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# Prostate cancer mortality following active surveillance versus immediate radical prostatectomy

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## Abstract

**Propose—**Active surveillance (AS) has been endorsed for low-risk prostate cancer, but information about long-term outcomes and comparative effectiveness of AS is lacking. The purpose of this study is to project prostate cancer mortality under AS followed by radical prostatectomy (RP) versus under immediate RP.

**Experimental Design—**A simulation model was developed to combine information on time from diagnosis to treatment under AS and associated disease progression from a Johns Hopkins AS cohort (n=769), time from RP to recurrence from cases in the CaPSURE database with T-stage ≤ T2a (n=3,470), and time from recurrence to prostate cancer death from a T-stage ≤ T2a Johns Hopkins cohort of patients whose disease recurred after RP (n=963). Results were projected for a hypothetical cohort aged 40–90 years with low-risk prostate cancer (T-stage ≤ T2a, Gleason score ≤ 6, and PSA level ≤ 10 ng/mL).

**Results—**The model projected that 2.8% of men on AS and 1.6% of men with immediate RP would die of their disease in 20 years. Corresponding lifetime estimates were 3.4% for AS and 2.0% for immediate RP. The average projected increase in life expectancy associated with immediate RP was 1.8 months. On average, the model projected that men on AS would remain free of treatment for an additional 6.4 years relative to men treated immediately.

**Conclusions—**AS is likely to produce a very modest decline in prostate-cancer-specific survival among men diagnosed with low-risk prostate cancer but could lead to significant benefits in terms of quality of life.

### Keywords

Active surveillance; radical prostatectomy; prostaticneoplasms; Gleason score

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## Introduction

Interest in active surveillance (AS) is increasing as an initial management approach for newly diagnosed, low-risk prostate cancer. In December 2011, the National Institutes of Health convened a State-of-the-Science Consensus Conference on the role of AS in the management of men with localized prostate cancer (http://consensus.nih.gov/2011/prostate.htm). The final statement from the conference panel concluded that forgoing immediate treatment with surgery or radiation, both of which can have serious side effects, and instead actively monitoring the disease is a "viable option" for many men diagnosed with low-risk prostate cancer. However, currently, most men with low-risk prostate cancer undergo immediate treatment (1). There are significant barriers to adoption (2), principally a paucity of comparative data evaluating cancer-specific outcomes among contemporary, low-risk cases undergoing immediate treatment versus AS. Indeed, the literature review commissioned for the consensus conference (3) did not find a single study reporting results from direct comparisons of AS with immediate treatment.

Although direct estimates of the impact of AS on prostate cancer mortality (PCM) are currently lacking, information is available on parts of the process from diagnosis to death under AS versus immediate treatment. Several AS studies are ongoing (4–8) and, although none are mature enough to assess PCM, they are now yielding distributions of times to treatment and the corresponding frequency of disease progression (e.g., biopsy upgrading). The implications of biopsy grade at treatment for disease recurrence are, in turn, well understood from cohort studies and nomograms (9, 10). And there are also several prognostic studies of the interval from disease recurrence to PCM (11, 12). Our goal is to integrate this information using a coherent model of the progression of disease through surveillance, treatment, recurrence, and death. Without modeling, any assessment of the effect of AS will necessarily depend on a direct assumption about the impact of AS on PCM (e.g., (13)). Such an assumption could critically influence inferences about the harms and benefits of AS.

In this article we present a model that logically combines results from AS and prognostic studies among prostate cancer patients receiving surgery. We use the model to project PCM among contemporary low-risk cases on AS, followed by radical prostatectomy (RP) if disease progresses, and we compare our projections with PCM had the cases received immediate RP. Our work provides a novel method for using data from AS cohorts to inform practices that favorably balance harms and benefits in low-risk prostate cancer cases.

## Methods

Our methods decompose the interval from diagnosis to PCM into phases, the duration of each of which can be projected based on published studies (Figure 1). Among men on AS, we model the time from diagnosis to RP, the time from RP to recurrence, and the time from recurrence to PCM. Among men treated immediately with RP, time spent in the first phase (AS) is zero. We use the same model for time to PCM after RP whether it is performed immediately or following AS. However, the outcomes differ in the two scenarios because we allow disease to progress on AS so that key prognostic predictors (i.e., Gleason score (GS) and PSA) used in the model of time from treatment to recurrence and time from recurrence to death may have different values when men are treated immediately versus after the delay induced by a period on AS.

