias por pensar en participar en un estudio de investigación de COVID-19. Por favor, haga TODAS las preguntas que tenga.



HARVARD CATALYST
Harvard Clinical & Translational Science Center



Opportunities: What can we do?



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...”

mrctcenter.org/diversity-in-clinical-trials



Practical Approaches to Improving Diversity in Clinical Trials

Wednesdays
11AM – 12noon ET

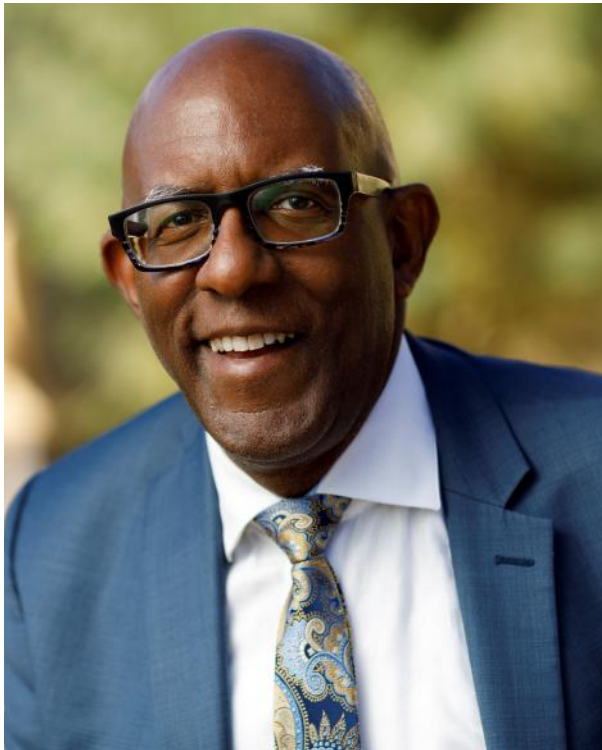


LEARNING IN: A WEBINAR SERIES

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



Today's speakers



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



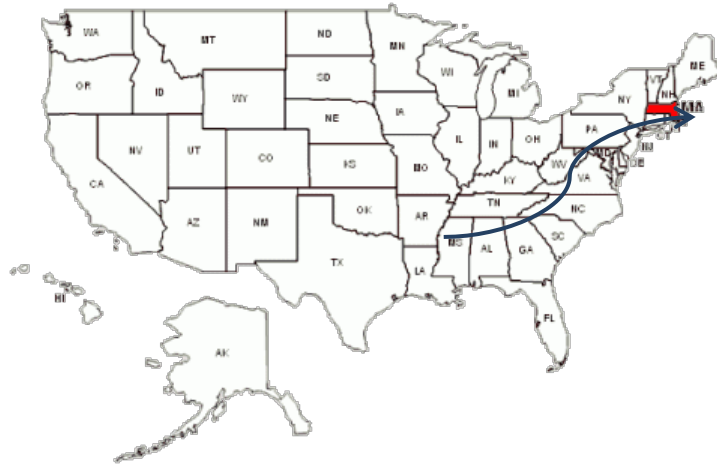
Faculty Disclosures

- *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

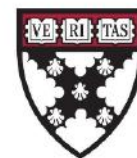
My Journey: Training and Education



My Journey: Training and Education and Practice



