U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Public Workshop to Enhance Clinical Study Diversity

November 29 - 30, 2023 / 10 a.m. - 2:00 p.m. EST

U.S. FOOD & DRUG ADMINISTRATION

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November 29 - 30, 2023 / 10 a.m. - 2:00 p.m. EST

FDA U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Meeting will begin at 10:00 a.m. EST

Day 1 Opening Remarks

Karen Hicks

M.D., FACC, Deputy Director, Office of Medical Policy (OMP)
Center for Drug Evaluation and Research (CDER)
US Food and Drug Administration (FDA)

Day 1 - Agenda

- Overview of clinical study diversity
  - Where we are now?
- Establishment of clinical study enrollment goals
  - Use of disease prevalence or incidence data
- Approaches to support the inclusion of historically underrepresented populations
  - Age, Sex, Race, Ethnicity, Pregnancy, Lactation, Disability
  - Overcoming barriers to participation

Post Comments to FDA Public Docket

FDORA Public Workshop to Enhance Clinical Study Diversity

A docket is open for the public to submit electronic or written comments related to the topics addressed during this workshop.

Link to provide comments to the docket

Docket Number: FDA-2023-N-2462

Comment Period Closes: January 29, 2024

Keynote Address

Patrizia Cavazzoni

Director, Center for Drug Evaluation and Research

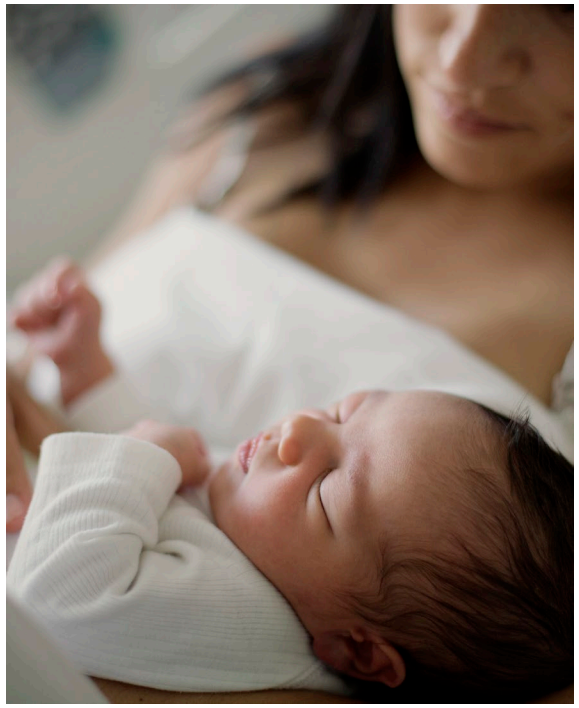
US Food and Drug Administration

Importance of Diversity and Inclusion in Clinical Trials

- Clinical trials provide critical evidence regarding whether a medical product is safe and effective.

- Clinical trials should, to the extent possible, enroll a population that is representative of the diversity of the population that will use the medical product, if approved.

- FDA is committed to increasing the participation of underrepresented populations in clinical trials through:
  - Issuing guidance(s)
  - Encouraging the use of innovative trial designs
  - Leveraging “fit-for-purpose” technology



FDA's Longstanding Commitment to Promote Diversity & Inclusion: Topics of Published *Guidances for Industry*

- Specific populations e.g.
  - Underrepresented racial and ethnic populations
  - Older adults
  - Pregnant individuals
  - Lactating individuals
  - Sex
- Innovative trial designs and technologies e.g.
  - Decentralized clinical trials
  - Digital health technologies
- And many others

A Balanced Approach is Needed

Timeline of Key Events

April 2022

- **Draft Diversity Plans Guidance**

June 2022

- **Diversity Plans Implementation Committee (DPIC)**

December 2022

- **Food and Drug Omnibus Reform Act (FDORA)**

Food and Drug Omnibus Reform Act

- December 2022 – the Food and Drug Omnibus Reform Act (FDORA) was passed.
- Sponsors will be required to submit Diversity Action Plans for Phase 3 or other pivotal trials.
- FDA to convene a public workshop to enhance clinical study diversity.
  - This two-day virtual public workshop is one of the deliverables to fulfill these FDORA requirements.
- FDA is required to update existing guidance or release new guidance on Diversity Action Plans

Common Goal

- Ensuring that the clinical study of a drug or device reflects the diversity of the population for which it is being developed is not only important for the patients who will ultimately use the drug or device after approval, but also of interest to:
  - industry
  - clinicians
  - study participants
  - health care systems
  - other interested parties

Moving Forward

- To achieve meaningful representation in clinical trials, it will take our combined effort.
  - FDA is only one piece of this puzzle.

- To obtain the data we need for the diverse population that will use the medical product, if approved, will take **ALL** of us working together:
  - sharing ideas
  - sharing experiences
  - sharing best practices

Key Takeaways

- FDA has a longstanding commitment to promote diversity and inclusion of underrepresented populations in clinical trials.
- Enrollment in clinical trials should, to the extent possible, reflect the diversity of the population that will use the medical product, if approved.
- A pragmatic approach that balances FDA's intent to increase diversity in clinical trials with bringing urgent medical treatments to patients as soon as possible is needed.
- To achieve meaningful representation in clinical studies, it takes the combined effort of all interested parties in the clinical trials enterprise.

U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Session 1: Clinical Study Diversity – Where Are We Now?

Moderator: RDML Richardae Araojo
Associate Commissioner for Minority Health and Director of the Office of Minority Health and Health Equity, FDA

Lola Fashoyin-Aje
Deputy Division Director & Associate Director, Oncology Center for Excellence, FDA

Eldrin Lewis
Professor of Cardiovascular Medicine, Stanford School of Medicine

Laura Mauri
Senior VP and COO, Medical and Regulatory Officer, Medtronic

Allison Cuff Shimooka
TransCelerate BioPharma

Ricki Fairley
The Black Breast Cancer Alliance

Clinical Study Diversity – A Brief Overview: Where are We Now?

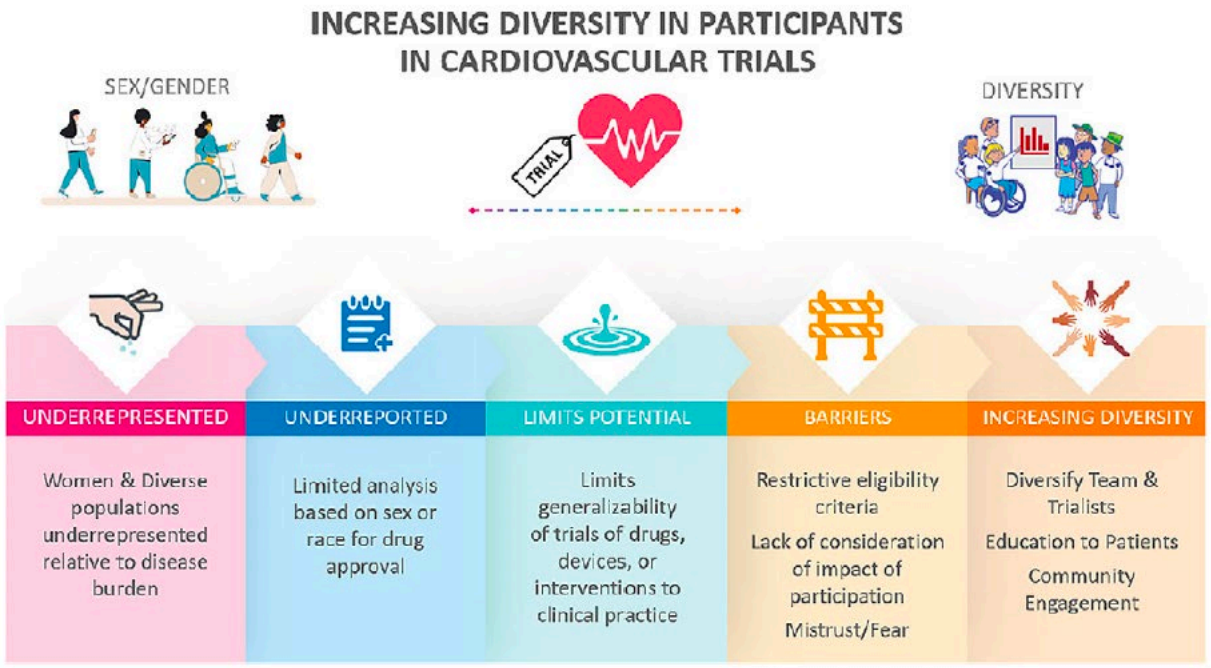
Eldrin F. Lewis, MD, MPH, FAHA
Simon H. Stertzer, MD Professor of Medicine
Chief, Cardiovascular Division
Stanford University

November 29, 2023

Disclosures

Novartis (Consulting, Institutional research support)
Akebia (Consulting, Institutional research support)
Merck (Consulting, Institutional research support)
Dal-Cor (Consulting)
Astra Zeneca (Consulting)

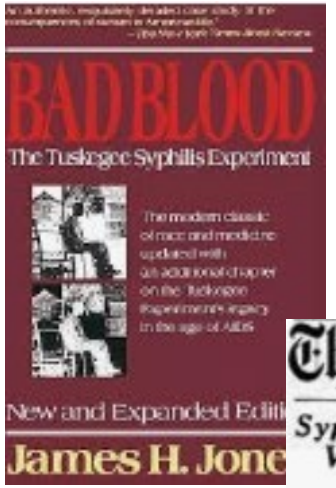
Barriers to Enrollment and Strategies

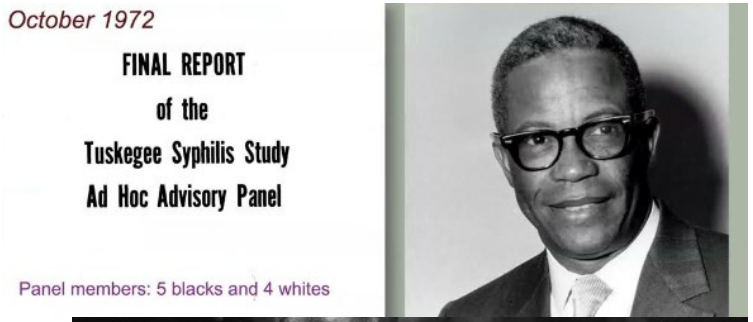


Levers: Trust and Publication Requirements

Michos ED et al. American Journal of Preventive Cardiology 8 (2021) 100250

Legacy of Tuskegee Experiment and "HeLa cells"






The New York Times

Syphilis Victims in U.S. Study Went Untreated for 40 Years

By JEAN HELLER

WASHINGTON, July 25—For 40 years the United States Public Health Service has conducted a study in which human beings with syphilis, who were induced to serve as guinea pigs, have gone without medical treatment for the disease and a few have died of its late effects, even though an effective therapy was eventually discovered.

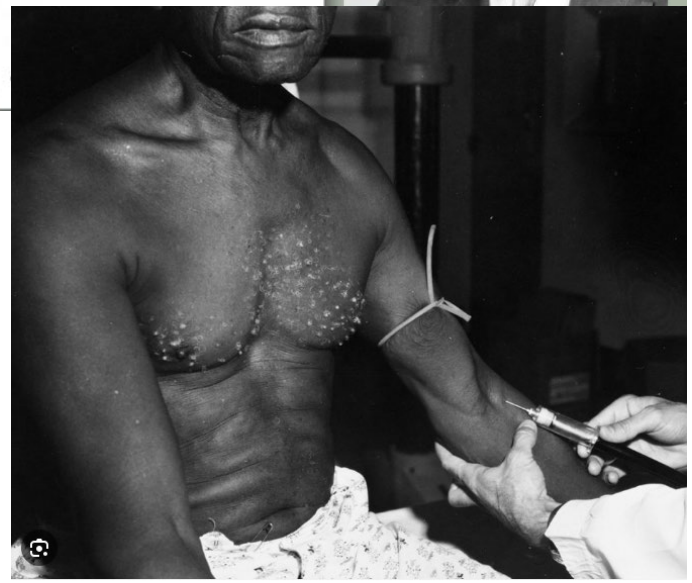
The study was conducted to determine from autopsies what the disease does to the human body.

Officials of the health service who initiated the experiment have long since retired. Current officials, who say they have serious doubts about the morality of the study, also say that it is too late to treat the syphilis in any surviving participants.

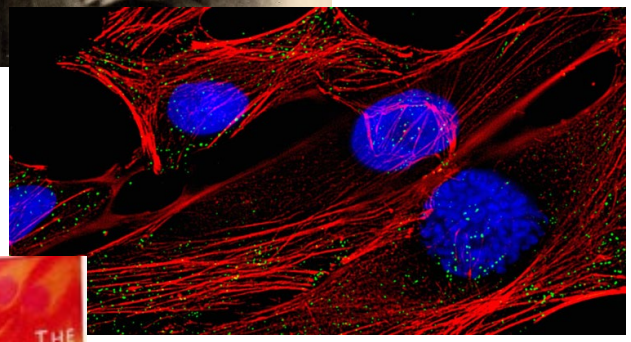
Doctors in the service say they are now rendering whatever other medical services they can give to the survivors while the study of the disease's effects continues.

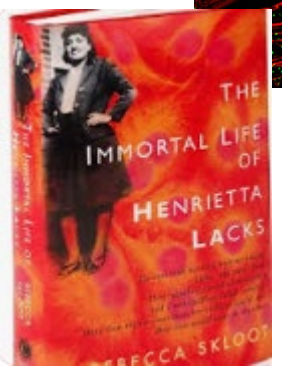
Dr. Merlin K. DuVal, Assistant Secretary of Health, Education and Welfare for Health and Scientific Affairs, expressed shock on learning of the study. He said that he was making an immediate investigation.

The experiment, called the Tuskegee Study, began in 1932 with about 600 black men



In Tuskegee, Painful History Shadows Efforts To Vaccinate African Americans – Houston Public Media





Foundation of Mistrust

Legacy of Tuskegee Experiment and “HeLa cells”

JANUARY 6, 2017

Stanford researchers explore legacy of Tuskegee syphilis study today

Stanford sophomore Javarcia Ivory (left) and Dr. Owen Garrick compare notes outside a clinic where volunteers receive medical checkups. Photo by Nicole Feldman.

“Researchers have found that the disclosure of the infamous Tuskegee syphilis study in 1972 is correlated with increases in medical mistrust and mortality among African-American men. Their subsequent Oakland project seeks to better understand African-American wariness of medicine and health care providers.”

https://news.stanford.edu/2017/01/06/stanford-researchers-explore-legacy-tuskegee-syphilis-study-today/#:~:text=Researchers%20have%20found%20that%20the,medicine%20and%20health%20care%20providers.

Strategies to Build Trust

Embed into the Community

Diversify the Workforce

Simplify Consent Forms

Structural Racism and Need for Race/Ethnicity Data

Are you even trying to stop racism if you don't collect data on race?

A Black Lives Matter protest in Berlin.

Image: REUTERS/Christian Mang

By **Amanda Shendruk** Published July 8, 2021

In the UK, US, and Canada, it is commonplace for public institutions—like the healthcare system, and the national census—to ask for your race or ethnicity. Because of this, they have robust statistics on the identities of their citizens. These nations, however, are the outliers.

Most of the world's wealthiest countries don't collect any data on the racial or ethnic identity of their people. In many cases, it's illegal. France doesn't keep official statistics of how many Black residents it

https://qz.com/2029525/the-20-countries-that-dont-collect-racial-and-ethnic-census-data

OECD
Organisation for Economic Co-operation and Development

SDD/DOC(2018)9

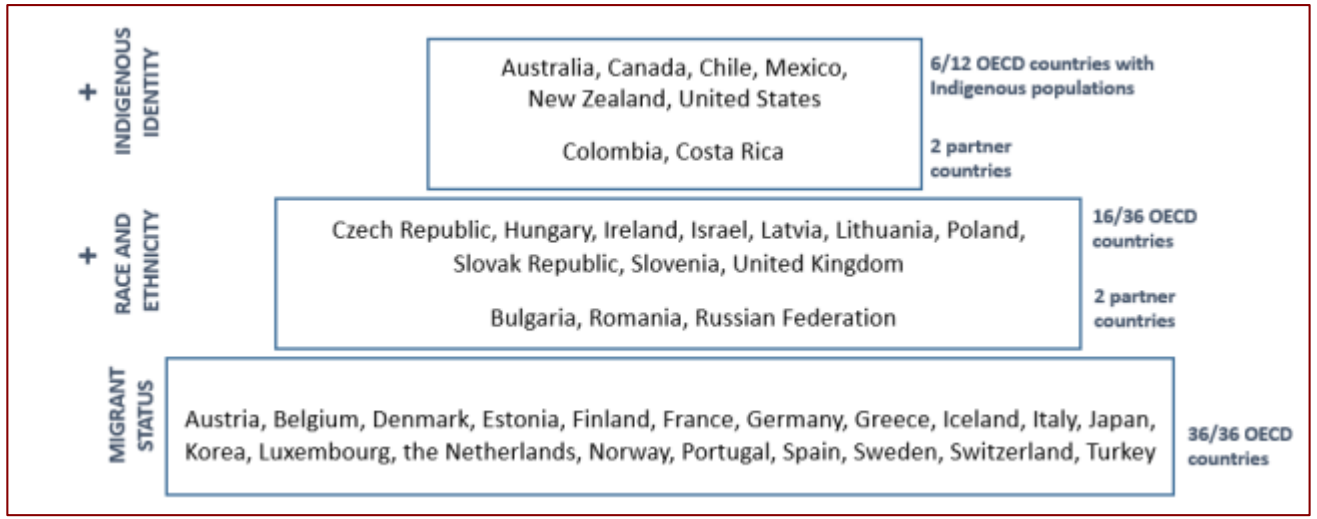
Unclassified | **English - Or. English**

8 November 2018

STATISTICS AND DATA DIRECTORATE

- Survey of OECD Countries
- Imputed for France/Estonia (non-response)

= No collection of ethnicity and race



Australia
Austria
Belgium
Czech Republic
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Israel
Italy
Japan
Korea
Latvia
Lithuania
Luxembourg
Netherlands
New Zealand
Norway
Poland
Portugal
Slovak Republic
Slovenia
Turkey
Spain
Sweden
Switzerland

Collection of Race and Ethnicity Data in Clinical Trials

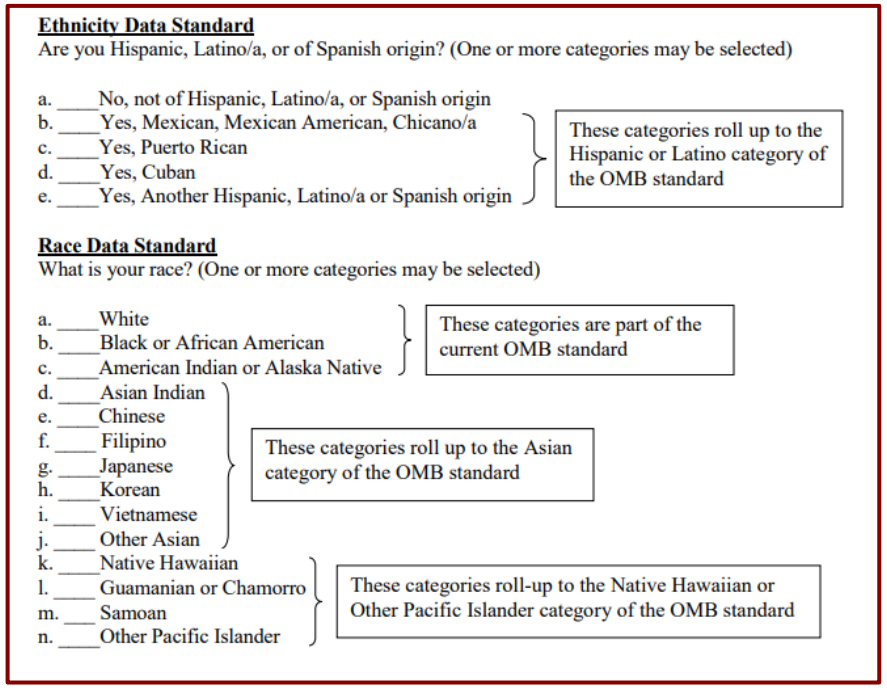
Guidance for Industry and Food and Drug Administration Staff

Document issued on October 26, 2016

For questions about this document, contact the FDA Office of Minority Health at 240-402-5084 or omh@fda.hhs.gov.

U.S. Department of Health and Human Services (HHS)
Food and Drug Administration (FDA)
Office of the Commissioner (OC)
Office of Minority Health (OMH)
Office of Women's Health (OWH)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiologic Health (CDRH)

October 2016
Clinical Medical



Ethnicity Data Standard
Are you Hispanic, Latino/a, or of Spanish origin? (One or more categories may be selected)

a. ____No, not of Hispanic, Latino/a, or Spanish origin
b. ____Yes, Mexican, Mexican American, Chicano/a
c. ____Yes, Puerto Rican
d. ____Yes, Cuban
e. ____Yes, Another Hispanic, Latino/a or Spanish origin

These categories roll up to the Hispanic or Latino category of the OMB standard

Race Data Standard
What is your race? (One or more categories may be selected)

a. ____White
b. ____Black or African American
c. ____American Indian or Alaska Native

These categories are part of the current OMB standard

d. ____Asian Indian
e. ____Chinese
f. ____Filipino
g. ____Japanese
h. ____Korean
i. ____Vietnamese
j. ____Other Asian

These categories roll up to the Asian category of the OMB standard

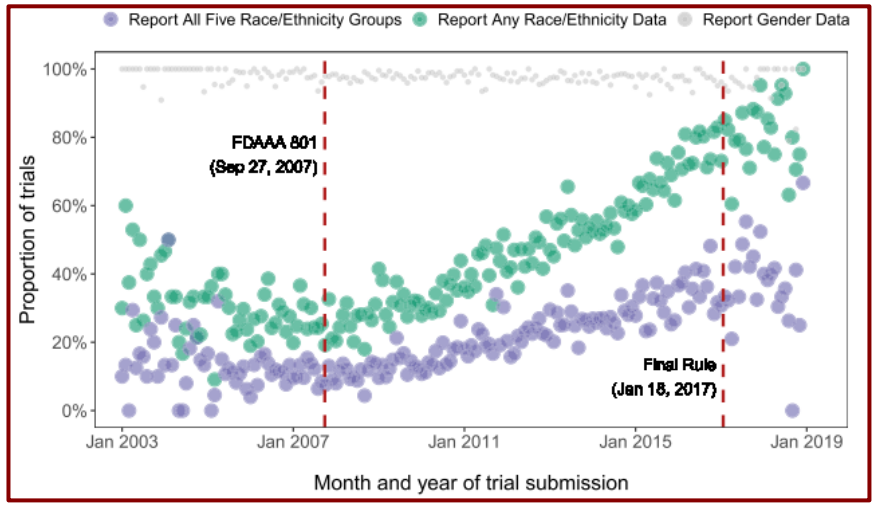
k. ____Native Hawaiian
l. ____Guamanian or Chamorro
m. ____Samoan
n. ____Other Pacific Islander

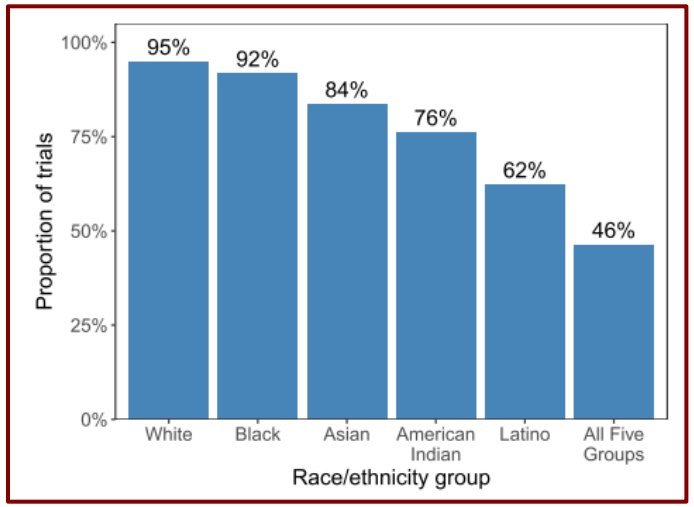
These categories roll-up to the Native Hawaiian or Other Pacific Islander category of the OMB standard

CDER and CBER Requirements

- Beginning in May 2017
- Presentation of demographic data (section 2.7.4.1.3 and table 2.7.4.2)
- Suggests a tabular display of demographic characteristics by treatment group

