Prostate Cancer Screening: A Decision Analysis

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Background. The issue of whether to screen men for prostate cancer is controversial. No randomized clinical trials have been completed to confirm the efficacy of screening for prostate cancer. We created a mathematical model of the clinical risks and benefits of screening for prostate cancer.

Methods. A Markov decision-analytic model evaluated the outcomes of annually screening asymptomatic men for prostate cancer beginning at age 50 years. The screening and testing algorithm included the digital rectal examination, transrectal ultrasound, and prostate-specific antigen test. A sample of 10 male patients with no history of prostate disease were interviewed to assess their utilities (preferences) regarding the various adverse outcomes of prostate cancer treatment.

Results. The model indicated that no screening was preferred to screening when patients' utilities were considered (24.14 vs 23.47 quality-adjusted life years expected). The optimal decision was sensitive to the utilities of impotence and urethral stricture, the most common adverse outcomes for patients under the age of 65 years. When adverse outcomes of treatment were ignored, screening was favored (24.86 vs 24.22 years of life expectancy).

Conclusions. When quality-of-life preferences of men are considered, the annual screening of asymptomatic patients for prostate cancer is not recommended.

Key words. Medical decision making; prostatic diseases; prostatic neoplasm; prostate cancer; diagnostic tests, routine; screening; utilities; quality of life; primary health care. (*J Fam Pract 1995; 41:33-41*)

Prostate cancer is the second leading cause of cancer deaths among men in the United States. There were at least 165,000 new cases diagnosed in 1993. In that year, more than 35,000 men died from the disease.[1] Screening for prostate cancer remains controversial, however, because it has never been demonstrated in a randomized clinical trial that an early diagnosis increases either length of survival or quality of life.[2-4] Treatment of prostate cancer may be effective for certain aggressive tumors that can be detected and treated in early and intermediate stages. However, currently available screening tests for prostate cancer may also detect in asymptomatic men microscopic cancers that will have no detrimental effect on the patient. Between 30% and 40% of men are found to have some microscopic form of prostate cancer at autopsy.[5] Treatment of prostate cancer is not without risk of adverse outcomes, including impotence, urinary incontinence, and even death. It is important to consider these outcomes in determining the appropriateness of screening for prostate cancer.

Decision analysis uses available data from the literature to produce a model of the possible outcomes and their probabilities of occurrence, facilitating the process of choosing among different strategies for the evaluation and treatment of disease. The optimal decision often depends on the individual patient's values and how that patient evaluates each potential outcome. Using an algorithm that includes the recently developed prostate-specific antigen (PSA) test, this study used decision anal-

Submitted, revised, February 10, 1995.

This paper was presented in part at the Agency for Health Care Policy and Research 3rd Annual Meeting in Atlanta, Georgia, January 1993, and at the 21st Annual Meeting of the North American Primary Care Research Group in San Diego, California, November 1993.

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ISSN 0094-3509

ysis to evaluate whether it is appropriate to annually screen men 50 years of age and older for prostate cancer. Rather than using preferences estimated by physicians, as has been done in previously published decision analyses of prostate cancer evaluation and treatment,[6,7] the utilities for the possible different outcomes were evaluated by assessing patient preferences based on a pilot sample of 10 middle-aged adult male family practice patients who were free of prostate disease.

Methods

A decision-analytic model of whether to screen annually for prostate cancer was created using probability and outcome data from the medical literature. We considered two screening-treatment strategies in our decision model; the method of treatment differed if prostate cancer was detected at the annual screening. The first strategy consists of treating stages A and B prostate cancer with radical prostatectomy, stage C with radiation, and stage D with hormonal therapy. The second strategy consists of treating stages A, B, and C with radiation therapy and treating stage D cancer with hormonal therapy. Both treatment strategies were initially considered because of inconclusive evidence that one treatment option is clinically superior to the other for the earlier stages of prostate cancer.[8–10]

As shown in Table 1, 23 different states were considered, based on stage of the cancer identified and the possibility of adverse treatment effects. Figure 1 displays a simplified state-transition diagram for the Markov process,[11] which was used in the decision analysis. Four basic states are shown in Figure 1: no cancer, cancer, posttreatment, and death. An arrow indicates movement from one state to another or remaining in a health state for a 1-year period. A hypothetical asymptomatic 50-year-old man begins in the no cancer or cancer state, progressing through the various health states until his death. Based on this model, we can compute the average amount of time a cohort of men spend in each of the health states to compute the life expectancy and quality-adjusted life expectancy of each of the potential strategies considered.

Screening Algorithm

We evaluated a screening algorithm similar to the one recommended by Cooner[12] (Figure 2). A digital rectal examination (DRE) and a prostate-specific antigen test (PSA) would initially be performed. If the physician found a nodule or if the PSA test was positive (>10 ng/mL), a biopsy would be performed. If both were normal, further testing would be postponed until the following year.

