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Cost-effectiveness of ferumoxtran-enhanced macrophage-specific-MRI and PSMA-PET/CT versus ePLND for nodal staging in primary prostate cancer: a decision analysis based on updated phase-3 trial data

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ABSTRACT

Background and objective: Accurate nodal staging in intermediate- to high-risk prostate cancer (PCa) is crucial for treatment decisions. While extended pelvic lymph node dissection (ePLND) is the standard, it is invasive and has a low diagnostic yield. A 2019 analysis suggested that non-invasive imaging such as PSMA-PET/CT and ferumoxtran-enhanced macrophage-MRI (m-MRI) is cost-effective, but at the possible expense of a small QALY loss compared to ePLND, based on limited evidence. Recent Phase 3 trials have provided new data, prompting a reevaluation. Therefore, the aim of this article is to update a model with recent trial data to assess the cost-effectiveness of m-MRI and PSMA-PET/CT versus ePLND in Germany.

Material and methods: We adapted a Markov model to simulate lifetime outcomes for men with intermediate- to high-risk PCa from a German insurer's perspective, with costs updated to 2025 level. Diagnostic accuracy data were derived from recent multicenter trials. Costs and QALYs were calculated using a 3% discount rate. Sensitivity analyses tested uncertainties. A practical interactive online-tool is provided for clinical decision-making and research purposes, which can incorporate various input data (https://macrophage-mri.app).

Results: Both imaging options were dominant over ePLND (€37,855; 18.11 QALYs). PSMA-PET/CT was €7,869 cheaper and gained 0.800 QALYs; m-MRI was €9,985 cheaper and gained 0.990 QALYs. m-MRI was superior, saving €2,116 and gaining 0.19 QALYs over PSMA-PET/CT. The probabilistic analysis showed that m-MRI was optimal over 95% of the time at an €80,000/QALY threshold; the probability of PSMA-PET/CT being optimal was less than 5%.

Conclusions: An imaging-first approach outperforms routine ePLND, with m-MRI as a cost-effective option. PSMA-PET/CT's low sensitivity limits its usefulness, though it is still cheaper than ePLND. These results support including m-MRI in guidelines for initial staging.

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1. Introduction

Accurate staging of pelvic lymph node (LN) involvement is a key component of managing men with intermediate- and high-risk prostate cancer (PCa), significantly affecting prognosis and treatment decisions[1]. In Germany alone, around 20,000 men are diagnosed each year with intermediate- to high-risk, non-metastatic disease, making the choice of the staging method a critical public health and economic concern[2,3].

The established reference standard, extended pelvic lymph node dissection (ePLND), is an invasive surgical procedure with a complication rate of up to 20%. Postoperative complications include pelvic

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lymphocele, lymphoedema, ileus, deep venous thrombosis, and pulmonary embolism. Among these, pelvic lymphocele is common, affecting up to 19% of symptomatic cases after extraperitoneal RARP[4]. Importantly, its diagnostic yield is low; about 84% of men undergoing ePLND are found to be node-negative, exposing most patients to surgical risks without therapeutic benefit[4]. This underscores the urgent clinical need for a non-invasive staging tool that accurately identifies patients with true nodal metastases, thereby helping to personalize treatment and prevent overtreatment.

Advanced molecular imaging has emerged to bridge this gap, with prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA-PET/CT) and ferumoxtran-enhanced macrophage-specific magnetic resonance imaging (m-MRI) being the leading techniques. Also, there is a significant interest in integrating image-based information from radiomics into the multiomics framework, aiming to combine biomolecular-level information with imaging data. The clinical application of radiomics involves identifying the relationship between the features extracted from images and the clinical outcome of interest[5]. PSMA-PET/CT targets a glycoprotein overexpressed on PCa cells and is more accurate than traditional imaging methods[6,7]. M-MRI utilizes ultrasmall superparamagnetic iron oxide nanoparticles (USPIOs) that are taken up by macrophages in healthy lymph node tissue[8]. This buildup causes normal lymph nodes to appear dark on T2*-weighted MRI, while metastatic deposits, which lack macrophages, stay bright and can be identified regardless of nodal size[8].

