The Use of Race Correction in Clinical Algorithms

UCLA Department of Urology Grand Rounds

9-15-21

UCLA Health | David Geffen School of Medicine

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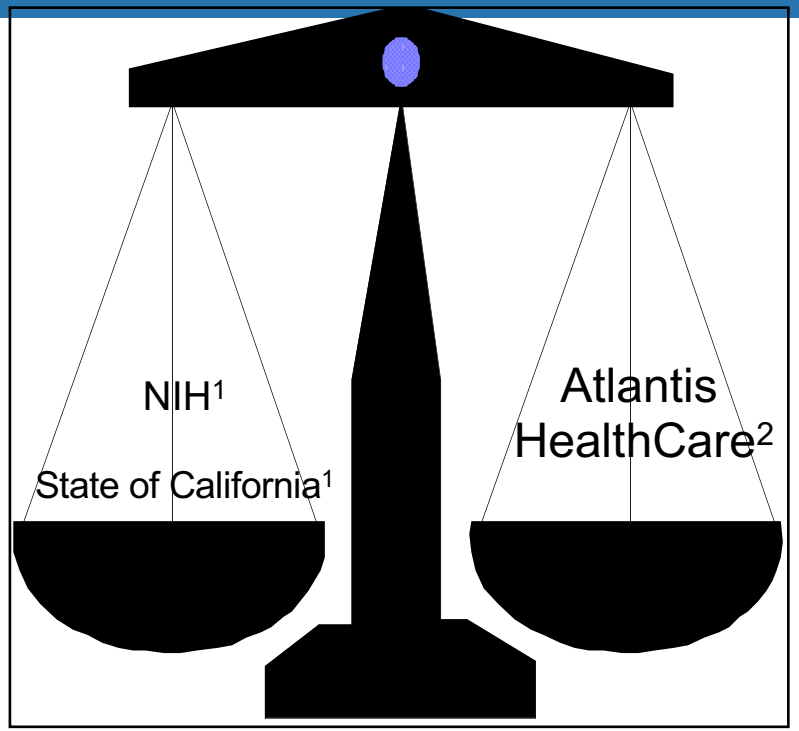
Building.Belonging.Becoming.

Disclosures/Potential Conflicts of Interest*#



* Activities within the last year

Grants: 1

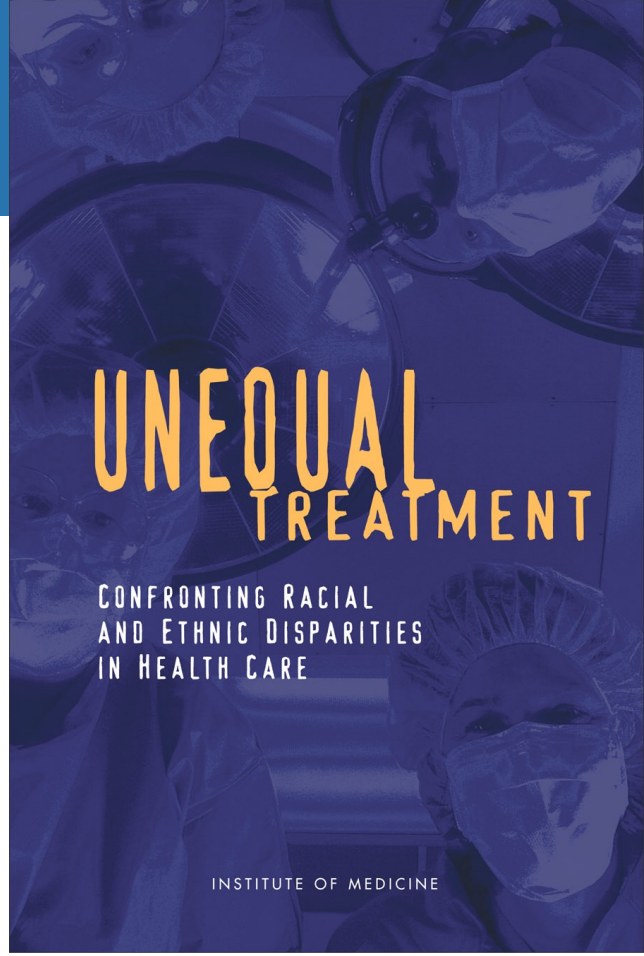
Consulting: 2

None related to this talk

I believe in a society grounded in Equity & Justice

I am not an expert in anything

Major Race-Based Inequities Exist in Society & in Medicine that lead to Disparities and Undermine the Research Advances and Optimal Care for All



Outline

- **The use of race in medical algorithms and formula for assessing kidney and urologic and other diseases**
- More appropriate use of race in research
- The Way Forward

Who is leading the race to remove race?

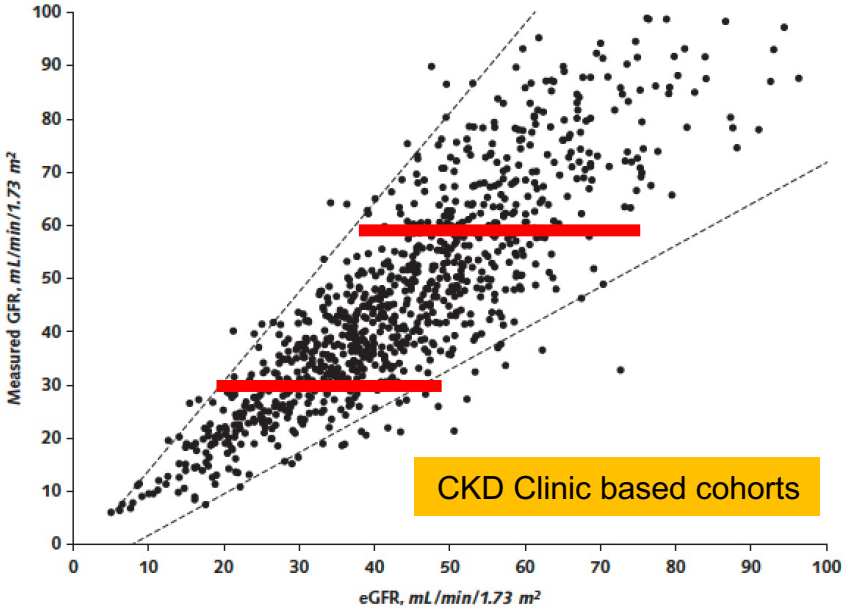
They say race is a social and not a biologic construct

