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Economic Analysis of Prostate-Specific Antigen Screening and Selective Treatment Strategies:

Everything in moderation

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Abstract

Importance—Prostate-specific antigen (PSA) screening for prostate cancer is controversial. Experts have suggested more personalized or more conservative strategies to improve benefit-risk tradeoffs, but the value of these strategies—particularly when combined with increased conservative management for low-risk cases—is uncertain.

Objective—To evaluate the potential cost-effectiveness of plausible PSA screening strategies, and to assess the value added by increased use of conservative management among low-risk screen-detected cases.

Design—Micro-simulation model of prostate cancer incidence and mortality under alternative PSA screening strategies and either (1) “contemporary” treatment practices based on age, stage, and grade observed in the Surveillance, Epidemiology, and End Results program in 2010 or (2) “selective” treatment practices where cases with Gleason sum <7 and clinical T-stage ≤T2a are treated only after clinical progression and all others are treated according to “contemporary” treatment practices.

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Reproducible Research Statement: *Study Protocol:* Screening and treatment strategies available from Mr. Gulati (e-mail, rgulati@fredhutch.org). *Statistical Code:* Cost-effectiveness analysis code available from Dr. Roth (e-mail, jroth@fredhutch.org). *Data/Model:* Model source code (languages: C and R) available from Mr. Gulati (e-mail, rgulati@fredhutch.org). A detailed model description is available at http://cisnet.cancer.gov/prostate/profiles.html and a high-level overview of the model is available at https://resources.cisnet.cancer.gov/registry/packages/psapc-fhcrc.

Setting—National and trial data on PSA growth, screening and biopsy patterns, incidence, treatment distributions, treatment efficacy, mortality, health-related quality of life, and direct medical expenditure.

Participants—A simulated contemporary cohort of U.S. men beginning at 40 years of age.

Interventions—18 screening strategies that vary by start and stop age, screening interval, and criteria for biopsy referral; "contemporary" or "selective" treatment practices.

Main Outcome Measures—Life years (LYs), quality-adjusted life years (QALYs), direct medical expenditure, and cost per LY and QALY gained.

Results—All screening strategies increased LYs (range 0.03–0.06) and costs ($300–$1,400) vs. no screening with cost per LY ranging from $7,300 to $21,600. With "contemporary" treatment, only strategies with biopsy referral when PSA >10.0 μg/L or age-dependent thresholds increased QALYs (0.002–0.004), and only quadrennial screening of ages 55–69 was potentially cost-effective in terms of cost per QALY (ICER=$92,400). With "selective" treatment, all strategies increased QALYs (0.002–0.004) and several strategies were potentially cost-effective in terms of cost per QALY (ICER=$70,800–$136,300).

Conclusions—For PSA screening to be cost effective it needs to be used conservatively and ideally in combination with a conservative management approach for low-risk disease.

Keywords

active surveillance; conservative management; cost-effectiveness; prostate cancer screening; prostatic neoplasms

INTRODUCTION

With the U.S. Preventive Services Task Force (USPSTF) recommendation against routine prostate-specific antigen (PSA) screening[1], and conservative guidance from other national panels[2–4], the future of PSA screening is uncertain. The recently updated guidelines relied heavily on results from two large trials conducted in the U.S. and Europe[5–7]. These results have been interpreted by some as demonstrating that PSA screening provides at most modest benefit, with unacceptable costs in terms of overdiagnosis and overtreatment[8,9]. However, over a long-term horizon, the lives saved by screening are likely to be considerably higher, and the fraction overdiagnosed considerably lower compared with the trials[10–13]. Rather than rejecting screening, we have recommended seeking more personalized (or "smarter") screening strategies that preserve benefit while reducing harms[13,14]. Unfortunately, these strategies are unlikely to be evaluated in randomized trials due to resource and logistical constraints. Therefore, we have used modeling to conduct simulated comparisons of candidate screening approaches.

In a recent study[15], we projected outcomes for a contemporary cohort of U.S. men using 35 screening strategies that varied by screening ages, inter-screening intervals, and criteria for biopsy referral. We identified several strategies that reduced screening harms by more than half yet retained the majority of lives saved relative to a "reference" annual screening strategy for men aged 50–74 years. These "smarter" strategies used longer inter-screening

intervals and more conservative criteria for biopsy referral in older men. Other investigators have also proposed screening policies with similar objectives, including: stopping screening at age 60 if PSA <1.0 μg/L[16], using baseline PSA at age 45–50 to identify men appropriate for less frequent screening[17], and referring to biopsy only when PSA >10.0 μg/L[9]. However, no studies to date have evaluated how these strategies alter the benefit-risk balance of PSA screening, or if they represent high-value alternatives to no screening[18].

