Medical Stereotypes?

Assessing the Use of Race as a Risk Factor

Graham Stratton, PGY3
Department of Family and Community Medicine
The Thomas Jefferson University

September 23, 2020

Discussion Objectives

- Introduction to issues of race as a risk factor (VBAC Calculator)
  - Race is a social construct, not genetic
  - Unclear causality of observed disparities
  - Possible medical consequences for patients
  - Patient and community trust/mistrust
- Evaluating the VBAC Calculator
- Theory/Research into Causes of Health Disparities
  - Ecosocial Theory
  - Racism as opposed to race
- Evaluating race use in eGFR algorithms
  - Evidence
  - Causal mechanism
  - Effect on health equity/patients
- Next steps

Case:
Z.P. was a 32yo G6P5005 at 36wks

No complaints but desiring a TOLAC.

She had had 4 previous SVDs, but most recently had a c-section for non-reassuring FHTs.

We did a TOLAC Informed Consent discussion and forms.

VAGINAL BIRTH AFTER CESAREAN

Height & weight optional; enter them to automatically calculate BMI

Maternal age	18 years
Height (range 54-80 in.)	in
Weight (range 80-310 lb.)	lb
Body mass index (BMI, range 15-75)	25 kg/m^2
African-American?	no
Hispanic?	no
Any previous vaginal delivery?	no
Any vaginal delivery since last cesarean?	no
Indication for prior cesarean of arrest of dilation or descent?	no

Calculate

Case:
Z.P. was a 32yo G6P5005 at 36wks

ZP is African-American and Hispanic.

Her VBAC percents:

As Hispanic: 52.4%

As African American: 52.7%

As neither: 68.5%

VAGINAL BIRTH AFTER CESAREAN

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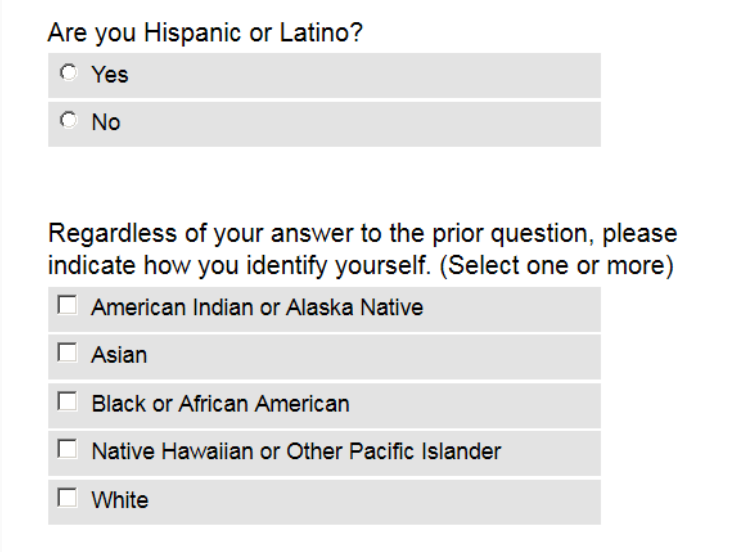
Calculate

Race as a risk factor

Issue 1:

- Race is a **social construct**, not biological category

  → 90-95% of genetic variation “occurs within, not among, continental populations” (Cooper, et al.)

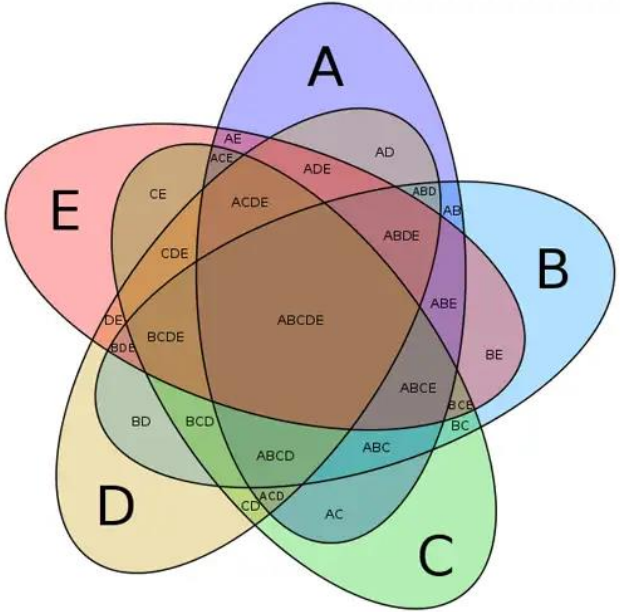


Race as a risk factor

Issue 2:

- The **unclear etiology** of disparities

  → Is race the most appropriate grouping or just convenient?

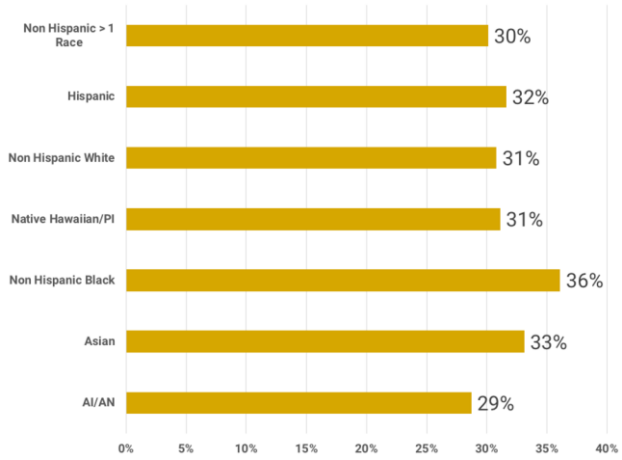


newscientist.com

Race as a risk factor

Issue 3:

- The **consequences** of differentiating healthcare based on race
  - For the patient
  - For health disparities

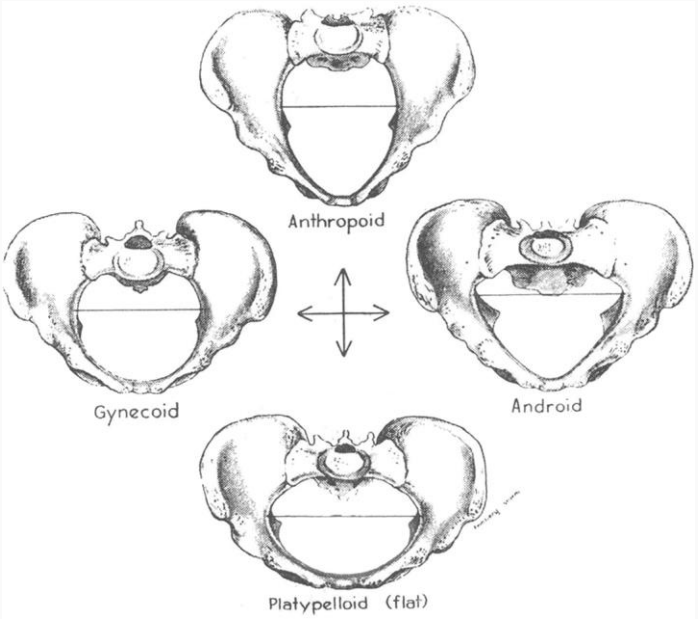


2018 C-section data from CDC
Graph from birthbythenumbers.org/

Race as a risk factor

Issue 4:

