PATIENT-REPORTED OUTCOME MEASUREMENT GROUP, OXFORD

A STRUCTURED REVIEW OF PATIENT-REPORTED OUTCOME MEASURES (PROMs) FOR PROSTATE CANCER

Report to the Department of Health, 2009

Patient-Reported

O U T C O M E

Measures

A STRUCTURED REVIEW OF PATIENT-REPORTED OUTCOME MEASURES FOR MEN WITH PROSTATE CANCER, 2009

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EXECUTIVE SUMMARY

Aims of the report

The aims of this report are to review the evidence of Patient-reported Outcome Measure (PROMs) for people with prostate cancer and provide a short-list of the most promising generic and cancer-specific instruments based on this evidence.

The methods of the review are described and the results of the search, including sources and search terms used to identify specific published research. Details of this evidence are presented firstly for generic and preference-based PROMs evaluated with people with prostate cancer, followed by condition-specific PROM results. The report concludes with discussion and recommendations.

Results

One generic instrument, which has been evaluated with people with prostate cancer, was identified in this review:

1. Medical Outcomes Study Health Survey instruments (SF-36 & SF-12).

Three preference-based measures were identified:

1 European Quality of Life Questionnaire (EuroQol EQ-5D)
2. Health Utilities Index (HUI)
3. Quality of Well Being Scale (QWB)

Two general cancer and 9 prostate cancer-specific specific PROMs were identified in the review

1. European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)
2. EORTC Prostate-specific module (QLQ-PR25)
3. Functional Assessment of Cancer Therapy – General (FACT-G)
4. Functional Assessment of Cancer Therapy – Prostate (FACT-P)
5. FACT Advanced Prostate Symptom Index (FAPSI-8)
6. Prostate Cancer Treatment Outcomes – Questionnaire (PCTO-Q)
7. University of California-Los Angeles Prostate Cancer Index (UCLA-PCI)
8. Expanded Prostate Index Composite (EPIC, revised version of UCLA-PCI)
9. Prostate Cancer – Quality of Life (PC-QoL)
10. Prostate Cancer Related Quality of Life
11. Patient Oriented Prostate Utility Scales (PORPUS)

Recommendations

Two instruments have been substantially examined and can be recommended for further piloting in the context of the NHS:

- SF-36
- EQ-5D

The EQ-5D has specific advantages if a short preference-based measure is needed.

Several condition-specific instruments have supportive evidence used in relation to prostate cancer:

- EORTC QLQ-C30 & PR25
- FACT-P (including the 4 domains from the FACT-G)
- UCLA-PCI & EPIC

However none of these condition-specific instruments clearly stands out as having considerably more supportive evidence.

In addition the absence of a well established instrument relevant to longer term survivorship in relation to prostate cancer needs to be noted.

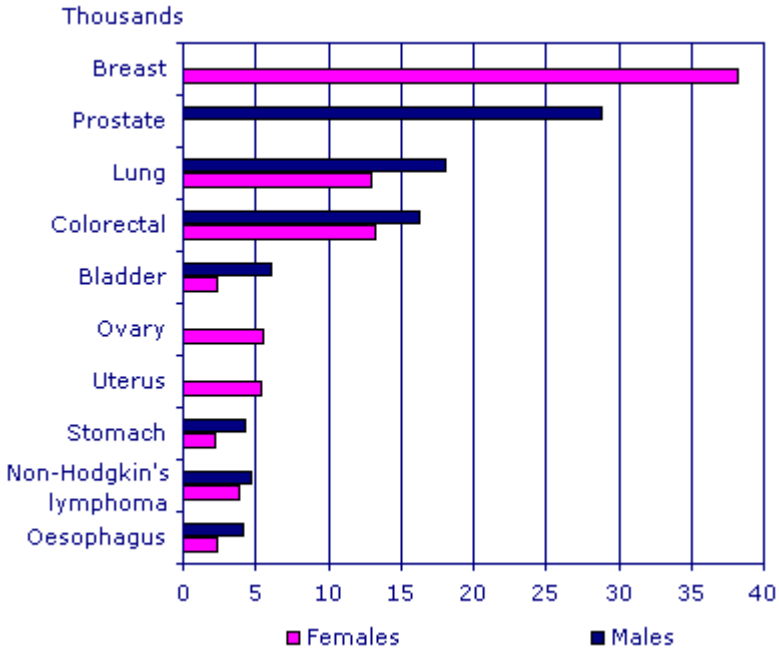
BACKGROUND

Patient-reported outcome measures (PROMs) offer enormous potential to improve the quality and results of health services. They provide validated evidence of health from the point of view of the user or patient. They may be used to assess levels of health and need in populations, and in users of services, and over time they can provide evidence of the outcomes of services for the purposes of audit, quality assurance and comparative performance evaluation. They may also improve the quality of interactions between health professionals and individual service users.

Lord Darzi's Interim Report on the future of the NHS recommends that patient-reported outcome measures (PROMs) should have a greater role in the NHS (Darzi 2007). The new Standard NHS Contract for Acute Services, introduced in April 2008, included a requirement to report from April 2009 on patient-reported outcome measures (PROMs) for patients undergoing Primary Unilateral Hip or Knee replacements, Groin Hernia surgery or Varicose Vein. Furthermore, Lord Darzi's report 'High Quality Care for All' (2008) outlines policy regarding payments to hospitals based on quality measures as well as volume. These measures include PROMs as a reflection of patients' experiences and views. Guidance has now been issued regarding the routine collection of PROMs for the selected elective procedures (DH, 2009) and since April 2009, the collection of PROMs for the selected elective procedures has been implemented and is ongoing.

In light of recent policy to include PROMs as an important quality indicator, the Department of Health now seek guidance on PROMs which can be applied in patients with cancer and have commissioned the Patient-reported Outcome Measurement Group, Oxford to review the evidence of PROMs for selected cancers. It is proposed that the most common cancers, as identified via the Office for National Statistics, should be the subject of review in terms of most promising PROMS. Breast, lung, colorectal and prostate cancer are highlighted as being the four most common cancers, accounting for half of the 239,000 new cases of malignant cancer (excluding non-melanoma skin cancer) registered in England in 2005 (Figure 1). On scrutinising cumulative incidence data from the cancer registry of the Oxford region, findings support that these four cancers are the most common. According to the Department of Health's Cancer Reform Strategy (2007), which aims to place the patient at the centre of cancer services, a 'vision 2012' has been created for each of these four cancer types, highlighting the progress that it is hoped will be made by 2012 in terms of the cancer pathway. Underlying these visions are the aims to achieve full implementation of improving outcomes guidance. In this context, PROMs are an important resource to monitor cancer outcomes.

Figure 1: Incidence of the major cancers, 2005, England (ONS, 2007)



PROSTATE CANCER

Prostate cancer is a tumour that forms in tissues of the prostate gland in the male reproductive system, found below the bladder and in front of the rectum. Prostate cancer symptoms may include urinary or erectile problems and pain; however the condition is often asymptomatic and only discovered through routine screening (PSA testing). Some of these cases will die with but not from prostate cancer. Once discovered, treatment options include watchful waiting, surgery, radiation therapy, hormone therapy and chemotherapy. All treatments carry risks of side effects including urinary, bowel and sexual dysfunction. The choice of treatment will depend on the stage of the cancer, physician recommendations and patient preferences.

Prostate cancer is the most common cancer in men in the UK – it accounts for nearly a quarter (24%) of all new male cancer diagnoses. Although there has been a huge rise in prostate cancer incidence over the last 20 years, the increase in mortality has been much less. Much of the rise in incidence is due to the increased detection of prostate cancer through the use of prostate specific antigen (PSA) testing and surgery for benign prostatic hyperplasia (BPH).

In 2004, there were 34,986 new cases of prostate cancer diagnosed in the UK. The lifetime risk of being diagnosed with prostate cancer is 1 in 14 for men in the UK. During the 1980s these rates rose consistently, with an acceleration of the trend in the early 1990s, followed by a brief leveling off in the mid-1990s and another rising trend in the late 1990s. Some of this increase may be due to a real increase in risk, but growing detection of the disease has almost certainly played a part. Whether there is a real increase in incidence or not, the numbers of cases of prostate cancer will rise as the population at risk (older men) expands due to increasing life expectancy. An increase has been seen in all age groups over 45 in Great Britain since the mid-1970s (Cancer Research UK, 2007).

METHODS

Structure of the report

The methods of the review are described and the results of the search, including sources and search terms used to identify specific published research. Details of this evidence are presented firstly for generic and preference-based PROMs evaluated with people with prostate cancer, followed by cancer-specific PROM results. The report concludes with discussion and recommendations.

Methods for the review

a) Inclusion criteria
Titles and abstracts of all articles were assessed for inclusion/exclusion by one reviewer and a selection agreement was checked by another reviewer. Included articles were retrieved in full. Published articles were included if they provided evidence of measurement and/or practical properties (Fitzpatrick et al., 1998).

Articles were retrieved, assessed for relevance and catalogued according to the PROM for which they provided evidence (note that a single paper frequently provided information on more than one measure). Papers were included if the patients were entirely or substantially diagnosed with prostate cancer and the questionnaires administered were in English language. Papers were excluded if the patients had Benign Prostatic Hyperplasia rather than cancer, or if the questionnaires were administered in languages other than English.

-Study design selection

- studies where a principal PROM is being evaluated;
- studies evaluating several PROMs concurrently;
- applications of PROMs with sufficient reporting of methodological issues.

-Specific inclusion criteria for generic and disease-specific instruments

- the instrument is patient-reported;
- there is published evidence of measurement reliability, validity or responsiveness following completion in the specified patient population;
- the instrument has been recommended for use with patients with prostate cancer;
- evidence is available from English language publications, and instrument evaluations conducted in populations within UK, North America, Australasia.

b) Exclusion criteria

- Clinician-assessed instruments

c) Search terms and results: identification of articles
The searches were conducted using three main sources.

