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Original Article

Trends in treatments for prostate cancer in the United States, 2010-2015

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Abstract: Although annual mortality trends for prostate cancer were stabilized in recent years, understanding the exact treatment changes is necessary for optimal management. Utilization of not-otherwise specified (NOS) treatments for prostate cancer was unclear. Thus, this study aimed to analyze trends in treatment for prostate cancer in the U.S. from 2010 to 2015 and examine whether the treatment for the prostate cancer in the U.S. is compliant with clinical practice guidelines. Using joinpoint regression models, we examined trends in the rate and proportion of age-standardized utilization (ASUR and ASUP) of treatments for prostate cancer diagnosed during 2010-2015 in the U.S. based on the data from the Surveillance, Epidemiology, and End Results (SEER, 2018 data-release, with linkage to active surveillance/watchful waiting [AS/WW]) cancer registry program. Among 316,690 men with prostate cancer diagnosed during 2010-2015, ASUR and ASUP for radical prostatectomy, radiotherapy, AS/WW and NOS treatment were 32.7, 34.4, 10.0 and 40.1 per 100,000, and 27.9%, 29.3%, 8.5% and 34.2%, respectively. Trends in the overall ASUR for prostate cancer treatments differed by cancer risk group, patients' age, race/ethnicity, Gleason score, insurance status, and the average education level, average poverty-level and foreign-born person percentage of the patient's residence-county, but not by rural-urban continuum or region. ASUP of radical prostatectomy decreased from 9.8% in 2010 to 4.8% in 2015 (annual percent change [APC] = -12.0%, 95% CI, -15.9 to -7.9%), and the decrease was observed in all different risk groups. ASUP of AS/WW increased from 16.4% in 2010 to 30.2% in 2013 (APC = 22.7%, 95% CI, 4.6 to 44.0%) and then remained stable through 2013 to 2015 (APC = 1.9%, 95% CI, -24.1 to 36.9%). The increasing tendency of AS/WW only occurred in the low-risk and intermediate-risk groups. The ASUP of NOS treatment has increased from 32.3% in 2010 to 36.8% in 2015 (P<0.01). In conclusion, ASUR and ASUP for prostate cancer treatments, including NOS treatment, had changed during 2010-2015. Their trends appeared to differ by cancer risk-group, age, race/ethnicity, Gleason score and socioeconomic factors. Future studies are warranted to understand the impacts of upward trends in ASUP of NOS treatments and AS/WW on patient survival and prostate cancer mortality.

Keywords: Prostate cancer, treatments, trends, joinpoint regression analysis, population-based study

Introduction

Prostate cancer is the most common cancer among men in the United States, with estimated 248,530 new cases and 34,130 deaths for 2021 [1]. Its race-adjusted age-standardized cause-specific mortality rates have been unchanged in recent years [2], which is largely due to the earlier detection through prostate-specific antigen (PSA) testing and advances in treatment [3, 4]. Treatment options for prostate cancer include active surveillance/watchful waiting (AS/WW), radiation therapy, brachytherapy, prostatectomy, androgen deprivation therapy, immunotherapy, and chemotherapy according to the 2010 and 2019 National Comprehensive Cancer Network (NCCN) guidelines. The treatment choice should be primarily

based on cancer risk group, which is influenced by patient's individual profile and choice [5, 6].

A study on Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry demonstrated that both undertreatment of high-risk disease and overtreatment of low-risk disease existed, with the latter appearing to be improving but the former worsening during 1990 and 2007 [7]. Thus, prostate cancer treatments could be better utilized or optimized to reduce prostate cancer deaths in the United States. Indeed, there was an increase in AS/WW use among low- or intermediate-risk prostate cancers over the years [8-13]. However, studies modeling the trends according to the guidelines for trend analysis are scarce [14], and identification of trend turning-point(s) and adjustment for potential confounders are required for proper trend analysis on population data [15, 16]. Furthermore, cases of unknown treatment were rarely included in these trend analyses [8-13], but may significantly change the percentage of patients with AS/WW. Therefore, this study aims to examine trends in the numbers and percentages of treatment utilization among U.S. prostate cancer patients by risk groups and potential confounders, focusing on potential turning points and inclusion of patients with unknown treatment status. The Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) was used as it is an authoritative population-based database and one of the largest cancer registry datasets in the world. We chose the years of 2010-2015 because these are the years when reliable AS/WW data were available in the SEER program at the time of study.

Methods

Data source and sample

This retrospective cross-sectional study was exempted from the Institutional Review Board (IRB). We examined data from a custom SEER*Stat Databases: November 2017 Submission (1973-2015) for all incident cases of prostate cancer from 2010 to 2015, which were the most recent and the most complete data at the time of analysis. We checked the following items in the SEER*Stat program (seer.cancer.gov/seerstat) by using their Standard Case Selection function. We selected only the microscopically confirmed cases, and the first primary cancer only. Any cases without histology, age-data or follow-up data in the SEER were excluded.

Variables and definitions

AS/WW was defined as no treatments identified in the patient within one year of the cancer diagnosis, as described before [8, 17]. Radical prostatectomy was defined as surgery code 50 without AS/WW. Radiotherapy was defined as using any of the radiation modality, without AS/WW and any of the prostatectomy (partial, segmental, simple or radical prostatectomy, *i.e.,* surgery codes 30, 50, 70 and 80). Not-otherwise-specified (NOS) treatments were grouped for the remainder of the cases. NCCN risk groups are widely used by U.S. physicians and were classified based on tumor's T category, PSA level and Gleason scores [18]. According to the American Joint Committee on Cancer (AJCC)-7 stage system [18] and the NCCN risk-group classification, which are overall consistent with those of D'Amico *et al.* [19] and the American Urological Association [20], we classified the cases of AJCC stage I into the low-risk group, those of stage IIA into intermediate-risk group, and those of stage IIB and above into high-risk group, respectively. The cases of unknown AJCC stage were assigned to the unknown risk group.

Geographic regions were grouped according to the U.S. Census Bureau's definitions [21]. We arranged the rural-urban continuum of the patient's location (county-level) according to the 2013 version of mitigating the potential changes across the years [22] and grouped the county-level data of the socioeconomic factors according to the 2011-2015 Census-Bureau American Community Survey (ACS) 5-year file [23]. PSA levels in the SEER database were not reliably recorded [24], and thus not subject to further exploration.

Data collection

The data collection for each case included age, year of diagnosis, the ALCC stage, treatment for prostate cancer, race/ethnicity, Census region, rural-urban continuum, high school education in the county, the poverty level in the county, foreign-born persons in the county, and insurance status.

Statistical analysis

The individual-based age-standardized utilization rate (ASUR) of a treatment modality was computed using SEER*Stat software (Surveillance Research Program, National Cancer Institute SEER*Stat program (seer.cancer.gov/seerstat) version <8.3.5>) with the 2000 U.S. standard population (19 age groups, Census P25-1130). We calculated proportion of the individual-based age-standardized utilization (ASUP) of a stratum using stratum's ASUR divided by the sum of all strata's ASUR (*i.e.*, proportion of a given modality's utilization in all patients/treatments). The Chi-square test was used to examine the difference in the distribution of age-standardized incidence cases among the subgroups. We stratified the ASUP and ASUR by risk group, age, diagnosis year, race, census regions, and rural-urban continuum, insurance status and socioeconomic attributes of the county where patents resided (for SEER18 data only), respectively. Finally, we examined the temporal trends of ASUP and ASUR of prostate cancer treatments using Stata (version 15, StataCorp LLC, College Station, TX) and Joinpoint program (Version 4.6.0.0., Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD), respectively [25].

Joinpoint regression was used to analyze potential trends and the joinpoint (*i.e.*, turning point). We used the following default parameters for trend analyses. First, the log transformation option was chosen. Then, the standard errors were used to provide the opportunity for Heteroscedastic Errors Option (Weighted Least Squares). Next, a grid search method was selected with two as the minimal number of observations from a joinpoint to either end of the data (excluding the first or last joinpoint if it falls on observation) and the minimum number of observations between the two joinpoints (excluding any joinpoint if it falls on an observation). The joinpoint model selection method was a permutation test with an overall significance level of 0.05 and 4499 permutations. We also chose "Fit an uncorrelated errors mode" for the autocorrelated errors option, and the parametric model option for the annual percentage change (APC)/Tau confidence intervals (CI) calculation [25]. On rare occasions, age-standardized rates were unavailable due to the lack of population data; case counts within the strata were used to calculate proportional utilization. Multiple comparison adjustment was considered, but deemed unnecessary and was not used since only 1 or 2 factors were included in the analyses each time according to the practice recommendations [26, 27]. We reported 2-sided *P* values and set $P<0.05$ as statistical significance.

Results

Baseline characteristics

Among the 316,690 men with invasive prostate cancer diagnosed during 2010-2015, 143,523 (52.4%), 69,073 (26.1%), 77,236 (27.7%) and 26,858 (10.9%) were categorized into high-risk, intermediate-risk, low-risk and unknown risk groups. The overall ASUR was 117.2 per 100,000; the ASUR was 32.7, 34.4, 10.0 and 40.1 per 100,000 for radical prostatectomy, radiotherapy, AS/WW and NOS treatments, respectively (**Table 1**). From 2010 to 2015, the overall ASUR of prostate cancer treatments had been reduced (from 142.2 per 100,000 in 2010 to 101.6 per 100,000 in 2015). The ASUR of radical prostatectomy and radiotherapy decreased during 2010-2015, while that of AS/WW increased during 2010-2013 and was then stabilized thereafter (**Table 1**). The utilization was associated with diagnosis year, cancer risk group/stage, age, race, rural-urban continuum, region and the socioeconomic factors of the patients' residency county (for strata comparison within their groups, $P<0.001$, **Table 1**).

Trends in treatments for prostate cancers by risk group

Trends in the ASUP differed by risk groups. While the overall ASUP was continuously decreasing for radical prostatectomy in all risk groups, except for unknown-risk group, there was a turning point for AS/WW treatment in intermediate- and low-risk groups, respectively, but not in the high- or unknown-risk groups (**Figure 1**). Strikingly, 35-45% of the patients in low-risk group and 77-84% of those in unknown risk group had NOS treatments.

Among U.S. men with low-risk prostate cancer, a trend-difference in the ASUP was observed in age groups of 65-74 (decreasing), 75-84

Table 1. Rate and proportion (%) of age-standardized utilization of treatments for prostate cancer diagnosed during 2010-2015 in the United States

	Total cases	Rate (per 100,000) and proportion (%) of age-standardized treatment utilization					*P* value*
		Radical prostatectomy	Radiotherapy AS/WW	AS/WW	NOS treatments	Total	
All, per 100,000	316690	32.7	34.4	10.0	40.1	117.2	
Year of diagnosis							<0.001
2010	59070	41.9 (29.5)	45.7 (32.1)	8.7 (6.1)	45.9 (32.3)	142.2 (100.0)	
2011	59915	41.1 (29.4)	43.8 (31.3)	10.2 (7.3)	44.5 (31.9)	139.6 (100.0)	
2012	51408	32.5 (28.0)	33.8 (29.2)	10.2 (8.8)	39.4 (34.0)	115.9 (100.0)	
2013	50124	29.0 (26.5)	30.4 (27.8)	11.5 (10.5)	38.6 (35.2)	109.5 (100.0)	
2014	46887	26.4 (26.5)	27.4 (27.5)	9.6 (9.6)	36.2 (36.3)	99.6 (100.0)	
2015	49286	26.9 (26.5)	27.6 (27.2)	9.7 (9.6)	37.4 (36.8)	101.6 (100.0)	
Risk group, per 100,000 (%)							<0.001
High-risk	143523	27.3 (52.1)	11.4 (21.7)	0.5 (1.0)	13.2 (25.2)	52.4 (100.0)	
Intermediate-risk	69073	3.0 (11.4)	13.7 (52.5)	2.2 (8.6)	7.2 (27.5)	26.1 (100.0)	
Low-risk	77236	2.2 (7.8)	7.7 (27.9)	6.8 (24.4)	11.0 (39.8)	27.7 (100.0)	
Unknown	26858	0.2 (2.0)	1.5 (13.8)	0.5 (4.2)	8.7 (80.0)	10.9 (100.0)	
Age, per 100,000 (%)							<0.001
<45 years	1679	0.7 (59.8)	0.2 (12.3)	0.1 (8.0)	0.2 (19.9)	1.2 (100.0)	
45-54 years	28853	42.4 (55.5)	12.8 (16.8)	6.2 (8.1)	14.9 (19.6)	76.3 (100.0)	
55-64 years	103615	148.9 (43.8)	82.1 (24.1)	31.6 (9.3)	77.5 (22.8)	340.1 (100.0)	
65-74 years	121728	183.0 (26.6)	237.5 (34.5)	65.0 (9.4)	202.3 (29.4)	687.8 (100.0)	
75-84 years	48363	30.9 (5.6)	202.5 (36.4)	40.4 (7.3)	282.4 (50.8)	556.2 (100.0)	
85+ years	12451	3.1 (0.8)	39.2 (10.0)	15.3 (3.9)	334.8 (85.3)	392.4 (100.0)	
Race/ethnicity, per 100,000 (%)							<0.001
NH White	211843	34.8 (30.6)	32.8 (28.9)	10.2 (9.0)	35.7 (31.5)	113.5 (100.0)	
API	14865	17.2 (30.2)	18.9 (8.9)	5.6 (33.3)	20.8 (33.3)	62.5 (99.9)	
Hispanic	29938	24.5 (25.7)	26.1 (27.3)	6.7 (7.0)	38.3 (40.0)	95.6 (100.0)	
NH Black	47771	42.9 (22.6)	65.0 (34.2)	14.2 (7.5)	67.8 (35.7)	189.9 (100.0)	
Unknown	12273	54.1 (7.6)	124.5 (17.4)	50.4 (7.0)	486.5 (68.0)	715.5 (100.0)	
Census region, per 100,000 (%)							<0.001
Midwest	31201	42.0 (31.8)	37.9 (28.7)	10.5 (7.9)	41.7 (31.6)	132.1 (100.0)	
Northeast	54612	35.5 (26.9)	46.8 (35.4)	10.0 (7.6)	39.8 (30.1)	132.1 (100.0)	
South	73780	32.7 (25.8)	40.6 (32.0)	7.9 (6.3)	45.5 (35.9)	126.7 (100.0)	
West	157097	30.5 (28.5)	27.8 (26.0)	10.7 (10.0)	38.0 (35.5)	107.0 (100.0)	
Rural-urban continuum in 2013, per 100,000 (%)							<0.001

