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

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ABSTRACT

**Context:** 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.

**Objective:** To determine the clinical scenarios (age, tumor grade, PSA) for which variations in patient preferences lead to different optimal treatments for localized prostate cancer, and those where the optimal treatment is unaffected by preferences.

**Design:** A decision model comparing four treatments: 1) Radical Prostatectomy (RP); 2) External Beam Radiation (EB); 3) Brachytherapy (BT); and 4) Watchful Waiting (WW). We use published data on treatment success rates, side effects, and non-cancer survival, and a patient survey using a time-tradeoff tool to elicit preferences in quality-adjusted life years (QALY’s).

**Patients:** 156 men with localized prostate cancer, who had not yet undergone treatment.

**Main Outcome:** Each treatment’s quality-adjusted life expectancy (QALE).

**Results:** Patient preferences are critical in determining treatment for low-risk cancers (Gleason \( \leq 6 \), PSA \( \leq 10 \)), and for patients 75 or older. In younger patients with more aggressive tumors, RP and EB were always superior to WW or BT, regardless of preferences (average QALE gain vs. WW for a 60 year-old with middle-risk tumor = +1.4 years for RP, +1.7 for EB; for high-risk tumor = +2.1 years for RP, +2.4 for EB). BT was an appropriate option for low-risk tumors, at any age. WW was only appropriate for patients 70 and older with low-risk tumors, or 80 and older with medium-risk tumors. Selecting treatment based on average preferences would lead to suboptimal choices for 30% of patients.
Conclusions: The optimal treatment for prostate cancer depends on both the clinical scenario – age and tumor aggressiveness – and the patient’s preferences. Decision analyses taking individualized preferences into account may be a useful adjunct to clinical decision-making.
INTRODUCTION

Selecting a treatment for clinically-localized prostate cancer remains an ongoing challenge for patients and providers. This is partially due to a lack of randomized controlled data, though a recent trial comparing radical prostatectomy to watchful waiting provided valuable evidence.\(^1\) But even if the medical literature provided perfect data, there would still be significant ambiguity regarding the best treatment for any particular patient, since tradeoffs between length of life and quality of life are inherent in prostate cancer treatments. Thus, the treatment of prostate cancer presents a clinical dilemma: even with perfect data, clinically similar patients should receive different therapies, given differences in their underlying preferences.

In this paper, we analyze 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 the average survey responses to quality-of-life measures for particular health states.\(^2\sim4\) However, for prostate cancer – and many other clinical 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 on individualized patient choices, rather than a hypothetical “average patient.”

OBJECTIVES

This study has two 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, independent of preferences.

2) Develop a decision model that: a) considers not only surgery, traditional radiation, and watchful waiting, but also brachytherapy (interstitial radiation), which previous models did not examine; b) incorporates evidence published since previous decision analyses were conducted; and c) explicitly accounts for variation in individual patient preferences.

METHODS

Decision Model

We constructed a decision model featuring four possible treatments for localized prostate cancer: 1) Radical Prostatectomy (RP); 2) External Beam Radiation (EB); 3) Brachytherapy (BT); and 4) Watchful Waiting (WW). The model employs a Markov framework, whose inputs transition probabilities from one state to another within a specified time period. The model’s health states are baseline health, metastatic-free survival but with one 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 two short-term parameters from previous studies: (1) age-adjusted excess 30-day mortality after RP, and (2) pain/inconvenience (“disutility”) of treatment. Disutility of initial treatment was estimated to be equivalent to losing two weeks of life expectancy for surgery, following Fleming et al. (1993), and was adjusted to one week following radiation – since the latter is less invasive but nonetheless imposes some short-term discomfort and inconvenience compared to WW.
The probability of metastatic progression in each treatment group was determined by Gleason score and PSA. Low-, medium-, and high-risk tumors were defined using two common classification approaches from the literature, described in Table 1. When a patient’s clinical data produced differing risk profiles depending on which approach was used, our results include the outcomes of the model for both approaches. Similarly, for patients reporting neither Gleason score nor PSA in their survey, our results include the outcomes of all three risk profiles for those patients.

