

# QUALITY OF LIFE AT THE END OF LIFE: TRENDS IN PATIENTS WITH METASTATIC PROSTATE CANCER

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## ABSTRACT

**Objectives.** To identify the rates of decline in health-related quality of life during the year before death in men with prostate cancer.

**Methods.** We studied men in a subset analysis within a longitudinal, observational cohort of patients with metastatic prostate cancer at the University of California, Los Angeles, Center for Health Sciences. The analysis included 23 patients who died and had submitted at least two health-related quality-of-life surveys in the final months before death. The outcomes were measured with the RAND 36-Item Health Survey, an established, validated instrument that includes physical and emotional domains. To gauge the effect of marital status, education, and income, we dichotomized these demographic variables.

**Results.** Most domains showed declines, many of them substantial. Patients who had a slower rate of decline in the physical domains tended to be married, better educated, and more affluent. We noted a trend toward a slower deterioration in the mental composite scores among patients who had less than a college degree and an annual household income of \$30,000 or less.

**Conclusions.** Patients dying of metastatic prostate cancer appear to experience declines in health-related quality of life during their final year of life. Further investigation may help identify specific patient characteristics associated with more rapid declines; this will help focus attention on enhancing patients' quality of life as death approaches. UROLOGY 59: 103–109, 2002. © 2002, Elsevier Science Inc.

Toward the end of life, maintaining the quality of life acquires obvious significance in many individuals. In patients with cancer, healthcare decisions often position quantity against quality of life. Recently, the focus on health-related quality of life (HRQOL) as it pertains to clinical outcomes and to its deterioration toward the end of life has been much greater. A slow, gradual decline in the quality of life of patients with cancer may begin up to 3 years before death,<sup>1</sup> and the vast majority of patients dying with cancer report deterioration in their physical quality of life within their final year.<sup>2</sup> There is also a recognized need to address psychosocial issues and the quality of personal relationships in the dying.<sup>3</sup>

Although prostate cancer is the second-leading cause of death in this country, its usually slow and

gradual progression allows physicians and patients to neglect the end-of-life planning issues. It is important to recognize that because some patients do die of their disease, their physicians must be equipped with the appropriate information to care for them throughout the course of their illness. We have previously shown that in patients with prostate cancer, the quality of life begins a steady, inexorable decline in the final 12 months of life.<sup>4</sup> In this analysis, our goal was to identify the rate of HRQOL deterioration during the year before death in men with prostate cancer. In particular, we wondered whether certain patient characteristics were associated with a more or less rapid HRQOL decline toward the end of life.

## MATERIAL AND METHODS

### PATIENTS

Eighty-one men were diagnosed with metastatic prostate cancer at the University of California, Los Angeles, from November 1993 through June 1996, of whom 78 agreed to be included in a longitudinal, observational cohort. Metastasis was confirmed with whole-body nuclear bone scanning. Patients completed confidential HRQOL questionnaires at baseline (before beginning androgen ablation therapy), at 3-month

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intervals for the first year, and subsequently at 6-month intervals for up to 5 years. For the baseline and follow-up surveys, patients were mailed the instrument and a prestamped return envelope. Telephone reminders were used for all patients who did not respond within 2 weeks. All patients who died during the course of their longitudinal follow-up (n = 36) were considered for inclusion in the present analysis. Only those patients who had submitted at least two surveys (n = 29) and whose last survey was received within 12 months of death were included, leaving 23 patients in the final subset analysis. The date of death was determined by the death notice in the hospital computer record system, the Los Angeles County Recorder's Office, or the Social Security Death Index (<http://ssdi.genealogy.rootsweb.com/cgi-bin/ssdi.cgi>). The cause of death could not be reliably determined in enough of the 23 subjects to conduct any meaningful analyses of those who died of, versus with, their cancer. Of the remaining 42 patients, 22 were still living after completing the 5-year study period, and 20 discontinued participation while still living.