- CV Clerkship director
- Recruitment
- STARS program



**HARVARD
BUSINESS SCHOOL**

Executive Education

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

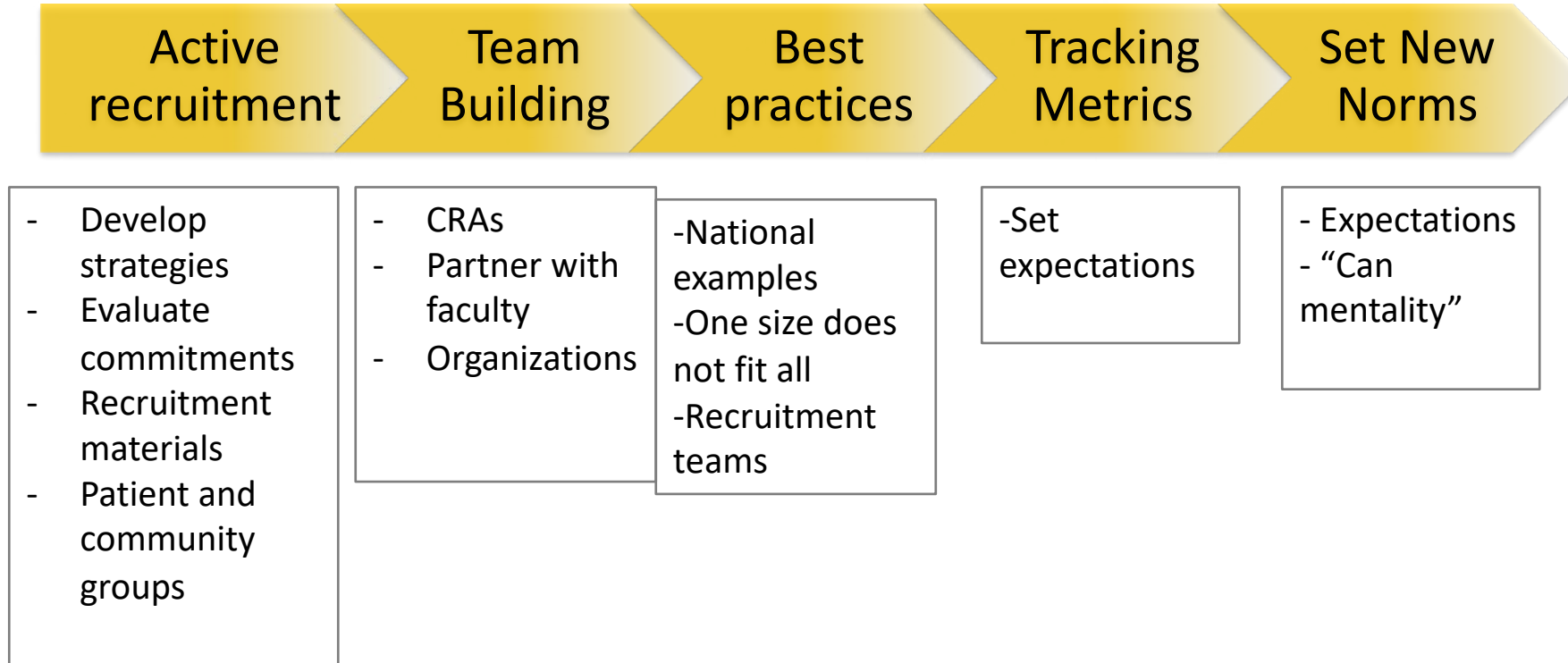
Management strategies

Disparities and Health Equity

Outline

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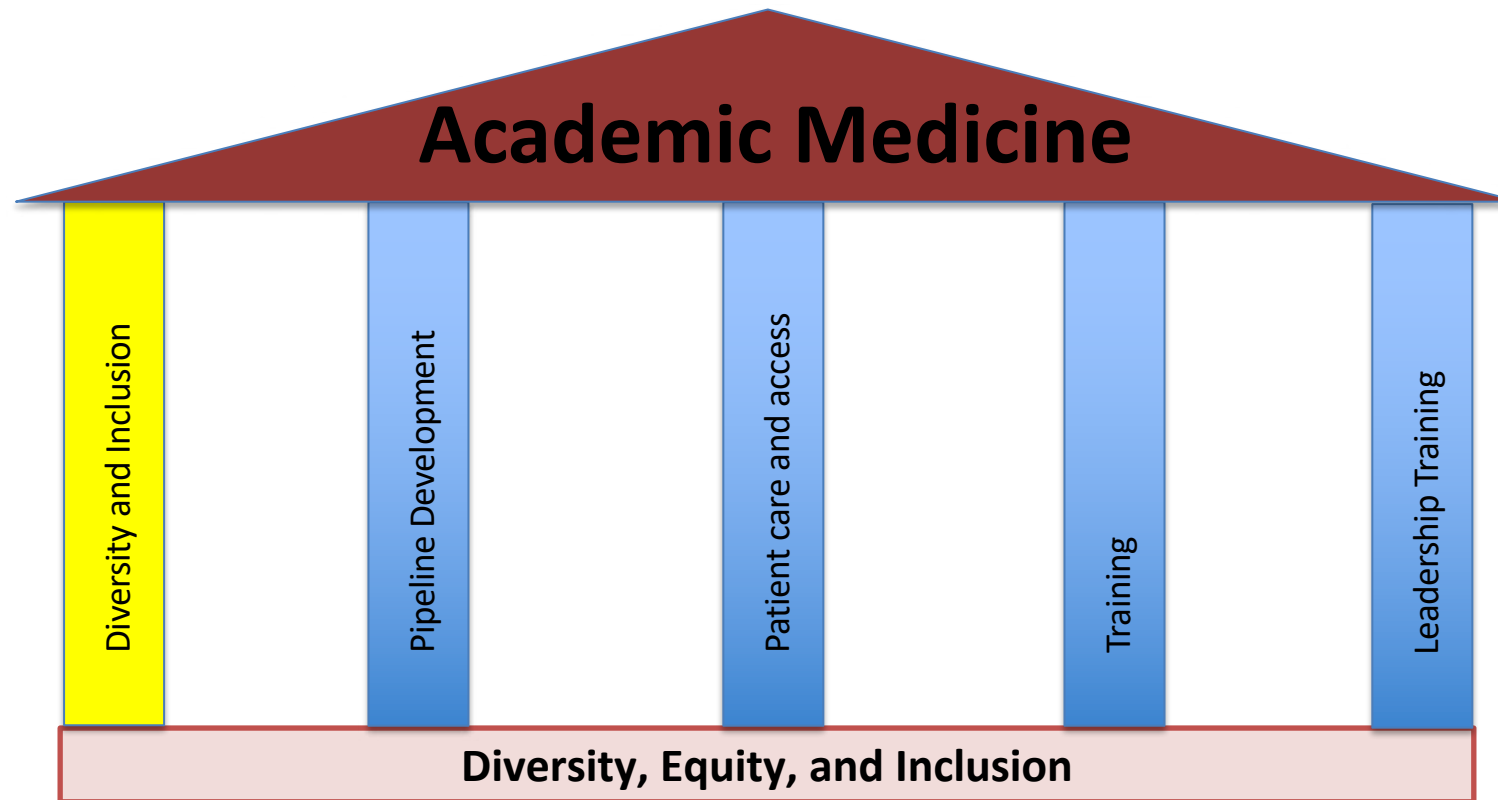
Perspective as an Investigator for Site Activities to Increase Diversity



