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PROSTATE CANCER (S PRASAD, SECTION EDITOR)

Quality of Life–Focused Decision-Making for Prostate Cancer

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Abstract

Purpose of Review Quality of life (QoL) outcomes have been reported in the literature and incorporated in decision-making in localized prostate cancer management for decades. Until recently, there was less emphasis on understanding the QoL effects of therapies for patients with advanced disease, possibly because there were fewer options for treatment. The purpose of this review is to summarize the key recent literature describing QoL outcomes for prostate cancer treatments in different disease settings.

Recent Findings Recent data demonstrate that men who undergo local therapy for prostate cancer have worse early QoL related to therapy in sexual, urinary, and bowel function domains compared with men who choose observation, though the effects become less divergent over time. In patients receiving systemic therapy for advanced prostate cancer, more effective treatment typically delays deterioration of various aspects of QoL as assessed by patient-reported outcomes.

Summary While there are multiple management options for localized and advanced prostate cancer, different treatment modalities affect QoL in distinct ways. Particularly in settings that lack head-to-head efficacy data between treatment options, clinicians can incorporate adverse effect profiles and effects on patient-reported outcomes describing QoL to inform patients as they make treatment decisions for prostate cancer.

Keywords Prostate cancer · Patient-reported outcomes · Quality of life · Radiotherapy · Prostatectomy · Anti-androgen

Introduction

Prostate cancer (PC) is the highest incident cancer among men in the USA, with an estimated 174,560 new cases in 2019 [1, 2]. However, there is significant heterogeneity among men who are diagnosed with and receive care for PC. The heterogeneity is present with respect to patient factors—such as age, performance status, and disease aggressiveness at time of diagnosis—and this affects disease outcomes both in terms of efficacy and the patient experience during treatment.

In patients with localized disease, the backbones of curative intent therapy are surgery and radiotherapy. In this setting, 5-year and 10-year prostate cancer-specific survival (PCSS) rates of patients approach 99% and 98% [3, 4], respectively, regardless of treatment modality. Due to excellent survival rates, patient preference and impact on quality of life (QoL) have always played key roles in decision-making for localized PC. Enhancing QoL by reducing unnecessary treatment is also a priority. Further, based on an individual's NCCN risk category and expected actuarial survival [5], it is recommended that select patients with low-risk cancer or limited life expectancy proceed with active surveillance as a means of reducing morbidity related to treatment.

In cases of advanced and metastatic PC, the mainstay of therapy is androgen deprivation therapy (ADT), even when castration resistance has developed [6]. Multiple additional systemic treatments target or manipulate the androgen axis, and there are several novel androgen receptor (AR) pathway–targeted drugs, as well as new indications for existing androgen axis–targeted therapies, that improve prostate cancer–specific and overall survival outcomes. While survival and oncologic outcomes are important for patients and clinicians, they are only one component of measuring therapy efficacy and safety. In fact, when patients with metastatic PC were surveyed at a single center, treatment efficacy was not among the top 3 factors considered by patients when deciding

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on PC therapy, while more value was placed on factors such as "feeling well enough to spend quality time with family" [7]. QoL is of particular importance in men receiving ADT, since it is associated with several long-term adverse effects (AE) [8, 9], and a substantial proportion of patients will experience long-term survival [4].

QoL considerations should be incorporated in shared decision-making about PC treatment options along with oncologic and survival outcomes. In this review, we will examine the latest high-quality trial data as it relates to QoL through patient-reported outcomes (PROs) and AEs in different PC disease settings.

What Is Quality of Life?

