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# Long-term Health-related Quality of Life After Primary Treatment for Localized Prostate Cancer: Results from the CaPSURE Registry

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## Abstract

***Background:*** Few studies have reported on late declines and long-term health-related quality of life (HRQOL) after prostate cancer (PCa) treatment.
***Objective:*** We assessed long-term HRQOL following various treatments for localized PCa.
***Design, setting, and participants:*** This cohort study of HRQOL up to 10 yr after treatment used a prospectively accrued, nationwide PCa registry that collects longitudinal patient-reported HRQOL.
***Intervention:*** Various primary treatments for localized PCa.
***Outcome measurements and statistical analysis:*** The Medical Outcomes Studies 36-item Short Form and the University of California, Los Angeles, Prostate Cancer Index characterized physical function, mental health, and sexual, urinary, and bowel function and bother. Repeated measures mixed-model analysis assessed change in HRQOL by treatment over time, and logistic regression was used to measure the likelihood of a clinically significant decline in HRQOL.
***Results and limitations:*** Among 3294 men, 1139 (34%) underwent nerve-sparing radical prostatectomy (NSRP), 860 (26%) underwent non-NSRP, 684 (21%) underwent brachytherapy, 386 (12%) underwent external beam radiotherapy, 161 (5%) underwent primary androgen deprivation therapy, and 64 (2%) pursued watchful waiting/active surveillance. Median follow-up was 74 mo (interquartile range: 50–102). Most treatments resulted in early declines in HRQOL, with some recovery over the next 1–2 yr and a plateau in scores thereafter. Surgery had the largest impact on sexual function and bother and on urinary function, radiation had the strongest effect on bowel function, and androgen deprivation therapy had the strongest effect on physical function. The main limitation was attrition among the cohort.
***Conclusions:*** Although most men experience initial declines in HRQOL in the first 2 yr after treatment, there is little change from 3 to 10 yr and most differences between treatments attenuated over time.
***Patient summary:*** Various treatments for prostate cancer result in a distinct constellation of adverse effects on health-related quality of life, which may have a long-term impact. These findings are helpful regarding shared decision making over choice of primary treatment.


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## 1. Introduction

Prostate cancer (PCa) is the most common malignancy among men in the United States, accounting for 27% ($n$ = 233 000) of estimated new cancers in 2014 [1]. Local treatments are associated with distinct constellations of treatment-related morbidity, primarily in domains of sexual, urinary, and bowel health-related quality of life (HRQOL) [2–5]. Consequently, the anticipated impact of treatment on HRQOL is an important driver of shared decision making.

The largest detriments in HRQOL occur within 1 yr of treatment with some improvement thereafter [2,3,5]. Surgery generally has the largest impact on erectile function and urinary continence, while radiation has the largest impact on bowel and urinary irritation. Although studies provide consistent short- to intermediate-term results, few have reported follow-up beyond 5 yr. A 2013 population-based study reported that declines in HRQOL persist 10–15 yr after treatment, although differences between treatments attenuate over time [6]. However, this study focused only on radiotherapy and surgical patients.

Given the variable options for primary treatment of PCa and the diverse array of adverse effects different treatments produce, we sought to compare long-term HRQOL after various forms of primary treatment in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE), a US nationwide PCa registry.

## 2. Methods

### 2.1. Patient selection

The CaPSURE registry enrolls men with biopsy-proven PCa from 45 predominantly community-based urology practices around the United States. During 1995–1998, both prevalent and incident cases were enrolled, and after 1998, all enrollment has been prospective. Participating urologists report initial and follow-up information, including risk assessment, treatment, and outcomes. Patients are treated per their clinicians' standards of care and observed until death or study withdrawal. All patients provide written informed consent under local and central institutional review board approval [7].

One of CaPSURE's core goals has been prospective collection of patient-reported HRQOL. Participants with localized PCa diagnosed from 1995 to 2011 and with a known primary treatment were selected. Men were excluded if they did not have HRQOL assessments at diagnosis and at least one follow-up. Primary treatment modalities included nerve-sparing radical prostatectomy (NSRP), non-NSRP, external beam radiotherapy (EBRT), brachytherapy (BT), primary androgen deprivation therapy (PADT), and watchful waiting/active surveillance (WW/AS). CaPSURE does not distinguish WW from AS, but men with no recorded management plan were excluded rather than assumed to be on WW/AS. Patients undergoing neoadjuvant, adjuvant, or salvage treatments were included, and analyses controlled for the receipt of these additional interventions.

### 2.2. Health-related quality of life assessment

At the time of enrollment in CaPSURE, men completed self-administered questionnaires on sociodemographics, clinical information, comorbidities, and HRQOL. HRQOL was reassessed at regular intervals using well-validated, self-reported questionnaires every 6 to 12 mo. We used the Medical Outcomes Studies Short Form-36 (SF-36) to provide measures of physical function and mental health [8], and the University of California, Los Angeles (UCLA) Prostate Cancer Index (PCI) to provide measures of sexual, urinary, and bowel function and bother [9,10]. Both instruments yield scores from 0 to 100, with higher scores denoting better function or less bother. A binary outcome was created denoting a clinically meaningful decline in function or bother, defined as a one-half standard deviation (SD) decrease from baseline [11–13]. Clinically meaningful declines were analyzed at 2, 5, and 10 yr after treatment.

