Recommended Patient-Reported Core Set of Symptoms to Measure in Prostate Cancer Treatment Trials

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The National Cancer Institute (NCI) Symptom Management and Health-Related Quality of Life Steering Committee convened four working groups to recommend core sets of patient-reported outcomes to be routinely incorporated in clinical trials. The Prostate Cancer Working Group included physicians, researchers, and a patient advocate. The group’s process included 1) a systematic literature review to determine the prevalence and severity of symptoms, 2) a multistakeholder meeting sponsored by the NCI to review the evidence and build consensus, and 3) a postmeeting expert panel synthesis of findings to finalize recommendations. Five domains were recommended for localized prostate cancer: urinary incontinence, urinary obstruction and irritation, bowel-related symptoms, sexual dysfunction, and hormonal symptoms. Four domains were recommended for advanced prostate cancer: pain, fatigue, mental well-being, and physical well-being. Additional domains for consideration include decisional regret, satisfaction with care, and anxiety related to prostate cancer. These recommendations have been endorsed by the NCI for implementation.

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In September 2011, a National Cancer Institute Clinical Trials Planning Meeting was convened to develop recommendations regarding a core set of patient-reported symptoms and health-related quality of life (HRQOL) domains to be assessed in clinical trials (1). This brief communication summarizes the process and recommendations of the Prostate Cancer Working Group, which is composed of a multidisciplinary team of physicians, researchers, and a patient advocate, as well as discussions regarding these recommendations from the planning meeting. Recognizing that patients with localized prostate cancer (who commonly receive treatments targeting the prostate) vs those with advanced/metastatic disease (who commonly receive systemic therapy and experience symptoms from metastases) may experience different types of HRQOL impact, the working group made separate recommendations for these two groups of patients.

A systematic literature review was conducted to determine the prevalence and severity of symptoms and HRQOL domains across published studies. A PubMed search was performed using the search terms “prostate cancer” and “quality of life” and the following search filters: 1) published from January 1, 2001, to December 31, 2011; 2) English language; 3) human subjects; 4) adult: 19+ years; and 5) subjects: cancer. This resulted in an initial list of 1164 articles; 295 articles without prostate cancer patient-reported outcomes (PROs) data were excluded. Further, we excluded studies with less than 200 patients, those not of prospective design or lacking pretreatment PRO assessment, and those from a single institution (Figure 1), resulting in 77 articles included for review and providing the basis for the working group’s considerations. The recommendations for core PRO domains were finalized through the multistakeholder planning meeting and subsequent consensus-building process, as described elsewhere (1).

Of 61 included articles for localized prostate cancer, 51 were prospective cohort studies, and 10 were clinical trials (references 43–88 are cited in Supplementary Table 1, available online). Studies reported PRO data in different formats, and those that reported the percentage of patients having each symptom in the different domains provided the level of detail needed by the working group.

In validated PRO instruments, urinary incontinence is measured as presence/absence of incontinence, incontinence frequency, and pad use (2–8). Incontinence is rare pretreatment, with less than 5% of patients using pads at baseline (9–11). Prostatectomy causes at least short-term incontinence in most men, with subsequent recovery over 1 to 2 years (9,10,12–14). At 2 months after operation, two-thirds of prostatectomy patients report pad use; this decreases to 20% by 2 years (9,14). However, up to 50% to 60% of patients report some degree of incontinence at 2 years after prostatectomy (10,13,15). The rates of pad use after external beam radiation and brachytherapy do not change dramatically with time, with 5% of patients reporting use at 2 years (9,10).

Urinary obstruction and irritation occur and change independently from incontinence; both domains should be assessed. In validated instruments, urinary obstruction and irritation is measured as ease/strength of urinary flow, nocturia, urinary frequency, urgency, and dysuria (2,3,5–8,16). At baseline, 10% to 15% of patients have weak urinary flow, and 15% report frequency (9). After prostatectomy, frequency is modestly more prevalent acutely (in one study, 17% to 24% of patients reported it at 2 months) (9), but obstructive symptoms improve, likely because of alleviation of benign prostatic hypertrophy (9). Up to one-third of external beam radiation patients and two-thirds of brachytherapy patients report acute obstructive and irritative symptoms (13,17), with resolution over 1 to 2 years to levels similar to baseline (9).

In validated instruments, bowel-related symptoms include diarrhea, bowel...
urgency, incontinence, frequency, pain with bowel movements, hematochezia, abdominal cramping, and tenesmus (2–8,16). Most bowel symptoms are uncommon pretreatment, except diarrhea (up to 15%) (10,14). Both external beam radiation and brachytherapy can cause symptoms: approximately 15% to 40% of patients report increased urgency, frequency, or diarrhea acutely after radiation (9,10,15), with recovery in brachytherapy patients (<10% report these symptoms at 2 years) and less so in external beam radiation patients. Five percent of external beam patients and 3% of brachytherapy patients report hematochezia at 2 years (9). Bowel incontinence is rare (13).