- The ugly legacy of race in medicine means that the use of racial categories has implications for **patient/community trust**, as well as whether the use of race is perpetuating this legacy.



nph.onlinelibrary.wiley.com

VBAC Calculator

OBSTETRICS & GYNECOLOGY

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ORIGINAL RESEARCH

Development of a Nomogram for Prediction of Vaginal Birth After Cesarean Delivery

Grobman, William A. MD, MBA[1]; Lai, Yinglei PhD[2]; Landon, Mark B. MD[3]; Spong, Catherine Y. MD[4]; Leveno, Kenneth J. MD[5]; Rouse, Dwight J. MD, MSPH[6]; Varner, Michael W. MD[7]; Moawad, Atef H. MD[8]; Caritis, Steve N. MD[9]; Harper, Margaret MD[10]; Wapner, Ronald J. MD[11]; Sorokin, Yoram MD[12]; Miodovnik, Menachem MD[13,14]; Carpenter, Marshall MD[15]; O'Sullivan, Mary J. MD[16]; Sibai, Baha M. MD[17]; Langer, Oded MD[18]; Thorp, John M. MD[19]; Ramin, Susan M. MD[20]; Mercer, Brian M. MD[21] Author Information

Obstetrics & Gynecology: April 2007 - Volume 109 - Issue 4 - p 806-812
doi: 10.1097/01.AOG.0000259312.36053.02

Logistic Regression Equation for Prediction of Achieving VBAC After a Trial of Labor

Predicted probability of successful VBAC=exp(w)/[1+exp(w)], where w=3.766−0.039(age)−0.060 (prepregnancy body mass index)−0.671 (African-American race)−0.680 (Hispanic race)+0.888 (any prior vaginal delivery)+1.003 (vaginal delivery after prior cesarean)−0.632 (recurring indication for cesarean)

VBAC Calculator

Bill Grobman, MD, MBA
Dept of OBGYN
Northwestern University

Race was “one of the factors that was most predictive… race/ethnicity is a socially determined variable. There’s no reason to think that those differences are biologically based.”

The NEW ENGLAND JOURNAL of MEDICINE

MEDICINE AND SOCIETY

Debra Malina, Ph.D., *Editor*

Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms

Darshali A. Vyas, M.D., Leo G. Eisenstein, M.D., and David S. Jones, M.D., Ph.D.

Do not ignore race.

“Distinguish between the use of race in descriptive statistics, where it plays a vital role in epidemiologic analyses, and in prescriptive clinical guidelines, where it can exacerbate inequities.”

Darshali A. Vyas. (now an Internist at Massachusetts General Hospital), Eisenstein LG, and Jones DS. “Hidden in Plain Sight-- Reconsidering the Use of Race Correction in Clinical Algorithms.” *NEJM*. August 2020.

“Defensible empirical logic” is not enough.

Proposes three questions for clinical algorithms:

1) Is the need for race correction based on robust evidence?
2) Is there a “plausible causal mechanism” for the racial difference?
3) Would the race correction relieve or exacerbate health equities?

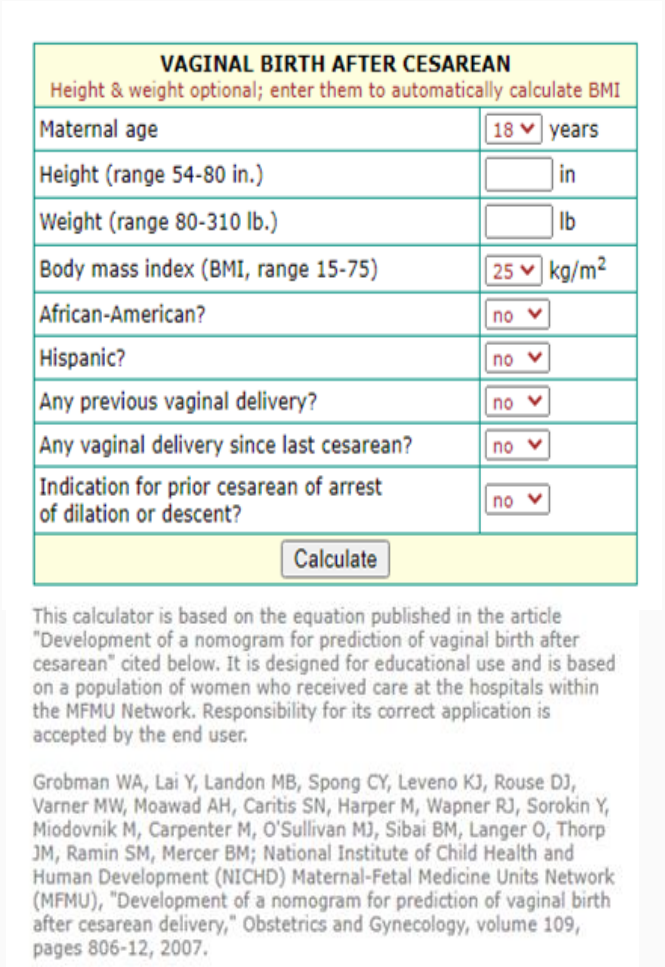
Vyas DA, Eisenstein LG, and Jones DS. “Hidden in Plain Sight-- Reconsidering the Use of Race Correction in Clinical Algorithms.” *NEJM*. August 2020.

Evaluating the MFMU VBAC Calculator:

1) Robust evidence?

2) Causal mechanism?

3) Effect on health equity?



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Calculate

This calculator is based on the equation published in the article "Development of a nomogram for prediction of vaginal birth after cesarean" cited below. It is designed for educational use and is based on a population of women who received care at the hospitals within the MFMU Network. Responsibility for its correct application is accepted by the end user.

