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Longitudinal Comparison of Patient-Level Outcomes and Costs Across Prostate Cancer Treatments With Urinary Problems

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Abstract

Prostate cancer (PCa) is the leading cancer in men in the United States. This study evaluated direct costs of treating urinary problems after PCa treatments and determined predictors of long-term costs for urinary problems. Data from the Cancer of Prostate Strategic Urologic Research Endeavor registry was analyzed for this study. Annual treatment costs for urinary problems for up to 14 years were compared among different primary PCa treatments, which included radical prostatectomy, external beam radiation therapy, brachytherapy, and watchful waiting. A multivariate generalized estimating equation (GEE) model with bootstrapping was estimated to identify the predictors associated with treatment costs for urinary problems. A total of 3,062 eligible patients were identified with a mean age of 65 years at diagnosis. Mean annual treatment cost for urinary problems across all patients with PCa was $118/patient. Those greater than 74 years old had the highest cost ($238/patient). Mean annual cost for urinary problems among only those with urinary problems was $432. Multivariate regression showed patients undergoing radical prostatectomy had significantly lower (−63%, $p = .01$) costs for urinary problems than those treated with watchful waiting. This study helps to understand the importance of treating urinary problems associated with different PCa treatments and highlights their medical care costs. The pattern of treatment costs for urinary problems across all PCa treatments suggests that clinicians need to offer treatment for urinary problems to all PCa patients over longer time periods, even to those choosing watchful waiting.

Keywords

American men, prostate cancer, urinary problems, treatment costs comparison

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Prostate cancer (PCa) is the leading cancer in men in the United States and accounts for 10% of all cancer mortality. For 2018, it is estimated that 164,690 new cases will be diagnosed and 29,430 men will die of PCa (American Cancer Society, 2018).

There are four standard treatments for PCa: (a) radical prostatectomy, a surgical procedure to remove the entire prostate gland; (b) external beam radiation therapy, which involves the delivery of radiation externally to target tumor cells; (c) brachytherapy, an internal radiation therapy procedure; and (d) watchful waiting, an alternative to definitive treatment for men with low-risk PCa (Abouassaly, Lane, Lakin, Klein, & Gill, 2006; Arredondo et al., 2008; Bill-Axelson et al., 2014; Sanda et al., 2008; Thompson et al., 2007). The Agency for Healthcare Research and Quality (AHRQ) systematic review of the

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treatment types concluded that no single therapy can be considered the preferred treatment due to limitations in the evidence weighing survival and adverse events. Surgical and radiation therapy for treating PCa affects the patient's urinary health significantly (Litwin, Pasta, Yu, Stoddard, & Flanders, 2000; Wallis et al., 2016), and health-related quality of life (HRQOL) was identified to be a major determinant of treatment selection and a major factor in the assessment of treatment outcomes for PCa (Arredondo et al., 2008; Hu, Elkin, Krupski, Gore, & Litwin, 2006; Lubeck, Litwin, Henning, & Carroll, 1997).

Urinary problems associated with PCa treatments are defined as (a) the functional dysfunctions and (b) bother that relate to urinary health, including urinary incontinence, urinary irritation (frequent urination, pain or burning with urination, urinary urgency, waking up to urinate, and blood in the urine), and urinary obstruction (Sanda et al., 2008). Urinary problems following treatment for localized PCa are as high as 80% with significant quality-of-life impact (Abouassaly et al., 2006; Grise & Thurman, 2001). The clinical outcomes of treating urinary problems in men after PCa surgery have been evaluated in the literature (Ellison, He, & Wood, 2013; Kimura et al., 2010; Lubeck et al., 1997; Robinson et al., 2006), but little has been done to assess the costs of treating urinary problems after PCa.

This study aimed first to determine the average 3-month direct treatment costs of urinary problems associated with PCa and compare them across four standard primary treatment types. Second, we used regression analyses to determine the predictors of these costs within and across treatments for PCa.

