ACTIVE SURVEILLANCE VS SURGERY IN LOW-RISK PROSTATE CANCER: A CLINICAL DECISION ANALYSIS

APPENDIX

EXTERNAL VALIDATION

To validate the radical prostatectomy arm of our model, we compared outcomes from a large modern era cohort of men[1] with low-risk disease treated with surgery, to outcomes from our model assuming excellent health and a matched age of diagnosis. Observed prostate cancer specific survival (PCSS) at 5 and 10 years was 99.8% and 99.7%, compared to 99.8% and 99.0% from the model. Observed metastasis-free survival at 5 and10 years was 99.6% and 99.0% compared to 99.2% and 97.8% from the model. Observed overall survival at 5 and 10 years was 97% and 91% compared to 96% and 90% from the model.

Though there is no long-term data of men managed with surveillance, men diagnosed and treated in the pre-PSA screening era are similar to men with screen-detected disease who delay intervention. Thus, to validate our active surveillance model, we compared outcomes of men from the RP arm of the SPCG-4 trial[2] to men in our model undergoing active surveillance. In our model, we assumed average health, starting age of 59 years, and median age at surgery of 65 years (matching the median age of men in the SPCG-4 trial). However, our model population includes a significant proportion of men who in the pre-screening era would never have been diagnosed or had symptomatic

disease. Thus, we adjusted our outcomes for an overdiagnosis rate of 45%[3]. Observed PCSM at 8 and 12 years was 5.5% and 12.5% compared to an adjusted PCSM of 5.5% and 10.4% from the model. Observed metastasis at 8 and 12 years was 11.5% and 19.3% compared to 11.5% and 17.6% from the model. Observed overall mortality at 8 and 12 years was 17.9% and 32.7% compared to 27% and 40% from the model, which could be due to better-than-average baseline health status of men participating in the RCT.

Finally, we compared results of our model against non-published results from the PIVOT trial[4]. For a cohort of 200,000 men aged 67 years at diagnosis (matching the mean age of diagnosis in the PIVOT cohort) and followed for 12 years, prostate cancer specific mortality in the active surveillance and surgery arms were 1.7% and 1.2%, respectively, compared to 2.7% and 4.1% as reported in the low-risk subgroup of the PIVOT trial, and overall mortality was 35.1% and 34.4%, as compared to 36.5% and 41.9% in the PIVOT trial. The absolute risk reductions in overall mortality and prostate cancer specific mortality found in our model (0.7% and 0.5% respectively) are well within the confidence intervals of the absolute risk reduction found in the low-risk subgroup of the PIVOT trial (-16.3% to 5.7% for overall mortality, -6.2% to 3.2% for PCSM).

MODEL OUTCOME: Quality Adjusted Life Expectancy (QALE)

For each simulated patient in our study, we multiply the utility (value between 0-1.0) of his health state by the duration of time in that state to generate quality-adjusted

life years (QALYs). The average number of QALYs per simulated patient in each arm (surgery or surveillance) is defined as the QALE.

It is unclear whether the high anchor point in most studies we derive our utilities from is "perfect health", or "best possible health". But "perfect health" is standard, and therefore we assume that our utilities are anchored at "perfect health" as 1. Thus, 1 quality adjusted life year (QALY) in our study is a year of life in perfect health.

In our study, we ignore health states other than prostate cancer states with or without treatment side effects. Thus, a man with asymptomatic prostate cancer and incontinence and impotence for one year at age 55 has the same number of QALYs as a man with asymptomatic prostate cancer and incontinence and impotence for one year at age 75, despite it being highly likely that the 75 yr old man has additional comorbidities that affect his quality of life. This would be problematic if we were comparing QALYs for a 55 yr old vs. QALYs for a 75 yr old. However, since we only compare QALYs between surgery and surveillance for men of the same age and comorbidity status (consistent with the patient perspective of our analysis), this simplifying assumption still allows us to make this direct comparison in a valid way.

MODEL PARAMETERS: LITERATURE SEARCH

Data sources for model parameters were determined by a Cochrane and Pubmed search, as well as review of a recent meta-analysis by Hayes, Ollendorf, and colleagues[5, 6]. Relevant papers were read and their references reviewed for additional sources. One author (DL) conducted the search, reviewed results with a

second author (HBC), and a joint decision was made on inclusion. Model parameter values and ranges are described in Appendix Table 2. Studies included in model parameter base values and sensitivity analysis ranges are described in Appendix Tables 3-12.

MODEL PARAMETERS: Transition probabilities

For the surgery model, we focused on disease progression probabilities from PSA-era cohorts of men with low-risk disease treated with radical prostatectomy (Appendix Table 3). However, there was a lack of data on disease progression from post-treatment biochemical evidence of disease (i.e. detectable PSA) to clinically metastatic disease in men with low-risk disease treated with radical prostatectomy in the PSA era. To estimate this parameter, we used an observed prostate cancer specific mortality outcome and the baseline value of all other transition probabilities to calculate a parameter value that would result in the desired outcome. We calculated a 20-yr prostate cancer specific mortality of 3.1-3.9% for men with low-risk prostate cancer treated with radical prostatectomy using long-term outcomes by pathologic Gleason score from a large multi-center study[7] and pathologic Gleason scores of men with low-risk disease treated with surgery in a large institutional database[8]. The resulting parameter values were checked and consistent with values calculated using outcomes from a separate cohort of men with low-risk disease[9].

For the surveillance model, we used data from existing active surveillance cohorts to determine the probability of progression to treatment (Appendix Tables 10, 11). There

is a lack of data to determine the increased risk of disease progression with delayed treatment, which is a key model parameter. We modeled the increased risk by assuming that all men who progressed to treatment on surveillance because of biopsy upgrades (e.g. from GS <= 6 to GS >= 7) had an increased rate of disease progression equivalent to the hazard rate ratio for prostate cancer mortality of men with intermediate risk disease vs. men with low-risk disease (D'Amico risk stratification[10]). Everyone else who progressed to treatment for other reasons (e.g. PSA increase, DRE exam change) was assumed to have the same risk of disease progression as their counterparts who had immediate surgery. The increased risk of disease progression for men on surveillance was calculated to be a weighted average based on the proportion of men on surveillance who progressed to treatment because of biopsy upgrade. For our model, we assumed that only men who progressed to treatment were at risk of further disease progression. To estimate the probability of progression to treatment and biopsy upgrading on surveillance, we used data from PSA-era low-risk active surveillance cohorts with at least 30 men at 5 years of follow-up[11-15] **(Appendix Tables 10, 11).** For our baseline values, we chose the highest observed values, i.e. 10% annual probability of progression to treatment, and 3.9% annual probability of biopsy upgrade (Appendix Table 2).

The age-specific probabilities of dying from competing causes of death were taken from Social Security life tables[16]. To simulate poor and excellent health status equivalent to 50% and 150% of the average life expectancy, average age-specific probabilities of death were modified by a constant factor for each age/health status combination. This constant factor was determined by a binary search[17], stopping when life expectancy was within 0.01 years of the target.

A shorter time to biochemical recurrence has been found to be associated with more rapid progression to metastatic disease, and therefore we estimated a factor to adjust this probability when time to biochemical recurrence was 2 years or less[18] (Appendix Table 8).