We use a micro-simulation modeling framework to project outcomes for the same cohort of cases under AS or immediate RP. We consider cases who are low-risk at diagnosis according to the most recent guidelines on prostate cancer from the National Comprehensive

Cancer Network (http://www.nccn.com/cancer-treatment/prostate-cancer/localized.html), namely T-stage ≤ T2a, GS ≤ 6, and PSA ≤ 10 ng/mL. This is generally consistent with ongoing AS cohort studies as summarized by the State-of-the-Science Conference draft statement.

## Data sources

To project the time to treatment under AS, we use data from the Johns Hopkins AS (JH-AS) program (6). Patients enrolled are those with T-stage ≤ T1c, GS ≤ 6, PSA density ≤ 0.15 ng/mL/cc, ≤ 2 prostate needle biopsy cores with cancer, and cancer involvement of ≤ 50% in any biopsy core. Cases are biopsied annually and referred to treatment based on any adverse change in prostate biopsy. Patient also self-refer for a variety of reasons, including rising PSA or anxiety. Using data for all cases in this program, we estimate time to treatment using a Kaplan-Meier curve and the frequency of biopsy GS progression under AS using a logistic regression of whether GS is ≥ 7 at the final biopsy before treatment. Covariates include age at diagnosis, PSA at biopsy, annual percent change in PSA between diagnosis and final biopsy, and time from diagnosis to treatment.

To project the time from RP to PSA recurrence or any secondary treatment (“recurrence”), we use data from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) database (14–16). CaPSURE was initiated in 1995 to document community trends in prostate cancer practice patterns, epidemiology, and outcomes. It is a longitudinal, observational database accruing data from 40 urologic practice sites over its history. There are currently 13,821 men enrolled in CaPSURE and CaPSURE collects approximately 1,000 clinical and patient-reported variables, including post-treatment PSA levels. We use data from cases diagnosed after 1994 because this was the year in which PSA screening rates in the population began to stabilize and cases diagnosed after this point are likely to be more reflective of contemporary diagnoses.

To model the time from recurrence to PCM, we use data from a Johns Hopkins PCM (JH-PCM) cohort, consisting of patients treated with RP who had a recurrence (i.e., PSA ≥ 0.2 ng/mL) and who were followed for PCM (12).Approximately 55% were treated with salvage radiation, hormonal therapy, or both at the time of recurrence. To be consistent with the model of time from RP to recurrence, we only consider patients who received RP after January 1994. To their data on time from recurrence to death we fit a Cox regression model adjusting for biopsy GS at the time of diagnosis and time from RP to recurrence (11, 17).

## A simulation model of time from diagnosis to PCM

The simulation model first generates a virtual population of 1 million patients representative of contemporary US prostate cancer cases by sampling age and PSA pairs from cases reported in the Surveillance, Epidemiology, and End Results (SEER) program (http://seer.cancer.gov/) with low-risk disease diagnosed after January 2004 (this was the date when PSA levels at diagnosis were added to the SEER database). For each simulated case we generate time to PCM under AS versus immediate RP.

Given age and PSA, we simulate the time from immediate RP to recurrence for each case using a Cox model fit to low-risk CaPSURE cases (T-stage ≤ T2a, GS ≤ 6, and PSA ≤ 10 ng/mL) and a time from recurrence to PCM from the Cox model fit to the JH-PCM data restricted to cases with T-stage ≤ T2a at RP. We use Weibull regression to extrapolate beyond the last observed failure times. We independently simulate times to other-cause mortality from life tables (http://www.mortality.org/) given age at diagnosis and birth year. The age at death is the minimum of the age at PCM and other-cause death, with cause of death assigned accordingly.