In validated instruments, sexual function is measured as libido, frequency of sexual activity, quality of erection, ability to get and keep an erection, and ability to achieve orgasm and ejaculation (2–8,16,18). In the literature, fewer prostatectomy patients than radiation patients have baseline sexual dysfunction (19,20), likely because of age and comorbidity differences in patients selected to undergo these different treatments. Approximately 15% of prostatectomy patients report baseline poor erections, compared with 30% to 40% of radiation patients (9). Acutely after prostatectomy, 80% to 90% of patients report difficulty with erections (9,10), but this proportion decreases to approximately 60% by 2 years (9,19,21). After radiation, erectile dysfunction increases with time and is reported by 50% to 60% of external beam radiation patients and 20% to 50% of brachytherapy patients at 2 years (9,10,13,19,22). Those who received radiation alone (without androgen deprivation therapy) had better outcomes (9). Most existing studies have not consistently captured use of sexual dysfunction therapies and how these therapies affect PROs.

In validated instruments, hormonal-related symptoms include hot flashes, breast tenderness or enlargement, depression, fatigue, and weight change (3,5–7). Depression and fatigue are reported by approximately 10% of patients at baseline. After external beam radiation or brachytherapy, fatigue affects 21% to 25% of patients at 2 months, but this rate decreases to 12% to 16% by 2 years (9). Hot flashes (1%), breast problems (1%), and weight change (4%) are uncommon at baseline and for patients who do not receive hormonal therapy (9).

PROs in advanced prostate cancer are less well studied. Of 16 included articles, two were prospective cohort studies, and 14 were clinical trials (references 89–98 are cited in Supplementary Table 2, available online).

In validated instruments, pain is measured as presence of pain, bother, and pain interfering with activities (18,23–25). Pain is common in advanced prostate cancer patients, reported by more than 70% in some studies (26–28). With systemic therapy or zoledronic acid, one-third or more of patients can experience a pain response (27–29).

In validated instruments, items in the fatigue domain include experiencing tiredness, or lack of energy or vitality (18,23–25). Items in the mental well-being domain include ability to perform activities of daily living, instrumental activities of daily living, and physical functioning. Some instruments include specific examples of these, including ability to work, perform strenuous activities, and take a walk (18,23,25).

The prevalence of symptoms in these domains is difficult to ascertain from existing literature. Studies that have reported PRO data in patients with advanced prostate cancer commonly include these measures and describe changes in domain scores (30) but do not report the prevalence of each symptom.

The Prostate Cancer Working Group recommends five domains for studies of localized prostate cancer patients (urinary incontinence, urinary obstruction and irritation, bowel-related symptoms, sexual dysfunction, and hormonal symptoms [if relevant for patients receiving hormonal therapy]) and four domains for advanced cancer (pain, fatigue, mental well-being, and physical well-being). Table 1 summarizes existing validated PRO instruments that can be used for these assessments.

These recommendations are in addition to those from the cross-cutting group, which apply to all cancer patients (1). Several points of discussion during the planning meeting deserve mention:

1. In the context of these recommendations, PRO incorporation in clinical trials should be hypothesis-driven and should measure symptoms appropriate for the treatments being assessed.
2. Symptoms experienced by patients with localized and advanced cancers

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**Figure 1.** Flowchart of the selection process of articles for the literature review.