MODEL PARAMETERS: Side Effects

For surgery, the most common and important post-treatment side effects affecting quality of life are incontinence and erectile dysfunction (ED)[19]. Typically, these symptoms are worse immediately after surgery, then improve up to 2 years after treatment[20]. To simplify the analysis, we ignored acute treatment side effects that resolved over time, and assumed side effects that began immediately after treatment and persisted thereafter, using rates of persistent ED and incontinence from the literature. We chose to use age-specific rates reported by Loeb et al[21](Appendix Table 2). To our knowledge, this is the only study specifically reporting outcomes on men with low-risk disease treated in the PSA era, and represents the side effect rates from a highly-specialized and experienced surgeon at an academic center, thus representing a best case scenario for treatment side effects. Average side effect rates were significantly higher in studies not used in this model[19, 20, 22-25] **(Appendix Table 9)**. These choices minimize the side effects from treatment and thus bias the model for surgery against surveillance.

Side effect rates for an age range (e.g. 50-59, 60-69 years) were assumed to be the rate for the median of that range (e.g. 55, 65 years), and rates for intervening ages were estimated by linear interpolation.

MODEL PARAMETERS: Utilities

The utility of the various disease states and side effect states ranged from 0 ("as good as dead") to 1 ("perfect health"), and were estimated based on a review of the literature since 2000, a date chosen to reflect modern management and understanding of prostate cancer and treatment side effects (Appendix Table 11). Only studies that elicited utilities using standard gamble or time tradeoff from prostate cancer patients or older men at risk for prostate cancer were included, and from studies that elicited both we used average values and the larger of the variances (a conservative approach). Studies eliciting utilities from individuals not at risk (e.g. spouses, clinicians) were excluded. In total, 10 studies were included[26-35]. For each utility we estimated an average and variance following previously published methods[36].

Prostate cancer rarely causes symptoms until it is metastatic and no longer responsive to hormonal therapy. Thus, utility of an asymptomatic prostate cancer health state represents the psychological toll of the threat of disease, rather than physical symptoms. Studies of utility of prostate cancer states to date have not adequately addressed utilities in well-informed men with low-risk disease who understand that their risk of dying from prostate cancer is low. In particular, the utility of the state of surveillance (with asymptomatic untreated disease potentially causing anxiety) has not been well-studied; however, Steineck and Johansson et al found that men randomized to no treatment and watchful waiting were comparable in worry, anxiety, and depression to men randomized to RP in the SPCG-4 trial[37, 38]. Therefore, asymptomatic disease states,

including surveillance, no evidence of disease (after treatment), and biochemical evidence of disease were assigned base-case utilities of 1, and allowed to vary up to 20% (down to .8) in the sensitivity analysis.

The utility of a given period of time in a simulated life is calculated as the product of the utility of the disease state and the utility of any side effects from treatment. We chose the multiplicative model rather than the additive model or a lexicographically ordered model because of the properties of the multiplicative model (e.g. ranges between 0 and 1, automatic scaling) and an assumption of qualitative equivalence between stage of disease and side effect quality of life adjustments. The number of QALYs for a simulated life was calculated by summing the products of utility and the time spent in that state for a given life, and QALE calculated as the average number of QALYs per life for a cohort.

MODEL SIMULATION: Time Frame and Analytic Horizon

Each management option was initiated at the time of prostate cancer diagnosis, and we used a lifetime analytic horizon, reflecting the fact that the adverse effects of prostate cancer and benefits of treatment are captured only with long-term follow up.

MODEL SIMULATION: Cycle Length and Discount Rate

We used a Markov model cycle length of 3 months to reflect the minimum time for an event or transition in our model, and a baseline discount rate of 3% per year for QALYs[39].

MODEL PARAMETERS: BIASES AGAINST SURVEILLANCE

We wanted to avoid biasing our model for surveillance. **Thus, we chose baseline model parameters for active surveillance that resulted in the worst survival outcomes (e.g. the highest rates of progression to treatment reported, the highest proportion of biopsy-progression, and the highest HR for intermediate risk vs. low risk disease). Further, we only included long-term surgical side effects and ignored short-term surgical side effects that resolved over time, and used side effect rates from a specialty center with low rates of sides effects relative to centers where most surgeries occur today[21]. As a result, we see significantly worse prostate cancer outcomes in our model for men on active surveillance, e.g. for a 65-yr old man in average health, initial surveillance vs. surgery results in lifetime prostate cancer specific mortality that is more than twice that under initial surgery (8.6% vs. 3.7%), or a relative risk of death in the surgery group of 0.43 (compared to 0.62 in the SPCG-4 trial for surgery vs. watchful waiting in men with more advanced disease). We feel that given current data, this can reasonably be considered a "worst-case" for active surveillance relative to surgery. Thus, in cases where our model concludes that surveillance is a better option than surgery, these conclusions are likely to be robust.**

THRESHOLD ANALYSES

Threshold ages above which surveillance resulted in greater expected QALYs compared to surgery were estimated by a linear interpolation between the two ages where the choice that optimized QALE changed, and rounded up to the nearest year.

SENSITIVITY ANALYSES

A range of values for each model parameter was generated, either reflecting the range of values found in the literature or allowing 20-50% variation, reflecting uncertainties in model parameters and variation in patient preferences. To determine the effects of uncertainty and variation in model parameters on the optimal choice of management strategy, we constructed a Tornado diagram for the base case of a 65 year old in average health **(Appendix Figure 2)**. Outcomes were generated for a cohort of 200,000 men under surgery and surveillance, varying each model parameter from the highest to lowest possible values within their range while holding all other parameters constant. These outcomes were examined to determine the model parameters in which uncertainty or variation caused the greatest difference between surveillance and surgery in QALE. We constructed additional Tornado diagrams for ages 50, 65, and 75 yrs in excellent, average, and poor health to examine the differences in sensitivity when age and health status varied.

To identify the patient preferences with the greatest effect on the choice of surgery vs surveillance, we calculated the change in difference in QALE between surveillance and surgery per 0.1 change in utility for each quality of life utility. We conducted this analysis for men aged 50, 65, and 75 yrs in excellent, average, and poor health **(Appendix Figure 3)**.

To assess the robustness of results to simultaneous uncertainty in model parameters and variation in patient preferences, we conducted a probabilistic sensitivity analysis[40-42] where all model parameters were allowed to vary. Each parameter was modeled as a pert distribution[43] (a modified beta distribution similar to a triangular distribution with smoothed curves) between the minimum and maximum value of its range, assuming the baseline parameter value was the mode of the distribution. For each simulation, a value for each parameter was sampled from its distribution, and a cohort of 10,000 men simulated with this new set of parameters. Five hundred simulations for each age and health status combination were run to generate a set of outcomes sampling from the space of all possible model parameters. These results were used to generate confidence intervals for outcomes, as well as determine the proportion of simulations where surveillance was more effective (i.e. had higher QALE) than surgery.

