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13. ABSTRACT ***(Maximum 200 Words)***

Purpose: We evaluated preferences for current urinary and sexual function following radical prostatectomy in men with clinically localized prostate cancer. We used utility assessment to quantify patient preferences.

Methods: We measured preferences in 209 community volunteers enrolled in a prostate cancer screening study who had radical prostatectomy between 1994 and 1998. We compared preferences in three outcome groups: (1) men who were bothered by both their current urinary and sexual functioning, (2) men who were only bothered by their current sexual functioning, and (3) men who were not bothered by either. Preferences were assessed via computer-based interview using time trade-off and standard gamble methods. Functioning was assessed via standardized questionnaire.

Results: Differences in utilities were found by outcome group, with median utilities high across groups (0.9 for TTO and Standard Gamble), indicating that men were not willing to give up much remaining life years (1 year or 10% risk of death) with current functioning to achieve ideal functioning.

Conclusion: Health related quality of life is generally good in patients treated for prostate cancer with radical prostatectomy; and those who have urinary and/or sexual dysfunction would not be willing to trade much of their remaining life span to have perfect functioning.

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Introduction

This project provides a novel opportunity to measure preferences for key health outcomes in a well-characterized cohort of men with prostate cancer detected via prostate-specific antigen (PSA) and treated with radical prostatectomy between 1994 and 1998. This project is innovative in that no previous investigators have assessed preferences for outcomes in a large cohort of men who were actually experiencing the post-treatment outcomes of interest. Because we had recently evaluated urinary and sexual function and bother in this cohort,[1] we were able to stratify our cohort to target men for further study that had experienced a range of outcomes in these domains. More specifically, we systematically measured preferences for living with a health state in men who were experiencing problems with urinary and/or sexual functioning, and men who were not experiencing problems in these domains. Final analysis indicates significant differences in preferences by outcome group. Ultimately, linking preferences for health states with current functioning will provide more accurate estimates of patient preferences for use in decision analysis models. These models are of critical importance because the proportion of men in the US being screened and treated for prostate cancer is increasing.[2] Although direct evidence from randomized controlled trials are likely to provide the most definitive estimate about the overall effectiveness of screening and treatment for prostate cancer, the results of such studies will not be available for many years. Decision makers- patients, physicians, and health policy makers – must act before these results are available. Supporting these decision makers requires a better understanding of how men feel about their quality of life after surgical management of their disease. These data will allow a more accurate evaluation of the immediate costs of screening in the absence of long-term data from randomized trials. Since the established risk factors for prostate cancer are non-modifiable, screening is the only currently viable method for affecting prostate cancer morbidity and mortality; therefore, we need to know how screening and resultant treatment affect quality of life.

Body

The following outlines the progress made during the funding period October 1, 1998 to March 31, 2002 with regard to each task outlined in our originally submitted "Statement of Work."

Task 1 "Development of computer-based health utility assessment module (months 1-6)"

Measures of health utilities are used to adjust estimates of life expectancy that are the endpoints of decision analysis models. Recently, interview and computer-based methods have been developed to measure health utilities in individual patients. These methods use techniques such as the standard gamble[3] or time trade off[4] to elicit utilities. Using these methods, preferences are derived implicitly based on the individual's response to decision situations.[5] For example, in the time trade-off method an individual is presented with a paired comparison in which he or she must choose between two alternatives. In the case of a chronic health condition (i.e., incontinence following surgical treatment for prostate cancer), one alternative is to live with the chronic condition for the remainder of life, the second alternative is to have a shorter life, but to live in the absence of the chronic condition. The individual is asked to choose between theses two alternatives, varying the length of the "shorter life" until the individual is indifferent between the two alternatives. The indifference point is the utility for the chronic condition. The less desirable the health condition, the greater the amount of life the individual will give up in order to be free of the chronic condition. In this instance, the chronic condition would have a low utility.

For the current project we have used the U-titer computer program[6] as the platform for building automated preference interviews. More specifically, we have successfully computerized both standard gamble and time trade-off methods for eliciting utilities for current health states in our patient groups. The final version of the interview was completed after testing preliminary programs with 25 pilot subjects (men with prostate cancer who were not eligible for the current study). To use the automated interview, the subject sits in front of the computer and answers a series of questions presented on the screen. The subject responds to questions using a track ball to select the appropriate answers. Overall, the computerized interview was well accepted by our subject population. The majority of subjects were able to complete the interview independently after a brief introduction by the research assistant. More specifically, only 11 of 237 (5%) interviews had to be excluded from the final analysis due to misordering of practice utilities indicating that the subject did not understand the format of the interview.

The second task completed in the initial 6 months was the development of databases and quality control procedures for data management. More specifically, databases were created to link the computerized interview data with the questionnaire responses measuring current urinary and sexual functioning.

Tasks 2 & 3 "Participant selection and data collection (months 7-24)"
"Statistical Analysis and write-up of results (months 25-42)."

Participants were recruited from our ongoing longitudinal study of outcomes in men with screen-detected prostate cancer (N=2,237).[7] Because these men were all originally enrolled in our PSA screening studies, we had extensive data regarding demographics, primary treatment, and cancer stage and grade. In addition, we also had extensive information regarding quality-of-life outcomes after treatment.[1] As per our original grant proposal, we selected for further study only those men who had cancer detected between 1994 and 1997, had radical prostatectomy as their primary treatment, and had returned a prior questionnaire measuring quality of life (N=432). We selected this time frame so that outcomes would be more likely attributed to the treatment and not to aging per se; we selected only surgery patients because this treatment is being increasingly used in the US. Additionally, within this cohort of 432 men we *a priori* defined positive, intermediate, and negative health states based on previous self-reports of urinary and sexual functioning. We defined these health states based on prior responses to questions regarding the level of bother associated with current urinary function and level of bother associated with current sexual function. More specifically, we selected for further study men from three categories of outcomes: (1) men who were bothered by both their current sexual and urinary functioning, (2) men who were bothered by their current sexual functioning, but not urinary functioning, and (3) men who were not bothered by either their current sexual or urinary functioning. By sampling men from these outcome categories, we hoped to obtain utilities from equal number of men within each of these health states; however, we also reassessed their current urinary and sexual functioning to monitor potential drift between outcome categories.

To serve as our sampling frame, we randomly selected approximately 80 men from each of the three outcome categories defined above. Within these groups, we again randomly selected men until we had recruited ~50 men in each group that had completed the interview and the reassessment of function and bother. Refusal rates ranged from 12-16% across groups. Of the men who agreed to participate, we also randomly selected a subset of 30 men to complete the computerized interview twice at two-week intervals to assess test-retest reliability of the computerized interview. We found an interclass correlation coefficient (ICC) of 0.8 for the time trade-off method and an ICC of 0.7 for the standard gamble method of assessment of utilities. These values were within the range of other computerized assessments of utilities[8] and indicated that the computerized measures had acceptable test-retest reliability.