Medical students lead effort to remove race from kidney function estimates

- When a lecturer described the use of black race as an adjustment in estimated glomerular filtration rate (eGFR) calculations, it made medical students uncomfortable.
  - One said the use of race as a proxy for muscle mass hearkened back to racist comments she'd heard suggesting that Black people have more muscle or are otherwise biologically different.
    - E.g. Lung function - Gould BA. Investigations in the military & anthropological statistics of American soldiers. New York: Hurd & Houghton, 1869.
- A growing movement led by US medical students across the country is working to eliminate the use of race as an adjustment in eGFR and more.

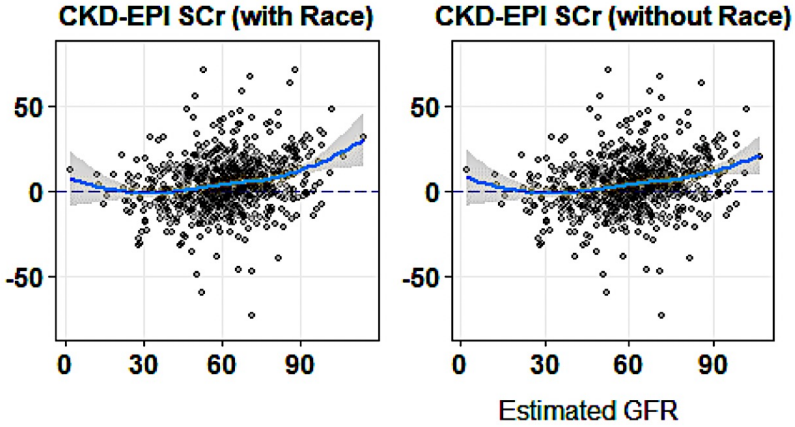
Medical students lead effort to remove race from kidney function estimates. Available at: https://www.kidneynews.org/kidney-news/current-issue/medical-students-lead-effort-to-remove-race-from-kidney-function-estimates. July 24, 2020

Relationship between iothalamate GFR and CKD-EPI eGFR, ml/min/1.73m^2



CKD Clinic based cohorts

The dashed lines represent 95% prediction intervals, by using quantile regression. Unpublished data are from 954 adult participants in the Chronic Renal Insufficiency Cohort study. CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR = estimated glomerular filtration rate.



Zhu X, Shafi T, Norris KC, Simino J, P, Griswold ME, PHD^2, Lirette S. Three new race-free, community-based equations to estimate GFR: the machine learning estimation of renal function (MLERF) equations. ASN Kidney Week 2021

Community based cohorts

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Sehgal AR. Race and the False Precision of Glomerular Filtration Rate Estimates. *Ann Intern Med.* 2020;173:1008-1009

Publication Date: 24 Aug 2021

ASN and NKF Commend Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases

In addition to the task force's interim report, NKF and ASN set forth the following objectives:

1. Equations to estimate kidney function should not include race modifiers.
2. Current race-based equations should be replaced by a suitable approach that is accurate, inclusive, and standardized in every laboratory in the United States.
3. Any such approach must not differentially introduce bias, inaccuracy, or inequalities.

NKF/ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases

NATIONAL KIDNEY FOUNDATION®

ASN American Society of Nephrology

August 2020

Reconsidering the Use of Race Correction in Urology

Tool & Clinical Utility	Input Variables	Use of Race
STONE Score Predicts ureteral stone risk in patients who present with flank pain	• Sex • Acute onset of pain • **Race: Black or non-Black** • Nausea or vomiting • Hematuria	A 13-point scale, with a higher score indicating a > risk of a ureteral stone; **3 points are added for non-Black race**, same as for hematuria
Urinary tract infection calculator estimates risk in 2–23 mo old children to guide urine testing decisions for definitive diagnosis (https://uticalc.pitt.edu/)	• Age <12 months • Max temp >39° C • **Race: Black Female or uncircumcised male** • Other fever source	**Assigns a lower UTI likelihood to a Black child (i.e., ~2.5-times increased risk vs. non-Black patients**

Vyas DA, et al. Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms. NEJM. 2020.

Social Justice vs. Race Based Medicine

We should not change “science” because people want social justice

vs.

We should not do less than our best “science” because we don’t understand race or how to use it in medicine

We often hear people say yes race is a social construct, but - and then proceed to use it as a biologic variable

Mohottige D, Diamantidis CJ, Norris KC, Boulware LE. Racism and Kidney Health: Turning Equity Into a Reality. Am J Kidney Dis. 2021 Jun;77(6):951-962

The Problem

1) First - we need to understand what race is and how race **should and should not** be used in medicine
2) Then we can determine what we should do with race in existing formulas/algorithms
    1) the rationale for why race as a variable has been included in algorithms
    2) whether race-based measurements are reproducible with fidelity at an individual level
3) We have taken a backward approach by assuming because race is in a formula/algorithm it is appropriate and now how do we work around it – rather than should it be there at all

Vyas DA, et al. Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms. NEJM. 2020.

- The use of race in medical algorithms and formula for assessing kidney disease
- **More appropriate use of race in research?**
- The Way Forward

A Few Definitions

What have we learned about race since 1950?

