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Robust Health Utility Assessment Among Long-term Survivors of Prostate Cancer: Results from the Cancer of the Prostate Strategic Urologic Research Endeavor Registry

Chang Wook Jeong[a,b,*], *Janet E. Cowan*[a], *Jeanette M. Broering*[a], *Renske M.T. ten Ham*[c,d], *Leslie S. Wilson*[c], *Peter R. Carroll*[a], *Matthew R. Cooperberg*[a,e]

[a] *Helen Diller Family Comprehensive Cancer Center, Department of Urology, University of California, San Francisco, CA, USA;* [b] *Department of Urology, Seoul National University Hospital, Seoul, Republic of Korea;* [c] *Health Policy and Economics, Department of Clinical Pharmacy, University of California, San Francisco, CA, USA;* [d] *Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands;* [e] *Department of Epidemiology & Biostatistics, University of California, San Francisco, CA, USA*

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Abstract

Background: Valid health utility values are essential for comparative effectiveness analyses. However, subjective utilities in long-term survivors of prostate cancer (PCa) with various oncological and functional outcomes have not been well described.
Objective: To quantify utilities in long-term survivors of PCa using the standard gamble method, generally regarded as the approach best grounded in economic theory.
Design, setting, and participants: We performed a cross-sectional study nested within a prospective cohort—Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE). Overall, 1884 (59.7%) of 3155 active participants across all disease states returned the questionnaire.
Intervention: Various primary treatments for PCa.
Outcome measurements and statistical analysis: Utility values for PCa health, sexual function, urinary function, bowel function, and overall health were measured, based on patients' conditions at the time of the survey. Bias correction methods were employed.
Results and limitations: After exclusion of incomplete or disqualified data, 1740 (92.3% of responding) patients were included in the final analysis. The mean age was 73.1 ± 8.2 yr at a median of 9 yr (interquartile range: 6–11) since diagnosis. Mean utilities for PCa health and overall health were 0.934 ± 0.120 and 0.960 ± 0.100, respectively. After bias correction by probability weighting function, utilities were 0.866 ± 0.154 and 0.897 ± 0.142, and by mixed model correction, 0.845 ± 0.186 and 0.884 ± 0.176, respectively. Measured utilities were similarly high for specific functional outcomes, even with bias corrections. Survivorship bias and skewed proportion of disease status due to natural history of PCa were potential limitations.
Conclusions: Standard gamble-based utilities in long-term survivors of PCa were much higher than those determined previously. The results indicate substantial human resilience: most PCa patients adapt to their health status over time even if they experience incomplete functional recovery and would not take risk in pursuit of better quality of life.
Patient summary: We elicited health utilities (measures of quality of life) among long-term survivors of prostate cancer using the most robust method. These were much higher than previously reported values that were based on theoretical scenarios or indirect methods. Long-term survivors of prostate cancer may adapt well to their health conditions over time even if they experience disease-specific or functional problems.

* Corresponding author. Department of Urology, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea.
E-mail address: drboss@snu.ac.kr (C.W. Jeong).

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1. Introduction

Comparative effectiveness studies frequently adjust years of life saved by a health utility score in an effort to quantify quality of life (QoL) outcomes. Perfect health is assigned a utility value of 1 and death a value of 0. Distinct from descriptive health-related QoL (HRQoL) measurements, which can be reported on a variety of scales, utilities are intended to be weighted as standardized values used to calculate quality-adjusted life years (QALYs) [1], which are critical for cost effectiveness and related analyses [2].

However, well-defined utilities for prostate cancer (PCa) health states are sparse in the literature. Typically, studies determine utility values either by indirect methods, using hypothetical scenarios among those without cancer, or using small numbers of patients with newly diagnosed disease [3–5]. In fact, most comparative effectiveness analyses in PCa cite a single 2005 study of 162 men, only half of whom had PCa [3]. Direct utility measurements in long-term cancer survivors are rare for all types of cancer [6]. Considering the growing number and importance of comparative effectiveness studies [2], reliable utility values for PCa generated by direct methods in large-scale studies are greatly needed.

The objective of the current study was to measure utility values directly from a large cohort of men with PCa with various disease states and functional outcomes, enrolled in a nationwide, prospective, multicenter cohort—Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE).

2. Patients and methods

2.1. Study design

CaPSURE is a nationwide, multicenter cohort of men with biopsy-proven PCa enrolled from 43 predominantly community-based urology practices across the USA since 1995 [7]. One of CaPSURE's major goals has always been to understand patients' HRQoL. To further this end, we executed a CaPSURE utility supplementary study (CaPSURE-USS) with a cross-sectional analysis using additional surveys.