Of the 155 who completed the interview and the questionnaire, approximately 40% drifted from their original outcome group when recategorized based on current urinary and sexual function. This was especially problematic for the group originally bothered by both urinary and sexual function. More specifically, based on the questionnaire responses at the time of the utilities assessment, 58% of these men drifted from their original group to either (1) having only bother associated with sexual function, or (2) not bothered by either sexual or urinary function. In the other two original study groups, only 30% of the men were recategorized based on current functioning. Overall, the utility for current health state was high when measured via either standard gamble or time trade-off (mean $\pm$ sd = .90 $\pm$ .25 and .86 $\pm$ .27, respectively). An analysis including all the completed interviews showed a significant difference in mean utilities assessed via standard gamble method when comparing the original groups (see Appendices, Table 1). Significant group differences for both the time trade-off and standard gamble utilities were also found when outcome groups were recategorized based upon most recent functioning (see Appendices, Table 2). Therefore, these preliminary results indicated that men with greater bother associated with sexual and urinary functioning were willing to give up more life to be in perfect health. These results support our original hypothesis. However, we were concerned that the sample size for the recategorized group for bother associated with both sexual and urinary function was too small (N = 26) to provide stable estimates of the mean utilities. Therefore we gained approval from the DOD to recruit additional men to increase the number of subjects in the group including men bothered by both sexual and urinary functioning (i.e., to increase the sample size to ~50 as proposed originally). We used the same eligibility criteria for recruiting new participants, except to extend the cutoff for treatment from 1997 through

1998. This change in the study criteria provided 82 additional participants (final N = 237). However, of the 237 men, 28 were excluded due to utility misorders (N=11), urinary dysfunction only (N=10), or the final outcome group could not be determined due to incomplete questionnaire (N=7). As shown in Table 3, significant group differences in both time trade-off and standard gamble utilities were also found with the expanded study sample, indicating that men with worse outcomes were willing to trade off more remaining life years to be in perfect health.

A manuscript that describes the study methods and reports the study results in detail has been accepted for publication in the Journal of Urology (anticipated date of publication May, 2002). A copy of this manuscript is included in Appendix C

Key Research Accomplishments

(1) Development of computerized interview for assessment of preferences for health states in men with prostate cancer.

(2) Achieved acceptable test-retest reliability for computerized interview.

(3) Achieved original and amended participant recruitment goals.

(4) Performed final data analysis showing that median utilities for quality-of-life outcomes after surgical management of prostate cancer were high ($\geq .9$), indicating that men were not willing to trade-off many remaining life years in the current state of health in order to be in perfect health. However, we did find differences in utility measures that corresponded with objective measures of functioning. More specifically, men bothered by their urinary and sexual functioning were more willing to trade-off time in the current state of health compared with men less bothered by their current functioning. These results supported our original hypothesis that men with worse disease-specific would report significantly lower utilities for their health states then men who were living with more positive outcomes.

Reportable Outcomes

(1) Development of a reliable computerized interview for assessment of preferences for health states in men with prostate cancer.

(2) Development of a database with preferences for health states linked to objective measures of quality of life and clinical data.

(3) Completed manuscript detailing methods and results of the study. This manuscript has been accepted for publication in the Journal of Urology.

(4) The manuscript resulting from this research grant also served as partial requirement for one author's (J. Krygiel) Doctor of Public Health degree from Saint Louis University School of Public Health.

Conclusions

The results of this study indicated significantly lower utilities for men bothered by both their current sexual and urinary functioning. However, the overall median utilities were high ($\geq$ .9), indicating that men who have undergone surgical management of prostate cancer are not willing to trade-off much to be in perfect health. This indicates that the quantification of quality-of-life outcomes may need to be reevaluated in decision analysis models. Measurement of patient preferences for health states following prostate surgery has never been performed in a large sample of men who were actually experiencing the outcomes of interest. In addition, the current study provides a link between utilities for health following surgical management of prostate cancer and more widely used measure of functional status and bother. Such a linkage will be of increased importance as outcomes studies employing these measures are used as the basis for decision analysis and cost-effectiveness analysis.

References

1. Smith DS, Carvalhal GF, Schneider K, Krygiel J, Yan Y, Catalona WJ. Quality-of-life outcomes for men with prostate carcinoma detected bly screening. Cancer 2000;88(6):1454.

2. Jacobson SJ, Katusic SK, Bergstralh EJ, Oesterling JE, Ohrt D, Klee GG, Chute CG, Lieber MM. Incidence of prostate cancer diagnosis in the eras before and after serum prostate-specific antigen testing. JAMA 1995;274:1445.

3. Von Neumann J, Morgenstern O. Theory of Games and Economic Behavior (3rd Edition). New York: Wiley & Sons, 1953.

4. Torrance GW, Thomas WH, Sackett DL. A utility maximization model for evaluation of health care programs. Health Serv Res 1972;7:118.

5. Torrance GW. Utility approach to measuring health-related quality of life. J Chron Dis 1987;40:593.

6. Sumner W, Nease RF Jr, LittenbergB, Kneeland t, O'Connor G. U-titer. A utility assessment tool. Med Decis Making 1991;11:327.

7. Smith DS, Catalona WJ, Herschman JD. Longitudinal screening for prostate cancer with prostate specific antigen. JAMA 1996;276:1309.

8. Nease RF Jr, Kneeland T, O'Connor G. Variation in patient utilities for outcomes of the management of chronic stable angina. Implications for clinical practice guidelines. JAMA 1995;273:1185.

Appendix A

Table 1

Mean and Median Time-Trade Off and Standard Gamble Utilities, Stratified by Original Outcome Group (Original Sample N = 155)

Outcome Group:	Bothered by Urinary and Sexual Functioning (N =55)	Bothered by Sexual Functioning (N=50)	Bothered by Neither (N=50)	P*
Time-Trade Off Method				
Mean (±SD)	.81 (±.31)	.90 (± .20)	.88(± .28)	0.3
Median	.92	94	.99	
Standard Gamble Method				
Mean (±SD)	.83 (± .31)	.96 (± .11)	.93 (± .26)	.002
Median	.94	.99	.99	

* = P values represent results for Kruskal-Wallis test.

Table 2

Mean and Median Time-Trade Off and Standard Gamble Utilities, Stratified by Recategorized* Outcome Groups (Original Sample N = 155)

Outcome Group:	Bothered by Urinary and Sexual Functioning (N =26)	Bothered by Sexual Functioning (N=62)	Bothered by Neither (N=57)	P**
Time-Trade Off Method				
Mean (±SD)	.74 (±.31)	.85 (± .24)	.92 (± .25)	0.001
Median	.82	.92	.99	
Standard Gamble Method				
Mean (±SD)	.79 (± .35)	.89 (± .25)	.96 (± .21)	0.0001
Median	.91	.99	.99	

* = Outcome groups were recategorized based on reassessment of bother associated with sexual and urinary function at the time of the computerized interview. Ten (10) men were excluded from the analysis because their original outcome group shifted from "bothered by both urinary and sexual function", or "bothered by sexual function only", to "bothered by urinary function only." The latter outcome group was not included in our original study in that proportionately very few men were bothered only by urinary functioning.

