Cost-Effectiveness of Magnetic Resonance Imaging and Targeted Fusion Biopsy for Early Detection of Prostate Cancer

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ABSTRACT

Objective: To determine how best to use MRI and targeted MR/ultrasound fusion biopsy for early detection of prostate cancer in men with elevated PSA and whether it can be cost-effective.

Methods: A Markov model of prostate cancer onset and progression was developed to estimate health and economic consequences of prostate cancer screening with MRI. Men were screened with prostate-specific antigen (PSA) from ages 55 to 69. Men with elevated PSA (>4 ng/mL) received an MRI, followed by targeted fusion or combined (standard + targeted fusion) biopsy on positive MRI, and standard or no biopsy on negative MRI. Prostate imaging reporting and data system (PI-RADS) score on MRI determined biopsy decisions. Deaths averted, quality-adjusted life years (QALYs), cost, and incremental cost-effectiveness ratio (ICER) were estimated for each strategy.

Results: With a negative MRI, standard biopsy was more expensive and had lower QALYs than performing no biopsy. The optimal screening strategy (ICER: $23,483/QALY) recommended combined biopsy for men with PI-RADS score ≥3 and no biopsy for men with PI-RADS score <3, and reduced the number of screening biopsies by 15%. Threshold analysis suggests MRI continues to be cost-effective when sensitivity and specificity of MRI and combined biopsy are simultaneously reduced by 19.0.

Conclusions: Our analysis suggests MRI followed by targeted MR/ultrasound fusion biopsy can be a cost-effective approach for early detection of prostate cancer.

1. Introduction

Concerns about the poor sensitivity and specificity of the prostate-specific antigen (PSA) test have led to recommendations to discontinue prostate cancer (PCa) screening in the United States.[1] A key factor

leading to this recommendation is that PSA does not distinguish between likely indolent and potentially lethal PCa.[2] As a result, many men who undergo PSA screening receive biopsies with negative results, which are associated with pain, anxiety, and the potential for infection.[3] Eliminating screening spares men from unnecessary biopsies; however, it also results in late detection of intermediate- and high-grade cancers, potentially leading to poor outcomes for these patients.[4]

Magnetic resonance imaging (MRI) recently has been proposed as a way to achieve early detection of high-grade cancer in a minimally invasive way. This would potentially reduce overtreatment by preferentially detecting intermediate- and high-grade cancers.[5,6,7,8] However, MRI is costly and there is limited evidence for its effectiveness as an intermediate test in patients being screened for PCa. Moreover, there are multiple ways to use MRI in a screening setting, and it is not clear which is best. For example, if an MRI does not detect lesions suspicious for prostate cancer, either no biopsy or a standard biopsy (which randomly samples cores of tissue from the entire prostate gland) can be performed. If an MRI detects suspicious lesions, a targeted MR/ultrasound fusion biopsy (i.e. targeted fusion biopsy) can be performed in which the MR images are used with real-time ultrasound to sample cores of tissue directly from suspicious lesions; alternatively, a combined approach can be used in which both standard and targeted fusion biopsies are performed during a single biopsy session. Since there are multiples ways to implement MRI in a screening setting, the optimal clinical pathway is unknown.

We used a Markov model to evaluate the cost-effectiveness of MRI in a screening setting. We used the model to predict outcomes based on simulation for five screening strategies and report the results on the basis of 1,000 men. The frequency of screening for each strategy was based on the American Urological Association (AUA) guideline for PSA screening. The first strategy employed standard biopsy for men with elevated PSA (>4 ng/mL).[10] The other four strategies performed MRI on men with elevated PSA, and the results were used to decide whether the men should be referred for no biopsy, standard biopsy, targeted fusion biopsy, or combined (standard + targeted fusion) biopsy. We estimated the number of deaths averted, quality-adjusted life years (QALYs) gained, and the total cost for each strategy. Additionally, we estimated the incremental cost-effectiveness ratios (ICERs).