Beyond "smarter" screening strategies, there is growing support for more selective treatment strategies. Active surveillance, which manages newly diagnosed patients conservatively with serial biopsies, is an increasingly common approach[19–21] for treating low-risk cases—which constitute the majority of newly diagnosed prostate cancers. However, few studies have projected screening outcomes under alternative treatment practices.

The primary objective of this modeling study is to investigate whether "smarter" PSA prostate cancer screening strategies have the potential to be effective and cost-effective relative to no screening. Additionally, we investigate the potential added value of combining screening and treatment strategies by also projecting outcomes under "selective" treatment practices with increased use of conservative management among men with screen-detected low-risk disease.

METHODS

Overview

The Fred Hutchinson Cancer Research Center (FHCRC) micro-simulation model of prostate cancer (summarized in the Supplement) was developed as part of the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET) prostate cancer working group[22]. The model is unique among prostate cancer models because it explicitly links cancer progression with individual PSA growth. This link is critical for evaluating screening strategies with PSA-dependent criteria for biopsy referral, inter-screening intervals, and/or early cessation. The model has been fit to U.S. incidence data (eFigure 1 in the Supplement), and has been used to study population incidence and mortality trends[23] and evaluate the comparative effectiveness of alternative PSA screening policies[15].

We expanded the FHCRC model to estimate quality-adjusted survival and costs for coordinated screening and treatment strategies from a U.S. healthcare payer perspective. For each strategy, the model simulated a cohort of men beginning at age 40 and projected prostate cancer outcomes over a lifetime horizon. We calculated outcomes using health state utility and cost weights applied to the person-years tallied in the healthy state and in the post-diagnosis states (eFigure 2 in the Supplement). Costs and survival outcomes were discounted at 3% per year in the base case, and cost outcomes are presented in 2014 USD. This modeling study was exempt from human subjects review.

Screening strategies

The strategies in our analysis (Figure 1) reflect promising strategies from our prior comparative effectiveness evaluation[15] and approximations to the National Comprehensive

Cancer Network recommendations (Strategy 2)[24], the American Urologic Association guidelines statement (Strategy 14)[2], and the commonest protocol used in the European Randomized Study of Screening for Prostate Cancer (Strategy 15)[25]. We also consider strategies that use a high PSA threshold (i.e., 10.0 μg/L) for referral to biopsy (Strategies 3–4, 9–12, and 16–18)—a value that would mandate a biopsy recommendation. Supplementing this selection, we also evaluated the cost-effectiveness of the superset of screening strategies comprising 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 (explained in the Supplement); and PSA threshold 3.0, 4.0, and 10.0 μg/L and two age-dependent PSA thresholds (explained in the Supplement).

Survival model

In the absence of screening and curative treatment, prostate cancer survival is based on observed survival for untreated cases diagnosed in SEER in 1983–1986, just before the PSA era. Frequencies of curative surgery and/or radiation are based on SEER trends by age, stage, and grade at diagnosis, and frequencies of adjuvant hormone use are based on patterns observed in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) database[26]. Effects of curative treatment are based on the Scandinavian randomized trial of prostatectomy vs. watchful waiting (HR=0.62)[27] and assuming similar efficacy for contemporary radiation therapy[28,29].

The model represents the effect of early detection on prostate cancer survival by assuming that would-be metastatic cases screen-detected at a local-regional stage have their survival changed to that associated with detection at the earlier stage. We previously showed that this effect is consistent with the published 21% mortality reduction reported in ERSPC[14,15]. Although the results of the U.S. Prostate, Lung, Colorectal, and Ovarian cancer screening trial[14,30,31] did not show a reduction in the screen arm, we showed that the extensive control arm contamination suggests that a mortality benefit of this magnitude cannot be ruled out[30].

In this study, the model was extended to track time spent in pre- and post-diagnosis states, including short- and long-term disease management states after receipt of curative treatment, a “no curative treatment” state for individuals not receiving curative treatment, and a two-year end-of-life state for men who die of prostate cancer. Cases with low-risk disease detected by screening may defer therapy until they progress to a point at which their disease would have become clinically apparent in the absence of screening. The Supplement summarizes health state definitions and durations.

