



NIH Collaboratory

Rethinking Clinical Trials®

Health Care Systems Research Collaboratory

NIH Collaboratory Grand Rounds , May 14, 2021

“Creating more diversity in clinical trial participants: why and how?”

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Professor, Medical Social Science
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No relevant disclosures



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Who Participates in Clinical Trials?





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FDA U.S. FOOD & DRUG
ADMINISTRATION

2015 - 2016

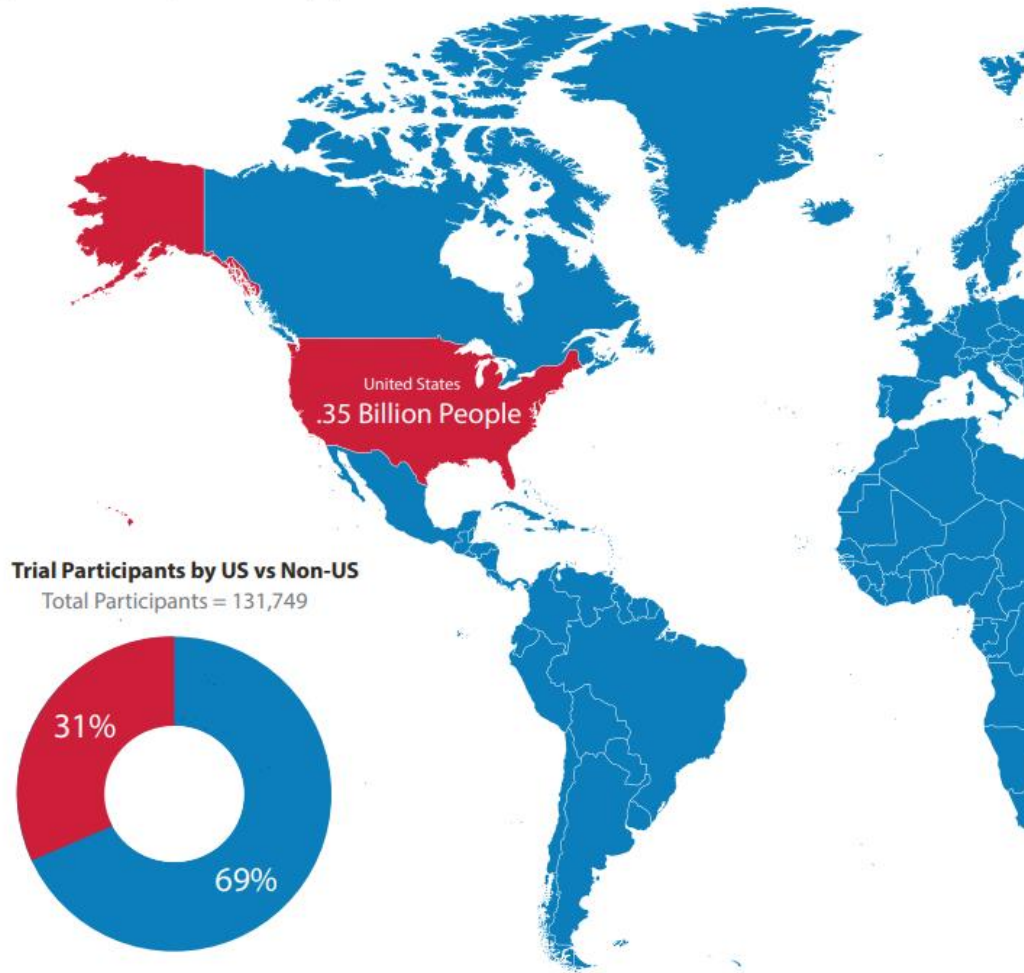
GLOBAL PARTICIPATION IN CLINICAL TRIALS REPORT



Geography

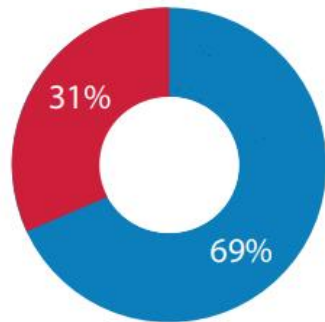
Where are Participants From?

The country contributing the most clinical trial participants was the United States. Compared to the population of the entire world (7.4 Billion), the US (0.35 Billion) makes up a little more than 4% of the world population.



