### Prostate cancer-specific HRQoL questionnaires

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th># of items</th>
<th>Domains</th>
<th>Original validation ref</th>
<th>Validity and Reliability</th>
<th>Examples of clinical trials where scale identified a treatment effect</th>
</tr>
</thead>
</table>
| EORTC QLQ-PR25 | Official EORTC module designed to supplement the QLQ-C30 for any application in prostate cancer | 25 | • urinary symptoms (9 items)  
• bowel symptoms (4 items)  
• treatment-related symptoms from surgery, radiotherapy and hormonal therapy (6 items)  
• sexual function (6 items) | None | Constructs v. Cronbach’s alpha*  
ICC coefficient ** | 1 |
| Quality of Life Module - Prostate 14 (QOLM-P14) | Developed for use with the EORTC QLQ-C30 in a trial of prednisone vs mitoxantrone and prednisone in men with hormone-resistant, metastatic prostate cancer | 14 | • pain impact on mobility  
• pain relief  
• drowsiness  
• hair loss  
• change in taste  
• urinary problems  
• sleep disturbance | None | | 2 |
| FACT-P | Includes the FACIT core measure, the FACT-G | 39 | • physical wellbeing  
• emotional wellbeing  
• social/family wellbeing  
• functional wellbeing  
• urinary symptoms (3 items) | | Discriminated men grouped by performance status, disease stage and baseline PSA;  
0.65-0.69 | 4-6 |
<table>
<thead>
<tr>
<th>Instrument</th>
<th>Description</th>
<th>52</th>
<th>7</th>
<th>8</th>
</tr>
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<tbody>
<tr>
<td>Prostate Cancer Quality of Life scale (PC-QOL)</td>
<td>Developed to assess HRQoL in prostate cancer patients with clinically localized disease.</td>
<td>Assesses severity, impact on functioning and concern relating to:</td>
<td>Discriminated groups: treatment (surgery vs radiotherapy vs watchful waiting). Subscales correlated with SF-36, PCI, Satisfaction with Life Scale, PANAS-N/P as expected.</td>
<td>0.70-0.90</td>
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<tr>
<td>Prostate Cancer Specific Quality of Life Instrument (PROSQOLI)</td>
<td>Developed to be an outcome measure for clinical trials in symptomatic men with advanced hormone-resistant prostate cancer. Includes the Present Pain Intensity item from the McGill Pain Questionnaire.</td>
<td>10</td>
<td>Relative efficiency statistics for PROSQOLI vs QLQ-C30 &amp; QOLM-P14 favoured the PROSQOLI for physical symptoms and physical function but the QLQ-C30 for emotional function, social function, and global perceptions; PROSQOLI pain scale most responsive.</td>
<td></td>
</tr>
<tr>
<td>Questionnaire</td>
<td>Description</td>
<td>Item Count</td>
<td>Subscales Correlation</td>
<td>Exploratory Factor Analysis</td>
</tr>
<tr>
<td>---------------</td>
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<tr>
<td>Unnamed questionnaire developed by Cleary et al. (1995)</td>
<td>Designed to assess HRQoL in men with metastatic prostate cancer undergoing surgery or hormonal treatment. Some domains were newly constructed; others were adapted from existing instruments (e.g., the SF-20)</td>
<td>29</td>
<td>general health perceptions (1 item) • pain (4 items) • emotional well-being (5 items) • vitality (3 items) • social functioning (2 items) • physical capacity (6 items) • sexual interest (3 items) • sexual functioning (3 items) • activity limitation (1 item) • bed disability (1 item)</td>
<td>Subscales generally correlated in ways hypothesised.</td>
</tr>
<tr>
<td>UCLA Prostate Cancer Index (PCI)</td>
<td>Designed for use with the RAND generic HRQoL measures in men treated for early stage prostate cancer. A 15 item version also exists but has not been extensively validated.</td>
<td>20</td>
<td>urinary function (5 items) • sexual function (8 items) • bowel function (4 items) • urinary bother (1 item) • sexual bother (1 item) • bowel bother (1 item)</td>
<td>Exploratory factor analysis identified 3 factors: urinary, sexual and bowel function. Subscale correlations with subscales of the SF-36 were broadly as hypothesised (r = 0.10-0.71); PCI and SF-26 subscales shared only 10% to 20% of variance, supporting their distinctness; the sexual function correlated with</td>
</tr>
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</table>
corresponding subscale on the CARES-SF ($r = 0.43$). Neither the PCI nor other measures distinguished men grouped according to tumour grade or stage.\textsuperscript{16}

Urinary and sexual function subscales correlated strongly with those of EPIC in Japanese men ($r = 0.85, 0.93$); bowel function subscale less so ($r = 0.47$).\textsuperscript{17}

In English and French-speaking Canadians, subscale correlations with subscales of the SF-36 supported their hypothesised distinctness ($r = 0.07-0.37$).\textsuperscript{18}

The PCI tracked changes during and after prostatectomy in sexual and urinary functioning.\textsuperscript{19}

Combined short forms of the PCI and SF-12 accounted for 85% correlation.