A 2020 health economic analysis by Scholte et al. suggested that both imaging strategies were cost-effective compared to ePLND, but at the expense of a small reduction in quality-adjusted life years (QALYs)[9]. However, this conclusion was based on preliminary evidence. Since then, the evidence landscape has undergone significant advancements. High-level evidence from prospective, multicenter Phase 3 registration trials is now available for both modalities. The PROSTAPROGRESS trial for m-MRI has provided solid data on its performance[10]. Simultaneously, the pivotal LIGHTHOUSE study for ^{18}F-rhPSMA-7.3 PET/CT has established new, definitive diagnostic accuracy parameters for modern PSMA imaging[6]. These trials offer strong, directly comparable data on diagnostic accuracy against the gold standard of histopathology/ePLND, prompting a reevaluation of the relative value of these technologies.

Considering these key advances, this study aims to update and reparameterize the validated decision-analytic model of Scholte et al. to assess the current cost-effectiveness of PSMA-PET/CT and m-MRI compared to ePLND. We conduct this analysis from the perspective of the German statutory health insurance payer for 2025, providing a current evidence base to guide clinical guidelines and reimbursement policies.

2. Methods

This health economic evaluation was performed and reported following the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 statement[11]. A supplementary table showing compliance with the CHEERS checklist is provided (Supplementary Table S2).

2.1. Model overview

This analysis used the structure of a previously published and validated economic health model, adapted to the German healthcare setting. The model combines a decision tree for the initial diagnostics and treatment decision-making with a state-transition Markov model to simulate long-term clinical and economic outcomes over a lifetime horizon as previously described[9]. After the initial staging decision, patients can move between five mutually exclusive health states: “no evidence of disease (NEOD)”, “biochemical recurrence (BCR)”, “salvage treatment”, “palliative care”, and “death” (from PCa or other causes).

2.2. Target population, setting, and perspective

The model simulates a hypothetical group of men with newly diagnosed, non-metastatic intermediate- to high-risk PCa who are candidates for curative therapy and have a pre-test probability of LN

metastases of ≥5%. The analysis is conducted from the perspective of the German statutory health insurance payer. The setting is within the German healthcare system, with all costs updated to 2025 euros (€).

2.3. Comparators and time horizon

Three different staging strategies were compared:

- ePLND Strategy: All patients undergo surgical staging with ePLND, which acts as the reference standard.
- PSMA-PET/CT Strategy: Patients undergo a PSMA-PET/CT scan first. Treatment decisions are then based on the imaging results.
- m-MRI Strategy: Patients undergo an m-MRI scan first. Treatment decisions are then based on the imaging results.

In the imaging-first strategies, patients with negative or oligometastatic findings on the scan proceed with curative-intent local treatment, while those with findings indicating multiple metastases are directed towards non-curative systemic therapies, avoiding unnecessary local treatment. A lifetime horizon was used to account for all relevant downstream costs and health outcomes.

2.4. Model inputs and data sources

Key input parameters were updated based on recent clinical trial data, German cost data, and published literature. Major parameters are summarized in Table 1. A comprehensive list of all model parameters is provided in Supplementary Table S1.

2.4.1. Diagnostic accuracy

A key update was the addition of new diagnostic accuracy data from prospective Phase-3 trials for both imaging methods.

- PSMA-PET/CT: Accuracy figures were taken from the prospective, multicenter Phase-3 LIGHTHOUSE study by Surasi et al. This trial reported a per-patient sensitivity of 24% and a specificity of 95% for detecting LNM[6].
- m-MRI (Ferumoxtran): Sensitivity and specificity were derived from the per-protocol analysis of the prospective, multicenter Phase-3 PROSTAPROGRESS trial[10]. This study showed a sensitivity of 67% and a specificity of 95% for detecting LNM equal to or larger than 5 mm, and a sensitivity of 35% when including LNM between 2 and 5 mm.
- ePLND: Recognizing that surgical dissection is not a perfect gold standard and may miss micro-metastases, this updated analysis uses a clinically realistic base-case assumption of 85% sensitivity for ePLND, a parameter tested thoroughly in sensitivity analyses. This is because there are no available, reliable data regarding the sensitivity of ePLND in the literature[12]. Since up to one third of the potential metastatic lymph nodes can be missed by ePLND, 85% sensitivity seems to be a more than realistic value[16]. Specificity was assumed to be 100%.