Metropolitan counties	282313	33.3 (28.1)	34.7 (29.3)	10.4 (8.8)	40.0 (33.8)	118.4 (100.0)	
Non-metropolitan counties	34194	28.3 (26.2)	31.9 (29.6)	6.8 (6.3)	40.9 (37.9)	107.9 (100.0)	
Unknown/missing/no match	183	11.2 (13.8)	18.9 (23.2)	1.5 (1.9)	49.7 (61.1)	81.3 (100.0)	
% of persons <high school education in the county (ACS 2011-2015, quartiles)							<0.001
<10 (Q1)	79702	35.2 (28.6)	38.0 (30.8)	10.9 (8.8)	39.1 (31.8)	123.2 (100.0)	
10-13.05 (Q2)	78444	32.0 (26.7)	38.3 (32.0)	12.0 (10.0)	37.6 (31.3)	119.9 (100.0)	
13.06-18.0 (Q3)	77775	32.6 (27.3)	35.7 (29.9)	9.8 (8.2)	41.3 (34.6)	119.4 (100.0)	
>18.1 (Q4)	80703	31.2 (29.0)	26.6 (24.8)	7.6 (7.1)	42.1 (39.2)	107.5 (100.1)	
% of persons <200% poverty level in the county (ACS 2011-2015, quartile)							<0.001
<26 (Q1)	77724	34.5 (27.7)	40.1 (32.2)	12.4 (10.0)	37.6 (30.2)	124.6 (100.0)	
26-33 (Q2)	79190	32.9 (29.3)	32.2 (28.6)	11.1 (9.8)	36.3 (32.3)	112.5 (100.0)	
33-40.45 (Q3)	65172	31.6 (26.0)	38.5 (31.6)	9.0 (7.4)	42.5 (34.9)	121.6 (100.0)	
>40.45 (Q4)	94538	31.8 (28.2)	29.3 (26.0)	7.9 (7.0)	43.8 (38.8)	112.8 (100.0)	
% of foreign-born persons in the county (ACS 2011-2015, quartile)							<0.001
<7 (Q1)	76127	33.1 (27.4)	36.0 (29.8)	8.0 (6.6)	43.7 (36.1)	*120.8 (100.0)*	
7-15 (Q2)	78309	35.9 (28.4)	39.1 (30.9)	10.7 (8.5)	40.7 (32.2)	*126.4 (100.0)*	
>15-24 (Q3)	84281	31.6 (28.1)	32.0 (28.5)	10.8 (9.6)	37.9 (33.8)	*112.3 (100.0)*	
>24 (Q4)	77907	30.9 (27.8)	31.2 (28.0)	10.3 (9.3)	38.9 (35.0)	*111.3 (100.1)*	
Insurance status, n (%)#							<0.001
Any Medicaid	16023	3857 (24.1)	4978 (31.1)	841 (5.2)	6347 (39.6)		
Insurance status unknown	43641	2342 (5.4)	9553 (21.9)	2516 (5.8)	29230 (67.0)		
Insured	203229	77466 (38.1)	58421 (28.7)	19839 (9.8)	47503 (23.4)		
Insured, but insurance provided not specified	49161	13601 (27.7)	16164 (32.9)	4155 (8.5)	15241 (31.0)		
Uninsured	4636	1361 (29.4)	1123 (24.2)	334 (7.2)	1818 (39.2)		

Note: Data were derived from the 18 registries of the Surveillance, Epidemiology, and End Results (SEER)-18. The data in the parentheses are the proportion of age-standardized treatments utilization (*i.e.* the percentages of different treatments among the overall treatment utilization) for prostate cancer. NOS, Not otherwise specified; AS/WW, active surveillance/watchful waiting; NH, non-Hispanic. API, Asian Pacific Islanders; ACS, the Census American Community Survey 5-year file. **P* values as determined by Chi-square test on the proportion of age-standardized treatment utilization in each subgroup. #No age-standardized utilization rate could be computed due to the lack of insurance-status data in the study population.

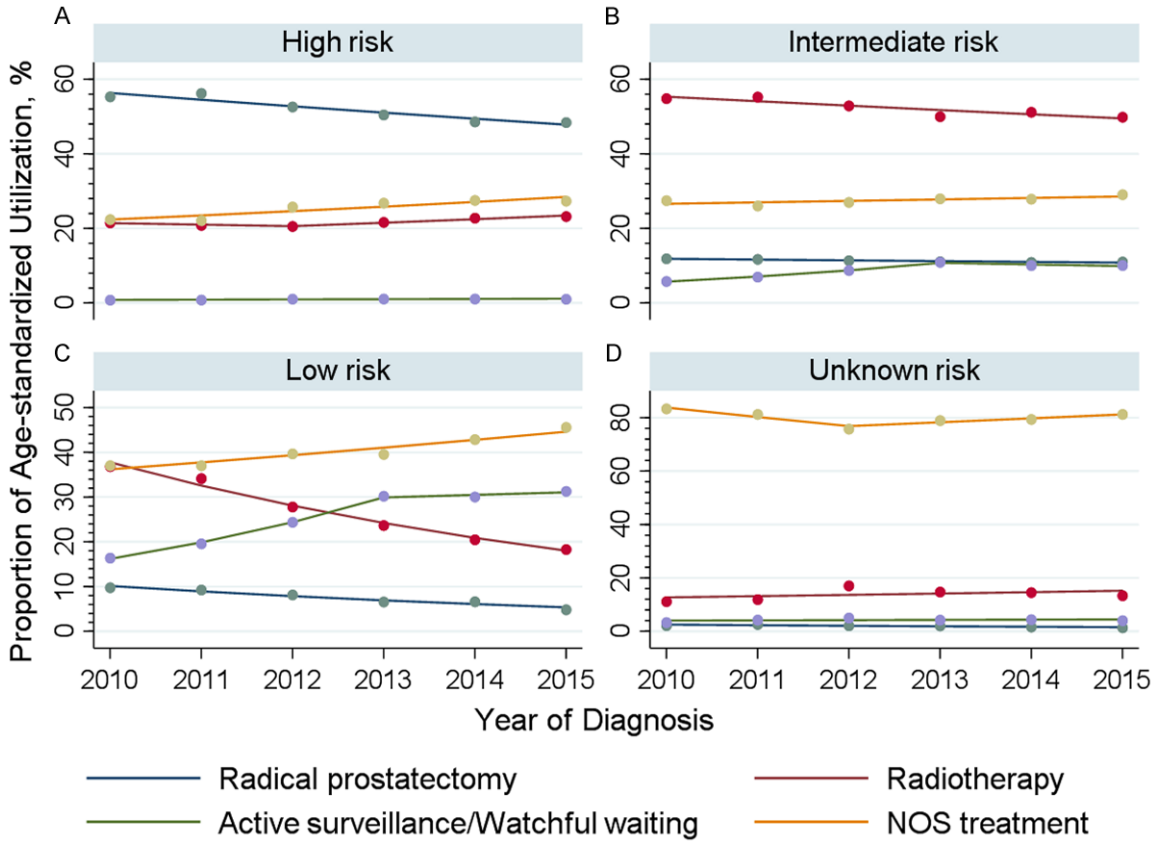

Figure 1. Trends in the proportion of age-standardized treatment utilization for prostate cancers diagnosed in the U.S. during 2010-2015 by cancer risk group. A. High-risk: There were a downward trend in radical proctectomy (annual percentage change [APC] = -3.2, *P* = 0.004) and an upward trend in not-otherwise-specified (NOS) treatments (APC = 4.9, *P* = 0.01), but no significant trends were identified in the other two treatment groups. B. Intermediate-risk: There were downward trends in radical proctectomy (APC = -1.8, *P* = 0.003) and radiotherapy (APC = -2.2, *P* = 0.01), and an upward trend in active surveillance/watchful waiting during 2010-2013 (APC = 23.5, *P* = 0.03) which was no longer present during 2013-2015 (*P* = 0.31). There was no significant trend of NOS treatment group. C. Low-risk: There were downward trends in radical proctectomy (APC = -12.0, *P* = 0.001) and radiotherapy (APC = -13.8, *P*<0.001), an upward trend in NOS treatment group (APC = 4.3, *P* = 0.003) and an upward trend in active surveillance/watchful waiting during 2010-2013 (APC = 22.7, *P* = 0.04) which was no longer present during 2013-2015 (*P* = 0.57). D. Unknown-risk group: Only radical prostatectomy had a significant trend (APC = -9.4, *P* = 0.04); all other treatment groups had no significant trends or turning points. Dots represent individual data points, while lines represent piecewise log-linear model computed using the joinpoint program.

(increasing) or 85+ (increasing) years for radical prostatectomy and in age groups of 55-64, 65-74, 75-84 or 85+ (stable) for AS/WW, with reference to the age of 45-54 years (**Table 2**). Compared with men in Midwest, different trends in ASUP were observed in the ones in Northeast (smaller upward trend) for AS/WW and in Northeast (no significant trend) and South (smaller upward trend) for NOS treatments. Compared with the men in a county with fewer foreign-born residents (first quartile), those in a county with more foreign-born residents (fourth quartile) had different trends in ASUP for both radiotherapy and AS/WW (**Table 2**). Compared with tumor of Gleason scores 2-6, there was a trend-difference of the ASUP in Gleason score 7 group for radical prostatectomy (**Table 2**).

Among U.S. men with intermediate-risk prostate cancer, trends in ASUP differed between those of unknown race/ethnicity and non-Hispanic white men for radical prostatectomy and AS/WW and between those in a county of more high-school graduates (fourth quartile) and the men in a county of fewer high-school graduates (first quartile) for radical prostatectomy and NOS treatments (**Table 3**). Similar to the low-

Table 2. Trends in the proportion (%) of age-standardized utilization of treatments for low-risk prostate cancers diagnosed during 2010-2015 in the U.S