<table>
<thead>
<tr>
<th>UCLA Prostate Cancer Index short form</th>
<th>The PCI-SF was co-validated with a shortened version of the</th>
<th>12</th>
<th>urinary function (3 items)</th>
<th>sexual function (3 items)</th>
<th>Mental health (3 items from SF-12)</th>
<th>0.72-0.90</th>
<th>0.92-0.99</th>
</tr>
</thead>
</table>

\textsuperscript{12}•

\textsuperscript{16}

\textsuperscript{17}

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<table>
<thead>
<tr>
<th>(PCI-SF) Expanded Prostate Cancer Index Composite (EPIC)</th>
<th>SF-12. Expanded from the PCI to enable a more comprehensive assessment of outcomes from radical prostatectomy, external beam radiation, brachytherapy and hormonal treatment in men with localised disease.</th>
<th>50</th>
<th>• Physical health (3 items from SF-12)</th>
<th>20 of full-scale variance.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary (23 items, see note): - Function (5 items) - Bother (7 items) - Incontinence (4 items) - Irritative/Obstructive (7 items)</td>
<td>21 Correlations between EPIC and SF-12 subscales supported distinctness (r = 0.17-0.56); moderate correlations between EPIC and FACT-P subscales (r=0.44-0.61) suggested greater overlap; strong correlation (r=0.77) as hypothesised between EPIC urinary subscale and IPSS. Sexual and hormonal domains discriminated progression-free men from those with increased prostate-specific antigen (PSA). Urinary and sexual function subscales correlated strongly with those of PCI in Japanese men (r = 0.85, 0.93); bowel function subscale less so (r = 0.47).</td>
<td>0.51-0.93</td>
<td>0.73-0.91</td>
<td></td>
</tr>
<tr>
<td>Bowel (14 items): - Function (7 items) - Bother (7 items)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual (13 items): - Function (9 items) - Bother (4 items)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormonal (11 items): - Function (5 items) - Bother (6 items)</td>
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<tr>
<td>Note: function and bother, and incontinence and irritative/obstructive items are combined.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Unnamed questionnaire, developed</th>
<th>Developed to assess HRQoL in men undergoing</th>
<th>35</th>
<th>• bowel function (12 items) • urinary function (11 items)</th>
<th>22 Principle components factor analysis identified</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.63-0.94</td>
</tr>
</tbody>
</table>
by Dale et al. (1999)

| external beam radiotherapy. | • sexual function (9 items) Plus an item for each domain asking how bothersome it is. | two subscales within each domain: BF, urgency and daily living; UF, urgency and weakness of stream; and SF, interest/satisfaction and impotence. Urinary and sexual function subscales discriminated men grouped according to tumour stage and grade. |

* While standards vary, Cronbach’s alphas of between 0.70 and 0.90 are widely accepted as an indication of satisfactory internal consistency.

** An intraclass correlation coefficient (ICC) > 0.70 is typically considered an indication of satisfactory test-retest reliability.
References

1. Buron C, Le Vu B, Cosset J-M, et al. Brachytherapy versus prostatectomy in localized prostate cancer: results of a French multicenter prospective medico-economic study. *International Journal of Radiation Oncology, Biology, Physics*. Mar 1 2007;67(3):812-822 PURPOSE: To prospectively compare health-related quality of life (HRQOL), patient-reported treatment-related symptoms, and costs of iodine-125 permanent implant interstitial brachytherapy (IB) with those of radical prostatectomy (RP) during the first 2 years after these treatments for localized prostate cancer. METHODS AND MATERIALS: A total of 435 men with localized low-risk prostate cancer, from 11 French hospitals, treated with IB (308) or RP (127), were offered to complete the European Organization for Research and Treatment of Cancer core Quality of Life Questionnaire QLQ-C30 version 3 (EORTC QLQ-C30) and the prostate cancer specific EORTC QLQ-PR25 module before and at the end of treatment, 2, 6, 12, 18, and 24 months after treatment. Repeated measures analysis of variance and analysis of covariance were conducted on HRQOL changes. Comparative cost analysis covered initial treatment, hospital follow-up, outpatient and production loss costs. RESULTS: Just after treatment, the decrease of global HRQOL was less pronounced in the IB than in the RP group, with a 13.5 points difference (p < 0.0001). A difference slightly in favor of RP was observed 6 months after treatment (-7.5 points, p = 0.0164) and was maintained at 24 months (-8.2 points, p = 0.0379). Impotence and urinary incontinence were more pronounced after RP, whereas urinary frequency, urgency, and urination pain were more frequent after IB. Mean societal costs did not differ between IB (8,019 euros at T24) and RP (8,715 euros at T24, p = 0.0843) regardless of the period. CONCLUSIONS: This study suggests a similar cost profile in France for IB and RP but with different HRQOL and side effect profiles. Those findings may be used to tailor localized prostate cancer treatments to suit individual patients' needs.

2. Osoba D, Tannock IF, Ernst DS, Neville AJ. Health-related quality of life in men with metastatic prostate cancer treated with prednisone alone or mitoxantrone and prednisone.[see comment]. *Journal of Clinical Oncology*. Jun 1999;17(6):1654-1663 PURPOSE: A combination of mitoxantrone plus prednisone is preferable to prednisone alone for reduction of pain in men with metastatic, hormone-resistant, prostate cancer. The purpose of this study was to assess the effects of these treatments on health-related quality of life (HQL). PATIENTS AND METHODS: Men with metastatic prostate cancer (n = 161) were randomized to receive either daily prednisone alone or mitoxantrone (every 3 weeks) plus prednisone. Those who received prednisone alone could have mitoxantrone added after 6 weeks if there was no improvement in pain. HQL was assessed before treatment initiation and then every 3 weeks using the European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire C30 (EORTC QLQ-C30) and the Quality of Life Module-Prostate 14 (QOLM-P14), a trial-specific module developed for this study. An intent-to-treat analysis was used to determine the mean duration of HQL improvement and differences in improvement duration between groups of patients. RESULTS: At 6 weeks, both groups showed improvement in several HQL domains, and only physical functioning and pain were better in the mitoxantrone-plus-prednisone group than in the prednisone-alone group. After 6 weeks, patients taking prednisone showed no improvement in HQL scores, whereas those taking mitoxantrone plus prednisone showed significant improvements in global quality of life (P =.009), four functioning domains, and nine symptoms (.001 < P < .01), and the improvement (> 10 units on a scale of 0 to100) lasted longer than in the prednisone-alone group (.004 < P <.05). The addition of mitoxantrone to prednisone after failure of prednisone alone was associated with improvements in pain, pain impact, pain relief, insomnia, and global quality of life (.001 < P <.003). CONCLUSION: Treatment with mitoxantrone plus prednisone was associated with greater and longer-lasting improvement in several HQL domains and symptoms than treatment with prednisone alone.