Under AS, we simulate a time to treatment from the distribution of treatment times in the JH-AS cohort. To capture the intuition that disease that progresses quickly to treatment under AS will also likely recur quickly after immediate RP, we generate the time to treatment under AS at a percentile corresponding to the percentile used to generate the time from immediate RP to recurrence. To extrapolate beyond the last observed failure time we assume a constant failure rate (i.e., an exponential distribution), with risk of failure (proceeding to treatment) estimated based on the final year of observation. To each patient initiating treatment, we randomly assign a PSA growth rate and use this to project the PSA level at the time of treatment. PSA growth rates among cancer cases in the absence of treatment are estimated via linear, mixed-effects models fit to serial PSA measurements among participants enrolled in the JH-AS cohort. We impute biopsy GS ($\leq 6$ or $\geq 7$) at treatment from the GS progression model fit to the JH-AS data. Among cases upgraded on AS, we assume that 86% have biopsy GS 7 at treatment and 14% have biopsy GS $\geq 8$ at treatment based on observed frequencies from the JH-AS cohort.

Once age, PSA, and GS have been updated for cases treated on AS, we simulate a time from treatment to recurrence for each treated case based on a Cox model fit to the cases in the CaPSURE cohort; we restrict to cases with T-stage $\leq$ T2a since cases still have early stage disease despite possible progression of PSA and grade. We correlate the times from diagnosis to treatment and from treatment to recurrence by generating them at the same percentile within their respective distributions. For cases that recur within their lifetimes, we simulate a time from recurrence to PCM from the Cox model fit to the JH-PCM data with T-stage $\leq$ T2a. We use Weibull regression to extrapolate beyond the last observed failure times in the models for time to recurrence and PCM respectively. Death due to competing causes is simulated independently using contemporary life tables.

Using the simulated data, we compute the cumulative incidence of PCM and the difference in life years overall and after treatment for each patient under AS versus immediate RP.

In addition, we conduct three sensitivity analyses to determine the robustness of our results to the model inputs and assumptions. The first two pertain to the delay in treatment and disease progression under AS, which we anticipate could influence the prognosis and survival of men under AS. The first considers outcomes given a different distribution of time to treatment under AS, representing a protocol with a different surveillance intensity. The JH-AS cohort represents a relatively intense surveillance protocol, and we consider a less intensive protocol, with the distribution of times to treatment modeled after that observed in the Toronto AS study (7). The second sensitivity analysis pertains to the extent of upgrading to GS 7 versus GS $\geq 8$ while on AS; we consider how PCM mortality following AS would change under more versus less extensive upgrading. The third sensitivity analysis varies the extent of the presumed correlation between time to treatment under AS and time to recurrence after RP using two methods. First, we generate time to recurrence after RP using a percentile that is close but not exactly equal to that used to generate time to treatment under AS. Second, we only match percentiles in these distributions to cases treated due to biopsy grade progression.

## Result

The JH-AS cohort included data on 769 cases with a median follow-up time of 2.7 years (range from 4 days to 15.0 years). Among these cases, PSA grew by 3.1% per year on average with a standard error of 0.5%. 253 patients initiated treatment by the time of analysis and another 66 had progressed but had not yet initiated treatment (and so are censored). The median time to treatment among those treated was 5.9 years; the failure rate in the last year of observation (0.10) was used for extrapolation beyond the last observed

treatment time. Table 1 presents the results of the model for GS progression by the time of treatment. A longer time to treatment and older age were associated with a greater chance of biopsy upgrade while on AS. PSA and the annual change in PSA from diagnosis to treatment were not significantly associated with biopsy upgrading, and excluding the PSA covariates did not materially change our projections. The majority of upgrades (86%) were to GS 7.

The T-stage ≤ T2a CaPSURE cohort for analysis of recurrence under delayed RP includes data on 3,470 men diagnosed after January 1994 and treated with RP, of whom 385 (11.1%) recurred after RP. The average age at diagnosis was 60.8 (range 39–80) years, and the median follow-up time was 3.6 years (range from 5 days to 15.3 years). The cumulative incidence of recurrence was 10.1% at 5 years and 11.1% at 10 years. The Weibull regression model used to extrapolate beyond the follow-up period had a median time to recurrence of 68.2 years. The low-risk CaPSURE cohort for analysis of recurrence under immediate RP includes data on 2,150 (62.0%) men, of whom 163 (7.6%) recurred after RP. The average age at diagnosis was 60.2 (range 39–79) years, and the median follow-up time was 3.7 years (range from 7 days to 15.3 years). The cumulative incidence of recurrence was 6.8% at 5 years and 7.6% at 10 years. The Weibull regression model used to extrapolate beyond the follow-up period had a median time to recurrence of 86.1 years. Table 2 summarizes the characteristics of the T-stage ≤ T2a CaPSURE cohort and low-risk CaPSURE cohort. Table 4 presents the Cox model results for recurrence following immediate and delayed RP.