"Scientists have reached general agreement in [recognizing] that mankind is one: that all men belong to the same species, Homo sapiens. The myth of 'race' has created an enormous amount of human and social damage. In recent years it has taken a heavy toll in human lives and caused untold suffering. It still prevents the normal development of millions of human beings and deprives [civilization] of the effective co-operation of productive minds."

In "The race question" UNESCO (United Nations Educational, Scientific and Cultural Organization) **1950**

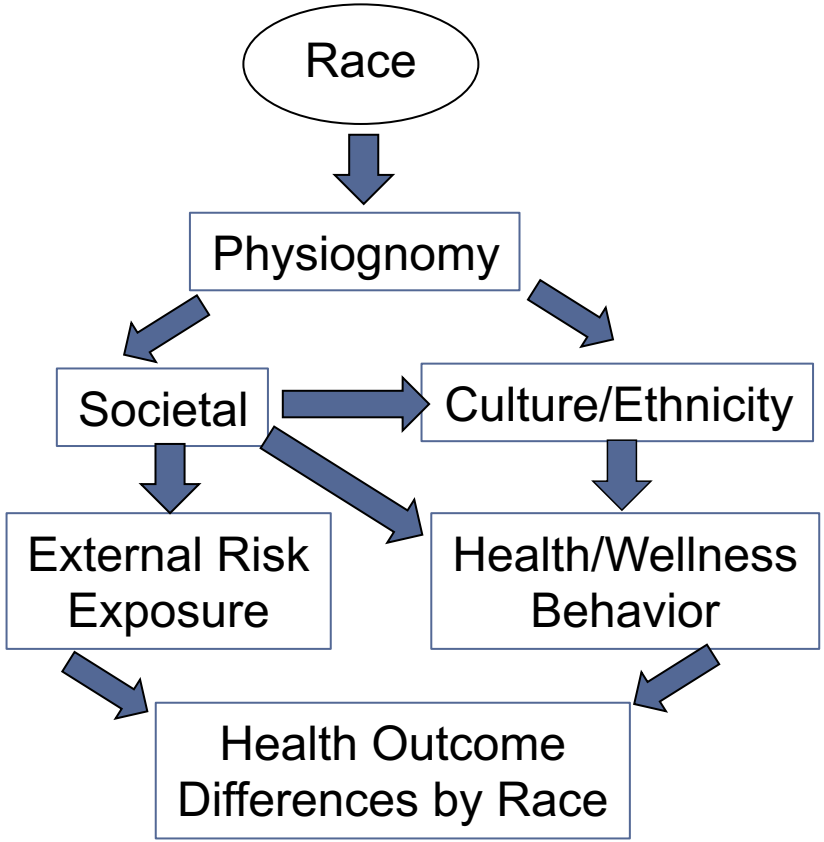
Race – social interpretation of how one looks in a "race"- conscious society

- A socio-political construct to control power based on how people look (race) and then expanded to marginalize other people (ethnicity - culture/language/religion)
  - *Derived from White supremacy ideology to justify and maintain American Indian genocide/oppression & chattel slavery*
    - *The ideology persists & the role of Medicine/Science has been to prove race is biologic*
  - Race is **indirectly** (**not directly)** related to ancestry
  - **As a research variable: race is a poor indicator of biology and strong indicator of exposure to racism**

Race is socially assigned = How society sees you and thinks of you

Jones CP. Confronting Institutionalized Racism. *Phylon.* 2002;50(1/2):7-22.
Bailey ZD, et al. How Structural Racism Works — Racist Policies as a Root Cause of U.S. Racial Health Inequities. New England Journal of Medicine. 2020.

Conceptual Model of Race in Research



Latent (unobserved & unmeasurable factor)

Manifest indicator (Mostly Skin Color)

Categorization into risk/behavior groups

Risk Exposure

Health Outcome

Adapted from La Veist TA. Why we should continue to study race...but do a better job: an essay on race, racism and health. Ethnicity & Disease. 1996;6(1-2):21-9.

Race & Biology

- Human Genome Projects, completed June 2020:
  - ***'race' is not a scientifically valid construct*** - Craig Venter, Head Celera Genomics
- Race does have biologic <u>associations</u>
  - Racism can affect health/illness & biology
  - Race is indirectly (**not directly**) related to biology/ancestry
    - Estimated that 85% of human genetic variation occurs between two persons from the same ethnic group, 8% occurs between tribes or nations, and 7% occurs between the so-called major races

#1 The number of people you would classify as having Asian Ancestry is
#2 The number of people you would classify as White race is
#3 The number of people you would classify as Black or African American race is
#4 The number of people with asymptomatic kidney stones is

Possible answers
0, 1, 2, 3, 4, 5, 6, don't know

Jones CP. Confronting Institutionalized Racism. *Phylon.* 2002;50(1/2):7-22.; Jones CP. Levels of racism: a theoretic framework and a gardener's tale. *Am J Public Health*. Aug 2000;90(8):1212-5.
Witzig R. The medicalization of race: scientific legitimization of a flawed social construct. Ann Int Med. 1996;125(8):675-9.

Race does not = Population or Continental Ancestry

- A person from Southern Africa, Northern Africa, Aboriginal Australian, U.S. slave descendent may be classified Black or African American.
- A person from China, India, Pakistan, Thailand, Afghanistan are each likely to be classified as being Asian
  - Yet these individuals have very distinct population ancestral characteristics.
- **Ancestry (has multiple definitions) is <u>not directly</u> associated with an individual's race or health**
- **Gene polymorphisms/biomarkers may have a direct health association –**
  - Use them (e.g. ALPL gene variants & kidney stones) and not race or population ancestry.
    - Oddsson A, et al. Common and rare variants associated with kidney stones and biochemical traits. Nat Commun. 2015
  - You should not guess a gene polymorphism/biomarker by looking at someone

What if we Replace Race Correction with Religion Correction in Urology (Exchanging Social Constructs)

Tool & Clinical Utility	Input Variables	Use of Race
STONE Score Predicts ureteral stone risk in patients who present with flank pain	• Sex • Acute onset of pain • **Religion: Baptist or non-Baptist** • Nausea or vomiting • Hematuria	A 13-point scale, with a higher score indicating a > risk of a ureteral stone; **3 points are added for non-Baptist religion**, same as for hematuria
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Adapted from Vyas DA, et al. Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms. NEJM. 2020.

