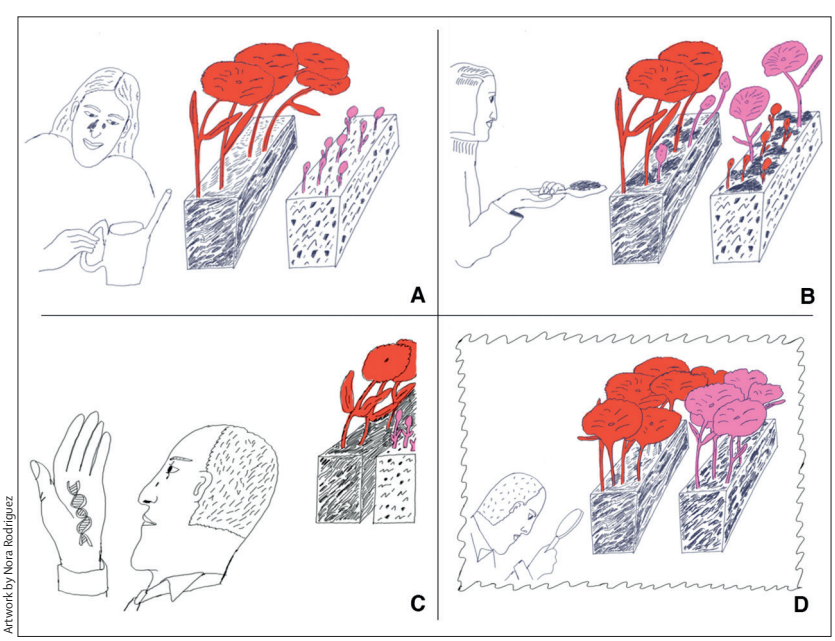
The art of medicine

The misuse of race in the search for disease-causing alleles

In her influential 2000 paper, *Levels of Racism: A Theoretic Framework and a Gardener's Tale*, Camara Phyllis Jones presented a theoretical framework for understanding racism through an allegory about a gardener with two flower boxes, one with rich and the other with poor soil. The gardener, who prefers red flowers, plants red blossoming seeds in fertile soil but pink blossoming seeds in poor soil (structural racism) and plucks pink blossoming seeds blown into fertile soil (personally mediated racism). The pink blossoming plants start to believe red blossoms are better and prefer red blossom pollination (internalised racism).

Here, we—a biocultural and medical anthropologist, a clinician researcher, and a genetic anthropologist—extend Jones's allegory to highlight how theories and beliefs about a biological meaning of race have engendered dangerous misconceptions with implications for disease treatment, research, and policy. There is often ambiguity surrounding the terms race (a sociopolitical invention), ethnicity (a cultural grouping), and genetic ancestry (estimates of continental origins), and it is unclear how precisely each correlates with disease-causing alleles. Despite these ambiguities and the extensive scholarship detailing the biased historical origins of these concepts, these terms continue to be poorly defined and used interchangeably as proxies for "genetic risk" and the basis for identifying disease-causing alleles. Research findings based on these terms inform clinical treatment decisions, disease surveillance frequency, and eligibility for disability claims.



Artwork by Nora Rodriguez

Figure: **Visual representation of the new gardener's tale allegory**
(A) Original gardener's preference for nurturing red plants in fertile soil. (B) A new gardener adding a layer of fertile soil to the top layer. (C) A botanist speculating on genetic differences driving growth differences, while ignoring the soil conditions. (D) A hypothetical future where the botanist examines the soil, leading to successful growth of both plant colours.