Grobman WA, Lai Y, Landon MB, Spong CY, Leveno KJ, Rouse DJ, Varner MW, Moawad AH, Caritis SN, Harper M, Wapner RJ, Sorokin Y, Miodovnik M, Carpenter M, O'Sullivan MJ, Sibai BM, Langer O, Thorp JM, Ramin SM, Mercer BM; National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units Network (MFMU), "Development of a nomogram for prediction of vaginal birth after cesarean delivery," Obstetrics and Gynecology, volume 109, pages 806-12, 2007.

Evaluating the MFMU VBAC Calculator:

1) Robust evidence?

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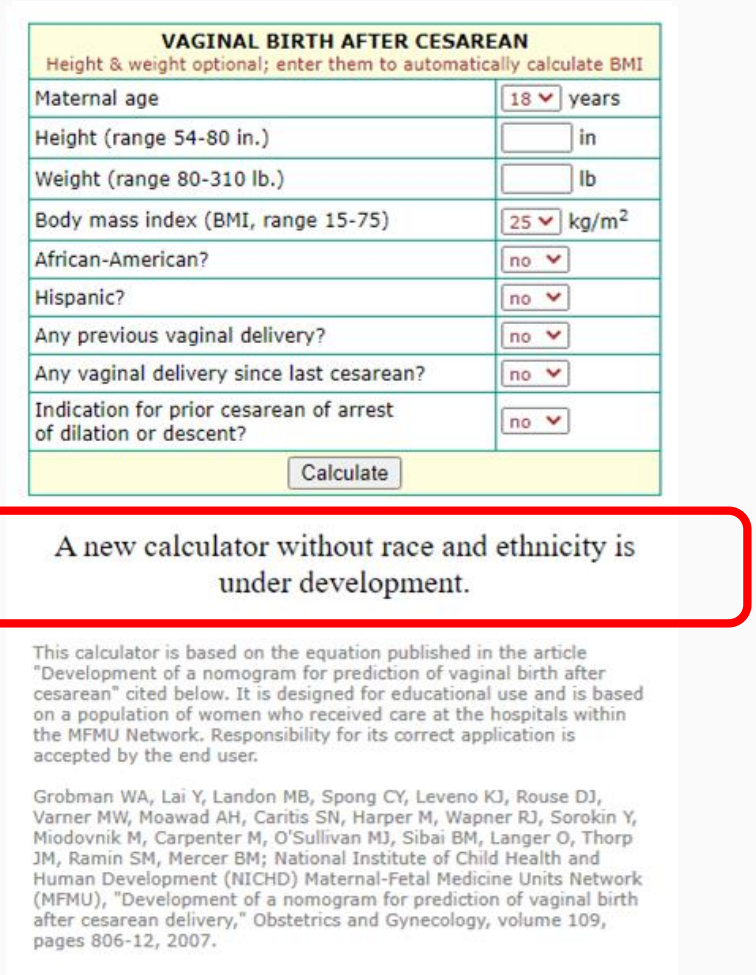

VAGINAL BIRTH AFTER CESAREAN

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Calculate

A new calculator without race and ethnicity is under development.

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1) Robust evidence?

2) Causal mechanism?

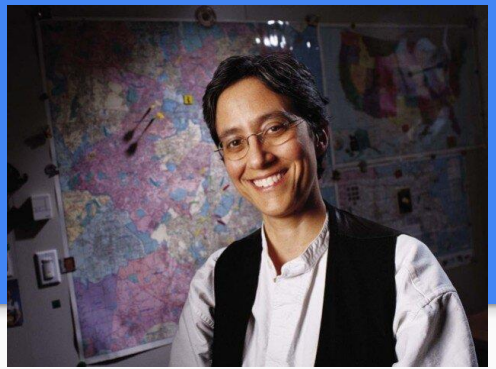
3) Effect on health equity?

- VBAC Calculator
- **Colon Cancer Screening Guidelines**
- ASCVD Score
- Heart Failure Risk Score
- Osteoporosis Risk Estimation (SCORE)
- FRAX Score
- STONE Score for ureteral stones
- Pediatric UTI Calculator
- USPSTF STI Screening Recommendations
- Pulmonary Function Tests
- eGFR
- Medication selection

… and many more algorithms and guidelines in primary and specialty care

Theory and Research on Racial Health Disparities

Ecosocial Theory

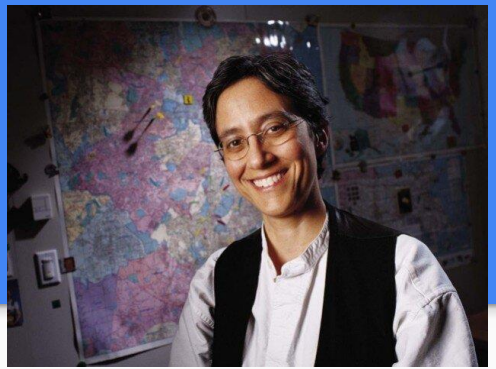


“People literally embody, biologically, their lived experience, in societal and ecological context, thereby creating population patterns of health and disease.”

“At issue are socially patterned exposure-induced pathogenic pathways, mediated by physiology, behavior, and gene expression…”

Nancy Krieger (an epidemiologist at the Harvard School of Public Health). “Methods for the Scientific Study of Discrimination and Health: An Ecosocial Approach.” Amer J of Public Health. May 2012.

Ecosocial Theory



Core Proposition #4:

Common diseases are more likely to have exogenous influences implicated in population disparities.

Rare diseases not so much.

"The more prevalent the health outcome, the greater the absolute burden… on those with less power and fewer resources, because they constitute the majority of the population; a corollary is that for more rare or infrequent (nonendemic) diseases, it cannot be presumed, in advance, whether social inequalities in the outcome exist, and, if they do, the direction of the gradient."

Krieger N. "Methods for the Scientific Study of Discrimination and Health: An Ecosocial Approach." Amer J of Public Health. May 2012.

Ecosocial causality beyond SES

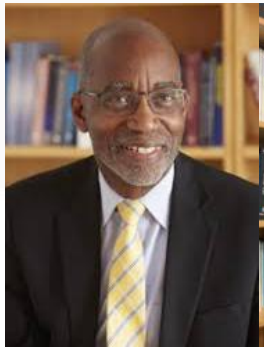
February 2020, at the sixth annual University of Pennsylvania Martin Luther King Jr. Health Equity Symposium

Discussing the complexity of social determinants as a major concern for the CDC Office of Minority Health and Health Equity:

The rate of **maternal mortality for Black women** “with at least a college degree… was five times as high as that of white women with similar education.”

"Maternal mortality is a barometer of our society's health.”