Ecological Fallacy

- “The relation between ecological (*group level, poorly defined, unordered social variables*) and individual correlations which is discussed in this paper provides a definite answer as to whether ecological correlations can validly be used as substitutes for individual correlations. **They cannot**. While it is theoretically possible for the two to be equal, the conditions under which this can happen are far removed from those ordinarily encountered in data. **From a practical standpoint, therefore, the only reasonable assumption is that an ecological correlation is almost certainly not equal to its corresponding individual correlation**.”

“I am aware that this conclusion has serious consequences, and that its effect appears wholly negative because it throws serious doubt upon the validity of a number of important studies made in recent years.”

Robinson, W.S. (**1950**). "Ecological Correlations and the Behavior of Individuals". *American Sociological Review*. **15** (3): 351–357.

Use of Race and Ethnicity in Medicine

- Race is a **complex** population-level social variable

- Research data on R/E is critical for population-level assessments that inform public health and community messaging, screening, monitoring progress in addressing disparities, modifying systems, creating policy recommendations, etc.

Jones CP. Race, racism, and the practice of epidemiology. Am J Epi. 2001;154(4):299-304.

Use of Race and Ethnicity in Medicine

- Racial and ethnic differences in health conditions and/or outcomes tell us there are important elements impacting socially assigned groups differently (outside of phenotype)

For kidney stones or UTI: the many factors that influence the relative risk for a condition being present may not be equally distributed across groups.

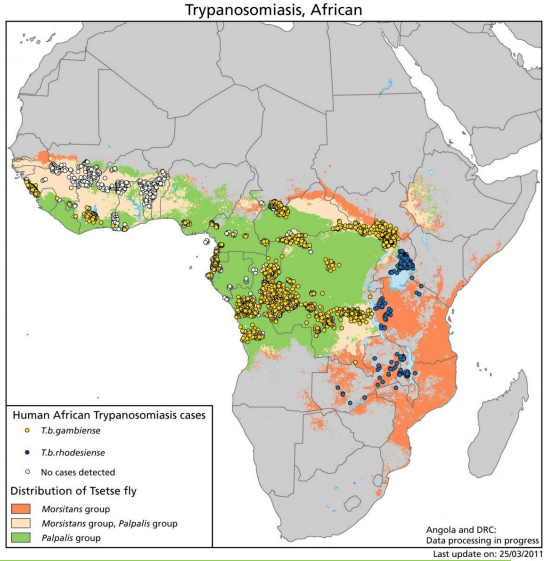
As researchers it is our role to now try to understand these factors.

Biomarkers & Race/Ethnicity: APOL1 CKD risk allele distribution in Nigeria

Wudil UJ, et al. Apolipoprotein-1 risk variants and associated kidney phenotypes in an adult HIV cohort in Nigeria. Kid Int. 2021;100(1):146-54.

APOL1 risk variants:
A disease of people whose family genealogy traces back to local areas where select APOL1 variants increased survival following exposure to trypanosomiasis

It has nothing to do with race
It has everything to do with understanding Kidney Dz



- **APOL1 risk variants**
  - Helps use understand:
  - race ≠ population genetics
  - population genetics ≠ precision for individuals (or for groups)
  - Group differences by race say close to nothing about individual group members

Thus, knowing a person's race gives essentially no insight into even the most well known and established gene variants

So, if Race is not directly related to biomarkers what is it directly related to?

Racism: a system of structuring opportunity and assigning value based on race

Racism by design

- 1) unfairly disadvantages some individuals/communities,
- 2) unfairly advantages other individuals/communities, and
- 3) saps the strength of the whole society through the waste of human resources.
  - ***Structural or Institutionalized racism****; personally mediated, internalized*

While Race is how society sees you and thinks of you

Racism = What society does to you based on how it sees you

Race is a risk factor for Racism, Racism is a risk factor for poor health

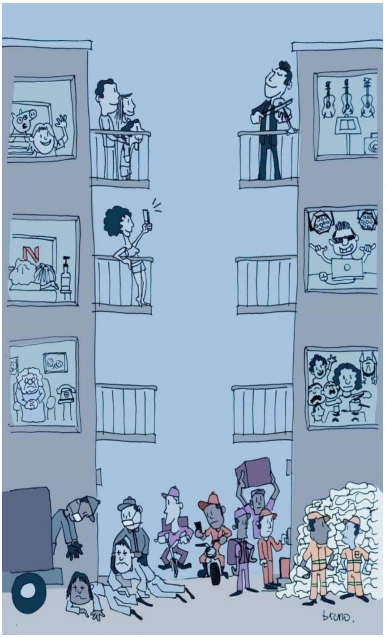
Jones CP. Confronting Institutionalized Racism. *Phylon.* 2002;50(1/2):7-22.
Jones CP. Levels of racism: a theoretic framework and a gardener's tale. *Am J Public Health.* Aug 2000;90(8):1212-5.

How Might we Examine and Appropriately Use Racial and/or Ethnic Group Differences and still move beyond Race-Based Medicine?