If the DRE was negative, but the PSA level was indeterminate (4 to 10 ng/mL), transrectal ultrasound (TRU) and the predicted PSA (PSA level divided by estimated prostate volume, also called PSA density) would be performed to determine whether a biopsy would be appropriate.[13] Even though most physicians would immediately perform a biopsy if the PSA level was in this range of intermediate values, the screening algorithm includes TRU and PSA density tests to avoid an unnecessary biopsy. Detection of cancer is not compromised with the use of these tests in the intermediate range of PSA values.[14] If the biopsy results were positive, indicating the presence of cancer, appropriate treatment (either radiation therapy or radical prostatectomy) would be considered. Clinical staging procedures, a significant part of the cancer evaluation and management process, are not considered in this model, which focuses on clinical effectiveness rather than monetary costs of screening.

Table 1. The 4 Basic and 23 Specific Health States Included in the Markov Model

NO CANCER
CANCER
Undetected stage A
Undetected stage B
Undetected stage C
Undetected stage D
POSTTREATMENT
Posttreatment States for No Cancer (False Positive)
No adverse effects
Impotence
Incontinence
Urethral stricture
Rectal injury
Posttreatment States for Stage A or B Cancer
No adverse effects
Impotence
Incontinence
Urethral stricture
Rectal injury
Posttreatment States for Stage C Cancer
No adverse effects
Impotence
Incontinence
Urethral stricture
Rectal injury
Posttreatment States for Stage D Cancer
Impotence
Gynecomastia
DEATH

NOTE: The 23 specific health states include the 21 indented states and NO CANCER and DEATH.

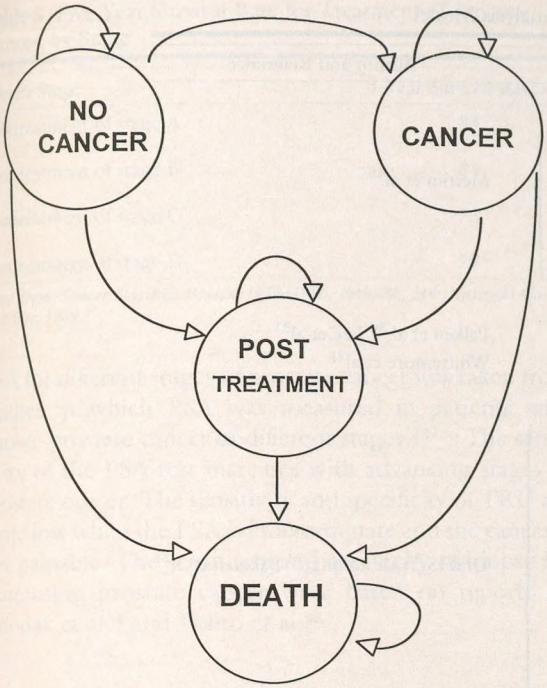

Figure 1. A simplified state-transition diagram modeling the health states of the prostate cancer decision model. Arrows indicate either movement from one state to another or remaining in one health state for a period of 1 year.

Probabilities

The assumptions and sources for all probability data can be found in Tables 2 and 3. We defined *prevalence* as the proportion of men in the asymptomatic screening population with clinically detectable prostate cancer. These include all cancers that are detectable with currently available screening methods but does not include histological cancers that are clinically undetectable. Based on data from the American Cancer Society National Prostate Cancer Detection Project adjusted for clinical understaging, the prostate cancer prevalence in an asymptomatic screening population was found to be 2.4%.[15] Thirty-two percent of cancers diagnosed as stage A or stage B on clinical examination are found to be stage C cancers at surgery.[15] Thus, of the 50-year-old men who have asymptomatic prostate cancer, 17% have stage A cancer; 44%, stage B; 37%, stage C; and 2%, stage D.

The annual transition probabilities between stages (A to B, B to C, and C to D) were calculated from 5-year cohort studies[16–18] using the appropriate transformation equation. The rates were recomputed in terms of annual probabilities based on the transformation

$$p = 1 - (1 - r)^{(1/t)}$$

where p is the annual transition probability, r is the rate, and t is the time interval of the study.[11] The progression of treated stage D disease to death (25% per year) was based on survival rates reported by the National Cancer Institute.[19]

The transition probability from no cancer to stage A cancer is the incidence rate of prostate cancer. Scardino[20] estimated that the annual incidence rate of prostate cancer in men over 50 years old is 0.0031 and may increase with age. We modeled increasing incidence by using the prevalence of prostate cancer at different ages at autopsy. Whittemore et al[21] stated that the mean incidence is approximately 0.017, and could increase to 0.023 in white men. We used an incidence of 0.003 for men 50 to 60 years old, 0.017 for men 61 to 70 years old, and 0.023 for men older than 70 years to reflect increasing incidence by age.

Age-specific mortality rates were obtained from United States life-table data.[22] Because we could not find in the literature an estimate of the probability that an advanced stage of prostate cancer would become symptomatic in a given year, we based our estimates of these probabilities on clinical judgment.