	Radical prostatectomy			Radiotherapy			AS/WW			NOS treatments		
	2010	2015	APC (95% CI)	2010	2015	APC (95% CI)	2010	2015	APC (95% CI)	2010	2015	APC (95% CI)
All	9.8	4.8	-12.0 (-15.9 to -7.9)	36.8	18.3	-13.8 (-16.1 to -11.4)	16.38	30.2#	22.7 (4.6 to 44.0)	37	45.6	4.3 (2.5 to 6.1)
							30.2#	31.3	1.9 (-24.1 to 36.9)			
Age												
<45 years	29.3	16.6	-13.4 (-23.2 to -2.3)	23.2	14.3	-8.7 (-15.0 to -1.8)	14.1	25.0*	59.2 (-40.6 to 327.0)	33.3	27.6#	-5.0 (-44.9 to 63.9)
							25.0*	26.7	-6.3 (-37.4 to 40.3)	27.6#	42.4	27.0 (-61.5 to 318.3)
45-54 years¶	26.0	9.9	-16.7 (-20.0 to -13.4)	30.4	17.6	-12.2 (-18.4 to -5.5)	13.6	33.4#	34.4 (8.3 to 66.9)	30.1	36.6	4.5 (1.0 to 8.1)
							33.4#	36.0	3.7 (-24.6 to 42.6)			
55-64 years	15.1	6.6	-15.5 (-19.6 to -11.1)	37.3	19.6	-12.9 (-15.1 to -10.6)	16.9	24.3#	24.9 (6.2 to 46.9)§	30.7	38.1	4.9 (2.9 to 6.9)
							24.3#	35.7	3.8 (-21.1 to 36.6)			
65-74 years	6.6	3.1	-11.0 (-17.9 to -3.6)§	41.7	20.1	-14.0 (-16.6 to -11.4)	17.4	27.0#	22.8 (-0.9 to 52.3)§	34.3	44.4	4.7 (2.3 to 7.2)
							27.0#	32.5	1.4 (-32.3 to 51.8)			
75-84 years	1.9	2.2	6.9 (-3.3 to 18.1)§	31.1	13.8	-15.5 (-19.7 to -11.0)§	15.2	20.5#	11.3 (0.3 to 23.6)§	51.9	65.0	5.1 (2.8 to 7.4)
							20.5#	19.0	-6.0 (-26.8 to 20.7)			
85+ years	1.8	5.2	10.9 (-17.4 to 48.8)§	6.7	1.9	-21.8 (-43.7 to 8.5)	11.1	9.7	-1.4 (-9.2 to 7.2)§	80.4	83.2	1.0 (-0.2 to 2.3)§
Race/ethnicity												
API	11.0	4.6	-18.6 (-26.3 to -9.9)§	37.0	19.5#	-18.8 (-27.4 to -9.2)§	22.3	37.1	12.4 (0.3 to 26.0)	29.7	37.8	5.1 (-0.6 to 11.1)
				19.5#	20.6	0.2 (-31.2 to 45.9)						
Hispanic	10.6	8.2	-5.6 (-12.5 to 1.9)	38.9	19.3	-14.4 (-17.8 to -10.8)	12.1	26.7#	29.5 (3.3 to 62.5)	38.4	44.7	3.8 (1.0 to 6.7)
							26.7#	27.8	1.1 (-33.7 to 54.4)			
NH Black	6.6	3.0	-13.0 (-21.4 to -3.6)	44.1	28.0	-9.5 (-10.9 to -8.0)§	14.1	26.9#	24.3 (19.9 to 28.8)	35.2	39.6	2.3 (0.4 to 4.4)§
							26.9#	29.5	5.0 (-1.6 to 11.9)			
NH White¶	10.7	5.1	-12.3 (-16.3 to -8.1)	36.2	17.3	-14.4 (-16.9 to -11.9)	16.9	31.1#	22.7 (15.1 to 30.7)	36.3	44.8	4.3 (2.8 to 5.9)
							31.1#	32.8	2.7 (-8.4 to 15.2)			
Other	1.9	1.6	-2.8 (-8.6 to 3.3)	17.6	4.7	-18.4 (-33.9 to 0.7)	17.4	18.2	2.1 (-8.0 to 13.4)	63.2	75.5	4.2 (-0.3 to 8.9)
Rural-urban continuum in 2013												
Metropolitan counties¶	9.9	4.8	-12.1 (-16.2 to -7.8)	36.6	17.5	-14.1 (-16.7 to -11.5)	17.2	31.3#	22.2 (1.9 to 46.5)	36.3	45.2	4.5 (2.3 to 6.7)
							31.3#	32.4	2.1 (-27.1 to 43.0)			
Non-metropolitan counties	8.4	5.1	-10.2 (-13.2 to -7.0)	38.9	24.7	-10.6 (-14.9 to -6.1)	9.9	21.3#	29.3 (18.3 to 41.3)	42.9	48.4	2.9 (1.5 to 4.3)
							21.3#	21.8	0.1 (-14.1 to 16.6)			
Census region												
Midwest¶	8.9	4.0	-9.9 (-21.9 to 4.0)	34.9	11.9	-18.8 (-22.6 to -14.9)	15.8	30.6	14.6 (7.2 to 22.6)	40.3	53.5	5.6 (2.1 to 9.3)
Northeast	10.3	5.2	-11.2 (-14.1 to -8.2)	46.6	26.0	-11.2 (-14.0 to -8.3)	11.7	36.7	26.2 (19.4 to 33.4)§	31.4	32.1	0.2 (-2.2 to 2.7)§
South	10.4	9.3*	-4.9 (-26.4 to 22.9)	41.1	22.9	-11.8 (-14.3 to -9.2)	9.3	22.9#	35.9 (9.6 to 68.6)	39.2	48.7	4.0 (1.2 to 6.9)§
	9.3*	5.0	-18.8 (-33.3 to -1.2)				22.9#	23.4	2.4 (-26.4 to 42.5)			
West	9.4	4.7	-12.3 (-17.6 to -6.6)	31.5	13.6	-16.3 (-19.4 to -13.1)	21.5	35.9#	17.8 (17.2 to 18.5)	37.6	48.0	5.4 (2.9 to 7.9)
							35.9#	33.7	-3.4 (-4.5 to -2.2)			

% of persons <high school education in the county (ACS 2011-2015, quartile)												
<10 (Q1)¶	9.9	4.9	-11.4 (-16.1 to -6.4)	35.4	18.3	-12.5 (-14.8 to -10.1)	16.5	30.6#	22.3 (17.4 to 27.3)	38.2	43.6	2.7 (0.5 to 5.0)
							30.6#	33.2	4.0 (-3.3 to 11.9)			
10-13.05 (Q2)	8.9	4.9	-10.5 (-14.7 to -6.0)	38.3	17.5	-14.5 (-17.0 to -12.0)	20.9	34.0#	18.9 (-33.7 to 113.3)	31.9	43.5	5.8 (2.8 to 8.8)
							34.0#	34.1	0.9 (-68.2 to 220.4)			
13.06-18.0 (Q3)	9.2	3.9	-13.6 (-17.7 to -9.4)	38.0	19.4	-14.0 (-17.4 to -10.5)	15.0	28.9#	25.9 (-27.1 to 117.2)	37.8	47.0	4.3 (2.3 to 6.4)
							28.9#	29.8	1.4 (-62.3 to 172.2)			
>18.1 (Q4)	11.2	5.7	-12.5 (-17.8 to -6.8)	35.5	18.0	-13.9 (-16.9 to -10.8)	12.7	27.9	15.3 (5.5 to 25.9)	40.6	48.4	4.3 (1.1 to 7.5)
% of persons <200% poverty level in the county (ACS 2011-2015, quartile)												
<26 (Q1)¶	9.1	5.0	-11.1 (-14.7 to -7.4)	37.1	19.6	-12.5 (-15.0 to -9.9)	19.8	34.8#	21.1 (-11.0 to 64.6)	34.0	41.0	3.4 (0.8 to 6.0)
							34.8#	34.5	0.4 (-44.3 to 80.8)			
26-33 (Q2)	9.7	4.6	-12.0 (-17.6 to -6.0)	34.8	13.9	-16.5 (-20.3 to -12.5)	20.6	36.4	13.4 (5.0 to 22.5)	34.9	45.1	4.9 (0.9 to 9.1)
33-40.45 (Q3)	9.9	4.6	-12.9 (-17.1 to -8.4)	39.9	21.0	-12.6 (-15.0 to -10.2)	11.3	25.3#	29.5 (-9.0 to 84.2)§			
							25.3#	28.0	4.7 (-42.4 to 90.5)	38.8	46.5	3.9 (1.4 to 6.4)
>40.45 (Q4)	10.3	5.2	-11.9 (-17.4 to -6.1)	36.1	18.7	-13.7 (-16.8 to -10.5)	13.3	24.8#	22.5 (-9.9 to 66.4)			
							24.8#	26.7	2.4 (-40.8 to 77.2)	40.4	49.5	4.5 (2.5 to 6.6)
Insurance status												
Insured¶	13.2	6.5	-12.9 (-16.9 to -8.6)	40.2	20.2	-14.1 (-17.0 to -11.1)	18.3	36.5#	25.6 (8.2 to 45.8)	28.4	34.5	4.3 (2.7 to 5.8)
							36.5#	38.8	2.9 (-19.9 to 32.1)			
Any Medicaid	9.9	4.0	-9.2 (-20.7 to 4.0)	42.8	21.0	-14.0 (-15.8 to -12.2)	9.4	28.4	22.3 (16.2 to 28.7)	38.0	46.5	4.1 (1.7 to 6.6)
Insurance status unknown	3.5	1.1	-16.7 (-31.9 to 1.9)	21.7	14.0	-8.6 (-15.6 to -1.0)§	7.9	15.5	15.3 (5.3 to 26.2)	67.0	62.#	-2.3 (-15.9 to 13.6)§
										62.#	69.4	5.4 (-22.9 to 44.1)
Insured/No specifics	9.6	8.8*	-3.8 (-32.1 to 36.4)	38.9	24.0#	-7.8 (-30.6 to 22.5)	19.6	31.0	11.4 (6.8 to 16.2)	32.0	37.1#	5.0 (-12.1 to 25.4)
	8.8*	4.8	-18.4 (-38.3 to 7.9)	24.0#	18.7	-18.0 (-36.3 to 5.4)				37.1#	45.4	11.2 (-20.8 to 56.1)
Uninsured	10.7	6.7	-14.3 (-27.5 to 1.2)	28.7	13.3	-14.5 (-22.8 to -5.3)	17.4	42.2	16.7 (10.1 to 23.7)	43.3	37.8	0.7 (-8.1 to 10.4)
% of foreign-born persons in the county (ACS 2011-2015, quartile)												
<7 (Q1)¶	10.3	4.7	-12.4 (-18.1 to -6.3)	38.1	22.0	-11.9 (-15.1 to -8.7)	11.6	23.3#	26.7 (4.2 to 54.0)	40.0	47.0	3.5 (1.8 to 5.1)
							23.3#	26.2	6.8 (-22.5 to 47.3)			
7-15 (Q2)	8.9	4.5	-11.9 (-17.8 to -5.6)	36.6	16.1	-14.2 (-17.3 to -10.9)	16.6	28.4#	20.7 (-25.9 to 96.5)§	38.0	40.8#	2.0 (1.8 to 2.2)
							28.4#	30.0	2.8 (-58.6 to 154.9)	40.8#	49.5	10.9 (10.3 to 11.4)
>15-24 (Q3)	8.9	5.1	-9.4 (-14.9 to -3.5)	34.2	15.4	-15.4 (-19.5 to -11.0)§	18.8	34.2	12.4 (4.7 to 20.6)	38.0	45.2	4.0 (0.1 to 8.1)
>24 (Q4)	11.2	5.1	-13.8 (-17.2 to -10.3)	38.6	20.3	-13.4 (-16.0 to -10.6)§	18.3	34.4#	24.7 (-38.5 to 152.6)§	32.0	39.8	4.1 (2.0 to 6.2)
							34.4#	34.9	0.5 (-73.6 to 282.3)			
Gleason score												
2-6¶	3.45	0.98	-22.7 (-27.6 to -17.5)	13.09	3.69	-24.3 (-29.3 to -18.9)	5.75	6.36	0.9 (-5.7 to 7.9)	12.17	8.64	-8.1 (-11.7 to -4.4)
7	0.46	0.18	-15.7 (-23.3 to -7.5)§							0.03	0.01	-14.5 (-42.4 to 26.8)
8-10	0.04	0.01	-21.5 (-33.8 to -6.9)									

Note: Data from the 18 registries of the Surveillance, Epidemiology, and End Results (SEER)-18 with data on active surveillance/watchful waiting. NOS, not otherwise specified; AS/WW, active surveillance/watchful waiting; NH, non-Hispanic. API, Asian Pacific Islanders; ACS, the Census American Community Survey 5-year file; APC, annual percentage change; CI, confidence interval; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile. ¶, the reference subgroup.§, not parallel to the reference subgroup ($P<0.05$ for testing parallelism). * indicates a joinpoint where the two trends intercept in 2012. # indicates a joinpoint where the two trends intercept in 2013.

Table 3. Trends in proportion (%) of age-standardized treatment rate for the intermediate-risk prostate cancers diagnosed during 2010-2015 in the U.S