The primary source of evidence was the bibliographic database compiled by the PROM group in 2002 with funding from the Department of Health and hosted by the University of Oxford (http://phi.uhce.ox.ac.uk/home). In 2005, it became the property of the NHS Information Centre for Health & Social Care. The most recent

bibliographic update is current to December 2005. The PROM bibliographic database comprises over 30,000 records relating specifically to PROMs. The content is based on systematic searches of published literature using a specially developed search strategy to identify PROMs across a broad spectrum of academic publications (further details of the strategy are provided in Appendix A).

A supplementary search was conducted using (i) Pubmed to take account of more recent publications, and 'name' searches were conducted for the commonly cited PROMs identified in the initial phase; (ii) NHS Database of Economic Evaluations (http://www.crd.york.ac.uk/crdweb) was used to identify the utility measures used in cost-effectiveness studies; (iii) 'hand-searches' of the reference lists of review papers and by checking the contents pages of Journal of Clinical Oncology, Medical Care, Health and Quality of Life Outcomes, and Quality of Life Research.

The number of relevant articles identified through each source is shown in Table 1.

Table 1 Number of articles identified by the literature review (after removal of duplicates)

Identified	**n**
Bibliography (until 2005)	79
Bibliography 2006/2007	34
Supplementary searches	84
Total	197
Reviewed	
Full text reviewed	186
Included in report	**76**

d) Data extraction

Data were extracted on the psychometric performance and operational characteristics of each PROM. Assessment and evaluation of the methodological quality of PROMs was performed independently by two reviewers adapting the London School of Hygiene appraisal criteria outlined in their review (Smith et al., 2005). These criteria were modified for our review (Appendix B).

The final short-listing of promising PROMs to formulate recommendations is based on these assessments and discussion between reviewers.

RESULTS: GENERIC INSTRUMENTS

One generic PROM was identified that had been used with patients with prostate cancer in English language populations, and for which adequate evidence of psychometric properties was available to enable appraisal.

Generic PROMs
1). Medical Outcome Short Form Health Survey Instruments (SF-36 & SF-12)

The SF-36 (Ware and Sherbourne, 1992) is a 36-item generic health status measure with eight dimensions: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, energy/vitality, pain, and general health perception. Fourteen papers contributed evidence on the performance of the Medical Outcome Short Form Health Survey Instruments. The SF-12 has been used in tandem with prostate cancer-specific instruments but the psychometric performance of the SF-12 itself has not been reported with sufficient detail to enable a full appraisal to be conducted. Hence, the performance of the SF-12 has not been reported separately.

Acceptable internal consistency has been demonstrated for all domains when using the SF-36 with men with prostate cancer, with Cronbach's alpha statistics for each domain ranging from 0.68-0.91 (Lev et al., 2004).

In terms of construct validity, the SF-36 domains for bodily pain, vitality, social functioning, mental health discriminated between disease status (remission versus progression) ($p<0.05$) (Albertsen et al., 1997). In the same study patients with progressive disease scored statistically significantly lower than general population on all domains, whilst patients in remission scored similarly to general population (Albertsen et al., 1997). Small differences were observed in all domains between patients undergoing first and second treatment, and the differences were statistically significant after adjusting for time (Arredondo et al., 2007). The role domain discriminated between disease status, and role, physical and emotional domains discriminated between patients with adverse side effects from treatment (Gall 2004). However, in patients undergoing radical prostatectomy, only the Pain domain discriminated between patients with prostate cancer and controls (data not shown) (Hoffman et al., 2004).

Poorer domain scores at follow up were reported to be associated with depressive symptoms at 4 weeks post-treatment (Monahan et al., 2007), and statistically significant correlations were reported between domain scores and symptoms one year after treatment except for pain, role and mental health (Clark et al., 1999). Physical function, emotional role, pain, general health and mental health were associated with psychosocial factors, whilst physical role general health, social function were associated with symptoms; age was also correlated with a small decrement in scores in physical domains (Lev et al., 2004). Poorer scores were found to be associated with turning to religion to cope (Gall 2004).

The summary PCS and MCS scores have been found to be broadly similar to population norms (Arredondo et al., 2008; Clark et al., 1999; Greene et al., 2005; Talcott et al., 2003); though the PCS was slightly lower than the norms (Arredondo et

al., 2008). The PCS was found to discriminate between patients receiving different surgical interventions (Hu et al., 2006), however, in another study, the PCS did not discriminate between patients receiving different modes of treatment (Soderdahl et al., 2005). Evidence of convergent validity can be found in that lower PCS scores were associated with poor bowel function (Talcott et al., 2003), and lower PCS and MCS scores were associated with bowel and sexual dysfunction assessed from symptom indices. Lower MCS scores associated with urinary dysfunction (Clark & Talcott 2001).

Small decreases in PCS scores initially with treatment returned to baseline level at one year (Kouba et al., 2007; Soderdahl et al., 2005; Talcott et al., 2003); MCS scores showed a trend of slight improvement after starting treatment (Kouba et al., 2007). PCS and physical domains modelled to decrease more than would be expected with aging alone in patients under watchful waiting (Arredondo et al., 2008). Scores of patients who were asymptomatic after one year were observed to increase, albeit with small effect sizes except in the Role domain which were moderate (ES=0.4) (Clark et al., 1999).

Three preference-based measures were identified:

1. European Quality of Life Questionnaire (EuroQol EQ-5D)
2. Health Utilities Index (HUI)
3. Quality of Well Being Scale (QWB)

These instruments are summarised in Appendix C.

1) EuroQol EQ-5D

The EQ-5D (EuroQol Group, 1990; Brazier et al., 1993) is a generic measure of health utility. There are five single item dimensions: mobility, self-care, usual function status, pain and/or discomfort, and anxiety and/or depression. The content of the EQ-5D is not relevant to effects of prostate cancer: urinary, sexual or bowel problems; this creates problems with face and content validity (Krahn et al., 2007). However, four papers were identified that reveal some evidence of the performance of the EQ-5D in this population.

However the instrument has been used with prostate cancer patients. Very small statistically non-significant change in utility (<0.02) was observed over 2-10 months with patients whose prognoses was expected to improve or decline. In the same study, larger and statistically significant changes were detected using condition-specific instruments (Krahn et al., 2007). Slightly greater, but still small, changes in utility (0.06-0.08) were observed by categorising patients by those whose QLQ-C30 scores changed by more or less than 0.5 SD; the effect sizes were moderate (0.4-0.5, not presented but calculated from data presented). Statistically significant decline in utility (>0.5) has been reported at 3, 6 and 9 months in patents with metastatic disease (Sullivan Andel et al., 2007). Small differences in utility have been reported in patients with prostate cancer who experience secondary skeletal problems such as fractures (Reed et al., 2004).

The EQ-5D also includes a visual analogue scale (VAS) 'feeling thermometer' to enable direct scaling by the respondent. Small changes in both VAS (0.06) and utilities (0.7-0.13) were reported following radiation to bone/fracture sites (moderate effect size, from 0.31-0.56); however this largely reflects changes in health status due to treatment of skeletal side-effects rather than prostate cancer itself (Weinfurt et al., 2005).

2). Health Utilities Index (HUI2 and HUI3)

The HUI2 and HUI3 are generic measures of health utility. The HUI2 classifies health states in the attributes: sensation, mobility, emotion, cognitive, self-care, pain, and fertility; the HUI3 assesses vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain. Therefore the content not particularly relevant to effects of prostate cancer creating problems with face and content validity (Krahn et al., 2007). Four papers contributed to the review.

HUI3 showed poor correlation with condition-specific instruments, (Albertsen et al., 1998), and did not discriminate between health states (metastatic versus non-metastatic disease) or treatment (radiotherapy versus other) (Ritvo et al., 2005). However, the HUI3 did discriminate (observed differences in utility) between patients who had received hormone therapy and radiotherapy (with or without hormone therapy) (Konski et al., 2005).

Small statistically non-significant change in utility (<0.02) was observed over 2-10 months with patients whose prognoses were expected to improve or decline; effect sizes were small for both versions (<0.1). In the same study, larger and statistically significant changes were detected using condition-specific instruments (Krahn et al., 2007). Slightly greater changes in utility (0.03-0.06) were observed by categorising patients by those whose QLQ-C30 scores changed by more or less than 0.5 SD. Effect sizes were small for both versions (~0.3, not presented but calculated from data presented) (Krahn et al., 2007).

3). Quality of Well Being Scale (QWB)

The QWB classifies health states using four attributes: mobility, physical activity, social activity, and symptoms/problems. Thus the content is only marginally relevant to effects of prostate cancer; sexual functioning is coded within social functioning and problems with specific symptoms could, in principle, be assessed. Two papers contributed to the review.

In terms of discriminative validity, small differences in utility were reported between patients who had received hormone therapy and radiotherapy with or without hormone therapy (Konski et al., 2005); and statistically significant differences in utility were seen in patients receiving radiotherapy versus other treatments (Ritvo et al., 2007). However QWB utility did not discriminate between metastatic versus non-metastatic disease (Ritvo et al., 2007).

Small, statistically non-significant changes in utility (<0.02) were observed over 2-10 months with patients whose prognoses were expected to improve or decline, except in the sub-group of patients undergoing treatment for who the fractionally larger change

in utility (0.03) was statistically significant. However, effect sizes were small (<0.2, not presented but calculated from data presented) (Krahn et al., 2007). In the same study, larger and statistically significant changes were detected using condition-specific instruments (Krahn et al., 2007). Marginally larger changes in utility (0.02-0.06) were observed by categorising patients by those whose QLQ-C30 scores changed by more or less than 0.5 SD, though the effect sizes were small to moderate (0.15-0.46, not presented but calculated from available data).

RESULTS: CANCER & PROSTATE CANCER -SPECIFIC INSTRUMENTS

Two general cancer-specific PROMs and 9 prostate cancer-specific PROMs were identified that had been used with patients with prostate cancer in English language populations, and for which adequate evidence of psychometric properties was available to enable appraisal.