| 1164 results returned | 295 search failure (no prostate cancer PRO) |
|-----------------------|--------------------------------------------|
| 869 with prostate cancer PRO data | 555 with less than 200 patients |
| 314 with at least 200 patients | 165 without prospective, pretreatment data |
| 149 with prospective, pretreatment data | 72 with data from one institution |
| 77 with data from multiple institutions | |
| First author (reference) | Instrument | Domains |
|--------------------------|------------|---------|
| Clark (2) | Prostate Cancer Symptom Indices (31 items) | - Urinary incontinence (3 items)  
- Incontinence bother (1 item)  
- Obstruction (5 items)  
- Obstruction bother (5 items)  
- Bowel problems (6 items)  
- Bowel problems bother (4 items)  
- Sexual dysfunction (5 items)  
- Sexual problems (2 items) |
| Litwin (4) | UCLA Prostate Cancer Index (20 items) | - Urinary function (5 items)  
- Urinary bother (1 item)  
- Sexual function (8 items)  
- Sexual bother (1 item)  
- Bowel function (4 items)  
- Bowel bother (1 item) |
| Wei (3) | Expanded Prostate Cancer Index Composite (EPIC) (50 items) | - Urinary incontinence (4 items)  
- Urinary irritation/obstruction (7 items)  
- Overall urinary (1 item)  
- Sexual function (9 items)  
- Sexual bother (4 items)  
- Bowel function (7 items)  
- Bowel bother (7 items)  
- Hormonal function (5 items)  
- Hormonal bother (6 items) |
| Szymanski (6) | EPIC–26 (26 items) | - Urinary incontinence (4 items)  
- Urinary irritation/obstruction (4 items)  
- Overall urinary (1 item)  
- Bowel (6 items)  
- Sexual (6 items)  
- Vitality or hormonal (5 items) |
| Chang (5) | EPIC–Clinical Practice (16 items) | - Urinary incontinence (3 items)  
- Urinary irritation/obstruction (3 items)  
- Overall urinary (1 item)  
- Bowel (3 items)  
- Sexual (3 items)  
- Vitality or hormonal (3 items) |
| van Andel (7) | EORTC QLQ-PR25 (25 items) | - Urinary symptoms (8 items)  
- Incontinence aid (1 item)  
- Bowel symptoms (4 items)  
- Hormonal symptoms (6 items)  
- Sexual activity (2 items)  
- Sexual function (4 items) |
| Esper (23) | FACT-G + FACT-P (47 items) | - Physical well-being (8 items)  
- Social/family well-being (8 items)  
- Relationship with doctor (3 items)  
- Emotional well-being (7 items)  
- Functional well-being (8 items)  
- Additional items: weight loss, appetite, pain (4 items), feel like a man, difficulty bowel, urinary (3 items), erection, QOL. |
| Yount (24) | FAPSI-6 (6 items)  
FAPSI-8 (8 items)  
– designed for advanced prostate cancer | FAPSI-6  
- Pain (3 items)  
- Fatigue/lack of energy  
- Weight loss  
- Worry  
FAPSI-8  
= FAPSI-6, plus…  
- Urination (2 items) |
| Victorson (25) | NCCN/FACT-P Symptom Index (17 items) – designed for advanced prostate cancer | Items are: lack of energy, fatigue, leg weakness, pain (3 items), difficulty urinating, weight loss, appetite, worry, sleep, nausea, trouble moving bowels, satisfied sex life, treatment side effects, enjoy life, QOL. |
| Stockler (41) | PROSQOLI (10 items) – designed for advanced prostate cancer | Present pain intensity (1–5)  
Linear-analog (0–100): pain, fatigue, appetite, constipation, passing urine, physical activity, mood, family/marriage/relationships, overall well-being |

*(Table continues)*
Table 1 (Continued).

| First author (reference) | Instrument | Domains |
|--------------------------|------------|---------|
| Farnell (16)             | LENT (22 items) – designed for radiation-related symptoms | - Rectum/Bowel (10 items) - Bladder/Urethra (9 items) - Sexual Function (3 items) |
| Cleary (18)              | (30 items) – designed for advanced prostate cancer | - Pain (4 items) - Emotional well-being (5 items) - Social functioning (2 items) - Vitality (6 items) - Physical capacity (6 items) - Sexual interest (3 items) - Sexual Functioning (4 items) - Overall health (1 item) |
| Rodrigues (8)            | Prostate Cancer Radiation Late Toxicity (29 items) – designed for radiation-related symptoms | - Bowel (12 items) - Urination (11 items) |
| Ritvo (42)               | Prostate Outcomes Record of Psychometric and Utility Self-Report (PORPUS; 10 items) | - Pain/disturbing body sensations - Energy - Family/friend support - Communication with doctor - Urinary frequency - Urinary incontinence - Sexual function - Sexual interest - Emotional well-being - Bowel problems |

* EORTC = European Organization for Research and Treatment of Cancer; FACT = Functional Assessment of Cancer Therapy; FAPSI = FACT Advanced Prostate Symptom Index; LENT = Late Effects in Normal Tissues; NCCN = National Comprehensive Cancer Network; PROSQOLI = Prostate Cancer Specific Quality of Life Instrument; UCLA = University of California—Los Angeles. Instruments that measure pain, fatigue, mental well-being, and physical well-being can be considered in clinical trials assessing advanced prostate cancer treatments. Instruments that measure urinary incontinence, urinary obstruction and irritation, bowel-related symptoms, sexual dysfunction, and hormonal symptoms (for patients receiving hormonal therapy) can be considered in clinical trials assessing localized prostate cancer treatments, including radical prostatectomy, radiation therapy, and other local therapies. Patient-reported outcome assessment in clinical trials should be hypothesis-driven, and patients with localized and advanced cancers may have overlapping symptoms depending on their disease status and prior treatments.

Table 2. Validated prostate-cancer specific patient-reported outcome instruments measuring decisional regret, satisfaction with care, and anxiety

| First author | Instrument | Number of items |
|--------------|------------|-----------------|
| Decisional regret | Clark (99) | 3 |
| Clark (100) | 5 |
| Satisfaction with care | Lubeck (101) | CaPSURE* satisfaction scale | 9 |
| Prostate cancer anxiety | Roth (102) | Memorial Anxiety Scale for Prostate Cancer | 18 |

* CaPSURE = Cancer of the Prostate Strategic Urologic Research Endeavor.

may overlap. For example, localized cancer patients can experience fatigue and physical well-being changes while receiving treatment. Similarly, advanced cancer patients may experience symptoms relating to their local (prostate) cancer or residual symptoms from prior treatment, as well as hormonal therapy symptoms. If appropriate, these additional domains can be included.

3. Longitudinal PRO measurement is important because of the time-dependent nature of symptom development and resolution after treatment. Investigators need to consider not only relevant domains and symptoms for inclusion but also appropriate measurement time points.