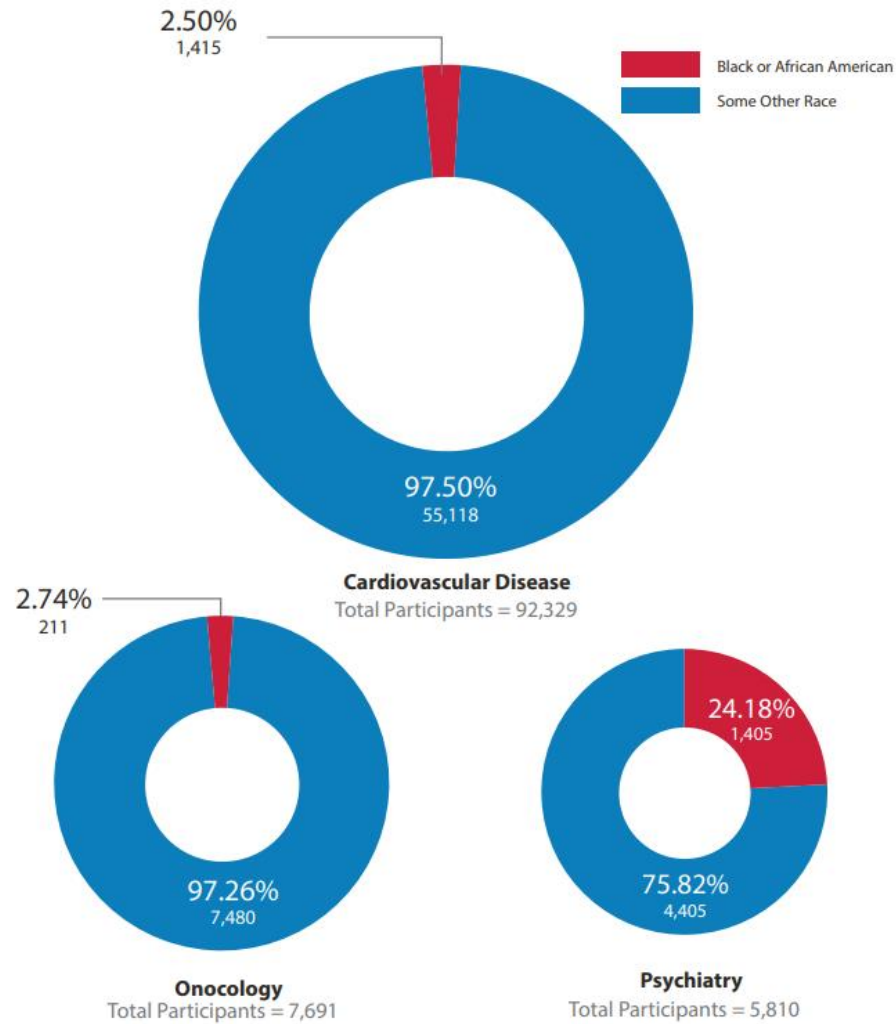
Trial Participants by US vs Non-US

Total Participants = 131,749



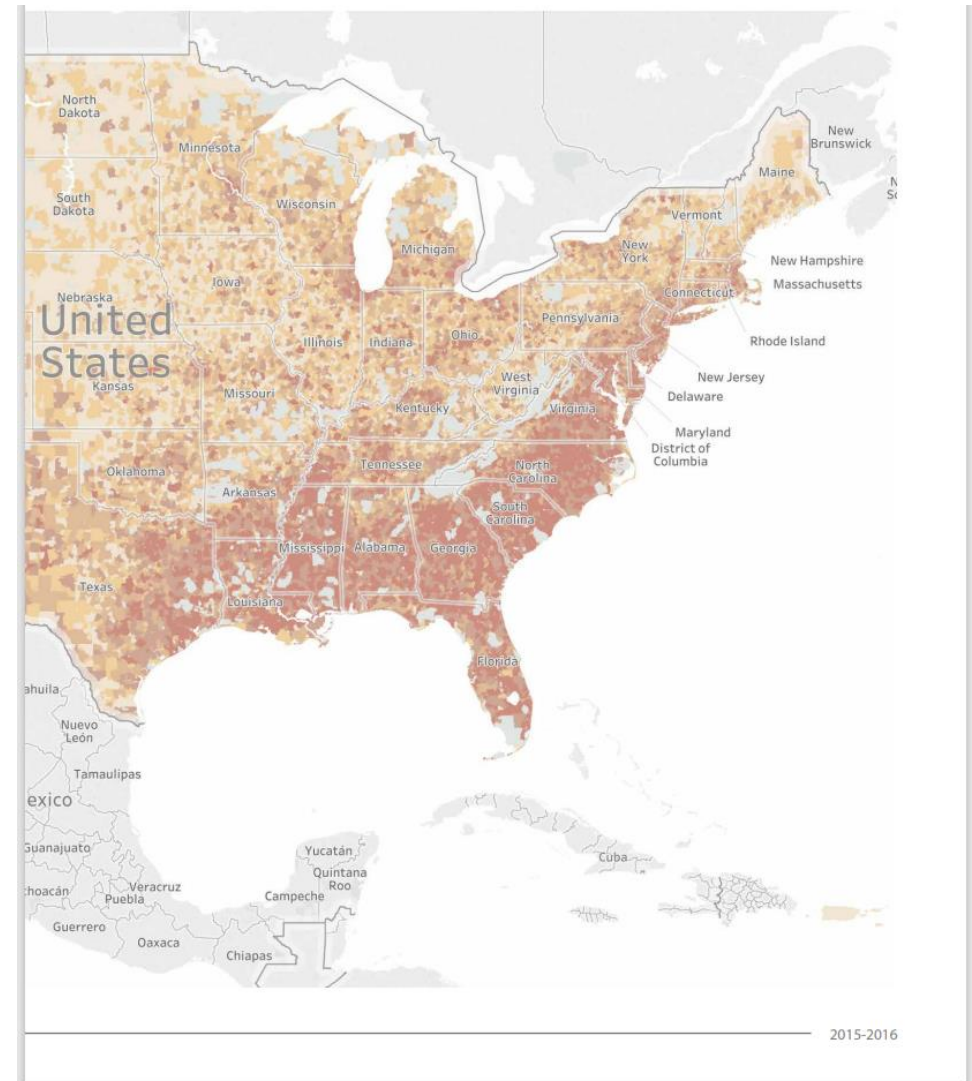
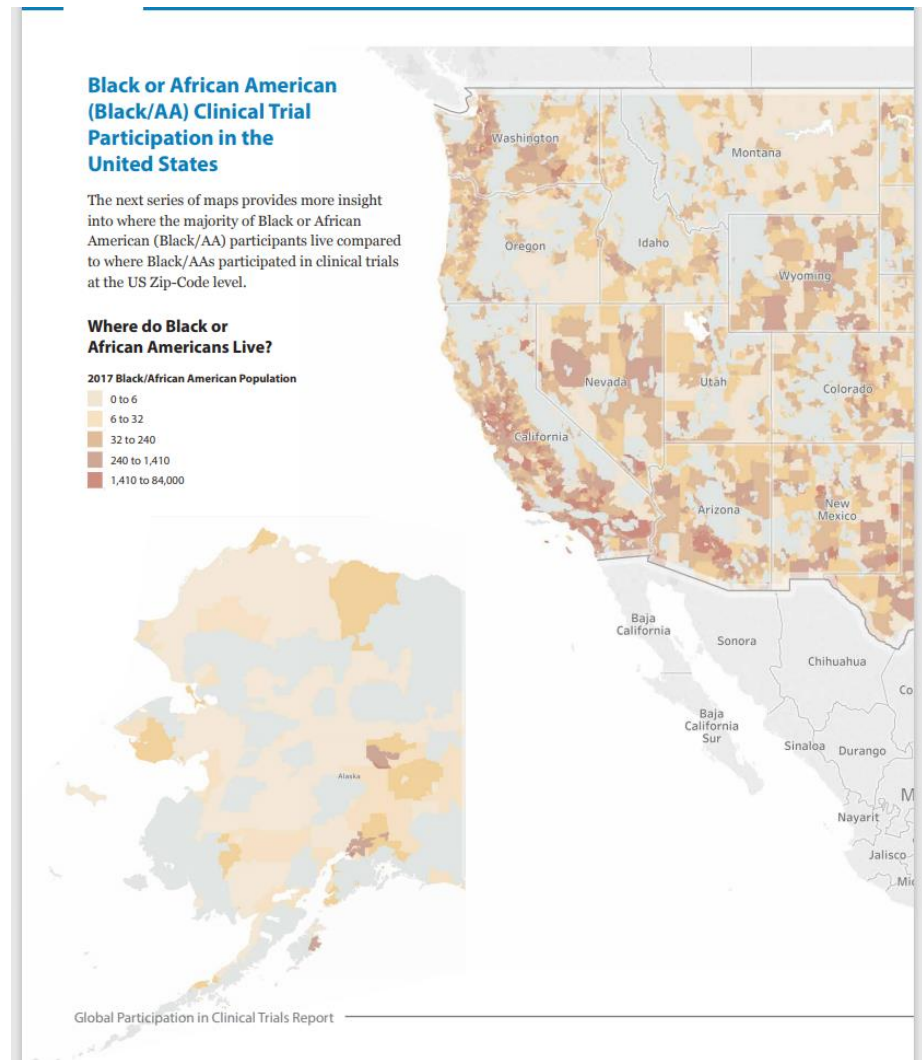
Participation of Black/AAs in Clinical Trials for Oncology, Cardiology, and Psychiatry