We define QoL as a composite of three aspects of the patient experience. These are PROs, such as fatigue and pain; clinician- and laboratory-collected adverse events (AEs), such as anemia; and the "X-factor," including time off of work and financial toxicity of treatment. PROs are a method by which qualitative data can be collected systematically and quantified to allow for comparison between patients, between therapies, and over time. PROs are measured using patient surveys and are complementary (though not always correlated) data points to AEs [10, 11]. AEs are collected by clinicians using the National Cancer Institute-Common Terminology Criteria for Adverse Events (CTCAE) as part of randomized trials, and these are not always accompanied by symptoms. The X-factor includes a number of factors that are not routinely measured or reported in clinical trials, but that affect patients and their treatment decisions. Examples include frequency and number of visits required for treatment, relative cost of treatment, time and cost of missed work, and amount and complexity of follow-up monitoring. A common scenario is the patient who lives over an hour away from the nearest academic center where a particular treatment option is available that is unavailable locally. One factor the patient may consider in making the choice to pursue this treatment or not is the extra travel burden that can affect the patient and loved ones and the risk of facing complications when the treatment team is far away.

Local Therapy

Management options for men diagnosed with nonmetastatic PC can be categorized broadly as observation, surgery, or radiotherapy [12]. Observation can be further categorized as watchful waiting or active surveillance. The former implies treatment only for symptomatic disease progression with palliative intent. The latter consists of routine monitoring of disease progression with regular PSA measurements, digital rectal exam, repeat prostate biopsies, and potentially imaging with multiparametric magnetic resonance imaging (MRI). Surgery is typically radical prostatectomy most commonly via a minimally invasive laparoscopic approach with robotic assistance. Radiotherapy consists of external beam radiotherapy (EBRT) or brachytherapy either alone or in combination, as well as concurrent androgen deprivation therapy (ADT) for intermediate- and high-risk disease. This section reviews each of these categories and relevant QoL considerations.

Observation Versus Surgery or Radiotherapy

The benefits of observation as an initial management for PC are realized in delaying or avoiding the adverse effects of treatment. In the Prostate Testing for Cancer and Treatment (ProtecT) trial, men with clinically localized PC were prospectively randomized to observation, radical prostatectomy, or EBRT, and PROs were collected for urinary, sexual, and bowel function as well as general QoL [13••]. In terms of urinary function, urinary incontinence symptoms were poorer in men undergoing surgery than radiation and active monitoring at all time points. At year 6, differences in pad use remained, with 17% of men in the prostatectomy group reporting pad use, vs 8% in the active monitoring group and 4% in the radiotherapy group. However, by two years post-treatment, the effect of this on QOL was similar between men treated with prostatectomy and the other groups. Erectile dysfunction was most severe in the group treated with prostatectomy at all time points, with 12% reporting erections firm enough for intercourse at 6 months and 21% at 36 months. In the radiotherapy group 22% had erections firm enough for intercourse, vs 52% in the active monitoring group. At 6 years, these numbers were 27% in radiotherapy, 30% in active monitoring, and 17% in the surgery group. Bowel symptoms were unchanged for patients receiving prostatectomy and active monitoring, but were worse for men receiving treatment with radiation. Symptoms were poorest in the radiation group at the 6 month time point. Importantly, symptoms reported by men in the observation arm may have been related to attrition from observation and subsequent local treatment, with local treatment delivered in 55% of patients during the course of the trial [13••].

However, after longer follow-up (6 years), men randomized to observation were noted to have similar bother scores related to urinary, sexual, and bowel issues as men in the treatment arms: 8.0% for lower urinary tract symptoms impacted their lives "somewhat / a lot," 37.4% for moderate or severe sexual dysfunction, and 3.5% for moderate or severe bowel symptoms [13••]. Men managed with observation experienced worse obstructive urinary symptoms relative to men treated with radical prostatectomy with prolonged follow-up, likely due to benign prostatic hyperplasia in an aging male population or local cancer progression [13••]. Similar findings were noted in an earlier randomized study comparing