Materials and Methods

Design

The Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™) PCa registry patient data were used for this study. This well-established national longitudinal registry was founded in 1995 and continues to enroll PCa patients treated with various types of therapy in the United States. The registry data include ongoing data of clinical risk and treatment information provided by physicians, as well as the health outcomes and healthcare utilization data collected from patient-reported questionnaires. Study data included data for men with PCa enrolled from 1995 through 2008 and follow-up data through 2012 (Lubeck et al., 1996). The initial CaPSURE registry collected clinical data continuously and quality-of-life data directly from participants at 3-month intervals, extended to every 6 months in 1999, and beginning in 2012, every 12 months (Lubeck et al., 1996). CaPSURE data include clinical data, treatments, cancer staging, medications prescribed and health services utilizations, as well as HRQOL questionnaire responses and have been described in detail previously (Litwin et al., 2000; Lubeck et al., 1996, 1997). This study has been approved by the University of California San Francisco Institutional Review Board (approval 10-02087).

Sample

Subjects for this study were selected from CaPSURE if they met the following inclusion criteria. First, they were diagnosed with PCa within 6 months of enrollment in CaPSURE; second, they provided a pretreatment HRQOL score; third, they had at least one follow-up interview; and finally, they had selected primary treatment with either radical prostatectomy, brachytherapy, external beam radiation therapy, or watchful waiting.

Variables

Cost variables. Total treatment costs associated with urinary problems were measured quarterly for each patient to keep cost data consistent with the variation in data collection time periods. If data were only available for every 6 or 12 months after 1999, these cost values were partitioned equally to each 3-month period during the 6 or 12 months. Treatment costs of urinary problems included utilization of corrective surgical procedures and medications that were used to reduce muscle spasms in the bladder and urinary tract. Surgical procedures were identified using *Current Procedural Terminology* (CPT) codes and *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) procedure codes, place of service, and length of stay to calculate the hospital treatment costs. Hospital length of stay per each type of procedure was recorded in CaPSURE and cost was applied for this analysis using Health Care Costs and Utilization Project (HCUP) national surgical procedure costs per day (AHRQ, 2012). Surgeries included the sling operation for correction of male urinary incontinence (CPT 53440), removal or revision of sling for male urinary incontinence (CPT 53442), and placement of inflatable urethral/bladder *neck sphincter*, including placement of pump, reservoir, and cuff (CPT 53445), and transurethral resection of the prostate (TURP) for lower urinary tract symptoms (LUTS) or direct vision urethrotomy (CPT 52276). For each surgical procedure, we also included the costs of two inpatient physician visits (CPT 99223/99235) and two outpatient physician visits (CPT 99204/99215), using costs from the Medical Fee Schedule for 2010. Consumer Price Index 2012 was used to convert 2010 costs to the 2012 dollar value by detailed categories (see Appendix). In CaPSURE, patients' medication regimens were collected from surveys and the

2012 cost of medications was calculated from the RED BOOK™ using lowest average wholesale price (AWP) minus 17% to match average drug costs. Total annual mean costs per person were calculated as the sum of four 3-month treatment periods and were calculated across all patients, whether or not they had a treatment for urinary problems (cost with zeros) and also for just those patients who incurred a treatment for urinary problems (cost without zeros). Total 3-month treatment costs for urinary problems across all patients were used as the dependent variable in the regression models.

Independent variables. Independent variables included type of primary PCa treatment, risk group, age, race/ethnicity, family relationships, body mass index (BMI) categories, comorbidity counts, pretreatment urinary function and urinary bother scores, and change in urinary function and urinary bother over time from pretreatment scores. These independent variables acted as potential predictors of long-term costs for treatment of urinary problems.

