ELSEVIER

Urologic Oncology: Seminars and Original Investigations 37 (2019) 575.e9−575.e18

UROLOGIC ONCOLOGY

Clinical-Prostate cancer

The current landscape of low-value care in men diagnosed with prostate cancer: what is the role of individual hospitals?

Marieke J. Krimphove, M.D.[a,b], Alexander P. Cole, M.D.[a], David F. Friedlander, M.D.[a], David-Dan Nguyen[a], Stuart R. Lipsitz, Sc.D.[c], Paul L. Nguyen, M.D.[d], Kerry L. Kilbridge, M.D., M.Sc.[e], Adam S. Kibel, M.D.[a], Luis A. Kluth, M.D.[b], Quoc-Dien Trinh, M.D.[a,*]

[a] *Division of Urological Surgery and Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, MA*
[b] *Department of Urology, University Hospital Frankfurt, Frankfurt am Main, Germany*
[c] *Division of General Internal Medicine and Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, MA*
[d] *Department of Radiation Oncology, Dana Farber Cancer Institute, Harvard Medical School, Boston, MA*
[e] *Department of Medical Oncology, Dana Farber Cancer Institute, Harvard Medical School, Boston, MA*

Received 22 January 2019; received in revised form 26 March 2019; accepted 8 April 2019

Abstract

Background: A considerable number of prostate cancer (PCa) patients eligible for expectant management receive definitive treatment. We aimed to investigate the hospital-level contribution to overtreatment in the United States.

Methods: Using the National Cancer Database we identified two nonoverlapping cohorts: (1) men with a life expectancy <10 years harbouring low or intermediate risk PCa (2) men with life expectancy ≥10 years with low-risk PCa. Multivariable mixed models with patient characteristics as fixed and hospital-level intercept as random effect were used to assess the hospital-level risk-adjusted probability of definitive treatment in both groups. Pearson's correlation coefficient was calculated to investigate the correlation between the hospitals probabilities of treating patients of both cohorts.

Results: We found 33,431 men with a life expectancy <10 years and 122,514 men with a life expectancy ≥10 years and low-risk PCa. In the latter, the probability of treatment ranged from 29.0% in the bottom to 90.0% in the top decile and from 35.0% to 88.0% for men with a life expectancy <10 years. Age and race were independent predictors of low-value treatment in both cohorts. The correlation between 1,225 hospitals treating men of both cohorts was strong (Pearson's $r = 0.66$, $P < 0.001$).

Conclusion: There is wide hospital-level variability in low-value treatment of men with limited life expectancies and low-risk PCa. Hospitals more likely to treat men with limited life expectancies were more likely to treat men with low-risk PCa and vice versa. Identifying drivers and modifying practice at these hospitals may represent an effective tool for reducing overtreatment.

Keywords: Prostate cancer; Overtreatment; Quality of health care; Public health; Active surveillance

1. Introduction

Prostate cancer (PCa) often represents indolent disease, as the majority of men diagnosed will die *with* PCa rather than *of* PCa. Aiming to balance harms and benefits of PCa treatment, active surveillance and watchful waiting became standard of care for men with low-risk disease [1] and for men with a life expectancy of less than 10 years, respectively [2,3]. While the use of active surveillance has generally increased in the past decade [4], many men continue to receive definitive treatment with significant hospital level variability [5−7]. Overtreatment of men unlikely to die from PCa leads to both treatment-associated morbidity and

*Corresponding author. Tel.: +1-617-525-7350; fax: + 1-617-525-6348.
E-mail addresses: qtrinh@bwh.harvard.edu, trinh.qd@gmail.com (Q.-D. Trinh).

https://doi.org/10.1016/j.urolonc.2019.04.001
1078-1439/

is also associated with significant costs with minimal medical benefit [8,9].

Factors influencing the choice of active surveillance versus definitive treatment are manifold ranging from the patients' personal preference, anxiety, and social environment to general health status and healthcare organization [10]. In terms of provider's contribution to variation in use of active surveillance, Loppenberg et al. showed a high practice and hospital level variation in the use of active surveillance for men with low-risk PCa [11].

To further characterize the role of hospitals as a potential catalyst for overtreatment in PCa, we aimed to investigate the hospitals' contribution to variation of definitive treatment for men eligible for active surveillance with localized PCa. We therefore evaluate the hospital-level variation of probability of definitive treatment for men with life expectancy of <10 years and low or intermediate risk PCa and for men with life expectancy ≥10 years diagnosed with low-risk PCa. Finally, we investigate correlation of the hospitals' probability of treating patients in either group.

2. Materials and methods

2.1. Data source

We obtained data from the National Cancer Database, which was established by the Commission on Cancer of the American Cancer Society [12]. All patients who were seen at any stage of their cancer diagnosis or treatment at one of 1,500 approved hospitals are included. It captures around 60 percent of PCa cases of the United States of America [13]. Trained data abstractors gather the data utilizing standardized methodology.

2.2. Study population

We identified men diagnosed with adenocarcinoma of the prostate between 2010 and 2015 using the International Classification of Diseases for Oncology, Third Edition, topography codes C.61. We then selected men who are eligible for expectant management for their disease and divided them into 2 cohorts according to their life expectancy and risk profile based on the d'Amico risk stratification for PCa [14]. Group 1: Men with a life expectancy <10 years harbouring low- or intermediate-risk PCa; group 2: men with life expectancy ≥10 years with low-risk PCa. If the cumulative incidence of other cause mortality within 10 years exceeded 50%, men were considered having a limited life expectancy. This was calculated accounting for age and Charlson Comorbidity Index (CCI) as previously described: age 66 to 69 years and a CCI ≥2, age 70 to 74 years and a CCI ≥1, or age >75 years [15,16]. Men with missing PSA, Gleason, TNM staging or treatment information were excluded, as well as men with nodal positive or metastatic disease. We also excluded men aged <40 years due to censoring by the National Cancer Data Base (NCDB) for confidentiality purposes (Fig. 1).