More insight into the participation rates of Black/AAs in clinical trials for Oncology, Cardiology, and Psychiatry are provided in the figures below.



Global Participation in Clinical Trials Report

Heat Map- Clinical Trial participants- Black



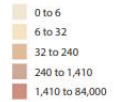
Heat Map- Clinical Trial Participants: All

22

Where do Black/AAs participate in Clinical Trials compared to Non-Black/AA Races? (Based on NMEs from 2015-16)

This map shows where Black/AAs participate in clinical trials compared to Non-Black/AA races. Roughly comparing the sites with Black/AA participants and sites with non-Black/AA participants, it seems to suggest clinical trials in the US are being conducted where Black/AAs live.

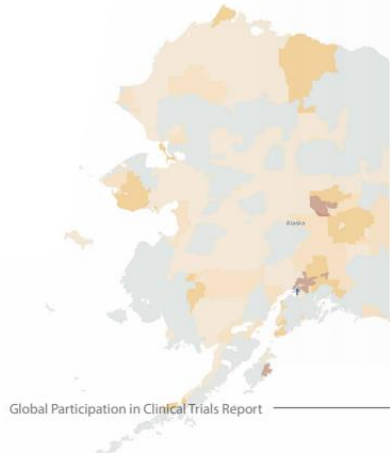
2017 Black/African American Population



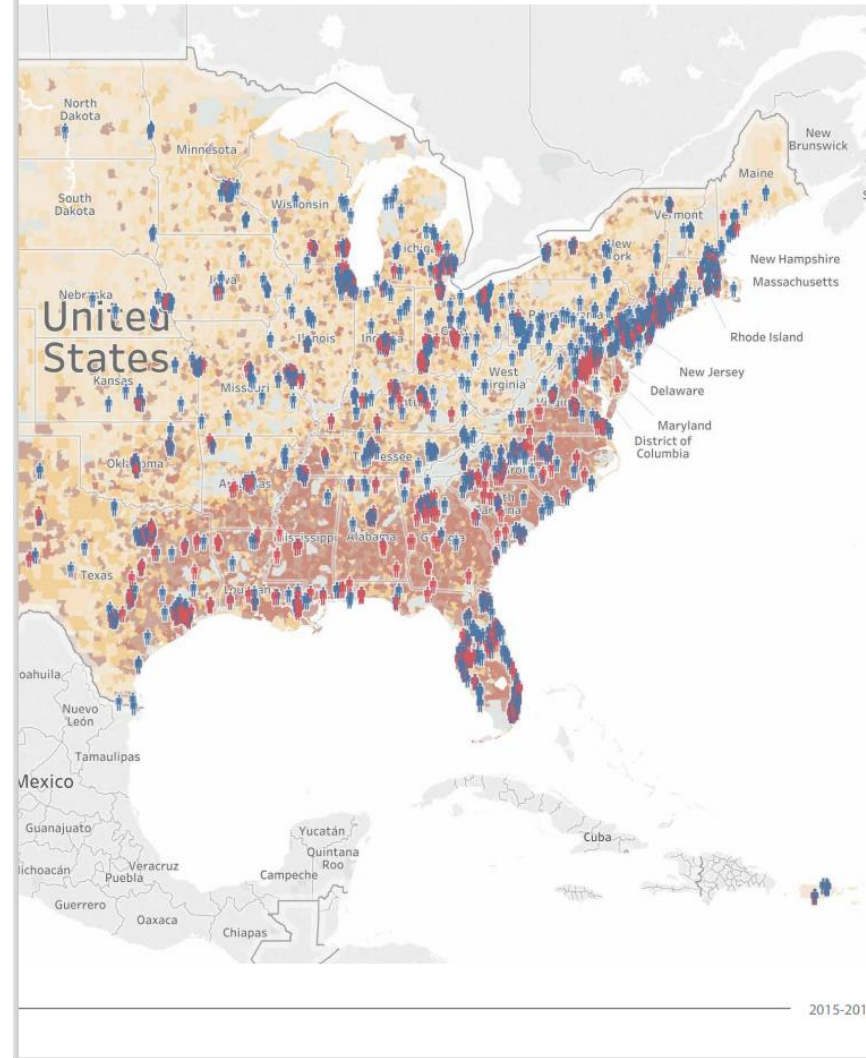
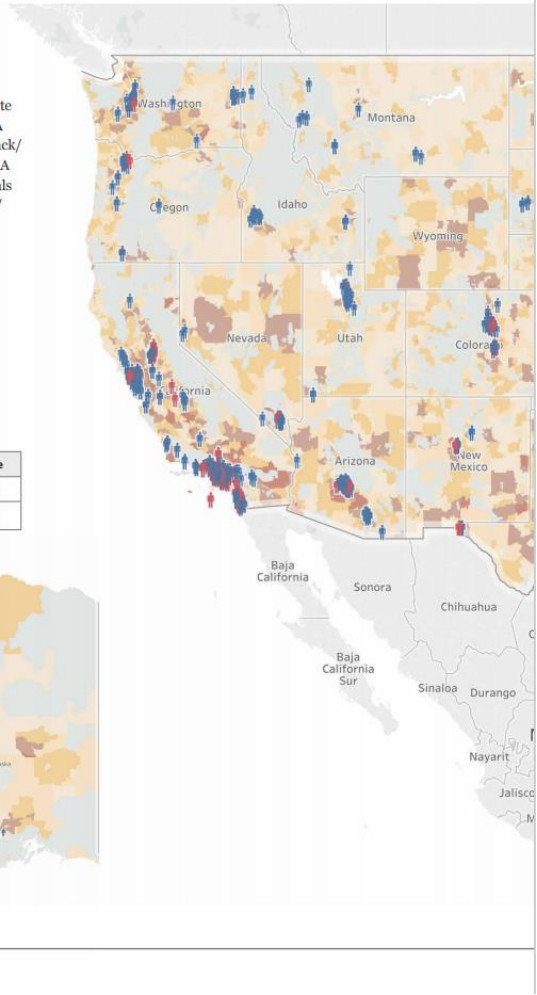
Race of Participant