Leandris Liburd, PhD, MPH, MA is the Associate Director for the Office of Minority Health and Health Equity at the CDC



ANNUAL REVIEWS

Annual Review of Public Health

Racism and Health: Evidence and Needed Research

David R. Williams,[1,2,3] Jourdyn A. Lawrence,[1] and Brigette A. Davis[1]

[1]Department of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Harvard University, Boston, Massachusetts 02115, USA; email: dwilliam@hsph.harvard.edu

[2]Department of African and African American Studies and Department of Sociology, Harvard University, Cambridge, Massachusetts 02138-3654, USA

[3]Department of Psychiatry and Mental Health, University of Cape Town, Cape Town, South Africa

Racism

"an overview of the evidence linking the primary domains of racism—structural racism, cultural racism, and individual-level discrimination—to mental and physical health outcomes"

TED TALK: How racism makes us sick

UNNATURAL CAUSES… is inequality making us sick?

David R. Williams, Lawrence JA, Davis BA. "Racism and Health: Evidence and needed research." Annu Rev Public Health 2019;40:105–25.

Berkeley medical students wrote a comprehensive manual and call to action.

https://belonging.berkeley.edu/race-medicine

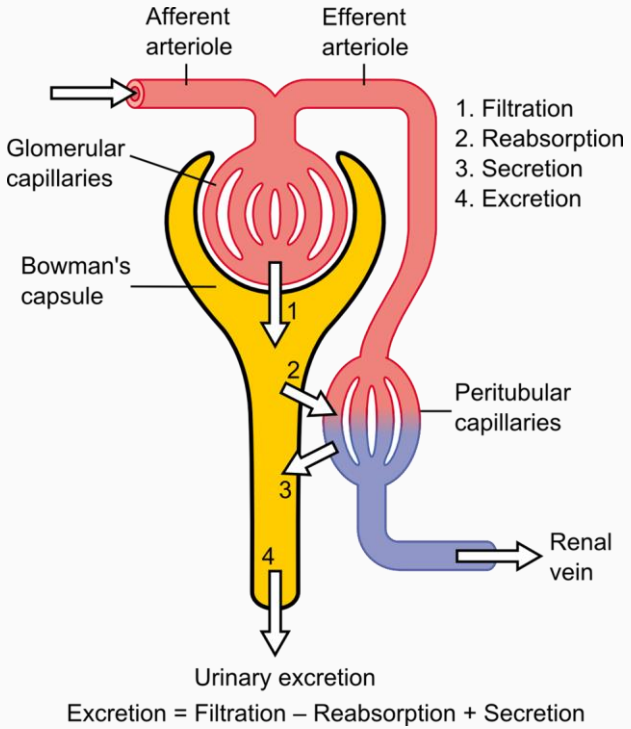
eGFR

Estimating GFR

The gold standard for measuring GFR is ^{125}I iothalamate clearance, but this is clinically impractical.

Instead, we estimate GFR using endogenous creatinine or cystatin C.

- 1973 Cockcroft-Gault Equation (for Cr Clearance)
- 1999 Modification of Diet in Renal Disease (MDRD)
  Suggested to only report eGFRs below 60 mL/min/1.73 m^2
- 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)



wikipedia.org



JAMA®

Viewpoint

June 6, 2019

Reconsidering the Consequences of Using Race to Estimate Kidney Function

Nwamaka Denise Eneanya, MD, MPH[1,2]; Wei Yang, PhD[3]; Peter Philip Reese, MD, MSCE[1,3]

Author Affiliations

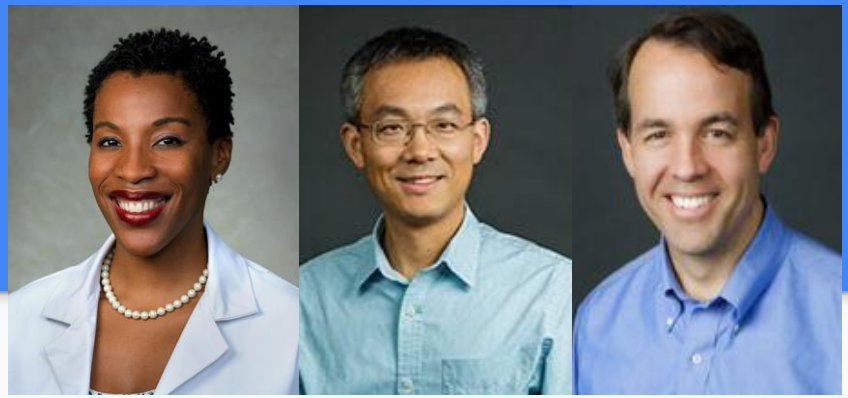
[1]Renal-Electrolyte and Hypertension Division, Perelman School of Medicine, University of Pennsylvania, Philadelphia

[2]Palliative and Advanced Illness Research Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia

