Decision Analysis Using Individual Patient Preferences to Determine Optimal Treatment for Localized Prostate Cancer

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BACKGROUND. Selecting treatment for clinically localized prostate cancer remains an ongoing challenge. Previous decision analyses focused on a hypothetical patient with average preferences, but preferences differ for clinically similar patients, implying that their optimal therapies may also differ.

METHODS. A decision model was constructed comparing 4 treatments for localized prostate cancer: 1) radical prostatectomy (RP); 2) external beam radiation (EB); 3) brachytherapy (BT); and 4) watchful waiting (WW). Published data were used regarding treatment success, side effects, and noncancer survival, and 156 men with prostate cancer were surveyed to elicit preferences in quality-adjusted life years (QALYs). The clinical scenarios were determined (age, tumor grade, and prostate-specific antigen [PSA]) for which variations in patient preferences led to different optimal treatments and those for which the optimal treatment was unaffected by preferences.

RESULTS. Patient preferences were critical in determining treatment for low-risk cancers (Gleason score $\leq$6, PSA $\leq$10 ng/mL) and for patients aged 75 years and older. In younger patients with more aggressive tumors, RP and EB were always superior to WW or BT, regardless of preferences (average gain in quality-adjusted life expectancy vs WW for a 60-year-old with a medium-risk tumor = +1.4 years for RP and +1.7 for EB; for a high-risk tumor = +2.1 years for RP and +2.4 for EB). BT was a reasonable option for low-risk tumors at any age. WW was only reasonable for patients aged 70 and older with low-risk tumors or those aged 80 years and older with medium-risk tumors. Selecting treatment based on average preferences leads to suboptimal choices for 30% of patients.

CONCLUSIONS. The optimal treatment for prostate cancer depends on both the clinical scenario (patient age and tumor aggressiveness) and the patient's preferences. Decision analyses taking individualized preferences into account may be a useful adjunct in clinical decision-making. ***Cancer*** **2007;110:2210–7.** © *2007 American Cancer Society.*

KEYWORDS: prostate cancer, decision analysis, quality-adjusted life year (QALY).

Selecting a treatment for clinically localized prostate cancer remains an ongoing challenge for patients and providers. This is partially because of a lack of randomized controlled data, although a recent trial comparing radical prostatectomy (RP) with watchful waiting (WW) provided valuable evidence.[1] However, even if the medical literature provided perfect data, there would still be significant ambiguity regarding the best treatment for any particular patient because prostate cancer treatments involve inherent tradeoffs between length of life and quality of life. Thus, the treatment of prostate cancer presents a clinical dilemma: even with perfect data,

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clinically similar patients should receive different therapies, given that their preferences differ.

In this study, we analyzed the role of patient preferences in determining the optimal individualized treatment for localized prostate cancer using a decision model and a survey of men recently diagnosed with the disease. Previously published decision analyses explore some of these tradeoffs, typically focusing on a representative patient, using average survey responses to quality-of-life measures.[2–4] However, for prostate cancer—and many other conditions—the 'average patient' in terms of preferences is merely a convenient concept, and a decision model using such a hypothetical person may lead to incorrect recommendations.[5] Our decision analysis focuses instead on individualized patient preferences.

Objectives

This study had 2 objectives: 1) Determine the clinical scenarios (age, prostate-specific antigen [PSA], and tumor grade) for which variations in patient preferences lead to different optimal treatments, and those for which the patient's clinical features alone are sufficient to dictate the optimal treatment. 2) Develop a decision model that: a) considers not only surgery, traditional radiation, and WW, but also brachytherapy (interstitial radiation), a treatment not examined in previous models; b) incorporates evidence published since previous decision analyses were conducted; and c) explicitly accounts for variation in individual patient preferences.

MATERIALS AND METHODS

Decision Model

We constructed a decision model featuring 4 treatments for localized prostate cancer: 1) RP; 2) external beam radiation (EB); 3) brachytherapy (BT); and 4) WW. The model employs a Markov framework, whose inputs are transition probabilities from 1 state to another within a specified time period. The model's health states are baseline health, metastatic-free survival but with 1 or more treatment side effects (erectile dysfunction [ED], urinary incontinence, and bowel discomfort), metastatic prostate cancer, and death. Baseline health, which for some patients includes erectile, urinary, and/or bowel symptoms, was assessed in the survey discussed in the next section.

