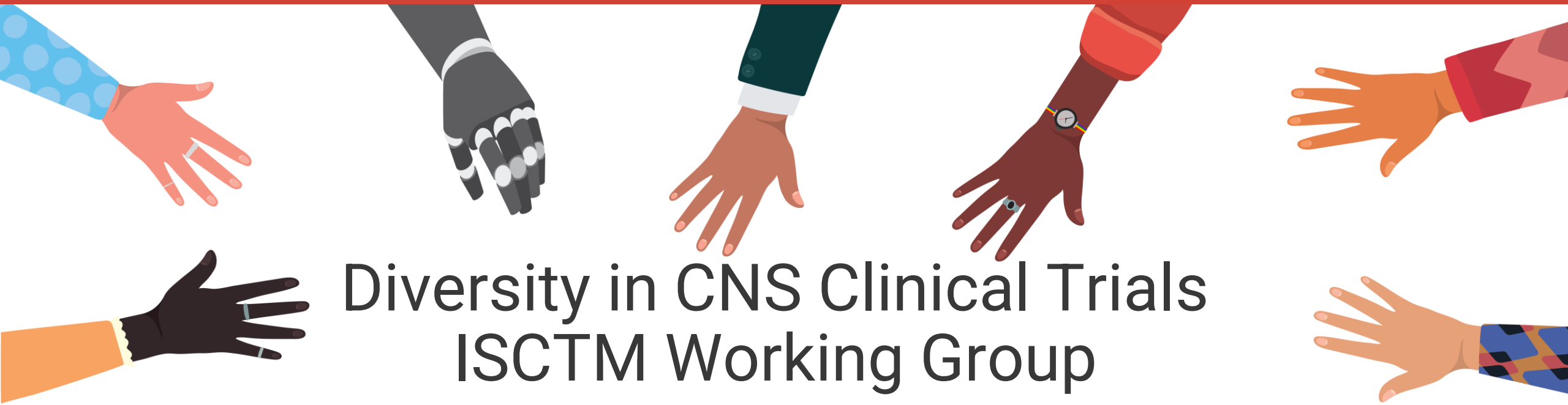
ISCTM

International Society for CNS Clinical Trials and Methodology



Diversity in CNS Clinical Trials
ISCTM Working Group

Feb 21 – 4.40-6.15 PM

Disclosures

Sian Ratcliffe

- Head of Global Clinical Operations, Analytics, Technology & Data Sciences
- Employee and shareholder of Biogen
- Shareholder of Pfizer
- Data presented today is not linked to any Biogen studies/trials
- Opinions = mine

Abhi Pratap

- Senior Clinical Program Leader, CNS
- Employed by Boehringer Ingelheim
- Data presented today is not linked to any Boehringer Ingelheim studies/trials
- Opinions = mine
- Examples from published research for educational purposes only

Academic Affiliations

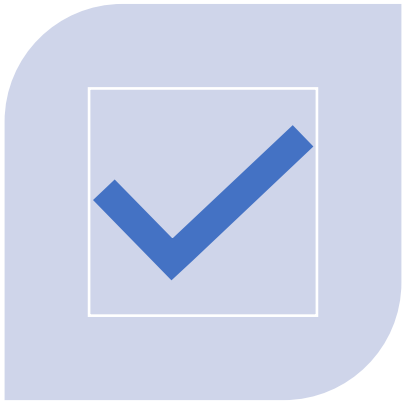
- Visiting fellow, Kings College London, UK
- Fellow, Boston University, USA
- Adjunct Faculty, University of Washington, USA

Agenda

- Introductions
- Goals & Logistics
- Diversity in CNS Trials
  - Representation & **Beyond**
  - Challenges
  - Solutions, real-world experiences and best practices
- Next Steps

Introductions

NAME, AFFILIATION



CURRENT FOCUS IN CNS

BRIEFLY, WHAT “DIVERSITY IN CNS” MEANS TO YOU

Key Goals

- Diversity in the context of CNS
- Real-world experiences / solutions
- Assess need for establishing a longer-term working group and setup deliverables

Logistics

NOTE-TAKERS

CURATING IDEAS

Agenda

- Introductions
- Goals & Logistics
- Diversity in CNS Trials
  - Representation & **Beyond**
  - Challenges
  - Solutions, real-world experiences and best practices
- Next Steps

Race/ethnicity reporting and representation in US clinical trials: A cohort study

Brandon E. Turner,[a,b,*] Jecca R. Steinberg,[a] Brannon T. Weeks,[a] Fatima Rodriguez,[c] and Mark R. Cullen[d]

N = 20,000+ trials

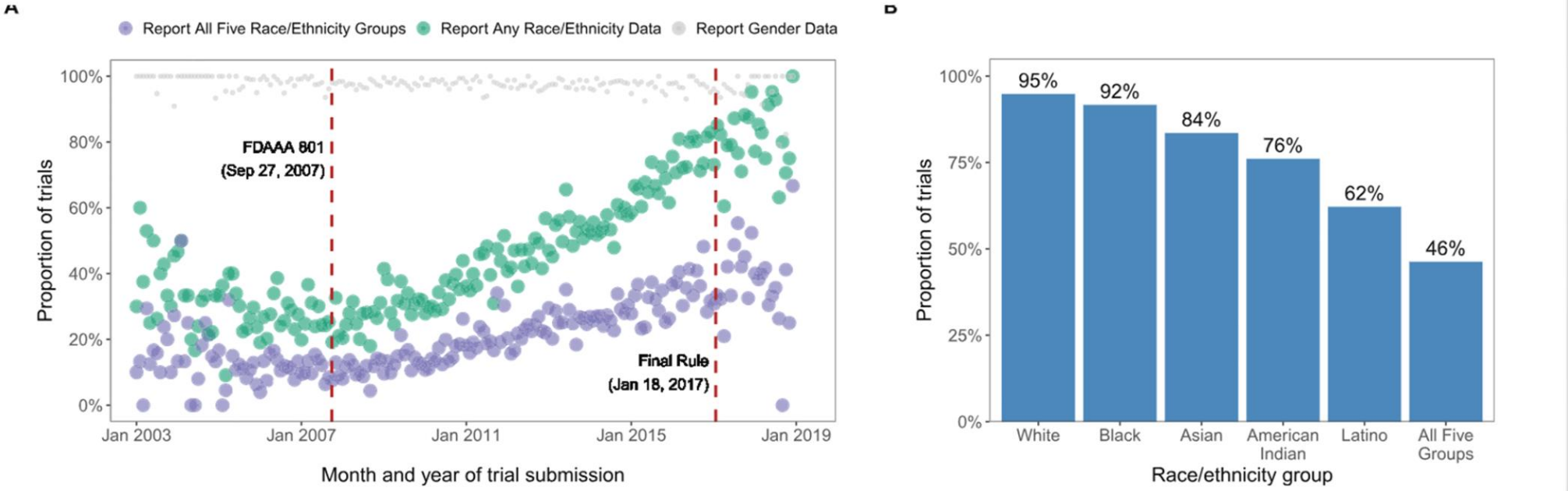


Figure 2. Race and ethnicity enrollment reporting in United States-based clinical trials registered on ClinicalTrials.gov.

Panel A shows change over time in proportion of trials reporting race/ethnicity enrollment data. All Five Race/Ethnicity Groups include White, Latino, Black, Asian (including Pacific Islander and Native Hawaiian), and American Indian (including Alaskan Native). *Panel B* shows the races/ethnicities that were reported among trials that included any race/ethnicity enrollment results data and the proportion of those trials that reported each individual race/ethnicity.

Clinical research need to reflect the growing social, racial and ethnic diversity of the US population

Underrepresentation of target population in medical product development can make generated evidence inapplicable to those who weren’t included in the trials and, therefore, biased

GUIDANCE DOCUMENT

Diversity Plans to Improve Enrollment of Participants From Underrepresented Racial and Ethnic Populations in Clinical Trials; Draft Guidance for Industry; Availability

Draft Guidance for Industry

APRIL 2022

Download the Draft Guidance Document | Read the Federal Register Notice

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NEWS | 16 February 2023

FDA to require diversity plan for clinical trials

US regulatory agency makes 'big change' to increase the number of participants from under-represented groups in drug testing.

Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials Guidance for Industry

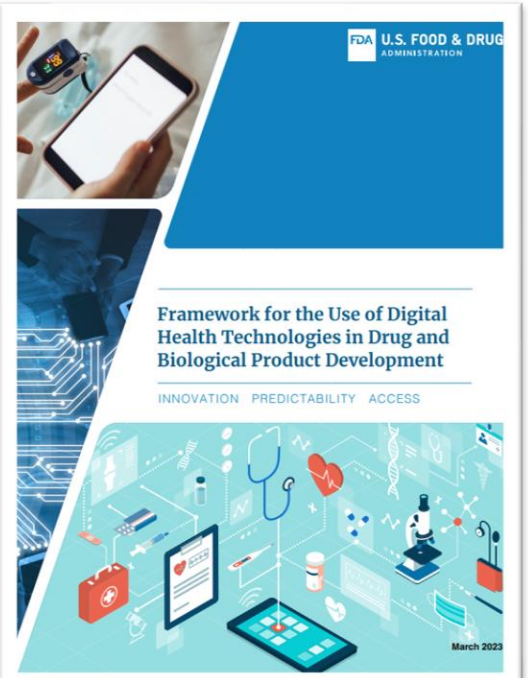
DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (OCE/CDER) Lola Fashoyin-Aje, 240-402-0205, (CBER) Office of Communication, Outreach, and Development, 800-835-4709, or 240-402-8010, or CDRHClinicalEvidence@fda.hhs.gov.