watchful waiting to surgery [14]. The ProtecT trial also failed to find differences in mental, physical, and overall QoL between the three treatment arms [13••]. Two recently published population-based, retrospective studies reported on QoL outcomes based on treatment type with the added benefit of more contemporary cohorts treated with more recently developed technologies and techniques [15, 16]. While these studies largely corroborate data from the ProtecT trial, they also assessed the different adverse effects of treatment based on baseline patient function. In terms of sexual function, both studies noted the largest differences in sexual function were reported by men with normal baseline erectile function who received surgery compared with observation. For instance, in one study, for men with normal baseline erectile function, worse erectile function at 2 years of follow-up was noted in 57% of men who underwent surgery, 27% who received EBRT, 34% who received brachytherapy, and 25% who initially underwent active surveillance [16]. Notably, overall QoL was similar between all three treatment arms over time.

Definitive treatment provides superior cancer control in patients with PC that is greater than low risk and remains the standard of care for these patients. However, men with low- and very low–risk prostate cancer should consider that these studies demonstrate that observation for low-risk localized PC is associated with better short-term QoL outcomes related to treatment-associated adverse effects, especially in terms of sexual function among men with normal baseline erectile function. With prolonged follow-up, functional domains are similar between men who received treatment or observation, providing hope to men that must undergo definitive local therapy for higher risk disease that they can achieve a similar QOL to untreated men over time.

Surgery Versus Radiotherapy

The ProtecT trial also illustrated important difference in terms of QoL outcomes between surgery and EBRT. Men randomized to surgery experienced worse initial issues with incontinence (29% completely continent at 6 months) while those randomized to EBRT experienced worse voiding symptoms such as nocturia (59% at 6 months; $p < 0.001$ for both overall comparisons) [13••]. Both groups, however, reported similar short- and long-term effects of urinary symptoms on QoL. The effect of treatment on sexual QoL was worse in the surgery group compared with the EBRT group across all time points (moderate or severe sexual dysfunction, 63.6% and 41.6% vs 45.5% and 33.5% at 6 months and 6 years, respectively; $p < 0.001$ for overall comparison). The effect of bowel symptoms on QoL was somewhat worse for those who received EBRT compared with those who received surgery (moderate or severe bowel symptoms, 10.4% vs 3.3% at 6 months). These findings were largely supported by previous work from a large prospective dataset [17]. Recent population-based data provide some additional information [15, 16]. At 3 months of follow-up, Prostate Cancer Symptom Index scores for bowel problems were generally worse for men who received EBRT (12.0, 95% CI 9.8–14.3) compared with brachytherapy (9.0, 95% CI 6.9–11.0) and surgery (6.7, 95% CI 5.5–7.8) [16]. Additionally, only men who were exposed to androgen deprivation therapy with EBRT (recommended for men with intermediate- and high-risk disease [12]) reported poorer hormonal function defined by hot flashes, breast tenderness, depression, lack of energy, and change in body weight which persisted for about 12 months after treatment [15, 18]. Compared with men who received androgen deprivation and EBRT, those who received EBRT alone did not experience significant worsening of sexual function in the first 12 months after treatment relative to men on observation.

Systemic Therapy

Systemic therapy options for men with PC have undergone a recent revolution, with new therapies being approved in a variety of disease settings, including chemotherapy, novel anti-androgens such as enzalutamide and apalutamide, and the biosynthesis inhibitor abiraterone. We evaluate recent literature describing the QoL effects of traditional ADT and these newer treatment modalities.

Hormone-Sensitive Prostate Cancer (HSPC)

The Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4) randomized 695 patients with localized PC to watchful waiting or treatment with radical prostatectomy [19]. Men in the prostatectomy arm received ADT for local recurrence, and men in either arm received ADT if investigators felt it was clinically indicated or if there was evidence of disseminated disease [20]. At 12.2 years of median follow-up, 349 surviving and willing study patients and 281 age-matched control patients without PC completed a study-specific questionnaire analyzing QoL in several domains. Patients receiving ADT in both groups reported more genitourinary symptoms than men who did not receive ADT. Men receiving ADT were less likely to have high QoL compared with men not receiving ADT. Men in the watchful waiting group not receiving ADT had similar likelihood of high QoL to that of healthy controls (44% vs 45%).