	Radical Prostatectomy			Radiotherapy			AS/WW			NOS Treatment		
	2010	2015	APC (95% CI)	2010	2015	APC (95% CI)	2010	2015	APC (95% CI)	2010	2015	APC (95% CI)
All	11.9	11	-1.8 (-2.6 to -1.0)	54.8	49.8	-2.2 (-3.6 to -0.8)	5.8	10.9#	23.4 (6.9 to 42.5)	27.5	29.1	1.4 (-0.5 to 3.4)
							10.9#	10.1	-4.0 (-26.9 to 26.0)			
Age												
<45 years	40.9	48.7	3.3 (-5.2 to 12.6)	27.0	10.9	-7.3 (-21.1 to 8.8)	2.5	3.4	NA	29.6	12.0#	-25.0 (-83.8 to 246.9)
										12.0#	37.0	72.6 (-95.8 to 6932.6)
45-54 years¶	39.8	32.4*	-10.5 (-34.5 to 22.3)	37.7	36.4	-1.1 (-3.6 to 1.4)	3.3	8.4	14.2 (-1.1 to 32.0)	19.2	23.6	5.0 (0.04 to 10.1)
	32.4*	31.6	-0.4 (-17.9 to 20.8)									
55-64 years	24.1	19.4	-5.1 (-7.3 to -2.8)	51.8	47.4	-2.1 (-3.6 to -0.5)	4.3	10.5#	32.7 (-48.1 to 239.1)	19.8	23.9	4.7 (2.6 to 7.0)
							10.5#	9.2	-6.0 (-79.8 to 338.1)			
65-74 years	10.0	9.0	-3.0 (-5.1 to -0.8)	61.7	54.8	-2.5 (-3.7 to -1.2)	5.3	10.3#	26.1 (-36.1 to 149.0)	23.0	26.0	2.6 (0.4 to 4.8)
							10.3#	10.2	-1.2 (-71.3 to 240.2)			
75-84 years	1.7	2.0	5.7 (-0.1 to 11.9)§	54.3	50.1	-2.2 (-4.4 to 0.0)	7.9	11.0	7.8 (-1.7 to 18.3)	36.2	36.9	0.9 (-1.1 to 3.0)
85+ years	0.6	0.5	NA	17.0	18.1	-0.2 (-8.8 to 9.0)	8.2	12.1	7.1 (-5.4 to 21.2)	74.2	69.4	-1.2 (-3.8 to 1.5)
Race/ethnicity												
API	13.6	9.4	-1.3 (-11.5 to 10.0)	59.0	53.9	-3.1 (-6.4 to 0.3)	7.1	12.8	14.9 (4.4 to 26.4)	20.3	24.0	2.9 (0.1 to 5.8)
Hispanic	11.8	11.3	-2.1 (-7.0 to 3.0)	50.9	44.1	-2.7 (-5.4 to -0.1)	5.4	9.1*	31.6 (-75.8 to 614.1)§	32.0	35.5	2.9 (-3.4 to 9.6)
							9.1*	9.1	-2.0 (-56.8 to 122.4)			
NH Black	7.5	8.3	0.5 (-6.3 to 7.8)	57.5	52.5	-1.5 (-2.4 to -0.6)	4.5	9.1	16.3 (2.8 to 31.5)	30.5	30.1	-1.0 (-4.9 to 3.0)
NH White¶	13.3	12.2	-1.8 (-2.9 to -0.7)	54.9	50.8	-2.0 (-3.7 to -0.2)	6.0	11.5#	24.2 (-17.8 to 87.7)	25.9	26.6	1.0 (-0.5 to 2.5)
							11.5#	10.4	-4.3 (-56.2 to 108.8)			
Other/Unknown	3.5	3.0#	-3.0 (-20.8 to 18.7)§	35.1	24.6	-7.5 (-16.1 to 2.1)	9.5	6.8	-6.6 (-14.6 to 2.2)§	51.9	62.7	5.2 (0.0 to 10.6)
	3.0#	6.0	36.7 (-5.5 to 97.7)									
Census region												
Midwest¶	10.4	9.6	-2.7 (-9.9 to 5.0)	55.0	49.7	-2.5 (-4.4 to -0.4)	5.2	10.7#	26.7 (26.0 to 27.5)	29.4	30.0	1.3 (-4.0 to 7.0)
							10.7#	10.7	-1.8 (-2.8 to -0.7)			
Northeast	11.3	10.6	0.2 (-5.3 to 6.0)	61.5	58.5	-0.9 (-3.4 to 1.6)	3.2	8.0	21.7 (5.3 to 40.7)	24.0	22.9	-2.4 (-8.0 to 3.6)§
South	10.3	12.0	2.6 (1.0 to 4.2)	55.2	49.0	-2.2 (-3.1 to -1.4)	3.5	7.4	15.7 (6.2 to 26.0)	31.0	31.6	0.1 (-2.1 to 2.4)
West	13.3	11.0	-4.5 (-7.0 to -1.9)	52.1	46.6	-2.9 (-4.7 to -1.0)	8.1	14.0#	20.0 (-11.7 to 62.9)	26.5	30.1	3.6 (1.3 to 5.9)
							14.0#	12.3	-6.5 (-50.3 to 76.0)			
Rural-urban continuum 2013												
Metropolitan Counties¶	12.0	11.3	-1.4 (-2.5 to -0.3)	55.3	49.4	-2.6 (-4.0 to -1.1)	6.0	11.0#	22.3 (13.5 to 31.7)	26.7	29.2	2.1 (-0.1 to 4.3)
							11.0#	10.2	-3.9 (-16.6 to 10.7)			
Nonmetropolitan Counties	11.1	9.0	-5.5 (-12.3 to 1.9)	51.1	48.1#	-1.6 (-15.5 to 14.6)§	4.7	9.3	16.2 (-0.6 to 35.7)	33.1	28.0	-3.0 (-4.8 to -1.3)
				48.1#	53.8	5.3 (-24.4 to 46.5)						
% of Persons <high school education in the county (ACS 2011-2015, quartile)												
<10 (Q1)¶	11.0	12.3#	3.8 (-3.6 to 11.8)	56.7	53.3	-1.3 (-3.1 to 0.6)	5.5	10.2	14.0 (-0.4 to 30.4)	26.8	24.5	-2.5 (-6.4 to 1.7)

	12.3#	12.0	-1.6 (-16.0 to 15.3)									
10-13.05 (Q2)	11.8	10.5	-1.9 (-4.7 to 1.1)	58.5	51.6	-2.7 (-3.6 to -1.9)	6.9	10.5	8.9 (-0.2 to 18.9)	22.8	23.1*	0.1 (-12.2 to 14.0)§
										23.1*	27.4	6.3 (-0.9 to 14.1)
13.06-18.0 (Q3)	11.2	9.9	-2.4 (-4.7 to -0.1)§	52.7	51.3	-1.3 (-3.8 to 1.3)	5.9	10.7#	23.7 (-46.0 to 183.8)	30.2	29.5	0.2 (-2.0 to 2.5)§
							10.7#	9.3	-7.9 (-82.6 to 386.5)			
>18.1 (Q4)	13.6	11.7	-5.1 (-9.8 to -0.1)§	51.0	42.1	-3.9 (-5.4 to -2.5)	5.0	9.3#	23.5 (4.5 to 45.9)	30.5	36.0	4.4 (1.2 to 7.7)§
							9.3#	10.2	4.1 (-22.8 to 40.5)			
% of Persons <200% Poverty level in the county (ACS 2011-2015, quartile)												
<26 (Q1)¶	10.8	10.2	0.5 (-5.9 to 7.4)	59.6	56.0	-1.6 (-3.7 to 0.5)	8.5*	9.6	21.9 (1.8 to 45.9)	23.0	24.3	0.6 (-2.3 to 3.7)
							27.1	12.1#	-9.8 (-37.4 to 29.9)			
26-33 (Q2)	13.6	11.2#	-5.7 (-11.8 to 0.8)	51.9	49.8	-1.5 (-4.0 to 1.1)	7.4	10.7	21.7 (-12.3 to 68.9)	12.1#	27.2	0.5 (-3.5 to 4.7)
	11.2#	12.3	5.3 (-9.8 to 23.0)				4.5	13.3#	-9.5 (-53.3 to 75.3)			
33-40.45 (Q3)	10.4	10.9	0.1 (-2.9 to 3.1)	56.4	48.4	-2.5 (-3.6 to -1.4)	13.3#	9.8	26.2 (-31.5 to 132.6)	28.7	31.0	0.8 (-1.6 to 3.3)
							4.6	9.4#	2.8 (-62.8 to 183.8)			
>40.45 (Q4)	12.6	10.8	-4.7 (-8.5 to -0.8)§	52.0	45.4	-3.3 (-5.5 to -1.1)§	9.4#	10.1	35.9 (14.3 to 61.5)	30.8	33.7	3.2 (-0.7 to 7.2)
							6.6	8.5*	6.4 (-1.1 to 14.5)			
Insurance status												
Insured¶	16.7	15.3	-2.2 (-4.1 to -0.3)	57.4	52.1	-2.2 (-3.6 to -0.8)	5.8	11.9#	27.1 (8.2 to 49.3)	20.2	21.2	1.5 (-0.7 to 3.8)
							11.9#	11.4	-2.6 (-26.3 to 28.6)			
Any Medicaid	10.2	11.5	0.7 (-5.5 to 7.2)§	53.7	50.3	-1.7 (-3.8 to 0.5)§	3.6	7.0	16.3 (-0.3 to 35.6)	32.6	31.2	-0.4 (-5.4 to 5.0)§
Insurance status unknown	3.1	2.9	2.9 (-6.8 to 13.6)	33.2	35.6	0.3 (-5.3 to 6.2)	3.6	6.8	13.6 (1.9 to 26.7)	60.2	51.7*	-8.1 (-48.4 to 63.6)
										51.7*	54.7	2.2 (-25.1 to 39.5)
Insured/No specifics	12.0	9.4	-4.3 (-8.3 to -0.1)	58.0	55.5	-1.3 (-2.6 to 0.1)	6.4	8.4	6.1 (-1.4 to 14.1)	23.7	26.7	3.0 (0.9 to 5.1)
Uninsured	13.5	11.0	-6.2 (-14.9 to 3.2)	53.7	38.3*	-15.5 (-37.8 to 14.7)	4.2	12.3#	44.1 (-14.4 to 142.7)	28.7	33.0	3.7 (-7.4 to 16.1)
				38.3*	47.3	6.1 (-14.7 to 31.9)	12.3#	8.8	-11.9 (-69.5 to 155.0)			
% of Foreign born persons in the county (ACS 2011-2015, quartile)												
<7 (Q1)¶	11.2	10.3	-2.4 (-6.4 to 1.7)	52.0	49.0#	-2.1 (-10.6 to 7.3)	4.7	8.2#	22.2 (-29.6 to 112.3)	32.1	30.5	-0.7 (-2.0 to 0.7)
				49.0#	51.4	2.3 (-16.7 to 25.8)	8.2#	7.8	-3.0 (-65.6 to 173.9)			
7-14 (Q2)	11.3	10.3	-2.1 (-3.5 to -0.6)	56.2	50.2	-2.1 (-4.2 to -0.1)	4.9	9.9#	25.2 (6.1 to 47.7)	27.7	28.8	0.9 (-3.6 to 5.7)
							9.9#	10.7	2.8 (-23.2 to 37.4)			
15-24 (Q3)	11.2	12.0	2.7 (-0.9 to 6.4)	54.7	47.6	-3.2 (-4.4 to -1.9)§	6.9	11.1	9.6 (-1.6 to 22.1)	27.3	29.3	1.6 (-1.6 to 5.0)
>24 (Q4)	14.3	11.7	-5.5 (-10.2 to -0.5)	56.4	50.4	-2.8 (-5.3 to -0.3)	6.9	13.0#	25.0 (-51.4 to 221.8)	22.4	27.3	4.8 (1.8 to 7.9)§
							13.0#	10.6	-8.1 (-86.2 to 511.5)			
Gleason score												
2-6 ¶	1.62	0.66	-18.2 (-23.0 to -13.2)	2.02	0.84	-17.9 (-22.5 to -13.0)	0.67	0.95#	11.5 (-10.2 to 38.4)	1.34	0.82	-10.1 (-12.2 to -8.0)
							0.95#	0.80	-7.9 (-36.7 to 34.0)			
7	3.36	2.63	-8.8 (-13.3 to -4.0)§	15.60	10.42	-9.5 (-13.9 to -4.8)	1.18	1.45	2.5 (-6.3 to 12.0)	7.43	5.67	-6.3 (-11.1 to -1.3)
8-10	0.25	0.22	-3.5 (-10.6 to 4.2)§									

Note: Data from the 18 registries of the Surveillance, Epidemiology, and End Results (SEER)-18 with data on active surveillance/watchful waiting. NA, Not available due to small number of cases; NOS, not otherwise specified; AS/WW, active surveillance/watchful waiting; NH, non-Hispanic. API, Asian Pacific Islanders; ACS, the Census American Community Survey 5-year file; APC, annual percentage change; CI, confidence interval; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile. ¶, the reference subgroup. §, not parallel to the reference subgroup (P<0.05 for testing parallelism). * indicates a joinpoint where the two trends intercept in 2012. # indicates a joinpoint where the two trends intercept in 2013.

risk group, there were different trends in ASUP between those in a county of more foreign-born residents and compared with the men in a county of fewer foreign-born residents (first quartile) for radiotherapy (third quartile group) and NOS (fourth quartile group). Surprisingly, age (except 75-84-age group) and other factors were not associated with trends in ASUP of various treatments (**Table 3**). Compared with men with tumor of Gleason scores 2-6, there was a trend-difference of the ASUP in those with tumor of Gleason score 7 or 8-10 for radical prostatectomy (**Table 3**).

Among U.S. men with high-risk prostate cancer, age, Gleason score and percentage of foreign-born residency in the patient's residency county were both associated with different trends in ASUP for radical prostatectomy and NOS treatment. Compared with non-Hispanic white men, Asian Pacific Islander and Non-Hispanic black men both had different trends in ASUP for radical prostatectomy (**Table 4**).

Similar trends were observed in ASUR of the four treatment modalities (Supplementary Tables 1, 2, 3). Detailed trend analyses by potential confounders were not possible for the unknown-risk group due to their small numbers of cases, and thus were not conducted.

Consistent with the overall trends, a trend joinpoint in 2012 or 2013 was noted in ASUP of AS/WW in some subgroups of age, race/ethnicity, census region, insurance status, rural-urban continuum and socioeconomic factors of patient's residency county, but only in low- and intermediate-risk groups (**Tables 2** and **3**). As a consequence, there should be a joinpoint in other treatment modalities. However, among men of low-risk group, trend joinpoints were identified only in ASUP of NOS treatment in some subgroups of age, insurance status and percentage of foreign-born person in the patient's residency county's, and in those of radical prostatectomy and radiotherapy among subgroups of insurance status (**Table 2**). Among men of intermediate-risk group, trend joinpoints were identified only in ASUP of NOS treatment in some subgroups of insurance status and percentage of high-school graduates in the patient's residency county's, and those of radical prostatectomy in some subgroups of age, race/ethnicity, and percentage of high-school graduates in the patient's residency county's (**Table 3**).

The differences in ASUR trends for AS/WW, radical prostatectomy, radiotherapy and NOS treatments were similar to those in ASUP trends (Supplementary Tables 1, 2, 3).