COVID19: The Makings of a Disparity

Minoritized groups are 2-4 times more likely to be hospitalized or die from COVID19

Structural Racism*
(e.g. residential segregation, underfunded school systems, poverty, chronic discrimination)



Increase Risk of Exposure	Service Jobs	Poor housing conditions	Public Transportation
High Chronic Disease Burden	DM/CKD	HTN/CVD	Asthma/COPD
Lack of Access to Quality Care	Early testing shortage	Poor preventative care	Low quality hospitals

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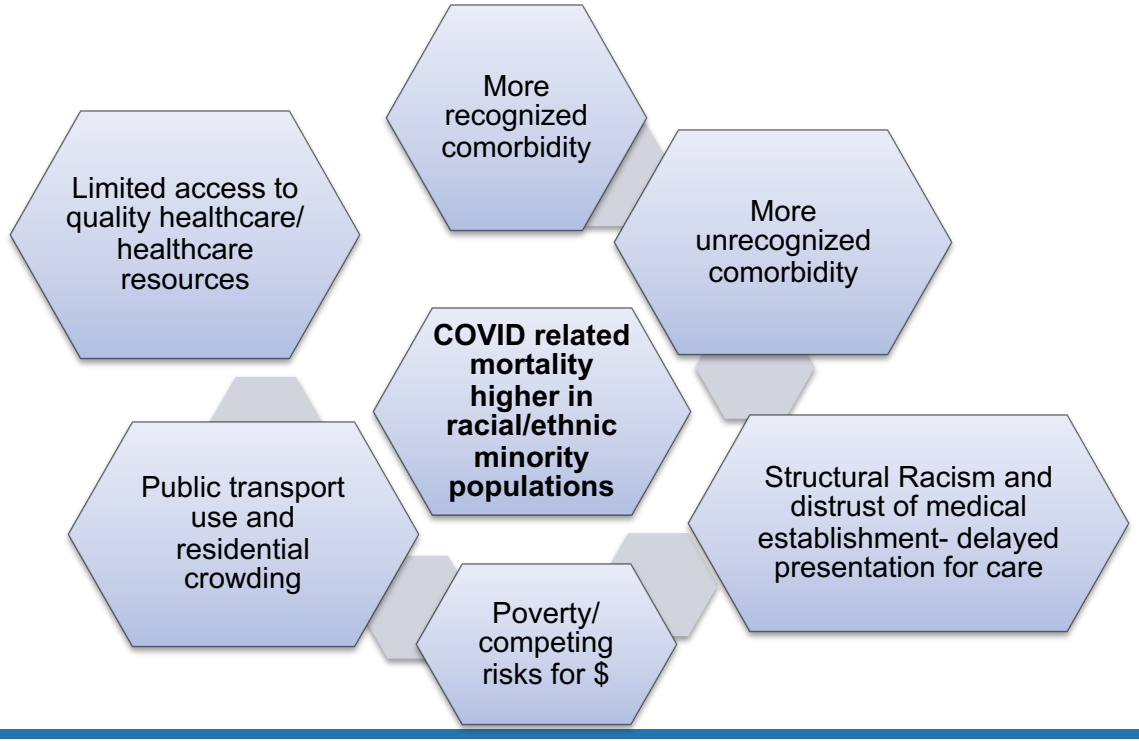
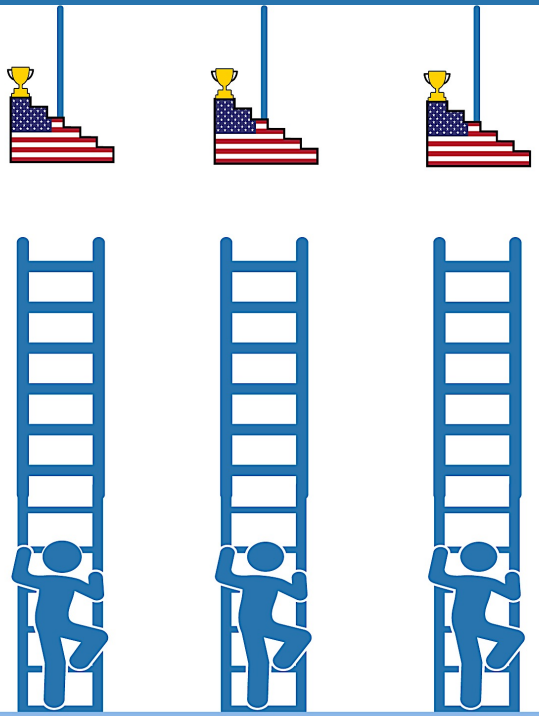
Every system is perfectly designed to achieve the results it gets - Don Berwick

How to use race/ethnicity in medicine

- For COVID we may find a given racial/ethnic group has ~ 3 times the rate of COVID infection, hospitalization and death vs. others
- We cannot say every person of that group is 3 times more likely to be hospitalized or die



Towards Achieving Equity and Justice to Eliminate Disparities



1. **Equality** imagines a world that is fair.

America has a **powerful** narrative–that it is a true meritocracy.

We hold these Truths to be self-evident that all Men are created equal, that they are endowed by their Creator with certain unalienable Rights that among these are Life, Liberty, and the Pursuit of Happiness.

