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E D I T O R I A L

Re-Examining Racial Disparities in Prostate Cancer Outcomes

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Prostate cancer incidence varies greatly across the world, reflecting disparate population genetic factors, dietary and other environmental influences, and local screening and diagnostic practices. Incidence is high in the United States, where prostate specific antigen (PSA) –based screening is relatively intense; the world age-standardized rate (ASR) for diagnosis in the United States in 2008 was 83.8 per 100,000, corresponding to a 10.8% lifetime risk of diagnosis. The ASR for mortality is 9.7, which is fairly average from the global perspective (although the mortality rate has been falling faster in the United States in the PSA screening era than in any other country).[1,2]

Most of the highest ASRs for mortality worldwide are found in western and southern Africa and in regions with large populations of African ancestry, most notably the Caribbean (ASRs up to 61.7).[1,3] Within the United States, mortality ASRs vary more than fivefold, from 9.5 for Asian/Pacific Islanders to 48.2 for African American men.[4] In fact, the mortality rate ratio between African American and white men is higher for prostate cancer than for any other malignancy.[5] African American men tend to present with higher-stage, more aggressive disease than those of other racial/ethnic groups, but tumor characteristics at diagnosis only partially explain the higher observed mortality rates in African American men.[6] Relatively few studies have examined racial variations in outcomes among men who are well-matched for grade, stage, PSA, tumor extent, and other parameters.

In the article that accompanies this editorial, Sundi et al[7] report an analysis of men in the Johns Hopkins University prostatectomy cohort who met institutional criteria for low-risk disease and could have been eligible for active surveillance but opted instead for immediate surgery. The authors found that, compared with white men, African American men meeting these strict low-risk criteria had higher rates of adverse pathology (defined as Cancer of the Prostate Risk Assessment [Post-Surgical] score ≥ 3, reflecting higher-grade and/or higher-stage disease) and biochemical recurrence. These results were not only statistically significant but clinically quite substantial; among contemporary-era (2004-present) men undergoing extended-pattern biopsy, African American men were more than six times as likely as whites to have adverse pathology on multivariable analysis.

This observation is an important one, with key potential implications for both clinical practice and future research. Whereas the independent association between race and prostate cancer outcomes has not been demonstrated consistently in previous studies—as reviewed by Sundi et al[7]—the observation of disparate results specifically for those with low clinical risk has been made at least once previously. A study from the Shared Equal Access Regional Cancer Hospital registry, representing multiple Veterans' Affairs centers with a relatively high proportion of African American men, found that among men with low-risk characteristics at time of surgery, African American men were substantially more likely to experience biochemical recurrence than others.[8]

Assuming, then, that the observations by Sundi et al[7] may represent a true phenomenon, two principal questions raised in the article are particularly salient. First, should African American men be considered ineligible for active surveillance on the basis of a higher rate of apparent undersampling? The answer is of course no, but these higher risks should be included in the information presented during decision-making counseling sessions with African American men newly diagnosed with clinically low-risk prostate cancer. The study authors suggest that existing risk instruments should be recalibrated for African American men, or that race/ethnicity should be included as an additional parameter in multivariable models. In fact, in development studies for pretreatment multivariable predictive models such as the Kattan nomogram and the Cancer of the Prostate Risk Assessment score, race was expressly examined but was not an independent predictor of outcome after adjustment for PSA, Gleason grade, stage, and biopsy details.[9,10] Others have shown that models predicting post-prostatectomy outcomes perform with comparable accuracy and calibration between African American and white men.[11]

Another possibility might be a relatively intense approach to surveillance for African American men, including, for example, earlier repeat biopsy and/or more use of adjunct imaging, such as multiparametric magnetic resonance imaging. Emerging biomarkers may be valuable for these men as well, although most such markers to date have been validated only in populations that are overwhelmingly white. Of note, recent studies have identified different expression levels of prostate cancer–related genes between African American and white men, even after adjustment for clinical parameters.[12,13] Finally, a lower threshold for intervention might be appropriate for African American men initially opting for active surveillance. Decisions for intervention should also be informed by the fact that from a psychological standpoint, African American men experience substantially greater traumatic stress symptoms after prostate cancer diagnosis than

white men, and these differences do not attenuate with time elapsed since diagnosis.[14]

At least as important as determining the extent to which surveillance protocols should be modified, however, is the more fundamental question posed in the paper and elsewhere: *why* are rates of undersampling so much higher among African American men? In other words, in what ways, anatomically or functionally, are prostate cancers fundamentally different across different populations? Incidence of prostate cancer, high-risk prostate cancer, and lethal prostate cancer are all higher among African American than other racial/ethnic groups in the United States. The explanations for this epidemiologic disparity are likely multiple, including genetics, dietary and lifestyle variation, and environmental exposures—with the latter perhaps including the chronic allostatic stress associated with low socioeconomic status.[15]

Although unequal access to care clearly plays a role in delayed diagnosis and treatment,[16] the interactions among access, quality of care, and genetic and environmental factors in driving outcomes are complex and incompletely understood. Men diagnosed in health care systems serving primarily low socioeconomic status populations tend to have significantly higher disease risk and stage at diagnosis than those seen in other settings with comparable ages, a phenomenon that does not seem possible to explain solely by racial distributions.[17-19]

African American men are systematically under-represented in most prostate cancer research studies. As Sundi et al[7] point out, few men of African descent are included in published North American or European active surveillance series. The same observation applies to most other prostate cancer research questions, including the PSA screening trials. Indeed, one of the most critical flaws in the 2012 "D" recommendation (by the US Preventive Services Task Force[20]) against all PSA screening was its disregard for variable risk not only of prostate cancer incidence but also of prostate cancer mortality across various subpopulations.

Ameliorating the disproportionate prostate cancer disease burden borne by African American men will clearly require a concerted, sustained, multidisciplinary effort. Education and screening programs should be targeted to men at greatest risk and must include access to appropriate and high-quality follow-up care. The higher risk that African American men face for disease progression should be included in treatment decision-making discussions. Perhaps most important for the long-term, prostate cancer must be recognized as a heterogeneous, global disease, and research on prostate cancer screening, risk assessment, treatment, and follow-up must include adequate representation of African American men and men in other high-risk groups who stand to gain the most from improved care.

AUTHOR'S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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