“Contemporary” and “selective” treatment practices

We consider two initial treatment scenarios. Under “contemporary” treatment practices, all cases receive curative treatment (prostatectomy or radiation therapy, with or without androgen deprivation therapy) based on the frequencies of treatment observed in the SEER program in the year 2010 by age, stage, and grade. We do not model the small proportion of localized cases who receive androgen deprivation therapy alone. In contrast, under “selective” treatment practices, screen-detected cases with Gleason score <7 and clinical T-stage ≤T2a disease initially receive conservative management and all other cases receive the

same treatments as under “contemporary” treatment practices. The Supplement describes extensions to the FHCRC model to identify cases eligible for conservative management and frequencies of immediate primary treatments (eTable 1).

We model a conservative management program in which curative treatment is offered once cases progress to the point of would-be clinical diagnosis in the absence of screening. Consequently, only non-overdiagnosed cases receive delayed curative treatment. This conservative version of active surveillance (AS) is modeled because there is no consensus around the appropriate conduct of AS, and the timing of progression to treatment under AS is therefore unclear. Further, the endpoint of would-be clinical diagnosis in the absence of screening is generated by the FHCRC model. We believe this represents a useful benchmark for comparison but acknowledge that under most contemporary AS approaches, curative therapy would likely be offered at an earlier time point.

Health-related quality of life and costs

Few studies have produced estimates of health state utilities for prostate cancer and its treatment. The health state utility for men without prostate cancer diagnosis was assumed to be 1.0 to represent full health. All other health state utilities were extracted from a prior U.S. study of 162 men aged ≥60 years or older that used standard gamble to elicit preferences for 19 prostate cancer health states (Table 1)[32]. Note that the short-term treatment health state utility decrement was applied for one year to localized cases receiving prostatectomy or radiation therapy, and reflects a weighted average of patients with and without major treatment side effects.

We obtained cost estimates related to PSA testing, office visits, and conservative management by micro-costing resource use with the Centers for Medicare and Medicaid Services 2014 reimbursement schedule[33]. Costs for surgical treatment and radiation therapy episodes were derived from a prior SEER-Medicare analysis that calculated the mean procedure-attributable cost for patients receiving either type of treatment[34]. Biopsy, distant stage initial treatment (one-time), long-term management, end-of-life, and treatment complication costs were derived from prior economic analyses in prostate cancer (Table 1)[28,35–37]. Treatment complication costs were applied to 12.5% and 4.2% of men receiving prostatectomy and radiation therapy, respectively, based on the rates of Grade 3/4 complications in a prior analysis.[28] Cost inputs were adjusted using the medical care component of the consumer price index to 2014 USD[38].

Model outcomes

We used the model to calculate prostate cancer diagnosis, treatment, death, unadjusted life years, quality-adjusted life years (QALYs), and cost for each screening strategy. The incremental cost-effectiveness ratio (ICER) was calculated as the ratio of the difference in costs between strategies to the difference in effects (e.g., QALYs) between strategies[38].

We calculated probabilistic outcomes using Monte Carlo simulation and conducted one-way sensitivity analyses to determine the inputs with the greatest influence on incremental QALY and cost outcomes[39].

Cost-effectiveness was evaluated at willingness-to-pay thresholds ranging from $50,000 to $150,000 per QALY[40–44]. This range reflects the implied willingness-to-pay for cancer treatments in the U.S. and is consistent with values used in prior analyses[40,44–46].

RESULTS

"Contemporary" treatment practices

Table 2 displays the results under "contemporary" treatment practices. Among the 18 screening strategies evaluated, all increased life years (range=0.03–0.06) compared with no screening, but only strategies with biopsy threshold at PSA >10.0 μg/L increased QALYs (range=0.002–0.004). Among this subset of strategies, cost per life year ranged from $12,000 to $21,000. Only quadrennial screening of ages 55–69 with a biopsy threshold at PSA >10.0 μg/L (Strategy 18) was potentially cost-effective in terms of cost per QALY ($92,446/QALY).

Corresponding results for the superset of screening strategies show that our selection of promising and policy-relevant strategies is representative of the range of cost-effectiveness outcomes (eFigure 3 in the Supplement). In general, only a small number of conservative screening strategies (4% of the superset) similar to those presented in Table 2 were potentially cost-effective at a willingness-to-pay of $150,000 or less per QALY.