CaPSURE-USS was designed to measure utility values and answer related questions such as comparability of different HRQoL instruments [8]. Thus, in addition to the routine questions, we sent a one-time supplemental questionnaire, which was a composite of nine instruments including a series of standard gamble (SG) exercises to CaPSURE participants (Supplementary Table 1).

We adapted a previously validated paper SG utility questionnaire for PCa [9,10]. In an SG utility questionnaire, a patient is asked what risk of immediate death he would accept to be assured of the resolution of a given health state. Patients were randomly assigned to receive either a survey version A (chance of cure first and risk of death later, utilities ordered high to low) or a survey version B (risk of death first and chance of cure later, utilities ordered low to high; Supplementary Appendix 1), with a block randomization design stratified by time since diagnosis (Supplementary Table 2).

2.2. Participants

A total of 3441 active CaPSURE participants were assessed for eligibility. Among them, 286 patients were excluded based on nonfluency in English, absence of a baseline survey, or inadequate follow-up, leaving 3155 (91.7%) participants eligible for the survey (Fig. 1).

2.3. Outcomes and measurements

"Response rate 2," defined by American Association for Public Opinion Research [11], was used to calculate the survey response rate.

We separately measured utility values for five domains (PCa status, sexual function, urinary function, bowel function, and overall health) based on each patient's own self-assessment (Supplementary Appendix 1). The utility value was defined as the midpoint of two neighboring probabilities of cure between which the preference changed (Supplementary Appendix 2). On the assumption that some participants would not have adequately understood the task, we also took steps to exclude irrational responses (Supplementary Appendix 2).

As prior evidence has suggested that expected utilities determined by SG can be upwardly skewed, we also calculated two bias-corrected values based on prospect theory [12–15], which describes how people differently estimate the value of losses versus gains and how they choose between alternative options [16,17]. The value function is concave for gains, usually convex for losses, and generally steeper for losses than for gains [16]. The first method is a one-parameter weighting correction based on probability transformations [14,15]. We used this function with the assumption probability weighting parameter γ for version A = 0.61 and the best matched γ for version B to minimize differences between mean utility values.

The second method is gain-and-loss mixed modeling using the probability equivalence method, further adjusting for loss aversion [12,15]. In the SG, gambles may be perceived as gain (cure/restoration of function) and loss (risk of death) at the same time. Thus, this model includes a probability weight for the loss and loss aversion parameter λ. We applied this model with λ for version A = 2.25 and the best-matched λ for version B with the same principle (Supplementary Appendix 3) [12,15].

2.4. Statistical analyses

We first compared demographic and clinical characteristics between responders and nonresponders. The comparison was performed using a χ^2 test for categorical variables and t test for continuous variables.

The main purpose of this study was description of the utility values. We summarized them as means with standard deviations. However, we also presented medians and 95% confidence intervals of utilities for future usage when needed. We calculated utility values in each disease status at the time of the survey. The disease states included (1) active surveillance (AS) without treatment, (2) watchful