1. European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)
2. EORTC Prostate-specific module (QLQ-PR25)
3. Functional Assessment of Cancer Therapy – General (FACT-G)
4. Functional Assessment of Cancer Therapy – Prostate (FACT-P)
5. FACT Advanced Prostate Symptom Index (FAPSI-8)
6. Prostate Cancer Treatment Outcomes – Questionnaire (PCTO-Q)
7. University of California-Los Angeles Prostate Cancer Index (UCLA-PCI)
8. Expanded Prostate Index Composite (EPIC, revised version of UCLA-PCI)
9. Prostate Cancer – Quality of Life (PC-QoL)
10. Prostate Cancer Related Quality of Life
11. Patient Oriented Prostate Utility Scales (PORPUS)

These instruments are summarised in Appendix D.

1). European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)

The EORTC QLQ-C30 (Aaronson et al., 1993) is a 30-item cancer-specific instrument. Multi-trait scaling was used to create five functional domain scales: Physical, Role, Emotional, Social and Cognitive; two items evaluate global QoL; in addition three symptom scales assess: fatigue, pain and emesis; and six single items assess further symptoms. Fourteen papers provided data for the review.

In men with prostate cancer, the Role, Social, and Emotional domains, and Global QoL, have been found to have adequate internal consistency (alpha >0.7); however the Physical and Cognitive domains showed lower consistency (alphas = 0.6) (Aaronson et al., 1993; Albertsen et al., 1997) Guttman coefficients for reproducibility and scalability (indicative of unidimensionality) for the Physical and Role domains were reported as good (>0.7) (Curran et al., 1997). Poor reliability between patients and clinicians-rated scores was noted for the symptom scales (Fromme et al., 2004).

Moderate correlations between QLQ-C30 domain scales has been shown, with higher correlation (convergence) for Physical and Fatigue, and lower correlation (divergence) for Physical and Emotional (Aaronson et al., 1993; Albertsen et al., 1997). QLQ-C30 Physical, Role, and Global QoL scales discriminated between known groups based on ECOG performance and weight loss (Aaronson et al., 1993; Albertsen et al., 1997), between disease status (remission/progressive) (Aaronson et al., 1993; Albertsen et al., 1997), (local/advanced) (Lintz et al., 2003); and between patients with different prognoses (Curran et al., 1997). The Physical, Emotional, Financial domains and Pain and Appetite symptom scales discriminated between disease status/prognosis in patients of low socioeconomic status (note that some participants in this study required assistance to complete questionnaires) (Knight et al., 1998). In the same study there

was strong convergence between QLQ-30 and FACT-G for the Physical, Emotional and Role/Functional domains (r ranging from 0.54 to 0.72); however the social functioning scales correlated poorly (r from 0.14 to 0.38) (Sharp et al., 1999).

In terms of responsiveness, statistically significant improvement was seen in the Emotional and Global QoL domains, but the change in scores was not statistically significant in other domains; the authors noted that change scores were strongly correlated with baseline scores (van Andel et al., 2008e). Statistically significant change in scores was reported for Physical, Role, and Global QoL, and for the Fatigue and Nausea symptom scales (Aaronson et al., 1993) but the effect sizes were low to moderate (<0.3) (not presented but calculated from data presented). Larger effect size (Guyatt's statistic=0.85) (Yount et al., 2003).

Statistically significant changes were observed in the Physical and Role scales, and symptom scores (Spry et al., 2006). The domain scales showed weak correlation with a global rating of change (Rodrigues et al., 2004). Small but statistically significant improvement in total scores were reported in a mixed cancer population (17% had prostate cancer) who underwent mindfulness training with small to moderate effect size (0.33) (not presented but calculated from data presented) (Carlson et al., 2003). Statistically significant decline in all scores have been reported at 3, 6 and 9 months in patents with metastatic disease, although symptom scores improved (Sullivan et al., 2007)

2). European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-PR25)

The EORTC QLQ-PR25 is a 25-item prostate cancer-specific scale intended to supplement, the EORTC QLQ-30. There are six prostate-specific domains: Urinary, Bowel, Use of Incontinence Aids, Treatment-Related Symptoms, Sexual Active and Sexual Function. Three papers are referenced in the review.

The QLQ-PR was initially developed in Sweden (Borghede & Sullivan 1996) and later evaluated using multi-language versions of which 13% of the study population completed English language versions (van Andel et al., 2008). The questionnaire takes approximately 15 minutes to complete, and some participants needed assistance, there was a high response to the baseline survey (80% of eligible population) but attrition to 57% response was recorded after 6 months.(van Andel et al., 2008). Some negative feedback was recorded from patients in relation to the Sexual Functioning items (van Andel et al., 2008).

The items were generated from interviews with clinicians and patients. Multi-trait scaling was used to produce domains, and acceptable item-total correlations were reported but these data were not presented. Only the Urinary Symptoms, Sexual Active and Sexual Function domains showed acceptable internal consistency (alpha>0.7), scale consistency was poorer for the Bowel domain (0.5) and Treatment-related symptoms (0.4) (van Andel et al., 2008). Some floor effect seen in all domains except Sexual Function, and the floor effect was worst for the Bowel domain (50% of patients had no problems) (van Andel et al., 2008).

The QLQ PR-25 discriminated between scores on the Karnofsky Performance Scale, and between curative and palliative patients; low correlations (<0.4) were seen with QLQ-C30 domain scales, suggesting these were different constructs (van Andel et al., 2008).

Statistically significant changes in scores in the expected direction were consistent with changes in Karnofsky score (the magnitude of change in score and raw data were not presented to enable calculation of effect size). Statistically significant changes in Sexual Active and Sexual Function scores (Spry et al., 2006).

3). Functional Assessment of Cancer Therapy – General Version (FACT-G)

The FACT-G (Cella et al., 1993) is a 27-item cancer-specific instrument with four domains: Physical, Social, Emotional, and Functional wellbeing, and a total score. Fifteen papers provided data for the review.

The items were devised with input from patients with lung, breast and colorectal cancer; but a small number of men with prostate cancer (2% of study population) were involved in initial testing of questionnaire (Cella et al., 1993). Internal consistency of scales has been reported in two studies, as acceptable for all domains (alphas >0.7) although slightly lower for the Emotional and Social domains (>0.6) (Cella et al., 1993); Yount et al., 2003). High internal consistency was reported for total scores (>0.8) (Yount et al., 2003). Test-retest reliability was observed to be good within one week for all domains (ICC>0.8) (Cella et al., 1993). Proxy reports by spouse showed poor inter-observer reliability except in the Functional domain (Knight et al., 2001).

In a mixed cancer population (only 2% had prostate cancer) FACT-G scales discriminated between disease status, and convergence was observed between similar scales (Cella et al., 1993). The physical and functional scales also discriminated well between health status using ECOG Performance Status Rating in men with prostate cancer (Yount et al., 2003). The Physical and total scores discriminated between disease status/prognosis in patients of low socioeconomic status who completed questionnaires (albeit some required administrator assistance) (Knight et al., 2001). In the same population strong convergence was reported with QLQ-C30 for the Physical, Emotional and Role/functional domains (r from 0.54 to 0.72) but the Social scales correlated poorly. Divergence was observed with dissimilar domains (r from 0.14 to 0.38) (Sharp et al., 1999). Statistically significant correlation has been reported between Total scores and symptom scales but the magnitude of correlation was not provided (Bradley et al., 2004). When used in conjunction with the prostate-specific module (FACT-P) the domain scales similarly discriminated between disease status (Esper et al., 1997; Rosenfeld et al., 2004; Shrader-Bogen et al., 1997). A moderate correlation has been reported with the EPIC summary scales, and higher correlation with FACT-P, and the SF-12 PCS and MCS (Wei et al.,2000). Scores have also been shown to be associated with co-morbidities, physical activity, and sleep functioning; differences by ethnicity were thought to be confounded by socio-economic variables (Penedo et al., 2006).

In terms of responsiveness, the proportion of patients scoring above or below a threshold of 30 points on the physical function scale changed for patients on a trial comparing radiation dosages, no changes were observed for the other domain scales

(Dearnaley et al., 2007). Large effect sizes (Guyatt's statistic=0.92) have been cited (Yount et al., 2003). The physical and social scales detected small but statistically significant improvement comparing an exercise programme versus no exercise programme during radiotherapy (Monga et al., 2007). The physical, social and function scales demonstrated statistically significant changes after cryosurgery but not the emotional or social/family scale; typical patterns of a sharp decline at 6 weeks, returning to baseline levels at one year was recorded) (Robinson et al., 1999). The same patterns were seen in patient undergoing brachytherapy (Lee et al., 2000; Robinson et al., 1999) (Lee et al., 1999; Robinson et al., 1999), and also in patients receiving other interventions (Lee et al., 1999; (Hoskin et al., 2007). When used in conjunction with the FACT-P, statistically significant improvement in physical and functional scales were only observed in patients with improved PSR, however only the total scores changed with PSA (Esper et al., 1997). Very small, but nonetheless statistically significant, changes in the emotional wellbeing were reported in patients with advanced cancer undergoing treatment (Kornblith et al., 2000). Statistically significant changes in physical, functional & emotional domains are noted in men undergoing brachytherapy with effect sizes range from 0.4 to 1 (not reported but calculated from data presented) (Lee et al., 2001). Regression to mean was generally observed, and a need to adjust for baseline scores and demographics recommended (Lee et al., 2001).

4).Functional Assessment of Cancer Therapy – Prostate Version (FACT-P)

The FACT-P is a 12-item prostate cancer-specific scale that supplements the general version (FACT-G). Scores can be produced from the 12 condition-specific items, the Prostate Cancer Score (PCS) and a Treatment Outcome Index (TOI) can be calculated by summing the FACT-G Physical and Functional domains and the PCS. Fourteen papers provided data for the review.

The items were developed and piloted with patients and in liaison with the developers of FACT-G (Esper et al., 1997). The questionnaire takes around 14 minutes to complete (Cella et al., 2008). Poor completion rates have been noted in drug trials (Canil et al., 2005; Stone et al., 2008). Acceptable internal consistency has been reported for the PCS (alpha = 0.65) but higher for the TOI and total score (alphas >0.7) (Esper et al., 1997).