	Participants	Percentage
Black/AAs	5,913	14.48%
Some Other Race	34,922	85.52%



Global Participation in Clinical Trials Report



2015-2016

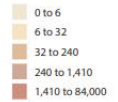
Heat Map- Clinical Trial Participants: All

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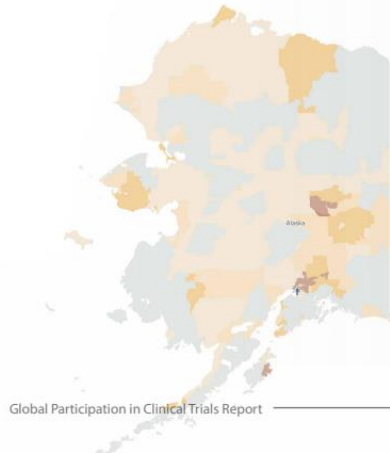
2017 Black/African American Population



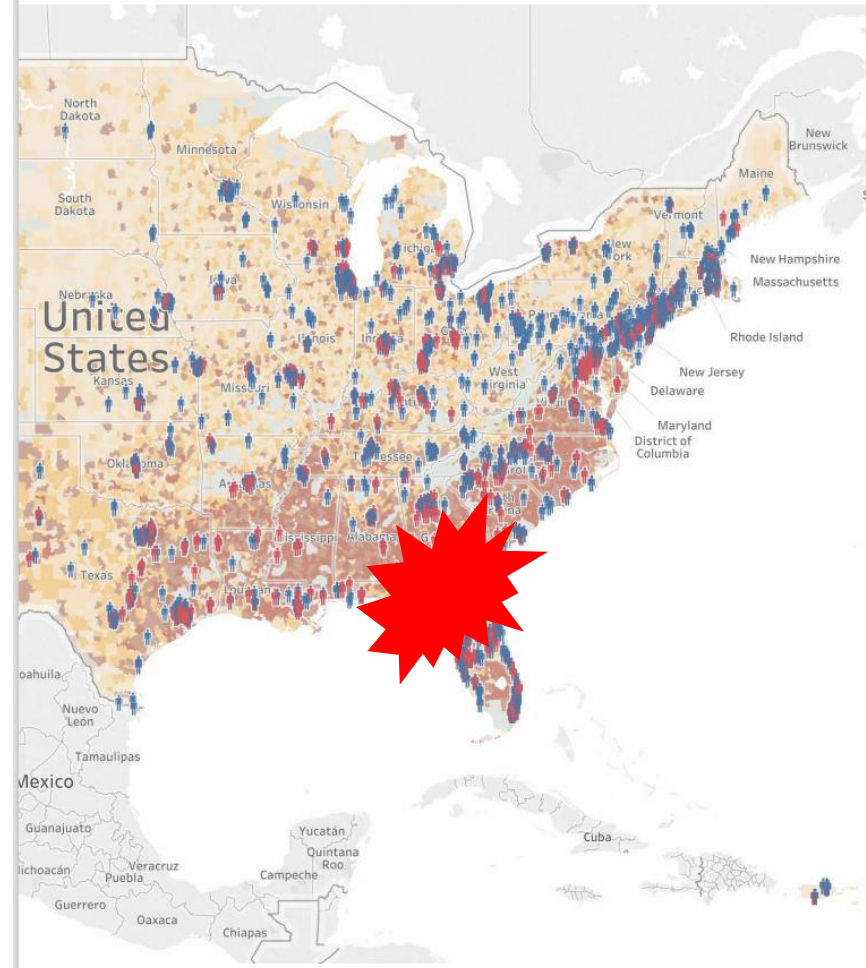
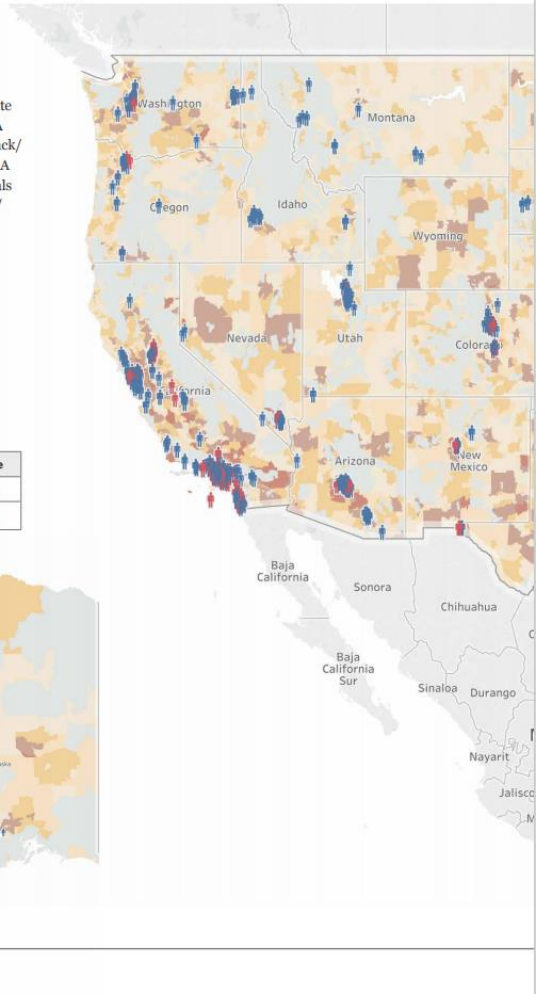
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Global Participation in Clinical Trials Report



