Optimal assessment of quality of life for patients with prostate cancer

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Abstract: The burden of cancer and oncologic treatment is reflected not only through morbidity and mortality, but also through impacts on patient quality of life (QoL). However, QoL has not been historically measured or addressed with the same rigorous methodology as traditional disease-related outcomes such as overall survival and progression, as these are driven by objective measurements and events. Prostate cancer (PCa) is one of the most prevalent non-cutaneous cancers in men around the world. Both the cancer and its treatment significantly impact patients’ physical, emotional, sexual, social, and overall QoL. Ensuring assessment and integration of QoL in research and clinical care enables improvement in treatment outcomes that matter most to patients while also facilitating alignment of healthcare priorities with reimbursements. Great strides toward this end have been made over the last decade, but significant room for improvement remains. To ensure high quality, reliable data collection, QoL assessment tools must be psychometrically validated, standardized, widely implemented across trials, and regularly assessed to allow internal and external validity, longitudinal comparative effectiveness research, and quality control. Additional consideration should be taken for instruments used to measure the aspects of QoL specific to minority, caregiver, and elderly populations. Open clinical questions include how providers should weight changes in different QoL subscales and how clinically meaningful difference thresholds should be defined. Review of ongoing clinical trials encouragingly reveals an increased focus on measuring and improving QoL for men with PCa which will inform the way we utilize QoL assessments. However, additional efforts herein described are needed to fully optimize these processes. In summary, this review will explain the rationale for QoL assessments in PCa populations, discuss requirements for effective implementation, describe considerations for vulnerable and under-evaluated populations, and summarize ongoing clinical trials assessing patient QoL.

Keywords: chemotherapy, complementary medicine, prostate cancer, quality of life, radiotherapy, hormone therapy

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Introduction
Prostate cancer (PCa) is the most prevalent solid-organ cancer, estimated to account for 27.3% of all new cancer diagnoses in men in the United States in 2022, and 10.7% of cancer deaths.1 Treatment for PCa is associated with disease-specific and treatment-related effects that significantly impact quality of life (QoL), including urinary and erectile function, and more general effects such as cancer-related fatigue, psychological distress, and chemotherapy-surgical-, radiation-induced complications, among others. Such effects due to PCa or its treatment resulted in 490,000 disability-adjusted life-years in the United States alone in 2011,2 contributing to significant annual productivity loss. Consequentially, physicians and policymakers alike have increasingly emphasized the importance of mitigating complications and toxicity associated with cancer and its treatment as well as improving patient QoL and survivorship care.3–6 For example, one component of the United
Nation’s Sustainable Development Goals aims to reduce worldwide cancer burden through prevention, treatment, and promotion of mental health and well-being. Furthermore, analysis of ‘what matters most’ to the patient in the setting of a cancer diagnosis and treatment has revealed that PCa patients are willing to compromise cancer-specific survival for improved QoL. Thus, with increasing emphasis on QoL as a stand-alone outcome of great importance, it is critical that the appropriate tools are used in the appropriate context.

There has been significant progress toward effective assessment and optimization of QoL for patients with PCa over the past 5–10 years, but there remains room for improvement in terms of consensus regarding standardization of measures and analytic approaches and personalization of measures to assess relevant effects and reduce patient burden in instrument completion. In this review, we will discuss the rationale for and benefits of measuring QoL in clinical practice and trials, choice of QoL assessments and analytic approaches, identification of under evaluated populations and outcomes that require further research and validation, and ongoing clinical trials.

Rationale for QoL assessments
There are several effective arguments for routinely measuring the QoL of PCa patients as part of routine clinical care and academic research. A primary reason is that it is impossible to improve on something that is not measured. Indeed, a recent collaborative review demonstrated that measuring outcomes for every patient is associated with improved PCa outcomes, including overall survival, functional outcomes (e.g. urinary, sexual, and bowel function), and health-related QoL (HRQoL). Implementing a common set of patient-reported outcomes measures (PROMs) in clinical trials is a first step toward standardized comparative effectiveness research across trials and enables a holistic evaluation of disease-related outcomes that includes survival and QoL. Integrating PROMs into clinical practices similarly enables quality assessment and improvement for the outcomes that matter most to the patient within practices or healthcare systems.