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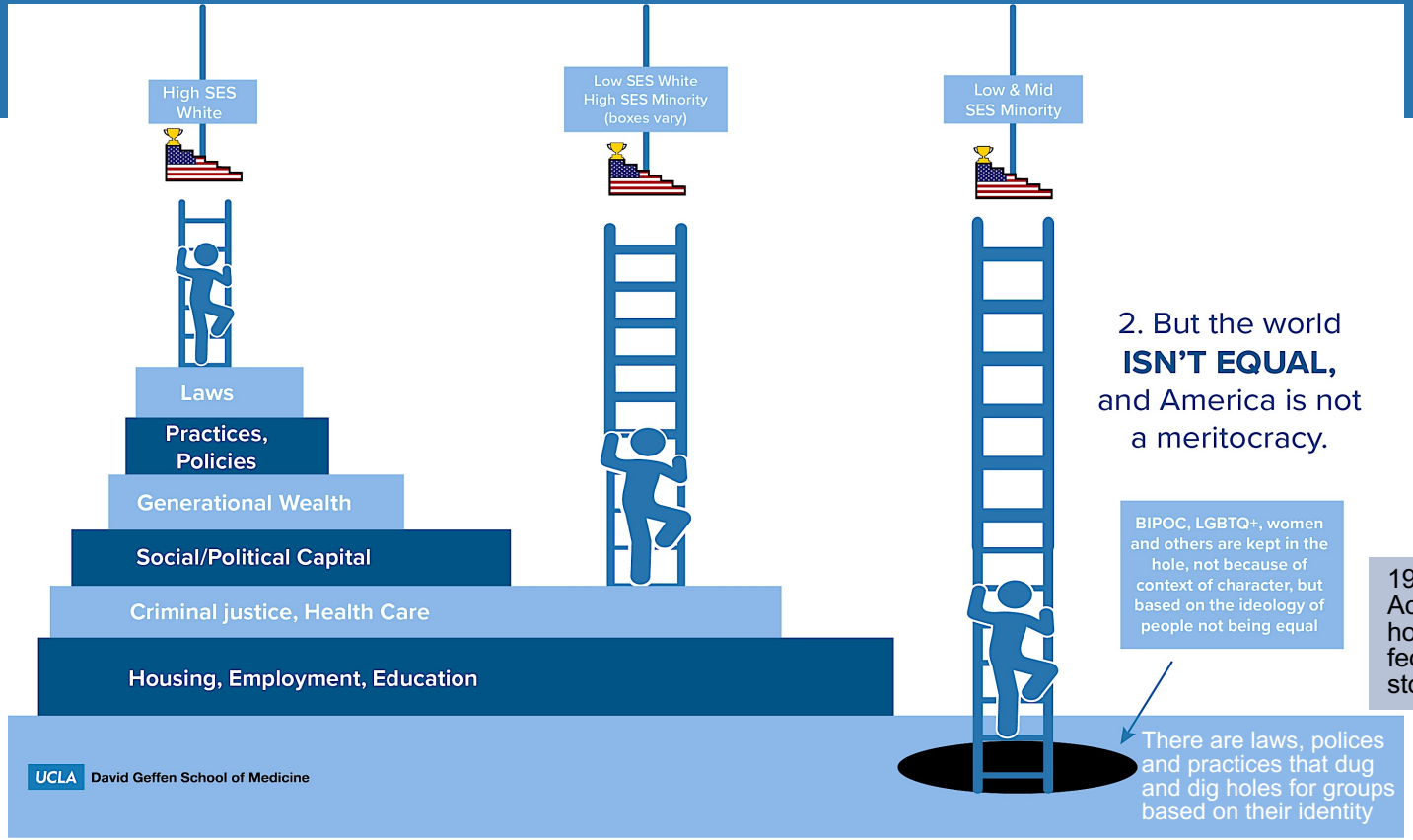
Norris K, Harris C, Seeman T. Adapted from the USC Center for Urban Education

Towards Achieving Equity and Justice to Eliminate Disparities



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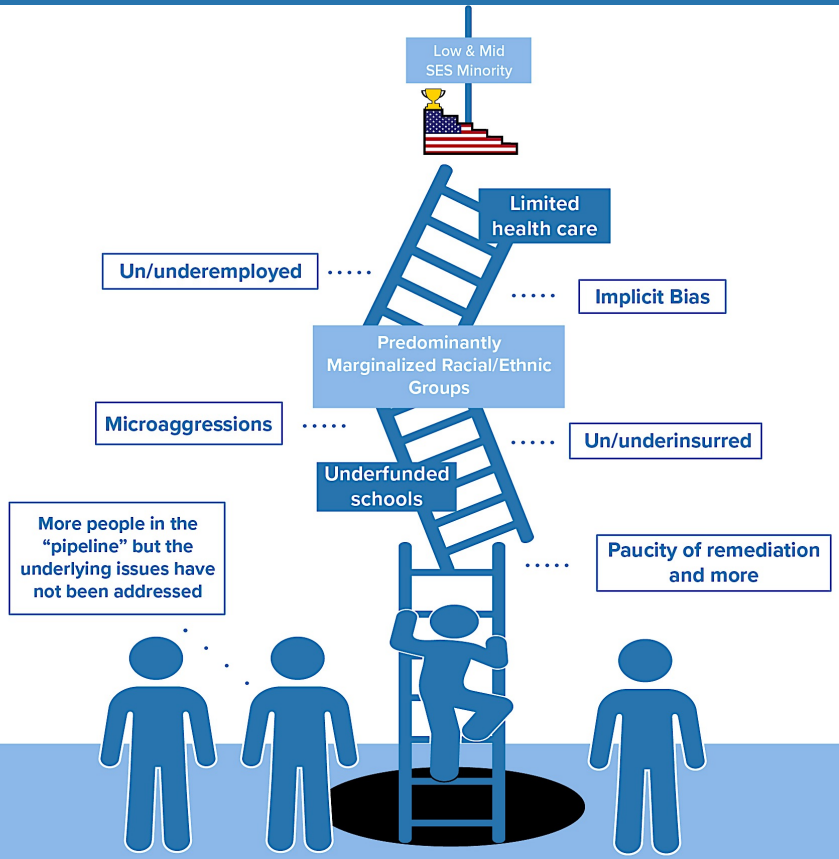
Towards Achieving Equity and Justice to Eliminate Disparities



3. And it has **BIAS AND SYSTEMIC RACISM.**

4. **DIVERSITY** only places more people from marginalized groups into an unequal pathway.

