Supplemental Appendix

## MODEL STRUCTURE AND PARAMETERS

To evaluate several screening strategies for the detection of prostate cancer (listed in manuscript Table 1), we developed a partially observable Markov model in which pretreatment states are not directly observable. The Markov model includes five pretreatment states that are not directly observable, including no prostate cancer, organ-confined prostate cancer based on Gleason score (<7, 7,>7), and extraprostatic or lymph node-positive cancer. This established model simulates the onset and progression of prostate cancer from age 40 years until end-of-life, and has been validated in Barnett et al. (*1*). This model was extended to estimate model to estimate outcomes for MRI-based screening strategies (*2*). Tests give (imperfect) information about the true state of the patient. The partially observable pretreatment states in the model include no prostate cancer, undetected organ-confined prostate cancers based on Gleason score (<7, 7, >7), and extraprostatic or lymph-node positive cancer (EPLN). The EPLN state aggregates these two conditions into one state because they are similarly associated with decreased survival. The states were selected because they distinguish patients on the basis of likely treatment options, outcomes, and survival.

Figure 1 displays the health states and possible state transitions for the model. As our model focuses on screening of the general population, the screening strategy terminates after initial biopsy and the patient continues to make state transitions in the absence of screening until reaching one of the absorbing states, all-other-cause mortality or prostate cancer mortality. The parameters used to calculate the transition probabilities are described in appendix Table 1.

Our QALY measurements account for disutilities of screening, biopsy, diagnosis, active surveillance, radical prostatectomy, recovery from radical prostatectomy, and metastasis; the

values of the disutilities with their sources are shown in Table 1, which also displays the values of our base case model parameters and their sources. The reward update function for QALYs was:

$$r_t(s_t, a_t) = 1 - \delta_{\text{Scr}} - \delta_{\text{Biop}} - \delta_{\text{Dia}} - \delta_{\text{Tre}} - \delta_{\text{Rec}} - \delta_{\text{AS}} - \delta_{\text{Met}}$$

where $r_t(s_t, a_t)$ is the reward a patient receives at age $t$, which is 1 minus the disutilities associated with screening, biopsy, diagnosis, treatment and the presence of metastatic cancer, as defined in Appendix Table 1. The arguments for the reward are the health state $s_t$ that defines the cancer status of the patient and the action, $a_t$, that defines whether a screening test or biopsy was performed. The total expected QALYs a patient receives in their lifetime is:

$$R = E^{\pi}[\sum_{t=40}^{T} r_t(s_t, a_t)]$$

where T denotes maximum lifespan and the expectation is with respect to the stochastic process induced by the screening strategy $\pi$ that defines the frequency of testing and the thresholds at which to perform biomarker tests and/or biopsies.

Supplemental Appendix Table 1. Parameters, their sources, and the specific values used in our base case and sensitivity analysis.

| Parameter | Symbol | Low Value(s) | Base Case Value(s) | High Value(s) | Source |
|---|---|---|---|---|---|
| Annual transition rate from No PCa to GS<7 | $w_t$ | Lower bound of 95% C.I. | 0.004-0.069 | Upper bound of 95% C.I. | (*3*) |
| Annual other-cause mortality rate | $d_t$ | -20% | 0.002-0.347 | +20% | (*4*) |
| Annual metastasis rate for patients with undiagnosed PCa | $e_t$ | -10% | 0.002-0.037 | +10% | Callibrated |
| Annual PCa-specific mortality rate given metastasized PCa | $z_t$ | -10% | 0.181-0.204 | +10% | (*5*) |
| Sensitivity of prostate biopsy procedure | $f$ | -10% | 0.8 | +10% | (*3*) |
| Annual transition rate from GS<7 to GS=7 | $o1o2$ | -10% | 0.101 | +10% | (*6*) |
| Annual transition rate from GS=7 to GS>7 | $o2o3$ | -10% | 0.087 | +10% | (*6*) |
| Annual transition rate from GS<7 to EPLN | $o1e$ | -10% | 0.029 | +10% | (*6*) |
| Annual transition rate from GS=7 to EPLN | $o2e$ | -10% | 0.081 | +10% | (*6*) |
| Annual transition rate from GS>7 to EPLN | $o3e$ | -10% | 0.097 | +10% | (*6*) |
| Probability of no possible recurrence following definitive treatment in state EPLN | $pnc$ | -10% | 0.468 | +10% | (*7*) |
| Proportion of patients detected with GS<7 who undergo active surveillance | $s$ | -10% | 0.485 | +10% | (*8*) |
| Annual metastasis rate for patients with possible recurrence after definitive treatment in EPLN | $g$ | -10% | 0.006 | +10% | (*9*) |

PCa = prostate cancer; GS = Gleason score; EPLN = extraprostatic or lymph-node positive cancer.

