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MRI in Prostate Cancer Screening: A Review and Recommendations, From the *AJR* Special Series on Screening

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Traditional PSA-based screening for prostate cancer (PCa) is challenged by an unfavorable benefit-to-harm ratio from underdiagnosis of clinically significant cancers, overdiagnosis of indolent cancers, and unnecessary biopsies, despite demonstrated reductions in PCa-associated mortality. Inclusion of MRI in screening algorithms helps address these limitations by improving risk stratification of men suspected of having PCa and by enabling targeted biopsies. The impact of MRI-based strategies on screening's benefit-to-harm ratio can be objectively assessed using ratios reflecting clinically significant cancers detected, indolent cancers detected, unproductive biopsies, and avoided biopsies. Of two overarching MRI-based screening strategies (sequential MRI after PSA testing and MRI alone), the sequential strategy is favored as a balanced and scalable approach. This Special Series Review provides a detailed analysis of the role of MRI in PCa screening, targeted to radiologists. Recommendations are provided for optimizing the use of MRI in PCa screening, including individualized risk assessments, tailored protocols, quality assurance for ensuring reliable and reproducible results, and consideration of new screening-specific scoring systems and biopsy thresholds. Ultimately, successful integration of MRI in PCa screening will require radiologists to actively engage in refining protocols, standardizing interpretations, and adopting emerging technologies. Such efforts will help maximize benefits while minimizing harms, enabling wider acceptance of PCa screening.

MRI-Based Prostate Cancer Screening

Prostate cancer (PCa) is a significant global health challenge, ranking as the most frequently diagnosed cancer among men in Europe and the United States [1]. In the United States, rates of PCa-associated mortality (hereafter, PCa mortality) surpass those of colorectal cancer, making PCa the second leading cause of cancer-related death in men, behind lung cancer, whereas in Europe the PCa mortality rate is positioned as the third leading cause of cancer-related death [1]. PCa mortality has increased in countries where screening has been scaled back. For example, in the United States, PCa mortality has increased for the first time since the early 1990s, coinciding with declining PSA screening rates [2]. This issue underscores the pressing need for effective screening strategies to detect clinically significant PCa at an early and treatable stage [3].

Benefits and Limitations of Traditional PCa Screening

Traditional PCa screening relies on PSA testing and untargeted systematic biopsy. Randomized trials using this approach have shown a reduction in mortality; however, consensus is lacking regarding population screening recommendations due to an unfavorable benefit-to-harm ratio [2].

Benefits—The most significant benefit of PSA-based screening is a reduction in PCa-specific mortality. The European Randomized Study of Screening for Prostate Cancer (ERSPC) showed a consistent 20% relative reduction in PCa mortality at 9–16 years of

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follow-up, by use of organized population-based PSA screening that is repeated every 2–4 years [3]. This reduction corresponds to the prevention of one PCa-related death for every 570 men invited to undergo screening at the 16-year mark. The U.S. Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial observed similar results after accounting for variations in biopsy compliance and cross-contamination [4].

Limitations—Population-based screening that uses PSA-promoted systematic biopsy at one time point fails to diagnose many high-risk cancers and thus does not reduce mortality [5]. Furthermore, estimates suggest that half of screening-detected cancers may be insignificant [6]. Thus, PSA screening results in many men being diagnosed and treated for cancers that would never have caused harm if they had gone undetected. Additionally, the low specificity of PSA testing results in many unnecessary systematic biopsies, which carry risks of bleeding, infection, pain, and discomfort.

Overall balance—In aggregate, the harm associated with PSA screening outweighs its benefits. High rates of underdiagnosis, overdiagnosis, unnecessary biopsies, and overtreatment affect the overall effectiveness and safety of traditional screening programs, accounting for the lack of PCa screening recommendations in many countries [7, 8].

Promise of MRI in PCa Screening

The emerging consensus is that selective and personalized strategies incorporating risk stratification, liquid biomarkers, MRI triage, and targeted biopsy are essential for optimizing PCa screening, enabling a more satisfactory balance between benefits and harm [9, 10]. MRI addresses the limitations of PSA testing (e.g., underdiagnosis and overdiagnosis) and the limitations of untargeted systematic biopsies (e.g., unproductive biopsies, undersampling of significant disease, and overdetection of indolent cancers) [11].

MRI-Based PCa Screening Approaches

The emerging consensus is that selective and personalized strategies that incorporate risk stratification, liquid biomarkers, MRI triage, and targeted biopsy are essential for optimizing PCa screening, enabling a more satisfactory balance between benefits and harm [9, 10]. MRI addresses the limitations of PSA testing (e.g., underdiagnosis and overdiagnosis) and the limitations of untargeted systematic biopsies (e.g., unproductive biopsies, undersampling of significant disease, and overdetection of indolent cancers) [11].

Among the various PCa screening pathways involving MRI that were investigated (Fig. 1), two distinct overarching approaches have emerged: a sequential PSA-based MRI strategy and an MRI-only strategy. Table 1 provides an overview of five studies of first-line MRI utilization (i.e., without PSA pretesting) [12–17] and eight studies of second-stage MRI utilization after PSA pretesting [18–22], including four studies of first screening rounds and four studies of repeat screening rounds [23–26]. As MRI outperforms all other biomarkers currently studied in PCa screening, such biomarkers are excluded from the scope of the current review [27, 28].

MRI as a first-line tool—Some clinically significant cancers do not cause elevated PSA levels and thus are missed by PSA testing [13]. For example, although hardly any clinically significant cancers occur below a PSA cutoff level of 1 ng/mL, a PSA cutoff level of 3 ng/mL misses approximately half of significant cancers [13, 15, 17]. The use of MRI as a first-line screening tool may help to identify these cancers. In addition, patients may be more inclined to undergo screening by MRI than by PSA; for example, the Swedish OPT (Organized Prostate Cancer Testing) screening trial reported that young men (age, 50 years) who received an invitation to undergo screening MRI had a response rate of 35% [22]. Most patients adhere to subsequent biopsy recommendations after abnormalities are found on MRI [12, 17].

> **Highlights**
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> - *Including MRI in prostate cancer screening addresses the screening limitations of overdiagnosis and underdiagnosis by enhancing risk stratification and enabling targeted biopsies, improving the benefit-to-harm ratio.*
> - *Among two distinct MRI-based screening strategies (sequential MRI after PSA testing and MRI alone), the sequential strategy is favored as a balanced and scalable approach.*
> - *Quality assurance in screening requires harmonized MRI equipment, acquisition, and interpretation protocols, including automation and artificial intelligence assistance, to ensure reliability and reproducibility of results.*

A key concern regarding the MRI-only approach is its cost-effectiveness given the high costs of MRI and the low prevalence of cancers with a grade group (GG) score of 2 or greater. Performing MRI on a large scale without prior risk stratification can yield a high proportion of negative results and associated unnecessary costs. This approach may also yield a high proportion of indeterminate results, especially in young men (as noted in the PROBASE (Risk-Adapted Prostate Cancer Early Detection Study Based on a Baseline Prostate-Specific Antigen Value in Young Men) and OPT trials [21, 22]), when assessed using conventional PI-RADS-based criteria. In contrast, when MRI is used after PSA testing, disease prevalence in tested men increases, yielding greater cancer detection rates.

MRI as a secondary-line tool after PSA testing—Restriction of MRI to men with a PSA screening examination exceeding a predetermined threshold level results in the population of men undergoing MRI to be variably enriched with high-grade PCa, depending on the PSA cutoff level. For example, the STHLM3-MRI (Prostate Cancer Detection Using the Stockholm3 Test and Magnetic Resonance Imaging) and Göteborg-2 trials reported detection rates of 21% and 14%, respectively, for PCa of GG 2 or greater, by use of a PSA cutoff level of 3 ng/mL or greater [18, 19] (Fig. 2). In the MRI-only PROSTAGRAM (Prostate Cancer Screening Trial Using a Group of Radiological Approaches Including MRI and Ultrasound), VISIONING, and ReIMAGINE (Refining Imaging and Molecular Analysis Guiding Individualized Navigation of Early Prostate Cancer) studies, detection rates for PCa graded as GG of 2 or higher were lower (3%, 8%, and 7%, respectively) [13, 15, 17]. The Göteborg-2 trial found PCa of GG 2 or greater in 5% of men with a PSA level between 1.8 and 3 ng/mL. These data indicate the need for further research to determine optimal PSA thresholds in

TABLE 1: Overview of MRI-Based Prostate Cancer (PCa) Screening Studies Using MRI As a First-Line or Second-Stage Stratification Tool in First and Repeat Screening Rounds

Study Approach and Name [Reference]	First Author	Year	Country	Inclusion Age (y)	Study Design	Objective	Key Points/Conclusion
MRI as first-line tool in first screening round							
MVP [12]	Nam	2022	Canada	≥ 50	RCT	Intervention: MRI-targeted and systematic biopsies for men with positive MRI; comparator: systematic biopsies for all men	MRI as a stand-alone screening test reduced the rate of prostate biopsy; more patients were willing to follow biopsy recommendations after positive MRI results
ReIMAGINE [13]	Moore	2023	United Kingdom	50–75	Prospective cohort, single arm	MRI-targeted and systematic biopsies for men with positive MRI	One in six screened men had a lesion on MRI; half of men with PCa of GG ≥ 2 on biopsy had a PSA level of < 3 ng/mL; 1% of screened men had GG 1 PCa overdiagnosed
IP1-PROSTAGRAM [14]	Eldred-Evans	2023	United Kingdom	50–69	Prospective cohort, paired	Systematic with possible MRI-targeted biopsies for all men	Trade-off exists between reducing excessive numbers of biopsies and maintaining rates of detection of PCa of GG ≥ 2; pathway that combines PSA level > 1 ng/mL and MRI score of 4 maintains detection of PCa of GG ≥ 2 with fewer biopsies than the standard pathway and would be the preferred strategy to evaluate in future studies at the first screening round
IP1-PROSTAGRAM [15]	Eldred-Evans	2021	United Kingdom	50–69	Prospective cohort, single arm	Systematic with possible MRI-targeted biopsies for all men	PI-RADS score of 4–5 resulted in more men being diagnosed with PCa of GG ≥ 2, compared with systemic biopsy, without increasing detection rates of GG 1 PCa; more than half of men with PCa of GG ≥ 2 had a PSA level of < 3 ng/mL
PROSA [16]	Messina	2024	Italy	49–69	RCT	Intervention: MRI-targeted biopsies for men with positive MRI; comparator: second-stage MRI-targeted biopsies for men with positive MRI	Noncontrast MRI can facilitate early diagnosis of PCa with a GG score ≥ 2 while reducing the number of unnecessary prostate biopsies and the detection of GG 1 PCa
VISIONING [17]	Wetteraurer	2024	Switzerland	50[a]	Prospective cohort, single arm	MRI-targeted biopsies for men with positive MRI and template biopsies for men with negative MRI; MRI performed for patients with PSA level > 10 ng/mL or with positive DRE in phase 1 and in patients with PSAD > 0.15 ng/mL^2 in phase 2	bpMRI as an opportunistic screening tool for PCa showed superior effectiveness in detecting PCa of GG ≥ 2 compared with PSA and DRE; optimizing the screening protocol with a PSA cutoff level of 1 ng/mL and excluding men with a negative family history could further decrease both detection of GG 1 PCa and negative biopsies, resulting in the detection of one PCa of GG ≥ 2 for every third man undergoing biopsy