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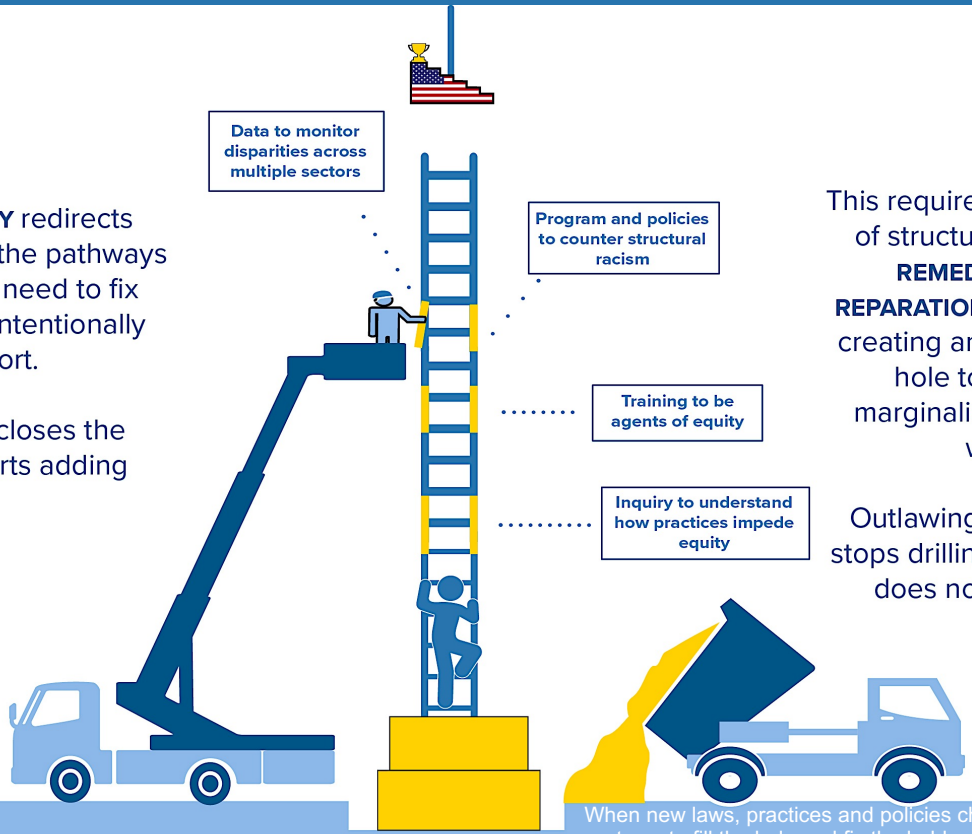
Norris K, Harris C, Seeman T. Adapted from the USC Center for Urban Education

Towards Achieving Equity and Justice to Eliminate Disparities

5. True **EQUITY** redirects resources to the pathways with greatest need to fix barriers and intentionally provide support.

And **JUSTICE** closes the holes and starts adding some boxes.



This requires the elimination of structural racism, and **REMEDIATION** and **REPARATIONS** to move from creating and maintaining a hole to making all marginalized Americans whole.

Outlawing discrimination stops drilling the hole, but it does not fill the hole.

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When new laws, practices and policies change structures and systems to fill the hole and fix the ladder then we can say structural racism is essentially over and reasonable equity has been achieved

Norris K, Harris C, Seeman T. Adapted from the USC Center for Urban Education

Structural Racism

- It is an American Problem
- **For R/E group kidney stone/UTI differences: ? differences due to types of jobs and hydration status, diet, increased stress and SNS activity, other?**
- Don't be afraid of names. No one in this room or zoom owned a slave or created Structural Racism
- But everyone can and does choose to support Structural Racism (actively or by doing nothing) or to help to dismantle it.
  - Many White people work to dismantle racism
  - Many non-White people actively support/promote white supremacy narratives and policies
  - Exchanging support for one "ism" as a cover to promote others (sexism, elitism, LGBTQ discrimination, etc.) is not real progress

From UCLA Health Care Workers rally for Black Lives Matter – June 2020

- The use of race in medical algorithms and formula for assessing kidney disease
- More appropriate use of race in research?
- **The Way Forward**

Summary: Medical students are right

- Medical students were right to request the removal of **race as an individual level modifier in formulas and algorithms**

- Not for social justice reasons

But because it is a poorly defined, unordered and unmeasurable social variable that is not directly related to health conditions - and

we want to do the best "science"

Arnold gets no eGFR modifier due to muscle mass

Actress Kerry Washington gets 16% added to her eGFR for her extra muscle mass

Medical students lead effort to remove race from kidney function estimates. Available at: https://www.kidneynews.org/kidney-news/current-issue/medical-students-lead-effort-to-remove-race-from-kidney-function-estimates. July 24, 2020

Summary

- Race" belongs in medicine because it is an essential part of the social history in the United States, **not because it approximates genotype.**
  - Race/ethnicity data can responsibly inform population-level analyses (e.g., monitoring disparities) and interventions.
  - Race/ethnicity should not be used as fixed biologic variables in clinical formulae or algorithms.

Summary

Do not generate and assign "race or ethnicity" created biologic values to individual patients

1. Ignores genetic and social heterogeneity within groups,
2. Obscures the mechanisms linking racism to health disparities,
3. Reinforces racist stereotypes,
4. Assumes each individual is exposed equally to the myriad of elements through which racism operates
5. Denies race is not a biologic variable
6. Generally lacks scientific rigor (e.g., ecologic fallacy and substantial aggregation bias) as well as an understanding that race is merely a risk factor for racism and not health.