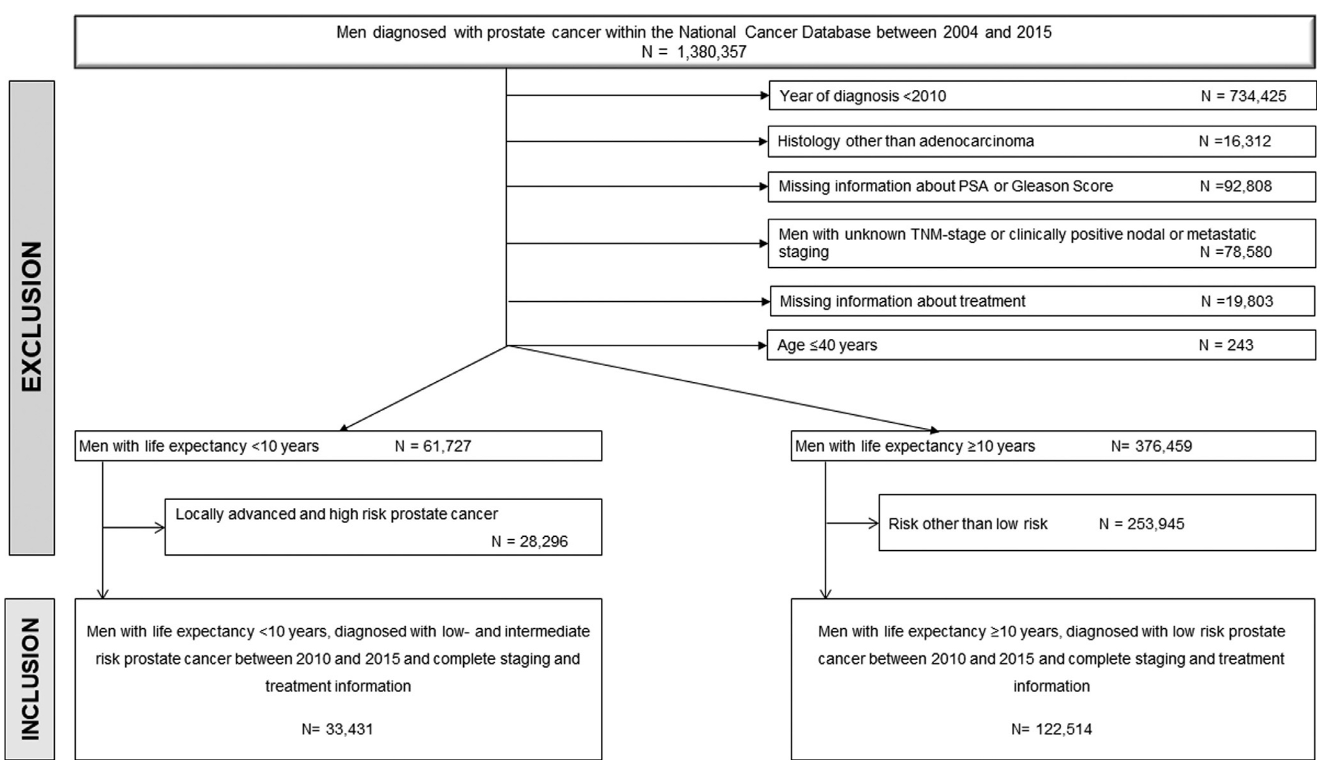

Fig. 1. Cohort selection.

2.3. Covariates

Patient level data were abstracted including age at diagnosis, race (White, Black, other, or unknown), year of diagnosis, CCI (categorized into 0,1, ≥2) as well as TNM staging information based on the American Joint Committee on Cancer 7th edition, PSA level (in ng/ml), and Gleason Score at diagnosis. Sociodemographic covariates included primary insurance carrier (private, Medicare, Medicaid, other government payer [TRICARE, Military, VA and Indian/Public Health Service], uninsured, and unknown), percentage of adults within patient's ZIP code without a high school diploma (<7%, 7−12.9%, 13−20.9%, ≥21%), ZIP code level median household income per year (<$38,000, $38,000−$47,999, $48,000−$62,999, or ≥$63,000), County type (metropolitan, urban, rural, or unknown), census geographical region, and distance to the hospital. Commission on Cancer (CoC) facility type was categorized as Community Cancer Program (CCP), Comprehensive Community Cancer Program (CCCP), Academic/Research Program (ACAD), Integrated Network Cancer Program (INCP), or Other/Unknown. Facility caseload was defined as the mean of the total volume of patients with PCa treated at the treating facility in the year of the patient's diagnosis using a previously described method, accounting for variation in facility caseload over time [17,18].

2.4. Main outcome measure

Our main outcome measure was the receipt of definitive treatment within 180 days of diagnosis. Receipt of treatment was defined as surgery (radical prostatectomy) or radiation therapy (e.g. external beam radiation therapy, brachytherapy) of the prostate and pelvis. Men, who received treatment beyond 180 days of diagnosis were considered observed, as their treatment may be due to upgrading or upstaging procedures during active surveillance.

2.5. Statistical analysis

Descriptive statistics were reported using frequencies and proportions for categorical variables. Chi square tests with a Rao-Scott adjustment to account for clustering were applied to compare differences between men who received treatment and those who did not [19,20]. Multivariable logistic regression analysis was used to account for confounding due to patient demographic and clinical variables [18].

We fit multivariable mixed-effects models for both cohorts to detect the association between treatment and patient characteristics as fixed effects and hospital-level intercept as random effect. The hospital level random intercept allowed us to estimate the contribution of unmeasured hospital level random effects. The random effect intercepts allowed us to estimated probabilities of receipt of treatment and 95% confidence intervals (CIs) for each hospital, whereas the fixed effects were held at their frequency in the overall population. Thus, we estimated each hospital's predicted rate of receipt of treatment based on the hospital level random intercepts. All hospitals were ranked from least- to most-likely to treat their patients and plotted against the probability of definitive treatment, using a previously used method [21,22]. The mean estimated probability of treatment in the top and bottom deciles with 95% CIs were compared.