STATISTICAL ANALYSIS

Typically, to generate 95% confidence intervals for an univariate outcome of Monte Carlo simulations, a probabilistic sensitivity analysis is performed and the 2.5th to 97.5th percentile of outcomes in those simulations are used[40]. However, we had multiple

outcomes. To generate 95% confidence intervals without making any assumptions about correlation of outcomes, we normalized each simulation outcome to a mean of 0 and standard deviation of 1, then plotted each simulation as a point on a n-dimensional (n = number of different outcomes) graph assuming each outcome was on an orthogonal axis centered at 0. We calculated a 95% "cloud" to contain the 95% of simulations with minimum distance from the origin of this graph, then used the minimum and maximum values in this cloud as the 95% confidence interval for each outcome. This was repeated for each age and health status combination. As compared to using the 2.5^{th} to 97.5^{th} percentile of all outcomes separately, this resulted in larger (i.e. more conservative) confidence intervals.

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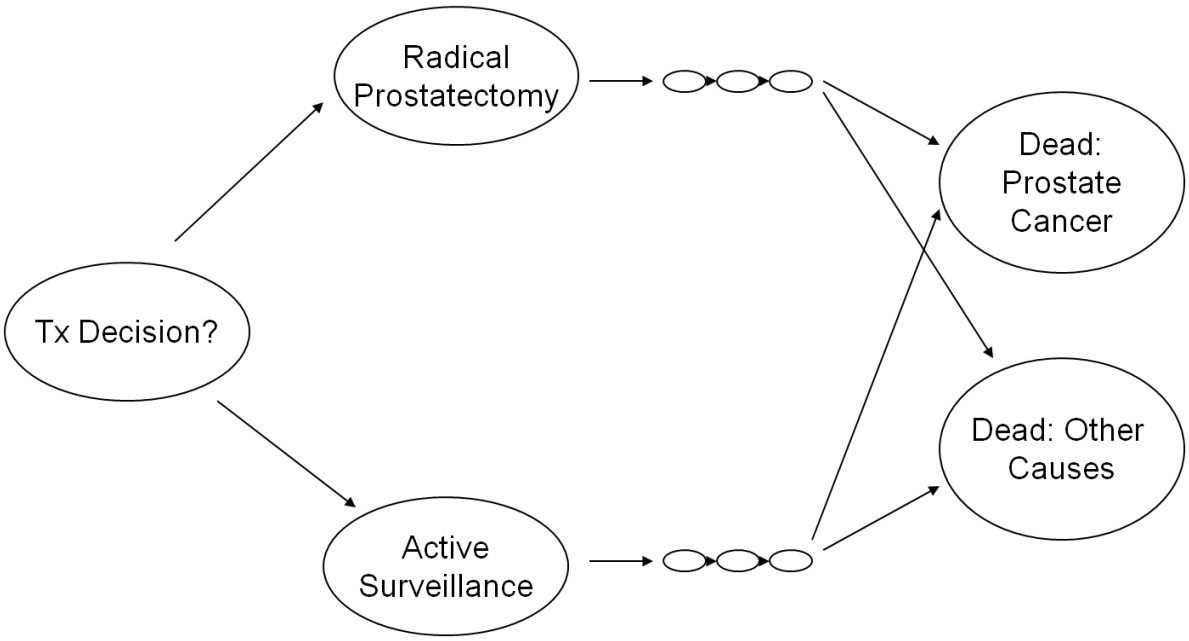
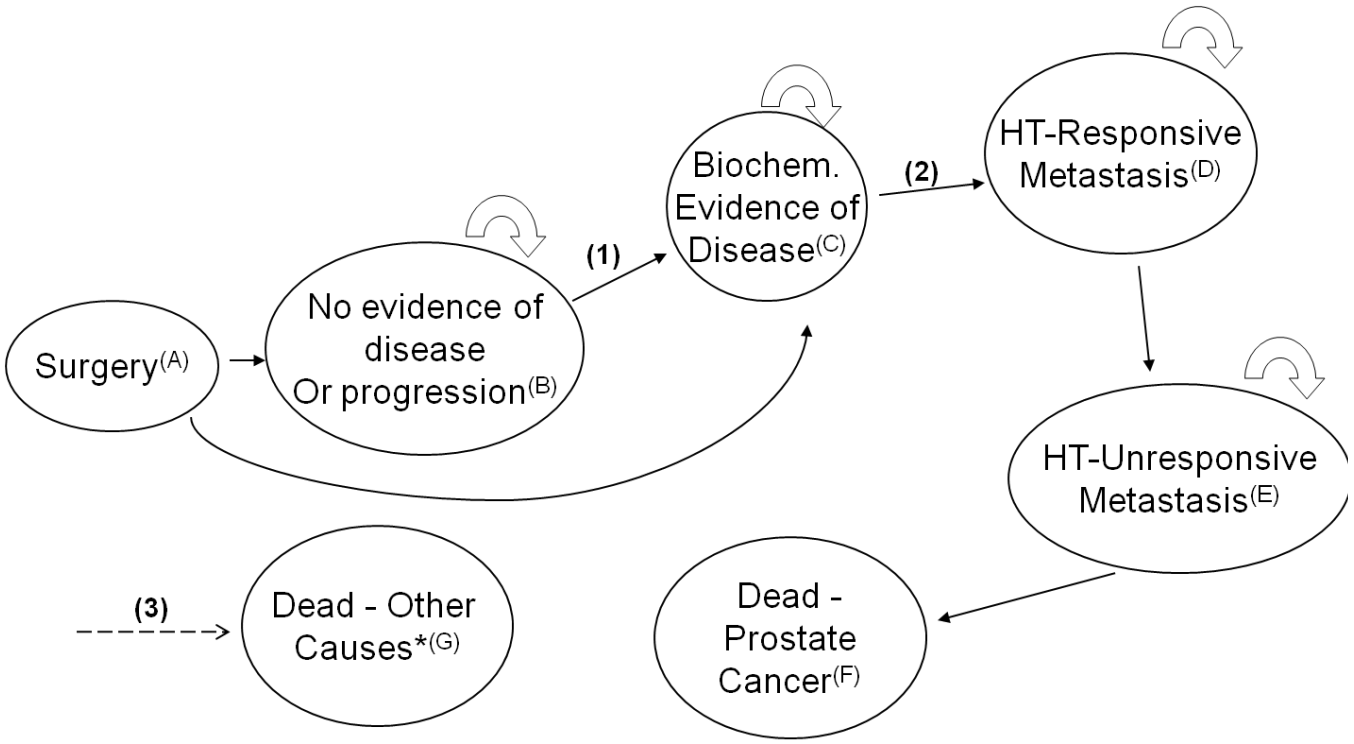
Appendix Figure 1a



