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# Cost-effectiveness evaluation of initial prostate cancer diagnosis using PSA and multiparametric magnetic resonance imaging in the Brazilian private sector: a comparison between systematic biopsy and MRI-first strategy

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### Abstract

**Background:** Prostate cancer is highly prevalent, and current PSA-only screening leads to overdiagnosis and unnecessary biopsies. Recent trials show that using multiparametric MRI (mpMRI) as triage before biopsy reduces invasive procedures without missing clinically significant tumors. **Objective:** To evaluate the cost-effectiveness of an MRI-first strategy vs. traditional systematic biopsy for initial prostate cancer diagnosis in the Brazilian private healthcare sector. **Methods:** A decision-tree model based on Göteborg-2 trial data was developed using TreeAge Pro®. The analysis adopted the private payer perspective, with a time horizon limited to the initial diagnostic episode. Effectiveness was defined as detection of clinically significant prostate cancer (ISUP  $\geq 2$ ). Direct medical costs were obtained from three sources: Delboni/Dasa (V1), Hospital Sírío-Libanês (V2), and an estimate for supplementary health operators (V3). Two scenarios were evaluated: Scenario A (mpMRI included in both strategies) and Scenario B (mpMRI only in the MRI-first arm). Deterministic sensitivity analyses varied MRI costs by  $\pm 20\%$ . **Results:** The MRI-first strategy was dominant across all scenarios and cost sources. In Scenario A (V1), mean costs were R\$ 6,000.20 (MRI-first) vs. R\$ 8,893.16 (systematic biopsy), with effectiveness of 0.35 vs. 0.17, respectively (ICER: dominated). In Scenario B (V1), costs were R\$ 6,000.20 vs. R\$ 6,159.24, maintaining higher effectiveness for MRI-first (0.35 vs. 0.17). Results remained robust across V2 and V3, and in sensitivity analyses with  $\pm 20\%$  variation in MRI costs. Within each cost source, the cost-effectiveness ratio (cost per clinically significant cancer detected) was consistently lower for the MRI-first strategy than for systematic biopsy (e.g., R\$ 17,143 vs. R\$ 52,313 for V1; R\$ 25,690 vs. R\$ 77,644 for V2; and R\$ 10,710 vs. R\$ 32,489 for V3 in Scenario A), confirming the superior efficiency of the MRI-first approach across all evaluated cost structures. **Conclusions:** The MRI-first approach is a cost-effective and dominant strategy for initial prostate cancer diagnosis in the Brazilian private setting across all evaluated scenarios, reducing unnecessary biopsies while optimizing detection of clinically significant tumors and promoting efficient resource allocation.

**Keywords:** Prostate cancer; Screening; Multiparametric magnetic resonance imaging; Prostate biopsy; Cost-effectiveness analysis; Health economics.

### Introduction

Prostate cancer (PC) is the most prevalent malignant neoplasm among men worldwide, with an estimated 1.4 million new cases annually, representing 14.1% of all male cancers.<sup>1</sup> In Brazil, PC is the second most common cancer in men, with approximately 65,840 new cases expected in 2023, corresponding to an estimated risk of 62.95 cases per 100,000 men.<sup>2,3</sup> Despite advances in early detection, PC remains a significant cause of morbidity and mortality, with an estimated 15,983 deaths in Brazil in 2021.<sup>2,4</sup> Regional inequalities in hospitalization rates and mortality from prostate cancer persist across Brazilian states, with marked differences in access to specialized oncological care.<sup>4</sup>

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While various randomized clinical trials on PC screening have been conducted, there is still no consensus in medical literature regarding the most appropriate population screening model.<sup>5,6</sup> The European Randomized Study of Screening for Prostate Cancer (ERSPC) demonstrated a 20% reduction in prostate cancer-specific mortality with PSA-based screening,<sup>7</sup> while the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial showed no mortality benefit.<sup>8</sup> This discrepancy has fueled ongoing debate about the net benefit of population-based PSA screening.

The main challenges lie in the overdiagnosis and overtreatment of indolent tumors, especially when prostate-specific antigen (PSA) is used in isolation for PC screening.<sup>9,10</sup> Studies estimate that 20-50% of screen-detected prostate cancers are clinically insignificant, leading to unnecessary treatment-related morbidity, including urinary incontinence and erectile dysfunction.<sup>11,12</sup> Furthermore, the risk of complications inherent to systematic prostate biopsies, including infection (0.5-6%), hematuria (up to 58%), and hematospermia (up to 37%), reinforces the need for more selective and precise strategies to better indicate this invasive procedure.<sup>13,14</sup>

In this context, the Göteborg-2 clinical trial<sup>15</sup> presents robust and potentially transformative evidence for prostate cancer screening. The study compared two diagnostic strategies based on PSA and multiparametric magnetic resonance imaging (mpMRI) of the prostate, demonstrating that introducing mpMRI as a triage tool for indicating targeted biopsy significantly reduced the detection of benign alterations and clinically insignificant neoplasms. Specifically, the MRI-first strategy reduced the number of biopsies by 46% while maintaining similar detection rates of clinically significant cancers (ISUP grade  $\geq 2$ ) compared to systematic biopsy.<sup>15</sup> The higher diagnostic accuracy of mpMRI—with sensitivity of 85-95% and specificity of 70-85% for clinically significant prostate cancer<sup>16,17</sup> allows to overcome overdiagnosis, the main obstacle for widespread population screening of PC. Therefore, mpMRI contributes to a decrease in unnecessary interventions, rationalizing the use of health resources without compromising the detection of clinically relevant tumors.

International cost-effectiveness studies have demonstrated favorable economic profiles for MRI-based screening strategies in high-income countries.<sup>18-20</sup> However, the economic impact of this strategy in the Brazilian private context remains poorly defined. The Brazilian private healthcare sector serves approximately 49.6 million beneficiaries (23.5% of the population) and operates under a unique reimbursement structure distinct from both public systems and international private markets.<sup>21</sup> Given this scenario, it is essential to analyze the cost-effectiveness of the mpMRI-first strategy (i.e., biopsy only in cases with suspicious findings on mpMRI) in the initial diagnosis of prostate cancer, considering the specificities of the Brazilian private healthcare system context.

