ESC Cardiovascular Round Table

ESC European Society of Cardiology

CRT Plenary Meeting

5-6 July 2023

Steigenberger Herrenhof Hotel Vienna

"The Future of Clinical Trials: towards Diversity and Inclusion"

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@NMHheartdoc


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The burden of
health inequities

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Original Investigation

May 16, 2023

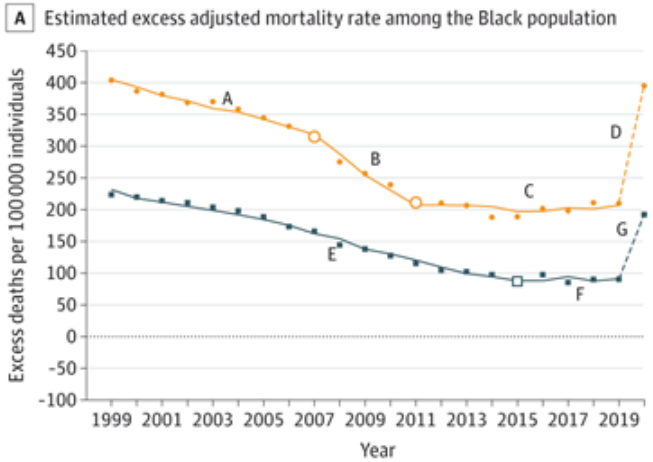
Excess Mortality and Years of Potential Life Lost Among the Black Population in the US, 1999-2020

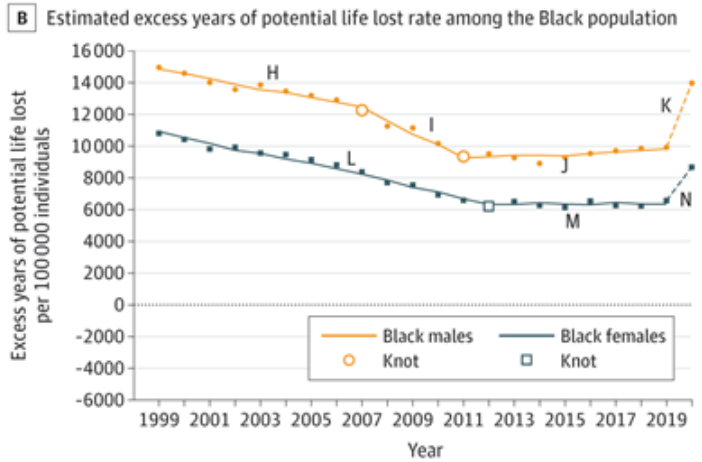
César Caraballo, MD[1,2]; Daisy S. Massey, BA[3]; Chima D. Ndumele, PhD[4]; et al

» Author Affiliations | Article Information

JAMA. 2023;329(19):1662-1670. doi:10.1001/jama.2023.7022

Figure 1. US Black Population Excess Age-Adjusted Mortality and Years of Potential Life Lost Rates, 1999-2020





Excess age-adjusted mortality rate

Period	Segment	Annualized rate of change (95% CI)	*P* value
Males			
1999-2007	A	-11.0 (-15.9 to -6.1)	<.001
2008-2011	B	-28.2 (-34.6 to -21.9)	<.001
2012-2019	C	-0.03 (-2.8 to 2.8)	.98
2020	D	185.3 (177.0 to 193.6)	<.001
Females			
1999-2015	E	-9.0 (-10.1 to -8.0)	<.001
2016-2019	F	0.9 (-3.9 to 5.8)	.71
2020	G	101.9 (96.3 to 107.5)	<.001

Excess years of potential life lost rate

Period	Segment	Annualized rate of change (95% CI)	*P* value
Males			
1999-2007	H	-304.2 (-389.5 to -218.9)	<.001
2008-2011	I	-797.6 (-952.0 to -643.2)	<.001
2012-2019	J	69.7 (-50.9 to 190.4)	.26
2020	K	4050.4 (2755.4 to 5345.5)	<.001
Females			
1999-2012	L	-349.7 (-389.6 to -309.8)	<.001
2013-2019	M	4.8 (-67.9 to 77.5)	.90
2020	N	2102.7 (904.3 to 3301.1)	<.001

To assess trends over time, the relationship between each metric and study year was graphically assessed, and time was modeled as a linear spline with knots that reflected the observed inflection points from 1999 to 2019. For excess mortality rates, these inflection points were from 2007 to 2011 for males and 2015 for females. For excess rates of years of potential life lost, the knots were 2007 and 2011 for males and 2012 for females. Rates that fall above the dotted line indicate rates higher than the White population and those that fall below, rates lower than the White population. Autoregressive integrated moving average models using a 1-year correlation were implemented to account for the serial correlation of annual rates. The 2019-2020 change was estimated using a *z* test.