(a) **Model of Treatment Decision at Diagnosis of Low-Risk Prostate Cancer**

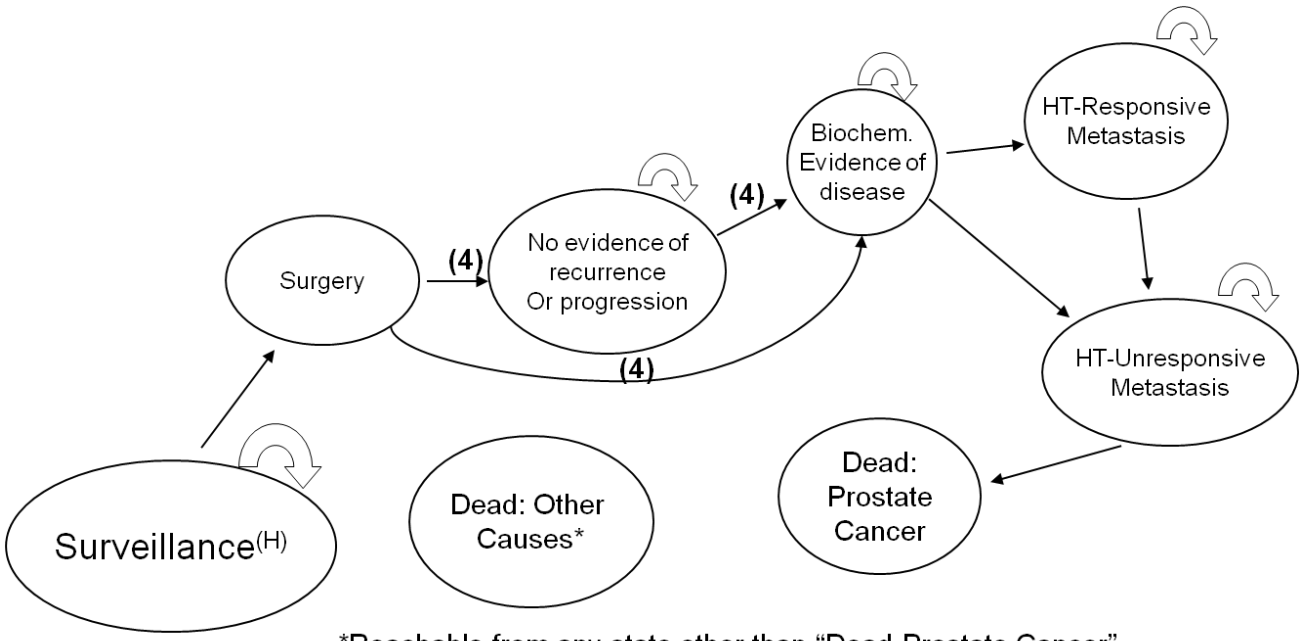
Overall Decision Model. All men who enter are diagnosed with biopsy-diagnosed, low-risk (GS < 7, PSA < 10.0 ng/ml, Stage T1c or T2a) disease and either undergo immediate surgery or begin surveillance. At the end of the simulation, everyone either has died from prostate cancer or from other causes.

Appendix Figure 1b



(b) **Radical Prostatectomy Model** – At diagnosis, men undergo surgery. After surgery, individuals can have undetectable disease (No Evidence of Disease or Progression), or have immediate residual, detectable disease (Biochemical Evidence of Disease). At each stage, an individual can experience disease progression, maintain their current state, or die from another cause of death. All transition probabilities are assumed to be constant except those noted.

Appendix Figure 1c



(c) **Active Surveillance Model** – At diagnosis, men begin a regimen of active surveillance. At signs of disease progression or patient choice, they undergo surgery, after which their disease states are analogous to the states of the radical prostatectomy model. All transition probabilities are the same as those of the radical prostatectomy model except those noted.

STATES:

(A) **Surgery:** Undergoing radical prostatectomy and recovering from the procedure.

(B) **No evidence of disease or progression**: Post-surgery, undergoing regular screening to detect recurrence of disease. No symptoms of disease.

(C) **Biochemical Evidence of Disease**: Despite surgery, PSA is detectable (either after a period of undetectability or never becoming undetectable after surgery, indicating residual or progressive disease). The disease is still asymptomatic.

(D) **Hormone-Therapy Responsive Metastasis**: Clinically evident metastatic disease

(e.g. bone lesions) whose manifestations/symptoms are controlled by hormonal castration therapy. No symptoms of disease other than those related to treatment.

(E) **Hormone-Therapy Unresponsive Metastasis**: Clinically evident metastatic disease with symptoms and manifestations no longer controlled by hormonal castration therapy.

(F) **Dead-Prostate Cancer**: Death from prostate cancer

(G) **Dead-Other Causes**: Death from any other causes (e.g. cardiovascular disease, other malignancy, trauma), reachable from any state.

(H) **Surveillance**: Under a protocol of active monitoring, including regular PSA tests, DREs, and biopsies, for signs of disease progression. No symptoms from disease.

Transition Notes:

(1) The probability of biochemical progression after 15 years of undetectable disease is assumed to be 0.

(2) The risk of disease progression from PSA-recurrence only to metastatic disease is associated with time from treatment to biochemical recurrence, with shorter times to recurrence associated with increased risk of progression. We used a threshold of 2 years [12]. Further, there was limited modern PSA-era low-risk population data for this model parameter. Therefore, we used a 20-yr prostate cancer specific mortality (PCSM) of 3.1%-3.9% for men median-age 58 years with low-risk disease treated with surgery[1] to back-calculate this parameter, assuming baseline values of all other model parameters (Appendix).

(3) The probability of dying from another cause of death (other than prostate cancer) is based on age and health status; age-specific Social Security life tables[10] were used for men in average health, and probabilities adjusted by a constant hazard ratio to yield 50%

and 150% of average life expectancy for men in "poor" and "excellent" health, respectively.

(4) For men managed initially with surveillance, an increased risk of disease progression is calculated as follows: men who have biopsy progression are assumed to have a hazard ratio of progression equivalent to the hazard ratio of prostate-cancer specific mortality of men diagnosed with intermediate-risk disease compared to low-risk disease. All other causes for intervention (e.g. changes in PSA level, density, DREs, patient choice) are assumed to bear the same probability of progression as if surgery had initially been chosen. Then, based on the proportion of the group of men receiving intervention who have biopsy-upgrades, a population-averaged hazard ratio for disease progression under surveillance is calculated. This hazard ratio is applied to the (converted to rate) probability of immediate residual disease after treatment and the probability of biochemical progression after treatment. The probability of having no evidence of disease after treatment (i.e. undetectable PSA) is simply the residual probability of not having immediate residual disease after treatment or dying from other causes of death.

Appendix Figure 2. Tornado Diagram: Results of One-way Sensitivity Analysis

"(p)" denotes probabilities

"(u)" denotes utilities (quality-of-life)

"(f)" denotes factors which modify transition probabilities

QALE(Surgery) = Quality Adjusted Life Expectancy under the strategy Radical Prostatectomy

QALE(Active Surveillance) = Quality Adjusted Life Expectancy under Active Surveillance