4. PRO measurement burden needs to be considered because substantial overburden may increase missing data. Among the attendees, there was general feeling that the working group’s recommended domains are not overly burdensome because validated instruments measuring these domains have been successfully incorporated in prior trials.

5. PRO use in clinical trials is changing over time. Not only are PROs commonly incorporated in current trials (31), but they have also been used as primary endpoints. For example, a randomized phase II trial (RTOG 0938) is comparing two different doses of stereotactic body radiation therapy for early prostate cancer. The primary goal is to assess the safety and tolerability of this treatment, as assessed by patient-reported bowel and urinary symptoms. Similar approaches can be applied to trials examining future surgical, radiation, and other treatment technologies.

The working group recognizes the rich literature in prostate cancer PROs and important methodologic advances over the past 20 years. However, the current literature is based mainly on cohort studies, which are limited by differential patient selection into treatment groups. Patients treated by prostatectomy are often younger, healthier, and have higher baseline sexual, bowel, and urinary function than those treated by radiation (9,10,32–36), thus making comparisons across groups
difficult. More PRO incorporation in trials and publication of PRO results simultaneously with the mortality and disease control outcomes (31) will help mitigate this limitation and provide important new information to patients and physicians.

Because the working group’s recommendations are based on a systematic literature review, they may not incorporate all possible side effects from newer systemic therapies. Hypothesis-driven additional measures may be needed in trials that use these therapies.

A continued challenge is interpretability of PRO data (19,37,38). Most published studies report average scores of symptom domains, usually ranging from 0 to 100 points, but the exact meaning of higher vs lower scores is unclear. The proportion of patients experiencing symptoms and severity of these symptoms cannot be ascertained from average scores. Further, a commonly used threshold of one-half standard deviation signifying clinically meaningful change (39) appears limited in that a statistical threshold is used to derive clinical meaning; however, few alternatives have emerged. Reporting the prevalence of individual symptoms in addition to summary scores (9) provides important and more tangible information. In addition, some studies have classified patients into different levels of function (eg, normal, intermediate, poor) (19,33,40), which can facilitate interpretation of “meaningful change” as a move from one clinical level to another. Further methodologic development is needed.

Although not included in the official recommendation, other PRO measures that investigators may consider include decisional regret, satisfaction with care, and anxiety or worry related to prostate cancer (Table 2). Further, although the charge of the working group was to make recommendations for clinical trials, these same considerations may also apply to observational studies.

References

1. Reeve B, Mitchell S, Dueck A, et al. Recommended core set of symptoms to measure adult oncology treatment trials. 2. Clark JA, Talcott JA. Symptom indexes to assess outcomes of treatment for early prostate cancer. Med Care. 2001;39(10):1118–1130. 3. Wei JT, Dunn RL, Litwin MS, et al. Development and validation of the expanded prostate cancer index composite (EPIC) for comprehensive assessment of health-related quality of life in men with prostate cancer. Urology. 2000;56(6):899–905. 4. Litwin MS, Hays RD, Fink A, et al. The UCLA Prostate Cancer Index: development, reliability, and validity of a health-related quality of life measure. Med Care. 1998;36(7):1002–1012. 5. Chang P, Szymanski KM, Dunn RL, et al. Expanded prostate cancer index composite for clinical practice: development and validation of a practical health related quality of life instrument for use in the routine clinical care of patients with prostate cancer. J Urol. 2011;186(3):865–872. 6. Szymanski KM, Wei JT, Dunn RL, et al. Development and validation of an abbreviated version of the expanded prostate cancer index composite instrument for measuring health-related quality of life among prostate cancer survivors. Urology. 2010;76(5):1245–1250. 7. van Andel G, Bottomley A, Fossa SD, et al. An international field study of the EORTC QLQ-PR25: a questionnaire for assessing the health-related quality of life of patients with prostate cancer. Eur J Cancer. 2008;44(16):2418–2424. 8. Rodrigues G, Bauman G, Lock M, et al. Psychometric properties of a prostate cancer radiation late toxicity questionnaire. Health Qual Life Outcomes. 2007;5:29. 9. Sarda MG, Dunn RL, Michalski J, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. N Engl J Med. 2008;358(12):1250–1261. 10. Madalinska JB, Essink-Bot ML, de Koning HH, et al. Health-related quality-of-life effects of radical prostatectomy and primary radiotherapy for screen-detected or clinically diagnosed localized prostate cancer. J Clin Oncol. 2001;19(6):1619–1628. 11. Gacci M, Carini M, Simonato A, et al. Factors predicting continence recovery 1 month after radical prostatectomy: results of a multicenter survey. Int J Urol. 2011;18(10):700–708. 12. Kubler HR, Tseng TY, Sun L, et al. Impact of nerve sparing technique on patient self-assessed outcomes after radical perineal prostatectomy. J Urol. 2007;178(2):488–492, discussion 492. 13. Buron C, Le Vu B, Cosset JM, et al. Brachytherapy versus prostatectomy in localized prostate cancer: results of a French multicenter prospective medico-economic study. Int J Radiat Oncol Biol Phys. 2007;67(3):812–822. 14. Talcott JA, Manola J, Clark JA, et al. Time course and predictors of symptoms after primary prostate cancer therapy. J Clin Oncol. 2003;21(12):3979–3986. 15. Talcott JA, Manola J, Clark JA, et al. Time course and predictors of symptoms after primary prostate cancer therapy. J Clin Oncol. 2003;21(12):3979–3986. 16. Farnell D, Mandall P, Anandadas C, et al. Development of a patient-reported questionnaire for collecting toxicity data following prostate brachytherapy. Radiother Oncol. 2010;97(1):136–142. 17. Merrick GS, Butler WM, Wallner KE, et al. Dysuria after permanent prostate brachytherapy. Int J Radiat Oncol Biol Phys. 2003;55(4):979–985. 18. Cleary PD, Morrissey G, Oster G. Health-related quality of life in patients with advanced prostate cancer: a multinational perspective. Qual Life Res. 1995;4(3):207–220. 19. Chen RC, Clark JA, Talcott JA. Individualizing quality-of-life outcomes reporting: how localized prostate cancer treatments affect patients with different levels of baseline urinary, bowel, and sexual function. J Clin Oncol. 2009;27(24):3916–3922. 20. Sanda MG, Dunn RL, Michalski J, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. New Engl J Med. 2008;358(12):1250–1261. 21. Ward NT, Parsons JK, Levinson AW, et al. prostate size is not associated with recovery of sexual function after minimally invasive radical prostatectomy. Urology. 2011;77(4):952–956. 22. Guedea F, Ferrer M, Pera J, et al. Quality of life two years after radical prostatectomy, prostate brachytherapy or external beam radiotherapy for clinically localised prostate cancer: the Catalan Institute of Oncology/Bellvitge Hospital experience. Clin Transl Oncol. 2009;11(7):470–478. 23. Esper P, Mo F, Chodak G, et al. Measuring quality of life in men with prostate cancer using the functional assessment of cancer therapy-prostate instrument. Urology. 1997;50(6):920–928. 24. Yount S, Cella D, Banik D, et al. Brief assessment of priority symptoms in hormone refractory prostate cancer: the FACT Advanced Prostate Symptom Index (FAPSI). Health Qual Life Outcomes. 2003;1:69.