The FACT-P scores discriminated between disease status (Rosenfeld et al., 2004), and between locoregional/metastatic disease on all domains except social wellbeing (Stone et al., 2008), and also between health status using Performance Status Rating (Yount et al., 2003). Moderate to high correlation has been reported between FACT-P scores with EPIC and with SF-12 PCS and MCS, and FACT-G (Wei et al., 2000).

A statistically significant improvement in total scores was reported in patients who were stable or had improved PSR and PSA (Esper et al., 1997). A large effect size (Guyatt's statistic=1.06) has been reported for the PCS (Yount et al., 2003). Effect sizes and meaningful change are estimated for the total score (effect size=0.47, meaningful change = 6-9), for the Treatment Outcome Index (effect size=0.48, meaningful change=2-3); and for the PCS (effect size=0.44, meaningful change=1-2) (Cella et al., 2008). In another study, no statistically significant changes overall after 22 weeks, however there were statistically significant changes in patients who rated

QoL better (effect size=0.25) or worse (effect size=0.32) (Stone et al., 2008). Total scores detected small but statistically significant improvement comparing exercise versus no exercise programme during radiotherapy (Monga et al., 2007); the total score also demonstrated statistically significant changes after cryosurgery (with a sharp decline at 6 weeks, returning to baseline levels at one year) (Robinson et al., 1999). The same pattern was seen in patient undergoing brachytherapy (Hoskin et al., 2007; Lee et al., 2000). A statistically significant change in FACT-P scores was reported in men undergoing brachytherapy (effect size 0.69, not reported but calculated from data presented) (Lee et al., 2000). A small, but statistically insignificant, change in total score has been reported in patients with advanced cancer undergoing treatment (Kornblith et al., 2000). Deterioration in item and TOI scores has been reported; however in this study no differences were seen between groups given adjuvant hormonal treatment (Stephens et al., 2007). Small but statistically significant decline in total score at 3, 6 and 9 months were observed in patents with metastatic disease (Sullivan et al., 2007). No differences were found between mean scores in patients treated with radiotherapy versus radiotherapy & brachytherapy after one year on any scale (Joseph et al., 2008).

5). FACT Advanced Prostate Symptom Index (FAPSI-8)

Specific to advanced prostate cancer, the eight FAPSI items, relating to pain, fatigue, weight loss, urinary difficulties, concern about getting worse, were a subset selected from the FACT-P considered of most importance by clinicians (Yount et al., 2003). Two papers provided data.

The internal consistency has been tested on 4 occasions and found to be acceptable (alphas ranging from 0.67-0.80). Tests of uni-dimensionality indicate that the items for difficulty urinating and 'urinating difficulties limiting activities' are not consistent with other 6 items, nevertheless eliminating these items did not improve internal consistency (Yount et al., 2003).

The FAPSI showed moderate to strong correlations with all FACT-G domains except social family wellbeing (lowest was emotional r=0.33); in addition strong correlations were reported with the FACT-P summary score and the EORTC global, pain and fatigue scales. The FAPSI discriminated between health status (using the Performance Status Rating) (Yount et al., 2003).

Large effect size (Guyatt's statistic >1.3) have been recorded (Yount et al., 2003). An effect size of 0.47 has been reported with a meaningful change estimated at 2-3 points (Cella et al., 2008).

6). Prostate Cancer Treatment Outcomes – Questionnaire (PCTO-Q)

The PCTO-Q is a 41-item prostate cancer-specific instrument. Domain scales assess the incidence and severity of specific changes in bowel, urinary, and sexual functions. Two papers provided data.

Pilot testing included examination of test-retest reliability which is reported as 91% but an ICC was not presented (Shrader-Bogen et al., 1997).

After adjustment for age, the domains for bowel, urinary and sexual function discriminated between patients receiving different treatments (prostatectomy versus radiotherapy). Worse bowel functioning was reported in the radiotherapy group and worse urinary and sexual function in the prostatectomy patients (Rodgers et al., 2006; Shrader-Bogen et al., 1997).

7). University of California-Los Angeles Prostate Cancer Index (UCLA-PCI)

The UCLA-PCI is a 20-item prostate cancer-specific measure of HRQoL experienced in the previous four weeks. There are six scales covering function and bother, separately, with in each of urinary, sexual and bowel domains. Twelve papers provided data for the review.

Focus groups held to generate pertinent issues and derive the items (Litwin et al., 1998). Factor analysis was used to create the domains; internal consistency was reported to be good for the sexual and urinary scales (alphas between 0.7 and 0.9) (Litwin et al., 1998) good but lower for the bowel domain (alpha 0.58). Test-retest reliability over four weeks was moderate (ICC=0.6) (Litwin et al., 1998). The questionnaire was estimated to take approximatemy12 minutes to complete (Litwin et al., 1998).

Moderate correlations between function and bother scales (Litwin et al., 1998); and low to moderate correlations with SF-36 scales, highest for urinary-fatigue, sexual-general health, bowel-general health (Litwin et al., 1998). A slight floor effect exists for the sexual domain (Greene et al., 2005) whereas a ceiling effect occurs for the urinary function and bother and bowel bother scales (Greene et al., 2005; Jayadevappa et al., 2005; Litwin et al., 1998).

The scales did not discriminate between tumour stages (Litwin et al., 1998). However there were differences in domain scores between patient receiving different treatments, such as prostatectomy and radiotherapy (Hu et al., 2006; Newton et al., 2006; Jayadevappa et al., 2005) and those undergoing second treatment (Arredondo et al., 2006). The scales also discriminated between patients with and without co-morbidities (Arredondo et al., 2006).

In longitudinal studies, the proportion of patients scoring +/-30 on the bowel and sexual scales changed for patients on trial comparing radiation dosage, but no changes were seen for the urinary scale (Dearnaley et al., 2007). Statistically significant decreases in urinary and sexual function and bother domains were reported one year after prostatectomy (Jayadevappa et al., 2005; Shikanov et al., 2008). A follow up study (6, 12, 24, 36 months) showed no statistically significant changes in bowel function and bother over time, small and larger statistically significant change over time for urinary and sexual domains respectively (Soderdahl et al., 2005; White et al., 2008). Small and statistically insignificant changes in urinary and sexual scores were reported with increasing experience of surgeons performing prostatectomy (Zorn et al., 2007). Deterioration in item scores, sexual scores, no differences between groups given adjuvant hormonal treatment (Stephens et al., 2007), physical and sexual domains modelled to decrease more than would be expected with aging alone in patients under watchful waiting (Arredondo et al., 2008), moderate to large decreases in urinary and sexual domains and small or no changes in bowel domains after

prostatectomy, deterioration in sexual function associated with co-morbidities (Arredondo et al., 2006).

8). Expanded Prostate Index Composite (EPIC)

The EPIC is a 36-item revised and expanded version of the UCLA-PCI incorporating issues that were missing from the previous version. As before, there are separate function and bother scales, and a summary scale for each of urinary, bowel, sexual and hormonal domains. Ten papers provided data for the review.

The revision of the content from the UCLA-PCI was conducted with input from patients and clinical experts. Response of approximately 80% has been recorded (Ash et al., 2007). Rest-retest reliability was acceptable for all scales (ICC>0.7) (Wei et al., 2000). A ceiling effect exists for the bowel domain (Ash et al., 2007;(Dahm et al., 2003; Simone et al., 2008). The function and bother scales for each domain correlated highly but not perfectly; low to moderate correlations were observed between domains and with the SF-12 PCS and MCS. A high correlation was noted between the Prostate Cancer Score from the FACT-P, and moderate correlations with FACT-G domain scores (Wei et al., 2000). The urinary scales correlated with International Prostate Symptom Score (IPSS) (coefficient not reported) (Ash et al., 2007). Bowel function and bother scales discriminated between two different doses of an endorectal radioprotector (Amifostine) (Simone et al., 2008). The sexual domains discriminated between nerve and non-nerve-sparing surgical techniques (Wiygul et al., 2005); a statistically significant association existed between sexual domains and age (</>67yrs). The sexual scales also discriminated between patients who were or were not receiving hormonal treatment when undergoing radiotherapy (Hollenbeck et al., 2004).

Statistically significant changes were seen in the urinary and sexual scales with patients undergoing brachytherapy, but not in the bowel domain (Ash et al., 2007). However, small but statistically significant changes were seen in bowel scale scores following prostatectomy (Dahm et al., 2003). Statistically significant changes (deterioration) were observed in all sexual and urinary function scores after prostatectomy (Wiygul et al., 2005). Increases (improvement) in the sexual summary score over 4 years exceeded 0.5 SD criterion for meaningful change (Hollenbeck et al., 2004). A large decrease in all domain scores was observed initially after prostatectomy (effect sizes not presented but >1 when calculated from data presented) (Yang et al., 2004). Substantial deterioration was noted after prostatectomy in all sexual scores, small decreases in urinary scores, and no change in bowel scores (Link et al., 2005; Tseng et al., 2006). Sexual scores deteriorated sharply after prostatectomy and recovery slightly more in patients who had nerve sparing surgery (Wiygul et al., 2005; Wagner et al., 2006).

9). Prostate Cancer – Quality of Life (PC-QoL) (Giesler et al. 2000)

The PC-QoL is a 52-item instrument with 10 domain scales: function, role activity limitations, and bother for each of urinary, bowel and sexual issues (Giesler et al., 2000). One other scale assesses worry/anxiety about having prostate cancer and treatment. Two papers provided data for the review.

The development paper describes a clear conceptual basis: physiologic function, bother, activity role limitations (Giesler et al., 2000). Items were generated from other instruments and clinicians, and refined with feedback from survey with 20 patients. Item reduction (52/120) was achieved through item analysis (removing items with floor/ceiling effects) and item-total correlations (data not presented). The PC-QoL is estimated to take 15 minutes to complete; a high response (90%) was reported with no missing data.