BR = Biochemical Recurrence

MP = Metastatic Progression

BRFS = Biochemical Recurrence Free Survival

HRR = Hazard Rate ratio

HT = Hormone Therapy

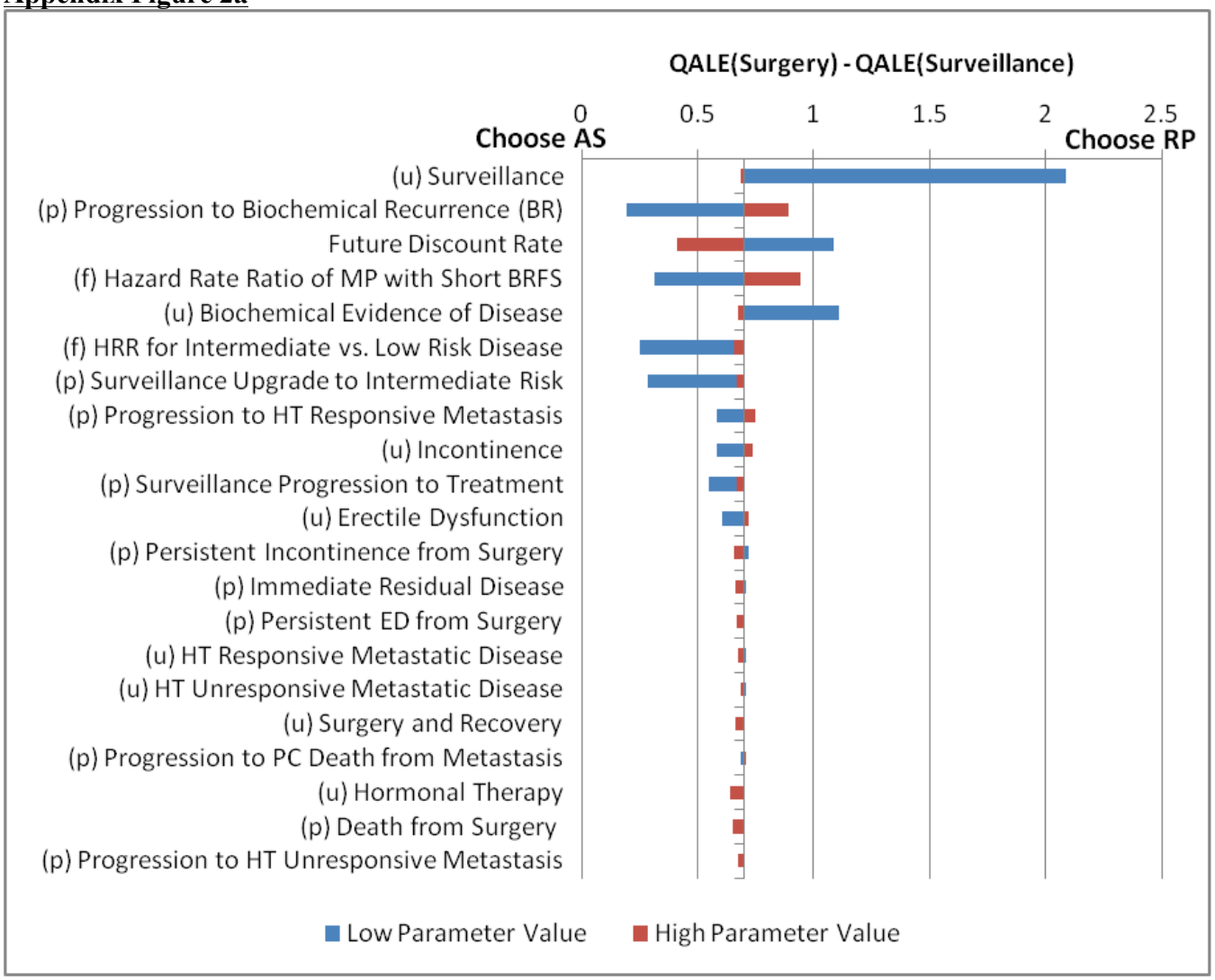
PC = Prostate Cancer

Vertical line denotes (QALE(Surgery) – QALE(Surveillance)) for baseline parameter values for men age 50, 65, and 75 years in average health. Red indicates (QALE(Surgery) – QALE(Surveillance)) given the highest value of each parameter within its range, and blue indicates the same calculation for the lowest. Model parameters are ordered by highest to lowest magnitude of (QALE(Surgery) - QALE(Surveillance))

Positive values imply that QALE (Surgery) > QALE (Surveillance), and hence surgery may be preferred. Negative values imply that QALE (Surgery) < QALE(Surveillance), and hence surveillance may be preferred.

Note that these represent ranges of outcomes given the low and high values of each model parameter as listed in Table 2. Ranges for utility of Erectile Dysfunction and Incontinence are the expanded "Individual" ranges (0.6 - 1.0)

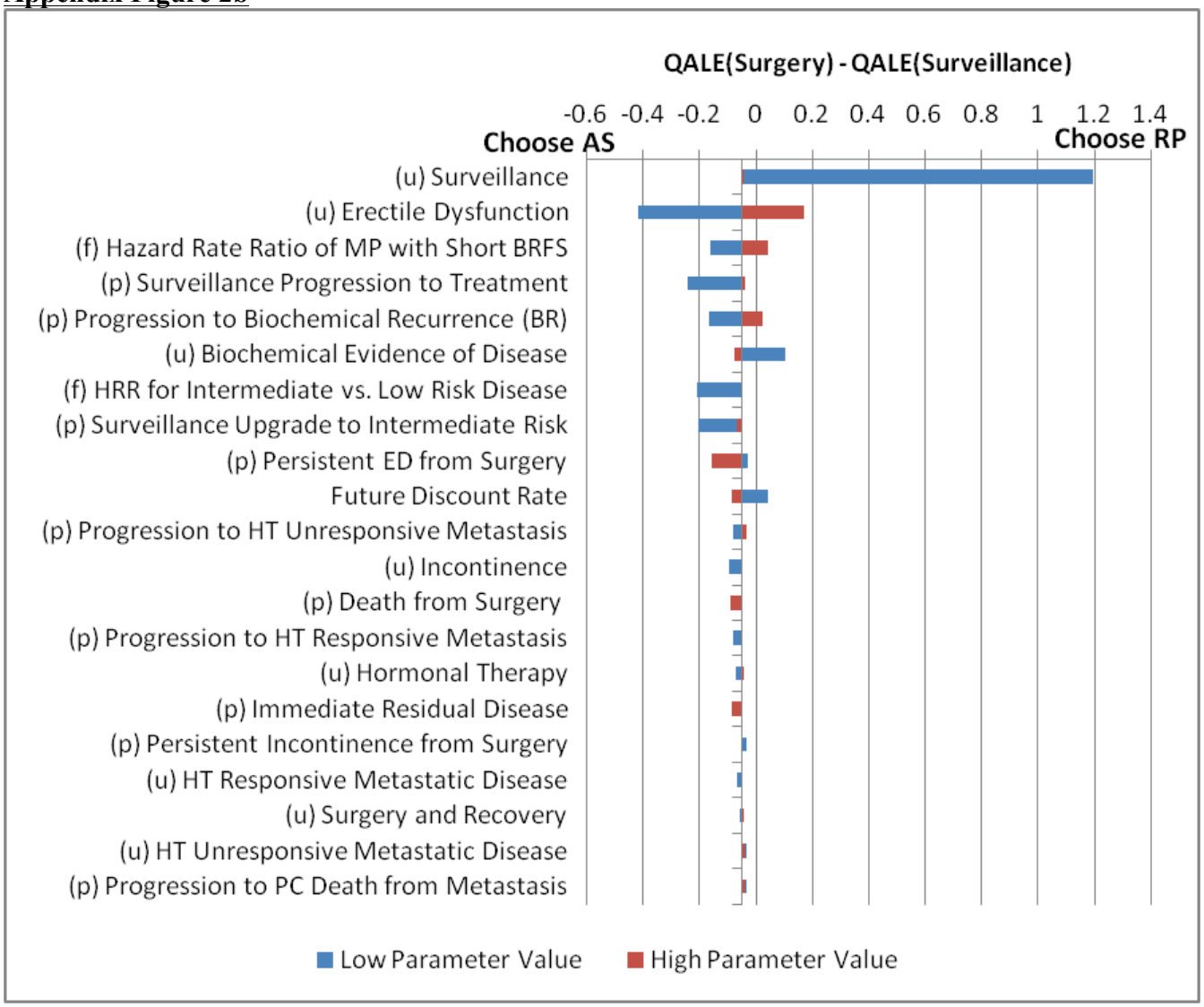
Appendix Figure 2a



(a) **Age 50 yrs, average health**

Note that no variation of any model parameter results in a switch from surveillance having greater QALE compared to surgery.