exceeds 330,000 in 1997, increasingly more men are faced with treatment choices for which there is no clear approach. At every stage of disease, these treatment choices may involve clinically equivalent modalities that differ in side effects and impact upon quality of life (QOL). Comprehensive, yet efficient, questionnaires are needed to measure QOL in patients with prostate cancer. METHODS: Developed as a disease-specific adjunct to the Functional Assessment of Cancer Therapy (FACT) measurement system, a 12-item prostate cancer subscale (PCS) was developed and tested in three independent samples: a subscale development sample (n = 43), validity sample 1 (n = 34), and validity sample 2 (n = 96). The 12 items ask about symptoms and problems specific to prostate cancer. These questions are added to the general (FACT-G) instrument, thereby comprising a 47-item questionnaire. RESULTS: Internal consistency of the PCS ranged from 0.65 to 0.69, with coefficients for FACT-G subscales and aggregated scores ranging from 0.61 to 0.90. Concurrent validity was confirmed by the ability to discriminate patients by disease stage, performance status, and baseline prostate-specific antigen (PSA) level. Sensitivity to change in performance status and PSA score over a 2-month period suggested that some subscales of the FACT-Prostate (P) (including the PCS) are sensitive to meaningful clinical change. CONCLUSIONS: Our findings support use of the FACT-P as a meaningful component of QOL evaluation in men undergoing therapy for prostate cancer.

4. Dearnaley DP, Sydes MR, Langley RE, et al. The early toxicity of escalated versus standard dose conformal radiotherapy with neo-adjuvant androgen suppression for patients with localised prostate cancer: results from the MRC RT01 trial (ISRCTN47772397). Radiotherapy & Oncology. Apr 2007;83(1):31-41 BACKGROUND: Five-year disease-free survival rates for localised prostate cancer following standard doses of conventional radical external beam radiotherapy are around 80%. Conformal radiotherapy (CFRT) raises the possibility that radiotherapy doses can be increased and long-term efficacy outcomes improved, with safety an important consideration. METHODS: MRC RT01 is a randomised controlled trial of 862 men with localised prostate cancer comparing Standard CFRT (64Gy/32f) versus Escalated CFRT (74Gy/37f), both administered with neo-adjuvant androgen suppression. Early toxicity was measured using physician-reported instruments (RTOG, LENT/SOM, Royal Marsden Scales) and patient-reported questionnaires (MOS SF-36, UCLA Prostate Cancer Index, FACT-P). RESULTS: Overall early radiotherapy toxicity was similar, apart from increased bladder, bowel and sexual toxicity, in the Escalated Group during a short immediate post-radiotherapy period. Toxicity in both groups had abated by week 12. Using RTOG Acute Toxicity scores, cumulative Grade 2 bladder and bowel toxicity was 38% and 30% for Standard Group and 39% and 33% in Escalated Group, respectively. Urinary frequency (Royal Marsden Scale) improved in both groups from pre-androgen suppression to 6 months post-radiotherapy (p<0.001), but bowel and sexual functioning deteriorated. This pattern was supported by patient-completed assessments. Six months after starting radiotherapy the incidence of RTOG Grade > or = 2 side-effects was low (<1%); but there were six reports of rectal ulceration (6 Escalated Group), six haematuria (5 Escalated Group) and eight urethral stricture (6 Escalated Group). CONCLUSIONS: The two CFRT schedules with neo-adjuvant androgen suppression have broadly similar early toxicity profiles except for the immediate post-RT period. At 6 months and compared to before hormone therapy, bladder symptoms improved, whereas bowel and sexual symptoms worsened. These assessments of early treatment safety will be complemented by further follow-up to document late side-effects and efficacy.

5. Hoskin PJ, Motohashi K, Bownes P, Bryant L, Ostler P. High dose rate brachytherapy in combination with external beam radiotherapy in the radical treatment of prostate cancer: initial results of a randomised phase three trial. Radiotherapy & Oncology. Aug 2007;84(2):114-120 BACKGROUND AND PURPOSE: A randomised phase III trial has compared external beam radiotherapy alone with a dose escalated schedule using high dose rate brachytherapy. Patients with histologically confirmed prostate cancer, no evidence of metastases, a PSA <50, no previous TURP and fit for general anaesthetic were included. METHODS: Patients were randomised to receive either standard radiotherapy 55 Gy in 20 fractions treating Monday to Friday over 4 weeks or a combined schedule comprising external beam treatment delivering 35.75 Gy in 13 fractions treating daily Monday to Friday over 2.5 weeks followed by a temporary high dose rate afterloading implant delivering 17 Gy in two
fractions over 24h. RESULTS: A total of 220 patients were randomised, balanced for important prognostic parameters including tumour stage, presenting PSA, Gleason score and use of adjuvant anti-androgens. With a median follow up of 30 months (range 3-91) a significant improvement in actuarial biochemical relapse-free survival is seen in favour of the combined brachytherapy schedule (p=0.03). A lower incidence of acute rectal discharge was seen in the brachytherapy group (p=0.025) and other acute and late toxicities were equivalent. Patients randomised to brachytherapy had a significantly better FACT-P score at 12 weeks (p=0.02). CONCLUSIONS: The use of high dose rate brachytherapy in combination with external beam radiotherapy resulted in an improved biochemical relapse-free survival compared to external beam radiotherapy alone with less acute rectal toxicity and improved quality of life in this randomised trial.