We then assessed the correlation of the hospital's probability of treating men with limited life expectancy and low-risk PCa. Each hospital's estimated probability of treating patients with limited life expectancy and low- or intermediate-risk PCa were plotted against hospitals' probability of treating patients with high life expectancy harbouring low-risk PCa. Pearson's correlation coefficient was calculated to investigate the correlation between the hospitals.

All statistical analyses were performed using Stata v.13.0 (StataCorp, College Station, TX). Two-sided statistical significance was defined as $P < 0.05$. An institutional review board waiver was obtained before the study was conducted.

3. Results

3.1. Baseline characteristics

We identified a total of 33,431 men diagnosed with low- and intermediate-risk localized PCa with a life expectancy of less than 10 years; 22,772 (68.1%) of these received either surgery or radiation therapy and 10,659 (31.9%) were observed. There were 122,514 men with a life expectancy ≥10 years, diagnosed with low-risk PCa, 84,140 (68.7%) received definitive treatment and 38,374 (31.3%) had active surveillance. In this cohort, almost 50% of the treated men were treated in 2010 and 2011. A summary of baseline characteristics of all PCa patients is available in Table 1.

3.2. Factors associated with receipt of treatment

In the cohort of men with a life expectancy <10 years, men with higher Gleason Scores were more likely to receive treatment (Gleason 7: Odds Ratio [OR] 3.06 95% CI 2.85−3.28, $P < 0.001$). In the cohort of men with a life expectancy ≥10 years, higher CCI (CCI ≥ 2: OR 1.24 95% CI 1.08−1.41, $P = 0.002$) and tumor stage cT2a (OR 1.26 95% CI 1.13−1.39, $P < 0.001$) were associated with higher odds of receipt of treatment.

In both cohorts older age and black race (group 1: OR 0.77 95% CI 0.69−0.85, $P < 0.001$|group 2: OR 0.85 95% CI 0.79−0.91, $P < 0.001$) were independently associated with lower odds of receipt of treatment. Comprehensive community cancer programs were associated with higher odds of receipt of definitive treatment compared to academic hospitals in both cohorts (Table 2).

Table 1
Baseline characteristics of men diagnosed with localized prostate cancer between 2010 and 2015

	Men with life expectancy <10 years				Men with life expectancy ≥10 years and low risk prostate cancer			
	Active surveillance N = 10,659 (31.9%)	Definitive treatment N = 22,772 (68.1%)	Total N = 33,431 (100%)	*P* value*	Active surveillance N = 38,374 (31.3%)	Definitive treatment N = 84,140 (68.7%)	Total N = 122,514 (100%)	*P* value*
Age group								
≤55	-/-	-/-	-/-	<0.001	6,657 (17.4)	19,861 (23.6)	26,518 (21.6)	<0.001
56−65	-/-	-/-	-/-		18,543 (48.3)	42,326 (50.3)	60,869 (49.7)	
66−75	3,990 (37.4)	10,993 (48.3)	14,983 (44.8)		13,174 (34.3)	21,953 (29,1)	35,127 (28.7)	
76−85	6,287 (59.0)	11,578 (50.8)	17,865 (53.4)		-/-	-/-	-/-	
≥ 85	382 (3.6)	201 (0.9)	583 (1.7)		-/-	-/-	-/-	
Race								
White	8,832 (82.9)	19,500 (86.0)	28,422 (85.0)	<0.001	31,011 (80.8)	70,072 (83.3)	101,083 (82.5)	<0.001
Black	1,329 (12.5)	2,328 (10.2)	3,657 (10.9)		5,473 (14.3)	11,136 (13.2)	16,609 (13.6)	
Other	498 (4.7)	854 (3.8)	1,352 (4.0)		1,890 (4.9)	2,932 (3.5)	4,822 (3.9)	
CCI								
0	6,733 (63.2)	12,918 (56.7)	19,651 (58.8)	<0.001	34,588 (90.1)	72,833 (86.6)	107,421 (87.7)	<0.001
1	2,824 (26.5)	7,070 (31.1)	9,894 (29.6)		3,391 (8.8)	10,253 (12.2)	13,644 (11.1)	
≥2	1,102 (10.3)	2,784 (12.2)	3,886 (11.6)		395 (1.0)	1,054 (1,3)	1,449 (1.2)	
PSA								
<10	8,077 (75.8)	18,058 (79.3)	26,135 (78.2)	<0.001				
10−20	2,582 (24.2)	4,714 (20.7)	7,296 (21.8)					
Gleason								
≤6	5,730 (53.8)	6,685 (29.4)	12,415 (37.1)	<0.001				
7	4,929 (46.2)	16,087 (70.6)	21,016 (62.9)					
Clinical T-stage								
cT1	9,009 (84.5)	17,946 (78.8)	26,955 (80.6)	<0.001	35,397 (92.2)	76,270 (90.7)	111,667 (91.2)	0.002
cT2a	1,214 (11.6)	3,233 (14.2)	4,474 (13.4)		2,977 (7.8)	7,870 (9.4)	10,847 (8.9)	
cT2b	409 (3.8)	1,593 (7.0)	2,002 (6.0)		-/-	-/-	-/-	
Year of diagnosis								
2010	1,920 (18.0)	4,415 (19.4)	6,335 (19.0)	<0.001	6,057 (15.8)	19,581 (23.3)	25,638 (20.9)	<0.001
2011	2,017 (18.9)	4,649 (20.4)	6,666 (19.9)		6,967 (18.2)	19,559 (23.3)	26,526 (21.7)	
2012	1,586 (14.9)	3,489 (15.3)	5,075 (15.2)		5,922 (15.4)	13,797 (16.4)	19,719 (16.1)	
2013	1,794 (16.8)	3,405 (15.0)	5,199 (15.6)		6,288 (16.4)	11,917 (14.2)	18,205 (14.9)	
2014	1,474 (13.8)	3,200 (14.1)	4,674 (14.0)		6,197 (16.2)	10,149 (12.1)	16,346 (13.3)	
2015	1,868 (17.5)	3,614 (15.9)	5,482 (16.4)		6,943 (18.1)	9,137 (10.9)	16,080 (13.1)	
Insurance								
Medicaid	193 (1.8)	258 (1.1)	451 (1.4)	<0.001	1,123 (2.9)	1.685 (2.0)	2,808 (2.3)	<0.001
Medicare	8,905 (83.5)	19,200 (84.3)	28,105 (84.1)		13,342 (34.8)	24,202 (28.8)	37,544 (30.6)	
Other Gov't	102 (1.0)	307 (1.4)	409 (1.2)		681 (1.8)	1,913 (2.3)	2,594 (2.1)	
Private	1,226 (11.5)	2,664 (11.7)	3,890 (11.6)		21,794 (56.8)	54,501 (64.8)	76,295 (62.3)	
No insurance	71 (0.7)	87 (0.4)	158 (0.5)		823 (2.1)	961 (1.1)	1,784 (1.5)	
Unknown	162 (1,5)	256 (1.1)	418 (1.3)		611 (1.6)	878 (1.0)	1,489 (1.2)	
Income[a]								
≥$63,000	3,442 (32.3)	7,599 (33.4)	11,041 (33.0)	0.523	15,660 (40.8)	31,368 (37.3)	47,028 (38.4)	0.008
$48,000−$62,999	2,931 (27.5)	6,286 (27.6)	9,217 (27.6)		9,812 (25.6)	22,682 (27.0)	32,494 (26.5)	
$38,000−$47,999	2,462 (23.1)	5,213 (22.9)	7,675 (23.0)		7,522 (19.6)	17,668 (21.0)	25,190 (20.6)	
<$38,000	1,789 (16.8)	3,609 (15.9)	5,398 (16.2)		5,258 (13.7)	12,209 (14.5)	17,467 (14.3)	
Unknown	35 (0.3)	65 (0.3)	100 (0.3)		122 (0.3)	213 (0.3)	335 (0.3)	
Education[a,b]								
Highest >21%	1,651 (15.5)	3,266 (14.3)	4,917 (14.7)	0.305	5,137 (13.4)	22,056 (13.1)	16,193 (13.2)	<0.001
13−20.9%	2,571 (24.1)	5,461 (24.0)	8,032 (24.0)		8,184 (21.3)	19,698 (23.4)	27,882 (22.8)	
7−12.9%	3,540 (33.2)	7,758 (34.1)	11,298 (33.8)		12,556 (32.7)	28,199 (33.5)	40,755 (33.3)	
Lowest <7%	2,867 (26.9)	6,237 (27.4)	9,104 (27.2)		12,401 (32.3)	25,012 (29.7)	37,413 (30.5)	
Unknown	30 (0.3)	50 (0.2)	80 (0.2)		96 (0.3)	175 (0.2)	271 (0.2)	
Distance to hospital								
First	6,201 (58.2)	13,247 (58.2)	19,448 (58.2)	0.543	19,406 (50.6)	40,184 (47.8)	59,590 (48.6)	0.029
Second	3,352 (31.5)	7,314 (32.1)	10,666 (31.9)		13,232 (34.5)	29,820 (35.4)	43,072 (35.2)	
Third	1,079 (10.1)	2,165 (9.5)	3,244 (9.7)		5,625 (14.7)	13,920 (16.5)	19,545 (16.0)	
Unknown	27 (0.3)	46 (0.2)	73 (0.2)		91 (0.2)	216 (0.3)	307 (0.3)	
Mean caseload[c]								