25. Victorson DE, Beaumont JL, Rosenbloom SK, et al. Efficient assessment of the most important symptoms in advanced prostate cancer: the NCCN/FACT-P Symptom Index. Psychooncology. 2011;20(9):977–981. 26. Saad F, Gleason DM, Murray R, et al. A randomized, placebo-controlled trial of zolodronic acid in patients with hormone-refractory metastatic prostate carcinoma. J Natl Cancer Inst. 2002;94(19):1458–1468. 27. Saad F, Eastham J. Zoledronic Acid improves clinical outcomes when administered before onset of bone pain in patients with prostate cancer. Urology. 2010;76(5):1175–1181. 28. Ernst DS, Tannock IF, Winquist EW, et al. Randomized, double-blind, controlled trial of mitoxantrone/prednisone and cladrolated versus mitoxantrone/prednisone and placebo in patients with hormone-refractory prostate cancer and pain. J Clin Oncol. 2003;21(17):3333–3342. 29. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med. 2004;351(15):1502–1512. 30. Berry DL, Moiinpour CM, Jiang CS, et al. Quality of life and pain in advanced stage prostate cancer: results of a Southwest Oncology...
Group randomized trial comparing docetaxel and estramustine to mitoxantrone and prednisone. J Clin Oncol. 2006;24(18):2828–2835.

31. Bruner DW, Bryan CJ, Aaronson N, et al. Issues and challenges with integrating patient-reported outcomes in clinical trials supported by the National Cancer Institute sponsored clinical trials networks. J Clin Oncol. 2007;25(12):3051–3057.

32. Chen RC, Clark JA, Talcott JA. Individualizing quality-of-life outcomes reporting: how localized prostate cancer treatments affect patients with different levels of baseline urinary, bowel, and sexual function. J Clin Oncol. 2009;27(24):3916–3922.

33. Pardo Y, Guedea F, Aguilo F, et al. Quality-of-life impact of primary treatments for localized prostate cancer in patients without hormonal treatment. J Clin Oncol. 2010;28(11):4687–4696.

34. Jayadevappa R, Schwartz JS, Chhatre S, et al. Satisfaction with care: a measure of quality of care in prostate cancer patients. Med Decis Making. 2010;30(2):234–245.

35. Ferrer M, Suírez JF, Guedea F, et al. Health-related quality of life 2 years after treatment with radical prostatectomy, prostate brachytherapy, or external beam radiotherapy in patients with clinically localized prostate cancer. Int J Radiat Oncol Biol Phys. 2008;72(2):421–432.

36. Downs TM, Sadesky N, Pasta DJ, et al. Health-related quality of life patterns in patients treated with interstitial prostate brachytherapy for localized prostate cancer—data from CaPSURE. J Urol. 2003;170(5):1822–1827.