LATITUDE was an international phase three randomized control trial in which 1199 men with high-risk metastatic HSPC (mHSPC) were randomized to treatment with ADT with or without abiraterone acetate [21••]. At median follow-up of 30.4 months, patients in the abiraterone group had longer time to worst pain intensity (HR 0.63; $p < 0.0001$) and time to pain interference progression (HR 0.67; $p < 0.0001$) than those in the placebo arm. The abiraterone arm also had

shorter time to worst fatigue intensity (HR 0.65; $p = 0.0001$) and time to fatigue interference progression (HR 0.59; $p < 0.0001$). Time to deterioration of the Functional Assessment of Cancer Therapy-Prostate (FACT-P) score was longer in the abiraterone group compared with the placebo group (12.9 vs 8.3 months; HR 0.85; $p = 0.032$), with the positive effect of abiraterone also seen in the PC-specific (8.3 vs 5.6 months; HR 0.81; $p = 0.0025$), pain-related (10.2 vs 6.5 months; HR 0.76; $p = 0.0001$), trial outcome index (18.4 vs 9.2 months; HR 0.73; $p = 0.0001$), and physical well-being (14.4 vs 7.4 months; HR 0.75; $p = 0.0001$) subscales [22]. There was no difference between groups with respect to time to deterioration of FACT-G general function, emotional, functional, social, and family well-being subscales. General health status scores and health utility scores (measured by the EuroQoL five-dimension, five-level [EQ-5D-5L]) also favored the abiraterone group.

The E3805 Chemohormonal Androgen Ablation Randomized Trial in Prostate Cancer (CHAARTED) is a phase three randomized controlled trial in which 790 men with mHSPC were randomized to treatment with ADT with or without six cycles of docetaxel [23•]. QoL data as measured by FACT-P, FACT-Taxane (FACT-T) [24], Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) [25], and Brief Pain Inventory-Short Form (BPI-SF) were collected at 3-month intervals for the first year of treatment. At 3 months during treatment with chemotherapy, FACT-P scores were 3.09 points better in the ADT-alone arm ($p = 0.02$). However, QoL by FACT-P was superior by 2.85 points for the chemohormonal therapy arm at the 12-month time point ($p = 0.04$). Differences at these time points did not meet criteria for clinically meaningful difference (10 point difference). Among the FACT-P subscales, functional and physical well-being subscales were significantly poorer in the chemohormonal therapy arm vs ADT alone, but were similar at other time points. FACIT-F scores were poorer in patients receiving chemohormonal therapy at 3 months (36.1 vs 40.4; $p < 0.001$), but were similar at later time points.

Nonmetastatic CRPC

Several trials have recently evaluated the benefit of novel antiandrogens in the setting of nonmetastatic castration-resistant prostate cancer (CRPC) (M0CRPC). PROSPER randomized 1401 patients with M0CRPC in a 2:1 fashion to receive enzalutamide or placebo, and the primary endpoint was metastasis-free survival [26]. Importantly in this generally asymptomatic population, there was no difference in time to FACT-P decline between the two groups with patients on enzalutamide reporting a similar good QoL as those on placebo during treatment. Time on treatment was significantly longer for patients receiving enzalutamide as they had a prolonged metastasis-free survival by 22 months vs men on placebo (time on treatment 18.4 vs 11.1 months for enzalutamide vs placebo, respectively). There was a significantly higher incidence ≥ grade 3 AEs for patients receiving enzalutamide vs placebo (31% vs 23%), including a higher incidence of fatigue (33% vs 14%), hot flush (13% vs 8%), hypertension (12% vs 5%), falls (11% vs 4%), and mental impairment.

