Prostate cancer in black men: It is time for personalized screening approaches?

Lauren P. Wallner, PhD, MPH,[1,2] and Steven J. Jacobsen, MD, PhD[2]

[1]University of Michigan, Departments of Medicine and Epidemiology

[2]Department of Research and Evaluation, Kaiser Permanente Southern California

Corresponding Author:

Lauren P. Wallner, PhD, MPH

Assistant Professor, Department of Medicine and Epidemiology, University of Michigan; Adjunct Investigator, Department of Research and Evaluation, Kaiser Permanente Southern California

North Campus Research Complex

2800 Plymouth Road, Building 16, 409E

Ann Arbor, MI 48109

Office: (734) 232-0788

Fax: (734) 232-0788

Email: lwallner@med.umich.edu

Running title: Prostate cancer screening in black men

Keywords: prostate cancer screening, prostate specific antigen, African American men, precision medicine

Disclosures: Dr. Wallner and Jacobsen report no conflicts of interest related to the topic of this manuscript.

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version record. Please cite this article as doi:10.1002/cncr.30685.

This article is protected by copyright. All rights reserved.

Accepted Article

Funding: The authors have no funding to disclose for this work.

Condensed Abstract: Evidence is accumulating that a “one size fits all” screening approach to prostate cancer may not be what is most appropriate. Therefore, the use of personalized screening approaches in higher risk men, particularly black men, warrants further policy consideration.

Accepted Article

Is prostate cancer different in black men? This is the question that Tsodikov and colleagues are trying to answer in their study published in this issue of *Cancer*. Their findings highlight some important racial differences in screening patterns and projected outcomes that suggest a more personalized approach to prostate cancer screening that is not “one size fits all”. Indeed, a more personalized approach to screening among black men would be an active move towards precision medicine that does not require the sequencing of germline or somatic DNA.

To inform this question, the authors estimated three independent models to compare the natural history of prostate cancer in black men as compared to the general population. To do this, they reconstructed prostate specific antigen (PSA) screening patterns in the US and then fit three independent simulation models using screening data from the National Health Interview Survey (NHIS) and prostate cancer incidence data from SEER. They found that 30-43% of black men develop preclinical prostate cancer by age 85, a risk that is 28-56% higher than the general population. The models predicted similar risks of prostate cancer diagnosis when comparing black men to the general population (35-49%).

This article is protected by copyright. All rights reserved.

Black men, however, were much more likely (44-75%) to progress to metastatic prostate cancer prior to diagnosis when compared to the general population.

This study is timely, as the US Preventive Services Task Force (USPSTF) is currently reviewing their 2012 Grade D recommendation against PSA screening[1] and are expected to release an updated one sometime in 2017. One of the key questions highlighted in the Research Plan released as part of this review, is evaluating whether the effectiveness of PSA screening varies by subpopulation or risk factor, including age, race/ethnicity, family history, and clinical risk assessment.[2] The 2012 USPSTF prostate cancer screening recommendations do not currently take into account race/ethnicity; the Grade D recommendation against screening applies to men of all races.[1] The appropriateness of these recommendations for higher-risk men, including black men, continues to be debated in the medical literature and in the media.[3-5] In addition, the clinical guidelines in this area also are not aligned when it comes to screening black men. While the American Urological Association and National Comprehensive Cancer Network guidelines both reference that African American race is a strong risk factor for prostate cancer and screening discussions should be individualized,[6, 7] they fall short of providing explicit guidance on incorporating race/ethnicity into screening recommendations and discussions. The American Cancer Society guidelines are the only ones to currently make specific screening recommendations for black men, as they recommend offering PSA screening to

Accepted Article

This article is protected by copyright. All rights reserved.

black men beginning at age 45.[8] Therefore, a lack of clarity continues around the appropriateness of using PSA to screen for prostate cancer in black men.

What is clear, however, is that prostate cancer disproportionally affects black men. In 2016 alone, 1 in 6 black men were diagnosed with prostate cancer and 1 in 23 died from their disease.[9] Black men are more likely to be diagnosed with prostate cancer at a younger age and higher stage, and have their disease progress after treatment when compared to white men.[9] While the incidence and mortality rates of prostate cancer in the US have been steadily decreasing over time, black men continue to remain significantly more likely to die from their prostate cancer.[9] The lifetime probability of a black man dying of prostate cancer is almost double that of a non-Hispanic White man (4.4% vs. 2.4%).[9]

This is not new news. African-American race is one of the strongest and most established risk factors for prostate cancer diagnosis and death. A wealth of literature exists in this area and it has spawned myriad studies aimed to elucidate the underlying causes of these disparities, including sociodemographics, genetics, environmental factors, health behaviors, differences in tumor biology, access to care issues, variation in screening, detection, treatment and post-treatment surveillance.[5, 10] And yet there remains a lack of data on the effectiveness of prostate cancer screening in black men. It is well established that black men are under represented in clinical trials of prostate cancer.[11] In the two large randomized control trials of prostate cancer screening on which the

Accepted Article

This article is protected by copyright. All rights reserved.