6. Monga U, Garber SL, Thornby J, et al. Exercise prevents fatigue and improves quality of life in prostate cancer patients undergoing radiotherapy. Archives of Physical Medicine & Rehabilitation. Nov 2007;88(11):1416-1422 OBJECTIVE: To show fatigue prevention and quality of life (QOL) improvement from cardiovascular exercise during radiotherapy. DESIGN: Prospective enrollment (n=21), randomized to exercise (n=11) and control groups (n=10), with pre- and post-radiotherapy between- and within-group comparisons. SETTING: Academic medical center. PARTICIPANTS: Localized prostate cancer patients undergoing radiotherapy. INTERVENTIONS: The interventional group received radiotherapy plus aerobic exercise 3 times a week for 8 weeks whereas the control group received radiotherapy without exercise. MAIN OUTCOME MEASURES: Pre- and post-radiotherapy differences in cardiac fitness, fatigue, depression, functional status, physical, social, and functional well-being, leg strength, and flexibility were examined within and between 2 groups. RESULTS: No significant differences existed between 2 groups at pre-radiotherapy assessment. At post-radiotherapy assessment, the exercise group showed significant within group improvements in: cardiac fitness (P<.001), fatigue (P=.02), Functional Assessment of Cancer Therapy-Prostate (FACT-P) (P=.04), physical well-being (P=.002), social well-being (P=.02), flexibility (P=.006), and leg strength (P=.000). Within the control group, there was a significant increase in fatigue score (P=.004) and a decline in social well-being (P<.05) at post-radiotherapy assessment. Between-group differences at post-radiotherapy assessment were significant in cardiac fitness (P=.006), strength (P=.000), flexibility (P<.01), fatigue (P<.001), FACT-P (P=.006), physical well-being (P<.001), social well-being (P=.002), and functional well-being (P=.04). CONCLUSIONS: An 8-week cardiovascular exercise program in patients with localized prostate cancer undergoing radiotherapy improved cardiovascular fitness, flexibility, muscle strength, and overall QOL and prevented fatigue.

7. Giesler RB, Miles BJ, Cowen ME, Kattan MW. Assessing quality of life in men with clinically localized prostate cancer: development of a new instrument for use in multiple settings. Quality of Life Research. 2000;9(6):645-665 BACKGROUND: Quality of life in prostate cancer patients with clinically localized disease has become the focus of increasing attention over the past decade. However, few instruments have been developed and validated to assess quality of life specifically in this patient population. OBJECTIVE: The purpose of this investigation was to create a comprehensive, multi-scale quality of life instrument that can be tailored to the needs of the clinician/investigator in multiple settings. DESIGN, SUBJECTS, AND MEASURES: Patients diagnosed with clinically localized prostate cancer were mailed a questionnaire consisting of new and previously validated quality of life items and ancillary scales. Data from returned questionnaires were analyzed and used to create a multiscale instrument that assesses the effects of treatment and disease on urinary, sexual, and bowel domains, supplemented by a scale assessing anxiety over disease course/effectiveness of treatment. The instrument was then mailed to a second sample of prostate cancer patients once and then again two weeks later to assess test retest reliability. To assess feasibility in clinical settings, the instrument was self-administered to a third patient sample during a urology clinic visit. RESULTS: All scales exhibited good internal consistency and test retest reliability, convergent and discriminant validity, and significant correlations with disease specific, generic health-related, and global measures of quality of life. Men with greater physiologic impairment reported more limitations in role activities and more bother. Scales were also able to differentiate patients undergoing different therapies. All scales exhibited negligible correlations with a measure of socially desirable responding.
Additionally, the instrument proved feasible when used as a self-administered questionnaire in a clinical setting. CONCLUSIONS: The current instrument possesses brief multi-item scales that can be successfully self-administered in multiple settings. The instrument is flexible, relatively quick, psychometrically reliable and valid, and permits a more comprehensive assessment of patients' quality of life.

8. Giesler RB, Given B, Given CW, et al. Improving the quality of life of patients with prostate carcinoma: a randomized trial testing the efficacy of a nurse-driven intervention. Cancer. Aug 15 2005;104(4):752-762 BACKGROUND: Treatments for clinically localized prostate carcinoma are accompanied by sexual, urinary, and bowel dysfunction and other sequelae that can result in significant distress and reduced well being. Methods capable of improving quality of life are needed that can be integrated into clinical practice. To address this need, a nurse-driven, cancer care intervention was developed and tested. METHODS: Within 6 weeks after completing treatment, 99 patients, along with their partners, were enrolled into a prospective, controlled trial and were randomized to receive the cancer care intervention or to receive standard care. Participants in the intervention arm met once each month for 6 months with an oncology nurse intervier, who helped patients identify their quality-of-life needs using an interactive computer program. The intervier then provided education and support tailored to participants' needs. Primary outcome variables included 1) disease-specific quality of life, including sexual, urinary, and bowel outcomes and cancer worry; 2) depression; 3) dyadic adjustment; and 4) general quality of life. Outcomes data were collected prior to randomization and again at 4 months, 7 months, and 12 months posttreatment. RESULTS: Patients in the intervention arm experienced long-term improvements in quality-of-life outcomes related to sexual functioning and cancer worry compared with patients who received standard care. Baseline depression moderated the impact of the intervention on several other quality-of-life outcomes. CONCLUSIONS: The findings of the current study indicated that a computer-assisted, nurse-driven intervention was capable of providing durable improvements in the quality of life of men who underwent treatment for clinically localized prostate carcinoma.