The model incorporates 2 short-term parameters: 1) age-adjusted excess 30-day mortality after RP,[6] and 2) pain/inconvenience ('disutility') of treatment. Disutility of initial treatment was estimated to be equivalent to losing 2 weeks of life expectancy for surgery, following Fleming et al.,[2] and was adjusted to 1 week after radiation because the latter is less invasive but nonetheless imposes some short-term discomfort and inconvenience compared with WW.

TABLE 1
Risk Stratification

	Low risk	Medium risk	High risk
Approach 1	Gleason score 2–4	Gleason score 5–7	Gleason score 8–10
Approach 2	Gleason score $\leq$6 *and* PSA <10 ng/mL	Meeting neither high-risk nor low-risk criteria	Gleason score $\geq$8

PSA indicates prostate-specific antigen.

The probability of metastatic progression after each treatment was determined by Gleason score and PSA. Low-risk, medium-risk, and high-risk tumors were defined using 2 common approaches from the literature, as described in Table 1. When a patient's clinical data produced differing risk profiles depending on the approach, our results include the model's outcomes for both approaches. Similarly, our results include the outcomes of all 3 risk profiles for patients reporting neither Gleason score nor PSA.

Baseline probabilities of metastatic progression at 5 and 10 years after RP come from Gerber et al.[7] and relative risks of disease progression for radiation therapies and WW are taken from D'Amico et al.[8] and Bill-Axelson et al.[1] These studies were chosen because they offered 3 major advantages. They were large multicenter studies, they compared multiple treatments simultaneously, and they stratified by tumor risk. Although recent research has demonstrated improved radiation therapy outcomes using higher EB dosing and newer BT techniques, to our knowledge these studies provided no direct comparisons with RP or WW.[9,10] These latter findings are included in our sensitivity analyses.

A significant methodological concern is that these data regarding posttreatment recurrence were largely collected in the pre-PSA era. Prior research documents a stage migration (toward younger patients with less aggressive tumors) over the past 20 years, associated with increased PSA screening.[11] However, our model controls explicitly for patient age, tumor grade, and PSA. This should minimize any bias from stage migration. We revisit this important topic later in the article. A related concern is grade migration. Currently, pathologists generally assign higher Gleason scores than they did in the 1990s.[12] This trend may bias our analysis toward recommending invasive treatment rather than WW for patients with 'medium-risk tumors' that 15 years ago would have been deemed 'low-risk.' Using PSA along with Gleason

score for risk categorization helps minimize this potential bias, but cannot eliminate it entirely.

In patients who develop metastatic disease, the median survival was estimated at 5 years.[13] For older individuals with an age-adjusted life expectancy of less than 5 years, the model uses the shorter life expectancy.

Among individuals remaining free of metastases, estimates of side effect risk for each treatment (defined by percentage impairment in function) were obtained primarily from a study by Talcott et al.,[14] selected for its prospective design and simultaneous analysis of all 3 treatments (RP, EB, and BT). Data concerning side effects with WW compared with RP come from Steineck et al.[15] Side effects from WW were assumed not to occur until 24 months after diagnosis, whereas side effects from other therapies were observed at 6 months, 12 months, and 24 months. Side effects for all therapies included ED (difficulty maintaining an erection sufficient for intercourse) and urinary incontinence (leakage more than once weekly). Side effects for radiation therapies also included bowel discomfort, such as diarrhea, stool leakage, and pain with defecation. The model allows multiple side effects to be present simultaneously, with each combination representing a unique health state, and the risk of each symptom calculated independently.

Each period in the model incorporates the age-adjusted male risk of dying from causes other than prostate cancer.[16] After 15 years, the model assumes no further risk of metastasis. Cancer-free survivors then return to normal age-adjusted life expectancy. Erectile, urinary, or bowel symptoms still present 2 years after treatment persist for the remainder of the individual's life.

The model's output is the set of quality-adjusted life expectancies (QALEs) for a particular patient, under each treatment. The QALE combines length of life and quality of life in each health state, according to each patient's survey responses. The quality of life for a year in a given state ranges from 0 for death to 1.0 for perfect health. This value is designated the quality-adjusted life year (QALY).[17] We define 'optimal' or 'reasonable' treatment(s) to be those providing the maximal QALE for a particular patient, or a QALE within 3% of the single best treatment.