** = P values represent results for Kruskal-Wallis test.

Table 3

Mean and Median Time-Trade Off and Standard Gamble Utilities, Stratified by Recategorized* Outcome Groups (Final Sample N = 209)

Outcome Group:	Bothered by Urinary and Sexual Functioning (N =40)	Bothered by Sexual Functioning (N=95)	Bothered by Neither (N=74)	P**
Time-Trade Off Method				
Mean (±SD)	.77 (±.31)	.87 (± .29)	.92 (± .21)	0.0007
Median	.88	.95	1.0	
Standard Gamble Method				
Mean (±SD)	.82 (± .27)	.90 (± .20)	.96 (± .17)	0.0001
Median	.94	.99	1.0	

* = Outcome groups were recategorized based on reassessment of bother associated with sexual and urinary function at the time of the computerized interview. Ten (10) men were excluded from the analysis because their original outcome group shifted from "bothered by both urinary and sexual function", or "bothered by sexual function only", to "bothered by urinary function only." The latter outcome group was not included in our original study in that proportionately very few men were bothered only by urinary functioning. An additional 11 men were excluded due to utility disorders, and 7 men were excluded because the final outcome group could not be determined due to an incomplete questionnaire

** = P values represent results for Kruskal-Wallis test.

Appendix B

Bibliography

Smith DS, Krygiel J, Nease RF, Sumner W, Catalona WJ. Patient preferences for outcomes associated with surgical management of prostate cancer. J Urol, in press.

Personnel Receiving Pay

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PATIENT PREFERENCES FOR OUTCOMES ASSOCIATED WITH SURGICAL MANAGEMENT OF PROSTATE CANCER

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ABSTRACT

Purpose: We used utility assessment to evaluate patient preferences for current urinary and sexual function following radical prostatectomy.

Materials and Methods: We measured preferences in 209 community volunteers enrolled in a prostate cancer screening study who underwent radical prostatectomy between 1994 and 1998. We compared preferences for three outcome groups: (1) men who were bothered by both their current urinary and sexual functioning, (2) men who were only bothered by their current sexual functioning, and (3) men who were not bothered by either their current sexual or urinary functioning. Preferences were assessed via computer-based interview using both time trade-off (TTO) and standard gamble (SG) methods. Current functioning was assessed via standardized questionnaire.

Results: Median utilities were high across outcome groups (0.9 for TTO and SG), indicating that men were not willing to give up much remaining life years (10% of remaining life expectancy) with current functioning to achieve ideal functioning. However, mean TTO and SG scores significantly decreased as burden increased (.77 and .82 for men bothered by both their current sexual and urinary function ; .87 and .89 for men bothered by their current sexual function only; .92 and .96 for men not bothered by either sexual or urinary function).

Conclusions: Health related quality of life was generally good in this observational study of patients treated for prostate cancer with radical prostatectomy. Additionally, those bothered by their urinary and/or sexual function would not be willing to trade much of their remaining life span to have perfect functioning. However, the perception of side effects was bothersome enough in some men that appropriate patient counseling regarding the potential risks and benefits is essential.

INTRODUCTION

Among U.S. men, prostate cancer is the most common non-skin cancer and the second leading cause of male cancer deaths.[1] Because the only well-established risk factors are age, African-American race, and positive family history, efforts directed toward primary prevention are not currently feasible. Therefore, secondary prevention, which includes both screening and early detection, has assumed heightened importance and controversy.

Currently, the two best methods for early detection of prostate cancer are digital rectal examination (DRE) and measurement of serum prostate-specific antigen (PSA) concentration.[2] Although a population-based study has shown changes consistent with stage migration from advanced to localized prostate cancer with the advent of increased PSA screening,[3] there is no direct evidence from randomized controlled trials that screening reduces disease-specific mortality rates. This lack of evidence, coupled with concerns about the negative effects of treatment on quality of life, has led to disagreement about the net benefits of screening and differing screening recommendations.[4]

Health-related quality of life refers to the physical, emotional, and social domains of health, which can be influenced by a person's experiences, beliefs, expectations, and perceptions.[5] The evaluation of quality of life in men with prostate cancer has evolved in parallel with the stage migration in prostate cancer created by increased PSA screening. More specifically, early published reports of health-related quality of life in men with prostate cancer have focused on those with metastatic disease.[6] However, given the controversy regarding the potential negative effects of early detection on quality of life, more recent reports have focused on men with localized prostate cancer undergoing aggressive treatments such as radical prostatectomy.[7-9] In general, these reports

have shown decrements in disease-specific health-related quality of life (i.e., sexual and urinary functioning) after treatment. However, general health-related quality of life does not appear to be decreased in men after aggressive treatment for prostate cancer.[7,8] This could be explained by the insensitivity of general quality of life instruments in detecting modest changes.

In addition to patient self-reports of changes in health-related quality of life (such as described above), it is also important to quantify patient preferences for outcomes (including outcomes such as changes in quality of life) that may result from medical interventions.[10] Therefore, not only are the outcomes themselves measured, but the *desirability* (or undesirability) of the outcome is also measured. The strength of a patient's preference for an outcome is also referred to as the patient's "utility" for a specific health outcome.[10] Consequently, standardized assessment of diverse patients' preferences for a range of outcomes may inform screening and treatment decisions.

In the current study, we compared preferences for current outcome states of urinary and sexual functioning in men with localized prostate cancer treated with radical prostatectomy.

MATERIALS AND METHODS

Study Participants.

Participants were recruited from our ongoing longitudinal study of outcomes in men with screen-detected prostate cancer (N = 2,237). The preliminary quality-of-life outcomes for men with cancer detected between 1989 and 1995 have been reported elsewhere.[11]

Patient selection included men who had cancer detected between 1994 and 1998, had radical prostatectomy as their primary treatment, and returned the original quality-of-life questionnaire (n = 594). We selected this time frame so that outcomes would be more likely attributed to the treatment and not to aging per se; we selected only surgery patients because this treatment is widely used in the US. Additionally, within this cohort of 594 men we defined *a priori* positive, intermediate, and negative health states based on previous self-reports of urinary and sexual functioning. We defined these health states based on prior responses to questions regarding the level of bother associated with current urinary function and level of bother associated with current sexual function. This was assessed using the question "Overall, how big a problem has your sexual (urinary) function been for you during the last 4 weeks?", where small, moderate or big problem were coded as sexual (urinary) bother. More specifically, we selected for further study men from three categories of outcomes: (1) men who were bothered by both their current urinary and sexual functioning (N=136), (2) men who were bothered by their current sexual functioning, but not urinary functioning (N=341), and (3) men who were not bothered by either their current sexual or urinary functioning (N=117). Very few men (8 patients) were bothered by their urinary function without also being bothered by their sexual function. Therefore, utilities for this pattern of outcomes were not evaluated. By randomly sampling approximately 125 men from the three outcome categories (N=387), we hoped to obtain completed utilities for at least 50 men within each of these health

