Proxy Assessment of Health-Related Quality of Life in African American and White Respondents With Prostate Cancer:

Perspective Matters

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Abstract

Objectives—An emerging issue in the proxy literature is whether specifying different proxy viewpoints contributes to different health-related quality of life (HRQL) assessments, and if so, how might each perspective be informative in medical decision making. The aims of this study were to determine if informal caregiver assessments of patients with prostate cancer differed when prompted from both the patient perspective (proxy-patient) and their own viewpoint (proxy-proxy), and to identify factors associated with differences in proxy perspectives (ie, the intraproxy gap).

Research Design and Methods—Using a cross-sectional design, prostate cancer patients and their informal caregivers were recruited from urology clinics in the Jesse Brown Veterans Affairs Healthcare System in Chicago. Dyads assessed HRQL using the EQ-5D visual analog scale (VAS) and EORTC QLQ-C30.

Results—Of 87 dyads, most caregivers were female (83%) and were spouses/partners (58%). Mean difference scores between proxy-patient and proxy-proxy perspectives were statistically

significant for QLQ-C30 physical and emotional functioning, and VAS (all $P < 0.05$), with the proxy-patient perspective closer to patient self-report. Emotional functioning had the largest difference, mean 6.0 (SD 12.8), an effect size = 0.47. Factors weakly correlated with the intraproxy gap included relationship (spouse) and proxy gender for role functioning, and health literacy (limited/functional) for physical functioning (all $P < 0.05$, $0.20 < r < 0.35$).

Conclusions—Meaningful differences between proxy-patient and proxy-proxy perspectives on mental health were consistent with a conceptual framework for understanding proxy perspectives. Prompting different proxy viewpoints on patient health could help clinicians identify patients who may benefit from clinical intervention.

Keywords

quality of life; proxy; prostate cancer; Veterans

According to the National Cancer Institute, there were 2 million prostate cancer survivors in the United States as of 2004, and the overall death rate from prostate cancer has dropped approximately 4% percent per year from 1994 to 2004.[1] Family caregivers, particularly spouses, often have a major role with the patient and physician in shared decision making related to the management of localized prostate cancer. Management choices for localized prostate cancer include radical prostatectomy, watchful waiting, radiotherapy, and hormonal therapy,[2,3] and impact on health-related quality of life (HRQL) can be a determining factor in choosing between treatment options.[4,5] Not only do treatment alternatives for prostate cancer vary in their impact on the patient's HRQL,[6–18] but these choices can also affect the caregiver's quality of life.[19,20] In more advanced stages of the cancer, a family caregiver may become the primary source of information for clinicians on patient HRQL (ie, as a proxy). For these reasons, the caregiver's perspective on the patient's HRQL can be important to prostate cancer treatment decision making and management at any stage of the disease.

Although numerous studies have explored the relationship between patient and proxy assessments of HRQL,[21] the proxy viewpoint from which patient HRQL is rated has only recently received attention. A framework for understanding proxy perspectives delineated 2 proxy perspectives, where proxies can assess HRQL as they believe the patient would report on their own experience (ie, proxy-patient perspective), or assess HRQL from their own proxy viewpoint (ie, proxy-proxy perspective).[22] The difference between HRQL assessments from the proxy-patient and proxy-proxy perspective has been referred to as the intraproxy gap, whereas the inter-rater gap refers to the difference between patient and proxy-patient perspective. Little is currently known about the magnitude of these differences in proxy perspectives or differences between patient and proxy perspectives that can serve as a clinical "red flag" for the treatment or care of the patient. In principle, when proxy assessment is performed for the purpose of eliciting surrogate judgments, the proxy-patient perspective is most appropriate. In this case, strong agreement between patient self-assessment and proxy assessment is desirable. In other circumstances, the proxy's view of patient HRQL may be different from patient self-assessment yet provide valuable information about the patient that is potentially relevant to clinical decision making. Studies in pediatric oncology have found that HRQL ratings by children and their parents often do not agree yet each perspective provides valid and important information.[23,24] HRQL assessments from the caregiver/proxy's viewpoint can provide useful information that is complementary to the patient perspective, particularly in cases where the patient viewpoint prevents the patient from receiving adequate clinical care, such as when the patient neglects or denies their condition or illness. In such contexts, agreement between ratings from each perspective is not a requisite criterion for validity.

In this study, we sought to empirically investigate aspects of a framework for understanding multiple proxy perspectives.[22] The goal of this study was to compare HRQL assessments from the patient, proxy-patient, and proxy-proxy perspectives in prostate cancer. We tested whether assessments by patient self-report differed from proxy-patient and proxy-proxy ratings of HRQL by informal caregivers of prostate cancer patients. Drawing from the conceptual framework by Pickard and Knight,[22] we hypothesized that the proxy-patient perspective would be closer to patient self-assessment than the proxy-proxy perspective. A secondary objective was to identify factors that explained the intraproxy gap (ie, differences in HRQL assessment between the proxy perspectives).

METHODS

Study Design

A cross-sectional study design was used to recruit prostate cancer patients and their proxies, preferably their spouse, or if not, a close family member or friend. Dyads were recruited from 2 urology clinics in the Chicago-based Jesse Brown VA system, Lakeside and Westside. IRB approval was obtained for each site. Patients had to have a histologically proven diagnosis of adenocarcinoma of the prostate. Patient and proxy had to be able to comprehend English language versions of the questionnaires and have no history of major psychiatric illness.