Baseline probabilities of metastatic progression at 5 and 10 years after RP comes from Gerber et al. (1996) and relative risks of progression for radiation therapies and WW are taken from D’Amico et al. (1998) and Bill-Axelson et al. (2005). These studies were chosen because they offered three major advantages. They were large, multi-center studies, they compared multiple treatments simultaneously, and they stratified by tumor risk. While recent research has found improved radiotherapy outcomes using higher EB radiation dosing and newer BT techniques, these studies provided no direct comparisons to RP or WW. These latter findings are included in our sensitivity analyses.

A potential concern is that these data on post-treatment recurrence were largely collected in the pre-PSA era. Prior research documents a stage migration – towards younger patients with less aggressive tumors – over the past 20 years, associated with increased PSA screening. However, our model controls explicitly for patient age, tumor grade, and PSA. This should minimize any bias from stage migration. We revisit this important later in the paper.

In patients developing metastatic disease, median survival was estimated at 5 years. For older individuals with age-adjusted non-cancer life expectancy less than five years, the model uses the shorter life expectancy.
Among individuals remaining free of metastases, estimates of side-effect risk for each treatment were obtained primarily from Talcott et al. (2003), selected for its prospective design and comprehensive analysis of all three treatments (RP, EB, BT) simultaneously.\textsuperscript{13} Data on side effects with WW relative to RP come from Steineck et al. (2002).\textsuperscript{14} Side effects from WW were assumed not to occur until 24 months after diagnosis, whereas side effects from other therapies were observed at 6, 12, and 24 months. Side effects for all therapies included ED (difficulty maintaining 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 for the presence of multiple side effects simultaneously, with each combination a unique health state, and the risk of each symptom calculated independently.

Each period in the model also incorporates the age-adjusted male risk of dying from causes other than prostate cancer.\textsuperscript{15} After 15 years, the model assumes no further risk of metastasis. Cancer-free survivors then return to normal age-adjusted life expectancy. Any erectile, urinary, or bowel symptoms persist for the remainder of the individual’s life.

The model’s output is the set of quality-adjusted life expectancies (QALE’s) for a particular patient, under each treatment. The QALE combines the length of life with estimates of the 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, and this value is designated the quality-adjusted life year (QALY).\textsuperscript{16} We define the optimal treatment(s) to be those providing the maximal QALE for a particular patient, or at least 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 on decision analysis.\textsuperscript{17}

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

* Progression to metastatic disease at 5 and 10 years for each treatment: baseline $\pm$ 20%.
* Progression to metastatic disease at 5 and 10 years for EB, reduced by 49% from baseline, based on a trial comparing high-dose radiation (79.2 Gy) with conventional dosing (70.2 Gy).\textsuperscript{10}
* Progression to metastatic disease at 10 years for BT, using improved PSA relapse-free survival at 8 years for high- and middle-risk tumors.\textsuperscript{9}
* Risk of each side effect for each treatment: baseline $\pm$ 20%.
* Surgical mortality: baseline age-adjusted mortality $\pm$ 20%.
* Short-term disutility for each treatment: baseline adjustment $\pm$ 20%.
* Discount rate: 0, 5%, and 10% annually.

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

**Patient Survey**

We surveyed patients with prostate cancer to elicit the following information: (1) preferences (QALY’s) regarding health states related to prostate cancer and its treatment; (2) demographic information; (3) health status – Gleason score, PSA, self-reported health, and pre-treatment presence of ED, urinary incontinence, and/or bowel discomfort; (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…” At this point the survey described one of the health states in the model. 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. This self-administered assessment of preferences using a time-tradeoff has been validated and shown reliable by previous research, yielding results comparable to other costlier and more intensive approaches.18

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:19-20 (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 #1–3 above.