(Table 1 continues on next page)

TABLE 1: Overview of MRI-Based Prostate Cancer (PCa) Screening Studies Using MRI As a First-Line or Second-Stage Stratification Tool in First and Repeat Screening Rounds (continued)

Study Approach and Name [Reference]	First Author	Year	Country	Inclusion Age (y)	Study Design	Objective	Key Points/Conclusion
MRI as second-stage tool in first screening round							
Göteborg-2, first round [18]	Hugosson	2022	Sweden	50–60	RCT	Intervention: MRI-targeted biopsies for men with positive MRI; comparator: systematic and possible MRI-targeted biopsies for all men	Avoidance of systematic biopsy for the MRI-targeted biopsy strategy reduced the risk of overdiagnosis by half at the cost of delaying the detection of intermediate-risk PCa in a small proportion of patients
STHLM3-MRI, first round [19]	Eklund	2021	Sweden	50–74	RCT	Intervention: MRI-targeted and systematic biopsies for men with positive MRI; comparator: systematic biopsies for all men	MRI with targeted and systematic biopsy for men with positive MRI results was noninferior to standard biopsy for detection of PCa with a GG score ≥ 2 but reduced the detection of GG 1 PCa
PROBASE, first round [20]	Arsov	2022	Germany	45 or 50	RCT	Intervention: delayed screening to age 50 y for all men; comparator: screening at age 45 y with systematic and MRI-targeted biopsies for all men; screening round represented baseline results	Screening-detected cancers were mainly low- or intermediate-risk (GG 1 or GG ≥ 2), and prevalence of PCa with a GG score ≥ 3 was very low; invitation acceptance rate was low (11%); indication for further diagnostic tests should be based on only two PSA values
PROBASE, first round [21]	Boschheidgen	2024	Germany	45	Prospective cohort, single arm	Systematic and possible MRI-targeted biopsies for all men; screening round represented baseline results	PCa prevalence was low due to young age; the proportion of indeterminate test results for young men was high; results were highly dependent on reader experience; central review decreased intermediate test results
OPT [22]	Bratt	2024	Sweden	50	Prospective cohort, single arm	Systematic and MRI-targeted biopsies for men with positive MRI or for men with PSAD > 0.15	Use of MRI and PSAD avoids biopsy in more than 50% of men with a PSA level ≥ 3 ng/mL; interregional differences in biopsy outcomes indicate the need to perform quality control of the MRI pathway components; results show the need for prospective outcome registration, analysis of diagnostic results, and governance

(Table 1 continues on next page)

TABLE 1: Overview of MRI-Based Prostate Cancer (PCa) Screening Studies Using MRI As a First-Line or Second-Stage Stratification Tool in First and Repeat Screening Rounds (continued)

Study Approach and Name [Reference]	First Author	Year	Country	Inclusion Age (y)	Study Design	Objective	Key Points/Conclusion
MRI as second-stage tool in repeat screening round							
Göteborg-2, second to fourth round [23]	Hugosson	2024	Sweden	50–60	RCT	Intervention: MRI-targeted biopsies for men with positive MRI; comparator: systematic and possible MRI-targeted biopsies for all men	Only 1.4% of men had PCa with a GG score ≥ 2 at 3.9 y of follow-up after a negative baseline MRI; omitting biopsy for patients with negative MRI results eliminated more than half of GG 1 PCa diagnoses
STHLM3-MRI, second round [24]	Nördstrom	2024	Sweden	50–74	Prospective cohort, single arm	MRI-targeted and systematic biopsies for men with positive MRI	A substantial proportion of men had elevated PSA levels during rescreening, and a considerable portion of MRI scans obtained lacked lesions suggestive of PCa; 3.2% of men had PCa of GG ≥ 2 at 2.4 y of follow-up after a negative baseline MRI
ERSPC-Rotterdam, fifth round (pilot study) [25]	Alberts	2018	Netherlands	71–75	Prospective cohort, paired	Intervention: systematic and possible MRI-targeted biopsies for all men; comparator: systematic biopsy for all men	Men who underwent repeated screening after age 70 y and who often had one previous biopsy still harbored high-grade PCa; the harm-to-benefit ratio of early PCa detection in older men by multivariable risk stratification and MRI was improved compared with a standard screening approach; avoidance of two-thirds of biopsies and of low-grade PCa diagnoses was realized while maintaining the high-grade PCa detection
Göteborg-1, 10th round (pilot study) [26]	Grenabo Bergdahl	2016	Sweden	69	Prospective cohort, paired	Intervention: systematic and possible MRI-targeted biopsies for all men; comparator: systematic biopsy for all men	Despite a heavily prescreened population, MRI detected more significant PCa compared with standard PSA screening; a new PCa screening strategy involving MRI appeared to be highly accurate in detecting significant PCa and minimizing unnecessary biopsies

Note—MVP = MRI Versus PSA in Prostate Cancer Screening, RCT = randomized controlled trial, ReIMAGINE = Refining Imaging and Molecular Analysis Guiding Individualized Navigation of Early Prostate Cancer, GG = grade group, IP1-PROSTAGRAM = IP1–Prostate Cancer Screening Trial Using a Group of Radiological Approaches Including MRI and Ultrasound, PROSA = Prostate Cancer Secondary Screening in Sapienza, DRE = digital rectal examination, PSAD = PSA density, bpMRI = biparametric MRI, STHLM3-MRI = Prostate Cancer Detection Using the Stockholm3 Test and Magnetic Resonance Imaging, PROBASE = Risk-Adapted Prostate Cancer Early Detection Study Based on a Baseline Prostate-Specific Antigen Value in Young Men, OPT = Organized Prostate Cancer Testing, ERSPC = European Randomized Study of Screening for Prostate Cancer.
[a]Forty-five years old if at high risk.

MRI-based risk-adapted screening [29]. The recently launched U.K. TRANSFORM (Transforming Prostate Cancer Screening) trial will compare several MRI study arms (no PSA threshold, PSA > 1 ng/mL, and PSA > 3 ng/mL) to address these issues [30].

The main role of MRI performed after PSA testing is to triage men for prostate biopsy. Men with highly suspicious lesions on MRI are recommended to undergo MRI-targeted biopsy, whereas those with negative or low-suspicion findings may avoid immediate biopsy. This approach enables a more selective and personalized biopsy approach, focusing on men considered at highest risk on the basis of PSA and MRI findings. For this approach, the key concern is delayed diagnosis of cancers of GG 2 or greater, relying on an inbuilt safety net of repeated screening rounds; such rounds mostly detect GG 2 cancers [23, 24].

MRI Benefits Outweigh Harms

Studies have shown that MRI progressively reduces unnecessary biopsies and detects fewer indolent cancers across a range of decreasing prevalences of cancer of GG 2 or greater, indicating a potential utility for screening [31, 32]. In screening trials, MRI helps avoid biopsies for men with negative or low-suspicion findings. For example, in a meta-analysis, an MRI-based screening pathway reduced biopsies by more than 3.5 times compared with a traditional pathway of only systematic biopsies (OR = 0.28) [33]. In addition, by targeting biopsies to suspicious areas only, MRI reduced the likelihood of detecting insignificant cancers by almost three times (OR = 0.34). Furthermore, the performance of MRI was more than four times better in detecting intermediate- and high-risk cancers (OR = 4.15), enabling more accurate risk stratification. Importantly, the MRI-based screening pathway and traditional pathway required biopsy of two and six men, respectively, to detect cancer of GG 2 or higher in one man.

Combined Measures of Benefit-to-Harm Ratio

Although available evidence suggests that MRI-guided strategies can enhance PCa screening, insufficient information addresses how to compare benefits and harms among MRI-based approaches. We thus propose four ratios as summary measures to compare strategies objectively. When these ratios are used, the context (e.g., individual early diagnosis vs population screening), the role of MRI in the pathway (e.g., MRI after PSA testing vs MRI alone), and definitions of clinically significant cancer must be considered (Fig. 2).

Ratios in men undergoing biopsy—The ratio of cancer of GG 2 or greater to GG 1 cancer reflects the screening strategy's selectivity for detecting cancers graded as GG 2 or higher while minimizing detection of GG 1 cancers (i.e., indolent cancers). A higher ratio indicates a more favorable balance between benefits and harm. Among traditional screening trials, estimates of overdiagnosis [6] were 43% in the ERSPC trial [3], 63% in the Nörrkoping trial [5], and 52% in the Stockholm trial [34], yielding ratios of 1.3, 0.6, and 0.9, respectively. The STHLM3-MRI and Göteborg-2 MRI-based screening trials showed improved balance, with ratios of 4.7 and 1.7, respectively. The significance of a favorable ratio using MRI should be interpreted cautiously given that clinically significant cancer remains not fully defined in the MRI era. Nonetheless, the ratio may help compare screening strategies.

The ratio of cancer graded as GG 2 or higher to the sum of GG 1 cancer and benign biopsies reflects the overall accuracy of a strategy. A higher ratio suggests fewer detected GG 1 cancers and fewer unproductive biopsies in men with positive MRI results. These benefits can be particularly relevant when comparing screening strategies that include different rates of men avoiding biopsy due to negative screening results.

Ratios for biopsy avoidance—Men with positive PSA results but negative MRI results may opt out of biopsy testing. These avoided biopsies are a benefit compared with a strategy of biopsy being performed for all men with positive PSA results. However, undetected cancers of GG 2 or greater in men with negative MRI results are a harm. The ratio of avoided biopsies to missed cancers of GG 2 or higher quantifies the trade-off between reducing unnecessary biopsies and reducing the risk of missed cancers graded as GG 2 or greater in men with negative MRI results. A higher ratio indicates that the strategy effectively avoids biopsies without substantially increasing the number of missed significant cancers. The number of undetected cancers of GG 2 or greater resulting from biopsy avoidance can be assessed through studies that separately investigated MRI-targeted and systematic nontargeted biopsies or that investigated men actively undergoing follow-up rescreening tests [18, 23, 24].

The ratio between biopsies avoided after negative MRI results and biopsies with benign findings after positive MRI results reflects the extent to which a strategy minimizes unproductive biopsies. This ratio could be a key driver of quality assurance programs. Use of a higher threshold for MRI positivity (e.g., a MRI suspicion score of 4 or greater rather than 3 or greater) to avoid more biopsies would substantially reduce unproductive biopsies, increasing the benefit-to-harm balance indicated by this ratio.

Screening Test Principles

MRI Performance Characteristics and Reproducibility

To optimize benefit-to-harm ratios and cost-effectiveness, population-based screening requirements favor abbreviated MRI approaches with shorter scanning times and higher biopsy thresholds. In contrast, to maximize cancer detection in individuals with suspected cancer, early-diagnosis protocols prioritize comprehensive examinations using full multiparametric protocols and lower biopsy thresholds. Both contexts are associated with variable image quality, acquisitions, and outcomes, as well as qualitative MRI assessments.