Risk group at diagnosis was determined using the D'Amico risk classification algorithm, which classified the PCa as mild, moderate, or severe based on a combination of PSA, Gleason Score, and T stage at diagnosis (D'Amico et al., 1998). Although there are other staging systems that more specifically differentiate early disease for mortality outcomes, this staging was used across all study years in the CaPSURE data set and is consistent with the study aims to determine general cost differences. Age at diagnosis of PCa was grouped as <55, 55–64, 65–74, and 75+ years. Race/ethnicity was White, African American, and other. Family relationships included living with spouse or partner, in a significant relationship, not in a significant relationship, and widowed. BMI was categorized using the Centers for Disease Control and Prevention (CDC) criteria as underweight (<18.5), normal (18.5–24.9), overweight (25–29.9), and obese (≥ 30).

Urinary function and urinary bother were measured using the University of California, Los Angeles (UCLA)-Prostate Cancer Index (PCI). The UCLA-PCI assesses disease-specific, organ-targeted HRQOL, including urinary function and urinary bother as subdomains. The scores for urinary function were evaluated based on several UCLA-PCI questionnaire items, including urine leakage, urinary control, pad counts, urine dripping, and urine leakage interfering with sexual activity. Urinary function does not, however, ask about urinary irritation, which can be an important side effect of primarily radiation therapies. The scores for urinary bother refer to patients' personal perception of overall urinary function. The UCLA-PCI uses a scale of 0 to 100 where higher scores indicate better function and less bother. A meaningful change in urinary function and bother from pretreatment was defined as a 0.5 standard deviation change (Guyatt, Osoba, Wu, Wyrwich, & Norman, 2002; Norman, Sloan, & Wyrwich, 2003).

Statistical Analysis

Descriptive analysis was conducted to compare patients' demographics and baseline clinical information between different treatment types. In Table 1, means for continuous measures were compared using one-way analysis of variance (ANOVA) to determine significant differences among primary treatment groups. Proportions for categorical measures of potential predictors of the costs of urinary problems were compared using a Pearson chi-square test. The distribution of cost data was tested and most closely fit a gamma distribution (Laird & Ware, 1982). Therefore, a GEE model with a gamma family and log link function was used to control for the skewed nature of the cost data (Lord & Asante, 1999). The GEE model controls for repeated observations from the same subject over time. Bootstrapped 3-month costs were calculated to obtain standard errors.

For analysis of the second aim to determine predictors of total costs of treatment for urinary problems, multivariate regressions of generalized estimating equations (GEE) models were used as a function with bootstrapped 3-monthly costs as the dependent variable and the previously described potential predictors as independent variables. The STATA's GEE method enables us to account for correlation across repeated observations from the same subject over time and to fit a multivariate linear model to compare the relative effects of primary treatment, risk group, age at diagnosis, change in urinary function and urinary bother, BMI, race/ethnicity, and family relationships on total 3-monthly treatment costs of urinary problems across all years (Marcus et al., 2005). The variables chosen for the regressions were those variables with statistical significance used in the regression models developed to predict urinary function change scores in a previous paper by the research team (Alemozaffar et al., 2011).

The watchful waiting patients were set as the reference group not only because this group of patients received active surveillance monitoring in CaPSURE but also because watchful waiting patients can act as a partial control for age-related changes in urinary function, since they have no active PCa treatment affecting their urinary function (Wilson et al., 2007). For other categorical independent variables, the youngest (age at diagnosis less than 55 years), low-risk group, no decline/improvement in urinary function and urinary bother change, living with spouse or partner, White race, and zero comorbidity, were used as reference groups in the multivariate regression models.

Table 1. Patient Demographic and Clinical Characteristics.