After doing quality science add a lens of social justice

Tool & Clinical Utility	Input Variables	Use of Race	Equity Concern
STONE Score Predicts ureteral stone risk in patients who present with flank pain	• Sex • Acute onset of pain • **Race: Black or non-Black** • Nausea or vomiting • Hematuria	A 13-point scale, with a higher score indicating a > risk of a ureteral stone; **3 points are added for non-Black race**, same as for hematuria	**By systematically reporting lower risk for Black patients, this calculator may steer clinicians away from aggressive evaluations of Black patients**
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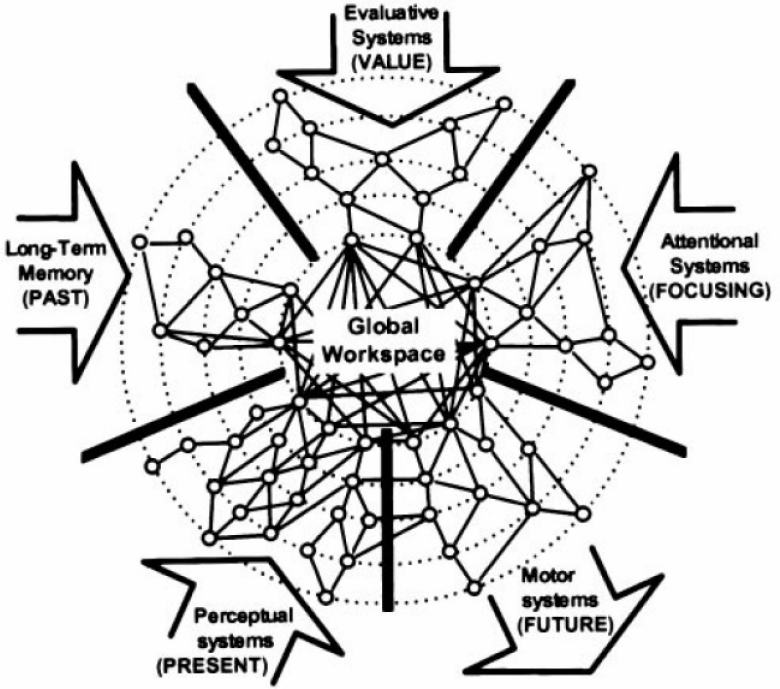
Vyas DA, et al. Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms. NEJM. 2020.

Psychosocial Stress (Poverty/Discrimination/More) & Cognitive Processing

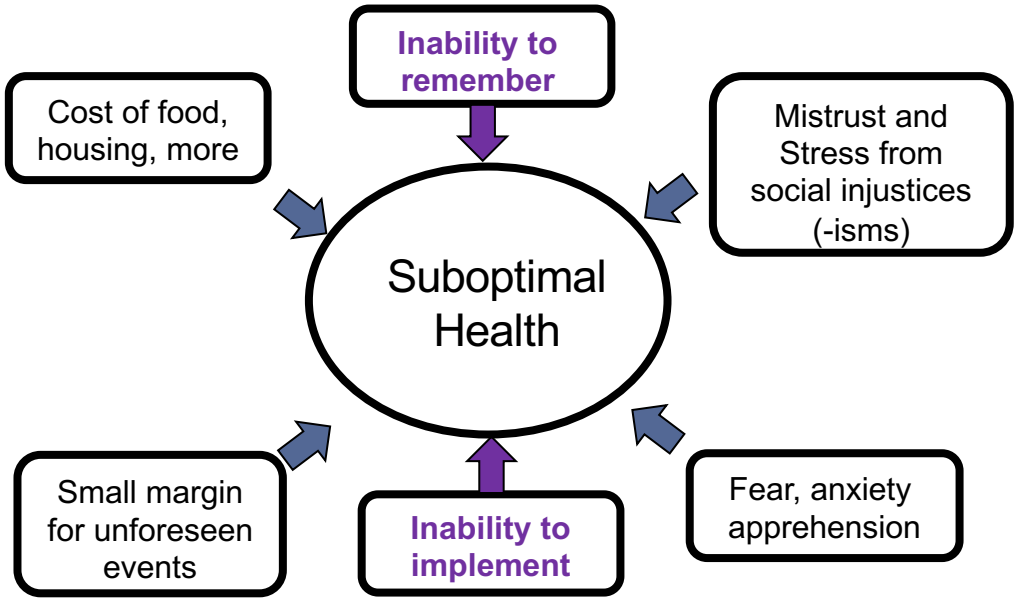
R/E disparities data says on average different groups are juggling more or fewer balls but not which ones



Stress (to survive) leads to realignment of workspaces that limits cognitive processing

Dehaene S, et al. A neuronal model of a global workspace in effortful cognitive tasks. PNAS. 1998 24;95(24):14529-34.

What might happen if/when an "under-resourced/marginalized" patient/study participant makes it to their visit & then goes home?



Which ball(s) are your under-resourced/marginalized and disproportionately minority patients/study participants likely to drop
-Rent, food, electricity, childcare, elder care or
-Provider recommendations/trial protocol, f/u visit, meds/other?

You can't assign a single group number to each member as they each have different balls to juggle

Caring for Marginalized Patients

What many "Marginalized" Patients have

- Discriminated Group status (reinforced by race modifiers)
- Limited Income
- Under and Un-Insured
- Low Educational Attainment
- Limited Access to Care
- Impaired Cognitive Processing
- Adverse Biologic Profile
- Multimorbidity

What many "Marginalized" Patients need

- High Quality Care
- Treated with Respect
- Our Empathy
- Our Compassion
- Our Support
- To Be Given Hope
- ~~Judgement~~
- ~~Ire~~
- ~~Lecture~~

Remember, at a group level: It's not what's wrong with them - it's what did we do to them

Don't assign a patient a group R/E modifier value - add that to their social history. Reinforces treating each person as an individual, like family - And not a number

"The greatest obstacle to discovery is not ignorance - it is the illusion of knowledge

-Daniel Boorstin