Patients were informed about the study by the clinic nurse or physician, and if interested, referred to the study research assistant who explained the purpose of the study. Patients who agreed to participate were asked to identify their family member who would serve as a proxy, and that person was approached to participate. Patients who were unaccompanied were given a form that briefly explained the purpose of the study and asked to invite their closest family member/friend to attend their next visit.

The project research assistants were trained in survey administration, human subject protection in research, protocols for obtaining informed consent, and specific procedures, such as reading the questionnaire to respondents with poor literacy. Subjects were paid $30 for their participation. The first 30 caregivers were also invited to participate in structured cognitive interviews conducted after the questionnaires were completed. This was done to clarify their responses and ensure the instructions and items were worded appropriately to each proxy perspective. For the proxy-patient perspective, instructions stated that "we are interested in how you think the patient would assess their health. Answer these questions as if you are the patient." For the proxy-proxy perspective, instructions read "we are interested in the patient's health and ability/capabilities from your perspective, which may or may not be the same as how the patient might view themselves."

Measures

Health literacy was assessed using the Rapid Estimate of Adult Literacy in Medicine (REALM), a health word recognition test designed for screening adult reading ability in medical settings.[25,26] Health literacy is an important issue in prostate cancer, particularly in a VA-based patient sample.[27] Scores on the REALM range from 0 to 66, where limited literacy has been defined as reading at or below 60 (ie, 8th grade reading level), and functional literacy defined as reading above 60 (ie, 9th grade reading level).[28] Both the patient and the caregiver completed the REALM.

HRQL was assessed with 2 widely used measures in cancer: European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30+3) - version 2, and EQ-5D. EORTC QLQ-C30 core subscales include emotional functioning (EF), physical functioning (PF), social functioning (SF), role functioning (RF), cognitive

functioning (CF), and global quality of life (QOL).[29] All scales and single item scores were transformed to a scale from 0 to 100, where higher scores represent better functioning. The EQ-5D is a brief, easy to administer questionnaire comprised of 2 components: a description of the respondent's own health using a health status classification system with 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and a rating of "own health" by means of a visual analogue scale (VAS). For the VAS, the patient's health today is rated on a 20-cm scale anchored by 0, "worst imaginable health" and 100, "best imaginable health."[30]

The Center for Epidemiological Studies-Depression (CES-D) scale is a short 20-item self-report scale designed to measure frequency of depressive symptoms experienced in the past week.[31] The instrument is scored by simple summation, with higher scores associated with more depressive symptoms. CES-D scale has been widely used in community-based studies, with a summary score of ≥16 used as a basis of referral for diagnosis of depression.[32,33]

Both EQ-5D and EORTC QLQ-30 were adapted for completion by proxy from each perspective. Questionnaires were administered as follows: REALM, EQ-5D, EORTC QLQ-30, and CES-D (only caregiver). Generic and condition-specific instrument ordering has been found to have little effect on responses to HRQL questionnaires.[34] Caregivers completed the HRQL measures both from the perspective of the patient (proxy-patient) as well as from their own perspective (proxy-proxy). The ordering of presentation of proxy perspective was alternated for every other dyad to test for presence of an ordering effect on proxy perspective-based assessments.

Data Analysis

Patient and caregiver characteristics were described and compared for differences using t tests or χ^2 tests. Internal consistency reliability was evaluated for each scale on the EORTC QLQ-C30 using Cronbach's α.

To evaluate whether there were differences between proxy perspectives, paired t tests were used, or if inappropriate, the nonparametric Wilcoxon signed ranks test. The magnitude of the difference between perspectives was quantified using the standardized response mean (SRM), a variant of effect size calculated by taking mean difference scores divided by the standard deviation of the difference scores. A standardized difference of 0.2 was interpreted as a small effect; 0.5 indicated a medium effect; and 0.8 interpreted as a large effect.[35]

The intraclass correlation coefficient (ICC)[36] was used to assess agreement between each perspective: patient self-assessment (A), proxy-patient (B), and proxy-proxy (C). Conventional benchmarks for the interpretation of ICC are >0.80 as excellent agreement, 0.61 to 0.80 as good agreement, 0.41 to 0.60 as moderate agreement and <0.40 as poor agreement.[37,38] Exact agreement was calculated based on 100% concordance for pair-wise comparison of perspectives.

Bivariate correlations were used to identify significant associations between patient and proxy characteristics and differences between proxy perspectives (ie, the intraproxy gap) for each HRQL measure. If the basic assumptions of parametric analysis were not met, nonparametric analyses such as Mann-Whitney U tests were performed to identify significant factors that explained the intraproxy gap. Finally, logistic regression was used to identify characteristics that were significant predictors of the presence of any difference between proxy perspectives for each HRQL subscale score (ie, failure to obtain 100% exact agreement).