"Selective" treatment practices

"Selective" treatment practices were implemented only for strategies with PSA thresholds below 10.0 μg/L because prostate cancer cases diagnosed with PSA >10.0 μg/L would not typically qualify as "low-risk" or candidates for delayed curative treatment. Among the 10 screening strategies evaluated (Table 2), Strategies 8, 14, and 15 compared most favorably with no screening, resulting in 0.041, 0.046, and 0.036 more life years, 0.004, 0.003, and 0.004 more QALYs, and $353, $397, and $262 greater cost, respectively. All of these strategies have an inter-screening interval of 2–4 years with PSA biopsy thresholds of 4.0, 3.0, and 3.0 μg/L; the ICERs for these strategies were $8,622, $7,335, and $8,600 per life year gained and $89,333, $70,831, and $120,952 per QALY gained, respectively.

Results for the superset of screening strategies with "selective" treatment practices, including those with biopsy threshold at PSA >10.0 μg/L, show that a large proportion of the strategies are potentially cost-effective at willingness-to-pay levels of $100,000 (43% of the superset) and $150,000 (70% of the superset) per QALY (eFigure 3 in the Supplement). The most cost-effective strategies in the superset are similar to the most cost-effective strategies in Table 2.

Sensitivity analysis

One-way sensitivity analyses focused on QALYs demonstrated that results were by far most sensitive to the health state utility in the conservative management state. One-way sensitivity analyses evaluating cost differences were most sensitive to the costs of prostate cancer death, radiation therapy, and PSA testing. All analyses were conditional on the assumed efficacy of curative treatment.

Under “contemporary” treatment practices, the probabilistic sensitivity analysis demonstrated a low probability of PSA screening cost-effectiveness at willingness-to-pay levels at or below $100,000 per QALY (Figure 2A). Only quadrennial screening of men age 55–69 with a PSA biopsy threshold of 10.0 μg/L had greater than a 50% probability of being potentially cost-effective at willingness-to-pay of $100,000 and $150,000 per QALY (Figure 2).

Under “selective” treatment practices, the probabilistic sensitivity analysis demonstrated that no strategies had a greater than 50% probability of being cost-effective at a willingness-to-pay of $50,000 per QALY, and only quadrennial screening of men age 55–69 with a PSA biopsy threshold of 3.0 μg/L (Strategy 15) and quadrennial screening of men age 50–74 with a PSA biopsy threshold of 4.0 μg/L (Strategy 8) had greater than a 50% probability of being potentially cost-effective at a willingness-to-pay of $100,000 per QALY (Figure 2). Several other relatively conservative strategies (7, 10, 13, and 14) were potentially cost-effective at a willingness-to-pay of $150,000 per QALY (Figure 2).

DISCUSSION

The value of PSA screening for prostate cancer is uncertain, as reflected by variable clinical guidelines. This study provides the first quantitative framework to evaluate the comparative effectiveness of PSA-based screening strategies and selective treatment approaches, and it addresses an urgent need for direction concerning the future of PSA screening in the U.S. Our work indicates strategies with conservative screening frequency (e.g., quadrennial) and/or a higher PSA biopsy threshold (e.g., 4.0 μg/L) are potentially cost-effective when combined with increased use of conservative management for low-risk cases, but are unlikely to be cost-effective under contemporary treatment practices.

Our findings have clear implications for the future of PSA screening in the U.S. Rather than stopping PSA screening, as recommended by the USPSTF, implementation of strategies that extend the inter-screening interval and/or utilize higher PSA biopsy thresholds have the potential to preserve substantial benefit while controlling harm and costs. Though higher-threshold policies (e.g., 10.0 μg/L) are unlikely to be clinically appealing, they reinforce the general conclusion that conservative patterns of screening and biopsy referral are important directions to consider if PSA screening is to be both clinically effective and cost-effective.

All strategies evaluated were potentially cost-effective in terms of cost per life year (range= $7,300–$21,600). However, that metric ignores the important health-related quality of life impacts of cancer diagnosis, treatment, and associated complications. For this reason, our primary analysis evaluated the impacts of PSA screening in terms of cost per QALY. In analyses with “contemporary” treatment practices, we demonstrated that only strategies with highly conservative PSA biopsy thresholds (i.e., 10.0 μg/L) are expected to increase QALYs relative to no screening, and among those strategies only the most conservative (quadrennial screening of ages 55–69) was potentially cost-effective.