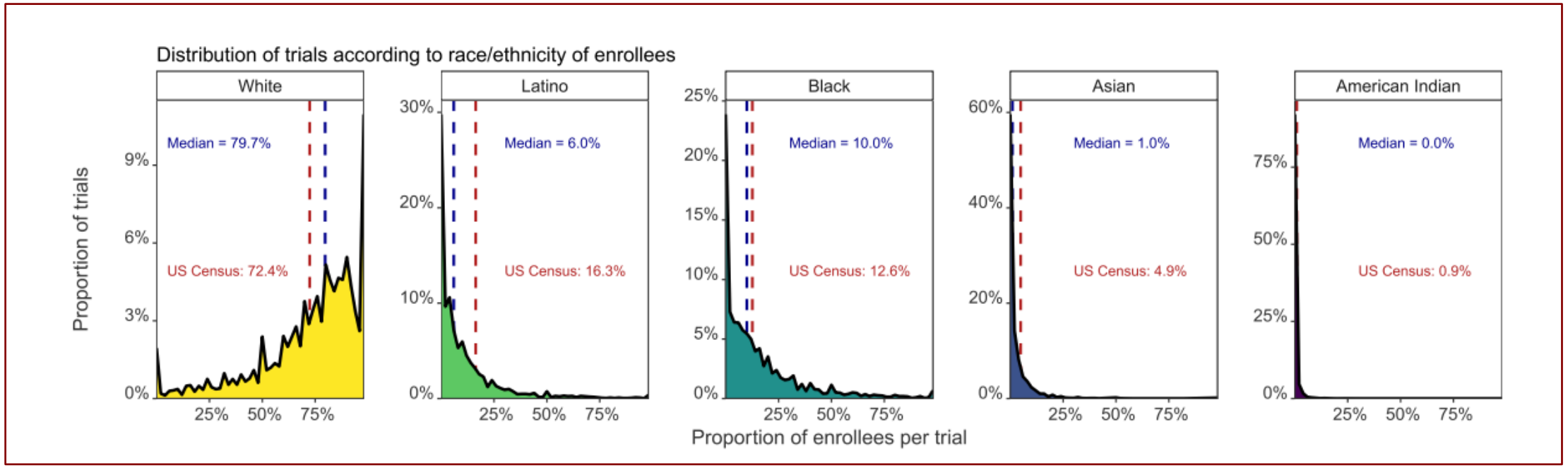
Race and ethnicity enrollment reporting in United States-based clinical trials registered on ClinicalTrials.gov





Turner BE et al. The Lancet Regional Health – Americas 2022;11: 100252

Distribution of trials and the representation of each racial/ethnic group organized by racial/ethnic category

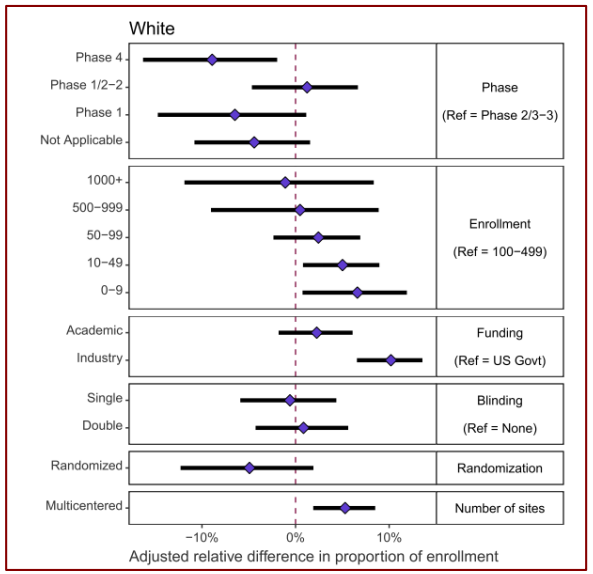


- 2010 Census
- Only trials reporting all 5 categories

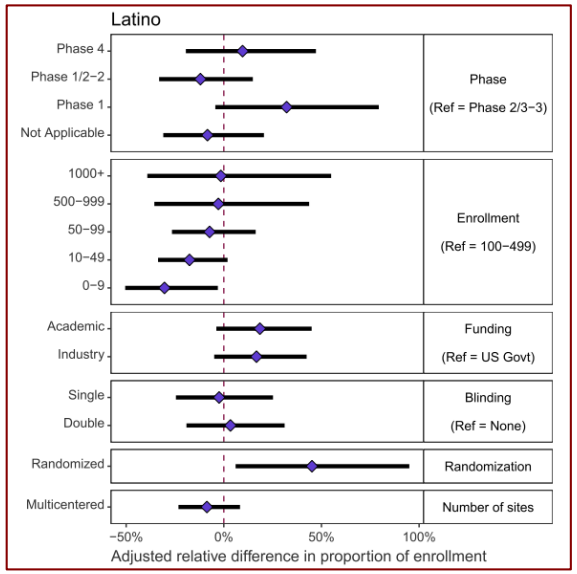
Turner BE et al. The Lancet Regional Health – Americas 2022;11: 100252

Distribution of trials and the representation of each racial/ethnic group organized by racial/ethnic category

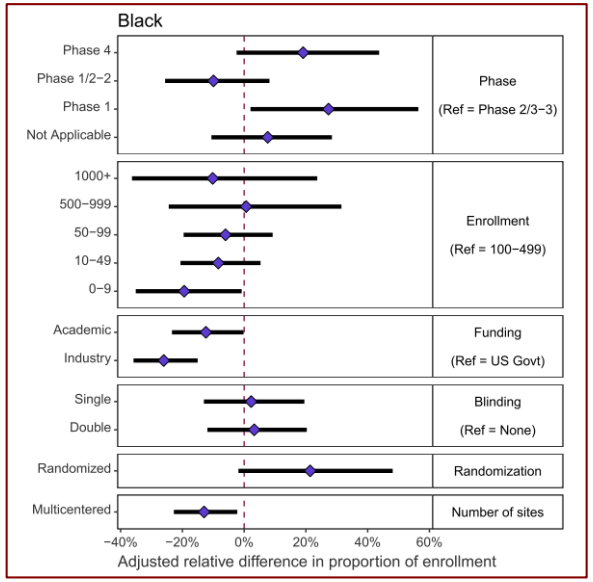
White Participants



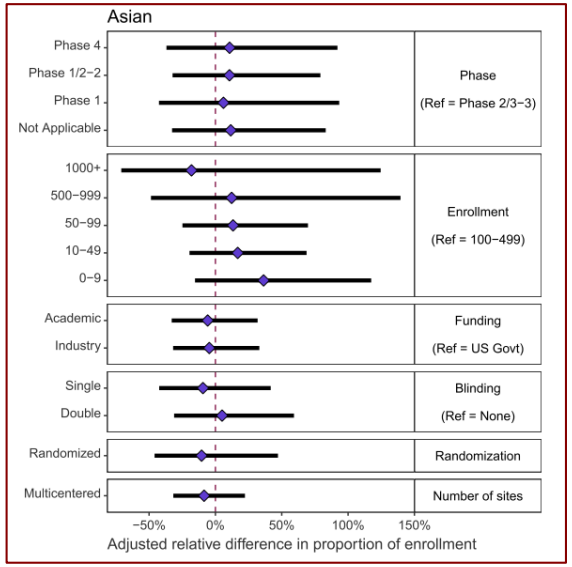
Latino Participants



Black Participants

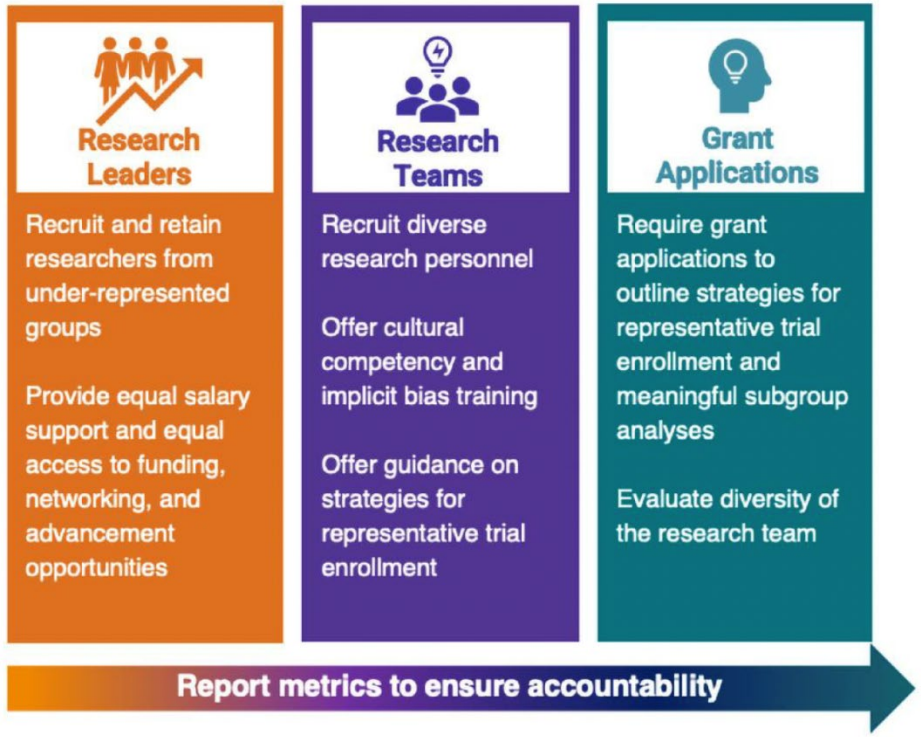


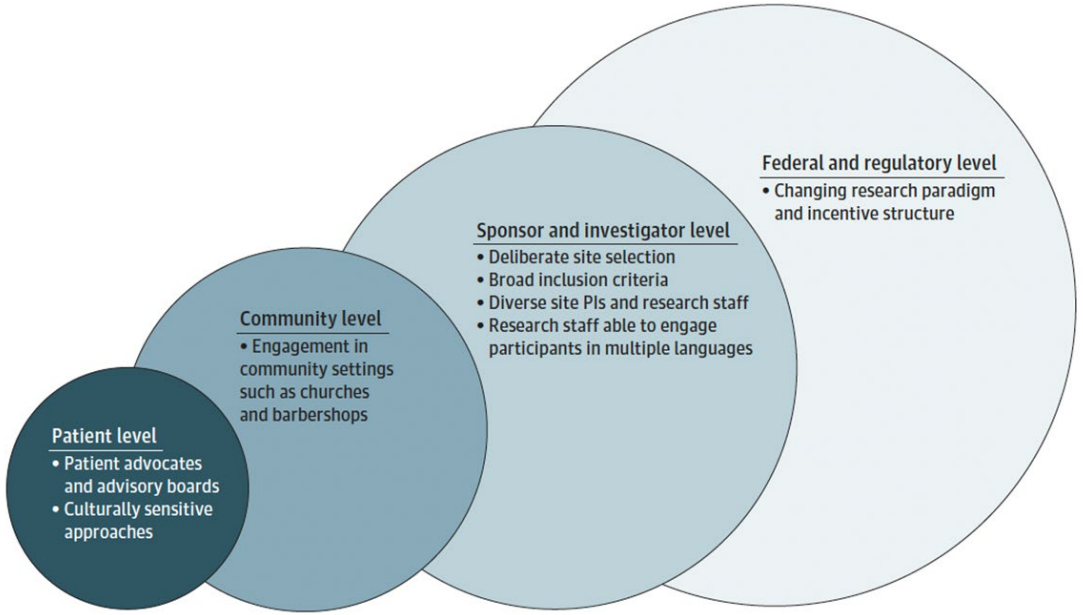
Asian Participants



Turner BE et al. The Lancet Regional Health – Americas 2022;11: 100252

Institutional and Regulatory Strategies





Publication Strategies

- N/A for non-reporting countries
- Standard reporting of demographics
- Diversity of teams
- SDoH elements

Filbey et al European Heart Journal (2023) 44, 921–930
DeFelippis EM et al JAMA Cardiol. 2022;7(5):540-548

Standardization for Health Equity Research

Circulation: Cardiovascular Quality and Outcomes
Volume 14, Issue 2, February 2021
https://doi.org/10.1161/CIRCOUTCOMES.121.007868

EDITORIAL

The Groundwater of Racial and Ethnic Disparities Research

A Statement From *Circulation: Cardiovascular Quality and Outcomes*

Khadijah Breathett, MD, MS, Erica S. Spatz, MD, MHS, Daniel B. Kramer, MD, MPH, Utibe R. Essien, MD, MPH, Rishi K. Wadhera, MD, MPP, MPhil, Pamela N. Peterson, MD, MSPH, P. Michael Ho, MD, PhD, and Brahmajee K. Nallamothu, MD, MPH

AHAjournals.org/health-equity

Circulation

EDITORIAL

Creation of the American Heart Association Journals' Equity, Diversity, and Inclusion Editorial Board: The Next Step to Achieving the 2024 Impact Goal

Eldrin F. Lewis, MD, MPH; Christine Beaty; Johannes Boltze, MD, PhD; Khadijah Breathett, MD, MS; Walter K. Clair, MD, MPH; Lisa de las Fuentes, MD, MS; Utibe R. Essien, MD, MPH; Heather Goodell; H.E. Hinson, MD, MCR; Kiarri N. Kershaw, PhD, MPH; Joshua W. Knowles, MD, PhD; Sula Mazimba, MD, MPH; Mahasin Mujahid, PhD, MS; Henry E. Okafor, MD; Kyung Woo Park, MD, PhD, MBA; Jonathan Schultz

ELEVATING the focus on:

- **Disparities**
- **Anti-racism**
- **Health equity**
- **Community-engaged/community-based participatory research**
- **Implementation science**

COLLECTIONS include:

- **Disparities and health equity**
- **Race, ethnicity, and health**
- **Social determinants of health**
- **Women's health, sex, and gender**

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

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Chief, Division of Cardiovascular Medicine

Stanford University School of Medicine

E-mail: eflewis1@Stanford.edu

@EldrinL

Website: med.stanford.edu/cvmedicine

U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Laura Mauri

Senior VP and COO
Medical and Regulatory Officer
Medtronic

The medical device industry is on a journey to increase diverse representation in clinical trials

Clinical evidence supports a wide range of medical devices:

Medtronic

Unique realities and opportunities in medical device trials

Study design

- Can be focused on well understood mechanisms, use surrogate endpoints, and/or single arm study designs
- Devices may directly collect physiologic data
- Regulatory balance toward post market for additional data on subgroups and indication expansion

Site selection

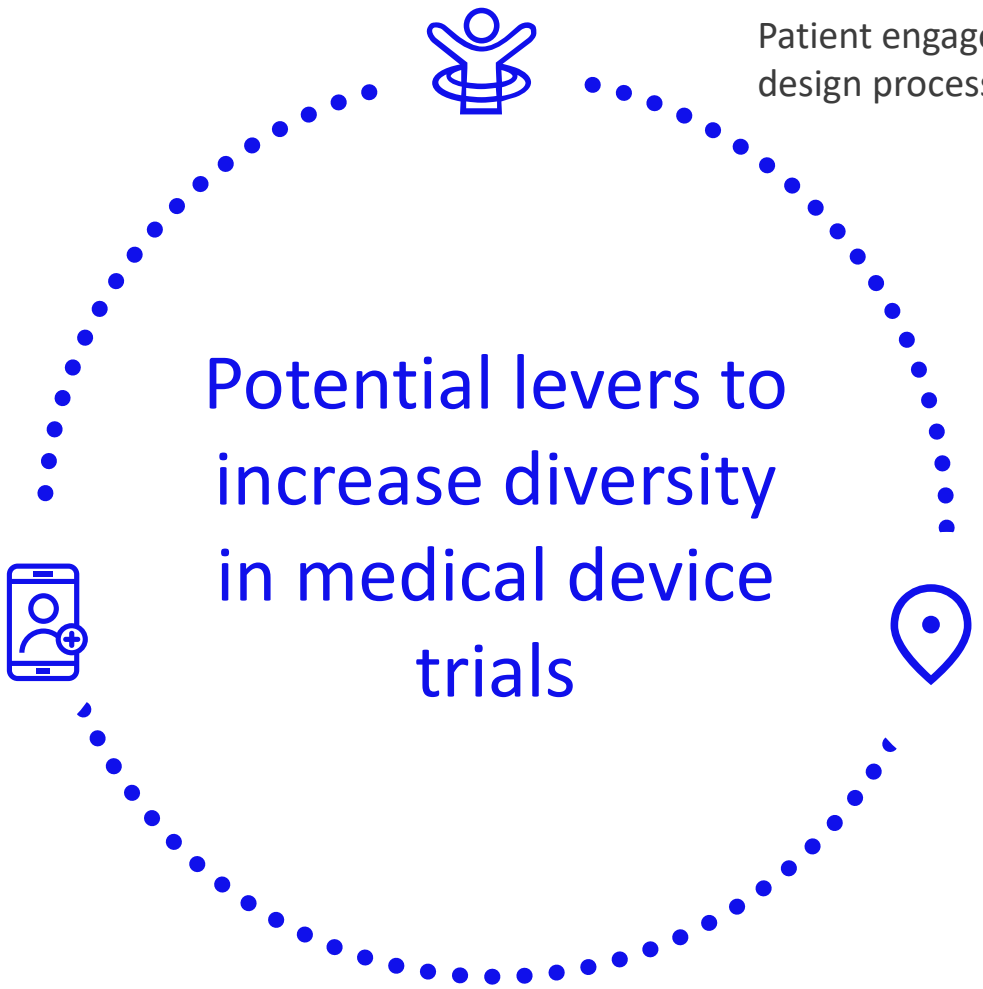
- High volume procedural centers are not evenly distributed across communities

Patient recruitment

- Investigators and recruitment through traditional referral pathways may not reach the eligible population

Medtronic

Potential levers to increase diversity in medical device trials



Patient engagement during study design process

Partnerships with community groups in locations with underrepresented populations

New approaches to patient recruiting, including direct-to-patient communication and social media

Medtronic

What got us here won’t get us there

The entire healthcare system has a shared role in driving forward progress

FDA Public Workshop to Enhance to Clinical Study Diversity

Clinical Study Diversity: A Brief Overview: Where are we now?

Allison Cuff Shimooka, COO, TransCelerate BioPharma Inc.

November 29th, 2023

TransCelerate was conceived to improve the health of people around the world by accelerating and simplifying the research and development of innovative new therapies

TransCelerate BIOPHARMA INC.
Accelerating Answers.

In 2012, R&D Leaders formed a non-profit to collaborate to tackle common operational challenges. Combining the words **"Transform"** and **"Accelerate"**, TransCeler ate was launched.

Member driven mission to collaborate across the global biopharmaceutical research and development community to **identify, prioritize, design, and facilitate** the implementation of solutions designed to drive the **efficient, effective and high-quality delivery of new medicines**.

TransCelerate has grown from **10 pioneering companies** to **22 Member Companies, fostering interactions** across ecosystem stakeholders, towards improvement in key value drivers in clinical research.

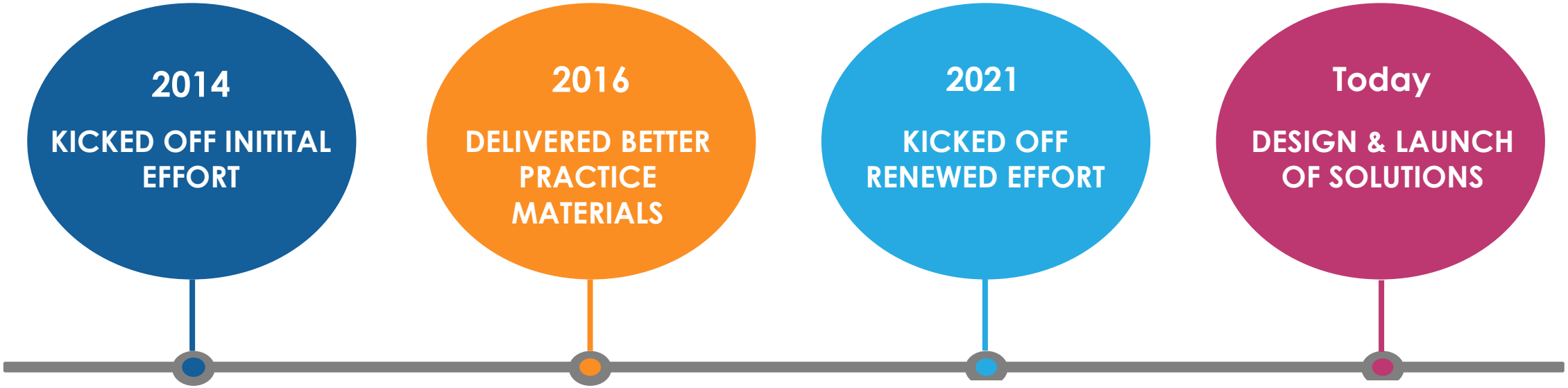
TransCelerate BIOPHARMA INC.

Diversity of Participants in Clinical Trials

Vision

V I S I O N

Focused on providing **tools & information** to organizations working to improve the **representation of patient populations in clinical trials** for which the studied drugs are intended to be prescribed/used.



Kicked off initial effort to bring awareness to need for diversity in clinical trials

Delivered targeted better practice materials for sites and sponsors

Focused on actionable tools and resources needed to improve outcomes for diversification of participants in clinical trials

Currently developing solutions in key areas of scope, including diversity roundtable events, assessment, and toolkits.

TransCelerate BIOPHARMA INC.

Diversity of Participants in Clinical Trials

Initiative Solutions

Reference Table and Landscape of Available Resources

Provides descriptions and links to publicly available resources for Patients, Sponsors, and Sites/HCPs. It also includes a visual landscape of the resources described and linked in the reference tables. Additionally, the landscape indicates resources that serve overlapping stakeholder communities.

Sponsor Toolkit Portfolio and Program-Level Considerations for Diversity, Equity and Inclusion of Participants in Clinical Trials (DEICT)

Consists of a set of considerations designed to support sponsors with improving diversity in clinical trials related to protocol design and development.

Diversity Community-Based Site Engagement and Capacity Building

Provides an aggregated collection of insights and perspectives from the attending organizations of a June 9 Roundtable Event, regarding considerations that sponsors, sites, and others have taken to enhance engagement and capacity building for community-based sites.

Sponsor Toolkit Site Engagement and Capacity Building Considerations for Diversity, Equity and Inclusion of Participants in Clinical Trials (DEICT)

This toolkit is comprised of a set of mitigation considerations designed to support efforts to sustainably partner with sites to enable the enrollment and retention of underrepresented patient populations in clinical trials. These mitigation considerations consist of perspectives from a series of stakeholder discussions and a Diversity Roundtable event and suggest considerations across different maturity levels.

Additional Solutions with US Focus: U.S. Regulatory Landscape, FDA Diversity Plan Early Insights and Considerations

TransCelerate BIOPHARMA INC.

touch

THE BLACK BREAST CANCER ALLIANCE

GET IN TOUCH!

MY STORY...


Kaiser Permanente
Certificate of Completion


WALKING IN BLESSINGS!


THRIVER


MAGIC TOUCH
MAGIC TOUCH
MAGIC TOUCH

The State of Black Breast Cancer

Breast cancer is the most fatal health issue for Black women. Our disease is different, unique and warrants special and focused attention. Black women diagnosed with breast cancer face:

41% **Higher mortality rate compared to white women.**

39% **Higher risk of breast cancer recurrence.**

71% **Higher relative risk of death compared to white women.**

THE STATE
OF BLACK BREAST CANCER

Black women under 35 get breast cancer at twice the rate and die at three times the rate.

Black women under 50 are twice as likely to die from breast cancer.

Black women are nearly twice as likely as White women to receive a breast cancer diagnosis at an advanced stage of the disease

Black women are 3 times more likely to have triple negative breast cancer. 40% of TNBC patients are under 40

Black women are more likely than White women to die of breast cancer at any age across any sub-type

Black women have the lowest 5-year relative breast cancer survival rate compared to all other racial/ethnic groups for every stage of diagnosis and every breast cancer subtype

The State of Black Breast Cancer

The physiology of Black women has not been a consideration in clinical trial research.

- The clinical trials for the current standard of care drugs have had little to no inclusion of Black women.
- The average Black women participation rate for current breast cancer clinical trials is less than 3%.

Clinical trial education, recruiting, and participation are not commensurate with the state of disease.

HOW IS THE ECOSYSTEM FAILING **BLACK WOMEN?**

Doctors don’t invite Black women to clinical trials.

When the patient brings up the conversation, they still walk away not sufficiently informed.

What Can the Ecosystem **Do Better?**

Educate with Cultural Agility!

Fear of the unknown!

Can’t continue to blame the fear on the earned medical mistrust and the social determinants of health.

“Don’t do a clinical trial! You will get the sugar pill and die.”

Metastatic Patient

Talking at them and about them

VERSUS

Talking to them and with them

What Can the Ecosystem **Do Better?**

Words like ***underserved and unrepresented*** should not be used in patient-facing language

Pronouns like **'you'** and **'they'** are disturbing and undermine trust

What Can the Ecosystem **Do Better?**

What's Black about it?

- Must show that you really care about the audience and are willing to invest in it.
- Must be intentional in every word and visual
- Patient voice is the voice of TRUST

How Is the Ecosystem Failing **Black Women?**

How Is The FDA Guidance Changing the Game?