RESULTS

Of 98 dyads who met the selection criteria, 11 declined to enroll and 87 dyads agreed to participate in the study. Most of the dyads who declined to participate did so because they either did not have the time or the caregiver wanted to minimize any real or perceived stress to the patient that might be associated with completing questionnaires about their health. The mean age of caregivers was 62 (SD 13.3), which was significantly lower than the patient mean age of 75 (SD = 9.0) ($P < 0.001$) (Table 1). Most caregivers were female (83%), and 63% were the spouse/partner of the patient. The majority of patients (71%) and their caregivers (70%) were African American. Approximately 70% of the patients and caregivers resided together. Although 73% of patients and 81% of caregivers reported at least a high school graduate level of education, limited health literacy was identified in 68% of patients and 46% of caregivers. Presence of depressive symptoms (CES-D score ≥16) was identified in 27% of caregivers.

Internal consistency reliability was generally acceptable for QLQ-C30 subscales. Cronbach's α ranged from 0.60 (cognitive functioning) to 0.88 (emotional functioning) for patient self assessment; from 0.76 (physical functioning) to 0.94 (social functioning) for assessments from the proxy-patient perspective; and 0.54 (cognitive functioning) to 0.94 (social functioning) from the proxy-proxy perspective.

For the 5 dimensions of the EQ-5D, the proportion of patients who self-reported "no problems" ranged from 61% for pain/discomfort to 89% for self-care (Table 2). The proportion of any problems (some or extreme) reported from the proxy-patient and proxy-proxy perspectives was similar for all dimensions except for anxiety/depression, where significantly more problems (50.6%) were reported from the proxy-proxy perspective than from the proxy-patient perspective (37.9%) ($P = 0.003$). ICCs demonstrated fair levels of agreement between patient self-report and each proxy perspective, and good agreement between proxy-patient and proxy-proxy perspectives. Exact agreement between proxy-patient and proxy-proxy perspectives was very good, ranging from 71% for usual activities to 91% for self-care. The more observable dimensions of HRQL such mobility and self-care tended to demonstrate higher levels of agreement compared with the more subjective dimensions like anxiety/depression.

In general, patient self-assessed mean scores on EQ-5D VAS and the 6 subscales of the QLQ-C30 were higher than the proxy-patient perspective, which in turn were higher than scores from the proxy-proxy perspective, except for the global QOL scale (Table 3). Consequently, differences between mean scores were larger between the patient and proxy-proxy perspective (ie, A/C) than between the patient and proxy-patient perspective (ie, A/B). In examining the intraproxy gap, statistically significant mean scores differences between proxy-patient and proxy-proxy assessments were identified for emotional functioning, physical functioning, and on the EQ-5D VAS (all $P < 0.05$). The magnitude of effect was largest for emotional functioning (SRM = 0.47).

Similar levels of agreement were observed between patient self-report and each proxy perspective (Table 4). Agreement between proxy perspectives was generally good to excellent based on the ICC (ie, ≥0.60). Exact agreement between proxy perspectives ranged from 42% on the QLQ-C30 emotional functioning scale to 72% on the social functioning scale.

Correlations between proxy characteristics and mean differences in proxy perspectives were absent to weak on the EQ-5D VAS and QLQ-C30 subscales (Table 5). Larger mean score differences between proxy perspectives of patient role function were associated with male caregivers ($P = 0.024$) and caregivers who were not spouses/partners of the patient ($P =$

0.015). Significantly smaller mean difference scores between proxy perspectives on physical functioning were associated with caregivers who had limited literacy ($P < 0.001$). In examining factors associated with exact agreement, presence of depressive symptoms in caregivers was associated with significantly lower odds of exact agreement between proxy perspectives for cognitive functioning (OR = 0.29; 95% CI = 0.09 – 0.87) and the EQ-5D VAS (OR = 0.26; 95% CI = 0.08 – 0.86). No other results were statistically significant.

DISCUSSION

Since the framework proposed by Pickard and Knight was published in 2005,[22] literature has begun to emerge that seeks to understand whether the viewpoint elicited from the proxy affects the rating provided by the proxy.[39–42] Similar to the present study, an empirical investigation by Lobchuk et al[40] reported evidence to support the conceptual basis for multiple proxy perspectives. The investigators were able to reduce caregiver discrepancy with the patient (the interrater gap) on symptom frequency, severity, distress, and total symptom distress using an "imagine-patient prompt," a variant of the proxy-patient perspective, in comparison to an imagine-self prompt, a derivative of the proxy-proxy perspective that involves a hypothetical process that caregivers might use when their own imagined experiences serve as a basis for estimating what the patient is experiencing. A recent article by Gundy and Aaronson[43] also investigated the proxy-patient and proxy-proxy viewpoints by randomly assigning the significant others of cancer patients to either the proxy-patient or proxy-proxy perspectives. No significant differences were identified between proxy perspectives, and little evidence was found to support the proxy-patient perspective as being more closely aligned with the patient perspective. Notably, the study design used by Gundy and Aaronson[43] did not introduce both proxy perspectives to the respondent, with respondents assigned to either one perspective or the other, precluding investigation of an intraproxy gap within subjects. Taken together, these studies suggest that may be necessary to clearly prompt/instruct each proxy to imagine/think about different proxy viewpoints in order for the intraproxy gap to be evident and to reduce rater the differences between patient and proxy when substituted judgment is desired.