The results of this study may support decisions of health insurers and inform current clinical protocols, providing economic evidence for the potential incorporation of mpMRI in the screening and early diagnosis of prostate cancer in Brazil.

## Methods

### Study Type and Design

An analytical decision model was developed in TreeAge Pro<sup>®</sup> software (TreeAge Software, Williamstown, MA, USA)<sup>22</sup> to estimate the cost and diagnostic effectiveness of two prostate cancer screening strategies, based on data from the Göteborg-2 study.<sup>15</sup> The model was structured as a decision tree, contemplating only the first screening round (Round 1), with a time horizon restricted to the diagnostic episode—from the PSA request to the issuance of the anatomopathological report.

The analysis adopted the perspective of the Brazilian private payer, considering only direct medical costs (consultations, laboratory and imaging exams, biopsies, and anatomopathological analyses). Costs or outcomes related to treatment, follow-up, or mortality were not included, as the primary objective was to evaluate only the economic impact of the initial diagnostic process. This restricted time horizon was chosen to reflect the decision-making context faced by private payers when evaluating reimbursement policies for initial diagnostic workup, independent of subsequent treatment costs.

All costs were expressed in 2024 Brazilian Reals (BRL/R\$). No discount rate was applied given the short time horizon (single diagnostic episode). The analysis followed the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines for reporting economic evaluations.<sup>23</sup>

### Compared Strategies

Two main diagnostic strategies were simulated, each representing an arm of the Göteborg-2 study:<sup>15</sup>

Group 1 (G1) – PSA + mpMRI + Targeted Biopsy (MRI-first/MRI-only): Multiparametric MRI is performed in all individuals with elevated PSA ( $\geq 3$  ng/mL); only those with suspicious findings (PI-RADS 3-5) undergo targeted biopsy guided by MRI findings.

Group 2 (G2) – PSA + Systematic Biopsy ( $\pm$  mpMRI): All individuals with elevated PSA ( $\geq 3$  ng/mL) undergo systematic transrectal biopsy (typically 10-12 cores), with or without prior mpMRI depending on the scenario evaluated.

Each strategy was modeled independently, allowing for the calculation of expected cost and effectiveness in each scenario.

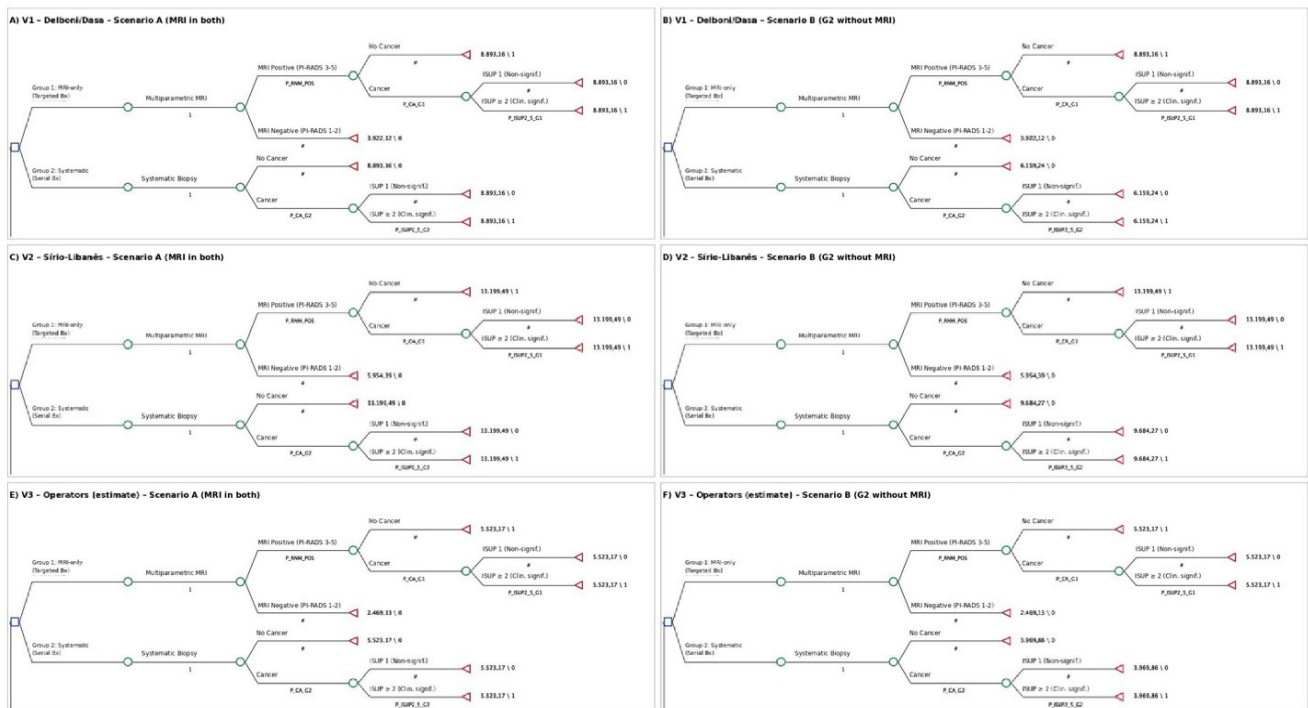
### Model Structure

The model was represented by a decision tree in TreeAge Pro® (Figure 1).

In Group 1 (MRI-first): The initial node corresponds to mpMRI, which can result in a positive (PI-RADS  $\geq 3$ ) or negative (PI-RADS 1-2) exam. Only cases with positive MRI proceed to the prostate biopsy node, with terminal outcomes of absence of cancer or presence of cancer. Cases with cancer are subdivided into clinically non-significant (ISUP grade 1), clinically significant (ISUP grade  $\geq 2$ ), and advanced disease.