The diversity evaluation process does not yet have proven metrics

OUR
When We Tri(al)
MOVEMENT

1. Acknowledges earned mistrust in medical research and re-establish trust.

2. Dispels myths about clinical trial research and educate around the basics and benefits of research.

3. Empowers Black breast cancer patients to advocate for themselves.

WHEN we Trial

COMMUNITY EVENTS

WHEN we Trial

touch
THE BLACK BREAST CANCER ALLIANCE

We Support Trials With:

Recruiting Consulting
Site Guidance And Training
Nurse Navigators To Support Patients

WHEN we Trial

touch
THE BLACK BREAST CANCER ALLIANCE

WEBSITE VISITS

126,999

39,118 unique visits

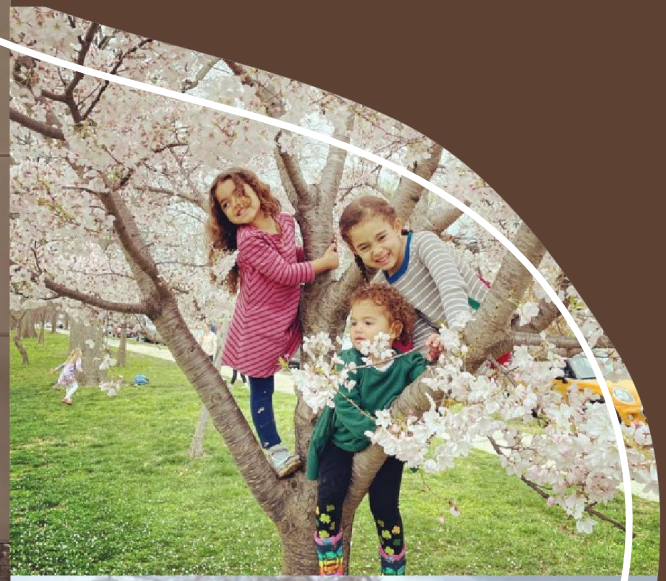
CLINICAL TRIALS SEARCH

14,572

The Golden Rule

Treat others the way YOU want to be treated.

THANK YOU!



Session 2: Establishment of Clinical Study Enrollment Goals & Use of Disease Prevalence or Incidence Data

Moderator: Dionne Price
Director Division of Biometrics IV, Office of Biostatistics, CDER, FDA

Scott Halpern
Professor of Medicine, Epidemiology, and Medical Ethics and Health Policy, Perelman School of Medicine, University of Pennsylvania

Dooti Roy
Director of Global Biostatistics and Data Sciences, Boehringer, Ingelheim, Inc

Bobby Bogaev Chapman
Vice President, Heart Failure, Abiomed

Michel Reid
Senior Director and Head, Global Demographics and Diversity, GlaxoSmithKline

Tom Fleming
Professor of Biostatistics, University of Washington

Matching measures to goals in efforts to promote clinical trial diversity

Scott D. Halpern, MD, PhD

John M. Eisenberg Professor of Medicine, Epidemiology, and Medical Ethics & Health Policy

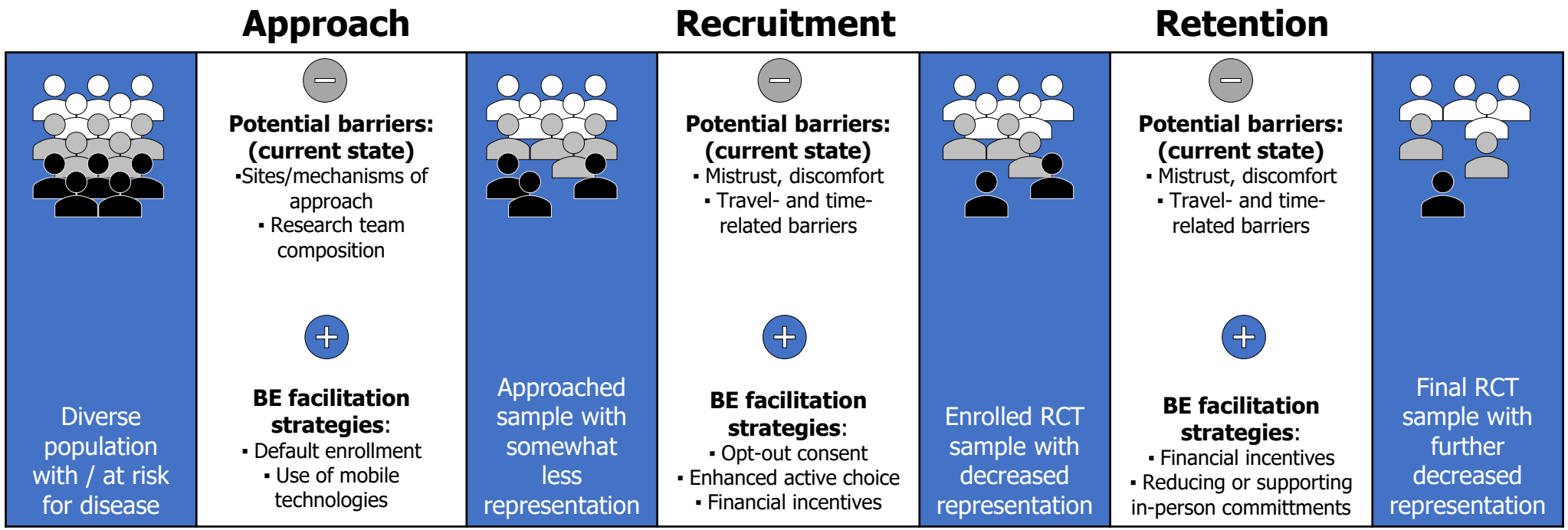
Director, Palliative and Advanced Illness Research (PAIR) Center

Director, Behavioral Economics to Transform Trial Enrollment Representativeness (BETTER) Center

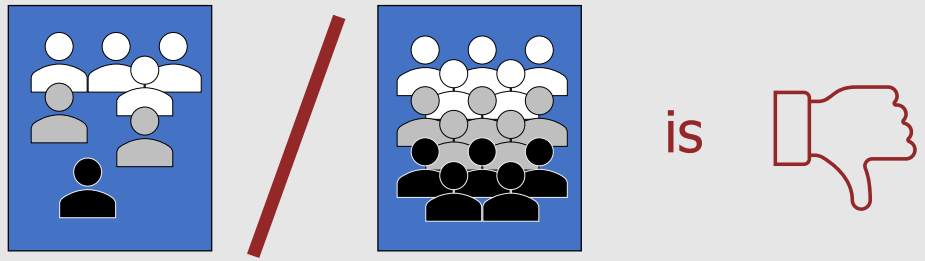
University of Pennsylvania Perelman School of Medicine

BETTER CENTER

Trial participation barriers and facilitators



Participation-to-Prevalence Ratio (PPR)



Virtues of Participation-to-Prevalence Ratio (PPR)

- Single metric that can be used across RCTs of different diseases
- Aligned with goal of equitably distributing potential benefits of trial participation

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Problems with sole reliance on Participation-to-Prevalence Ratio (PPR)

- Accurate prevalence data across groups are often unavailable
- Geographic heterogeneity – population prevalence where?
- PPR can be "gamed"
  - Selectively recruiting from sites with high %s of underrepresented groups
  - Oversampling underrepresented patients
- Improving equity of opportunity may or may not improve PPR
- Poorly aligned with goal of augmenting biomedical knowledge

BETTER CENTER

Why Diverse Clinical Trial Participation Matters

Aaron L. Schwartz, M.D., Ph.D., Marcella Alsan, M.D., Ph.D., Alanna A. Morris, M.D., and Scott D. Halpern, M.D., Ph.D.

N ENGL J MED 388;14 NEJM.ORG APRIL 6, 2023

Goals of Increasing Diversity in Clinical Trials.

Goal	Key Challenges	Implications
Building trust in medical research and institutions	Distrust of medical and scientific professions can be an important obstacle to receiving effective medical care.	The effect on public trust of the design and conduct of clinical trials can be as important to public health as trials' results. Investments should be made in elucidating how clinical trial practices affect public trust.
Promoting fairness for potential participants and their communities	Opportunities to participate in trials are limited. Preferences, resources, and trust all affect willingness to participate in trials. Health systems' capacities to conduct trials vary among communities.	Overcoming unjust barriers to participation for disenfranchised groups will require affirmative outreach and recruitment actions. Grading trials on inclusive outreach and recruitment practices, rather than solely enrollment demographics, may better reflect recruitment equity. Investing in trial capacity in marginalized communities may benefit such communities broadly by improving adoption of innovations.
Generating biomedical knowledge	Sample sizes are often too small to permit assessment of treatment efficacy within particular subgroups. Clinically significant differences in treatment efficacy between groups that are underrepresented and those that are overrepresented in trials may not be common. Efforts to diversify trials address only some of the barriers to efficient patient recruitment.	Investigators should acknowledge that more inclusive trials may not show whether a treatment is effective for certain patient subgroups or meaningfully shift estimates of the treatment's efficacy. Shifting the focus of trials to diseases that disproportionately affect marginalized groups may more effectively generate knowledge benefiting these groups. Future meta-research could clarify the importance and detectability of heterogeneous treatment effects.

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JAMA Internal Medicine | Original Investigation

Effectiveness and Ethics of Incentives for Research Participation
2 Randomized Clinical Trials

Scott D. Halpern, MD, PhD; Marzana Chowdhury, PhD; Brian Bayes, MS; Elizabeth Cooney, MPH; Brian L. Hitsman, PhD; Robert A. Schnoll, PhD; Su Fen Lubitz, MPH; Celine Reyes, MA; Mitesh S. Patel, MD, MBA, MS; S. Ryan Greysen, MD, MHS, MA; Ashley Mercede, MPH; Catherine Reale; Frances K. Barg, PhD, MEd; Kevin G. Volpp, MD, PhD; Jason Karlawish, MD; Alisa J. Stephens-Shields, PhD

Parent RCT 1: 4-arm trial of smoking cessation interventions among outpatients with depression

Parent RCT 2: gamification intervention vs. usual care to promote ambulation among inpatients

Main effectiveness outcome: signed consent to participate in parent trial

Ethical safety outcomes: undue* & unjust inducement

BETTER CENTER

Equalized racial enrollment in a real smoking cessation trial with incentives without adverse ethical safety outcomes in any group

Incentive	Black patients	White patients
$0	17%	30%
$200	36%	36%
$500	46%	49%

Recommendations

- Academic-Industry partnerships to test representativeness-promoting interventions in real RCTs
    - Outcomes fit for purpose: e.g., group-specific enrollment fractions
- Real-world and survey experiments exploring how interventions impact ethical safety outcomes (undue inducement) and trust
- All trials should fully capture the characteristics of all approached patients, not just those who consent
- Get over concerns about paying people to participate – or at least be open to further tests

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Diversity in Clinical Trials

On the path to create health equity

Dooti Roy, PhD.

FDA Public Workshop to Enhance Clinical Study Diversity

November 29, 2023

Boehringer Ingelheim

“You have to dream before your dreams can come true.” - A. P. J. Abdul Kalam

Boehringer Ingelheim is committed to impact 50 million people in underserved communities by 2030 by empowering our employees, partners and social entrepreneurs to help co-create healthy, inclusive and sustainable communities.

Boehringer Ingelheim

The Bigger Picture

Equitable access

Innovation to address unmet medical needs

Equitable analyses

Community engagement

Availability of healthcare solution

Engagement and infrastructure

Vestibulum

Promoting a diverse healthcare workforce

Training

Diversity

RWE generation

Expanded geographic footprint

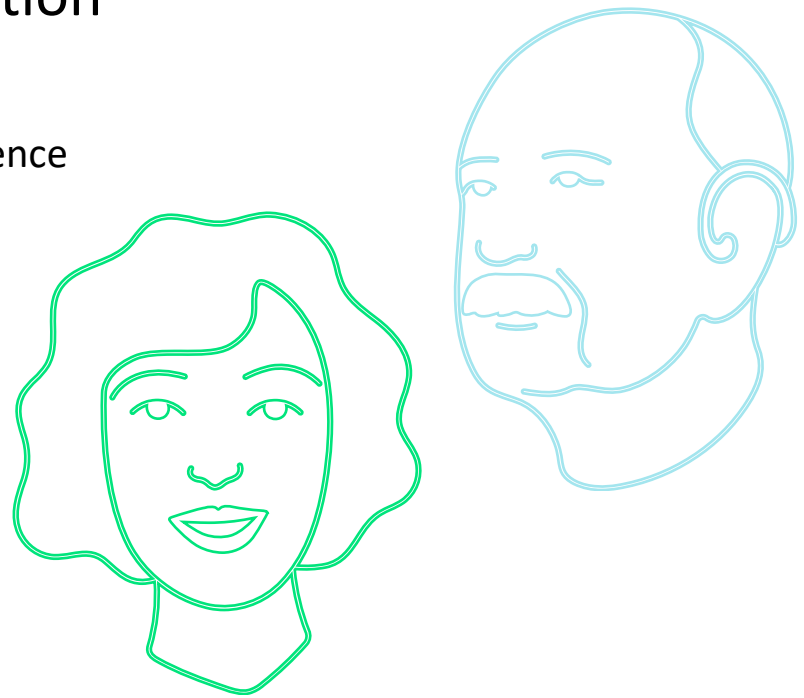
Education and Prevention

Advocacy and policy

Ensuring treatment adherence

Awareness

“Health equity is achieved when everyone can attain their full potential for health and well-being” (WHO)



Boehringer focuses on clinical trial diversity as a part of eliminating healthcare disparities for people and animals in vulnerable communities.

Boehringer Ingelheim

The regulatory context

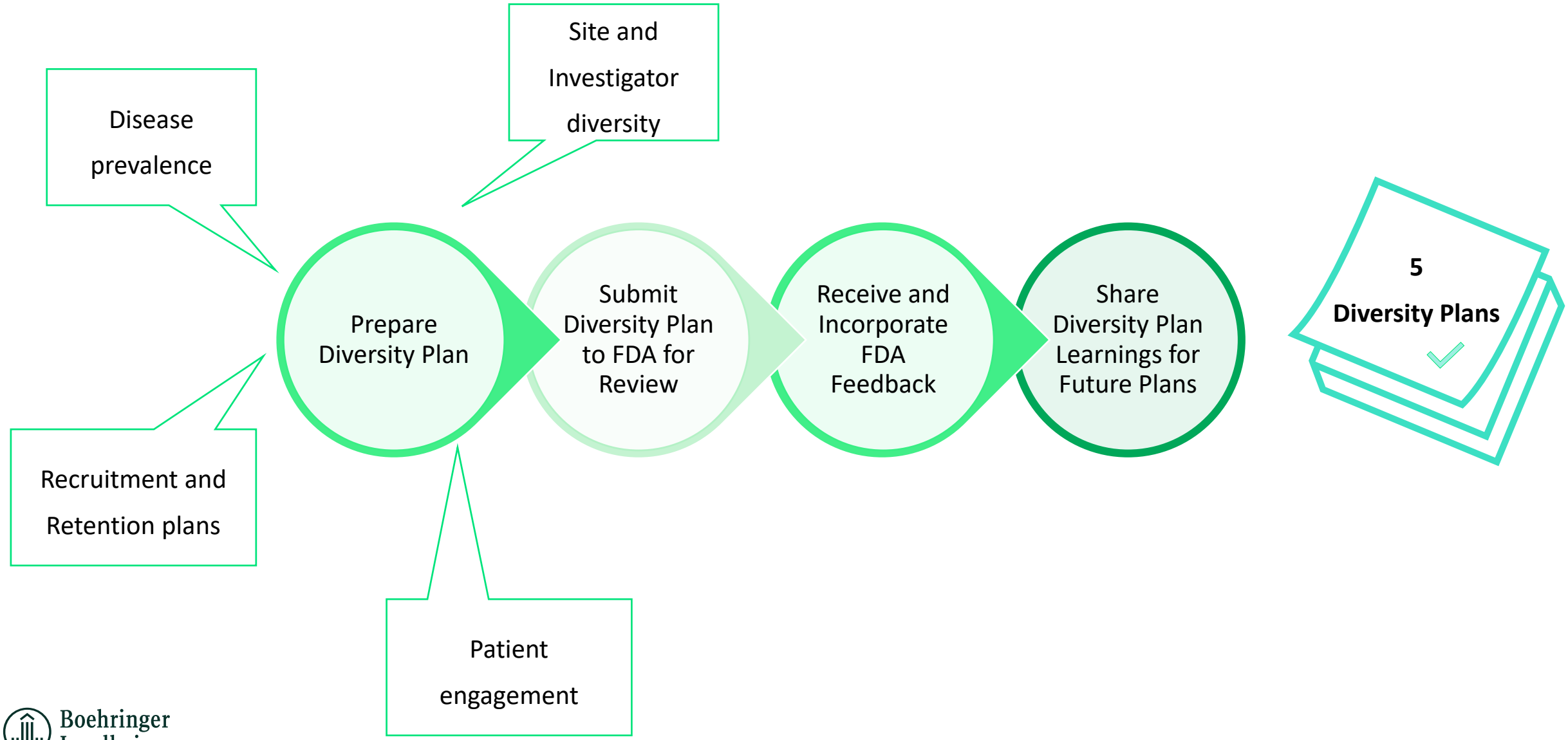
In response to publication of FDA guidance, Boehringer Ingelheim developed a "Diversity Plan Working Group"

- Cross-functional
- Established Business Practice and Diversity Plan Template documents to ensure teams were working similarly across therapeutic areas and development programs
- Created mechanisms for sharing completed plans and lessons learned
- Provided educational sessions

Future focused: New Clinical Trial Diversity Lead and Team of Diversity Strategists

Boehringer Ingelheim

Diversity Plan in Action



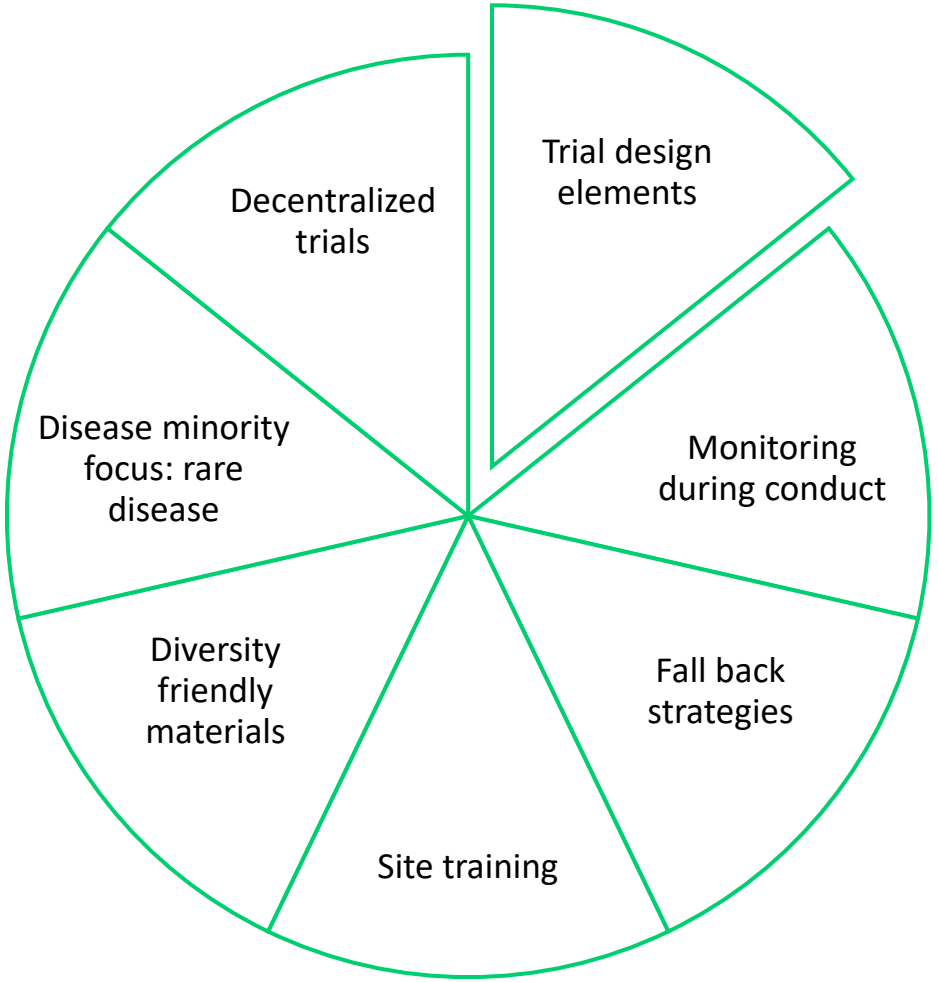
Boehringer Ingelheim

From Plan → Action: Operations at work

Ensuring diversity in clinical trial is a multi-faceted, nuanced endeavor

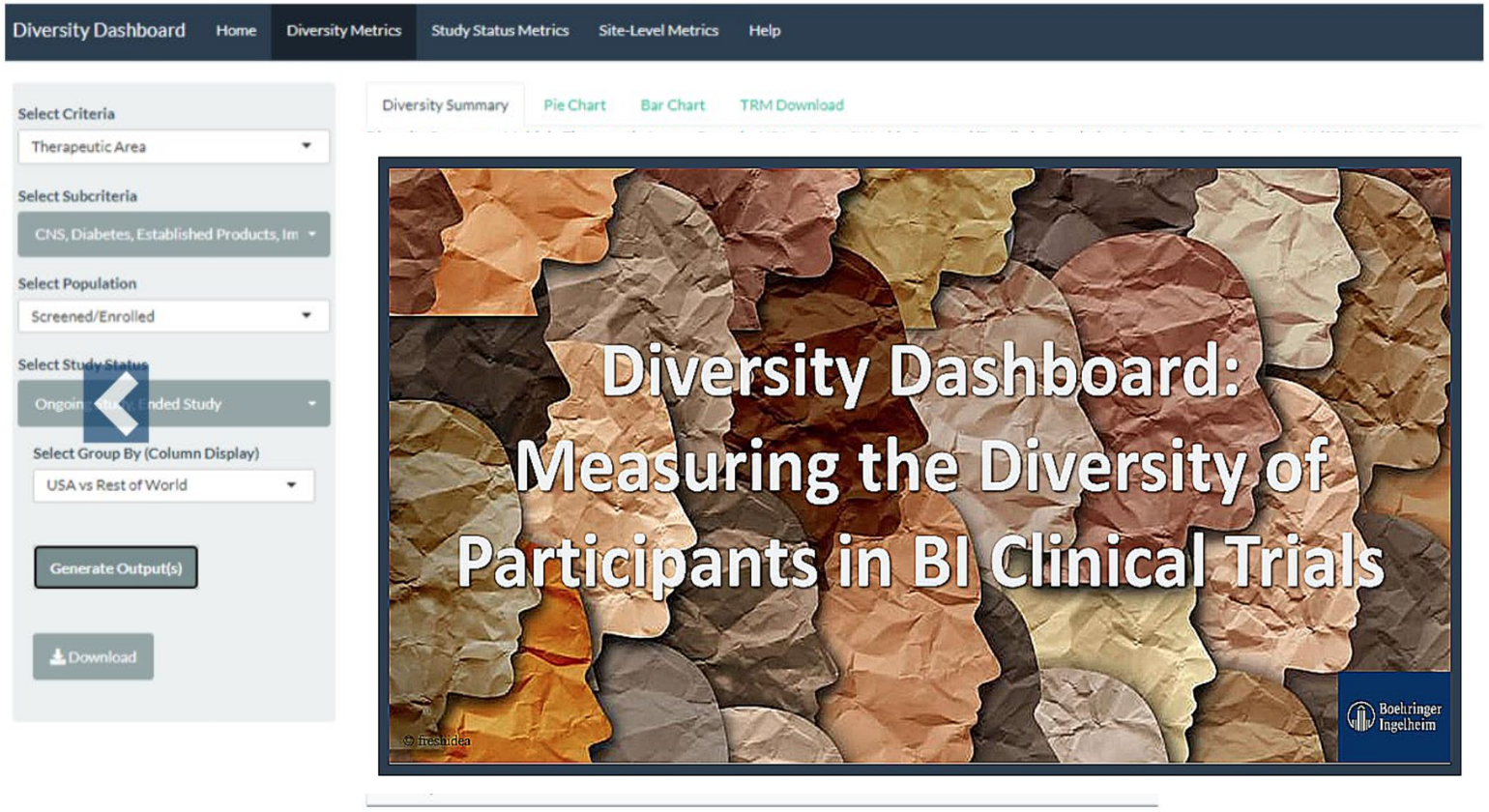
Focused commitment, strategy and execution at a broad spectrum of correlated topics are critical components for success

Learn ← → adapt



Boehringer Ingelheim

Monitoring diversity during trial conduct



- A R-Shiny based interactive data visualization dashboard has been implemented
- Site and trial level monitoring
- Enables during conduct real time tracking of diversity metrics
- Keeps teams on target and focused
- Insights for future use

Patients at the center

Diversity and Inclusion Patient Council[3]

- Standing committee of diverse patients
- Direct input into a variety of topics e.g., clinical trial materials, design considerations
- EMPA-ASi trial

Yale Diversity Study[2]

- Oncology
- Cross-industry
- Understand facilitators and barriers to participation in early phase clinical trial
- Focus on underrepresented patients

Hear Your Heart[1]

- Empower Black and Latina women with heart failure who experience a higher mortality rate
- Encourage patients to prioritize their heart health

Co-creating solutions together with the under-served patient community: goal of turning those solutions back to the communities to create **impact for generations.**

1 Heart Failure: Health Disparities & Inequities for Women | BI US (boehringer-ingelheim.com)

2 Confronting health disparities in clinical trials | Boehringer Ingelheim US (boehringer-ingelheim.com)

3 Achieving Health Equity: The Importance of Patient Input at Every Phase of Care | Boehringer Ingelheim US (boehringer-ingelheim.com)

Boehringer Ingelheim

Boehringer Ingelheim

It really takes a village.