### 2.3. Statistical analysis

Men were grouped according to primary treatment. Baseline clinical and demographic data were compared using the chi-square test for categorical variables and analysis of variance (ANOVA) for continuous variables. Baseline mean summary scores in each HRQOL domain were compared using ANOVA. Mixed-model repeated measures analysis compared HRQOL change over time within each treatment group and compared trends between treatments. These scores were adjusted for patient age; year of treatment; number of comorbidities; medical insurance status; cancer progression risk at diagnosis, as measured by the well-validated Cancer of the Prostate Risk Assessment (CAPRA) score [14]; and receipt of any secondary treatments, and were plotted over time. Models assessing sexual function and bother also controlled for phosphodiesterase inhibitor (PDE-I) use after treatment. Logistic regression assessed the impact of different treatments on the likelihood of clinically meaningful declines in HRQOL over time. These models were adjusted for similar variables as well as baseline scores in each HRQOL domain and used men undergoing NSRP as the reference group for comparison. To include the impact of secondary therapies on our observations, we repeated the analyses without controlling for adjuvant or salvage treatments.

Biased censorship was assessed by comparing baseline characteristics between the final cohort and men excluded for lack of follow-up HRQOL data. In addition, a sensitivity analysis using multiple imputation was performed to estimate missing domain-specific summary scores for patients with sufficient clinical follow-up (ie, those who could have completed additional HRQOL assessments based on their last clinical follow-up date). Patients with missing HRQOL and clinical data were censored at last follow-up. Summary scores were estimated with paired mean matching using baseline characteristics, and 200 datasets were imputed. Parallel mixed-model repeated measures and logistic regression analyses were performed on the imputed dataset as a secondary analysis.

## 3. Results

The final cohort consisted of 3294 patients (Fig. 1). Among these men, 1139 (34%) underwent NSRP, 860 (26%) underwent non-NSRP, 684 (21%) underwent BT, 386 (12%) underwent EBRT, 161 (5%) underwent PADT, and 64 (2%) pursued WW/AS. The median follow-up time was 74 mo (interquartile range: 50–102 mo). Surgical patients were younger, with less comorbidity, lower clinical risk, and more PDE-I therapy use after treatment (Table 1). Excluded patients had a somewhat higher proportion of African Americans and men treated with PADT and WW/AS, compared to the final cohort (Supplementary Table 1).

Reflecting the age and comorbidity variances across treatments, RP patients reported the highest mean scores at baseline in all HRQOL domains but mental health (Table 2). At 2 yr, 2676 men (81%) provided HRQOL data, and 1607 (49%) and 394 (12%) provided data at 5 and 10 yr,

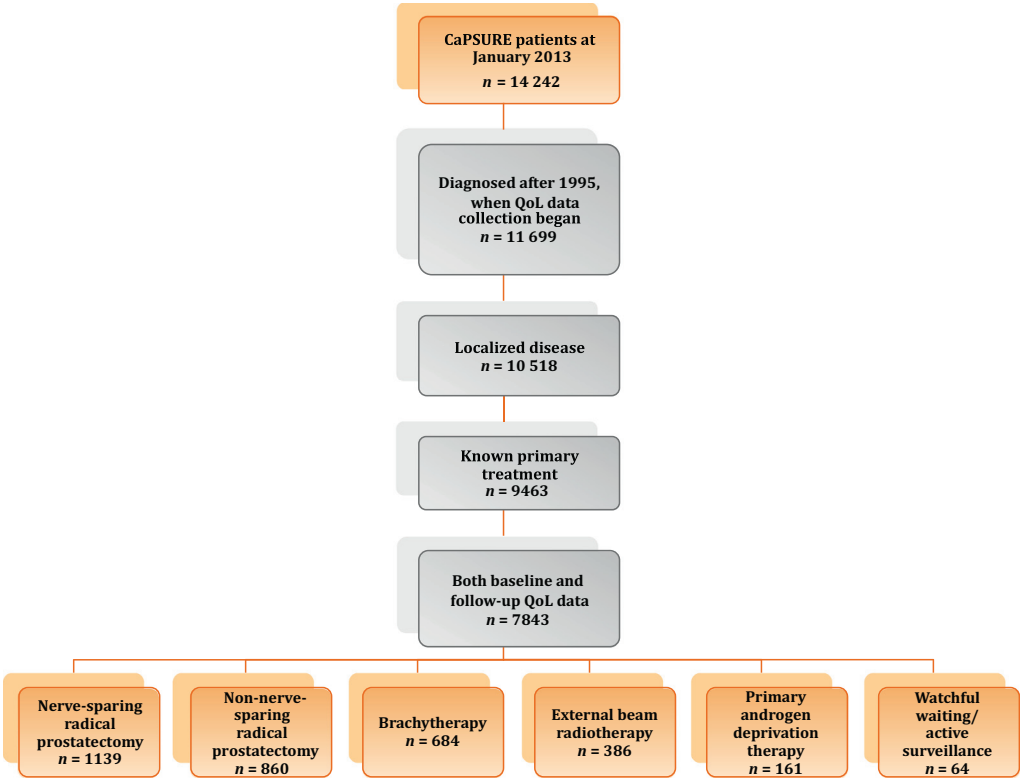


**Fig. 1 – Patient flow chart.**
**CaPSURE = Cancer of the Prostate Strategic Urologic Research Endeavor; QoL = quality of life.**

respectively. Table 3 displays the unadjusted proportion of men who experienced a clinically meaningful decline in HRQOL at 2, 5, and 10 yr.