A follow-up study was performed exploring PROs in more depth in the PROSPER trial [27]. Investigators used the BPI-SF, FACT-P, European Organisation for the Treatment of Cancer QoL Questionnaire Prostate Module (EORTC QLQ-PR25), and EQ-5D-5L to collect PROs. Median follow-up was 18.5 months in the enzalutamide group vs 15.1 months in the placebo group. Most pain outcomes were the same between the two groups, though the enzalutamide group took longer for an increase in pain severity (HR 0.75; $p = 0.028$). Time to bowel (33.2 vs 29.5 months; HR 0.75; $p = 0.0018$) and urinary symptom (36.9 vs 25.9 months; HR 0.58; $p < 0.0001$) worsening in the EORTC QLQ-PR25 favored enzalutamide over placebo, though time to hormonal treatment–related symptoms favored the placebo group (36.8 vs 33.2 months; HR 1.29; $p = 0.035$). FACT-P total scores remained stable through the duration of treatment in both groups, but there were differences in time to deterioration of FACT-P scores (22.1 vs 18.4 months; HR 0.83; $p = 0.037$) and emotional well-being (36.7 vs 29.5 months; HR 0.69; $p = 0.0008$) and PC-specific (18.4 vs 14.7 months; HR 0.79; $p = 0.0042$) subscales of the FACT-P. Patients in the enzalutamide group had longer time to deterioration in their health status measured by EQ-visual analog scale (22.2 vs 14.8 months; HR 0.75; $p = 0.0013$).

SPARTAN randomized 1207 patients with M0CRPC in a 2:1 fashion to receive either apalutamide or placebo, and the primary endpoint was time to metastasis-free survival [28]. Apalutamide was associated with a 24-month prolongation of metastasis-free survival as compared with placebo. Of note, the time to symptomatic progression favored the apalutamide group (HR 0.45; $p < 0.001$), though the median was not reached in either group. Using FACT-P and EQ-5D-3L as PROs, the trial demonstrated stable QoL in both groups. AEs occurring more frequently in the apalutamide group include fatigue (30% vs 21%), hypertension (25% vs 20%), rash (24% vs 6%), diarrhea (20% vs 15%), weight loss (16% vs 6%), arthralgia (16% vs 8%), falls (16% vs 9%), fractures (12% vs 7%), dizziness (9% vs 6%), hypothyroidism (8% vs 2%), mental impairment (5% vs 3%), and seizure (0.2% vs 0%).

ARAMIS randomized 1509 patients with M0CRPC and a PSA doubling time ≤ 10 months in a 2:1 fashion to receive treatment with the AR inhibitor darolutamide or placebo [29]. Like the other AR-targeted therapies, darolutamide was associated with a 22-month prolongation in metastasis-free survival when compared with placebo. PROs were collected using

FACT-P, EQ-5D-3L, and the EORTC QLQ-PR25. BPI-SF was used to determine time to pain progression, one of the study's secondary endpoints. Median time to pain progression (40.3 vs 25.4 months; HR 0.65; $p < 0.001$) and time to first symptomatic skeletal event (medians not reached; HR 0.43 $p = 0.01$) both favored the darolutamide group. Overall, QoL was similar between the two groups during the duration of the trial. FACT-P, BPI-SF, and EORTC-QLQ-PR25 urinary symptom subscale favored darolutamide; however, the thresholds for minimally important difference were not met. AEs occurring more frequently in the darolutamide group included fatigue (12% vs 9%), pain in the extremity (6% vs 3%), rash (3% vs 1%), and heart failure (1.9% vs 0.9%). AEs occurring more frequently in the placebo group included urinary retention (7% vs 4%) and memory impairment (1.3% vs 0.5%).