(*continued*)

Table 1 (***Continued***)

	Men with life expectancy <10 years				Men with life expectancy ≥10 years and low risk prostate cancer			
	Active surveillance N = 10,659 (31.9%)	Definitive treatment N = 22,772 (68.1%)	Total N = 33,431 (100%)	*P* value*	Active surveillance N = 38,374 (31.3%)	Definitive treatment N = 84,140 (68.7%)	Total N = 122,514 (100%)	*P* value*
1st Quartile	3,358 (31.5)	7,446 (32.7)	10,804 (32.3)	<0.001	8,428 (22.0)	19,387 (23.0)	27,815 (22.7)	<0.001
2nd Quartile	2,388 (22.4)	5,977 (26.3)	8,365 (25.0)		7,339 (19.1)	21,005 (25.0)	28,344 (23.1)	
3rd Quartile	2,524 (23.7)	5,497 (24.1)	8,021 (24.0)		9,343 (24.4)	20,735 (24.6)	30,078 (24.6)	
4th Quartile	2,389 (22.4)	3,852 (16.9)	6,241 (18.7)		13,264 (34.6)	23,013 (27.4)	36,277 (29.6)	
County								
Metro	8,424 (79.0)	18,025 (79.2)	26,449 (79.1)	0.844	31,827 (82.9)	67,945 (80.8)	99,772 (81.4)	0.009
Urban	1,754 (16.5)	3,707 (16.3)	5,461 (16.3)		5,029 (13.1)	12,579 (15.0)	17,608 (14.4)	
Rural	261 (2.5)	528 (2.3)	789 (2.4)		611 (1.6)	1,596 (1.9)	2,207 (1.8)	
Unknown	220 (2.1)	512 (2.3)	732 (2.2)		907 (2.4)	2,020 (2.4)	2,927 (2.4)	
Location								
Northeast	2,364 (22.2)	4,711 (20.7)	7,075 (21.2)	0.233	10,721 (27.9)	17,418 (20.7)	28,139 (23.0)	<0.001
South	3,374 (31.7)	7,954 (34.9)	11,328 (33.9)		11,644 (30.3)	31,833 (37.8)	43,477 (35.5)	
Midwest	3,243 (30.4)	6,690 (29.4)	9,933 (29.7)		2,652 (25.2)	23,746 (28.2)	33,398 (27.3)	
West	1,678 (15.7)	3,417 (15.0)	5,095 (15.2)		6,357 (16.6)	11,143 (13.2)	17,500 (14.3)	
Facility type								
Academic	3,957 (37.1)	6,882 (30.2)	10,839 (32.4)	<0.001	20,157 (52.5)	32,876 (39.1)	53,033 (43.3)	<0.001
Community Cancer Program	1,338 (12.6)	2,320 (10.2)	3,658 (10.9)		2,938 (7.7)	5,565 (6.6)	8,503 (6.9)	
Comprehensive Community Cancer Program	4,418 (41.5)	11,354 (49.9)	15,772 (47.2)		12,161 (31.7)	36,962 (43.9)	49,123 (40.1)	
Integrated Network Cancer Program	946 (8.9)	2,216 (9.7)	3,162 (9.5)		3,118 (8.1)	8,737 (10.4)	11,855 (9.7)	