Inspired by Jones's allegory, we return to the garden when a new gardener has taken over (figure). Over this time, the wind has carried a few pink blossoming seeds from their original poor soil to the fertile soil, where they took root and flourished as well as possible in the shade of the towering red flowers. Some bees pollinate pink blossoms with red pollen and vice versa, resulting in plant blossoms that take on every shade between the original bubblegum pink and scarlet red blossoms. The new gardener notes the differences in soil between the two flower boxes but does not feel responsible for the decisions of her predecessor and just adds a layer of the same fertile soil to the top of each flower box. One day a young botanist happens by and observes how the red blossoming plants are flourishing and the scrawniness of the pink blossoming plants. He suspects the growth disparity is due to the colour of the blossoms and wonders if the plants are even from the same progenitor. Although he sees the variable shades of blossoms and plant heights, he thinks scrawniness is related to pink blossom origins. He reasons that because blossom colour is inherited, so must be the ability to grow. The new gardener suspects the same and provides the botanist with generous funds to isolate the specific genes that prevent the pink flowers from growing. He begins his analysis by extracting and sequencing the DNA of the red and pink plants. The genomes are 99·9% identical so he determines they must share the same origin, but he is confident that the 0·1% difference will explain scrawniness. Given the varying shades of blossoms and increasing criticism that referring to plant blossoms by their colour is crude and unscientific, the botanist decides it would be more precise to categorise the plants by what percentage of their DNA corresponds to their colour. He finds that, on average, the higher the percentage of pink DNA, the scrawnier the plant and concludes that pink DNA is a risk factor for scrawniness. The new gardener, intrigued by these findings, provides more funding to allow the botanist to continue his work, to the exclusion of work examining the original flower box environments. Eventually, the botanist discovers a genetic variant that appears to be associated with growth in the red plants and a slightly different variant in the pink plants. He recommends investigations to determine how the variant contributes to growth and gene manipulation experiments to target and modify the pink mutation.

This botanist is akin to researchers focused on identifying race-specific disease-causing alleles. This focus is often justified by the observation of single-gene disorders, such as sickle cell disease and Tay-Sachs disease with predominance

among African and Ashkenazi Jewish populations, without acknowledging the regional geographical origins of both diseases. Neither is it usually acknowledged that racial patterns in complex diseases like hypertension and cancer arise through multiple gene interactions with surrounding conditions, such as nutrition, toxic environmental exposures, and psychosocial stress. The botanist begins with an attempt to show the plants are not even of the same progenitor—similar to how scientists and physicians during the 18th and 19th centuries attempted to prove races were biologically distinct subspecies and not merely sociopolitical inventions. Next, he made a conscious a-priori decision to stratify his analysis by colour, on the basis of his assumption that blossom colour is genetically linked to growth. Although blossom colour is inherited, there was no evidence that blossom colour is genetically linked to growth, independent of soil conditions. In much the same way, modern geneticists often stratify by socially assigned race at the start of genome-wide association studies to search for disease-causing alleles, reasoning that because the phenotypic characteristics used to define race are inherited and worse outcomes appear in specific racial categories, race must be a reasonable proxy for disease-causing alleles. But, as depicted in this allegory, no evidence suggests that alleles encoding characteristics such as skin colour and hair texture also encode specific disease phenotypes. In fact, no genetic causation can be attributed to any phenotypic presentation unless the populations in question have shared the same environment—a situation precluded by the disparate soil environments for the plants in this allegory and by structural racism for human populations.

The botanist's decision to rename the blossoms not on the basis of colour but rather according to the percentages of pink or red DNA resembles how modern researchers have rebranded language from "race" to "ancestry". Many researchers claim that ancestry is a more refined and specific alternative to race because ancestry estimates are inferred from objective informative markers in the genome, rather than by self-report. However, these markers are derived from living reference populations being treated as "ancestors" and are often defined by whole continents—for instance, Africa and Europe—which historically have served as delineations for racial categorisations. Therefore, defining percentages of African ancestry and European ancestry cannot be independent of the phenotypic presentations of those continental regions, especially since the phenotypic presentations reflect decisions that result in structural, personally mediated, and internalised racism. One cannot assume that a higher proportion of African ancestry is evidence of a genomic contribution to a complex disease, since these associations are confounded by the experiences of racism that are also associated with African ancestry and darker skin colour.