2. Methods

We extended a recently validated partially observable Markov model to estimate outcomes for MRI-based screening strategies.[9] The extended Markov model included five pretreatment states that are not directly observable, including no prostate cancer, organ-confined prostate cancers based on Gleason score (GS<7, GS=7, GS>7), and extraprostatic or lymph-node positive cancer (EPLN). This established model simulates the onset and progression of prostate cancer from age 40 until end-of-life, and has been validated in Barnett et al. [9] We incorporated the five biopsy strategies and updated the annual metastasis rate to calibrate our model based on estimates from the literature.[11] Our revised model estimates for expected life-years gained and QALYs gained from PSA screening have external validity relative to

another recent cost-effectiveness study of PSA screening.[12] For each strategy, we used 30,000,000 samples of biopsy-naïve men who were screened every two years from age 55 to 69 according to the AUA guideline. In strategy 1, a standard biopsy was recommended for elevated PSA (>4 ng/mL). The decision rule diagram for strategies 2 through 5 is shown in Figure 1. Each strategy from 2–5 recommended MRI for elevated PSA, while actions based on the MRI results depended on the strategy as defined in Table 1. Our model focuses on initial biopsy decisions; thus, the screening strategy terminates after the patient receives an initial biopsy or two negative MRIs. However, the patient continues to make state transitions in the absence of screening until all-other-cause mortality or clinical detection and subsequent mortality of PCa.

The model was comprised of discrete health states based on Gleason score, which are not directly observable but can be inferred from PSA and MRI subject to published estimates of sensitivity and specificity. In our model, we considered clinically significant disease to be any Gleason score ≥7. For standard biopsy, the results were randomly sampled as either positive or negative for any prostate cancer, assuming a sensitivity of 80.0.[13] If the biopsy result was positive, the probability that the biopsy provides an incorrect grading at diagnosis was based on data reported by Epstein et al.[14] For targeted fusion and combined biopsy, we used the values of sensitivity and specificity to high-grade cancer (high volume Gleason 3+4 or ≥ Gleason 4+3) reported in Siddiqui et al: 77.0 and 68.0, respectively, for targeted fusion biopsy, and 85.0 and 49.0, respectively, for combined biopsy.[5] Based on Medicare infection rates reported in Loeb et al, 1.1% of biopsies performed led to hospitalization for post-biopsy infection.[3,15]

In addition to detection of PCa through routine screening, the model incorporated the clinical detection of symptomatic PCa. For each patient, we randomly sampled a lead time from an elevated PSA measurement of ≥3 ng/mL to clinical diagnosis of PCa from a distribution developed by Savage et al.[16] If a patient had PCa and a PSA score ≥3 ng/mL for their lead time[16] and had not yet been diagnosed with PCa in the model, it was assumed the patient was clinically detected due to symptoms.

2.1 Treatment

Patients with PSA >20 ng/mL or a Gleason score ≥8 received a bone scan and a computed tomography scan for staging.[17,18] Patients with a biopsy result of Gleason score ≥7 received radical prostatectomy. Based on practice patterns reported in Liu et al.[19], we assumed that 48.5% of patients diagnosed with Gleason score 6 PCa received active surveillance, while the rest received radical prostatectomy. If a patient was clinically detected to have PCa after age 80, we assumed they received watchful waiting.

Men on active surveillance received an annual PSA test and a biopsy every two years and continued to progress through the natural history of the disease. If any biopsy indicated progression in Gleason score, the patient received radical prostatectomy. For men with no indication of progression within 10 years, survival was consistent with survival for men with untreated PCa.[9] Men treated via radical prostatectomy

had survival consistent with a treated population, [20] with the potential for progression to metastatic PCa and PCa mortality. Other-cause mortality was based on estimates from CDC life tables.[21]