U.S. Department of Health and Human Services



Proceedings of a Workshop

STRATEGIES FOR ENSURING DIVERSITY, INCLUSION, AND MEANINGFUL PARTICIPATION IN CLINICAL TRIALS

Patient-Focused Drug Development: Methods to Identify What Is Important to Patients

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

February 2022
Procedural

[Virtual Public Workshop to Enhance Clinical Study Diversity (FDORA) - CTTI (ctti-clinicaltrials.org)]

Advancing the Landscape: Increasing Diversity in Clinical Trials

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Key Takeaways

FDA

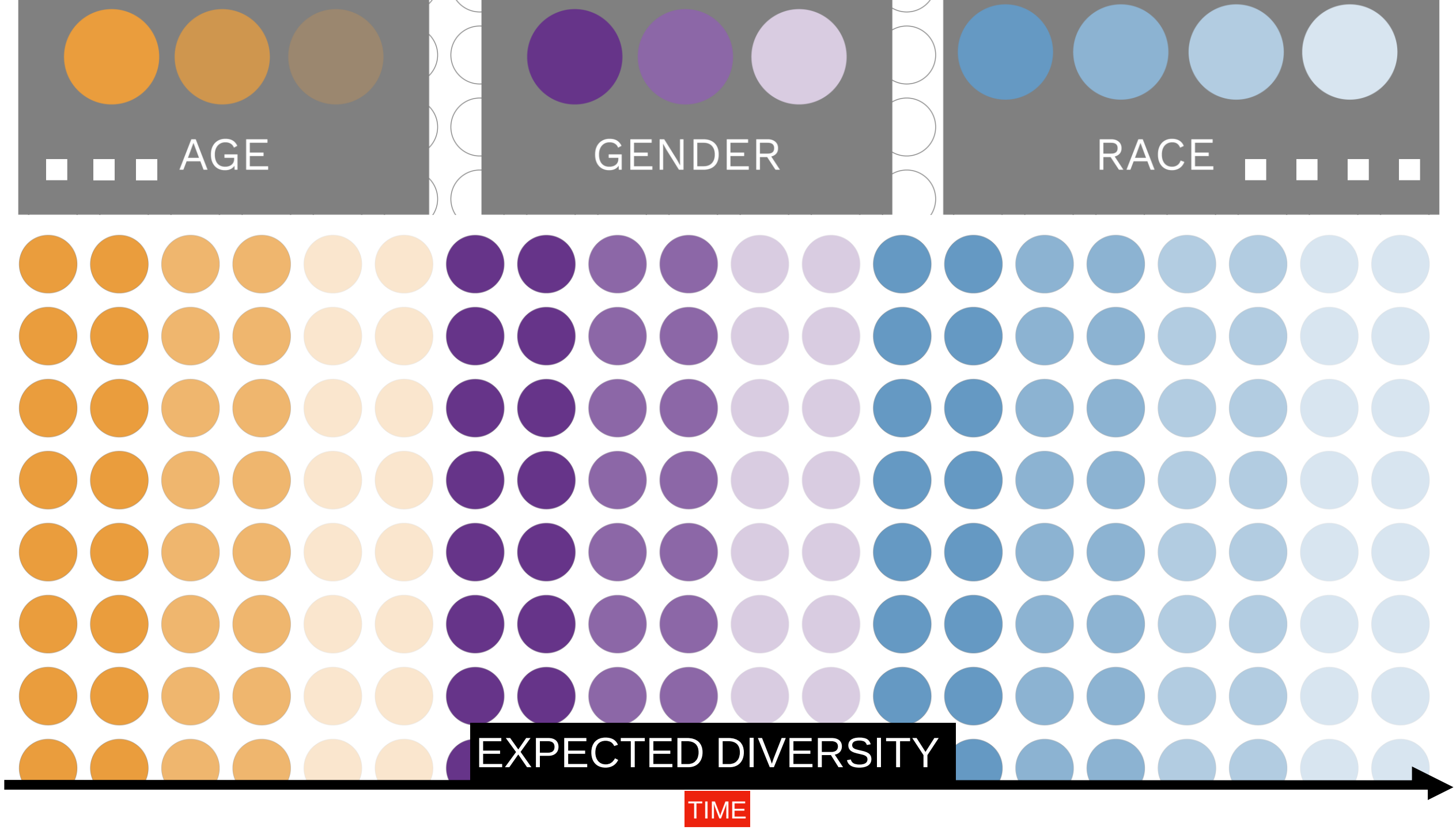
- FDA has a longstanding commitment to promote diversity and inclusion of underrepresented populations in clinical trials.
- Enrollment in clinical trials should, to the extent possible, reflect the diversity of the population that will use the medical product, if approved.
- A pragmatic approach that 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.

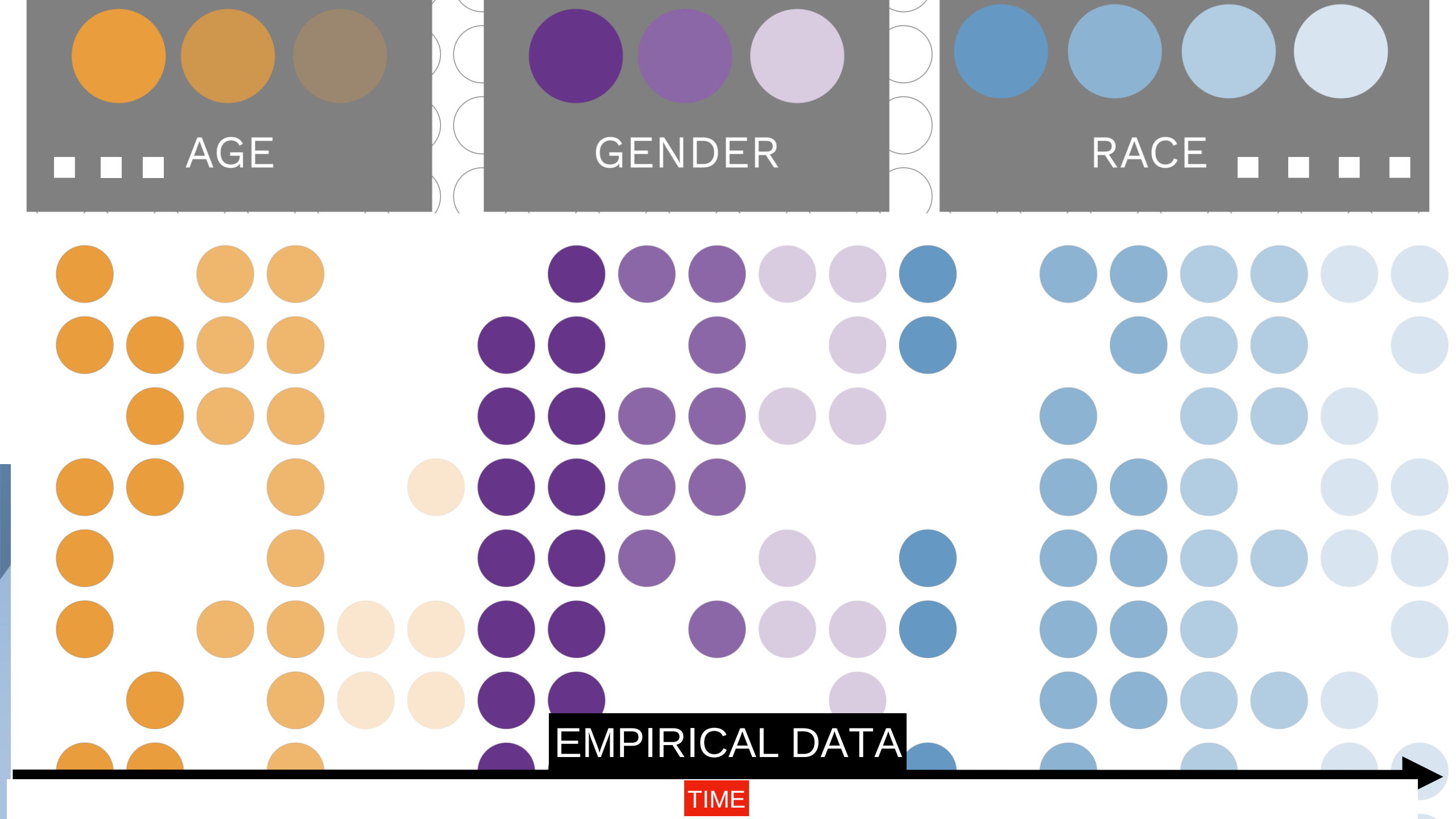
Various Potential for Biases in Clinical Trials

- Site selection
- Patient Reach
- Recruitment
- Retention
- Data analysis
- Inference
- ……..