2015-2016



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**Why is diversity in clinical trial
recruitment important?**

Cardiovascular Disease Disparities



Perspective

Racial Disproportionality in Covid Clinical Trials

Daniel B. Chastain, Pharm.D., Sharmon P. Osae, Pharm.D., Andrés F. Henao-Martínez, M.D., Carlos Franco-Paredes, M.D., M.P.H., Joanna S. Chastain, Pharm.D., and Henry N. Young, Ph.D.



Article **Figures/Media**

Metrics

August 27, 2020

N Engl J Med 2020; 383:e59

DOI: 10.1056/NEJMp2021971

5 References 29 Citing Articles Letters



This Issue

Views 149,171 | Citations 552 | Altmetric 1847 | Comments 4



Viewpoint



April 15, 2020

More ▾

COVID-19 and African Americans

Clyde W. Yancy, MD, MSc¹

» [Author Affiliations](#) | [Article Information](#)

JAMA. 2020;323(19):1891-1892. doi:10.1001/jama.2020.6548

JACC: CARDIOVASCULAR INTERVENTIONS

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VOL. 12, NO. 10, 2019

Racial Disparities in the Utilization and Outcomes of TAVR

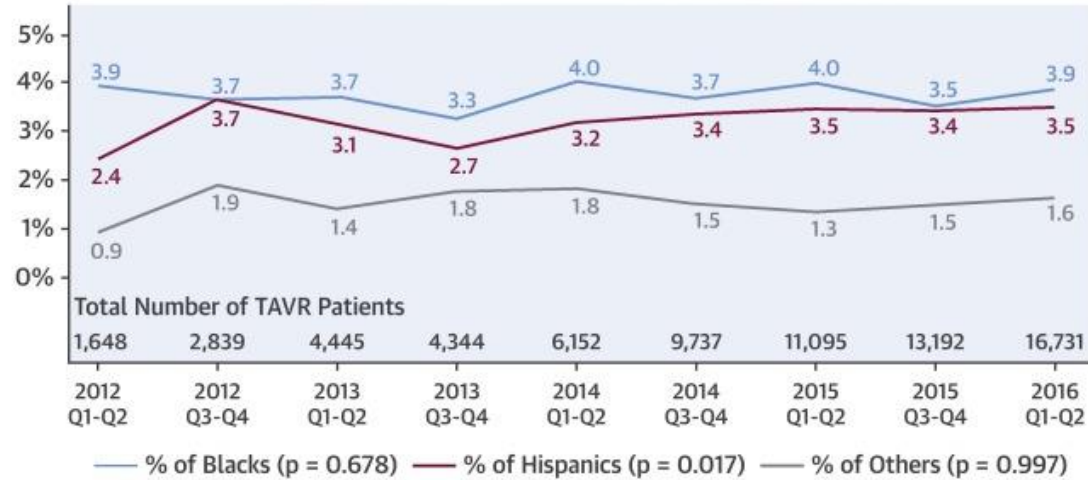


TVT Registry Report

Mohamad Alkhouli, MD,^{a,b,*} David R. Holmes, JR, MD,^{a,*} John D. Carroll, MD,^c Zhuokai Li,^d Taku Inohara, MD, PhD,^d
Andrzej S. Kosinski,^d Molly Szerlip, MD,^e Vinod H. Thourani, MD,^f Michael J. Mack, MD,^g
Sreekanth Vemulapalli, MD^{d,h}

CENTRAL ILLUSTRATION: Race-Stratified Differences in the Use and Outcomes of TAVR in the United States

Utilization of TAVR Among Racial Minorities



Baseline Characteristics Non-White vs. White	In-Hospital Outcomes Non-White vs. White	One Year Outcomes Non-White vs. White
Younger Age	Death ↔	Death ↔
More Females	Myocardial Infarction ↔	Myocardial Infarction ↔
More Medicare Insurance	Stroke ↔	Stroke ↔
Longer 5-Meter Walk Distance	Major Bleed ↔	Major Bleed ↑ Black
Higher STS Score	Pacemaker ↔	Valve Interventions ↔
More Aortic Insufficiency	Vascular Complications ↔	HF Hospitalizations ↑ Black, Hispanic
More Non-Elective TAVR		

Alkhouli, M. et al. J Am Coll Cardiol Interv. 2019;12(10):936-48.