Discussion

We here show different trends in ASUP of treatments for prostate cancer by risk group in the United States from 2010 to 2015, including NOS treatments. ASUPs of radical prostatectomy and radiotherapy had a downward trend in all risk groups, except the unknown-risk group. On the other hand, there was an upward trend in the ASUP of AS/WW during 2010-2013 among men with low- or intermediate-risk group, which plateaued during 2013-2015. Surprisingly and alarmingly, there was an upward trend of NOS treatments (*i.e.*, treatments other than radical prostatectomy, radiotherapy and AS/WW) in low-, intermediate and high-risk groups, but there were no significant trends in unknown-risk group. We also analyzed trends in the ASUR and ASUP of various treatments by subgroups of age, race/ethnicity, census region, rural-urban continuum, insurance status, tumor's Gleason score, and socioeconomic factors of the patient's residency county.

Although several previous studies have investigated utilization of treatments for prostate cancer, few included NOS treatments [8-13]. The plausible reasons are the lack of reliable sources to further classify these treatments, and its likely small proportion of all treatments. However, we here show that NOS treatments were present in 25.2% of high-risk group, 27.5 of intermediate-risk group, 39.8 of low-risk group and 80.0% of unknown-risk group. Therefore, omission of NOS treatment may lead to a bias (overestimation) on the proportional utilization of treatment modalities for prostate cancer. Indeed, our trend analysis including NOS treatment group showed that trends in ASUP of AS/WW plateaued after 2013 in men with low- or intermediate-risk prostate cancer, while previous studies without such a category showed a continued upward trend during 2013-2015 [8, 9]. Moreover, there was an upward trend in ASUP of NOS treatments in low- and high-risk groups, which even-

Table 4. Trends in the proportion (%) of age-standardized treatments for the high-risk prostate cancers diagnosed during 2010-2015 in the U.S

	Radical Prostatectomy			Radiotherapy			AS/WW			NOS Treatment		
	2010	2015	APC (95% CI)	2010	2015	APC (95% CI)	2010	2015	APC (95% CI)	2010	2015	APC (95% CI)
All	55.3	48.1	-3.2 (-4.7 to -1.7)	21.5	20.5*	-1.9 (-21.6 to 22.7)	0.8	1.1	6.7 (-0.3 to 14.2)	22.4	27.3	4.9 (1.7 to 8.2)
				20.5*	23.5	4.4 (-7.5 to 17.9)						
Age												
<45 years	85.3	83.1	-0.1 (-2.3 to 2.2)§	7.3	5.7	-5.4 (-22.9 to 16.0)	NA	NA		7.3	11.3	8.9 (-0.6 to 19.3)
45-54 years¶	86.1	79.5	-1.8 (-2.4 to -1.1)	7.0	8.7	5.7 (2.0 to 9.6)	0.1	0.5	23.4 (-20.3 to 91.3)	6.9	11.3	11.5 (5.7 to 17.5)
55-64 years	78.3	71.4	-2.3 (-3.5 to -1.1)§	11.8	14.1	4.5 (2.0 to 7.0)	0.4	0.6	9.5 (1.4 to 18.2)	9.5	13.9	10.1 (3.6 to 17.1)
65-74 years	57.2	52.5	-2.1 (-3.2 to -1.0)	25.6	25.7	0.4 (-1.8 to 2.6)	0.6	1.2	14.8 (5.0 to 25.6)	16.7	20.6	5.0 (1.2 to 8.9)
75-84 years	11.2	11.7	-0.9 (-5.6 to 4.0)	40.5	39.1	-0.4 (-2.6 to 1.8)	1.7	1.9	4.1 (-10.5 to 21.0)	46.6	47.6	0.6 (-1.5 to 2.7)§
85+ years	0.9	0.6	-9.3 (-16.8 to -1.0)§	14.5	17.1	2.3 (-3.7 to 8.7)	2.9	1.6	-6.5 (-15.5 to 3.5)	81.7	83.6#	0.8 (0.5 to 1.2)§
Race/ethnicity												
API	49.6	44.2	-2.7 (-4.5 to -0.8)§	25.4	27.6	1.5 (-4.3 to 7.7)	1.5	1.0	-6.9 (-20.0 to 8.4)	23.5	27.1	4.1 (-0.2 to 8.5)
Hispanic	47.6	46.6	-1.3 (-3.7 to 1.1)	24.2	20.7	-1.8 (-5.8 to 2.4)§	0.8	1.1	10.2 (-4.9 to 27.7)	27.5	31.6	3.1 (-0.3 to 6.6)
NH Black	44.9	41.9	-1.9 (-3.1 to -0.7)§	24.8	23.4*	-2.2 (-19.1 to 18.2)	0.9	1.2	9.2 (-7.9 to 29.5)	29.5	30.6	1.2 (-0.7 to 3.2)
				23.4*	26.3	3.8 (-6.2 to 14.9)						
NH White¶	59.2	51.0	-3.4 (-4.8 to -2.1)	20.1	19.4*	-1.2 (-10.2 to 8.7)	0.7	1.0#	13.6 (-0.7 to 30.0)	20.0	25.4	5.8 (2.4 to 9.3)
				19.4*	22.5	5.2 (-0.1 to 10.8)	1.0#	1.0	-1.2 (-24.1 to 28.5)			
Other/Unknown	33.6	32.7	-1.8 (-7.5 to 4.2)	20.4	28.6*	19.6 (-79.7 to 603.7)§	1.2	1.4	-3.1 (-22.9 to 21.8)	44.8	49.5	3.5 (-1.2 to 8.5)
				28.6*	16.4	-15.7 (-66.0 to 109.1)						
Census region												
Midwest¶	56.9	53.6	-1.7 (-4.2 to 0.7)	21.1	21.7	0.8 (-1.5 to 3.2)	0.6	0.9	11.4 (-9.5 to 37.0)	21.4	23.8	3.3 (-1.3 to 8.1)
Northeast	55.8	46.9	-3.4 (-5.2 to -1.6)	23.8	26.7	2.8 (-0.1 to 5.7)	0.5	0.9	13.5 (-5.1 to 35.9)	20.0	25.6	4.8 (0.8 to 8.9)
South	50.8	46.0	-2.7 (-4.3 to -1.0)	23.1	20.5*	-4.8 (-5.7 to -3.8)	0.6	0.8	9.3 (-7.7 to 29.6)	25.5	28.7	3.3 (-0.1 to 6.8)
				20.5*	24.5	5.6 (5.0 to 6.2)						
West	56.8	48.9	-3.7 (-5.4 to -1.9)	20.1	21.7	2.0 (-0.1 to 4.1)	1.0	1.3	4.8 (-4.0 to 14.5)	22.1	28.1	6.0 (2.1 to 10.0)
Rural-urban continuum 2013												
Metropolitan Counties¶	56.2	48.7	-3.4 (-4.8 to -1.9)	21.4	20.5*	-2.0 (-31.1 to 39.3)	0.8	1.1	7.0 (-0.5 to 15.1)	21.6	27.0	5.3 (2.2 to 8.6)
				20.5*	23.1	4.6 (-13.6 to 26.7)						
Nonmetropolitan Counties	48.6	46.0	-2.0 (-4.0 to 0.1)§	22.3	23.7	1.0 (-1.3 to 3.4)	0.8	0.7	4.1 (-10.3 to 20.8)	28.3	29.5	2.3 (-2.0 to 6.9)
Other/Unknown	27.0	9.2	-21.0 (-32.8 to -7.3)	21.6	38.4	9.8 (-17.5 to 46.2)			NA	51.4	52.4	11.1 (-4.1 to 28.8)
% of Persons <high school education in the county (ACS 2011-2015, quartile)												
<10 (Q1)¶	56.2	48.0	-3.4 (-5.3 to -1.5)	21.6	25.0	3.2 (1.3 to 5.1)	0.7	1.0	12.5 (-0.9 to 27.7)	21.6	26.0	4.5 (1.9 to 7.3)
10-13.05 (Q2)	54.4	46.1	-3.8 (-5.3 to -2.3)	23.9	23.9	1.0 (-1.7 to 3.7)	1.2	1.4	3.5 (-2.7 to 10.2)	20.5	28.5	6.9 (3.4 to 10.6)
13.06-18.0 (Q3)	55.0	48.0	-3.4 (-5.0 to -1.7)	21.0	24.5	3.4 (1.0 to 5.9)	0.7	0.9	7.4 (-3.2 to 19.1)	23.3	26.5	3.7 (-0.8 to 8.3)
>18.1 (Q4)	55.7	51.4	-2.4 (-4.2 to -0.5)	19.7	17.4*	-5.3 (-12.1 to 2.1)	0.6	1.1*	28.4 (17.0 to 40.8)	24.0	28.3	4.7 (0.7 to 8.9)
				17.4*	19.5	3.5 (-0.8 to 8.0)	1.1*	0.9	-6.6 (-10.8 to -2.1)			
% of Persons <200% Poverty level in the county (ACS 2011-2015, quartile)												
<26 (Q1)¶	57.0	46.6	-4.1 (-5.4 to -2.8)	22.5	25.5	2.9 (0.5 to 5.4)	0.9	1.1	5.2 (-5.4 to 16.9)	19.6	26.7	6.6 (4.3 to 8.9)
26-33 (Q2)	56.2	49.4	-3.3 (-5.4 to -1.3)	20.6	23.3	3.4 (0.7 to 6.2)	1.1	1.1	3.6 (-9.8 to 19.0)	22.2	26.2	4.2 (1.8 to 6.7)

33-40.45 (Q3)	53.3	46.6	-3.3 (-4.9 to -1.7)	22.8	21.3#	-2.6 (-37.4 to 51.6)	0.5	1.2	15.3 (1.9 to 30.4)	23.4	27.9	5.2 (0.0 to 10.7)
				21.3#	24.4	7.6 (-56.6 to 166.7)						
>40.45 (Q4)	54.6	50.2	-2.3 (-4.0 to -0.6)	20.8	20.5	0.2 (-3.2 to 3.8)	0.7	0.9	5.9 (-11.2 to 26.2)	24.0	28.4	4.2 (0.7 to 7.9)
Insurance status												
Insured¶	67.1	59.1	-2.9 (-4.1 to -1.7)	17.5	19.7	3.1 (0.1 to 6.1)	0.6	1.0#	17.2 (-52.2 to 187.3)	14.8	20.3	7.4 (3.8 to 11.1)
							1.0#	0.9	-2.7 (-82.0 to 425.2)			
Any Medicaid	38.4	41.0	0.4 (-3.7 to 4.7)	27.0	22.3	-3.2 (-4.8 to -1.6)	0.9	1.1	6.7 (-11.2 to 28.3)§	33.8	35.6	1.8 (-2.2 to 5.9)§
Insurance status unknown	29.9	22.2	-5.2 (-10.4 to 0.3)	22.9	28.3	3.4 (-0.5 to 7.4)	1.2	1.4	6.5 (-3.6 to 17.7)	46.0	51.6*	5.3 (-17.4 to 34.1)§
										51.6*	48.1	-2.1 (-13.3 to 10.4)
Insured, not specified	51.5	45.7	-3.3 (-5.6 to -1.0)	24.0	26.7	2.4 (-0.3 to 5.3)	0.8	0.9	6.9 (-6.4 to 22.2)	23.7	26.7	3.9 (-0.3 to 8.3)
Uninsured	50.2	40.4	-5.3 (-8.7 to -1.7)	18.7	21.9	4.2 (-0.5 to 9.2)	0.2	0.9	7.3 (-42.4 to 99.9)	30.9	36.7	4.1 (0.6 to 7.8)
% of Foreign born persons in the county (ACS 2011-2015, quartile)												
<7 (Q1)¶	51.5	49.1	-1.6 (-3.3 to 0.0)	22.5	22.9	0.7 (-3.0 to 4.6)	0.8	0.8	5.9 (-9.1 to 23.5)	25.2	27.2	2.4 (-0.4 to 5.2)
7-14 (Q2)	56.4	48.2	-3.5 (-5.0 to -1.9)	21.9	23.7	2.0 (0.6 to 3.4)	0.8	1.1	9.9 (2.0 to 18.4)§	21.0	27.1	5.7 (2.9 to 8.5)
15-24 (Q3)	55.2	47.0	-3.8 (-5.4 to -2.1)§	21.0	20.2*	-2.3 (-52.6 to 101.5)	0.8	1.4	8.4 (-3.9 to 22.4)§	23.0	28.3	5.5 (1.8 to 9.4)§
				20.2*	23.4	5.4 (-28.9 to 56.3)						
>24 (Q4)	58.1	49.8	-3.7 (-5.7 to -1.7)§	20.6	22.7	2.4 (0.1 to 4.8)§	0.9	1.4#	19.8 (-51.7 to 197.1)§	20.5	26.6	6.2 (1.7 to 11.0)§
							1.4#	0.9	-20.3 (-89.9 to 531.0)			
Gleason score												
2-6¶	16.37	6.02	-19.9 (-24.1 to -15.4)	0.88	0.38	-17.6 (-22.7 to -12.3)	0.16	0.22	13.1 (-14.2 to 49.2)	1.00	0.82*	-3.8 (-21.4 to 17.9)
							0.22	0.21	-2.3 (-37.5 to 52.6)	0.82*	0.68	-10.5 (-19.9 to -0.1)
7	23.43	17.67	-6.9 (-11.0 to -2.7)§	2.63	1.79#	-12.3 (-36.4 to 20.8)	0.10	0.12	3.1 (-2.7 to 9.2)§	2.20	1.73	-5.4 (-8.9 to -1.8)§
				1.79#	1.90	4.7 (-45.9 to 102.6)§						
8-10	5.99	6.41	0.5 (-2.9 to 4.1)§	9.25	8.02	-3.4 (-7.9 to 1.4)§	0.21	0.13	-9.2 (-11.5 to -6.7)§	7.98	7.26#	-3.1 (-8.9 to 3.0)
										7.26#	7.49	1.5 (-9.8 to 14.3)§

Note: Data from the 18 registries of the Surveillance, Epidemiology, and End Results (SEER)-18 with data on active surveillance/watchful waiting. NA, Not available due to small number of cases; NOS, not otherwise specified; AS/WW, active surveillance/watchful waiting; NH, non-Hispanic. API, Asian Pacific Islanders; ACS, the Census American Community Survey 5-year file; APC, annual percentage change; CI, confidence interval; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile. ¶, the reference subgroup. §, not parallel to the reference subgroup ($P<0.05$ for testing parallelism). * indicates a joinpoint where the two trends intercept in 2012. # indicates a joinpoint where the two trends intercept in 2013.

tually reached to 45% of men in low-risk group. Thus, nearly half of the men with low-risk prostate cancer had a treatment other than radical prostatectomy, radiotherapy and AS/WW by 2015. Furthermore, little is known about the NOS treatments although we suspect that many of them would be androgen deprivation therapy and others as suggested by others [28]. Additional studies are needed to further examine trends and related factors of NOS treatment utilization.