Implications of “Underrepresentation”

- Non-uniform representation
- Non-uniform data collection
- Non-generalizable inference -> Non-generalizable treatments
- Moving beyond guidance – methodological aspects
  - Imputation – pros/cons

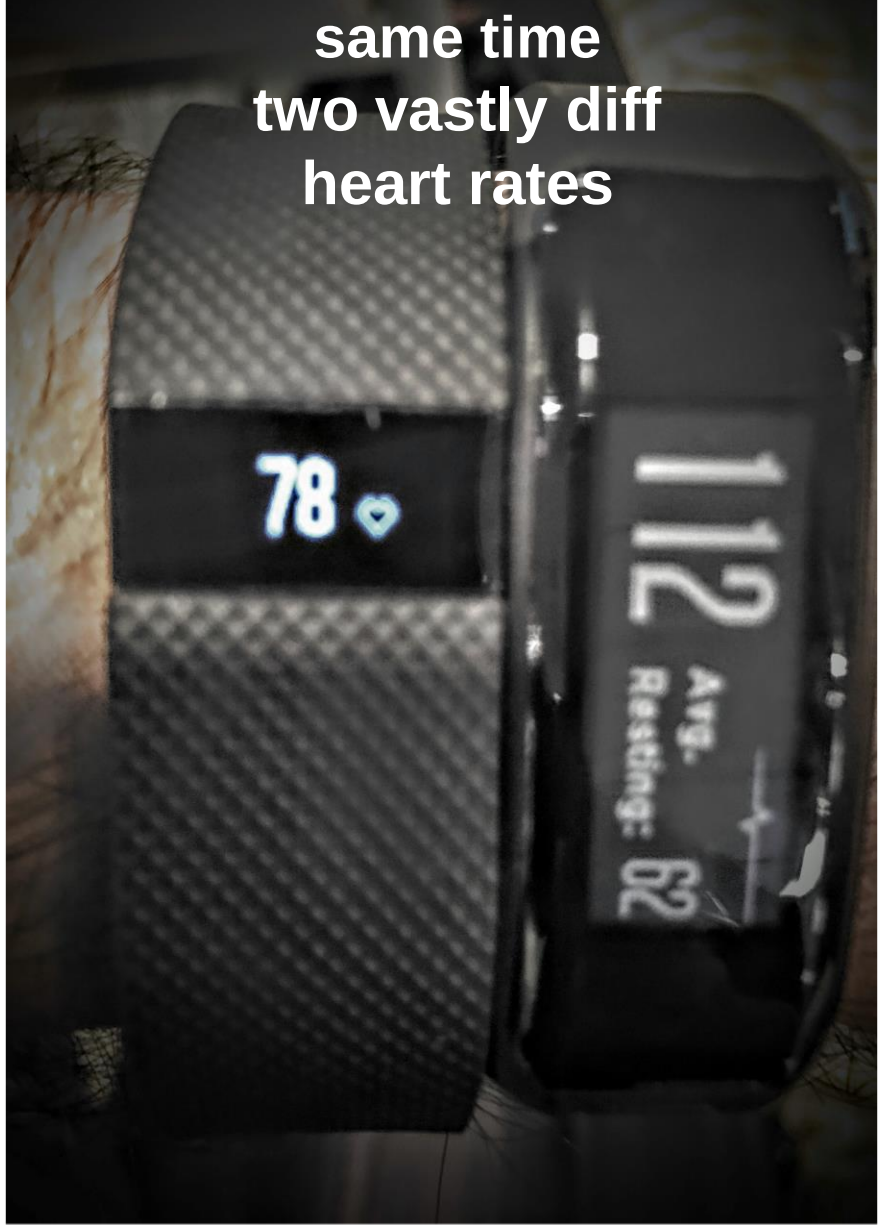

AGE
GENDER
RACE
EXPECTED DIVERSITY
TIME


AGE
GENDER
RACE
EMPIRICAL DATA
TIME

AGE

RACE

same time
two vastly diff
heart rates



EMPIRICAL DATA

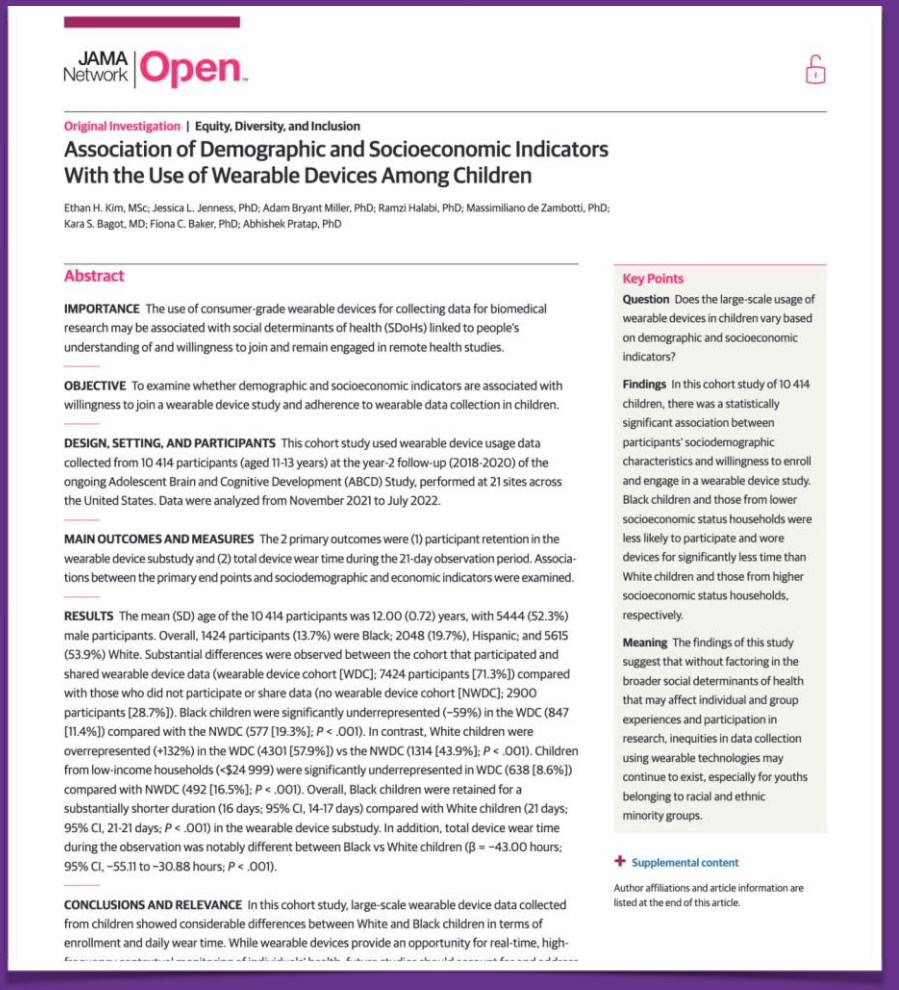
TIME

Wearable devices may not be adopted or worn equitably by a diverse population

ABCD Study in Brief

- N = 10,000+
- Healthy kids representatively sampled across US
- Data collection = ePROs + Wearables(Fitbits)

Adolescent **B**rain **C**ognitive **D**evelopment
The ABCD Study® is the largest long-term study of brain development and child health in the United States.



JAMA Network | Open

Original Investigation | Equity, Diversity, and Inclusion

Association of Demographic and Socioeconomic Indicators With the Use of Wearable Devices Among Children

Ethan H. Kim, MSc; Jessica L. Jenness, PhD; Adam Bryant Miller, PhD; Ramzi Halabi, PhD; Massimiliano de Zambotti, PhD; Kara S. Bagot, MD; Fiona C. Baker, PhD; Abhishek Pratap, PhD

Abstract

IMPORTANCE The use of consumer-grade wearable devices for collecting data for biomedical research may be associated with social determinants of health (SDoHs) linked to people's understanding of and willingness to join and remain engaged in remote health studies.

OBJECTIVE To examine whether demographic and socioeconomic indicators are associated with willingness to join a wearable device study and adherence to wearable data collection in children.

DESIGN, SETTING, AND PARTICIPANTS This cohort study used wearable device usage data collected from 10 414 participants (aged 11-13 years) at the year-2 follow-up (2018-2020) of the ongoing Adolescent Brain and Cognitive Development (ABCD) Study, performed at 21 sites across the United States. Data were analyzed from November 2021 to July 2022.

MAIN OUTCOMES AND MEASURES The 2 primary outcomes were (1) participant retention in the wearable device substudy and (2) total device wear time during the 21-day observation period. Associations between the primary end points and sociodemographic and economic indicators were examined.

RESULTS The mean (SD) age of the 10 414 participants was 12.00 (0.72) years, with 5444 (52.3%) male participants. Overall, 1424 participants (13.7%) were Black; 2048 (19.7%), Hispanic; and 5615 (53.9%) White. Substantial differences were observed between the cohort that participated and shared wearable device data (wearable device cohort [WDC]; 7424 participants [71.3%]) compared with those who did not participate or share data (no wearable device cohort [NWDC]; 2900 participants [28.7%]). Black children were significantly underrepresented (−59%) in the WDC (847 [11.4%]) compared with the NWDC (577 [19.3%]; $P < .001$). In contrast, White children were overrepresented (+132%) in the WDC (4301 [57.9%]) vs the NWDC (1314 [43.9%]; $P < .001$). Children from low-income households (<$24 999) were significantly underrepresented in WDC (638 [8.6%]) compared with NWDC (492 [16.5%]; $P < .001$). Overall, Black children were retained for a substantially shorter duration (16 days; 95% CI, 14-17 days) compared with White children (21 days; 95% CI, 21-21 days; $P < .001$) in the wearable device substudy. In addition, total device wear time during the observation was notably different between Black vs White children (β = −43.00 hours; 95% CI, −55.11 to −30.88 hours; $P < .001$).