Assessing the facets of QoL: PROMs and beyond
The WHO defines QoL as ‘an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns.’ Thus, it is generally accepted that the patient’s perspective should be prioritized in assessing QoL, usually through the use of standardized PROMs. In addition to using PROMs to evaluate QoL, we propose that QoL also includes complications from treatment, cancer, and other life events, as are measured by the Common Terminology Criteria for Adverse Events in clinical trials. In addition, QoL includes X factors associated with the patient experience that are not routinely measured, including patient perceptions regarding time and energy spent on treatment or cancer related activities, as well as underlying preferences and beliefs. QoL can thus be described as the following general constellation of factors: QoL = [PROs – AE] * X factors.

Although there is consensus that the patient’s perspective should be prioritized via the use of PROMs, there is heterogeneity in the integration of various PROMs in clinical trials, as well as in the timing and analytic approach used to report the data. Several PROMs commonly used for patients with PCa include the Functional Assessment of Cancer Therapy – Prostate (FACT-P), Expanded Prostate Cancer Index Composite (EPIC), University of California-Los Angeles Prostate Cancer Index (UCLA-PCI), International Index of Erectile Function (IIEF), and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Prostate Cancer 25 (EORTC QLQ-PR25). Some of these scales such as the FACT-P, or the EORTC QLQ-C30 plus the EORTC QLQPR-25 measure PCa-related symptoms as well as general QoL with broad and widely relevant metrics. Others, such as the EPIC or UCLA-PCI investigate PCa-specific symptoms specifically associated with treatment of localized PCa. The differences between some of the more common tools are detailed in Table 1.

With so many options to choose from, investigators designing clinical trials should choose the PROM that most thoroughly assesses the domains of interest that are expected to differ between treatment arms in the study being performed. Other objective measures of physical or functional performance measures such as frailty assessments, six-minute walk test, sarcopenia, or VO2 max could also be considered to augment these PROMs to provide a more thorough reflection of aspects of
### Table 1. Commonly used assessment tools for QoL in PCa.

| Abbreviation | Name                                              | Summary                                                                                   |
|--------------|---------------------------------------------------|-------------------------------------------------------------------------------------------|
| PROMs EPIC   | EPIC Expanded Prostate Cancer Index Composite     | 16-item questionnaire to measure urinary incontinence, urinary irritation, and the bowel, sexual, and hormonal HRQoL domains |
| EORTC QLQ-C30| European Organization for Research and Treatment of Cancer Quality of Life core 30 | Five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), a global health status/QoL scale, and six single items (dyspnea, loss of appetite, insomnia, constipation, diarrhea, and perceived financial impact) |
| EORTC QLQ-PR25| EORTC QLQ-prostate cancer 25                    | Nine items for urinary symptoms, four for bowel symptoms, six for treatment-related symptoms, and six for sexual functioning |
| FACT-P       | Functional Assessment of Cancer Therapy – Prostate| 39 items in five subscales (physical, social, emotional and functional well-being, and additional concerns) |
| IIEF         | International Index of Erectile Function         | 15 questions to assess erectile dysfunction and treatment outcomes in clinical trials |
| PROMIS       | Patient-Reported Outcomes Measurement Information System | 70 domains measuring pain, fatigue, depression, anxiety, sleep disturbance, physical function, social function, sexual function, and more to assess physical, mental, and social health |
| PQH9         | Patient Health Questionnaire                      | 9 items to screen for depression                                                        |
| SF-36        | 36-item Short-Form health survey                 | 36 questions covering eight domains of health (limitations in physical activities due to health problems, limitations in social activities due to physical or emotional problems, limitations in usual role activities due to physical health problems, bodily pain, general mental health, limitations in usual role activities because of emotional problems, vitality [energy and fatigue], and general health perceptions) |
| UCLA-PCI     | University of California–Los Angeles Prostate Cancer Index | 20 items covering six domains (exploring function and bother, separately, with in each of urinary, sexual, and bowel domains) to assess PCa-specific HRQoL |
| CROMs CRA    | Caregiver Reaction Assessment                    | 24 items covering five domains of caregiving (impact on schedule, impact on finances, lack of family support, impact on health, and self-esteem) |
| CQOLC        | Caregiver Quality of Life Index – Cancer         | 35-item cancer-specific instrument that assesses the caregiver’s QoL over four domains (physical functioning, emotional functioning, family functioning, and social functioning) |
| LMAT         | Locke’s Marital Adjustment Test                  | 15-item measure designed to assess marital adjustment in married couples, assessing agreement between partners on several issues including sex, leisure, and money |

