Viewpoint: Why health care based on race is so problematic

Choosing a medical treatment based on patient traits historically used to define races is fundamentally flawed, because race in the context of humans is a social construct, while medicine is based on biology. Race-based prescribing robs some individuals of drugs that could help them, while prescribing them to people who likely will not respond, or even be harmed. Fortunately, the practice of basing treatment decisions on the superficial traits used to define human races is on the decline.

Blood thinners and blood pressure medications have for decades dominated discussions of race-based prescribing. A more recent example of the dangers of using superficial features as guidelines for providing appropriate care is flawed interpretation of a standard measure of kidney function, used to prioritize patients for kidney transplants. Due to a fudge factor of sorts, until very recently Blacks have been given lower priority on the lists for organs.

Perhaps the starkest example I've encountered of race obscuring delivery of adequate health care comes from California-based pediatrician Richard Garcia, who wrote in The Chronicle of Higher Education in 2003 "The Misuse of Race in Medical Diagnosis":

> *My childhood friend Lela wasn't diagnosed with cystic fibrosis until she was 8 years old. Over the years, her doctors had described her as a '2-year-old black female with fever and cough' and 'a 4-year-old black girl with another pneumonia. Lela is back.' Had she been a white child, or had no visible 'race' at all, she would probably have gotten the correct diagnosis and treatment much earlier. Only when she was 8 did a radiologist, who had never seen her face to face, notice her chest X-ray and ask, 'Who's the kid with CF?'*

Today, Lela would have been diagnosed and treated much sooner, because all newborns in the US are screened for CF. Although Dr. Garcia's essay was published two decades ago, I still hear newscasters, actors in TV medical dramas, and others say that sickle cell disease (SCD) is a black disease and cystic fibrosis a white disease.

Of course people of shared ancestry tend to look somewhat alike if they have children within their group, restricting the range of gene variants. Another force for similarity within groups is that genes that are near each other on a chromosome tend to be inherited together. But at the single gene level, a sequence of DNA building blocks that encodes a salt channel (CF) or a blood protein (SCD) doesn't consider the color of a person's skin or shapes of facial features. It follows Mendel's first law.

And so a Black child can have CF and a white child sickle cell disease. Garcia offered another example. "I know that Ashkenazic Jews get Tay-Sachs, but the only baby I ever saw with Tay-Sachs was a Mexican

child.”

Until recently, prescribing drugs to treat hypertension was the classic example of how race-based medicine can do harm. The story is more complex than for single-gene conditions like CF and SCD because individual differences in blood pressure are more influenced by environmental factors than are salt channels and blood proteins.

The BiDil saga

Hypertension is the #1 cause of cardiovascular disease in the US and damages the kidneys. It affects 45% of Blacks, 32% of non-Hispanic whites, 30% of Hispanics, and 25% of Asians. Although many genes and environmental factors elevate blood pressure, one hypothesis for the prevalence among Blacks today goes back to their ancestors who were captured in Africa and crammed into ships for their journey to enslavement. Perhaps survivors were more likely to have gene variants that enabled their kidneys to conserve salt, combating fluid loss in the hellish conditions. Their descendants might face higher risk of hypertension from fluid retention.

Despite the fact that the genetic underpinnings of hypertension are complex and not well understood, race has been used in treating the condition.

In 2005, the FDA approved the first race-based drug, a pill called BiDil that paired existing drugs (hydralazine and isosorbide dinitrate) that lower blood pressure and widen blood vessels, relieving congestive heart failure to a degree. Prescribing BiDil for Blacks was based on several small, flawed studies that tested heart function in Black participants but not in members of other groups. The studies also didn’t consider the social determinants of health, nor identify gene variants that might contribute to or cause hypertension.

BiDil, the first “racialized” drug, was marketed to “self-identified” Black people. That was still true when I looked at ads a year ago. But googling BiDil now returns a warning: potential security risk ahead. Clearly, something is up.

Eventually, epidemiologists and geneticists began to question the designation of a “Black drug.” One follow-up study looked at 100 white patients given the anti-hypertensive part of BiDil and 100 Black patients NOT given the drug. Results were telling: 48 white patients did not respond to the drug and 41 Black patients did respond. That’s only slightly better than a coin toss! Diet has a large effect on hypertension risk, and that has nothing to do with race.

A vast medical literature chronicles the BiDil chapter of race-based medicine. See this study in JAMA Cardiology JAMA Cardiology from 2021. Yet the current description at GoodRx indicates that the legacy of race-based prescribing of BiDil may persist:

> *BiDil is a combination medication that can help certain patients with heart failure feel better and live longer. BiDil … was specifically studied in Black people and was shown to improve heart failure symptoms. It is not a first-choice drug, but can be added to other heart failure*

medications.

Kidney failure and the transplant list

Blacks account for 13% of the US population, but account for more than 30% of patients with end-stage kidney disease. However, since 2009 and until recently, reliance on a race-tweaked measurement of how fast the kidneys filter urine – estimated glomerular filtration rate (eGFR) – led to Blacks being less likely to receive kidney transplants.

The level of creatinine in the blood is used to estimate eGFR. This is a measure of the normal and constant breakdown of muscle and protein metabolism.

On average, Blacks have higher blood creatinine concentrations than do whites. But "race-based algorithms" applied to adjust blood test results to account for the population-level difference made some Black individuals appear to have healthier kidneys than they actually do. And they ended up lower on the lists for life-saving kidney transplants than they should have been.

In "The quagmire of race, genetic ancestry, and health disparities" in The Journal of Clinical Investigation from 2021, Giorgio Sirugo, Sarah A. Tishkoff, and Scott M. Williams pointed out another flaw in the reasoning is that most Blacks do not know how much African ancestry they actually have. And like the BiDil story, lumping all Blacks into one group using a "'race'-based correction" can lead to both under- and over- treatment. "Ultimately, precision medicine based on individual genetic risk factors should supersede simple racial classifications," they concluded.

I became aware of the race-based kidney function situation as a technical editor for the *Journal of the American Society of Nephrology*. That organization, with the National Kidney Foundation, formed the Task Force on Reassessing the Inclusion of Race In Diagnosing Kidney Diseases in 2020 to address the situation. I edited their *Perspective* in The New England Journal of Medicine. As a result of the task force's actions, race-based measurements that impact priority for kidney transplants are a thing of the past. A new calculator tool for eGFR was announced in September 2021. And the recommendations are already being wildly implemented, said Paul Palevsky, past president of the National Kidney Foundation and a professor at the University of Pittsburgh.

Coda

In everyday life, we designate race based on appearance, and that has societal repercussions. But thinking as a geneticist, I've pondered a "what if" scenario for dividing people according to *other* traits that have a genetic component.

What if everyone over a certain height would be designated as belonging to a separate race?

People with an extra finger or toe?

Individuals with type AB blood?

This simple thought exercise, which I've had my students do, starkly reveals the absurdity of race as a biological measure of anything. It certainly shouldn't enter into prescribing decisions, like BiDil, or access to life-saving interventions, like kidney transplants.

BiDil and eGFR are not the only examples of the fallacy of race-based medicine. Expanded DNA testing – exomes, genomes, and RNA – will, I hope, dim the misplaced, historical focus on appearances.

I wish that astute pediatrician Richard Garcia had published his account of his friend Lela, dismissed as having cystic fibrosis because of the color of her skin, in a medical journal rather than in *The Chronicle of Higher Education*. We need more health care providers to focus on the genotype and other non-biased metrics, not the phenotype.

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