Active Surveillance for Low-Risk Prostate Cancer in Black Patients: A United States Population-Based Analysis

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ABSTRACT

Purpose: Evidence from clinical trials supports conservative management with Active Surveillance/Watchful Waiting (AS/WW) as an acceptable alternative to definitive therapy for low-risk prostate cancer (LRPC). However, given concern for underlying aggressive disease and the underrepresentation of Black men in AS/WW clinical trials, expert panels currently advise caution with AS/WW in Black men. We therefore sought to characterize recent trends in AS/WW use across race.

Methods: The novel Surveillance, Epidemiology, and End Results (SEER) Program Prostate with AS/WW Database queried 50,302 men with LRPC (clinical T1c-T2a, prostate-specific antigen [PSA] <10 ng/mL, Gleason 6) and known management type, diagnosed from 2010-2015 in the United States (N=5218 Black). Trends in AS/WW use over time were determined, stratified by race (Black versus non-Black). The Cochran-Armitage test evaluated trends in initial management over time. Multivariable logistic regression defined adjusted odds ratios (aOR) and 95% confidence intervals (CI) for receipt of AS/WW (versus definitive RP or RT), with race as the primary independent variable of interest. The validated Yost-index adjusted for socioeconomic status (SES).

Results: From 2010 to 2015, AS/WW use increased from 12.6% to 36.4% (+23.8%) among Black men and from 14.8% to 43.3% (+28.5%) among non-Black men (P_trend<0.001), with the absolute difference in rates across race increasing from 2.2% to 6.9%. Black men had lower odds of receiving AS/WW compared to non-Black men before adjusting for SES and insurance status (aOR 0.93 [95% CI, 0.88–0.99], P=0.02), but not after adjustment (aOR 1.01 [95% CI, 0.95–1.07], P=0.86). The aOR of AS/WW for Black versus non-Black men (ref.) went from 1.06 (95% CI, 0.89-1.25, P=0.52) in 2010 to 0.84 (95% CI, 0.73-0.98, P=0.02) in 2015 (P_trend=0.02), even after full multivariable adjustment.

Conclusions: Using a population-based cohort containing the largest number of Black LRPC patients to-date to have quality-assured data on AS/WW in the United States, this report demonstrates that AS/WW use nearly tripled for both Black and non-Black men from 2010-2015, but that Black men were still managed with less AS/WW overall. This treatment disparity seemed to be largely accounted for by racial differences in SES and insurance status; nonetheless, differences in AS/WW use still widened over time and Black race appears to have emerged as an independent predictor of definitive treatment over AS/WW. There is currently no Level I evidence to support these trends, and future randomized trials will be needed to examine the safety and efficacy of AS/WW in Black men.
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GLOSSARY OF ABBREVIATIONS

aOR: adjusted odds ratio

AS/WW: Active Surveillance/Watchful Waiting

CI: Confidence Interval

LRPC: Low-risk prostate cancer

SEER: Surveillance, Epidemiology, and End Results

SES: Socioeconomic status

PSA: Prostate-Specific Antigen

Ref: Referent
SCHOLARLY PROJECT QUESTION AND CONTRIBUTIONS

Question: What have been the recent trends in use of active surveillance/watchful waiting (AS/WW) for Black patients with low-risk prostate cancer in the United States?

Specific Aims: Using a novel Surveillance, Epidemiology, and End Results (SEER) Program Prostate with Active Surveillance/Watchful Waiting (AS/WW) Database, we aimed to establish the following:
   1. Trends in AS/WW utilization by race (Black versus non-Black).
   2. Multivariable analysis for the likelihood of initial management with AS/WW, with race (Black versus non-Black [referent]) as the primary independent variable of interest.
      a. Analyzed both before and after adjustment for socioeconomic status and insurance status;
      b. Analyzed both over the entire study period (2010-2015) and year-by-year.

Contributions
Santino S. Butler researched the relevant literature on conservative management and racial disparities in low-risk prostate cancer, and—with guidance and editing by mentors Brandon A. Mahal, MD (Harvard Radiation Oncology Program) and Paul L. Nguyen, MD (Department of Radiation Oncology, Brigham and Women’s Hospital/Dana-Farber Cancer Institute)—completed all of the statistical analyses described in the manuscript.

Specifically, Stata/SE 15.1 (StataCorp, College Station, TX, USA) was used for all statistical analyses, including the rate of initial management types over time by race, with Cochran-Armitage testing for trends over time; additionally, logistic regression modeling was used on multivariable analysis and repeated with the inclusion of a multiplicative interaction term to test for trend over time.