CROM, caregiver-reported outcome measure; HRQoL, health-related QoL; PCa, prostate cancer; PROM, patient-reported outcome measure; QoL, quality of life.
function that may be important to patients. However, while such measures may provide objective data that can predict a variety of useful outcome measures,\textsuperscript{12-17} it is unclear how changes in these measures may affect QoL from an individual patient’s perspective. Furthermore, there are a variety of considerations including cost, patient acceptance, feasibility, ease of administration, accuracy, and degree of validation that make it difficult to establish consensus regarding which of these measures are most appropriate in a given setting. Thus, physical or functional performance measures should not be used to replace patient reported assessments of QoL, but may be valuable additions to a series of assessments to fully characterize QoL.\textsuperscript{18} Additional clinician-reported assessments of functional performance may similarly add to understanding of patient QoL. However, it should be noted that clinician measures of performance status can be subject to bias and high inter-observer variability.\textsuperscript{19}

Consensus efforts are underway to resolve the significant heterogeneity in use of different PROMs. For example, Ratti et al. recently performed a high-quality assessment of the most common PROMs used in localized PCa to move toward consensus and standardize use of PROMs.\textsuperscript{20} This 2021 systematic review identified the 27 most common PROMs and evaluated their psychometric properties and methodological quality using the Consensus-based Standards for the Selection of Health Measurement Instruments methodology and rated each based on their internal consistency and content validity.\textsuperscript{20,21} The authors found that the EORTC QLQ-C30 (a general cancer QoL module that does not directly assess PCa-specific issues) demonstrated high internal consistency but low content validity and the QLQ-Prostate 25 module (which assesses PCa-specific HRQoL) demonstrated moderate content validity and internal consistency. Compared to other tools, the authors concluded that the combination of these two modules (EORTC QLQ-C30 + QLQ-PR25) demonstrated the best psychometric properties and feasibility for use in routine practice and research settings, and thus should be considered for integration in future clinical trials including patients with localized PCa.\textsuperscript{20,22,23} A separate study further demonstrated superior patient acceptability of the EORTC QLQ-C30, with 82% of patients strongly agreeing/agreeing to the importance of all items for the QLQ-C30, whereas they only strongly agreed/agreed to 62% of questions included in the Patient-Reported Outcomes Measurement Information System measure and 56% of items in the Supportive Care Needs Survey Short Form 34 (\(p=0.05\)).\textsuperscript{24} It should be noted that while there is evidence for the incorporation of the EORTC QLQ-C30 + QLQ-PR25 in studies of patients with localized PCa, no such consensus has been established for patients with metastatic PCa. Furthermore, while the EORTC QLQ-C30 + QLQ-PR25 scores highly on internal consistency, content validity, and psychometric principles, there is still significant heterogeneity in QoL assessment tools utilized in practice, and feasibility concerns due to instrument length and clinical teams’ abilities to follow-up on concerning findings. Thus, further work is needed to standardize use and optimize integration of such instruments into practice such that results are more externally valid and comparable across sites and studies.

Special considerations in PROM collection
An important aspect of reporting QoL data for patients is ensuring that the data provide a comparison of QoL between treatment arms at specified timepoints and a characterization of QoL over time. To provide longitudinal data, PROMs should be consistently assessed at intervals over time. In routine clinical care, longitudinal evaluation of QoL on a patient by patient basis alerts the clinician to domains of QoL that are negatively affected by a given treatment or disease progression over time so that efforts can be made to improve them.\textsuperscript{8} Standardized assessments over time can also provide a meaningful comparative quality check between physicians, practices, geographic regions, or even countries based on metrics that are important to patients. Standardized assessment and reporting of PROMs may provide a method of comparing ‘scores’ that could result in quality improvement efforts or other incentives to enhance patient outcomes, or could assist patients who are searching for a health care team.

