AUA 2026 Washington, DC MAY 15-18

052IC - AUA Guidelines on Early Detection of Prostate Cancer: Maximizing Benefits, Minimizing Harm

Sunday, May 17

Faculty

Simpa S. Salami, MD

Sigrid V. Carlsson, PhD

Daniel A. Barocas, MD

Kara Watts, MD

Wayne Brisbane, MD

052IC - AUA Guidelines on Early Detection of Prostate Cancer: Maximizing Benefits, Minimizing Harm

Sunday May 17, 2026
4:00 PM – 6:00 PM

2026 AUA Annual Meeting, Washington DC

Course Directors: Simpa S. Salami, MD, MPH (simpa@med.umich.edu)
Sigrid Carlsson, MD, PhD, MPH (carlssos@mskcc.org)

Course Faculty:
Daniel Barocas, MD (dan.barocas@vumc.org)
Wayne Brisbane, MD (WBrisbane@mednet.ucla.edu)
Kara L. Watts, MD (KWATTS@montefiore.org)

Presentation Outline:

Time	Duration	Topic	Presenter	AUA Guideline statements
4:00 – 4:10	10 min	Introduction • Announcements, disclosures, learning objectives, course outline. • AUA Guideline flow-charts. • Pre-test (MCQs).	Salami	
4:10 – 4:20	10 min	Prostate Cancer Screening	Brisbane	1, 3 - 5
4:20 – 4:30	10 min	Use of PSA, PSA Isoforms and Risk Calculators (+ STHLM3)	Brisbane	2, 6 - 11
4:30 – 4:45	15 min	Biomarkers and Germline Genetic Testing	Salami	17, 24-25
4:45 – 4:50	5 min	Q&A	All	
4:50 – 5:05	15 min	MRI	Barocas	13-16, 30-34
5:05 – 5:10	5 mins	Integration of Biomarkers and MRI	Barocas	
5:10 – 5:35	25 min	Prostate Biopsy Techniques	Watts	11, 12, 18-23, 26-29, 35
5:35 – 5:50	15 min	Case Discussion, Q&A	Salami/Barocas	
5:50 – 5:55	5 mins	What is on The Horizon ?	Watts	
5:55 – 6:00	5 min	Wrap Up	Salami	

APPROVED BY THE AUA BOARD OF DIRECTORS FEBRUARY 2026

Authors' disclosure of potential conflicts of interest and author/staff contributions appear at the end of the article.

EARLY DETECTION OF PROSTATE CANCER: AUA/SUO GUIDELINE (2023, AMENDED 2026)

Guideline Panel

John T. Wei, MD, MS; Daniel Barocas, MD; Sigrid Carlsson, MD, PhD, MPH; Fergus Coakley, MD; Scott Eggener, MD; Ruth Etzioni, PhD; Samson W. Fine, MD; Misop Han, MD; Badrinath R. Konety, MD; Martin Miner, MD; Kelvin Moses, MD, PhD; Merel G. Nissenberg, JD; Peter A. Pinto, MD; Simpa S. Salami, MD, MPH; Lesley Souter, PhD; Ian M. Thompson, MD; Daniel W. Lin, MD

Amendment Panel

Daniel W. Lin, MD; Sigrid Carlsson, MD, PhD, MPH; Christopher P. Filson, MD, MS; Badrinath R. Konety, MD; Andrei S. Purysko, MD

Amendment Staff and Consultants

Sennett K. Kim; Erin Kirkby, MS; Lesley H. Souter, PhD

SUMMARY

Purpose

The recommendations discussed on the early detection of prostate cancer provide a framework to facilitate clinical decision-making in the implementation of prostate cancer screening and follow-up.

Methodology

The systematic review of this Guideline was based on searches in Ovid MEDLINE and Embase and Cochrane Database of Systematic Reviews (January 1, 2000 – November 21, 2022). Searches were supplemented by reviewing reference lists of relevant articles. Criteria for inclusion and exclusion of studies were based on the Key Questions (KQs) and the populations, interventions, comparators, outcomes, timing, types of studies and settings (PICOTS) of interest. The target population was persons without a diagnosis of prostate cancer undergoing prostate-specific antigen (PSA) screening, or patients without prostate cancer who have a suspicious finding indicating possible clinically significant prostate cancer who are undergoing or considering an initial or repeat biopsy. In 2025, the Early Detection of Prostate Cancer Guideline was updated through the American Urological Association (AUA) amendment process. This process involved reviewing and integrating newly published literature into previously established Guidelines. The methodologist updated the original Guideline search strategy to systematically search Ovid MEDLINE and Embase for new evidence published between November 2022 and December 2024.