According to the 2010, 2019 and 2021 NCCN guidelines [5, 6, 29], radical prostatectomy and radiotherapy are reasonable options for the men with high- or intermediate-risk prostate cancer and those with a life expectancy of greater than 10 years if there are no serious comorbid conditions. In the present study, ASUR of radical prostatectomy steadily decreased in all risk groups during 2010-2015, and that of radiotherapy steadily decreased in low- and intermediate-risk groups. This finding is consistent with previous reports [8, 10, 11, 13, 30], but the absolute trends appear smaller than those in the previous reports due to the inclusion of NOS treatments. The downward trend may be associated with recommendations against PSA screening for prostate cancer in 2012 [31], and seems to be driven by decrease of new cases, new biopsies and reverse stage migration [3, 32, 33]. Our data show that it may be also driven by the reduction in radical prostatectomy for tumors of low Gleason scores but high T category or PSA levels. Decreasing utilization of radical prostatectomy and radiotherapy, which have reduced medial and socioeconomic burdens of surgery and radiotherapy, would have provided fewer training opportunities for urology and radiation-oncology residents, respectively. However, the ultimate outcomes of the decreasing utilization of radical prostatectomy and radiotherapy on high- and intermediate-risk groups are largely unknown. Interestingly, the age-standardized race-adjusted mortality of prostate cancer has not been changed in the United States during 2013-2017 [2] and 2013-2018 [1]. Thus, more studies are required to determine the impact of these downward trends in radical prostatectomy and radiotherapy on individual-level overall survivals and population-level mortality of prostate cancer.

We here provide the early evidence that ASUP and ASUR of AS/WW increased from 2010 to 2013, then plateaued thereafter in low- and intermediate-risk groups, but not changed in high- and unknown-risk groups. This is in contrast to previous studies, which all showed a straight upward trend [8, 9, 13, 34, 35]. According to previous and present NCCN guidelines [5, 6, 29], AS/WW is recommended for men with very-low-risk prostate cancer and life expectancy at least 20 years, men with low-risk prostate cancer and life expectancy at least ten years, or some men with favorable prostate cancer [6]. However, we here show an overutilization of AS/WW in the intermediate- and high-risk groups, which might result in a worse survival and higher mortality rate in these patients. Indeed, the rates of metastases and disease progression are higher in the men with AS/WW than those with surgery [36]. The reason for the appearance of the turning point in AS/WW trends at 2013 is unclear, but may be associated with embracing of AS/WW in U.S. urologists [28]. It is understandable that patient age was associated with the utility of treatments for prostate cancers, since the NCCN guidelines recommend treatments partially based on age. However, AS/WW is not recommended for treating high-risk prostate cancers. We thus concern about the upward trend in AS/WW utilization among some age-groups (55-64 years and 65-74 years) with high-risk prostate cancer although the proportion of ASUR remained under 2%. This trend indeed suggests an increase in the incompliance of treatments with NCCN guidelines for these patients, which may have led to unintended adverse outcomes. Therefore, more educations are warranted to reduce the inappropriate use of AS/WW in these patients.

In the present study, trends in ASUP of various treatments for prostate cancer were associated with patients' socioeconomic status. Moreover, there were significant differences in the ASUP among various races/ethnicities and census regions. These findings are in agreement with previous studies reporting that the race and socioeconomic status affected the management of prostate cancer in the United States [37-39]. These differences should be better understood and addressed in future studies, and ideally eliminated *via* healthcare policies or unified guidelines-implementation.

The present study has several strengths and unique features. First, the AS/WW status in the SEER database has been rigorously validated using a clear definition and widely used [9, 35, 40], and thus our findings on the utilization of AS/WW are reliable. Second, the Joinpoint regression model used in the present study has been used to identify the turning point with the trend slopes intercept and APC to assess the rate difference [2, 41], which is also recommended by the guidelines on trend analysis [14] and can rigorously describe the treatment utilization trends [42, 43]. Third, age-standardization, which is critical for long-term trend analysis, was applied in the present study to define ASUR and the ASUP [2, 14-16]. To the best of our knowledge, this is the first study to conduct trend analyses on ASUR for prostate cancer. Fourth, we for the first time explored the treatment trends in the unknown risk group, in which the staging information was essentially missing. Unsurprisingly, a large proportion of the cases had NOS treatments likely due to missing data, while the significant downward trend in ASUR of radiotherapy in this group supports the similar observations in other risk groups. Finally, the present study covers all risk groups and found concerning trends in treatment utilization in intermediate-, high- and unknown-risk groups, whereas most other studies only focus on the very-low-risk or low-risk groups [9, 24, 35, 40, 44].

There were a few limitations in the present study. First, the study period was only six years. We had to choose this period because rigorously validated data on AS/WW, Gleason score, and PSA became available only in 2010 and was updated to 2015 as of the date of the present study. Second, no detailed information was available on NOS treatments, although nearly 45% of low-risk cancers fell into this group by 2015. The NOS treatment would include a significant proportion of androgen deprivation therapy as shown before [28] and the guidelines [5, 6]. Third, there were variations in grading tumor (Gleason scores) by local pathologists. A centralized pathology review will be needed in further studies to address the issue. Fourth, prostate cancer patients with long-term follow-up (≥10 years) should have been included for survival analyses. However, we were not able to include them in this study for two reasons: 1) This study focuses on the utilization of treatments which is not closely related to the follow-up (time); 2) The longest follow-up time for the cohorts with available AS/WW data was only about 7 years, which does not permit analyses on the long-term follow-up (≥10 years). Fifth, data of treatment, demographics and clinical indices in the unknown-risk group are very difficult to collect and likely unreliable if present. We therefore only examined the overall trend and did not conduct detailed trend-analyses as we did with low-, intermediate- and high-risk groups. Caution should be used when interpreting these data. Finally, although we discussed trends of treatments for prostate cancer, the impacts of those trend changes on patient survival are unclear, but are beyond the scope of the present study. They should be subject to future research.

Conclusion

The ASUP and ASUR of treatments for prostate cancer had changed by during 2010-2015. Their trends appeared to differ by prostate cancer risk-group, age, race/ethnicity, and socioeconomic factors, which should be closely monitored. There was concerning incompliance with treatments guidelines among the patients with intermediate- or high-risk cancer during 2010-2015. More studies are warranted to monitor and understand the reported treatment trends.

Disclosure of conflict of interest

None.

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Supplementary Table 1. Trends in age-standardized utilization of treatments for the low-risk prostate cancers diagnosed during 2010-2015 in the US

	Radical Prostatectomy, per 100,000				Radiotherapy, per 100,000				WW/AS, per 100,000				NOS treatment, per 100,000			
	2010	2015	APC (95% CI)	*P*	2010	2015	APC (95% CI)	*P*	2010	2015	APC (95% CI)	*P*	2010	2015	APC (95% CI)	*P*
All	2.1	0.6	**-22.5 (-27.2 to -17.4)**		8.0	2.3	**-24.0 (-29.1 to -18.5)**		3.5	3.9	0.9 (-5.8 to 8.2)		8.0	5.7	**-8.1 (-11.4 to -4.6)**	
Age																
<45 years	0.1	0.0	**-21.9 (-31.3 to -11.1)**		0.1	0.0	**-17.9 (-29.6 to -4.3)**		0.1	0.1*	64.6 (-71.2 to 841.3)		0.1	0.1	**-7.5 (-14.0 to -0.5)**	
									0.1*	0.1	-25.1 (-65.9 to 64.7)					
45-54 years	5.9	1.6	**-23.2 (-27.6 to -18.5)**	r	6.9	2.9	**-19.2 (-27.5 to -9.8)**	r	3.1	5.8	10.8 (-0.4 to 23.2)	r	6.8	5.9	**-3.9 (-7.2 to -0.5)**	r
55-64 years	17.1	4.8	**-24.0 (-30.2 to -17.3)**		42.1	14.2	**-21.6 (-26.5 to -16.4)**	^	19.0	25.9	4.6 (-2.3 to 11.9)	^	34.6	27.6	**-5.5 (-8.3 to -2.5)**	
65-74 years	15.9	4.0	**-22.8 (-27.3 to -18.0)**		100.4	26.3	**-25.1 (-30.0 to -19.9)**	^	41.9	42.5	-0.5 (-7.2 to 6.8)	^	82.4	58.2	**-8.6 (-13.0 to -4.0)**	^
75-84 years	2.7	1.6	-9.0 (-18.6 to 1.7)	^	45.4	9.8	**-27.9 (-34.7 to -20.5)**	^	22.1	13.4	**-10.2 (-17.1 to -2.8)**		75.8	46.0	**-10.3 (-13.5 to -6.9)**	^
85+ years	0.8	1.4	-1.3 (-28.1 to 35.5)		3.1	0.5	**-31.2 (-50.9 to -3.5)**		5.2	2.6	**-13.3 (-20.1 to -5.8)**		37.5	22.5	**-11.0 (-14.4 to -7.5)**	^
Race																
NH White	3.9	1.1	**-22.9 (-26.9 to -18.7)**	r	13.3	3.6	**-24.7 (-29.9 to -19.2)**	r	6.2	6.9	1.0 (-5.1 to 7.5)	r	13.3	9.4	**-8.0 (-11.9 to -4.0)**	r
API	1.8	0.4	**-29.6 (-36.9 to -21.4)**		6.1	1.7	**-24.9 (-29.7 to -19.8)**		3.7	3.0	-3.0 (-13.5 to 8.9)		4.9	3.0	**-9.2 (-15.6 to -2.4)**	
Hispanic	3.0	1.2	**-17.6 (-23.4 to -11.3)**	^	11.1	2.9	**-25.2 (-29.6 to -20.5)**		3.5	4.2	1.5 (-9.4 to 13.7)		11.0	6.7	**-9.6 (-12.0 to -7.0)**	
NH Black	3.4	0.9	**-23.1 (-33.1 to -11.6)**		22.3	8.3	**-19.9 (-25.0 to -14.4)**	^	7.1	8.7	2.0 (-6.9 to 11.8)		17.8	11.7	**-9.7 (-13.7 to -5.4)**	
[OTHER]	3.9	2.9	**-8.6 (-14.7 to -2.1)**		36.2	8.3	**-25.0 (-38.3 to -8.9)**		35.8	32.3	-3.8 (-13.1 to 6.4)		130.1	134.0	-1.2 (-11.0 to 9.7)	
Rural-urban contiuum 2013																
Metropolitan Counties	3.7	1.0	**-22.9 (-27.7 to -17.7)**	r	13.5	3.7	**-24.6 (-29.7 to -19.0)**	r	6.4	6.8	0.3 (-6.4 to 7.4)	r	13.4	9.5	**-8.0 (-11.5 to -4.4)**	r
Nonmetropolitan Counties	2.7	1.0	**-19.6 (-24.9 to -13.8)**		12.5	4.8	**-19.7 (-25.8 to -13.3)**		3.2	4.3	5.1 (-3.2 to 14.2)		13.8	9.5	**-7.6 (-11.0 to -4.1)**	
Census region																
Midwest	3.3	0.8	**-22.2 (-33.7 to -8.8)**	r	13.0	2.5	**-29.9 (-35.3 to -24.2)**	r	5.9	6.4	0.4 (-3.6 to 4.5)	r	15.0	11.2	-7.8 (-16.0 to 1.2)	r
Northeast	4.5	1.4	**-21.7 (-25.7 to -17.4)**		20.3	6.9	**-21.7 (-28.0 to -14.9)**		5.1	9.8	12.3 (7.8 to 16.9)	^	13.6	8.5	**-11.4 (-16.6 to -5.8)**	^
South	4.0	1.3	**-20.6 (-26.0 to -14.8)**		16.0	5.9	**-19.6 (-24.2 to -14.6)**	^	3.6	6.0	9.9 (-2.1 to 23.5)	^	15.2	12.5	**-5.2 (-8.3 to -1.9)**	
West	3.1	0.8	**-23.8 (-29.1 to -18.2)**		10.5	2.4	**-27.3 (-32.1 to -22.1)**		7.2	5.9	-4.9 (-12.8 to 3.6)		12.5	8.4	**-8.5 (-10.8 to -6.0)**	
% of Persons <high school education in the county (ACS 2011-2015), quartile																
Q1	3.9	1.1	**-22.3 (-27.5 to -16.8)**	r	14.1	4.1	**-23.1 (-27.3 to -18.7)**	r	6.6	7.4	1.4 (-3.2 to 6.2)	r	15.2	10.2#	-13.1 (-41.1 to 28.2)	r
													10.2#	9.8	-2.1 (-58.2 to 129.2)	
Q2	3.5	1.1	**-22.0 (-25.4 to -18.4)**		15.2	3.8	**-25.6 (-30.0 to -20.9)**		8.3	7.4	-2.3 (-8.8 to 4.6)		12.7	9.5	**-7.6 (-13.4 to -1.3)**	
Q3	3.4	0.8	**-23.8 (-28.6 to -18.7)**		14.0	4.2	**-24.0 (-30.3 to -17.1)**		5.5	7.7#	10.0 (-31.0 to 75.4)	^	14.0	10.2	**-7.8 (-11.8 to -3.7)**	
									7.7#	6.5	-9.0 (-60.7 to 111.1)					
Q4	3.4	1.0	**-22.1 (-29.0 to -14.5)**		10.7	3.3	**-23.2 (-28.8 to -17.1)**		3.8	5.1	2.2 (-8.4 to 14.1)		12.2	8.8	**-7.2 (-9.2 to -5.1)**	^
% of Persons <200% Poverty level in the county (ACS 2011-2015), quartile																
Q1	3.8	1.2	**-22.2 (-27.1 to -17.1)**	r	15.4	4.6	**-23.5 (-28.9 to -17.7)**	r	8.2	8.1	-1.4 (-7.4 to 5.0)	r	14.2	9.6	**-9.4 (-14.1 to -4.5)**	r
Q2	3.4	0.9	**-23.6 (-28.3 to -18.6)**		12.3	2.6	**-27.6 (-32.3 to -22.6)**		7.3	6.9	-1.1 (-7.7 to 6.0)		12.4	8.5	**-8.5 (-13.9 to -2.8)**	
Q3	3.9	1.0	**-23.2 (-28.0 to -18.1)**		15.8	4.8	**-22.9 (-27.0 to -18.5)**		4.5	6.4	5.0 (-3.6 to 14.4)	^	15.3	10.6	**-8.1 (-11.0 to -5.2)**	^
Q4	3.2	1.0	**-21.3 (-27.8 to -14.2)**		11.3	3.6	**-22.6 (-28.7 to -16.0)**		4.2	5.2	2.0 (-6.0 to 10.6)		12.7	9.6	**-6.4 (-9.5 to -3.2)**	^
% of Foreign born persons in the county (ACS 2011-2015), quartile																
Q1	3.7	1.1	**-21.6 (-26.9 to -15.9)**	r	13.8	5.0	**-20.7 (-26.6 to -14.5)**	r	4.2	5.9	**6.8 (1.1 to 12.9)**	r	14.5	10.6	**-6.8 (-9.4 to -4.1)**	r