2.2 PSA and MRI sensitivity and specificity

A published statistical model from the PCa prevention trial was used to sample age-dependent and cancer onset-dependent PSA scores.[22] The outcome of MRI was based on prostate imaging reporting and data system (PI-RADS) scores, between 1 and 5, with an increasing score indicating an increasing likelihood of the presence of clinically significant cancer.[23] We considered two PI-RADS thresholds to trigger biopsy: 3 and 4. A PI-RADS threshold of ≥3 had a sensitivity and specificity to clinically significant PCa (i.e., cancer core involvement of ≥6 mm or the presence of any Gleason pattern 4) of 96.5 (95% CI: 86.8–99.4) and 59.7 (95% CI: 51.2–67.7), respectively, and a PI-RADS threshold of ≥4 had sensitivity and specificity values of 78.9 (95% CI: 65.8–88.2) and 78.9 (95% CI: 69.9–84.1), respectively.[24]

2.3 Costs and quality of life

We estimated the difference in costs and QALYs for each combination of the five screening strategies and the two PI-RADS score thresholds. Cost and QALY estimates with their sources are shown in Table 2 and our assumptions were similar to those of previous studies.[26,27,29] The post-recovery period for radical prostatectomy was assumed to last 9 years.[29] Li et al. reported the disutility for hospitalization due to post-biopsy infection to be 0.28,[31] which we assumed lasted for three weeks.[29] Grann et al.[30] reported the disutility for MRI as 0.04, which we assumed lasted for one week.[29]

2.4 Cost-effectiveness

Future costs and QALYs were discounted to net present value using an annual discount rate of 3%.[32] Net costs per QALY gained were calculated for strategies 1 through 5 relative to no screening as the incremental costs of the screening strategy divided by the incremental QALYs of the screening strategy.

We identified the efficient strategies by removing dominated strategies (i.e., strategies that are more expensive and less effective than another strategy) as well as strategies ruled out by extended dominance (i.e., strategies that have higher ICERs than a more effective strategy).[32] The ICERs of the efficient policies were calculated as the incremental costs divided by the incremental health gains compared to the next most effective strategy. If the ICER is under $100,000/QALY, the screening strategy is considered cost-effective.[33]

2.5 Sensitivity analysis

To evaluate the robustness of our results, we performed one-way sensitivity analysis on the net costs per QALY gained relative to no screening for the optimal screening strategy. Ranges of the QALY disutilities appear in Table 2. Cost estimates and other-cause mortality rates were varied by ±20%.[21] The sensitivity

and specificity of PI-RADS threshold 3 were varied using the 95% confidence intervals reported in Grey et al.[24] The annual metastasis rate for patients with undiagnosed PCa was varied within the 95% confidence interval reported in Johansson et al.[11] Finally, we varied the annual PCa incidence rate within the 95% confidence interval reported in Haas et al.[13] Threshold analysis was also performed on the sensitivity and specificity of MRI and combined biopsy under the optimal strategy. Base case values of the sensitivity and specificity of MRI were 96.5 and 59.7, respectively, and base case values of the sensitivity and specificity of combined biopsy were 85.0 and 49.0, respectively. During threshold analysis, we simultaneously reduced the sensitivity and specificity of MRI and combined biopsy until it was no longer cost-effective to use MRI for screening.

2.6 *Role of the Funding Source* and Conflicts of Interest

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3. Results

3.1 Base case analysis

Table 3 presents the deaths averted, life years and QALYs gained, number of screening biopsies, costs, and cost-effectiveness estimates for each screening strategy. The largest 95% confidence interval for QALY and cost per patient reflecting Monte Carlo statistical error was less than 1% of the corresponding sample mean point estimate. The net discounted costs per QALY gained compared with no screening for each screening strategy was below $100,000/QALY. Strategy 5 with a PI-RADS threshold of 3 maximized expected QALYs and number of PCa death averted, and had the lowest net cost per QALY gained at $33,953/QALY. For every strategy, a PI-RADS threshold of 3 gained more QALYs than a PI-RADS threshold of 4. This difference was statistically significant for Strategies 3 – 5. Additionally, performing a combined biopsy after positive MRI (strategies 4 and 5) resulted in additional QALY gains compared to performing a targeted fusion biopsy alone (strategies 2 and 3), and these differences were statistically significant.