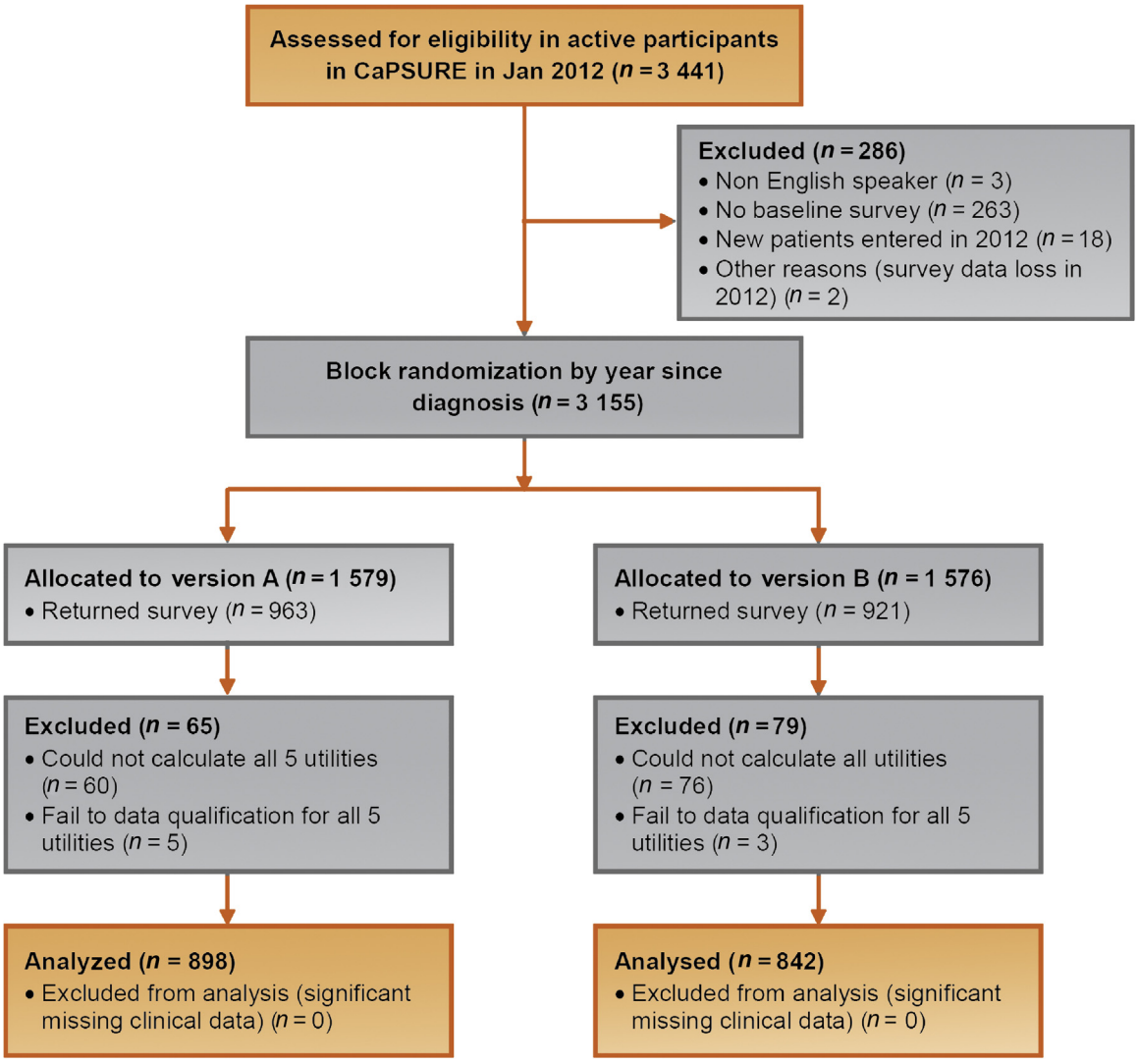

Fig. 1 – Patient flow diagram.
CaPSURE = Cancer of the Prostate Strategic Urologic Research Endeavor.

waiting without treatment, (3) no evidence of disease (NED) after definitive treatment, (4) biochemical recurrence (BCR) without metastasis after definitive treatment, (5) remission, (6) androgen deprivation therapy (ADT) without known metastasis, and (7) metastatic disease. BCR was defined as either rising prostate-specific antigen (PSA; two consecutive PSA values of ≥0.2 ng/ml after radical prostatectomy, or PSA failure by Phoenix criteria of two increases after nadir PSA following radiation or cryotherapy) or initiation of any salvage treatment. We separately defined remission status from BCR as controllable disease after secondary definitive treatment for BCR without current use of long-term ADT. We also included disease controlled with temporary, primary ADT without its ongoing use. However, off-ADT states during long-term intermittent ADT were not included.

We also calculated utility values categorized by functional status. Urinary function was characterized by continence status and urinary symptoms by International Prostate Symptom Score total or QoL score. Sexual function was characterized by potency as reported by EPIC-26 question 9 and general function by Sexual Health Inventory for Men score. Bowel function was determined using EPIC-26 question 7.

We also evaluated utility values by initial treatment. Finally, effects of treatment history such as radical prostatectomy or radiation therapy regardless of initial treatment were evaluated. Comparison between utilities was performed using *t* test or analysis of variance (ANOVA) test. All statistical analyses were performed using R for Windows, version 3.5.1 (http://www.r-project.org/).