MR Image Quality

High-quality MRI is critical for accurate diagnosis. Substantial variability in quality across centers stems from patient motion, susceptibility artifacts, variable compliance with PI-RADS technical standards, suboptimal scanner hardware and software, and inadequate personnel training [35–37]. Before MRI interpretation, scan quality should be benchmarked for diagnostic use [35]. Unfortunately, published MRI-based screening literature rarely reports image quality (Table 2).

MRI Equipment

MRI-based screening studies show marked variability in deployed MRI equipment (Table 2). Variations in field strength, receiver coil sensitivity, gradient strength, and acquisition parameters substantially affect image contrast, particularly for DWI. Vendors use different reconstruction algorithms, which also contributes to variability. Use of a single scanner type and coil configuration may help address challenges posed by equipment variation. Multivendor solutions are more complex and may use an accreditation approach, such as the standardized qualification program proposed by the American College of Radiology that involves regular reassessments to maintain certification [35].

MRI Protocols and Patient Preparations

Standardized protocols are crucial for reducing variation in scanning procedures and patient preparation. Harmonized imaging parameters should be used for the same sequence type (Table 2). Instructions for rectal cleaning and dietary restrictions should be clarified.

Requirements for Optimizing Protocols

MRI screening protocols should use ultrafast sequences, which have shown promise in early detection settings [38, 39]. A short, simple, and smart model should be considered for screening.

Short—A quick examination is fundamental to the feasibility of PCa screening programs, increasing availability and patient acceptance while lowering costs. Ideally, acquisition times should be 10 minutes at most [40]. Use of fewer acquisitions, focusing on axial (or 3D) sequences, shortens scanning times [38, 41]. Deep learning algorithms that expedite denoising and k-space filling can accelerate acquisitions [42, 43]. Omission of contrast media and antiperistalsis agents shortens procedures and alleviates safety concerns.

Simple—A simple protocol is essential for broader implementation of MRI-based screening. The protocol should use well-defined, widely available, nonproprietary sequences to ensure consistency across MRI systems [44]. This need is particularly important for DWI, where variations in b values are common (Table 2) and can impact results.

Smart—A smart protocol leverages automation and AI tools to standardize and optimize radiologic processes from image acquisition to interpretation. AI-assisted acquisitions can accelerate scanning and enable real-time imaging adaptation based on likely image quality. Deep learning computer-aided detection algorithms can evaluate images to assist radiologists in identifying suspicious lesions, segmenting the prostate, and assigning suspicion scores for detected lesions. These tasks can enhance efficiency, accuracy, and consistency of interpretation, especially for less-experienced readers [45]. Furthermore, AI levels of suspicion can be combined with radiologic assessments and clinical metadata to help personalize biopsy decision-making and planning [46].

Reliable MRI Results

Standardization of training, implementation of quality-control measures, and application of technologic advances such as AI hold promise for improving reliability and reproducibility of MRI results.

Interobserver variability—Radiologists have different training backgrounds and familiarity with prostate MRI interpretation criteria, contributing to interpretation variability. Prostate MRI interpretation involves a learning curve, with more-experienced radiologists showing higher accuracy and agreement. Radiologists specializing in urogenital imaging or with extensive prostate MRI experience typically show greater consistency in interpretation.

The ProScreen study found fair-to-moderate agreement among nine radiologists in reporting index lesions on MRI (kappa coefficient of 0.40 and 0.60 for lesions reported as having a PI-RADS score of ≥ 3 and ≥ 4, respectively) [47]. That study observed significant differences in sensitivity and specificity among radiologists, potentially impacting screening precision. Radiologists' agreement was good for detecting GG 4 and GG 5 cancers; however, disagreements were common regarding detecting GG 1 cancer.

Agreement is typically high for negative MRI findings, with more substantial variability seen for positive findings [48]. Disagreements regarding positive cases result in more total biopsies, more unproductive biopsies, and more indolent cancer detection, contributing to inconsistent

TABLE 2: Overview of MRI-Based Characteristics in Prostate Cancer Screening Studies

Study Approach and Name [Reference]	Quality Check Before Recruitment	No. of MRI Sites	MRI Protocol	MRI Duration (min)	Scanner Field Strength and Coil[a]	Planes for T2-Weighted Image	DWI b Values (s/mm²)	Patient Preparation[b]	MRI Interpretation	Interpretation System	MRI Score for Positive Test
MRI as first-line tool in first screening round											
MVP [12]	NR	1	bpMRI	15	3 T (Magnetom Prisma, Siemens Healthineers); six-channel pelvic phased-array coil	Ax Sag Cor	50, 200, 400, 600, 1000, 1600[c]	NR	Single reader	PI-RADS v2.0	4–5
ReIMAGINE [13]	NR	1	bpMRI	< 10	3 T (Achieva, Philips Healthcare); 32-channel pelvic phased-array coil	Ax	2000	NR	Blinded double readings; third reader for disagreement	NR	NR
IP1-PROSTAGRAM [15]	Centrally reviewed at two sites	2	bpMRI	< 15	1.5 T (Magnetom Aera, Siemens Healthineers) or 3 T (Magnetom Verio, Siemens Healthineers); pelvic phased-array coil	Ax Sag	0, 150, 400, 1000, 1500[c]	NR	Blinded double readings; third reader for disagreement	PI-RADS v2.1	3–5
PROSA [16]	NR	1	bpMRI	NR	3 T (Discovery 750, GE Healthcare; Magnetom Vida; Siemens Healthineers); 32-channel surface phased-array pelvic coil	Ax Cor	100, 800, 1000, 2000[c]	Microenema (1 h), low-fiber diet (3 d)	Blinded double readings; third experienced reader for disagreement	PI-RADS v2.1	3–5
VISIONING [17]	NR	1	bpMRI	10	3 T (Magnetom Prisma, Siemens Healthineers)	Ax	0, 800	NR	Blinded double readings, followed by consensus	PI-RADS v2.1	3–5

(Table 2 continues on next page)

TABLE 2: Overview of MRI-Based Characteristics in Prostate Cancer Screening Studies (continued)

Study Approach and Name [Reference]	Quality Check Before Recruitment	No. of MRI Sites	MRI Protocol	MRI Duration (min)	Scanner Field Strength and Coil[a]	Planes for T2-Weighted Image	DWI b Values (s/mm^2)	Patient Preparation[b]	MRI Interpretation	Interpretation System	MRI Score for Positive Test
MRI as second-stage tool in first screening round											
Göteborg-2, first round [18]	External validation of MRI interpretations in sample of 100 examinations	1	mpMRI	NR	3 T; pelvic phased-array coil	Ax Sag Cor	0, 100, 1000, 1500[c]	Fasting (4 h), microenema (2 h)	Blinded double readings, followed by consensus	PI-RADS v2.0 and v2.1	3–5
STHLM3-MRI, first round [19]	NR	2	bpMRI	< 16	1.5 T (Magnetom Aera, Siemens Healthineers) or 3 T (Signa Architect, GE Healthcare)	Ax Sag Cor	100, 450, 800, 1500[c]	Fasting (6 h), microenema, antispasmodic agent (glucagon)	2–3 Centralized readers	PI-RADS v2.0 and v2.1	3–5
PROBASE, first round [20]	NR	4	mpMRI	NR	3-T scanners	Ax Sag Cor	0 or 50, 500, 1000, 1400[c]	NR	Local readers at each site	PI-RADS v2.0 and v2.1	3–5
OPT [22]	No central review	18[d]	NR	NR	1.5-T or 3-T scanners	NR	NR	NR	NR	PI-RADS v2.1	4–5[e]
MRI as second-stage tool in repeat screening round											
Göteborg-2, second to fourth round [23]	NR	1	bpMRI	NR	3 T; pelvic phased-array coil	Ax Sag Cor	0, 100, 1000, 1500[c]	Fasting (4 h), microenema (2 h)	Double blinded readings, followed by consensus	PI-RADS v2.0 and v2.1	3–5
STHLM3-MRI, second round [24]	NR	2	bpMRI	< 10	1.5 T (Magnetom Aera, Siemens Healthineers) or 3 T (Signa Architect, GE Healthcare)	Ax Sag Cor	100, 450, 800, 1500[c]	Fasting (6 h), microenema, antispasmodic agent (glucagon)	2–3 Centralized readers	PI-RADS v2.1	3–5
ERSPC-Rotterdam, fifth round (pilot study) [25]	NR	1	mpMRI	NR	3 T (Discovery, GE Healthcare); 32 pelvic phased-array coil	Ax Sag	0 or 50, 400, 800, 1000[c]	NR	Double readings, followed by consensus	PI-RADS v2.0	3–5
Göteborg-1, 10th round (pilot study) [26]	NR	1	mpMRI	NR	3 T (Achieva, Philips Healthcare); 32 cardiac phased-array coil	Ax Sag Cor	0, 1000	NR	Triple readings, followed by consensus	PI-RADS v2.0	3–5

Note—MVP = MRI Versus PSA in Prostate Cancer Screening, NR = not reported, bpMRI = biparametric MRI (without IV contrast media), Ax = axial, Sag = sagittal, Cor = coronal, v2.0 = version 2.0, ReIMAGINE = Refining Imaging and Molecular Analysis Guiding Individualized Navigation of Early Prostate Cancer, IP1-PROSTAGRAM = IP1–Prostate Cancer Screening Trial Using a Group of Radiological Approaches Including MRI and Ultrasound, v2.1 = version 2.1, PROSA = Prostate Cancer Secondary Screening in Sapienza, mpMRI = multiparametric MRI, STHLM3-MRI = Prostate Cancer Detection Using the Stockholm3 Test and Magnetic Resonance Imaging, PROBASE = Risk-Adapted Prostate Cancer Early Detection Study Based on a Baseline Prostate-Specific Antigen Value in Young Men, OPT = Organized Prostate Cancer Testing, ERSPC = European Randomized Study of Screening for Prostate Cancer.

[a]Coil not reported in all studies.

[b]Values in parentheses indicate time before MRI examination, if reported in study.

[c]Not used in ADC map calculation.

[d]Sites or units.

[e]Score of 3 if PSA density is greater than 0.15 ng/mL^2.