	Treatment type					
	All	Radical prostatectomy (*n*, %)	Brachytherapy (*n*, %)	External beam radiation therapy (*n*, %)	Watchful waiting (*n*, %)	
Characteristic	*N* = 3,062	2,018 (66%)	568 (19%)	408 (13%)	68 (2%)	*p* value
Age at diagnosis (median, IQR)	65 (59–70)	62 (56–67)	69 (64–4)	72 (67–76)	73.5 (68–78.5)	<.001*
Age group (*n*, %)						
<55	383 (13%)	353 (17%)	24 (4%)	5 (1%)	1 (1%)	
55–64	1,167 (38%)	964 (48%)	133 (23%)	60 (15%)	10 (15%)	
65–74	1,204 (39%)	668 (33%)	293 (52%)	216 (53%)	27 (40%)	
75+	308 (10%)	33 (2%)	118 (21%)	127 (31%)	30 (44%)	
Race (*n*, %)						.06
White	2,794 (92%)	1,855 (92%)	513 (91%)	366 (91%)	60 (90%)	
African American	167 (5%)	101 (5%)	27 (5%)	33 (8%)	6 (9%)	
Other	81 (3%)	53 (3%)	22 (4%)	5 (1%)	1 (1%)	
Risk group (*n*, %)						<.001*
Low risk	1,467 (51%)	991 (52%)	331 (62%)	107 (27%)	38 (63%)	
Intermediate risk	955 (33%)	635 (33%)	155 (29%)	149 (37%)	16 (27%)	
High risk	483 (17%)	288 (15%)	46 (9%)	143 (36%)	6 (10%)	
Number of comorbidities (*n*, %)						<.001*
0	472 (16%)	382 (19%)	52 (9%)	34 (8%)	4 (6%)	
1	892 (30%)	639 (32%)	151 (27%)	90 (22%)	12 (18%)	
2	824 (27%)	528 (27%)	162 (29%)	115 (29%)	19 (29%)	
3+	817 (27%)	436 (22%)	188 (34%)	162 (40%)	31 (47%)	
Urinary function						
Pretreatment						
Mean (*SD*)	93 (12.75)	93 (12.29)	92 (12.39)	91 (13.54)	89 (20.42)	<.001*
Min–max	7–100	7–100	28–100	26.67–100	16.67–100	
Change						
Mean (*SD*)	−14 (21.08)	−19 (22.33)	−6.59 (16.04)	−3 (12.74)	−5 (13.07)	<.001*
Min–max	−93.89 to 90	−94 to 88	−65 to 90	−45 to 46.67	−54.58 to 34	
Urinary bother						
Pretreatment						
Mean (*SD*)	86 (22.76)	87 (21.24)	86 (22.65)	81 (27.25)	80 (31.29)	<.001*
Min–max	0–100	0–100	0–100	0–100	0–100	
Change						
Mean (*SD*)	−8 (26.91)	−8 (27.32)	−11.03 (24.75)	−3 (27.23)	−3 (25.18)	<.001*
Min–max	−100 to 100	−100 to 100	−100 to 100	−100 to 100	−100 to 75	
BMI at pretreatment (*n*, %)						.139
Normal	763 (26%)	480 (24%)	152 (28%)	111 (29%)	20 (31%)	
Overweight	1,546 (52%)	1,065 (54%)	268 (49%)	183 (48%)	30 (46%)	
Obese	661 (22%)	428 (22%)	127 (23%)	91 (24%)	15 (23%)	
Relationship status (*n*, %)						<.001*
Living with spouse or partner	2,677 (90%)	1,824 (92%)	479 (87%)	320 (81%)	54 (82%)	
In a significant relationship	97 (3%)	57 (3%)	26 (5%)	13 (3%)	1 (2%)	
Not in a significant relationship	157 (5%)	89 (4%)	29 (5%)	33 (8%)	6 (9%)	
Widowed	72 (2%)	23 (1%)	17 (3%)	27 (7%)	5 (8%)	
PSA level at pretreatment (median, IQR)	5.6 (4.3–8.0)	5.3 (4.2–7.3)	5.6 (4.4–7.4)	7.7 (5.2–12.9)	5.6 (4.1–8.1)	<.001*

Note. BMI = body mass index; IQR = interquartile range.
*$p < .05$.