### OUTCOME MEASURES

We measured general HRQOL with the RAND 36-Item Health Survey 1.0 (SF-36).<sup>5</sup> It is a self-administered, 36-item questionnaire that quantifies the general HRQOL using eight different multi-item scales: physical function, social function, bodily pain, emotional well-being, energy/fatigue, general health perceptions, role limitations due to physical health problems, and role limitations due to emotional problems. In addition, two summary scales, the physical (PCS) and mental (MCS) health composites, may be calculated to provide more global assessments of the HRQOL in those domains. The domains are scored separately from 0 to 100, with higher scores representing better outcomes. The SF-36 has been extensively tested and validated and has been shown to be both reliable and valid (test-retest reliability coefficients of 78% or more and internal consistency Cronbach's alpha coefficient<sup>6</sup> of 0.78 to 0.93 in various populations).<sup>7</sup>

Sociodemographic and comorbidity data were collected at the time of the baseline survey with a separate instrument that included relevant questions and a medical history checklist based on an established comorbidity rating scale.<sup>8</sup>

### STATISTICAL ANALYSIS

The mean scores for the domains were calculated for the final two surveys submitted before death. For each domain, a rate of change in the score was determined by calculating the slope of the line between the two time points and analyzed for significance from 0 (alpha = 0.05). In addition, the rates for the PCS and MCS were stratified by three dichotomized demographic variables (marital status, education, and income) to determine any differences between these groups.

## RESULTS

Table I lists the clinical characteristics of our study sample. At baseline, the mean age was 73.8 ± 4.4 years (range 67 to 82), with 16 patients aged 70 years or older. Most patients were white (75%), married or living with a partner (73%), and unemployed or retired (80%). Only 35% had at least a college degree, and 45% had an annual household income over \$30,000. Seventy percent of patients reported comorbidities. Prior radical prostatectomy or external beam irradiation were each reported by 31% of the respondents. The primary treatment of metastatic prostate cancer at baseline

**TABLE I. Demographic characteristics of the study sample**

Characteristic	n (%)
Sample size	23 (100)
Age (yr)	
<70	5 (22)
≥70	18 (78)
Race	
White	15 (65)
Black	4 (17)
Latino	3 (13)
Asian	1 (5)
Education	
Some college or less	13 (62)
College graduate or more	8 (38)
Annual household income	
≤\$30,000	12 (57)
>\$30,000	9 (43)
Employment	
Working full or part-time	4 (19)
Unemployed/retired	17 (81)
Comorbidities	
None	6 (29)
One or more	15 (71)
Marital status	
Married or living with partner	16 (73)
Unmarried or no partner	6 (27)
Primary treatment	
Bilateral orchiectomy	6 (26)
Chemical androgen ablation	14 (61)
Observation	3 (13)
Prior radical prostatectomy	7 (30)
Prior external beam irradiation	8 (35)
Average time between last and second-to-last survey (mo)	6.7 ± 3.6 (3–18)
Time between last survey and death (mo)	7.0 ± 3.5 (2–12)

Data for last two items presented as the mean ± SD, with the range in parentheses.

included chemical androgen ablation with leuprolide and flutamide (64%), bilateral orchiectomy (22%), or observation (14%).

The average length of time between the last survey received and death was 7.0 ± 3.5 months (range 2 to 12). The mean number of months between the last and the next-to-last survey was 6.7 ± 3.6 (range 3 to 18).

Table II shows the rates of change in each domain for the final two surveys received before death, as well as the actual quality-of-life scores on the final survey. Not every participant submitted complete data in every domain. The scores and rates are presented for the total cohort, as well as for the dichotomized variables of marital status, education, and income. A trend showing a decline in the HRQOL was seen in most domains in the overall analysis, as well as in the dichotomized analyses, with a few domains registering a positive rate of change. Significant declines were noted in

**TABLE II. HRQOL scores and their rates of decline for last two surveys before death, stratified by marital status, education, and income**