2.4.2. Costs and utilities

All costs were determined from the payer perspective, updated to 2025 Euros (€), and adjusted for inflation where needed. Key costs included ePLND (€11,500), radical prostatectomy with ePLND (€11,780), PSMA-PET/CT (€1,800), and m-MRI (€790). Health-state utilities were derived from published literature[13]. A crucial parameter is the reduction in quality of life associated with morbidity from the ePLND procedure. Based on expert opinion and existing studies, this was modelled as a one-time utility reduction, equivalent to a lifetime loss of 0.30 QALYs for all patients undergoing the procedure[14]. Both costs and QALYs were discounted at an annual rate of 3.0%.

Table 1. Key input parameters for the cost-effectiveness model.

Parameter	Base-case value	Range for DSA	Distribution (for PSA)	Source
Population Parameters				
Prevalence of N1 disease	16%	10–25%	Beta	Godoy et al.[12]
Proportion oligometastatic (of N1)	80%	70–90%	Beta	Godoy et al.[12]
Diagnostic Performance				
ePLND				
Sensitivity	85%	70–100%	Beta	Assumption
Specificity	100%	Fixed	Fixed	By definition
PSMA-PET/CT				
Sensitivity	24.0%	15–35%	Beta	Surasi et al.[5]
Specificity	95.0%	92–99%	Beta	Surasi et al.[5]
m-MRI (Ferumoxtran)				
Sensitivity	67.0%	75–90%	Beta	PROSTAPROGRESS Trial[10]
Specificity	95.0%	80–92%	Beta	PROSTAPROGRESS Trial[10]
Costs (€, 2025)				
Cost of ePLND	€11,500	±20%	Gamma	Model assumption
Cost of PSMA-PET/CT	€1800	±20%	Gamma	Model assumption
Cost of m-MRI	€790	±20%	Gamma	Model assumption
Utilities & Disutilities				
QALY loss from ePLND (lifetime)	0.30	0.0 – 0.5	Beta	Assumption
Discount Rate				
Costs & QALYs (annual)	3.0%	0–5%	Fixed	Guideline

Abbreviations: DSA, Deterministic Sensitivity Analysis; N1, Lymph node positive; PSA, Probabilistic Sensitivity Analysis; QALYs, Quality-Adjusted Life Years.

2.4.3. Transition probabilities

The yearly probabilities of disease progression between health states (e.g. from NEOD to BCR) were updated using recent long-term follow-up data from large clinical cohorts, stratified by nodal status (N0, oligometastatic, polymetastatic)[15].

2.5. Cost-effectiveness and sensitivity analysis

The primary outcomes were the mean per-patient lifetime costs and QALYs for each strategy. Incremental cost-effectiveness ratios (ICERs) were calculated where appropriate. A strategy was deemed dominant if it was both less costly and more effective (yielded more QALYs) than its comparator.

To evaluate the effect of parameter uncertainty, we performed extensive sensitivity analyses: Deterministic Sensitivity Analysis (DS-A): One-way sensitivity analyses assessed the impact of changing individual key parameters within plausible ranges on the model outcomes and Probabilistic Sensitivity Analysis (PS-A): A probabilistic sensitivity analysis was conducted using 10,000 Monte Carlo simulations to examine the effect of simultaneous uncertainty across multiple parameters. Appropriate probability distributions (e.g. Beta for probabilities and utilities, Gamma for costs) were assigned to each parameter (Table 1). The results were displayed on a cost-effectiveness plane and a cost-effectiveness acceptability curve (CEAC), with a willingness-to-pay (WTP) threshold of €80,000 per QALY gained, a common but unofficial benchmark in Germany. The CEAC shows the probability of each intervention being the most cost-effective option across different WTP thresholds, helping identify the best strategy at the €80,000/QALY benchmark.