3. Results

3.1. Survey results and data processing

Among all 3155 eligible participants, 1884 men returned the survey. After exclusion of incalculable or otherwise disqualified utility responses (Supplementary Appendix

2), 1740 patients were included in the final analyses (Fig. 1). Thus, response rates of the CaPSURE-USS survey overall and SG utility questionnaire were 59.7% (1884/3155) and 55.2% (1740/3155), respectively. Supplementary Table 3 shows the distribution of patients grouped by questionnaire version (A or B) and time since diagnosis in the final analyses. Response rates were not statistically significantly different between versions (version A 56.9% [898/1579] vs version B 53.4% [842/1576], $p = 0.056$).

Comparisons of basic characteristics between the responders and nonresponders are presented in Table 1. Cancer characteristics were not different. Responders reported fewer comorbidities and higher income and education levels, and a greater proportion underwent radical prostatectomy.

3.2. Utilities and related results in total study population

Table 2 presents the results of uncorrected utility values and rating scales in each utility stratified by version. Version A had slightly higher PCa health utility than version B (mean difference 0.025, 95% confidence interval 0.013–0.037). However, other utilities did not differ between groups. We did not find any significant differences by duration since diagnosis (ANOVA test, all $p > 0.05$). Urinary utility value was significantly associated with younger age (ANOVA test,

Table 1 – Basic characteristics of the patients.

	Responders ($N = 1740$)	Nonresponders ($N = 1415$)	p-Value
Age at diagnosis (yr)	63.7 ± 7.7 (64.0, 58.0–9.0)	64.1 ± 8.2 (64.0, 58.0–70.0)	0.112
Age at survey (yr)	73.0 ± 8.2 (73.0, 67.0–79.0)	73.5 ± 9.2 (74.0, 69.0–80.0)	0.139
Duration from diagnosis (yr)	8.9 ± 4.0 (9.0, 6.0–11.0)	8.8 ± 4.3 (9.0, 6.0–11.0)	0.878
Duration from diagnosis (yr), *n* (%)			0.292
0–1	72 (4.1)	78 (5.5)	
2–4	42 (2.4)	41 (2.9)	
5–7	574 (33.0)	437 (30.9)	
8–10	600 (34.5)	469 (33.1)	
11–15	303 (17.4)	266 (18.8)	
16–30	149 (8.6)	124 (8.8)	
Questionnaire version, *n* (%)			0.056
A (utility high to low)	898 (51.6)	681 (48.1)	
B (utility low to high)	842 (48.4)	734 (51.9)	
Insurance, *n* (%)			0.240
Medicare supplement[a]	485 (27.9)	414 (29.3)	
Medicare only	179 (10.3)	163 (11.5)	
Private	961 (55.2)	758 (53.6)	
Veterans affairs	53 (3.0)	28 (2.0)	
Other/unknown	62 (3.6)	52 (3.7)	
Income ($/yr), *n* (%)			<0.001
≤30 000	241 (13.9)	234 (16.5)	
30 000–50 000	353 (20.3)	263 (18.6)	
50 000–75 000	360 (20.7)	240 (17.0)	
≥75 000	554 (31.8)	413 (29.2)	
Unknown	232 (13.3)	265 (18.7)	
Marital/relationship status, *n* (%)			0.004
Partnered	1479 (85.0)	1151 (81.3)	
Single	113 (6.5)	94 (6.6)	
Unknown	148 (8.5)	170 (12.0)	
Education level, *n* (%)			<0.001
Some high school	85 (4.9)	98 (6.9)	
High school graduate	334 (19.2)	303 (21.4)	
Some college	306 (17.6)	248 (17.5)	
≥College graduate	882 (50.7)	607 (42.9)	
Unknown	133 (7.6)	159 (11.2)	
Race, *n* (%)			0.255
White	1624 (93.3)	1297 (91.7)	
Black	76 (4.4)	84 (5.9)	
Latino	13 (0.7)	11 (0.8)	
Other	27 (1.6)	23 (1.6)	
Number of comorbid conditions, *n* (%)			0.008
0	301(17.3)	229 (16.2)	
1–2	902 (51.8)	687 (48.6)	
≥3	393 (22.6)	334 (23.6)	
Unknown	144 (8.3)	165 (11.7)	
PSA at diagnosis (ng/ml)	7.7 ± 10.3 (5.6, 4.4–7.9)	10.3 ± 56.2 (5.8, 4.4–8.1)	0.096
ISUP grade group, *n* (%)			0.436
1	1151 (66.1)	921 (65.1)	
2	291 (16.7)	235 (16.6)	
3	135 (7.8)	116 (8.2)	
4	77 (4.4)	54 (3.8)	
5	42 (2.4)	36 (2.5)	
Unknown	44 (2.5)	53 (3.7)	