	n*	QOL on Last Survey Before Death	Rate of Decline in QOL Points Monthly	P Value for Rate of Decline (vs. Slope = 0)
Total sample	23			
General health perception	21	44 ± 23	-1.27 ± 3.99	0.16
Physical function	22	54 ± 32	-1.45 ± 5.15	0.20
Role physical	22	33 ± 40	-2.71 ± 10.4	0.23
Role emotional	23	45 ± 48	-1.05 ± 9.86	0.62
Social function	23	59 ± 32	-1.80 ± 5.00	0.10
Emotional well-being	22	68 ± 23	-0.82 ± 3.79	0.32
Bodily pain	23	60 ± 29	-1.52 ± 7.05	0.31
Energy/fatigue	22	48 ± 25	0.30 ± 4.95	0.77
Physical composite score	19	36 ± 12	-0.84 ± 2.07	0.10
Mental composite score	19	44 ± 12	-0.28 ± 2.39	0.62
Marital status				
Married or in relationship	16			
General health perception	15	43 ± 24	-1.50 ± 2.86	0.06
Physical function	16	55 ± 29	-0.22 ± 5.14	0.87
Role physical	16	34 ± 42	-0.87 ± 6.31	0.59
Role emotional	16	40 ± 49	-0.81 ± 7.56	0.67
Social function	16	55 ± 34	-1.93 ± 5.52	0.18
Emotional well-being	15	62 ± 24	-0.53 ± 3.13	0.03 <sup>†</sup>
Bodily pain	16	56 ± 29	-2.75 ± 4.70	0.52
Energy/fatigue	15	44 ± 23	-0.50 ± 3.12	0.55
Physical composite score	14	35 ± 10	-0.68 ± 1.56	0.13
Mental composite score	14	42 ± 13	-0.31 ± 2.15	0.60
Single	6			
General health perception	5	43 ± 21	-2.58 ± 4.84	0.30
Physical function	5	41 ± 38	-5.67 ± 3.41	0.02 <sup>†</sup>
Role physical	5	15 ± 22	-9.16 ± 18.7	0.34
Role emotional	6	50 ± 46	-3.70 ± 14.8	0.57
Social function	6	60 ± 26	-1.74 ± 4.25	0.36
Emotional well-being	6	81 ± 14	-0.33 ± 4.69	0.86
Bodily pain	6	63 ± 26	-0.67 ± 10.2	0.87
Energy/fatigue	6	52 ± 25	-0.14 ± 5.41	0.95
Physical composite score	4	33 ± 15	-2.18 ± 3.00	0.24
Mental composite score	4	49 ± 10	-0.32 ± 3.76	0.87
Education				
College graduate or more	13			
General health perception	12	46 ± 23	-2.07 ± 2.94	0.03 <sup>†</sup>
Physical function	12	48 ± 28	-1.23 ± 3.65	0.27
Role physical	12	29 ± 37	-0.81 ± 6.61	0.67
Role emotional	13	49 ± 50	-1.42 ± 4.01	0.22
Social function	13	56 ± 29	-1.98 ± 3.24	0.05 <sup>†</sup>
Emotional well-being	12	65 ± 22	-1.00 ± 2.88	0.02 <sup>†</sup>
Bodily pain	13	62 ± 26	-2.32 ± 4.75	0.10
Energy/fatigue	12	35 ± 23	-0.83 ± 3.62	0.44
Physical composite score	10	34 ± 11	-0.80 ± 1.89	0.21
Mental composite score	10	43 ± 13	-0.52 ± 1.66	0.35
Some college or less	7			
General health perception	7	35 ± 21	-2.23 ± 3.40	0.13
Physical function	7	66 ± 32	0.06 ± 6.89	0.98
Role physical	7	32 ± 47	-4.76 ± 13.5	0.39
Role emotional	7	29 ± 49	-3.18 ± 16.9	0.64
Social function	7	52 ± 38	-1.93 ± 8.34	0.56
Emotional well-being	7	65 ± 27	0.10 ± 4.84	0.96
Bodily pain	7	45 ± 32	-4.52 ± 7.85	0.17
Energy/fatigue	7	57 ± 15	0.00 ± 4.56	1.00
Physical composite score	7	36 ± 11	-1.17 ± 2.31	0.23
Mental composite score	7	41 ± 12	-0.25 ± 3.52	0.86

Continued on page 106

TABLE II. Continued

	n*	QOL on Last Survey Before Death	Rate of Decline in QOL Points Monthly	P Value for Rate of Decline (vs. Slope = 0)
Income				
> \$30,000	9			
General health perception	8	40 ± 25	-0.72 ± 2.63	0.46
Physical function	9	48 ± 30	-0.48 ± 3.69	0.71
Role physical	9	25 ± 33	-1.08 ± 5.41	0.57
Role emotional	9	15 ± 34	-4.52 ± 5.94	0.05 <sup>†</sup>
Social function	9	49 ± 26	-2.05 ± 1.54	0.00 <sup>†</sup>
Emotional well-being	9	52 ± 21	-1.71 ± 1.81	0.03 <sup>†</sup>
Bodily pain	9	62 ± 27	-1.70 ± 2.93	0.11
Energy/fatigue	9	32 ± 21	-1.15 ± 2.78	0.28
Physical composite score	7	34 ± 7	-0.25 ± 0.80	0.43
Mental composite score	7	34 ± 7	-1.37 ± 1.11	0.02 <sup>†</sup>
≤\$30,000	11			
General health perception	11	43 ± 22	-3.15 ± 2.98	0.01 <sup>†</sup>
Physical function	10	62 ± 31	-1.00 ± 6.05	0.61
Role physical	10	35 ± 46	-3.33 ± 12.4	0.42
Role emotional	11	64 ± 50	-0.00 ± 12.42	0.99
Social function	11	59 ± 36	-1.89 ± 7.2	0.41
Emotional well-being	11	74 ± 21	0.21 ± 4.44	0.88
Bodily pain	11	52 ± 30	-4.23 ± 7.50	0.09 <sup>†</sup>
Energy/fatigue	11	52 ± 21	-0.08 ± 4.61	0.96
Physical composite score	10	35 ± 13	-1.44 ± 2.47	0.10
Mental composite score	10	48 ± 12	0.26 ± 3.00	0.78