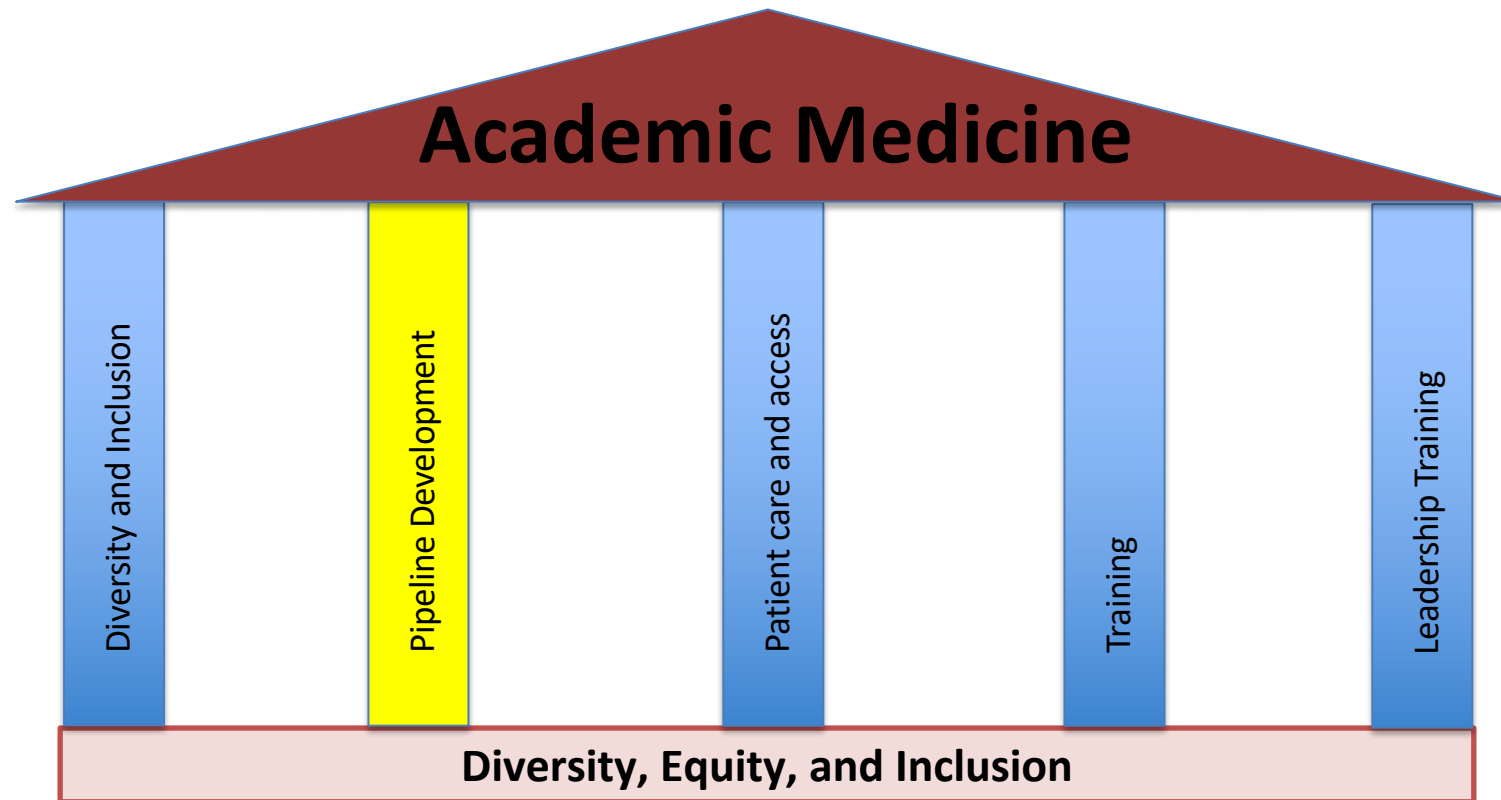
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