The contrasting cost-effectiveness results of the “contemporary” vs. “selective” treatment practices demonstrates the importance of conservative management of low-risk prostate

cancer and the potential for increased use of active surveillance to make the benefit-risk tradeoffs and cost-effectiveness of screening acceptable. For example, quadrennial screening of men age 55–69 with biopsy threshold at 3.0 μg/L (Strategy 15) and quadrennial screening of men age 50–74 with biopsy threshold at 4.0 μg/L (Strategy 8) were both dominated under "contemporary" treatment practices but had ICERs of $89,300 and $70,800 per QALY under "selective" treatment practices, respectively. These favorable results in the "selective" treatment scenario are due to low-risk men on conservative management having better health-related quality of life, lower cost, and similar survival compared with low-risk men who receive immediate curative treatment. Additionally, we observed in the supplemental analysis of the superset of 150 screening strategies that the high PSA biopsy threshold (e.g., 10.0 μg/L) found to be favorable under "contemporary" treatments has similar value under "selective" treatments because men diagnosed with high PSA are more promising candidates for immediate treatment[47] and are generally ineligible for surveillance programs.

There has been substantial discussion of the need for cost-effectiveness analyses exploring emerging PSA screening strategies, but few such studies have been reported in the literature[48,49]. A recent study used another CISNET micro-simulation model to evaluate the cost-effectiveness of a range of screening strategies in a European setting[50]. Their most cost-effective strategy screened men ages 55–59 at 2-year intervals, which is consistent with our conclusions that conservative use of the test is imperative. The authors concluded that shorter inter-screening intervals are more cost-effective than longer intervals when they examined strategies with cessation around age 60. In contrast, when they examined strategies with higher cessation ages, they found that longer screening intervals were more cost-effective. For example, quadrennial screening to age 69 or 74 achieved much lower additional costs but similar QALYs gained compared to biennial or annual screening (Figure 2B in that study). It should be noted that their model reflects a European setting with very different costs for many services, and with a lower frequency of curative treatments relative to the U.S. Additionally, several post-diagnosis utility values (e.g., active surveillance=0.97 and 1 year after initial primary treatment=0.95) were more favorable than ours (0.92 for both states). Nevertheless, despite these differences, and differences in how the two models represent and estimate prostate cancer natural history[5152], there is broad agreement between their study and ours that only a highly conservative PSA screening strategy will be cost-effective.

This analysis has several limitations that should be noted. First, this is a micro-simulation study that uses the best available evidence to project the comparative effectiveness of PSA screening strategies vs. no screening. Ideally, the comparative effectiveness of the PSA screening strategies would be evaluated head-to-head in "real world" settings prior to implementation. However, this is unlikely given the resource demands and complexity of designing studies to evaluate dozens of screening strategies. As a result, rigorously developed and validated disease models play an important role in projecting the comparative effectiveness of alternative PSA screening strategies. Nonetheless, our model evaluates a long-term time horizon, and there like to be is increasing uncertainty around model-projected results over time.

Few studies have elicited health state utilities for the PSA screening, making cost-effectiveness analyses challenging in this setting. As a result, we assume equivalence between several health states and those noted in prior studies (e.g., our conservative management utility was assumed to be equivalent to that of prostate cancer patients with a 20% chance of cancer spread not currently receiving treatment)[53]. However, we do allow a fraction of those cases to later receive curative treatment, and their utilities are modified accordingly at that time. We do not model the health-related quality of life impacts of biopsies. Neither do we model the impact of an elevated PSA (say 4.0 μg/L) that is still below the threshold for biopsy referral (say 10.0 μg/L) owing to a lack of data in this setting. Further, our analysis does not reflect the substantial costs of several recently approved systemic treatments for advanced prostate cancer. To the extent that screening reduces metastasis and castrate resistance, inclusion of these new treatments could improve screening cost-effectiveness outcomes relative to those projected in this study. Our previous studies have discussed other technical limitations of the FHCRC model[15].

We recognize that the modeled conservative management program in the “selective” treatment scenario reflects a highly conservative approach to active surveillance. There is not a standard protocol for active surveillance, but most contemporary programs would likely identify and treat progressive cases before they progressed to clinically detected disease (when cases are treated in the model). Thus, the “selective” treatment scenario results might underestimate survival and costs compared with contemporary active surveillance protocols.