Within research, the longitudinal assessment of PROMs alongside traditional objective outcome measures is equally important. Just as longitudinal assessments of progression-free, cancer-specific, or overall survival have allowed comparative assessment of various cancer-related therapeutics, similar assessment of QoL will inform the same purpose. Indeed, HRQoL deterioration-free survival was a concept initially explored in relation to metastatic pancreatic cancer\textsuperscript{25,26} and has since been implemented in many cancer populations including advanced colorectal cancer.\textsuperscript{27}
gastric adenocarcinoma, and newly diagnosed glioblastoma. It was first used within the study of PCa in the ENZAMET trial comparing the addition of enzalutamide with androgen deprivation therapy (ADT) ± docetaxel to nilutamide, flutamide, or bicalutamide with ADT ± docetaxel. Due to the use of a longitudinal approach to PROM collection, analysis, and reporting, the study demonstrated that the enzalutamide arm experienced inferior deterioration free survival in the physical function, fatigue, and cognitive function domains at 3 months, but improved deterioration-free survival for physical functioning, cognitive functioning, and overall HRQoL (all \( p < 0.01 \)) over 3 years. Thus, tracking QoL longitudinally allows a more nuanced view of QoL including changes over time that may be related to treatment effects and/or disease progression.

Ongoing analyses continue to investigate patient preferences and cancer-related characteristics that may allow for nuanced understanding of different aspects of QoL for specific populations. Watson et al. demonstrated differences between the way patients with low versus high risk localized PCa weigh the risks and benefits of treatment, time to return to normal activities, and absolute improvements in urinary and sexual function. This work suggests that it will be important to define clinically meaningful difference thresholds for PROMs for different disease settings and populations to appropriately account for changes that may be meaningful to patients who have differences in symptom burden at baseline. For example, the majority of patients with localized disease or biochemical recurrence are relatively asymptomatic and may be more sensitive to small changes in PROM measures than those with more advanced PCa who may have a higher symptom burden at baseline. Similarly, patients that choose active surveillance (AS) for low-risk PCa predictably have improved QOL and decreased symptom burden than patients who received treatment, but at the same time AS patients could suffer from increased psychological distress, as has been reviewed previously. Thus, the minimal clinically important difference for untreated patients who are asymptomatic may be smaller than for patients with advanced symptomatic PCa who have learned to live with symptoms over time.

From an implementation perspective, it is critical that QoL assessment tools are easy to use and set up in a way that adds value to the patient-clinician experience, rather than being an extra burden that detracts from limited face-to-face clinic time. Toward this end, QoL assessments may be integrated with digital health technologies that automate this process. For example, electronic intake forms can collect such information from patients and integrate with the electronic healthcare record to deliver the information to the clinician in a user-friendly way. One such platform collected patient preferences and integrated these with clinical factors to help patients and providers rank PCa treatment options, reducing decisional conflict by 37% \( (p < 0.0001) \) increasing patient-reported involvement (88% versus 57%, \( p = 0.01 \)) and increasing responsibility for the treatment decision (94% versus 52%, \( p < 0.0001) \) compared to patients who received usual care. Chatbots, which use machine learning algorithms to impersonate human interaction, can be used to collect similar information and even provide patient education. For example, the chatbot iDecide promotes informed PCa screening decisions among racial minorities. Furthermore, digital health technology can also provide remote monitoring of PROMs at home. While less extensive evidence exists within the PCa literature, there is strong evidence that monitoring PROs and chemotherapy toxicities during other cancer treatments improves outcomes such as the number of emergency admissions, hospitalizations, and quality-adjusted survival. Monitoring of PROs of patients on chemotherapeutic treatment for advanced PCa or even hormonal treatments for localized PCa could help physicians identify complications earlier, prevent toxicities, and optimize medication and dosing regimens to maximize efficacy while minimizing detrimental effects on QoL. Monitoring sexual and functional continence QoL scores at home could help flag patients who need additional follow-up treatment after radical prostatectomy or radiation, given the persistent prevalence of patient reported lower urinary tract symptoms years after local therapies. Further work in this area is needed to assess how monitoring ambulatory QoL and other PROMs could benefit patients with PCa.