Q2	3.6	1.1	**-22.4 (-28.7 to -15.5)**		14.7	3.8	**-24.4 (-28.3 to -20.3)**		6.7	7.1	0.7 (-3.5 to 5.1)	^	15.3	11.8	**-6.6 (-12.5 to -0.4)**	
Q3	3.2	1.0	**-21.2 (-25.8 to -16.3)**		12.1	3.0	**-26.4 (-33.2 to -19.0)**	^	6.7	6.7	-2.5 (-11.2 to 7.0)		13.4	8.8	**-9.4 (-12.7 to -5.9)**	
Q4	3.8	0.9	**-24.6 (-29.0 to -20.0)**	^	13.1	3.7	**-24.2 (-29.5 to -18.5)**		6.2	8.5#	9.4 (-10.7 to 34.1)	^	10.9	7.3	**-9.3 (-13.4 to -4.9)**	^
									8.5#	6.4	-13.5 (-41.2 to 27.1)					

Note: Data from the 18 registries of the Surveillance, Epidemiology, and End Results (SEER)-18 with data on watchful waiting/active surveillance. WW/AS, watchful waiting/active surveillance; NH, non-Hispanic; NOS, not otherwise specified. API, Asian Pacific Islanders; ACS, the Census American Community Survey (ACS) 5-year file; APC, annual percentage change; CI, confidence interval; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile. *P* values were calculated using test for parallelism of the Joinpoint program. ^ indicates a *P*<.05 and different trends in the examined and the reference subgroups, r indicates the reference group and blanks indicate no difference in trends identified. * indicates a joinpoint where the two trends intercept in 2012, while # indicates a joinpoint in 2013; otherwise no joinpoints were identified. Bolded APCs indicate statistically significant trends (*P for linearity* <0.05).

Supplementary Table 2. Trends in age-standardized utilization of treatments for the intermediate-risk prostate cancers diagnosed during 2010-2015 in the US

	Radical Prostatectomy, per 100,000				Radiotherapy, per 100,000				WW/AS, per 100,000				NOS treatment, per 100,000			
	2010	2015	APC (95% CI)	*P*	2010	2015	APC (95% CI)	*P*	###	2015	APC (95% CI)	*P*	2010	2015	APC (95% CI)	*P*
All	2.4	1.6	**-10.0 (-14.4 to -5.3)**		11.2	7.1	**-10.4 (-14.9 to -5.7)**		1.2	1.4	2.9 (-5.1 to 11.6)		**5.6**	**4.2**	**-6.9 (-11.1 to -2.6)**	
Age																
<45 years	0.06	0.06	-7.5 (-18.6 to 5.1)		0.04	0.01	**-18.3 (-30.3 to -4.1)**		0	0	NA		0.05	0.01#	-31.5 (-58.6 to 13.3)	
													0.01#	0.04	59.6 (-55.3 to 469.4)	
45-54 years	4.98	3.3	**-9.2 (-13.4 to -4.8)**	r	4.72	3.81	**-5.8 (-9.5 to -2.1)**	r	0.4	0.88	8.9 (-7.2 to 27.7)	r	2.4	2.47	0.1 (-6.4 to 7.0)	r
55-64 years	18.1	11.48	**-10.3 (-14.9 to -5.4)**		38.8	28.1	**-7.4 (-10.5 to -4.2)**		3.2	5.46	9.1 (-3.2 to 22.8)		14.8	14.2	-0.9 (-3.9 to 2.3)	
65-74 years	21	13.59	**-10.6 (-15.8 to -5.0)**		130	82.9	**-10.1 (-14.1 to -5.8)**		11	15.3	5.4 (-2.8 to 14.3)		48.4	39.4	-5.3 (-9.9 to -0.4)	
75-84 years	3.32	2.5	**-6.1 (-11.8 to -0.1)**		109	61.2	**-13.6 (-20.2 to -6.4)**	^	16	13.4	-4.6 (-12.0 to 3.5)	^	72.5	45	**-10.6 (-15.6 to -5.4)**	^
85+ years	0.41	0.17	NA		11.2	6.27	-13.8 (-26.2 to 0.5)		5.4	4.18	-7.7 (-18.4 to 4.3)		48.9	25.6#	-20.3 (-42.2 to 9.8)	^
													25.6#	24	-3.4 (-55.6 to 110.2)	
Race																
NH White	4.1	2.7	**-9.7 (-14.5 to -4.7)**	r	16.8	11.1	**-9.8 (-15.0 to -4.4)**	r	1.8	2.3	3.3 (-6.0 to 13.6)	r	7.9	5.8	**-7.0 (-11.0 to -2.8)**	r
API	2.3	1.0	**-12.9 (-19.3 to -6.1)**		9.8	5.8	**-13.5 (-22.0 to -4.1)**		1.2	1.4	2.5 (-5.1 to 10.7)		3.4	2.6	**-8.2 (-15.1 to -0.8)**	
Hispanic	2.9	1.8	**-12.0 (-19.0 to -4.3)**		12.6	7.0	**-12.7 (-17.2 to -7.9)**		1.3	1.4	-2.7 (-12.8 to 8.5)		7.9	5.6	**-7.0 (-13.1 to -0.4)**	
NH Black	4.6	3.5	-7.6 (-15.2 to 0.8)		35.1	21.9	**-9.7 (-11.5 to -7.7)**		2.7	3.8	6.2 (-3.7 to 17.1)		18.6	12.6	**-9.0 (-15.2 to -2.4)**	
[OTHER]	5.4	7.5	5.7 (-11.3 to 25.8)	^	54.5	30.9	**-13.8 (-22.0 to -4.7)**		14.8	8.5	**-12.3 (-18.1 to -6.1)**	^	80.7	78.7	-0.5 (-10.1 to 10.2)	
Rural-urban continuum 2013																
Metropolitan Counties	3.9	2.6	**-9.6 (-14.1 to -4.9)**	r	18.0	11.3	-10.7 (-15.3 to -6.0)	r	1.9	2.3	2.1 (-6.0 to 10.8)	r	8.7	6.7	**-6.3 (-10.8 to -1.5)**	r
Nonmetropolitan Counties	3.3	1.9	**-12.9 (-21.3 to -3.7)**		15.1	10.7#	-11.6 (-48.6 to 52.1)		1.4	2.0	7.4 (-4.9 to 21.2)		9.7	5.9	**-10.6 (-14.0 to -6.9)**	
					10.7#	11.3	2.3 (-67.4 to 220.5)									
Census region																
Midwest	4.4	2.7	**-12.5 (-21.1 to -3.1)**	r	23.3	14.1	**-11.9 (-17.4 to -6.1)**	r	2.2	3.0	3.4 (-5.8 to 13.5)	r	12.4	8.5	**-8.3 (-15.1 to -1.0)**	r
Northeast	3.8	3.0	**-5.5 (-10.3 to -0.3)**		20.8	16.6	-6.8 (-13.3 to 0.2)	^	1.1	2.3	15.2 (3.2 to 28.6)	^	8.1	6.5	**-7.8 (-17.6 to 3.1)**	
South	3.8	3.3	**-4.3 (-8.2 to -0.2)**	^	20.5	13.5	**-8.9 (-12.6 to -5.1)**	^	1.3	2.0	7.9 (0.7 to 15.6)		11.5	8.7	**-6.6 (-11.0 to -1.9)**	
West	3.7	2.0	**-13.6 (-18.8 to -8.0)**		14.7	8.6	**-12.1 (-16.4 to -7.5)**		2.3	2.3	-1.2 (-10.1 to 8.5)		7.4	5.5	**-6.2 (-9.0 to -3.3)**	
% of Persons <high school education in the county (ACS 2011-2015), quartile																
Q1	3.8	3.2	**-5.5 (-10.2 to -0.5)**	r	19.7	14.1	**-8.3 (-13.7 to -2.7)**	r	1.9	2.7	6.0 (-5.0 to 18.2)	r	9.3	6.5	**-9.1 (-17.2 to -0.3)**	r
Q2	4.1	2.4	**-10.6 (-13.8 to -7.2)**		20.4	11.9	**-11.4 (-14.6 to -8.2)**		2.4	2.4	-1.0 (-9.4 to 8.2)		7.9	6.3	**-5.2 (-9.5 to -0.8)**	^
Q3	3.8	2.3	**-11.0 (-16.0 to -5.8)**	^	17.8	11.9	**-9.9 (-15.8 to -3.7)**		2.0	2.2	0.8 (-8.3 to 10.7)		10.2	6.8	**-8.6 (-11.1 to -6.0)**	

Q4	3.6	2.2	**-13.0 (-20.2 to -5.1)**	^	13.5	7.8	**-12.0 (-15.9 to -8.0)**		1.3	1.9	5.7 (-0.2 to 12.0)		8.1	6.7	**-4.2 (-7.7 to -0.6)**	
% of Persons <200% Poverty level in the county (ACS 2011-2015), quartile																
Q1	3.8	2.6	**-8.1 (-13.2 to -2.8)**	r	21.3	14.1	**-10.0 (-15.4 to -4.2)**	r	2.4	2.4	-0.5 (-10.6 to 10.7)	r	8.2	6.1	**-7.7 (-13.8 to -1.2)**	r
Q2	4.2	2.6	**-10.2 (-15.7 to -4.4)**		15.9	10.7	**-9.8 (-14.7 to -4.6)**		2.3	2.3	-0.3 (-11.0 to 11.7)		8.3	5.8	**-7.7 (-13.7 to -1.2)**	
Q3	3.6	2.8	**-7.3 (-13.9 to -0.2)**		19.7	12.4	**-9.8 (-13.4 to -6.1)**		1.6	2.5	8.0 (1.9 to 14.4)		10.0	7.9	-6.4 (-13.1 to 0.8)	
Q4	3.7	2.1	**-13.0 (-18.9 to -6.6)**	^	15.2	9.0	**-11.6 (-16.0 to -6.9)**		1.4	2.0	5.4 (-2.4 to 13.9)		9.0	6.7	-5.7 (-8.4 to -2.9)	
% of Foreign born persons in the county (ACS 2011-2015), quartile																
Q1	3.8	2.5	-10.1 (-14.8 to -5.0)	r	17.6	12.3	-8.1 (-12.7 to -3.3)	r	1.6	2.1#	9.6 (9.3 to 9.8)	r	10.8	7.3	-8.2 (-11.4 to -4.9)	r
Q2									2.1#	1.9	-5.5 (-5.9 to -5.2)					
Q3	4.4	2.8	-10.4 (-14.3 to -6.2)		21.7	13.5	-10.5 (-14.4 to -6.3)	^	1.9	2.9	6.0 (-1.3 to 13.9)		10.7	7.8	-7.3 (-14.2 to 0.2)	
Q4	3.4	2.6	-5.1 (-9.0 to -1.0)	^	16.5	10.5	-10.6 (-15.5 to -5.5)		2.1	2.4	0.9 (-10.4 to 13.8)		8.2	6.5	-6.0 (-10.5 to -1.3)	
	3.9	2.2	-14.3 (-22.0 to -5.8)		15.5	9.3	-12.1 (-17.8 to -5.9)	^	1.9	2.0	0.7 (-8.5 to 10.8)		6.1	5.0	-5.1 (-9.1 to -1.0)	

Note: Data from the 18 registries of the Surveillance, Epidemiology, and End Results (SEER)-18 with data on watchful waiting/active surveillance. WW/AS, watchful waiting/active surveillance; NH, non-Hispanic; NOS, not otherwise specified. API, Asian Pacific Islanders; ACS, the Census American Community Survey (ACS) 5-year file; APC, annual percentage change; CI, confidence interval; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile. *P* values were calculated using test for parallelism of the Joinpoint program. ^ indicates a *P*<.05 and different trends in the examined and the reference subgroups, r indicates the reference group and blanks indicate no difference in trends identified. # indicates a joinpoint in 2013; otherwise no joinpoints were identified. Bolded APCs indicate statistically significant trends (*P for linearity* <0.05).