Our results primarily provided support for the framework for domains concerning mental health and emotional well-being. The difference between proxy perspectives for emotional functioning exceeded what would be considered minimally important difference for the EORTC QLQ-C30,[34] (ie, an effect size approximating 0.5).[44] Consistent with our hypothesis, mean scores for emotional functioning were highest for patient self-assessment, and scores from the proxy-patient perspective were significantly higher than from the proxy-proxy perspective. This finding was corroborated by the EQ-5D anxiety/depression dimension, where patients reported the lowest proportion of problems, while the highest proportion of problems was reported from the proxy-proxy perspective.

Substantial differences in the assessment of emotional functioning between the patient and proxy perspectives could be rationalized in several ways. Although patient report is typically considered the goal standard for emotional well-being in the absence of diagnosis, self-report of problems with emotional functioning/mental health may be difficult for elderly males such as American veterans due to the stigma of reporting mental health issues.[45] In the situation where a patient underreports emotional problems due to stigma, the caregiver's independent assessment of the patient's mental health may provide a report that more accurately reflects the patient's psychologic distress, thereby contributing to appropriate care. This result requires further investigation, as clinician discussions with caregivers to gain insight into the mental health of patients by using prompts from proxy-patient and proxy-proxy perspectives are an avenue to identify and address treatable mental health issues.

Several characteristics were identified as significant factors that explained differences between proxy perspectives; however, no factors were significantly correlated with the intraproxy gap for emotional functioning. Three variables (ie, relationship between caregivers and patients, caregivers' gender, literacy level) were weakly correlated with the intraproxy gap on certain domains of HRQL. For role functioning, proxies who were female and who were spouse/partners of the patient had smaller difference scores between proxy perspectives than males and nonpartners, perhaps because they had more insight into patients' daily activities and leisure time activities and felt their perspective on the patient's role functioning was similar to the patient's perspective.

Proxies with depressive symptoms were less likely to provide exact agreement between proxy-patient and proxy-proxy perspectives when rating patient cognitive functioning and overall health according to the EQ-5D VAS. Several studies have reported poorer agreement between proxy and patient assessments when proxies have depressive symptoms,[46,47] but this result is novel in that the association between depressive symptoms and poor agreement arose between assessments within the proxy. This systematic association raises concern about the validity of assessment of cognitive functioning and valuation of overall health by proxies with depressive symptoms. Results would support recommendations that assessments by proxies with depressive symptoms be cautiously interpreted due to potential for bias on the less observable domains of HRQL.[48]

The majority of previous research in proxies has focused on the level of agreement and/or bias when proxy and patient evaluations are compared, with one of the main findings being that proxies tend to overestimate the level of patient disability or symptoms.[21,49–52] Our study results were consistent with this literature, as the both the proxy-patient and proxy-proxy perspective were significantly lower or demonstrated a trend towards lower mean scores than patient self-assessment for most domains of HRQL.

The most useful proxy perspective to clinical decision making may depend on the specific condition(s) and the mental acuity or maturity of the patient. For circumstances where the patient's self-assessment of their HRQL lacks validity, the proxy-proxy perspective would be expected to be more useful to the clinical management of the patient because replication of the patient's self-assessment is undesirable when it does not represent the patient's true state. The relevance of the proxy-patient and proxy-proxy perspective to the clinicians who must develop plans of care for the patient may not be best realized by choosing between the proxy-proxy and proxy-patient perspectives, but instead by asking the caregiver for both perspectives and discussing reasons for those differences when they arise for domains where actionable patient management options exist. For group-level decision making where substituted judgment would be desirable (eg, minimizing bias associated with use of proxies to substitute for patients in clinical trials), the proxy-patient perspective was significantly closer to the patient's own view, particularly for domains related to mental health/emotional functioning.

It is beyond the scope of this study to fully appreciate and understand the implications of the difference between proxy assessments from each perspectives and how it might be acted upon in terms of clinical decision making. A limitation of the overall generalizability of the study is that a large proportion of the patients and caregivers were African American, but this can be also viewed as a study strength, as African Americans are often underrepresented in health services research. Race did not seem to be an important factor in proxy perceptions of the HRQL of the patient. The role of patient gender was not examined, as all prostate cancer patients were male. It is unclear whether the importance of proxy viewpoint in the assessment of emotional functioning generalizes to other conditions and types of cancers, nor can results be generalized to conditions where patients are cognitively impaired.

CONCLUSIONS

When eliciting proxy assessments of HRQL in prostate cancer, perspective can systematically influence the proxy rating provided, particularly for emotional functioning. Sig nificant divergence in ratings based on the proxy-patient and proxy-proxy perspective suggest that each perspective may be clinically relevant to decisions related to emotional well-being. At the group level, results for emotional functioning indicate that inferential power may be improved if the proxy-patient perspective is clearly delineated as the desired perspective from the proxy respondent for clinical trials in conditions where proxy respondents are used. Results also reinforce that clarification of the proxy perspective may reduce undesired variance in proxy assessments of HRQL and support the recommendation that standardized proxy versions of HRQL questionnaires be framed for each proxy perspective. Future research that focuses on understanding and using complementary HRQL assessments provided by proxies according perspective to inform medical decision-making will generate further insight into the contexts in which caregivers can positively contribute to the care of patients.