The sensitivity and specificity of each test (DRE, PSA, TRU) were determined by calculating the weighted means of several studies that evaluated both asymptomatic and symptomatic patients.[13,15,23–33] The sensitivity of

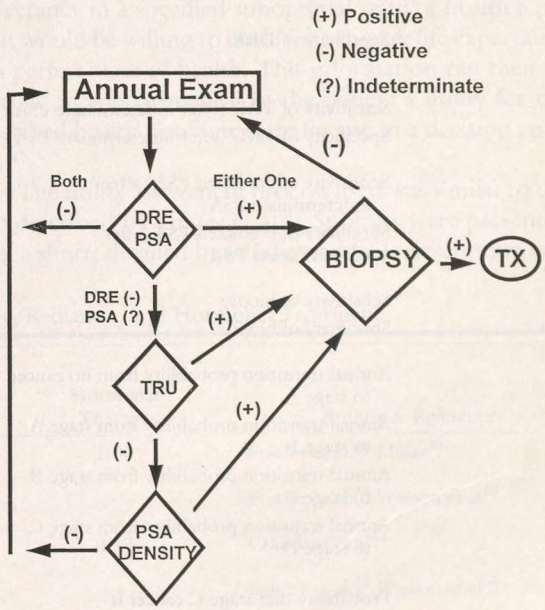

Figure 2. The annual screening algorithm evaluated by the decision analysis model. This algorithm is slightly modified from the one suggested by Cooner,[12] who recommends a second PSA test if the original was indeterminate.

Table 2. Probability Variables Used in the Decision Analysis Model

Variable	Value	Author and Reference
Prevalence of clinically detectable prostate cancer in asymptomatic 50-year-old men	0.024	
Proportion of cancers that are stage A	0.170	Mettlin et al[15]
Proportion of cancers that are stage B	0.442	
Proportion of cancers that are stage C	0.368	
Proportion of cancers that are stage D	0.020	
Proportion of patients without cancer with PSA level >4 ng/mL	0.1313	Palken et al,[30] Lee et al[31]
with PSA level 4–10 ng/mL	0.1107	Whittemore et al[21]
Proportion of stage A patients with PSA level >4 ng/mL	0.488	
with PSA level 4–10 ng/mL	0.3636	
Proportion of stage B patients with PSA level>4 ng/mL	0.66	
with PSA level 4–10 ng/mL	0.3947	DHHS,[22] Oesterling,[23] Babaian et al[24]
Proportion of stage C patients with PSA level >4 ng/mL	0.85	
with PSA level 4–10 ng/mL	0.2295	
Proportion of stage D patients with PSA level >4 ng/mL	0.99	
with PSA level 4–10 ng/ML	0.1584	
Specificity of PSA test	0.8687	Palken et al,[30] Lee et al[31]
Sensitivity of DRE	0.5406	Partin et al,[25] Lange et al,[26] Babaian et al,[27,28] Lee et al[29]
Specificity of DRE	0.9436	Mettlin et al,[15] Partin et al,[25] Babaian et al,[27,28] Lee et al[29]
Sensitivity of TRU (after indeterminate PSA)	0.107	Palken et al[30]
Specificity of TRU (after indeterminate PSA)	0.766	
Sensitivity of predicted PSA (after indeterminate PSA)	0.70	Lee et al[13]
Specificity of predicted PSA (after indeterminate PSA)	0.88	
Sensitivity of biopsy	0.98	Cooner et al,[32] Kane et al[33]
Specificity of biopsy	0.98	
Annual transition probability from no cancer to stage A	By age (see text)	Fleming et al[6]
Annual transition probability from stage A to stage B	0.066	Morse and Resnick,[16] Hanash,[17] Cantrell et al[18]
Annual transition probability from stage B to stage C	0.082	
Annual transition probability from stage C to stage D	0.46	Hanash[17]
Probability that stage C cancer is symptomatic	0.4	Estimate by investigators
Probability that stage D cancer is symptomatic	0.8	

PSA denotes prostate-specific antigen; DRE, digital rectal examination; TRU, transrectal ultrasound.

Table 3. Five-Year Survival Rate for Treatment of Prostate Cancer, by Stage

Cancer Stage	5-Year Survival Rate (%)
Posttreatment of stage A	84
Posttreatment of stage B	84
Posttreatment of stage C	73
Posttreatment of stage D	29

Data from Cancer Statistics Review 1973–1986. Bethesda, Md: National Cancer Institute, 1989.[19]

PSA for different stages of prostate cancer was taken from studies in which PSA was measured in patients with known prostate cancer of different stages.[23–26] The sensitivity of the PSA test increases with advancing stages of prostate cancer. The sensitivity and specificity of TRU are quite low when the PSA is indeterminate and the cancer is not palpable. The sensitivity and specificity of biopsy for diagnosing prostate cancer were based on reports by Chodak et al[34] and Polito et al.[35]