Responses to these items were converted into QALY’s by the following formula:

\[ \text{QALY} = \frac{10 - \text{years sacrificed}}{10} . \]

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 four outpatient sites – two radiation oncology and two urology – at Boston-area hospitals. Inclusion criteria were (1) patients with clinically-localized prostate cancer (stages T1, N0, M0 or T2, N0, M0); and (2)
patients who had not yet undergone treatment (surgery, radiation, or hormonal therapy) at the
time of the survey. Exclusion criteria were inability to read English, or impaired decision-
making. Subjects satisfying inclusion and exclusion criteria were given a brief explanation of
the study, and individuals interested in participating were then identified. Informed consent was
obtained, and patients were given a blank survey 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.

RESULTS

Descriptive Statistics

Surveys were distributed to 377 patients, of which 48.0% responded. Of submitted
surveys, 16 did not complete the QALY items, and 3 included inappropriate responses (e.g.,
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. Table 2 provides descriptive statistics for the sample. The average age was
61.7 years. Many patients experienced symptoms prior to treatment: 36% reported ED and 10%
urinary incontinence at baseline. Using Gleason score to classify risk, 80% were medium-risk,
with the remainder nearly evenly divided between high- and low-risk. Using both Gleason score
and PSA, low-risk was most common (47%), with nearly 40% medium-risk, and 10% high-risk.
The reason for this difference between classification systems was the high prevalence of tumors
with Gleason scores of 5-6 and PSA < 10, which were medium-risk under Approach 1 but low-risk under Approach 2.

**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 variation in preferences across the sample. Second, the sample included a significant number of respondents (26 of 156, or 16.7%) who expressed preferences that maximized life expectancy regardless of side effects – with QALY’s of 1.0 for each state. Third, these average QALY’s are comparable to previously published values in general magnitude and feature the same ordering of side effects from most acceptable to least.\(^\text{21}\)

**Decision Model Results**

Table 4 provides the QALE’s predicted by the model for each treatment, for a variety of clinical scenarios (i.e. 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 medium- and high-risk tumors, RP and EB are optimal, even in 80 year-old patients. WW is appropriate only for older patients with low- or medium-risk tumors.

But these results, like virtually all results in the literature, are based on a hypothetical patient with average 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 more importantly the sample’s full range of QALY’s. Clinical scenarios that yielded the same
optimal treatment(s) regardless of patient preferences are shown in white. Clinical scenarios in which the optimal treatment(s) varied, depending on patient preferences, are labeled in shades of gray. Light gray indicates where three treatments were potentially optimal, and darker gray is employed when all four 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 may lead to suboptimal therapy, we determined the percentage of patients in our sample that would have had a different optimal therapy (i.e. 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 produce an average loss of 0.13 QALY’s, a significant loss that translates into just over 1.5 months of perfect health.

**Sensitivity Analysis:**

To test how robust these results were, we repeated the analysis in Table 4 while allowing the model’s parameters to vary as discussed in the “Methods” section. Our results were highly sensitive to changes in the following parameters: rate of metastatic progression after treatment for all four modalities, incidence of ED after all four treatments, and incidence of urinary incontinence after surgery. The results were also affected, though to a lesser degree, by changes in surgical mortality, short-term disutility of surgery, and the discount rate (lower discounting
favored RP and EB, whereas higher rates favored WW). Altering the following parameters did not affect the results: Rates of bowel symptoms after radiotherapy, urinary incontinence after radiotherapy or WW, and the short-term disutility of radiotherapy.