An interactive, publicly accessible Excel-based tool was created to enable users to modify key parameters and analyze their impact on cost-effectiveness under different scenarios (https://macrophage-mri.app).

3. Results

3.1. Base-case analysis

In the deterministic base-case analysis, both m-MRI and PSMA-PET/CT were found to be dominant over the ePLND strategy. The ePLND strategy had a lifetime cost of €37,855 and provided 18.110 QALYs. The m-MRI strategy offered the best value, with a lifetime cost of €27,870 (saving €9,985) and an effectiveness of 19.10 QALYs (a gain of 0.990 QALYs) compared to ePLND.

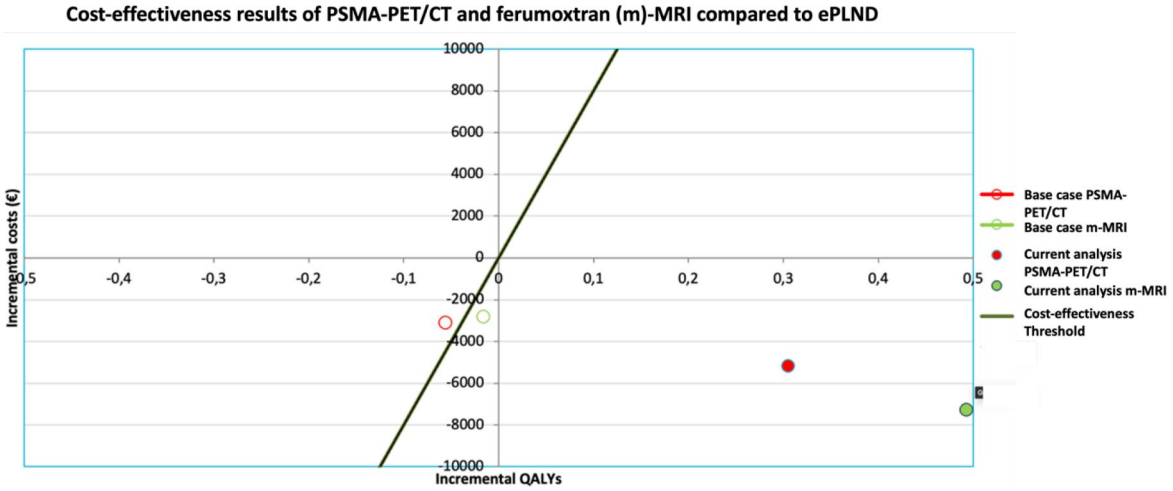

Figure 1. Cost-effectiveness plane (probabilistic sensitivity analysis). The cost-effectiveness plane from the PSA (10,000 simulations) comparing m-MRI and PSMA-PET/CT to ePLND. The x-axis represents incremental QALYs, and the y-axis represents incremental costs (€). The origin (0,0) represents ePLND. The dense clustering of simulation points for both imaging strategies in the southeast quadrant indicates dominance (lower costs, higher QALYs).

To enable a comparison with the Phase 3 trial of Surasi et al. we used the sensitivity for LNs larger than 5 mm as input, since LNM smaller than 5 mm are difficult to detect with PSMA-PET/CT[6]. After updating with these Phase 3 accuracy data, the PSMA-PET/CT strategy had a lifetime cost of €29,986 and yielded 18.91 QALYs. Compared with ePLND, this resulted in a significant cost saving of €7,869 and a health gain of 0.800 QALYs, confirming its dominance over surgical staging (Table 2). When directly compared, the m-MRI strategy was dominant over the PSMA-PET/CT strategy. The difference in diagnostic accuracy between the two methods provided a meaningful clinical and economic advantage for m-MRI, leading to additional cost savings of €2,116 and an effectiveness gain of 0.19 QALYs relative to PSMA-PET/CT (Table 3). Additional calculations can be easily performed using the online interactive tool (https://macrophage-mri.app/). Using this tool, we have calculated the outcome when applying the sensitivity of m-MRI for LNMs below 5 mm (Supplementary Figure S1).