KEY: HRQOL = health-related quality of life, QOL = quality of life

\* Not every patient submitted data for each demographic variable.

<sup>†</sup> P ≤ 0.05.

several areas. Patients who were married or in a relationship showed significant declines in emotional well-being ( $P = 0.03$ ), while single men showed faster declines in physical function ( $P = 0.02$ ). Those with at least a college degree had faster declines in their general health perceptions ( $P = 0.03$ ), social function ( $P = 0.05$ ), and emotional well-being ( $P = 0.02$ ); those with less education did not decline significantly in any single domain. Those with annual household incomes over \$30,000 showed a faster deterioration in role limitations due to emotional function ( $P = 0.05$ ) and social function ( $P < 0.01$ ), and those with a lower income had faster declines in general health perception ( $P = 0.01$ ). The domain of role limitations due to physical health problems was consistently the lowest-scoring domain in each analysis for both surveys, except in those with less than a college degree, for whom the scores were lowest in the role limitations due to emotional problems.

Overall, trends toward declines in both the PCS and the MCS ( $P = 0.10$ ) during the time between the final two surveys were noted. When the population was stratified by marital status and education, the rate of decline for the PCS was steeper than for the MCS, although the small sample size did not allow a demonstration of statistical significance. When dichotomized income was exam-

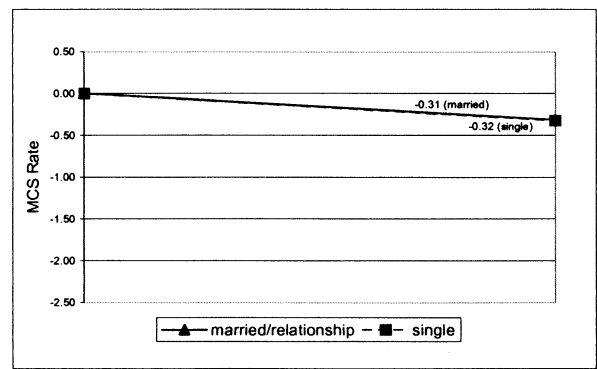
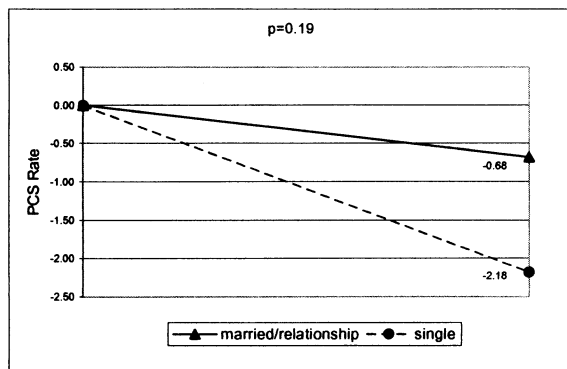
ined, more affluent patients had significantly worse declines in the MCS ( $P = 0.02$ ), while those with a lower income had a trend toward lower PCSs ( $P = 0.10$ ).

Figure 1 suggests several trends noted from examining the associations between the dichotomized variables and each of the composite summary scales, although the small sample size did not allow a demonstration of statistical significance. For the physical domains, married men had a slower rate of decline than did single men ( $P = 0.10$ ); marital status was not associated with differences in the emotional scales ( $P = 0.99$ ). Patients with higher incomes had a better trend on the PCS ( $P = 0.18$ ) and a worse one on the MCS ( $P = 0.14$ ) than those with annual incomes of \$30,000 or less.

