

Race and Medicine: A Genomics Policy Lens

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Disclaimer

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Opinions expressed are my own and should not be construed as the views of my affiliate institutions or collaborators

Session Aims

1. Clinician researchers
 - a) Challenges using genomics (instead of race) in clinical care
 - b) What are the risks and benefits of using race in medicine?
 - c) Report physician perspectives on using race in drug prescribing
2. Cancer biology researchers
 - a) Why is genomics failing on diversity?



Genomics is failing on diversity : Nature News

Challenges using genomics (instead of race) in clinical care – What we know



“human beings are 99.9 percent identical in their genetic makeup. Differences in the remaining 0.1 percent hold important clues about the causes of diseases.”

“Any two sub-Saharan Africans are more likely to be genetically different from each other than from an individual of European or Asian ancestry”

Science

Current Issue First release papers Archive About

HOME > SCIENCE > VOL. 371, NO. 6529 > COMPLICATED LEGACIES: THE HUMAN GENOME AT 20

POLICY FORUM | HUMAN GENOME ANNIVERSARY



Complicated legacies: The human genome at 20

KATHRYN MAXSON JONES, ROBERT COOK-DEEGAN, CHARLES N. ROTIMI, SHAWNEEQUA L. CALLIER, AMY R. BENTLEY, HALLAM STEVENS, KATHRYN A. PI

JEROEN P. JANSEN, CHRISTOPHER F. WEYANT, [...], AND MAYA WANG +7 authors [Authors Info & Affiliations](#)

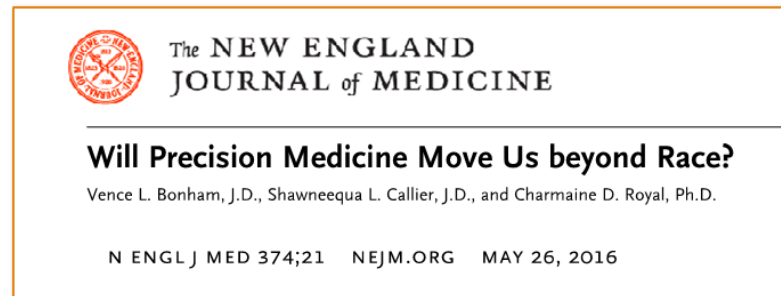
SCIENCE • 5 Feb 2021 • Vol 371, Issue 6529 • pp. 564-569 • DOI: 10.1126/science.abg5266

1,850 7



Challenges using genomics (instead of race) in clinical care – Practical concerns

- Since the 1700s we have not moved far away from Linnaeus' racial classification system despite knowledge that we are **99.9%** the same and that there is more diversity within populations than between them.
- Further, clinicians *usually* do not have the time or tools to assess ancestry and genomics and researchers have expended most of their energy studying people from Europe.

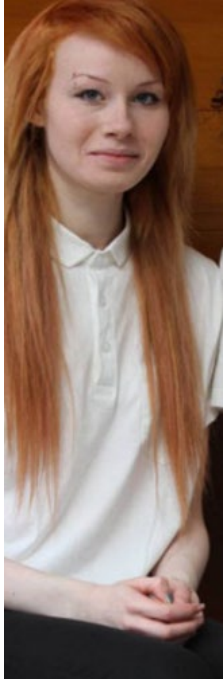


Species	1	2	3	4	5
Americanus	Red, choleric (bad-tempered), straight	Straight, black and thick hair; gaping nostrils; freckled face; beardless chin	Unyielding, cheerful, free	Paints himself in a maze of red lines	Governed by traditional practices
Europaeus	White, sanguine (cheerful), muscular	Plenty of yellow hair; blue eyes	Light, wise, inventor	Protected by tight clothing	Governed by religion
Asiaticus	Sallow, melancholic (sad), stiff	Blackish hair, dark eyes	Stern, haughty, greedy	Protected by loose garments	Governed by opinions
Africanus	Black, phlegmatic (unemotional), lazy	Dark hair, with many twisting braids; silky skin; flat nose; swollen lips; Further descriptions of sexual characteristics	Sly, sluggish, neglectful	Anoints himself with fat	Governed by choice

linnean.org

“The brevity of current clinical encounters coupled with the cost and time”

What race is this individual?



Inspiration: Video (11:20 min to 21 minutes in): Law, Genomic Medicine & Health Equity Conference/Webcast -- Consuelo Wilkins, Md,
<https://www.youtube.com/watch?v=8dHWZUw8DOQ>

What race is this individual?



The Conservation of Races by W.E.B. Du Bois (1897):

- “Many criteria of race differences have in the past been proposed, as color, hair, cranial measurements and language. . . Unfortunately for scientists, however, these criteria of race are most exasperatingly intermingled.”



Sendhil Ramamurthy



Beyoncé

What is race?

“Race is a concept without a generally agreed upon definition.”

“Racial groups have no defined boundaries, but have a blurry and imprecise relationship with human genetic variation and population groups across the world.”

-Vence Bonham, JD



National Human Genome
Research Institute

What is race?

Racial categories in the United States

- free, white or other, slave (1790)
- white, black, mulatto (1860)
- White, black, Mulatto, Chinese, Indian, Quadroon Octoroon, Japanese (1890)
- White, Black (of Negro Descent), Chinese, Indian, Japanese (1900)

Racial categories have changed in meaning over time

What is race?