[a] ZIP-code level variable.
[b] Percentage of residents in home county with no high school degree from 2012 American County Survey Data.
[c] Facility caseload was calculated as the mean of the total volume of patients with prostate cancer treated at the treating facility in the year of the patient's diagnosis (Cases/Year: 1st quartile:1−82; 2nd quartile: 83−153; 3rd quartile: 154−277; 4th quartile: 278−1472).Abbreviations: CCI = Charlson Comorbidity Index; PSA = prostate specific antigen.

3.3. Hospital-level probability of treatment

We found 1,230 unique hospitals where men with a life expectancy of less than 10 years received care for localized PCa (Fig. 2a). The hospitals' adjusted mean probability of treatment ranged from 35.0% (95% CI 33.8%−36.2%) in the bottom decile to 88.0% (95% CI 87.5%−89.3%) in the top decile.

1,287 unique hospitals cared for men with a life expectancy ≥10 years and a diagnosis of low-risk PCa (Fig. 2b). The adjusted mean of their probability of treatment was more than three-fold higher in the top decile (90.0% 95% CI 89.7%−90.4%) compared to the bottom decile (29.0% 95% CI 27.7%−30.2%).

3.4. Correlation of hospitals' probability of treatment for men with low-risk PCa and men with life expectancy <10 years

We identified 1,225 hospitals that cared for both patient groups (*Fig. 3*). The correlation between hospitals treating men with a life expectancy of less than 10 years and those treating men with a life expectancy ≥10 years diagnosed with low-risk PCa is strong and statistically significant (Pearson's Rho 0.66, $P < 0.001$).

4. Discussion

Our study demonstrated significant hospital-level variability in treatment of men unlikely to die from PCa. This encompassed both men with life expectancy less than 10 years, and men with life expectancy of 10 or more years, but with low-risk PCa. In addition to significant between-hospital variability, we found that there was correlation across these 2 categories. Facilities more likely to treat men with short life expectancies were also more likely to treat men with normal life expectancies and low-risk PCa, and vice versa.

The institution's contribution to overtreatment of PCa cannot simply be explained by different patient demographics. Indeed, our methods are specifically designed to control for patient characteristics and create estimates based only on hospital level effects. These findings further strengthen the hypothesis that hospital-level factors play a significant role in explaining variations in PCa management. These results echo findings from earlier research: In a previous retrospective, CoC-accredited hospital-based

Table 2
Multivariable logistic regression predicting definitive treatment of men diagnosed with localized prostate cancer between 2010 and 2015

	Men with life expectancy <10 years			Men with life expectancy ≥10 years and low risk prostate cancer		
	Odds ratio	95% confidence interval	*P* value	Odds ratio	95% confidence interval	*P* value
Age group						
≤55	-/-	-/-	-/-	Ref.		
56−65	-/-	-/-	-/-	0.74	0.70−0.78	<0.001
66−75	Ref.			0.56	0.52−0.61	<0.001
76−85	0.61	0.57−0.66	<0.001	-/-	-/-	-/-
≥85	0.15	0.12−0.18	<0.001	-/-	-/-	-/-
Race						
White	Ref.			Ref.		
Black	0.77	0.69−0.85	<0.001	0.85	0.79−0.91	<0.001
Other	0.86	0.70−1.06	0.161	0.82	0.72−0.93	0.002
CCI						
0	Ref.			Ref.		
1	1.05	0.96−1.14	0.280	1.38	1.29−1.48	<0.001
≥2	1.02	0.92−1.15	0.630	1.24	1.08−1.41	0.002
PSA						
<10	Ref.					
10-20	0.85	0.80−0.90	<0.001			
Gleason						
≤6	Ref.					
7	3.06	2.85−3.28	<0.001			
Clinical T-stage						
cT1	Ref.			Ref.		
cT2a	1.26	1.13−1.36	<0.001	1.26	1.13−1.39	<0.001
cT2b	1.62	1.42−1.84	<0.001	-/-	-/-	-/-
Year of diagnosis						
2010	Ref.			Ref.		
2011	0.99	0.91−1.07	0.752	0.87	0.82−0.91	<0.001
2012	0.86	0.78−0.95	<0.001	0.69	0.65−0.73	<0.001
2013	0.72	0.66−0.80	<0.001	0.56	0.52−0.60	<0.001
2014	0.80	0.72−0.88	<0.001	0.48	0.44−0.53	<0.001
2015	0.70	0.63−0.77	<0.001	0.40	0.36−0.43	<0.001
Insurance						
Medicaid	Ref.			Ref.		
Medicare	1.51	1.22−1.87	<0.001	1.22	1.09−1.37	0.001
Other Gov't	1.84	1.31−2.58	<0.001	1.45	1.24−1.69	<0.001
Private	1.56	1.23−1.96	<0.001	1.41	1.26−1.58	<0.001
No insurance	0.94	0.63−1.41	0.774	0.62	0.50−0.76	<0.001
Unknown	1.13	0.82−1.55	0.445	0.85	0.68−1.07	0.171
Income[a]						
≥$63,000	Ref.			Ref.		
$48,000−$62,999	0.92	0.84−1.01	0.097	0.99	0.90−1.08	0.762
$38,000−$47,999	0.93	0.81−1.06	0.267	0.93	0.82−1.05	0.226
<$38,000	0.94	0.79−1.12	0.450	0.98	0.85−1.12	0.721
Unknown	0.99	0.34−2.88	0.980	0.64	0.34−1.22	0.176
Education[a,b]						
Highest >21%	Ref.			Ref.		
13−20.9%	1.03	0.92−1.14	0.617	1.04	0.97−1.12	0.288
7−12.9%	1.04	0.91−1.18	0.567	0.99	0.89−1.09	0.795
Lowest <7%	1.01	0.87−1.18	0.887	0.93	0.82−1.06	0.268
unknown	0.75	0.21−2.71	0.656	0.85	0.34−2.16	0.740
Distance to hospital						
First	Ref.			Ref.		
Second	1.00	0.93−1.09	0.885	1.13	1.07−1.20	<0.001
Third	1.00	0.83−1.20	0.974	1.41	1.23−1.60	<0.001
unknown	0.94	0.43−2.05	0.875	1.45	0.64−3.30	0.372
Mean caseload[c]						
1st quartile	Ref.			Ref.		
2nd quartile	0.99	0.86−1.15	0.933	1.11	0.98−1.27	0.098