CONCLUSIONS AND RELEVANCE In this cohort study, large-scale wearable device data collected from children showed considerable differences between White and Black children in terms of enrollment and daily wear time. While wearable devices provide an opportunity for real-time, high-

Key Points

Question Does the large-scale usage of wearable devices in children vary based on demographic and socioeconomic indicators?

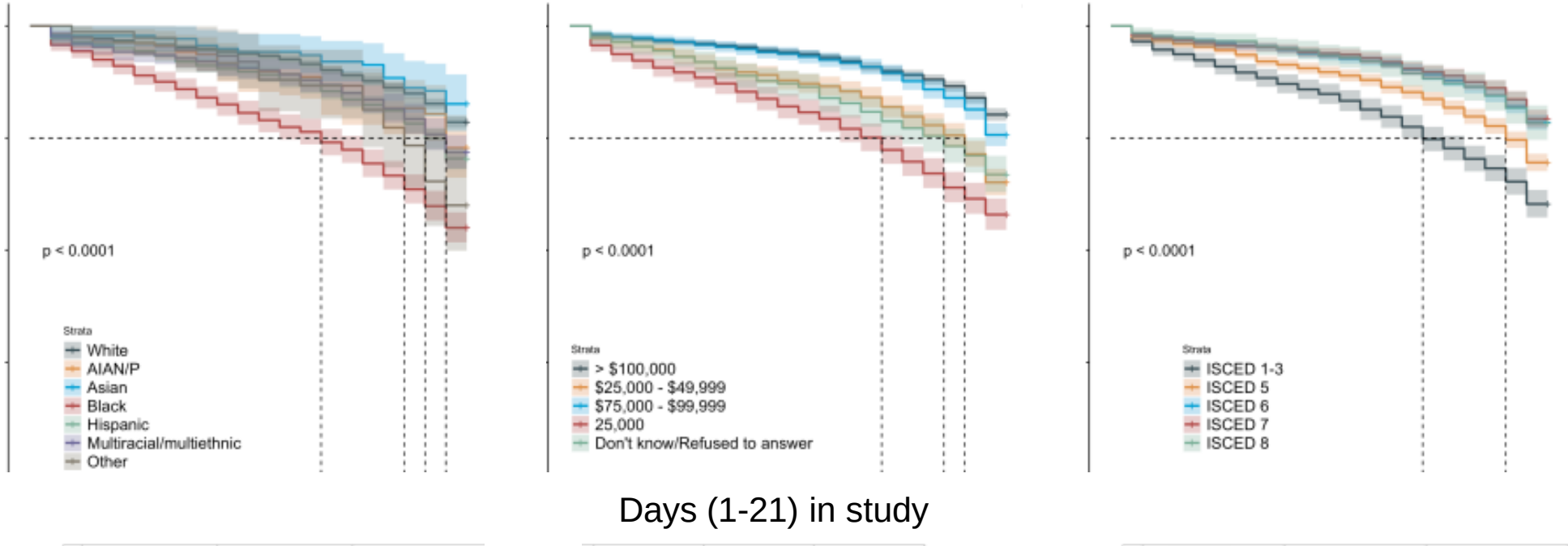
Findings In this cohort study of 10 414 children, there was a statistically significant association between participants' sociodemographic characteristics and willingness to enroll and engage in a wearable device study. Black children and those from lower socioeconomic status households were less likely to participate and wore devices for significantly less time than White children and those from higher socioeconomic status households, respectively.

Meaning The findings of this study suggest that without factoring in the broader social determinants of health that may affect individual and group experiences and participation in research, inequities in data collection using wearable technologies may continue to exist, especially for youths belonging to racial and ethnic minority groups.

Supplemental content

Author affiliations and article information are listed at the end of this article.