Acknowledgement:

Elizabeth Meissner
Dr. Yabing Mai
Julie Shah
Dr. Hilary Wilson
Marie-Claude Raymond
Keri Yale
Dr. Lisa Crose
Kathleen Collins
Vanessa Boulanger
Lesli Nordstrom
Shannon Darbouze
Sharon Attick
Paul Petraro
Christian Niyonkuru

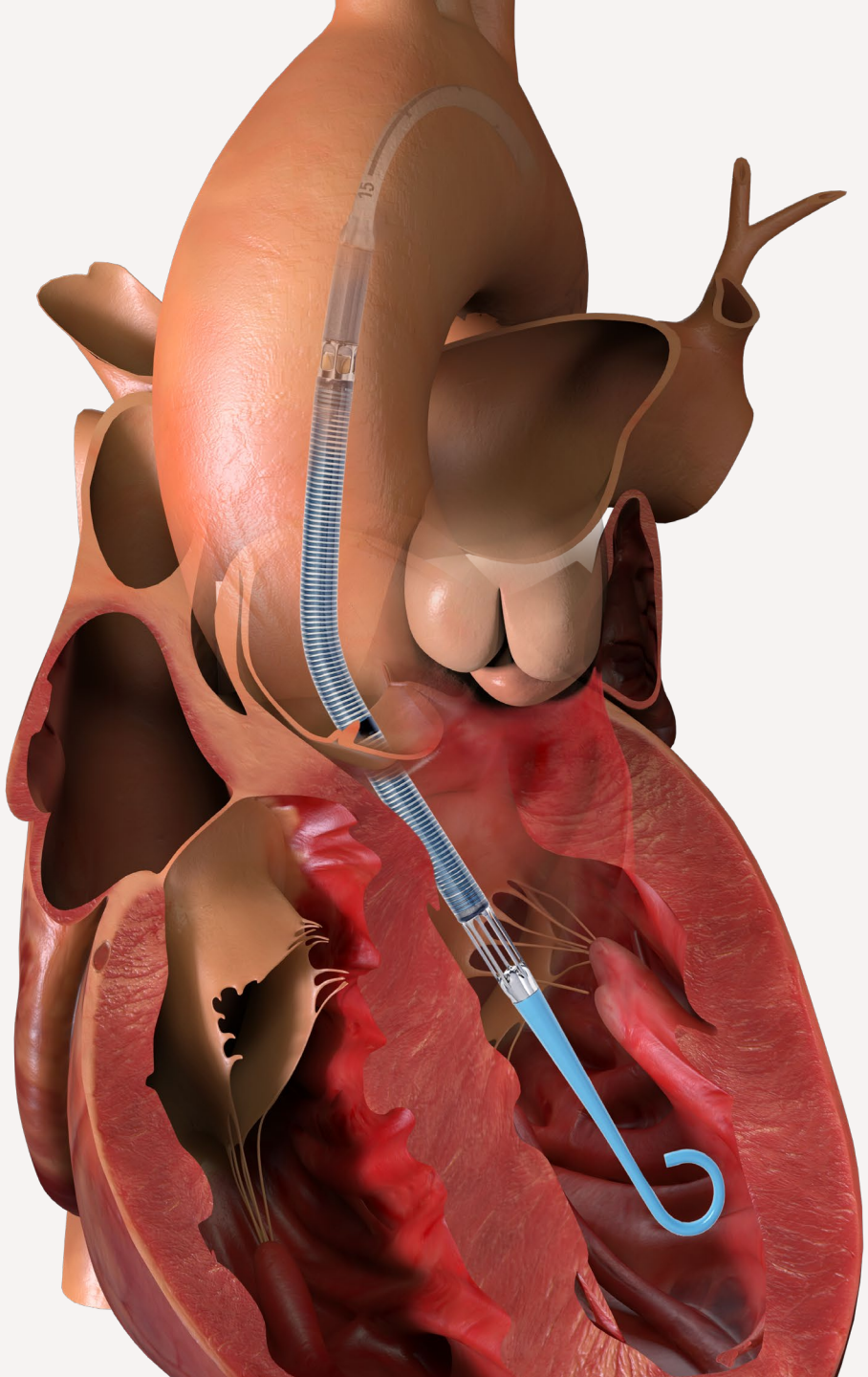
Establishment of Clinical Study Enrollment

Goals & Use of Disease Prevalence or Incidence Data

FDA Workshop
November 29, 2023

Bobbi Bogaev Chapman, MD
Vice President, Heart Failure

Johnson&Johnson
MedTech



Disclosures

Bobbi Bogaev Chapman, MD
Vice President, Heart Failure

Full time employee for Abiomed

Prevalence of Disease and Enrollment Targets

Published clinical trial data

Observational registries

Real world evidence

Human Factors Consideration in Device Design

1980s

- Large, heavy durable pulsatile pumps
- Invasive sternotomy

Heartmate XVE

1990s

- Lighter durable axial blood pumps
- Invasive sternotomy pumps

Heartmate II

2000s

- Smaller durable magnetically levitated centrifugal pumps
- Thoracotomy option

HVAD

2010s

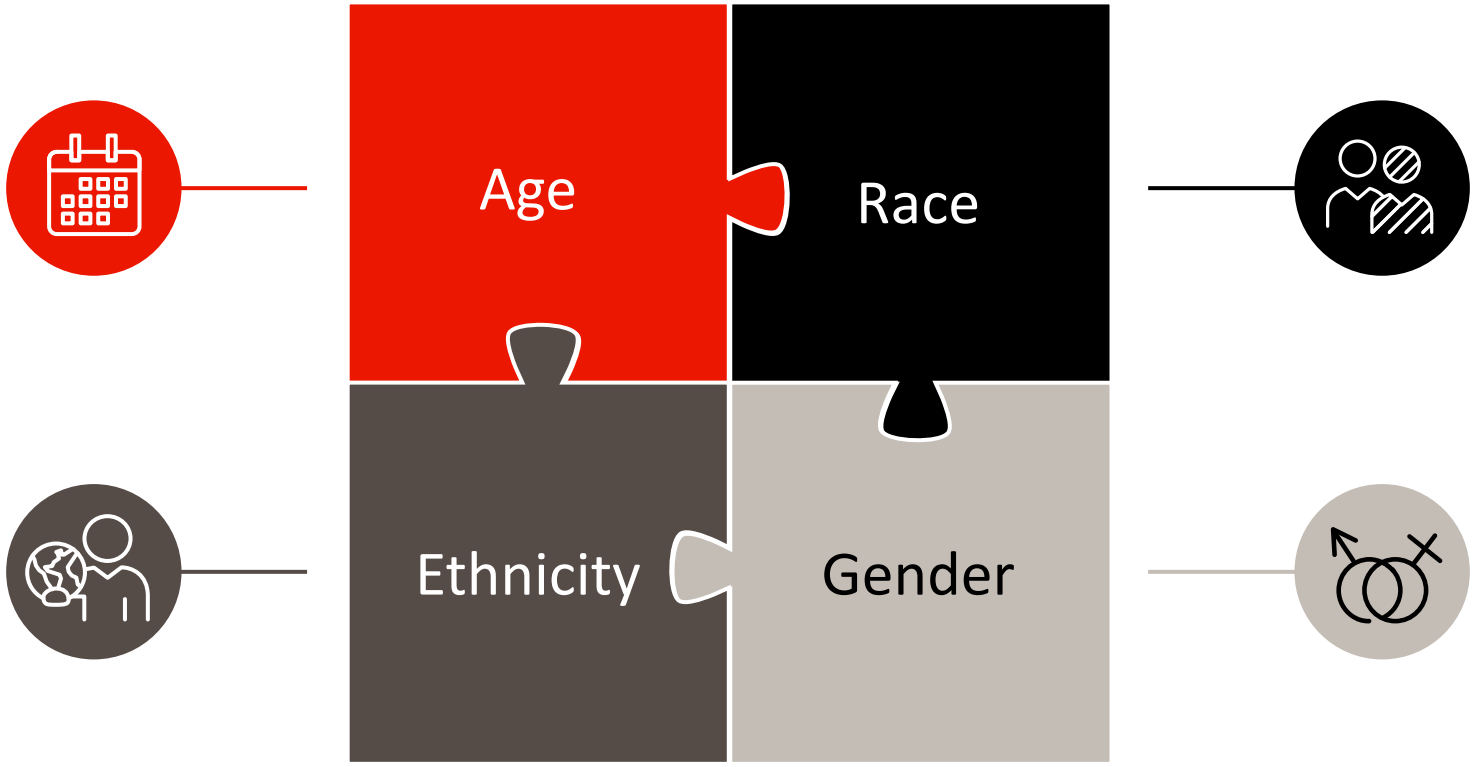
Heartmate III

2022

The world's first minimally invasive, intravascular durable LVAD

Impella BTR

Enrollment Targets

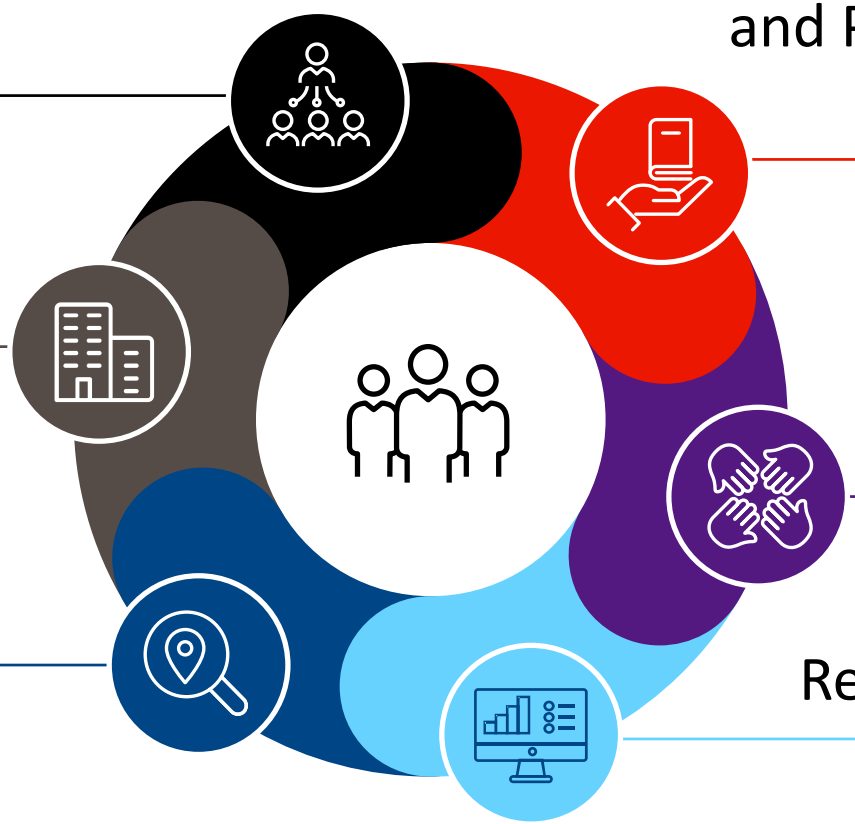


Strategies to Diversify Enrollment

Clinical Trial Leadership

Site Selection

Site Principal Investigators



Education to Patients and Primary Providers

Community Engagement

Remote Monitoring

Community Engagement: Patient Advisory Group

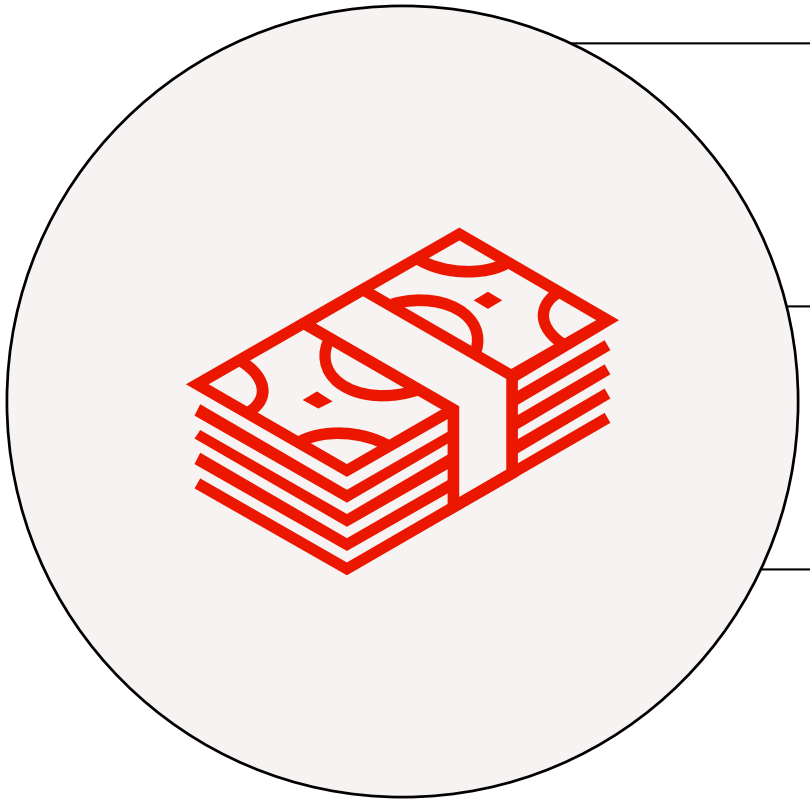
Patients

Caregivers

Research Coordinators

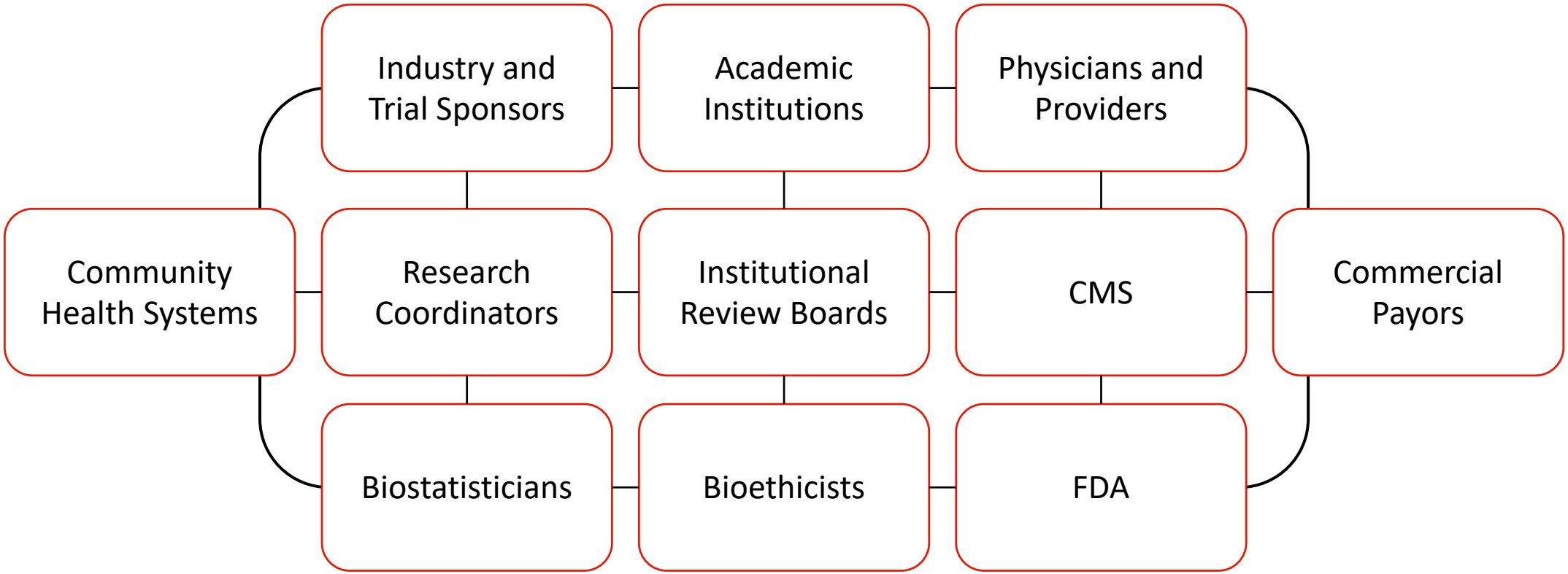
Physician Principal Investigators

Reimbursement Challenges to Equitable Enrollment



- Caregiver and Travel Reimbursement
- Category B CMS Reimbursement
- Variable IRB Policies

Multi-stakeholder Alignment is Needed to Enhance Diversity, Equity, and Inclusion in Clinical Trials



Thank you

If you have more questions, please contact:

Bobbi Bogaev Chapman, MD
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Johnson&Johnson
MedTech

FDA Public Workshop

Enhancing Clinical Study Diversity:

Introductory Comments

November 29, 2023

Thomas R. Fleming, Ph.D.
Professor, Dept. of Biostatistics
University of Washington

The FDA has made "*critically important contributions*" to the
"*pursuit and implementation of evidence-based approaches for the prevention & treatment of diseases*" *

* Fleming TR, DeMets DL, McShane LM. "The Role, Position and Function of the FDA—The Past, Present and Future". *Biostatistics* 18(3): 417-421, 2017

FDA Public Workshop

Enhancing Clinical Study Diversity

Objectives of this Session:

Discuss the establishment of goals for enrollment in clinical trials,
including the relevance of the estimated U.S. prevalence or incidence of the disease
or condition for which the drug or device is being developed

Discuss how and when to collect and present the prevalence or incidence data
on a disease or condition by demographic subgroup,
possible sources for such data and methodologies for assessing such data

Enhancing Clinical Study Diversity

Enhancing evidence-based medicine is of central importance

Clinical Trials should be properly designed and conducted

Among key design and conduct considerations are:

✓ *Having proper primary & secondary endpoints:*
'Feels, functions, survives' measures or validated biomarkers

✓ *Being randomized, when possible, to enhance reliability*

✓ *Use of Controls receiving a proper version of Standard-of-Care*

✓ *Ensuring evidence-based generalizability of results*

- Enabling properly informative descriptive presentations by important baseline characteristics

Enhancing Clinical Study Diversity

Ensuring proper generalizability of clinical trial results:

Quality Research: *Active* rather than *Passive* Approaches are Needed

✓ *Establishing of enrollment targets in clinical trials, including proper engagement of often underrepresented populations*

- Targets enlightened by the prevalence or incidence data for a disease or condition by demographic subgroup

✓ *Creative proactive approaches to increase ability to achieve targets*

- Selection of sites that increase diversity of enrollees
- Ensure adequate engagement of North American sites

CRDAC-O'Neill

✓ *Monitoring enrollment diversity throughout trial conduct*

- Shared responsibilities of the study sponsor and the DMC

Enhancing Clinical Study Diversity
—An important role of Data Monitoring Committees

Data Monitoring Committee (DMC) Mission:

"*Safeguard the interests of study participants as well as to preserve the integrity and credibility of clinical trials, enabling them to achieve both timely and reliable evaluations of experimental interventions for the benefit of the broader clinical community.*"

✓ *DMCs: Enhancing engagement of often underrepresented populations*

"There is need for proper diversity in clinical trial leadership, in DMC membership, and in patients enrolled in the clinical trial. Not only should DMCs have inclusion of diverse members, but DMCs also should monitor the composition of the trial cohort… DMC's have an opportunity throughout trial conduct to examine the representation of the enrolled cohort, and to make recommendations to enhance enrollment of specific groups that may be under-represented in the trial. This may include considerations around geography, race, sex, age, and other populations of interest." (HFC Article: To be submitted)

Conclusions: Enhancing Clinical Study Diversity

Ensuring proper generalizability of clinical trial results:

Quality Research: *Active* rather than *Passive* Approaches are Needed

✓ *Establishing of enrollment targets in clinical trials, including proper engagement of often underrepresented populations*

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Session 3A: Approaches to Support the Inclusion of Underrepresented Populations and to Encourage Clinical Study Participation – Age, Race, Ethnicity, Sex, Pregnancy, and Lactation

Moderator: Larissa Aviles-Santa
Director, Division of Clinical and Health Services Research, NIMHD, NIH

Rose Blackburne
VP, Global Therapeutic Area Head, General Medicine & Women's Health, Medical Science & Strategy (MSS) PPD, Thermo Fisher Scientific Company

Anne Lyerly
Professor of Social Medicine, The University of North Carolina at Chapel Hill

Michelle Kipke
Professor of Pediatrics, Associate VP of Strategic Health Initiatives, Keck School of Medicine, University of Southern California

Jennifer Jones-McMeans
Divisional VP of Global Clinical Affairs, Abbott

Dawn Corbett
Inclusion Policy Officer, Office of Extramural Research, NIH

FDORA Virtual Public Workshop to Enhance Clinical Study Diversity convened by CTTI and FDA November 2023

Session 3A: Approaches to Support the Inclusion of Underrepresented Populations and to Encourage Clinical Study Participation – Age, Race, Ethnicity, Sex, Pregnancy and Lactation

Rose Blackburne, MD, MBA

Vice President, Global Head, General Medicine and Women's Health, Medical Science and Strategy
PPD, part of Thermo Fisher Scientific

The world leader in serving science

Approach to Developing Strategies to Increase Diversity in Clinical Trials

ThermoFisher SCIENTIFIC

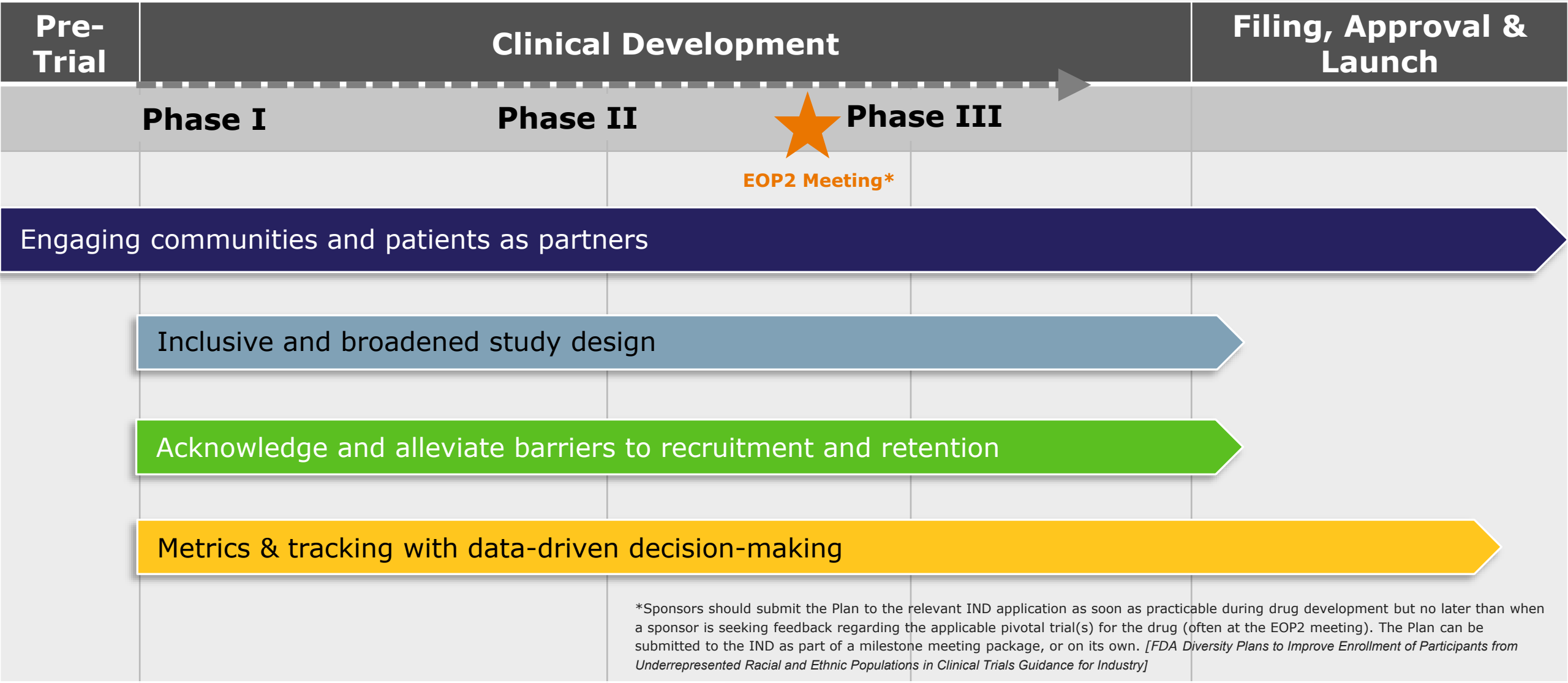
Identified Barriers to Achieving Proper Diversity in Clinical Trials