3.2. Sensitivity analysis

The one-way deterministic sensitivity analysis showed that the model results were most sensitive to the QALY loss associated with the ePLND procedure and the assumed sensitivity of ePLND itself. However, across all plausible ranges of input parameters, the conclusion that m-MRI was the most cost-effective strategy remained robust.

The probabilistic sensitivity analysis confirmed the robustness of the base-case findings. The cost-effectiveness plane (Figure 1) shows that the vast majority of simulated incremental cost-effectiveness pairs for both imaging strategies, relative to ePLND, fall in the southeast quadrant, confirming their dominance.

The cost-effectiveness acceptability curve (Figure 2) confirmed the deterministic results. At the willingness-to-pay threshold of €80,000 per QALY, the probabilistic analysis showed that m-MRI was the optimal strategy in over 95% of the 10,000 simulations. Conversely, the probability that PSMA-PET/CT was the best choice was less than 5%, a result similar to that of the ePLND strategy.

3.3. Comparison of m-MRI vs PSMA-PET/CT

Comparing m-MRI and PSMA-PET/CT in terms of QALYs, m-MRI was superior, gaining 0.19 QALYs over PSMA-PET/CT. Regarding costs, m-MRI was also superior, saving €2,116 over PSMA-PET/CT. The probabilistic analysis showed that m-MRI was optimal more than 95% of the time at an €80,000/QALY threshold; the probability that PSMA-PET/CT was optimal was less than 5%.

Table 2. Base-case cost-effectiveness results vs. ePLND (lifetime horizon).

Strategy	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	Result vs. ePLND
ePLND (Reference)	€37,855	18.110	–	–	–
PSMA-PET/CT	€29,986	18.910	−€7869	+0.800	Dominant
m-MRI	€27,870	19.100	−€9985	+0.990	Dominant

Abbreviations: QALYs, Quality-Adjusted Life Years; ePLND, extended pelvic lymph node dissection; PSMA-PET/CT, prostate-specific membrane antigen positron emission tomography/computed tomography; m-MRI, ferumoxtran-enhanced magnetic resonance imaging.

Table 3. Incremental cost-effectiveness analysis: m-MRI versus PSMA-PET/CT.

Comparison	Incremental costs (€)	Incremental QALYs	Incremental cost-effectiveness ratio (ICER)	Conclusion
m-MRI vs. PSMA-PET/CT	−€2116	+0.19	N/A	m-MRI is dominant

Abbreviations: QALYs, Quality-Adjusted Life Years; PSMA-PET/CT, prostate-specific membrane antigen positron emission tomography/computed tomography; m-MRI, ferumoxtran-enhanced magnetic resonance imaging.