Results

Pretreatment Characteristics

From the overall 13,801 CaPSURE participants by 2008, 3,276 patients who met all study inclusion criteria were selected. After excluding patients with combination PCa treatments, 3,062 patients were analyzed. The mean follow-up from the inception of the study was 4 years and maximum was 12.8 years. For the 2,018 (66%) patients who underwent radical prostatectomy procedure, the mean follow-up time was 4.0 years (range, 0.25–12.8 years); for the 568 (19%) patients who had brachytherapy procedure, the mean follow-up time was 4.0 years (range, 0.25–11.8 years); for the 408 (13%) patients who had external beam radiation therapy procedure, the mean follow-up time was 3.8 years (range, 0.25–11.5 years); and for the 68 (2%) patients who underwent watchful waiting, the mean follow-up time was 2.9 years (range, 0.5–9. 5 years). The overall median age was 65 years, with 2,796 (92%) Caucasians. The distribution of PCa treatment types, demographics characteristics, and clinical measures are shown in Table 1.

Annual Treatment Costs of Urinary Problems

The annual mean treatment cost of urinary problems per person across all patients and PCa treatment types was $118. Brachytherapy had the highest annual cost of urinary problems, $304, while radical prostatectomy had the lowest at $46 per patient. The youngest age group had lowest annual cost of urinary problems, $28, and the oldest age group had the highest at $238. Annual mean cost of urinary problems of those actually incurring urinary problems costs (excluding zero values) was high ($432/patient), considering the average treatment time was 4 years. Treatment costs for urinary problems across PCa treatment types and age groups were statistically significant across all patients and also were statistically significant across PCa treatment types for just those incurring costs for urinary problems (Table 2).

Costs Differences by Urinary Function and Urinary Bother Scores

We found that urinary function and bother scores both became worse 3 months after the pretreatment and improved from 6 months to 9 months, remaining relatively stable up to 3 years (see figure in supplement). Then, urinary function and bother scores became variable at later life years for PCa patients. Correspondingly, treatment costs for urinary problems increased to the highest right after the pretreatment, dropped to a lower cost, and then maintained a relatively stable cost level throughout the follow-up years for those with radical prostatectomy and external beam radiation therapy. Meanwhile, 3-month treatment costs for urinary problems for brachytherapy and watchful waiting increased after pretreatment and varied but kept an upward trend for the entire follow-up period. We also reported urinary function and bother with related urinary problems costs by age groups across all PCa treatment types, showing that younger ages recover more and are associated with lower urinary problems cost than older men.

Predictors of Treatment Cost for Urinary Problems Within and Across PCa Treatments

The individual predictors found significant in bivariate models were included in the multivariate bootstrapped GEE model to predict urinary treatment costs (Table 3). The results demonstrated that radical prostatectomy had a statistically significant negative effect on the 3-month treatment costs of urinary problems with a 62.99% cost reduction ($p = .01$) compared to watchful waiting. The patient's age didn't have additional effects on these costs. Being overweight (50.25%, $p = .044$), having three or more comorbidities (99.56%, $p = .03$), and a worsening change in urinary bother (119.24%, $p < .001$) had significant positive effects, while having a pretreatment urinary function deficit and greater bother scores (2.89%, $p = .024$ and 0.84%, $p = .031$), respectively, had significant negative effects on 3-month treatment costs for urinary problems cost. Being overweight increased these costs by 50.25%, while pretreatment urinary function deficits and greater bother scores led to cost reductions of 2.89% and 0.84%, respectively.