Santino S. Butler was responsible as the primary author of all work designated under the Scholarly Project. This involved writing of the original manuscript draft (i.e Abstract, Introduction, Methods, Results, and Discussion sections) data curation, investigation, formal analysis, and visualization. Brandon A. Mahal, MD performed first draft revisions and provided major assistance with conceptualization, data curation, methodology, formal analysis, data interpretation, and supervision. All other coauthors contributed via input on methodology and analysis, data interpretation, and review and editing of the final manuscript.
CITATION AND LINK TO PUBLISHED WORK


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To the Editor: Conservative management (active surveillance or watchful waiting) for low-risk prostate cancer is an increasingly used alternative to definitive radiation therapy or radical prostatectomy.\textsuperscript{1,2} Given the underrepresentation of black patients in clinical trials and concern about underlying aggressive disease,\textsuperscript{3,4} expert panels advise caution when applying conservative management to black patients.\textsuperscript{1} Therefore, we examined recent trends in the use of active surveillance or watchful waiting in black men, as compared with nonblack men, with low-risk prostate cancer in the United States.

The Surveillance, Epidemiology, and End Results Prostate with Watchful Waiting Database identified patients with low-risk prostate cancer (defined as a clinical stage of T1 to T2a [indicating early-stage disease], a Gleason score of \( \leq 6 \) [on a scale from 2 to 10, with scores of \( \leq 6 \) indicating low-risk cancer], and a prostate-specific antigen level of less than 10 ng per milliliter) for which the management type was known and that had been diagnosed between 2010 and 2015.\textsuperscript{5} Additional details about this cohort and the study design are provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

We used the Cochran–Armitage test to evaluate trends in initial management over time. Multivariable logistic regression was used to define adjusted odds ratios and 95% confidence intervals for the receipt of active surveillance or watchful waiting as compared with definitive treatment, with race as the primary independent variable. We used the validated Yost index to adjust for socioeconomic status.\textsuperscript{5} Information regarding all the variables that were included in the models is provided in the Supplementary Appendix.

Of 50,302 patients, 7517 (14.9%) were black and 42,785 (85.1%) were nonblack. (The baseline characteristics of the patients are shown in the Supplementary Appendix.) From 2010 through 2015, the use of radical prostatectomy and definitive radiotherapy decreased from 41.4% and 46.0% to 28.8% and 34.8%, respectively, among black men and from 48.5% and 36.7% to 31.8% and 24.9% among nonblack men (\( P<0.001 \) for trend). In contrast, the use of active surveillance or watchful waiting increased from 12.6% to 36.4% among black men and from 14.8% to 43.3% among nonblack men (\( P<0.001 \) for trend) (Fig. 1A).

In an analysis that was not adjusted for socioeconomic status or insurance status, black men had lower odds of receipt of active surveillance or watchful waiting than nonblack men (adjusted odds ratio, 0.93; 95% confidence interval [CI],
However, race was no longer significantly associated with receipt of active surveillance or watchful waiting after the analysis was adjusted for socioeconomic status and insurance status (adjusted odds ratio among black men, 1.01; 95% CI, 0.95 to 1.07; P=0.86) (see the Supplementary Appendix). For the years from 2010 through 2015, the multivariable-adjusted odds ratios for receipt of active surveillance or watchful waiting among black men as compared with nonblack men were as follows: 1.06 (95% CI, 0.89 to 1.25; P=0.52) in 2010; 1.24...
(95% CI, 1.07 to 1.44; P = 0.004) in 2011; 0.97 (95% CI, 0.84 to 1.13; P = 0.72) in 2012; 1.01 (95% CI, 0.88 to 1.17; P = 0.86) in 2013; 0.92 (95% CI, 0.79 to 1.08; P = 0.31) in 2014; and 0.84 (95% CI, 0.73 to 0.98; P = 0.02) in 2015 (P = 0.02 for trend) (Fig. 1B).

From 2010 through 2015, the use of active surveillance or watchful waiting nearly tripled among both black men and nonblack men. Multivariable analyses suggest that racial differences in the receipt of active surveillance or watchful waiting may be driven by differences in socioeconomic status. Still, black men were less likely than nonblack men to receive active surveillance or watchful waiting by 2015, even after adjustment for socioeconomic status — a finding that suggests a possible lower relative uptake of active surveillance or watchful waiting over time for black men. Studies with additional years of data collection, distinction between active surveillance and watchful waiting, and information on delayed radical interventions will be needed to monitor for trends in racial differences in conservative management.

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Omadacycline for Bacterial Infections

TO THE EDITOR: Stets et al. (Feb. 7 issue) report that omadacycline was effective for the treatment of Legionnaires’ disease. The diagnostic method used for at least 76% of cases of the disease involved serologic testing only, with just 17% of cases diagnosed with the more specific test of...