Figure 2 shows the discounted incremental effectiveness in QALYs versus the discounted incremental cost for each strategy relative to no screening. Dominated strategies were simultaneously more expensive and less effective than at least one other strategy. Interestingly, all four schemas that performed a standard biopsy after a negative MRI (strategies 2 and 4, with PI-RADS thresholds of 3 or 4) were dominated by strategies that performed no biopsy after negative MRI (strategies 3 and 5). The efficient strategies were strategy 1, strategy 5 with PI-RADS threshold of 4 with an ICER of

$14,031/QALY, and strategy 5 with PI-RADS threshold of 3 with an ICER of $23,483/QALY. Thus, we found strategy 5 (i.e., MRI if PSA >4 ng/mL, combined biopsy if MRI positive, no biopsy if MRI negative) with PI-RADS threshold of 3 to be optimal under a willingness-to-pay threshold of $100,000/QALY. This strategy performed 15% fewer screening biopsies than the strategy that uses PSA alone (strategy 1).

3.2 Sensitivity analysis

Figure 3 shows the one-way sensitivity analysis on the net costs per QALY gained relative to no screening for strategy 5 with a PI-RADS threshold of 3. We performed one-way sensitivity analysis on all model parameters; Figure 3 shows the parameters that varied the net costs per QALY gained by at least $5,000/QALY when using the low and high values. The three model parameters that had the greatest impact were: (1) the metastasis rate for undiagnosed PCa; (2) the annual QALY disutility for the 9-year post-radical prostatectomy recovery period; and (3) the annual QALY disutility for living with metastasis. In the sensitivity analysis, the only scenario that has a cost per QALY gained relative to no screening over $100,000/QALY is the case with a substantially lower risk of developing metastases compared to the base case, suggesting that our results are robust for most patients and cost-effective under a willingness-to-pay threshold of $100,000/QALY. Threshold analysis shows that strategy 5 with a PI-RADS threshold of 3 remains cost-effective under a willingness-to-pay threshold of $100,000/QALY when sensitivity and specificity of MRI and combined biopsy to high-grade cancer are all simultaneously reduced by 19.0. In particular, it is still cost-effective when sensitivity and specificity of MRI are ≥77.5 and ≥40.7, respectively, and sensitivity and specificity of combined biopsy are ≥66.0 and ≥30.0, respectively.

4. Conclusions

Based on our study, MRI as an intermediate test in the screening of men for PCa is cost-effective assuming a willingness-to-pay threshold of $100,000/QALY threshold. The most efficient strategy was the use of MRI if PSA >4 ng/mL, followed by combined biopsy if MRI was positive and no biopsy if MRI was negative, using a PI-RADS threshold of 3 to indicate a positive MRI. These results were robust over a range of sensitivity analyses and were maintained even if the sensitivity and specificity of MRI and combined biopsy were reduced by 19 percentage points. Additionally, this MRI strategy reduced the number of screening biopsies by 15% compared to using PSA alone to trigger standard biopsy.

Although MRI has recently been proposed as an effective way to achieve early detection of PCa, evidence in support of the use of MRI for early detection of PCa in biopsy-naïve men is sparse. Ahmed et al. showed that MRI could be effective from a clinical perspective by reducing primary biopsy and clinically insignificant cancer diagnoses, but did not consider the cost-effectiveness.[34] Willis et al. performed clinical decision analysis and De Rooij et al. performed cost-effectiveness analysis;[35,36] however, both studies assumed a fixed sensitivity and specificity of MRI and assumed that positive MRI is automatically followed by a targeted fusion biopsy, while negative MRI automatically results in no biopsy. Thus, they evaluated one clinical pathway compared to the standard of care. Our study evaluated