We also looked at the cost predictors within each treatment and these varied across treatments (Table 4). Having had a radical prostatectomy and being 65–74 years old rather than younger increased cost by 159% ($p = .035$); being an overweight or obese BMI increased cost by 112% ($p = .029$) and 163% ($p = .020$), respectively. Urinary bother significantly worse from baseline (146%, $p < .001$) had significant increasing effects on the 3-month treatment costs for urinary problems, showing that each 1-unit increase in urinary bother score change from baseline was associated with an increased cost of 146%. In those whose PCa was treated with brachytherapy, only the number of comorbidities had a significant positive effect on the 3-month treatment cost of urinary problems. In those with external beam radiation therapy, pretreatment urinary bother also had a statistically significant negative effect on 3-month treatment cost for urinary problems. Pretreatment urinary function and bother scores had negative effects on 3-month treatment costs for urinary problems in patients

Table 2. Annual Mean Cost Per Patient for Treatment of Urinary Problems.

	All	Radical prostatectomy (*n*, %)	Brachytherapy (*n*, %)	External beam radiation therapy (*n*, %)	Watchful waiting (*n*, %)	
	3,062	2,018 (66%)	568 (19%)	408 (13%)	68 (2%)	*p* value
Mean annual cost per person (with zero values)						
Mean (*SD*)	118.31 (341.84)	45.91 (215.26)	304.26 (417.53)	207.02 (558.9)	231.17 (332.59)	<.001*
Min–max	0–8,680.50	0–4,290.33	0–2,729.26	0–8,680.50	0–1,398.00	
Cost by age group						
<55, *n*	383	353	24	5	1	
Mean (*SD*)	28.53 (118.37)	16.64 (88.77)	188.49 (273.34)	105.56 (203.4)	0	<.001*
Min–max	0–904.2	0–904.2	0–860.8	0–466.27	0	
55–64, *n*	1,167	964	133	60	10	
Mean (*SD*)	79.96 (273.04)	38.00 (200.98)	345.84 (488.61)	150.93 (269.94)	207.28 (331.69)	<.001*
Min–max	0–3,742.89	0–3,742.89	0–2,729.26	0–1,273.73	0–968.40	
65–74, *n*	1,204	668	293	216	27	
Mean (*SD*)	153.41 (417.06)	71.36 (273.73	281.48 (386.52)	231.94 (692.42)	226.12 (379.99)	<.001*
Min–max	0–8,680.5	0–4,290.33	0–2,043.91	0–8,680.5	0–1,398.8	
>75+, *n*	308	33	118	127	30	
Mean (*SD*)	238.07 (384.78)	74.89 (176.06)	337.51 (425.23)	195.14 (390.33)	251.38 (299.12)	.001*
Min–max	0–2,219.18	0–768.69	0–1,984.29	0–2,219.18	0–941.50	
Mean annual cost per person (without zero values)						
n (% of total)	838 (27.4%)	275 (13.6%)	371 (65.3%)	162 (39.7%)	30 (44.1%)	
Mean (*SD*)	432.31 (539.85)	336.89 (492.67)	465.82 (437.83)	521.39 (790.4)	523.98 (311.19)	.002*
Min–max	1.14–8,680.50	2.12–4,290.33	1.14–2,729.26	8.43–8,680.50	7.15–1,398.80	

Note. *$p < .05$.

who underwent radical prostatectomy, brachytherapy, and external beam radiation therapy (Table 4).

Discussion

The current study had several important findings. First, this is the first study to determine the costs of treatments for urinary problems after PCa by different PCa treatment types, age, and urinary function and bother longitudinally. Direct cost of treating urinary problems per patient estimated in this study was $118 annually across all treatment types. This is only 1% of the annual PCa treatment cost ($12,527/patient, 2012 USD; Roehrborn & Black, 2011), only 2% of the annual direct cost ($5,555/patient, 2012 USD) of treating all-cause institutional urinary incontinence (UI), and only 14% ($832/patient, 2012 USD) of UI treatment cost in the community dwelling (Wilson, Brown, Shin, Luc, & Subak, 2001). If we only look at the cost for patients who actually seek medical attention for their urinary problems, the annual cost/patient across all treatment types was $432 based on the analysis. This cost is 3.4% of the average cost of treating PCa and 52% of the cost of treating all-cause UI. The variability observed in the limited literature describing the costs of treatments for urinary problems likely reflects the different populations and reasons for urinary problems. Most existing costs estimates are for UI across all causes and in female populations, unlike the current study costs, which focus on urinary problems in men and those resulting from a PCa treatment effect along with male aging. Our study contributes to the literature on cost analysis by including treatment costs of urinary problems for the first time and is highly relevant to the management of PCa treatment choices.