Slight ceiling effects were seen only for bowel function and bowel role activity limitation. Internal consistency was good (alphas 0.7-0.9) (Giesler et al., 2000). Test-retest reliability after 2 weeks for each domain was generally high (ICC>0.7), but slightly lower for the scales for cancer worry and bowel activity limitations (Giesler et al., 2000).

Strong convergence was noted for the function, bother and role activity limitation scales within each of the urinary, sexual and bowel categories; however strong divergence was observed between each of the urinary, sexual and bowel category scales (Giesler et al., 2000). There was strong convergence between PC-QoL function and bother scales with the Prostate Cancer Index (PCI), although the moderate correlations between the PCI and role activity limitation scales are indicative of divergence (Giesler et al., 2000). Appropriate convergence and divergence was reported with SF-36 domains (data not presented). The function scales discriminated between surgical and radiation treated patients. The role activity limitation and bother scales correlated moderately with a life satisfaction scale, and more strongly than physiologic function scales. The cancer worry domain scores converged moderately with a negative emotion scale (from PANAS), but more strongly than other scales. Lower domain scores at follow up were associated with depressive symptoms at 4 weeks post-treatment (Monahan et al., 2007). Evidence has been presented that the PC-QoL scales are more precise than single-item scores. No evidence of responsiveness of the PC-QoL was available.

A revised 46-item version of this instrument has also been published, with supporting evidence of adequate internal consistency and test-retest reliability, and discriminative, convergent and divergent validity (Befort et al., 2005).

10). Prostate Cancer Related Quality of Life

The Prostate Cancer Related Quality of Life instrument includes domains for urinary control, sexual intimacy, sexual confidence, marital affection, masculine self-esteem, health worry, PSA concern, cancer control, informed decision, regret, and outlook. Three papers provided data for the review.

The items were created based on themes from qualitative work, including focus groups with men with prostate cancer who were less than 24 months since diagnosis (Clark et al., 1997; Clark et al., 2003). Principal components analysis was used to define the domain scales, and item-total correlations were acceptable (all >0.4). The scales were internally consistent (all alphas >0.7) (Clark et al., 1997; Clark et al., 2003) except the scale for PSA concern (alpha=0.6) (Clark et al., 2003). A floor effect was noted for ‘regret’; and ceiling effects for urinary control and marital affection (>40% at extreme of scale) (Clark et al., 2003)

Appropriate convergence was reported between the urinary and sexual domains and standard symptom indices (Clark et al., 2003). The 'masculine self-esteem' and 'health worry' scales correlated highly with the SF-12 MCS ($r > 0.5$) (Clark et al., 2003). The scales for 'urinary control', 'sexual intimacy', 'sexual confidence', 'masculine self-esteem', and 'PSA concern' all discriminated between patients (prostate cancer and non-patients) (all $p<0.05$) (Clark et al., 2003).

11). Patient Oriented Prostate Utility Scales (PORPUS)

The PORPUS is a 10-item health state classification with 4-6 levels designed to measure prostate cancer-specific health status (profile) and utility. There are five broad items: pain, energy, psychosocial and social wellbeing, relationship with doctor; and five prostate-specific items: sexual function and desire, urinary frequency and incontinence, and bowel function. Three papers provided data for the review.

Items derived from literature review, consultation with clinicians, interviews/ranking with 80 patients; final draft version also endorsed by patients and clinicians in interviews. Acceptable test-retest reliability (ICC=0.81) has been reported for the profile score, however the scaled utility scores are less stable (ICC=0.66). (Krahn et al., 2007)

Appropriate convergence has been shown between PORPUS and the HUI, FACT-P, UCLA-PCI scale scores (Ritvo et al., 2005). The profile scale discriminated between disease states whereas the utility scale did not (Ritvo et al., 2005). However, different utility scores were derived from patients who had different treatments (hormone therapy with or without radiotherapy) (Konski et al., 2005).

In terms of responsiveness, changes in utility scores were statistically significant and larger than were detected by the generic instruments (HUI and EQ-5D) the effect sizes were large (>0.8) (Krahn et al., 2005).

Several instruments were identified but subsequently excluded as they were either not used in the English language, were dimension-specific, or too few data on psychometric performance was available to enable an appraisal to be conducted (Table 2).

Table 2 Excluded PROMs

PROM	Number of papers
Generic	
Nottingham Health Profile	1
General Health Index & Mental Health Index	2
Cancer Rehabilitation Evaluation System	2
Functional Living Index – Cancer	1
Standard gambles/Time Trade-Off	5
Cancer specific	
Prostate Cancer Radiation Toxicity Questionnaire	2
Coping with Cancer Instrument	1
Quality of Life Module – Prostate 14	1
PROSQOLI	2
Dimension-specific	
Profile of Moods Scale	1
Psychosocial Adjustment to Illness Scale	1
International Index of Erectile Function	3
Symptom checklists	5

CONCLUSIONS AND RECOMMENDATIONS

The full-text articles for 186 papers were retrieved and reviewed. Those papers describing studies not used in English language populations or were dimension-specific instruments or symptom checklists or clinician ratings were discarded. There were 76 papers identified that provided useful data for the review.

One generic, three preference based, two cancer-specific and nine prostate cancer-specific PROMs were identified that had been used with patients with prostate cancer in English language populations, and for which adequate evidence of psychometric properties was available to enable appraisal (Tables 3 and 4).

Of the generic PROMs the SF-36 is the only multidimensional instrument that has been used extensively with men with prostate cancer. The other generic PROMs are utility preference based instruments and none has face validity for the very specific urinary, sexual and bowel problems experienced with this condition. The EQ-5D appears to be sensitive to changes in the latter stages of the disease and side-effects of treating metastatic bone disease and co-morbidities. The EQ-5D could be further considered on the basis of using the data for comparison with the outcomes of other conditions.

The instruments included in this review have been used with patients for people with recent diagnosis or undergoing treatment, principally to evaluate the effectiveness of interventions. However, as more patients are living longer following treatment, there is increasing interest in measuring quality of life amongst the long-term survivors of cancer. In this context, our recommendations regarding generic instruments will likely remain appropriate, but the content of condition-specific instruments may lose face validity as the predicament of survivorship is different to undergoing treatment. Pearce et al. (2008) identified and appraised several instruments which have been specifically developed for long-term survivors of cancer. Although some instruments have been tested in samples including survivors of prostate cancer, the general conclusion of their review is that no instrument has been well established in this different context and that there is a need for an instrument to be developed and validated, to be broadly relevant across a range of cancers and addressing issues of health-related quality of life for the period one to five years after diagnosis.

There are several contenders amongst the cancer and prostate cancer-specific instruments. The available literature is weighted in favour of the EORTC and FACT instruments merely on quantity of evidence. Both of these systems have a multidimensional structure and prostate cancer-specific modules. The UCLA-PCI and its subsequent incarnation, the EPIC, have also been fairly extensively evaluated.

One important difference between the instruments is that the EORTC, UCLA-PCI and EPIC have different scales for urinary, bowel and sexual functioning, whilst the FACT-P combines these issues in a single total ‘prostate’ score. The PC-QoL includes three sub-scales for physiologic function, bother, and associated role limitations, for each of urinary, bowel and sexual domains. Hence the PC-QoL provides a comprehensive assessment of the key prostate cancer-specific problems with nine potential sub-domain scores and a summary score. However, the PC-QoL has not been

tested in terms of responsiveness and this limitation would need to be evaluated before the instrument could be recommended.

Taken together, the evidence from this review is not compelling in favour of any single condition-specific PROM. In making any selection, consideration should be given to the number, type and level of detail of total and domain scores that are desirable.

Recommendations

Two instruments have been substantially examined and can be recommended for further piloting in the context of the NHS and potentially more routine use:

- SF-36
- EQ-5D

The EQ-5D has specific advantages if a short preference-based measure is needed. Several condition-specific instruments have supportive evidence used in relation to prostate cancer:

- EORTC QLQ-C30 & PR25
- FACT-P (including the 4 domains from the FACT-G)
- UCLA-PCI & EPIC

However none of these condition-specific instruments clearly stands out as having considerably more supportive evidence.

In addition the absence of a well established instrument relevant to longer term survivorship in relation to prostate cancer needs to be noted.

Table 3: Appraisal of psychometric and operational performance of generic PROMs used with prostate cancer

PROM	Reproducibility	Internal consistency	Validity: Content	Construct	Responsiveness	Interpretability	Floor/ceiling/ precision	Acceptability	Feasibility
SF-36	0	++	+	++	+	0	0	0	0
EQ-5D	0	n/a	-	0	+	+	0	0	0
HUI	0	0	-	+	+	+	0	0	0
QWB	0	0	0	+	+	+	0	0	0

0 not reported — no evidence in favour + some limited evidence in favour ++ some good evidence in favour ++ + good evidence in favour.

Table 4: Appraisal of psychometric and operational performance of cancer & prostate cancer-specific PROMs

Instrument (n of studies)	Reproducibility	Internal consistency	Validity: Content	Construct	Responsiveness	Interpretability	Floor/ceiling/ precision	Acceptability	Feasibility
EORTC QLQ-C30 (15)	+	+	+	+++	++	0	0	0	0
EORTC QLQ-PR25 (3)	0	+	++	+	+	0	-	0	+
FACT-G (15)	+	++	+	+++	+++	++	0	0	0
FACT-P (14)	0	+	++	++	+++	+	0	-	+
FAPSI-8 (2)	0	+	+	+	+	+	0	0	+
PCTO-Q (2)	+	0	0	++	0	0	0	0	0
UCLA-PCI (12)	+	+	++	+++	++	+	-	0	0
EPIC (10)	+	0	++	++	++	++	-	+	0
PC-QoL (2)	+	+	++	++	0	0	-	+	+
PCRQL (3)	0	++	+	++	0	0	-	0	0
PORPUS (3)	+	0	+	+	+	0	0	0	0

0 not reported — no evidence in favour + some limited evidence in favour ++ some good evidence in favour ++ + good evidence in favour.