strategies that performed targeted fusion biopsy or combined biopsy on positive MRI, as well as the option to perform a standard biopsy or no biopsy on negative MRI. Thus, our study evaluated eight MRI-based clinical pathways (two PI-RADS thresholds for each of the four MRI-based strategies) compared to screening with PSA alone, allowing us to estimate the effects of varying PI-RADS thresholds and biopsy techniques on the cost-effectiveness of using MRI for PCa screening. More recently, Pahwa et al. performed cost-effectiveness of using MRI in biopsy-naïve men; however, this study is a decision tree that did not consider various PI-RADS scores and did not account for sequential PSA testing or progression of cancer over time.[37] Additionally, their study does not incorporate other-cause mortality, which is an important consideration when studying a disease like prostate cancer, which can be slow-growing. Finally, to our knowledge, our study is the first to focus on the use of MRI in a screening setting in combination with PSA and incorporates lifetime costs and health outcomes, rather than assessing short-term outcomes. Including long-term costs and health impacts enabled us to assess the potentially negative impact of detecting low-risk cancers related to harm from biopsy(-ies) and overtreatment. Prior studies did not account for the costs and harms associated with biopsy complications, resulting in an overestimation of the benefit from screening and an underestimation of the costs.

Heijnsdijk et al.[12] evaluated the cost-effectiveness of several PSA screening policies in the absence of MRI, and our models produced similar expected outcomes for PSA screening. The net cost per QALY gained we present for PSA screening is lower than the results reported in Heijnsdijk et al.[12] because we include more costs in our model, including the significant cost of a PCa-related death. Faria et al. recently published a cost-effectiveness study based on the Prostate MR Imaging Study (PROMIS) based in the UK and found that performing an mpMRI followed by up to two targeted transrectal ultrasound-guided biopsies is a cost-effective approach to early detection of prostate cancer [CITATION], reaching a similar conclusion to our study.[44]

Using MRI for PCa screening resulted in health benefits for the patient compared to both no screening and screening using PSA alone. For example, the screening strategy where men with a PI-RADS score ≥3 were recommended for combined biopsy (i.e., strategy 5) resulted in 5.9 PCa deaths averted, 60.7 QALYs gained, and 72.6 life-years gained per 1,000 men compared to no screening. For every screening strategy, a PI-RADS threshold of 3 outperformed a threshold of 4 in terms of QALYs, while also resulting in lower costs. Our results also suggest that performing a combined biopsy after a positive MRI outperforms performing a targeted fusion biopsy in terms of QALYs. However, there does not appear to be a benefit to performing standard biopsy on negative MRI, because it results in additional costs and disutility to the patient without added health benefits. This conclusion has been supported in the literature. For example, Hansen et al.[38] concluded that biopsies may not be necessary for men with elevated PSA and nonsuspicious MRI because the negative predictive value for excluding Gleason score ≥7 disease on MRI was very high. Our study adds additional evidence in support of this conjecture.

The results are sensitive to the choice of disutility estimates used to compute QALYs. Since we assumed patients undergoing definitive treatment will have surgery, the results do not necessarily apply to those patients that may receive radiation treatment. This is due to the fact that disutility estimates for radiation treatment are not readily available. However, other authors have noted the similarity in the disutility for these alternative treatment options.[42]

It is important to note that the cost figures used in this study are from the United States and the cost and ICER threshold used to define willingness to pay will vary depending on the specific healthcare setting. For example, in the United Kingdom the threshold is typically £20,000–£30,000 per QALY gained.[43]

Given the wide variability in the quality of radiology reporting and interpretation of MRI results, we performed threshold analysis on the sensitivity and specificity of MRI and combined biopsy. These analyses found this approach to be a cost-effective method of early detection even if the sensitivity and specificity were substantially lower than estimates reported in the literature, suggesting that our results may be relevant in a community setting where sensitivity and specificity may be lower than specialized medical centers where most previous MRI studies have been conducted. Despite these encouraging findings, minimizing variation in radiologist reporting remains a critical unmet need.[40, 41] The minimum thresholds we found for sensitivity and specificity of MRI in our sensitivity analysis are within the range of clinical possibility. Prospective tracking of outcomes data stratified by indication and PI-RADS v2 scoring is necessary to ensure performance within the range of values we studied can be achieved.