Outcomes

For each stage of prostate cancer identified, the declining exponential approximation of life expectancy[36] was used to calculate mortality rates based on 5-year survival rates reported by the National Cancer Institute.[19] The operative mortality rate from radical prostatectomy was assumed to be 1% for patients of all ages, which is consistent with that found by Lu-Yao et al.[37]

Treatment of prostate cancer has a significant risk of adverse outcomes with known probabilities of occurrence. The likelihood of each of these adverse treatment effects was determined from the literature and is presented in Table 4. We incorporated two sets of rates to reflect different adverse outcome rates for patients less than and more than 65 years of age at time of surgery.[38] The most common adverse effect for patients under the age of 65 years is impotence, which occurs in over 40% of patients treated with radiation and 31% treated with radical prostatectomy.[39,40] Other adverse consequences of treatment include urinary incontinence, urethral stricture, rectal injury, and gynecomastia.[40–43] We did not consider outcomes of living with untreated prostate cancer in its various stages because we assumed that once a man became symptomatic, he would seek evaluation and treatment.

Quality of Life

Outcomes for the decision-analytic model were expressed in quality-adjusted life years. Rather than use physicians' estimates of how adverse outcomes would affect quality of life, we recruited 10 married couples from The University of Texas Medical Branch at Galveston Family Medicine Center for the purpose of assessing the preferences of patients and their spouses. These couples included men who were approximately 50 years of age, were in good health, and gave informed consent to participate in the study. Although outcomes were evaluated for each partner separately and for the couple together, only the husbands' responses were used in this analysis. A comparison of marital concordance of outcome evaluation can be found in a companion analysis.[44]

Preferences regarding possible outcomes of prostate cancer treatment were assessed using the time trade-off method,[45] which is used to determine the amount of life expectancy in a specified suboptimal state of health a patient would be willing to trade for a shorter life expectancy in a perfect state of health. This information can then be used as an approximation of the patient's utility for the described health outcome state for use in a decision analysis.[46]

The utility assessment process used was similar to the one described by Singer et al.[47] Subjects were presented with a short, detailed but understandable description of a

Table 4. Probabilities of Adverse Effects Caused by Radical Prostatectomy, Radiation, and Hormonal Treatment

Treatment Adverse Effects	Radical Prostatectomy Patient Age, y		Radiation Therapy	Hormonal Therapy	Author & Reference
	<65	≥65			
Impotence	0.31	0.89	0.40	1.00	Fowler et al,[38] Millar[41]
Incontinence	0.06	0.47	0.01	—	Fowler et al,[38] Wasson et al[40]
Gynecomastia	—	—	—	0.13	Crawford et al[42]
Urethral stricture	0.124	0.20	0.045	—	Fowler et al,[38] Wasson et al[40]
Rectal injury	0.013	0.013	0.023	—	Wasson et al[40]
Death	0.01	0.01	0.002	—	Wasson et al,[40] Catalona and Avioli[43]

NOTE: *The probability data in this table were used as the baseline values in the decision analysis.*

Table 5. Quality-Adjustment Weights for Prostate Cancer Treatment Complications in 10 Subjects

Outcome	Quality-Adjustment Weight Mean (SE)
Incontinence	0.68 (0.10)
Impotence	0.74 (0.09)
Urethral stricture	0.60 (0.10)
Rectal injury	0.45 (0.10)
Gynecomastia	0.61 (0.11)

NOTE: *The quality-adjustment weights were used in the decision-analysis model to adjust for quality-of-life considerations for the adverse treatment outcomes.*

possible adverse outcome of cancer treatment. Each subject was then asked if he would prefer to live 10 more years with the adverse condition described, or 1 more year in perfect health. If the subject responded that he would rather live 10 years with the adverse condition, the number of years in perfect health was increased by 1, and the question was asked again. This sequence was repeated until an indifference point was determined. The procedure was repeated for each of five adverse outcomes. After evaluating all five outcomes, study subjects were able to review their responses to check for consistency and accuracy.

The subjects' mean utility values for each of the assessed outcomes were used in the decision analysis to compute the quality-adjusted life expectancy for each of the management strategies. The management strategy that yielded the maximum quality-adjusted life expectancy was identified as the optimal screening strategy.

We performed statistical analysis of the quality-of-life measures using SPSS-Windows.[48] We performed the decision analysis using SMLTREE.[49] We performed one-way sensitivity analysis by varying each probability and utility parameter independently to determine whether the optimal strategy would remain unchanged. Two-way sensitivity analysis was also performed on the most common adverse outcomes of treatment.

Results

There was some variation in the subjects' preferences for the possible adverse health outcomes. Table 5 presents the mean and standard error of the subjects' quality-adjustment weights. These weights can be interpreted as the fractional portion of 1 year in perfect health that a patient evaluates as equivalent to 1 year in the reduced health state. For example, for impotence, the mean of responses indicated that 12 months of impotence would be equivalent to 9 months (approximately 0.74 of a year) in perfect health. Other than death, rectal injury was perceived as the worst of the possible adverse outcomes of prostate cancer treatment.