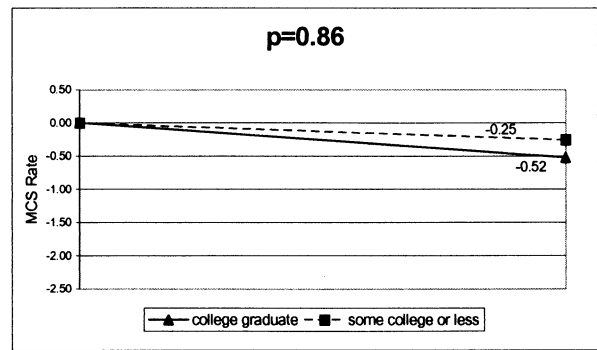
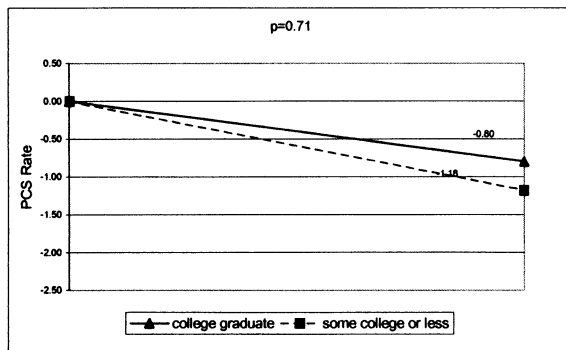
#### COMMENT

Our study has two important findings. First, marital status appears to be associated with rates of decline in the physical and emotional domains of the HRQOL in different ways toward the end of life. Married men tended to decline in the physical domains at a slower rate than did single men. The declines in the emotional domains, however, appear unrelated to marital status; both married and unmarried men have reason to become depressed

(a) marital status



(b) income



(c) education

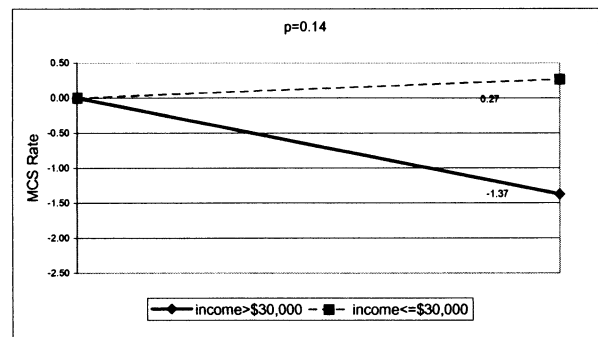
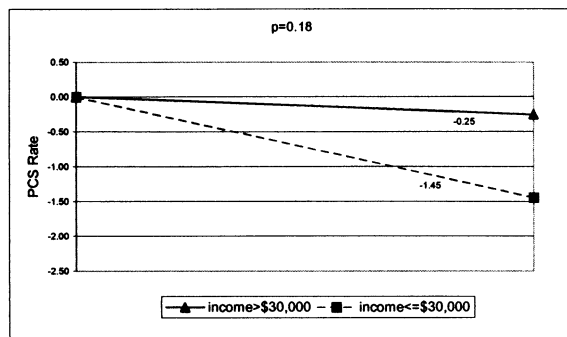


FIGURE 1. Rates of change of HRQOL (unadjusted PCS and MCS) dichotomized by (a) marital status, (b) income, and (c) education. The distance between the two points on the x-axis represents the time between the last and the next-to-last survey.

toward the end of life. Loneliness may have a significant impact on the emotional well-being of single men as death approaches. On the other hand, men who are married or in a relationship might compare their deteriorating health status to that of

their partner and subsequently suffer mentally and emotionally. These patients may also be more depressed than single men if they believe they are a burden to family members. This may explain in part why these men are slower to decline in the

physical domains; they are more motivated to remain physically functional so as to avoid troubling a spouse.

Second, socioeconomic status, measured as education level and annual household income, also appeared to be associated with changes in the physical and emotional domains in opposing directions. A lower socioeconomic status appeared to be associated with a more rapid decline in the physical domains but a slower deterioration in the emotional domains. Patients with a college degree had significant declines in their emotional well-being, social function, and general health perceptions, and those with higher incomes had significant declines in their rates of emotional well-being and social function. These patients may have had greater expectations than those with a lower socioeconomic status, resulting in greater disappointment and even depression when these expectations were not realized. They may also have had greater access to ancillary health services, which helped slow the deterioration of their physical domains.