TABLE 3: Distribution of MRI Results in MRI-Based Prostate Cancer Screening Studies

Study Approach and Name [Reference]	No. of Patients Undergoing MRI for Given Indication	MRI Not Performed	Nondiagnostic MRI	PI-RADS Score				
				1–2	3	4–5	4	5
MRI as first-line tool in first screening round								
MVP [12]	246	NA	NA	189 (77)	32 (13)	25 (10)	22 (9)	3 (1)
ReIMAGINE [13]	303	NA	NA	NR	NR	NR	NR	NR
IP1-PROSTAGRAM [15]	408	NA	NA	336 (82)	29 (7)	43 (11)	NR	NR
PROSA [16]	175	NA	NA	155 (89)	9 (5)	11 (6)	11 (6)	0 (0)
VISIONING [17]	229	NA	NA	152 (66)	13 (6)	64 (28)	55 (24)	9 (4)
MRI as second-stage tool in first screening round								
Göteborg-2, first round (reference) [18]	405	21 (5)	2 (0)	240 (59)	41 (10)	101 (25)	85 (21)	16 (4)
Göteborg-2, first round (experimental) [18]	796	34 (4)	7 (1)	488 (61)	65 (8)	202 (25)	150 (19)	52 (7)
PROBASE, first round [20]	149	37 (25)	0 (0)	43 (29)	61 (41)	45 (30)	35 (23)	10 (7)
STHLM3-MRI, first round [19]	929	83 (9)	0 (0)	521 (56)	175 (19)	150 (16)	85 (9)	65 (7)
PROSA [16]	61	0 (0)	0 (0)	52 (85)	5 (8)	4 (7)	4 (7)	0 (0)
OPT [22]	696	51 (7)	0 (0)	409 (59)	137 (20)	99 (14)	67 (10)	32 (5)
MRI as second-stage tool in repeat screening round								
STHLM3-MRI, second round [24]	667	50 (7)	0 (0)	533 (80)	51 (8)	33 (5)	23 (3)	10 (1)
ERSPC-Rotterdam, fifth round (pilot study) [25]	167	9 (5)	0 (0)	110 (66)	20 (12)	28 (17)	15 (9)	13 (8)
Göteborg-1, 10th round (pilot study) [26]	77	12 (16)	NR	44 (57)	NR	NR	NR	NR

Note—Except where otherwise indicated, data are number with percentage in parentheses. MVP = MRI Versus PSA in Prostate Cancer Screening, NA = not applicable, ReIMAGINE = Refining Imaging and Molecular Analysis Guiding Individualized Navigation of Early Prostate Cancer, NR = not reported, IP1-PROSTAGRAM = IP1–Prostate Cancer Screening Trial Using a Group of Radiological Approaches Including MRI and Ultrasound, PROSA = Prostate Cancer Secondary Screening in Sapienza, PROBASE = Risk-Adapted Prostate Cancer Early Detection Study Based on a Baseline Prostate-Specific Antigen Value in Young Men, STHLM3-MRI = Prostate Cancer Detection Using the Stockholm3 Test and Magnetic Resonance Imaging, OPT = Organized Prostate Cancer Testing, ERSPC = European Randomized Study of Screening for Prostate Cancer.

management. Radiologists trained in settings with a high prevalence of PCa may overinterpret findings in screening populations with a lower prevalence.

Efforts to support MRI test performance—Standardized training programs are needed to apply MRI-based screening criteria consistently. Double readings with adjudication can help mitigate variability and improve accuracy, pending the introduction of AI into workflows [49, 50]. Regular continuing education programs and feedback mechanisms, including follow-up of biopsy pathology results, can enhance reader performance. A screening certification process for radiologists can help ensure minimum competency levels and potentially reduce variability [51].

AI algorithms have shown potential for standardizing interpretation, reducing human error, and mitigating observer variability in MRI-based detection. However, appropriate training, calibration, and validation are needed before AI can be used in screening. No AI algorithms have been trained for population screening or have been integrated into screening studies, and a precise AI-based screening workflow has yet to be defined (Table 2).

MRI Interpretation in Screening

PI-RADS, which is optimized for multiplanar multiparametric MRI examinations [52], guides the definition of a suspicious examination in diagnostic settings. PI-RADS has been used in screening studies (Table 3), but it may not be appropriate or optimal in this setting. Given that MRI results guide biopsy decisions, clear definitions of MRI risk scoring are mandatory.

Negative MRI results—Based on PI-RADS descriptors, a score of 1 or 2 suggests that clinically significant cancer is very unlikely. Patient-level rates of detection of cancer of GG 2 or greater after a negative MRI result are low in the screening setting. In the reference arm of the Göteborg-2 trial, nine clinically significant cancers were detected in men undergoing systematic biopsy after negative MRI results [18]. These were all GG 2 cancers; six had less than 5% of Gleason pattern 4, thus having low to favorable intermediate risk. In the Göteborg-2 trial of repeat screening after 3.9 years, the detection rate for cancers graded as GG 2 or greater in men with negative MRI results at initial screening was not substantially different between men who previously underwent systematic biopsy (reference arm: 3.2%) and men who did not (experimental arm: 2.6%) [23]. Similarly, in the STHLM3-MRI trial of repeat screening, the detection rate of cancer of GG 2 or higher after 2.4 years of follow-up was only 3.9% in men with negative MRI results at initial screening; these were predominantly GG 2 cancers [24]. Therefore, an MRI suspicion score of 1 or 2 should be categorized as a negative screening test result. If PSA density exceeds 0.12–0.15 ng/mL/cm^3, then the screening test may be considered positive despite the negative MRI result [13, 22]. A clinically significant cancer not detected by MRI at initial screening may become visible on MRI at repeat screening.

In diagnostic settings, approximately 40% of MRI examinations are assessed as having a PI-RADS score of 1 or 2 [53]. In the screening setting, when MRI is performed after PSA testing, this frequency is approximately 60% (e.g., OPT, 59%; STHLM3-MRI, 56%; Göteborg-2 control arm, 59%; Göteborg-2 experimental arm, 61%) [18, 19, 22] (Table 3). The increase in PI-RADS scores of 1 or 2 is expected given the lower prevalence of cancer in a screening population. The frequency of negative MRI results increases further in trials that use MRI as a first-line screening examination without PSA pretesting (range, 66–89%) [12, 15–17].

Positive MRI results—A PI-RADS score of 4 or 5 suggests a high likelihood of clinically significant cancer. For PI-RADS scores of 4 and 5 in diagnostic settings, patient-level detection rates for cancers of GG 2 or greater are 55% (95% CI, 43–65%) and 83% (95% CI, 78–88%), respectively [54]. Thus, a suspicion score of 4 or 5 should be categorized as an MRI-positive result in the screening setting.

In diagnostic settings, PI-RADS scores of 4 and 5 each have frequencies of approximately 20% [54]. In the screening setting, when MRI is used after PSA testing, the estimated frequency of a PI-RADS score of 4 is approximately 15% (range, 7–23%), and that of PI-RADS score 5 is 4–7%. Thus, screening tends to yield fewer and smaller suspicious lesions (Table 3).

Indeterminate MRI results—In early diagnosis, an indeterminate result (i.e., a PI-RADS score of 3) accounts for 20% of MRI interpretations and has a 20% (95% CI, 15–26%) chance of yielding cancer of GG 2 or greater on biopsy [54]. In the screening setting, when MRI is used after PSA testing, similar or even higher rates of PI-RADS score 3 are observed (range, 8–41%) (Table 3). A PI-RADS score of 3 is reported excessively in young men (ProScreen, 41%; OPT, 20%), who generally have a low prevalence of PCa [22, 27]. This high proportion substantially influences MRI test performance.

To preserve the benefits of population screening, screening participants should not be designated patients on the basis of indeterminate MRI results. Thus, the indeterminate category (PI-RADS score, 3) generally should not be used in screening, as significant cancer is very unlikely. Managing men with indeterminate results should, by default, lean toward biopsy avoidance with a return to screening, as suggested by the Swedish OPT protocol [22]. If necessary, multiplanar and contrast-enhanced sequences can improve lesion characterization, reducing indeterminate risk categories [55]. Biopsy decisions should be guided by risk factors such as PSA density and patient preferences [56, 57].

Nondiagnostic MRI results—Low-quality examinations can negatively affect accuracy. Poor image quality can cause challenges in lesion identification and characterization [58, 59]. Poor quality can also cause greater uncertainty in interpreting findings, yielding a higher rate of equivocal lesions and a lower rate of negative results. Inadequate images also contribute to diagnostic errors. Screening units must adopt benchmark thresholds for nondiagnostic or low-quality examinations. A poor-quality examination should not be reported as indeterminate [60]. Among published studies (Table 3), only the Göteborg-2 trial reported separate results for patients with nondiagnostic MRI examinations and patients not undergoing MRI [18].

Screening programs should implement standardized criteria and protocols for recalling patients to repeat individual sequences or, possibly, the entire examination. These criteria should explicitly outline when an examination is nondiagnostic and requires repeat imaging [61].

Rescanning protocols should include adjustments to improve image quality. These measures should seek to address identified challenges such as hip prostheses and may include repeating specific sequences that were deemed nondiagnostic. Modifications could include obtaining contrast-enhanced sequences (e.g., in patients with hip prostheses), obtaining sequences in additional planes, and obtaining motion-insensitive sequences through radial k-space filling. Low-residue diets, bowel preparation, and antispasmodic agents may also be used. Real-time quality control allows immediate repetition of nondiagnostic sequences but requires on-table image quality monitoring. Patients with claustrophobia or anxiety may require a wide-bore scanner or antianxiety medications.

Alternative MRI scoring systems for screening—Although screening studies have adopted PI-RADS scoring, PI-RADS was not intended to screen populations with a low prevalence of disease or to evaluate uniplanar biparametric examinations. Image descriptors, interpretation algorithms, and thresholds for biopsy should be reconsidered in the screening context. The definition of a positive examination may warrant a new scoring system tailored specifically for PCa screening.

The ReIMAGINE study used a staged MRI interpretation approach whereby readers first performed a simplified assessment of only axial T2-weighted images and high-b-value DWI (disregarding ADC maps) for the presence or absence of a suspicious lesion [13, 61]. Only cases with a detected lesion were entered into a second evaluation stage using PI-RADS, incorporating multiplanar sequences and ADC maps. With this approach, the PPV for cancer of GG 2 or higher was 52% and 90% after the first and second stages, respectively [13]. The rate of overdiagnosis of GG 1 cancer was only 1% [13]. If confirmed, these data suggest that streamlined MRI interpretation may mitigate the complexities and interreader variability associated with PI-RADS scoring while lowering false-positive rates.

Next Steps After MRI Screening

In a screening setting, positive MRI results should be followed by further diagnostic workup. MRI has relatively low specificity in the diagnostic setting, yielding many false-positive results. After a positive MRI screening examination, the goal of further diagnostic workup is to direct biopsies to detect clinically significant cancers.

Positive MRI results—Several screening studies support defining a positive MRI result as a PI-RADS score of 4 or greater rather than a score of 3 or greater [12, 22] (Table 2). This higher threshold reduces unnecessary biopsies and detects fewer GG 1 cancers and fewer GG 2 cancers having favorable intermediate risk. Additionally, use of a threshold score of 4 to select patients for biopsy leads to an increase in the rate of negative MRI screening results from approximately 63% (range, 62–65%) to approximately 75% (range, 70–85%) (Table 4).

Further diagnostic workup after positive MRI screening should be performed in dedicated diagnostic units with multidisciplinary expertise. When targeted biopsy is performed, MRI-guided prebiopsy planning with organ and target segmentations is essential. Biopsy protocols should be standardized, specifying the number and placement of cores. The safest biopsy route should be selected on the basis of lesion location and patient factors. MRI-based screening programs have used diverse biopsy approaches.