9. Stockler MR, Osoba D, Goodwin P, Corey P, Tannock IF. Responsiveness to change in health-related quality of life in a randomized clinical trial: a comparison of the Prostate Cancer Specific Quality of Life Instrument (PROSQOLI) with analogous scales from the EORTC QLQ-C30 and a trial specific module. European Organization for Research and Treatment of Cancer. Journal of Clinical Epidemiology. Feb 1998;51(2):137-145 INTRODUCTION: The Prostate Cancer Specific Quality of Life Instrument (PROSQOLI) was developed to be a pragmatic outcome measure for clinical trials in symptomatic men with advanced hormone-resistant prostate cancer. DESIGN AND SETTING: A comparative assessment of responsiveness was made with longitudinal data from a positive multicenter randomized trial of palliative chemotherapy in 161 symptomatic men with advanced hormone-resistant prostate cancer. INSTRUMENTS: The PROSQOLI, the European Organisation for Research and Treatment of Cancer (EORTC) core quality of life questionnaire (QLQ-C30), and a specific quality of life module for advanced prostate cancer [QLM-P14] were administered every 3 weeks while patients received their allocated treatment. FINDINGS: Sixteen of the 19 health-related quality of life (HRQL) scales demonstrated improvements in palliative responders. All three pain scales detected a beneficial effect of palliative chemotherapy. The relative efficiency statistics favored the PROSQOLI for physical symptoms and physical function but the QLQ-C30 for emotional function, social function, and global perceptions. The PROSQOLI linear analog scale was the most responsive measure of pain. Bootstrap confidence intervals for the relative efficiency statistics were wide. CONCLUSIONS: Both the PROSQOLI and the analogous scales from the QLQ-C30 were responsive to improvements in HRQL. Differences between the instruments were generally subtle. The PROSQOLI is a short, simple, responsive measure of HRQL in men receiving systemic treatment for advanced hormone-resistant prostate cancer.

that was designed to be an outcome measure for clinical trials in advanced hormone-resistant prostate cancer. The cross-sectional validity of the PROSQOLI was assessed using baseline data from a randomized trial in which HRQL was also assessed with the European Organisation for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (QLQ-C30) and a trial-specific quality of life module (QLM-P14). Convergent validity was assessed with the multitrait-multimethod matrix approach; discriminative validity was assessed according to conventional clinical criteria; and predictive validity was assessed by the ability to predict survival duration. These assessments provided strong support for the validity of all PROSQOLI scales except those for family/marriage relationships and passing urine; modifications of these two scales are under evaluation. The strength, consistency, and independence of the prognostic information provided by the HRQL scales were striking. Differences between the instruments were generally subtle. These data support validity of the PROSQOLI and the analogous scales from the QLQ-C30 and QLM-P14 in symptomatic men with advanced hormone resistant prostate cancer. The PROSQOLI is a short, simple, and valid measure of HRQL in this setting.

11. Cleary PD, Morrissey G, Oster G. Health-related quality of life in patients with advanced prostate cancer: a multinational perspective. Quality of Life Research. Jun 1995;4(3):207-220 To explore the value of antiandrogen therapy for advanced prostate cancer, two clinical trials of similar design were recently conducted in six countries throughout Europe. A total of 550 patients with previously untreated metastatic prostate cancer were randomized either to treatment with an antiandrogen or castration. While time to treatment failure, objective tumour response and survival were expected to be similar between study treatments, their effects on health-related quality of life (HRQOL) were expected to differ and were therefore a focus of concern in this trial. To assess these effects, we developed a brief self-administered patient questionnaire covering 10 domains of HRQOL (general health perceptions, pain, emotional well-being, vitality, social functioning, physical capacity, sexual interest, sexual functioning, activity limitation and bed disability), which we translated from English into several other languages. In this paper, we describe the development, content and translation of this survey instrument and report on its reliability and validity in six countries based on data collected for the first 487 patients to complete questionnaires at study entry.

12. Kaisary AV, Tyrrell CJ, Beacock C, Lunglmayr G, Debruyne F. A randomised comparison of monotherapy with Casodex 50 mg daily and castration in the treatment of metastatic prostate carcinoma. Casodex Study Group. European Urology. 1995;28(3):215-222 Casodex (Bicalutamide, ICI 176,334) is a potent, non-steroidal, selective anti-androgen with a long half-life allowing once-daily oral administration. In this randomised, open, multicentre study, Casodex 50 mg monotherapy was compared with castration (medical, using goserelin acetate, [Zoladex], or surgical) in 245 patients with advanced prostate cancer. Primary end-points were time to treatment failure, time to objective disease progression and survival. Subjective responses, quality of life and tolerability were also evaluated. There was no significant difference between the groups in terms of objective progression or subjective responses. Treatment failed in 59 of 119 patients (50%) randomised to Casodex and in 61 of 126 patients (48%) randomised to castration (no statistically significant difference). An updated analysis showed that survival was similar in the two groups. Casodex was well tolerated with a low incidence of diarrhoea and sexual dysfunction. On the basis of this study, Casodex monotherapy is an effective alternative to castration in the treatment of metastatic prostate cancer.

13. Chodak G, Sharifi R, Kasimis B, Block NL, Macramalla E, Kennealey GT. Single-agent therapy with bicalutamide: a comparison with medical or surgical castration in the treatment of advanced prostate carcinoma. Urology. Dec 1995;46(6):849-855 OBJECTIVES. Single-agent therapy with bicalutamide, a nonsteroidal antiandrogen, was compared with castration, either surgical or medical, in patients with untreated Stage D2 prostate cancer. METHODS. In an open, randomized, multicenter trial, patients were randomized to treatment with 50 mg bicalutamide (n = 243) once daily or to castration (n = 243), either orchiectomy or depot injection of goserelin acetate every 28 days. Primary efficacy endpoints were times to treatment failure and objective disease progression and survival. Assessments included review of measurable metastases, prostate dimensions, Eastern Cooperative Oncology Group performance status, pain, analgesic requirements, and quality of life responses. RESULTS. The
median duration of therapy was 39 weeks for bicalutamide-treated patients and 42 weeks for castrated patients; treatment failure occurred in 53% and 42% and disease progression in 43% and 33%, respectively. Treatment effects favored castration for both endpoints (P < or = 0.002), with hazard ratios (bicalutamide:castration) of 1.54 (95% confidence interval [CI], 1.18 to 2.00) for time to treatment failure and 1.6 (95% CI, 1.19 to 2.15) for time to disease progression. From the 1-year survival analysis, the hazard ratio for probability of death was 1.29 (95% CI, 0.96 to 1.72). Thus far, with a median follow-up of 86 weeks, median survival has not been reached in either group. Changes from baseline in several quality of life variables were significantly different (P < or = 0.01) between treatment groups periodically from months 1 to 6, and all favored bicalutamide. Overall, the antiandrogen was well tolerated compared with castration; with bicalutamide, hot flushes occurred less often and breast tenderness and gynecomastia more often. CONCLUSIONS. Although a dosage of 50 mg of bicalutamide once daily was not as effective as castration, the favorable quality of life outcomes and the low incidence of nonhormonal adverse events provide reasons to evaluate bicalutamide, as a single therapeutic agent, at higher doses.