[3]Department of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia

JAMA. 2019;322(2):113-114. doi:10.1001/jama.2019.5774

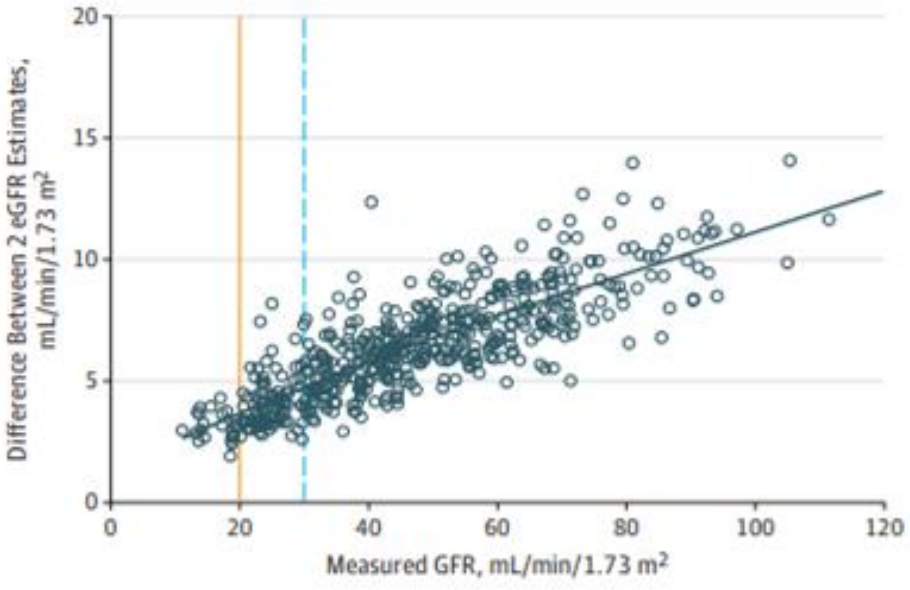
Challenging eGFR

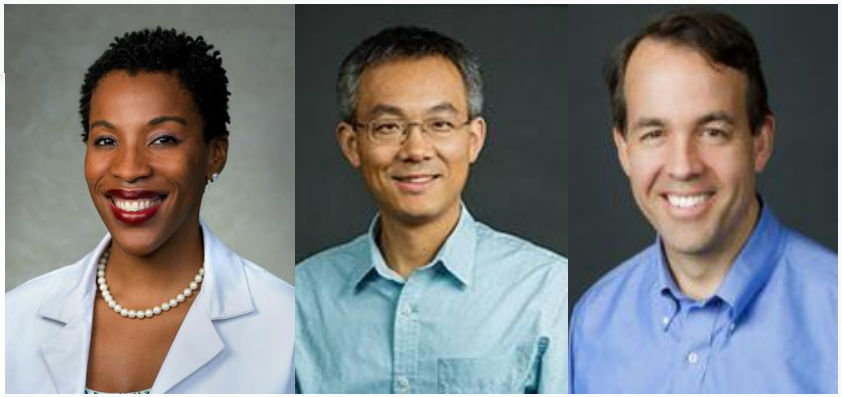


“The use of kidney function estimating equations that include race as a variable cause problems for transparency and unduly restrict access to care in some cases, yet offer only modest benefits to precision.”

Nwamaka Denise Eneanya (nephrologist at UPenn), Yang W, Reese PP. Reconsidering the consequences of using race to estimate kidney function. JAMA. 2019

Figure. Relationship Between Racial Categories and Estimation of Kidney Function Across the Spectrum of Chronic Kidney Disease

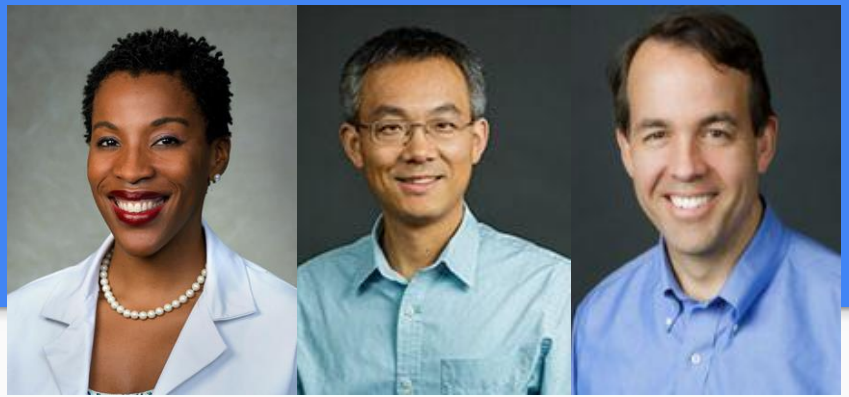


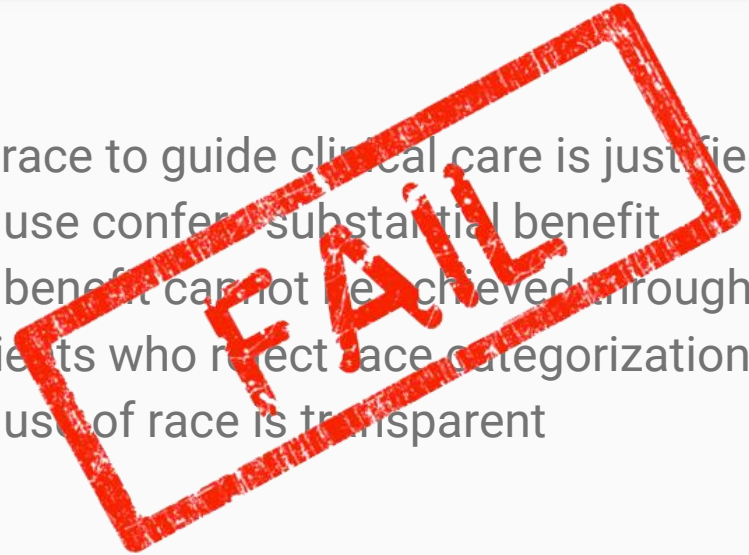


Circles indicate how much higher estimated glomerular filtration rate (eGFR) is for patients when assigned black race instead of nonblack race. eGFR was calculated twice for self-identified black adults, first by assigning them black race and then assigning them nonblack race. Patients must have kidney function lower than (ie, to the left of) the solid orange line to be eligible for the kidney transplant waiting list. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend nephrology referral for all patients with kidney function lower than (left of) the dashed blue line. Data are from 534 adult participants in the Chronic Renal Insufficiency Cohort who underwent urinary ^{125}I-iothalamate clearance testing, a gold-standard measurement of kidney filtration function. Estimated GFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Eneanya ND, Yang W, Reese PP. Reconsidering the consequences of using race to estimate kidney function. JAMA. 2019

Challenging eGFR

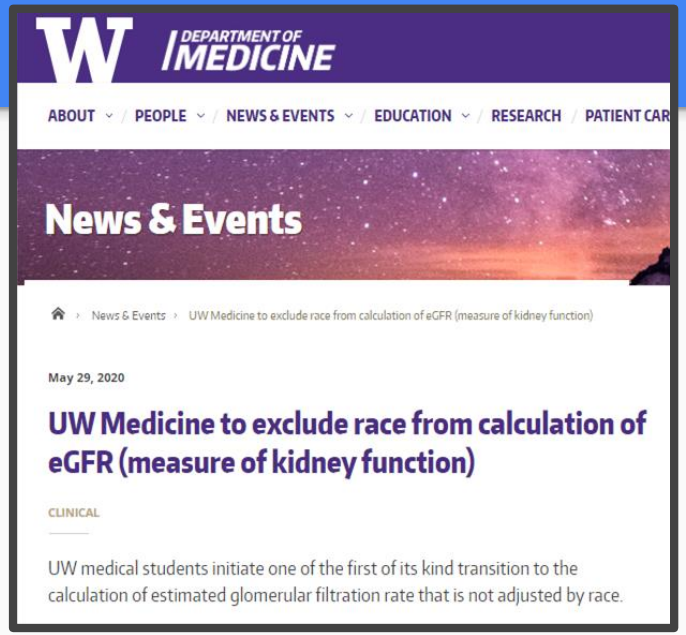




Using race to guide clinical care is justified only if:
1) the use confers substantial benefit
2) the benefit cannot be achieved through other feasible approaches
3) patients who reject race categorization are accommodated fairly
4) the use of race is transparent

Eneanya ND, Yang W, Reese PP. Reconsidering the consequences of using race to estimate kidney function. JAMA. 2019

clipart-library.com
pennmedicine.org



Naomi Nkinsi, an MD/MPH student in the University of Washington Anti-Racism Action Committee

"The use of race in the biomedical environment is an imprecise variable and does not meet the scientific rigor UW Medicine expects of diagnostic tools."

medicine.uw.edu/

Evaluating the eGFR algorithm:

1) Robust evidence?