37. Frank SJ, Pieters LL, Davis J, et al. An assessment of quality of life following radical prostatectomy, high dose external beam radiation therapy and brachytherapy iodine implantation as monotherapies for localized prostate cancer. J Urol 2007;177(6):2151–2156; discussion 2156.

38. Krupski TL, Kwan L, Affi AA, et al. Geographic and socioeconomic variation in the treatment of prostate cancer. J Clin Oncol. 2005;23(11):7881–7888.

39. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Med Care. 2003;41(5):582–592.

40. Potosky AL, Davis WW, Hoffman RM, et al. Five-year outcomes after prostatectomy or radiotherapy for prostate cancer: the prostate cancer outcomes study. J Natl Cancer Inst. 2004;96(18):1358–1367.

41. Stockler MR, Oseba D, Corey P, et al. Convergent discriminative, and predictive validity of the Prostate Cancer Specific Quality of Life Instrument (PROSQUAL) assessment and comparison with analogous scales from the EORTC QLQ-C30 and a trial-specific module. European Organisation for Research and Treatment of Cancer. Core Quality of Life Questionnaire. J Clin Epidemiol. 1999;52(7):653–666.

42. Rito P, Irvine J, Naglie G, et al. Reliability and validity of the PORPUS, a combined psychometric and utility-based quality-of-life instrument for prostate cancer. J Clin Epidemiol. 2005;58(5):466–474.

43. Jacobsen NE, Moore KN, Estey E, et al. Open versus laparoscopic radical prostatectomy: a prospective comparison of postoperative urinary incontinence rates. J Urol. 2007;177(2):615–619.

44. Moore KN, Truong V, Estey E, et al. Urinary incontinence after radical prostatectomy: can men at risk be identified preoperatively? J Urol. 2004;171(3):720–729; quiz 280–281.

45. Korfage IJ, Essink-Bot ML, Madalinska JB, et al. Measuring disease specific quality of life in localized prostate cancer: the Dutch experience. Qual Life Res. 2003;12(4):459–464.

46. Korfage IJ, Essink-Bot ML, Borsboom GJ, et al. Five-year follow-up of health-related quality of life after primary treatment of localized prostate cancer. Int J Cancer. 2005;116(2):291–296.

47. Talcott JA, Clark JA, Manola J, et al. Brining prostate cancer quality of life research back to the bedside: translating numbers into a format that patients can understand. J Urol. 2006;176(4 Pt 1):1558–1563; discussion 1563–1564.

48. Jayadevappa R, Johnson JC, Chhatre S, et al. Ethnic variation in return to baseline values of patient-reported outcomes in older prostate cancer patients. Cancer. 2007;109(11):2229–2238.

49. Jayadevappa R, Chhatre S, Wein AJ, et al. Predictors of patient reported outcomes and cost of care in younger men with newly diagnosed prostate cancer. Prostate. 2009;69(10):1067–1076.

50. Jayadevappa R, Schwartz JS, Chhatre S, et al. The burden of out-of-pocket and indirect costs of prostate cancer. Prostate. 2010;70(11):1255–1264.

51. Penson DF, Stoddard ML, Pasta DJ, et al. The association between socioeconomic status, health insurance coverage, and quality of life in men with prostate cancer. J Clin Epidemiol. 2001;54(4):350–358.

52. Mehta SS, Lubeck DP, Pasta DJ, et al. Fear of cancer recurrence in patients undergoing definitive treatment for prostate cancer: results from CaPSURE. J Urol. 2003;170(5):1931–1933.

53. Hu JC, Elkin EP, Pasta DJ, et al. Predicting quality of life after radical prostatectomy: results from CaPSURE. J Urol. 2004;171(2 Pt 1):703–707; discussion 707–708.

54. Litwin MS, Sadesky N, Pasta DJ, et al. Bowel function and bother after treatment for early stage prostate cancer: a longitudinal quality of life analysis from CaPSURE. J Urol. 2004;172(2):515–519.

55. Anst J, Sadesky N, Pasta DJ, et al. The impact of obesity on health related quality of life before and after radical prostatectomy (data from CaPSURE). J Urol. 2005;173(4):1132–1138.

56. Arredondo SA, Elkin EP, Marr PL, et al. Impact of comorbidity on health-related quality of life in men undergoing radical prostatectomy: data from CaPSURE. Urology. 2006;67(3):559–565.

57. Latini DM, Chan JM, Cowan JE, et al. Health-related quality of life for men with prostate cancer and diabetes: a longitudinal analysis from CaPSURE. Urology. 2006;68(6):1242–1247.

58. Knight SJ, Latini DM, Hart SL, et al. Education predicts quality of life among men with prostate cancer cared for in the Department of Veterans Affairs: a longitudinal quality of life analysis from CaPSURE. Cancer. 2007;109(9):1769–1776.

59. Bellizzi KM, Latini DM, Cowan JE, et al. Fear of recurrence, symptom burden, and health-related quality of life in men with prostate cancer. Urology. 2008;72(6):1269–1273.