Once the botanist finds the growth gene variant, he attributes it to differing ancestries and goes down a path of gene therapy, rather than considering that interaction with the environment has altered gene expression and activity. In short, this example represents the way in which researchers suggest ancestry can serve as a proxy for disease-causing alleles and capture the contribution of structural racism to health outcomes, but without actually testing any specific measures of structural racism. This shortcut perpetuates a misguided assumption that every person within a population experiences the same aspects of racism to the same degree—without consideration of individual exposure to social determinants of health driven by racism in its various forms, such as whether or how long an individual has lived in a neighbourhood where they are disproportionately exposed to pollution or whether or how long an individual is exposed to personally mediated racism and their physiological response to it.

The new gardener represents how opinions and ideologies are passed down through generations without question and then reinforced by skewed funding for genetics research. This inherited dogma follows on the heels of the original gardener who created the hierarchy based on blossom colour, just as colonisation historically rooted in White supremacy created political hierarchies based upon race and skin colour. These political hierarchies are still felt today because they shaped institutions such as the prison and educational systems and housing and job markets that perpetuate systems of inequity—all of which affect health. The insufficient research on developing measures to assess structural and institutional levels of racism and the inadequate funding dedicated to research focused on structural racism are reflective of the bias inherent in biomedical research.

Imagine the outcome had the botanist thought to approach his research by investigating how the flower boxes differ from one another. From there he would have discovered the soil as the true source of the growth disparity. With further examination, he would find proximity to poor soil directly and inversely correlates with plant growth, which would have led to the solution that would resolve the disparity: replacing the poor soil and subpar environment with fertile soil and conditions that allowed the red plants to flourish. What if researchers today did the same and focused their attention on resolving the structures of racism that created our disparities, instead of continuing a fruitless quest to find a genetic culprit? Doing so will require that the biomedical sciences abandon the notion of "race" and its derivations and recognise that these terms are nothing more than products of White supremacist ideology. Imagine that.

*Vanessa Grubbs, Jessica P Cerdeña, Amy L Non
Department of Ambulatory and Preventive Medicine, Alameda Health System, Oakland, CA 94602, USA (VG); Yale School of Medicine and Department of Anthropology, Yale University, New Haven, CT, USA (JPC); Department of Anthropology, University of California, San Diego, La Jolla, CA, USA (ALN)
drvanessa@thenephrologist.com

Further reading

Bailey ZD, Feldman JM, Bassett MT. How structural racism works—racist policies as a root cause of US racial health inequities. *N Engl J Med* 2021; **384:** 768–73

Carnethon MR, Kershaw KN, Kandula NR. Disparities research, disparities researchers, and health equity. *JAMA* 2020; **323:** 211–12

Cerdeña JP, Plaisime MV, Tsai J. From race-based to race-conscious medicine: how anti-racist uprisings call us to act. *Lancet* 2020; **396:** 1125–28

Graves JL Jr. Human biological variation and the "normal". *Am J Hum Biol* 2021; **33:** e23658

Jones CP. Levels of racism: a theoretic framework and a gardener's tale. *Am J Public Health* 2000; **90:** 1212–15

Krieger N. Stormy weather: race, gene expression, and the science of health disparities. *Am J Public Health* 2005; **95:** 2155–60

Krieger N, Boyd RW, DeMaio F, Maybank A. Medicine's privileged gatekeepers: producing harmful ignorance about racism and health. Health Affairs Blog 2021; published online April 20. https://doi.org/ 10.1377/hblog20210415.30548

Mohottige D, Boulware LE, Ford CL, Jones C, Norris KC. Use of race in kidney research and medicine: concepts, principles, and practice. *Clin J Am Soc Nephrol* 2022; **17:** 314–22

Vyas DA, Eisenstein LG, Jones DS. Hidden in plain sight: reconsidering the use of race correction in clinical algorithms. *N Engl J Med* 2020; **383:** 874–82