2) Causal mechanism?

3) Effect on health equity?

MDRD equation:

$$eGFR = 175 \times (SCr)^{-1.154} \times (age)^{-0.203} \times 0.742 \text{ [if female]} \times 1.212 \text{ [if AA]}$$

Evaluating the eGFR algorithm:

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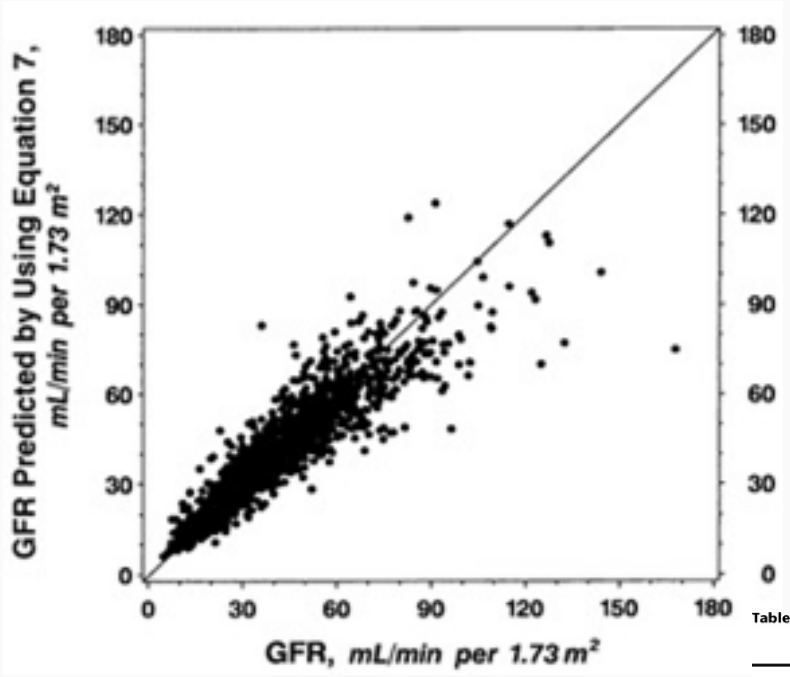

Table 3. Comparison of Equations To Predict Glomerular Filtration Rate (mL/min per 1.73 m²) from Serum Creatinine Concentration*

Equation 1: Serum creatinine
GFR = 0.69 × [100/P_{cr}]
Equation 2: Cockcroft–Gault formula
GFR = 0.84 × [Cockcroft–Gault formula]
Equation 3: Creatinine clearance
GFR = 0.81 × [C_{cr}]
Equation 4: Average of creatinine and urea clearance
GFR = 1.11 × [(C_{cr} + C_{urea})/2]
Equation 5: Creatinine clearance, urea clearance, and demographic variables
GFR = 1.04 × [C_{cr}]$^{+0.751}$ × [C_{urea}]$^{+0.226}$ × [1.109 if patient is black]
Equation 6: Demographic, serum, and urine variables
GFR = 198 × [P_{cr}]$^{-0.858}$ × [Age]$^{-0.167}$ × [0.822 if patient is female] × [1.178 if patient is black] × [SUN]$^{-0.293}$ × [UUN]$^{+0.249}$
Equation 7: Demographic and serum variables only
GFR = 170 × [P_{cr}]$^{-0.999}$ × [Age]$^{-0.176}$ × [0.762 if patient is female] × [1.180 if patient is black] × [SUN]$^{-0.170}$ × [Alb]$^{+0.318}$

Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130(6):461-470.

Evaluating the eGFR algorithm:

1) Robust evidence?

2) Causal mechanism?

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AA-correction factor was derived from the ***AASK trial*** in 2000:

1,094 participants

29% current smokers (23%)

41% did not graduate HS (25%)

48% reported income <$15k

(19% declined to report income)

Norris KC, Greene T, Kopple J, et al. Baseline predictors of renal disease progression in the African American Study of Hypertension and Kidney Disease. J Am Soc Nephrol. 2006;17(10): 2928–2936.

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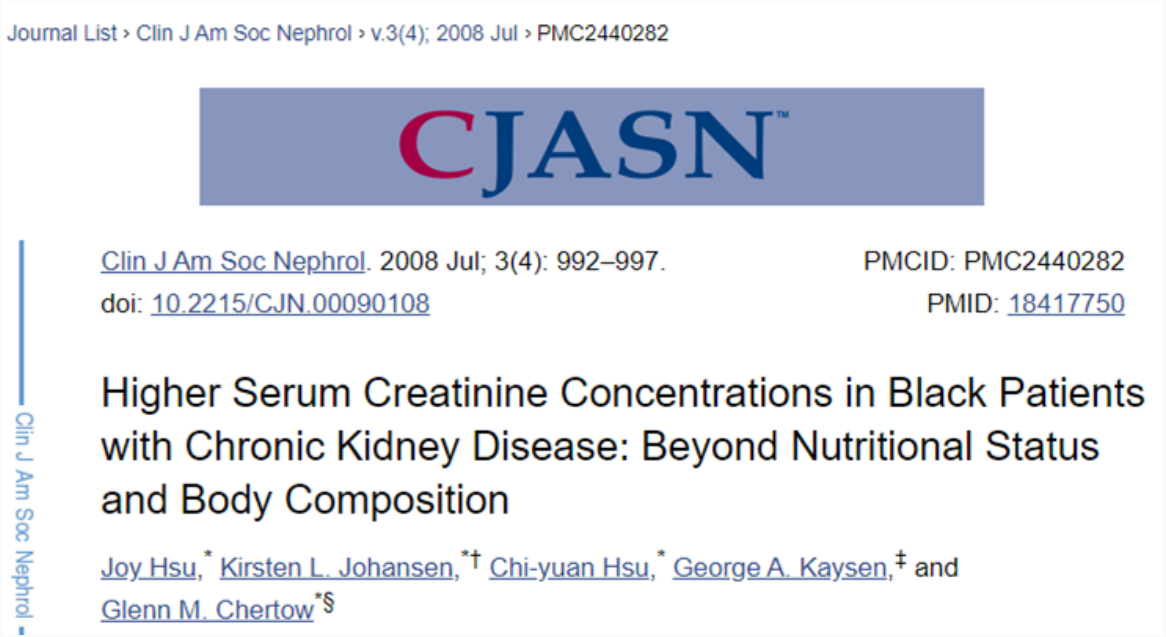