60. Lee IH, Sadesky N, Carroll PR, et al. The impact of treatment choice for localized prostate cancer on response to phosphodiesterase inhibitors. J Urol. 2008;179(3):1072–1076; discussion 1076.

61. Sadesky N, Lubeck DP, Pasta DJ, et al. Insurance and quality of life in men with prostate cancer: data from the Cancer of the Prostate Strategic Urological Research Endeavor. BJU Int. 2008;101(6):691–697.

62. van de Poll-Franse LV, Sadesky N, Kwan L, et al. Severity of cardiovascular disease and health-related quality of life in men with prostate cancer: a longitudinal analysis from CaPSURE. Qual Life Res. 2008;17(6):845–855.

63. Wright JL, Lin DW, Cowan JE, et al. Quality of life in young men after radical prostatectomy. Prostate Cancer Prostatic Dis. 2008;11(1):67–73.

64. Wu AK, Cooperberg MR, Sadesky N, et al. Health related quality of life in patients treated with multimodal therapy for prostate cancer. J Urol. 2008;180(6):2415–2422; discussion 2422.

65. Sadesky N, Hubbard A, Carroll PR, et al. Predictive value of serial measurements of quality of life on all-cause mortality in prostate cancer patients: data from CaPSURE (cancer of the prostate strategic urologic research endeavor) database. Qual Life Res. 2009;18(8):1019–1027.

66. Le JD, Cooperberg MR, Sadesky N, et al. Changes in specific domains of sexual function and sexual bother after radical prostatectomy. BJU Int. 2010;106(7):1022–1029.

67. Daskivich TJ, van de Poll-Franse LV, Kwan L, et al. From bad to worse: comorbidity severity and quality of life after treatment for early-stage prostate cancer. Prostate Cancer Prostatic Dis. 2010;13(4):320–327.

68. Hong YM, Hu JC, Paciorek AT, et al. Impact of radical prostatectomy positive surgical margins on fear of cancer recurrence: results from CaPSURE. Urol Oncol. 2010;28(3):268–273.

69. Huang GJ, Sadesky N, Penson DF. Health related quality of life for men treated for localized prostate cancer with long-term follow-up. J Urol. 2010;183(6):2206–2212.
70. Sadetsky N, Greene K, Cooperberg MR, et al. Impact of androgen deprivation on physical well-being in patients with prostate cancer: analysis from the CaPSURE (Cancer of the Prostate Strategic Urologic Research Endeavor) registry. Cancer. 2011;117(19):4406–4413.

71. Namiki S, Ishidoya S, Saito S, et al. Natural history of voiding function after radical retropubic prostatectomy. Urolgy. 2006;68(1):142–147.

72. Namiki S, Saito S, Tochigi T, et al. Impact of salvage therapy for biochemical recurrence on health-related quality of life following radical prostatectomy. Int J Urol. 2007;14(3):186–191.

73. Namiki S, Kwan L, Kagawa-Singer M, et al. Sexual function following radical prostatectomy: a prospective longitudinal study of cultural differences between Japanese and American men. Prostate Cancer Prostatic Dis. 2008;11(3):298–302.

74. Namiki S, Kwan L, Kagawa-Singer M, et al. Urinary quality of life after prostatectomy or radiation for localized prostate cancer: a prospective longitudinal cross-cultural study between Japanese and U.S. men. Urolgy. 2008;71(6):1103–1108.

75. Namiki S, Kwan L, Kagawa-Singer M, et al. Distress and social dysfunction following prostate cancer treatment: a longitudinal cross-cultural comparison of Japanese and American men. Prostate Cancer Prostatic Dis. 2009;12(1):67–71.

76. Namiki S, Ishidoya S, Kawamura S, et al. Quality of life among elderly men treated for prostate cancer with either radical prostatectomy or external beam radiation therapy. J Cancer Res Clin Oncol. 2010;136(3):379–386.

77. Alemozaffar M, Regan MM, Cooperberg MR, et al. Prediction of erectile function following treatment for prostate cancer. JAMA. 2011;306(1):1205–1214.

78. Reeve BB, Potosky AL, Smith AW, et al. Impact of cancer on health-related quality of life of older Americans. J Natl Cancer Inst. 2009;101(12):860–868.

79. Lepore SJ, Helgeson VS, Eton DT, et al. Improving quality of life in men with prostate cancer: a randomized controlled trial of group education interventions. Health Psychol. 2003;22(3):443–452.

80. Northouse LL, Mood DW, Schafanacker A, et al. Randomized clinical trial of a family intervention for prostate cancer patients and their spouses. Cancer. 2007;110(12):2809–2818.

81. Moinpour CM, Hayden KA, Unger JM, et al. Health-related quality of life results in pathologic stage C prostate cancer from a Southwest Oncology Group trial comparing radical prostatectomy alone with radical prostatectomy plus radiation therapy. J Clin Oncol. 2008;26(1):112–120.

82. Bolla M, de Reijke TM, Van Tienhoven G, et al. Duration of androgen suppression in the treatment of prostate cancer. N Engl J Med. 2009;360(24):2516–2527.