The model uses a 3% annual discount rate for the base case, following recommendations from a U.S. Public Health Services panel regarding decision analysis.[18]

One-way sensitivity analyses are conducted with the model's parameters varied as follows:

- Progression to metastatic disease at 5 years and 10 years for each treatment: baseline $\pm$ 20%.
- Progression to metastatic disease at 5 years and 10 years for EB, reduced by 49% from baseline, based on a trial comparing high-dose radiation (79.2 grays [Gy]) with conventional dosing (70.2 Gy).[10]
- Progression to metastatic disease at 10 years for BT, using improved PSA-recurrence-free survival at 8 years for high-risk and medium-risk tumors.[9]
- Risk of each side effect for each treatment: baseline $\pm$ 20%.
- Surgical mortality: baseline $\pm$ 20%.
- Short-term disutility for each treatment: baseline $\pm$ 20%.
- Disutility caused by anxiety under WW: QALYs for all nonmetastatic health states reduced by 10% under WW.[19]
- Discount rate: 0, 5%, and 10% annually.

The model was constructed using Microsoft Excel 11.3, and is available in a user-friendly electronic format upon request.

Patient Survey

We surveyed patients with prostate cancer to elicit the following information: 1) preferences (QALYs) regarding health states related to prostate cancer; 2) demographic information; 3) Gleason score, PSA, and self-reported health, as well as the pretreatment presence of ED, urinary incontinence, and/or bowel discomfort; and 4) whether the individual had chosen a treatment by the time of the survey and, if so, which treatment(s).

The survey elicited patient preferences using a time-tradeoff approach. Participants were asked to consider the following hypothetical situation: "Imagine you have 10 years to live. You are in excellent health, except that you have the following condition. . .." The survey then described 1 of the health states in the model. Separate questions were presented for each combination of health states. Then the respondent was asked, "How many years of your life, ranging from 0 to 10 years, would you be willing to sacrifice to achieve ideal health without this condition?" Respondents answered using a combination of years and/or months, allowing respondents to sacrifice partial years. This self-administered preference assessment using a time-tradeoff has been validated and shown reliable by previous research, yielding results comparable to more intensive approaches.[20]

The following survey descriptions of health states were drawn from the Patient-Oriented Prostate Utility Scale and a shared decision-making guide for prostate cancer[21,22]: 1) Erectile dysfunction—"unable

to maintain an erection firm enough to have sexual intercourse, even with the use of medication." 2) Urinary problems—"frequently leaking urine or losing bladder control, interfering with some activities," possibly requiring the individual to "wear pads to help deal with wetness." 3) Bowel problems—"frequent diarrhea, rectal discomfort (pain, burning, or irritation), or constipation." 4) Metastatic prostate cancer—"The disease and its treatment can cause severe bone pain, back pain, hot flashes, nausea, water retention, lack of sexual desire, problems getting erections, weakness, weak bones leading to fractures, and weight gain." 5) Four additional health states consisted of all possible combinations of Items 1–3 above.

Responses to these items were converted into QALYs by the following formula: QALY = (10 − years sacrificed)/10. For example, sacrificing 1 year and 6 months from a 10-year life expectancy to avoid incontinence yields a QALY of 0.85.

Our sample consisted of patients with prostate cancer recruited from 4 outpatient sites (2 radiation oncology and 2 urology sites) at Boston-area hospitals. Inclusion criteria were a diagnosis of clinically localized prostate cancer (T1N0M0, or T2N0M0 disease), and not yet having undergone treatment (surgery, radiation, or hormonal therapy) at the time of the survey. Exclusion criteria were inability to read English or impaired decision-making as judged by the patient's physician. Subjects satisfying the study criteria were given a brief explanation of the research and individuals interested in participating were then identified. Informed consent was obtained and patients were given surveys after the office visit. Surveys were completed at the patient's discretion and submitted anonymously by mail using a preaddressed stamped envelope.

The protocol was approved by Institutional Review Boards at all participating sites.