Acknowledgments

REFERENCES

1. National Institute of Cancer. [Accessed May 24, 2008] Available at: http://www.cancer.gov/cancertopics/cancer-advances-in-focus/prostate

2. Kutikov A, Guzzo TJ, Malkowicz SB. Clinical approach to the prostate: an update. Radiol Clin North Am. 2006; 44:649–663. [PubMed: 17030218]

3. Pickard AS, Hung SY, McKoy JM, et al. Opportunities for disease state management in prostate cancer. Dis Manag. 2005; 8:235–244. [PubMed: 16117718]

4. Echlin KN, Rees CE. Information needs and information-seeking behaviors of men with prostate cancer and their partners: a review of the literature. Cancer Nurs. 2002; 25:35–41. [PubMed: 11838718]

5. Davison BJ, Gleave ME, Goldenberg SL, et al. Assessing information and decision preferences of men with prostate cancer and their partners. Cancer Nurs. 2002; 25:42–49. [PubMed: 11838719]

6. Beard CJ, Propert KJ, Rieker PP, et al. Complications after treatment with external-beam irradiation in early-stage prostate cancer patients: a prospective multiinstitutional outcomes study. J Clin Oncol. 1997; 15:223–229. [PubMed: 8996146]

7. Litwin MS, Hays RD, Fink A, et al. Quality-of-life outcomes in men treated for localized prostate cancer. JAMA. 1995; 273:129–135. [PubMed: 7799493]

8. Clark JA, Rieker P, Propert KJ, et al. Changes in quality of life following treatment for early prostate cancer. Urology. 1999; 53:161–168. [PubMed: 9886606]

9. Fowler FJ Jr, Barry MJ, Lu-Yao G, et al. Patient-reported complications and follow-up treatment after radical prostatectomy. The National Medicare Experience: 1988–1990 (updated June 1993). Urology. 1993; 42:622–629. [PubMed: 8256394]

10. Fowler FJ Jr, Barry MJ, Lu-Yao G, et al. Effect of radical prostatectomy for prostate cancer on patient quality of life: results from a Medicare survey. Urology. 1995; 45:1007–1013. discussion 13–15. [PubMed: 7771002]

11. Helgason AR, Fredrikson M, Adolfsson J, et al. Decreased sexual capacity after external radiation therapy for prostate cancer impairs quality of life. Int J Radiat Oncol Biol Phys. 1995; 32:333–339.

12. Litwin MS, Flanders SC, Pasta DJ, et al. JM. Sexual function and bother after radical prostatectomy or radiation for prostate cancer: multivariate quality-of-life analysis from

CaPSURE. Cancer of the Prostate Strategic Urologic Research Endeavor. Urology. 1999; 54:503–508. [PubMed: 10475362]

13. Litwin MS, McGuigan KA, Shpall AI, et al. Recovery of health related quality of life in the year after radical prostatectomy: early experience. J Urol. 1999; 161:515–519. [PubMed: 9915438]

14. Litwin MS, Pasta DJ, Yu J, et al. Urinary function and bother after radical prostatectomy or radiation for prostate cancer: a longitudinal, multivariate quality of life analysis from the Cancer of the Prostate Strategic Urologic Research Endeavor. J Urol. 2000; 164:1973–1977. [PubMed: 11061894]

15. Lubeck DP, Kim H, Grossfeld G, et al. Health related quality of life differences between black and white men with prostate cancer: data from the cancer of the prostate strategic urologic research endeavor. J Urol. 2001; 166:2281–2285. [PubMed: 11696752]

16. Potosky AL, Knopf K, Clegg LX, et al. Quality-of-life outcomes after primary androgen deprivation therapy: results from the Prostate Cancer Outcomes Study. J Clin Oncol. 2001; 19:3750–3757. [PubMed: 11533098]

17. Potosky AL, Legler J, Albertsen PC, et al. Health outcomes after prostatectomy or radiotherapy for prostate cancer: results from the Prostate Cancer Outcomes Study. J Natl Cancer Inst. 2000; 92:1582–1592. [PubMed: 11018094]

18. Schapira MM, Lawrence WF, Katz DA, et al. Effect of treatment on quality of life among men with clinically localized prostate cancer. Med Care. 2001; 393:243–245. [PubMed: 11242319]

19. Maliski SL, Heilemann MV, McCorkle R. From "death sentence" to "good cancer": couples' transformation of a prostate cancer diagnosis. Nurs Res. 2002; 51:391–397. [PubMed: 12464759]

20. Davison BJ, Goldenberg SL, Gleave ME, et al. Provision of individualized information to men and their partners to facilitate treatment decision making in prostate cancer. Oncol Nurs Forum. 2003; 30:107–714. [PubMed: 12515988]

21. Sneeuw KC, Sprangers MA, Aaronson NK. The role of health care providers and significant others in evaluating the quality of life of patients with chronic disease. J Clin Epidemiol. 2002; 55:1130–1143. [PubMed: 12507678]

22. Pickard AS, Knight SJ. Proxy evaluation of health-related quality of life: a conceptual framework for understanding multiple proxy perspectives. Med Care. 2005; 43:493–499. [PubMed: 15838415]

23. Feeny D, Furlong W, Barr RD. Multiattribute approach to the assessment of health-related quality of life: Health Utilities Index. Med Pediatr Oncol. 1998; (Suppl 1):54–59. [PubMed: 9659947]