USPSTF based their recommendations,[12, 13] the proportion of black men included was extremely low. In the Prostate, Lung. Colorectal and Ovarian Cancer Screening Trial (PLCO), only 4% of the study population was African American. While the European Randomized Study of Screening for Prostate Cancer (ERSPC) did not publish their race data, the countries included are mostly Caucasian.[5, 13] Given the lack of prospective screening data in black men, additional observational studies that include more diverse populations are necessary to inform future screening strategies.

In addition, further consideration of more tailored prostate cancer screening guidelines is urgently needed. Recently, multiple studies suggest the 2012 USPSTF guidelines have resulted in a marked decrease in PSA screening rates in the US. These decreases in screening rates have been seen among all age ranges.[14-16] In addition, studies have also noted decreases in the rates of diagnosis of early-stage disease[15, 17] Disturbingly, early data suggest there may be an increase in high-risk disease,[18] but utilization associated with PSA, including subsequent referrals, urology visits and treatments may not have changed much.[16, 19] While it is possible that this may be due to more discriminate use of PSA screening in men who physicians believe are most likely to benefit from early-detection, it is concerning that the current recommendations may result in decreased screening and diagnosis rates in higher-risk men who are most likely benefit from early-detection and need subsequent treatment.

Accepted Article

This article is protected by copyright. All rights reserved.

Importantly, the impact of these recommendations on metastatic and mortality rates still remains largely unknown. Using predictive modeling approaches, Gulati and colleagues previously estimated that by eliminating PSA screening, the number of patients with metastatic disease would double and mortality would increase between 13-25% by 2025.[20] Two recent studies suggest the incidence of later-stage or metastatic disease may be increasing since the release of the recommendations, particularly in younger men.[21, 22] However, given that prostate cancer takes years to progress in most men, it is likely still too soon to fully appreciate the impact of the guidelines on the rates of metastatic prostate cancer and prostate cancer death. If the wide de-implementation of PSA screening does turn out to increase metastatic and fatal prostate cancer rates in the US, it is likely that this burden will disproportionately affect black men. Therefore, data to inform policy discussions as to whether or not PSA screening guidelines should differ is black men, as is presented in this issue of *Cancer*, are important.

The results from Tsodikov and colleagues further inform the ongoing discussion about whether or not screening practices in black men need to be adapted to better align with the fact that they are much more likely to progress to metastatic disease and subsequently die from their cancer. In light of the findings from their study, the authors question whether or not it is time to consider alternative screening approaches in black men specifically. However, there are some potential limitations to their study that warrant consideration when interpreting their results. The use of predictive modeling has inherent limitations, including

Accepted Article

This article is protected by copyright. All rights reserved.

the reliance on the assumption, in this case, that prostate cancer is progressive. This resulted in the exclusion of indolent prostate cancers from these models, which make up a large proportion of the prostate cancer diagnosed as a result of PSA screening. The authors did, however, use three different modeling strategies that relied on varying assumptions in an effort to increase the robustness of their results. In addition, the data used to reconstruct PSA screening were retrospective and age at first PSA was self-reported from the NIHS in 2005, which was then combined with claims from SEER-Medicare to estimate the intervals between screening tests. The older age of patients in SEER-Medicare may also have screening intervals that differ from younger men, which is relevant as the author's recommendations about the policy implications of their work focus on screening black men at younger ages.

At the end of the day, however, the findings from this study imply that the risk/benefit trade-offs of PSA screening may be quite different for black men when compared to the general population. As such, whether current general population PSA screening guidelines should apply to this high-risk group warrants further policy consideration. Given the issues of overdiagnosis and treatment of indolent prostate cancer that arose from prior ubiquitous screening practices, any recommendations to change current screening approaches need to be carefully considered and based on empirical evidence. While more evidence on the downstream mortality effects of PSA screening in black men would be ideal to inform these policies, it is worth contemplating whether we

Accepted Article

This article is protected by copyright. All rights reserved.

have now reached a critical tipping point in PSA screening in black men. In the growing era of precision medicine and personalized health initiatives, it is important that we consider that precision medicine approaches can be applied more broadly than the use genetic or genomic data. These approaches can be applied to better tailor screening practices to men who will indeed benefit from early-detection of prostate cancer. As the evidence is accumulating that a “one size fits all” screening approach to prostate cancer may not be what is most appropriate, it may be time for the conversation around PSA screening to really focus on more personalized approaches to screening in high-risk black men.

Accepted Article

This article is protected by copyright. All rights reserved.