GUIDELINE STATEMENTS

PSA Screening

1. Clinicians should engage in shared decision-making (SDM) with people for whom prostate cancer screening would be appropriate and proceed based on a person's values and preferences. (*Clinical Principle*)
2. When screening for prostate cancer, clinicians should use PSA as the first screening test. (*Strong Recommendation; Evidence Level: Grade A*)
3. For people with a newly elevated PSA, clinicians should repeat the PSA prior to a secondary biomarker, imaging, or biopsy. (*Expert Opinion*)
4. Clinicians may begin prostate cancer screening and offer a baseline PSA test to people between ages 45 to 50 years. (*Conditional Recommendation; Evidence Level: Grade B*)
5. Clinicians should offer prostate cancer screening beginning at age 40 to 45 years for people at increased risk of developing prostate cancer based on the following: Black race, germline mutations, strong family history of prostate cancer. (*Strong Recommendation; Evidence Level: Grade B*)
6. Clinicians should offer regular prostate cancer screening every 2 to 4 years to people aged 50 to 69 years. (*Strong Recommendation; Evidence Level: Grade A*)
7. Clinicians may personalize the re-screening interval, or decide to discontinue screening, based on patient preference, age, PSA, prostate cancer risk, life expectancy, and general health following SDM. (*Conditional Recommendation; Evidence Level: Grade B*)
8. Clinicians may use digital rectal examination (DRE) alongside PSA to establish risk of clinically significant prostate cancer. (*Conditional Recommendation; Evidence Level: Grade C*)
9. For people undergoing prostate cancer screening, clinicians should not use PSA velocity as the sole indication for a secondary biomarker, imaging, or biopsy. (*Strong Recommendation; Evidence Level: Grade B*)
10. Clinicians and patients may use validated risk calculators to inform the SDM process regarding prostate biopsy. (*Conditional Recommendation; Evidence Level: Grade B*)
11. When the risk of clinically significant prostate cancer is sufficiently low based on available clinical, laboratory, and imaging data, clinicians and patients may forgo near-term prostate biopsy. (*Clinical Principle*)

Initial Biopsy

12. Clinicians should inform patients undergoing a prostate biopsy that there is a risk of identifying a cancer, with a sufficiently low risk of mortality, that could safely be monitored with active surveillance (AS) rather than treated. (*Clinical Principle*)
13. Clinicians may use magnetic resonance imaging (MRI) prior to initial biopsy to increase the detection of Grade Group (GG)2+ prostate cancer. (*Conditional Recommendation*; *Evidence Level: Grade A*)
14. Radiologists should utilize Prostate Imaging Reporting and Data System (PI-RADS) in the reporting of multi-parametric magnetic resonance imaging (mpMRI). (*Moderate Recommendation; Evidence Level: Grade C*)
15. For biopsy-naïve patients who have a suspicious lesion on MRI, clinicians should perform targeted biopsies of the suspicious lesion and may also perform a systematic template biopsy. (*Moderate Recommendation [targeted biopsies]/Conditional Recommendation [systematic template biopsy]; Evidence Level: Grade C)*

16. For patients with both absence of suspicious findings on MRI and elevated risk for GG2+ prostate cancer, clinicians should proceed with a systematic biopsy. (*Moderate Recommendation; Evidence Level: Grade C*)
17. Clinicians may use adjunctive urine or serum markers when further risk stratification would influence the decision regarding whether to proceed with biopsy. (*Conditional Recommendation*; *Evidence Level: Grade C*)
18. For patients with a PSA > 50 ng/mL and no clinical concerns for infection or other cause for increased PSA (e.g., recent prostate instrumentation), clinicians may omit a prostate biopsy in cases where biopsy poses significant risk or where the need for prostate cancer treatment is urgent (e.g., impending spinal cord compression). (*Expert Opinion*)