TABLE 2
Descriptive Statistics for the Sample (N = 156)

Average age (SE), y	61.7 (8.6)
Tumor risk (Gleason score only)	
Low risk (2–4)	9.0%
Medium risk (5–7)	79.5%
High risk (8–10)	7.1%
Unknown	4.5%
Tumor risk (Gleason plus PSA)	
Low risk	46.8%
Medium risk	39.1%
High risk	9.6%
Unknown	4.5%
Pretreatment conditions	
Erectile dysfunction	35.6%
Urinary incontinence	10.9%
Bowel/rectal discomfort	5.1%
Self-reported health	
Excellent	48.1%
Good	44.9%
Fair/poor	7.1%
Race	
White non-Hispanic	89.0%
Black	7.1%
White Hispanic	1.3%
Asian	1.3%
Other	1.3%
Education	
No HS diploma or GED	2.6%
HS diploma/GED	13.5%
Some college	10.3%
College graduate	35.9%
Graduate/professional school	37.8%
Income	
<$30,000	11.1%
$30,000 to $50,000	24.2%
>$50,000	64.7%
Treatment decision*	
Undecided	19.9%
Radical prostatectomy	35.9%
External beam	17.9%
Brachytherapy	25.0%
Watchful waiting	3.8%

SE indicates standard error; PSA, prostate-specific antigen; HS, high school; GED, General Educational Development.

* Indicates the percentage of respondents reporting that they planned to receive a given treatment. Percentages sum to greater than 100% because some patients chose multiple treatments.

RESULTS

Descriptive Statistics

Surveys were distributed to 377 patients, 48.0% of whom responded. Of those who submitted surveys, 16 did not complete the QALY items, and 3 included inappropriate responses (eg, giving up more than 10 years of a 10-year life expectancy to eliminate a side effect); these surveys were excluded from our analysis. Six additional surveys were excluded because they indicated that they were completed after the patient had undergone treatment. This yielded a final sample of 156 patients, the results of which are summarized in Table 2. The average age of the patients was 61.7 years. Many patients experienced symptoms before treatment: 36% reported ED and 10% reported urinary incontinence at baseline. Using the Gleason score to classify risk, 80% were medium-risk, with the remainder nearly evenly divided between high-risk and low-risk. Using both Gleason score and PSA, low-risk was most common (47%), with nearly 40% of patients having medium-risk and 10% having high-risk prostate cancer. The high prevalence of tumors with Gleason scores of 5 to 6 and a PSA level <10 ng/mL, which were considered medium-risk

TABLE 3
Survey Results of QALYs for Disease and Side Effect Health States (N = 156)

	Average QALY	10th–90th percentile
Urinary incontinence	0.905	0.735–1.000
ED	0.921	0.700–1.000
Bowel/rectal discomfort	0.859	0.500–1.000
ED plus urinary incontinence	0.874	0.600–1.000
ED plus bowel discomfort	0.842	0.500–1.000
Bowel discomfort plus urinary incontinence	0.835	0.500–1.000
ED, bowel, and urinary symptoms	0.800	0.500–1.000
Metastatic prostate cancer	0.650	0.200–1.000

QALYs indicates quality-adjusted life-years; ED, erectile dysfunction.

under Approach 1 but as low-risk under Approach 2, accounted for these differences.

QALY Survey Responses

Table 3 presents the survey's 10th and 90th percentiles and average QALY estimates for each health state. Three features are notable. First, the 10th and 90th percentiles indicate wide variations in preferences across the sample. Second, the sample included a significant number of respondents (26 of 156 respondents, or 16.7%) who expressed preferences that maximized life expectancy regardless of side effects, with QALYs of 1.0 for each state. Third, these average QALYs are comparable to previously published values in general magnitude and feature the same ordering of conditions from most to least acceptable.[23]

Decision Model Results

Table 4 provides the QALEs predicted by the model for each treatment, for a variety of clinical scenarios (ie, combinations of age and tumor risk), for a hypothetical patient with the sample's average preferences. BT is an optimal treatment for low-risk tumors at any age. RP and EB are reasonable alternatives for younger patients with low-risk tumors. For patients with medium-risk and high-risk tumors, RP and EB are optimal, even in patients aged 80 years. WW is reasonable only for older patients with low-risk or medium-risk tumors.

