Racism Does Not Cause Prostate Cancer, It Causes Prostate Cancer Death

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Race and Prostate Cancer Outcomes

One of the most prominent findings in prostate cancer epidemiology is higher risk for men self-identifying as Black race, with a larger relative difference for mortality (per 100,000: 38.7 *v* 18.0 for non-Hispanic white Americans; relative risk, 2.15) versus incidence (173.0 *v* 97.1; relative risk, 1.78).[1] There are four major possible explanations.

1. Genetics: A genetic mutation in the Black population that increases the risk of either prostate cancer in general or aggressive prostate cancer more specifically.
2. Behavior: Racial differences in lifestyle factors such as diet or exercise.
3. Direct effects of racism: Factors such as the social stress of discrimination in everyday life or discriminatory medical treatment at the point of care.
4. Indirect effects of racism: Factors such as poorer access to care for Black men because of socioeconomic factors.

We can first discount explanation (2). Even if we assume that some lifestyle exposures are causally linked to prostate cancer, which has not been firmly established, the effect sizes and differences between populations are far too small to have any explanatory value. Take an exposure, such as a dietary influence, with an overall prevalence of 35%. If we assume that the exposure increases risk by about 10%—what seems to be at the higher end of the estimate for the link between lifestyle factors and prostate cancer[2,3]—and is as much as 50% more common in Black men, this would lead to only about a 1.5% difference in incidence, compared with the 75% difference we actually see.

The question remaining is, therefore, how much of the difference in mortality and incidence we should attribute to explanation (1) genetics versus explanations (3) and (4), the combined effects of racism. We will take each of mortality and incidence in turn.

Race and Prostate Cancer Mortality

There is clear and compelling evidence that racism strongly influences a man's risk of death after he develops prostate cancer. Black American patients receive poorer care than white patients, and, moreover, mortality differences generally disappear after adjusting for access to care. For instance, survival in the United States is worse in Black men diagnosed with low-grade prostate cancer (adjusted hazard ratio, 1.95; 95% CI, 1.42 to 2.67), but not with high-grade disease (hazard ratio, 1.01; 95% CI, 0.87 to 1.16; $P < .001$ for interaction). This is clearly indicative of disparities in care because true low-grade disease is not associated with mortality, suggesting under-ascertainment of high-grade disease in Black men.[4] There is direct evidence that Black men do not get standard-of-care diagnostic workup, with rates of magnetic resonance imaging–guided prostate biopsy being approximately half those of white men.[5] There is also compelling evidence that lower socioeconomic status in Black men and disparities in treatment are important drivers of observed differences in survival.[6] Critically, even after adjusting for sociodemographic factors and disease characteristics, Black patients are less likely to receive surgery or radiotherapy (adjusted odds ratio, 0.60; 95% CI, 0.56 to 0.64; $P < .001$). Moreover, although curative therapy is less common in Black men both among insured and uninsured patients, the difference is greater in the latter.[7]

Such differences disappear when studying men receiving equivalent care and in equal access settings. For instance, Dess et al[8] compared a population-based cohort with patients receiving care in two equal access settings, the Veteran's Administration and National Cancer Institute randomized trials. After adjusting for demographic characteristics (such as socioeconomic status) and oncologic risk (stage, grade, and prostate-specific antigen), excess mortality was seen for Black men in the population-based cohort but not in the equal access Veteran's Administration and National Cancer Institute cohorts. Similarly, excess mortality in Black men is not seen in prostate cancer clinical trials, where care is determined by protocol, including in studies of chemotherapy,[9] radiopharmaceuticals,[10] and hormonal therapies.[11]

In this respect, prostate cancer survival is like numerous other areas of medicine, where we can directly attribute racial differences in outcomes to racial disparities in care, a consequence of the direct and indirect effects of racism.

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on December 15, 2022 and published at ascopubs.org/journal/jco on January 24, 2023: DOI https://doi.org/10.1200/JCO.22.02203

TABLE 1. Summary of Arguments Why Racial Differences in Prostate Cancer Incidence Are Largely Due to Genetic Factors Rather Than the Direct or Indirect Effects of Racism

Argument	Evidence
Racism cannot affect the prostate uniquely	If prostate cancer is excluded, overall cancer rates are lower in Black *v* white Americans
	One example: cancer of the bladder, which sits directly above the prostate, is twice as common in white Americans
No plausible mechanism for racism-induced prostate cancer	Clear preponderance of evidence that psychosocial stress does not increases the risk of cancer
	Stress-related behaviors that cause some cancers, such as smoking and drinking, are not associated with prostate cancer risk
	Diet and exercise could explain, at best, only a small fraction of the observed racial differences in incidence
	Prostate cancer—compared with cervical or colorectal cancer—is not medically preventable
Prostate cancer, but not racism, varies by geographical origin in Africa	Prostate cancer rates vary between recent US immigrants from West *v* East Africa
	West African immigrants have rates similar to African American population
	East African immigrants have rates similar to US white population
Direct evidence of genetic risk factors that are correlated with self-identified race	Men of African ancestry have a high incidence of genetic variants associated with prostate cancer
	Generic mutations associated with prostate cancer have been identified that are only found in men of West African ancestry, a group that includes the majority of US Black men