Table 1 (*Continued*)

	Responders (*N* = 1740)	Nonresponders (*N* = 1415)	*p*-Value
Clinical T stage at diagnosis, *n* (%)			0.082
T1	922 (53.0)	722 (51.0)	
T2	694 (39.9)	579 (40.9)	
T3	30 (1.7)	14 (1.0)	
T4	0 (0)	1 (0.1)	
Tx	94 (5.4)	99 (7.0)	
Clinical N stage at diagnosis, *n* (%)			0.406
N0	363 (20.9)	281 (19.9)	
N1–3	6 (0.3)	2 (0.1)	
Nx	1371 (78.8)	1132 (80.0)	
Clinical M stage at diagnosis, *n* (%)			0.954
M0	574 (33.0)	474 (33.5)	
M1	6 (0.3)	5 (0.4)	
Mx	1160 (66.7)	936 (66.1)	
Primary treatment, *n* (%)			0.010
AS	63 (3.6)	82 (5.8)	
WW	12 (0.7)	11 (0.8)	
Radical prostatectomy	1115 (64.1)	813 (57.5)	
EBRT	149 (8.6)	143 (10.1)	
Brachytherapy	184 (10.6)	163 (11.5)	
Cryotherapy	67 (3.9)	66 (4.7)	
ADT	97 (5.6)	89 (6.3)	
Others/unknown	53 (3.0)	48 (3.4)	
Disease status at survey, *n* (%)			0.045
AS without Tx	45 (2.6)	61 (4.3)	
WW without Tx	10 (0.6)	9 (0.6)	
NED	1237 (71.1)	1014 (71.7)	
BCR	82 (4.7)	51 (3.6)	
Remission	264 (15.2)	195 (13.8)	
ADT without metastasis	25 (1.4)	11 (0.8)	
Metastasis	27 (1.6)	27 (1.9)	
Unknown	50 (2.9)	47 (3.3)	
Prior prostatectomy before survey, *n* (%)			<0.001
No	566 (32.5)	548 (38.7)	
Yes	1124 (64.6)	820 (58.0)	
Unknown	50 (2.9)	47 (3.3)	
Prior radiation therapy before survey, *n* (%)			0.267
No	1189 (68.3)	948 (64.6)	
EBRT	230 (13.2)	166 (11.7)	
Brachytherapy	231 (13.3)	211 (14.9)	
EBRT + brachytherapy	40 (2.3)	43 (3.0)	
Unknown	50 (2.9)	47 (3.3)	

ADT = androgen deprivation therapy; AS = active surveillance; BCR = biochemical recurrence; EBRT = external beam radiation therapy; ISUP = International Society of Urological Pathologists; NED = no evidence of disease; PSA = prostate-specific antigen; Tx = treatment; WW = watchful waiting.
Continuous variables are expressed as mean ± standard deviation (median, interquartile range), whereas categorical variables are expressed as *n* (%).
[a] Medicare supplement or Medicare plus other insurance.

Table 2 – Uncorrected utility values and rating scales according to versions.[a].

	Overall	Version A	Version B	Mean difference (95% confidence interval)	*p*-Value
Prostate cancer health					
Utility	0.934 ± 0.120	0.946 ± 0.108	0.921 ± 0.130	0.025 (0.013–0.037)	<0.001
Rating scale	0.849 ± 0.173	0.850 ± 0.174	0.848 ± 0.172	0.002 (−0.016 to 0.019)	0.832
Sexual function					
Utility	0.946 ± 0.117	0.948 ± 0.122	0.945 ± 0.112	0.003 (−0.009 to 0.015)	0.613
Rating scale	0.349 ± 0.263	0.358 ± 0.263	0.340 ± 0.264	0.018(−0.010 to 0.045)	0.206
Urinary function					
Utility	0.971 ± 0.079	0.971 ± 0.079	0.971 ± 0.079	0 (−0.008 to 0.008)	0.984
Rating scale	0.749 ± 0.216	0.754 ± 0.207	0.744 ± 0.225	0.010 (−0.012 to 0.032)	0.375
Bowel function					
Utility	0.975 ± 0.074	0.972 ± 0.082	0.979 ± 0.064	−0.007 (−0.014 to 0.001)	0.075
Rating scale	0.860 ± 0.166	0.854 ± 0.167	0.867 ± 0.165	−0.013 (−0.030 to 0.004)	0.146
Overall health					
Utility	0.960 ± 0.100	0.961 ± 0.099	0.960 ± 0.102	0.001 (−0.010 to 0.010)	0.982
Rating scale	0.795 ± 0.157	0.796 ± 0.153	0.793 ± 0.160	0.003 (−0.013 to 0.018)	0.753

Data are expressed as mean ± standard deviation.