14. Schellhammer P, Sharifi R, Block N, et al. A controlled trial of bicalutamide versus flutamide, each in combination with luteinizing hormone-releasing hormone analogue therapy, in patients with advanced prostate cancer. Casodex Combination Study Group. [see comment]. Urology. May 1995;45(5):745-752 OBJECTIVES. To compare the efficacy and safety of bicalutamide and flutamide, each used in combination with luteinizing hormone-releasing analogue (LHRH-A) therapy, in patients with untreated metastatic (Stage D2) prostate cancer. METHODS. Randomized, double-blind (for antiandrogen therapy), multicenter study with a 2 x 2 factorial design. Eight hundred thirteen patients were allocated 1:1 to bicalutamide (50 mg once daily) and flutamide (250 mg three times daily) and 2:1 to goserelin acetate (3.6 mg every 28 days) and leuprolide acetate (7.5 mg every 28 days). RESULTS. With a median duration of follow-up of 49 weeks, time to treatment failure, the primary endpoint, was significantly (P = 0.005) better for the bicalutamide plus LHRH-A group than for the flutamide plus LHRH-A group. Patients in the flutamide plus LHRH-A group were 34% more likely to fail treatment over the given time period, as indicated by the hazard ratio of 0.749 (95% confidence interval, 0.61 to 0.92) for bicalutamide plus LHRH-A to flutamide plus LHRH-A. Results for secondary endpoints (survival, quality of life, and subjective response) were similar between groups. Diarrhea occurred in 24% of patients in the flutamide plus LHRH-A group, compared with 10% of patients in the bicalutamide plus LHRH-A group (P < 0.001). CONCLUSIONS. In patients with metastatic prostate cancer, bicalutamide plus LHRH-A is well tolerated and provides superior efficacy to flutamide plus LHRH-A with respect to time to treatment failure. Assessment of the effects of these regimens on longer term survival requires additional time for follow-up.

15. Litwin MS, McGuigan KA. Accuracy of recall in health-related quality-of-life assessment among men treated for prostate cancer. Journal of Clinical Oncology. Sep 1999;17(9):2882-2888 PURPOSE: To determine the accuracy of patient recall of health-related quality of life (HRQOL) in men who have undergone radical prostatectomy for early-stage prostate cancer. PATIENTS AND METHODS: Patients enrolled onto a longitudinal, observational cohort study of HRQOL after radical prostatectomy for early-stage prostate cancer were asked to assess their baseline HRQOL before surgery. They were later asked to recall their baseline HRQOL at intervals of 7 to 37 months after surgery. The two views of baseline HRQOL (actual and recall) were compared. HRQOL was measured with established instruments (the RAND 12-Item Short-Form Health Survey and a validated short form of the University of California Los Angeles Prostate Cancer Index) that addressed impairment in the physical, mental, urinary, bowel, and sexual domains. RESULTS: Overall, recall was poor. Patients tended to remember their baseline HRQOL as being better than it actually was. This effect was particularly striking for urinary and sexual function. Greater education and younger age diminished this effect in some domains. The effect did not vary with time since surgery. CONCLUSION: Men undergoing radical prostatectomy for early-stage prostate cancer do not accurately recall their pretreatment HRQOL when asked several months or years later. This recall bias is constant throughout a period of 6 months to 3 years after surgery. By collecting data before treatment and observing subjects longitudinally, investigators can ensure
that HRQOL changes are analyzed in the context of any impairment that may have been present at baseline. If a longitudinal study is not feasible, then great caution must be used if patients are asked to recall their pretreatment HRQOL.

16. Litwin MS, Hays RD, Fink A, Ganz PA, Leake B, Brook RH. The UCLA Prostate Cancer Index: development, reliability, and validity of a health-related quality of life measure. *Medical Care*. 1998;36(7):1002-1012. Objectives. The need for accurate measures of health-related quality of life (HRQOL) in men treated for prostate cancer is of paramount importance because patients may survive for many years after their diagnosis. Hence, interest has increased in choosing treatments that optimize both the quality and quantity of life in patients with this disease. This study sought to develop and evaluate a self-administered, multi-item, disease-specific instrument to capture the health concerns central to the quality of life of men treated for early stage prostate cancer.

Methods. After focus group analysis and pilot testing, the instrument was tested with a large retrospective, cross-sectional survey. Exploratory factor analysis and multitrait scaling analysis were used to facilitate the formation of six scales containing 20 disease-targeted items that address impairment in the urinary, bowel, and sexual domains. The psychometric properties of the new scales were assessed by measuring test-retest reliability, internal consistency reliability, and construct validity. Performance on the new scales was compared with scores on other established cancer-related health-related quality of life instruments. Two hundred fifty-five long-term survivors of prostate cancer treatment and 273 age-matched and ZIP code-matched comparison subjects without prostate cancer from a large managed care population in California were studied. Mean age was 72.7 years. In addition to the new scales, the RAND 36-Item Health Survey (SF-36) was used as a generic core measure, and a cancer-related health-related quality of life instrument (the Cancer Rehabilitation System-Short Form) was used to provide construct validity.