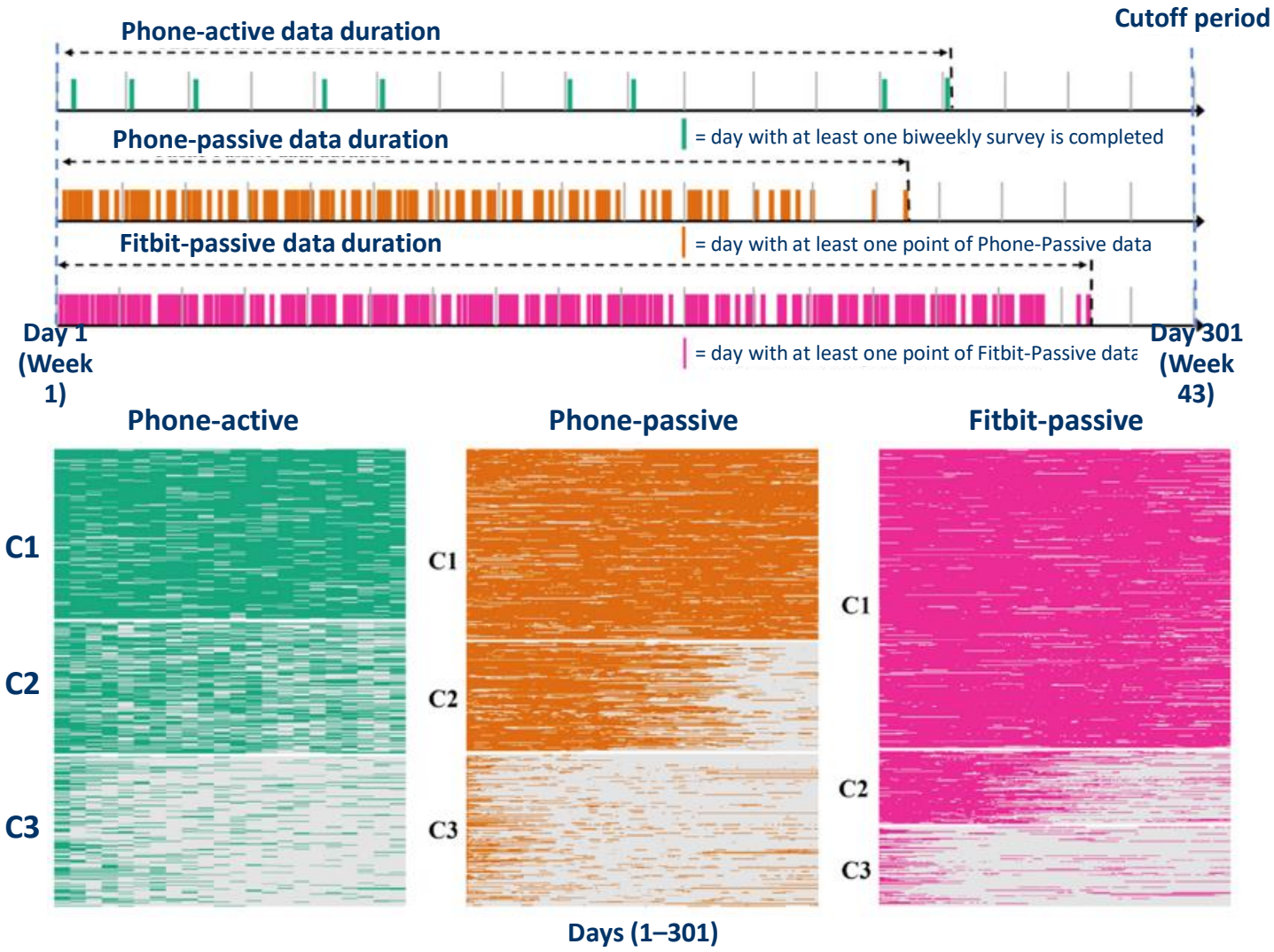
Participant Retention

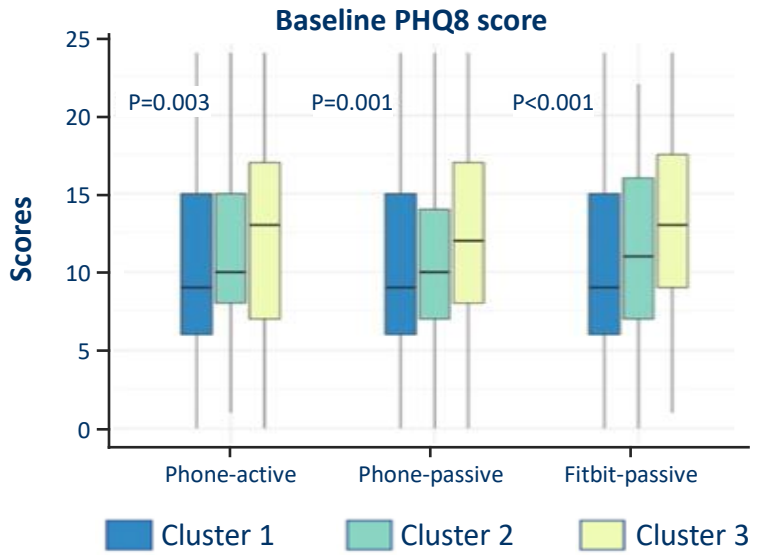


Days (1-21) in study

nic

Differential biases in real-world data collection

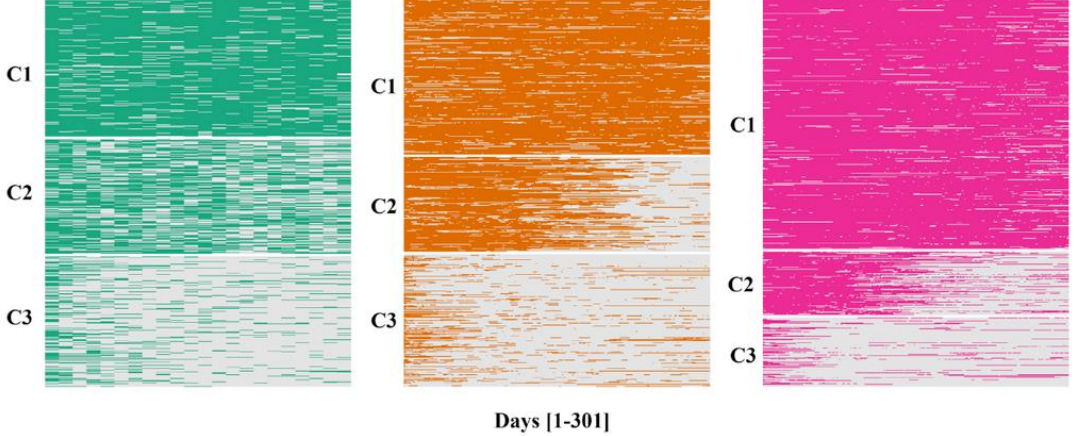




PHQ-8, eight-item Patient Health Questionnaire depression scale.
Zhang Y, et al. NPJ Digit Med 2023;6: 25.

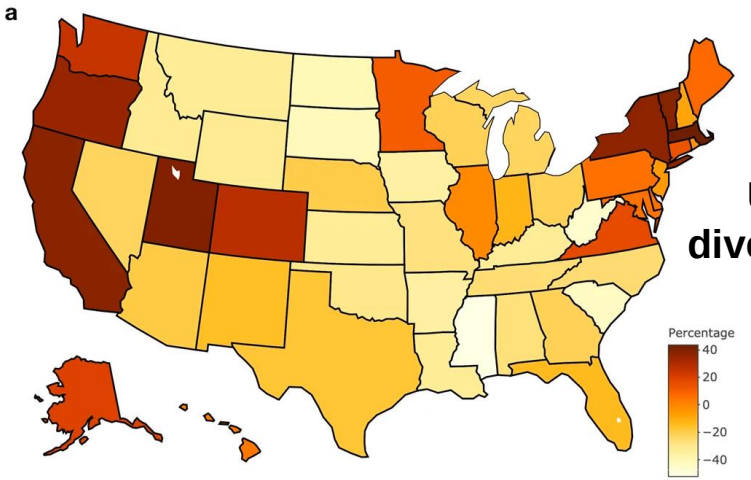
Study in brief

Clinical condition = depression
N = >600
Region = UK, Spain and The Netherlands
Data collection = smartphone (active and passive) + wearable (Fitbit



Understanding variation in technology usage by devices, sociodemographics & disease characteristics

Zhang, Y., **Pratap, A.**, Folarin, A.A. *et al.* Long-term participant retention and engagement patterns in an app and wearable-based multinational remote digital depression study. *npj Digit. Med.* **6**, 25 (2023). https://doi.org/10.1038/s41746-023-00749-3

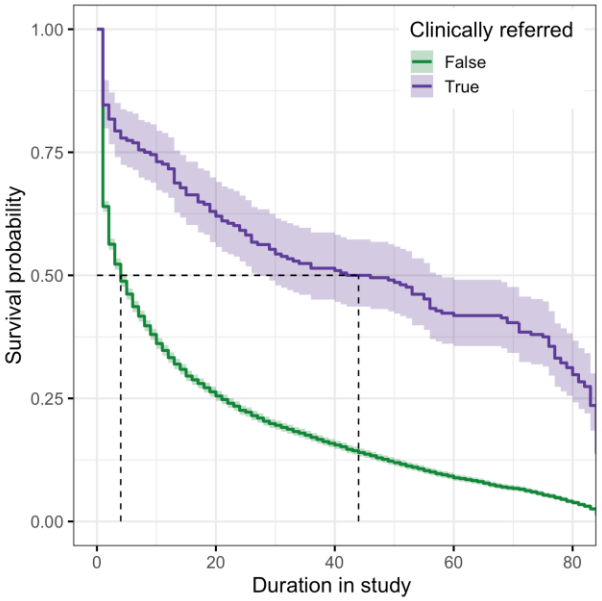


Understanding geospatial diversity & potential bias can be critical

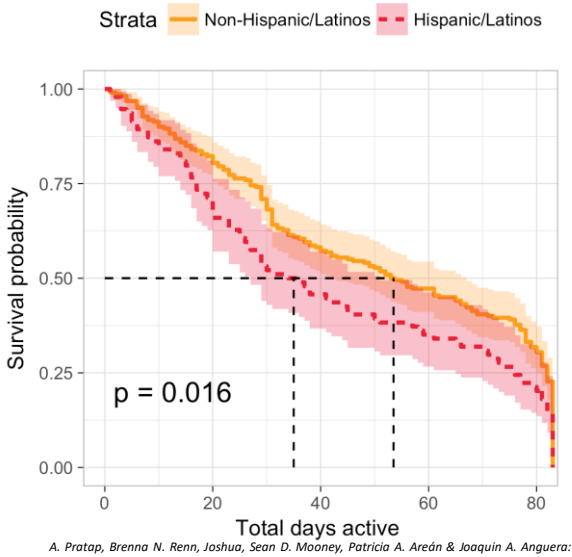
A Pratap, E Neto, P Snyder, C Stepnowsky, N Elhadad, D Grant, M Mohebbi, S Mooney, C Suver, J Wilbanks, L Mangravite, P Heagerty, P Arean, L Omberg - Indicators of retention in remote digital health studies: A cross-study evaluation of 100,000 participants **| Nature Digital Medicine, 2020**

PDTx

Provider referral matters



Need to engage minorities

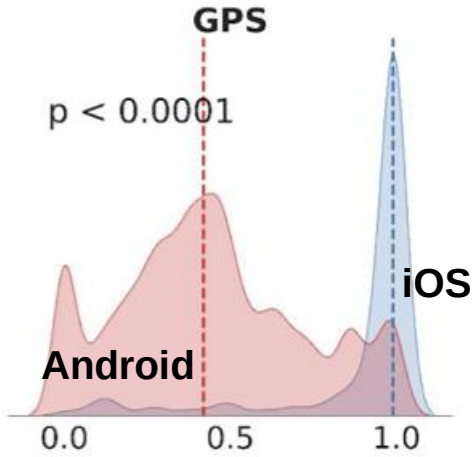


A. Pratap, Brenna N. Renn, Joshua, Sean D. Mooney, Patricia A. Areán & Joaquin A. Anguera: Using mobile apps to assess and treat depression in Hispanics and Latinos: Results from a fully remote and randomized clinical trial (JMIR, 2018)

Heterogeneity in real-world cohorts

Li SX, Halabi R, Selvarajan R, Woerner M, Fillipo IG, Banerjee S, Mosser B, Jain F, Areán P, Pratap A Recruitment and Retention in Remote Research: Learnings From a Large, Decentralized Real-world Study JMIR Form Res 2022;6(11):e40765

Device heterogeneity can impact evidence generation



Missing data ratio

Understanding real-world behavior using methods that are acceptable to the target population remains critical and is often missed

ORIGINAL RESEARCH ARTICLE

Using Real-world Data for Decision Support: Recommendations from a Primary Care Provider Survey

Patricia A Areán, PhD[1,2]; Emily C Friedman, MID, CPE[2]; Abhishek Pratap, PhD[3]; Ryan Allred, BA[1]; Jaden Duffy, BA[1]; Sara Gille, MPH[4]; Shelley Reetz, BS[4]; Erin Keast, MPH[4]; Gregory Clarke, PhD[4]

Perm J 2021;25:20.213

E-pub: 03/01/2021

https://doi.org/10.7812/TPP/20.213

JAMA Network | Open

Original Investigation | Health Informatics

Contemporary Views of Research Participant Willingness to Participate and Share Digital Data in Biomedical Research

Abhishek Pratap, MS; Ryan Allred, BA; Jaden Duffy, BA; Donovan Rivera, MSW; Heather Sophia Lee, PhD; Brenna N. Renn, PhD; Patricia A. Areán, PhD

Understanding Participant Needs for Engagement and Attitudes towards Passive Sensing in Remote Digital Health Studies

Samantha Kolovson,
Human Centered Design & Engineering, University of Washington

Abhishek Pratap,
Biomedical Informatics & Medical Education, University of Washington Sage Bionetworks