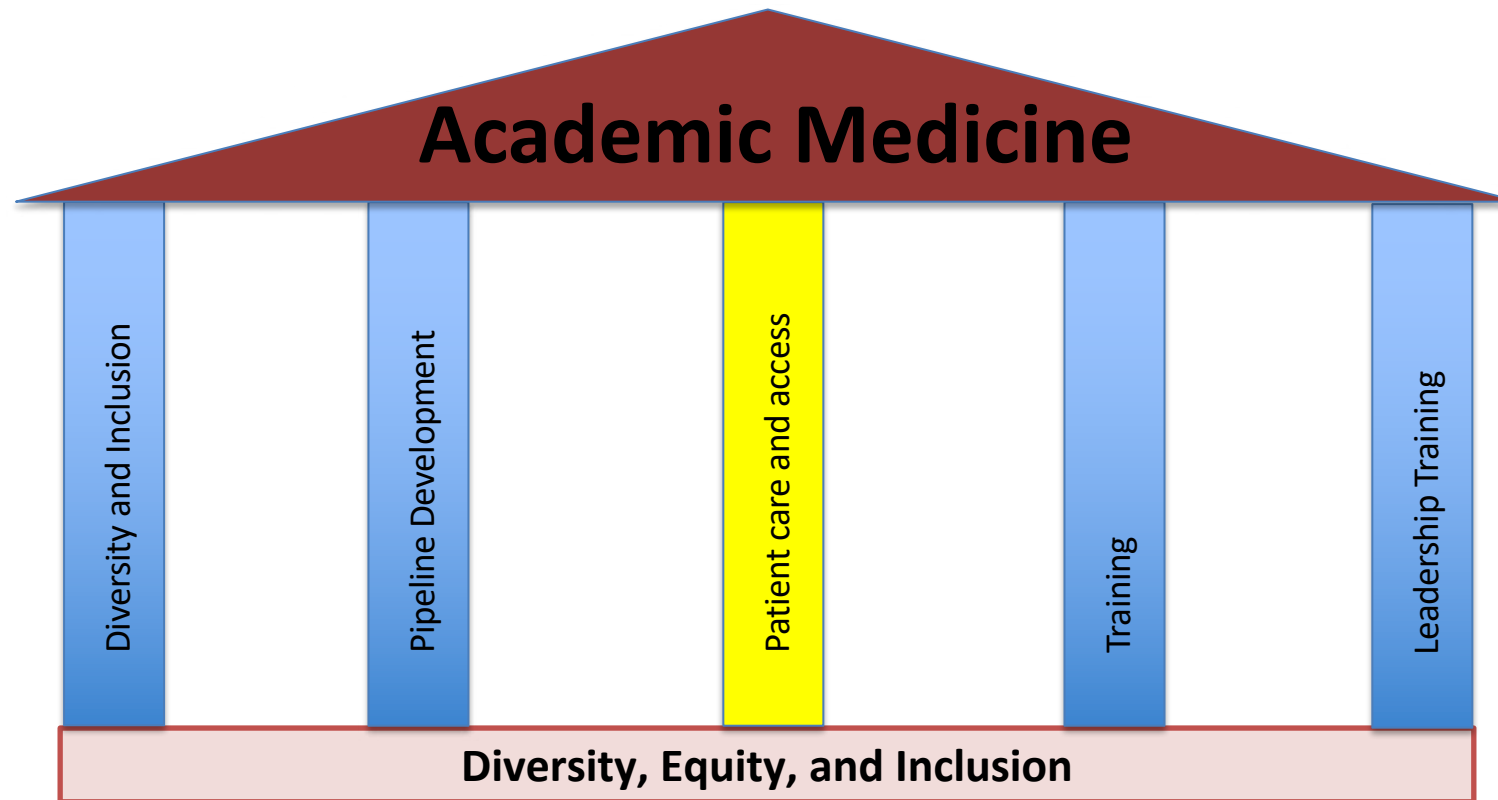
Pillars of Workforce Development in Research and Medicine