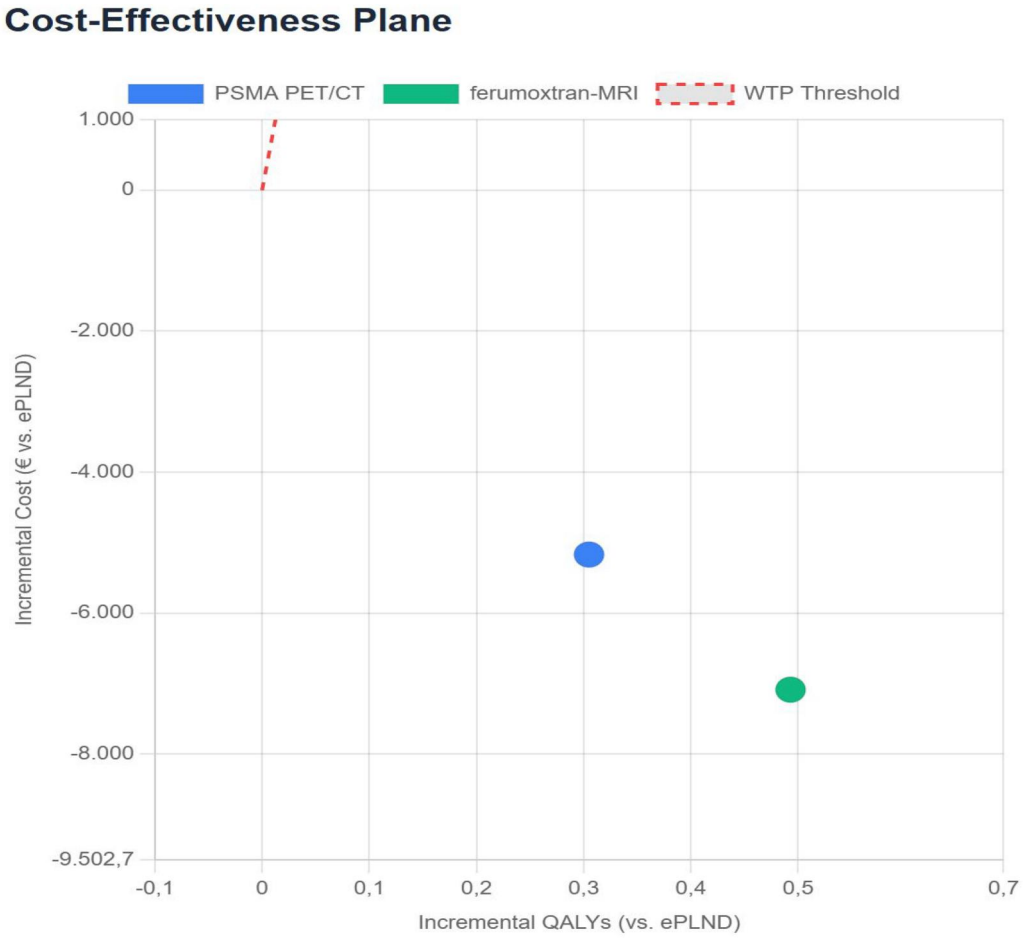

Figure 2. Cost-effectiveness plane for m-MRI vs. ePLND. The cost-effectiveness acceptability curve demonstrated that at a WTP threshold of €80,000 per QALY, m-MRI was the most cost-effective strategy in over 95% of the 10,000 simulations. The probability of PSMA-PET/CT being the optimal choice fell to below 5%, like that of the ePLND strategy.

4. Discussion

This updated health economic analysis, based on the latest prospective Phase 3 clinical trial data for both advanced imaging modalities, demonstrates a significant evolution in the value assessment of nodal staging for primary prostate cancer. The current findings suggest that an imaging-first approach is unequivocally superior to a universal ePLND strategy, offering better health outcomes at significantly lower lifetime costs in the German health system. However, the analysis reveals a crucial new finding: the choice of imaging modality is not equivalent, with m-MRI showing a clear and significant cost-

effectiveness advantage over PSMA-PET/CT for the specific indication of pelvic nodal staging. The robustness of this conclusion is emphasized by the probabilistic analysis, where m-MRI was identified as the optimal strategy in over 95% of simulations at a standard €80,000/QALY threshold. This high probability indicates that the dominance of m-MRI remains consistent despite parameter uncertainty, providing strong evidence for its preferred use in this clinical setting. Also, this is still true even with lower sensitivity (35% instead of 67%) for m-MRI when very small LNMs (2–5 mm) – which are below the detection threshold of PSMA-PET/CT – are included (Supplementary Figure S1). In this regard, the online interactive tool (https://macrophage-mri.app) provides a powerful and reliable method for modelling outcomes with different input data. The provision of such an interactive model serves as a key tool for decision-makers. It allows hospital administrators, guideline developers, and payers in different regions to input local cost data and diagnostic accuracy statistics from their own institutions. This adaptability transforms our analysis from a static report into a dynamic decision-support tool, facilitating localized cost-effectiveness evaluations and promoting evidence-based adoption of advanced imaging technologies.

These findings mark a significant development from the 2020 analysis by Scholte et al. who found imaging to be cost-saving but slightly less effective[9]. The reversal of this conclusion is driven by two key updates in our model: the inclusion of high-level diagnostic accuracy data and the use of more realistic assumptions about morbidity (QALY loss) and the imperfect sensitivity of ePLND. However, the most effective change is the inclusion of new Phase-3 data for PSMA-PET/CT and m-MRI, which fundamentally changes their relative positioning.