states; however, we reassessed their current urinary and sexual bother so that utility measures could be compared across the most current outcome group. More specifically, based on results from our pilot study, we anticipated that approximately 40% of the men originally sampled for one study category would drift to another category based on reassessment of their urinary and sexual bother. Since we also needed to build in extra potential subjects to account for refusals/deceased, we thought it would be prudent to randomly sample extra men for each category (i.e., 125 sampled to eventually obtain a sample of at least 50 men in each outcome group). The 387 men identified as potential participants were mailed a letter introducing the study and stating that they may be called in the future to set up an appointment to complete the study questionnaire and interview. Within each outcome group, men were called in random order to ask if they would like to participate in the study and to set up a time for them to complete the study instruments. When called by the research assistant, 25 of the 387 (6%) men refused and 8 of the 387 (2%) men were found to be deceased. Additionally, 117 of the 387 (30%) were deemed "extra" if their anticipated study group already had at least 50 subjects that had completed the study instruments; these men were therefore not contacted further. Therefore, 237 of the original 387 potential participants completed the study instruments as described below. Informed consent was obtained from all study participants.

Study Instruments.

Quality-of-life questionnaire. Items from the self-administered questionnaire included: (a) the RAND 36-Item Health Survey 1.0 (a global quality-of-life measure);[12] (b) current urinary and sexual function and bother scales (developed in men with localized prostate cancer by researchers at UCLA);[8] and (c) current comorbid medical conditions. Current comorbidities were assessed by asking participants to indicate Yes or No regarding whether they were currently being treated for common medical conditions including diabetes, hypertension, heart disease, or

malignancies other than prostate cancer. The total number of comorbidities was the simple sum of "Yes" responses.

Computer-based measures of patient preferences. We used standard reference gamble[13] and time trade-off[14] to elicit individual patient health utilities. Using these methods, preferences were derived implicitly based on the individual's response to decision situations.[10] For example, in the time trade-off method (TTO), an individual is presented with a paired comparison in which he must choose between two alternatives. In the case of a chronic health condition (i.e., incontinence following radical prostatectomy), one alternative is to live with the chronic condition for the remainder of his life, the second alternative is to have a shorter life, but to live in the absence of the chronic condition. When the patient becomes indifferent between the two choices, the utility score is calculated. This value is the ratio, on a scale from 0 to 1, of the number of life years chosen free of the chronic condition to the number of life years offered with the chronic condition. The format for the standard gamble (SG) technique differs in that it also incorporates risk. The individual is asked if he would be willing to take a "magic pill" that results in either cure or sudden death with varying probability, versus living in his current state of health. The less desirable the health condition, the greater the risk of death the individual will tolerate in order to be free of it. It should be noted that SBG utilities are often greater than TTO utilities when assessed in the same participants.

Our assessment employed U-Titer, a platform for building automated preference interviews.[15] In introductory screens, ideal and current health states were defined within the context of sexual and urinary functioning (see Figures 1-4). The interviews were self-administered via computer after a brief introduction and practice session overseen by a research assistant. The practice session asked participants to provide utilities (TTO and SG) for monocular blindness versus

binocular blindness. Eleven (11) participants who "misordered" these utilities (i.e., binocular blindness was given a higher utility compared with monocular blindness in either TTO or SG) were excluded from the analysis due to concern regarding their understanding of the task.

All participants completed the computer-based measure first and then the quality-of-life questionnaire second, so as not to bias the responses to the computer-based measure. Final outcome groups (both urinary and sexual bother , sexual bother only , or neither urinary or sexual bother) were determined based on the responses to the quality-of-life questionnaire obtained at the time of the computerized interview.

Statistical Analysis.

Demographic and clinical data were compared between those randomly selected and those not selected for the study. Demographic data included age, race, marital status, education, employment status, and interval between surgery and recruitment for the study. We did not include a specific measure of socioeconomic status given the significant positive correlation between education and income found in our preliminary analyses (data not shown). Preliminary analysis also showed that men with <=24 months interval since surgery (N= 24) compared to those with > 24 months interval since surgery (N=185) did not significantly differ in either mean TTO or SG utilities (p values > 0.3) and therefore no further distinctions were made in these groups for the remainder of the analyses. Clinical data included preoperative serum prostate-specific antigen (PSA) level, clinical and pathological stage, and whether or not surgery was performed at our institution. We also compared the demographic and clinical data for men who were deemed "extra", refused, or were deceased, compared with those who participated. We also compared those who completed part of the study instruments but were excluded (i.e., misorders, those with urinary

dysfunction only, and those whose outcome group could not be determined from questionnaire response) versus those included in the final sample. Demographic and clinical data and mean urinary and sexual functioning scores were also compared between final outcome groups. T-tests or chi-square tests were used for each of the aforementioned comparisons. Kruskal-Wallis test was used for comparison of utilities between the three outcome groups. Wilcoxon post-hoc comparisons were used for pairwise comparisons of utilities by outcome group. We also compared utilities by number of comorbid medical conditions, race, and age. SAS version 8 was used for all analyses.

Power.

With a sample size of approximately 50 men in each study group (alpha = .05 with 2-tailed tests), power was $\geq$ 80% to detect a difference of 0.1 scale points between outcome groups. This difference translates into being willing to give up 10% more of remaining life to be in ideal health compared to the current health state.

RESULTS

Comparison of Demographic and Clinical Data for Study Participants versus Non-Participants.

Among the total sample of 594 eligible participants, 387 were randomly selected for potential recruitment into the study. It was not necessary to recruit the remaining 207 in order to meet our sample goals (see Table 1). Chi-square analyses revealed no significant difference by recruitment status for demographic or clinical variables (Table 1). However, a t-test revealed a statistically significant, but not clinically significant, difference in the interval since surgery (mean number of months since surgery = 34.1 for those not recruited vs. 35.7 for those recruited, p = .02).

Among the sample originally randomly selected (n=387), we also compared clinical and demographic variables between those who participated (n=237) and those who were deemed extra, refused or were deceased (n=150) [see Table 1]. There was a statistically significant difference with respect to race (p=.03), with African-Americans more likely to participate (Table 1).

Among the sample excluded from the final analyses (outcome group could not be determined [n=7]; urinary dysfunction only [n=10], or utility misorder [n=11]) versus those who remained in the analyses (n=209), there was a statistically significant difference with respect to marital status (p=.009), with those currently married more likely to be included. Location of surgery (p=.005) was also associated with inclusion in the final analysis, with those who underwent surgery at Washington University more likely included in the final analysis.

Comparison of Demographics and Clinical Data by Outcome Group.

Demographic and clinical data stratified by outcome group are shown in Table 2. Statistically significant differences were found for number of comorbidities (p=.01) and pre-operative PSA level (p=.03). More specifically, men with ≥ 2 comorbid medical problems were more likely to report either sexual bother or sexual and urinary bother . Men with pre-operative

PSA ≥ 4.0 ng/mL were more likely to report neither urinary or sexual bother . As shown in Table 2, sexual and urinary mean function scores were significantly greater (higher scale score = greater functioning) in those men who reported being bothered by neither urinary or sexual function and significantly lower in those who were bothered by both urinary and sexual functioning (p values<.0001).