After incorporating the patients' mean utility values into the model, we found that of the two screening-treatment strategies, radiation was barely preferable to surgical treatment for the early stages of cancer (23.47 vs 23.46 quality-adjusted life years). The optimal treatment decision, if screening should occur, was relatively insensitive to variations in the model's values.

The no-screening strategy was preferred to the screening strategy by 8 quality-adjusted life months (24.14 vs 23.47 quality-adjusted life years). The one-way sensitivity analysis indicated that the decision not to screen was generally insensitive to changes to the model parameters except for changes in the prevalence of detectable cancer: if the prevalence of detectable asymptomatic prostate cancer was as high as 30.5%, the optimal decision would be to screen asymptomatic men.

Two-way sensitivity analysis was performed, varying patients' utilities for impotence and urethral stricture, which are the most likely adverse outcomes for patients under the age 65 years. As shown in the top right corner of Figure 3, if the patient's disutility for impotence and urethral stricture is negligible, screening is the optimal decision. If the maximization of life expectancy is the criterion used for decision-making, ie, if quality-of-life considerations are disregarded, screening is preferred to no screening (24.86 vs 24.22 years of life expectancy). Thus, the decision to screen is sensitive to changes in the patient's preferences regarding adverse effects of treatment.

Discussion

The appropriateness of performing a screening test is based on three criteria: the effectiveness of treatment if the disease is found, the burden of suffering caused by the disease, and the accuracy of the screening test.[50] Part of the difficulty in deciding whether screening for prostate cancer is appropriate is that not all these criteria are clearly fulfilled. The burden of suffering with prostate cancer is significant; however, the accuracy of the screening tests and the effectiveness of treatment are not ideal. The lack of clear benefits of screening has led to conflicting recommendations by the American Cancer Society and the United States Preventive Services Task Force.[51,52] We conducted this decision analysis, in part, in an attempt to shed new light on the screening controversy.

This research is an extension of the prostate cancer model analyzed by Mold et al.[7] In this paper, we have modified the original model of Mold et al as suggested by

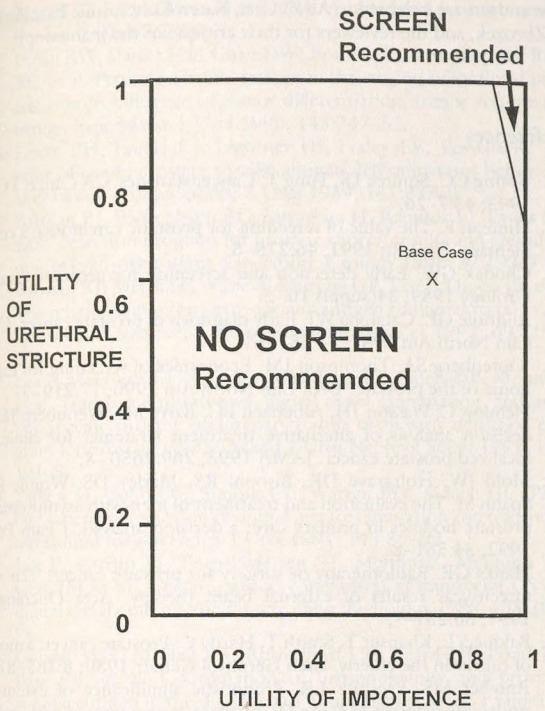

Figure 3. Two-way sensitivity analysis on the utilities of the most likely adverse outcomes of treatment, impotence and urethral stricture. If preferences fall below the threshold line, as in the base case, screening is not indicated. If preferences fall above the line, as would occur in cases where quality-of-life preferences are not considered (top right corner of figure), screening is indicated.

our previous recommendations.[53] These suggestions include the use of the new screening tests (PSA and PSA density) as well as the implementation of a structured algorithm for annual screening.

The critical variable in the decision analysis is the baseline prevalence of clinically rather than histologically detectable prostate cancer in asymptomatic 50-year-old men. Although 28% of 50-year-old men show evidence of prostate carcinoma on autopsy, most of these cases are microscopic, clinically undetectable, and of unknown clinical significance.[54,55] Our base case prevalence of 2.4% in asymptomatic 50-year-old men represents prostate cancer cases that are clinically relevant and therefore would appear to be the appropriate value for use in the decision-analytic model.

Other data for baseline prevalence appears in the literature but may not be appropriate for use in the current model. In particular, Krahn et al[56] used regression analysis to compute a prevalence of clinically detectable prostate cancer of 0.6% for 50-year-old men. Voss[57] and Scardino et al[20] cite prevalence rates of 6% to 12% and 6% to 9%, respectively. However, because the latter ranges are based on pathologic findings, the prevalence of detectable cancer should be lower. The sensitivity analysis showed that the screening strategy would be optimal only if the prevalence of clinically detectable cancer is greater than 30.5%. All available references suggest that the prevalence of clinically detectable prostate cancer is much lower than this threshold.