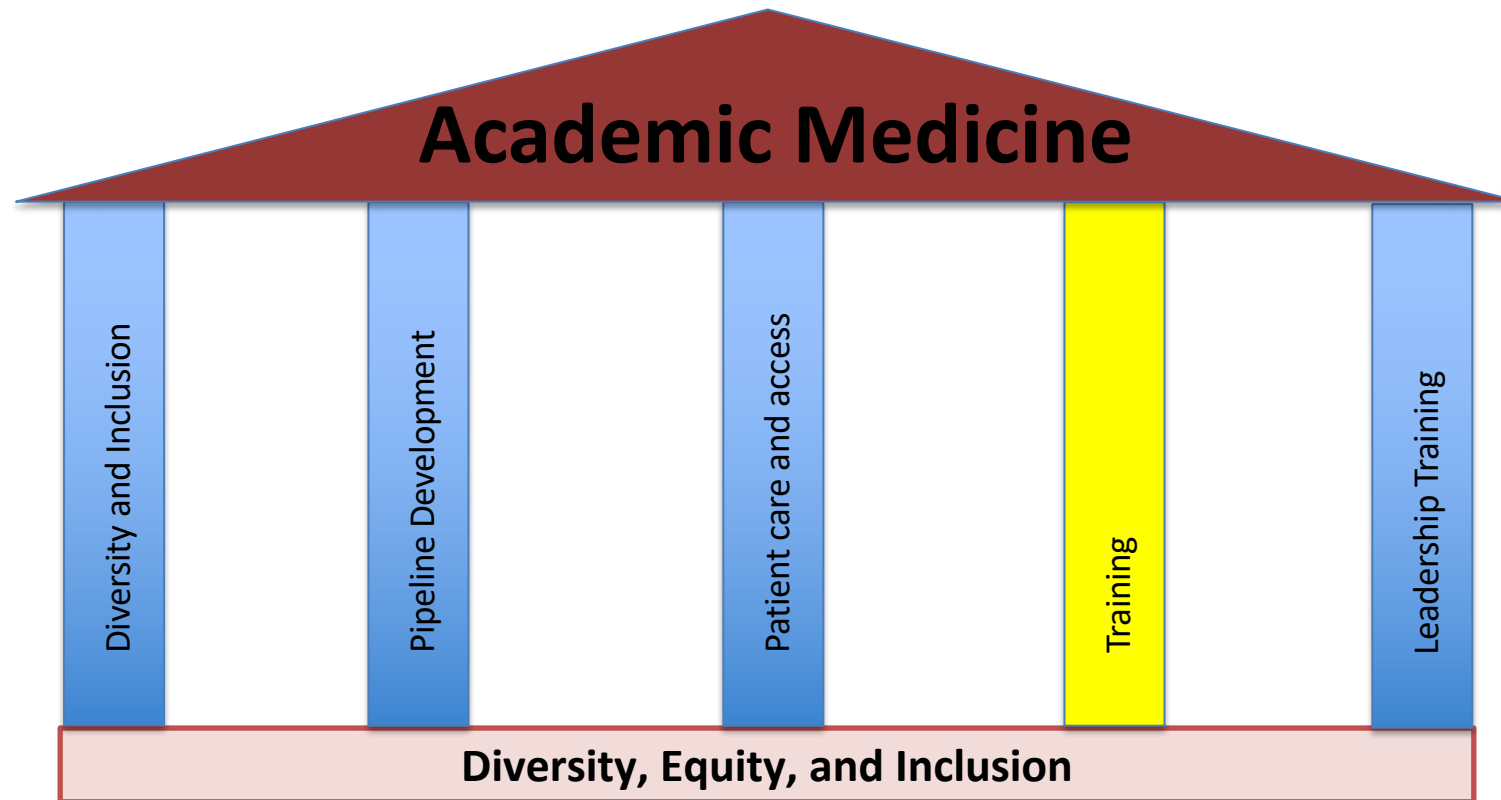
Pillars of Workforce Development in Research and Medicine