Journal List › Clin J Am Soc Nephrol › v.3(4); 2008 Jul › PMC2440282

CJASN

Clin J Am Soc Nephrol. 2008 Jul; 3(4): 992–997.
doi: 10.2215/CJN.00090108

PMCID: PMC2440282
PMID: 18417750

Higher Serum Creatinine Concentrations in Black Patients with Chronic Kidney Disease: Beyond Nutritional Status and Body Composition

Joy Hsu,[*] Kirsten L. Johansen,[*†] Chi-yuan Hsu,[*] George A. Kaysen,[‡] and Glenn M. Chertow[*§]

Clin J Am Soc Nephrol

Among other things, study used Bioelectrical Impedance Analysis to see if higher SCr among Black HD patients could be explained by muscle mass.

Evaluating the eGFR algorithm:

1) Robust evidence?

2) Causal mechanism?

3) Effect on health equity?

MDRD equation:

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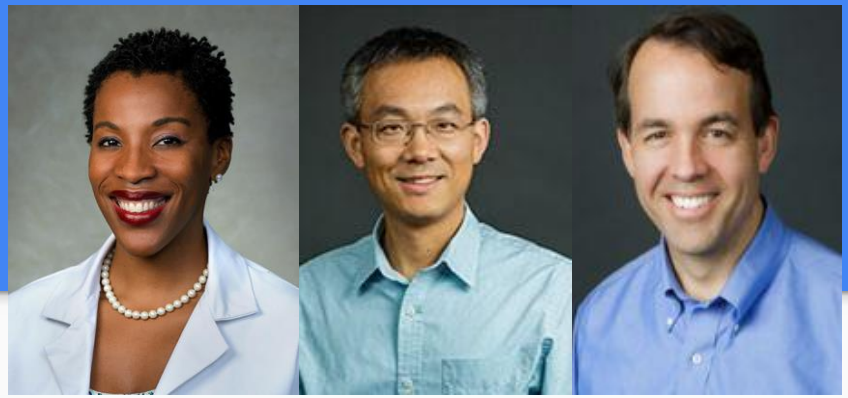
Challenging eGFR



"The use of kidney function estimating equations that include race as a variable cause problems for transparency and unduly restrict access to care in some cases, yet offer only modest benefits to precision."

Eneanya ND, Yang W, Reese PP. Reconsidering the consequences of using race to estimate kidney function. JAMA. 2019

JAMA Internal Medicine

Research Letter

March 16, 2020

Estimation of Glomerular Filtration Rate With vs Without Including Patient Race

Andrew S. Levey, MD[1]; Hocine Tighiouart, MS[2]; Silvia M. Titan, MD, PhD[1,3]; et al

» Author Affiliations

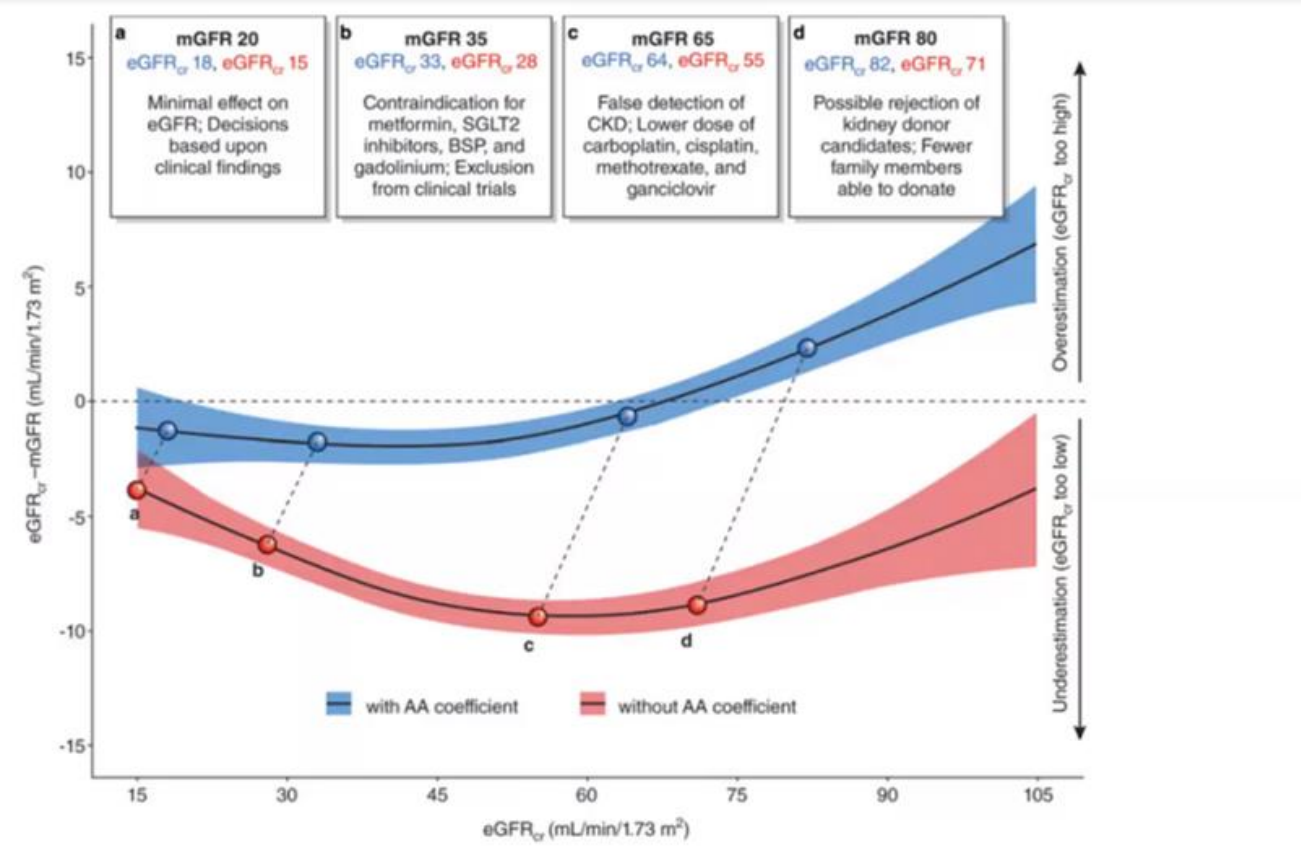
JAMA Intern Med. 2020;180(5):793-795. doi:10.1001/jamainternmed.2020.0045

Andrew S. Levey
Division of Nephrology
Tufts University

Responding to Eneanya et al.