Race in a Genetic World

MAY-JUNE 2008

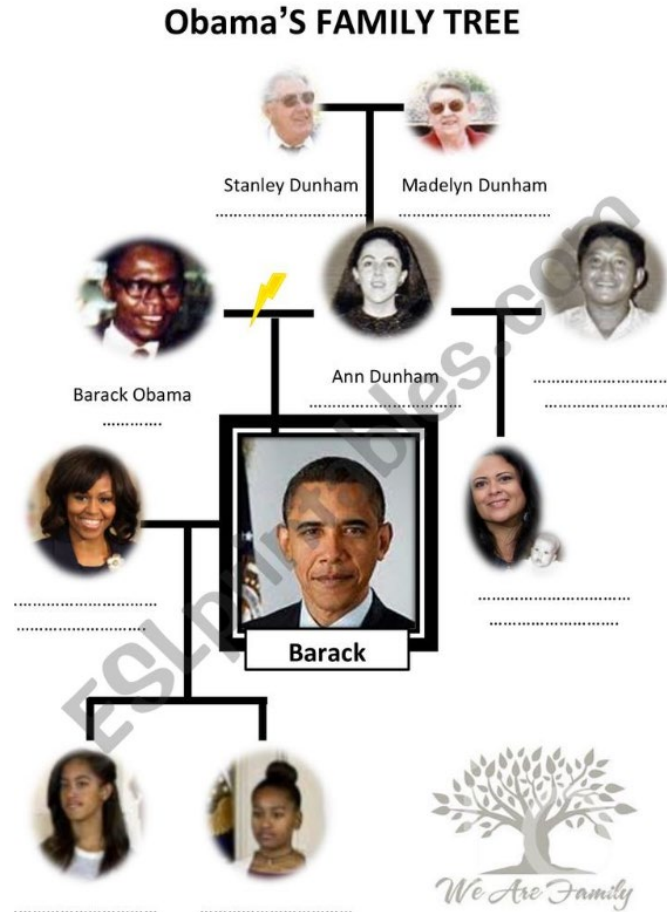
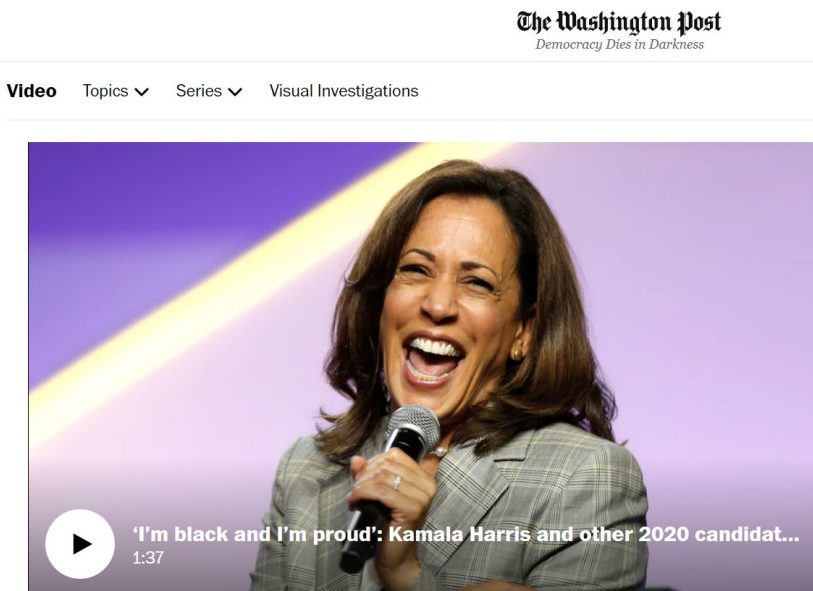
HARVARD
MAGAZINE

Dr. Duana Fullwiley
Anthropologist
Stanford University

(Harvard Magazine, 2008).

“I AM AN African American,” says Duana Fullwiley, “but in parts of Africa, I am white.” To do fieldwork as a medical anthropologist in Senegal, she says, “I take a plane to France, a seven- to eight-hour ride. My race changes as I cross the Atlantic. There, I say, ‘*Je suis noire*,’ and they say, ‘Oh, okay—*métisse*—you are mixed.’ Then I fly another six to seven hours to Senegal, and I am white. In the space of a day, I can change from African American, to *métisse*, to *tubaab* [Wolof for “white/European”]. This is not a joke, or something to laugh at, or to take lightly. It is the kind of social recognition that even two-year-olds who can barely speak understand. ‘*Tubaab*,’ they say when they greet me.”

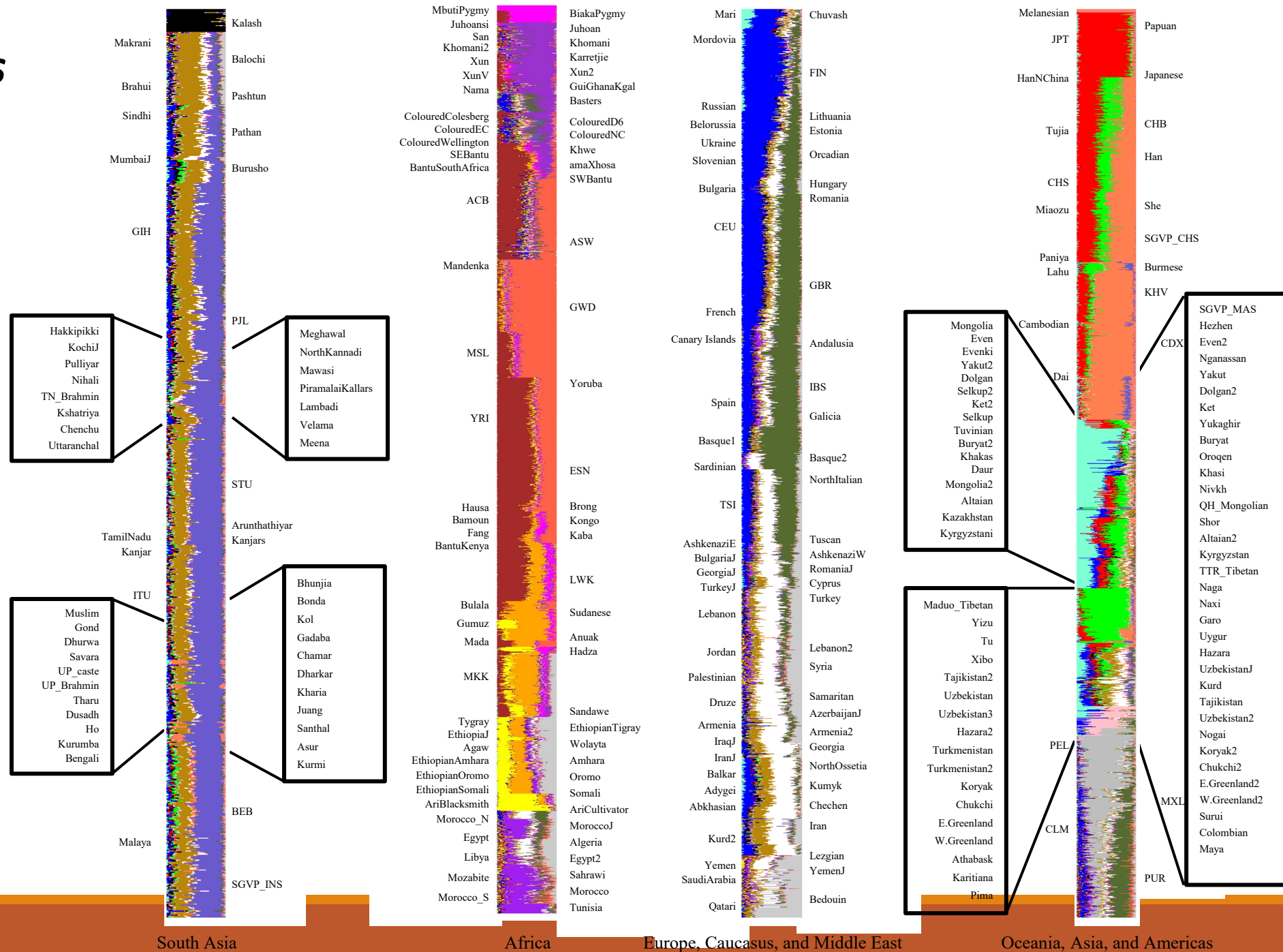
What are the risks and benefits of using race in medicine?