### 3.1. *Generalized health-related quality of life*

#### 3.1.1. *Physical and mental health*

All treatments experienced a decline in adjusted physical function, with PADT exhibiting the largest over 10 yr (Fig. 2a). Compared to NSRP, all other treatments except WW/AS experienced higher odds of meaningful declines in physical function at 2 yr, but no significant differences between NSRP and nonsurgical treatments existed by 5 yr (Table 4).

Mental health remained stable over time with little difference across treatments (Fig. 2b). Compared to NSRP, EBRT and PADT had higher likelihoods of decline at 2 yr. By 10 yr, there were no significant differences between treatments (Table 4).

### 3.2. *Disease-specific health-related quality of life*

#### 3.2.1. *Sexual function and bother*

Adjusted mean sexual function decreased the first year after most treatments, with surgery having the most pronounced effect (Fig. 2c). Some recovery occurred in the second year after most treatments, albeit not back to baseline on average, and then scores began to plateau. As anticipated, NSRP showed better recovery of function than non-NSRP. At 2 yr, all nonsurgical treatments were associated with lower odds of a meaningful decline compared to NSRP. However, this lessened over time and by 5 yr, only WW/AS had lower odds. Compared to NSRP, non-NSRP was associated with worse functional decline at all time points (Table 4).

Sexual bother displayed a similar trend (Fig. 2d). Again, RP had the most pronounced effect early. There was no difference in sexual bother recovery between non-NSRP and NSRP patients. By 2 yr, only WW/AS had a lower likelihood of meaningful worsening in sexual bother compared to NSRP and by 5 yr, there were no significant differences between NSRP and nonsurgical treatments (Table 4).

#### 3.2.2. *Urinary function and bother*

Surgery had the most pronounced impact on urinary function at 1 yr (Fig. 2e). There was some recovery in the second year, after which scores began to plateau, but they consistently remained lower than nonsurgical treatments. All nonsurgical treatments had lower likelihood of meaningful declines in urinary function at 2 and 5 yr than NSRP. By 10 yr, only EBRT had a lower likelihood of a clinically meaningful decline in urinary function (Table 4). We saw no association between nerve sparing and urinary function (Fig. 2e; Table 4).

Urinary bother decreased in the first year after surgery and BT (Fig. 2f). Otherwise scores remained relatively stable over time for the surgical and radiotherapy groups. We found no significant differences between treatments in the likelihood of declines in urinary bother (Table 4).

**Table 1 – Patient demographics and clinical characteristics of 3294 men with localized prostate cancer by primary treatment modality**

| Clinical characteristic | NSRP | Non-NSRP | BT | EBRT | PADT | WW/AS |
|---|---|---|---|---|---|---|
| Age at diagnosis, yr, mean (SD) | 60.0 (6.8) | 62.9 (6.6) | 68.3 (7.2) | 71.3 (6.2) | 73.6 (8.1) | 72.5 (7.9) |
| Follow-up time, mo, median (IQR) | 73 (51–100) | 76 (51–103) | 83 (52–104) | 71 (48–100) | 62 (41–95) | 58 (32–89) |
| CAPRA clinical risk, *n* (%) | | | | | | |
| Low (0–2) | 763 (73) | 418 (56) | 406 (65) | 118 (35) | 55 (40) | 38 (73) |
| Intermediate (3–5) | 253 (24) | 267 (35) | 181 (29) | 148 (44) | 53 (38) | 12 (23) |
| High (6–10) | 23 (3) | 70 (9) | 34 (6) | 71 (21) | 30 (22) | 2 (4) |
| Comorbidity, *n* (%) | | | | | | |
| None | 228 (20) | 148 (18) | 61 (9) | 31 (8) | 15 (10) | 4 (7) |
| 1 | 384 (34) | 249 (29) | 168 (25) | 85 (22) | 25 (16) | 12 (19) |
| 2 | 309 (28) | 226 (27) | 202 (31) | 110 (29) | 33 (21) | 18 (29) |
| ≥3 | 201 (18) | 224 (26) | 233 (35) | 155 (41) | 85 (53) | 28 (45) |
| Relationship status, *n* (%) | | | | | | |
| Partnered | 1067 (95) | 789 (93) | 604 (91) | 322 (86) | 129 (83) | 52 (84) |
| Single | 58 (5) | 61 (7) | 61 (9) | 53 (14) | 26 (17) | 10 (16) |
| PDE5-I use after treatment, *n* (%) | | | | | | |
| None | 430 (38) | 468 (54) | 511 (75) | 337 (88) | 146 (91) | 59 (92) |
| <1 yr | 625 (55) | 336 (39) | 113 (16) | 28 (7) | 4 (2) | 2 (3) |
| 1–2 yr | 58 (5) | 40 (5) | 35 (5) | 9 (2) | 6 (4) | 3 (5) |
| ≥3 yr | 26 (2) | 16 (2) | 25 (4) | 12 (3) | 5 (3) | 0 (0) |
| Neoadjuvant ADT, *n* (%) | | | | | | |
| No | 1096 (96) | 783 (91) | 410 (60) | 128 (33) | 160 (99) | 64 (100) |
| Yes | 43 (4) | 77 (9) | 274 (40) | 258 (67) | 1 (1) | 0 (0) |
| Adjuvant treatments, *n* (%) | | | | | | |
| None | 1079 (95) | 765 (89) | 509 (74) | 206 (53) | 118 (73) | 64 (100) |
| RT | 44 (4) | 76 (9) | 120 (18) | 180 (47) | 43 (27) | 0 (0) |
| ADT | 12 (1) | 8 (1) | 42 (6) | 0 (0) | 0 (0) | 0 (0) |
| RT plus ADT | 4 (<1) | 11 (1) | 13 (2) | 0 (0) | 0 (0) | 0 (0) |
| Salvage treatments, *n* (%) | | | | | | |
| None | 1085 (95) | 763 (89) | 624 (91) | 310 (80) | 114 (71) | 58 (90) |
| ADT | 31 (3) | 60 (7) | 60 (9) | 69 (18) | 39 (24) | 3 (5) |
| Local | 23 (2) | 37 (4) | 0 (0) | 6 (2) | 8 (5) | 3 (5) |