In conclusion, our work adds to a growing consensus[50,54,55] that highly conservative use of the PSA test and biopsy referral is necessary if PSA screening is to be cost-effective. Among the strategies considered, less frequent screening and more restrictive criteria for biopsy resulted in greater chances of PSA screening being cost-effective—particularly when combined with “selective” treatment strategies that do not immediately treat low-risk screen-detected cases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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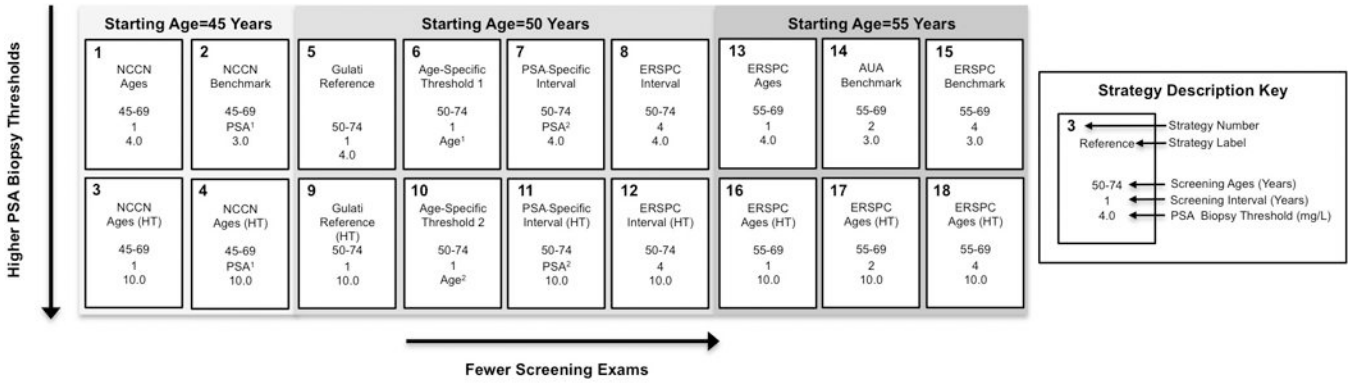

Figure 1. Candidate PSA screening strategies

Strategies were suggested by published screening studies, approximation to a trial protocol, approximation to a clinical recommendation statement from a national organization, or a combination of sources. All strategies are compared to no screening.

NCCN=National Comprehensive Cancer Network

ERSPC=European Randomized Study of Screening for Prostate Cancer

AUA=American Urological Association

PSA^1-dependent screening interval is every 1 year if PSA >3.0 μg/L and every 2 years otherwise.

PSA^2-dependent screening interval is every 2 years if PSA >1.0 μg/L and every 4 years otherwise.

Age^1-dependent PSA thresholds for biopsy referral are 3.5, 4.5, and 6.5 μg/L for ages 50–59, 60–69, and 70–74 y.

Age^2-dependent PSA thresholds for biopsy referral are 4.5, 5.5, and 8.5 μg/L for ages 50–59, 60–69, and 70–74 y.

HT=high threshold

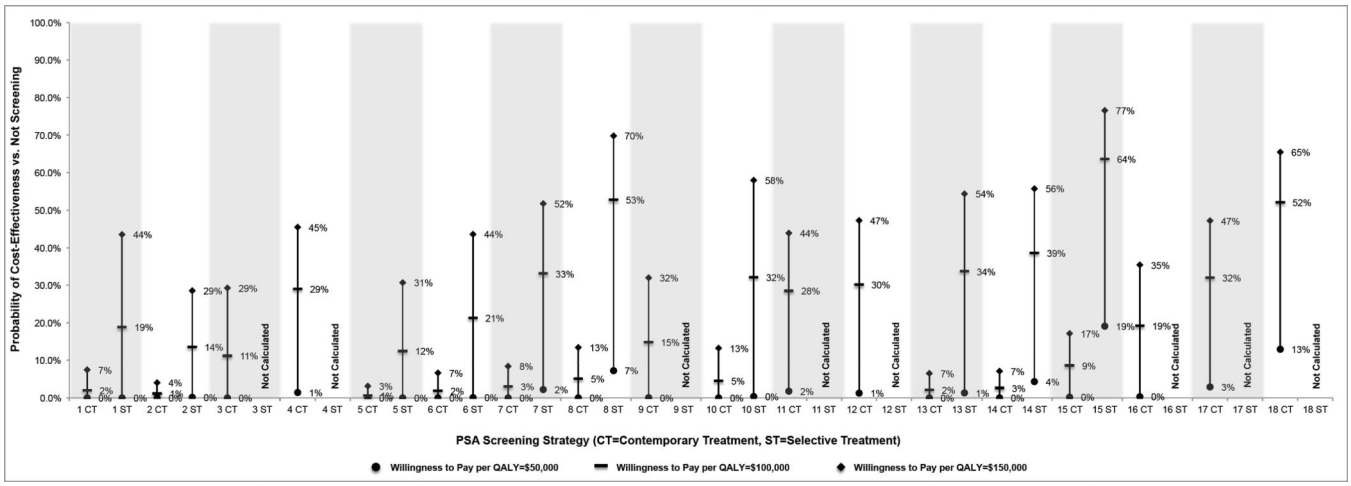

Figure 2.