APPENDIX A: SEARCH STRATEGY & SOURCES

Databases searched

- PROMS Bibliography
- AMED: Allied and Complementary Medicine Database.
- Biological Abstracts (BioAbs).
- BNI: British Nursing Index Database, incorporating the RCN (Royal College of Nursing) Journals Database.
- CINAHL: Cumulative Index to Nursing and Allied Health Literature.
- Econlit - produced by the American Economic Association.
- EMBASE - produced by the scientific publishers Elsevier.
- MEDLINE - produced by the US National Library of Medicine.
- PAIS: Public Affairs Information Service.
- PsycINFO (formerly PsychLit) - produced by the American Psychological Association.
- SIGLE: System for Information on Grey Literature in Europe.
- Sociofile: Cambridge Scientific Abstracts Sociological Abstracts Database.
- In addition, all records from the journal 'Quality of Life Research' are downloaded via Medline.

Search strategies

1. For records to December 2005

((acceptability or appropriateness or (component$ analysis) or comprehensibility or (effect size$) or (factor analys$) or (factor loading$) or (focus group$) or (item selection) or interpretability or (item response theory) or (latent trait theory) or (measurement propert$) or methodol$ or (multi attribute) or multiattribute or precision or preference$ or proxy or psychometric$ or qualitative or (rasch analysis) or reliabilit$ or replicability or repeatability or reproducibility or responsiveness or scaling or sensitivity or (standard gamble) or (summary score$) or (time trade off) or usefulness$ or (utility estimate) or valid$ or valuation or weighting$)

AND

((COOP or (functional status) or (health index) or (health profile) or (health status) or HRQL or HRQoL or QALY$ or QL or QoL or (qualit$ of life) or (quality adjusted life year$) or SF-12 or SF-20 or SF?36 or SF-6) or ((disability or function or subjective or utilit$ or (well?being)) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire$ or profile$ or scale$ or score$ or status or survey$))))

OR

((bibliograph$ or interview$ or overview or review) adj5 ((COOP or (functional status) or (health index) or (health profile) or (health status) or HRQL or HRQoL or QALY$ or QL or QoL or (qualit$ of life) or (quality adjusted life year$) or SF-12 or SF-20 or SF?36 or SF-6) or ((disability or function or subjective or utilit$ or (well?being)) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire$ or profile$ or scale$ or score$ or status or survey$))))

2. For records from January 2006 to 2007

(((acceptability or appropriateness or component$ analysis or comprehensibility or effect size$ or factor analys$ or factor loading$ or feasibility or focus group$ or item selection or interpretability or item response theory or latent trait theory or measurement propert$ or methodol$ or multi attribute or multiattribute or precision or preference$ or proxy or psychometric$ or qualitative or rasch analysis or reliabilit$ or replicability or repeatability or reproducibility or responsiveness or scaling or sensitivity or valid$ or valuation or weighting$)

AND

(HRQL or HRQoL or QL or QoL or qualit$ of life or quality adjusted life year$ or QALY$ or disability adjusted life year$ or DALY$ or COOP or SF-12 or SF-20 or SF-36 or SF-6 or standard gamble or summary score$ or time trade off or health index or health profile or health status or ((patient or self$) adj (rated or reported or based or assessed)) or ((disability or function$ or subjective or utilit$ or well?being) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire$ or profile$ or scale$ or score$ or status or survey$))))

OR

((bibliograph$ or interview$ or overview or review) adj5 (HRQL or HRQoL or QL or QoL or qualit$ of life or quality adjusted life year$ or QALY$ or disability adjusted life year$ or DALY$ or COOP or SF-12 or SF-20 or SF-36 or SF-6 or standard gamble or summary score$ or time trade off or health index or health profile or health status or ((patient or self$) adj (rated or reported or based or assessed)) or ((disability or function$ or subjective or utilit$ or well?being) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire$ or profile$ or scale$ or score$ or status or survey$)))))

APPENDIX B: APPRAISAL CRITERIA

The methods that will be used for assessing the performance of PROMs were developed and tested against multi-disciplinary consensus and peer review. They focus on explicit criteria to assess reliability, validity, responsiveness, precision, acceptability and feasibility. A pragmatic combination of the criteria developed and used in previous reports to DH by the Oxford and LSHTM groups will be used.

The appraisal framework focuses on psychometric criteria and PROMs must fulfil some or all to be considered as a short-listed instrument. Practical or operational characteristics are also assessed (acceptability and feasibility) (Appendix B: Appraisal framework).

Once evidence has been assessed for eligibility, records considered as inclusions will be assembled for each PROM identified. Measurement performance and operational characteristics will be appraised using the following rating scale independently by two reviewers and inter-rater reliability calculated.

Psychometric and operational criteria	
0	*not reported*
—	*no evidence in favour*
+	*some limited evidence in favour*
++	*some good evidence in favour*
+++	*good evidence in favour*

Appraisal criteria (adapted from Smith et al., 2005 and Fitzpatrick et al., 1998; 2006)

PROM	Reproducibility	Internal consistency	Validity: Content	Construct	Responsiveness	Interpretability	Floor/ceiling/ precision	Acceptability	Feasibility

Appraisal component	Definition/test	Criteria for acceptability
Reliability		
Reproducibility/Test-retest reliability	The stability of a measuring instrument over time; assessed by administering the instrument to respondents on two different occasions and examining the correlation between test and re-test scores	Test re-test reliability correlations for summary scores 0.70 for group comparisons
Internal consistency	The extent to which items comprising a scale measure the same construct (e.g. homogeneity of items in a scale); assessed by Cronbach's alpha's and item-total correlations	Cronbach's alphas for summary scores ≥0.70 for group comparisons Item-total correlations ≥ 0.20
Validity		
Content validity	The extent to which the content of a scale is representative of the conceptual domain it is intended to cover; assessed qualitatively during the questionnaire development phase through pre-testing with patients. Expert opinion and literature review	Qualitative evidence from pre-testing with patients, expert opinion and literature review that items in the scale represent the construct being measured Patients involved in the development stage and item generation
Construct validity	Evidence that the scale is correlated with other measures of the same or similar constructs in the hypothesised direction; assessed on the basis of correlations between the measure and other similar measures	High correlations between the scale and relevant constructs preferably based on a priori hypothesis with predicted strength of correlation

Construct validity (continued)	The ability of the scale to differentiate known-groups; assessed by comparing scores for sub-groups who are expected to differ on the construct being measured (e.g a clinical group and control group)	Statistically significant differences between known groups and/or a difference of expected magnitude
Responsiveness	The ability of a scale to detect significant change over time; assessed by comparing scores before and after an intervention of known efficacy (on the basis of various methods including t-tests, effect sizes (ES), standardised response means (SRM) or responsiveness statistics	Statistically significant changes on scores from pre to post-treatment and/or difference of expected magnitude. The recommended index of responsiveness is the effect size, calculated by subtracting the baseline score from the follow up score and dividing by the baseline SD. Effect sizes can be graded as small (<0.3), medium (~0.5), or large (>0.8).
Floor/ceiling effects	The ability of an instrument to measure accurately across full spectrum of a construct	Floor/ceiling effects for summary scores <15%
Practical properties		
Acceptability	Acceptability of an instrument reflects' respondents' willingness to complete it and impacts on quality of data	Low levels of incomplete data or non-response
Feasibility/burden	The time, energy, financial resources, personnel or other resources required of respondents or those administering the instrument	Reasonable time and resources to collect, process and analyse the data.

APPENDIX C:
GENERIC INSTRUMENTS

This Appendix provides a brief description of the generic PROMs included in this review.

a) SF-36: Medical Outcomes Study 36-item Short Form Health Survey (Ware and Sherbourne, 1992; Ware et al.,, 1994; Ware, 1997)

The Medical Outcomes Study (MOS) Short Form 36-item Health Survey (SF-36) is derived from the work of the Rand Corporation during the 1970s (Ware and Sherbourne, 1992; Ware et al.,, 1994; Ware, 1997). It was published in 1990 after criticism that the SF-20 was too brief and insensitive. The SF-36 is intended for application in a wide range of conditions and with the general population. Ware et al.,, (1994; 1997) proposed that the instrument should capture both mental and physical aspects of health. International interest in this instrument is increasing, and it is by far the most widely evaluated measure of health status (Garratt et al.,, 2002a).

Items were derived from several sources, including extensive literature reviews and existing instruments (Ware and Sherbourne, 1992; Ware and Gandek, 1998; Jenkinson and McGee 1998). The original Rand MOS Questionnaire (245 items) was the primary source, and several items were retained from the SF-20. The 36 items assess health across eight domains (Ware, 1997), namely bodily pain (BP: two items), general health perceptions (GH: five items), mental health (MH: five items), physical functioning (PF: ten items), role limitations due to emotional health problems (RE : three items), role limitations due to physical health problems (RP: four items), social functioning (SF: two items), and vitality (V: four items), as shown in Table 3.1. An additional health transition item, not included in the final score, assesses change in health. All items use categorical response options (range: 2-6 options). Scoring uses a weighted scoring algorithm and a computer-based programme is recommended. Eight domain scores give a health profile; scores are transformed into a scale from 0 to 100 scale, where 100 denotes the best health. Scores can be calculated when up to half of the items are omitted. Two component summary scores for physical and mental health (MPS and MCS, respectively) can also be calculated. A version of the SF-36 plus three depression questions has been developed and is variously called the Health Status Questionnaire (HSQ) or SF-36-D.

The SF-36 can be self-, interview-, or telephone-administered.

b) SF-12: Medical Outcomes Study 12-item Short Form Health Survey (Ware et al.,, 1995)

In response to the need to produce a shorter instrument that could be completed more rapidly, the developers of the Medical Outcomes Study (MOS) 36-item Short Form Health Survey (SF-36) produced the 12-item Short Form Health Survey (SF-12) (Ware et al.,, 1995).