ADT = androgen deprivation therapy; BT = brachytherapy; CAPRA = Cancer of the Prostate Risk Assessment Score; EBRT = external beam radiotherapy; IQR = interquartile range; NSRP = nerve-sparing radical prostatectomy; PADT = primary androgen deprivation therapy; PDE5-I = phosphodiesterase type 5 inhibitor; RT = radiotherapy; SD = standard deviation; WW/AS = watchful waiting/active surveillance.

**Table 2 – Mean health-related quality of life summary scores at baseline for 3294 men in the study cohort by primary treatment modality**

| Health domain | NSRP | Non-NSRP | BT | EBRT | PADT | WW/AS |
|---|---|---|---|---|---|---|
| SF-36 | | | | | | |
| Physical function | 93 (14) | 88 (19) | 82 (22) | 78 (23) | 74 (24) | 71 (29) |
| Mental health | 79 (16) | 78 (16) | 79 (15) | 81 (15) | 80 (16) | 77 (19) |
| UCLA PCI | | | | | | |
| Sexual function | 65 (26) | 54 (28) | 43 (30) | 35 (28) | 32 (26) | 32 (28) |
| Sexual bother | 71 (34) | 61 (37) | 54 (39) | 53 (40) | 55 (41) | 44 (41) |
| Urinary function | 93 (12) | 93 (13) | 92 (13) | 91 (14) | 90 (16) | 87 (22) |
| Urinary bother | 89 (19) | 85 (24) | 83 (24) | 81 (27) | 79 (28) | 77 (33) |
| Bowel function | 90 (12) | 88 (14) | 88 (14) | 87 (13) | 84 (17) | 86 (17) |
| Bowel bother | 93 (16) | 90 (20) | 88 (21) | 86 (23) | 83 (25) | 87 (22) |

BT = brachytherapy; EBRT = external beam radiotherapy; NSRP = nerve-sparing radical prostatectomy; PADT = primary androgen deprivation therapy; SF-36 = Medical Outcomes Studies 36-item Short Form; UCLA PCI = University of California, Los Angeles, Prostate Cancer Index; WW/AS = watchful waiting/active surveillance.
Data are shown as mean (standard deviation).

#### 3.2.3. *Bowel function and bother*

There was modest change in bowel function scores over time, with very little difference between treatments (Fig. 2 g). Compared to NSRP, EBRT displayed a higher likelihood of a decline in bowel function at 2, 5, and 10 yr, while BT displayed a higher likelihood at both 5 and 10 yr (Table 4). Both of these associations increased in magnitude over time.

Bowel bother remained stable, with PADT and WW/AS displaying the largest declines over 10 yr (Fig. 2 h). At 2 yr, BT, EBRT, and PADT all displayed a higher likelihood of meaningful declines in bowel bother compared to NSRP. At 5 and 10 yr, there were no significant differences among treatments (Table 4).

After performing multiple imputation for missing data in patients with sufficient clinical follow-up, 3145 patients

**Table 3 – Unadjusted proportion of 3294 men who experienced a clinically meaningful decline in health-related quality of life of at least half standard deviation from baseline to 2, 5, and 10 yr by primary treatment modality**