JACC: CARDIOVASCULAR
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Racial
Outcomes
TVT Registry

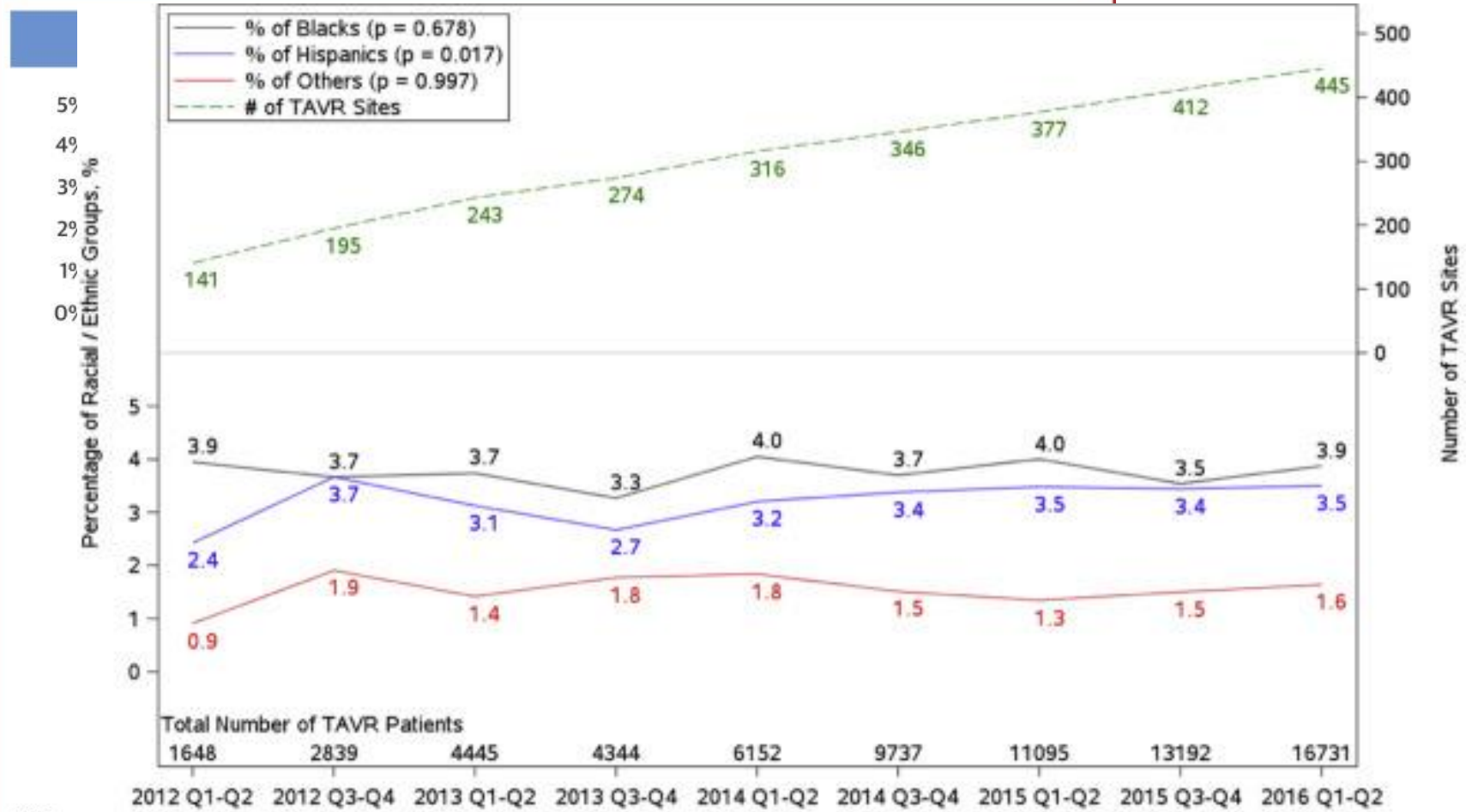
Mohamad Alkhouli
Andrzej S. Kosinski
Sreekanth Vemuri

CENTRAL ILLUSTRATION: Race-Stratified Differences in the Use and Outcomes of TAVR in the United States

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**Racial
 Outcomes
 TAVR Regi**