- **Historic lack of trust and cultural competency**
  - Unconscious biased towards patients and their willingness to participate in clinical trials
- **Limited health literacy and clinical trial awareness**
  - Historic unethical clinical research practices
- **Limited access to clinical trials**
  - Varying levels of understanding, ICF reading level too high
  - Traditional sites lack proper training and experience recruiting minority patients
- **Overly restrictive eligibility criteria and complicated protocol design**
  - Eligibility criteria inadvertently excluding minorities due to comorbidities and lab values ranges
- **Financial toxicity and burden in personal life**
  - Distance to site, child/senior care, impact on work schedules, logistical cost

Key Innovative Solutions to Address Diversity in Clinical Trials

- **Targeted minority patient engagement plans**
- **Enhanced site and patient educational materials and decentralized trial tools**
- **Digital tools, SiteCoach, data-driven feasibility and site placement**
- **Protocol optimization, broadened and inclusive study design recommendations**
- **Patient concierge, travel and transportation reimbursement**

Diversity in Every Phase of Clinical Development



*Sponsors should submit the Plan to the relevant IND application as soon as practicable during drug development but no later than when a sponsor is seeking feedback regarding the applicable pivotal trial(s) for the drug (often at the EOP2 meeting). The Plan can be submitted to the IND as part of a milestone meeting package, or on its own. *[FDA Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials Guidance for Industry]*

Engaging Communities and Patients as Partners

ThermoFisher SCIENTIFIC

Establish Rapport

- Get to know community well ahead of a trial
- Attend/sponsor community events
- Host open house events for community members to tour research sites

Build Shared Values

- Host focus groups for patients and community members to share perspectives
- Establish patient advisory boards and steering committees
- Elicit feedback to understand the factors that impact recruitment and retention

Support and Train

- Invite community members and patient champions as consultants throughout the study lifecycle
- Use patient and community input to develop culturally appropriate health and research materials

Stay Involved

- Thank-you letters for trial participation; disseminate study results to participants and community
- Collect feedback from patients and caregivers after participation has ended
- Maintain authentic relationships and stay involved in community

Inclusive and Broadened Study Design

Many populations are inadvertently excluded, including and not limited to:

- People with cognitive and physical disabilities
- People living with HIV, hepatitis
- People with co-morbidities
- People with substance use disorders
- Individuals with laboratory values that can vary by race and ethnicity (e.g., serum creatinine)

Example I/E Criteria Considerations

Investigator Judgment	Serum Creatinine Reference Level	WBC/ANC Reference Levels	Comorbidities	HIV and HBC/HCV	Minimum Age
Opportunities					
Avoid vague criteria and **specify exclusionary characteristics**. **Document** and **track** reasons for screen fail.	**Assess via CrCl**. If renal toxicity and clearance of IP is not of concern: CrCl values of >30mL/min should be used for inclusion.	**Provide race-specific WBC and ANC reference intervals** for proper diagnosis and clinical research.	**Offer clear guidance** on comorbidities that are exclusionary and follow for every patient and avoid the use of investigator judgment when possible.	**Clearly define exceptions for HIV patients** that utilize treatment and/or maintain a low viral load. **Reexamine types of studies** where HBV/HCV patients on an effective non-conflicting anti-viral or other effective therapy are excluded.	**When appropriate, consider the inclusion of adolescents** (ages 12-17) in disease and/or target-appropriate adult clinical trials at all stages of development.

It is important to assess and broaden eligibility criteria where possible, to ensure certain populations are not unintentionally excluded

Acknowledge and Alleviate Barriers to Recruitment and Retention

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Patient Concierge, Travel and Transportation Reimbursement

Culturally Competent and Inclusive Study Materials

Digital Technologies and Broadband/ WiFi Access

Support to Address Individual Site-Level Barriers

Strategies must consider the languages and varying levels of health/digital literacy, broadband access for digital tools, and accessibility among potential participants to enable inclusive and equitable participation

Metrics and Tracking with Data-Driven Decision-Making

- ✓ **Collect and track relevant demographic data in real time** (e.g., race and ethnicity, sex, socioeconomic measures) and conduct ongoing data-driven assessment
- ✓ For relevant studies, **collection of sexual orientation and gender identity (SOGI) data** should be considered
  - **Current gender identity** (Person's current internal sense of gender.) "How do you describe yourself?"
  - **Sex assigned at birth** (Sex perceived at birth based typically on genitalia and listed on their birth certificate.)
  - **Sexual orientation** (Person's romantic, relational and sexual orientation toward one or multiple genders.) "Do you think of yourself as …"
- ✓ **Clearly define and track KPIs** to monitor program performance and refine strategies to effectively reach target patient populations

Sample KPIs: Monitoring and Measuring Program Performance

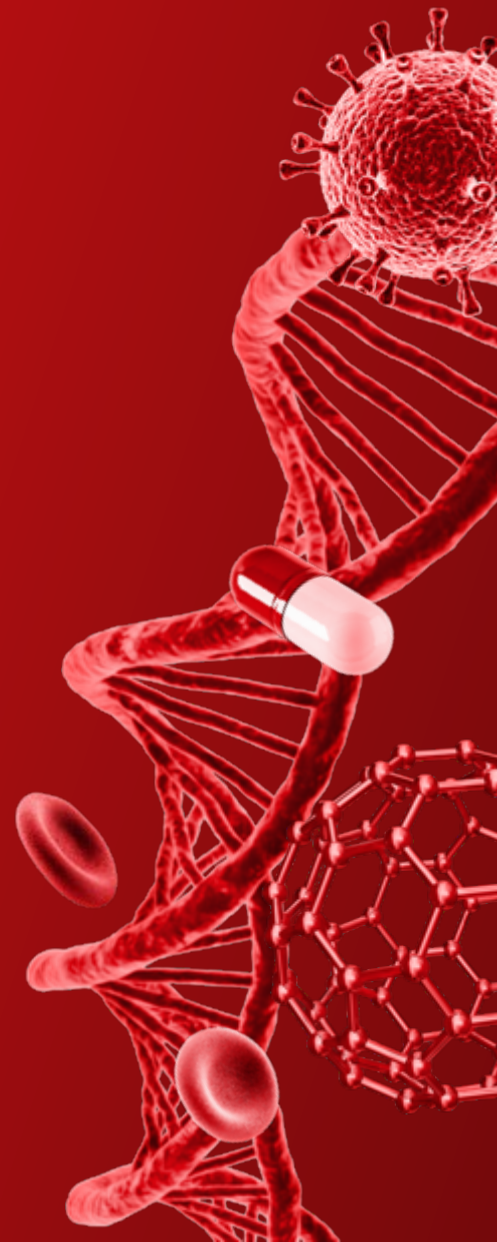
KPI	Metric Definitions
Site has staff with language capabilities matching patients	Site has staff/translators to include diverse populations of the community (Spanish, Creole, Tagalog, Mandarin, etc.)
Site assessed for accessibility standards (mobility, sensory, vision, audio, etc.)	Site is inclusive of and accessible to patients with disabilities
Site staff trainings (e.g., unconscious bias, cultural competence, psychological safety)	Site (investigators, CRCs, etc.) participates in diversity training
Site staff demographics reflect community diversity demographics	Site staff demographics reflects the community they serve
Specific plan per site/study to enroll and retain diverse participants	Numerical, percentage or ratio recruitment goal set for ethnicity, gender unique to each site and the surrounding community that matches overall study recruitment goal

Everyone should be able to see themselves represented in clinical trial data collection, with no penalty for those who opt out of sharing their personal information

Reference: Inclusion of Sexual Orientation and Gender Identity in Clinical Trials Is Necessary for Health Equity, Chen *et al.* *Int J Radiation Oncol Biol Phys*, Vol. 116, No. 1, pp. 118–121, 2023

Thank you

https://www.ppd.com/how-we-help/patient-diversity-in-clinical-trials/



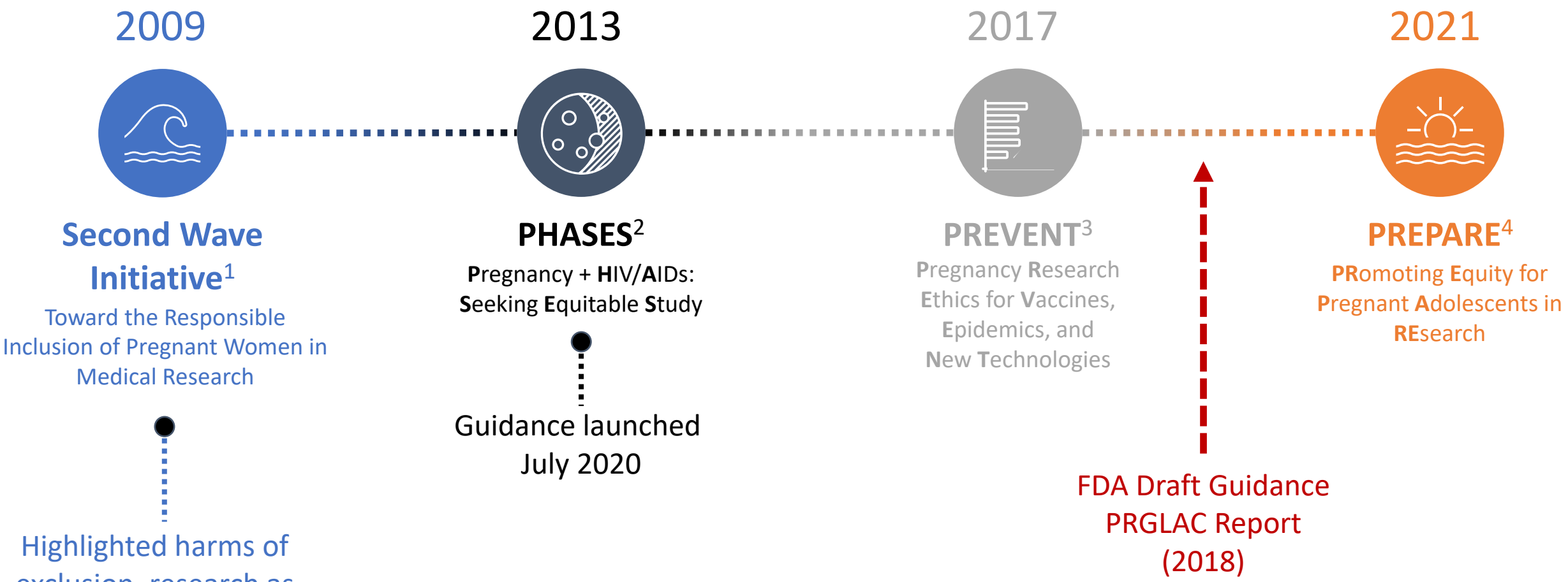
Ethical Considerations for Inclusion of Pregnant Persons in Biomedical Research

Anne Drapkin Lyerly, MD, MA
Professor, Departments of Social Medicine and Ob-Gyn
Center for Bioethics

Public Workshop to Enhance Clinical Study Diversity

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Toward a Paradigm of Inclusion



Harms of Exclusion from Research

Ineffective treatment	Undertreatment/toxicity, exposure to disease
Inappropriate risk	Treatment unsafe for fetus or pregnant person
Reticence	Avoidance of beneficial drugs
Exclusion from beneficial trials	“Protected to death”

Barriers


Drug development and approval pathway
Risk reasoning
Protectionism
Lack of training and experience
Legal and logistical challenges
Justificatory asymmetry
Myths and misconceptions

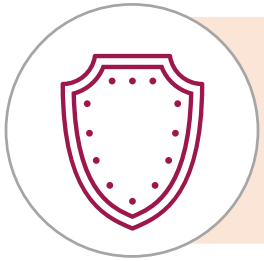
In a few words, what do you think is the greatest barrier to including pregnant women in clinical trials?

Wordcloud poll, Rheumapreg 2023

Conceptual Shifts Toward Inclusion

Exclusion

Vulnerable population



Protection *from* research

Presumptive exclusion

Inclusion

PHASES
PREGNANCY + HIV/AIDS
SEEKING EQUITABLE STUDY

Conceptual Shifts Toward Inclusion

Exclusion	Inclusion
Vulnerable population	*Complex* population
Protection *from* research	Protection *through* research
Presumptive exclusion	Fair inclusion

PHASES
PREGNANCY + HIV/AIDS
SEEKING EQUITABLE STUDY

Ethical Foundations of Research in Pregnancy

Protection
from intervention-related risks

Access
to the benefits of new technologies

Respect
for pregnant people's own health

PHASES
PREGNANCY + HIV/AIDS
SEEKING EQUITABLE STUDY

Strategies to advance ethical inclusion

Affirm
the need for research with pregnant populations

Enhance training
of those involved in conduct and evaluation of research

Design
for inclusion, integrating pregnant people and gathering pregnancy-specific data

Evaluate
for inclusion, and require justification for exclusion

Center
pregnant persons throughout the design, evaluation and conduct and reporting of trials

Work from the PHASES and PREPARE Projects supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under award number R01AI108368. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

hivpregnancyethics.org

@pregnancyethics

Session 3B: Approaches to Support the Inclusion and Clinical Study Participation of Individuals with Disabilities Including Intellectual or Developmental Disabilities

Moderator: David Resnik
Bioethicist, National Institute of Environmental Health Sciences, NIH

Willyanne Decormier Plosky
Program Director, Multi-Regional Clinical Trials Center Harvard University

Kellie Malloy Foerter
VP, Global Trial Management, Immunology, Cardiovascular and Neuroscience, BMS

Ari Ne'eman
PhD Candidate, Harvard University

Alison Barkoff
Performing the Duties of the ACL Administrator and Assistant Secretary for Aging

MULTI-REGIONAL CLINICAL TRIALS

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

Session 3B: Approaches to Support the Inclusion and Clinical Study Participation of Individuals with Disabilities Including Intellectual or Developmental Disabilities

Public Workshop to Enhance Clinical Study Diversity

November 29, 2023

Disclaimer

- This material and opinions expressed here are not intended to represent the position of Brigham and Women's Hospital, Mass General Brigham, Harvard University, HHS, FDA, or any organization, institution, or entity.
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The Multi-Regional Clinical Trials Center (MRCT Center)

The MRCT Center is a research and policy center focused on addressing the conduct, oversight, ethics, and regulatory environment of clinical trials.

Our Vision

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

Our Mission

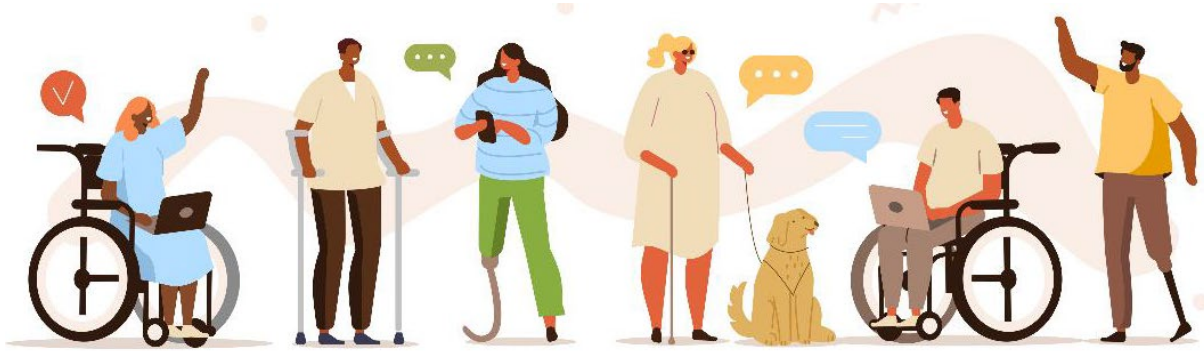
Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.

Brigham and Women's Hospital
Founding Member, Mass General Brigham

HARVARD UNIVERSITY

“We are regular people. We should have the same health care as others.”

- 1 billion people and 240 million children globally have a disability.
- There are many different kinds disabilities. People can identify as having more than one.
- Federal laws like Section 504 of the Rehabilitation Act and Section 1557 of the Affordable Care Act (ACA) prohibit discrimination against people with disabilities and require equal access to healthcare.
- Diversity Action Plans are now required f or Phase 3 and later trials. Guidance from the Food and Drug Administration (FDA) focuses on race and ethnicity but does mention disability. People with disabilities are the largest minority group in the US (1 in 4 adults; 1 in 3 Black and Hispanic adults).



“Medical Workers Must Treat Us Equally.”

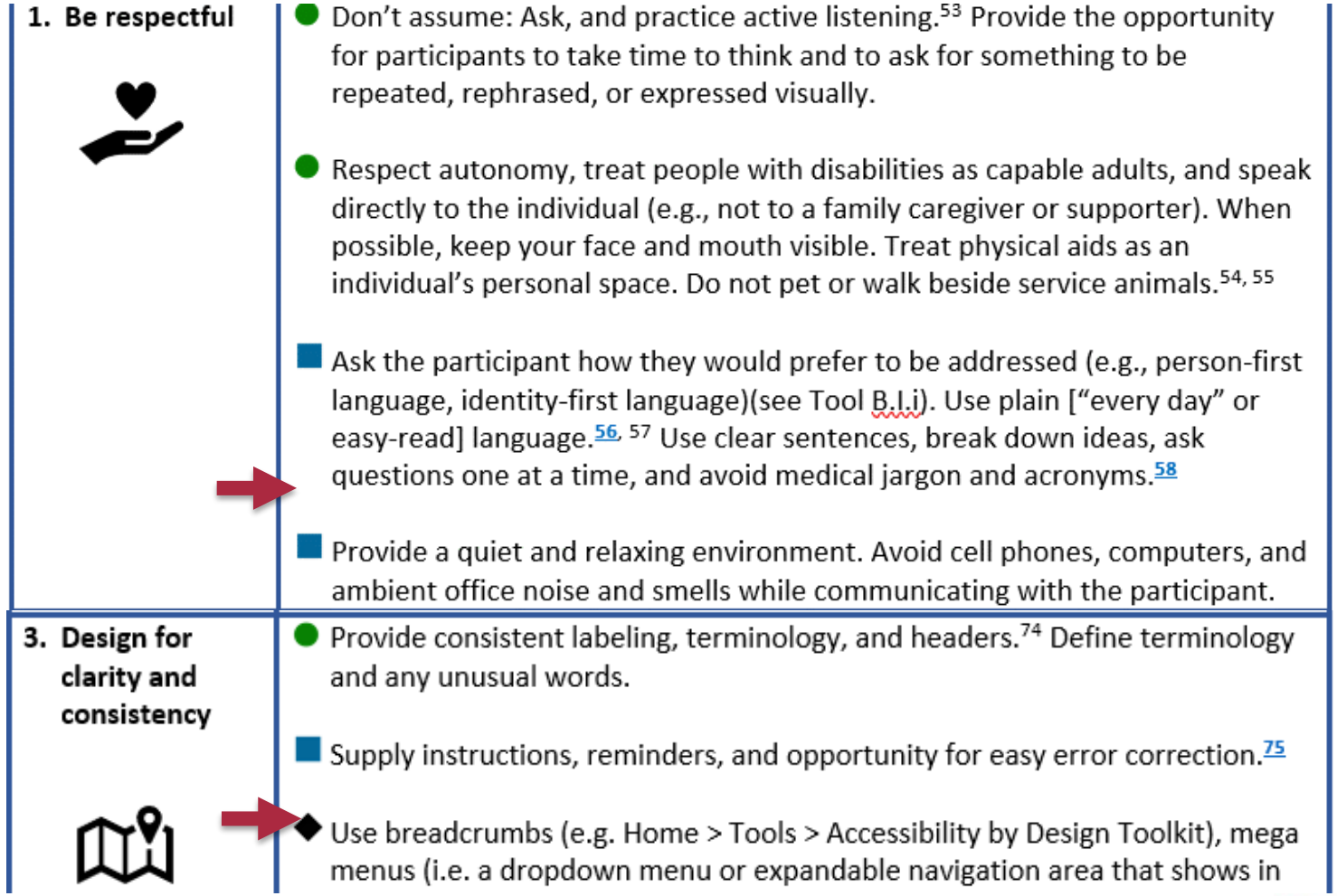
- 99% of studies required informed consent.
- 85% allowed for investigator discretion to exclude people.
- Only 24% of the exclusions had a listed justification. The listed justifications were often very broad.
- People with cognitive and intellectual/developmental disabilities were excluded in 42% of overall studies (dementia, depression, diabetes, lung cancer), and in approximately 90% of dementia studies.

https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2022.00520

“We have the right to information in a way we can understand. Buildings must have a way for us to get in. We have the right to get the help we need.”

Accessibility by Design in Clinical Research Toolkit website:

https://mrctcenter.org/diversity-in-clinical-research/tools/**abd_toolkit/**



1. Be respectful	● Don’t assume: Ask, and practice active listening.[53] Provide the opportunity for participants to take time to think and to ask for something to be repeated, rephrased, or expressed visually. ● Respect autonomy, treat people with disabilities as capable adults, and speak directly to the individual (e.g., not to a family caregiver or supporter). When possible, keep your face and mouth visible. Treat physical aids as an individual’s personal space. Do not pet or walk beside service animals.[54, 55] ■ Ask the participant how they would prefer to be addressed (e.g., person-first language, identity-first language)(see Tool B.I.i). Use plain [“every day” or easy-read] language.[56, 57] Use clear sentences, break down ideas, ask questions one at a time, and avoid medical jargon and acronyms.[58] ■ Provide a quiet and relaxing environment. Avoid cell phones, computers, and ambient office noise and smells while communicating with the participant.
3. Design for clarity and consistency	● Provide consistent labeling, terminology, and headers.[74] Define terminology and any unusual words. ■ Supply instructions, reminders, and opportunity for easy error correction.[75] ◆ Use breadcrumbs (e.g. Home > Tools > Accessibility by Design Toolkit), mega menus (i.e. a dropdown menu or expandable navigation area that shows in

“Society must break down the walls that keep us from having the same rights as everyone else. Discrimination is one wall.”

- Revise eligibility criteria in study protocols. Provide justification for exclusions.
- Expect to provide reasonable accommodations, and clearly state they will be available.

Problematic	Preferred
Subject is judged by (or is in the opinion of) the Investigator inappropriate for the study.	Subject is documented by the Investigator to be inappropriate for the study due to the following specific scientific, safety, or ethical reasons: [Specify] (e.g., subject has a cochlear implant and can’t complete the necessary MRI for safety reasons).
Subject has any condition that confounds the ability to interpret data from the study.	Subject has a physical or mental condition, as predetermined by the study team, that is expected to significantly impact study data interpretation: [Specify] Predetermination of significant impact is due to the following specific scientific reasons: [Specify] (e.g., subject has a condition documented to be associated with atypical enzyme [X] function).
Participant lacks capacity to consent for themselves.	Participant lacks the cognitive capacity to consent for themselves, as determined [when capacity is questionable] by a capacity assessment conducted with a supporter and any other accommodations desired by the participant.

"We have the right to make decisions about our lives."

- Supported decision-making.
- Participation as researchers: RE4ALL: Accessible Research Ethics Education for Community Research Partners. Available from: https://re4all.org/

Supported Decision-Making

A Guide for Supporting Clinical Trial Participants With Cognitive or Communication Challenges

People who take part in research are called **participants**. Supported decision-making is a strategy that lets participants choose **supporters** to assist them.

Supporters can be family members or friends. Others may be allowed, but it depends on the state law.

Supporters assist participants to learn more about the study and explain to researchers what they need and want.

Q: What Can I Do?

A supporter who is assisting with supported decision-making can:

- Discuss what actions might help the participant make decisions.
- Explain new things in easier ways for the participant, such as with stories or pictures.
- Work with the participant to think through the good and bad things about each option.
- Talk with the participant about their questions and concerns.
- Help access the participant's health, financial, school, and other information. You can do this without a special "ok" (permission) if that is the rule in your state.
- If the participant needs or wants you to, help the participant tell the research team about their questions and decisions. Check that the research team understands.