Cost-effectiveness acceptability results for the "contemporary" and "selective" treatment scenarios at willingness to pay levels of $50,000–$150,000 per quality-adjusted life year gained. The strategy numbers relate to the strategies in Table 2. The percentages noted in the figure relate to the proportion of simulation runs in which the cost per quality-adjusted life year was less than or equal to the given willingness to pay.

We do not report results for strategies with PSA threshold for biopsy of 10.0 μg/L in the "selective" treatment scenario because cases detected by screening are unlikely candidates for conservative management with delayed curative treatment.

Table 1

Health state utility and direct medical expenditure model inputs

The expenditure values below are presented as reported in the original publications. All costs were analyzed in 2014 USD.

Parameter	Point Estimate	Low Value	High Value	Distribution	Reference (Reference Number)
Direct Medical Expenditure Inputs					
PSA Test Cost (Per Procedure)	$27	$22	$32	Normal	CMS Reimbursement Schedule (33)
Biopsy Cost (Per Procedure)	$688	$550	$826	Normal	Hayes, Ann Int Med, 2013 (35)
Conservative Management Cost (Per Year) *	$476	$381	$571	Normal	CMS Reimbursement Schedule (33)
Mean Prostatectomy Cost (Per Procedure)	$10,600	$6,410	$10,684	Normal	Wang, Med Care, 2014 (34)
Mean Radiation Therapy Cost (Full Course of Treatment)	$22,515	$18,012	$27,018	Normal	Wang, Med Care, 2014 (34)
Androgen Deprivation Therapy Cost (Per Year)#	$2,267	$1,814	$2,720	Normal	Cooperberg, BJU Int, 2013 (28)
Distant Stage Initial Treatment Cost (Full Course of Treatment)&	$15,773	$12,618	$18,927	Normal	Cooperberg, BJU Int, 2013 (28)
Distant Stage Management Cost (Per Year)&	$2,212	$1,106	$4,424	Normal	Cooperberg, BJU Int, 2013 (28)
End-of-Life Cost (Last Year), Prostate Cancer Death	$40,807	$20,404	$81,614	Normal	Cooperberg, BJU Int, 2013 (28)
End-of-Life Cost (Last Year), Other Cause Death	$5,000	$4,000	$6,000	Normal	Mobley, MDM, 2006 (37)
Surgical Complication Cost (Per Event)	$709	$567	$851	Normal	Cooperberg, BJU Int, 2013 (28)
Radiation Therapy Complication Cost (Per Event)	$230	$184	$276	Normal	Cooperberg, BJU Int, 2013 (28)
Office Visit Cost^	$80	$64	$96	Normal	CMS Reimbursement Schedule (33)
Health State Utility Value Inputs					
Healthy, Utility	1.00	0.90	1.00	Beta	Assumption
Symptomatic, Utility Decrement	0.11	0.05	0.17	Beta	Stewart, Med Care, 2005 (32)
Surveillance, Utility Decrement	0.08	0.02	0.14	Beta	Stewart, Med Care, 2005 (32)
Short-Term Treatment, Utility Decrement	0.25	0.19	0.31	Beta	Stewart, Med Care, 2005 (32)
Long-Term Treatment, Utility Decrement	0.08	0.02	0.14	Beta	Stewart, Med Care, 2005 (32)
Distant Stage, Utility Decrement	0.25	0.22	0.28	Beta	Stewart, Med Care, 2005 (32)
End-of-Life, Utility Decrement	0.67	0.57	0.77	Beta	Stewart, Med Care, 2005 (32)

*Conservative management was assumed to consist of an annual office visit, annual PSA test, and a biennial biopsy.

#Men receiving initial curative treatment involving androgen deprivation therapy with prostatectomy or radiation therapy were assumed to receive one year of treatment.

[&] The "distant stage initial treatment cost" was a one-time cost of initial treatment applied to men diagnosed with distant stage disease. The "distant stage management cost" reflects the ongoing cost of care in the distant stage state and was applied to all years in that state.