## REFERENCES


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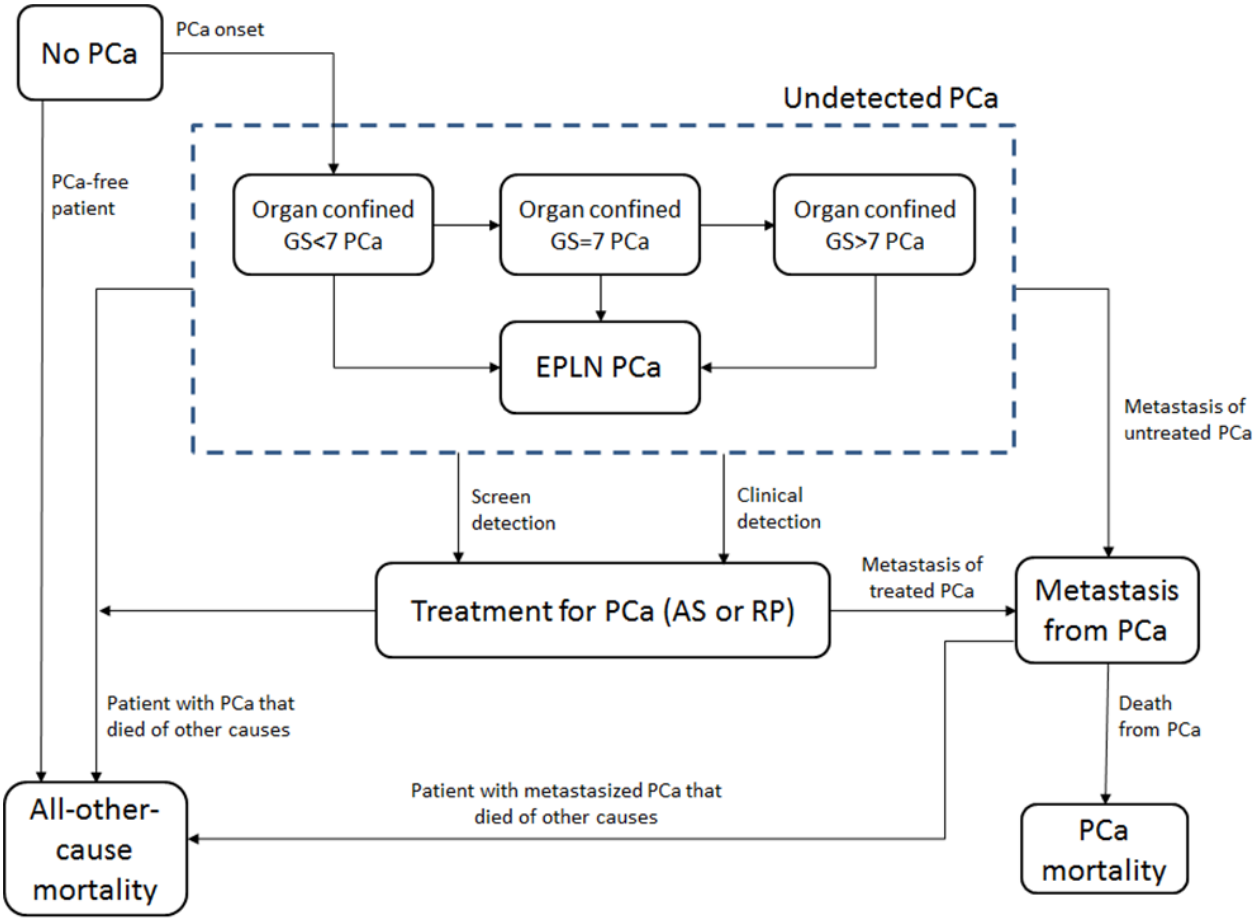
Supplemental Appendix Figure 1. State transition diagram.




Health states and progression paths in the Markov model are shown, where transitions between states are represented by arrows. Patients who are detected with prostate cancer (PCa) are treated immediately with radical prostatectomy (RP) or active surveillance (AS). GS = Gleason score; EPLN = extraprostatic or lymph-node positive cancer.