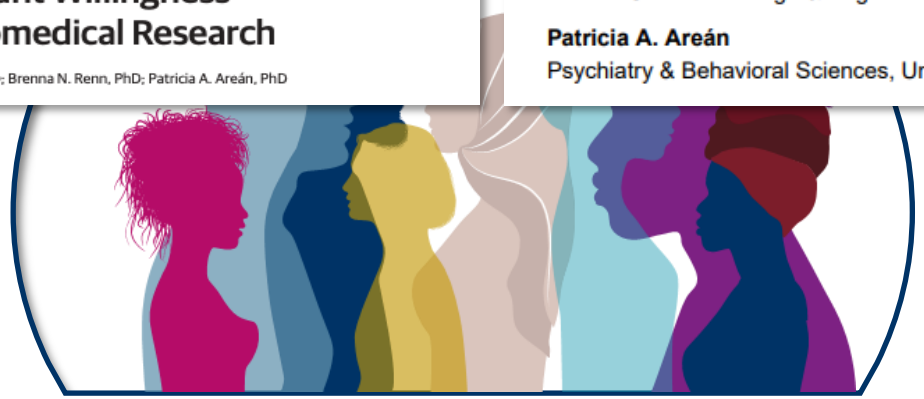
Jaden Duffy,
Psychiatry & Behavioral Sciences, University of Washington

Ryan Allred,
Psychiatry & Behavioral Sciences, University of Washington

Sean A. Munson,
Human Centered Design & Engineering, University of Washington

Patricia A. Areán
Psychiatry & Behavioral Sciences, University of Washington

Background noise levels



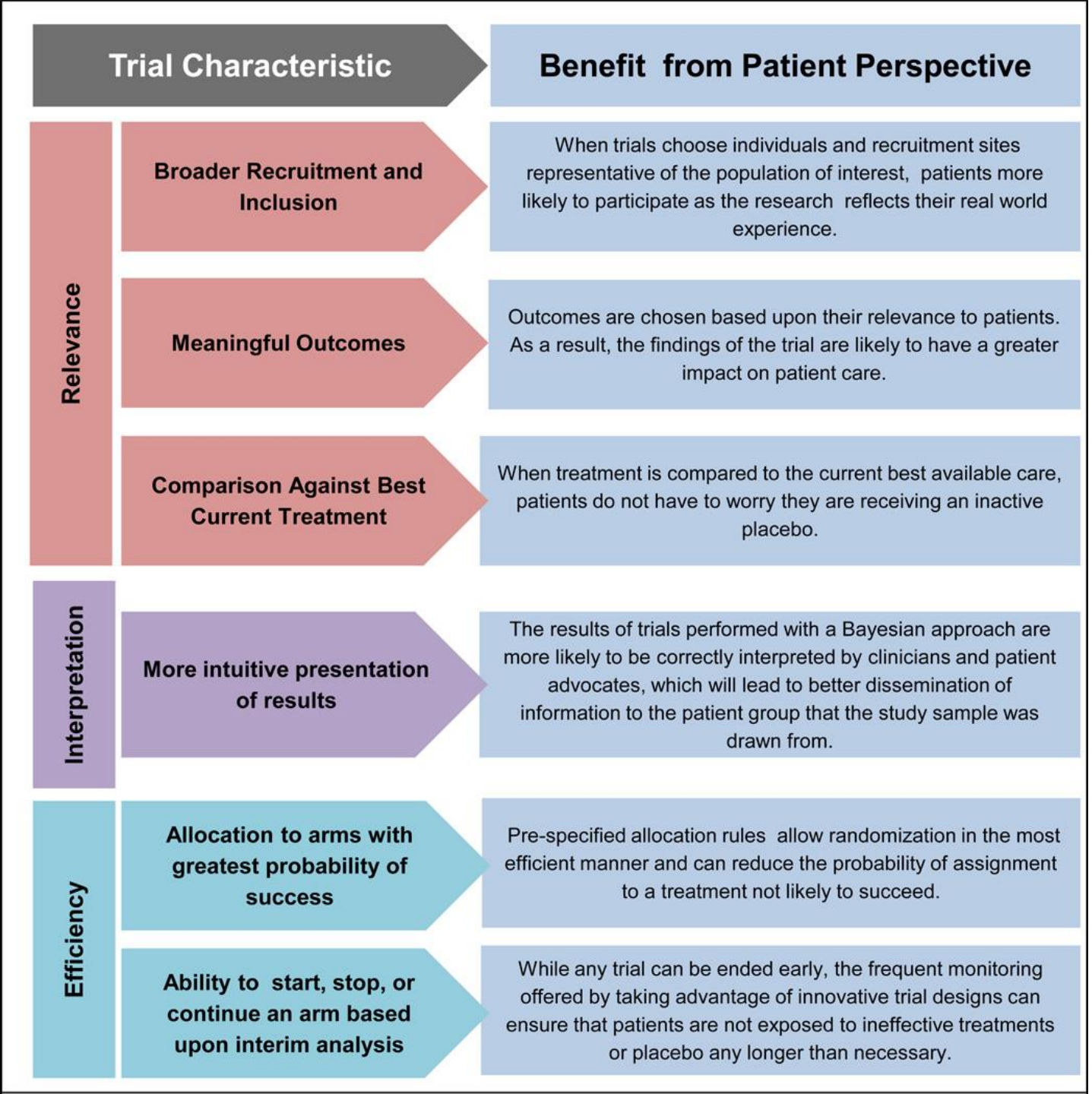
Air quality

Step counts/day

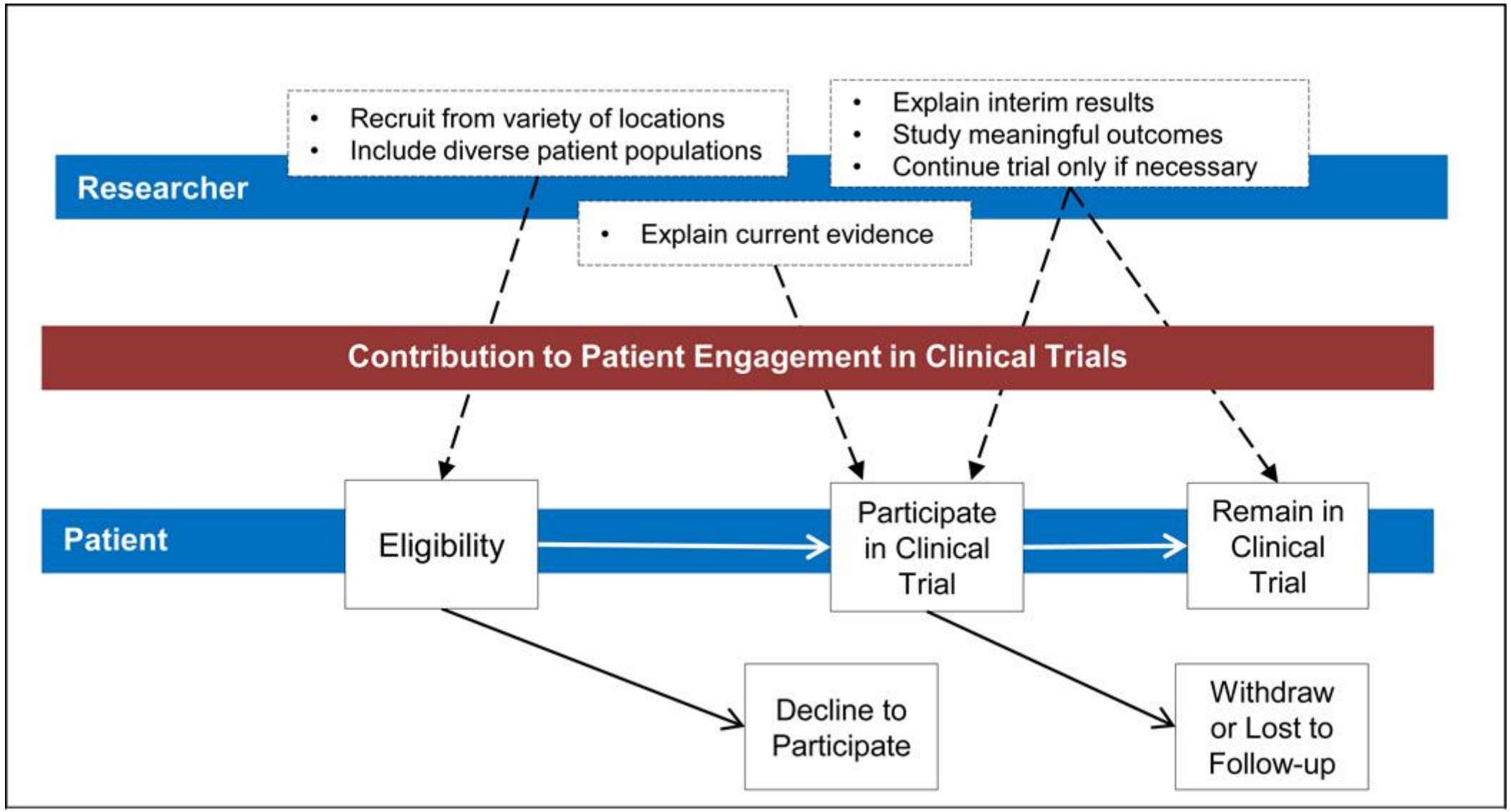
Areán PA, et al. Perm J 2021;20:213; Pratap A, et al. JAMA Netw Open 2019;2:e1915717; Kolovson S, et al. Int Conf Pervasive Comput Technol Healthc 2020;2020:347–362.