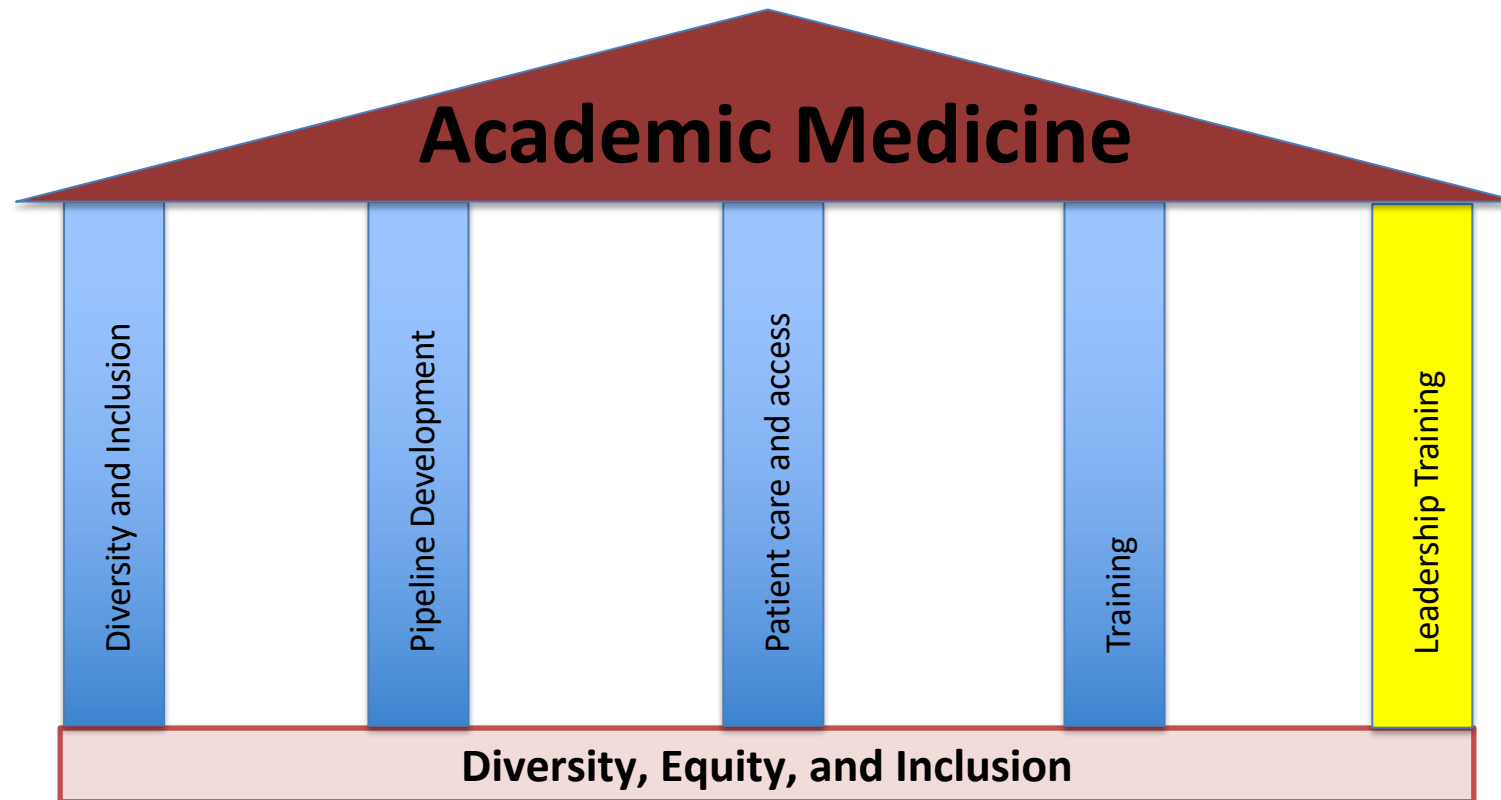
Pillars of Workforce Development in Research and Medicine



Pillars of Workforce Development in Research and Medicine



Pillars of Workforce Development in Research and Medicine



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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



Eldrin F. Lewis, MD, MPH, FAHA, FACC

Professor of Medicine

Chief, Division of Cardiovascular Medicine

Advanced Heart Failure Transplant Cardiology

Stanford University School of Medicine

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