| HRQOL domain | Treatment modality | Proportion with decline at 2 yr, *n/n* (%) | Proportion with decline at 5 yr, *n/n* (%) | Proportion with decline at 10 yr, *n/n* (%) |
|---|---|---|---|---|
| SF-36 | | | | |
| Physical function | NSRP | 84/923 (9) | 84/591 (14) | 28/140 (20) |
| | Non-NSRP | 104/688 (15) | 82/424 (19) | 49/119 (41) |
| | BT | 109/537 (20) | 94/322 (29) | 31/83 (37) |
| | EBRT | 80/292 (27) | 62/165 (38) | 16/34 (47) |
| | PADT | 48/116 (41) | 23/52 (44) | 5/9 (56) |
| | WW/AS | 16/48 (33) | 8/18 (44) | 1/1 (100) |
| Mental health | NSRP | 107/924 (12) | 105/594 (18) | 33/140 (24) |
| | Non-NSRP | 85/693 (12) | 79/422 (19) | 25/119 (21) |
| | BT | 82/550 (15) | 81/315 (26) | 25/83 (30) |
| | EBRT | 57/295 (19) | 59/158 (37) | 10/33 (30) |
| | PADT | 24/113 (21) | 10/51 (20) | 2/9 (22) |
| | WW/AS | 6/47 (13) | 4/19 (21) | 1/1 (100) |
| UCLA PCI | | | | |
| Sexual function | NSRP | 590/919 (64) | 367/594 (62) | 96/137 (70) |
| | Non-NSRP | 461/681 (68) | 282/421 (67) | 83/116 (72) |
| | BT | 204/513 (40) | 136/305 (45) | 53/80 (66) |
| | EBRT | 106/277 (38) | 64/158 (41) | 18/34 (53) |
| | PADT | 49/109 (45) | 27/51 (53) | 4/8 (50) |
| | WW/AS | 10/44 (23) | 6/17 (35) | 1/1 (100) |
| Sexual bother | NSRP | 550/905 (61) | 300/578 (52) | 74/133 (56) |
| | Non-NSRP | 359/671 (54) | 207/411 (51) | 53/115 (46) |
| | BT | 212/503 (42) | 123/297 (41) | 30/76 (39) |
| | EBRT | 104/270 (39) | 56/152 (37) | 10/33 (30) |
| | PADT | 42/103 (41) | 21/46 (46) | 4/8 (50) |
| | WW/AS | 8/43 (19) | 4/15 (27) | 1/1 (100) |
| Urinary function | NSRP | 499/921 (54) | 349/592 (59) | 100/144 (69) |
| | Non-NSRP | 370/680 (54) | 247/419 (59) | 68/115 (59) |
| | BT | 194/536 (36) | 137/312 (44) | 44/82 (54) |
| | EBRT | 70/295 (24) | 61/166 (37) | 19/36 (53) |
| | PADT | 28/118 (24) | 17/52 (33) | 6/9 (67) |
| | WW/AS | 12/46 (26) | 5/19 (26) | 1/1 (100) |
| Urinary bother | NSRP | 279/926 (30) | 180/598 (30) | 49/142 (35) |
| | Non-NSRP | 214/683 (31) | 116/416 (28) | 49/112 (44) |
| | BT | 191/533 (36) | 99/310 (32) | 33/85 (39) |
| | EBRT | 69/298 (23) | 43/163 (26) | 17/36 (47) |
| | PADT | 24/114 (21) | 19/50 (38) | 3/8 (38) |
| | WW/AS | 11/47 (23) | 3/19 (16) | 0/1 (0) |
| Bowel function | NSRP | 179/934 (19) | 112/601 (19) | 30/142 (21) |
| | Non-NSRP | 162/696 (23) | 93/426 (22) | 35/115 (30) |
| | BT | 146/539 (27) | 87/314 (28) | 28/84 (33) |
| | EBRT | 91/296 (31) | 46/164 (28) | 15/35 (43) |
| | PADT | 33/118 (28) | 17/53 (32) | 4/9 (44) |
| | WW/AS | 12/47 (26) | 6/19 (32) | 1/1 (100) |
| Bowel bother | NSRP | 160/930 (17) | 106/598 (18) | 29/141 (21) |
| | Non-NSRP | 139/689 (20) | 90/426 (21) | 32/116 (28) |
| | BT | 153/538 (28) | 76/317 (24) | 29/84 (35) |
| | EBRT | 100/295 (34) | 46/162 (28) | 8/34 (24) |
| | PADT | 49/118 (42) | 17/54 (31) | 5/9 (56) |
| | WW/AS | 15/47 (32) | 8/19 (42) | 1/1 (100) |

BT = brachytherapy; EBRT = external beam radiotherapy; HRQOL = health-related quality of life; NSRP = nerve-sparing radical prostatectomy; PADT = primary androgen deprivation therapy; SF-36 = Medical Outcomes Studies 36-item Short Form; UCLA PCI = University of California, Los Angeles, Prostate Cancer Index; WW/AS = watchful waiting/active surveillance.

(95%) had data at 2 yr, 2328 patients (71%) had data at 5 yr, and 494 patients (15%) had data at 10 yr. Repeat analyses using the imputed data showed no clinically significant differences in results or trends compared to the observed data (Supplementary Fig. 1, Supplementary Table 2). Repeating the analyses without adjusting for adjuvant and salvage treatments showed minimal change to the logistic regression results (Supplementary Table 3), while the longitudinal analysis revealed no significant differences (data not shown).

## 4. Discussion

We analyzed men who underwent various treatments for localized PCa and provided long term HRQOL follow-up. Most impacts on HRQOL occurred in the first year, with some