However, these results, similar to virtually all results in the literature, are based on a hypothetical patient with average preferences, and should not be directly applied to any particular patient without first assessing his individual preferences. Figure 1 shows the optimal treatment based on the decision model as a function of age and risk profile, taking into account not only average preferences but also the

TABLE 4
QALE for Prostate Cancer Treatment of a Patient With Average Preferences*

	Expected QALE under each treatment, ±3%			
Clinical scenario	**RP**	**EB**	**BT**	**WW**
Age 50 y, low-risk tumor	**15.9 ± −0.5**†	**16.3 ± 0.5**	**16.3 ± 0.5**	15.1 ± 0.5
Age 50 y, mid-risk tumor	**13.2 ± 0.4**	**13.6 ± 0.4**	11.0 ± 0.3	11.0 ± 0.3
Age 50 y, high-risk tumor	**11.2 ± 0.3**	**11.5 ± 0.3**	8.0 ± 0.2	8.0 ± 0.2
Age 60 y, low-risk tumor	**12.8 ± 0.4**	**13.2 ± 0.4**	**13.2 ± 0.4**	12.4 ± 0.4
Age 60 y, mid-risk tumor	**11.1 ± 0.3**	**11.4 ± 0.3**	9.7 ± 0.3	9.7 ± 0.3
Age 60 y, high-risk tumor	**9.6 ± 0.3**	**9.9 ± 0.3**	7.5 ± 0.2	7.5 ± 0.2
Age 70 y, low-risk tumor	9.4 ± 0.3	**9.8 ± 0.3**	**9.8 ± 0.3**	9.4 ± 0.3
Age 70 y, mid-risk tumor	**8.6 ± 0.3**	**8.8 ± 0.3**	8.0 ± 0.2	8.0 ± 0.2
Age 70 y, high-risk tumor	**7.7 ± 0.2**	**7.9 ± 0.2**	6.7 ± 0.2	6.7 ± 0.2
Age 80 y, low-risk tumor	6.2 ± 0.2	**6.4 ± 0.2**	**6.5 ± 0.2**	**6.4 ± 0.2**
Age 80 y, mid-risk tumor	**5.9 ± 0.2**	**6.1 ± 0.2**	**5.9 ± 0.2**	**5.9 ± 0.2**
Age 80 y, high-risk tumor	5.5 ± 0.2	**5.7 ± 0.2**	5.3 ± 0.2	5.4 ± 0.2

QALE indicates quality-adjusted life expectancy; RP, radical prostatectomy; EB, external beam radiation; BT, brachytherapy; WW, watchful waiting.

* This analysis considers the hypothetical average patient, but does not incorporate the study sample's full range of patient preferences. Accordingly, this table should *not* be used to guide individual patient treatment choices.

† QALEs in bold type indicate the optimal treatment(s). When multiple treatments are in bold type, it indicates that >1 treatment resulted in a QALE within 3% of the optimal treatment.

sample's full range of QALYs. Clinical scenarios yielding the same optimal treatment(s) regardless of patient preferences are shown in white. Clinical scenarios in which the optimal treatment(s) varied, depending on preferences, are labeled in shades of gray. Light gray indicates areas in which 3 treatments were potentially optimal and darker gray is employed when all 4 treatments (including WW) were optimal for some patient preferences.

The overall picture shows, literally, a large gray zone—clinical scenarios in which patient preferences are critical to determining the optimal therapy. In general, patient preferences matter more when dealing with low-risk tumors or older patients. In younger patients with more aggressive tumors, RP and EB were always superior to WW and BT, regardless of preferences.

To document how often using average preferences leads to suboptimal therapy, we determined the percentage of patients in our sample that had a different optimal therapy (ie, the single QALE-maximizing treatment) than a patient with the same clinical features but average preferences. In our sample, 30% had a different optimal treatment than the average patient. Treating these patients based on average preferences, instead of their own, would sacrifice 0.13 QALYs on average, a significant loss of 1.5 months of perfect health.

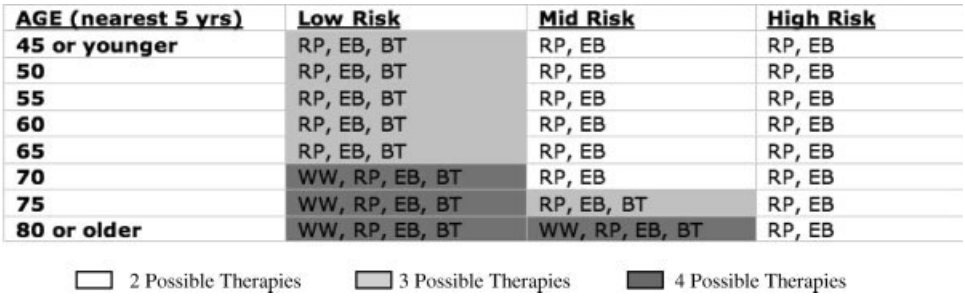

FIGURE 1. Range of optimal treatments based on age and tumor risk profile, across all patient preferences. Each cell contains the set of treatments that were optimal for at least 1 patient in the sample; optimal treatment(s) were defined as any treatment resulting in a quality-adjusted life expectancy (QALE) within 3% of the single best treatment. RP indicates radical prostatectomy; EB, external beam radiation; BT, brachytherapy; WW, watchful waiting.