In Group 2 (systematic biopsy): The initial node represents direct prostate biopsy, independent of the MRI result (in Scenario A, MRI is performed but does not affect the decision to biopsy). The outcomes follow the same hierarchical structure as Group 1.

Each terminal node incorporates the expected cost and the probability of the outcome, allowing the calculation of the weighted average cost per screened individual in each strategy.



**Figure 1.** Decision trees of the cost-effectiveness model (private sector), by cost source and scenario. V1 = Delboni/Dasa; V2 = Hospital Sírio-Libanês; V3 = supplementary health operators estimate. Scenario A = mpMRI included in both strategies; Scenario B = mpMRI in the MRI-first arm only. Terminal node values are shown as cost (R\$) \ effectiveness.

### Clinical Parameters and Data Sources

The primary clinical parameters used to populate the decision-tree model were derived from the proportions observed in Round 1 of the Göteborg-2 clinical trial,<sup>15</sup> which enrolled 38,366 men aged 50-60 years in Sweden between 2015 and 2021. The baseline clinical probabilities incorporated into the model were as follows: a prevalence of elevated PSA ( $\geq 3$  ng/mL) of 6.4% (0.064); a 58.0% (0.58) proportion of positive mpMRI (PI-RADS 3-5) among men with elevated

PSA; a detection rate of clinically significant prostate cancer (ISUP  $\geq 2$ ) of 35.0% (0.35) for the MRI-first (targeted biopsy) strategy; and a detection rate of clinically significant cancer of 17.0% (0.17) for the traditional systematic biopsy strategy. Biopsy-related complication rates were not factored into the initial diagnostic episode horizon. All clinical probabilities are thus fully detailed within the decision-tree structure, while cost parameters are presented in Table 1.

**Table 1.** Unit costs of diagnostic procedures by cost source (V1, V2, V3). The BRL/USD exchange rate was approximately R\$ 5.20 = US\$ 1.00 at the time of data collection (June 2024).

Procedure	V1 (R\$)	V2 (R\$)	V3 (R\$)
PSA	163.20	234.06	99.31
Complete Blood Count (Hemograma)	110.00	148.45	64.61
Creatinine	89.00	113.78	50.69
Coagulogram	166.24	258.00	106.06
Urinalysis (Urina 1)	80.00	126.78	51.69
Urine Culture	82.80	199.38	70.54
Transrectal Prostate Ultrasound	724.90	1,305.11	507.50
Multiparametric Prostate MRI	2,645.02	3,401.44	1,511.61
Biopsy + Anatomopathological	4,532.00	6,512.49	2,761.12
Urologist Consultation	300.00	900.00	300.00

**Note:** V1 = Delboni/Dasa; V2 = Hospital Sírio-Libanês; V3 = Supplementary health operators estimate (mean of V1 and V2 with 50% discount).

### Cost Parameters

Direct medical costs included all components of the diagnostic process: urological consultations, laboratory exams, imaging exams, prostate biopsies, and anatomopathological analyses. All individuals evaluated, regardless of the screening strategy, underwent serum PSA and creatinine dosage, the latter being necessary for renal function evaluation before administering the contrast used in mpMRI. For patients undergoing prostate biopsy, pre-procedure laboratory exams recommended in clinical practice—complete blood count, coagulogram, urinalysis (Type I), and urine culture, were also incorporated.

Reference values were obtained directly from two major private diagnostic services in Brazil through institutional fee schedules accessed in June 2024:

V1 (Delboni/Dasa): Largest private diagnostic network in Brazil, representing high-volume private laboratory pricing

V2 (Hospital Sírio-Libanês): Premium tertiary hospital in São Paulo, representing high-end private healthcare pricing

In the V1 scenario, the value of the urological consultation was defined based on the fee stipulated by the Brazilian Medical Association (AMB) Hierarchical Classification of Medical Procedures (CBHPM)<sup>24</sup> to standardize professional costs and reduce variability associated with private practice medical consultation fees.

For comparative analysis, a third cost source was defined:

V3 (Supplementary Health Operators Estimate): Calculated as the arithmetic mean of V1 and V2 values, with a subsequent 50% discount applied. This approach was adopted to realistically simulate the reimbursement pattern practiced by supplementary health operators in Brazil, who typically remunerate procedures at values substantially lower than those practiced in direct private care.<sup>25</sup>

Additionally, two distinct analytical scenarios were evaluated:

Scenario A: The cost of prostate mpMRI was included in both the MRI-first and systematic biopsy strategies, faithfully reproducing the Göteborg-2 study protocol.<sup>15</sup>

Scenario B: Both the cost of mpMRI and the costs associated with renal function evaluation (creatinine dosage), mandatory for contrast administration—were excluded from the systematic biopsy strategy, simulating clinical practice where the decision for biopsy occurs without prior realization of this exam.

The definition of these two scenarios allowed for a systematic evaluation of the impact of including or not including mpMRI—and its mandatory accessory exams—on the total estimated cost of the systematic biopsy strategy, expanding the robustness of the comparative analysis.

All costs are expressed in 2024 Brazilian Reals (R\$). At the time of data collection, the exchange rate was approximately R\$ 5.20 = US\$ 1.00. The unit costs used in the model are presented in Table 1.

### Outcome Measures

**Effectiveness:** Defined as the probability of detecting clinically significant prostate cancer, corresponding to tumors classified as International Society of Urological Pathology (ISUP) grade  $\geq 2$ <sup>24</sup>, according to Göteborg-2 study data.<sup>15</sup> This outcome measure was chosen because ISUP grade  $\geq 2$  tumors are generally considered to require active treatment, whereas ISUP grade 1 tumors are often candidates for active surveillance.<sup>26</sup>

**Cost:** Mean cost per patient screened, calculated as the sum of all direct medical costs weighted by the probability of each pathway through the decision tree.