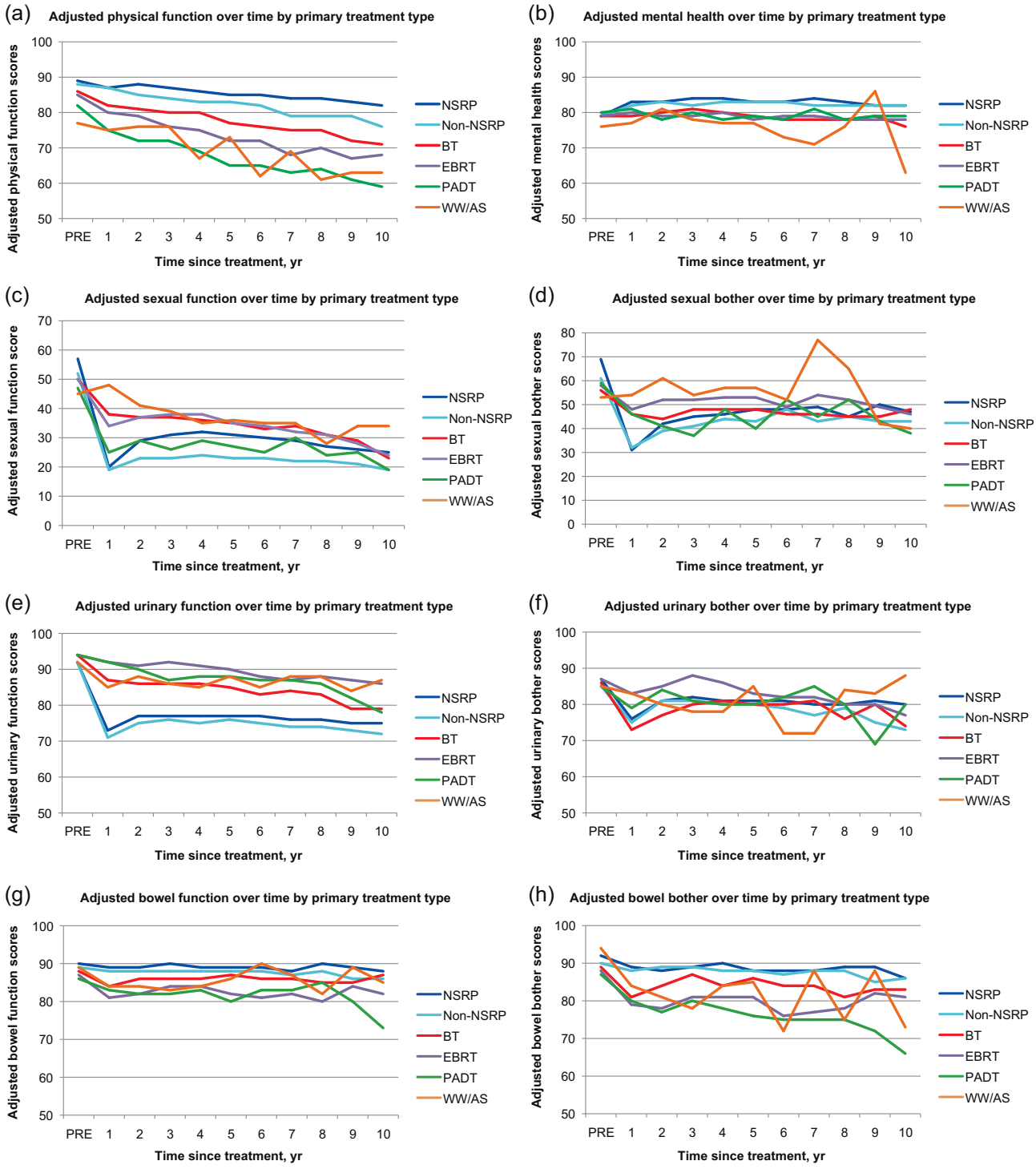


**Fig. 2 – Adjusted mean summary scores for the Medical Outcomes Studies 36-item Short Form (a) physical function and (b) mental health, and for the University of California, Los Angeles, Prostate Cancer Index (c) sexual function, (d) sexual bother, (e) urinary function, (f) urinary bother, (g) bowel function, and (h) bowel bother are displayed over time by primary treatment type among 3294 men in the study cohort.**
**BT = brachytherapy; EBRT = external beam radiotherapy; NSRP = nerve-sparing radical prostatectomy; PADT = primary androgen deprivation therapy; PRE = before treatment; WW/AS = watchful waiting/active surveillance.**

recovery in the following 1–2 yr. After 3 yr, most treatment groups experienced a plateau in scores or some mild decline over time. Surgery had the most pronounced effect on sexual function, sexual bother, and urinary function, while radiation had the most pronounced effect on bowel function and PADT on physical function. In most HRQOL domains, the differences among treatments attenuated over time.

We observed a late, mild decrease in scores for sexual, urinary, and physical function, which might be attributable to aging; without a non-PCa control group, we cannot assess

**Table 4 – Adjusted likelihood of a clinically significant decline in health-related quality of life of at least half standard deviation from baseline to 2, 5, and 10 yr by primary treatment modality among 3297 men in the study cohort**