(*continued*)

Table 2 (***Continued***)

	Men with life expectancy <10 years			Men with life expectancy ≥10 years and low risk prostate cancer		
	Odds ratio	95% confidence interval	*P* value	Odds ratio	95% confidence interval	*P* value
3rd quartile	0.89	0.74−1.07	0.222	0.90	0.77−1.05	0.172
4th quartile	0.72	0.57−0.91	0.005	0.80	0.63−1.02	0.067
County						
Metro	Ref.			Ref.		
Urban	0.94	0.81−1.11	0.500	0.93	0.83−1.04	0.185
Rural	0.90	0.69−1.18	0.457	0.84	0.70−1.01	0.062
unknown	1.08	0.87−1.35	0.488	1.07	0.90−1.27	0.450
Location						
Northeast	Ref.			Ref.		
South	1.17	0.98−1.40	0.079	1.47	1.17−1.84	0.001
Midwest	1.02	0.86−1.21	0.810	1.39	1.10−1.74	0.005
West	0.92	0.74−1.15	0.477	0.92	0.67−1.25	0.579
Facility type						
Academic	Ref.	0.75−1.21	0.708	Ref.	0.90−1.40	0.293
Community Cancer Program	0.96			1.13		
Comprehensive Community Cancer Program	1.33	1.11−1.60	0.002	1.68	1.41−2.00	<0.001
Integrated Network Cancer Program	1.19	0.94−1.51	0.155	1.54	1.21−1.96	<0.001

[a] ZIP-code level variable.
[b] Percentage of residents in home county with no high school degree from 2012 American County Survey Data.
[c] Facility caseload was calculated as the mean of the total volume of patients with prostate cancer treated at the treating facility in the year of the patient's diagnosis (Cases/Year: 1st Quartile:1-82; 2nd Quartile: 83-153; 3rd Quartile: 154-277; 4th Quartile: 278-1472).Abbreviations: CCI, Charlson Comorbidity Index; PSA, prostate specific antigen.

cohort of men diagnosed with PCa between 2010 and 2014, 91% of the unexplained variations in the use of active surveillance were attributable to facility-related factors such as the facility type, facility volume, and institution [7,11]. In 2013, Baldwin et al. looked at differences in treatment rates between patients treated in rural and urban hospitals and observed that adjusted definitive treatment rates were lower for rural than urban patients [23].

Past efforts have focused on selective screening, patient education, physician education, and adoption of guidelines. Hospital-level factors, as demonstrated by our study, could be the target of such initiatives seeking to further optimize care. These include hospital culture, financial solvency, reimbursement incentives, practice patterns, legal fears, and other organizational factors. For example, in a retrospective cohort study, Hoffman et al. found that men were more likely to receive definitive therapy if the physicians billed for the treatment [24] − although this impacts physician variation, this remains hospital-level and system-level policy. Similarly, increased use of radiation therapy was observed at institutions owning integrated intensity-modulated radiation therapy devices, possibly attributable to the fixed costs associates with the purchase of these devices [25]. Then again, the ownership of expensive devices is influenced by regional competition. For instance, the risk ratio of undergoing robotic surgery for prostate cancer was 2.64 in highly competitive markets compared to noncompetitive markets [26].

Our work provides further evidence for the role of hospital factors in treatment variability. Further investigation is needed to determine which specific features influence hospital-level attitudes regarding PCa treatment.

Our findings must be considered within the context of the study design. A limitation is the possibility of unmeasured patient confounders including physician-level contribution to overtreatment of PCa. These limitations are always a factor in retrospective research. Our use of a multilevel model with a hospital-level random intercept should account for unmeasured hospital characteristics *at the level of the hospital* or hospital-level differences in patient populations receiving definitive therapy or not. Although the NCDB captures a majority of patients with PCa in the United States, it relies on reports from 1,500 CoC-accredited US hospitals which may not be representative of the reality of other hospitals. For example, if the database underrepresents poor-performing rural hospitals, then our results might underestimate the differences in low-value definitive therapy for PCa management. Furthermore, we did not include hormonal treatment in our analyses for 2 reasons: (1) It is not considered definitive treatment for localized PCa and (2) the NCDB does not capture the specific type or duration of hormonal therapy. Finally, we did not use the code for active surveillance in NCDB, because it does not distinguish between active surveillance and watchful waiting. Patients who were treated within 180 days from diagnoses were considered being over