**Considerations for minority and other under-studied populations**

Intentional efforts to recruit minority PCa patients to evaluate potential differences in QoL outcomes in distinct populations are needed. There is evidence that Black men experience cancer care differently, and some successful mitigating strategies
have already been identified. For example, Berry et al. observed that Black race was associated with significantly higher decision regret ($p < 0.01$) among men recently diagnosed with PCa, but that use of the personal patient profile-prostate (a personalized decision support intervention) was associated with significantly decreased decisional regret among Black men ($p = 0.037$). In an RCT examining the effect of a tablet-delivered psycho-social intervention on disease-specific distress among men with advanced PCa, Bouchard et al. found that cognitive behavioral stress management improves PCa-related anxiety to a greater degree among Black patients compared to non-Hispanic White patients. Furthermore, while Davis et al. found no benefit to a technology-assisted symptom monitoring system (versus control) among early-stage PCa survivors, there was a significant interventional benefit among the African American men who received the intervention (versus control) on doctor/patient communication ($p < 0.05$), general HRQoL ($p < 0.06$), and sexual function ($p < 0.05$). Finally, Campbell et al. randomized 40 African-American PCa survivors and their partners to dyadic coping skills training versus usual care, and observed that the intervention significantly improved survivor QoL in multiple domains ($p < 0.05$) and there was a trend toward significant improvement in partner's QoL in multiple domains. In general, however, underrepresented minority patients are recruited to studies at disproportionately low levels and these kinds of racial analyses are not adequately powered. Thus, future studies should ensure that diverse cohorts are recruited.

There is also growing appreciation for the importance of caregiver-reported outcome measures (CROMs). The burden of cancer and its treatment extends beyond the patient, causing detrimental impacts to the QoL and psychological well-being of caregivers, partly driven by the cancer patient’s distress, sexual concerns and physical QoL. This is not only of personal importance to the caregiver/partner, but may also impact the burden of cancer on society through a 23% work productivity loss, as well as some influence on patient outcomes. There has been limited exploration of CROMs to date, reflected by how few studies measure CROMs. As evidenced by a systematic review that aimed to identify all instruments measuring the impact of caregiving and subsequently search for any psychometric testing of such instruments in cancer caregivers, no psychometrically validated cancer CROM exists.

The review identified eight CROM tools that were tested for at least one of the following psychometric components: content validity, construct validity, internal consistency, test–retest reliability, precision, responsiveness, and acceptability. Of those eight, there was the strongest evidence for the Caregiver Reaction Assessment and Caregiver Quality of Life Index – Cancer. A systematic review of 16 RCTs assessing psychological interventions for PCa survivors and their caregivers did not include these CROMs. Instead, the included studies measured between 2 and 12 other CROMs each, most often related to relationships, general- and cancer-specific distress. While included studies were generally effective at improving caregiver-reported outcomes (CROs) including relationship outcomes, sexuality outcomes, and mental health, there were no improvements in CROs in any of the studies, and nearly half actually produced poorer outcomes for the caregiver, perhaps because the interventions were predominantly focused on the PCA survivor’s needs rather than the caregiver/partner. Nevertheless, further work is needed to both to psychometrically validate tools to measure caregiver outcomes and to develop dually patient- and caregiver-centric interventions that may be effective in improving both PROMs and CROMs.