Metastatic CRPC

Therapy for metastatic CRPC (mCRPC) includes several different therapies available and indicated in multiple settings, including novel anti-androgens, biosynthesis inhibitors, radium-223, and chemotherapy. Alpharadin in Symptomatic Prostate Cancer Patients (ALSYMPCA) randomized 921 patients with symptomatic metastatic mCRPC to receive radium-223 or placebo [30]. Radium-223 (Ra-223) improved survival by 3 months compared with placebo and lengthened time to first symptomatic skeletal event (15.6 vs 9.8 months; HR 0.66; $p < 0.001$). Adverse effects were largely similar, but notably, patients in the placebo group were more likely to experience bone pain (16% vs 10%). Compared with the placebo group, a higher percentage of patients experienced improvement in QoL using FACT-P scores in the Ra-223 group (25% vs 16%; $p = 0.02$). A follow-up study of PROs among patients in ALSYMPCA confirmed these findings and demonstrated that a higher percentage of patients in the Ra-223 group experienced an improvement in EQ-5D utility scores (29% vs 19%; $p = 0.004$) [31].

Two trials have evaluated enzalutamide in the mCRPC setting. A Study Evaluating the Efficacy and Safety of the Investigational Drug MDV3100 (AFFIRM) randomized 1199 patients with mCRPC who had received prior chemotherapy in a 2:1 fashion to receive enzalutamide or placebo; enzalutamide improved median survival by 5 months vs placebo [32]. Patients receiving enzalutamide also experienced a clinically meaningful improvement in FACT-P scores at higher rates than those in the placebo group (81% vs 64%; $p < 0.001$). The total number of adverse effects was similar between the two groups, though fatigue (34% vs 29%), diarrhea (21% vs 18%), hot flushes (20% vs 10%), and headaches (12% vs 6%) occurred more frequently in the enzalutamide group. PREVAIL randomized 1717 patients with chemotherapy-naïve mCRPC to enzalutamide or placebo; enzalutamide improved median survival by 2 months and median radiographic progression-free survival by at least 15 months [33]. Enzalutamide also improved median time to decline in FACT-P (11.3 vs 5.6 months; HR 0.63; $p < 0.001$). Adverse events occurring more frequently in enzalutamide were fatigue (36% vs 26%), back pain (27% vs 22%), hot flush (18% vs 8%), and falls (12% vs 5%).

Two trials contributed to the approval of abiraterone acetate in mCRPC. COU-AA-301 randomized 1195 men with mCRPC previously treated with docetaxel to abiraterone and prednisone or placebo and prednisone; abiraterone improved median survival by 4 months [34]. Notable adverse events occurring more frequently in the abiraterone group included fluid retention (31% vs 22%) and hypokalemia (17% vs 8%). COU-AA-302 randomized 1088 men with chemotherapy-naïve mCRPC to abiraterone and prednisone or placebo and prednisone; abiraterone improved radiographic progression-free survival by 8 months and overall survival [35]. Abiraterone led to an increase in time to opiate use for cancer pain (HR 0.69; $p < 0.001$), increase in time to pain of 30% based on BPI-SF (26.7 vs 18.4 months; HR 0.82; $p = 0.049$), and time to a clinically meaningful decline in FACT-P scores (12.7 vs 8.3 months; HR 0.78; $p = 0.003$). Adverse events occurring more frequently in the abiraterone group included fluid retention (28% vs 24%), hypokalemia (17% vs 13%), hypertension (22% vs 13%), hot flushes (22% vs 18%), and fatigue (39% vs 34%).