Mohamad Alkhouli
 Andrzej S. Kosinski
 Sreekanth Vemuri



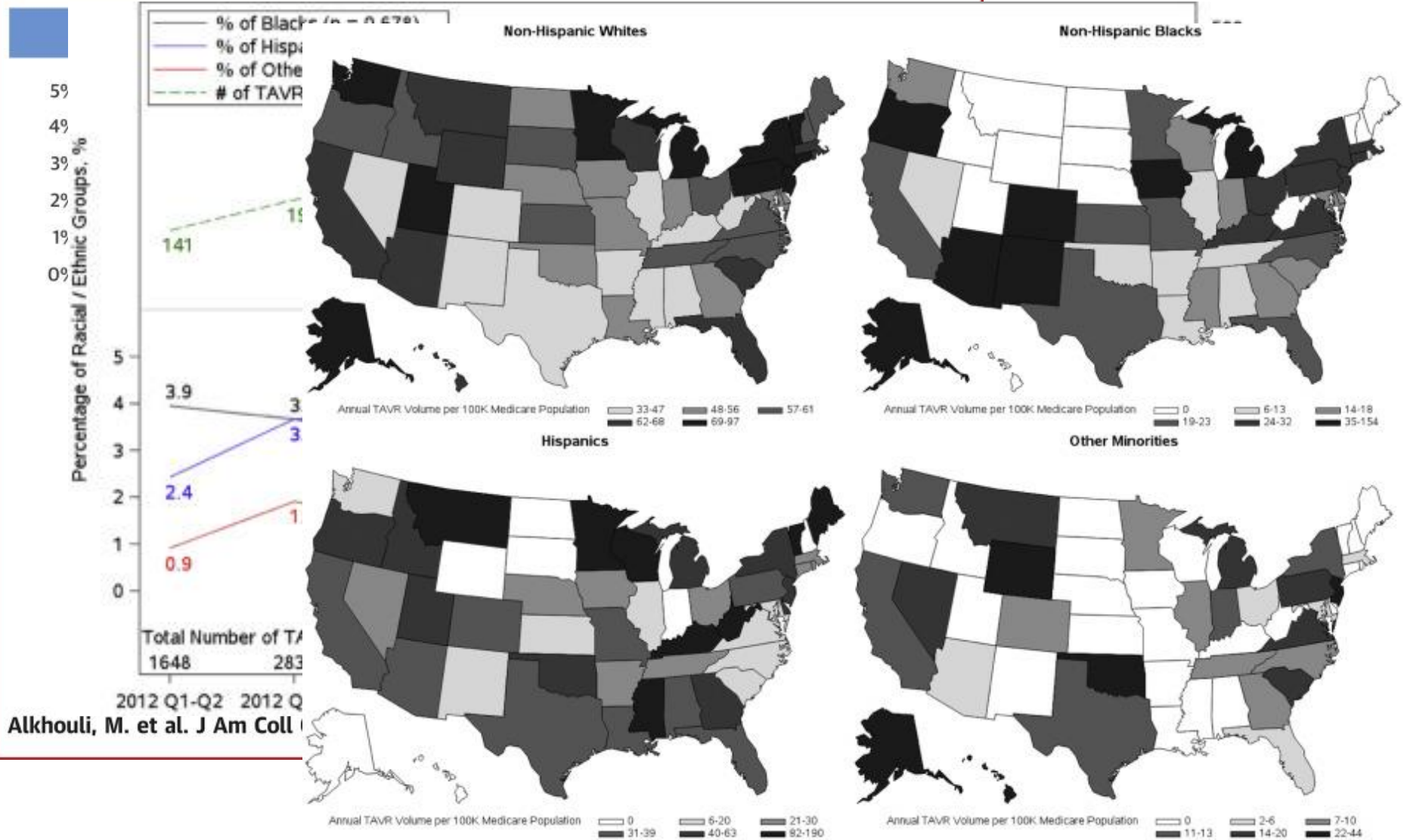
Alkhouli, M. et al. J Am Coll Cardiol Intv. 2019;12(10):936-48.

CENTRAL ILLUSTRATION: Race-Stratified Differences in the Use and Outcomes of TAVR in the United States

JACC: CARDIOVASCULAR INTERVENTIONS
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Racial and Ethnic Disparities in TAVR Outcomes

Mohamad Alkhouli
Andrzej S. Kosinski
Sreekanth Vemuri



Alkhouli, M. et al. J Am Coll



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**Can we change the way
we evolve evidence?**

Targeting Diversity in Clinical Trials



A relevant database-

Overcoming Lack of Diversity in Cardiovascular Clinical Trials

A New Challenge and Strategies for Success

Rebecca F. Ortega, Clyde W. Yancy, Roxana Mehran, Wayne Batchelor ✉

Originally published 18 Nov 2019 | <https://doi-org.ezproxy.galter.northwestern.edu/10.1161/CIRCULATIONAHA.119.041728> | Circulation. 2019;140:1690–1692

”While it may be argued that patient heterogeneity is a nuanced, rather than critical, component of drug or device efficacy, it is unquestionable that the current standard of care emanates from randomized controlled trials that have failed to fully represent elderly patients, minorities, and women.¹ The lack of adequate data for these relevant subgroups challenges the integrity of our evidence-based care algorithms and questions the replication of favorable safety and outcomes across all populations. These persistent missteps in our evidence-based generation could permit less than ideal health outcomes as a function of sex, age, race, and ethnicity.”

The Path Forward:

Ortega RF, Yancy CW,
Mehran R, Batchelor W.
*Overcoming Lack of Diversity
in Cardiovascular Clinical
Trials: A New Challenge
and Strategies for Success.*
Circulation.
2019 Nov 19;140(21):1690-1692.

- Consideration of economic incentives (or penalties) by the FDA (or payers) that would enable greater inclusion of diverse patients in clinical trials.
- Commitment by industry and the clinical science community to revisit the design of trials, selection of investigators and sites, and geographic balance of US and non-US subjects.
- Engagement with peer investigators outside of the United States to target more race/ethnicity diversity and gender balance in clinical trial recruitment.
- Exploration of enhanced cohort recruitment in phase IV or postapproval studies to address important safety and implementation questions.

The Path Forward:

*Ortega RF, Yancy CW,
Mehran R, Batchelor W.
Overcoming Lack of Diversity
in Cardiovascular Clinical
Trials: A New Challenge
and Strategies for Success.
Circulation.
2019 Nov 19;140(21):1690-1692.*

- Recruitment and training of more diverse coordinator and investigator research teams.
- Incorporation of novel information technology strategies, including use of electronic health data, social media, gamification, and other digital health technologies as unique steps to expand the pool of potential research subjects.
- Revision of the informed consent process, assuring that language matches literacy levels and that consent is culturally sensitive.
- Education at the societal level to advance the overall “research IQ” of the populace, thus overcoming a legacy of mistrust of the research enterprise and reducing barriers to participation in clinical trials.