Using regression analysis, 12 items were selected that reproduced 90% of the variance in the overall Physical and Mental Health components of the SF-36 (Table 3.1). The same eight domains as the SF-36 are assessed and categorical response scales are used. A computer-based scoring algorithm is used to calculate scores: Physical Component Summary (PCS) and Mental (MCS) Component Summary scales are generated using norm-based methods. Scores are transformed to have a mean value of 50, standard deviation (SD) 10, where scores above or below 50 are above or below average physical or mental well-being, respectively. Completion by UK city-dwellers reporting the absence of health problems yielded a mean PCS score of 50.0 (SD 7.6) and MCS of 55.5 (SD 6.1) (Pettit et al.,, 2001). Although not recommended by the developers, Schofield and Mishra (1998) report eight domain scores and two summary scores. The SF-12 may be self-, interview-, or telephone-administered.

Several authors have proposed simplification of the scoring process and revision of the SF-12 summary score structure, where norm-based weighting is replaced by item summation to facilitate score interpretation (Resnick and Nahm, 2001; Resnick and Parker, 2001).

c) EuroQol-EQ-5D (The EuroQol Group, 1990; revised 1993)

The European Quality of Life instrument (EuroQol) was developed by researchers in five European countries to provide an instrument with a core set of generic health status items (The EuroQol Group, 1990; Brazier et al.,, 1993). Although providing a limited and standardized reflection of HRQL, it was intended that use of the EuroQol would be supplemented by disease-specific instruments. The developers recommend the EuroQol for use in evaluative studies and policy research; given that health states incorporate preferences, it can also be used for economic evaluation. It can be self or interview-administered.

Existing instruments, including the Nottingham Health Profile, Quality of Well-Being Scale, Rosser Index, and Sickness Impact Profile were reviewed to inform item content (The EuroQol Group, 1990). There are two sections to the EuroQol: the EQ-5D and the EQ thermometer. The EQ-5D assesses health across five domains: anxiety/depression (AD), mobility (M), pain/discomfort (PD), self-care (SC), and usual activities (UA), as shown in Table 3.1. Each domain has one item and a three-point categorical response scale; health 'today' is assessed. Weights based upon societal valuations of health states are used to calculate an index score of –0.59 to 1.00, where –0.59 is a state worse than death and 1.00 is maximum well-being. A score profile can be reported. The EQ thermometer is a single 20 cm vertical visual analogue scale with a range of 0 to 100, where 0 is the worst and 100 the best imaginable health.

d) Health Utilities Index (Furlong et al., 1992; Horsman et al., 2003)

The Health Utilities Index (HUI) currently has two versions (HUI2 and HUI3). Both systems use a classification system for health states and are scaled using standard gamble techniques with a random sample from a population in Canada. The utility of health states are derived from a multiplicative model resulting in a scale ranging from 0 (dead) to 1 (perfect health). The health states classified differ slightly in each system. The HUI3 includes eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain/discomfort. The HUI2 includes attributes for self-care, emotion focusing on anxiety/worry, and fertility. An excellent summary of the development of the HUI measures can be found in Feeny et al.,, (1996).

e) Quality of Well-Being Scale (formerly the Index of Well-Being) (Kaplan et al.,, 1976; Kaplan et al.,, 1984; Kaplan et al.,, 1993)

The Index of Well-Being was modified and renamed the Quality of Well-Being scale (QWB) to emphasize the focus on quality of life evaluation (Kaplan et al.,, 1993; McDowell and Newell, 1996, 2006).

The QWB uses a three-component model of health (Kaplan and Anderson, 1988, cited by McDowell and Newell, 1996) comprising: 1) functional assessment, 2) a value reflecting the utility or desirability of each functional level, and 3) an assessment of illness prognosis to anticipate future health-care need, which may describe positive health. The QWB is interview-administered.

Completion corresponds to the three-component model. First, three domains of self-reported function are assessed, namely mobility and confinement (MOB: three categories), physical activity (PAC: three categories), and social activity (SAC: five categories). Respondents select the most appropriate category to describe their perceived functional level. Domain categories give 45 possible combinations (3 x 3 x 5); with the inclusion of death, 46 function levels are defined for the second stage of completion (McDowell and Newell, 1996). In addition, respondents select from a list of 27 items symptoms or medical problems experienced over the previous eight days.

Social preference weights for each possible health state have been derived from empirical studies. At the second stage, the assignment of an appropriate weight, or utility, to a health state or functional level gives the QWB index score from 0 to 1, where 0 equates to death and 1 to complete well-being. A negative score may be generated, representing a state 'worse than death'. QWB index scores can be converted into Quality-Adjusted Life-Years (QALYs), supporting their application in economic and policy analysis.

Stage three of the QWB addresses issues of prognosis to produce well-life expectancy score (McDowell and Newell, 1996). This stage is not necessary for calculating the QWB index.

A self-administered version has been developed: the QWB-SA (Andersen et al.,, 1995). Following a review of QWB items, five items were added to a mental health section and three self-rated health items were included. The QWB-SA has five domains: symptoms and problem complexes (58 acute and chronic items), self-care (two items), mobility, physical functioning (11 items for these two), and performance of usual activity (three items). For the first domain, respondents indicate the presence or absence ('yes' or 'no') of chronic (18), acute physical (25), and mental health symptoms (11) over the previous three days. The remaining four domains all use a three-day recall response option. The total number of items is inconsistent, ranging from 71 to 74. Symptom/problem weights for the QWB-SA are based on the original QWB weighting system. The focus of the original QWB is utility measurement and quality of life; the focus of the QWB-SA is symptoms and assessment of function. The QWB-SA has been recommended for self-completion by older adults (Andersen et al.,, 1995).

Summary of generic instruments

:

Instrument	*Domains (no. items)*	*Response options*	*Score*	*Completion (time in minutes)*
SF-36: MOS 36-item Short Form Health Survey (36)	Bodily pain (BP) (2), General health (GH) (5) Mental health (MH) (5), Physical functioning (PF) (10) Role limitation-emotional (RE) (3), Role limitation-physical (RP) (4), Social functioning (SF) (2), Vitality (V) (4)	Categorical: 2-6 options Recall: standard 4 weeks, acute 1 week	Algorithm Domain profile (0-100, 100 best health) Summary: Physical (PCS), Mental (MCS) (mean 50, sd 10)	Interview (mean values 14-15) Self (mean 12.6)
SF-12: MOS 12-item Short Form Health Survey (12)	Bodily pain (BP) (1), Energy/Vitality (V) (1), General health (GH) (1), Mental health (MH) (2), Physical functioning (PF) (2), Role limitation-emotional (RE) (2), Role limitation-physical (RP) (2), Social functioning (SF) (1)	Categorical: 2-6 options Recall: standard 4 weeks, acute 1 week	Algorithm Domain profile (0-100, 100 best health) Summary: Physical (PCS), Mental (MCS) (mean 50, sd 10)	Interview or self
European Quality of Life Questionnaire (EuroQol-EQ5D) (5+1)	EQ-5D Anxiety/depression (1), Mobility (1), Pain/discomfort (1), Self-care (1), Usual activities (1) EQ-thermometer Global health (1)	EQ-5D Categorical: 3 options *EQ-thermometer* VAS Current health	EQ-5D Summation: domain profile Utility index (–0.59 to 1.00) *Thermometer* VAS (0-100)	Interview or self
Health Utility Index 3 (Feeny et al, 1995) (8)	Vision, Hearing, Speech, Ambulation, Dexterity, Emotion, Cognition, Pain	Four domains have five response options and five have six response options	Global Utility index and single attribute utility scores for the eight separate dimensions	Self report (10 minutes), or interview (2-3 minutes)
Quality of Well-being Scale (QWB) (30)	Mobility and confinement (MOB) (3 categories) Physical activity (PAC) (3 categories) Social activity (SAC) (5 categories) Symptoms and medical problems (27)	Categorical: yes/no Recall 6 days Symptoms 8 days	Algorithm Index 0-1, 1 complete well-being	Interview Telephone (mean 17.4, range 6-30)

Summary of generic instruments: health status domains *(after Fitzpatrick et al.,, 1998)*

Instrument	*Instrument domains*							
	Physical function	**Symptoms**	**Global judgement**	**Psychol. well-being**	**Social well-being**	**Cognitive functioning**	**Role activities**	**Personal construct**
SF-36	x	x	x	x	x		x	
SF-12	x	x	x	x	x		x	
EQ-5D	x	x	x	x	x		x	
HUI	x			x		x		
QWB	x				x			

APPENDIX D: CANCER & PROSTATE CANCER-SPECIFIC PROMs

CANCER-SPECIFIC INSTRUMENTS

a) European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) Aaronson et al., 1993

The EORTC QLQ-C30 (Aaronson et al.,, 1993) is a 30-item cancer-specific measure of health status and HRQoL. There are five functional domain scales: physical, role, emotional, social and cognitive; two items evaluate global QoL; three symptom scales assess: fatigue, pain and emesis; and six single items to assess symptoms such as dyspnoea, sleep disturbance, appetite, diarrhoea and constipation, and financial impact. The scales for global health and HRQoL comprise seven-point Likert scales; the other 28 items use four-point Likert scales ranging from 'not at all' to 'very much'. Each domain scale is transformed to a scale of 0-100. For the functional and global rating scales higher scores represent a better level of functioning; conversely, for the symptom-oriented scales, higher scores represent more severe symptoms.

b) European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Prostate Module (EORTC QLQ-PR25) (Borghede & Sullivan 1996; van Andel et al., 2008)

The EORTC QLQ-PR25 is a 25-item prostate cancer-specific instrument that can be to supplement the EORTC QLQ-30. It was initially developed in Sweden (Borghede & Sullivan 1996), though published in English, and subsequently evaluated in multi-language versions of which 13% of participants answered English questionnaires (van Andel et al., 2008). There are six scales: urinary, bowel, and treatment-related symptoms; use of incontinence aids; and sexual active and sexual function. Item scores are summed and transformed to a 0-100 scale; higher scores represent higher functioning for the two sexual domains but, conversely, higher scores represent more symptoms (i.e. worse HRQoL) for the symptom scales.