TABLE 4: Cancer Detection Outcomes and Benefit-to-Harm Ratios in MRI-Based Prostate Cancer (PCa) Screening Studies

Study Approach and Name [Reference]	Men With Negative MRI[a]	No. of Men With Positive MRI[b]	Results of Targeted and Systematic Biopsy in Men With Positive MRI, by PCa Type			Ratio		
			No PCa	GG 1	GG ≥ 2	GG ≥ 2 to GG 1	GG ≥ 2 to GG 1 or No PCa	Avoided Biopsy to Benign Biopsies
MRI as first-line tool in first screening round								
MVP[c] [12]	221 (90)	24	4 (17)	4 (17)	11 (46)	2.8	1.4	55
IP1-PROSTAGRAM [15]	334 (82)	65	44 (68)	7 (11)	14 (22)	2.0	0.3	7.6
VISIONING [17]	152 (66)	77	48 (62)	8 (10)	21 (27)	2.6	0.4	3.2
ReIMAGINE[d] [13]	255 (84)	48	4 (8)	2 (4)	25 (52)	13	4.2	64
PROSA[d] [16]	155 (89)	10	4 (40)	2 (20)	4 (40)	2.0	0.7	39
MRI as second-stage tool in first screening round								
Göteborg-2, first round (reference) [18]	240 (63)	130	47 (36)	31 (24)	59 (45)	1.9	0.8	5.1
STHLM3-MRI, first round [19]	1207 (65)	297	79 (27)	35 (12)	183 (62)	5.2	1.6	15
Göteborg-2, first round[d] (experimental) [18]	488 (65)	261	98 (38)	59 (23)	104 (40)	1.8	0.7	5.0
IP1-PROSTAGRAM[b] [15]	31 (76)	9	3 (33)	0 (0)	6 (67)	NA	2.0	10
OPT [22]	409 (63)	221	84 (38)	44 (20)	93 (42)	2.1	0.7	4.9
VISIONING [17]	23 (45)	30	15 (50)	2 (7)	13 (43)	6.5	0.8	1.5
PROBASE, first round [20]	43 (29)	89	48 (54)	13 (15)	28 (31)	2.2	0.5	0.9
PROSA[d] [16]	52 (85)	6	4 (67)	2 (33)	0 (0)	NA	NA	13

Note—Except where otherwise indicated, data are expressed as number with percentage in parentheses. GG = grade group, MVP = MRI Versus PSA in Prostate Cancer Screening, IP1-PROSTAGRAM = IP1–Prostate Cancer Screening Trial Using a Group of Radiological Approaches Including MRI and Ultrasound, ReIMAGINE = Refining Imaging and Molecular Analysis Guiding Individualized Navigation of Early Prostate Cancer, PROSA = Prostate Cancer Secondary Screening in Sapienza, STHLM3-MRI = Prostate Cancer Detection Using the Stockholm3 Test and Magnetic Resonance Imaging, NA = not applicable, OPT = Organized Prostate Cancer Testing, PROBASE = Risk-Adapted Prostate Cancer Early Detection Study Based on a Baseline Prostate-Specific Antigen Value in Young Men.
[a]PI-RADS score of 1 or 2; biopsy avoided.
[b]PI-RADS score of 3–5; biopsy performed.
[c]Positive MRI result defined as PI-RADS score of 4 or 5 (instead of a score of 3–5).
[d]Only targeted biopsy was performed (no systematic biopsy).

Rates of detection of clinically significant cancers can be increased by obtaining multiple cores from the area surrounding the lesion [62]. However, perilesional sampling has not been systematically incorporated into screening protocols, and perilesional sampling strategies warrant further investigation. The combination of targeted and perilesional sampling, without complete systematic sampling of the prostate, may be sufficient for establishing a diagnosis [62]; however, even if it does not change overall diagnoses, this approach risks missing sites of cancer in patients with multifocal disease, impacting treatment planning [63].

The addition of systematic biopsy to targeted biopsy should be discouraged in screening, as a meta-analysis did not find benefit from systematic biopsy in detecting additional cancers [62]. Specifically, additional systematic biopsy did not yield significantly greater detection of cancer of GG 2 or greater (OR = 1.07, p = .07) or cancer of GG 3 or higher (OR = 1.06, p = .43), but it yielded significantly greater detection of GG 1 cancer (OR = 1.16, p = .01). Thus, in a low-prevalence population, systematic biopsies likely increase overdiagnosis.

Negative MRI results—Follow-up data from the STHLM3-MRI and Göteborg-2 trials provide valuable insights for determining screening intervals after negative MRI screening results [23, 24]. In repeat screening rounds, the STHLM3-MRI trial reported a strikingly high proportion of negative MRI examinations: 80% and 88% when defining a negative result as a PI-RADS score of 2 or less and 3 or less, respectively. Even in the Gotebörg-1 and ERSPC MRI-based pilot studies, which included men without prior MRI examinations, 70% and 82% of men had a negative MRI result when it was defined as a PI-RADS score of 2 or less and 3 or less, respectively [25, 26]. These high percentages of negative MRI results support the safety of extending the rescreening interval beyond the current 2-year standard. Indeed, data from the Göteborg-2 trial strongly indicate that most cancers become visible on MRI before becoming incurable and that men with a previously negative MRI result after a positive PSA result do not develop incurable or advanced cancers on rescreening [23]. Extended screening intervals could translate into more resource-efficient screening protocols. Optimal screening intervals remain under investigation and may vary depending on individual risk factors and evolving evidence [64].

Patient-tailored management—Management should be tailored on the basis of a patient's risk status and preferences. Men with an elevated PSA level or PSA density, a family history of PCa, or other risk factors may benefit from a lower threshold for biopsy. Men with strong biopsy-averse preferences may choose monitoring of a lesion assessed as having a PI-RADS score 4 or 5 after carefully considering their risks and benefits. These patient-tailored biopsy approaches require harmonization of postscreen-

TABLE 5: Overview of Recommendations in MRI-Based Prostate Cancer (PCa) Screening

Category	Recommendations
Recommendations for MRI-based PCa screening	
MRI test performance characteristics	• Use PI-RADS–compliant imaging parameters to ensure consistency across MRI systems • Harmonize MRI equipment within accredited medical centers or dedicated screening centers to ensure consistent image quality • Implement a standardized quality scoring system to ensure auditable, optimal image quality across all participating sites • Standardize acquisitions and patient preparations to ensure consistent image quality • Limit scanning times to 5–10 min for higher throughput, adoption, acceptance, and cost reduction - Use only axial (or 3D) sequences to shorten acquisition times - Remove dynamic contrast-enhanced imaging and antiperistaltic agents from MRI protocols to alleviate safety concerns and minimize the active supervision of scans • To guarantee high-quality scans, perform regular quality checks of MRI equipment, protocols, and acquisitions before, during, and after patient participation
MRI test reliability	• Measure interobserver agreement or disagreement among radiologists interpreting MRI-based screening studies • Use double reading by experienced readers to help mitigate variability and improve diagnostic accuracy • Standardize training programs and establish a certification process for radiologists to ensure consistent application of image-based criteria and levels of competency • Implement regular continuing education programs and multidisciplinary feedback to further enhance reader performance
MRI test interpretation	• Install clear definitions of MRI risk scoring (e.g., two-, three-, or five-tiered score; yes vs no based on PI-RADS) • If five-tier scoring is used, categorize - Any suspicion score of 1 or 2 on an MRI-negative screening - Any suspicion score of 4 or 5 on an MRI-positive screening • Refer only MRI-positive screenings to postscreening testing or biopsy • Manage patients with score of 3 by use of agreed-upon protocols for surveillance and biopsy. Biopsies are highly likely to be unproductive in screening of the general population, whereas high-risk men with a score of 3 (including those with high PSA densities) may require biopsies. Surveillance can include repeat MRI scans to reduce overdiagnosis and enhance the benefit-to-harm ratio. • Benchmark results of low-suspicion scores (1 or 2), indeterminate scores (3), and high-suspicion scores (4 or 5), to ensure appropriate MRI test performance • To reduce overdiagnosis, do not report a nondiagnostic (score 0) or low-quality scan as indeterminate (score 3), as unnecessary biopsies are heavily weighted as a harm of screening • To reduce diagnostic errors, install thresholds of nondiagnostic or low-quality scans, particularly for excluding clinically significant cancers • Standardize rescanning or recalling definitions when an MR image is considered nondiagnostic and address quality issues (e.g., technical failures, artifacts, or patient factors)
Postscreening test options	• Perform diagnostic workup of all MRI-positive screenings in dedicated diagnostic units with multidisciplinary expertise; MRI is most effective when integrated into a comprehensive multistep diagnostic pathway, including risk assessments, targeted and perilesional biopsies, and follow-up strategies • Standardize biopsy procedures to minimize failures and ensure accuracy, utilizing MRI-guided prebiopsy planning with segmentations for precise lesion localization and targeting, specifying the number and location of cores and selecting the safest biopsy route • To support a positive benefit-to-harm ratio, do not obtain systematic biopsy cores on top of the targeted biopsy strategy in screening settings • Extend rescreening intervals for men who avoid biopsy after an MRI-negative screening • Predefine the potential level of accuracy of the MRI screening tests to benchmark the performance of the MRI screening pathway • Install robust quality-control measures throughout the postscreening diagnostic pathway, from risk assessment to biopsy procedures and pathology review, by use of standardized protocols, ongoing audits, and feedback mechanisms, to help ensure accuracy and consistency in diagnosis and management • Include performance indicators that monitor key aspects of program implementation, patient satisfaction surveys, and outcomes, to assess adherence to established protocols and guidelines, identify improvement areas, and implement corrective actions

(Table 5 continues on next page)

TABLE 5: Overview of Recommendations in MRI-Based Prostate Cancer (PCa) Screening (continued)

Category	Recommendations
Research suggestions in MRI-based PCa screening	
MRI test	• Explore the interplay between PSA and MRI thresholds (or other risk stratification tools) to develop screening algorithms that maximize the detection of clinically significant PCa while minimizing unnecessary interventions and costs • Analyze ultrafast MRI protocols that have shown promise in early detection settings (e.g., leveraging deep learning software), ensuring an accessible, efficient, and reliable screening process • Use double reading by validated and calibrated AI systems to help mitigate variability and improve diagnostic accuracy • Leverage AI tools to automate and optimize the radiologic process, from image acquisition to interpretation, to ensure accuracy and consistency of interpretations (e.g., AI-aided scanning, MRI interpretation, and biopsy decisions) • To optimize the balance of the benefit-to-harm ratio, develop and validate an MRI scoring classification that is specifically tailored to the screening context (e.g., criteria for MRI-positive vs MRI-negative screenings), including image descriptors, interpretation algorithms, scoring systems, and biopsy thresholds • Stipulate robust quality-scoring systems to ensure high-quality scans and screen pathway performance
Postscreening test options	• Investigate MRI-targeting and perilesional biopsy strategies at accredited centers to ensure quality and expertise in an MRI-based screening program • Estimate the detection rate for PCa of GG ≥ 2 in men with indeterminate MRI results • Explore alternative definitions of clinically significant PCa that are unique to MRI, including MRI visibility, tumor size, and level of suspicion • Investigate patient-tailored MRI biopsy thresholds (e.g., in men with biopsy-averse preferences or in men with elevated risk due to such factors as high PSA density or strong family history of PCa), to further improve the benefit-to-harm balance • To guide men with different risk profiles during follow-up, investigate rescreening time intervals that are optimized for an individual's risk factors, previous MRI screening test results, and evolving evidence, through modeling and simulation that incorporates data from screening and diagnostic settings • Use benefit-to-harm ratios and net benefit analysis to potentially provide a more comprehensive and nuanced understanding of the clinical utility and cost-effectiveness of different PCa screening strategies

Note—AI = artificial intelligence, GG = grade group.

ing pathways across diagnostic units, to further investigate and improve the benefit-to-harm balance of various approaches.