### Cost-Effectiveness Analysis

The analysis compared the mean cost per screened patient and the diagnostic effectiveness of each strategy. Absolute differences in cost ( $\Delta C$ ) and diagnostic effectiveness ( $\Delta E$ ) between strategies were calculated. The incremental cost-effectiveness ratio (ICER) was determined by the ratio between  $\Delta C$  and  $\Delta E$ :

$$ICER = (Cost\_G2 - Cost\_G1) / (Effectiveness\_G2 - Effectiveness\_G1)$$

The ICER represents the additional cost necessary for each additional unit of diagnostic effectiveness obtained. Results with a negative ICER were interpreted as dominance, indicating that one strategy presented simultaneously lower cost and higher diagnostic effectiveness.

The net monetary benefit (NMB) was calculated using a willingness-to-pay threshold of R\$ 0 per unit of effectiveness, reflecting the fact that both strategies represent diagnostic approaches without direct health outcome gains measurable in monetary terms:

- $NMB = (Effectiveness \times WTP) - Cost$

The cost-effectiveness ratio (C/E) was calculated as:

- $C/E = Cost / Effectiveness$

Lower C/E ratios indicate better cost-effectiveness.

### Sensitivity Analysis

Deterministic one-way sensitivity analyses were performed to assess the robustness of the base-case results to variations in key parameters. The cost of multiparametric MRI was varied by  $\pm 20\%$  from the base-case value, as this represents the parameter with the greatest potential impact on the relative cost-effectiveness of the two strategies. Sensitivity analyses were conducted for all three cost scenarios (V1, V2, V3) and both clinical scenarios (A and B).

Probabilistic sensitivity analysis and extended sensitivity analyses on clinical parameters were not performed due to the exploratory nature of this initial economic evaluation.

### Ethical Aspects

As this study uses secondary data from the public domain without individual identification, it was exempted from submission to the Research Ethics Committee, in accordance with Brazilian National Health Council Resolution nº 510/2016.<sup>27</sup>

## Results

Overall, the MRI-first strategy (G1) demonstrated superior economic performance compared to systematic biopsy (G2) in all analyzed scenarios, characterizing itself as a dominant strategy regardless of the cost profile adopted. The results are detailed below according to each cost scenario.

In the cost-effectiveness analysis using V1 values (Dasa/Delboni), the MRI-first strategy (G1) proved dominant over systematic biopsy (G2) in both evaluated scenarios (Table 2).

**Table 2.** Cost and Effectiveness Results V1.

Scenario	Strategy	Mean Cost (R\$)	Efficacy (Prob.)	$\Delta$ Cost (Incr.)	$\Delta$ Efficacy (Incr.)	ICER (IC/IE)	NMB	C/E
A	G1 (Targeted Biopsy)	6,000.20	0.35	—	—	Dominant	-6,000.20	17,143.43
A	G2 (Systematic Biopsy)	8,893.16	0.17	2,892.96	-0.18	-16,072.00	-8,893.16	52,312.71
B	G1 (Targeted Biopsy)	6,000.20	0.35	-159.04	0.18	Dominant	-6,000.20	17,143.43
B	G2 (Systematic Biopsy)	6,159.24	0.17	—	—	—	-6,159.2	36,230.82

**Notes:**  $\Delta$  = incremental; ICER = incremental cost-effectiveness ratio; NMB = net monetary benefit; C/E = cost-effectiveness ratio. "Dominant" indicates lower cost and higher effectiveness simultaneously. Negative ICER indicates dominated strategy.

Scenario A (MRI included in both strategies): The mean cost per patient was R\$ 6,000.20 for G1 and R\$ 8,893.16 for G2, representing an incremental cost of R\$ 2,892.96 for the systematic biopsy approach. Effectiveness was 0.35 for G1 and 0.17 for G2, indicating an incremental effectiveness of -0.18 (i.e., G2 detected fewer clinically significant cancers). This resulted in a negative ICER of R\$ -16,072.00, characterizing G1 as the dominant strategy (lower cost, higher effectiveness).

Scenario B (MRI only in G1): Simulating clinical practice where G2 does not include MRI, the mean cost of systematic biopsy was R\$ 6,159.24 compared to R\$ 6,000.20 for G1, with effectiveness remaining at 0.17 vs. 0.35, respectively. G1 maintained dominance with an incremental cost of R\$ -159.04 and incremental effectiveness of 0.18.

The cost-effectiveness ratio (C/E) was consistently more favorable for G1 in both scenarios: R\$ 17,143.43 per unit of effectiveness in G1 compared to R\$ 52,312.71 (Scenario A) and R\$ 36,230.82 (Scenario B) in G2.

In the analysis using V2 values (Sírío-Libanês), the MRI-first strategy (G1) was dominant over systematic biopsy (G2) in both scenarios (Table 3).

**Table 3.** Cost and Effectiveness Results V2.

Scenario	Strategy	Mean Cost (R\$)	Efficacy (Prob.)	Δ Cost (Incr.)	Δ Efficacy (Incr.)	ICER (IC/IE)	NMB	C/E
A	G1 (Targeted Biopsy)	8,991.55	0.35	—	—	Dominant	-8,991.5	25,690.14
A	G2 (Systematic Biopsy)	13,199.49	0.17	4,207.94	-0.18	-23,377.4	-13,199.49	77,644.06
B	G1 (Targeted Biopsy)	8,991.55	0.35	-692.72	0.18	Dominant	-8,991.5	25,690.14
B	G2 (Systematic Biopsy)	9,684.27	0.17	—	—	—	-9,684.27	56,966.29

**Notes:** Δ = incremental; ICER = incremental cost-effectiveness ratio; NMB = net monetary benefit; C/E = cost-effectiveness ratio. "Dominant" indicates lower cost and higher effectiveness simultaneously. Negative ICER indicates dominated strategy.