Khalaf et al. randomized 202 patients with mCRPC to receive abiraterone or enzalutamide to understand their relative impact on QoL, mood, and cognitive function [36••]. QoL was measured with FACT-P, mood symptoms were measured using Patient Health Questionnaire-9 (PHQ-9), and cognitive function was measured with the Montreal Cognitive Assessment (MoCA). In a post hoc analysis of the subset of patients 75 or older, adjusted mean FACT-P scores were better in patients receiving abiraterone compared with enzalutamide (7.89 vs 0.54; $p = 0.003$). Among all patients, adjusted mean scores for the physical well-being (0.29 vs −0.97; $p = 0.007$) and prostate cancer pain score (1.26 vs 0.33; $p = 0.017$) favored abiraterone. Patients in the enzalutamide group were more likely to experience worsening in the functional well-being (39% vs 23%; $p = 0.015$) and physical well-being (37% vs 21%; $p = 0.013$) than those in the abiraterone group. PHQ-9 change from baseline was worse in the enzalutamide group during treatment weeks 4 ($p = 0.007$), 8 ($p = 0.019$) and 12 ($p = 0.039$), and a higher percentage of patients had abnormal PHQ-9 scores from weeks 4 to 16 in the enzalutamide group ($p < 0.05$). MoCA scores were similar between the two groups. Grade 2 or greater fatigue was much more prevalent in patients receiving enzalutamide (39% vs 20%).

FIRSTANA randomized 1168 patients with mCRPC to cabazitaxel 20 mg/m^2 (C20), cabazitaxel 25 mg/m^2 (C25), or docetaxel 75 mg/m^2 (D75) [37]. Overall survival was similar for all three groups. There were no statistically significant

differences between the three groups with respect to pain progression or pain response. Effect of treatment on time to deterioration of FACT-P scores was similar for all groups, except for the physical well-being subscale, which favored C20 when compared with D75 (14.9 vs 11.3 months; HR 0.76; $p = 0.013$). Adverse events occurred with the same frequency in all groups, though grade 3 or greater AEs occurred more frequently in C25 (60%) compared with C20 (41%) and D75 (46%). Neutropenic fever, neutropenia, hematuria, and diarrhea all occurred more frequently in C25. D75 was associated with a higher incidence of peripheral neuropathy, stomatitis, alopecia, and nail disorders.

Conclusions

Men who elect observation as their initial management for localized PC may delay the adverse effects of surgery or radiotherapy. Most notable adverse effects for surgery include declines in sexual function and urinary incontinence, while those for radiotherapy include worsening voiding symptoms and bowel dysfunction. Hormonal and sexual adverse effects are additional considerations for men who receive adjuvant ADT. Men on observation experience slow declines in these domains as they undergo more treatment following attrition from observation. Most notably, overall QoL measurements do not differ substantially from any one treatment over the other.

Whereas much of the treatment burden and QoL differences for patients treated with local therapy are due to local symptoms from surgery, RT, or local progression, systemic therapies alter QoL in different ways. Considering these factors when making treatment decisions can more accurately match a patient with the treatment that best matches his preferences for side effects in situations in which disease control is similar. Ultimately, there are multiple acceptable options for managing PC at each stage, and the landscape will only be more complex with several new treatment strategies and pharmacotherapies emerging. Clinicians should discuss not only the efficacy of various PC treatment options but also what patients should expect for their QoL with these different options. Discussions of management options incorporating QoL data comprised of patient-reported outcomes and adverse event data can empower a patient to make the most informed decision possible that is also the best choice for him as an individual.

Compliance with Ethical Standards

Conflict of Interest Jeffrey Shevach and Adam Weiner each declare no potential conflicts of interest. Alicia K. Morgans reports personal fees from Astellas, Bayer, Sanofi, Genentech, AstraZeneca, and Janssen and a research grant from Bayer.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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13. •• Donovan JL, Hamdy FC, Lane JA, Mason M, Metcalfe C, Walsh E, et al. Patient-reported outcomes after monitoring, surgery, or radiotherapy for prostate cancer. N Engl J Med. 2016;375(15):1425–37 **This prospective randomized study of 1643 men illustrates the**

effects that the three major localized PC management strategies have on QoL. Surgery was associated with worse urinary continence and sexual function while radiotherapy was associated with worse long-term bowel function. Urinary and sexual symptoms were better in the active monitoring group initially, but gradually worsened over time with disease progression and subsequent local therapy.

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