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

**DISCUSSION**

This study presents a decision model for localized prostate cancer that takes into account the range of preferences among a sample of men recently diagnosed with the disease. We find that the optimal treatment often depends on the individual patient’s preferences, not merely the clinical scenario (i.e. 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 for older patients. Traditional decision analyses using “average” QALY’s – 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 an equally valid – and in many cases preferred – treatment as the more traditional therapies, EB and RP. For patients 70 and older with low-risk tumors, and patients 80 and older with low- and medium-risk tumors, WW is also sometimes an optimal choice, depending on preferences. However, for patients younger than 70 with medium- or high-risk tumors, only RP and EB were appropriate options – even when taking into account our sample’s full spectrum of preferences. In fact, for high-risk tumors, even
patients 80 years and older expressed preferences indicating they would benefit from EB or RP. While the model predicts that surgery may be an acceptable alternative for some patients over 75, this would be an unusual treatment that many surgeons may 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 in 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, and high-risk tumors until age 80.\textsuperscript{4} However, unlike that study, we also find a benefit in quality-adjusted life expectancy from potentially-curative therapy, compared to WW, in low-risk tumors up to age 70. This is likely due to our model’s use of recently published data showing significant benefit 10 years after treatment, compared to WW.\textsuperscript{1}

Our analysis has several limitations. First, absent evidence from randomized controlled trials, the model relies on observational data for treatment effectiveness and side effects for radiotherapies. 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 does not consider combinations of therapies, such as radiation plus surgery, since adequate data for comparisons across such treatments are lacking.

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 the risk-profile of each patient’s disease, based on age, Gleason...
score, and PSA, which limits the bias of stage migration. It is still possible, however, that the risk posed by clinically-detected tumors may differ from the risk from tumors detected by PSA screening, even controlling for these variables. In that case, our model would overestimate the benefits of radiotherapy and surgery, relative to 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 an appropriate choice for many 80 year-old men even with high-risk tumors, and for men as young as 60 with low-risk tumors. Ongoing randomized controlled trials on PSA screening should help clarify these issues in the coming years.  

Third, our model does not factor in non-prostate 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).

Lastly, our survey has two potential limitations: (1) The assessment of QALY’s may be sensitive to the modality used, raising the possibility that our data will not generalize to other assessment tools. Fortunately, this concern is diminished because in addition to having used a validated instrument, the average QALY values in our study are comparable to previously published values assessed using an interactive standard-gamble computer program. (2) Our sample was non-random and was drawn from a patient population obtaining specialty care at academic medical centers. This may have created a bias towards more intervention-oriented patients, as compared to a sample drawn from a primary care setting that would include some patients who refuse specialty referral after diagnosis. Additionally, on average, our sample was relatively young and of higher socioeconomic status than prostate cancer patients in general. Lastly, there may be geographic patterns in preferences, and all of our patients received care in
the same city. If anything, these biases towards 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 the optimal treatment will vary widely, even among patients whose clinical presentations are similar.

**Conclusions:**

We draw two primary conclusions: First, given the wide variability in preferences in our sample, treatment decisions for 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 this study we did not incorporate our model into 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. Currently, many patient decisions regarding prostate cancer treatment are based on anecdote, friends’ experiences, or popular misconceptions, and physician recommendations for therapy depend on the specialty of the physician in question. These factors indicate that there is potentially significant benefit to be gained through using an impartial, evidence-based decision model that explicitly accounts for the preferences of each individual patient.
Authorship Contributions:

Study concept and design: Sommers, D’Amico, Zeckhauser

Acquisition of data: Sommers, Beard, Dahl, Kaplan, Richie

Data analysis and interpretation: Sommers, Beard, D’Amico, Dahl, Kaplan, Richie, Zeckhauser

Drafting of manuscript: Sommers, Zeckhauser

Critical revision of manuscript: Sommers, Beard, D’Amico, Dahl, Kaplan, Richie, Zeckhauser

Statistical Analysis: Sommers, Zeckhauser

Study Supervision: Sommers, Beard, D’Amico, Dahl, Kaplan, Richie, Zeckhauser

Dr. Sommers had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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TECHNICAL APPENDIX: DETAILS ON DESIGN OF THE DECISION MODEL

**BT vs. WW:** Rates of progression for medium- and high-risk tumors treated with BT reported in D’Amico et al. (1998) were higher than those reported for WW in Bill-Axelson et al. (2005). This is likely due to differences in their respective study populations. Given the biologic implausibility of this ordering, in the model, we normalized the metastatic risk after BT to be no worse than the risk under watchful waiting.