Outcome group by Utility.

Table 3 shows a statistically significant difference between utility score by outcome groups for both the time trade off method (p=.0007) and standard gamble method (p<.0001), with decreased utility scores with increased level of bother . Similar analyses showed no significant difference with respect to race, number of comorbid medical conditions, and age.

Wilcoxon pairwise post-hoc comparisons showed significant differences between the mean TTO utilities for men with sexual bother only versus those bothered by neither sexual nor urinary function (.87 versus .92, p=.0002). Similar results were found for mean SG utilities (.89 versus .96, respectively, p<.0001) indicating that bother associated with sexual function after radical prostatectomy resulted in patients being willing to both give up a larger amount of remaining life span and take a greater risk of dying to have ideal functioning compared with those with no bother associated with function. Significant differences in mean TTO and SG utilities were also found for men with both urinary and sexual bother compared with those men bothered by neither sexual nor urinary function (mean TTO =.77 versus .92, p=.02, and mean SG = .82 versus .96, p<.0001, respectively). Pairwise comparisons also revealed a statistically significant difference between mean SG utilities for men with both urinary and sexual bother compared with men with sexual bother only (p=.05), with a significant mean difference of approximately 8% of remaining life years between these two groups.

DISCUSSION

Overall, we found that mean utility for disease-specific health states after radical prostatectomy was high (mean = .9), indicating that on average, men would not be willing to trade much of current life to be in perfect health. Our results were comparable to those found in a previous study of prostate cancer patients for TTO scores of current sexual dysfunction, relative to no sexual dysfunction (mean=.89) and current urinary troubles, relative to no urinary troubles (mean=.89).[16] Our results also compare favorably to those found in other cancer patient groups. For example, patients with stage I rectal or stage I/II colon cancer undergoing removal of colorectal carcinoma had a mean SG utility of .74 for stage-dependent outcome states after surgery.[17] However, this comparison is limited in that colorectal surgery most likely has a greater impact on disease-specific survival compared with radical prostatectomy. Although beyond the scope of the current study, comparison of utilities for radiation therapy, brachytherapy, and radical prostatectomy would be important due to the similar survival outcomes for these various treatments.

In our study, we also found that burden as assessed by utility assessment was independent of race, comorbid medical conditions, and age; therefore, utilities for current health states were not unduly influenced by these factors. However, we also found that as level of bother increased (and as actual function decreased as shown by the incremental relationship between function scores and level of bother), so did the impact on the patient. More specifically, men with both urinary and sexual bother and men with sexual bother alone had significantly lower mean utilities (.77 to .89) compared to men not bothered by urinary or sexual function (.92 to .96). That is, the men with increased burden were willing to give up at least 10% more of remaining life to be in perfect health as defined by ideal urinary and sexual functioning. To put such a difference in context, among patients with visual impairment, previous studies have found that the average difference in utilities

for monocular and binocular blindness was 0.36,[18] the difference between utility for mild angina symptoms and severe angina symptoms was 0.22,[19] and a gain in utility for vision from cataract extraction of 0.07.[20] However, there was a smaller difference in the burden carried by the patient between having both urinary and sexual bother (.77 TTO and .82 SG) compared with those only with sexual bother (.87 TTO and .89 SG).

Although participants were chosen randomly from *a priori* outcome groups, our study sample included a higher proportion of men who underwent surgery at Washington University. Washington University is a major prostate cancer surgery center. Patients seeking care at this center may have higher expectations or greater risk aversion than patients treated at other locations. These patients' utilities may systematically differ from those of a broader population.

Our study is limited in that we have only evaluated utilities in men who have continued to cooperate in our research program; therefore, we may be missing those who are unhappy with their outcomes. Additionally, since our cohort includes only those men who actively sought screening for prostate cancer, assessment of health utilities in our cohort may result in preferences for outcomes different from those found in men who did not proactively seek cancer screening. Also, since our study is a cross-sectional design, we cannot assess whether utilities will change over time.

Finally, a more global limitation is that some authors (e.g. Torrance) have suggested that, for certain purposes, utility assessment should be taken from the general population as opposed to patients who have experienced that health state. Further, patients will necessarily have an emotional stake in their decision to have surgery and this potentially violates some of the underlying principles of utility theory. In addition, these results describe patients' utilities for current sexual and urinary functioning, and do not explicitly distinguish harms specific to surgical treatment from harms related to the general effects of aging. In spite of the correlation of utilities with symptoms,

it remains possible that there is little utility to be gained by improvements in surgical technique. Therefore, our results are limited in terms of their application to decision-analytic models for health care policy. Further work is needed to evaluate utilities in the general population, and to distinguish the contribution of specific harms to utility for current health.

CONCLUSIONS

Health-related quality of life is generally good in this observational study of men treated for prostate cancer with radical prostatectomy. Additionally, those who are bothered by urinary and/or sexual dysfunction would not be willing to trade much of their remaining life span to have perfect functioning. However, the perception of side effects is bothersome enough in some men that appropriate patient counseling regarding the potential risks and benefits is essential. These results have important implications for patients contemplating aggressive treatment for prostate cancer.

REFERENCES

1. Greenlee, R. T., Murray, T., Bolden, S. et al.: Cancer statistics, 2000. CA Cancer J Clin, **50:** 7, 2000

2. Catalona, W. J., Richie, J. P., Ahmann, F. R. et al.: Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6,630 men. J Urol, **151:** 1283, 1994

3. Jacobsen, S. J., Katusic, S. K., Bergstralh, E. J. et al.: Incidence of prostate cancer diagnosis in the eras before and after serum prostate-specific antigen testing. JAMA, **274:** 1445, 1995

4. Barry, M. J.: Prostate-specific-antigen testing for early diagnosis of prostate cancer. N Engl J Med, **344:** 1373, 2001

5. Testa, M. A., Simonson, D. C.: Assesment of quality-of-life outcomes. N Engl J Med, **334:** 835, 1996

6. Herr, H. W., Kornblith, A. B., Ofman, U.: A comparison of the quality of life of patients with metastatic prostate cancer who received or did not receive hormonal therapy. Cancer, **71:** 1143, 1993

7. Braslis, K. G., Santa-Cruz, C., Brickman, A. L. et al.: Quality of life 12 months after radical prostatectomy. Br J Urol, **75:** 48, 1995

8. Litwin, M. S., Hays, R. D., Fink, A. et al.: Quality-of-life outcomes in men treated for localized prostate cancer. JAMA, **273:** 129, 1995

9. Litwin, M. S., McGuigan, K. A., Shpall, A. I. et al.: Recovery of health related quality of life in the year after radical prostatectomy: early experience. J Urol, **161:** 515, 1999