Table 3 – Bias-corrected utility values and parameter assumptions.

	One-parameter weighting correction				Gain and loss mixed model			
	Version A[a]	Version B	γ for version B	p-Value	Version A[b]	Version B	λ for version B	p-Value
Prostate cancer health	0.865 ± 0.150	0.866 ± 0.159	0.69	0.957	0.845 ± 0.188	0.845 ± 0.184	1.51	0.971
Sexual function	0.877 ± 0.152	0.876 ± 0.155	0.62	0.886	0.860 ± 0.189	0.860 ± 0.189	2.04	1.000
Urinary function	0.915 ± 0.120	0.915 ± 0.125	0.60	0.952	0.906 ± 0.150	0.905 ± 0.156	2.38	0.984
Bowel function	0.919 ± 0.121	0.919 ± 0.119	0.57	0.905	0.910 ± 0.150	0.910 ± 0.154	2.97	0.994
Overall health	0.897 ± 0.138	0.896 ± 0.146	0.59	0.838	0.884 ± 0.171	0.884 ± 0.182	2.45	0.994

The utility values are expressed as mean ± standard deviation.
[a] $\gamma = 0.61$.
[b] $\lambda = 2.25$.

$p = 0.003$), but the others were not. Table 3 shows bias-corrected utility values and their parameter assumptions. Distribution of bias-corrected utility values (one-parameter weighting function) is illustrated in Fig. 2.

3.3. Utilities by disease status, initial treatment, and functional outcome

Uncorrected and bias-corrected utility values by disease status are presented in Supplementary Table 4. Most patients (86.3%, 1501/1740) were in remission or NED. Progressive disease had lower PCa health and overall health utilities without statistical significance (ANOVA test, all $p > 0.05$). AS without treatment had the highest and metastatic disease had the lowest PCa health utility. However, even metastatic disease had a relatively high overall health utility. Supplementary Table 5 summarizes utility values by conditions in sexual, urinary, and bowel function. Dysfunction in terms of QoL status was significantly associated with lower utility values.

3.4. Utilities by initial treatment and treatment effect

Overall health utility was significantly different by the type of initial treatment, and radical prostatectomy had the highest value (Supplementary Table 6). History of radical prostatectomy (as initial or salvage treatment) was associated with higher utility values in urinary function, bowel function, and overall health (Supplementary Table 7). Meanwhile, utilities were lower, but not significantly so, for patients who underwent combined external beam radiation therapy and brachytherapy (Supplementary Table 7).

4. Discussion

PCa and its treatments are associated with various disease or treatment-related adverse outcomes [18,19], consequences that may be magnified by the prolonged natural history of the disease [20]. Thus, the long-term QoL of PCa survivors is highly relevant and merits close attention [21]. Identifying optimal management strategies from among the various treatment alternatives remains a source of considerable ongoing controversy, and in fact, the US National Academy of Medicine identified localized PCa treatment among the top 25 questions most in need of