**RP vs. EB:** D’Amico et al. (1998) found no statistically significant difference in metastatic progression between RP and EB, across all three risk groups. Accordingly, the model uses equivalent risk progressions for these two treatments.

**Time to Metastasis:** The model assumes no metastasis occurred in the first year after treatment. From years 10 until 15, the model assumes the same rate of progression per year as between years 5 and 10. After year 15, there is no additional risk of metastasis.

**Prognosis by Risk Profile:** Bill-Axelson et al. (2005) performed subgroup analyses and found no significant differences in the relative risk of disease-specific survival between WW and RP, based on Gleason score and PSA. The other studies did find differences in relative risk across these risk profiles, and the model reflects their findings. In classifying our sample into risk profiles, for surveys that did not include sufficient information to use one of the classification systems (e.g., patients only reporting the Gleason score but not PSA), the other classification system was used.

**Persistence of Side Effects:** Two years after treatment, the prevalence of major treatment or tumor related side effects appears to be fairly stable, with the possible exception that erectile dysfunction may worsen over time in EB patients. Given the lack of conclusive data

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along these lines, we followed the general evidence that recovery of function and/or development of new symptoms would occur by 2 years and afterwards be stable.

**Appendix Figure A-1: Markov Model Transitions from Diagnosis until 24 Months**
Appendix Figure A-2: Markov Model Transitions After 24 Months

- Baseline Health
- Bowel Discomfort
- Urinary Incontinence
- Erectile Dysfunction
- Bowel, Erectile, Urinary Symptoms
- Bowel & Urinary Symptoms
- Bowel & Erectile Symptoms
- Erectile & Urinary Symptoms
- Metastatic Prostate Cancer
- Death
REFERENCES


7 - Gerber, Glenn S. MD; Thisted, Ronald A. PhD; Scardino, Peter T. MD; et al., 1996. Results of Radical Prostatectomy in Men With Clinically Localized Prostate Cancer: Multi-institutional Pooled Analysis. JAMA. Vol 276(8): 615-619.

8 - D’Amico AV; Whittington R; Malkowicz SB; Schultz D; Blank K; Broderick GA; Tomaszewski JE; Renshaw AA; Kaplan I; Beard CJ; Wein A. 1998. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA Vol 280(11):969-74.


14 - Steineck G; Helgesen F; Adolfsson J; et al., 2002. Quality of Life after Radical Prostatectomy or Watchful Waiting. NEJM. Vol 347(11): 790-796.


<table>
<thead>
<tr>
<th>Approach 1:</th>
<th>Low Risk</th>
<th>Medium Risk</th>
<th>High Risk</th>
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<tr>
<td></td>
<td>Gleason score 2-4</td>
<td>Gleason score 5-7</td>
<td>Gleason score 8-10</td>
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<tr>
<td>Approach 2:</td>
<td>Gleason score ≤ 6 AND PSA &lt; 10</td>
<td>Meeting neither high nor low risk criteria</td>
<td>Gleason score ≥ 8 OR PSA ≥ 20</td>
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### TABLE 2: DESCRIPTIVE STATISTICS FOR THE STUDY SAMPLE (N = 156)