Appendix Figure 2b

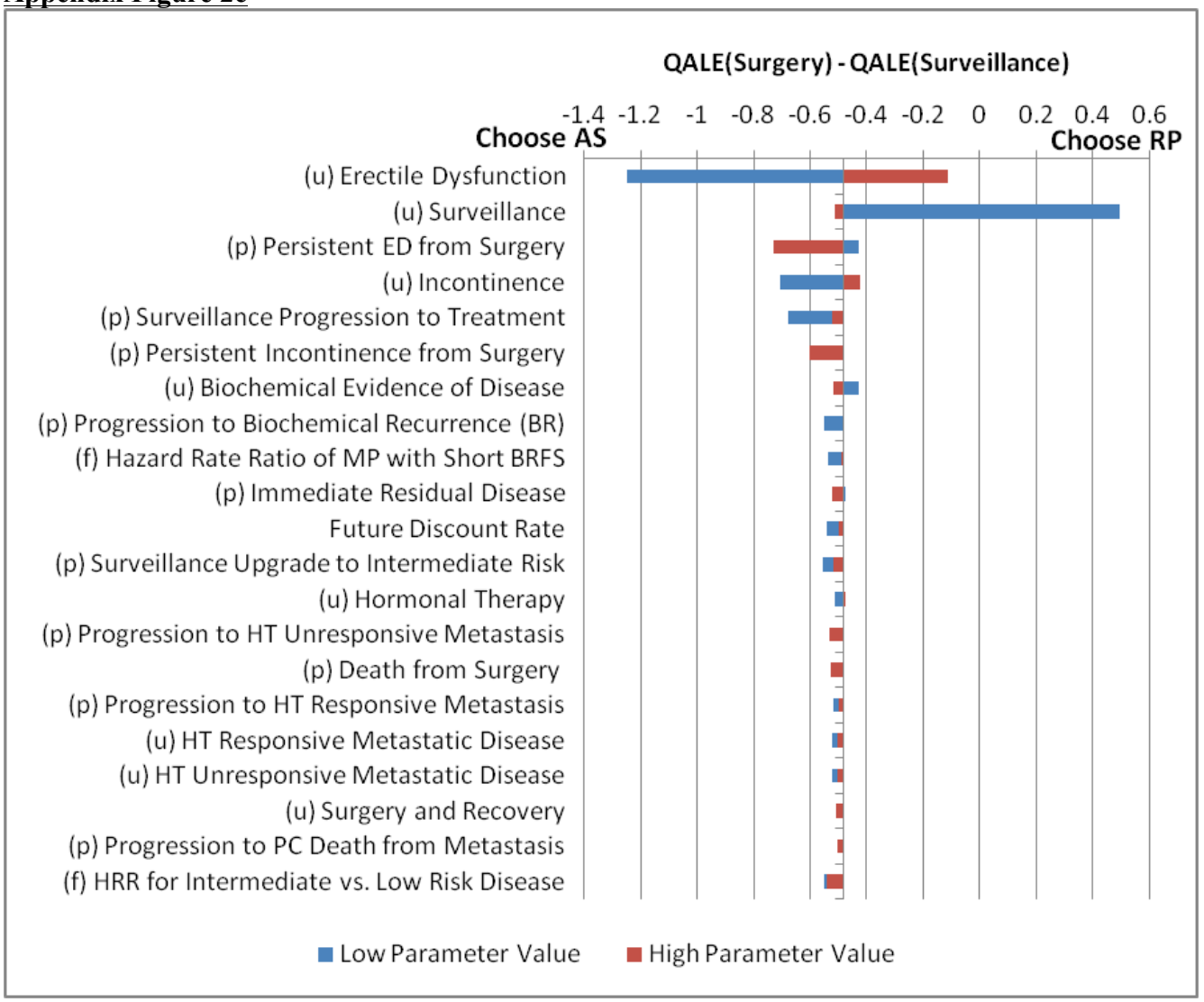


(b) **Age 65 yrs, average health**

At baseline, the difference in QALE between surgery and surveillance is virtually 0.

Thus, choice of optimal management strategy is sensitive to variation in several model parameters.