Although based on the German payer perspective, the core findings of this analysis regarding the clinical and economic benefits of an imaging-first approach, especially with high-sensitivity m-MRI, have broader relevance. Healthcare systems worldwide face high costs and overtreatment concerns in prostate cancer. The demonstrated QALY gains and cost savings suggest that payers in other countries should consider similar assessments. Key cost-effectiveness drivers – avoiding invasive surgery in node-negative patients and better risk stratification – are not Germany-specific and could be replicated elsewhere, though actual savings may differ.

4.1. Direct comparison of m-MRI and PSMA-PET/CT

Our updated model, incorporating definitive Phase-3 evidence, identifies a substantial, clinically significant cost-effectiveness advantage of m-MRI over PSMA-PET/CT for pelvic nodal staging[6,10]. The previous finding of marginal superiority is now replaced by clear dominance, primarily driven by the superior diagnostic profile of m-MRI in diagnostic sensitivity (67% for m-MRI vs. 24% for PSMA-PET/CT) with equally high specificity (95% and 96%)[6,9,10].

This outcome directly results from the model's structure mirroring clinical reality. The high specificity of both imaging techniques (95% and 96%) minimizes false-positive results, thereby preventing a large cohort of node-negative patients from undergoing unnecessary, costly, and morbid ePLND procedures. Given that approximately 95% of patients in this risk category are truly node-negative, the ability to correctly identify them and spare them from surgery is a powerful driver of both cost savings and quality-of-life preservation. The model demonstrates that the QALYs and costs saved by avoiding this overtreatment far outweigh the downstream consequences of the increased number of false negatives, which are typically identified later upon biochemical recurrence and can still receive effective salvage therapy.

The lower sensitivity of PSMA-PET/CT (24% vs 67%) causes a higher rate of false negatives compared to m-MRI, leading to more patients being initially undertreated. In the model, these patients progress faster to biochemical recurrence and more severe disease, leading to increased downstream treatment costs and, importantly, a reduction in quality-adjusted life years. This decline in QALYs mainly drives the widening value gap between the two imaging options.

The underlying clinical and biological mechanisms support this modeling outcome. The Surasi et al. study itself acknowledges that sensitivity is a known challenge for PSMA-PET agents, especially when detecting metastatic deposits in small lymph nodes that are smaller than 5 mm. These LNs fall below the resolution limits of PET scanners[6]. In contrast, m-MRI is a size-independent technique that identifies metastases by their failure to absorb iron oxide nanoparticles, a characteristic of nodes where healthy

macrophage-rich tissue has been replaced by tumor cells. This enables m-MRI to detect metastases in normal-sized nodes, including those as small as 2 mm[10].

4.2. Policy implications

The results of this analysis strongly support a fundamental change in how intermediate- and high-risk prostate cancer is managed in Germany. For about 20,000 men each year, the current standard, ePLND, is more expensive and less effective than a non-invasive imaging-first approach. Using either m-MRI or PSMA-PET/CT as the primary staging method would improve patient outcomes and lead to significant cost savings for the healthcare system.

However, our findings suggest a more nuanced policy. While both imaging tests surpass ePLND in effectiveness, they are not interchangeable in terms of value for pelvic staging. The evidence now strongly favors m-MRI as the most cost-efficient initial staging method. With an NPV of 86%, a negative m-MRI scan offers strong confidence to safely skip ePLND, saving most patients from potential surgical complications while better identifying those who need intensified therapy.

It is essential to contextualize these findings. This model specifically examines the cost-effectiveness of pelvic nodal staging. A key limitation, noted in the original analysis, is that it does not include the additional benefit of PSMA-PET/CT in detecting distant, extra-pelvic metastases (M1 disease), a capability demonstrated in the LIGHTHOUSE trial[6]. The clinical decision between m-MRI and PSMA-PET/CT may therefore involve a trade-off: better pelvic nodal staging with m-MRI versus comprehensive whole-body staging with PSMA-PET/CT. The optimal approach may depend on the specific clinical question for each patient. It should be noted that whole-body imaging is also possible with m-MRI for evaluating the axial skeleton.