Recommendations and Ongoing Initiatives

Figure 3 presents trade-offs between the standard-of-care MRI pathway and the MRI-only pathway, highlighting the comparative strengths and limitations. The standard-of-care MRI pathway is favored for immediate adoption as a balanced and scalable established screening strategy, with the MRI-only pathway reserved for research settings and specific high-risk populations. Table 5 provides additional recommendations for use of MRI in PCa screening [65]. These recommendations focus on optimizing the benefits and mitigating the harms of PCa screening. Specifically, they aim to reduce unnecessary biopsies and overdetection of indolent cancers while maintaining or increasing detection of clinically significant cancers. The recommendations emphasize the importance of standardized protocols, equipment, and radiologist training programs, to ensure consistent and reliable results. Furthermore, the recommendations encourage research into new scoring systems and screening intervals tailored to an individual's risk factors and an evolving understanding of PCa behavior.

European initiatives are investigating use of MRI in PCa screening programs. For example, MRI is a critical component of the Prostate Cancer Awareness and Initiative for Screening in Europe (PRAISE-U), implemented by the European Association of Urology. The initiative involves pilot studies of population-based risk-adapted PCa screening, aiming to inform creation of cost-effective screening algorithms suitable for diverse health care systems across Europe [66]. PRAISE-U will also help to develop relevant clinical performance indicators and quality-assurance protocols. The TRANSFORM project is comparing the use of MRI as a first-line screening investigation versus as a second-stage screening tool in men with elevated PSA levels [30]. This project will provide insights into the strategy's long-term outcomes, including PCa incidence and mortality.

Conclusion

This review provides a detailed analysis of the role of MRI in PCa screening, targeted to radiologists. Implementing MRI in PCa screening requires meticulous attention to image quality, acquisition protocols, and interpretation criteria, to mitigate variability and ensure reliable results. Ultimately, the successful integration of MRI in PCa screening will require radiologists to engage in refining protocols, standardizing interpretations, and adopting emerging technologies. Such efforts will help to maximize benefits while minimizing harms, thereby enabling wider acceptance of PCa screening.

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References

1. International Agency for Research on Cancer, WHO website. Data visualization tools for exploring the global cancer burden in 2022. gco.iarc.fr/today/en. Published 2022. Accessed Dec 12, 2024
2. Ilic D, Neuberger MM, Djulbegovic M, Dahm P. Screening for prostate cancer. *Cochrane Database Syst Rev* 2013; 2013:CD004720

3. Hugosson J, Roobol MJ, Månsson M, et al.; ERSPC investigators. A 16-yr follow-up of the European Randomized Study of Screening for Prostate Cancer. *Eur Urol* 2019; 76:43–51
4. Tsodikov A, Gulati R, Heijnsdijk EAM, et al. Reconciling the effects of screening on prostate cancer mortality in the ERSPC and PLCO trials. *Ann Intern Med* 2017; 167:449–455
5. Kjellman A, Akre O, Norming U, Törnblom M, Gustafsson O. 15-year follow-up of a population based prostate cancer screening study. *J Urol* 2009; 181:1615–1621; discussion, 1621
6. Voss T, Krag M, Martiny F, Heleno B, Jørgensen KJ, Brandt Brodersen J. Quantification of overdiagnosis in randomised trials of cancer screening: an overview and re-analysis of systematic reviews. *Cancer Epidemiol* 2023; 84:102352
7. Grossman DC, Curry SJ, Owens DK, et al.; U.S. Preventive Services Task Force. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *JAMA* 2018; 319:1901–1913
8. European Union website. Council updates its recommendation to screen for cancer. www.consilium.europa.eu/en/press/press-releases/2022/12/09/council-updates-its-recommendation-to-screen-for-cancer/. Published Dec 9, 2022. Accessed Dec 12, 2024
9. Getaneh AM, Heijnsdijk EAM, de Koning HJ. The comparative effectiveness of mpMRI and MRI-guided biopsy vs regular biopsy in a population-based PSA testing: a modeling study. *Sci Rep* 2021; 11:1801
10. Science Advice for Policy by European Academies. Improving cancer screening in the European Union. Scientific Advice Mechanism website. scientificadvice.eu/advice/improving-cancer-screening-in-the-european-union/. Published Sep 2022. Accessed Dec 12, 2024
11. Padhani AR, Godtman RA, Schoots IG. Key learning on the promise and limitations of MRI in prostate cancer screening. *Eur Radiol* 2024; 34:6168–6174
12. Nam R, Patel C, Milot L, et al. Prostate MRI versus PSA screening for prostate cancer detection (the MVP study): a randomised clinical trial. *BMJ Open* 2022; 12:e059482
13. Moore CM, Frangou E, McCartan N, et al. Prevalence of MRI lesions in men responding to a GP-led invitation for a prostate health check: a prospective cohort study. *BMJ Oncol* 2023; 2:e000057
14. Eldred-Evans D, Tam H, Sokhi H, et al. An evaluation of screening pathways using a combination of magnetic resonance imaging and prostate-specific antigen: results from the IP1-PROSTAGRAM study. *Eur Urol Oncol* 2023; 6:295–302
15. Eldred-Evans D, Burak P, Connor MJ, et al. Population-based prostate cancer screening with magnetic resonance imaging or ultrasonography: the IP1-PROSTAGRAM study. *JAMA Oncol* 2021; 7:395–402
16. Messina E, La Torre G, Pecoraro M, et al. Design of a magnetic resonance imaging-based screening program for early diagnosis of prostate cancer: preliminary results of a randomized controlled trial—Prostate Cancer Secondary Screening in Sapienza (PROSA). *Eur Radiol* 2024; 34:204–213
17. Wetterauer C, Matthias M, Pueschel H, et al. Opportunistic prostate cancer screening with biparametric magnetic resonance imaging (VISIONING). *Eur Urol Focus* 2024; 10:332–338
18. Hugosson J, Månsson M, Wallström J, et al.; Göteborg-2 Trial Investigators. Prostate cancer screening with PSA and MRI followed by targeted biopsy only. *N Engl J Med* 2022; 387:2126–2137
19. Eklund M, Jäderling F, Discacciati A, et al.; STHLM3 Consortium. MRI-targeted or standard biopsy in prostate cancer screening. *N Engl J Med* 2021; 385:908–920
20. Arsov C, Albers P, Herkommer K, et al. A randomized trial of risk-adapted screening for prostate cancer in young men: results of the first screening round of the PROBASE trial. *Int J Cancer* 2022; 150:1861–1869
21. Boschheidgen M, Albers P, Schlemmer HP, et al. Multiparametric magnetic resonance imaging in prostate cancer screening at the age of 45 years: results from the first screening round of the PROBASE trial. *Eur Urol* 2024; 85:105–111
22. Bratt O, Godtman RA, Jiborn T, et al. Population-based organised prostate cancer testing: results from the first invitation of 50-year-old men. *Eur Urol* 2024; 85:207–214
23. Hugosson J, Godtman RA, Wallstrom J, et al. Results after four years of screening for prostate cancer with PSA and MRI. *N Engl J Med* 2024; 391:1083–1095
24. Nordström T, Annerstedt M, Glaessgen A, et al. Repeated prostate cancer screening using prostate-specific antigen testing and magnetic resonance imaging: a secondary analysis of the STHLM3-MRI randomized clinical trial. *JAMA Netw Open* 2024; 7:e2354577
25. Alberts AR, Schoots IG, Bokhorst LP, et al. Characteristics of prostate cancer found at fifth screening in the European Randomized Study of Screening for Prostate Cancer Rotterdam: can we selectively detect high-grade prostate cancer with upfront multivariable risk stratification and magnetic resonance imaging? *Eur Urol* 2018; 73:343–350
26. Grenabo Bergdahl A, Wilderäng U, Aus G, et al. Role of magnetic resonance imaging in prostate cancer screening: a pilot study within the Göteborg randomised screening trial. *Eur Urol* 2016; 70:566–573
27. Rannikko A, Leht M, Mirtti T, et al. Population-based randomized trial of screening for clinically significant prostate cancer ProScreen: a pilot study. *BJU Int* 2022; 130:193–199
28. Nordström T, Discacciati A, Bergman M, et al.; STHLM3 Study Group. Prostate cancer screening using a combination of risk-prediction, MRI, and targeted prostate biopsies (STHLM3-MRI): a prospective, population-based, randomised, open-label, non-inferiority trial. *Lancet Oncol* 2021; 22:1240–1249
29. Möller F, Månsson M, Wallström J, Hellström M, Hugosson J, Arnsrud Godtman R. Prostate cancers in the prostate-specific antigen interval of 1.8–3 ng/ml: results from the Göteborg-2 Prostate Cancer Screening Trial. *Eur Urol* 2024; 86:95–100
30. Prostate Cancer UK website. TRANSFORM trial. prostatecanceruk.org/research/transform-trial/. Published 2024. Accessed Dec 12, 2024
31. Elkhoury FF, Felker ER, Kwan L, et al. Comparison of targeted vs systematic prostate biopsy in men who are biopsy naive: the Prospective Assessment of Image Registration in the Diagnosis of Prostate Cancer (PAIREDCAP) study. *JAMA Surg* 2019; 154:811–818
32. Klotz L, Chin J, Black PC, et al. Comparison of multiparametric magnetic resonance imaging-targeted biopsy with systematic transrectal ultrasonography biopsy for biopsy-naive men at risk for prostate cancer: a phase 3 randomized clinical trial. *JAMA Oncol* 2021; 7:534–542
33. Fazekas T, Shim SR, Basile G, et al. Magnetic resonance imaging in prostate cancer screening: a systematic review and meta-analysis. *JAMA Oncol* 2024; 10:745–754
34. Sandblom G, Varenhorst E, Rosell J, Löfman O, Carlsson P. Randomised prostate cancer screening trial: 20 year follow-up. *BMJ* 2011; 342:d1539
35. Purysko AS, Zacharias-Andrews K, Tomkins KG, et al.; ACR Prostate MR Image Quality Improvement Collaborative. Improving prostate MR image quality in practice-initial results from the ACR Prostate MR Image Quality Improvement Collaborative. *J Am Coll Radiol* 2024; 21:1464–1474
36. Fleming H, Dias AB, Talbot N, et al. Inter-reader variability and reproducibility of the PI-QUAL score in a multicentre setting. *Eur J Radiol* 2023; 168:111091
37. Giganti F, Ng A, Asif A, et al.; PRIME Quality Improvement Group. Global variation in magnetic resonance imaging quality of the prostate. *Radiology* 2023; 309:e231130