[^] The cost of office visits was applied once annually in men without prostate cancer diagnosis.

Table 2

Results in the “contemporary” and “selective” treatment scenarios. The PSA screening strategy results are listed in descending order of quality-adjusted life years in the “contemporary treatment” scenario

We do not report results for strategies with PSA threshold for biopsy 10.0 μg/L in the “selective” treatment scenario because cases detected by screening are unlikely candidates for conservative management with delayed curative treatment.

PSA Screening Strategy Number	Screening Ages (Years)	Inter-Screening Interval (Years)	PSA Threshold for Biopsy Referral (μg/L)	"Contemporary Treatment" Scenario					"Selective Treatment" Scenario				
				Total Life Years	Total QALYs	Total Cost	Cost Per Life Year Gained	Cost Per QALY Gained	Total Life Years	Total QALYs	Total Cost	Cost Per Life Year Gained	Cost Per QALY Gained
No Screening	-	-	-	36.302	21.504	$4,708	Reference	Reference	36.302	21.504	$4,708	Reference	Reference
4	45–69	PSA[1]	10	36.347	21.508	$5,391	$15,344	$184,074	-	-	-	-	-
18	55–69	4	10	36.329	21.508	$5,022	$11,977	$92,446	-	-	-	-	-
12	50–74	4	10	36.338	21.507	$5,246	$15,123	$170,195	-	-	-	-	-
11	50–74	PSA[2]	10	36.348	21.507	$5,357	$14,209	$209,338	-	-	-	-	-
9	50–74	1	10	36.357	21.507	$5,698	$18,160	$330,065	-	-	-	-	-
17	55–69	2	10	36.338	21.507	$5,197	$13,734	$170,981	-	-	-	-	-
3	45–69	1	10	36.345	21.507	$5,590	$20,761	$326,292	-	-	-	-	-
16	55–69	1	10	36.343	21.506	$5,371	$16,347	$300,884	-	-	-	-	-
15	55–69	4	3	36.343	21.502	$5,315	$14,977	Dominated	36.338	21.508	$4,971	$7,335	$70,831
8	50–74	4	4	36.348	21.502	$5,513	$17,466	Dominated	36.343	21.508	$5,062	$8,622	$89,333
10	50–74	1	Age[2]	36.361	21.502	$5,818	$19,006	Dominated	36.355	21.509	$5,329	$11,838	$124,564
1	45–69	1	4	36.361	21.499	$5,919	$20,751	Dominated	36.354	21.509	$5,404	$13,409	$163,214
7	50–74	PSA[2]	4	36.359	21.499	$5,730	$17,983	Dominated	36.352	21.508	$5,160	$9,098	$136,332
6	50–74	1	Age[1]	36.363	21.498	$5,928	$19,972	Dominated	36.357	21.508	$5,364	$11,906	$166,784

PSA Screening Strategy Number	Screening Ages (Years)	Inter-Screening Interval (Years)	PSA Threshold for Biopsy Referral (μg/L)	"Contemporary Treatment" Scenario					"Selective Treatment" Scenario				
				Total Life Years	Total QALYs	Total Cost	Cost Per Life Year Gained	Cost Per QALY Gained	Total Life Years	Total QALYs	Total Cost	Cost Per Life Year Gained	Cost Per QALY Gained
13	55–69	1	4	36.355	21.498	$5,688	$18,645	Dominated	36.350	21.508	$5,187	$9,985	$128,680
14	55–69	2	3	36.353	21.498	$5,597	$17,390	Dominated	36.349	21.508	$5,105	$8,600	$120,952
5	50–74	1	4	36.366	21.494	$6,079	$21,649	Dominated	36.360	21.507	$5,411	$12,293	$243,768
2	45–69	PSA[1]	3	36.360	21.494	$5,835	$19,622	Dominated	36.353	21.506	$5,269	$11,028	$313,214

PSA[1]-dependent screening interval is every 1 year if PSA >3.0 μg/L and every 2 years otherwise.

PSA[2]-dependent screening interval is every 2 years if PSA >1.0 μg/L and every 4 years otherwise.

Age[1]-dependent PSA thresholds for biopsy referral are 3.5, 4.5, and 6.5 μg/L for ages 50–59, 60–69, and 70–74 y.

Age[2]-dependent PSA thresholds for biopsy referral are 4.5, 5.5, and 8.5 μg/L for ages 50–59, 60–69, and 70–74 y.

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