24. Davis TC, Long SW, Jackson RH, et al. Rapid estimate of adult literacy in medicine: a shortened screening instrument. Fam Med. 1993; 25:391–395. [PubMed: 8349060]

25. Davis TC, Michielutte R, Askov EN, et al. Practical assessment of adult literacy in health care. Health Educ Behav. 1998; 25:613–624. [PubMed: 9768381]

26. Kim SP, Knight SJ, Tomori C, et al. Health literacy and shared decision making for prostate cancer patients with low socioeconomic status. Cancer Invest. 2001; 19:684–691. [PubMed: 11577809]

27. Parker RM, Baker DW, Williams MV, et al. The test of functional health-literacy in adults: a new instrument for measuring patients' literacy skills. J Gen Intern Med. 1995; 10:537–541. [PubMed: 8576769]

28. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993; 85:365–376. [PubMed: 8433390]

29. Brooks R. EuroQol: the current state of play. Health Policy. 1996; 37:53–72. [PubMed: 10158943]

30. Locke, BA. Center for Epidemiological Studies Depression Scale, Epidemiology and Psychopathology Research Branch. Division of Epidemiology and Services Brance, Public Health Service, National Institutes of Health, National Institutes of Mental Health; 1971.

31. Radloff LS. The CES-D scale: a self-report depression scale for research in general population. Appl Psychol Meas. 1977; 1:385–440.

32. Weissman MW. Assessing depressive symptoms in five psychiatric populations: a validation study. Am J Epidemiol. 1977; 106:203–214. [PubMed: 900119]

33. McColl E, Eccles MP, Rousseau NS, et al. From the generic to the condition-specific: instrument order effects in Quality of Life Assessment. Med Care. 2003; 41:777–790. [PubMed: 12835602]

34. Guyatt GH, Osoba D, Wu AW, et al. Methods to explain the clinical significance of health status measures. Mayo Clin Proc. 2002; 77:371–383. [PubMed: 11936935]

35. Sneeuw KC, Aaronson NK, Osoba D, et al. The use of significant others as proxy raters of the quality of life of patients with brain cancer. Med Care. 1997; 35:490–506. [PubMed: 9140337]

36. Shrout PE. Intraclass correlations: uses in assessing rater reliability. Psychol Bull. 1979; 86:420–428. [PubMed: 18839484]

37. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977; 33:159–174. [PubMed: 843571]

38. Cicchetti DV, Sparrow SA. Developing criteria for establishing interrater reliability of specific items: applications to assessment of adaptive behavior. Am J Ment Defic. 1981; 86:127–137. [PubMed: 7315877]

39. Lobchuk MM, McClement SE, Daeninck PJ, et al. Caregiver thoughts and feelings in response to different perspective-taking prompts. J Pain Symptom Manage. 2007; 33:420–433. [PubMed: 17397703]

40. Lobchuk MM, McClement SE, Daeninck PJ, et al. Asking the right question of informal caregivers about patient symptom experiences: multiple proxy perspectives and reducing interrater gap. J Pain Symptom Manage. 2007; 33:130–145. [PubMed: 17280919]

41. Mittal V, Rosen J, Govind R, et al. Perception gap in quality-of-life ratings: an empirical investigation of nursing home residents and caregivers. Gerontologist. 2007; 47:159–168. [PubMed: 17440121]

42. Kutner JS, Bryant LL, Beaty BL, et al. Symptom distress and quality-of-life assessment at the end of life: the role of proxy response. J Pain Symptom Manage. 2006; 32:300–310. [PubMed: 17000347]

43. Gundy CM, Aaronson NK. The influence of proxy perspective on patient-proxy agreement in the evaluation of health-related quality of life: an empirical study. Med Care. 2008; 46:209–216. [PubMed: 18219250]

44. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Med Care. 2003; 41:582–592. [PubMed: 12719681]

45. Hirschfeld RM, Keller MB, Panico S, et al. The National Depressive and Manic-Depressive Association consensus statement on the undertreatment of depression. JAMA. 1997; 277:333–340. [PubMed: 9002497]

46. Rothman ML, Hedrick SC, Bulcroft KA, et al. The validity of proxygenerated scores as measures of patient health status. Med Care. 1991; 29:115–124. [PubMed: 1994145]

47. Sneeuw KC, Aaronson NK, Sprangers MA, et al. Comparison of patient and proxy EORTC QLQ-C30 ratings in assessing the quality of life of cancer patients. J Clin Epidemiol. 1998; 51:617–631. [PubMed: 9674669]

48. Hung SY, Pickard AS, Witt WP, et al. Pain and depression in caregivers affected their perception of pain in stroke patients. J Clin Epidemiol. 2007; 60:963–970. [PubMed: 17689813]

49. Magaziner J, Bassett SS, Hebel JR, et al. Use of proxies to measure health and functional status in epidemiologic studies of community-dwelling women aged 65 years and older. Am J Epidemiol. 1996; 143:283–292. [PubMed: 8561163]

50. Magaziner J, Simonsick EM, Kashner TM, et al. Patient-proxy response comparability on measures of patient health and functional status. J Clin Epidemiol. 1988; 41:1065–1074. [PubMed: 3204417]