Original Investigation

November 17, 2021

Racial, Ethnic, and Socioeconomic Disparities in Access to Transcatheter Aortic Valve Replacement Within Major Metropolitan Areas

Ashwin S. Nathan, MD, MS[1,2,3]; Lin Yang, MS[2,3]; Nancy Yang, BA[2,3]; et al

» Author Affiliations

JAMA Cardiol. 2022;7(2):150-157. doi:10.1001/jamacardio.2021.4641

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For each $1000 decrease in median household income, the number of TAVR procedures performed per 100 000 Medicare beneficiaries was 0.2% (95% CI, 0.1%-0.4%) lower (P = .002). For each 1% increase in the proportion of patients who were dually eligible for Medicaid services, the number of TAVR procedures performed per 100 000 Medicare beneficiaries was 2.1% (95% CI, 1.3%-2.9%) lower (P < .001). For each 1-unit increase in the Distressed Communities Index score, the number of TAVR procedures performed per 100 000 Medicare beneficiaries was 0.4% (95% CI, 0.2%-0.5%) lower (P < .001). Rates of TAVR were lower in zip codes with higher proportions of patients of Black race and Hispanic ethnicity, despite adjusting for socioeconomic markers, age, and clinical comorbidities.

Editor's Note

November 17, 2021

Race Bias in Transcatheter Aortic Valve Replacement

Are We Sure?

Clyde W. Yancy, MD, MSc[1,2]; Ajay Kirtane, MD, SM[3,4]

» Author Affiliations

JAMA Cardiol. 2022;7(2):158. doi:10.1001/jamacardio.2021.4647

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Houston, we *still* have a problem.

T O P A

Can we change the way we evolve evidence?

- Targeting Diversity in Clinical Trials

A relevant commentary-

Overcoming Lack of Diversity in Cardiovascular Clinical Trials

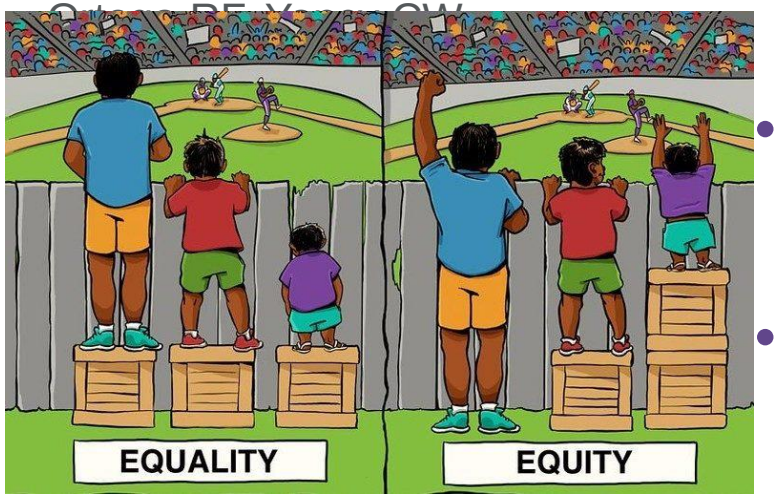
A New Challenge and Strategies for Success

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:



- Consideration of economic incentives (or penalties) by the **FDA (& 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 community cohort** recruitment in phase IV or postapproval studies to address important safety and implementation questions.