Scenario A: With MRI included in both strategies, the mean cost per patient was R\$ 8,991.55 for G1 and R\$ 13,199.49 for G2, representing an incremental cost of R\$ 4,207.94. With effectiveness of 0.35 vs. 0.17, the systematic strategy showed a negative incremental effectiveness of -0.18, resulting in an ICER of R\$ -23,377.44, indicating clear dominance of the MRI-first strategy.

Scenario B: Without mpMRI in G2, the systematic biopsy cost was R\$ 9,684.27 compared to R\$ 8,991.55 for G1, with effectiveness remaining at 0.17 vs. 0.35. G1 maintained dominance with an incremental cost of R\$ -692.72.

The magnitude of cost differences was more pronounced in V2 compared to V1, reflecting the higher unit costs in premium healthcare settings. The cost-effectiveness ratio for G1 was R\$ 25,690.14 compared to R\$ 77,644.06 (Scenario A) and R\$ 56,966.29 (Scenario B) for G2.

Using estimated supplementary health operator reimbursement values (V3), G1 was dominant in both scenarios (Table 4).

**Table 4.** Cost and Effectiveness Results V3.

Scenario	Strategy	Mean Cost (R\$)	Efficacy (Prob.)	Δ Cost (Incr.)	Δ Efficacy (Incr.)	ICER (IC/IE)	NMB	C/E
A	G1 (Targeted Biopsy)	3,748.64	0.35	—	—	Dominant	-3,748.64	10,710.40
A	G2 (Systematic Biopsy)	5,523.17	0.17	1,774.53	-0.18	-9,858.50	-5,523.17	32,489.24
B	G1 (Targeted Biopsy)	3,748.64	0.35	-221.22	0.18	Dominant	-3,748.64	10,710.40
B	G2 (Systematic Biopsy)	3,969.86	0.17	—	—	—	-3,969.86	23,352.12

**Notes:** Δ = incremental; ICER = incremental cost-effectiveness ratio; NMB = net monetary benefit; C/E = cost-effectiveness ratio. "Dominant" indicates lower cost and higher effectiveness simultaneously. Negative ICER indicates dominated strategy.

Scenario A: Mean cost was R\$ 3,748.64 for G1 and R\$ 5,523.17 for G2, with an incremental cost of R\$ 1,774.53. The systematic strategy had lower effectiveness (0.17 vs. 0.35), resulting in a negative ICER of R\$ -9,858.50, characterizing dominance.

Scenario B: Systematic biopsy cost was R\$ 3,969.86 compared to R\$ 3,748.64 for G1, with effectiveness remaining at 0.17 vs. 0.35. G1 maintained dominance with an incremental cost of R\$ -221.22.

The cost-effectiveness ratio for G1 was R\$ 10,710.40 compared to R\$ 32,489.24 (Scenario A) and R\$ 23,352.12 (Scenario B) for G2, demonstrating that the dominance of the MRI-first strategy persists even in contexts of reduced reimbursement typical of supplementary health operators.

Deterministic sensitivity analyses were performed varying the cost of multiparametric MRI by ±20% to assess the robustness of the base-case results. The MRI-first strategy maintained dominance across all scenarios and cost sources.

With a 20% reduction in MRI cost (Table 5), the MRI-first strategy maintained or strengthened its dominant position across all cost sources and scenarios.

**Table 5.** Results of the deterministic sensitivity analysis with a 20% reduction in the cost of magnetic resonance imaging (scenarios A and B).

Center / Payer	Strategy	Mean Cost (R\$)	Effectiveness (Prob.)	Δ Cost (Incremental)	Δ Effectiveness (Incremental)	ICER (IC/IE)	NMB	C/E
<b>Delboni</b>								
A	G1 (Targeted)	5,475.98	0.35	—	—	Dominant	-5,475.98	15,645.66
	G2 (Systematic)	8,364.16	0.17	2,888.18	-0.18	-16,045.44	-8,364.16	49,200.94
B	G1 (Targeted)	5,475.98	0.35	—	—	Dominant	-5,475.98	15,645.66
	G2 (Systematic)	6,159.24	0.17	—	—	—	-6,159.24	36,230.82
<b>Sírio-Libanês</b>								
A	G1 (Targeted)	8,309.80	0.35	—	—	Dominant	-8,309.80	23,742.29
	G2 (Systematic)	12,519.20	0.17	4,209.40	-0.18	-23,960.83	-12,519.20	73,642.35
B	G1 (Targeted)	8,309.80	0.35	—	—	Dominant	-8,309.80	23,742.29
	G2 (Systematic)	9,684.27	0.17	1,374.47	-0.18	-7,823.73	-9,684.27	56,966.29
<b>Private</b>								
A	G1 (Targeted)	3,446.44	0.35	—	—	Dominant	-3,446.44	9,846.97
	G2 (Systematic)	5,220.84	0.17	1,774.40	-0.18	-9,857.78	-5,220.84	30,710.82
B	G1 (Targeted)	3,446.44	0.35	—	—	Dominant	-3,446.44	9,846.97
	G2 (Systematic)	3,969.86	0.17	523.42	-0.18	-2,907.89	-3,969.86	23,352.12

**Scenario A:** MRI performed in both strategies (faithful to Göteborg-2 protocol). **Scenario B:** MRI performed only in MRI-first strategy (systematic biopsy without MRI). Costs are expressed in 2024 Brazilian reais (R\$). Negative ICERs indicate a dominated strategy. 'Dominant' indicates lower cost and higher effectiveness simultaneously.

V1 (Dasa/Delboni): In Scenario A, G1 cost decreased to R\$ 5,475.98 while G2 cost decreased to R\$ 8,364.16, maintaining G1 dominance. In Scenario B, G1 cost remained at R\$ 5,475.98 while G2 cost (without MRI) stayed at R\$ 6,159.24, further strengthening G1 advantage.