Compared to the US and other countries, Germany has a similar approach to lymph node management in prostate cancer, with local differences due to health policies. In Germany, PLND is usually extended (ePLND) for better staging, but use has become more selective. In the US, ePLND mainly aids staging, not survival. Worldwide guidelines agree (e)PLND is for staging, not treatment. EAU recommends using nomograms such as the Briganti nomogram to assess lymph node invasion risk and avoid dissection if the risk is very low. PSMA-PET/CT is mainly used in Germany for high-risk patients and is also recommended by the AUA for similar risk groups, though access and insurance coverage vary in the US. European urologists favour PSMA PET-CT for its accuracy, but limited infrastructure leads some countries to rely on conventional imaging. Since m-MRI uses existing MRI infrastructure, it is a cost-effective alternative[17,18].

Approximately 20–40% of patients face biochemical recurrence (BCR) – a rising PSA – within 10 years after radical prostatectomy and ePLND, mostly within 5 years[19]. Although imaging struggles to detect microscopic lymph node metastases below resolution, its low invasiveness allows repeated use during follow-up without impacting QUALYs.

4.3. Limitations

This study presents several limitations. First, as a modelling study, it inherently relies on assumptions and synthesized data from multiple sources, although key parameters were derived from high-quality Phase 3 clinical trials. Second, the analysis was performed from the perspective of the German healthcare payer, which may limit the generalizability of cost inputs to other healthcare systems. Third, the model does not capture the potential added value of PSMA-PET/CT in detecting distant metastases; such a capability could affect its utility in comprehensive staging scenarios. Fourth, this analysis does not constitute a direct comparison within a single clinical trial, necessitating caution when interpreting outcomes across different studies due to possible heterogeneity in patient populations and study protocols. Fifth, the reported sensitivity for both m-MRI and PSMA-PET/CT in these Phase 3 trials is lower than the figures commonly cited in the literature, likely reflecting the rigorous study design and stringent quality control inherent to Phase 3 registration trials. Also, the percentage of micro metastases in this study was higher than in most other studies: 35% of LNM were < 2 mm, and 52% were 2–5 mm. Finally, 73% of m-MRI-positive LNs were left behind after ePLND, thereby reducing m-MRI sensitivity.

Notably, these trials are more representative of typical 'real-world' clinical practice. Final limitations include the reliance on modelled long-term outcomes, as randomized controlled trial data comparing the long-term survival of imaging-guided strategies versus routine ePLND are still developing. Furthermore, while we used assumed parameters reflecting real-world ePLND sensitivity (85%), variations in surgical technique can influence this; however, sensitivity analysis confirmed the robustness of the results.

5. Conclusion

This economic evaluation, updated with the strongest available Phase-3 evidence, confirms that a non-invasive imaging-first approach for nodal staging in primary prostate cancer is superior to the surgical standard of ePLND. More importantly, it demonstrates that the chosen imaging method has crucial effects on both patient outcomes and healthcare costs. Due to its high specificity and better sensitivity to detect pelvic lymph node metastases, ferumoxtran-enhanced m-MRI is the dominant and most cost-effective strategy, surpassing both ePLND and PSMA-PET/CT. While PSMA-PET/CT remains a cost-effective alternative to ePLND, its low sensitivity for detecting nodal disease limits its usefulness in this specific clinical setting. These findings provide a strong, evidence-based reason to consider incorporating m-MRI as the primary tool for pelvic nodal staging in guidelines, thereby helping to improve treatment for men with intermediate- and high-risk prostate cancer.

Transparency

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Author contributions

Patrik Zamecnik: Conceptualization; Formal analysis; Methodology; Writing – original draft; Writing – review & editing. Jürgen Feuerstein: Conceptualization; Methodology; Writing – review & editing. Michael Berghahn: Methodology; Writing – review & editing. Jelle Barentsz: Conceptualization; Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

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