Thank you

Please note: All quotes in the slide headings were drawn from “We Have Human Rights” A Handbook for People with Developmental Disabilities. From the Harvard Law School Project on Disability. Available at: https://hpod.law.harvard.edu/pdf/we-have-human-rights.pdf

Closing remarks

Sally Okun

Executive Director,
Clinical Trials Transformation Initiative (CTTI)

U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Public Workshop to Enhance Clinical Study Diversity

November 29 - 30, 2023 / 10 a.m. - 2:00 p.m. EST

U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Public Workshop to Enhance Clinical Study Diversity

November 29 - 30, 2023 / 10 a.m. - 2:00 p.m. EST

FDA U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Meeting will begin at 10:00 a.m. EST

Day 2 Opening remarks

CDR Mathilda Fienkeng

Director, Division of Medical Policy Development

Office of Medical Policy

Center for Drug Evaluation and Research

FDA

Day 2 - Agenda

- Approaches to support the inclusion of individuals with mental illness
  - Approaches to enhance inclusion in clinical studies
  - Overcoming informed consent barriers

- Study elements that may enhance trial diversity
  - Decentralized studies
  - Digital health tools
  - Clinical endpoints
  - Biomarker selection
  - Study analyses

- Public dissemination of demographic enrollment data

- Community engagement

- Moving forward

Post Comments to FDA Public Docket

FDORA Public Workshop to Enhance Clinical Study Diversity

A docket is open for the public to submit electronic or written comments related to the topics addressed during this workshop.

Link to provide comments to the docket

Docket Number: FDA-2023-N-2462

Comment Period Closes: January 29, 2024

Session 3C: Approaches to Support the Inclusion and Clinical Study Participation of Individuals with Mental Illness

Moderator: Paul Appelbaum
Professor of Psychiatry, Medicine & Law
Columbia University

Patricia Areán
Director, Division of Services and Intervention Research, NIMH

Allissa Torres
Director of Mental Health Equity, Mental Health America

Scott Kim
Senior Investigator, Department of Bioethics, NIH Clinical Center

Eric Lenze
Professor and Head, Department of Psychiatry, Washington University School of Medicine

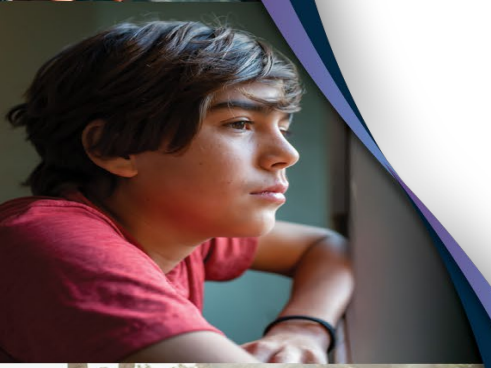
NATIONAL INSTITUTE OF MENTAL HEALTH
75 YEARS
RESEARCH. DISCOVERY. HOPE.

Including people with mental illnesses in clinical trials.

Patricia A. Areán, PhD.

Director, NIMH Division of Services and Interventions Research

NIH National Institute of Mental Health



Importance of inclusion

- Rates of mental illness in US adults is ~20%, with 7% suffering from severe mental illness. [1]
- People with diabetes are 2-3 times more likely to suffer from depression than those without diabetes; nearly half of people with bipolar disorder suffer from diabetes. [2-3]
- 8-15% of people with cancer suffer from depression. [3]
- 23% of people with epilepsy suffer from depression and anxiety. [4]
- People with Autism also tend to suffer from many chronic health conditions.

Impact of mental illness on health.

- People with severe mental illness die 25 years earlier, with leading health cause being heart disease. [5]
- Mild depression increases healthcare cost two-fold, and major depression three-fold, compared to those without depression. [6]
- Mental illness can attenuate the effectiveness of physical health conditions (diabetes, heart disease). [6]

People with mental health conditions often experience health care disparities and are very often excluded from clinical trials. [7]

- Lack of guidelines for clinicians.
- Limits to generalizability.
- Safety of drugs or devices ignores the risk to those with mental health risks.
- Is an example of discriminatory practice against a large group of people in the US.

National Institute of Mental Health

Why do we exclude?

- Assumptions about capacity to consent to research.
- Concerns about retention rates or interrupted participation owing to hospitalization.
- Lack of guidance as to how to measure, monitor and manage psychiatric symptoms in the context of physical health.
- Institutional Review Board variation in whether people with mental illnesses are vulnerable populations.

Citations

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4. Fiest KM, Dykeman J, Patten SB, et al. Depression in epilepsy: a systematic review and meta-analysis. *Neurology*. 2013;80(6):590-599.
5. Viron MJ, Stern TA. The impact of serious mental illness on health and healthcare. Psychosomatics. 2010 Nov-Dec;51(6):458- 65. doi: 10.1176/appi.psy.51.6.458. PMID: 21051676.
6. Schousboe JT, Vo TN, Kats AM, Langsetmo L, Diem SJ, Taylor BC, Strotmeyer ES, Ensrud KE. Depressive Symptoms and Total Healthcare Costs: Roles of Functional Limitations and Multimorbidity. J Am Geriatr Soc. 2019 Aug;67(8):1596-1603. doi: 10.1111/jgs.15881. Epub 2019 Mar 23. PMID: 30903701; PMCID: PMC6684454.
7. Shepherd, V., Wood, F., Griffith, R. *et al.* Protection by exclusion? The (lack of) inclusion of adults who lack capacity to consent to research in clinical trials in the UK. *Trials* 20, 474 (2019). https://doi.org/10.1186/s13063-019-3603-1

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Patricia Areán, PhD

Division Director NIMH Services and Interventions

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nimh.nih.gov

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NIH National Institute of Mental Health

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CLINICAL TRIALS TRANSFORMATION INITIATIVE

Session 4: Appropriate Use of Decentralized Studies, Digital Health Tools, and Other Trial Elements to Support the Inclusion of Underrepresented Populations in Clinical Studies

Moderator: Craig Tendler
Vice President, Oncology Clinical Development, Diagnostics, & Global Medical Affairs Janssen

Craig Lipset
Co-Founder and Co-Chair, Decentralized Trials and Research Alliance

Laura Esserman
Professor of Surgery & Radiology, School of Medicine, University of California, San Francisco

Luther T. Clark
Deputy Chief Patient Officer, Merck

Alanna Morris
Associate Professor, Department of Medicine, Emory University School of Medicine

Ivor Horn
Director of Health Equity and Product Inclusion, Google

Appropriate Use of Decentralized Studies to Support the Inclusion of Underrepresented Populations

Craig H Lipset
@craiglipset
30 November 2023

Views expressed do not necessarily represent my current affiliations

Decentralized Clinical Trials [DCT]: Defined

Clinical trial where some or all of the trial-related activities occur at locations other than traditional clinical trial sites

FDA Draft Guidance: "Decentralized Clinical Trials for Drugs, Biological Products, and 2 Devices " May 2023

- Inclusive of hybrid and fully-remote
- Create optionality and choice

- May be at home
- Or may be pharmacy, community centers, local health providers, pop-up sites, mobile units, etc.

Decentralized Clinical Trials [DCT]: Defined

Source	Definition
FDA Draft Guidance May 2023	…some or all of the trial-related activities occur at locations other than traditional clinical trial sites.
EMA Recommendations December 2022	…using procedures conducted outside the traditional 'clinical trial site'.
CTTI	… those in which some or all study assessments or visits are conducted at locations other than the investigator site via any or all …DCT elements.
DTRA	…utilizing technology, processes, and/or services that create the opportunity to reduce or eliminate the need for participants to physically visit a traditional research site.
IMI Trials@Home	…make use of digital innovations and other related methods to make them more accessible to participants; by moving clinical trial activities to the participant's home or to other local settings this minimises or eliminates physical visits to a clinical trial centre.

Different words / Same themes:

- Umbrella term inclusive of hybrid and fully-remote approaches
- Represents a collection of decentralized methods and tools (both processes and technologies)
- Focus on providing options for participation outside of a traditional "site"

Reasons to Decentralize Trials

Patient Factors

Experience & Access

Representation & Equity

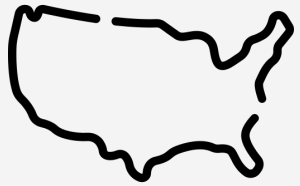
Business Continuity

Maintaining trials in an unpredictable environment

Sustainability

Support Green Trials and ESG commitments

Decentralized as a Tool for Diversity Plans



Rural / Frontier

Leverage DCT to manage distance

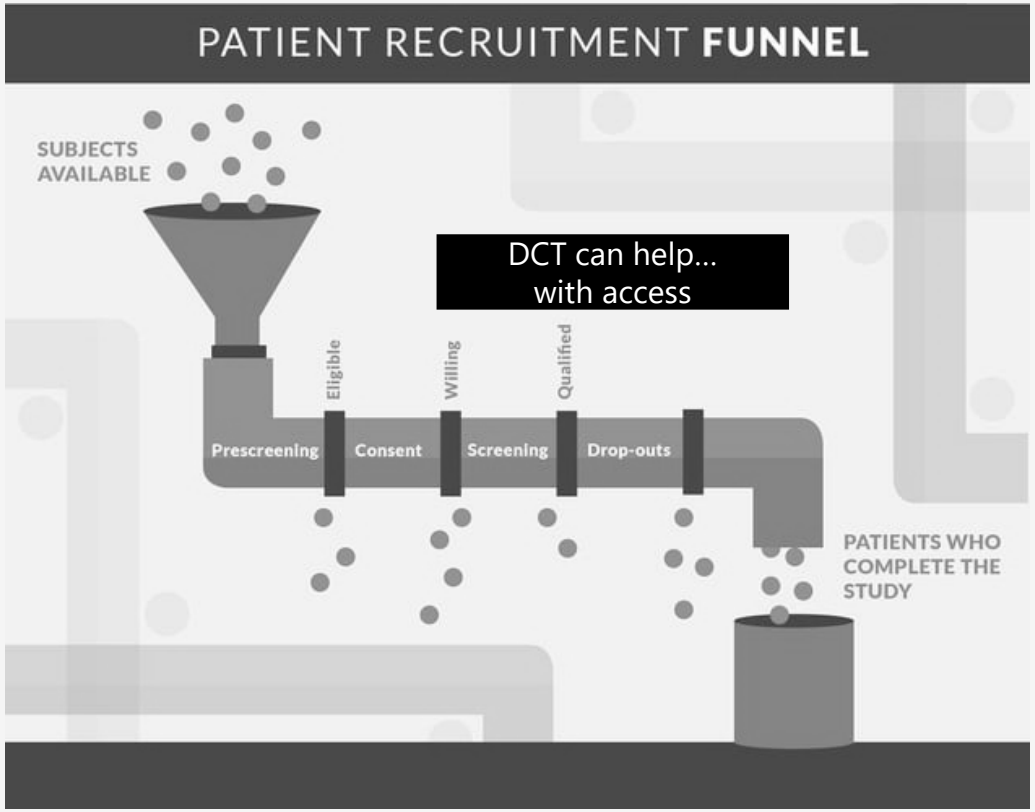
Underserved

Leverage DCT to address barriers with time & travel

Ability Issues

Leverage DCT to support those physically unable to reach a site

Decentralized Contributes to Access [but may also Unlocks the "HCP"]



Investigator Delegation of Activities

FDA

- When permitted by the trial protocol, investigators may delegate trial-related activities to local HCPs to perform trial-related procedures that require in-person interactions with trial participants
- A critical consideration when delegating trial-related activities to local HCPs is the potential for variability in the approach across different practices
- Videoconferencing and other technologies may be useful to allow investigators to oversee trial personnel performing activities described in the trial protocol at participants' locations

Documentation: Investigators, Subinvestigators, Local HCPs

FDA

- Drug trials (Form 1572)
  - When trial personnel contribute directly and significantly to the trial data, they should be included on Form FDA 1572 as subinvestigators
  - Local HCPs (as defined in the draft guidance) should not be listed on Form FDA 1572 as subinvestigators. However, local HCPs should be included in a task log.
- For device trials, local HCPs are generally not considered investigators and should not be included in the IDE list of investigators. However, these local HCPs should be included in a task log

More Investigators Can Bring More Diversity, But Does Not Address Equitable Access

Without addressing the barriers to stimulating referrals into research studies,

"More investigators" (diverse investigators in diverse communities) may help research sponsors enroll more diverse patients

But will not address equitable research access for all.

Access will still be based on serendipity.

For equitable access, we need all providers to have pathways to stimulate referrals

And the draft DCT guidance language on a role for HCPs in research is the right start.

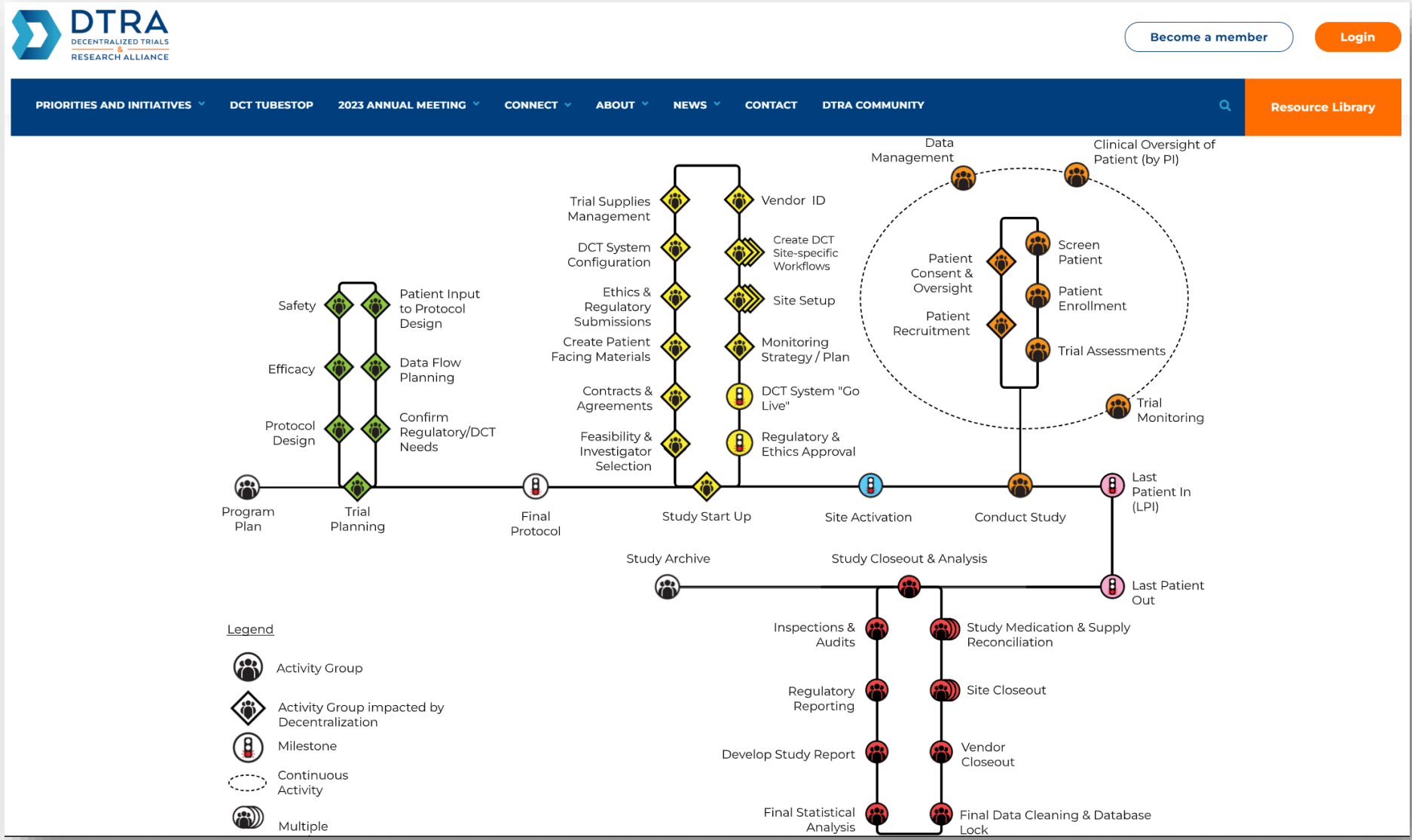
Special Considerations for DCT to Support Diversity

Not a silver bullet
DCT supports access, but still require DAP to ensure representative patients are being invited to participate

Digital divide
Must ensure participation is feasible for those without technology or bandwidth and help support digital literacy

General considerations
- Representative patient insights
- Proper investigator oversight
- Appropriate role for HCPs
- Aspire to optionality and choice
- Patients should feel more connected to care and support

Research Community Resources for DCT at DTRA.org



The Wisdom Study

Laura Esserman, MD MBA
on behalf of the WISDOM consortium

Revolutionizing Breast Cancer Screening
to Ensure that tomorrow will be better than today

Wisdom

A Few Important Things to Know About Screening

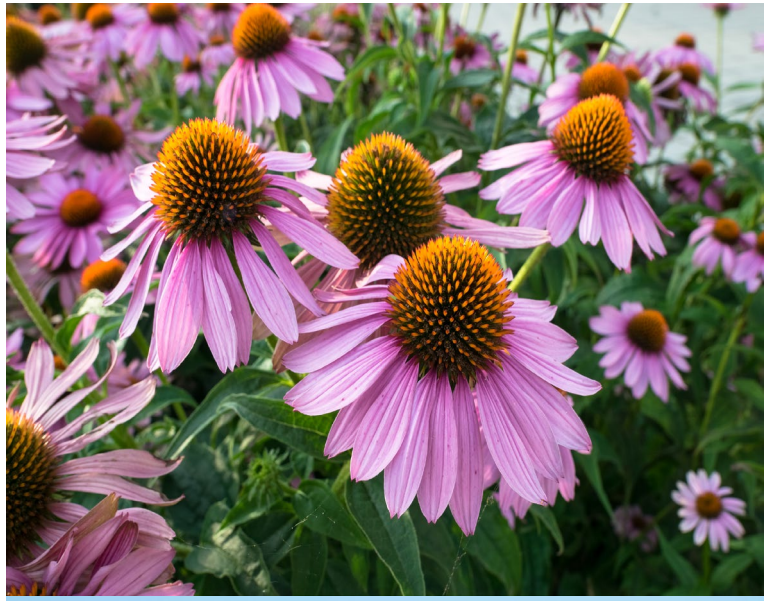
- Screening every year vs every other year has gotten politicized
- Finding cancers under 2cm, equally treatable with identical outcomes
  - Stage 1 cancers HR+, molecularly low risk get endocrine therapy
  - Stage 1 cancers that are Her2+, TNBC- less aggressive
- Mortality is not impacted up to 2cm because of improvement in treatments and outcomes

Wisdom

Where Has Screening Fallen Short?

- 42,370 women still die every year despite screening
- We are not finding the fast growing tumors at earlier stages
  - In the I-SPY TRIAL (stage 2/3 cancers)- the vast majority are NOT screen detected
- We treat stage 0 cancers (DCIS) like stage 1 cancer (likely overtreatment)
- Call back rates are high (especially for women in the 40's)
- We are not using the tools we have to PREVENT breast cancer
  - 276,480 diagnosed in 2021

Wisdom



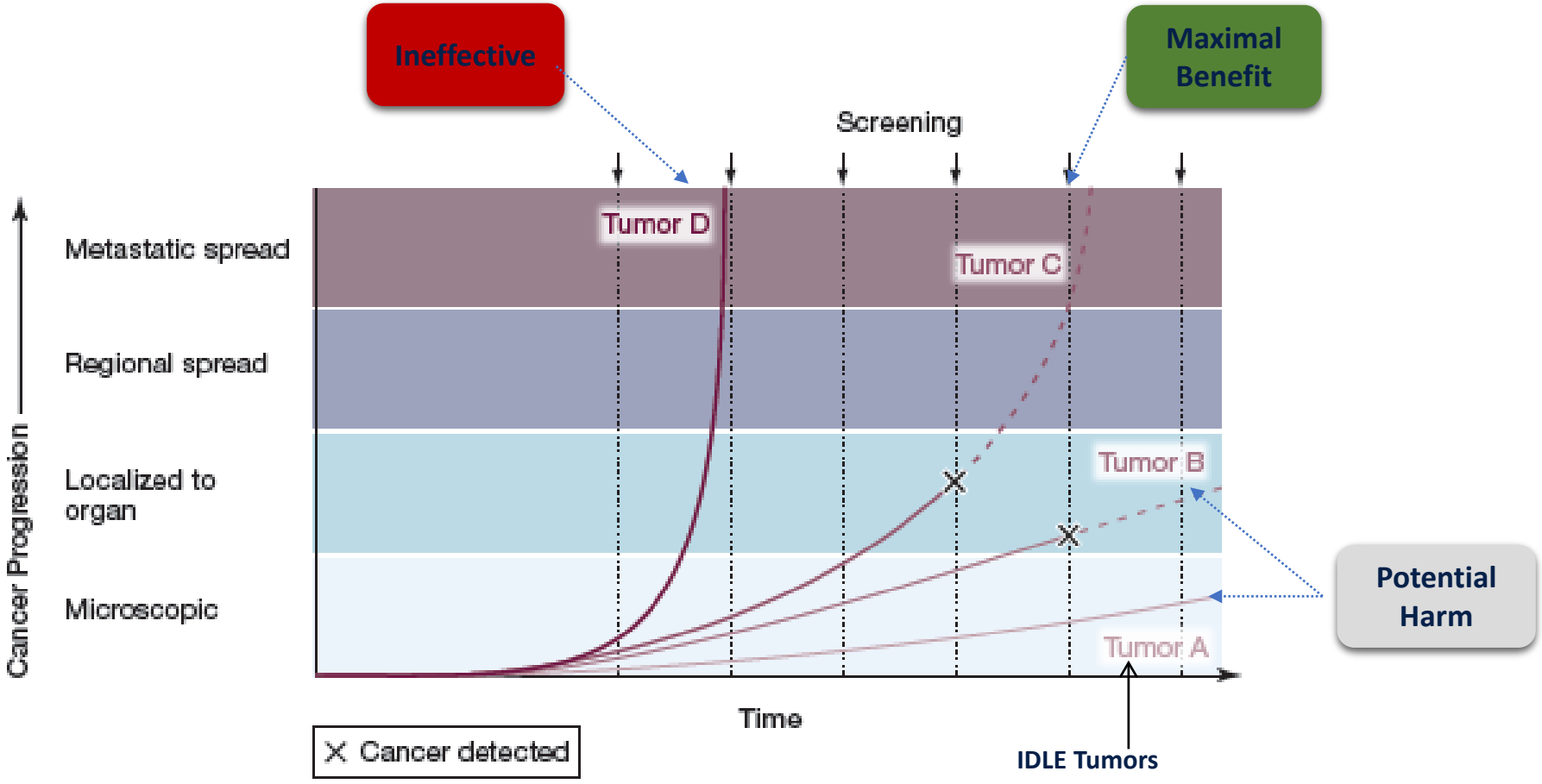

ragweed
allergy


Allergy


1
2

Breast cancer is not a single disease

Rate of tumor progression explains benefit (lack of) from screening



More for the people who need it, less for those who do not

Wisdom

What is the solution? Improve our screening algorithm

- ✓ Integrate risk assessment, screening, and **prevention**
- ✓ Allow women to join regardless of where they get their care
- ✓ Test a strategy where everyone is not screened the same
- ✓ *Improve identification of women at risk for fast growing and "interval" cancers (WISDOM 2.0)*

Wisdom

Wisdom

(Women Informed to Screen Depending on Measures of risk)

A study of women aged 40-75 without a history of breast cancer that compares:

- Personalized breast screening
- Standard (annual) screening

Study Questions

1. **Safety** – Is it just as good at avoiding high risk cancers?
2. **Morbidity** – Will it reduce biopsies & false positives?
3. **Prevention** – Will it encourage prevention in high-risk women?
4. **Acceptance** – Is it accepted by women?
5. **Value** – Is it better?