V2 (Sírio-Libanês): Similar patterns were observed, with G1 costs of R\$ 8,309.80 in both scenarios, compared to G2 costs of R\$ 12,519.20 (Scenario A) and R\$ 9,684.27 (Scenario B).

V3 (Operators Estimate): G1 cost decreased to R\$ 3,446.44, compared to G2 costs of R\$ 5,220.84 (Scenario A) and R\$ 3,969.86 (Scenario B).

The cost-effectiveness ratios for G1 improved across all scenarios, ranging from R\$ 9,846.97 to R\$ 23,742.29, while G2 ratios ranged from R\$ 23,352.12 to R\$ 73,642.35.

Deterministic sensitivity analyses varying MRI costs by ±20% confirmed the robustness of the MRI-first strategy's dominance (Tables 5 and 6). Even with a 20% cost increase for mpMRI, G1 remained dominant in most scenarios, with favorable ICERs in the remaining cases (R\$ 283 to R\$ 2,029 per additional significant cancer detected). These results demonstrate that the economic advantage of MRI-first is not sensitive to moderate fluctuations in MRI pricing.

With a 20% increase in MRI cost (Table 6), the MRI-first strategy maintained dominance in most scenarios, though cost differences narrowed in some cases.

V1 (Dasa/Delboni): In Scenario A, G1 cost increased to R\$ 6,524.42 while G2 increased to R\$ 9,422.16, maintaining G1 dominance. In Scenario B, G1 cost was R\$ 6,524.42 compared to G2 cost of R\$ 6,159.24, resulting in a small incremental cost of R\$ 365.18 but maintaining substantially higher effectiveness (0.35 vs. 0.17), with an ICER of R\$ 2,028.78.

**Table 6.** Results of the deterministic sensitivity analysis with a 20% increase in the cost of magnetic resonance imaging (scenarios A and B).

Center / Payer	Strategy	Mean Cost (R\$)	Effectiveness (Prob.)	Δ Cost (Incremental)	Δ Effectiveness (Incremental)	ICER (IC/IE)	NMB	C/E
<b>Delboni</b>								
A	G1 (Targeted)	6,524.42	0.35	—	—	Dominant	-6,524.42	18,641.20
	G2 (Systematic)	9,422.16	0.17	2,897.74	-0.18	-16,098.56	-9,422.16	55,424.47
B	G1 (Targeted)	6,524.42	0.35	365.18	0.18	2,028.78	-6,524.42	18,641.20
	G2 (Systematic)	6,159.24	0.17	—	—	—	-6,159.24	36,230.82
<b>Sírio-Libanês</b>								
A	G1 (Targeted)	9,670.38	0.35	—	—	Dominant	-9,670.38	27,629.66
	G2 (Systematic)	13,879.78	0.17	4,209.40	-0.18	-23,860.63	-13,879.78	81,645.76
B	G1 (Targeted)	9,670.38	0.35	—	—	Dominant	-9,670.38	27,629.66
	G2 (Systematic)	9,684.27	0.17	13.89	-0.18	-78.08	-9,684.27	56,966.29
<b>Private</b>								
A	G1 (Targeted)	4,020.83	0.35	—	—	Dominant	-4,020.83	11,488.09
	G2 (Systematic)	5,825.49	0.17	1,804.66	-0.18	-10,253.75	-5,825.49	34,267.59
B	G1 (Targeted)	4,020.83	0.35	50.97	0.18	283.17	-4,020.83	11,488.09
	G2 (Systematic)	3,969.86	0.17	—	—	—	-3,969.86	23,352.12

**Scenario A:** MRI performed in both strategies (faithful to Göteborg-2 protocol). **Scenario B:** MRI performed only in MRI-first strategy (systematic biopsy without MRI). Costs are expressed in 2024 Brazilian reais (R\$). Negative ICERs indicate a dominated strategy. 'Dominant' indicates lower cost and higher effectiveness simultaneously.

V2 (Sírio-Libanês): G1 costs increased to R\$ 9,670.38 in both scenarios, compared to G2 costs of R\$ 13,879.78 (Scenario A) and R\$ 9,684.27 (Scenario B). In Scenario B, costs were nearly identical (R\$ 9,670.38 vs. R\$ 9,684.27), but G1 maintained substantially higher effectiveness.

V3 (Operators Estimate): G1 cost increased to R\$ 4,020.83, compared to G2 costs of R\$ 5,825.49 (Scenario A) and R\$ 3,969.86 (Scenario B). In Scenario B, G1 had a small incremental cost of R\$ 50.97 but maintained higher effectiveness, with an ICER of R\$ 283.17.

Even with a 20% increase in MRI costs, the cost-effectiveness ratios for G1 remained favorable, ranging from R\$ 11,488.09 to R\$ 27,629.66, compared to G2 ratios of R\$ 23,352.12 to R\$ 81,645.76.

## Discussion

This study evaluated the cost-effectiveness of prostate cancer screening strategies based on multiparametric magnetic resonance imaging, comparing an mpMRI-first approach (G1) to traditional systematic biopsy (G2) across different health financing scenarios in the Brazilian private healthcare context. The results demonstrate that the MRI-first strategy presents consistently superior economic performance, characterized as a dominant strategy (lower cost, higher effectiveness) in the vast majority of evaluated scenarios.

The MRI-first strategy demonstrated dominance across all three cost scenarios (V1, V2, V3) and both clinical scenarios (A and B), with mean costs ranging from R\$ 3,749 to R\$ 8,992 compared to R\$ 3,970 to R\$ 13,199 for systematic biopsy, while maintaining substantially higher diagnostic effectiveness (0.35 vs. 0.17). This translates to a 106% improvement in detection of clinically significant prostate cancer (ISUP ≥ 2) with simultaneous cost reduction or minimal cost increase.