- Doctors are assessing race but racialized individuals have diverse ancestries.
- Self-identified race is **not** a reliable indicator of genotype or variation **locally**.
- Asking about family history and ancestry may help but many patients do not know their ancestry

Concerns

Baker, J.L., Rotimi, C.N. & Shriner, D. Human ancestry correlates with language and reveals that race is not an objective genomic classifier. *Sci Rep* 7, 1572 (2017).



South Asia

Africa

Europe, Caucasus, and Middle East

Oceania, Asia, and Americas

Ethical Concerns: Drug Prescribing

REVIEW ARTICLE

GENOMIC MEDICINE

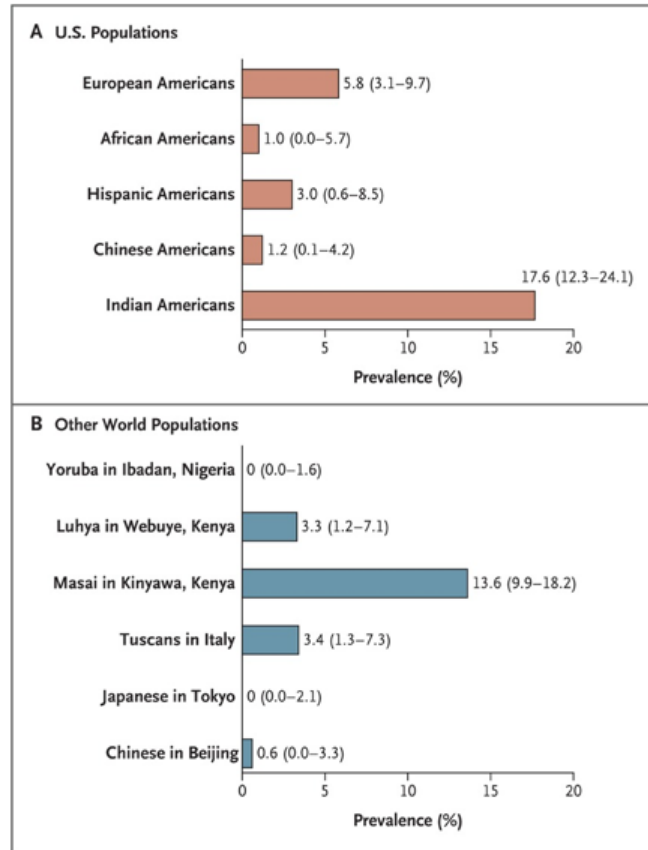
W. Gregory Feero, M.D., Ph.D., and Alan E. Guttmacher, M.D., Editors

Ancestry and Disease in the Age of Genomic Medicine

Charles N. Rotimi, Ph.D., and Lynn B. Jorde, Ph.D.

Public Health Implications Genetic Screening to Prevent Hypersensitivity Reaction to Abacavir

*Labels such as Black or African
"obscure biomedically relevant
variation and could lead to less
vigilance among physicians . . ."*