Our model is based on available evidence but there are a number of noteworthy limitations. One potential limitation is that there is the potential for bias in the data we used to estimate MRI results because the population used includes patients with previous negative biopsies in addition to biopsy-naïve patients; however, by using the estimates based on the larger patient population we were able to obtain better estimates of sensitivity and specificity. Our sensitivity analysis further confirms our conclusions are not sensitive to this assumption. Another possible limitation is the inconsistent definition of clinically significant PCa in the literature. For example, Siddiqui et al.[5] defined clinically significant disease as high-volume Gleason 3+4, or Gleason ≥4+3, while Grey et al.[24] defined clinically significant disease to be cancer core involvement ≥6 mm or the presence of any Gleason pattern 4. In our model, we considered clinically significant disease to be any Gleason score ≥7. Additionally, the only curative treatment included in our model was radical prostatectomy, because it is the most common curative treatment, and patients undergoing radiation therapy have similar health outcomes.[39] Our model uses many different sources of data; however, given the long-term evaluation period needed for PCa screening, randomized trials are unlikely to be able to assess long-term QALYs and costs. We considered multiple ways of using MRI for early detection, but MRI may also play an important role in active surveillance. We have not attempted to incorporate this aspect of MRI into the model because of the complexity of decisions and evidence related to the use of MRI for active surveillance. These limitations notwithstanding, we believe this study

provides important evidence in support of the use of MRI for early detection of PCa in biopsy-naïve men, both from a health benefit and cost perspective.

Our results show that incorporating MRI into PCa screening in biopsy-naïve men is cost-effective under a willingness-to-pay threshold of $100,000/QALY. The strategies that performed a standard biopsy on negative MRI were more expensive and less effective than strategies that perform no biopsy on negative MRI. The screening strategy where men with PI-RADS score ≥3 were recommended for combined biopsy, while men with PI-RADS score <3 were recommended for no biopsy was optimal and cost-effective with an ICER of $23,483/QALY. Our results were also robust with respect to sensitivity analysis. Therefore, MRI appears to be a viable approach for early detection of prostate cancer from a cost-effectiveness perspective.

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Figure Legends

Figure 1: Decision rule diagram for screening strategies 2–5. All of the decision rules were compared to no screening and the case of standard biopsy for PSA greater than 4 ng/mL.

Figure 2: Incremental health benefits and costs associated with alternative screening strategies relative to no screening. Costs and QALYs are discounted at a rate of 3%. Each point is labeled with the screening strategy and PI-RADS threshold. Screening strategies are defined in Table 1. Lines connecting points representing two efficient screening strategies indicate the incremental cost-effectiveness ratio (ICER). QALY = quality-adjusted life years; PI-RADS = prostate imaging reporting and data system.

Figure 3: Tornado diagram of one-way sensitivity analysis on the net costs per QALY gained of strategy 5 with a PI-RADS threshold of 3 relative to no screening. Costs and QALYs are discounted at a rate of 3%. QALY = quality-adjusted life years; PCa = prostate cancer; RP = radical prostatectomy; GS<7 = Gleason score <7.

Table 1: Definitions of five screening strategies.

Screening strategy	PSA > 4 ng/mL	Positive MRI	Negative MRI
1	Standard Biopsy	-	-
2	MRI	Targeted Fusion Biopsy	Standard Biopsy
3	MRI	Targeted Fusion Biopsy	No Biopsy
4	MRI	Combined Biopsy	Standard Biopsy
5	MRI	Combined Biopsy	No Biopsy

Table 2: Costs considered in our cost-effectiveness analysis and annual disutilities for health states. Costs from the literature have been updated to 2016 US dollars based on inflation.