Several investigators have examined the quality of life immediately and in the year before death, although few have done so using validated HRQOL instruments. Overall, the quality of life in the last year of life of older adults was shown to be better in 1993 than in 1986 when looking at variables such as the number of hospital days, the number and length of disability in five activities of daily life, and the duration of impairment in cognitive function.<sup>9</sup> Some studies have shown that although decline is expected in the year before death, it is neither universal across all areas of the HRQOL nor sweeping in commonality among all patients. In terminally ill cancer patients, Morris *et al.*<sup>10</sup> found that the decline was gradual, with an accelerated deterioration between 3 weeks and 1 week before death, although up to 20% of patients did not exhibit poor HRQOL even in the week before death. A study of 150 living elderly people matched with proxy-completed surveys of decedents from the same community showed that although various features of HRQOL declined in the months before death, most of the decedents experienced significant "positive-quality" months in their last year.<sup>11</sup>

Attempts have been made to characterize those patients experiencing more rapid declines in their HRQOL before death. Bortz<sup>12</sup> looked at the functionality of patients at various points in the last year of life and noted that patient age did not correlate with dysfunction. Morris and Sherwood<sup>13</sup> were unable to identify a subgroup with better HRQOL in the last 12 weeks of life among patients dying of cancer.

Several studies have investigated the impact of various clinical characteristics of patients dying of cancer on morbidity and mortality. Culling data

from the National Health Interview Survey, Liao and colleagues<sup>14</sup> found that educational level was inversely associated with morbidity and disability. They also found that after accounting for education, blacks had greater morbidity than did whites.<sup>15</sup> In both these studies, quality of life was not quantified by a validated HRQOL survey but rather was defined by long-term limitation of activity, number of chronic conditions, number of bed days, number of doctor visits, and days of short hospital stay. Krongrad *et al.*<sup>16</sup> found that married patients with prostate cancer survived longer than did single patients and proposed that in prostate cancer, the quality of life determines the quantity of life. In a Norwegian cohort of men with prostate cancer, Harvei and Kravdal<sup>17</sup> found a 20% higher incidence of prostate cancer in ever-married men and with a higher education. Mortality, however, was lower in these groups.

Our study had several limitations. First, our sample size was small, limiting our ability to stratify our population further to make group comparisons based on other variables such as race. Second, we did not standardize the time between the last two surveys or between the last survey and death. Although the time of death is obviously unpredictable, it may behoove future investigations to endeavor to assess the HRQOL as close to death as possible to quantify the rates of decline leading during demise. Third, we did not consider the effect of treatment on HRQOL. For example, some patients may have had ongoing or just-completed irradiation therapy that would depress their HRQOL further than it would have been because they were approaching death. Fourth, our population was predominantly white, married, and treated at a tertiary medical center, thus limiting the ability to generalize our results. Additionally, patients who responded to the surveys toward the end of life may not represent the typical man dying of prostate cancer. Responder bias might have selected for the more functional patients with higher HRQOL scores. Alternatively, the surveys might have been filled out by proxies. Finally, although we have no evidence that the analyzed subset differed from the entire sample under study, patients who chose not to participate or were otherwise ineligible may have had HRQOL outcomes that were either better or worse than the men in our cohort. Also, future studies may benefit from study designs that allow for the collection of uniform baseline patient information to explore more fully how demographic variables such as marital status affect the quality of life.

Despite these limitations, our study is unique in that it quantifies the rates of change of HRQOL before death using validated instruments based on patients' own self-assessment. Our goal was to

identify which patients are likely to have a more rapid decline toward death, as well as to delineate in these patients the specific domains of HRQOL more likely to deteriorate during the last year of life. We hope this study will be followed by others with greater statistical power to assess the predictive values of patient characteristics with the prospect of targeting interventional strategies at improving HRQOL in patients dying of metastatic prostate cancer. Such studies may elucidate the impact of marital status and social support on men dying of, or with, this malignancy. Ultimately, the important clinical issues revolve not around simply identifying which dying men are depressed but what can be done to help them cope better.

This work underscores the importance of increased attention to quality-of-life issues in men dying of, or with, prostate cancer, particularly in those who are unmarried, less educated, and less affluent. Involving experts in palliative care is certainly appropriate for these men; however, all clinicians who care for patients with cancer should be well-versed in end-of-life issues, such as advance directives, hospice care, and the importance of strong social support.

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