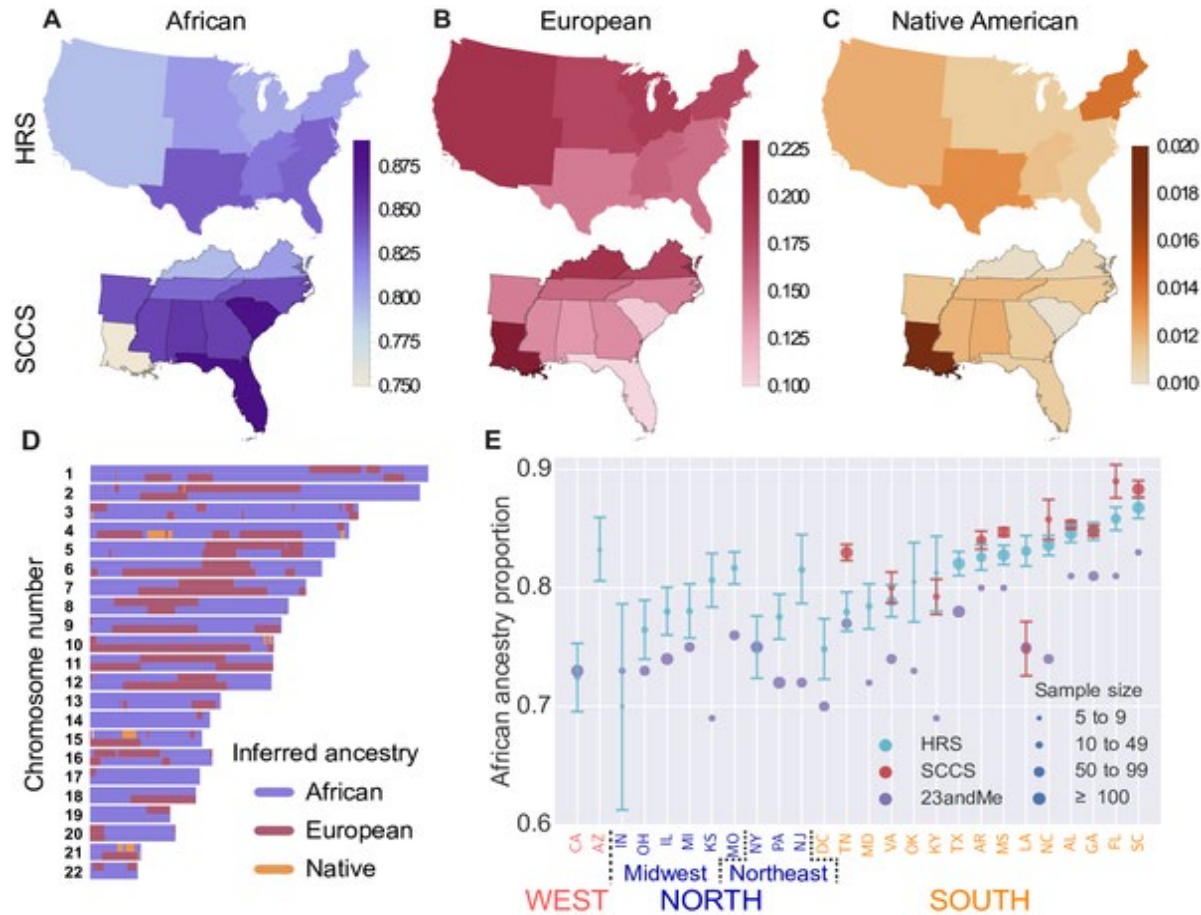


Rotimi CN, Jorde LB. *N Engl J Med* 2010;363:1551-1558.

THE NEW ENGLAND
JOURNAL OF MEDICINE

Figure 1. Variation in the HLA-B*5701 Locus in 11 HapMap Samples.

Fig 1. Inferred regional ancestry proportions for the HRS and SCCS cohorts: (A) African, (B) European, and (C) Native American ancestries.



“African-Americans have been under-represented in genetic studies, and relatively little is known about nation-wide patterns of genomic diversity in the population”

(Baharian et al., 2016)

Race as a proxy for racism

**Socioeconomic disparities
rank Iowa as third worst
state for Black Americans**

A recent study ranked Iowa as the third worst state in the U.S. for Black Americans on an index of various socioeconomic factors.



The Daily Iowan

THE INDEPENDENT NEWSPAPER OF THE UNIVERSITY OF IOWA COMMUNITY SINCE 1868

Race Correction

- “. . . . the system by which research characterising race as an essential, biological variable, translates into clinical practice, leading to inequitable care.”

Jessica P. Cerdeña et al., “From Race-Based to Race-Conscious Medicine: How Anti-Racist Uprisings Call Us to Act.” *The Lancet* 396, no. 10257 (2020): 1125-1128.

Race Correction

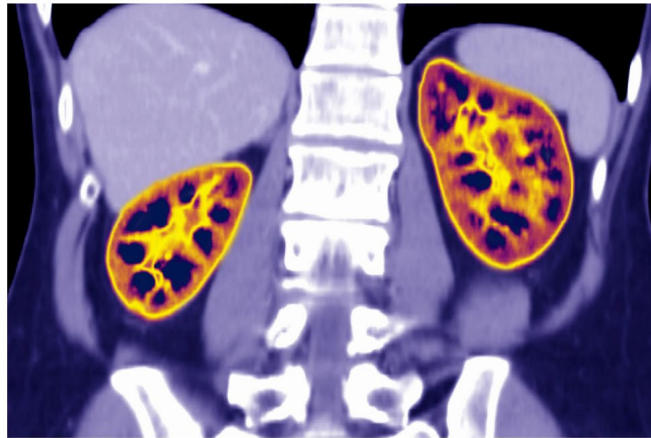
Report	
GLUCOSE	<p>**In accordance with recommendations from the NKF-ASN Task force,**</p> <p>Labcorp is in the process of updating its eGFR calculation to the 2021 CKD-EPI creatinine equation that estimates kidney function without a race variable.</p>
BUN	
CREATININE	
EGFR IF NONAFRICN AM	
EGFR IF AFRICN AM	

(National Kidney Foundation, n.d.)

Race Correction: Concerns

How an Algorithm Blocked Kidney Transplants to Black Patients

A formula for assessing the gravity of kidney disease is one of many that is adjusted for race. The practice can exacerbate health disparities.