| Domain | Treatment | Decline 0–2 yr | | Decline 0–5 yr | | Decline 0–10 yr | |
|---|---|---|---|---|---|---|---|
| | | OR (95% CI) | *p* value | OR (95% CI) | *p* value | OR (95% CI) | *p* value |
| SF-36 | | | | | | | |
| Physical health | NSRP | 1 | | 1 | | 1 | |
| | Non-NSRP | 1.6 (1.1–2.3) | <0.01 | 1.1 (0.7–1.6) | 0.7 | 2.7 (1.3–5.3) | <0.01 |
| | BT | 1.9 (1.3–2.8) | <0.01 | 1.2 (0.8–1.8) | 0.5 | 1.3 (0.5–3.0) | 0.6 |
| | EBRT | 2.3 (1.5–3.8) | <0.01 | 1.3 (0.7–2.1) | 0.4 | 1.0 (0.3–3.4) | 1.0 |
| | PADT | 3.8 (2.1–6.6) | <0.01 | 1.7 (0.8–3.5) | 0.2 | 1.0 (0.2–6.2) | 1.0 |
| | WW/AS | 1.8 (0.7–4.3) | <0.01 | 1.7 (0.6–5.1) | 0.4 | – | |
| Mental health | NSRP | 1 | | 1 | | 1 | |
| | Non-NSRP | 0.9 (0.7–1.3) | 0.8 | 1.1 (0.8–1.6) | 0.6 | 0.8 (0.4–1.7) | 0.6 |
| | BT | 1.4 (0.9–2.0) | 0.1 | 1.9 (1.3–2.9) | <0.01 | 1.7 (0.8–4.0) | 0.2 |
| | EBRT | 1.7 (1.0–2.8) | 0.04 | 2.6 (1.5–4.4) | <0.01 | 1.3 (0.4–4.3) | 0.6 |
| | PADT | 2.0 (1.1–3.7) | 0.03 | 1.3 (0.6–3.1) | 0.5 | 1.9 (0.2–15.2) | 0.5 |
| | WW/AS | 0.9 (0.3–2.7) | 0.8 | 0.8 (0.2–3.8) | 0.8 | – | |
| UCLA PCI | | | | | | | |
| Sexual function | NSRP | 1 | | 1 | | 1 | |
| | Non-NSRP | 1.6 (1.2–2.1) | <0.01 | 2.0 (1.4–2.8) | <0.01 | 3.6 (1.5–8.6) | <0.01 |
| | BT | 0.5 (0.4–0.7) | <0.01 | 0.8 (0.5–1.2) | 0.2 | 0.9 (0.3–2.6) | 0.8 |
| | EBRT | 0.5 (0.3–0.8) | <0.01 | 0.8 (0.4–1.3) | 0.3 | 0.7 (0.2–3.4) | 0.7 |
| | PADT | 0.6 (0.3–1.0) | 0.05 | 0.8 (0.4–1.8) | 0.6 | 0.3 (0.0–3.5) | 0.3 |
| | WW/AS | 0.1 (0.0–0.3) | <0.01 | 0.2 (0.1–0.9) | 0.03 | – | |
| Sexual bother | NSRP | 1 | | 1 | | 1 | |
| | Non-NSRP | 1.0 (0.7–1.2) | 0.7 | 1.4 (1.0–1.9) | 0.03 | 1.1 (0.6–2.1) | 0.8 |
| | BT | 0.7 (0.5–1.0) | 0.06 | 1.2 (0.8–1.7) | 0.4 | 1.2 (0.5–2.9) | 0.7 |
| | EBRT | 0.7 (0.4–1.0) | 0.07 | 1.1 (0.6–1.9) | 0.7 | 0.5 (0.2–1.8) | 0.3 |
| | PADT | 0.8 (0.4–1.3) | 0.3 | 1.3 (0.6–2.9) | 0.5 | 1.1 (0.1–8.3) | 0.9 |
| | WW/AS | 0.2 (0.1–0.7) | <0.01 | 0.5 (0.1–1.9) | 0.3 | – | |
| Urinary function | NSRP | 1 | | 1 | | 1 | |
| | Non-NSRP | 1.0 (0.8–1.2) | 0.7 | 1.0 (0.7–1.3) | 0.8 | 0.7 (0.4–1.2) | 0.2 |
| | BT | 0.4 (0.3–0.6) | <0.01 | 0.5 (0.3–0.7) | <0.01 | 0.5 (0.3–1.1) | 0.07 |
| | EBRT | 0.3 (0.2–0.4) | <0.01 | 0.3 (0.2–0.5) | <0.01 | 0.2 (0.1–0.6) | <0.01 |
| | PADT | 0.2 (0.1–0.4) | <0.01 | 0.2 (0.1–0.5) | <0.01 | 0.8 (0.1–5.6) | 0.8 |
| | WW/AS | 0.3 (0.1–0.7) | <0.01 | 0.2 (0.1–0.6) | <0.01 | – | |
| Urinary bother | NSRP | 1 | | 1 | | 1 | |
| | Non-NSRP | 1.1 (0.8–1.4) | 0.5 | 0.8 (0.6–1.1) | 0.2 | 1.8 (1.0–3.4) | 0.06 |
| | BT | 1.3 (1.0–1.8) | 0.08 | 1.0 (0.7–1.5) | 0.8 | 1.2 (0.6–1.7) | 0.6 |
| | EBRT | 0.8 (0.5–1.2) | 0.3 | 0.8 (0.5–1.3) | 0.3 | 1.3 (0.5–3.7) | 0.6 |
| | PADT | 0.6 (0.3–1.0) | 0.07 | 1.3 (0.6–2.8) | 0.4 | 1.5 (0.2–9.9) | 0.7 |
| | WW/AS | 0.5 (0.2–1.3) | 0.2 | 0.4 (0.1–1.5) | 0.2 | – | |
| Bowel function | NSRP | 1 | | 1 | | 1 | |
| | Non-NSRP | 1.1 (0.8–1.4) | 0.7 | 1.1 (0.8–1.5) | 0.7 | 1.6 (0.8–3.1) | 0.2 |
| | BT | 1.3 (1.0–1.8) | 0.08 | 1.6 (1.0–2.3) | 0.03 | 3.3 (1.4–7.4) | <0.01 |
| | EBRT | 1.8 (1.2–2.7) | <0.01 | 1.8 (1.0–3.0) | 0.03 | 4.0 (1.3–11.7) | 0.01 |
| | PADT | 1.4 (0.8–2.3) | 0.3 | 1.8 (0.9–3.9) | 0.1 | 4.5 (0.8–26.5) | 0.09 |
| | WW/AS | 1.1 (0.5–2.7) | 0.8 | 1.5 (0.5–4.5) | 0.5 | – | |
| Bowel bother | NSRP | 1 | | 1 | | 1 | |
| | Non-NSRP | 1.0 (0.8–1.4) | 0.7 | 1.1 (0.7–1.5) | 0.8 | 1.1 (0.6–2.2) | 0.7 |
| | BT | 1.6 (1.1–2.2) | <0.01 | 1.1 (0.7–1.6) | 0.8 | 2.3 (1.0–5.2) | 0.05 |
| | EBRT | 2.3 (1.5–3.5) | <0.01 | 1.5 (0.9–2.6) | 0.2 | 1.1 (0.3–3.5) | 0.9 |
| | PADT | 3.1 (1.9–5.2) | <0.01 | 1.9 (0.9–4.0) | 0.1 | 5.1 (0.9–30.5) | 0.07 |
| | WW/AS | 2.0 (0.9–4.2) | 0.09 | 2.0 (0.7–5.7) | 0.2 | – | |