The magnitude of dominance was particularly pronounced in Scenario A (where both strategies include MRI), with incremental cost savings ranging from R\$ 1,775 to R\$ 4,208 per patient screened across the three cost sources. This finding indicates that the primary cost driver is not the MRI itself, but rather the high cost associated with systematic prostate biopsies and their complications. By using MRI as a triage tool, the MRI-first strategy reduces unnecessary biopsies by approximately 46%, as demonstrated in the Göteborg-2 trial,<sup>15</sup> without compromising detection of clinically significant cancers.

Even in Scenario B, which simulates clinical practice where systematic biopsy is performed without prior MRI (representing current standard practice in many Brazilian settings), the MRI-first strategy maintained cost-effectiveness. In V1 and V3, G1 remained dominant with small incremental costs (R\$ –159 and R\$ –221, respectively), while in V2, costs were nearly identical (R\$ 8,992 vs. R\$ 9,684) but with substantially higher effectiveness. This demonstrates that incorporating MRI into the diagnostic pathway is economically justified even when compared to the current standard of care without MRI.

Our findings align with and extend the growing international evidence base supporting MRI-based prostate cancer screening strategies. The PROMIS trial<sup>28</sup> demonstrated that mpMRI had superior sensitivity (93%) and specificity (41%) compared to transrectal ultrasound-guided biopsy (48% and 96%, respectively) for detecting clinically significant prostate cancer. The PRECISION trial<sup>29</sup> showed that MRI-targeted biopsy detected 12% more clinically significant cancers than systematic biopsy while detecting 13% fewer clinically insignificant cancers.

Economic evaluations from high-income countries have consistently demonstrated favorable cost-effectiveness profiles for MRI-based strategies. A UK-based analysis<sup>18</sup> found that MRI-targeted biopsy was cost-effective compared to systematic biopsy, with an ICER of £1,072 per additional clinically significant cancer detected. A US-based study<sup>19</sup> demonstrated that MRI-first strategies could reduce costs by \$189–\$497 per patient while improving quality-adjusted life years. A Dutch analysis<sup>20</sup> found that MRI-targeted biopsy was dominant over systematic biopsy in 78% of probabilistic sensitivity analysis iterations.

Our study extends these findings to the Brazilian private healthcare context, demonstrating that the economic advantages of MRI-first strategies are maintained—and in some cases amplified—in a middle-income country setting with distinct cost structures and reimbursement patterns. The dominance of the MRI-first strategy across all evaluated scenarios (including the conservative Scenario B) suggests that these findings may be generalizable to other Latin American and middle-income country contexts with similar healthcare financing structures. Comparative epidemiological analyses of cancer mortality between Brazil and high-income countries reveal marked differences shaped by undernotification, population heterogeneity, and differential access to novel therapies,<sup>30</sup> reinforcing the need for context-specific economic evaluations rather than direct extrapolation from international models.

#### Economic Mechanisms Underlying Cost-Effectiveness

The superior cost-effectiveness of the MRI-first strategy is driven by several interconnected mechanisms:

**Reduction in unnecessary biopsies:** By using MRI as a triage tool, approximately 46% of biopsies can be avoided,<sup>15</sup> directly reducing procedure costs, anatomopathological analysis costs, and costs associated with biopsy complications (infection, bleeding, hospitalization).

**Improved diagnostic accuracy:** The higher sensitivity and specificity of MRI-targeted biopsy<sup>16,17,28</sup> result in better detection of clinically significant cancers while avoiding detection of indolent tumors, optimizing the diagnostic yield per invasive procedure performed.

**Reduced overdiagnosis and overtreatment:** By detecting fewer clinically insignificant cancers (ISUP grade 1), the MRI-first strategy reduces downstream costs associated with unnecessary active surveillance, repeat biopsies, and potential overtreatment.<sup>11,12</sup>

**Economies of scale for MRI:** As MRI technology becomes more widely available and MRI acquisition times decrease with technological advances,<sup>31</sup> the unit cost of mpMRI is likely to decrease further, strengthening the economic case for MRI-first strategies.

The sensitivity analyses demonstrated that these economic advantages are robust to substantial variations ( $\pm 20\%$ ) in MRI costs, indicating that the conclusions are stable even in the face of uncertainty about future MRI pricing or variations across different Brazilian regions and healthcare providers.

#### Implications for Brazilian Healthcare Policy

These findings have important implications for healthcare policy and reimbursement decisions in the Brazilian private sector:

**Reimbursement policy:** Supplementary health operators should consider prioritizing reimbursement for mpMRI in men with elevated PSA, as this strategy is economically dominant even under conservative reimbursement scenarios (V3).

**Clinical guidelines:** Brazilian urological societies and supplementary health regulatory agencies should consider updating clinical practice guidelines to incorporate MRI-first strategies as the preferred approach for prostate cancer diagnosis in men with elevated PSA.

**Healthcare resource allocation:** The demonstrated cost savings could be redirected to expand screening coverage, improve MRI technology and expertise, or invest in other preventive health services. The substantial economic burden of oncological hospitalizations in Brazil—estimated at billions of reais annually for individual cancer types<sup>32</sup>—underscores the systemic importance of early detection strategies capable of reducing unnecessary high-cost invasive procedures.

**Quality of care:** Beyond economic considerations, the MRI-first strategy improves patient quality of life by reducing unnecessary invasive procedures and their associated complications, anxiety, and recovery time.

The fact that dominance was maintained across V1 (high-volume diagnostic network), V2 (premium hospital), and V3 (operator reimbursement estimate) suggests that the economic case for MRI-first strategies is robust across the diverse landscape of Brazilian private healthcare provision.