A score known as eGFR aims to reflect the seriousness of a patient's kidney disease. PHOTOGRAPH: JAMES CAVALLINI/SCIENCE SOURCE

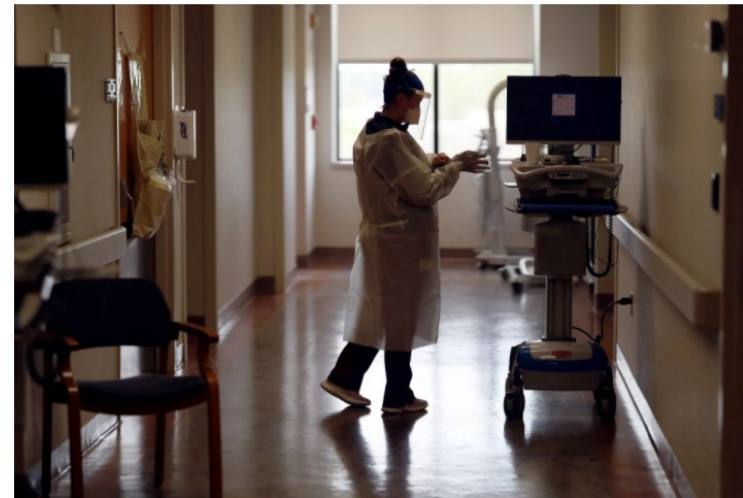
WIRED

(Simonite, 2020; Kolta, 2020)

The New York Times

Many Medical Decision Tools Disadvantage Black Patients

Doctors look to these digital calculators to make treatment decisions, but they can end up denying black patients access to certain specialists, drugs and transplants.



Race Correction



<https://www.hollywoodreporter.com/>

Race correction causes people who could benefit from a therapy or intervention not to receive it.

Waiting time adjustment approved for kidney transplant candidates affected by race-based calculation

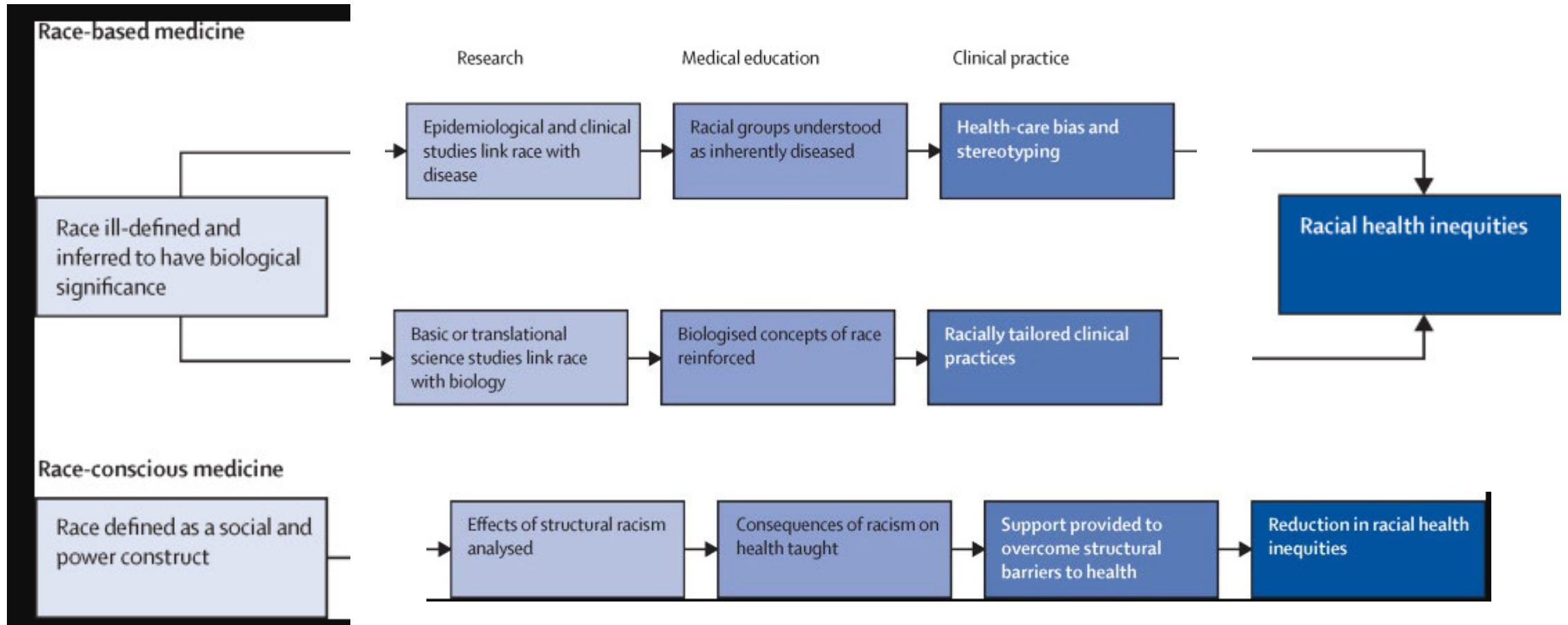
United Network for Organ Sharing

We are the private, non-profit organization that manages the nation's organ transplant system under contract with the federal government. [Learn more.](#)

Jan 5, 2023 | Equity, Kidney/pancreas, News, Patient, Trending



Race Correction: Concerns



Physician perspective in using race in drug prescribing

Arguments in favor of race correction and race-based drug prescribing

- Racial and ethnic categories correlate with continental ancestry
 - **(Growing agreement that this view ignores subcontinental diversity)**
- The benefits of relying on race may outweigh the potential harms
 - **(We shouldn't treat diverse groups from around the world as if they only have European ancestries)**
- It would be unwise to abandon the use of race in medicine because we have limited evidence about the benefits of using ancestry
 - **(Another way of saying, we don't know enough about diverse people to use ancestry instead of race; and we do not know enough about genomic diversity to use genomics)**



By Sonja Soo, Ph.D.

NIH study finds that failing to account for mixed genetic lineages could lead to inaccuracies

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

NOVEMBER 11, 2004

VOL. 351 NO. 20

**Combination of Isosorbide Dinitrate and Hydralazine in Blacks
with Heart Failure**

Anne L. Taylor, M.D., Susan Ziesche, R.N., Clyde Yancy, M.D., Peter Carson, M.D., Ralph D'Agostino, Jr., Ph.D.,
Keith Ferdinand, M.D., Malcolm Taylor, M.D., Kirkwood Adams, M.D., Michael Sabolinski, M.D.,
Manuel Worcel, M.D., and Jay N. Cohn, M.D., for the African-American Heart Failure Trial Investigators*

BiDil – Support

- NitroMed Supporters
 - National Association for the Advancement of Colored People (NAACP)
 - National Medical Association
 - Association of Black Cardiologists
 - Congressional Black Caucus
- Arbor Pharmaceuticals Partnership
 - Shaquille O’Neal
- “ Representatives from the ABC, NAACP, CBC, and members of the black community regarded BiDil as an appropriate response to race-based health disparities in the U.S. and even as, according to Susan Reverby, ‘reparations for racial wrongs’ like the Public Health Service Syphilis Study at Tuskegee.”