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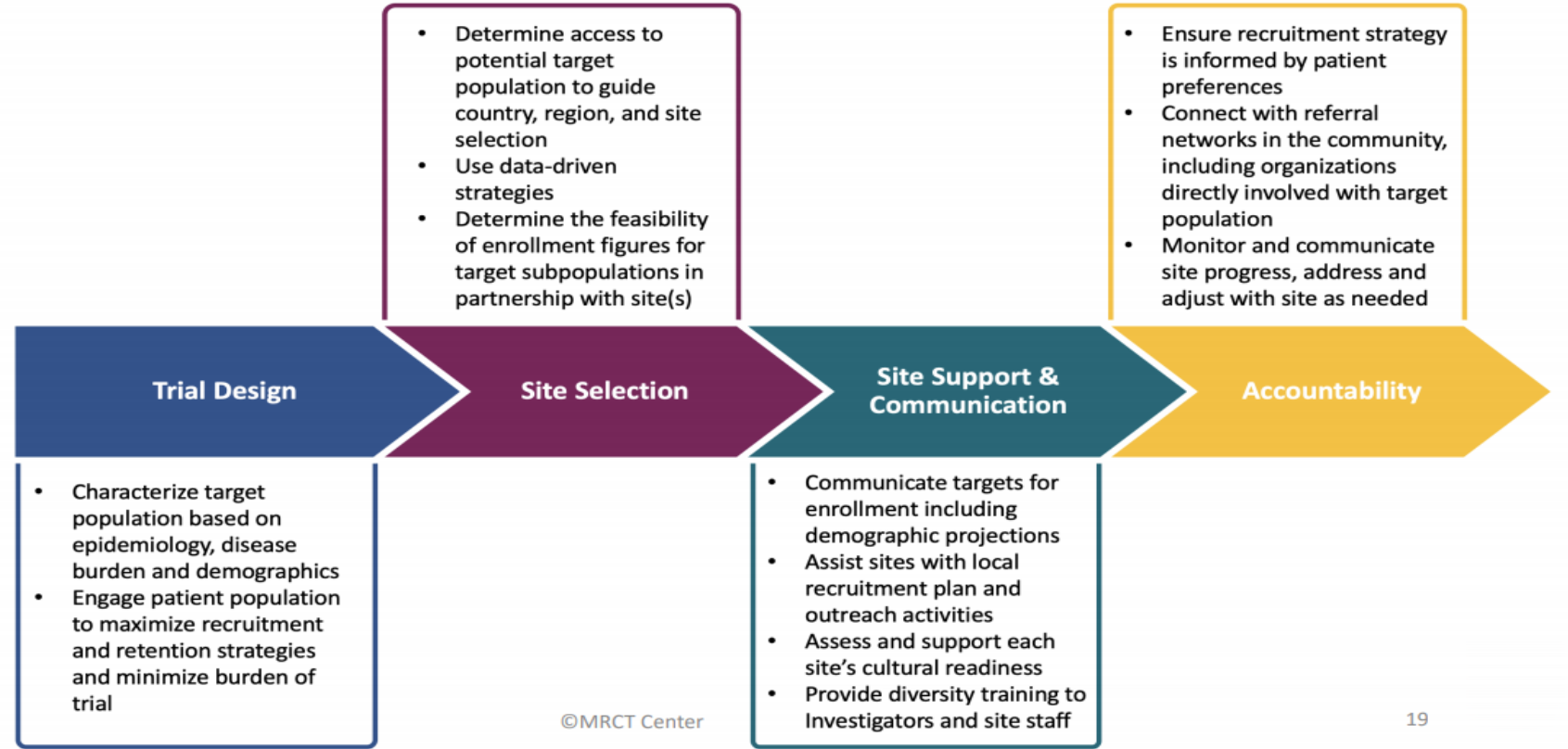
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Are there concordant points of view?



Achieving Diversity, Inclusion, Equity In Clinical Research

Opportunities: What can we do?



22 September 2020
FDA-hosted Launch

©MRCT Center

19

Multi-Regional
Clinical Trials Center

The MRCT Center
is supported by
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contributions
(www.MRCTCenter.org)
and grants

Proceedings from
FDA-hosted launch
9/22/2020

Brigham & Womens
Faculty Director:
Barbara E. Bierer, MD

FDA Guidance to Enhance Diversity in Clinical Trials, November 9, 2020

- **Inclusive Trial Practices**

- *Developing protocols intentionally to support inclusion*
- *Expanding recruitment criteria from phase II to phase III trials*
- *Recruitment of subjects who represent the target **marketing** population*
- *Explicit inclusion of women to support important sex/gender analyses*
- *Inclusion of racial minorities with concomitant detailed sociodemographic data*

- **Trial Design and Methodological Approaches**

- *Include genomics*
- *Consider adaptive trial design to accommodate alterations in clinical trial population based on real-time enrollment data*

FDA Guidance to Enhance Diversity in Clinical Trials, November 9, 2020

- **Broadening Eligibility Criteria in Trials**
 - *Enrichment strategies' emphasizing recruitment of targeted populations*
- **Making trial participation less burdensome**
 - *Support for transportation, parking other fees associated with logistics*
 - *Access for those with disabilities*
 - *Use of digital health tools*
- **Adopt enrollment and retention practices that enhance inclusiveness**
 - *Start with community engagement and public outreach; focus groups and community-based participatory research (engaging community members and leaders in the design and execution of the research)*



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How do we create accountability?



Diversity in Clinical Trial Leadership

May, 2021

JACC: HEART FAILURE

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EDITOR'S PAGE



Promoting Diversity in Clinical Trial Leadership: A Call to Action



JoAnn Lindenfeld, MD, *Deputy Editor, JACC: Heart Failure*,
Mona Fiazat, PHARM.D, *Executive Editor, JACC: Heart Failure*,
Christopher O'Connor, MD, *Editor-in-Chief, JACC: Heart Failure*



- First, we need to be more engaged and intentional in choosing site-based principal investigators with an eye toward diversity.
- Second, as journal editors we need to take an active role in inquiring and considering why a design or results paper of a large-scale clinical trial does not have significant representation of female or Black physicians in positions of leadership.
- The authors must explain the diversity of the study's leadership (PIs, committees, core labs, etc.) and author list in the Methodology section of the manuscript. If there is a lack of diversity, an explanation of this must be stated in the Limitations section of the manuscript.

SUMMARY

- Diversity in Clinical Trials is important as a meaningful action addressing ongoing cardiovascular health disparities
- Advancing Diversity in Clinical Trials involves:
 - Policy
 - Outreach
 - A priori intentions to support inclusion with trial design/protocol
 - Lessening barriers and improving access
 - ***Diversifying Clinical Trial Leadership***
 - Accountability
 - FDA
 - Sponsors
 - Journal Editors