Appendix Figure 2c



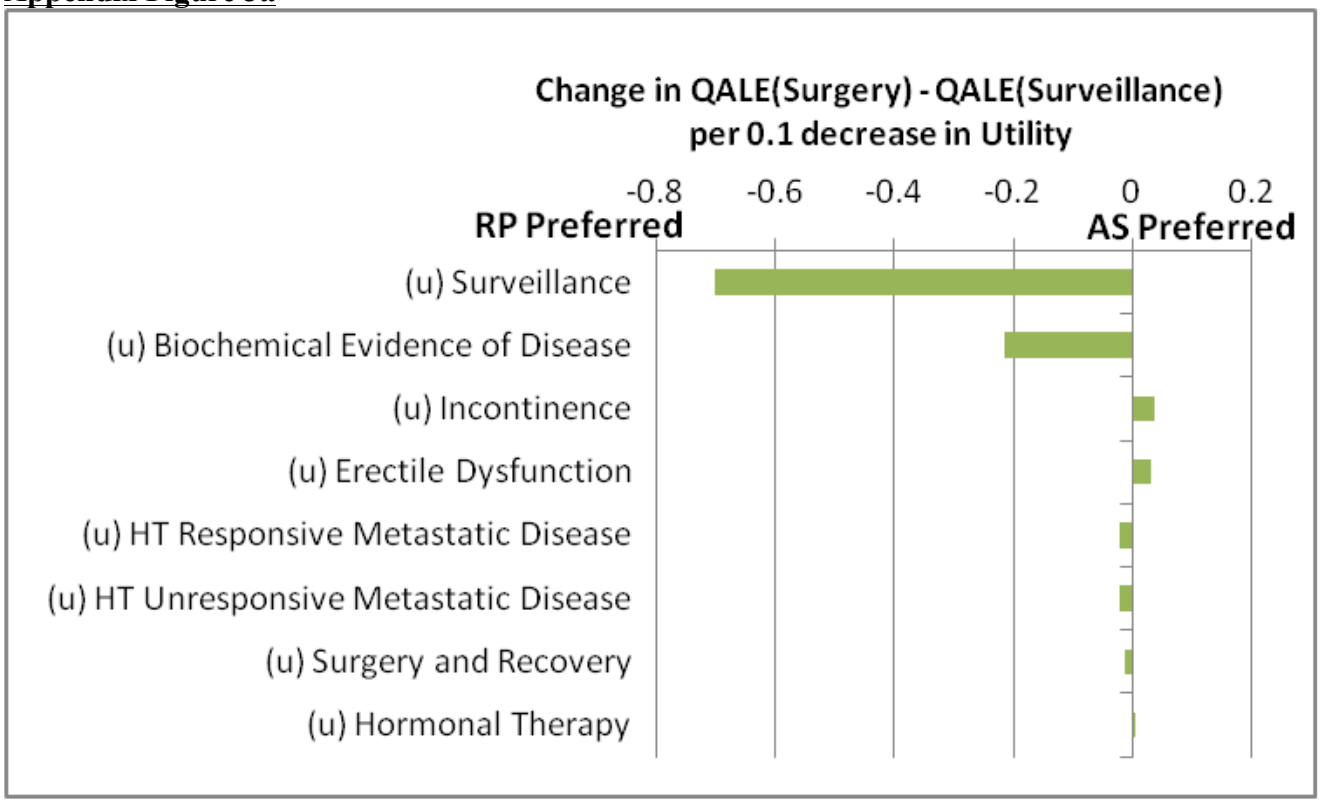
(c) **Age 75 yrs, average health**

Note that the optimal management strategy is sensitive only to variation in utility of surveillance, with surgery preferred if utility of surveillance is low. Otherwise, surveillance is preferred.

Appendix Figure 3 Relative Importance of Utilities to Choice of Optimal Management

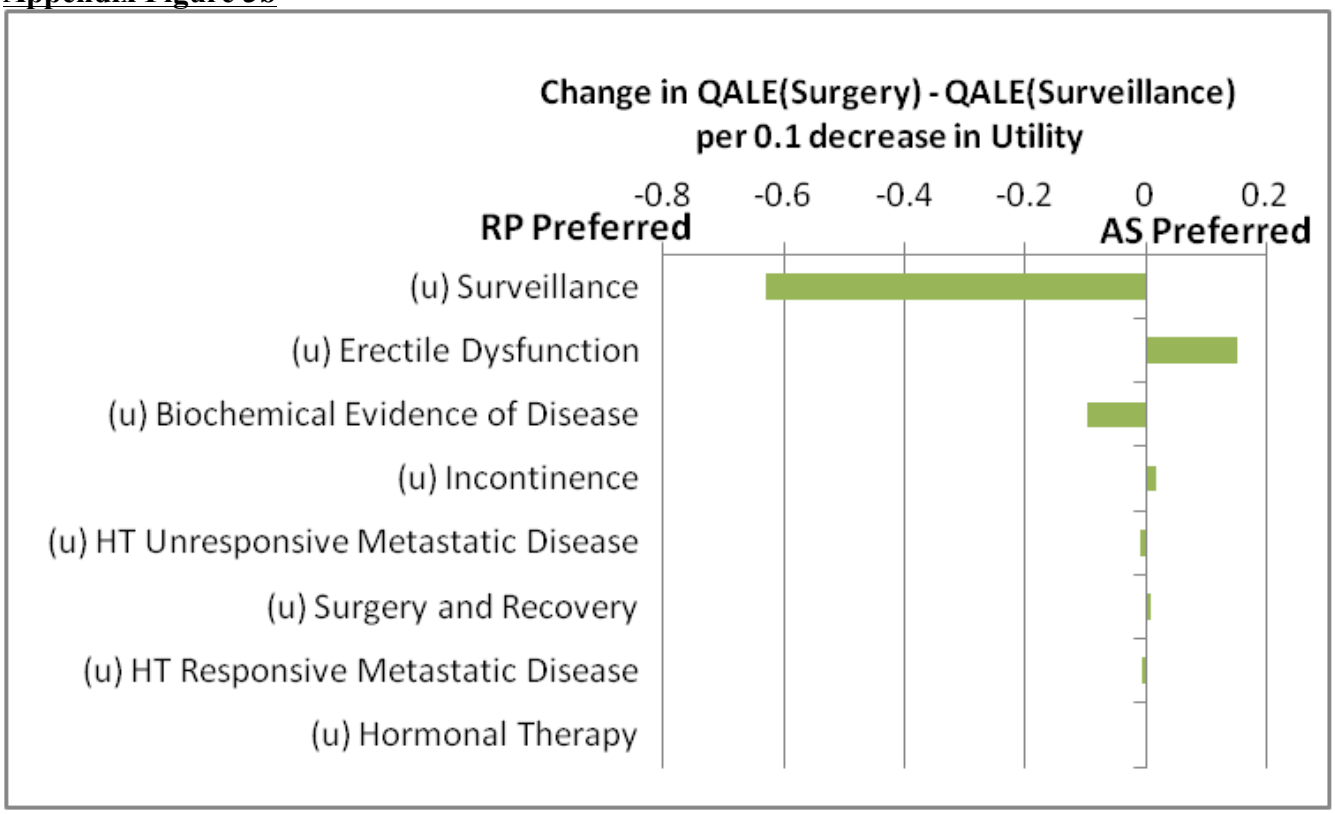
The bars delineate how much a 0.1 decrement in the specified utility affects the difference in QALE between surveillance and surgery. A 0.1 decrement in the utility of life associated with surveillance (e.g. anxiety with untreated disease) has by far the strongest effect in all ages, decreasing the QALE of surveillance by 0.5-0.7 QALYs relative to surgery. Quality of life with biochemical evidence of disease is important for younger ages, and quality of life with side effects is more important at higher ages.