Rusert BM, Royal CD. Grassroots marketing in a global era: more lessons from BiDil. *J Law Med Ethics*. 2011;39(1):79-90.

15 August 2006

BiDil: From Another Vantage Point

Despite criticisms of BiDil, its clinical benefits for African Americans have held up to scientific scrutiny.

by Gary Puckrein

“Critics of BiDil’s approval as a race-based treatment have expressed concern about the medical and scientific validity of the concept of race. This concern is valid but, under present circumstances, impractical. Current research and medical practices recognize racial and other crude distinctions, in the absence of more precise information, every day.”



Race and Genetic Ancestry in Medicine — A Time for Reckoning with Racism

Luisa N. Borrell, D.D.S., Ph.D., Jennifer R. Elhawary, M.S., Elena Fuentes-Afflick, M.D., M.P.H., Jonathan Witonsky, M.D., Nirav Bhakta, M.D., Ph.D., Alan H.B. Wu, Ph.D., Kirsten Bibbins-Domingo, Ph.D., M.D., José R. Rodríguez-Santana, M.D., Michael A. Lenoir, M.D., James R. Gavin, III, M.D., Ph.D., Rick A. Kittles, Ph.D., Noah A. Zaitlen, Ph.D., [et al.](#)

2021

“The largest genetic clusters of people correspond to geographic regions and specific populations in Africa, Europe, Asia, Oceania, and the Americas, suggesting that continental-level ancestry captures the greatest population differences in genetic variation. **Ancestry assessment within continents can provide information on a finer scale**”

“**However, before ancestry adjustment is widely adopted, it is important to demonstrate that it provides results at least as accurate as those of race adjustment.**”

Cardiologists' Perspectives on BiDil and the Use of Race in Drug Prescribing

Shawneequa L. Callier^{1,2} · Perry W. Payne Jr.³ · Deborah Akinniyi⁴ · Kaitlyn McPartland⁵ · Terry L. Richardson⁶ · Mark A. Rothstein⁷ · Charmaine D. M. Royal⁸

- 2010 cross-sectional online survey, Association of Black Cardiologists, 59 respondents
 - BiDil not prescribed purely based on race but race influential due to A-HeFT
 - 59.2% viewed race as biological (2010)
 - Doctors did not refer patients to patient payment assistant programs

Cardiologists' Perspectives on Race-Based Drug Labels and Prescribing Within the Context of Treating Heart Failure

Shawneequa L. Callier , Brooke A. Cunningham, Jill Powell, Mary Anne McDonald, and Charmaine D.M. Royal

Published Online: 22 May 2019 | <https://doi.org/10.1089/heaq.2018.0074>

Health Equity, Vol. 3, No. 1 | Original Article

Semi-structured interviews at an American College of Cardiology Annual meeting to assess cardiologists' and cardiology fellows' attitudes toward the use of race in drug prescribing.

Table 2. Participant Demographics (N=81)

		n (%)
Race/Ethnicity	Asian	14 (17)
	Black or African American	15 (19)
	Hispanic/Latino	3 (4)
	White	44 (54)
	Middle Eastern	4 (5)
	Other	1 (1)
	Missing	1 (1)
Age	35 or younger	21 (26)
	36–45	18 (22)
	46–65	35 (43)
	Over 65	5 (6)
	Missing	2 (2)
Gender	Male	73 (90)
	Female	8 (10)
Practice environment (some cardiologists practice in more than one type of environment)	Hospital	17 (21)
	Group/private practice/clinic	48 (60)
	Academic	31 (38)
	Community	30 (37)
	Government	1 (1)
Years of practice	Missing	11 (14)
	1–5	30 (37)
	6–10	5 (6)
	11–20	9 (11)
	20+	31 (38)
	Missing	6 (7)

Results

A-Heft study presented an important opportunity to address health disparities

- “A lot of the studies, at least the older studies, really haven’t addressed the race issues in terms of differences in morbidity and mortality in terms of the disease state, so I think that we have a lot to learn about it. This was one of the earlier studies that seemed to indicate that there was an advantage in blacks so I don’t have a problem with it.”

Labeling the drug as “African American” is justified if it will lead doctors to prescribe this drug sooner to African American patients

The health outcome is more important than the racial label

- “At the end of the day, my job as a physician is to help people live their lives better, keep them healthy, have them live longer if that’s what they want. And if this [race-based drug prescribing] works for patients that are black, then for my patients that come see me, it’s something that I certainly should consider as a physician.”

Results

Non-Black patients may benefit

- “.we see it time and time again with BiDil. Even though it’s labeled to benefit African Americans more, Caucasian patients do benefit from it.”

Race is too simple a category

- “I think it is too simplistic to do race-based therapy. whoever made that trial, made it in such a way that they were not giving us an opportunity to select more specifically who should and shouldn’t get it”
- A variety of biological and medical factors contribute to heart failure morbidity and mortality, and a more rigorous trial would have taken other factors into account to better inform prescribing (i.e., comorbidities)

Other treatment options may be ignored

- “Well, I think the problem is that it sort of has gotten pigeon holed into, here’s what’s good for African Americans, here’s what’s good for white people, to the point that maybe you are excluding the other therapies, which probably should not be done.”

Results

Nearly half of all participants expressed skepticism or strongly disapproved of race-based drug labels and the use of race in drug prescribing. Yet, most participants stated that they continue to consider race when prescribing isosorbide dinitrate and hydralazine hydrochloride

Are race-based drugs and guidelines effective?