The JH-PCM cohort includes 1,745 men, of whom 963 (55.2%) received RP after January 1994 and had T-stage ≤ T2a. The average age at diagnosis was 58.7 (range 39–74) years. 63 (6.5%) men died of prostate cancer and the cumulative incidence of PCM was 3.4% at 5 years and 5.9% at 10 years after recurrence. The Weibull regression model used to extrapolate beyond the follow-up period had a median time to PC death of 122.4 years. Table 3 summarizes the JH-PCM data, and Table 4% presents the results of our model of PCM. Table 4 shows the strong association between time to recurrence and PCM, with each additional year of recurrence-free survival reducing the risk of PCM following recurrence by 35%.

Our distributions of age and PSA at diagnosis were based on low-risk cases diagnosed after 2004 in SEER (mean age 60.6; mean PSA 4.9 ng/mL). The model projected that 63.7% of cases on JH-AS would progress to treatment before they died of other causes. The projected 20-year cumulative incidence of PCM was 2.78% under AS and 1.64% under immediate RP. The reduced incidence of PCM under immediate RP amounted to an average of 1.8 months of life saved per case (Table 5). Compared to men initially treated with RP, men on AS had on average 6.4 more years of life free from treatment and its side effects.

As a sensitivity analysis of the intensity of surveillance, we modified the simulated time to treatment on AS by a hazard ratio of 0.5 to lengthen the interval from diagnosis to treatment. Our goal was to approximate a less intensive surveillance regimen; the hazard ratio of 0.5 was motivated by the published time to treatment on the Toronto AS study (7), which reported 84%, 72%, and 62% remaining on surveillance at 2, 5, and 10 years respectively versus 81%, 56% and 34% respectively in the JH-AS cohort. Under this setting, the model projected that about 54.8% patients would progress to treatment within their lifetimes (versus 63.7% projected for the JH-AS cohort), and the corresponding 20-year PCM would increase from 2.78% to 2.82%.

As a second sensitivity analysis, we altered the assumed fraction upgrading to GS ≥ 8 while on AS. In our baseline model, projections of post-treatment survival assume that 14% of upgraded cases are treated with GS ≥ 8, based on the observed grade distribution at

treatment in the JH-AS cohort. In our sensitivity analysis, we changed this fraction to 25% and, as a consequence, projected that 20-year PCM would increase from 2.75% to 3.04%.

Our third sensitivity analysis relaxed the correlation between the time to treatment under AS and the time to recurrence following surgery. Under baseline assumptions, the Spearman correlation was 0.94. We projected that 20-year PCM under AS would decrease to 2.38% with a correlation of 0.5 and to 1.69% with no correlation, resulting in a more comparable survival outcome relative to immediate RP. When we only correlate times in these phases for cases on AS who were treated due to biopsy upgrading (Spearman correlation 0.94), we projected that 20-year PCM under AS would decrease to 2.08%.

All sensitivity analyses produced only modest differences in cumulative PCM under AS, and supported our projections that AS would have minimal impact on life expectancy for low-risk prostate cancer cases.

## Discussion

The recent results from the Prostate cancer Intervention Versus Observation Trial (PIVOT) have reinforced the notion that men diagnosed with low-risk prostate cancer may not need to be treated for their disease (18). In this article, we have presented a novel modeling framework for projecting the long-term outcomes and comparative effectiveness of active surveillance, the emerging approach of choice for low-risk prostate cases. Several studies (8, 13, 19) have suggested that AS may produce PCM similar to that under immediate treatment. In contrast, our modeling framework does not make any quantitative assumptions about the likely impact of AS on PCM; rather, the estimated impact arises as a mechanistic consequence of the timing of treatment and extent of disease progression under AS.