This model evaluates the decision to screen an asymptomatic patient in the primary care setting rather than in a specialty clinic. The prior probability of prostate cancer will be higher in a patient seen in a urology specialty clinic because of selection bias based on self- or physician referral. Thus, our conclusions may not apply in the specialty setting.

Our simplified Markov model based on cancer stage did not stratify tumors by grade (eg, poorly, moderately, or well differentiated). An alternative model based on tumor grade is plausible but adds much complexity and data unavailability problems. In particular, if tumor grades had been used, the number of health states and required probability parameters would have more than doubled. Most prostate cancer growth rates and test sensitivity rates would have to be estimated and not be taken directly from the literature. Therefore, we chose to model the screening decision by stratifying tumors according to stage.

This analysis is different from previously published decision analyses of the evaluation and treatment of prostate cancer. Mold et al[7] analyzed the management strategies of radical prostatectomy and radiation therapy after a nodule had been identified by DRE. Their conclusion was that even with the best possible treatment, the patient would be better off if the nodule were left alone. Similarly, Fleming et al[6] evaluated different possible treatment strategies, including radical prostatectomy, radiation therapy, and watchful waiting, for localized cancer of the prostate. They concluded that once a prostate nodule is found, watchful waiting is a reasonable clinical management strategy. The conclusions of these papers may not go far enough; ie, if watchful waiting is a viable alternative, what is to be gained by screening?

In another recently published study, Krahn et al[56] analyzed the monetary costs and health benefits of *one-time* screening for prostate cancer. Our results are consistent with their conclusions, but go a step further by showing the ineffectiveness of *annual* screening.

Many of the assumptions made in our analysis were biased to favor screening over not screening. For example, we did not include several other potential complications of prostate cancer treatment, including respiratory failure and myocardial infarction. In addition, we did not incorporate any adjustments for short-term adverse effects on quality of life, such as time spent recovering from surgery,

or acute effects associated with radiation therapy. Nevertheless, the optimal strategy in the decision analysis was not to screen.

Our analysis did not consider the issue of monetary cost. A screening strategy certainly would be more costly than a strategy not to screen. If screening offers no health benefit measured in quality-adjusted life expectancy, a cost-effectiveness analysis would show that not screening is a dominant strategy, ie, it yields fewer health benefits at a greater cost.

Unlike previous analyses, the utility data used in this decision analysis were obtained from patients rather than physicians. Although the subjects in the pilot sample were not known to have prostate cancer, their lack of "medical" biases should provide a more accurate reflection of the values of real patients. While it is certainly possible that an individual's utilities may change over time, current preferences are the best possible approximation of future utilities.[58]

The number of quality-adjusted life years will be an appropriate utility scale under the following conditions: utility independence of quality and quantity of life, the existence of the proportional trade-off property, and risk neutrality in life years.[46] These assumptions, not usually restated in applications of decision analysis, may not actually hold true for patients, a possibility that potentially compromises the validity of our results. Nevertheless, these assumptions may be reasonable approximations for the true preferences of patients.

We recognize that we assessed utilities on a small sample of asymptomatic patients. However, the sensitivity analysis showed that with reasonable variation, the optimal decision is dependent on the patient's quantitative evaluation of the adverse outcomes.

This decision analysis shows that when average patient utility data are incorporated into a model that seeks to maximize quality-adjusted life expectancy, prostate cancer screening is not recommended. Individual patient preferences regarding possible adverse consequences of treatment, particularly impotence and urethral stricture, are important in this controversial clinical decision. If life expectancy is the only criterion for decision-making, and cost is not a consideration, screening may extend a patient's life expectancy by a few months. When quality-of-life factors are included, however, screening men for prostate cancer is not indicated.

Acknowledgments

This research was funded in part by the Bureau of Health Professions, Health Resources and Services Administration, grant No. D32-PE16033.

The authors are indebted to Alvah Cass, Karen Kuntz, Julie Pass, Arthur Zbrozek, and the reviewers for their critique of the manuscript.