83. Fransson P, Lund JA, Damber JE, et al. Quality of life in patients with locally advanced prostate cancer given endocrine treatment with or without radiotherapy: 4-year follow-up of SPCG-7/SFUO-3, an open-label, randomised, phase III trial. Lancet Oncol. 2009;10(4):370–380.

84. Morey MC, Snyder DC, Sloane R, et al. Effects of home-based diet and exercise on functional outcomes among older, overweight long-term cancer survivors: RENEW: a randomized controlled trial. JAMA. 2009;301(18):1883–1891.

85. Sandler HM, Liu PY, Dunn RL, et al. Reduction in patient-reported acute morbidit in prostate cancer patients treated with 81-Gy Intensity-modulated radiotherapy using reduced planning target volume margins and electromagnetic tracking: assessing the impact of the margin reduction study. Urolgy. 2010;75(5):1004–1008.

86. Warde P, Mason M, Ding K, et al. Combined androgen deprivation therapy and radiation therapy for locally advanced prostate cancer: a randomised, phase 3 trial. Lancet. 2011;378(9809):2104–2111.

87. Al-Mamgani A, van Putten WL, van der Wielen GJ, et al. Dose escalation and quality of life in patients with localized prostate cancer treated with radiotherapy: long-term results of the Dutch randomized dose-escalation trial (CKTO 96-10 trial). Int J Radiat Oncol Biol Phys. 2011;79(4):1004–1012.

88. Beckendorf V, Guerif S, Le Priére E, et al. J 70 Gy versus 80 Gy in localized prostate cancer: 3-year results of GETUG 06 randomised trial. Int J Radiat Oncol Biol Phys. 2011;80(4):1056–1063.

89. Spry NA, Kristjanson L, Hooton B, et al. Adverse effects to quality of life arising from treatment can recover with intermittent androgen suppression in men with prostate cancer. Eur J Cancer. 2006;42(8):1083–1092.

90. Sullivan PW, Mulani PM, Fishman M, et al. Quality of life findings from a multicenter, multinational, observational study of patients with metastatic hormone-refractory prostate cancer. J Clin Oncol. 2006;24(8):1083–1092.

91. De Puy V, Anstrom KJ, Castel LD, et al. Effects of skeletal morbidities on longitudinal patient-reported outcomes and survival in patients with metastatic prostate cancer. Support Care Cancer. 2007;15(7):869–876.

92. Carducci MA, Padley RJ, Breul J, et al. Effect of endothelin-A receptor blockade with atrasentin on tumor progression in men with hormone-refractory prostate cancer: a randomized, phase II, placebo-controlled trial. J Clin Oncol. 2003;21(4):679–689.

93. Sullivan PW, Nelson JB, Mulani PM, et al. Quality of life as a potential predictor for morbidity and mortality in patients with metastatic hormone-refractory prostate cancer. Qual Life Res. 2006;15(8):1297–1306.

94. Cella D, Nichol MB, Eton D, et al. Estimating clinically meaningful changes in quality of life following treatment for early prostate cancer. J Clin Oncol. 2003;21(8):1293–1296.

95. Berthold DR, Pond GR, Roessner M, et al. Treatment of hormone-refractory prostate cancer with docetaxel or mitoxantrone: relationships between prostate-specific antigen, pain, and quality of life response and survival in the TAX-327 study. Clin Cancer Res. 2008;14(9):2763–2767.

96. Arai Y, Akaza H, Deguchi T, et al. Evaluation of quality of life in patients with previously untreated advanced prostate cancer receiving maximum androgen blockade therapy or LHRHa monotherapy: a multicenter, randomized, double-blind, comparative study. J Cancer Res Clin Oncol. 2008;134(12):1385–1396.

97. Calais da Silva FE, Bono AV, Whelan P, et al. Intermittent androgen deprivation for locally advanced and metastatic prostate cancer: results from a randomised phase 3 study of the South European Urological Group. Eur Urol. 2009;55(6):1269–1277.

98. Shamash J, Powles T, Sarker SJ, et al. A multicentre randomised phase III trial of dexamethasone vs dexamethasone and diethylstilbestrol in castration-resistant prostate cancer: immediate vs deferred diethylstilbestrol. Br J Cancer. 2011;104(6):620–628.

99. Clark JA, Wray N, Brody B, et al. Dimensions of quality of life expressed by men treated for metastatic prostate cancer. Soc Sci Med. 1997;45(8):1299–1309.

100. Clark JA, Bokhour BG, Inui TS, et al. Measuring patients’ perceptions of the outcomes of treatment for early prostate cancer. Med Care. 2003;41(8):923–936.

101. Labreck DP, Litwin MS, Henning JM, et al. An instrument to measure patient satisfaction with healthcare in an observational database: results of a validation study using data from CaPSURE. Am J Manag Care. 2006;10(1):70–76.

102. Roth AJ, Rosenfeld B, Kornblith AB, et al. The memorial anxiety scale for prostate cancer: validation of a new scale to measure anxiety in men with prostate cancer. Cancer. 2003;97(11):2910–2918.

Notes
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