The impact of AS on PCM arises by connecting the phases in the model, each of which is informed by published data that we consider to be sufficiently mature and high quality for modeling purposes. We have used specific data sources and inputs to inform the model and produce the specific findings reported; however, the framework developed is designed to be applicable for use with other data sources and in other settings. In particular, we plan to use this framework to explore the consequences of a variety of AS approaches, varying the surveillance intervals and criteria for referral to treatment. In the present article, we used data from the CaPSURE cohort to model the interval from RP to recurrence because of its size, quality, and multi-site nature. Detailed information on disease progression under AS is necessary for modeling and this was available in the JH-AS data. Finally, we used information on disease progression after recurrence from the JH-PCM cohort. Although studies of these cohorts are highly cited and they are recognized as valuable, high-quality data sources, they are subject to limitations. The JH-AS cohort includes very-low-risk cases (6) with PSA density ≤ 0.15 ng/mL/cc and very-low-volume disease. Consequently, our inferences about the risk of progression and PCM based on the JH-AS data may be lower than what would be expected for other low-risk AS cohorts. The JH-PCM cohort reflects a single clinical site and may not be broadly representative. Our sensitivity analyses indicate that our conclusions appear to be relatively robust, but further investigation of the impacts of different inputs and data sources will be important to confirm this result.

Our main finding is that the absolute difference between the projected PCM under AS or immediate RP is likely to be very modest, corresponding to a number needed to harm (NNH) of 88 after 20 years. The difference in PCM averages approximately 1.8 months of life saved per individual, but men on AS are able to live an average of 6.4 years longer without treatment than those treated immediately. Ultimately, the model projects that approximately 64% of men on AS would be treated within their lifetimes under a

surveillance protocol similar to the JH-AS cohort. Thus, under AS, 36% of men could avoid being treated.

We focus on PCM rather than all-cause mortality because RP is an intervention designed to reduce PCM and other-cause death is so much more frequent than PCM in this cohort. As a result, analyses of all-cause mortality are generally not sensitive to real differences in PCM under RP versus AS.

We did not explicitly model quality of life because well-validated utilities under AS are not yet available. However, if there was no loss in quality of life under AS and the impacts of treatment on quality of life were to be included, the post-treatment utility would only have to be 0.9 or less each year in the five years following treatment for immediate RP to have a lower quality-adjusted life expectancy than AS (19.2 years versus 19.3 years respectively).

The model rests on several key assumptions. The first is that the risk of disease recurrence following RP is not affected by the AS process itself so that the likelihood of recurrence depends similarly on measured prognostic variables whether RP is performed immediately or after surveillance. This conditional independence assumption is a key underpinning of our model. We assume that, conditional on prognostic variables measured at the time of RP, time from RP to recurrence does not depend on whether RP was done at diagnosis or after AS. An additional assumption is that the fate of a tumor under AS is linked with the fate of that tumor once it is treated. While this is a reasonably intuitive assumption, the way in which we operationalize it in the model (by simulating times to treatment and recurrence using similar percentiles within their respective distributions) is only one method of quantitatively representing this intuition. We note that results are somewhat sensitive to the resulting correlation between time to treatment and time to recurrence, with 20-year PCM varying from 1.67% to 2.78% as the correlation ranges from 0 to 0.94.

Our results are similar to those from the PIVOT study (18), which found modest absolute difference in 12-year PCM in (primarily GS ≤ 6) cases treated immediately with RP (4.4%) or assigned to watchful waiting (7.4%). They also reflect the findings of another modeling study (20) which projected 0–1% absolute difference in PCM at 15 years under conservative management versus immediate curative treatment (we estimate 1.14% at 20 years). Our projected mortality under immediate RP (1.64% over 20 years) is lower than population-based results for low-risk cases diagnosed after 1994 in the SEER registry who received immediate RP (3.4% died of prostate cancer within 14 years), possibly reflecting selection of cases with more favorable risk profiles into the CaPSURE and JH-PCM cohorts.

The final statement from the 2011 NIH Consensus Conference on Active Surveillance (http://consensus.nih.gov/2011/prostate.htm) concluded that AS has emerged as a viable option that should be offered to patients with low-risk cancer, but that there are many unanswered questions that require further research. Answering these questions via prospective, randomized studies is infeasible. Despite their limitations, alternative types of studies will have to be used and modeling should play an important role in this setting. The present work exemplifies how the power of modeling can be harnessed to project the long-term outcomes of AS and should be useful in determining best practices for men with low-risk prostate cancer.