### Limitations

This study has several limitations that should be considered when interpreting the results:

**Model structure and time horizon:** The analysis used a simple decision-tree model with a time horizon limited to the initial diagnostic episode. This approach does not capture long-term outcomes such as cancer-specific mortality, quality-adjusted life years, or costs associated with treatment, follow-up, and management of overdiagnosed cancers. While this limitation is appropriate for evaluating the initial diagnostic decision faced by payers, future studies should incorporate extended time horizons and Markov or microsimulation models to capture the full lifetime costs and health outcomes of different screening strategies.<sup>33</sup>

**Effectiveness measure:** The effectiveness outcome was defined as probability of detection of clinically significant cancer, rather than health outcomes such as mortality reduction or quality-adjusted life years. While detection of ISUP  $\geq 2$  cancers is a clinically meaningful intermediate outcome,<sup>26,34</sup> it does not directly measure impact on patient survival or quality of life. Future studies should incorporate longer-term health outcomes when sufficient data become available.

**Clinical probabilities:** All clinical transition probabilities were derived from the Göteborg-2 trial,<sup>15</sup> which was conducted in a Swedish population of men aged 50–60 years. While this is the most robust randomized trial comparing MRI-first and systematic biopsy strategies, the probabilities may not perfectly reflect the Brazilian population due to differences in prostate cancer epidemiology, PSA testing patterns, and healthcare-seeking behavior. Sensitivity analyses on clinical parameters would strengthen confidence in the generalizability of findings.

**Absence of probabilistic sensitivity analysis:** The study performed only deterministic one-way sensitivity analyses on MRI costs. Probabilistic sensitivity analysis (PSA) simultaneously varying all model parameters according to appropriate probability distributions would provide a more comprehensive assessment of parameter uncertainty and generate cost-effectiveness acceptability curves.<sup>35</sup> The absence of PSA limits our ability to quantify the probability that MRI-first is cost-effective at various willingness-to-pay thresholds.

**Complications and adverse events:** The model did not explicitly incorporate costs and health outcomes associated with biopsy complications (infection, bleeding, urinary retention, hospitalization). Including these would likely strengthen the economic case for MRI-first strategies, as reducing biopsy volume directly reduces complication-related costs and morbidity.<sup>13,14</sup>

**MRI quality and expertise:** The model assumes that mpMRI is performed and interpreted at the quality level demonstrated in the Göteborg-2 trial, with experienced radiologists using standardized PI-RADS reporting.<sup>35</sup> The cost-effectiveness of MRI-first strategies in real-world practice depends critically on maintaining high-quality MRI acquisition and interpretation, which may require investment in training and quality assurance programs.

**Generalizability to public sector:** This analysis focused exclusively on the Brazilian private healthcare sector. The findings may not be directly generalizable to the Brazilian public sector (Sistema Único de Saúde, SUS), which operates under different cost structures, resource constraints, and organizational models. Future studies should evaluate the cost-effectiveness of MRI-first strategies in the SUS context. Recent ecological analyses of perioperative outcomes and government reimbursements for urological procedures in the Brazilian public health system<sup>36</sup> demonstrate that cost structures, procedure volumes, and clinical outcomes differ substantially between public and private settings, reinforcing the importance of separate economic analyses for each context.

**Discounting and inflation:** Although no discount rate was applied due to the short time horizon, future studies with extended time horizons should incorporate appropriate discount rates for costs and health outcomes. Additionally, while all costs were expressed in 2024 values, inflation adjustments should be applied when comparing to costs from different time periods.

Despite these limitations, the consistency of findings across multiple cost scenarios, clinical scenarios, and sensitivity analyses provides confidence in the robustness of the conclusion that MRI-first strategies are economically favorable in the Brazilian private healthcare context.

#### Future Research Directions

Several important questions remain for future research:

**Extended time horizon modeling:** Markov or microsimulation models incorporating lifetime costs, quality-adjusted life years, cancer-specific mortality, and treatment outcomes would provide a more comprehensive economic evaluation.

**Real-world implementation studies:** Pragmatic trials or observational studies evaluating the cost-effectiveness of MRI-first strategies in routine Brazilian clinical practice would complement the trial-based modeling approach used here.

**Public sector evaluation:** Cost-effectiveness analysis from the SUS perspective, considering public sector costs, resource constraints, and budget impact.

**Optimal PSA threshold:** Evaluation of different PSA thresholds (e.g., 2.5, 3.0, 4.0 ng/mL) for triggering MRI to identify the optimal screening algorithm for the Brazilian population.

**Risk-stratified approaches:** Evaluation of incorporating additional risk factors (age, family history, genetic markers, prostate health index) to further refine patient selection for MRI.

**Budget impact analysis:** Assessment of the financial impact on supplementary health operators and healthcare systems of transitioning from systematic biopsy to MRI-first strategies at the population level.

**Implementation science:** Studies evaluating barriers and facilitators to implementing MRI-first strategies in Brazilian clinical practice, including radiologist training needs, MRI capacity, and guideline dissemination.

## Conclusions

This cost-effectiveness analysis demonstrates that the MRI-first strategy for prostate cancer diagnosis is economically dominant compared to traditional systematic biopsy across all evaluated scenarios in the Brazilian private healthcare sector. The strategy simultaneously reduces costs (or increases costs minimally) while substantially improving detection of clinically significant prostate cancer (ISUP  $\geq 2$ ). These findings were robust to  $\pm 20\%$  variations in MRI costs and consistent across diverse cost structures representing high-volume diagnostic networks, premium hospitals, and supplementary health operator reimbursement patterns.

The economic advantages of the MRI-first approach are driven primarily by reduction in unnecessary biopsies and improved diagnostic accuracy, rather than by the cost of MRI itself. These findings support policy recommendations for Brazilian supplementary health operators to prioritize reimbursement for mpMRI in men with elevated PSA and for clinical practice guidelines to incorporate MRI-first strategies as the preferred diagnostic approach.

While this analysis focused on the initial diagnostic episode, the demonstrated economic and clinical advantages suggest that MRI-first strategies represent an important opportunity to modernize prostate cancer screening in Brazil, reconciling clinical efficiency, patient quality of life, and economic rationality. Future research incorporating extended time horizons, real-world implementation studies, and public sector perspectives will further inform evidence-based policy decisions regarding prostate cancer screening in Brazil.

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