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<th>Average Age (Standard Error)</th>
<th>61.7 (8.6)</th>
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<tr>
<td></td>
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<td>- White Non-Hispanic 89.0%</td>
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<td></td>
<td>- Black 7.1%</td>
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<td></td>
<td></td>
<td>- White Hispanic 1.3%</td>
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<tr>
<td>Tumor Risk (Gleason only)</td>
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<td>- Asian 1.3%</td>
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<tr>
<td>- Low Risk (2-4)</td>
<td>9.0%</td>
<td>- Other 1.3%</td>
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<tr>
<td>- Medium Risk (5-7)</td>
<td>79.5%</td>
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<td>- High Risk (8-10)</td>
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<tr>
<td>- Unknown</td>
<td>4.5%</td>
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<td>Tumor Risk (Gleason+PSA - see Table 1)</td>
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<td>- Medium Risk</td>
<td>39.1%</td>
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<td>Pretreatment Conditions</td>
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<td>- Erectile Dysfunction</td>
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<td>- Urinary Incontinence</td>
<td>10.9%</td>
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<td>- Bowel / Rectal Discomfort</td>
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<td>Self-Reported Health</td>
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<td>7.1%</td>
<td>- Radical Prostatectomy 35.9%</td>
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<td>- Brachytherapy 25.0%</td>
</tr>
<tr>
<td>- $30,000 to $50,000</td>
<td>24.2%</td>
<td>- Watchful Waiting 3.8%</td>
</tr>
<tr>
<td>- Greater than $50,000</td>
<td>64.7%</td>
<td></td>
</tr>
</tbody>
</table>

*Note: Treatment Decision categories sum to greater than 100%, because some patients indicated that they had decided to receive more than one treatment simultaneously.*
<table>
<thead>
<tr>
<th>Health State</th>
<th>Average QALY</th>
<th>10th percentile - 90th percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary Incontinence</td>
<td>0.905</td>
<td>0.735 - 1.000</td>
</tr>
<tr>
<td>Erectile Dysfunction (ED)</td>
<td>0.921</td>
<td>0.700 - 1.000</td>
</tr>
<tr>
<td>Bowel / Rectal Discomfort</td>
<td>0.859</td>
<td>0.500 - 1.000</td>
</tr>
<tr>
<td>ED + Urinary Incontinence</td>
<td>0.874</td>
<td>0.600 - 1.000</td>
</tr>
<tr>
<td>ED + Bowel Discomfort</td>
<td>0.842</td>
<td>0.500 - 1.000</td>
</tr>
<tr>
<td>Bowel Discomfort + Urinary Incontinence</td>
<td>0.835</td>
<td>0.500 - 1.000</td>
</tr>
<tr>
<td>ED, Bowel, + Urinary Symptoms</td>
<td>0.800</td>
<td>0.500 - 1.000</td>
</tr>
<tr>
<td>Metastatic Prostate Cancer</td>
<td>0.650</td>
<td>0.200 - 1.000</td>
</tr>
</tbody>
</table>
**TABLE 4: QUALITY-ADJUSTED LIFE EXPECTANCY (QALE) FOR PROSTATE CANCER TREATMENT OF A PATIENT WITH AVERAGE PREFERENCES**

This table should *not* be used to guide individual patient treatment choices.*

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>RP</th>
<th>EB</th>
<th>BT</th>
<th>WW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 60, Low Risk Tumor</td>
<td>12.8</td>
<td>13.2</td>
<td>13.2</td>
<td>12.4</td>
</tr>
<tr>
<td>Age 60, Mid Risk Tumor</td>
<td>11.1</td>
<td>11.4</td>
<td>9.7</td>
<td>9.7</td>
</tr>
<tr>
<td>Age 60, High Risk Tumor</td>
<td>9.6</td>
<td>9.9</td>
<td>7.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Age 70, Low Risk Tumor</td>
<td>9.4</td>
<td>9.8</td>
<td>9.8</td>
<td>9.4</td>
</tr>
<tr>
<td>Age 70, Mid Risk Tumor</td>
<td>8.6</td>
<td>8.8</td>
<td>8.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Age 70, High Risk Tumor</td>
<td>7.7</td>
<td>7.9</td>
<td>6.7</td>
<td>6.7</td>
</tr>
<tr>
<td>Age 80, Low Risk Tumor</td>
<td>6.2</td>
<td>6.4</td>
<td>6.5</td>
<td>6.4</td>
</tr>
<tr>
<td>Age 80, Mid Risk Tumor</td>
<td>5.9</td>
<td>6.1</td>
<td>5.9</td>
<td>5.9</td>
</tr>
<tr>
<td>Age 80, High Risk Tumor</td>
<td>5.5</td>
<td>5.7</td>
<td>5.3</td>
<td>5.4</td>
</tr>
</tbody>
</table>

*Notes: RP = Radical Prostatectomy, EB = External Beam Radiation, BT = Brachytherapy, WW = Watchful Waiting
QALE’s in bold indicate the optimal treatment(s). Where multiple treatments are in bold, it indicates that more than one treatment resulted in a QALE within 3% of the optimal treatment.