BT = brachytherapy; CI = confidence interval; EBRT = external beam radiotherapy; NSRP = nerve-sparing radical prostatectomy; OR = odd ratio; PADT = primary androgen deprivation therapy; SF-36 = Medical Outcomes Studies 36-item Short Form; UCLA PCI = University of California, Los Angeles, Prostate Cancer Index; WW/AS = watchful waiting/active surveillance.

whether these declines are greater or less than that of a similar age group of men without PCa. A previous report suggested that men older than 60 yr experienced more accelerated declines in urinary function after RP compared to their younger counterparts, suggesting that age may be a driver of late declines in functional scores [15].

The recent Prostate Cancer Outcomes Study (PCOS) reported that surgery had the most profound impact on sexual HRQOL [6]. Although we noticed a similar pattern, these differences appeared smaller in magnitude. This may reflect a more contemporary surgical cohort in CaPSURE. Furthermore, nerve sparing during surgery is known to be associated with better sexual function [2], and the use of NSRP as our reference group could explain smaller differences between surgery and other treatments. We saw very little difference in the unadjusted proportion of NSRP and non-NSRP patients who experienced a decline in sexual function at 2 yr. Men undergoing NSRP had higher baseline

sexual function scores, which may have resulted in them being more likely to cross our threshold for a clinically significant decline of one-half SD from baseline. After adjustment for factors such as age, comorbidity, and baseline function, we found that men who underwent NSRP were less likely to experience a decline in sexual function compared to their nonNSRP counterparts.

Both our study and PCOS [6] report worse declines in urinary function after surgery. However, both studies measured urinary function using the UCLA PCI, which focuses primarily on urinary incontinence rather than irritating or obstructive symptoms, and, therefore, reflects the impact of surgery on urinary function to a greater extent than that of radiation or local tumor progression. Studies using other measures, such as the Expanded Prostate Cancer Index Composite (EPIC) [16], have reported consistently that surgery resulted in more incontinence but less irritating and obstructive symptoms [2,5]. As of 2012, CaPSURE has switched to using EPIC to provide a more comprehensive assessment of urinary HRQOL.

Another interesting finding was the long-term impact of radiotherapy on bowel function. Although other studies reported similar findings at short to intermediate follow-up [5], we found this deficit in bowel function after radiotherapy persisted for the long term and increased in magnitude over time. This differs from PCOS, where differences in bowel function attenuated over time [6]. These findings require further validation.

Men in this prospective database provided longitudinal HRQOL follow-up. However, one of the main limitations was attrition. We used multiple imputation to estimate HRQOL summary scores where data that should have been available were missing. Repeat analyses on the imputed data found that overall trends and results did not change significantly. However, we fully acknowledge a potential for biased censorship that can affect the validity of these findings. This is most true among PADT or WW/AS patients, for whom data in the latter years were sparse, questioning the long-term findings in these men.

There is no standard approach for reporting nerve sparing among CaPSURE sites, which leaves a potential for misclassification of nerve-sparing surgery that may affect the outcomes witnessed from this procedure. CaPSURE uses a one-half SD decline from baseline to represent a meaningful decline in HRQOL. Although there is literature to support this definition to assess HRQOL change among PCa patients [13], we acknowledge that this outcome relies heavily on the SD of scores within the cohort, thereby questioning the true clinical significance of this definition. CaPSURE does not differ between men undergoing WW versus AS. Therefore, this cohort may include men who are untreated due to significant competing risks of mortality. It is possible that many of these patients on WW may have local or distant tumor progression, which may be responsible for declines in HRQOL. Although we attempted to control for many of these factors, given the observational nature of the study, there is always a potential for unmeasured confounding.

The study has several strengths. In addition to providing longitudinal patient-reported HRQOL using validated questionnaires, this study offers the longest follow-up to date among men undergoing a variety of treatments, including PADT and WW/AS. Furthermore, we differentiated between various forms of radiation and accounted for nerve sparing. Finally, the patients represented here come primarily from community-based urologic practices, suggesting the findings are more generalizable to the majority of men being treated for localized PCa in the United States.

## 5. Conclusions

We compared long-term HRQOL after various treatments for localized PCa. Most of the detriments in various HRQOL domains occurred in the first year after treatment, followed by some recovery in the next 1–2 yr, with different treatments resulting in a distinct constellation of adverse effects. After 3 yr, HRQOL scores tended to plateau and any further declines may have reflected aging rather than the impact of treatment. These results may help men understand the long-term implications of their treatment decisions.

***Author contributions:*** Matthew R. Cooperberg had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Study concept and design:* Punnen, Cooperberg, Carroll.
*Acquisition of data:* Punnen, Cowan, Cooperberg, Carroll.
*Analysis and interpretation of data:* Punnen, Cowan, Chan, Cooperberg, Carroll.
*Drafting of the manuscript:* Punnen.
*Critical revision of the manuscript for important intellectual content:* Punnen, Cowan, Chan, Cooperberg, Carroll.
*Statistical analysis:* Punnen, Cowan.
*Obtaining funding:* Cooperberg, Chan, Carroll.
*Administrative, technical, or material support:* Cooperberg, Chan, Carroll.
*Supervision:* Cooperberg, Carroll.
*Other* (specify): None.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eururo.2014.08.074.

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