10. Torrance, G. W.: Utility approach to measuring health-related quality of life. J Chronic Dis, **40:** 593, 1987

11. Smith, D. S., Carvalhal, G. F., Schneider, K. et al.: Quality-of-life outcomes for men with prostate carcinoma detected by screening. Cancer, **88:** 1454, 2000

12. Hays, R. D., Sherbourne, C. D., Mazel, R. M.: The RAND 36-Item Health Survey 1.0. Health Econ, **2:** 217, 1993

13. von Neumann, J., Morgenstern O.: Theory of Games and Economic Behavior (3rd Edition). New York: Wiley & Sons, 1953

14. Torrance, G. W., Thomas, W. H., Sackett, D. L.: A utility maximization model for evaluation of health care programs. Health Serv Res, **7:** 118, 1972

15. Sumner, W., Nease, R. F., Jr., Littenberg, B. et al: U-titer. A utility assessment tool. Med Decis Making, **11:** 327, 1991

16. Albertsen, P. C., Nease, R. F., Jr., Potosky, A. L.: Assessment of patient preferences among men with prostate cancer. J Urol, **159:** 158, 1998

17. Ness, R. M., Holmes, A. M., Klein, R. et al.: Utility valuations for outcome states of colorectal cancer. Am J Gastroenterol, **94:** 1650, 1999

18. Kneeland, T., Nease, R., Littenberg, B.: Results of a computer-based utility assessment tool in 244 patients. Med Decis Making, **13:** 390, 1993

19. Nease, R. F., Jr., Kneeland, T., O'Connor, G. T. et al.: Variation in patient utilities for outcomes of the management of chronic stable angina. Implications for clinical practice guidelines. Ischemic Heart Disease Patient Outcomes Research Team. JAMA, **273:** 1185, 1995

20. Amin, A. N., Nease, R. F., Jr., Amin, S. S. et al: Determinants of the cost-effectiveness of cataract extraction. Med Decis Making, **16:** 455, 1996

Figure 1. Example Utility Screen for Ideal Sexual and Urinary Functioning Definitions

With IDEAL SEXUAL & URINARY FUNCTIONING, you would:

- have NO PROBLEM with sexual functioning
  - VERY GOOD ability to get an erection firm enough for intercourse
  - VERY GOOD ability to reach orgasm (climax)
  - Have an erection WHENEVER you wanted one
  - NO NEED for devices or medicine (e.g., Viagra) to have an erection

- NEVER have a problem controlling your bladder
  - NEVER leak urine
  - Have COMPLETE control over your bladder
  - NEVER need pads/adult diapers

Think about what you might trade to have IDEAL SEXUAL & URINARY FUNCTIONING.

Go Back Continue

Figure 2. Example Utility Screen for Current Sexual and Urinary Functioning Definitions