Intervention	**Unit costs in $**	**Source**
PSA screening	33.86	Medicare data
MRI	964.21	Medicare data
Standard prostate biopsy *	2,953.67	Medicare data
Targeted fusion prostate biopsy †	3,018.35	Medicare data
Combined prostate biopsy †	3,018.35	Medicare data
Post-biopsy infection-related hospitalization	6,361.31	Adibi et al (25) Gonzalez et al (3)
Staging	1,059.28	Medicare data
Active surveillance – standard biopsy (per year) ‡	1,642.58	Medicare data
Active surveillance – targeted biopsy (per year) ‡	1,674.92	Medicare data
Active surveillance – combined biopsy (per year) ‡	1,674.92	Medicare data
Radical prostatectomy	15,752.37	Aizer et al (26)
Distant-stage initial treatment	17,831.29	Roth et al (27)
Distant-stage management (per year)	2,500.65	Roth et al (27)
Other cause of death	5,975.15	Mariotto et al (28)
Prostate cancer death (age <65)	103,884.24	Mariotto et al (28)
Prostate cancer death (age ≥65)	69,256.16	Mariotto et al (28)
Health State	**Annual disutility (range)**	**Source**
PSA screening	0.00019 (0.0-0.00019)	Heijnsdijk et al (29)
MRI	0.00077 (0.00038-0.0012)	Grann et al (30) Heijnsdijk et al (29)
Biopsy	0.00577 (0.00346-0.0075)	Heijnsdijk et al (29)
Post-biopsy infection	0.0161 (0.00969-0.0291)	Li et al (31) Heijnsdijk et al (29)
Diagnosis	0.0167 (0.0125-0.0208)	Heijnsdijk et al (29)
Radical prostatectomy	0.247 (0.0917-0.323)	Heijnsdijk et al (29)
Post-radical prostatectomy recovery	0.05 (0.0-0.07)	Heijnsdijk et al (29)

Active surveillance	0.03 (0.0-0.15)	Heijnsdijk et al (29)
Palliative therapy	0.4 (0.14-0.76)	Heijnsdijk et al (29)
Terminal illness	0.3 (0.3-0.38)	Heijnsdijk et al (29)

* Includes professional, technical, and facility fees, pathology costs, and office visit

† Includes professional, technical, and facility fees, pathology costs, office visit, and 3D reconstruction

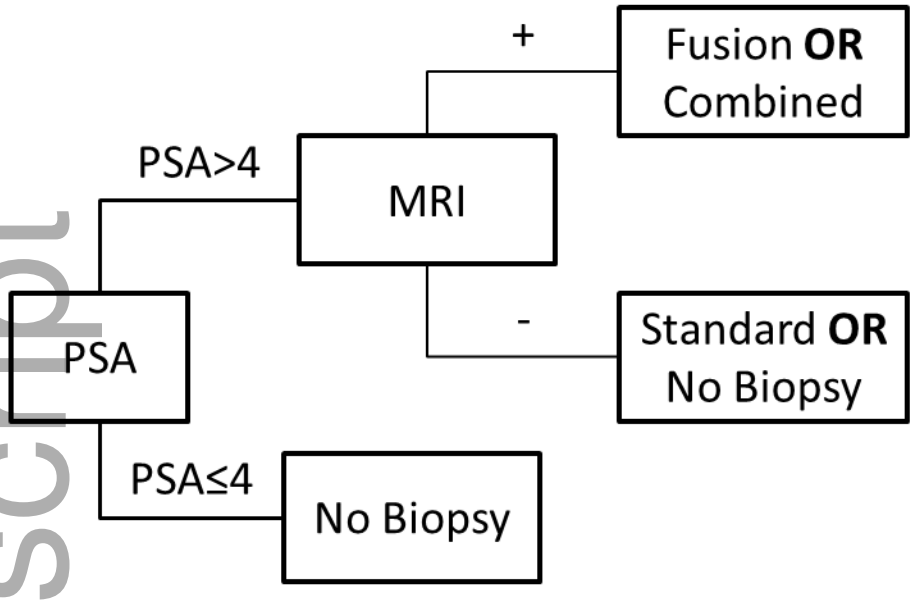
‡ Assumed to include an annual office visit, annual PSA test, and a biopsy every two years

Table 3: Predicted effects, costs, and cost-effectiveness for various screening strategies per 1000 men. Screening strategies are defined in Table 1. Effects and costs are shown without discount. The cost-effectiveness is calculated at 3% discount rate for costs and QALYs. In 2016 US dollars.