References

1. Boring CC, Squires TS, Tong T. Cancer statistics. CA Cancer J Clin 1993; 43:7–26.
2. Hinman F. The value of screening for prostatic carcinoma: a commentary. Urol Int 1991; 46:275–8.
3. Chodak GW. Early detection and screening for prostatic cancer. Urology 1989; 34(suppl):10–2.
4. Andriole GL, Catalona WJ. Early diagnosis of prostate cancer. Urol Clin North Am 1987; 14:657–61.
5. Optenberg SA, Thompson IM. Economics of screening for carcinoma of the prostate. Urol Clin North Am 1990; 17:719–37.
6. Fleming C, Wasson JH, Albertsen PC, Barry MJ, Wennberg JE. A decision analysis of alternative treatment strategies for clinically localized prostate cancer. JAMA 1993; 269:2650–8.
7. Mold JW, Holtgrave DR, Bisonni RS, Marley DS, Wright RA, Spann SJ. The evaluation and treatment of men with asymptomatic prostate nodules in primary care: a decision analysis. J Fam Pract 1992; 34:561–8.
8. Hanks GE. Radiotherapy or surgery for prostate cancer? Ten and fifteen-year results of external beam therapy. Acta Oncologica 1991; 30:231–7.
9. Balducci L, Khansur T, Smith T, Hardy C. Prostate cancer: a model of cancer in the elderly. Arch Gerontol Geriatr 1989; 8:165–87.
10. Anscher MS, Prosnitz LR. Prognostic significance of extent of nodal involvement in stage D1 prostate cancer treated with radiotherapy. Urology 1992; 39:39–43.
11. Sonnenberg FA, Beck JR. Markov models in medical decision making: a practical guide. Med Decis Making 1993; 13:322–38.
12. Cooner WH. Rectal examination and ultrasonography in the diagnosis of prostate cancer. Prostate 1992; 4:3–10.
13. Lee F, Littrup PJ, Loft-Christensen L, Kelly BS, McHugh TA, Siders DB, et al. Predicted prostate specific antigen results using transrectal ultrasound gland volume. Cancer 1992; 70:211–20.
14. Bazinet M, Meshref AW, Trudel C, Aronson S, Peloquin F, Nachabe M, et al. Prospective evaluation of prostate-specific antigen density and systematic biopsies for early detection of prostatic carcinoma. Urology 1994; 43:44–52.
15. Mettlin C, Lee F, Drago J, Murphy GP. The American Cancer Society National Prostate Cancer Detection Project. Cancer 1991; 67:2949–58.
16. Morse RM, Resnick MI. Detection of clinical occult prostate cancer. Urol Clin North Am 1989; 16:635–55.
17. Hanash KA. Natural history of prostatic cancer: imaging techniques, radiotherapy, and management issues. Prog Clin Biol Res 1987; 243B:289–320.
18. Cantrell BB, DeKlerk DP, Eggleston JC, Boitnott JK, Walsh PC. Pathological factors that influence prognosis in stage A prostatic cancer: the influence of extent versus grade. J Urol 1981; 125:516–20.
19. Cancer Statistics Review 1973–1986. Bethesda, Md: National Cancer Institute, 1989. National Institutes of Health publication No. 89-2789.
20. Scardino PT. Early detection of prostate cancer. Urol Clin North Am 1989; 16:635–55.
21. Whittemore AS, Keller JB, Betensky R. Low-grade, latent prostate cancer volume: predictor of clinical cancer incidence? J Natl Cancer Inst 1991; 83:1231–5.
22. National Center for Health Statistics. Vital Statistics of the United States, 1988. Vol 2. Mortality, part A. Washington, DC: Public Health Service, 1991. DHHS publication No. (PHS) 91-1101.
23. Oesterling JE. Prostate specific antigen: a critical assessment of the most useful tumor marker for adenocarcinoma of the prostate. J Urol 1991; 145:907–23.
24. Babaian RJ, Camps JL, Frangos DN, Ramirez EI, Tenney DM,