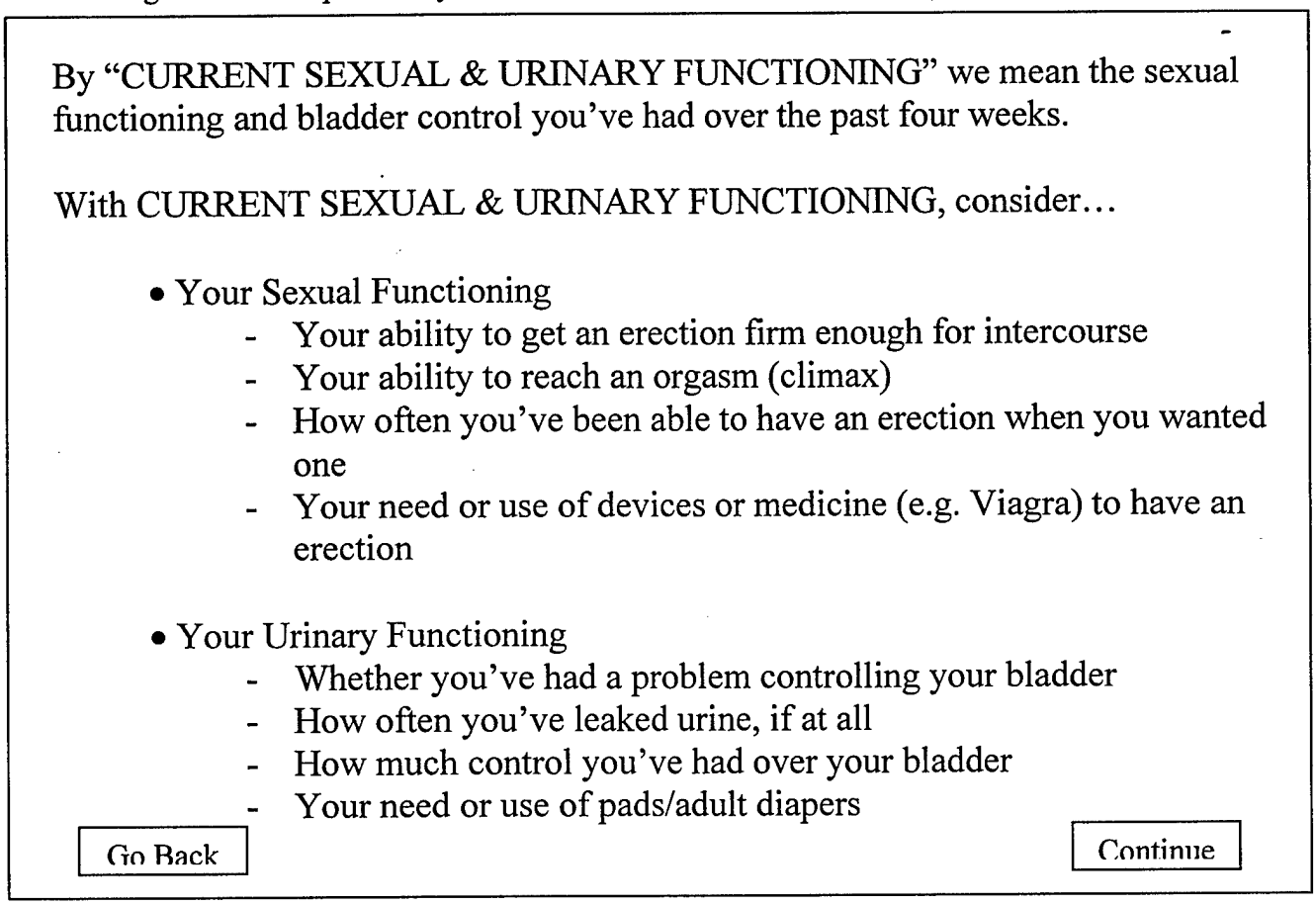

Figure 3. Example Utility Screen for Time Trade Off Measure

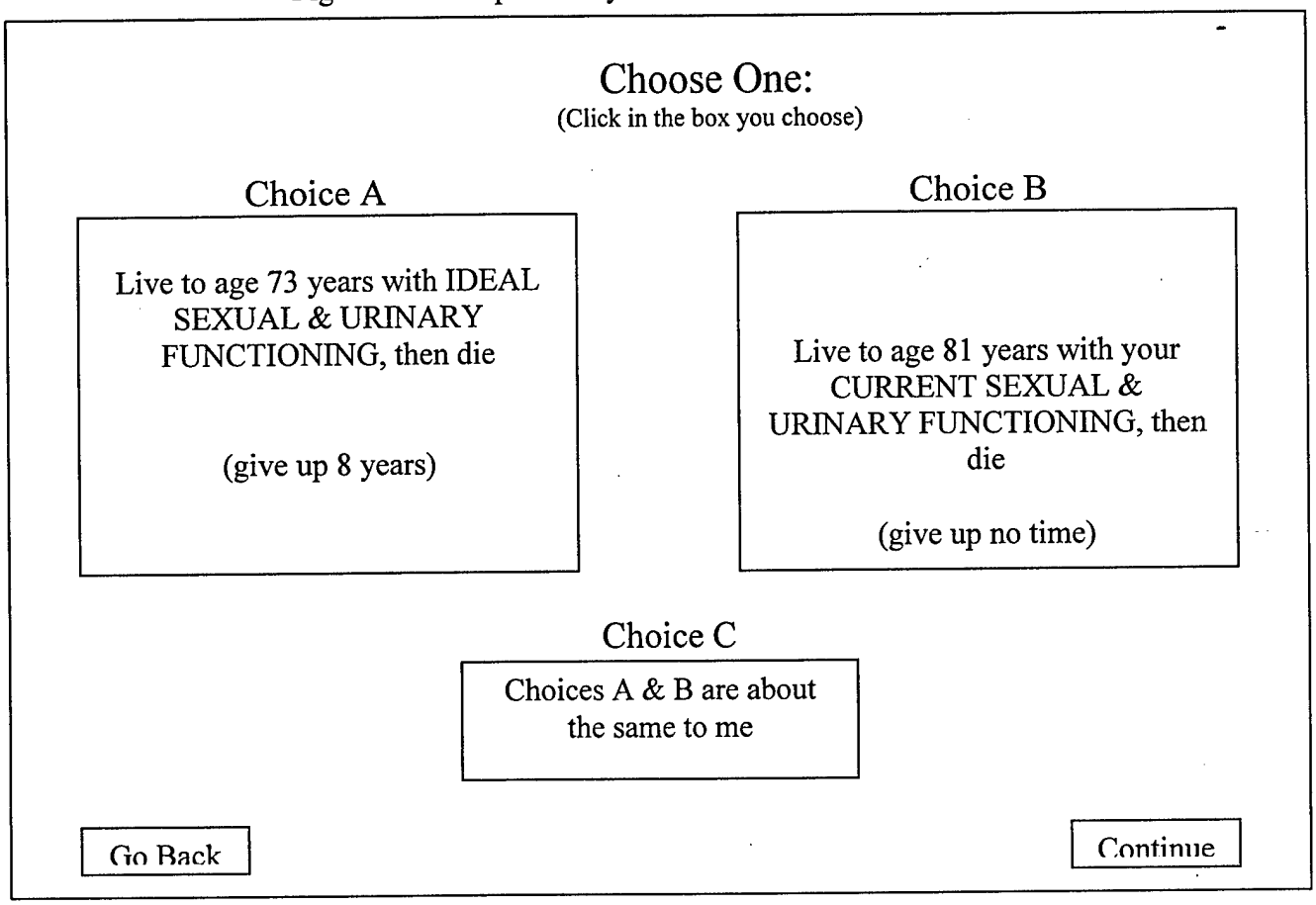

Figure 4. Example Utility Screen for Standard Gamble Measure

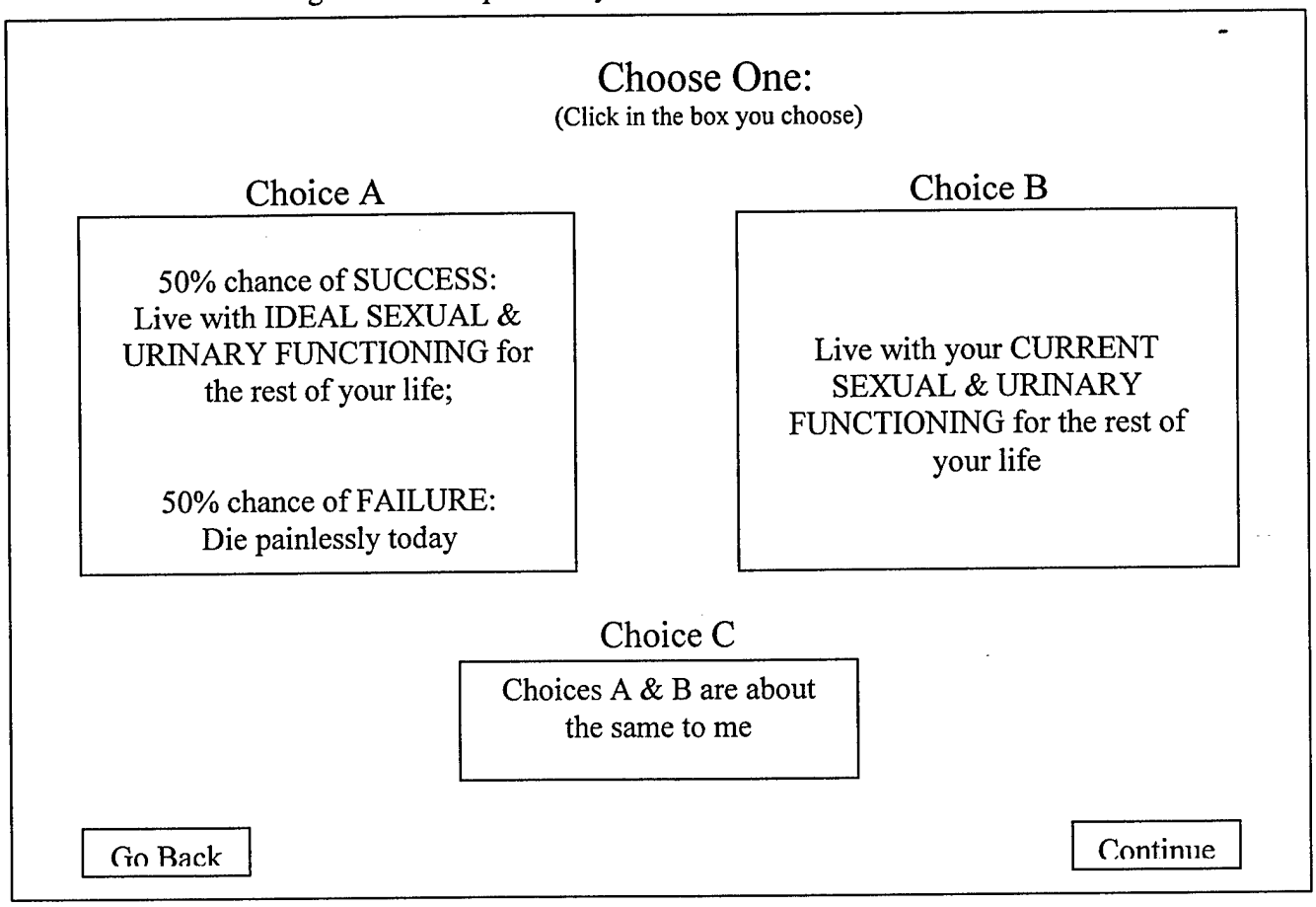

Table 1. Chi Square* and T-Test† Analyses of Sample Selection of Eligible Radical Prostatectomy Patients