The Path Forward:

- 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.
- 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,

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)*

April, 2022

FDA NEWS RELEASE

FDA Takes Important Steps to Increase Racial and Ethnic Diversity in Clinical Trials

Agency's Focus on Inclusion in Trials for All Medical Products Aligns with Biden Administration's Cancer Moonshot Goal of Addressing Inequities and Beyond

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“The U.S. population has become increasingly diverse, and ensuring meaningful representation of racial and ethnic minorities in clinical trials for regulated medical products is fundamental to public health,” said FDA Commissioner Robert M. Califf, M.D. “Going forward, achieving greater diversity will be a key focus throughout the FDA to facilitate the development of better treatments and better ways to fight diseases that often disproportionately impact diverse communities…”

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

"... recommends that sponsors of medical products develop and submit a Race and Ethnicity Diversity Plan to the agency early in clinical development, based on a framework outlined in the guidance."

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What the guidance document states:

"The contents of this document do not have the force and effect of law and are not meant to bind…"

What the guidance document should state to ACCELERATE progress?

- "The contents of this document have the force and effect of law and are meant to bind…"

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Academic Guidance

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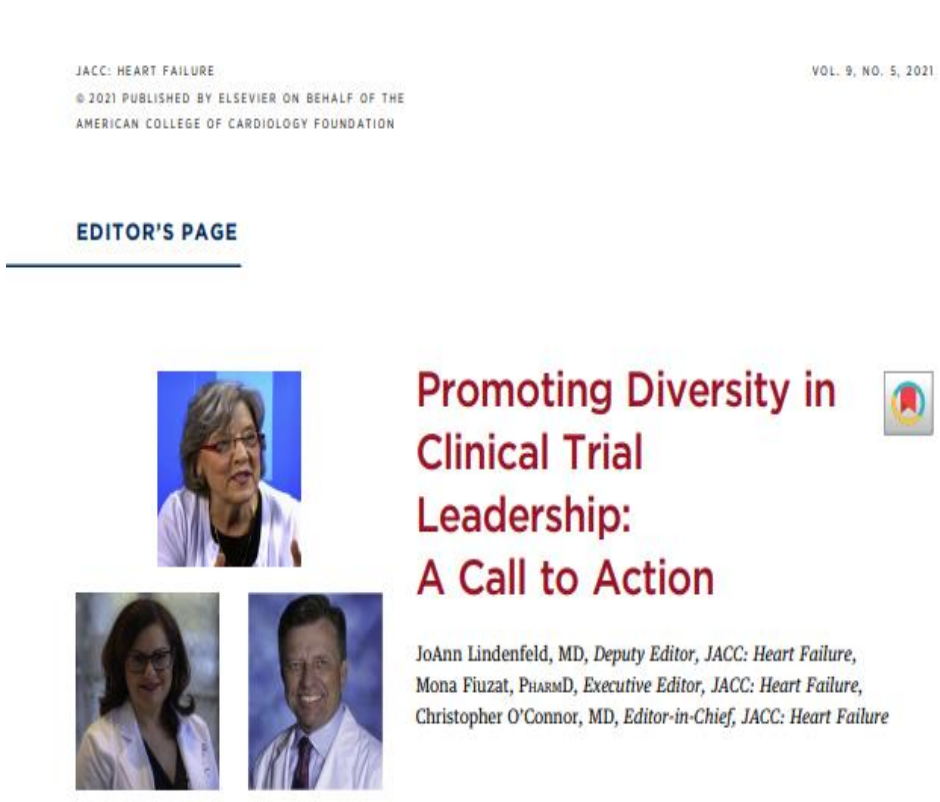
Diversity in Clinical Trial Leadership

- **May, 2021**



JACC: HEART FAILURE VOL. 9, NO. 5, 2021

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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 Fiuzat, PharmD, *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
- Accelerating Diversity in Clinical Trials
  - Patent protection/extension – US Patent Office
  - ENFORCEABLE Public Policy- FDA, CMS
- Advancing Diversity in Clinical Trials
  - Outreach; decentralization of sites; community engagement
  - A priori intentions to support inclusion with trial design/protocol
  - *Diversifying Clinical Trial Leadership*


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The Question of the Day?
Are you biased?


What? I'm not biased!


WARNING
BLIND SPOT AHEAD


Northwestern Medicine®
Overcoming Bias
What you can do today
P
Pay attention
A
Acknowledge your assumptions
U
Understand your perspective
S
Seek different perspectives
E
Examine your options and make a decision

“Thank you”

Clyde W. Yancy, MD, MSc

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