Screening strategy	PCa deaths averted *	Life-years gained *	QALYs gained * (95% CI)	Number of Screening Biopsies
No screening	-	-	-	-
Strategy 1	4.7	58.7	47.8 (47.2 – 48.3)	151
Strategy 2, PI-RADS ≥3	5.2	64.1	53.0 (52.4 – 53.5)	151
Strategy 2, PI-RADS ≥4	5.1	63.0	51.9 (51.3 – 52.5)	151
Strategy 3, PI-RADS ≥3	5.2	64.3	53.9 (53.3 – 54.5)	128
Strategy 3, PI-RADS ≥4	4.9	60.3	50.9 (50.3 – 51.4)	107
Strategy 4, PI-RADS ≥3	5.8	71.4	59.2 (58.6 – 59.8)	151
Strategy 4, PI-RADS ≥4	5.5	68.7	56.8 (56.2 – 57.5)	151
Strategy 5, PI-RADS ≥3	5.9	72.6	60.7 (60.1 – 61.3)	128
Strategy 5, PI-RADS ≥4	5.5	67.8	57.2 (56.6 – 57.8)	107

PCa = prostate cancer; QALY = quality-adjusted life year; CI = confidence interval; PI-RADS = prostate imaging reporting and data system.

* Compared with no screening



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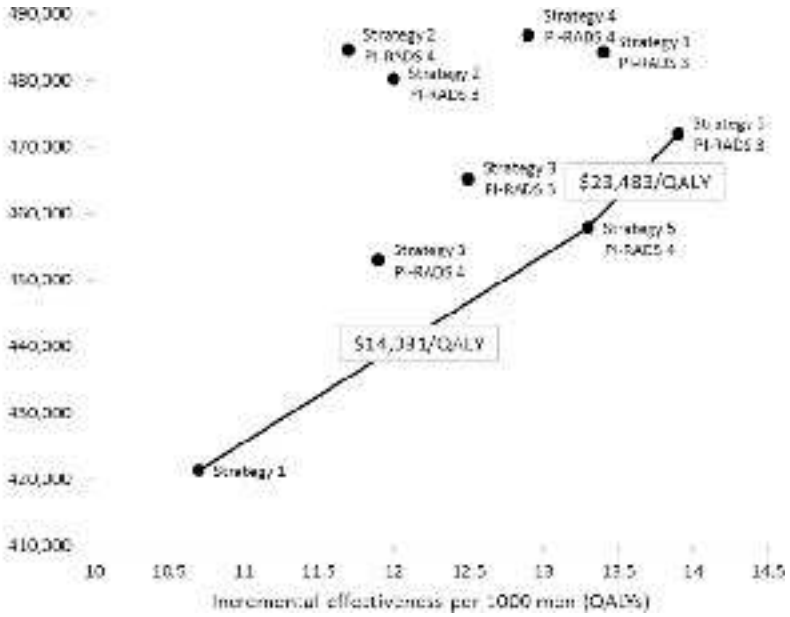

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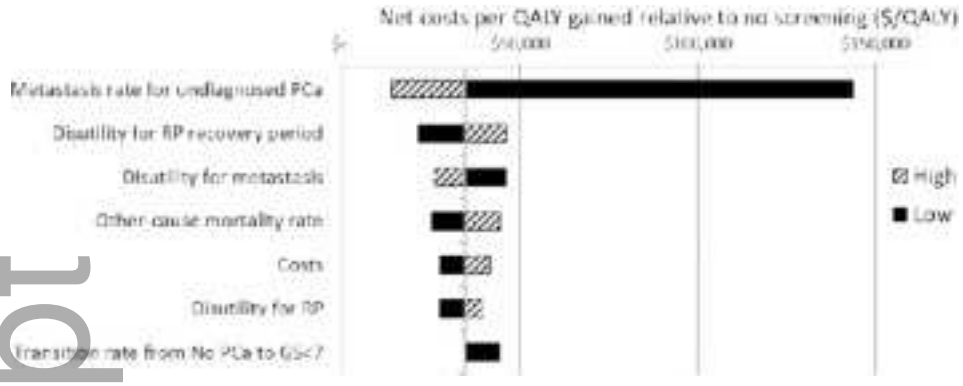

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