38. Russo F, Mazzetti S, Regge D, et al. Diagnostic accuracy of single-plane biparametric and multiparametric magnetic resonance imaging in prostate cancer: a randomized noninferiority trial in biopsy-naive men. *Eur Urol Oncol* 2021; 4:855–862
39. Padhani AR, Schoots IG, Barentsz JO. Fast magnetic resonance imaging as a viable method for directing the prostate cancer diagnostic pathway. *Eur Urol Oncol* 2021; 4:863–865
40. Oerther B, Engel H, Nedelcu A, et al. Performance of an ultra-fast deep-learning accelerated MRI screening protocol for prostate cancer compared to a standard multiparametric protocol. *Eur Radiol* 2024; 34:7053–7062
41. van der Leest M, Israël B, Cornel EB, et al. High diagnostic performance of short magnetic resonance imaging protocols for prostate cancer detection in biopsy-naive men: the next step in magnetic resonance imaging accessibility. *Eur Urol* 2019; 76:574–581
42. van Lohuizen Q, Roest C, Simonis FFJ, et al. Assessing deep learning reconstruction for faster prostate MRI: visual vs. diagnostic performance metrics. *Eur Radiol* 2024; 34:7364–7372
43. Johnson PM, Tong A, Donthireddy A, et al. Deep learning reconstruction enables highly accelerated biparametric MR imaging of the prostate. *J Magn Reson Imaging* 2022; 56:184–195
44. Boss MA, Malyarenko D, Partridge S, et al. The QIBA profile for diffusion-weighted MRI: apparent diffusion coefficient as a quantitative imaging biomarker. *Radiology* 2024; 313:e233055
45. Ponsiglione A, Stanzione A, Minieri A, et al. Impact of software-assisted structured reporting on radiology residents approaching prostate MRI. *Eur J Radiol* 2025; 183:111889
46. Schrader A, Netzer N, Hielscher T, et al. Prostate cancer risk assessment and avoidance of prostate biopsies using fully automatic deep learning in prostate MRI: comparison to PI-RADS and integration with clinical data in nomograms. *Eur Radiol* 2024; 34:7909–7920
47. Hietikko R, Kilpeläinen TP, Kenttämies A, et al. Expected impact of MRI-related interreader variability on ProScreen prostate cancer screening trial: a pre-trial validation study. *Cancer Imaging* 2020; 20:72
48. Westphalen AC, McCulloch CE, Anaokar JM, et al. Variability of the positive predictive value of PI-RADS for prostate MRI across 26 centers: experience of the Society of Abdominal Radiology prostate cancer disease-focused panel. *Radiology* 2020; 296:76–84
49. Brembilla G, Dell'Oglio P, Stabile A, et al. Interreader variability in prostate MRI reporting using Prostate Imaging Reporting and Data System version 2.1. *Eur Radiol* 2020; 30:3383–3392
50. Frazer HML, Peña-Solorzano CA, Kwok CF, et al.; BRAIx Team. Comparison of AI-integrated pathways with human-AI interaction in population mammographic screening for breast cancer. *Nat Commun* 2024; 15:7525
51. de Rooij M, Israël B, Tummers M, et al. ESUR/ESUI consensus statements on multi-parametric MRI for the detection of clinically significant prostate cancer: quality requirements for image acquisition, interpretation and radiologists' training. *Eur Radiol* 2020; 30:5404–5416
52. Turkbey B, Rosenkrantz AB, Haider MA, et al. Prostate Imaging Reporting and Data System version 2.1: 2019 update of Prostate Imaging Reporting and Data System version 2. *Eur Urol* 2019; 76:340–351
53. Eldred-Evans D, Connor MJ, Bertoncelli Tanaka M, et al. The rapid assessment for prostate imaging and diagnosis (RAPID) prostate cancer diagnostic pathway. *BJU Int* 2023; 131:461–470
54. Oerther B, Nedelcu A, Engel H, et al. Update on PI-RADS version 2.1 diagnostic performance benchmarks for prostate MRI: systematic review and meta-analysis. *Radiology* 2024; 312:e233337
55. Schoots IG, Barentsz JO, Bittencourt LK, et al. PI-RADS Committee position on MRI without contrast medium in biopsy-naive men with suspected prostate cancer: narrative review. *AJR* 2021; 216:3–19
56. Schoots IG, Padhani AR. Risk-adapted biopsy decision based on prostate magnetic resonance imaging and prostate-specific antigen density for enhanced biopsy avoidance in first prostate cancer diagnostic evaluation. *BJU Int* 2021; 127:175–178
57. Rajendran I, Lee KL, Thavaraja L, Barrett T. Risk stratification of prostate cancer with MRI and prostate-specific antigen density-based tool for personalized decision making. *Br J Radiol* 2024; 97:113–119
58. Cheng Y, Zhang L, Wu X, Zou Y, Niu Y, Wang L. Impact of prostate MRI image quality on diagnostic performance for clinically significant prostate cancer (csPCa). *Abdom Radiol (NY)* 2024; 49:4113–4124
59. Hötker AM, Dappa E, Mazaheri Y, et al. The influence of background signal intensity changes on cancer detection in prostate MRI. *AJR* 2019; 212:823–829
60. de Rooij M, Allen C, Twilt JJ, et al. PI-QUAL version 2: an update of a standardised scoring system for the assessment of image quality of prostate MRI. *Eur Radiol* 2024; 34:7068–7079
61. Marsden T, Lomas DJ, McCartan N, et al.; ReIMAGINE Study Group. ReIMAGINE prostate cancer screening study: protocol for a single-centre feasibility study inviting men for prostate cancer screening using MRI. *BMJ Open* 2021; 11:e048144
62. Sanguedolce F, Lauwers CNG, Tedde A, et al.; EAU Section of Urological Imaging (ESUI). Regional versus systematic biopsy in addition to targeted biopsy: results from a systematic review and meta-analysis. *Eur Urol Oncol* 2025; 8:534–543
63. Gandaglia G, Pellegrino A, Montorsi F, Briganti A. Prostate cancer: is there still a role for systematic biopsies? Yes. *Eur Urol Open Sci* 2022; 38:10–11
64. Woo S, Vargas HA, Padhani AR. Prostate cancer screening with MRI: lessons learned from repeat rounds of the GÖTEBORG-2 and STHLM3-MRI trials. *Korean J Radiol* 2024; 25:1033–1035
65. Dobrow MJ, Hagens V, Chafe R, Sullivan T, Rabeneck L. Consolidated principles for screening based on a systematic review and consensus process. *CMAJ* 2018; 190:E422–E429
66. Chandran A, van Harten M, Singh D, et al. Risk-stratified approach to implementing population-based prostate cancer screening in five pilot sites in the European Union: a protocol for the PRAISE-U Project. *European Urol Open Science* 2024; 70:8–17
67. Van Poppel H, Roobol MJ, Chapple CR, et al. Prostate-specific antigen testing as part of a risk-adapted early detection strategy for prostate cancer: European Association of Urology position and recommendations for 2021. *Eur Urol* 2021; 80:703–711

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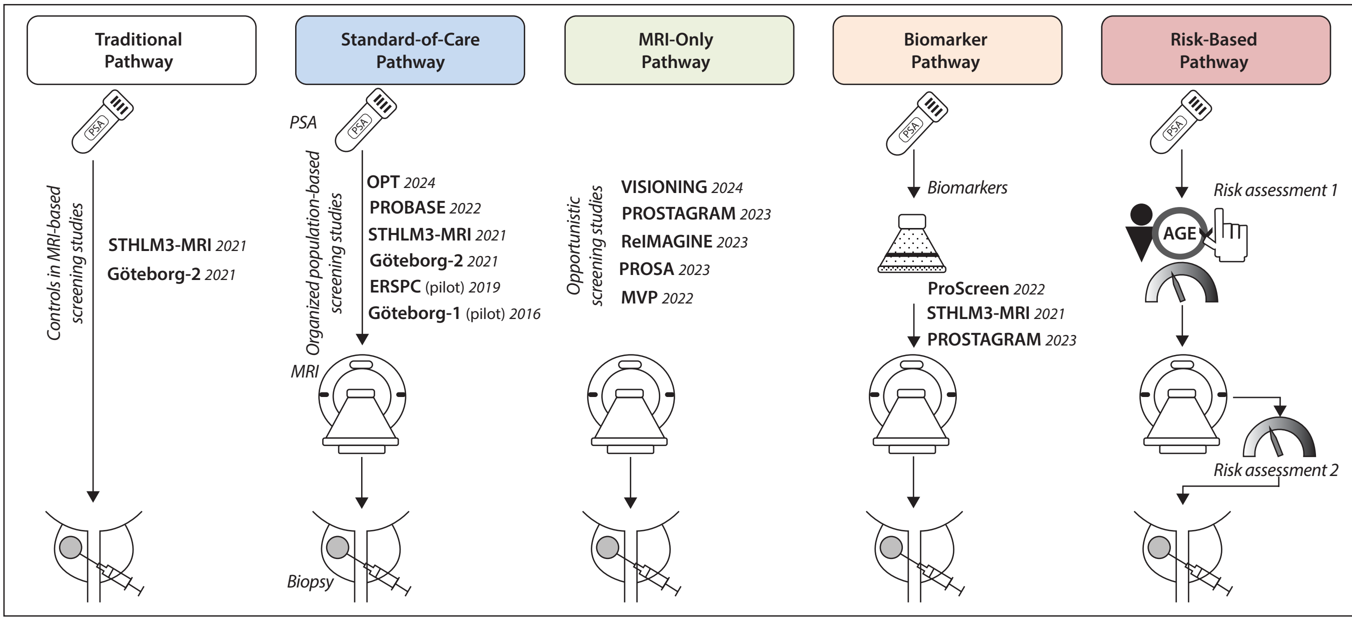

Fig. 1—Schematic shows prostate cancer screening pathways with varying incorporation of MRI. In traditional pathway, men with positive PSA screening examination undergo systematic biopsy. In standard-of-care MRI pathway, men with positive PSA screening examination undergo MRI, and those with positive MRI result also undergo MRI-targeted biopsy; systematic biopsy may also be performed either for all men with positive PSA screening examination or for men with positive MRI result. In MRI-only pathway, men undergo MRI; only those with positive MRI result undergo MRI-targeted biopsy. In biomarker pathway, men with positive PSA screening examination undergo additional testing, such as 4Kscore Test (BioReference Laboratories, OPKO Health; example of blood test for assessing probability of aggressive prostate cancer) or polygenic risk score testing, before undergoing MRI; those with positive MRI results also undergo MRI-targeted biopsy. In risk-based pathway, men with positive PSA screening examination are assessed for additional risk factors (e.g., age, ethnicity, family history, digital rectal examination results) to assess need for MRI [67]; second risk assessment is performed after MRI to assess need for MRI-targeted biopsy. Schematic provides names of trials evaluating various pathways, along with associated years of publication. Four pathways that include MRI represent two distinct overarching approaches: sequential MRI after PSA testing (standard-of-care MRI pathway, biomarker pathway, and risk-based pathway) and MRI alone (i.e., MRI-only pathway). STHLM3-MRI = Prostate Cancer Detection Using the Stockholm3 Test and Magnetic Resonance Imaging, OPT = Organized Prostate Cancer Testing, PROBASE = Risk-Adapted Prostate Cancer Early Detection Study Based on a Baseline Prostate-Specific Antigen Value in Young Men, ERSPC = European Randomized Study of Screening for Prostate Cancer, PROSTAGRAM = Prostate Cancer Screening Trial Using a Group of Radiological Approaches Including MRI and Ultrasound, ReIMAGINE = Refining Imaging and Molecular Analysis Guiding Individualized Navigation of Early Prostate Cancer, PROSA = Prostate Cancer Secondary Screening in Sapienza, MVP = MRI Versus PSA in Prostate Cancer Screening.