Group discussion

- What works
- How
- Real-world examples

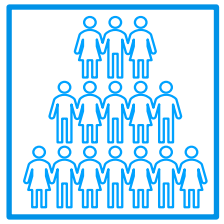


Mullins CD, Vandigo J, Zheng Z, Wicks P. Patient-centeredness in the design of clinical trials. Value Health. 2014 Jun;17(4):471-5. doi: 10.1016/j.jval.2014.02.012. Epub 2014 May 5. PMID: 24969009; PMCID: PMC4497570.



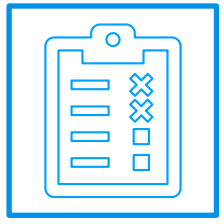
Mullins CD, Vandigo J, Zheng Z, Wicks P. Patient-centeredness in the design of clinical trials. Value Health. 2014 Jun;17(4):471-5. doi: 10.1016/j.jval.2014.02.012. Epub 2014 May 5. PMID: 24969009; PMCID: PMC4497570.

Data-Driven Approach To Set Trial Targets



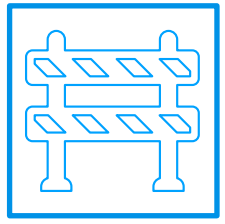
Study-level diversity goals depend on having best available data

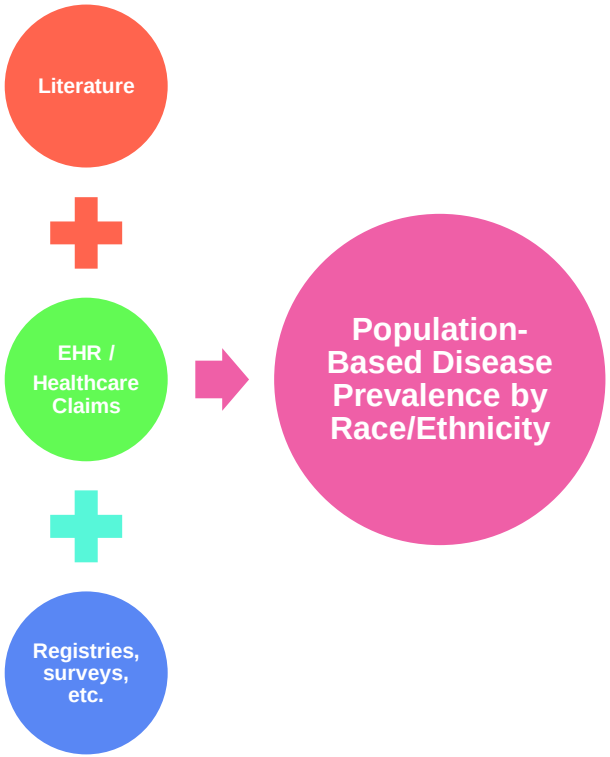
Examining previous performance with a firm eye on the future



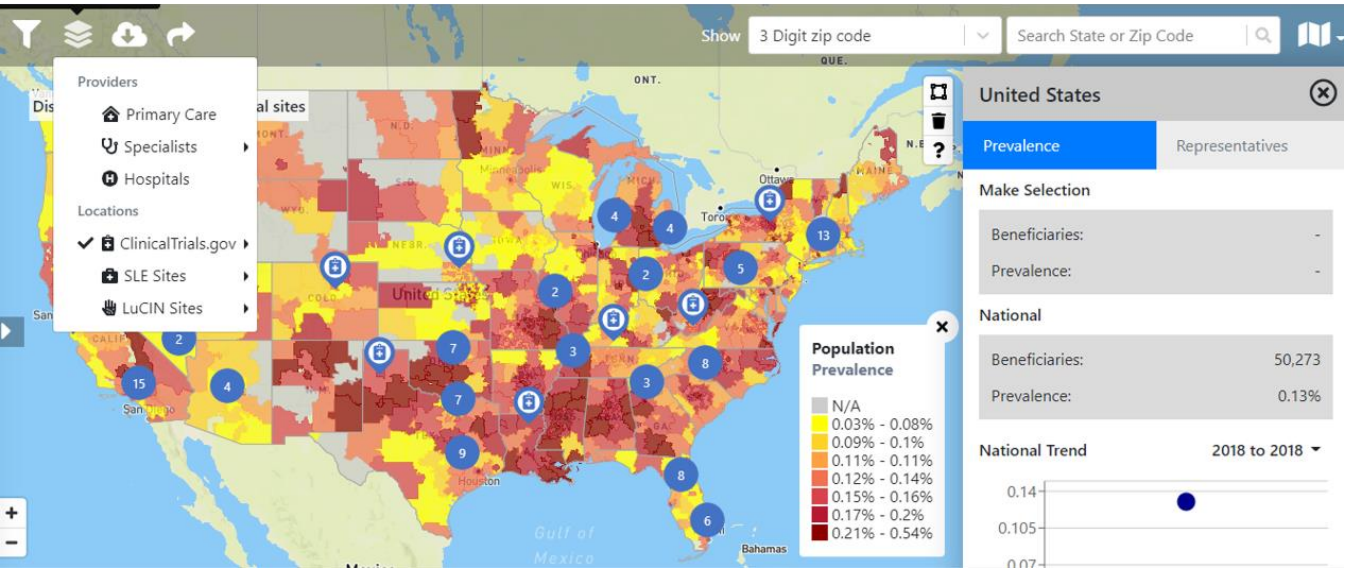
Rare Disease = Bigger Challenges

Data feed into dashboards to measure progress





Clinical Trial Index: Leveraging geographic and social determinants of health data to support clinical trial site selection



Purpose

The CTLC is designed to overcome the barriers that have historically plagued minority accrual in neurological clinical trials.

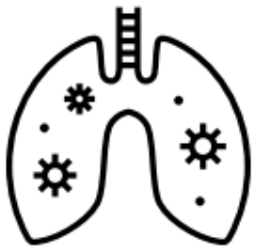
Visualizations

Users Identify treated populations by geography (zip code, county, state, metropolitan statistical areas, and state and congressional legislative districts), by demographic cohort (age, gender, race and ethnicity), and by provider (primary and specialty care, hospital, clinic and pharmacy).

Applications

Using data derived from the CT Index and advisors, an action plan was to help match clinical trial operations activities to the needs of the diverse patient populations at the community level. Initiatives may relate to site selection, clinical trial enrollment and retention.

Inclusion provides equal opportunities



Addressing serious unmet medical needs is a key priority in medical research
Unmet needs are typically not confined to:
-age
-ethnicity
-comorbidity
-residency

Most unmet medical needs are universal

Some patients will view trial participation as an opportunity:
- Potentially effective therapy (no promise of positive benefit/risk)
- Access to therapies that are not reimbursed
- Contribute to research and future patients

The hope and opportunity should not per default be confined to specific patient populations

Initiatives and structures that promote equity is needed
Some patients have special needs that should be addressed, for example
- Travel for patient and family to site
- Language barriers
- Poor health literacy

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**

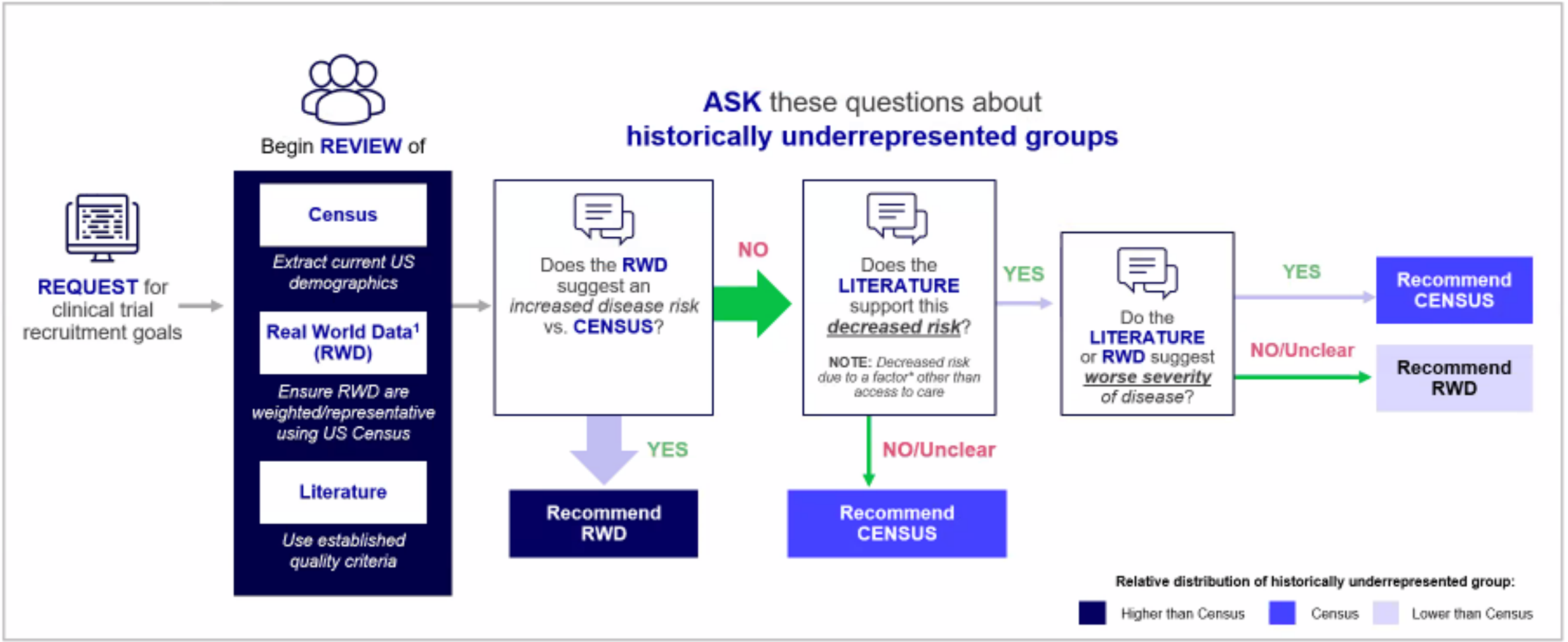
Perspective

New Federal Incentives for Diversity in Clinical Trials

Thomas J. Hwang, M.D., and Otis W. Brawley, M.D.