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**Translational Relevance**

Men diagnosed with low-risk prostate cancer face an agonizing decision about whether to be treated or to opt for active surveillance. Their dilemma is made even more challenging by the lack of information about the clinically relevant outcomes of active surveillance—primarily its effect on their risk of prostate cancer death. Ongoing active surveillance programs are not mature enough to provide results concerning disease-specific mortality. Also, they are single-arm studies so there is no comparison group to enable inferences about the comparative effectiveness of active surveillance. In this study we utilize the results from one of the leading active surveillance cohorts and, using a computer model as a virtual laboratory for translational research, we project disease-specific deaths under active surveillance versus immediate treatment. This information should enable patients and their clinicians to make better informed decisions about the most appropriate approach for managing newly-diagnosed, low-risk prostate cancer.

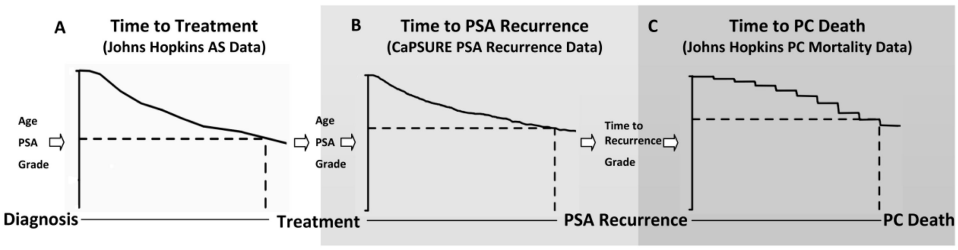


**Figure 1.**

Framework for modeling of prostate cancer mortality following active surveillance versus immediate radical prostatectomy. Under immediate treatment, we model time to recurrence (B) followed by time from recurrence to prostate cancer mortality (C). Under active surveillance, these are preceded by a model of time to treatment (A). The figures show Kaplan-Meier curves for the relevant endpoints from the three data sets used in the model.

## Table 1

Logistic regression model of biopsy upgrading for active surveillance patients who were diagnosed after 1995 and underwent treatment (n=237).

| Covariate | Coefficient | Odds ratio | Standard error | P-value |
|---|---|---|---|---|
| Intercept | −7.91 | 0.00 | 1.99 | < 0.001 |
| Age at diagnosis | 0.10 | 1.11 | 0.03 | < 0.001 |
| PSA at diagnosis | 0.01 | 1.01 | 0.05 | 0.821 |
| Time to treatment (years) | 0.21 | 1.23 | 0.08 | 0.008 |
| Annual change of PSA | 0.06 | 1.06 | 0.07 | 0.372 |

## Table 2

Characteristics of T-stage ≤ T2a and low-risk (T-stage ≤ T2a, Gleason score ≤ 6, and PSA level ≤ 10 ng/mL) CaPSURE patients diagnosed after 1994.

| | T-stage ≤ T2a (n=3,470) | | Low risk (n=2,150) | |
|---|---|---|---|---|
| **Characteristic** | **No. patients** | **Percent** | **No. patients** | **Percent** |
| Age | | | | |
| < 40 | 1 | 0.03 | 1 | 0.05 |
| 40–49 | 189 | 5.45 | 122 | 5.67 |
| 50–59 | 1256 | 36.20 | 856 | 39.82 |
| 60–69 | 1677 | 48.33 | 1008 | 46.88 |
| 70–79 | 344 | 9.91 | 163 | 7.58 |
| ≥ 80 | 3 | 0.08 | – | – |
| Gleason score | | | | |
| ≤ 6 | 2545 | 73.34 | 2150 | 100.00 |
| 7 | 738 | 21.27 | – | – |
| ≥ 8 | 121 | 3.49 | – | – |
| Missing | 66 | 1.90 | – | – |
| PSA at diagnosis (ng/mL) | | | | |
| 0–2.5 | 203 | 5.85 | 162 | 7.54 |
| 2.51–4.0 | 362 | 10.43 | 287 | 13.35 |
| 4.1–6.0 | 1369 | 39.45 | 1031 | 47.95 |
| 6.1–10.0 | 953 | 27.46 | 670 | 31.16 |
| > 10.0 | 451 | 13.00 | – | – |
| Missing | 132 | 3.81 | – | – |

**Table 3**

Characteristics of T-stage T2a JH-PCM data diagnosed after 1994 (n=963).