Results. For the new scales, test-retest reliability ranged from 0.66 to 0.93, and internal consistency ranged from 0.65 to 0.93. Disease-targeted measures of function and bother in the three domains correlated substantially with one another. Scale scores correlated well with related, established scales. Men undergoing prostatectomy or pelvic irradiation demonstrated the expected differences in performance on the disease-specific health-related quality of life scales when compared with each other or with comparison subjects. Age was inversely related to sexual and bowel function.

Conclusions. The UCLA Prostate Cancer Index performed well in this population of older men with and without prostate cancer. It demonstrated good psychometric properties and appeared to be well understood and easily completed. The high response among patients suggests that these men especially are interested in addressing both the general and disease-specific concerns that impact their daily quality of life.

17. Namiki S, Takegami M, Kakehi Y, Suzukamo Y, Fukuhara S, Arai Y. Analysis linking UCLA PCI with Expanded Prostate Cancer Index Composite: an evaluation of health related quality of life in Japanese men with localized prostate cancer. *Journal of Urology*. Aug 2007;178(2):473-477; discussion 477. PURPOSE: We evaluated the correspondence between UCLA PCI and the Extended Prostate Cancer Index Composite for Japanese patients with localized prostate cancer. MATERIALS AND METHODS: A total of 385 patients treated with retropubic radical prostatectomy, external beam radiation, hormonal therapy or select watchful waiting from 2002 to 2006 were enrolled. For this study we used equipercentile linking, a technique that identifies scores on the 2 measures that have the same percentile rank. RESULTS: Urinary and sexual functions showed a strong correlation (r = 0.85 and 0.93, respectively, p <0.0001). In contrast, the correlation for bowel function was relatively weak (r = 0.47, p <0.0001). The correlations of each Extended Prostate Cancer Index Composite bother domain with UCLA PCI were 0.6 (p <0.0001). The linking between each scale of the Extended Prostate Cancer Index Composite and UCLA PCI domains showed that an Extended Prostate Cancer Index Composite urinary function score of 73 was equivalent to a UCLA PCI score of 60. With regard to urinary bother an Extended Prostate Cancer Index Composite score of 69 to 84 was equivalent to a UCLA PCI score of 75. A sexual function score of 18 on UCLA PCI corresponded to an Extended Prostate Cancer Index Composite score of 12 and a sexual bother score of 50 on UCLA PCI corresponded to an Extended Prostate Cancer Index Composite score of 56 to 88. CONCLUSIONS: The urinary and sexual domains of UCLA PCI and the Extended Prostate Cancer...
Index Composite showed strong correlations. In contrast, the correlation for the bowel domain was relatively weak. The results of the linking analysis between UCLA PCI and the Extended Prostate Cancer Index Composite may have implications useful for their interpretation.


OBJECTIVES: To explore the impact of cross-cultural differences on University of California, Los Angeles, Prostate Cancer Index (PCI) reliability and validity, which is unknown. The PCI represents the most widely used prostate cancer-specific health-related quality-of-life assessment tool.

METHODS: The PCI sexual and urinary scales, the RAND SF-36 survey, and the Prostate Outcomes Research Team (PORT) prostate cancer treatment complication profile were self-administered. The principal sample consisted of 2415 men (anglophone 256, francophone 2159) treated with radical prostatectomy in Quebec between 1988 and 1996. An additional 35 men (anglophone 17, francophone 18) formed the retest sample. RESULTS: The PCI demonstrated excellent internal consistency and test-retest reliability in tests based on the entire cohort and in tests addressing the two linguistically different groups. The instrument showed a lack of convergence with the SF-36 scales, confirming the distinctness of the generic and prostate cancer-specific constructs. The PCI sexual scales converged with the aggregate PORT sexual items \( r = 0.8 \), and the PCI urinary scales were strongly related to the aggregate PORT urinary items \( r = 0.7 \). Convergence between PCI urinary bother and function was strong \( r = 0.8 \), but only moderate convergence was noted between PCI sexual bother and function \( r = 0.4 \). The relation between bother and function in both urinary and sexual domains was weaker in anglophone participants relative to their francophone counterparts. CONCLUSIONS: The PCI is reliable and, at best, only modestly affected by cultural differences when administered to culturally distinct English-speaking men or when translated into French.


PURPOSE: We investigate the longitudinal recovery of quality of life after radical prostatectomy in men with localized prostate cancer. MATERIALS AND METHODS: We assessed the self-reported health related quality of life in 247 men undergoing radical prostatectomy for prostate cancer. Patients were assessed at baseline before surgery and postoperatively every 3 months for 1 year and then every 6 months for up to 48 months (median 30). We measured general and prostate specific health related quality of life with the RAND 36-Item Health Survey 1.0 SF-36 and University of California, Los Angeles Prostate Cancer Index. The Cox proportional hazards regression model was used to determine whether some patients were more likely than others to have a successful return to baseline functioning after treatment. RESULTS: In the SF-36 60% of patients reached baseline in all domains by 3 months. By 12 months, greater than 90% of patients reached baseline in all domains. Mean recovery time for these domains was about 4(1/2) months. The recovery of urinary function to baseline was 21% at 3, 56% at 12 and 63% at 30 months, respectively. About 80% of patients recovered to baseline urinary bother. In the urinary domains patients who recovered did so at an average of 7 to 8 months, and there was little additional recovery after 18 months. By 1 year postoperatively, approximately a third of patients reached baseline sexual function and about half recovered to baseline sexual bother. At 2 years postoperatively, sexual function and bother returned to baseline in 40% and 60% of patients, respectively. Mean recovery time was about 11 months for sexual function and about 9 months for sexual bother. There was little additional recovery in the sexual domains after 18 to 24 months. In the bowel domains more than two thirds of patients returned to baseline by 3 months, and greater than 90% recovered by 12 months, with a mean recovery of 4.8 months. Unmarried men were more likely than those married to regain baseline sexual function \( p = 0.03 \) and urinary function \( p = 0.07 \). Patients who were 65 years and older were more likely than those younger to return to baseline sexual bother \( p = 0.03 \). There were trends that showed patients with higher incomes as well as those who were white were more likely to recover baseline scores for urinary function and the physical component summary. Another trend suggested that men with a higher education were less likely to regain urinary function \( p = 0.08 \). CONCLUSIONS: Most quality of life recovery occurs early after radical prostatectomy, except in several
domains, including urinary and sexual, which continue to improve even beyond 2 years postoperatively. Patients should be encouraged that recovery may continue for months or years after surgery.