Sensitivity Analysis

To test our model's robustness, we repeated the analysis in Table 4 while varying the model's parameters as discussed earlier. Our results were highly sensitive to changes in the following parameters: rate of metastatic disease progression after all 4 treatments, incidence of ED after all 4 treatments, and incidence of urinary incontinence after surgery. The results were also affected, to a lesser degree, by changes in surgical mortality, short-term disutility of surgery, anxiety under WW (a 10% decrease in QALYs because of anxiety rendered WW inferior for all clinical scenarios), and the discount rate (lower rates favored RP and EB, whereas higher rates favored WW). Altering the following parameters did not affect the results: short-term disutility of radiation therapy, rates of bowel symptoms after radiation therapy, and urinary incontinence after radiation therapy or WW.

Table 5 summarizes these findings, indicating for a patient with average preferences whether a treatment for a particular clinical scenario was potentially appropriate in all, some, or none of the sensitivity analyses.

TABLE 5
Sensitivity Analysis—When Is Each Treatment Potentially Appropriate for a Patient With Average Preferences?*

Clinical scenario	RP	EB	BT	WW
Age 50 y, low-risk tumor	+	++	+	+
Age 50 y, mid-risk tumor	+	+	–	–
Age 50 y, high-risk tumor	+	+	–	–
Age 60 y, low-risk tumor	+	++	+	+
Age 60 y, mid-risk tumor	+	++	–	–
Age 60 y, high-risk tumor	+	+	–	–
Age 70 y, low-risk tumor	+	++	++	+
Age 70 y, mid-risk tumor	+	++	+	–
Age 70 y, high-risk tumor	+	+	–	–
Age 80 y, low-risk tumor	+	++	++	+
Age 80 y, mid-risk tumor	+	++	+	+
Age 80 y, high-risk tumor	+	+	+	+

RP, radical prostatectomy; EB, external beam radiation; BT, brachytherapy; WW, watchful waiting; +, a particular treatment was an appropriate option for the "average patient" in at least some of the sensitivity analyses; ++, a particular treatment was an appropriate option for the "average patient" across all sensitivity analyses; –, a particular treatment was never appropriate for the "average patient" in any of the sensitivity analyses.

* This analysis considers the hypothetical average patient to assess the model's robustness, but does not incorporate the study sample's full range of patient preferences. Accordingly, this table should *not* be used to guide individual patient treatment choices.

Sensitivity analyses included variations in disease progression, side effects, discount rate, surgical mortality, anxiety, and short-term treatment disutility. Appropriate treatment options are those that produce a quality-adjusted life expectancy (QALE) within 3% of the single best treatment.

DISCUSSION

The current study presents a decision model for localized prostate cancer that incorporates the range of preferences among a sample of men recently diagnosed with the disease. We found that the optimal treatment often depends on individual patient preferences, not merely the clinical scenario (age and tumor aggressiveness). Tradeoffs between quantity and quality of life, as well as among different side effects, often determine which treatment would be optimal for a specific patient. This is especially true for less-aggressive tumors and older patients. Traditional decision analyses using 'average' QALYs—or analogously, clinician advice based on generalizations about patient preferences—will not provide appropriate guidance for many patients.

Our model suggests that for low-risk tumors BT is equally as valid as, and in many cases preferred to, the more traditional therapies, EB and RP. For patients aged 70 years and older with low-risk tumors, and patients aged 80 years and older with low-risk and medium-risk tumors, WW is also sometimes a preferred choice, depending on preferences. However, for patients aged younger than 70 years

with medium-risk or high-risk tumors, only RP and EB were optimal, even when taking into account our sample's full spectrum of preferences. In fact, for high-risk tumors, even patients aged 80 years and older expressed preferences indicating they would benefit from EB or RP. Although the model predicts that surgery may be an acceptable alternative for some patients aged older than 75 years, this would be an unusual treatment that many surgeons might not consider appropriate, and would need to be considered on a case-by-case basis.