Given that PCa is the leading cause of cancer death in men over 85, the question of assessing QoL in older adults is essential to the holistic care of PCa patients. Furthermore, QoL in older patients with PCa must be understood in the context of their aging, potential frailty, and other comorbidities, and national guidelines for the care of older adults with cancer emphasize the importance of understanding the intersection of QoL and function in this population. In trials of comprehensive geriatric assessment where secondary outcomes include QoL, authors use previously described such as the FACT and QLQ-C30, though in these study populations, QoL must be integrated into the context of broader geriatric syndromes such as comorbidities, incontinence, falls, and social supports. The relationship between PCa treatment and QoL in the older adult population is particularly complex due to the interplay of functional status and comorbidities in these patients. Though comprehensive geriatric assessments have been shown to reduce nursing home admissions and falls in patients with cancer, there has been no consistent association with QoL improvements, and further study is needed in older men with PCa.
Finally, given how these questionnaires generally query a wide range of physical, functional, emotional, social, and familial factors, it follows that other sociodemographic factors beyond race, age, and caregiver status could have significant and predictable impacts on the ways that patients respond. For example, health literacy has been shown to affect many aspects of the PCa care continuum, from PSA screening rates or shared decision-making regarding treatment options, but little work has been done to assess differences in how health literacy affects patients’ response to QoL questionnaires. Song et al. found that after controlling for sociodemographic variables among 1581 American men with localized PCa, higher health literacy was associated with better mental well-being as measured by the SF12 ($p < .005$), though not physical well-being. Goodwin et al. similarly demonstrated that among 565 Australian men with PCa, health literacy factors had greater association with mental than physical health status. Thus, poor health literacy appears to have a detrimental effect on mental more so than physical QoL, which could provide a basis for targeted intervention. Other sociodemographic variables, such as religious affiliation, marital status, employment, income, etc., may create additional, predictable variability in responses to QoL questionnaires and should be studied.

**Current ongoing clinical trials related to patient QoL**

There are numerous ongoing clinical trials that may inform the way PROMs are utilized in clinical practice. To outline some of the ongoing efforts, a search of registered clinical trials was performed on Clinicaltrials.gov with the keywords ‘prostate cancer’ together with ‘patient reported outcomes’ or ‘quality of life’. Only studies performed exclusively with PCa patients that included HRQoL/PROMs as the primary outcome are discussed below; there were innumerable trials that were collecting QoL data as a secondary objective. Furthermore, only currently active trials, or those completed within the past 5 years (but yet to have results published), were included. Most studies were currently recruiting, reflecting the level of attention in the field of health outcomes research in PCa. Table 2 offers a brief outline of the trials.

Two prospective observational studies incorporate PROMs into electronic medical records to longitudinally track patients’ QoL along their PCa journey, with a special focus on treatment toxicity and survivorship (NCT04694924 and NCT04357925). Indeed, obtaining QoL information can help guide treatment decision-making at the localized stage, a concept that has been explored in several large trials but remains an area of ongoing research. For example, a trial is evaluating QoL after prostatectomy with the aim of identifying prevalent symptoms that can guide specific interventions to reduce these symptoms in future care delivery (NCT03035500). Likewise, another trial is monitoring patients’ anxiety and depressive symptoms associated with their PCa diagnosis to establish their prevalence and determine whether mental well-being can affect cancer outcomes (NCT04647474).

Multiple trials aimed at preventing or relieving treatment-related toxicity have been developed. The interventions are frequently pharmacologic in nature, whether it is testosterone replacement to improve sexual function after radical prostatectomy (NCT03716739), alpha blockers for radiation-induced urinary symptoms (NCT02220829), modafinil to combat fatigue caused by radiation and ADT (NCT03772834), or oxybutynin to improve the burden of hot flashes caused by ADT (NCT04600336). In addition, interventional approaches like adaptive radiation techniques to preserve erectile function are also being studied (NCT04861194). Lastly, non-pharmacologic interventions, such as exercise and physical activity, are being evaluated to improve fatigue brought on by ADT (NCT03421782) or to improve symptoms related to palliative radiotherapy (NCT04556045).

The role of QoL in helping decide between treatment options at the metastatic stage is the focus of several large studies, some of which have been mentioned before. Ongoing studies are specifically evaluating the effects of oral antiandrogens in cognitive function and fatigue. For instance, a trial is evaluating differences in cognitive side effects between abiraterone and enzalutamide (NCT03016741), with other objectives including overall HRQoL and fatigue. Another similar study is assessing the cognitive issues associated with enzalutamide by comparing full dose with reduced dosing of enzalutamide, although the primary outcome is fatigue and not directly effects on cognition (NCT03927391). Lastly, a pair of recently completed studies evaluated the effects of radium-223 on QoL, particularly its effects on bone-specific symptoms.
Table 2. Current trials on HRQoL in PCa patients.