Race and Prostate Cancer Incidence

The effects of racism are also asserted to be strongly explanatory for differences in prostate cancer incidence. One recent review claimed that "critical influencers of prostate cancer incidence [include the] physiological response to psychosocial stressors, such as racism and segregation."[12] An empirical study of racial differences in prostate cancer incidence concluded that further research should examine how "perceived racism and social stress … contribute to high-risk prostate cancer,"[13(p411)] hypothesizing that an important cause is the "experience of racism through individual- and neighborhood-level social stressors across the life course that 'get under the skin.'"[13(p409)] Other researchers have even proposed specific molecular mechanisms whereby psychosocial stress caused by racism, or indirectly related to racism via low socioeconomic status, increases the risk of prostate cancer.[14]

These speculations are intuitively appealing because they mirror established science on racial disparities in other diseases. For instance, psychosocial stress is known to influence cardiovascular disease,[15] and racial differences in the incidence of cardiovascular disease can be directly attributed to higher levels of psychosocial stress experienced by Black Americans, starting in pregnancy.[16] However, cardiovascular disease and cancer are etiologically distinct, and a causal association between racism and prostate cancer incidence is directly contradicted by several findings (summarized in Table 1). First, age-adjusted rates of cancers other than prostate cancer are actually lower in Black compared with white Americans: about 280 per 100,000 versus approximately 365.[1] Part of this difference, around 20 cases per 100,000, is due to melanoma, which is rare in Black Americans and part of the difference likely due to overdiagnosis of several cancers in the white population. Nonetheless, cancer is not generally more prevalent in Black Americans and so it would remain to be explained why psychosocial stressors, such as racism and segregation, seem so specifically to target the prostate. It is notable, for instance, that cancer of the bladder, the organ immediately proximal to the prostate, is about half as common in Americans who identify as Black.[17] Second, best evidence suggests that psychosocial stress does not directly cause cancer, and although it can lead to behaviors, such as smoking and drinking, that raise cancer risk,[18,19] prostate cancer is not importantly influenced by these exposures.[20,21] Moreover, unlike cervical or colon cancer, prostate cancer is not preventable if caught at a premalignant state and hence limited access to medical care cannot affect prostate cancer risk.

An epidemiologic finding of particular importance is that prostate cancer varies within the Black population.[17] Recent immigrants from East Africa have very similar age-adjusted rates of prostate cancer mortality to white Americans (19.3 *v* 17.8 per 100,000), whereas immigrants from West and Central Africa have rates closer to the African American population (32.7 *v* 41.0 per 100,000). These data are hard to explain under the hypothesis of a carcinogenic effect of racism. There is no reason to believe that racism is experienced differently depending on geographical origin in men who appear Black, and there is no evidence that secondary effects of racism, such as depressed socioeconomic status, differ by West versus East African ancestry.[22] Although the end point here is mortality, not incidence, clearly large differences in one imply large differences in the other. The mortality end point is, incidentally, a possible explanation for the difference between African American population and recent immigrants from West and Central Africa: Mortality is affected by medical care, and African immigrants generally

have higher socioeconomic status and thus access to good medical care than the African American population.[22]

There is also direct evidence to support the hypothesis that genetics is the major cause of increased prostate cancer risk in Black men. A transancestry genome-wide association study identified a total of 269 prostate cancer variants, of which 71 had an odds ratio of at least 1.1. These were more common in men of African compared with European ancestry.[23] For instance, a variant near the microsatellite marker *DG8S737* is associated with an increased risk of prostate cancer across racial groups but is more common in Black men (30% *v* 13% for white men[24]). Prostate cancer risk variants have been reported that are only found in men of African ancestry, including at *8q24*[25] and *HOXB13*,[26] loci that have been strongly associated with prostate cancer.[27,28] This last variant, *rs77179853*, is particularly interesting because it is found only in West Africa—where most Black Americans trace their ancestry because of the slave trade—with zero prevalence in East and South Africa. These germline changes have downstream consequences for tumor biology. Although comparison of somatic genomes by race is methodologically challenging, because of possible confounding by racial differences in cancer stage, there is good evidence that men of African ancestry have a greater number of acquired genetic alterations in their tumors than men of European ancestry, and African ancestry-specific genomic subtypes of prostate cancer have been identified.[29] There are racial differences in the frequency of SPOP mutations,[30] *TMPRSS2-ERG* fusions,[30,31] and expression of GSTP1[32] and long non-coding RNAs such as *PVT1*,[33] *PCAT1* and *PCAT10/CTBP1-AS*.[30]

Hence, there is clear evidence that from both epidemiologic and genetic studies that the primary cause of increased incidence of prostate cancer in Black men is genetic.

In conclusion, the best evidence is that racism does not cause prostate cells to become cancers, but once that malignant transformation takes place, the effects of racism influence the chances the patient will die as a result.

Despite our title, we are not trying to be absolutist. It is entirely plausible that germline genetic differences in the Black population explain a small part of differences in prostate cancer survival and, comparably, that direct and indirect effects of racism do have a minor impact on carcinogenesis. But to best address racial differences in prostate outcomes, we have to know where to focus and what to prioritize. Understanding the distinction between carcinogenesis and survival will best help both research into prostate cancer disparities and practical efforts to alleviate those disparities.

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SUPPORT

Supported in part by the National Institutes of Health/National Cancer Institute (NIH/NCI) with a Cancer Center Support Grant to Memorial Sloan Kettering Cancer Center (P30 CA008748), a SPORE grant in Prostate Cancer to Dr H. Scher (P50-CA92629), the Sidney Kimmel Center for Prostate and Urologic Cancers and David H. Koch through the Prostate Cancer Foundation.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/JCO.22.02203.

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Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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No other potential conflicts of interest were reported.