| Characteristic | No. patients | Percent |
|---|---|---|
| Age | | |
| < 40 | 1 | 0.10 |
| 40–49 | 71 | 7.37 |
| 50–59 | 440 | 45.69 |
| 60–69 | 431 | 44.76 |
| 70–79 | 20 | 2.08 |
| Gleason score | | |
| ≤ 6 | 468 | 48.60 |
| 7 | 366 | 38.01 |
| ≥ 8 | 128 | 13.29 |
| Missing | 1 | 0.00 |
| PSA at diagnosis (ng/mL) | | |
| 0–2.5 | 30 | 3.12 |
| 2.51–4.0 | 54 | 5.61 |
| 4.1–6.0 | 247 | 25.65 |
| 6.1–10.0 | 316 | 32.81 |
| > 10.0 | 316 | 32.81 |
| Time to recurrence | | |
| ≤ 3 years | 636 | 65.01 |
| > 3 years | 337 | 34.99 |

**Table 4**

Cox proportional hazards regression model for recurrence following immediate and delayed RP based on CaPSURE data and for prostate cancer death based on T-stage ≤ T2a JH-PCM data. The immediate RP model was fit to 2,150 cases with low-risk disease (T-stage ≤ T2a, Gleason score ≤ 6, and PSA level ≤ 10 ng/mL); the delayed RP model, used to simulate times to recurrence following AS, was fit to 3,470 cases with T-stage ≤ T2a disease.

| End Point | Covariate | Coefficien | Hazard ratio | 95% CI | p-value |
|---|---|---|---|---|---|
| Recurrence under immediate RP | Age | 0.01 | 1.01 | (0.98, 1.03) | 0.527 |
| (Fit to low-risk CaPSURE cohort) | PSA | 0.15 | 1.16 | (1.07, 1.25) | < 0.001 |
| Recurrence under delayed RP | Age | 0.01 | 1.01 | (1.00, 1.03) | 0.187 |
| (Fit to T-stage ≤ T2a CaPSURE cohort) | PSA | 0.03 | 1.03 | (1.02, 1.03) | < 0.001 |
| | Gleason score | | | | |
| | ≤ 6 | ref | | | |
| | 7 | 0.47 | 1.59 | (1.25, 2.03) | < 0.001 |
| | ≥ 8 | 1.43 | 4.16 | (2.92, 5.93) | < 0.001 |
| Prostate cancer mortality | Time to recurrence | −0.44 | 0.65 | (0.51, 0.82) | < 0.001 |
| | Gleason score | | | | |
| | ≤ 6 | ref | | | |
| | 7 | 0.56 | 1.75 | (0.96, 3.17) | 0.066 |
| | ≥ 8 | 0.89 | 2.43 | (1.21, 4.86) | 0.012 |

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## Table 5

Comparison of outcomes of following active surveillance or immediate radical prostatectomy. Outcomes are based on 1 million simulated patients.

| | Immediate RP | Active surveillance |
|---|---|---|
| Treated | 100.00% | 63.68% |
| Treated with Gleason score ≤ 6 | 100.00% | 40.69% |
| Treated with Gleason score 7 | 0.00% | 19.76% |
| Treated with Gleason score ≥ 8 | 0.00% | 3.23% |
| Time to treatment | | |
| ≤ 3 years | – | 27.75% |
| > 3 years | – | 35.93% |
| PSA at treatment (ng/mL) | | |
| 0–2.5 | 14.43% | 14.55% |
| 2.51–4.0 | 14.05% | 13.73% |
| 4.1–6.0 | 43.23% | 30.09% |
| 6.1–10.0 | 28.29% | 30.42% |
| > 10.0 | 0.00% | 11.21% |
| Cumulative incidence of recurrence from diagnosis | | |
| 20-year | 24.54% | 31.13% |
| Lifetime | 29.38% | 37.61% |
| Cumulative incidence of prostate cancer death | | |
| 20-year | 1.64% | 2.78% |
| Lifetime | 2.00% | 3.40% |
| Cumulative incidence of other cause death | | |
| 20-year | 51.60% | 51.13% |
| Lifetime | 98.00% | 96.60% |
| Years of life per person from treatment | 19.66 | 13.30 |
| Total years of life per person from diagnosis | 19.66 | 19.50 |
| Years of life per person lost due to prostate cancer | 0.25 | 0.40 |