- Respondents in both studies prescribed BiDil and the generics but were skeptical about their own drug prescribing behaviors
- There is continued skepticism about the FDA's approval of BiDil for one race
- Some physicians may disregard race-based guidelines; the debate could cost lives

Clinicians are not prescribing BiDil

Adv Ther (2017) 34:1976–1988
DOI 10.1007/s12325-017-0584-x



ORIGINAL RESEARCH

Fixed-Dose Versus Off-Label Combination of Isosorbide Dinitrate Plus Hydralazine Hydrochloride: Retrospective Propensity-Matched Analysis in Black Medicare Patients with Heart Failure

Elizabeth Ofili · Inder Anand · Richard Allen Williams · Ola Akinboboye ·

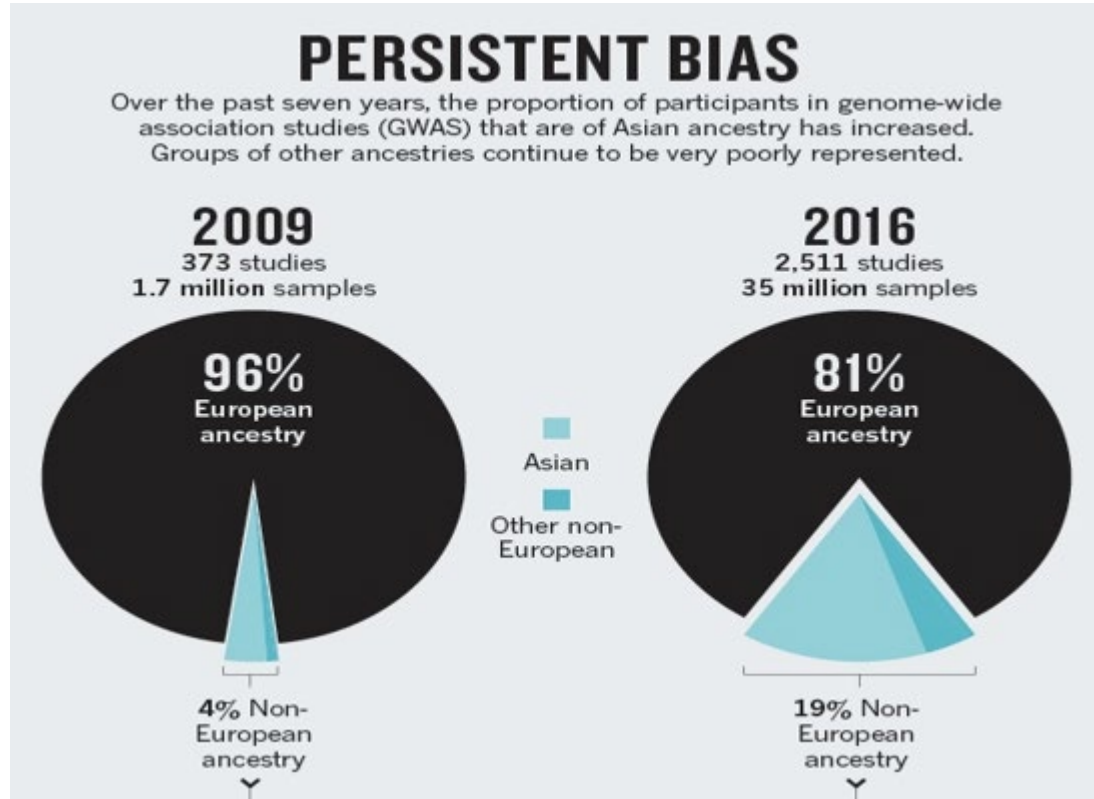
Liou Xu · Gary Puckrein

Received: May 19, 2017 / Published online: July 13, 2017
© The Author(s) 2017. This article is an open access publication

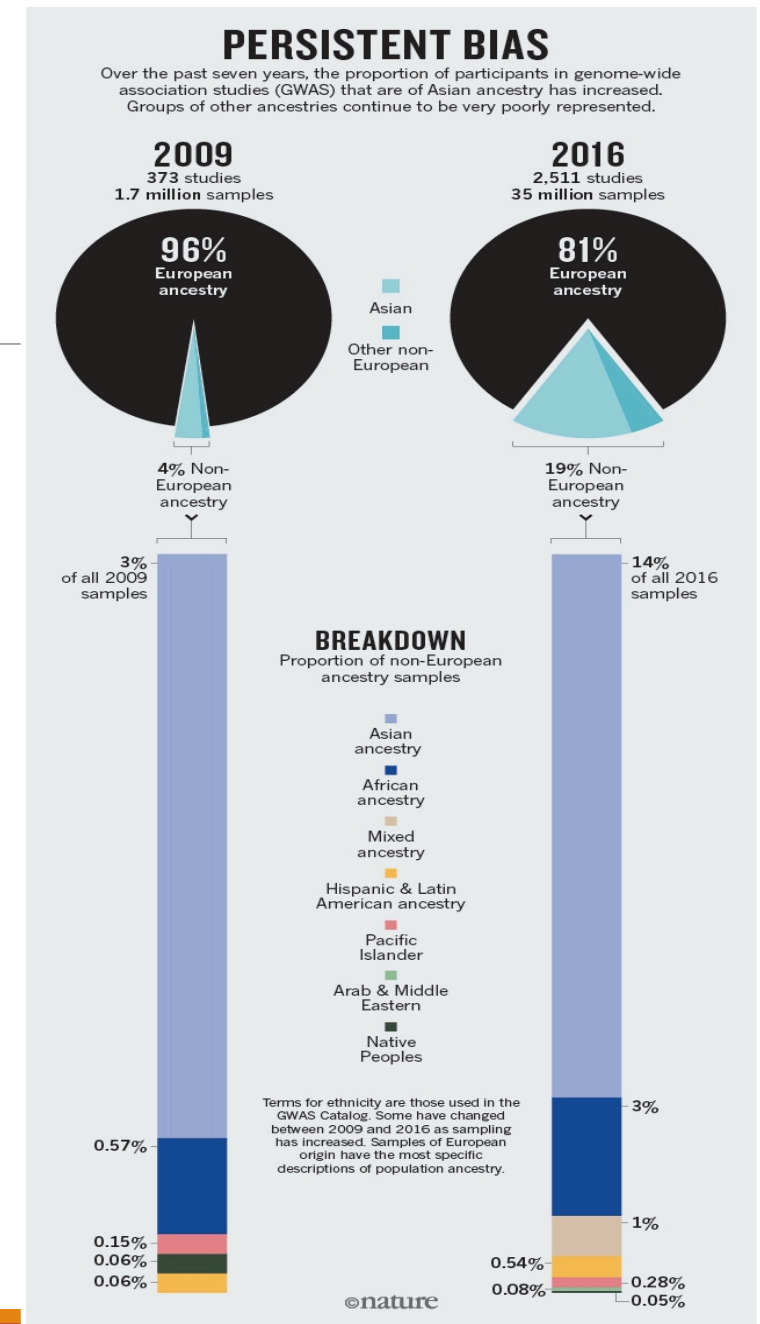
“In the absence of more specific indicators, the appropriate clinical approach is to heed evidence in prescribing a life-saving therapy.”

