Supplementary Online Content


eMethods. Microsimulation Model and Definitions

eFigure 1. Observed and Projected Prostate Cancer Incidence Rates per 100,000 Men Ages 50-84 Years for Calendar Years 1975-2010

eFigure 2. Schematic Illustration of Individual Health States and Prostate Cancer Treatment Interventions in the Extended FHCRC Model

eFigure 3. Additional Costs, Life-years (LYs) Gained, and Quality-Adjusted Life-years (QALYs) Gained Under 150 Candidate Screening Strategies Relative to No Screening

eTable. Frequencies of Immediate Curative Treatment Under Contemporary and Selective Treatment Practices for 2 Screening Strategies and Under No Screening

This supplementary material has been provided by the authors to give readers additional information about their work.
eMethods. Microsimulation Model and Definitions

Prostate cancer natural history in the FHCRC model

The FHCRC prostate cancer model links age-dependent PSA levels in healthy men and in cancer cases with prostate cancer onset, progression from a localized to a metastatic stage, and progression from a preclinical state to clinical presentation. Rates of increase in PSA levels, and within- and between-individual variability, are based on PSA test results from the placebo arm of the Prostate Cancer Prevention Trial (PCPT) (1). Risks of cancer onset and of high grade disease increase with age, and risks of progression to metastatic and clinically detected disease increase with PSA. To identify the progression risks we superimpose US screening patterns (2) on a population of simulated disease natural histories. We then determine values of the risks for which model-projected incidence patterns best match observed incidence by age (50–84), stage (local-regional and distant), grade (Gleason 2–7 and 8–10), and year (1975–2000) as observed in the Surveillance, Epidemiology, and End Results (SEER) program. The calibrated model closely reproduces observed prostate cancer incidence patterns (eFigure 1).

Model extensions to identify cases eligible for conservative management

To identify cases eligible for conservative management, the model partitioned cases with Gleason score 2–7 into those with Gleason score 2–6 vs. 7 based on grade-specific PSA growth rates in the PCPT (3). Cases with faster PSA growth had a higher probability of having Gleason score 7. The model also partitioned local-regional stage at diagnosis into clinical T-stage ≤T2a vs. >T2a based on a logistic regression model fit to cases in the CaPSURE database by age, grade, and PSA level (3). Cases with older age, higher grade, or higher PSA level at diagnosis had a higher probability of having T-stage >T2a.

Health state definitions and durations

All individuals enter the modeled population in the healthy state, which spans the initial age at entry (age 40 years) until prostate cancer diagnosis or non-prostate cancer death (eFigure 2). Individuals with clinical presentation of non-metastatic cancer who receive curative treatment first enter a 1-year short-term treatment state and then transition into a long-term effects state until either non-prostate cancer death or until they enter a 2-year end-of-life state leading to prostate cancer death. Counterparts who do not receive curative treatment enter a long-term management state, and counterparts with metastatic cancer at diagnosis (not shown) enter a distant stage state, for this phase. Under “contemporary” treatment practices, transitions through health states are similar for individuals with screen-detected cancer. Under “selective” treatment practices, individuals with screen-detected low-risk (Gleason score <7 and clinical T-stage ≤T2a) cancers enter a conservative management state, which lasts until non-prostate cancer death or the point at which the cancer would have presented clinically in the absence of screening (with similar transitions through subsequent health states). For individuals with
screen-detected high-risk cancers, transitions through health states are similar to those under “contemporary” treatment practices.

**Frequencies of immediate primary treatments under “contemporary” and “selective” treatment practices**

Frequencies of primary treatments immediately following diagnosis projected by the model depend on patient age and tumor characteristics, screening strategy, and treatment practices (eTable 1). Results under two selected screening strategies are stratified for “low-risk” (screen-detected cancers with Gleason score < 7 and clinical T-stage ≤ T2a) or “high-risk” (all other) non-metastatic cancers. Under “selective” treatment practices, low-risk cancers initially receive conservative management but may receive delayed curative treatment if they progress to clinical presentation.

**Cost-effectiveness of the superset of screening strategies**

To supplement the selection of screening strategies evaluated in the main text, we also evaluated the cost-effectiveness of all 150 combinations of starting ages 45, 50, and 55; cessation ages 69 and 74; inter-screening intervals 1, 2, and 4 years and two PSA-dependent intervals (every 1 year if PSA > 3.0 ng/mL and every 2 years otherwise; every 2 years if PSA > 1.0 ng/mL and every 4 years otherwise); and PSA threshold 3.0, 4.0, and 10.0 ng/mL and two age-dependent PSA thresholds (2.5, 3.5, 4.5, and 6.5 μg/L for ages 45–49, 50–59, 60–69, and 70–74; 3.5, 4.5, 5.5, and 8.5 ng/mL for ages 45–49, 50–59, 60–69, and 70–74). For each screening strategy, we calculated cost per LY and per QALY under “contemporary” and “selective” treatment practices (eFigure 3).

**eReferences**


eFigure 1. Observed and Projected Prostate Cancer Incidence Rates per 100,000 Men Ages 50-84 Years for Calendar Years 1975-2010

PSA=reconstructed prostate-specific antigen screening patterns in the US population
eFigure 2. Schematic Illustration of Individual Health States and Prostate Cancer Treatment Interventions in the Extended FHCRC Model
eFigure 3. Additional Costs, Life-years (LYs) Gained, and Quality-Adjusted Life-years (QALYs) Gained Under 150 Candidate Screening Strategies Relative to No Screening

(A) “contemporary” and (B) “selective” treatment practices

A) Cost-effectiveness under “contemporary” treatment practices

B) Cost-effectiveness under “selective” treatment practices

Screening strategies presented in the main text are superimposed as blue dots.
# eTable. Frequencies of Immediate Curative Treatment Under Contemporary and Selective Treatment Practices for 2 Screening Strategies and Under No Screening

<table>
<thead>
<tr>
<th>Screening strategy</th>
<th>Risk group</th>
<th>“Contemporary” treatments</th>
<th>“Selective” treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gulati et al.</td>
<td>Low</td>
<td>CM 18% RP 42% RT 40%</td>
<td>CM 100% RP 0% RT 0%</td>
</tr>
<tr>
<td>reference</td>
<td>High</td>
<td>CM 36% RP 24% RT 40%</td>
<td>CM 36% RP 24% RT 40%</td>
</tr>
<tr>
<td>ERSPC benchmark</td>
<td>Low</td>
<td>CM 14% RP 51% RT 35%</td>
<td>CM 100% RP 0% RT 0%</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>CM 37% RP 24% RT 39%</td>
<td>CM 37% RP 24% RT 39%</td>
</tr>
<tr>
<td>No screening</td>
<td>Any</td>
<td>CM 42% RP 19% RT 39%</td>
<td>CM 42% RP 19% RT 39%</td>
</tr>
</tbody>
</table>

CM=conservative management, with or without systemic therapy
RP=radical prostatectomy, with or without systemic therapy
RT=radiation therapy, with or without systemic therapy