In June 2022, the U.S. House of Representatives passed legislation intended to increase the diversity of the populations enrolled in clinical trials of new drugs. Under this bill, study sponsors would be required to submit a diversity action plan — including goals for study enrollment according to demographic group and steps for achieving those goals — for phase 3 or pivotal studies of new drugs. These diversity provisions, considered as part of a broader reauthorization of user-fee funding of the Food and Drug Administration (FDA), would codify recent FDA draft guidance recommending that clinical trial sponsors develop and submit diversity plans for enrolling participants from historically underrepresented racial and ethnic populations.[1]

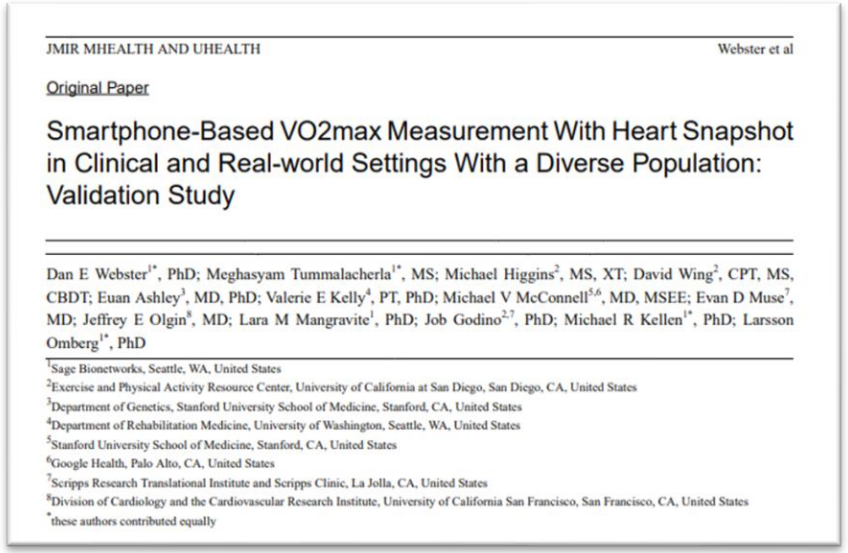
Result: A process that is scientifically rigorous, flexible, and based the disease epidemiology



* *E.g., due to a biological factor.*

1. Real world data refer to in-house, recent analyses of the demographic distribution of diseases targeted by Pfizer's medicines, from sources such as disease registries, surveys, electronic health records, and claims.

Include diversity as part of study design when it matters most



JMIR MHEALTH AND UHEALTH — Webster et al

Original Paper

Smartphone-Based VO2max Measurement With Heart Snapshot in Clinical and Real-world Settings With a Diverse Population: Validation Study

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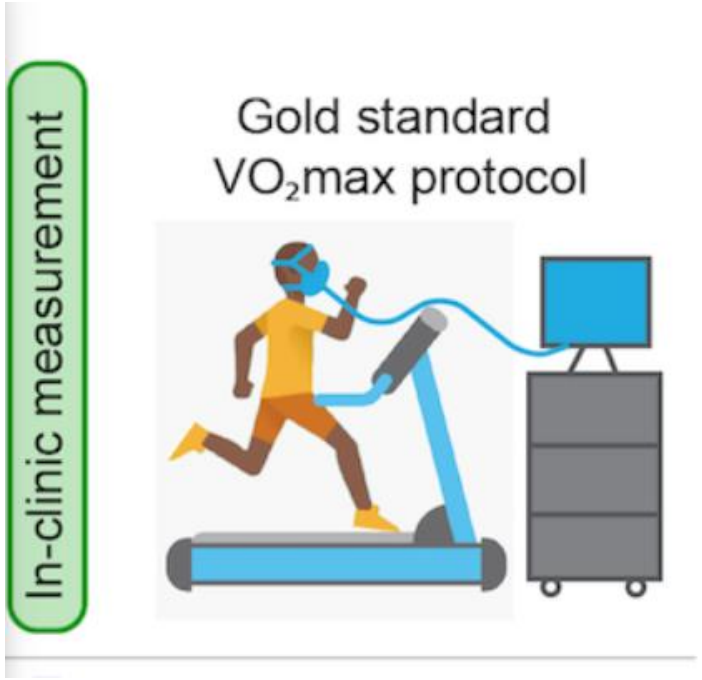

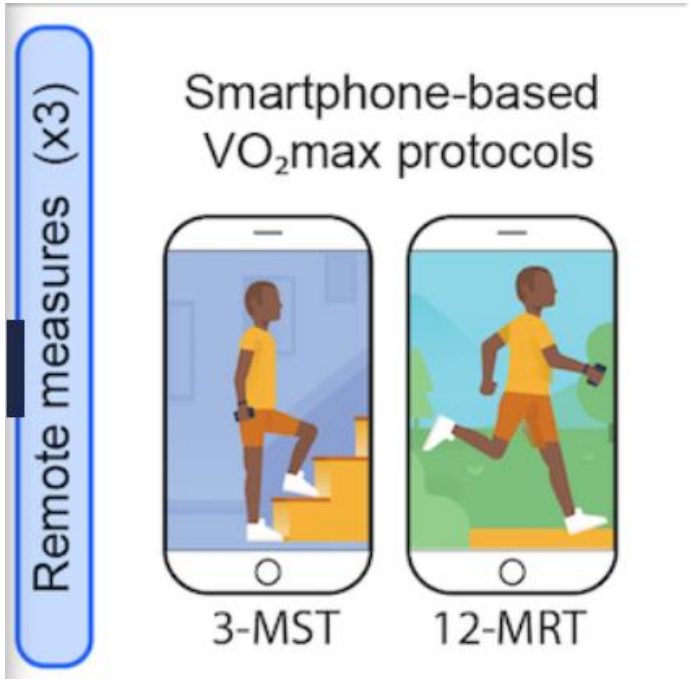

….recruit six different skin types were asked to participate in this study. We aimed to recruit an equal ratio of male and female participants, **as well as an equal number of participants with each skin type, as determined by the Fitzpatrick scale.**

VISIBLE: Filling in the gaps within dermatology with a first-of-its-kind skin of color (SoC) dedicated study

OVERVIEW

- Phase 3b study investigating the efficacy/safety of an investigational compound vs placebo in SoC patients with mod-sev PsO
- Aims to build a Skin of Color Image repository and gain novel scientific insights into issues like PIPA

CHALLENGE

- **Low utilization of dermatological services** amongst skin of color
- **Lack of clinical benchmarks & accurate presentation of dermatologic diseases on skin of color**
- **Darker skin tones** may present with less noticeable skin reddening, **making it difficult to truly assess active disease / inflammation**
- **Scalp psoriasis is very prevalent among non-white PsO patients,** yet representation remains low **(~10% of trial population)**

DEI Metrics

Recruit 200 self-identified non-white who are bio-naïve or experienced across all skin tones (I-VI)

100% Skin of Color

DEI FOCUSED TACTICS

Leveraging Data

To **identify sites**, we **utilized our MSL network** and to identify potential diverse sites

Conducted site feasibility with questions regarding **SoC experience** and communicated early on diverse enrollment requirements.

Targeted **geographic locations** across the United States based on diversity, target population.

Instilling Training & Tech

Created training decks for MSLs to empower prepare them for **challenging DEI conversations** with potential and selected Dermatology HCPs

Leveraging **colorimeter technology** to independently quantify skin tones – **aids in measuring pigmentation (melanin) and erythema**

Impactful Engagement

Leveraged **skin of color appropriate images and recruitment materials** to support HCPs, **drive referrals**, and **educate patients about the VISIBLE trial – we ensured that complex study details were written in layman terms for greater understanding**

Leveraged insights from diverse advisory boards of >30 leading SOC experts to refine our protocol and study elements that are equitable and more inclusive of the target demographic

Janssen has also partnering with leading medical and patient organizations (*e.g., AAD & Skin of Color Society*) to increase training and raise awareness of PsO as well as clinical research

CURRENT IMPACT

180 — **Patients screened:** 104 Body, 24 Scalp, and 52 Both

113 — **Patients randomized:** 35 FST I-III and 78 FST IV-VI

53% — **Randomized patients are Hispanic –** other top demographics are Asian (22%) and Black (13%)

AllofUS Recruitment Effort

The “All of Us” Research Program | NEJM

Thank you!