| Trial identifier | Intervention | Population | Primary outcome | Study instrument | Status            |
|------------------|--------------|------------|-----------------|------------------|------------------|
| NCT02220829      | Silodosin    | Localized, planned for EBRT | Urinary symptoms | IPSS             | Recruiting       |
| NCT02398526      | N/A, observational | Metastatic, undergoing radium-223 | Pain | BPI-SF | Completed         |
| NCT0301674       | Abiraterone versus enzalutamide | Metastatic | Cognitive function | Cogstate | Recruiting       |
| NCT03035500      | Survivorship care plan | Localized, post-RP | Treatment related toxicity | EPIC | Active, not recruiting |
| NCT03421782      | Exercise ± CBT | Advanced, on ADT | Fatigue | PROMIS | Recruiting       |
| NCT03716739      | Testosterone | Localized, post-RP | Sexual activity | Psychosexual Daily Questionnaire | Recruiting       |
| NCT03772834      | Methylphenidate | Localized, planned for XRT with ADT | Fatigue | FACIT-F | Recruiting       |
| NCT03927391      | Enzalutamide | Metastatic, frail | Fatigue | FACIT-F | Recruiting       |
| NCT04357925      | N/A, observational | All | Overall HRQOL | EORTC QLQ-C30 | Recruiting       |
| NCT04556045      | Exercise | Metastatic, palliative XRT | Overall HRQOL | PROMIS | Recruiting       |
| NCT04600336      | Oxybutynin  | All, on ADT | Hot flashes | Hot flash scores | Recruiting       |
| NCT04647474      | N/A, observational | Localized | Mental well-being | PHQ-9, GAD-7 | Recruiting       |
| NCT04694924      | N/A, observational | Non-metastatic | Overall HRQOL | EORTC QLQ-C30 | Recruiting       |
| NCT04861194      | Neurovascular sparing XRT | Localized, undergoing XRT | Erectile dysfunction | International Index of Erectile Function | Recruiting       |
| NCT04995614      | N/A, observational | Metastatic, undergoing radium-223 | Overall HRQOL | EORTC QLQ-C30 | Completed       |

ADT, androgen deprivation therapy; BPI-SF, Brief Pain Inventory - Short Form; CBT, Cognitive Behavioral Therapy; EORTC QLQ, European Organization for Research and Treatment Core Quality of Life questionnaire; EPIC, Prostate Cancer Index Composite; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; GAD, General Anxiety Disorder; HRQoL, health-related quality of life; IPSS, International Prostate Symptom Score; N/A, Not Applicable; PCa, prostate cancer; PHQ, Patient Health Questionnaire; PROMIS, Patient-Reported Outcomes Measurement Information System; QoL, quality of life; XRT, external radiation therapy.

(NCT04995614) as well as pain associated with skeletal events (NCT02398526).

Conclusion
Researchers and clinicians have increasingly stressed the importance of assessing QoL among patients with PCa in addition to more traditional metrics such as morbidity and mortality. Such assessment allows for study of, and intervention on, that which matters most to the patient. Great strides toward this end have been made over the last decade to study and address patient QoL, and current clinical trials seek to further optimize these processes. However, there remains significant room for improvement in investigating QoL and incorporating PROMs in clinical trials and practice in the most effective manner. Future research must continue to evaluate QoL complications that have been inadequately assessed as well as complications of novel therapies that have different toxicity profiles than previously used treatments. Defining minimal clinically important differences in patient populations across the disease continuum is also needed to ensure an appropriate degree of difference in QoL according to the
baseline symptom burden of each population. Furthermore, we must validate PROMs in minority, caregiver, and older adult populations to better characterize the unique aspects of QoL that are affected during PCa treatment. Ongoing trials will continue to inform this area of research and clinical care for many years to come, demonstrating the ways in which the ‘soft’ science of QoL can improve ‘hard’ clinical outcomes as well as the lived experience of PCa patients around the world.

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Not Applicable.

Consent for publication
Not Applicable.

Author contribution[s]

Logan G Briggs: Conceptualization; Methodology; Project administration; Writing – original draft; Writing – review & editing.

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