Accrual ended February 2023; Read out of Trial Feb 2025; WISDOM 2.0 started July 2023

Wisdom

Personalized Screening Group

RISK FACTORS

- **Mammogram**
  -breast density
- **Health Questionnaire**
  -family history, comorbidities, previous biopsies, age, race/ethnicity
- **Genomic profiling**
  -9 Gene Panel, SNPs
  -saliva collection

SCREENING RECOMMENDATIONS (based on risk)

Guidelines-based Frequencies

- No screening until age 50
- Every other year (biennial) mammos
- Annual mammograms
- Annual mammograms + MRI

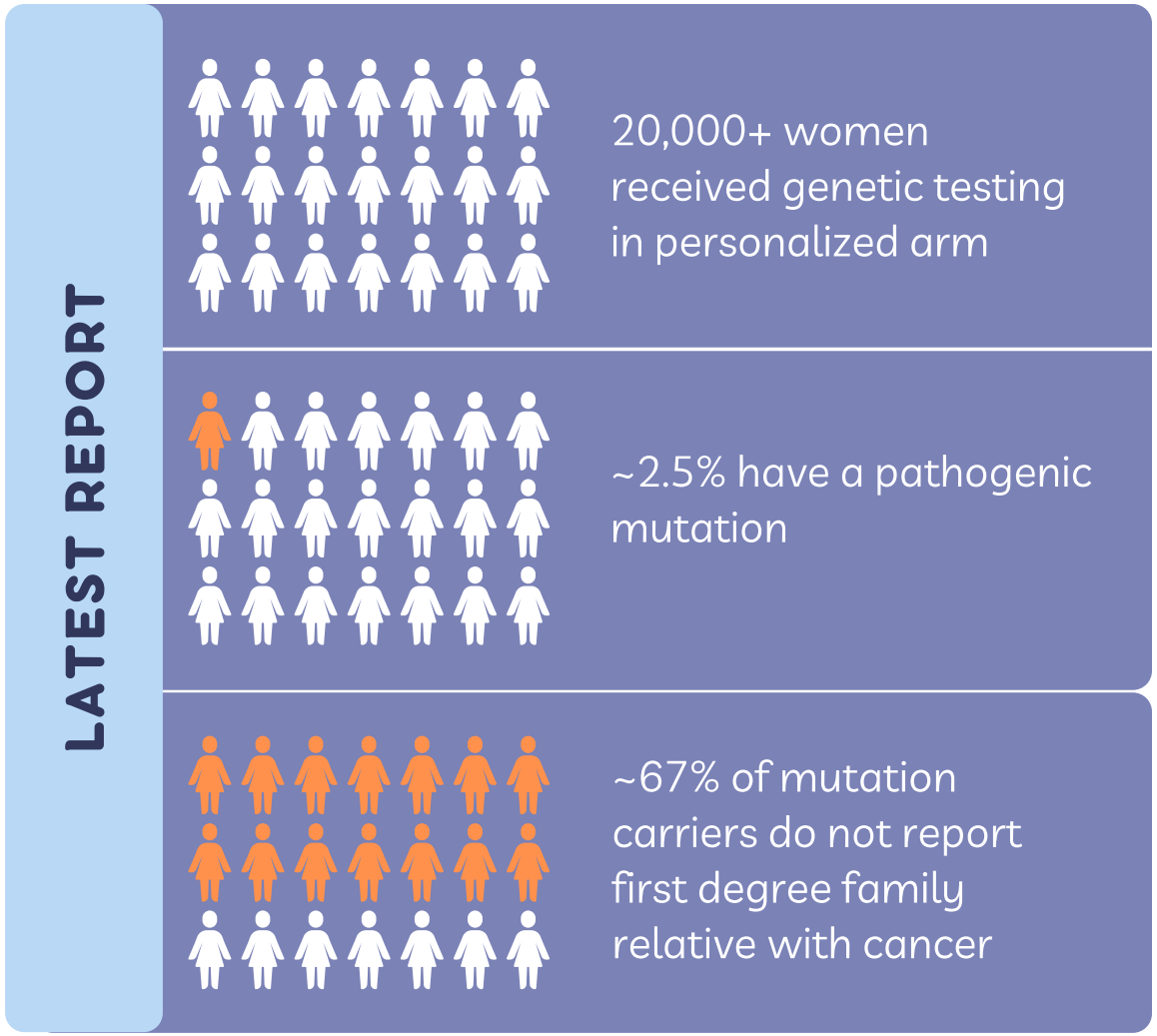
ADDITIONAL SERVICES

(for highest risk cohorts)

- 1:1 Breast Health Specialist
- Breast Health Decisions Tool

Wisdom

WISDOM: Genetic testing

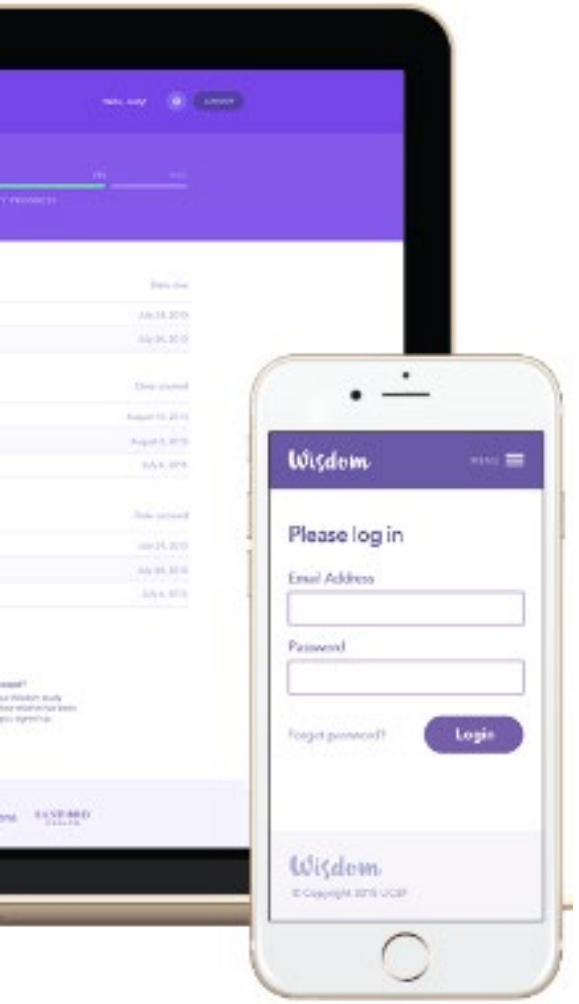


Family history is not the best way to find women who inherit a mutation-

We have a simple test to find these errors- rare but critical and we should look starting at age 30

Wisdom

How do patients participate?



Women enroll and participate online

- No requirement to travel to a recruitment center
- **Study website wisdomstudy.org**
- Mobile, tablets, computers

All study services are rendered virtually

- Breast Health Specialist available telehealth
- No additional visits

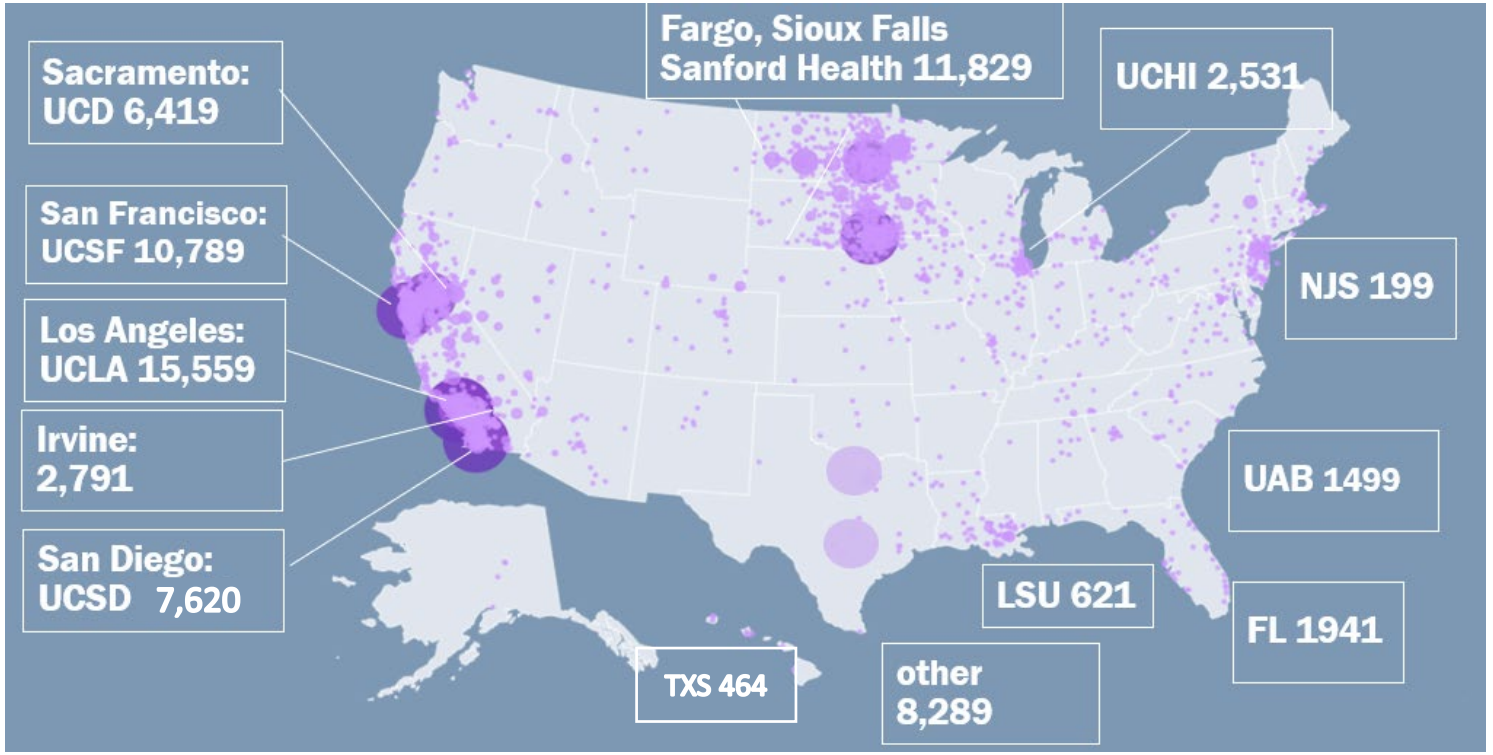
Provide information back to participants

- Deliver screening assignments and reports to personal participant account

Personal and Confidential

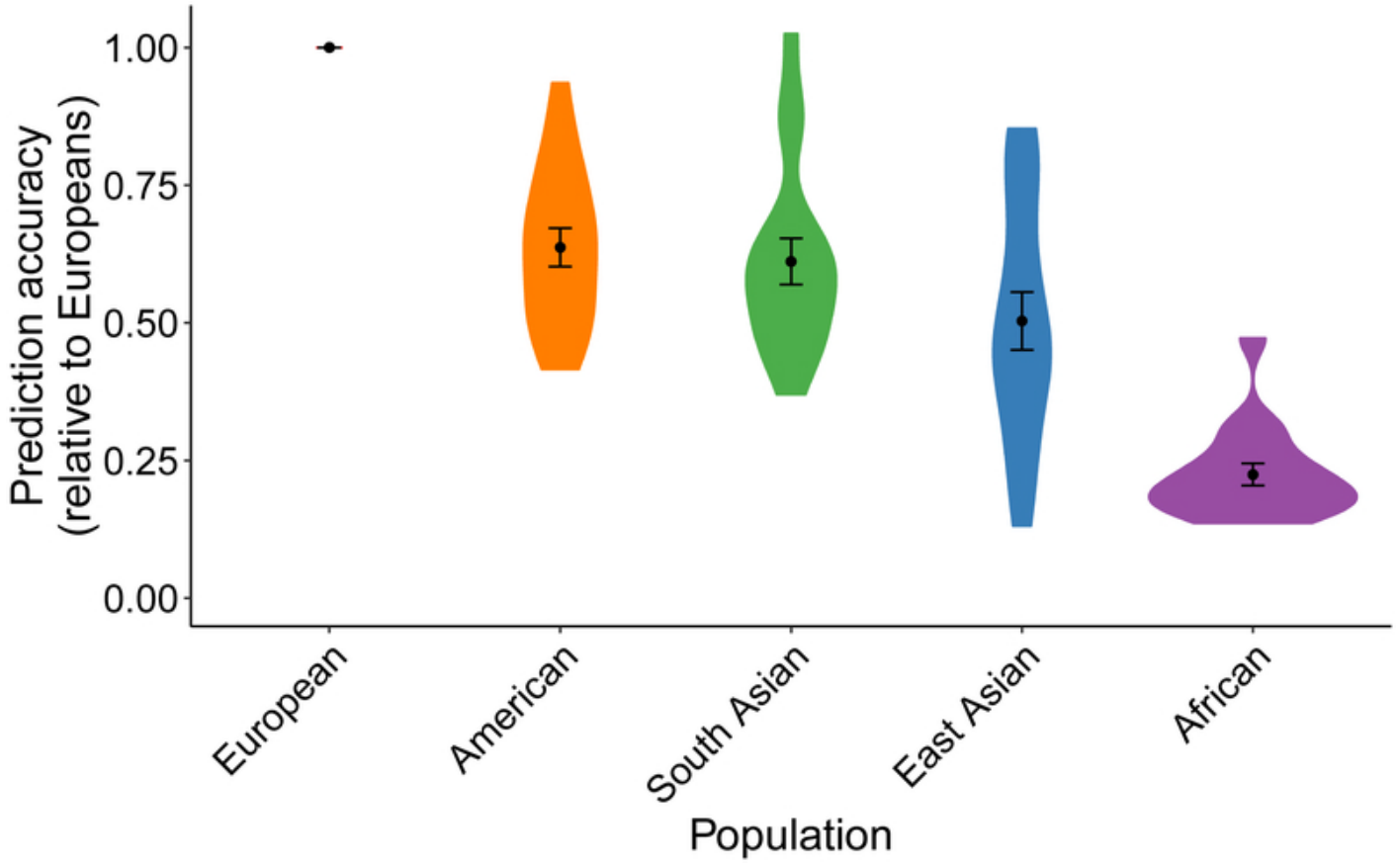
Wisdom impact to date

- Over 55k women across the US have joined
- Women from every state in the US
- Over 20,000 learned their genetic risk for breast cancer
- Over 2,000 learned they are at elevated risk and received counseling from us
- We've identified over 500 active cancers in women who didn't know they had it
    - Self report highly accurate (based on registry, EMR)



Wisdom

Current risk models perform poorly in non-White groups



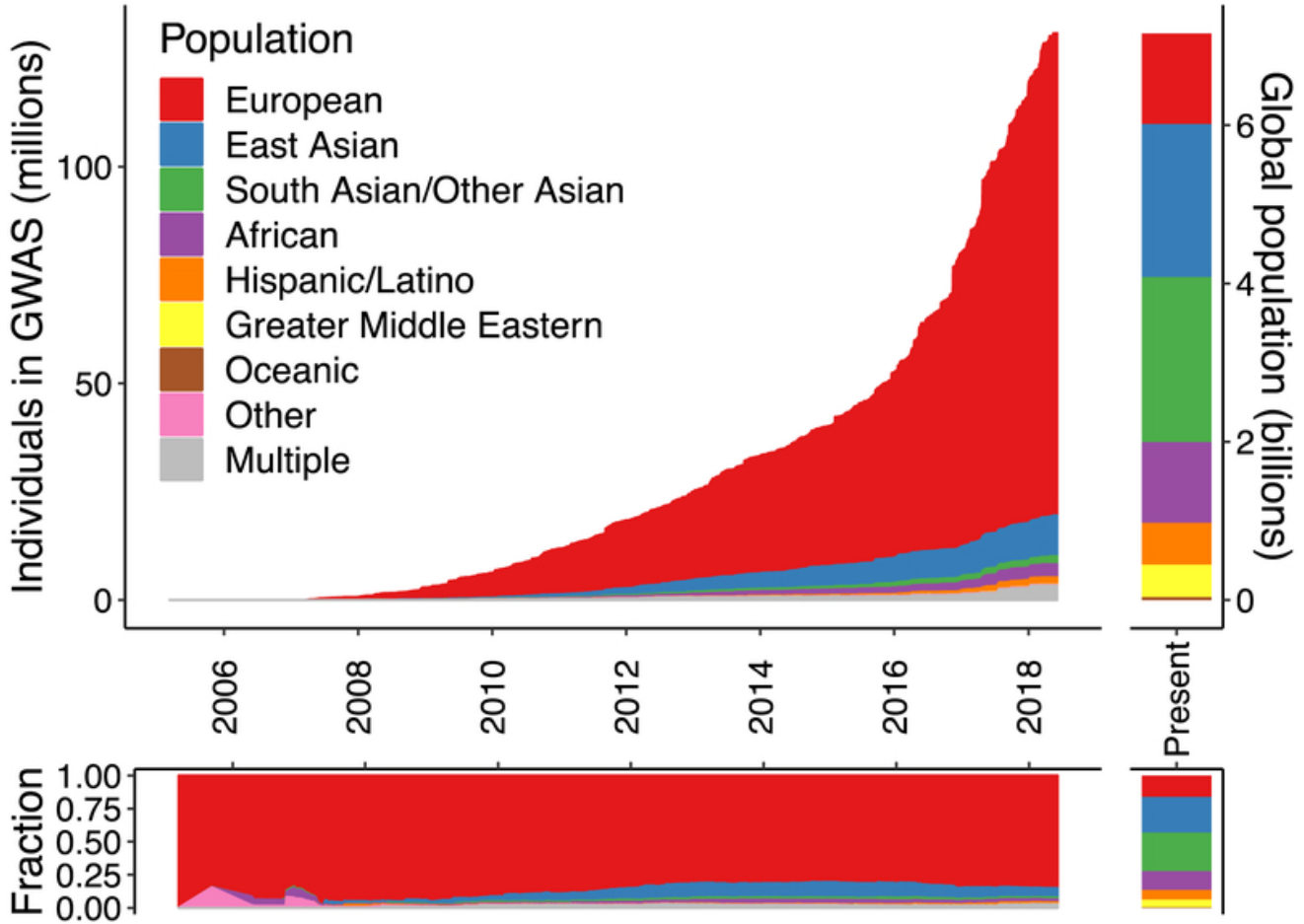
Prediction accuracy relative to European ancestry for 17 quantitative traits
(Martin et al, 2019 Nat Genet.)

Decline in performance with increasing genetic divergence from the training population

In WISDOM- we have ancestry specific SNPs

Wisdom

Low representation of non-White groups



Ancestry of participants in risk studies over time
(Martin et al, 2016 Nat Genet.)

Persons of European ancestry are ~16% of global population but make up 70% of risk studies

- **Availability**
- **Accessibility**
- **Participation**

Wisdom

Improvements in Racial and Ethnic Diversity

- Significant improvement in representation since 2020
- 1.7% Black/African American participants through 2019; in Q4 2022, WISDOM included over 16% Black/AA participants
- Overall study numbers show gradual improvement each quarter and year

Year/Timeframe	White alone, non-Hispanic or Latino	Black or African American alone non-Hispanic or Latino	American Indian and Alaskan Native alone non-Hispanic or Latino	Asian alone, non-Hispanic or Latino	Native Hawaiian and Other Pacific Islander alone, non-Hispanic or Latino	Two or More Race, non-Hispanic or Latino	Hispanic or Latino	Unknown, Prefer not to answer, some other race not listed	Total N
Start-2019	81.4%	1.7%	0.2%	4.5%	0.2%	2.9%	7.9%	1.3%	21,399
2020	74.2%	4.2%	0.3%	6.0%	0.1%	3.4%	10.5%	1.3%	7,725
2021	73.4%	8.1%	0.3%	4.0%	0.1%	0.3%	10.1%	0.8%	10,053
2022	67.1%	11.9%	0.5%	4.6%	0.1%	3.7%	11.5%	0.8%	10,108
Q1 2023	57.9%	18.1%	0.1%	5.6%	0.7%	3.8%	12.2%	1.6%	1,076
All Time	**75.3%**	**5.7%**	**0.3%**	**4.7%**	**0.2%**	**3.2%**	**9.5%**	**1.1%**	**50,300**
US Population	*60.1%*	*13.4%*	*1.3%*	*5.9%*	*0.2%*	*2.8%*	*18.5%*	*n/a*	

Available in English and Spanish

Join now Login En Español

- **Spanish**
  - Printed Materials
  - All study communications, questionnaires, education for high-risk participants, letters

- **Plain-language**
  - Materials tailored to make sure they are understandable to everyone

Supporting the Inclusion of Underrepresented Populations in Clinical Studies: Clinical Endpoints & Study Analysis

Luther T. Clark, MD, FACC
Executive Director
Patient Innovation & Engagement
Global Medical and Scientific Affairs
Merck Research Laboratories
Rahway, NJ, USA

FDA/CTTI Workshop to Enhance Clinical Study Diversity;
Session Number: 4
Appropriate Use of Decentralized Studies, Digital Health Tools, and Other Trial Elements to Support the Inclusion of Underrepresented Populations in Clinical Studies

Thursday, November 30, 2023; 10:35-11:35 AM EST

Barriers to Inclusion in Clinical Trials

Critical Barriers

- Lack of Awareness
- Access
- Mistrust
- Logistical and Resource Constraints
- Shortage of Sites, Networks, and Investigators in Underrepresented Communities

Key Stakeholders

- Patients & Community Members
- Healthcare Providers
- Investigators
- Coordinators, Clinical Sites
- Sponsors

Clark et al. Curr Probl Cardiol 2019; 44:148-172

Bierer B.E., White S.A., Meloney L.G., Ahmed H.R., Strauss D.H., Clark L.T., (2021). Achieving Diversity, Inclusion, and Equity in Clinical Research Guidance Document and Supplementary Toolkit Version 1.2. Available at: https://mrctcenter.org/diversity-in-clinical-trials/

Clinical Trial Endpoints

Endpoints

- Measures designed to test the efficacy and safety of study medications (mortality, disease progression, other clinical events, measures of function, etc.)

Patient-Centered Endpoints

- Outcomes or measures relevant and meaningful to patients, aligned with patient preferences, needs, and priorities (quality of life, knowledge and satisfaction, caregiver burden, etc.)

"The Patient Matters in the End(point)"*

Patient engagement early in trial design, including identification of endpoints that matter to them, can help overcome critical barriers, including mistrust and SDOH, leading to more patient-centered trials, better participant recruitment, retention and outcomes

Clark et al. Curr Probl Cardiol 2019; 44:148-172.

*Griffiths P, Rofail D, Lehner R, Mastey V. The Patient Matters in the End(point). Adv Ther. 2022;39(11):4847-4852.

Clark L. Increasing Diversity in Medicines Discovery, Development, Access & Utilization: The Critical Role of Community Partnerships and Collaborations". *Clinical Leader* (October 6, 2020).

Bierer BE, et al. Achieving Diversity, Inclusion, and Equity in Clinical Research Guidance Document and Supplementary Toolkit Version 1.2. Available at: https://mrctcenter.org/diversity-in-clinical-trials/.

Patient Engagement, Community Partnerships, and Collaborations

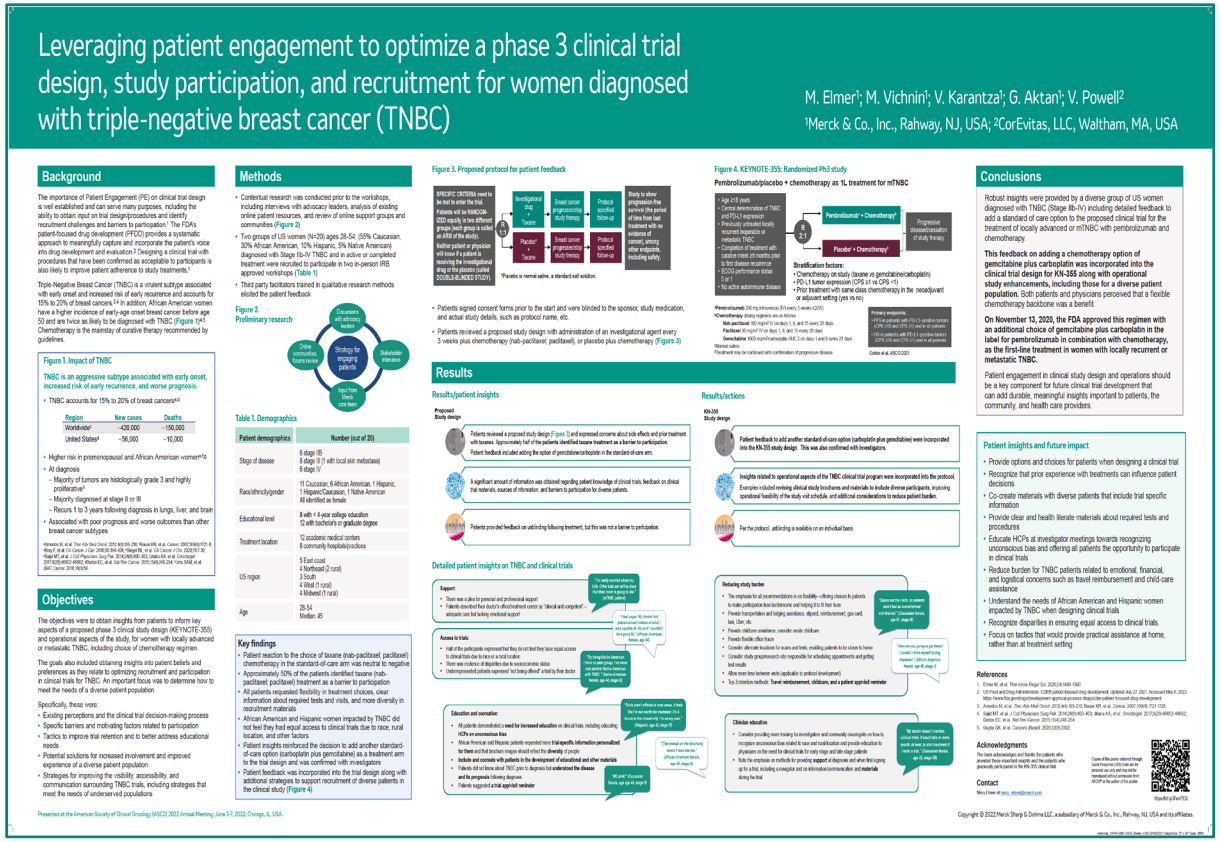
Patient-Centered Research and Outcomes

- Patients, caregivers, and patient advocates advising on all aspects of the research, including patient-relevant, patient-centered endpoints and outcomes

Successful Patient/Community Engagement

- Establishing meaningful partnerships
- Demonstrating mutual benefits
- Collaborating early and often

Patient insights and feedback impacting study design and conduct



Leveraging patient engagement to optimize a phase 3 clinical trial design, study participation, and recruitment for women diagnosed with triple-negative breast cancer (TNBC)

M. Elmer[1]; M. Vichnin[1]; V. Karantza[1]; G. Aktan[1]; V. Powell[2]

[1]Merck & Co., Inc., Rahway, NJ, USA; [2]CorEvitas, LLC, Waltham, MA, USA

Background

Methods

Objectives

Results

Conclusions

Patient insights and future impact

References

Acknowledgments

Contact

Presented at the American Society of Clinical Oncology (ASCO) 2022 Annual Meeting: June 3-7, 2022; Chicago, IL, USA.