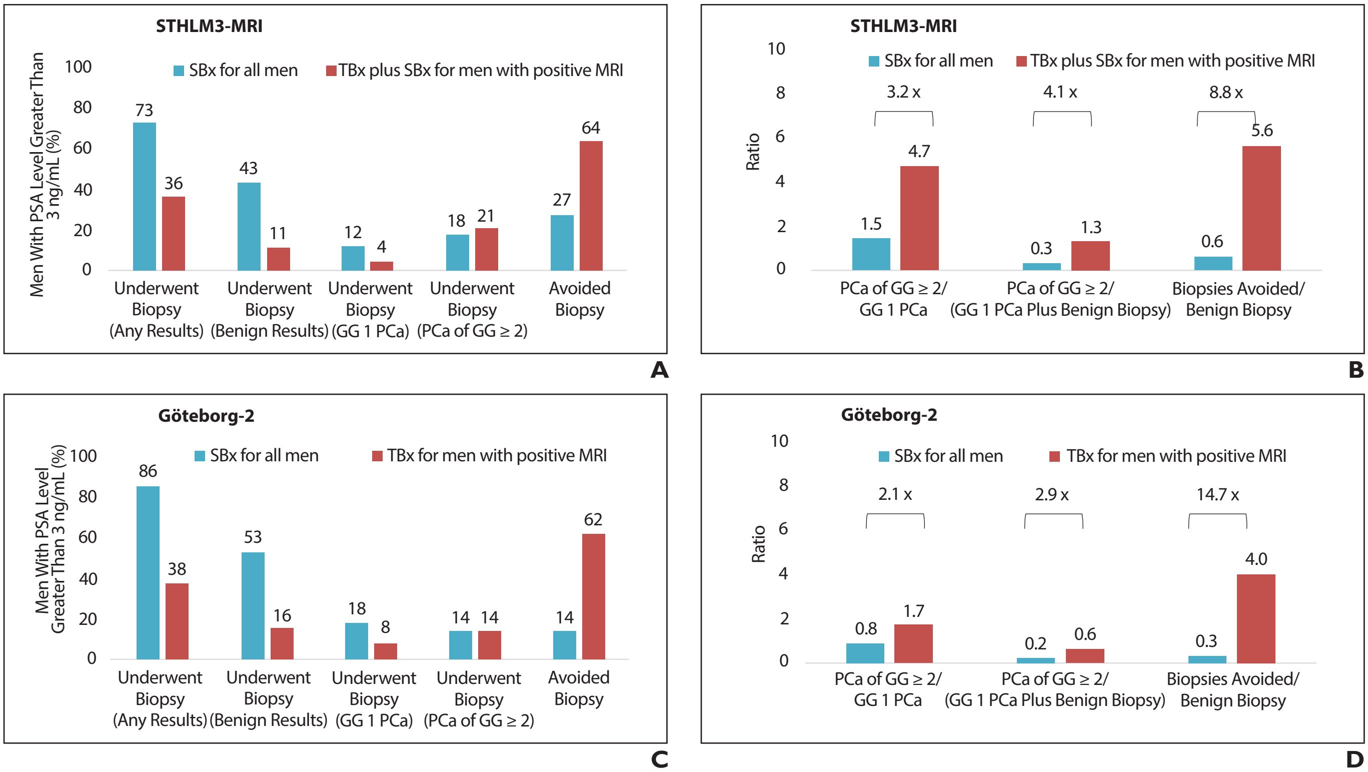

Fig. 2—Benefit-to-harm ratios in two screening trials. Trial compared traditional pathway (systematic biopsy after positive PSA screening examination) and standard-of-care MRI pathway (MRI after positive PSA screening examination; additional MRI-targeted biopsy for men with positive MRI result). STHLM3-MRI = Prostate Cancer Detection Using the Stockholm3 Test and Magnetic Resonance Imaging, SBx = systematic biopsies, TBx = MRI-targeted biopsies, GG = grade group, PCa = prostate cancer.

A–D, Graphs **A** and **B** show results from STHLM3-MRI trial [19]. In this trial, in standard-of-care arm, men with positive MRI also underwent systematic biopsy. Graphs **C** and **D** show results from Göteborg-2 trial [18]. In this trial, in standard-of-care MRI arm, men with positive MRI did not undergo systematic biopsy. For each trial, graphs at left (**A** and **C**) indicate percentage of patients for each pathway who underwent biopsy, who had biopsy showing benign results (i.e., who underwent unproductive biopsy), who had biopsy showing GG 1 PCa, who had biopsy showing PCa of GG 2 or greater, and who avoided biopsy (i.e., due to negative results of MRI screening examination). For each trial, graphs at right (**B** and **D**) indicate ratios of men in trial with different screening outcomes, which were used to assess benefit-to-harm ratios. In STHLM3-MRI trial, in standard-of-care MRI pathway, 21% of men had PCa graded as GG 2 or higher, and 4% had GG 1 cancer, leading to ratio of 4.7 for cancer of GG 2 or greater to GG 1 cancer. Corresponding ratio in traditional pathway was 1.5. Findings indicate approximately threefold greater benefit-to-harm ratio for standard-of-care MRI pathway relative to traditional pathway. In Göteborg-2 trial, in standard-of-care MRI pathway, 14% of men had PCa of GG 2 or greater, and 8% had GG 1 PCa, leading to ratio of 1.7 for PCa of GG 2 or above to GG 1 PCa. Corresponding ratio for traditional pathway was 0.8. Findings indicate approximately twofold greater benefit-to-harm ratio for standard-of-care MRI pathway relative to traditional pathway. In STHLM3-MRI and Göteborg-2 trials, 11% and 16% of men, respectively, in standard-of-care MRI pathway had benign biopsies. These findings indicate results of 1.3 and 0.6 for ratio of men with PCa graded as GG 2 or greater to men with GG 1 PCa and for ratio of men with PCa of GG 2 or higher to benign biopsy for two trials, respectively. Corresponding ratios in traditional pathway were 0.3 and 0.2 for two trials, respectively. Findings indicate greater efficacy for standard-of-care MRI pathway in STHLM3-MRI trial than in Göteborg-2 trial, possibly relating to difference in biopsy strategies. Nonetheless, in two trials, benefit-to-harm ratio was greater for standard-of-care MRI pathway than for traditional pathway by approximately fourfold and threefold, respectively. In STHLM3-MRI and Göteborg-2 trials, 64% and 62% of men, respectively, in standard-of-care MRI pathway avoided biopsy due to negative MRI screening examination. These findings indicate results of 5.6 and 4.0 for ratio of men who avoided biopsy to men with benign biopsy in two trials, respectively. Corresponding ratios in traditional pathway were 0.6 and 0.3 for two trials, respectively. Thus, in two trials, benefit-to-harm ratio was greater for standard-of-care MRI pathway than for traditional pathway by approximately ninefold and 13-fold, respectively.

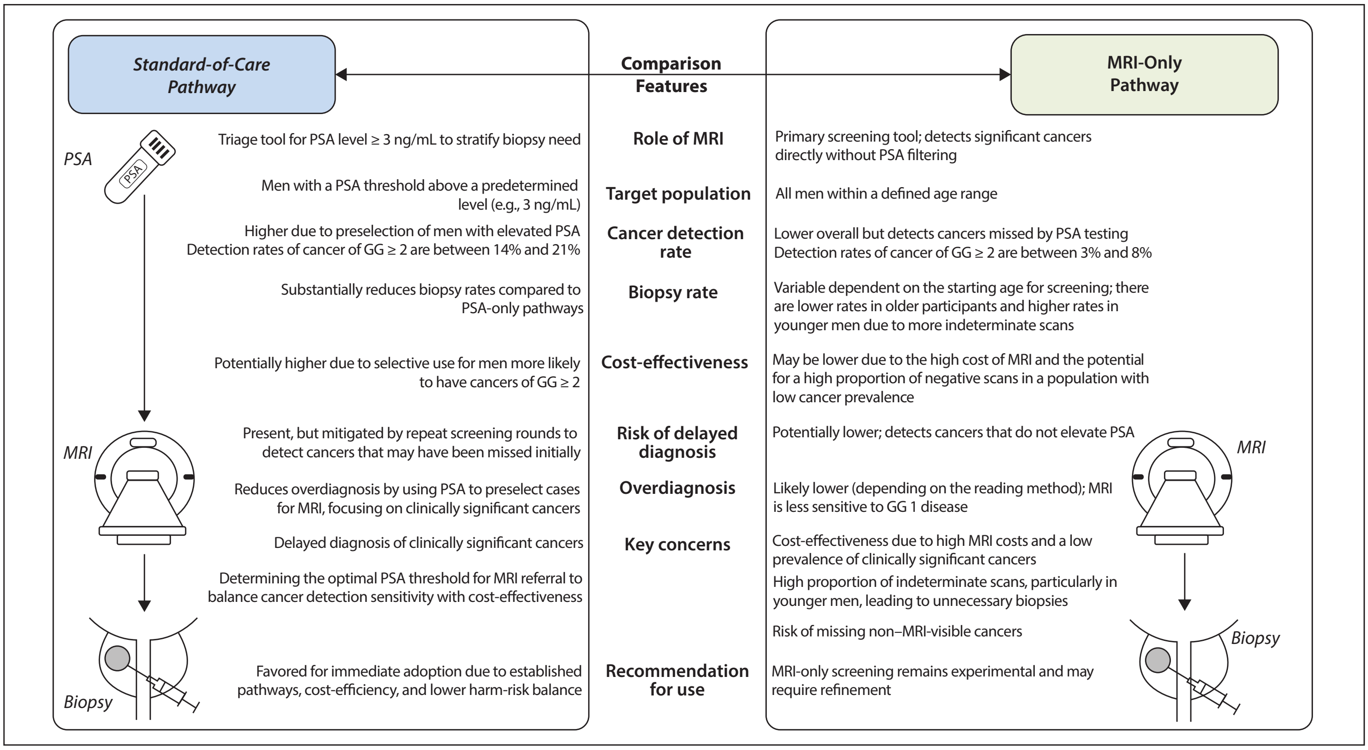

Fig. 3—Trade-offs between standard-of-care MRI pathway (i.e., performing MRI for men with positive PSA screening examination) versus MRI-only pathway (i.e., implementing upfront MRI broadly for prostate cancer [PCa] screening). Figure highlights comparative strengths and limitations of each pathway for PCa screening with respect to risk stratification, cancer detection rates, biopsy rates, cost-effectiveness, and risks of delayed diagnosis or overdiagnosis. Standard-of-care MRI pathway leverages PSA pretesting to enrich biopsy yield, optimizing cost-effectiveness and reducing overdiagnosis while potentially missing cancer in men with low PSA levels. MRI-only pathway prioritizes broad cancer detection, identifying MRI-visible cancers in men with normal PSA levels; this pathway allows reduced biopsy rates but is associated with higher costs and is particularly susceptible to variable MRI interpretations. Current recommendations favor standard-of-care MRI pathway (i.e., sequential MRI after initial PSA screening) as balanced and scalable screening strategy, with MRI-only pathway (i.e., without initial PSA screening) reserved for research settings and specific high-risk populations. GG = grade group.