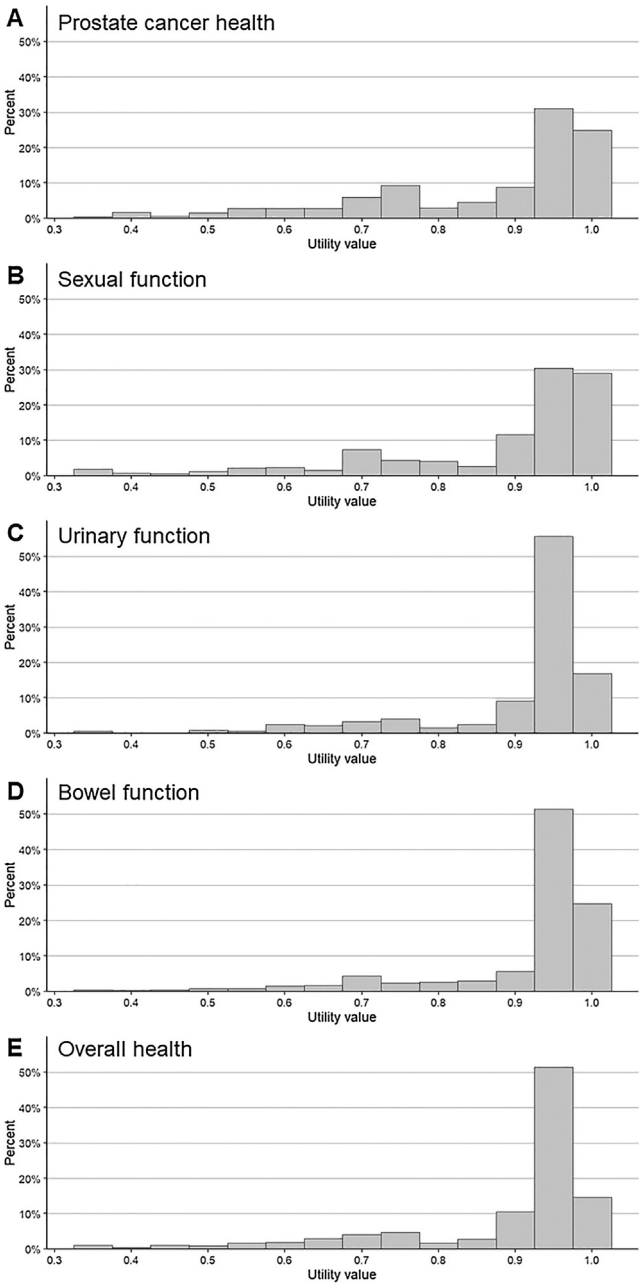

Fig. 2 – Distribution of each bias-corrected utility value (one-parameter weighting function): (A) prostate cancer health, (B) sexual function, (C) urinary function, (D) bowel function, and (E) overall health.

better comparative effectiveness research [22]. Comparative effectiveness and cost effectiveness analyses are driven in part by comparisons in expected QALYs between treatments [23,24].

Utility measurement methods can be categorized into three groups: direct valuation such as SG and time trade-off, indirect measurement using a multiattribute utility instrument such as EQ-5D, and lastly estimation using mapping formulas from HRQoL questionnaires [24,25]. For most purposes, direct measurements are more desirable than indirect methods because conversion formulas must be validated extensively in relevant patient populations, which is rarely done. Assessments in those unaffected by the disease using hypothetical health status may generate lower utilities than in those with the disease who uniquely understand the relevant health states by living through them [26]. Moreover, with long-term exposure to some health conditions, patients may well adapt to these conditions, with reduced psychological distress over time [6,13,21,27]. Since most existing reference utility values for PCa are based on these imprecise methods and small participant numbers, we undertook a large-scale, direct measurement of utility based on patients' own conditions, using SG methods in a well-described nationally representative registry.

Quantifying utility is further complicated by natural human resilience and adaptation. If asked how much probability of death he would accept to cure erectile dysfunction, a 30-yr-old man might answer very differently from a 70-yr-old. Likewise, a 50-yr-old man asked the same question may answer differently the week before and the week after a diagnosis of a high-grade, life-threatening cancer. Among men actually living with erectile dysfunction, some are highly bothered and some are minimally so.

This concept is critical for understanding the much higher utility scores that we calculated compared with prior studies. The most commonly cited utilities for PCa health states were derived from a single SG study of 162 men, 84 of whom had PCa, published in 2005. Details of the patients' treatment history or personal health states were not provided [3]. The utilities from this study were generally low: for example, 0.67 for living with asymptomatic progressive disease and 0.25 for metastatic disease [3]. In our study, by contrast, the utility was 0.91 for men with biochemically progressive disease and 0.89 for those with established metastases.

One explanation is that, in the 2005 study, metastatic cancer was described to participants as a terminal, painful state that typically characterizes only the final months of the lives of most men living with metastatic PCa. However, more fundamentally, the older utility scores may not accurately reflect the subjective experience. Men with rising PSA or receiving ADT for early metastatic disease would naturally prefer to be cured, but how many would actually accept a one-in-three chance of sudden death in pursuit of cure (which is what a utility of 0.67 implies)?

Actual long-term cancer survivors may adapt well to their health status [6,28]. Another study previously suggested that elderly men with relatively short life expectancies, irrespective of PCa, may consider a trade-off for death in the SG to be a more serious possibility, and may therefore be more conservative and risk averse [28]. Older men's subjective experience of HRQoL impairments may also reflect less bother than that of younger men [29].