“Eliminating race… may have unintended consequences in African American individuals, such as inappropriate early transplant or dialysis initiation, overdiagnosis of CKD, overestimation of the association of the risk of adverse outcomes with reduced GFR, inadequate dosing of drugs… and limited access to tests (eg, some imaging procedures) and treatments… including living kidney donation. Better methods are needed to improve accuracy of GFR assessment without requiring specification of race.”

Levey AS, Tighiouart H, Titan SM, Inker LA. Estimation of glomerular filtration rate with vs without including patient race. JAMA Intern Med. 2020;180(5):793-795.

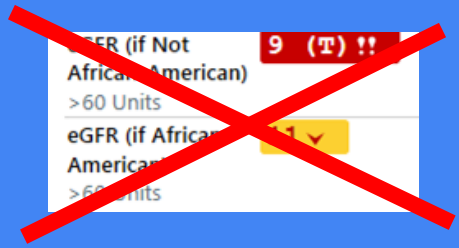


Levey AS, Titan SM, Powe NR, Coresh J, Inker LA. Kidney disease, race, and GFR estimation. Clin J Am Soc Nephrol. 2020;15(8):1203-1212. (and in JAMA Internal Medicine 2020)

Moving forward

Until we have a better method for evaluating renal function, what should we do?

A team at TJUH led by
Dr. Omar Maarouf and Dr. Traci Trice
is working to eliminate the AA-correction variable



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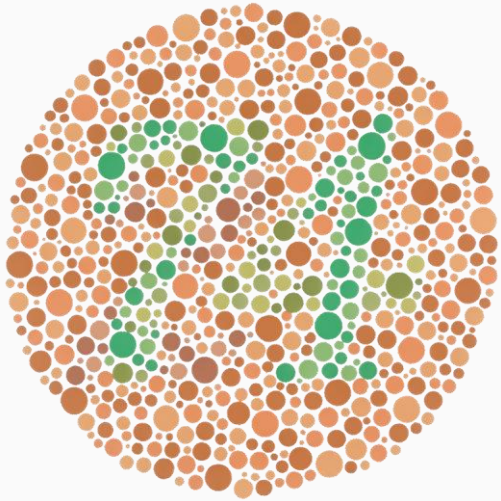
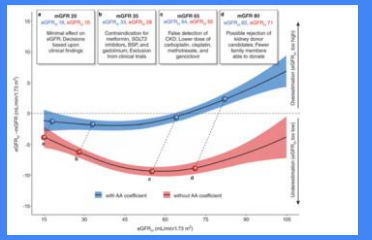


The result is an eGFR algorithm developed from a dataset that specifically excluded participants who identified as African American.

If the equation was based on the African American study participants with a correction factor for non-AA patients… would we be eliminating this correction factor?

$$eGFR = 212 \times (SCr)^{-1.154} \times (age)^{-0.203} \times 0.742 \text{ [if female]} \times 1.210 \text{ [if not AA]}$$

$$eGFR = 212 \times (SCr)^{-1.154} \times (age)^{-0.203} \times 0.742 \text{ [if female]} \times 0.825 \text{ [if not AA]}$$



For a 50 y.o. white cisman with Cr=1.3, eGFR = 58,
but, *without* the race correction variable, eGFR= 71.

Recent studies have found no increased eGFR accuracy with the AA-correction factor in Brazil, South Africa, the Democratic Republic of the Congo, Ghana, and Côte d'Ivoire.

Bukabau JB, Sumaili EK, Cavalier E, et al. Performance of glomerular filtration rate estimation equations in Congolese healthy adults: The inopportunity of the ethnic correction. *PLoS One*. 2018;13(3):e0193384.

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Alternatively, we could reaggregate the data and develop a new algorithm without a race variable, instead of defaulting to the non-African American algorithm.

Take-Home Points

In the future, how will you use the VBAC calculator, interpret eGFR values, or counsel patients regarding colon cancer screening, etc?

- Critically evaluate any use of race in medicine
  - Evidence
  - Causal mechanism
  - Effect on health equity/patients
- Race is not genetic and is a crude proxy for other factors (investigate them)
- Be transparent with patients and allow them to self-identify and share decision making
- Be cautious not to ignore race altogether

For eGFR specifically:

- GFR should be considered a range and not a numeric value
- Rate of change in eGFR should be considered when values are low
- Race correlations are complex and should not be systematized into our eGFR algorithms

Thank you!

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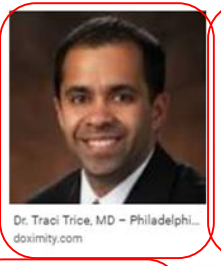
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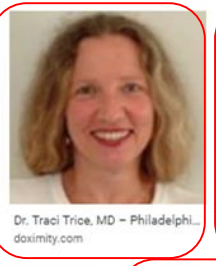
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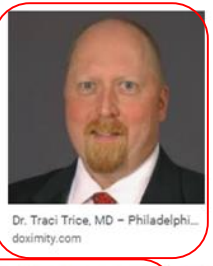
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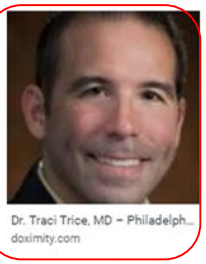
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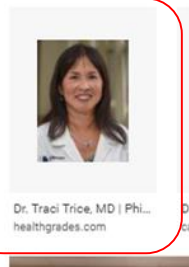
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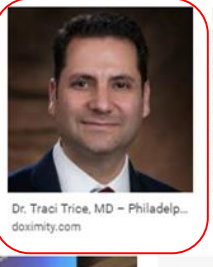
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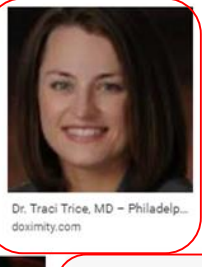
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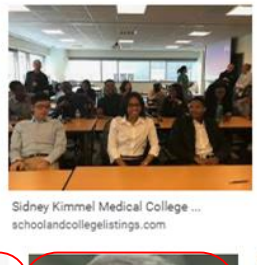
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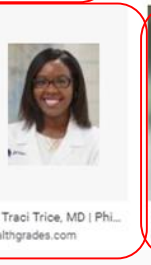
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