20. Lebeau T, Perrotte P, Valiquette L, et al. Validation of prostate cancer index and SF-12 short forms. Canadian Journal of Urology. Dec 2005;12(6):2873-2879 BACKGROUND: Assessment of prostate cancer (PCa) specific and generic health-related quality-of-life (HRQOL) is frequently omitted due to several obstacles, such as respondent burden and infrastructure-related limitations. We attempted to reduce the number of items of two commonly used HRQOL assessment tools, namely the UCLA PCa Index (PCI) and the RAND SF-12, with the intent of generating the most parsimonious, yet psychometrically valid and reliable HRQOL assessment tool. METHODS: The PCI and SF-12 were administered to 2415 radical prostatectomy patients, and re-tested in a convenience sample of 35 men with PCa. Multivariate linear regression models defined the most predictive and item-reduced SF-12 and PCI item combinations. These were subjected to standard psychometric reliability and validity tests. RESULTS: The 8-item PCI sexual function (SF) scale was reduced to three items. The 5-item PCI urinary function (UF) scale was reduced to three items. The 6-item SF-12 mental health scale was reduced to three items, and the 6-item SF-12 physical scale was also reduced to three items. The total number of items was reduced from 27 to 12 (44%). The item-reduced scales accounted for over 85% of full-scale variance. All reliability and validity tests yielded highly satisfactory results. CONCLUSION: We developed SF-12 and PCI short-forms, which consist of 12 of 27 (44%) original items and can be completed by most men within 2 minutes. The short-forms represent a valid substitute for the full scales, as they provide over 85% of full-scale information and demonstrate excellent reliability statistics. The short forms have the potential for decreasing respondent burden and infrastructure-related requirements, which may in turn promote HRQOL assessment after radical prostatectomy.

21. Wei JT, Dunn RL, Litwin MS, Sandler HM, Sanda MG. 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. Dec 20 2000;56(6):899-905 OBJECTIVES: Health-related quality of life (HRQOL) is an increasingly important endpoint in prostate cancer care. However, pivotal issues that are not fully assessed in existing HRQOL instruments include irritative urinary symptoms, hormonal symptoms, and multi-item scores quantifying bother between urinary, sexual, bowel, and hormonal domains. We sought to develop a novel instrument to facilitate more comprehensive assessment of prostate cancer-related HRQOL. METHODS: Instrument development was based on advice from an expert panel and prostate cancer patients, which led to expanding the 20-item University of California-Los Angeles Prostate Cancer Index (UCLA-PCI) to the 50-item Expanded Prostate Index Composite (EPIC). Summary and subscale scores were derived by content and factor analyses. Reliability and validity were assessed by test-retest correlation, Cronbach's alpha coefficient, interscale correlation, and EPIC correlation with other validated instruments. RESULTS: Test-retest reliability and internal consistency were high for EPIC urinary, bowel, sexual, and hormonal domain summary scores (each r >/=0.80 and Cronbach's alpha >/=0.82) and for most domain-specific subscales. Correlations between function and bother subscales within domains were high (r >0.60). Correlations between different primary domains were consistently lower, indicating that these domains assess distinct HRQOL components. EPIC domains had weak to modest correlations with the Medical Outcomes Study 12-item Short-Form Health Survey (SF-12), indicating rationale for their concurrent use. Moderate agreement was observed between EPIC domains relevant to the Functional Assessment of Cancer Therapy Prostate module (FACT-P) and the American Urological Association Symptom Index (AUA-SI), providing criterion validity without excessive overlap. CONCLUSIONS: EPIC is a robust prostate cancer HRQOL instrument that complements prior instruments by measuring a broad spectrum of urinary, bowel, sexual, and hormonal symptoms, thereby providing a unique tool for comprehensive assessment of HRQOL issues important in contemporary prostate cancer management.

psychometrically valid and clinically useful questionnaire to assess health-related quality of life (HRQOL) in patients with prostate cancer (PCa) undergoing external beam radiotherapy. The most important factors in three dimensions (bowel function [BF], urinary function [UF], and sexual function [SF]) were identified by patient survey. METHODS: Three HRQOL dimensions were assessed using Likert-type questions. Responses were analyzed by factor analysis to create HRQOL scales. Reliability and validity of the scales were assessed. Because patients can suffer symptoms yet not report their lives to be affected, the scales were compared with patient-reported bother. RESULTS: Two scales were identified within each dimension: BF, urgency and daily living; UF, urgency and weakness of stream; and SF, interest/satisfaction and impotence. Cronbach's alpha for the scales ranged from 0.63 to 0.94, and item-scale correlations and item-scale divergence correlations supported scale validity. Rising median scores correlated with rising levels of perceived bother. CONCLUSIONS: The questionnaire is a suitable tool for assessing HRQOL in three distinct dimensions for patients undergoing radiotherapy for PCa. Six dimensions of HRQOL were found to be related to bother, suggesting important relationships to be monitored for patients. Urgency of bowel movements, urgency of urination, and level of interest/satisfaction in sex correlated most strongly with bother.