51. Lobchuk MM, Degner LF. Symptom experiences: perceptual accuracy between advanced-stage cancer patients and family caregivers in the home care setting. J Clin Oncol. 2002; 20:3495–3507. [PubMed: 12177111]

52. McPherson CJ, Addington-Hall JM. Judging the quality of care at the end of life: can proxies provide reliable information? Soc Sci Med. 2003; 56:95–109. [PubMed: 12435554]

TABLE 1

Characteristics of Patients and Caregivers

Characteristic	Patient (N, %)	Caregiver (N, %)
Age, mean (SD)[*]	75.0 (9.0)	61.6 (13.3)
Gender (%)		
Male	87 (100)	15 (17)
Female	0 (0)	72 (83)
Race (n = 86)		
Black	61 (71)	60 (70)
White	24 (27)	22 (26)
Hispanic black	0 (0)	1 (1)
Hispanic white	0 (0)	1 (1)
Native American	1 (3)	2 (2)
Educational attainment (n = 86)[†]		
Some high school or less	23 (27)	16 (19)
High school graduate or GED	25 (29)	29 (34)
Military (trade school)	6 (7)	0 (0)
Vocational college or some college	22 (26)	26 (30)
College degree	7 (8)	12 (14)
Advanced or graduate training	3 (3)	0 (0)
Patient marital status (n = 86)		
Married	57 (66)	—
Separated	6 (7)	—
Divorced	7 (8)	—
Widowed	11 (13)	—
Single	5 (6)	—
Employment status (n = 86, 87)[†]		
Retired	73 (85)	45 (52)
Employed	9 (11)	21 (24)
Student	0 (0)	1 (1)
Homemaker	0 (0)	12 (14)
Seeking work	0 (0)	2 (2)
Other	4 (5)	6 (7)
No. persons living with patient, mean (SD)	2.5 (1.5)	—
Proxy lives with patient	—	60 (69)
Relationship of proxy to patient (n = 87)		
Spouse/partner	—	55 (63)
Other	—	32 (37)
Health literacy (n = 87/72)[†]		
Limited literacy (REALM score ≤60)[*]	59 (68)	33 (46)
Functional literacy (REALM score >60)	28 (32)	39 (54)

Characteristic	Patient (N, %)	Caregiver (N, %)
Caregiver depression		
Presence of symptoms (CES-D score ≥16)	—	24 (27)

[*]$P < 0.001$; based on independent t test or χ^2 test.

[†]$P < 0.01$; based on independent t test or χ^2 test.

REALM indicates rapid estimate of adult literacy in medicine; CES-D, Center for Epidemiological Studies Depression Scale.

TABLE 2

Responses to EQ-5D Dimensions and Agreement Between Rater Perspectives

EQ-5D Dimension	Patient (A) (n = 81) n, %	Proxy-Patient (B) (n = 87) n, %	Proxy-Proxy (C) (n = 87) n, %	ICC (95% CI) A/B	ICC (95% CI) A/C	ICC (95% CI) B/C	Exact Agreement (%) A/B	Exact Agreement (%) A/C	Exact Agreement (%) B/C
Mobility				0.46 (0.28–0.62)	0.44 (0.25–0.60)	0.73 (0.61–0.81)	72	66	86
No problem	50 (61.7)	44 (50.6)	42 (48.3)						
Some problems	30 (37.0)	43 (49.4)	45 (51.7)						
Confined to bed	1 (1.2)	0 (0.0)	0 (0.0)						
Self-care				0.53 (0.35–0.67)	0.44 (0.25–0.60)	0.62 (0.47–0.73)	86	76	91
No problem	72 (88.9)	71 (81.6)	71 (81.6)						
Some problems	7 (8.6)	15 (17.2)	16 (18.4)						
Unable to wash/dress	2 (2.5)	1 (1.2)	0 (0.0)						
Usual activities				0.44 (0.24–0.60)	0.38 (0.18–0.55)	0.57 (0.41–0.70)	61	56	71
No problem	58 (71.6)	52 (59.8)	55 (63.2)						
Some problems	20 (24.7)	30 (34.5)	26 (29.9)						
Unable to perform	3 (3.7)	5 (5.8)	5 (5.8)						
Pain/discomfort				0.37 (0.16–0.54)	0.46 (0.26–0.62)	0.70 (0.58–0.80)	62	58	82
No problem	49 (60.5)	34 (39.1)	38 (43.7)						
Some problems	28 (34.6)	48 (55.2)	43 (49.4)						
Extreme problems	4 (4.9)	4 (4.6)	6 (6.9)						
Anxiety/depression *				0.29 (0.09–0.47)	0.33 (0.08–0.54)	0.61 (0.44–0.73)	64	54	77
No problem	68 (84.0)	54 (62.1)	43 (49.4)						
Some problems	10 (12.4)	33 (37.9)	41 (47.1)						
Extreme problems	3 (3.7)	0 (0.0)	3 (3.5)						

*
$P < 0.01$, Wilcoxon test comparing responses between proxy perspectives.

A indicates patient perspective; B, proxy-patient perspective; C, proxy-proxy perspective; ICC, intraclass correlation coefficient.