* This analysis considers the hypothetical average patient, but does not incorporate our sample’s full range of patient preferences. Accordingly, this table should *not* be used to guide individual patient treatment choices.
**FIGURE 1: RANGE OF OPTIMAL TREATMENT CHOICES BASED ON AGE & TUMOR RISK PROFILE, ACROSS ALL PATIENT PREFERENCES**

<table>
<thead>
<tr>
<th>AGE (nearest 5 yrs)</th>
<th>Low Risk</th>
<th>Mid Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>45 or younger</td>
<td>RP, EB, BT</td>
<td>RP, EB</td>
<td>RP, EB</td>
</tr>
<tr>
<td>50</td>
<td>RP, EB, BT</td>
<td>RP, EB</td>
<td>RP, EB</td>
</tr>
<tr>
<td>55</td>
<td>RP, EB, BT</td>
<td>RP, EB</td>
<td>RP, EB</td>
</tr>
<tr>
<td>60</td>
<td>RP, EB, BT</td>
<td>RP, EB</td>
<td>RP, EB</td>
</tr>
<tr>
<td>65</td>
<td>RP, EB, BT</td>
<td>RP, EB</td>
<td>RP, EB</td>
</tr>
<tr>
<td>70</td>
<td>WW, RP, EB, BT</td>
<td>RP, EB</td>
<td>RP, EB</td>
</tr>
<tr>
<td>75</td>
<td>WW, RP, EB, BT</td>
<td>RP, EB, BT</td>
<td>RP, EB</td>
</tr>
<tr>
<td>80 or older</td>
<td>WW, RP, EB, BT</td>
<td>WW, RP, EB, BT</td>
<td>RP, EB</td>
</tr>
</tbody>
</table>

- 2 Possible Therapies
- 3 Possible Therapies
- 4 Possible Therapies

*Notes: RP = Radical Prostatectomy, EB = External Beam Radiation, BT = Brachytherapy, WW = Watchful Waiting*

Each cell contains the set of treatments that were optimal for at least one patient in the sample; optimal treatment(s) were defined as any treatment resulting in a QALE within 3% of the maximum QALE across all four treatments.
TABLE 5: SENSITIVITY ANALYSIS – WHEN IS EACH TREATMENT APPROPRIATE FOR A PATIENT WITH AVERAGE PREFERENCES?

This table should *not* be used to guide individual patient treatment choices.*

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>RP</th>
<th>EB</th>
<th>BT</th>
<th>WW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 60, Low Risk Tumor</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Age 60, Mid Risk Tumor</td>
<td>+</td>
<td>++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Age 60, High Risk Tumor</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Age 70, Low Risk Tumor</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Age 70, Mid Risk Tumor</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Age 70, High Risk Tumor</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Age 80, Low Risk Tumor</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Age 80, Mid Risk Tumor</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Age 80, High Risk Tumor</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*Notes: RP = Radical Prostatectomy, EB = External Beam Radiation, BT = Brachytherapy, WW = Watchful Waiting

* This analysis considers the hypothetical average patient in order to assess the model’s robustness, but does not incorporate our 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, and short-term disutility of treatment. Appropriate treatment options are defined as those that produce a QALE within 3% of the single best treatment.

++ Indicates that a particular treatment was an appropriate option for the "average patient" across all scenarios in the sensitivity analysis.

+ Indicates that a particular treatment was an appropriate option for the "average patient" in at least some scenarios in the sensitivity analysis.

– Indicates that a particular treatment was never appropriate for the "average patient" in any scenarios in the sensitivity analysis.