Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Butler S, Muralidhar V, Chavez J, et al. Active surveillance for low-risk prostate cancer in black patients. N Engl J Med 2019;380:2070-2. DOI: 10.1056/NEJMc1900333

SUPPLEMENTAL APPENDIX

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METHODS:

Study Cohort

The novel US Surveillance, Epidemiology, and End Results (SEER) Prostate AS/WW Database identified patients with low-risk prostate cancer (LRPC) (clinical T1-T2a, prostate-specific antigen [PSA] <10 ng/mL, Gleason 6 disease) and known management type, diagnosed between 2010–2015.[1,2] Cases were designated as "Active Surveillance/Watchful Waiting" (AS/WW) by treating facilities if both of the following requirements for conservative management were fulfilled: (1) Initial management plans were documented as either AS or WW, and (2) patients did not receive initial curative treatment within one year of diagnosis.[1] Data on AS/WW metrics were collected as a North American Association of Central Cancer Registries (NAACCR) item and quality-assured by SEER. "AS/WW" was designated by treating facilities and captured by SEER as one variable given the distinction between AS and WW was only recently made during the study period.[3] Definitive management, defined by SEER, included RP or RT (including external beam radiotherapy and/or brachytherapy). Changes to definitive therapy after initial AS/WW within one year of diagnosis, for reasons excluding disease progression, were captured as the definitive therapy received.

Exclusion criteria included unknown T stage, PSA, or Gleason score. The inclusion period of this study was determined by the first and last year in which all SEER Prostate with AS/WW data were available (January 2010 – December 2015). Race was collected and documented by SEER registries as 'White,' 'Black' or 'other' via information from medical records, face sheets, provider notes, photographs, and any other medical record sources available to registries. We dichotomized race as Black versus non-Black given that the primary focus of this study was to determine the rates and outcomes of AS/WW among Black compared with non-Black patients. Insurance status was classified as Medicaid, Uninsured, non-Medicaid insurance, and unknown insurance. Socioeconomic (SES) status was measured by SEER using the validated Yost

Index,[4] which is based on the composite factor analysis of census-tract level median household income, median house value, median rent, percent below 150% of poverty line, education index, percent working class, and percent unemployed (higher Yost Index scores correspond with higher SES). Number of positive cores data were provided by SEER. SEER does not report on the percentage by volume of core cancer involvement.

We obtained access to this data via a proposal to the SEER custom data group.

Statistical Analyses

Initial management type over time was examined for Black and non-Black patients; the Cochran-Armitage test evaluated trends. Multivariable logistic regression defined adjusted odds ratios (AOR) and 95% confidence intervals for receipt of AS/WW (versus definitive therapy [RP or RT]), with race as the primary independent variable of interest. The validated Yost-index adjusted for census-tract level socioeconomic status (SES);[1,4] additional variables included in the model are listed in **Supplemental Table 2**. The multivariable analysis (including adjustment for SES and insurance status) was repeated on a year-by-year basis from 2010-2015; a race*year of diagnosis interaction term was applied to test for trend.

P-values were two-sided, with α=0.05. Stata/SE 15.1 (StataCorp, College Station, TX, USA) was used for analyses. This study was limited by lack of information on percent of a core involved and PSA density. The Dana-Farber/Harvard Cancer Center Institutional Review Board granted permission for the performance of this study.

Supplemental Table 1. Distribution of baseline characteristics by race (Black versus non-Black) [a] and initial management type (AS/WW versus initial definitive treatment with radical prostatectomy or radiation therapy) among 50,302 patients in the U.S. diagnosed with low-risk prostate cancer (clinical T1-T2a, prostate-specific antigen [PSA] <10 ng/mL, Gleason 6 disease) from 2010-2015.

Characteristic [b]		Black, AS/WW (N=1835)	Black, RP or RT (N=5682)	Non-Black, AS/WW (N=11,649)	Non-Black, RP or RT (N=31,136)
Initial Management Type, N (%) [c]					
	AS/WW	1835 (100)	-	11649 (100)	-
	Radical Prostatectomy	-	2643 (46.5)	-	17,869 (57.4)
	Radiation Therapy	-	3039 (53.5)	-	13,267 (42.6)
Age (median with IQR, years)		62 (56-67)	59 (54-65)	64 (59-69)	62 (57-67)
PSA (median with IQR, ng/mL)		5.5 (4.4-6.9)	5.3 (4.3-6.7)	5.4 (4.4-6.8)	5.2 (4.3-6.6)
Number Positive Cores, N (%)					
	≤2	1190 (64.8)	2106 (37.1)	7646 (65.6)	12,315 (39.6)
	≥3	403 (22.0)	2175 (38.3)	2281 (19.6)	10,904 (35.0)
	Unknown	242 (13.2)	1401 (24.7)	1722 (14.8)	7917 (25.4)
Year of Diagnosis, N (%)					
	2010-2012	764 (41.6)	3551 (62.5)	5010 (43.0)	20,681 (66.4)
	2013-2015	1071 (58.4)	2131 (37.5)	6639 (57.0)	10,455 (33.6)
Insurance Status, N (%)					
	Non-Medicaid Insured	1637 (89.2)	4819 (84.8)	10,513 (90.2)	28,358 (91.1)
	Medicaid	86 (4.7)	353 (6.2)	285 (2.4)	898 (2.9)
	Uninsured	39 (2.1)	106 (1.9)	120 (1.0)	242 (0.8)
	Unknown	73 (4.0)	404 (7.1)	731 (6.3)	1638 (5.3)
Yost-Index (median with IQR)		10.91 (10.42-11.48)	10.84 (9.63-11.37)	11.37 (10.82-11.63)	11.20 (10.62-11.58)