Supplementary Table 3. Trends in age-standardized utilization of treatments for the high-risk prostate cancers diagnosed during 2010-2015 in the US

	Radical Prostatectomy, per 100,000				Radiotherapy, per 100,000				WW/AS, per 100,000				NOS treatment, per 100,000			
	2010	2015	APC (95% CI)	*P*	2010	2015	APC (95% CI)	*P*	2010	2015	APC (95% CI)	*P*	2010	2015	APC (95% CI)	*P*
All	10.8	7.4	**-9.1 (-13.3 to -4.7)**		4.2	3.5	-4.1 (-8.8 to 0.8)		0.2	0.2	0.4 (-2.8 to 3.8)		4.4	4.2	-1.2 (-2.6 to 0.1)	
Age																
<45 years	0.8	0.5	**-11.2 (-16.8 to -5.2)**		0.1	0.0	-15.1 (-35.2 to 11.3)		0.0	0.0	NA		0.1	0.1	-2.3 (-16.8 to 14.8)	
45-54 years	44.5	27.2	**-10.7 (-14.5 to -6.7)**	r	3.6	2.7#	-8.1 (-25.0 to 12.7)	r	0.0	0.2	13.4 (-24.2 to 69.5)	r	3.5	3.9	1.5 (-3.4 to 6.8)	r
					2.7#	3.0	4.5 (-32.0 to 60.8)									
55-64 years	159.5	102.7	**-9.9 (-14.4 to -5.3)**		24.0	19.0*	-11.1 (-28.0 to 9.7)		0.9	0.8	1.2 (-3.0 to 5.6)		19.4	20.1	1.9 (-0.7 to 4.5)	
					19.0*	20.3	1.5 (-9.0 to 13.3)									
65-74 years	190.1	138.0	**-7.8 (-12.1 to -3.4)**		85.2	67.5	**-5.3 (-9.7 to -0.7)**		1.9	3.0	**8.2 (1.3 to 15.6)**		55.4	54.2	-1.1 (-3.0 to 0.9)	^
75-84 years	28.3	26.6	-3.5 (-10.9 to 4.5)	^	####	78.6#	-8.9 (-42.5 to 44.2)		4.3	3.6	-4.1 (-6.3 to -1.9)		117.7	100.9#	-5.1 (-10.0 to 0.0)	
					78.6#	88.9	7.6 (-56.3 to 165.1)						100.9#	108.2	3.1 (-7.2 to 14.6)	
85+ years	1.9	1.2	**-11.2 (-17.6 to -4.2)**		31.1	25.1#	-7.3 (-42.1 to 48.5)		6.2	3.1	-8.9 (-17.8 to 0.9)		175.0	154.0	-2.2 (-4.6 to 0.2)	
					25.1#	32.7	13.7 (-53.7 to 179.1)									
Race																
NH White	36.7	24.1	**-9.7 (-13.9 to -5.1)**	r	12.4	10.7	-3.7 (-8.7 to 1.7)	r	0.5	0.5	1.0 (-1.1 to 3.2)	r	12.4	11.6#	-2.2 (-14.3 to 11.6)	r
													11.6#	12.0	1.9 (-21.3 to 31.9)	
API	17.4	12.7	**-8.4 (-13.4 to -3.1)**		8.9	7.9	-4.0 (-12.9 to 5.8)		0.5	0.3	-12.3 (-24.3 to 1.8)		8.3	7.8	-1.9 (-3.9 to 0.2)	^
Hispanic	23.4	17.9	**-6.9 (-11.2 to -2.3)**		11.9	8.6*	-14.1 (-40.4 to 23.9)		0.4	0.4	3.4 (-9.7 to 18.5)		13.5	12.2	-2.7 (-5.5 to 0.2)	^
					8.6*	8.0	-2.7 (-19.8 to 18.2)									
NH Black	44.9	33.0	**-7.1 (-10.5 to -3.6)**		24.8	20.0*	-10.8 (-60.4 to 101.2)		0.9	0.9	3.2 (-11.1 to 19.8)		29.4	24.1	-4.1 (-5.0 to -3.2)	^
					20.0*	20.7	0.6 (-33.2 to 51.6)									
[OTHER]	48.8	55.0	0.4 (-9.5 to 11.4)		29.7	41.8*	**17.8 (16.5 to 19.1)**		1.7	2.3	-1.9 (-25.5 to 29.2)		65.1	83.1	6.3 (-2.5 to 16.0)	^

					41.8*	27.6	**-12.6 (-13.1 to -12.1)**									
Rural-urban continuum 2013																
Metropolitan Counties	35.1	23.5	**-9.3 (-13.5 to -4.9)**	r	13.4	10.4#	-9.0 (-35.1 to 27.8)	r	0.5	0.5	0.5 (-3.6 to 4.9)	r	13.5	13.0	-0.9 (-2.4 to 0.6)	r
Nonmetropolitan Counties	28.1	21.7	**-6.7 (-11.4 to -1.8)**		10.4#	11.2	5.0 (-46.4 to 105.6)		0.5	0.3	-1.4 (-13.8 to 12.8)		16.4	13.9	**-2.6 (-4.6 to -0.5)**	
Unknown/missing/no match (Alaska or Hawaii-Entire State)	14.1	2.8	**-25.4 (-35.7 to -13.5)**		12.9	11.2	-3.8 (-8.8 to 1.6)						26.8	16.0	3.5 (-23.1 to 39.3)	
					11.3	11.7	-2.6 (-21.6 to 20.9)									
Census region																
Midwest	42.9	30.5	**-7.9 (-11.7 to -3.8)**	^	15.9	12.2*	-13.0 (-39.1 to 24.3)	^	0.5	0.5	4.3 (-14.2 to 26.9)	^	16.1	12.5*	**-12.7 (-14.1 to -11.2)**	^
					12.2*	12.4	-0.2 (-17.6 to 20.8)						12.5*	13.5	3.7 (2.8 to 4.6)	
Northeast	35.7	24.5	**-8.5 (-12.8 to -4.0)**		15.2	14.0	-2.4 (-7.3 to 2.8)		0.3	0.5	8.3 (-7.3 to 26.6)		12.8	13.4	-0.4 (-4.5 to 3.8)	
South	31.6	23.8	**-7.2 (-11.4 to -2.9)**		14.3	12.7	-3.0 (-8.9 to 3.4)		0.4	0.4	4.3 (-12.1 to 23.8)		15.8	14.8	-1.5 (-3.1 to 0.2)	
West	33.6	21.6	**-10.2 (-14.8 to -5.3)**		11.9	9.3*	-12.1 (-53.0 to 64.3)		0.6	0.6	-2.3 (-9.0 to 4.9)		13.1	12.4	-1.0 (-1.9 to 0.0)	^
					9.3*	9.6	0.2 (-27.6 to 38.5)									
% of Persons <high school education in the county (ACS 2011-2015), quartile																
Q1	36.2	24.9	**-8.8 (-13.6 to -3.8)**	r	13.9	10.0#	-8.5 (-39.8 to 39.1)	r	0.4	0.5	6.3 (-1.7 to 15.0)	r	13.9	11.6#	-6.1 (-11.7 to 0.0)	r
					10.0#	13.0	9.1 (-51.2 to 144.0)						11.6#	13.5	8.1 (-4.0 to 21.7)	
Q2	35.0	22.2	**-10.3 (-14.8 to -5.5)**		15.4	11.7*	-13.5 (-36.0 to 16.8)		0.8	0.7	-3.1 (-10.2 to 4.6)		13.2	13.7	0.1 (-2.5 to 2.8)	
					11.7*	11.5	-0.4 (-15.2 to 16.8)									
Q3	34.8	23.2	**-9.2 (-13.0 to -5.3)**		13.3	11.9	-2.7 (-6.8 to 1.6)		0.5	0.4	0.7 (-6.8 to 8.9)		14.7	12.8	-2.6 (-4.5 to -0.6)	
Q4	31.4	22.8	**-8.0 (-12.2 to -3.5)**		11.1	8.6	**-5.6 (-10.4 to -0.5)**	^	0.4	0.4	-1.7 (-12.4 to 10.3)	^	13.6	12.6	-1.3 (-2.3 to -0.2)	^
% of Persons <200% Poverty level in the county (ACS 2011-2015), quartile																
Q1	36.6	23.7	**-9.8 (-14.0 to -5.4)**	r	14.5	11.1#	-8.9 (-39.5 to 37.1)	r	0.6	0.6	-1.0 (-8.1 to 6.7)	r	12.6	13.6	0.7 (-2.7 to 4.1)	r
					11.1#	13.0	8.1 (-51.3 to 139.9)									
Q2	35.4	23.4	**-9.8 (-14.6 to -4.6)**		13.0	11.0	-3.3 (-6.6 to 0.2)		0.7	0.5	-3.2 (-14.9 to 10.0)		14.0	11.9#	-5.2 (-11.4 to 1.4)	^
													11.9#	12.4	2.1 (-10.6 to 16.6)	
Q3	32.4	22.5	**-8.5 (-12.5 to -4.4)**		13.8	11.8	-4.2 (-10.4 to 2.4)		0.3	0.6	9.6 (-3.4 to 24.3)		14.3	13.5	**-0.3 (-2.6 to 2.0)**	
Q4	32.6	23.3	**-8.1 (-12.3 to -3.8)**		12.4	9.2*	-13.9 (-40.9 to 25.4)	^	0.4	0.4	-0.6 (-14.9 to 16.0)		14.4	13.2	**-1.9 (-2.8 to -1.0)**	
					9.2*	9.5	0.0 (-18.2 to 22.1)									
% of Foreign born persons in the county (ACS 2011-2015), quartile																
Q1	32.3	24.9	**-6.6 (-10.7 to -2.4)**	r	14.1	10.3*	-14.4 (-69.9 to 143.4)	r	0.5	0.4	0.4 (-13.0 to 15.9)	r	15.8	14.1#	-3.8 (-8.9 to 1.6)	r
					10.3*	11.6	2.7 (-40.0 to 75.7)						14.1#	13.8	-1.0 (-11.1 to 10.3)	
Q2	38.6	25.2	**-9.6 (-14.4 to -4.6)**	^	15.0	11.3#	-9.1 (-34.8 to 26.8)		0.5	0.6	3.3 (-1.0 to 7.8)		14.3	12.5#	-4.6 (-20.2 to 14.0)	
					11.3#	12.4	4.6 (-46.1 to 103.2)						12.5#	14.2	6.2 (-24.7 to 49.8)	^
Q3	33.0	22.5	**-9.2 (-13.6 to -4.6)**	^	12.6	9.8#	-8.8 (-54.8 to 84.1)		0.5	0.7	2.4 (-10.3 to 17.0)		13.8	13.6	-0.2 (-1.4 to 1.0)	
					9.8#	11.2	7.1 (-72.5 to 316.4)									
Q4	33.6	21.1	**-10.4 (-14.3 to -6.3)**	^	11.9	9.7	**-4.5 (-8.3 to -0.6)**		0.5	0.6#	9.1 (-39.6 to 97.3)		11.9	11.3	-1.0 (-3.3 to 1.3)	
									0.6#	0.4	-23.0 (-78.3 to 172.8)					

Note: Data from the 18 registries of the Surveillance, Epidemiology, and End Results (SEER)-18 with data on watchful waiting/active surveillance. WW/AS, watchful waiting/active surveillance; NH, non-Hispanic; NOS, not otherwise specified. NA, not available; API, Asian Pacific Islanders; ACS, the Census American Community Survey 5-year file; APC, annual percentage change; CI, confidence interval; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile. *P* values were calculated using test for parallelism of the Joinpoint program. ^ indicates a *P*<.05 and different trends in the examined and the reference subgroups, r indicates the reference group and blanks indicate no difference in trends identified. * indicates a joinpoint where the two trends intercept in 2012, while # indicates a joinpoint in 2013; otherwise no joinpoints were identified. Bolded APCs indicate statistically significant trends (*P for linearity* <0.05).