Our results differ from previous decision analyses, first and foremost with regard to our attention to individual preferences. For the hypothetical patient with average preferences, our results are largely consistent with the most recent published model, which found that RP and EB provided a benefit over WW for medium-risk tumors until age 75 years, and high-risk tumors until age 80 years.[4] However, unlike that study, we also find a benefit in quality-adjusted life expectancy from potentially curative therapy, compared with WW, for low-risk tumors up to age 70 years. This is likely because our model uses recently published data showing significant benefit 10 years after treatment compared with WW.[1]

Our analysis has several limitations. First, absent evidence from randomized controlled trials, the model relies on observational data for the effectiveness and side effects of radiation therapy. Furthermore, these data come from different patient populations, some from Europe (randomized trials of RP vs WW), and some from the U.S. (observational studies of EB, BT, and RP). However, this limitation is the reality for clinicians and patients, who must make treatment decisions with existing, albeit imperfect, data. We have used the most appropriate observational data available, featuring large multicenter studies and multivariate adjustment, and we have conducted sensitivity analyses to determine when and to what extent our results hinge on these data. Our model also did not consider combinations of therapies, such as radiation therapy plus surgery, or hormonal therapy and radiation, because adequate data for comparisons across such treatments are lacking. Finally, the model did not include obstructive/irritative urinary symptoms after radiation, which may have biased the analysis in favor of radiation therapy. However, previous research suggests that such symptoms are generally limited to the first 3 months after treatment and thus are unlikely to significantly bias our results.[14]

A second concern is the stage migration associated with PSA screening, and the fact that our model uses outcomes data largely collected in the pre-PSA era. As discussed earlier, our model explicitly accounts for each patient's risk-profile, based on age, Gleason score, and PSA, which limits any bias from stage migration. However, it is still possible that the risk posed by clinically detected tumors may differ from the risk from tumors detected by PSA screening, even after controlling for these variables. In that case, our model would overestimate the benefits of radiation therapy and surgery compared with WW. Our sensitivity analysis helps measure the potential magnitude of this bias. If the risk of metastasis with WW were 20% lower than in our baseline case, WW would be a reasonable choice for many 80-year-old men, even those with high-risk tumors, and for men as young as 60 years with low-risk tumors. Ongoing randomized controlled trials on PSA screening should help clarify these issues in the coming years.[24]

Third, our model does not factor in nonprostate comorbidities, instead using age-adjusted mortality for the average American male. Therefore, our results are not directly applicable to patients significantly above or below average in health for their age (apart from prostate cancer).

Our survey has some additional limitations: First, the assessment of QALYs may be sensitive to the modality used, raising the possibility that our data will not generalize to other assessment tools.[25] In particular, the single-item time-tradeoff approach may be subject to framing bias or a ceiling effect, given that 17% of respondents provided QALYs of 1.0 for every state.[26] Fortunately, these concerns are diminished because in addition to having used a validated instrument, the average QALY values in the current study are comparable to previously published values assessed using an interactive standard-gamble approach.[23] Second, our sample was nonrandom and was drawn from a patient population obtaining specialty care at academic medical centers. This may have created a bias toward intervention-oriented patients compared with a sample drawn from a primary care setting that would include some patients who refuse specialty referral after diagnosis. In addition, our sample was younger and of higher socioeconomic status than prostate cancer patients in general. Lastly, there may be geographic patterns in preferences, and all our patients received care in the same city. If anything, these biases toward homogeneity in our sample would lead us to underestimate the true extent of variation in preferences among men with prostate cancer, further supporting our contention that optimal treatments vary widely, even among patients whose clinical presentations are similar.

Conclusions

Based on the results of the current study, we draw 2 primary conclusions. First, given the wide variability in preferences in our sample, treatment decisions for patients with localized prostate cancer should be crafted in response to individual preferences. Second, the decision-making process can be facilitated by decision analyses that take individual preferences into account. In the current study, we did not use our model in actual patient care. However, previous research on similar interventions for other conditions (intended to supplement but not supplant thoughtful discussions between patients and physicians) suggests that this sort of decision aid may significantly benefit patients facing difficult treatment choices.[27] Currently, many patient decisions regarding prostate cancer treatment are based on anecdotes, friends' experiences, or popular misconceptions, and physician treatment recommendations depend on the specialty of the physician in question.[28,29] These factors indicate that there are potentially significant benefits to be gained through using an impartial, evidence-based decision model that explicitly accounts for the preferences of each individual patient.

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