High cost of urinary problems is ideally the result of adequate treatment of urinary problems, which may lead to improved urinary function and lower urinary bother, while low or absent costs for urinary problems is likely the result of either good PCa clinical outcomes or inadequate treatment for urinary problems. For example, in the current study, radical prostatectomy patients (mean 55–64 years old) are normally younger than other PCa-treated patients. They usually have lower disease risk and they have the worst posttreatment urinary function but worry the least (high urinary bother scores) about their urinary health. Also, they have the lowest treatment costs for urinary problems. This implies radical prostatectomy patients have less concern about the amount of urinary problems they have and given their low urinary function score, they may not have been offered enough treatment for their urinary problems. External beam radiation therapy patients are the second oldest (65–74 years)

Table 3. Multivariate GEE Model of Predictors for Treatment Costs for Urinary Problems.

Variables	Observed coef.	Bootstrapped *SE*	*p* value	95% CI Lower	95% CI Upper	$(e^{(coef.)} - 1) \times 100$ (%)
Constant	5.34	1.130	<.000***	3.130	7.550	
Treatment types						
Radical prostatectomy ($N = 2{,}019$)	−0.99	0.386	.010**	−1.751	−0.237	−62.99
Brachytherapy ($N = 568$)	0.53	0.351	.134	−0.161	1.214	69.3
External beam radiation therapy ($N = 408$)	0.23	0.397	.562	−0.548	1.008	25.85
Watchful waiting ($N = 68$)		Reference group				
Age at diagnosis						
55–64	0.42	0.423	.323	−0.412	1.248	51.93
65–74	0.71	0.419	.09	−0.112	1.530	103.23
75+	0.79	0.464	.089	−0.12	1.699	120.33
<55		Reference group				
BMI at pretreatment						
Overweight	0.41	0.202	.044*	0.011	0.803	50.25
Obese	0.37	0.264	.156	−0.143	0.892	45.47
Normal		Reference group				
Number of comorbidities						
1	0.53	0.388	.169	−0.226	1.294	70.52
2	0.45	0.345	.190	−0.224	1.127	57.08
3+	0.69	0.318	.030*	0.068	1.314	99.56
0		Reference group				
Pretreatment UF	−0.02	0.011	.024*	−0.045	−0.003	−2.39
Pretreatment UB	−0.01	0.004	.031*	−0.016	−0.001	−0.84
UB changes[a]	0.78	0.188	<.000***	0.416	1.154	119.24

Note. BMI = body mass index; GEE = generalized estimating equation; UB = urinary bother; UF = urinary function.
[a]This change represented urinary bother score change using 0.5 standard deviation from baseline.
*$p < .05$. **$p < .01$. ***$p < .001$.

compared to other PCa patients in this study; they have the highest disease risk and the best posttreatment urinary function and bother, but they have the second highest treatment costs for urinary problems. Similar to patients receiving external beam radiation therapy, the brachytherapy group has relatively older patients than those receiving radical prostatectomy with good posttreatment urinary function and bother but the highest treatment costs for urinary problems. This is because radiation patients may be receiving effective treatment for their urinary problems. Meanwhile, watchful waiting patients were the oldest patient group; they have similar disease risk as radical prostatectomy patients and better urinary function than radical prostatectomy patients, but the worst urinary bother among all the PCa treatment options and they have the second lowest cost of urinary problems in our study. This may indicate a likely aging effect for their urinary problems and those watchful waiting patients may be undertreated.