Although it is generally regarded as the method best grounded in economic theory for eliciting utility, SG may have weaknesses due to the complex psychological process it asks of participants [17]. We considered multiple systemic biases, including risk aversion, loss aversion, probability weighting, framing effect, and possible scale compatibility [12–15]. Thus, we also applied the two most commonly used bias-correction methods based on prospect theory to overcome this potential weakness [12,14,15]. Currently, there is no consensus on which method is best for bias correction. Health utilities are typically used for comparative analysis. Thus, we suggest that researchers be consistent in the selection of utility values from any method across studies. Table 4 shows one choice of utilities by

Table 4 – Bias-corrected utility values by disease status and function conditions (one-parameter weighting function).

	N	Mean ± SD	95% confidence interval
Prostate cancer health utility			
Active surveillance without treatment	38	0.907 ± 0.121	0.867–0.946
Watchful waiting without treatment	10	0.796 ± 0.166	0.677–0.914
No evidence of disease	1100	0.869 ± 0.151	0.860–0.878
Biochemical recurrence	68	0.838 ± 0.173	0.796–0.880
Remission	224	0.865 ± 0.156	0.844–0.885
ADT without metastasis	19	0.833 ± 0.187	0.743–0.923
Metastasis	23	0.826 ± 0.190	0.744–0.908
Sexual function			
Potent	308	0.901 ± 0.132	0.886–0.916
Impotent	1065	0.870 ± 0.159	0.861–0.880
Urinary function			
Continence (no pad/d)	1230	0.922 ± 0.116	0.916–0.929
Incontinence (≥1 pad/d)	280	0.886 ± 0.141	0.870–0.903
Bowel function			
No problem	1419	0.923 ± 0.114	0.917–0.929
With problem	50	0.822 ± 0.195	0.766–0.877

ADT = androgen deprivation therapy; SD = standard deviation.

common disease status and function conditions, but there is no consensus on choice. The values were bias corrected by a probability weighting function. In this table, we can notice that utilities of having to undergo ADT or having a BCR are similar to the utility of having metastatic PCa. It means that ADT or recurrence affect QoL a lot, similar to metastasis.

Potential limitations to the interpretation of our findings should be considered as well. First, there is potential for a survivorship bias. The majority of patients had no evidence of active disease, and the proportion of those with clinically progressed or metastatic disease was relatively small due to the natural history of PCa [2,18,20]. Therefore, we also could not elicit utility values for subgroups within metastatic disease, such as castration-resistant PCa. Next, there were comparatively small proportions of young or recently diagnosed patients, as CaPSURE is a mature registry and accrual has intentionally slowed in recent years [7,30]. Only 6.5% (114) were diagnosed within 5 yr since initial diagnosis, and only 5.1% (88) were younger than 60 yr. Thus, we could not reliably evaluate acute effects of treatment, changes over time, and age. Furthermore, <7% of respondents were non-White, suggesting potentially limited generalizability to other racial/ethnic groups. The cohort is entirely based in US practices, and men in other countries or cultures may assess the relative value of survival versus HRQoL differently. Finally, unmeasured confounding or other methodological problems may also contribute to our consistently high observed utility values and the lack of substantial measured differences between conditions.

Despite the aforementioned limitations, the current study has many advantages. We directly measured utility values with the most accurate methods from actual long-term PCa survivors on a large scale. Our study cohort was 10-fold larger than the largest previous study of PCa utilities, and such a large number of patients have rarely been surveyed using SG in any cancer population.

5. Conclusions

These results provide the most reliable reference utility values to date for a wide range of health states among long-term survivors of PCa. SG utilities were much higher than those of previous studies that were based on theoretical scenarios or indirect methods. We do not imply that differential impacts of various PCa treatments on HRQoL are not meaningful or important, but rather that long-term survivors of PCa may adapt well to their health conditions over time even if they continue to experience disease-specific or functional problems. Surviving PCa patients would not take the risk of death in pursuit of better HRQoL compared with what previous studies have suggested, and this remarkable human resilience—as reflected in the new utility values provided here–should be considered in future comparative effectiveness research.

Author contributions: Chang Wook Jeong and Matthew R. Cooperberg 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.

Study concept and design: Cooperberg, Broering, ten Ham, Wilson, Carroll, Jeong.
Acquisition of data: Broering, Cowan, Cooperberg, Carroll.
Analysis and interpretation of data: Jeong, Cooperberg.
Drafting of the manuscript: Jeong.
Critical revision of the manuscript for important intellectual content: All authors.
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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.eururo.2019.07.012.

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