Elmer, Mary E; Karantza, Vassiliki; Vichnin, Michelle; Aktan, Gursel; Powell, Valerie J (American Society of Clinical Oncology, 2022-06-01).

Bloom D, et al. The Rules of Engagement: CTTI Recommendations for Successful Collaborations Between Sponsors and Patient Groups Around Clinical Trials. Ther Innov Regul Sci. 2018 Mar;52(2):206-213.

Bierer BE, et al. Achieving Diversity, Inclusion, and Equity in Clinical Research Guidance Document and Supplementary Toolkit Version 1.2. Available at: https://mrctcenter.org/diversity-in-clinical-trials/.

Collins SP, et al. Incorporating Patient and Caregiver Experiences Into Cardiovascular Clinical Trial Design. JAMA Cardiol. 2017:1263-1269.

MERCK

Enhancing Clinical Trial Relevance, Value, and Equity for Underrepresented Populations

Study Relevance and Value

- Results relevant to and understood by participants and communities
- Consistency of treatment benefits and/or risk differences
- Participant experience and feedback to improve design of future trials

"Underrepresented groups acutely feel the disconnect between trial efficacy and real-world effectiveness both because they do not see themselves in trials and because under-representation can affect trial results"

"…enrolling a diverse population provides the best opportunity for an informed analysis of important subgroups, illuminating potential signals of disproportionate benefit or risk…"

Study Attrition: Indicator of Social Vulnerability

- Representative clinical trials includes recruitment, enrollment and equity in trial completion
- Differential attrition of participants can lead to bias and limit generalizability of results
- Participant attrition may be associated with financial resource strain and/or other vulnerability indicators, independent of race or gender
- Understanding differential attrition may help advance patient care, outcomes and equity

Shah SJ, Essien UR. Equitable Representation in Clinical Trials: Looking Beyond Table 1. Circ Cardiovasc Qual Outcomes. 2022 May;15(5).

Bierer B.E., White S.A., Meloney L.G., Ahmed H.R., Strauss D.H., Clark L.T., (2021). Achieving Diversity, Inclusion, and Equity in Clinical Research Guidance Document and Supplementary Toolkit Version 1.2. Cambridge and Boston, MA: Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center). Available at: https://mrctcenter.org/diversity-in-clinical-trials/.

Collins SP, Levy PD, Holl JL, Butler J, Khan Y, Israel TL, Fonarow GC, Alikhaani J, Sarno E, Cook A, Yancy CW. Incorporating Patient and Caregiver Experiences Into Cardiovascular Clinical Trial Design. JAMA Cardiol. 2017 Nov 1;2(11):1263-1269. doi: 10.1001/jamacardio.2017.3606. PMID: 29049526.

Relationship Between Social Vulnerability Indicators and Trial Participant Attrition: Findings From the HYVALUE Trial
Kamal H. Henderson, MD, MSc, Laura J. Helmkamp, MS, John F. Steiner, MD, MPH, Edward P. Havranek, MD, Suma X. Vupputuri, PhD, Rebecca Hanratty, MD, Irene V. Blair, PhD, Julie A. Maertens, PhD, Miriam Dickinson, PhD, Stacie L. Daugherty, MD, MSPH

National Academies of Sciences, Engineering, and Medicine. 2022. Envisioning a Transformed Clinical Trials Enterprise for 2030: Proceedings of a Workshop. Washington, DC: The National Academies Press. https://doi.org/10.17226/26349.

Equitable Clinical Trial Representation Beyond Recruiting and Enrollment: Gateway to Innovative Therapies

Advancing science, health care solutions, health outcomes, confidence in trial results and equity

Schwartz AL, et al. Why Diverse Clinical Trial Participation Matters. N Engl J Med 2023; 388:1252-1254.
Bierer BE, et al., Achieving Diversity, Inclusion, and Equity in Clinical Research Guidance Document and Supplementary Toolkit Version 1.2. Available at: https://mrctcenter.org/diversity-in-clinical-trials/
Collins SP et al. JAMA Cardiol. 2017;2(11):1263-1269.
Henderson KH, et al. Circ Cardiovasc Qual Outcomes. 2022 May;15(5).
National Academies of Sciences, Engineering, and Medicine. 2022. Envisioning a Transformed Clinical Trials Enterprise for 2030: Proceedings of a Workshop. Washington, DC: https://doi.org/10.17226/26349.

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Achieving Increased Clinical Trial Inclusion and Participation

Patient-Centered

- Patient and community awareness, education, training, partnerships and collaborations
- Achieving optimal outcomes with minimal added burden to patients
- Meaningful, ongoing patient engagement
- Earning and building trust and trustworthiness

Inclusive Study Design and Conduct

- Meaningful, relevant, measurable & equitable endpoints and outcomes for patients and communities

Sustainability

- Demonstration of benefits, implications and relevance of study findings for impacted individuals and communities
- Equitable representation beyond recruiting and enrollment
- Recognition and addressing social determinants of health (SDOH) and vulnerability indicators

Thank you

Session 5A: Post-Approval Dissemination of Clinical Study Enrollment Demographic Data to Public

Moderator: James Hildreth
President and CEO,
Meharry Medical College

Paula Boyles
External Clinical Trial Data Sharing Program Lead, Pfizer

Cynthia Chauhan
Patient Representative/Advocate, Independent

Tarek Hammad
VP, Head of Medical Safety, Marketed Products, GPSE, Takeda Pharmaceutical Company

Barbara Bierer
Professor of Medicine, Center for Bioethics, Harvard Medical School

FDA / CTTI Workshop to Enhance Clinical Study Diversity

Post-Approval Dissemination of Clinical Study Enrollment Demographic Data to the Public

Presented by Paula Boyles

Health information equity helps improve patient outcomes

Health information equity is the sharing of information in a way that is accessible and **understandable to all people**, allowing everyone to **reach their full potential for health**.[1]

Studies show that **low health literacy** (the degree to which individuals can understand and use information to inform health-related decisions)[2] can **increase mortality rates**.[3-5]

People with the knowledge needed to become **actively engaged in their health care** have **better outcomes, according to research.**[6]

To achieve **better health outcomes**, we must produce patient-facing **content that is easy to read, understand** and act on.[7]

[1]Berkman https://doi.org/10.1002/aris.1440370112

Information Equity – Introduction to design Equity (umn.edu)

Health equity Leadership & Exchange Network, 2020

[2]What Is Health Literacy? | Health Literacy | CDC

[3]Berkman ND, Sheridan SL, Donahue KE, et al. low health literacy and health outcomes: an updated systematic review. *Ann Intern Med*. 2011;155(2):97-107. doi: 10.7326/0003-4819-155-2-201107190-00005

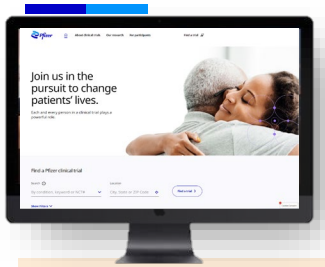
[4]Mitchell SE, Sadikova E, Jack BW, Paasche-Orlow MK. Health literacy and 30-day post discharge hospital utilization. *J Health Commun.* 2012;17(suppl 3):325-338. doi: 10.1080/10810730.2012.715233

[5]Bostock S, Steptoe A. Association between low functional Health health literacy and mortality in older adults: longitudinal cohort study. BMJ. 2012;344; e1602. doi:10.1136/bmj.e1602

[6]CDC: Patient Engagement | Health Literacy | CDC

[7]Shoemaker SJ, Wolf MS, Brach C. Development of the Patient Education Materials Assessment Tool (PEMAT): a new measure of understandability and actionability for print and audiovisual patient information. Patient Educ Couns. 2014;96(3):395-403. doi: 10.1016/j.pec.2014.05.027

Pfizer



The Pfizer Clinical Trials Ecosystem delivers a World Class consumer experience for Participants

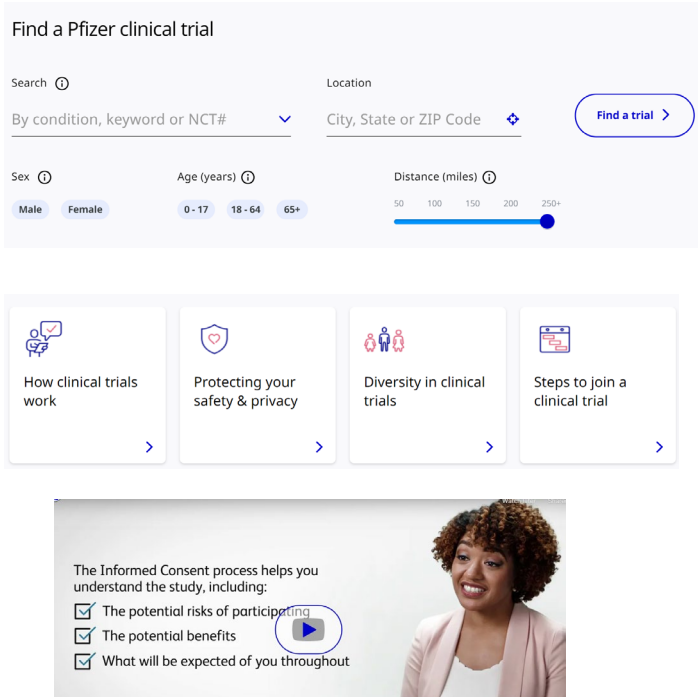
Information Seekers

Awareness → Education → Action

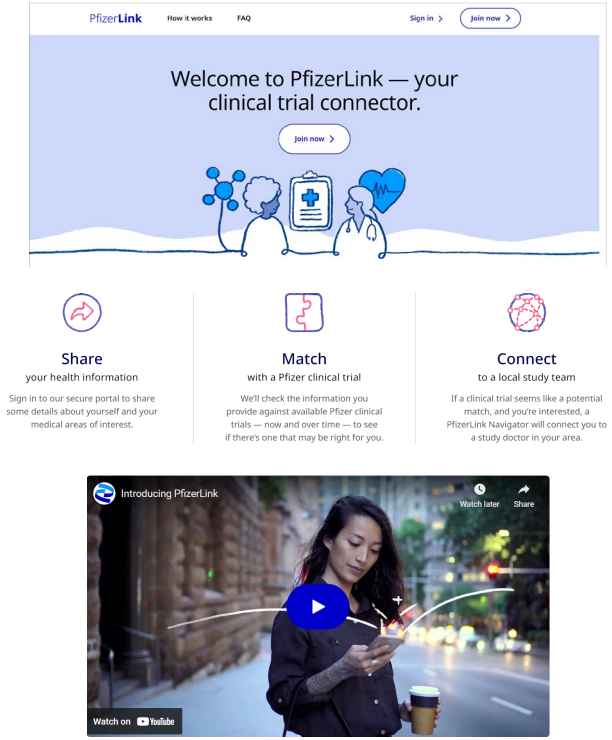
Former Participants

→ Get back

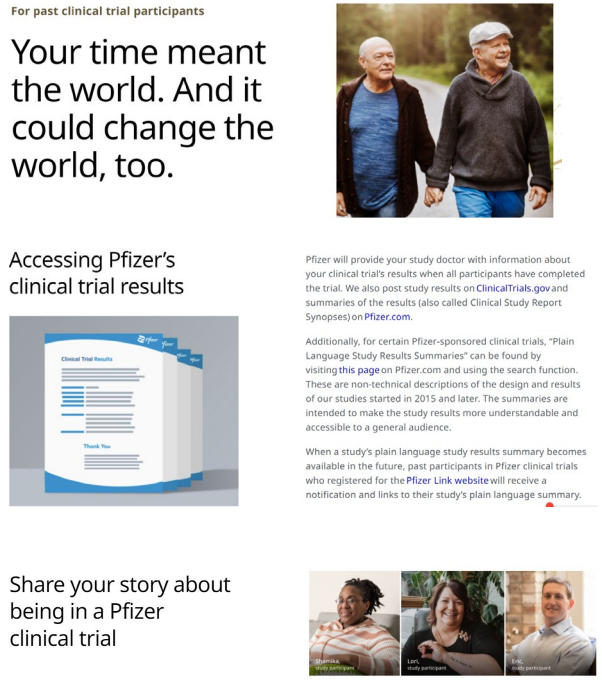
PfizerClinicalTrials.com



PfizerLink.com

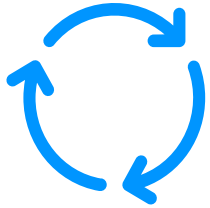


PfizerClinicalTrialAlumni.com

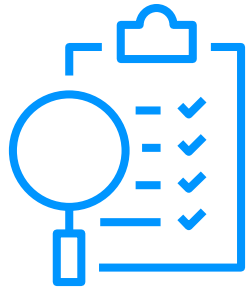


Pfizer is committed to Health Equity via Participant Data Return

Fulfill our social contract with participants by **enabling** response to any data requests and allowing patients to **opt-in** to data return



Empower participants with data based upon accepted health literacy principles to make more informed healthcare decisions by providing necessary context to their clinical trial data, and **facilitate** continued care beyond trial



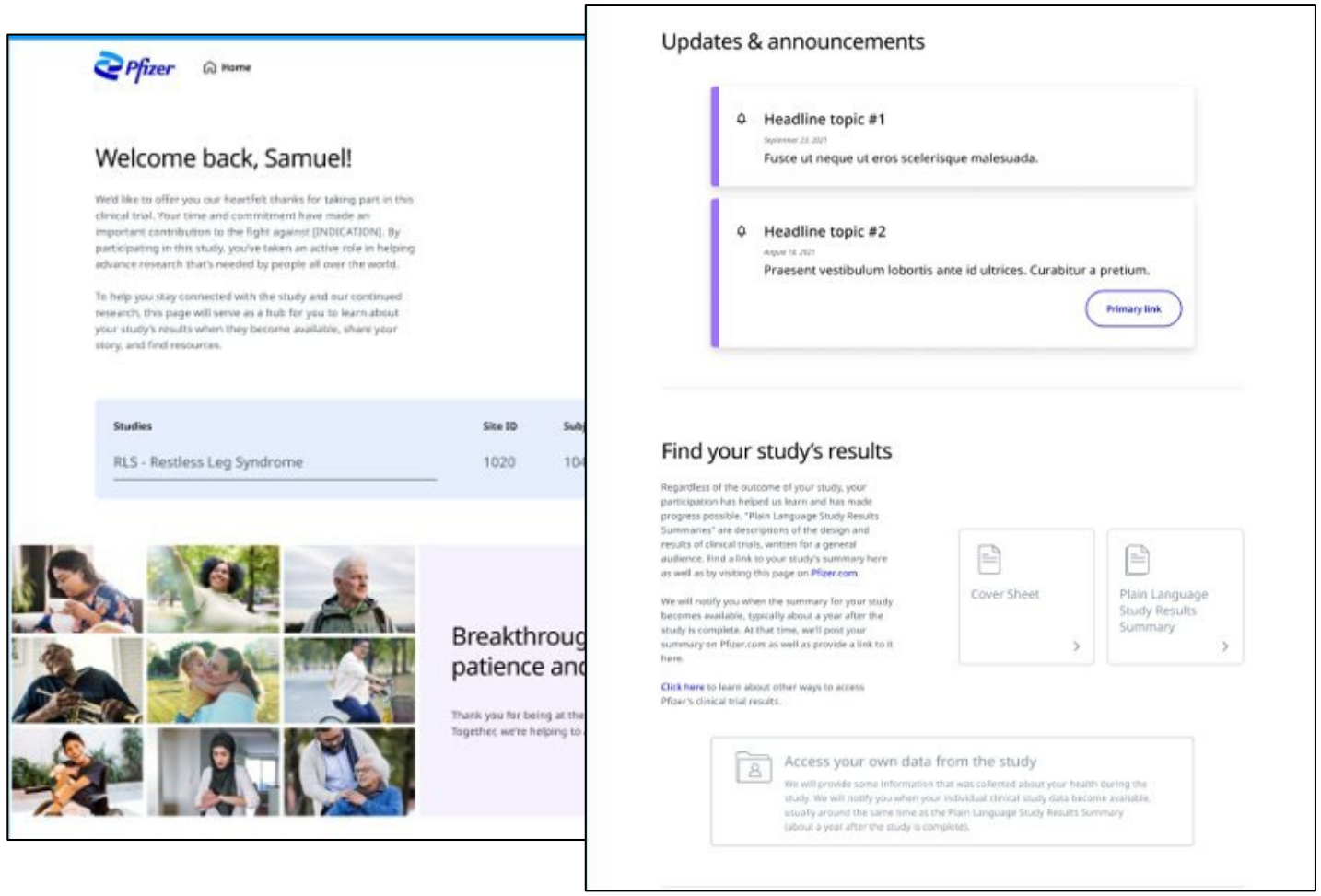
Maintain engagement with participants to **improve** trial experience, and in turn **optimize** trial adherence and retention

Clinical Trial Participants have **demanded** the ability to **Access, Visualize,** and **Share** their data, and Clinical Researchers have a responsibility to provide more Transparency and Engagement with participants

Pfizer Clinical Trial Alumni Site (PCTA)

PfizerClinicalTrialAlumni.com is an opt-in portal that helps Pfizer clinical trial participants find information, resources, and data related to their current or prior study.

PCTA allows participants to feel connected to Pfizer and their trial, well after their study has completed.



TransCelerate's Individual Participant Data Return (iPDR) initiative is developing solutions to support flexible processes for the planned, intentional, and meaningful return of pre-defined individual data to participants who choose to receive it

Participant Data Return Resource Pack [PUBLICLY AVAILABLE]

A document that provides access to a consolidated set of resources from across the clinical research ecosystem that can assist with returning individual data globally.

Individual Participant Data Return Package [COMING SOON]

Considerations Guide

Provides considerations for implementing the return of individual data

Template

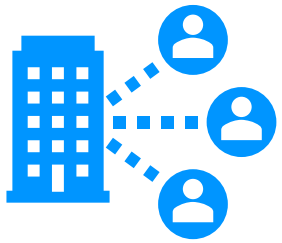
Provides a customizable template example of how a study team might capture important operational details for enabling individual data return at a study or program level

Socialization Presentation

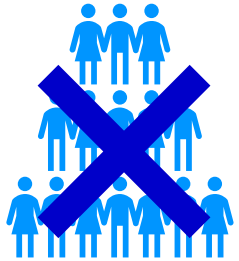
A presentation to educate key internal stakeholders of the potential value of returning participant data in clinical studies and to obtain support to operationalize within sponsor organization

TransCelerate BIOPHARMA INC.

Conclusion



Common efforts across industry



Solutions are **NOT “one size fits all”**

Ensure we reach **ALL populations globally**

U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Session 5B: Community Engagement

Moderator: Tesheia Johnson
Deputy Director and COO, Yale Center for Clinical Investigation

Ileana Pina
Professor of Medicine, Thomas Jefferson University

B. Angeloe Burch, Sr.
African American Community Collaborative, Inc.

Reed Tuckson
Managing Director, Tuckson Health Connections, LLC

Perla Nunes
Perla Nunes, Consulting

Billy Caceres
Assistant Professor, Columbia University School of Medicine

Kali Zhou
Assistant Professor of Clinical Medicine, Keck School of Medicine, University of Southern California

Enhance Clinical Study Diversity

The Role of Community

- The Definition of Community
  - Geographical
  - Racial
  - Ethnicity
  - Sex
  - Age

Whose responsibility to enroll or support diversity in clinical trials.

Need to bring the patients into the clinic environment prior to enrollment in clinical trials.

Pts in clinic make the best participants in RCT's

Who to train?

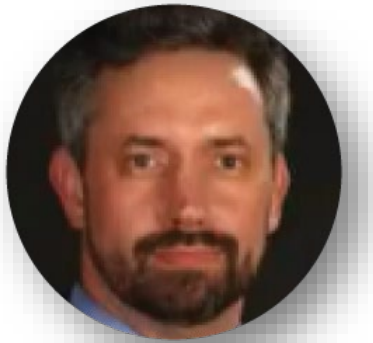
Session 6: Moving Forward

Moderator: Nakela Cook
Executive Director, Patient-Centered Outcomes Research Institute

Peter Marks
Director, Center for Biologics Evaluation and Research, FDA

Jeff Shuren
Director, Center for Devices and Radiological Health, FDA

Peter Stein
Director, Office of New Drugs, Center for Drug Evaluation and Research, FDA



Marc Theoret
Deputy Director, Oncology Center for Excellence, FDA

Meghan McKenzie
Patient Inclusion and Health Equity, Chief Diversity Office, Genentech

Day 2 Closing Remarks

Karen Hicks

Deputy Director, Office of Medical Policy
Center for Drug Evaluation and Research
FDA

Public Workshop to Enhance Clinical Study Diversity

CLOSING REMARKS
Day 2

Karen A. Hicks, M.D., FACC
Deputy Director, Office of Medical Policy
Center for Drug Evaluation and Research
Food and Drug Administration

November 30, 2023

FDA has a longstanding commitment to promote diversity in clinical trials

- Let's not wait for Congress to pass additional legislation to move the needle
- Responsive guidelines that are informed by the community
- Engagement and communication
  - Sharing ideas
  - Sharing experiences
  - Sharing best practices
- Implementation of innovative approaches
  - **"What got us here won't get us there"**

Patients First

- Acknowledge earned mistrust and establish trust
- Address the fear
- Invite patients to participate
- Simplify informed consent
- “Treat others the way ***YOU*** want to be treated”
- Create clinical trial environments that reflect love and care
  - Warm blankets
  - Patient concierges (travel and transportation reimbursement, coordinate appointments, more)
- Eliminate the enrollment gaps
  - Remuneration
  - Other strategies
- Meet patients where they are
- Shift paradigm from protecting patients ***from*** research to protecting patients ***through*** research
- Include patients and trial participants as ***trusted partners in research***

Understand the Demographics and the Reasons

- All approached patients
  - Those not enrolled in the trial
    - Screen Failures
      - "Physician Discretion"
      - Scientific basis for exclusion/safety concern
    - Eligible patients that do not sign the informed consent
  - Those enrolled in the trial
    - Patients that discontinue from the trial or withdraw consent for participation

Monitor Enrollment Diversity throughout Trial Conduct

- Sponsors
  - Diversity Dashboards
- Data Monitoring Committees

Diversity is needed every step of the way

- FDA
- Industry
- Academic Institutions
- Institutional Review Boards
- Clinical Investigators
- Trial personnel
- Clinicians
- Participants
- Patient Advocacy Groups
- Health care systems
- Other members of the diversity community

Training and Education are Critical

FDA is committed to enhancing diversity in clinical trials

Our policies:

- Focus on the diversity of the **population** that will use the medical product, if approved
- Support a pragmatic **approach**
- Encourage the use of **clinical trial designs** that **minimize complexity and reduce burden**
- Leverage **innovative "fit for purpose" technology**
- Incorporate **learnings** from innovative trial designs and lessons learned from public health emergencies
- Promote **fit-for-purpose** approaches as well as innovations in design and technologies
- Encourage **better informed consent process**
- Facilitate the utilization of available **healthcare infrastructure,** processes, and workforce

To Achieve Meaningful Representation in Clinical Trials

It Takes a Village!

Post Comments to FDA Public Docket

FDORA Public Workshop to Enhance Clinical Study Diversity

A docket is open for the public to submit electronic or written comments related to the topics addressed during this workshop.

[Link to provide comments to the docket]

Docket Number: FDA-2023-N-2462

Comment Period Closes: January 29, 2024


FDA
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