TABLE 3

EQ-5D and QLQ-C30 Mean Scores and Mean Differences Between Each Rater Perspectives

	Patient (A) Mean (SD)	Proxy-Patient (B) Mean (SD)	Proxy-Proxy (C) Mean (SD)	Difference Between A/B		Difference Between A/C		Difference Between B/C	
				Mean (SD)	SRM	Mean (SD)	SRM	Mean (SD)	SRM
QLQ-C30									
Physical function	72.8 (31.3)	65.8 (30.0)	62.7 (31.5)	7.4 (29.7)*	0.25	10.5 (30.2)	0.35	3.1 (13.4)†	0.23
Role function	82.4 (27.1)	77.0 (30.3)	76.6 (29.6)	5.6 (27.4)	0.21	6.0 (27.5)	0.22	0.4 (18.3)	0.02
Emotional function	87.5 (19.9)	84.1 (19.6)	78.1 (21.4)	3.5 (19.5)	0.18	9.6 (21.9)‡	0.44	6.0 (12.8)‡	0.47
Cognitive function	87.4 (16.6)	85.4 (19.8)	83.5 (19.6)	2.1 (23.0)	0.09	4.1 (23.6)	0.17	1.9 (12.3)	0.15
Social function	87.0 (23.8)	80.3 (28.3)	80.3 (29.8)	7.0 (29.1)	0.24	6.8 (30.9)	0.22	0.0 (13.0)	0.00
QOL	72.5 (24.1)	69.1 (22.8)	70.7 (22.5)	4.0 (28.3)	0.14	2.2 (27.7)	0.08	−1.6 (15.9)	−0.10
EQ-5D VAS	73.4 (20.2)	69.4 (20.3)	67.3 (19.1)	3.8 (21.8)	0.19	6.5 (21.3)†	0.31	2.3 (12.8)*	0.18

*$P < 0.05$, Wilcoxon test comparing proxy perspectives.

†$P < 0.01$, Wilcoxon test comparing proxy perspectives.

‡$P < 0.001$, Wilcoxon test comparing proxy perspectives.

QLQ-C30 indicates European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire; VAS, visual analogue scale; A, patient perspective; B, proxy-patient perspective; C, proxy-proxy perspective; SRM, standardized response mean.

TABLE 4

Level of Exact Agreement on Quality of Life Assessments Between Rater Perspectives

| | Exact Agreement, n (%) | | | ICC (95% Confidence Interval) | | |
Measure	Patient (A) and Proxy-Patient (B)	Patient (A) and Proxy-Proxy (C)	Proxy-Patient and Proxy-Proxy (B/C)	A/B	A/C	B/C
QLQ-C30						
Physical function	37 (43)	37 (43)	57 (67)	0.51 (0.34–0.65)	0.51 (0.33–0.65)	0.90 (0.85–0.94)
Role function	34 (40)	38 (44)	54 (63)	0.54 (0.37–0.67)	0.52 (0.35–0.66)	0.82 (0.73–0.88)
Emotional function	31 (36)	31 (36)	37 (42)	0.51 (0.34–0.65)	0.37 (0.17–0.54)	0.77 (0.67–0.85)
Cognitive function	42 (49)	37 (43)	57 (66)	0.21 (0.00–0.40)	0.15 (−0.06–0.35)	0.80 (0.71–0.87)
Social function	39 (44)	43 (49)	62 (72)	0.36 (0.16–0.53)	0.33 (0.13–0.51)	0.90 (0.85–0.93)
QOL	13 (15)	12 (14)	45 (53)	0.27 (0.06–0.45)	0.30 (0.09–0.48)	0.75 (0.65–0.83)
EQ-5D VAS	19 (22)	17 (20)	43 (49)	0.42 (0.22–0.59)	0.39 (0.18–0.56)	0.79 (0.69–0.86)

QLQ-C30 indicates European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire; QOL, quality of life; VAS, visual analogue scale; ICC, intraclass correlation coefficient; A, patient perspective; B, proxy-patient perspective; C, proxy-proxy perspective.

TABLE 5

Bivariate Correlation Between Proxy Characteristic and Mean Difference Score Between Proxy-Patient and Proxy-Proxy Perspectives (ie, Intraproxy Gap)

	Intraproxy Gap						
	QLQ-C30						
Proxy Characteristic	Physical Function	Role Function	Emotional Function	Cognitive Function	Social Function	Quality of Life	EQ-5D VAS
Relationship (spouse/partner, other)	−0.06	−0.23 *	−0.01	−0.08	0.01	−0.04	−0.07
Gender (female, male)	0.06	−0.24 *	−0.07	−0.08	0.02	−0.08	0.10
Literacy (functional literacy, limited literacy)	0.36 †	−0.02	−0.07	0.07	0.16	0.09	0.14
Depressive symptoms (CES-D; continuous scale)	0.10	0.13	0.18	0.05	0.15	0.04	0.01
Depressive symptoms (CES-D score <16, 16, or higher; scale dichotomized)	0.06	0.01	0.11	0.03	0.15	0.08	0.08
Race (African American, white)	−0.05	0.08	−0.16	−0.05	−0.03	−0.11	−0.08
Ordering effect	−0.05	−0.07	0.08	−0.15	−0.00	−0.16	−0.15

*
$P < 0.05$;
$P < 0.01$ Kendall's τ-b correlation coefficient.

QLQ-C30 indicates European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire; CES-D, Center for Epidemiological Studies Depression Scale.