The use of GEE regression models enables us to determine important predictors for treatment costs of urinary problems. The current study shows radical prostatectomy is a predictor of lower treatment costs for urinary problems. This may be because most patients are younger compared to patients who undergo other treatment options. Also, not like with other PCa treatments, urinary function and bother scores after radical prostatectomy decline and then improve substantially and remain stable afterward. This observation is also found in the literature (Litwin et al., 2000). Therefore, the long-term treatment cost for urinary problems after radical prostatectomy was lower than other treatment options despite the patients' low urinary function scores and perhaps because of their lack of bother about their urinary problems. Within the individual treatments, age group 65–74 years, BMI, and urinary bother change were associated with long-term treatment costs for urinary problems after radical prostatectomy s (Litwin et al., 2000).

The observed high treatment costs of urinary problems with better urinary function and bother scores should be interpreted in the light of one limitation. Urinary irritation was not able to be measured in CaPSURE because it is not included in the urinary function HRQOL questionnaire, so the urinary function scores in our study were

Table 4. GEE Models for Urinary Problems Cost Within PCa Treatment Type.

Treatment, variable	Observed coef.	Bootstrap *SE*	*p* value	95% CI Lower	95% CI Upper	$(e^{(coef.)} - 1) \times 100$ (%)
Radical prostatectomy						
Constant	5.34	1.098	.000*	3.191	7.494	
Age groups						
55–64	0.17	0.500	.737	−0.813	1.149	18.27
65–74	0.95	0.452	.035*	0.065	1.838	159.05
75+	1.00	0.825	.227	−0.619	2.614	171.17
<55			Reference group			
BMI level						
Overweight	0.75	0.345	.029*	0.076	1.428	112.20
Obese	0.97	0.416	.020*	0.152	1.783	163.15
Normal			Reference group			
Pretreatment UF	−0.04	0.011	.000***	−0.062	−0.0205	−4.04
UB change[a]	0.90	0.230	.000***	0.451	1.354	146.50
Brachytherapy						
Constant	5.00	0.343	.000***	4.330	5.673	
Number of comorbidity						
1	0.41	0.252	.107	−0.086	0.9006	50.12
2	0.61	0.262	.019*	0.102	1.128	84.91
3+	0.83	0.260	.001***	0.317	1.335	128.44
0			Reference group			
Pretreatment UB	−0.01	0.003	.000***	−0.018	−0.008	−1.27
External beam radiation therapy						
Constant	5.82	0.510	.000***	4.816	6.816	
Number of comorbidity						
1	−0.28	0.506	.586	−1.266	0.715524	−24.06
2	−0.07	0.493	.892	−1.033	0.899765	−6.46
3+	0.33	0.411	.418	−0.473	1.139	39.53
0			Reference group			
Pretreatment UB	−0.02	0.005	.000***	−0.028	−0.011	−1.93

Note. BMI = body mass index; GEE = generalized estimating equation; UB = urinary bother; UF = urinary function.
[a]This change represented urinary bother score change using 0.5 standard deviation from baseline.
*$p < .05$. **$p < .01$. ***$p < .001$.

probably overestimated for nonsurgical patients, who have less irritation. However, the urinary irritation treatments were captured in the health-care utilization and the cost of urinary irritation was included in the costs for treating urinary problems, so derived costs could be higher than the urinary function indicates.

In general, urinary problems can occur with any form of PCa treatment. By understanding the costs of medical care for urinary problems, clinicians and patients can weigh the long-term cost versus clinical benefit of each PCa treatment. Furthermore, this study can remind clinicians to offer treatment for urinary problems to all PCa patients, even those choosing watchful waiting, and also across a longer time period than their immediate recovery from the primary PCa treatment. Future study of cost-effectiveness analysis could further quantify the effectiveness of urinary problems treatment and provide valuable evidence for decision makers on selection of the PCa treatment.

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