[a] Race was defined via the SEER "Race Recode" variable as Black versus non-Black (including White, other, and unknown races) for the purposes of this study. Race was collected and documented by SEER registries via information from medical records, face sheets, provider notes, photographs, and any other medical record sources available to registries.

[b] P-value <0.05 for all patient characteristics when comparing across race and initial management type subgroups.

[c] Among Black patients, 24.4% (N=1,835) were managed with AS/WW, 35.2% (N=2,643) with RP and 40.4% (N=3,039) with definitive RT. Among non-Black patients, 27.2% (N=11,649) were managed with AS/WW, 41.8% (N=17,869) with RP and 31.0% (N=13,267) with RT. Patients with unknown T stage, PSA, or Gleason score were excluded from the study. For men managed with AS/WW, there were 6.2% (N=122/1957) Black versus 7.5% (N=941/12,590) non-Black men excluded for unknown T stage, PSA, or Gleason score (P=0.05). For men managed with either RP or RT, there were 10.7% (N=684/6366) Black versus 10.4% (N=3599/34,735) non-Black men excluded for unknown T stage, PSA, or Gleason (P=0.36).

Abbreviations: AS/WW, Active Surveillance/Watchful Waiting; IQR interquartile range; N, number; ng/mL, nanograms per milliliter; %, percentage (percentages may not add to 100% due to rounding); PSA, prostate-specific antigen; RT, radiation therapy; RP, radical prostatectomy

Supplemental Table 2. Multivariable-adjusted odds for receipt of AS/WW compared to definitive therapy (radical prostatectomy or any radiation therapy) among 50,302 patients in the U.S diagnosed with NCCN low-risk prostate cancer from 2010-2015, including one model with and one model without adjustment for Yost-index (socioeconomic status) and insurance status.

Characteristic		**Without Adjustment for Yost-Index/SES or Insurance status**		**With Adjustment for Yost-Index/SES and Insurance Status**	
		AOR (95% CI)	P	AOR (95% CI)	P
Race [a]					
	Non-Black	1.0 (Ref)		1.0 (Ref)	
	Black	0.93 (0.88–0.99)	0.02	1.01 (0.95-1.07)	0.86
Yost-Index (for socioeconomic status) [b]					
	Top 50 percentile Yost-Index	Not Adjusted For		1.0 (Ref)	
	Bottom 50 percentile Yost-Index	-		0.68 (0.66-0.71)	<0.001
Age at Diagnosis (per year increase)		1.038 (1.035–1.041)	<0.001	1.040 (1.037-1.043)	<0.001
PSA (ng/mL increase)		1.00 (0.99–1.02)	0.45	1.01 (0.99-1.02)	0.32
Number of Positive Cores					
	≥3	1.0 (Ref)		1.0 (Ref)	
	≤2	3.16 (3.00–3.32)	<0.001	3.16 (3.01-3.33)	<0.001
	Unknown	1.17 (1.10–1.25)	<0.001	1.20 (1.12-1.28)	<0.001
Year of Diagnosis					
	2010-2012	1.0 (Ref)		1.0 (Ref)	
	2013-2015	2.60 (2.49–2.71)	<0.001	2.64 (2.53-2.75)	<0.001
Insurance Status					
	Non-Medicaid Insured	Not Adjusted For		1.0 (Ref)	
	Medicaid	-		0.84 (0.74–0.95)	0.005
	Uninsured	-		1.57 (1.28–1.92)	<0.001
	Unknown	-		0.87 (0.79–0.95)	0.002

[a] Race was defined via the SEER "Race Recode" variable as Black versus non-Black (including White, other, and unknown races) for the purposes of this study. Race was collected and documented by SEER registries via information from medical records, face sheets, provider notes, photographs, and any other medical record sources available to registries.

[b] Socioeconomic (SES) status was captured at the census tract level using the validated Yost-index[4]—a continuous composite numerical score based on median household income, median house value, median rent, percent below 150% of poverty line, education index, percent working class, and percent unemployed (where higher Yost-index scores correspond with higher SES). Yost-index values in this study ranged from 8.18 – 11.83 (8.18-11.82 for Black men and 8.18-11.83 for non-Black men), with a median of 11.18 and interquartile range of 10.60-11.57. For the purposes of this study, the Yost-index was stratified at the median.

Abbreviations: AS/WW, Active Surveillance/Watchful Waiting; AOR, Adjusted Odds Ratio; CI, Confidence Interval; N, number; P, P-value; PSA, prostate-specific antigen; ng/mL, nanograms per milliliter; Ref, Referent; SES, Socioeconomic status

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