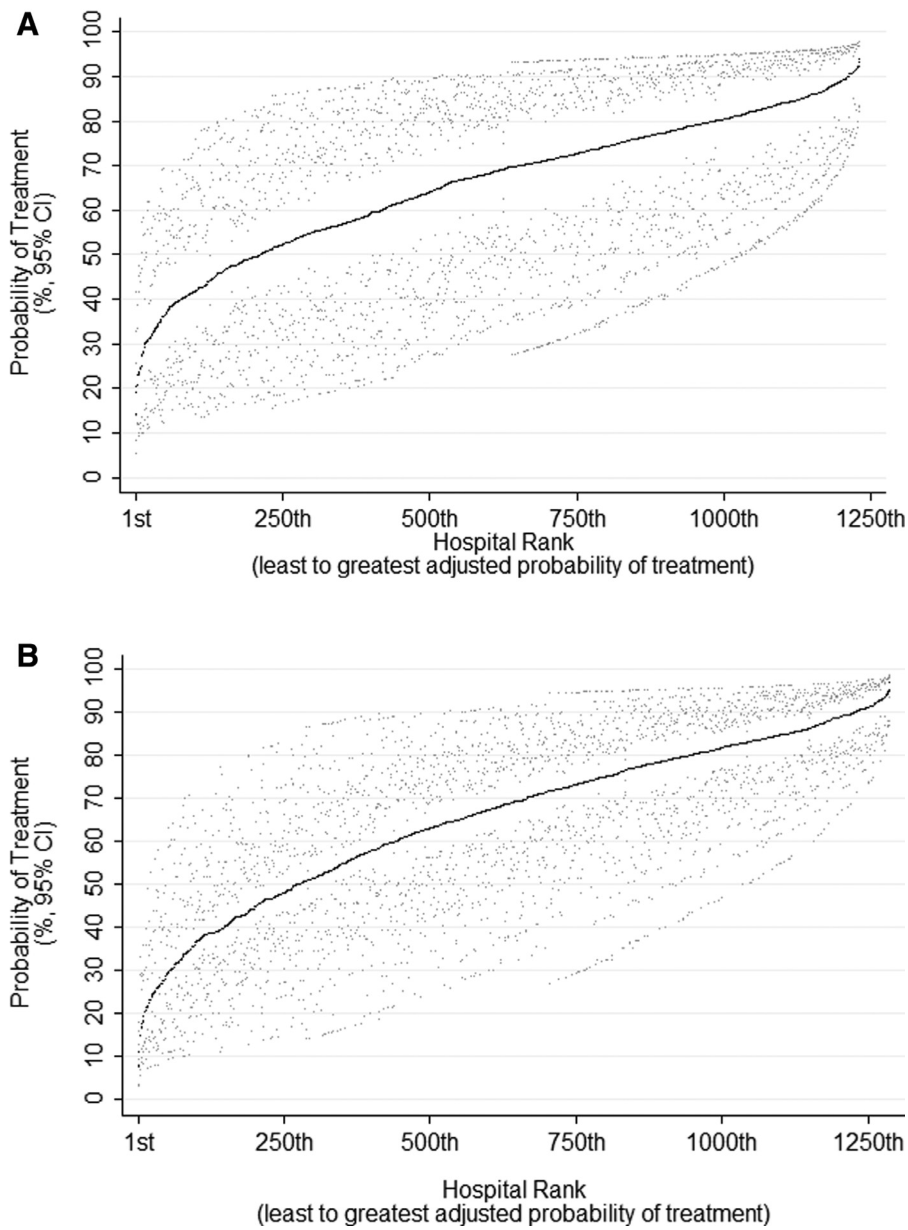

Fig. 2. (A−B) Risk-Adjusted hospital-level probability of treatment. (A) Patients with low- and intermediate-risk prostate cancer and a life expectancy <10 years. (B) Patients with low-risk prostate cancer and life expectancy ≥10 years.

treated; however, variation amongst active surveillance protocols may be an important contributor to hospital level variation seen in our study. For example, some would advocate for immediate confirmatory testing with MRI, genetic panels, re-biopsy after diagnosis of low-risk disease and often result in upgrading in risk within 180 days.

5. Conclusion

We found a wide variation of treatment pattern for men with localized PCa between hospitals and a strong correlation of hospitals treating men with low-risk and with a limited life expectancy. Underlying hospital factors may represent a modifiable target for interventions to reduce low-value care in PCa.

Conflicts of interest

Quoc-Dien Trinh reports honoraria from Astellas, Bayer, Janssen and Intuitive Surgical. ASK reports consulting fees from Sanofi, Dendreon, Tokai, and Profound. Paul L. Nguyen reports consulting fees from Janssen, Augmenix, Ferring, Bayer, Astellas, research funding from Astellas and Janssen, and equity in Augmenix.

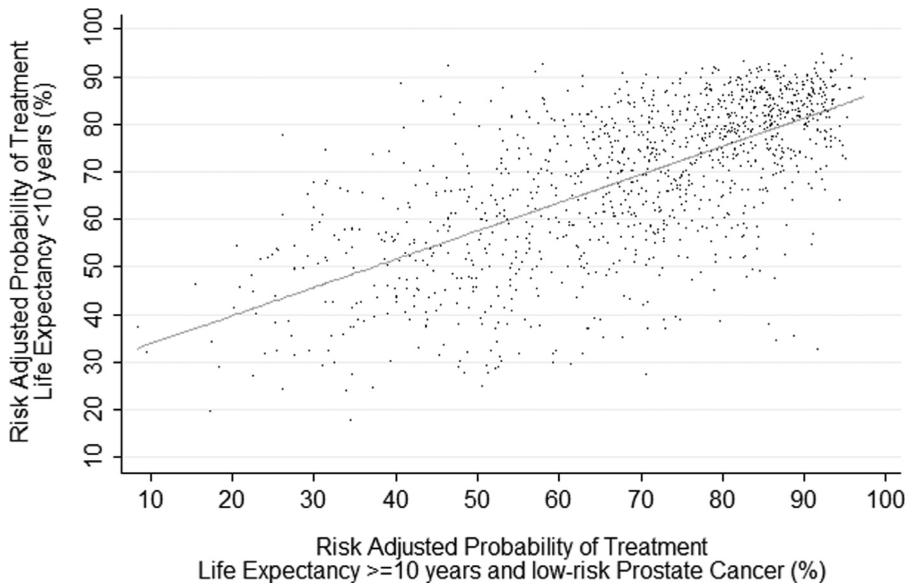

Fig. 3. Correlation of hospital-level probabilities of treatment for men with localized prostate cancer eligible for expectant management.