Hassell JS, et al. Monoclonal PSA in untreated prostate cancer. Cancer 1991; 67:2200–6.
25. Partin AW, Carter HB, Chan DW, Epstein JI, Oesterling JE, Rock RC, et al. Prostate specific antigen in the staging of localized prostate cancer: influence of tumor differentiation, tumor volume and benign hyperplasia. J Urol 1990; 143:747–52.
26. Lange PH, Ercole CJ, Lightner DJ, Fraley EE, Vessella R. The value of serum prostate specific antigen determinations before and after radical prostatectomy. J Urol 1989; 141:873–9.
27. Babaian RJ, Eschenbach AC, Miyashita H, Ramirez EI, Evans RB. Early detection program for prostate cancer: results and identification of high-risk patient population. Urology 1991; 37:193–7.
28. Babaian RJ, Mettlin C, Kane R, Murphy GP, Lee F, Drago JR, et al. The relationship of prostate-specific antigen to digital rectal examination and transrectal ultrasonography. Cancer 1992; 69:1195–200.
29. Lee F, McHugh TA, Solomon MH, Dorr RP, Siders DB, Kirscht L, et al. Transrectal ultrasound, digital rectal examination, and prostate specific antigen: preliminary results of an early detection program for prostate cancer. Scand J Urol Nephrol Suppl 1991; 137: 101–5.
30. Palken M, Cobb OE, Simons CE, Warren BH, Aldape HC. Prostate cancer: comparison of digital rectal examination and transrectal ultrasound for screening. J Urol 1991; 145:86–92.
31. Lee F, Littrup PJ, Torp-Pedersen ST, Mettlin C, McHugh TA, Gray JM, et al. Prostate cancer: comparison of transrectal US and digital rectal examination for screening. Radiology 1988; 168:389–94.
32. Cooner WH, Mosley BR, Rutherford CL, Beard JH, Pond HS, Bass RB, et al. Coordination of urosonography and prostate-specific antigen in the diagnosis of nonpalpable cancer. J Endourol 1989; 3:193–9.
33. Kane RA, Littrup PJ, Babaian R, Drago JR, Lee F, Chesley A, et al. Prostate-specific antigen levels in 1695 men without evidence of prostate cancer. Cancer 1992; 69:1201–7.
34. Chodak GW, Steinberg GD, Bibbo M, Wied G, Straus FS, Vogelzang NJ, et al. The role of transrectal aspiration biopsy in the diagnosis of prostate cancer. J Urol 1986; 135:299–302.
35. Polito M, Alberti G, Muzzonigro G, Baldi A, Diambrini M, Vecchi A. Fine needle aspiration biopsy of the prostate gland: our experience concerning 101 cases with histological follow-up. Prostate 1990; 17:85–94.
36. Beck JR, Kassirer JP, Pauker SG. A convenient approximation of life expectancy (the DEALE): 1. validation of the method and 2. use in medical decision making. Am J Med 1982; 73:883–8, 889–97.
37. Lu-Yao GL, McLerran D, Wasson J, Wennberg JE. An assessment of radical prostatectomy. Time trends, geographic variation, and outcomes. JAMA 1993; 269:2633–6.
38. Fowler FJ, Barry MJ, Lu-Yao G, Roman A, Wasson J, Wennberg JE. Patient-reported complications and follow-up treatment after radical prostatectomy: the National Medicare experience: 1988–1990 (updated June 1993). Urology 1993; 42:622–9.
39. Narayan P, Jajodia P. Prostatic oncology. Clin Geriatr Med 1990; 6:131–61.
40. Wasson JH, Cushman CC, Bruskewitz RC, Littenberg B, Mulley AG, Wennberg JE, et al. A structured literature review of treatment for localized prostate cancer. Arch Fam Med 1993; 2:487–93.
41. Millar JGB. Drug induced impotence. Practitioner 1979; 223:634–9.
42. Crawford ED, Eisenberger MA, McLeod DG, Spaulding JT, Benson R, Dorr FA, et al. A controlled trial of leuprolide with and without flutamide in prostatic carcinoma. N Engl J Med 1989; 321:419–24.
43. Catalona WJ, Avioli LV. Diagnosis, staging, and surgical treatment of prostatic carcinoma. Arch Intern Med 1987; 147:361–3.
44. Volk RJ, Cantor SB, Spann SJ, Cardenas MP, Warren MM. Husbands' and wives' quality of life considerations in the decision to screen for prostate cancer. Med Decis Making 1993; 13:400.
45. Read JL, Quinn RJ, Berwick DM, Fineberg HV, Weinstein MC. Preferences for health outcomes: comparison of assessment methods. Med Decis Making 1984; 4:315–29.
46. Pliskin JS, Shepard DS, Weinstein MC. Utility functions for life years and health status. Operations Res 1980; 28:206–24.
47. Singer PA, Tasch ES, Stocking C, Rubin S, Siegler M, Weichselbaum R. Sex or survival: trade-offs between quality and quantity of life. J Clin Oncol 1991; 9:328–34.
48. SPSS for Windows, version 6. Chicago, Ill: SPSS, Inc, 1993.
49. Hollenberg J. SMLTREE, version 2.9. New York, NY: J Hollenberg, 1989.
50. Fletcher RH, Fletcher SW, Wagner EH. Clinical epidemiology: the essentials. Baltimore, Md: Williams & Wilkins, 1988:159–60.
51. American Cancer Society. Guidelines for the cancer-related checkup: recommendations and rationale. CA Cancer J Clin 1980; 30:4.
52. US Preventive Services Task Force. Guide to clinical preventive services: an assessment of the effectiveness of 169 interventions. Baltimore, Md: Williams & Wilkins, 1989.
53. Cantor SB, Volk RJ, Cardenas MP. Asymptomatic prostate nodules [letter]. J Fam Pract 1992; 35:368.
54. Franks LM. Latent carcinoma of the prostate. J Pathol Bacteriol 1954; 69:603–6.
55. McNeal JE. Origin and development of carcinoma of the prostate. Cancer 1969; 23:24–6.
56. Krahn MD, Mahoney JE, Eckman MH, Trachtenberg J, Pauker SG, Detsky AS. Screening for prostate cancer. A decision analytic view. JAMA 1994; 272:773–80.
57. Voss JD. Prostate cancer, screening, and prostate-specific antigen: promise or peril? J Gen Intern Med 1994; 9:468–74.
58. Christensen-Szalanski JJJ. Discount functions and the measurement of patients' values: women's decisions during childbirth. Med Decis Making 1984; 4:47–58.