c) Functional Assessment of Cancer Therapy – General Version (FACT-G) Cella et al., 1993

The FACT-G (Cella et al.,, 1993) is a 27-item cancer-specific measure of health status and HRQoL. There are four domains: physical, social, emotional, functional, and a total well-being score. The FACT-G is appropriate for use with any form of cancer; furthermore a number of organ-specific modules have been developed to supplement the core scales (see below for details of the prostate cancer module, FACT-P). Item responses are indicated on five-point Likert scales ranging from 'Not at all' to 'Very Much', in the context of 'the past 7 days'. Each item is scored from 1-4; for negatively-phrased item the scores are reversed. Item scores are summed to produce domain scores for which the range varies by domain. Higher scores represent better health and HRQoL.

d) Functional Assessment of Cancer Therapy – Prostate Version (FACT-P) (Esper et al., 1997)

The FACT-P is a 12-item prostate cancer-specific instrument that can be used to supplement the general version (FACT-G); hence 39 items in total., There is an optional additional global rating on a 10-point Likert scale of how the prostate-specific issues are affecting HRQoL. Responses to all items range from 'Not at all' to 'Very much so'. The twelve prostate-specific items use 5-point Likert scales of 1 (not at all) to 4 (very much); the scores are summed to produce a summary prostate cancer score (PCS). A Treatment Outcome Index (TOI) score is calculated by summing the FACT-G physical and functional domains and the PCS.

e) FACT Advanced Prostate Symptom Index (FAPSI-8) (Yount et al., 2003)

The FAPSI is an 8-item single scaled instrument containing a subset of the FACT-P (see above). Items selected were those considered most important by clinicians for patients with advanced disease. A summary score is calculated from responses to items relating to pain, fatigue, weight-loss, urinary difficulties, and concern about the condition getting worse.

f) Prostate Cancer Treatment Outcomes – Questionnaire (PCTO-Q) (Shrader-Bogen et al., 1997)

The PCTO-Q is a 41-item prostate cancer-specific instrument. Domain scales assess patients' perceptions of the incidence and severity of specific changes in three domains bowel (10 items), urinary (22 items), and sexual (9 items) functions. Items have either four or five response options, scores are summed for each domain; higher scores represent better HRQoL.

g) University of California-Los Angeles Prostate Cancer Index (UCLA-PCI) (Litwin et al., 1997)

The UCLA-PCI is a 20-item prostate cancer-specific instrument that assesses problems experienced in the previous four weeks. There are six scales covering function and bother, separately, in each of urinary, sexual and bowel domains. The function scales are multi-item whereas the bother scales are single items. Responses to items are solicited on Likert scales which have varying numbers of options (from 3-5 response options). Item scores are summed for the function scales and all six domain scores are transformed to a 0-100 scale where higher scores represent better HRQoL.

h) Expanded Prostate Index Composite (EPIC) (Wei et al., 2000)

The EPIC is a 26 or 50-item prostate cancer-specific measure of HRQoL; it is a revised and expanded version of the UCLA-PCI that incorporates key issues that were considered to be missing from the previous version. There are separate function and bother scales for urinary, bowel, sexual and hormonal domains, and also a summary score for each domain. As with the UCLA-PCI, responses to items are solicited on Likert scales which have varying numbers of options (from 3-5). Item scores are

summed for the function scales and all six domain scores are transformed to a 0-100 scale where higher scores represent better HRQoL.

i) Prostate Cancer – Quality of Life (PC-QoL) (Giesler et al., 2000)

The PC-QoL is a 52-item prostate cancer-specific instrument which assesses problems experienced in the preceding four weeks. There are 10 domain scales: function, role activity limitations, and bother for each of urinary, bowel and sexual issues. A further domain scale assesses worry/anxiety about having prostate cancer and treatment received. A well argued conceptual justification for the scales is provided. Each item has a 5-point Likert response scale; item scores are summed and transformed to produce domain scores (0-100) where higher scores represent better HRQoL.

j) Patient Oriented Prostate Utility Scales (PORPUS-P and PORPUS-U_I) (Krahn et al., 2000)

The PORPUS is a 10-item health state classification designed to measure prostate cancer-specific health utility. There are five generic items: pain, energy, psychosocial and social wellbeing, relationship with doctor; and five prostate cancer-specific items: sexual function and desire, urinary frequency and incontinence, and bowel function. An un-weighted profile score (PORPUS-P) can be calculated, or a range of utility scores (PORPUS-U) created using a variety of preference weighting systems (all scaled 0-1). The methods for eliciting direct scaling with patients are complex and inappropriate for the current review. Indirect scaling uses the preferences of a Canadian sample of patients with prostate cancer (PORPUS-U_I).

Summary of cancer and prostate cancer-specific instruments

Instrument	*Domains (no. items)*	*Response options*	*Scoring*	*Administration/ Completion (time)*
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)	30-items: five multi-item functional subscales: physical, role, emotional, social and cognitive functioning; three multi-item symptom scales measure fatigue, pain and emesis; global health/quality of life subscale; and six single items to assess financial impact and symptoms such as dyspnoea, sleep disturbance, appetite, diarrhoea and constipation.	28 four-point Likert reponse options of 1 (not at all) to 4 (very much), and 2 seven-point Likert scales for the global health and QoL domain of 1 (very poor) to 7 (excellent).	0 to 100. For functional and global QoL scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score means more severe symptoms.	Under 10 minutes.
Functional Assessment of Cancer Therapy – General Version (FACT-G)	27-items, four dimensions: physical, social, emotional, and functional well-being.	5-point Likert response options of 0 (not at all) to 4 (very much).	Higher scores represent better global QoL or better well-being on each of the dimensions.	Self-completed in 5-10 minutes.
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Prostate Module (EORTC QLQ-PR25)	25-items, six domains: urinary, bowel, and treatment-related symptoms; use of incontinence aids; and sexual active and sexual function.	4-point Likert response options of 1 (not at all) to 4 (very much),	Item scores are summed and transformed to a 0-100 scale; higher scores represent higher functioning for the two sexual domains but, conversely, higher scores represent more symptoms (i.e. worse HRQoL) for the symptom scales	Self-completed in 5-10 minutes
Functional Assessment of Cancer Therapy – Prostate Version (FACT-P)	12-item prostate cancer-specific scale supplementing FACT-G domains.	5-point Likert response options of 1 (not at all) to 4 (very much).	Item scores are summed to produce a summary prostate cancer score (PCS). A Treatment Outcome Index (TOI) score is calculated by summing the FACT-G physical and functional domains and the prostate-specific score	Self-completed in 8-10 minutes.

Instrument	*Domains (no. items)*	*Response options*	*Scoring*	*Administration/ Completion (time)*
FACT Advanced Prostate Symptom Index (FAPSI-8)	8-item scale, sub-set of FACT-P	5-point Likert response options of 1 (not at all) to 4 (very much).	summary score is calculated from responses to items relating to pain, fatigue, weight-loss, urinary difficulties, and concern about the condition getting worse	Self-completed in 8-10 minutes.
Prostate Cancer Treatment Outcomes – Questionnaire (PCTO-Q)	41-item prostate cancer-specific instrument assessing incidence and severity of changes in bowel, urinary and sexual functions.	Dichotomous (yes/no) or 4-5 point Likert response options.	Item scores are summed for each domain; higher scores represent better HRQoL.	Self-completed in 8-15-20 minutes.
University of California-Los Angeles Prostate Cancer Index (UCLA-PCI)	20-item prostate cancer-specific instrument, six domains covering function and bother in urinary, sexual and bowel domains. Function scales are multi-item; the bother scales are single items.	3-5 point Likert response options.	Item scores are summed for the function scales and all six domain scores are transformed to a 0-100 scale where higher scores represent better HRQoL.	Self-completed in 8-10 minutes.
Expanded Prostate Index Composite (EPIC)	50-item prostate cancer-specific instrument, separate function and bother scales for urinary, bowel, sexual and hormonal domains, summary score for each domain	3-5 point Likert response options.	Item scores are summed for the function scales and all six domain scores are transformed to a 0-100 scale where higher scores represent better HRQoL	Self-completed in 8-15-20 minutes.
Prostate Cancer – Quality of Life (PC-QoL)	52-item prostate cancer-specific instrument, 10 domain scales: function, role activity limitations, and bother for each of urinary, bowel and sexual issues, and a scale assessing worry/anxiety about prostate cancer.	3-7 point Likert response options assessing frequency or how much of a problem.	Item scores are summed and transformed to produce domain scores (0-100) where higher scores represent better HRQoL.	Self-completed in 15 minutes
Patient Oriented Prostate Utility Scales (PORPUS-P and PORPUS-U_I)	10 item instrument, five generic items: pain, energy, psychosocial and social wellbeing, relationship with doctor; five prostate cancer-specific items: sexual function and desire, urinary frequency and incontinence, and bowel function.	4-6 point Likert response options	Profile or utility (0-1) scales	Self-completed in 5-10 minutes

Summary of cancer and prostate cancer-specific instruments: health status domains

Instrument	Physical function	Symptoms	Global judgment	Psychological well-being	Social well-being	Cognitive functioning	Role activities	Personal constructs	Treatment satisfaction
EORTC QLQ-C30	X	X	X	X		X	X		
FACT-G	X		X	X	X		X		
EORTC QLQ-PR25	X	X							
FACT-P		X							
FAPSI-8		X							
PCTO-Q	X	X		X			X	X	X
UCLA-PCI	X	X					X		
EPIC	X	X		X			X		
PC-QoL	X	X					X		X
PORPUS	X	X			X				X

APPENDIX E: LICENSING & CONTACT DETAILS

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) & Prostate Module (EORTC QLQ-PR25)
EORTC Headquarters
Quality of Life Department
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http://groups.eortc.be/qol/questionnaires_qlqc30.htm
http://groups.eortc.be/qol/questionnaires_modules.htm

Functional Assessment of Cancer Therapy – General Version (FACT-G) & Prostate Version (FACT-P) & Advanced Prostate Symptom Index (FAPSI-8)
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