What should Cancer biology researchers understand?

Lack of Diversity & Inclusion



(Popejoy et al., 2016)



What are the potential pitfalls of precision medicine?

Gwasdiversitymonitor.com

- The “Preferred Cohort” Effect and Flawed Comparisons
 - “the vast majority of the well-characterized, well-studied genomic research cohorts are of European ancestry populations.”
- Bentley et al. 2017



Mills et al. 2020. *Nature genetics* 52, (3) (03): 242-2

Ethical Concerns: Lack of D&I in Research Analysis



nature

Don't ignore genetic data from minority populations

Efforts to build representative studies are defeated when scientists discard data from certain groups. Instead, researchers should work to balance statistical needs with fairness.

Sun, R., Hleap, J. S., Diaz-Papkovich, A., Munter, H. M., Grant, A. V., Dupras, C., & Gravel, S. (2020).

What are the potential pitfalls of precision medicine?

- “Limitations in current genotyping technology to adequately capture variation among diverse individuals”
- “Investing in overcoming the analytical challenges of studying diverse populations”
- Bentley et al. 2017

> J Natl Cancer Inst. 2022 Mar 17;djac054. doi: 10.1093/jnci/djac054. Online ahead of print.

Lower Exome Sequencing Coverage of Ancestrally African Patients in the Cancer Genome Atlas

Daniel P Wickland ¹, Mark E Sherman ¹, Derek C Radisky ², Aaron S Mansfield ^{3 4}, Yan W Asmann ^{1 4}

HEALTH
IT ANALYTICS
xelligent HEALTHCARE MEDIA
(<https://healthitanalytics.com/>)

Analytics in Action News

Black Cancer Patients Have Lower Quality Genomic Sequencing Data

Mayo Clinic found significant differences in genomic sequencing data among racial groups, specifically lower quality data for Black patients in one of most used cancer research datasets.



Ethical Concerns: Lack of diversity in research has clinical implications



HealthAffairs

Lack Of Diversity In Genomic Databases Is A Barrier To Translating Precision Medicine Research Into Practice

Latrice G. Landry, Nadya Ali, David R. Williams, Heidi L. Rehm, and Vence L. Bonham

AFFILIATIONS ▾

PUBLISHED: MAY 2018 No Access

<https://doi.org/10.1377/hlthaff.2017.1595>

(Grady, 2016 & Landry, et al., 2018)

Ethical Concerns: Encouragement of race-based drug approval processes

Race is used as a genetic category to obtain patent protection and drug approval.

Race-specific patent language has served as a foundation for conducting clinical trials, developing and marketing drugs, and raising capital.

Kahn, J. Patenting race. *Nat Biotechnol* **24**, 1349–1351 (2006).

Table 1 Racial and ethnic categories mentioned in US patent filings, 1976–present

From: [Patenting race](#)

Category	Issued patents		Patent applications filed since 2001
	1976–1997	1998–2005	
Race	0	2	15
Ethnic	0	0	2
African-American/black	0	4	11
Alaska native	0	0	0
Asian	0	0	13
Caucasian/white	0	6	18
Hispanic/Latino	0	0	3
Native American	0	0	2
Pacific Islander	0	0	1
Total	0	12	65

Use of Race, Ethnicity, and Ancestry as Population Descriptors in Genomics Research

National Academies of Sciences, Engineering, and Medicine ad hoc committee (2022)

Perspective

Box 5

Bold predictions for human genomics by 2030

“Research in human genomics will have moved beyond population descriptors based on historic social constructs such as race.”

Green, E.D., Gunter, C., Biesecker, L.G. *et al.* Strategic vision for improving human health at The Forefront of Genomics. *Nature* **586**, 683–692 (2020). <https://doi.org/10.1038/s41586-020-2817-4>



What can you do

- Increase your awareness of the debate and read about new guidelines and discussions about the use of race in cancer research and care.
- Attend webinars and encourage journal club meetings in your workplace
- Ask yourself, every time, why you are using race as a variable in clinical care or research and whether there are other measurable variables that you could use instead
 - i.e., racism and epigenetics, educational attainment, genetic similarity
- If you must use race, explain in all of your papers and talks that race is a poor proxy for variation that does not reflect genetic variation and then go on to provide the justifications for why you are using racial categories in your work
- Final additional points
 - Ethnic groups also experience ancestry and genetic diversity. Provide the same justifications for using ethnicity which could include geographical isolation or location (Nigeria vs. Kenya), community and cultural factors, political factors, or genetic variants prevalent in a particular ethnic group (Luya vs. Maasi).
 - Engage with historians, anthropologists, and ELSI researchers

Questions

Prof. Shawneequa Callier

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