Acknowledgments

Quoc-Dien Trinh is supported by the Brigham Research Institute Fund to Sustain Research Excellence, the Bruce A. Beal and Robert L. Beal Surgical Fellowship, the Genentech Bio-Oncology Career Development Award from the Conquer Cancer Foundation of the American Society of Clinical Oncology, a Health Services Research pilot test grant from the Defense Health Agency, the Clay Hamlin Young Investigator Award from the Prostate Cancer Foundation and an unrestricted educational grant from the Vattikuti Urology Institute.

The NCDB is a joint project of the CoC of the American College of Surgeons and the American Cancer Society. The CoC's NCDB and the hospitals participating in the CoC NCDB are the source of de-identified data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors. Quoc-Dien Trinh and Marieke J Krimphove had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

References

[1] Leapman MS, Cowan JE, Nguyen HG, et al. Active surveillance in younger men with prostate cancer. J Clin Oncol 2017;35:1898–904.

[2] Albertsen PC. Observational studies and the natural history of screen-detected prostate cancer. Curr Opin Urol 2015;25:232–7.

[3] Mohler JL, Kantoff PW, Armstrong AJ, et al. Prostate cancer, version 2.2014. J Natl Compr Cancer Netw 2014;12:686–718.

[4] Cooperberg MR, Carroll PR. Trends in management for patients with localized prostate cancer, 1990-2013. JAMA 2015;314:80–2.

[5] Kariburyo F, Wang Y, Cheng IE, et al. Observation versus treatment among men with favorable risk prostate cancer in a community-based integrated health care system: a retrospective cohort study. BMC Urol 2018;18:55.

[6] Moschini M, Fossati N, Sood A, et al. Contemporary management of prostate cancer patients suitable for active surveillance: a North American population-based study. Eur Urol Focus 2018;4:68–74.

[7] Loppenberg B, Sood A, Dalela D, et al. Variation in locoregional prostate cancer care and treatment trends at commission on cancer designated facilities: a National Cancer Data Base Analysis 2004 to 2013. Clin Genitourin Cancer 2017;15:e955–68.

[8] Aizer AA, Gu X, Chen MH, et al. Cost implications and complications of overtreatment of low-risk prostate cancer in the United States. J Natl Compr Cancer Netw: JNCCN 2015;13:61–8.

[9] Kariburyo F, Wang Y, Cheng IE, et al. Healthcare costs among men with favorable risk prostate cancer managed with observation strategies versus immediate treatment in an integrated healthcare system. J Med Econ 2017;20:825–31.

[10] Kinsella N, Stattin P, Cahill D, et al. Factors influencing men's choice of and adherence to active surveillance for low-risk prostate cancer: a mixed-method systematic review. Eur Urol 2018;74:261–80.

[11] Loppenberg B, Friedlander DF, Krasnova A, et al. Variation in the use of active surveillance for low-risk prostate cancer. Cancer 2018;124:55–64.

[12] Cole AP, Friedlander DF, Trinh QD. Secondary data sources for health services research in urologic oncology. Urol Oncol 2017;36:165–73.

[13] Lerro CC, Robbins AS, Phillips JL, Stewart AK. Comparison of cases captured in the national cancer data base with those in population-based central cancer registries. Ann Surg Oncol 2013;20:1759–65.

[14] D'Amico AV, Whittington R, Malkowicz SB, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA 1998;280:969–74.

[15] Daskivich TJ, Kwan L, Dash A, Saigal C, Litwin MS. An age adjusted comorbidity index to predict long-term, other cause mortality in men with prostate cancer. J Urol 2015;194:73–8.

[16] Friedlander DF, von Landenberg N, Loppenberg B, et al. Facility level variation in rates of definitive therapy for low risk prostate cancer in men with limited life expectancy: an opportunity for value based care redesign. J Urol 2019;201:728–34.

[17] Rosen JE, Hancock JG, Kim AW, Detterbeck FC, Boffa DJ. Predictors of mortality after surgical management of lung cancer in the National Cancer Database. Ann Thorac Surg 2014;98:1953–60.

[18] Cole AP, Trinh QD. Secondary data analysis: techniques for comparing interventions and their limitations. Curr Opin Urol 2017;27:354–9.

[19] Rao J, Scott A. On simple adjustments to chi-square tests with sample survey data. Ann Stat 1987: 385–97.

[20] Lipsitz SR, Fitzmaurice GM, Sinha D, Hevelone N, Giovannucci E, Hu JC. Testing for independence in contingency tables with complex sample survey data. Biometrics 2015;71:832–40.

[21] Cole AP, Leow JJ, Chang SL, et al. Surgeon and hospital level variation in the costs of robot-assisted radical prostatectomy. J Urol 2016;196:1090–5.

[22] Leow JJ, Cole AP, Seisen T, et al. Variations in the costs of radical cystectomy for bladder cancer in the USA. Eur Urol 2017;73:374–82.

[23] Baldwin LM, Andrilla CH, Porter MP, Rosenblatt RA, Patel S, Doescher MP. Treatment of early-stage prostate cancer among rural and urban patients. Cancer 2013;119:3067–75.

[24] Hoffman KE, Niu J, Shen Y, et al. Physician variation in management of low-risk prostate cancer: a population-based cohort study. JAMA Intern Med 2014;174:1450–9.

[25] Mitchell JM. Urologists' use of intensity-modulated radiation therapy for prostate cancer. N Engl J Med 2013;369:1629–37.

[26] Wright JD, Tergas AI, Hou JY, et al. Effect of regional hospital competition and hospital financial status on the use of robotic-assisted surgery. JAMA Surg 2016;151:612–20.