	N=594			N=387			N=237		
	Recruited N=387	Not Recruited N=207	P value	Participated N=237	Extra/ Refused/ Deceased N=150	P value	Included N=209	Excluded N=28	P value
Age at recruitment	67.4 (6.3)	67.2 (6.0)	.4	67.8 (5.9)	66.8 (6.7)	.1	67.6 (5.9)	68.9 (6.7)	.3
Months from surgery to recruitment	35.7 (11.1)	34.1 (9.6)	.02	35.7 (10.5)	35.6 (11.9)	.09	35.4 (10.2)	37.6 (12.8)	.08
Race									
Afri.American/Other	33 (9)	10 (5)	.09	26(11)	7(5)	.03	20(10)	6(21)	.06
White	354 (91)	197 (95)		211(89)	143(95)		189(90)	22(79)	
Marital Status									
Married	342 (88)	186 (90)	.5	206 (87)	136 (91)	.3	186 (89)	20 (71)	.009
Not Married	45 (12)	20 (10)		31 (13)	14 (9)		23 (11)	8 (29)	
Education									
high school or less	107 (28)	53 (26)	.9	60 (25)	47 (32)	.5	51 (25)	9 (32)	.5
some college	99 (26)	54 (26)		62 (26)	37 (25)		57 (27)	5 (18)	
college	73 (19)	38 (19)		45 (19)	28 (19)		38 (18)	7 (25)	
postgrad	104 (27)	60 (29)		69 (29)	35 (24)		62 (30)	7 (25)	
Employment									
Retired	220(57)	120(59)	.8	140(59)	80(54)	.4	122(59)	18(64)	.6
Working	163(43)	85(41)		96(41)	67(46)		86(41)	10(36)	
Comorbidities									
0	202(53)	108(53)	.3	118(50)	84(58)	.3	107(52)	11(39)	.2
1	118(31)	54(27)		76(32)	42(29)		67(32)	9(32)	
2+	60(16)	41(20)		41(18)	19(13)		33(16)	8(29)	
Pre-opp PSA									
<4	170(44)	84(41)	.4	96(41)	74(49)	.09	82(39)	14(50)	.3
>=4	217(56)	123(59)		141(59)	76(51)		127(61)	14(50)	
Clinical Stage									
T1	293(76)	153(75)	.7	176(74)	117(79)	.3	158(76)	18(64)	.2
T2	93(24)	52(25)		61(26)	32(21)		51(24)	10(36)	
Pathology Stage									
T2	293(76)	155(76)	.9	181(76)	112(75)	.7	158(76)	23(82)	.4
T3	94(24)	50(24)		56(24)	38(25)		51(24)	5(18)	
In-house Surgery									
Yes	323(84)	157(77)	.06	196(83)	127(85)	.7	178(86)	18(64)	.005
No	63(16)	46(23)		40(17)	23(15)		30(14)	10(36)	

*Numbers (percentages); Numbers may not add up to totals due to missing information; Percentages may not add up to 100 due to rounding.

† Means (standard deviations)

Table 2 . Chi Square* and T-Test† Analyses of demographic and clinical characteristics for patients who underwent a radical prostatectomy, stratified by level of bother at time of interview (N=209)

	Both Sexual and Urinary Bother N=40	Sexual Bother Only N=95	Neither Sexual or Urinary Bother N=74	p value
Age at recruitment	68.2 (6.4)	67.5 (5.7)	67.4 (5.8)	.8
Months from surgery to recruitment	37.4 (9.8)	33.7 (9.7)	36.6 (10.8)	.07
Mean Function Score$				
Sexual	26.1 (21.5)	32.3 (22.3)	58.7 (30.2)	<.0001
Urinary	43.3 (22.1)	84.1 (15.8)	87.8 (14.4)	<.0001
Race				
African American/Other	4 (10)	7(7)	9(12)	.6
White	36 (90)	88(93)	65(88)	
Marital Status				
Married	34 (85)	87 (92)	65 (88)	.5
Not Married	6 (15)	8 (8)	9 (12)	
Education				
high school or less	14 (35)	22 (23)	15 (20)	
some college	15 (38)	26 (28)	16 (22)	.08
college	2 (5)	18 (19)	18 (24)	
postgrad	9 (23)	28 (30)	25 (34)	
Employment				
Retired	26(65)	54(57)	42(57)	.7
Working	14(35)	40(43)	32(43)	
Comorbidities				
0	17(43)	46(49)	44(60)	.01
1	10(25)	34(36)	23(32)	
2+	13(33)	14(15)	6(8)	
Pre-opp PSA				
<4	15(37)	46(48)	21(28)	.03
>=4	25(63)	49(52)	53(72)	
Clinical Stage				
T1	30(75)	75(79)	53(72)	.5
T2	10(25)	20(21)	21(28)	
Pathology Stage				
T2	30(75)	72(76)	56(76)	.9
T3	10(25)	23(24)	18(24)	
In-house Surgery				
Yes	34(85)	79(84)	65(88)	.8
No	6(15)	15(16)	9(12)	

*Numbers (percentages); Numbers may not add up to totals due to missing information; Percentages may not add up to 100 due to rounding.

† Means (standard deviations)

$ Scale ranges from 0-100, with lower scores indicating greater impairment.

Table 3: Kruskal-Wallis Analyses and Wilcoxon Post-Hoc Comparisons of Outcome group, Race, and Comorbidity by Mean Utilities

	TTO				SG			
	N	Mean	SD	p value	N	Mean	SD	p value
Level of Bother								
Both Sexual and Urinary	40	.767[a]	.310	.0007	40	.822[c,d]	.272	<.0001
Sexual Only	95	.869[b]	.209		95	.898[c,e]	.199	
Neither	74	.923[a,b]	.205		74	.956[d,e]	.165	
Race								
African American/Other	20	.841	.312	.6	20	.955	.078	.1
White	189	.871	.227		189	.899	.218	
Comorbidities								
0	107	.863	.252		107	.903	.218	.3
1	67	.894	.208	.3	67	.913	.215	
2+	33	.843	.227		33	.901	.155	
Age at recruitment								
<70	134	.882	.218	.07	134	.918	.191	.2
≥70	75	.844	.264		75	.879	.237	

a Both versus Neither, TTO ; p=.015
b Sexual versus Neither, TTO; p=.0002
c Both versus Sexual, SG; p=.05
d Both versus Neither, SG; p<.0001
e Sexual versus Neither, SG; p<.0001