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Reply to Letter to the Editor Re: Generalizability of Prostate-Specific Antigen (PSA) Screening Trials in a “Real World” Setting: A Nationwide Survey Analysis

To the Editor:

We thank the authors for sharing their insight on our work. The Prostate, Lung, Colorectal and Ovarian cancer (PLCO) trial had important shortcomings directly affecting the interpretation of the trial, including the underrepresentation of African American (AA) men. As the authors allude to, this was one of the key findings of our study.¹ We agree with the authors that the United States Preventive Services Task Force (USPSTF) recommendations decreased the nationwide prostate-specific antigen (PSA) screening rates² and potentially led to men being diagnosed later with more aggressive prostate cancer (CaP).³ What is equally concerning is the fact that these “missed” diagnoses may have been even more in AA men, based on a recent nationwide survey data linked with Surveillance, Epidemiology and End Results registries.⁴ Indeed, most professional society guidelines explicitly acknowledge that AA men are higher risk for prostate cancer, with PSA screening guidelines tailored accordingly.⁵⁻⁷ Similar concerns exist for men with family history of CaP: more contemporary National Health Interview Survey data reveals a much higher prevalence of PSA screening in these men compared to their representation in the PLCO trial.¹ Extrapolation of Level 1 data from the European PSA screening studies suggested mortality benefit of PSA screening these men,^{8,9} yet, given the small number of these men in the United States-based PLCO trial, the USPSTF guidelines deemed the evidence insufficient. These findings, combined with our results above, make a strong case for adopting a more nuanced approach, and perhaps a different set of national guidelines for men at higher

risk of CaP. While we do not necessarily agree with the authors suggestion of annual PSA screening (given its potential for overdiagnoses), we certainly believe that more tailored guidelines, such as mid-life PSA based regimens, biennial screening, or tools incorporating life expectancy, will be the most judicious way forward.

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