Accepted Article

References

1. US Preventive Services Task Force. Final Recommendation Statement: Prostate Cancer: Screening. Available from URL: https://http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prostate-cancer-screening [accessed 02/01/2017].

2. US Preventive Services Task Force. Final Research Plan: Prostate Cancer: Screening. Available at URL: https://www.uspreventiveservicestaskforce.org/Page/Document/final-research-plan/prostate-cancer-screening1 [accessed 02/01/2017].

3. Brooks DD. Prostate cancer screening in black men--new questions, few answers. Cancer. 2013;119: 2206-2208.

4. Bokhorst LP, Roobol MJ. Ethnicity and prostate cancer: the way to solve the screening problem? BMC Medicine. 2015;13: 179.

5. Shenoy D, Packianathan S, Chen AM, Vijayakumar S. Do African-American men need separate prostate cancer screening guidelines? BMC Urology. 2016;16: 19.

6. American Urological Association. Psa testing for the pretreatment staging and posttreatment management of prostate cancer: 2013 revision of 2009 best practice statement. Available from URL: https://http://www.auanet.org/education/guidelines/prostate-specific-antigen.cfm [accessed 02/01/2017].

7. National Comprehensive Cancer Network. Prostate Cancer Early Detection, 2014.

8. American Cancer Society. Prostate Cancer: Early Detection. Available from URL: http://www.cancer.org/cancer/prostatecancer/moreinformation/prostatecancerearlydetection/prostate-cancer-early-detection-toc [accessed 02/01/2017].

This article is protected by copyright. All rights reserved.

9. American Cancer Society. Cancer Facts & Figures for African Americans 2016-2018. Available from URL: http://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/cancer-facts-and-figures-for-african-americans/cancer-facts-and-figures-for-african-americans-2016-2018.pdf [accessed 01/23/2017].

10. Powell IJ. Epidemiology and pathophysiology of prostate cancer in African-American men. J Urol. 2007;177: 444-449.

11. Ahaghotu C, Tyler R, Sartor O. African American Participation in Oncology Clinical Trials--Focus on Prostate Cancer: Implications, Barriers, and Potential Solutions. Clin Genitourin Cancer. 2016;14: 105-116.

12. Andriole GL, Crawford ED, Grubb RL, et al. Mortality results from a randomized prostate-cancer screening trial. Available from URL: http://dx.doi.org/10.1056/NEJMoa0810696 360].

13. Schroder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. Available from URL: http://dx.doi.org/10.1056/NEJMoa0810084 360].

14. Drazer MW, Huo D, Eggener SE. National Prostate Cancer Screening Rates After the 2012 US Preventive Services Task Force Recommendation Discouraging Prostate-Specific Antigen–Based Screening. Journal of Clinical Oncology. 2015;33: 2416-2423.

15. Etzioni R, Gulati R. Recent trends in psa testing and prostate cancer incidence: A look at context. JAMA Oncology. 2016;2: 955-956.

16. Wallner LP, Hsu JW, Loo RK, Palmer-Toy DE, Schottinger JE, Jacobsen SJ. Trends in Prostate-specific Antigen Screening, Prostate Biopsies, Urology Visits, and Prostate Cancer Treatments From 2000 to 2012. Urology. 2015;86: 498-505.

17. Jemal A, Ma J, Siegel R, Fedewa S, Brawley O, Ward EM. Prostate cancer incidence rates 2 years after the us preventive services task force recommendations against screening. JAMA Oncology. 2016;2: 1657-1660.

18. Banerji JS, Wolff EM, Massman JD, 3rd, Odem-Davis K, Porter CR, Corman JM. Prostate Needle Biopsy Outcomes in the Era of the U.S. Preventive Services Task Force Recommendation against Prostate Specific Antigen Based Screening. J Urol. 2016;195: 66-73.

19. Hutchinson R, Akhtar A, Haridas J, Bhat D, Roehrborn C, Lotan Y. Testing and referral patterns in the years surrounding the US Preventive Services Task Force recommendation against prostate-specific antigen screening. Cancer. 2016;122: 3785-3793.

Accepted Article

This article is protected by copyright. All rights reserved.

20. Gulati R, Tsodikov A, Etzioni R, et al. Expected population impacts of discontinued prostate-specific antigen screening. Cancer. 2014;120: 3519-3526.

21. Weiner AB, Matulewicz RS, Eggener SE, Schaeffer EM. Increasing incidence of metastatic prostate cancer in the United States (2004-2013). Prostate Cancer Prostatic Dis. 2016;19: 395-397.

22. Hoffman RM, Meisner AL, Arap W, et al. Trends in United States Prostate Cancer Incidence Rates by Age and Stage, 1995-2012. Cancer Epidemiol Biomarkers Prev. 2016;25: 259-263.

Accepted Article

This article is protected by copyright. All rights reserved.