Appendix Figure 3a



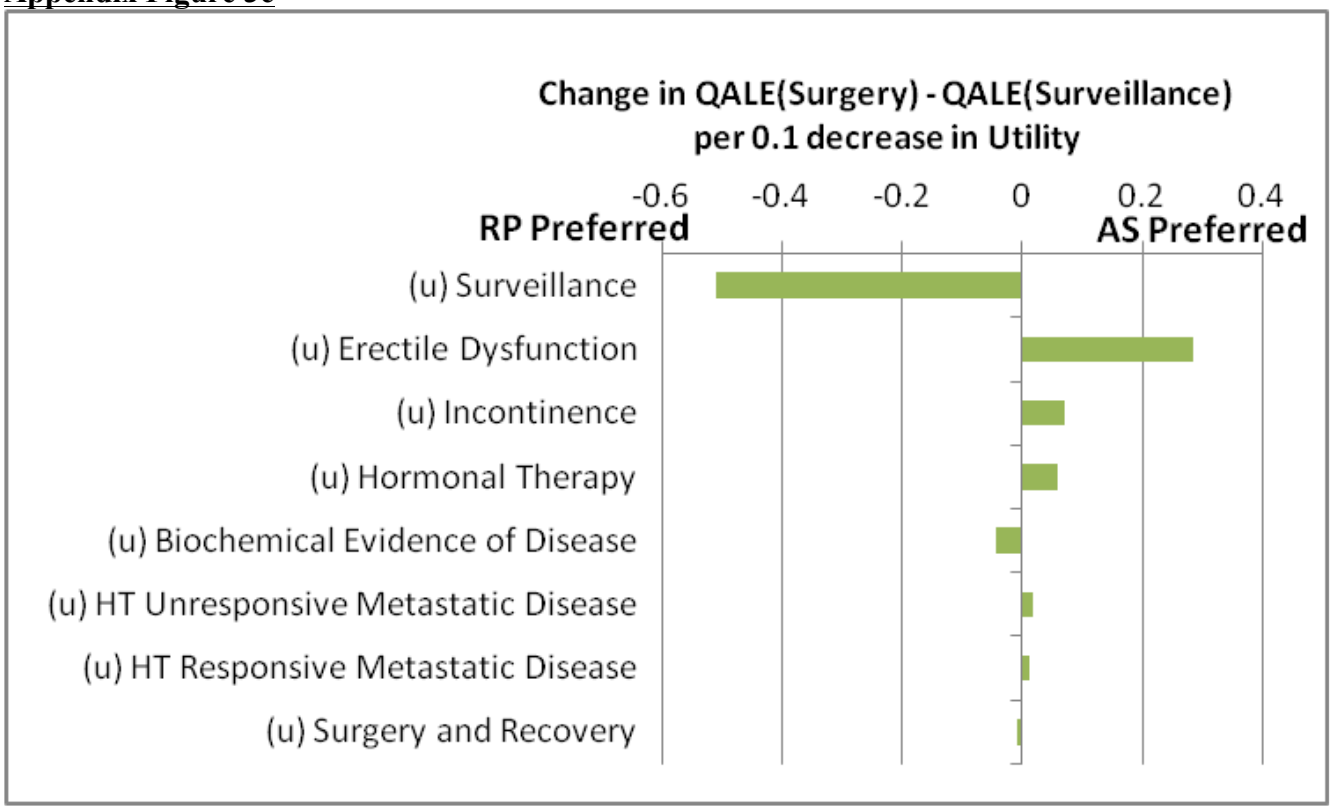
(a) **Age 50, average health**

Appendix Figure 3b



(b) **Age 65, average health**

Appendix Figure 3c



(c) **Age 75, average health**

Appendix Table 1 Major assumptions of model for low-risk prostate cancer

Model Assumption	**Rationale and Source**
Men must have biochemical recurrence and clinically metastatic disease (both hormone-responsive and unresponsive) before dying from prostate cancer.	Relatively indolent progression of disease in this population[3]; assumption of appropriately frequent diagnostics and treatment.
Disease recurrence after treatment is initially biochemical.	Assumption of appropriate frequency of monitoring for recurrence; indolent disease[3]
Men are at no further risk of disease progression 15 years after definitive treatment if disease has not recurred.	(Expert Opinion)
Men who have clinical metastases after biochemical recurrence without salvage hormone therapy have hormone therapy responsive metastases	True for vast majority of men[41, 42]
Men with hormone therapy responsive metastases do not die of prostate cancer.	Assumption that men with disease responsive to treatment are getting appropriate therapies.
Disease progression after clinical metastasis is independent of prior treatment	(Expert Opinion)

No man diagnosed with low-risk prostate cancer will die of prostate cancer within 1 year of diagnosis	Low prostate-cancer mortality risk in this population (2% PCM at 15 years[3])
Curative treatment after active surveillance is radical prostatectomy	No evidence that any other treatment results in improved outcomes; rates of RP have increased in men aged 65-84[43]
Age only impacts the probability of dying from other causes of death, and does not impact the probability of progression from disease.	Xu DD found that disease progression after RP was associated with age only in a high risk subset[44]. Sun et al found that age was not associated with disease progression in a multivariate model[45].
No salvage or adjuvant therapy	Less than 15% received salvage RT or hormonal therapy in similar populations[46, 47]. Benefits of salvage therapy are uncertain in this population[2, 48]. Less than 10% low risk prostate cancer patients have positive RP margins[49, 50]

Appendix Table 2 Model Parameters

Annual Probabilities (unless otherwise indicated)	**Base Case Estimate**	**Range for Sensitivity Analyses**	**Sources**
Disease progression probabilities			
Progression to Biochemical Recurrence (BR)	0.021 (< 15 yrs after treatment) 0.0 (>= 15 years after treatment)	0.006-0.049	[37, 51-55].
Progression from BR to Hormone Therapy Responsive Metastasis (HRM)	0.0145	0.0125 - 0.0165	Calculated using 3.1-3.9% prostate-cancer specific mortality at 20 years (Appendix)
Progression from HRM to Hormone Therapy Unresponsive Metastasis (HURM)	0.341	0.286 - 0.347	[41, 42, 56]

Death from prostate cancer after development of HURM	0.421	0.409 - 0.423	[57, 58]
Probability of never reaching undetectable PSA (i.e. residual disease) after treatment	0.011	0.0055 – 0.0165	[59]
One year rate ratio of metastatic progression for BR <= 2 yrs vs. BR > 2 yrs	2.8	1.4 – 4.2	[12]
Active Surveillance			
Annual probability of treatment	0.100	0.056 - 0.100	[5-9]
Progression to Intermediate Risk Disease with delayed treatment	0.039	0.018 - 0.039	[5, 7-9]
Rate ratio of prostate cancer specific mortality for men with intermediate-risk disease compared to low-risk disease	6.3	3.0 - 6.3	[3, 37, 60]
General			
Competing Causes of Mortality	(age-specific)		2005 Social Security Life Tables[10]

Health Status	(1.5× age-specific life expectancy)	0.5 - 1.5× age-specific life expectancy	2005 Social Security Life Tables[10]
Discount Rate (per year)	0.03	0.015-0.045	[32]
Complications and Side Effects			
Peri-operative Mortality	0.004	0.003-0.005	[61]
Long-term Incontinence		-20% -	[13-19]
Age 40-49	0.05	+50%	
Age 50-59	0.04		
Age 60-69	0.06		
Age 70+	0.15		
Long-term Erectile Dysfunction		-20% -	[13-19]
Age 40-49	0.07	+50%	
Age 50-59	0.20		
Age 60-69	0.32		
Age 70+	0.52		
Utilities			
Health States			
Undergoing radical prostatectomy	0.715	0.625 -0.715	[21]

No evidence of disease (post-treatment)	1.00		Assumed relative best health state.
Biochemical evidence of disease	1.00	0.8 - 1.0	Expert Opinion
Metastasis – HT responsive	0.649	0.649 - 0.703	[21, 25, 28, 29]
Metastasis – HT unresponsive	0.279	0.279 - 0.345	[21, 22, 25, 28, 29]
Surveillance (pre-treatment)	1.00	0.8 - 1.0	[31]
Side Effects			
Incontinence	0.864	(Population) 0.805 - 0.864 (Individual) 0.6-1.0	[20-22, 24-26, 29]
Erectile dysfunction (ED)	0.855	(Population) 0.814 - 0.855 (Individual) 0.6-1.0	[20-22, 24-26, 29]
Incontinence with ED	0.739		Product of utility of ED and incontinence
Hormonal Therapy	0.787	0.787 - 0.846	[21, 23]