Repeat Biopsy

19. Clinicians should communicate with patients following biopsy to review biopsy results, reassess risk of undetected or future development of GG2+ disease, and mutually decide whether to discontinue screening, continue screening, or perform adjunctive testing for early reassessment of risk. (*Clinical Principle*)
20. Clinicians should not discontinue prostate cancer screening based solely on a negative prostate biopsy. (*Strong Recommendation; Evidence Level: Grade C*)
21. After a negative biopsy, clinicians should not solely use a PSA threshold to decide whether to repeat the biopsy. (*Strong Recommendation; Evidence Level: Grade B*)
22. If the clinician and patient decide to continue screening after a negative biopsy, clinicians should re-evaluate the patient within the normal screening interval (two to four years) or sooner, depending on risk of clinically significant prostate cancer and life expectancy. (*Clinical Principle*)
23. At the time of re-evaluation after negative biopsy, clinicians should use a risk assessment tool that incorporates the protective effect of prior negative biopsy. (*Strong Recommendation; Evidence Level: Grade B*)
24. After a negative initial biopsy in patients with low probability for harboring GG2+ prostate cancer, clinicians should not reflexively perform biomarker testing. (*Clinical Principle*)
25. After a negative biopsy, clinicians may use blood-, urine-, or tissue-based biomarkers selectively for further risk stratification if results are likely to influence the decision regarding repeat biopsy or otherwise substantively change the patient’s management. (*Conditional Recommendation; Evidence Level: Grade C*)
26. In patients with focal (one core) high-grade prostatic intraepithelial neoplasia (HGPIN) on biopsy, clinicians should not perform immediate repeat biopsy. (*Moderate Recommendation; Evidence Level: Grade C*)
27. In patients with multifocal HGPIN, clinicians may proceed with additional risk evaluation, guided by PSA/DRE and mpMRI findings. (*Expert Opinion*)
28. In patients with atypical small acinar proliferation (ASAP), clinicians should perform additional testing, which may include repeat biopsy. (*Moderate Recommendation; Evidence Level: Grade C*)
29. In patients with atypical intraductal proliferation (AIP), clinicians should perform additional testing. (*Expert Opinion*)
30. In patients undergoing repeat biopsy with no prior prostate MRI, clinicians should obtain a prostate MRI prior to biopsy. (*Strong Recommendation; Evidence Level: Grade C*)
31. In patients with indications for a repeat biopsy who do not have a suspicious lesion on MRI, clinicians may proceed with a systematic biopsy. (*Conditional Recommendation; Evidence Level: Grade B*)
32. In patients undergoing repeat biopsy and who have a suspicious lesion on MRI, clinicians should perform targeted biopsies of the suspicious lesion and may also perform a systematic template biopsy. (*Moderate Recommendation [targeted biopsies]/Conditional Recommendation [systematic template biopsy]; Evidence Level: Grade C)*

Biopsy Technique

33. Clinicians may use software registration of MRI and ultrasound images during fusion biopsy, when available. (*Expert Opinion*)
34. Clinicians should obtain at least two needle biopsy cores per target in patients with suspicious prostate lesion(s) on MRI. (*Moderate Recommendation; Evidence Level: Grade C*)
35. Clinicians may use either a transrectal or transperineal biopsy route when performing a biopsy. (*Conditional Recommendation; Evidence Level: Grade B*)

INTRODUCTION

Background

Prostate cancer is the most commonly diagnosed noncutaneous malignancy in American men. It is estimated that 333,830 patients will be diagnosed with prostate cancer, and 36,320 deaths from prostate cancer will occur in the United States (U.S.) in 2026.[1] There was an estimated 1,414,259 new cases of prostate cancer and 375,304 deaths worldwide in 2020.[2] Significant advances have been made in early detection, especially with the increasing availability and usage of biomarkers and mpMRI. This Guideline is based on a systematic review of recently published literature and addresses early detection with an emphasis on PSA-based screening, considerations for initial and repeat biopsy, and biopsy technique, with the goal of identifying clinically significant prostate cancer.

Terminology and Definitions

This Guideline provides recommendations for prostate cancer screening in different groups based on their age range and risk criteria, with an emphasis on SDM. SDM is particularly necessary as there is no universally accepted standard definition of low versus elevated risk for prostate cancer detection. In practice, clinicians often resort to an elevated PSA level based on laboratory, prostate size, or age-based "norms" as a surrogate for an elevated prostate cancer risk, but such definitions, while easy to apply, do not suffice for all people and circumstances. Thus, clinicians may tailor the definitions of elevated risk and elevated PSA to the clinical situation at hand. Some examples that may elevate risk of clinically significant prostate cancer are Black race, germline mutations, strong family history of prostate cancer, polygenic risk scores (numerical estimate of an individual's genetic predisposition for developing a specific condition [e.g., prostate cancer]),[3, 4] and other factors that may be indicated by risk calculators (e.g., total PSA, PSA density [PSAD], percent free PSA, age). More importantly, this Guideline emphasizes potential benefit in using validated risk calculators and provides recommendations for the timing and methodology for screening.

This Guideline underscores the goal of detecting "clinically significant" cancer for initial and repeat biopsy. The risk of mortality in patients with GG1 prostate cancer is extremely low.[5, 6] Thus, this Guideline defines clinically significant prostate cancer as GG2 or higher (GG2+) prostate cancer and will use "clinically significant prostate cancer" and "GG2+" interchangeably throughout. However, the Panel acknowledges there are various definitions of "clinically significant" as not all "clinically significant" cancers are destined to impact quality or quantity-of-life, and it is patient-specific. The Guideline recommends utilizing validated risk calculators, particularly calculators that incorporate previous negative biopsy and mpMRI use in the repeat biopsy setting. It also addresses the significance of non-cancerous, yet potentially significant, pathologic findings identified from the biopsy. With the emergence of mpMRI and novel biomarkers, the Panel evaluated the current evidence to develop recommendations on how best to incorporate these into clinical practice. In certain clinical scenarios, additional data are needed to make definitive recommendations for the optimal biopsy approach. An abnormal MRI, for the purpose of this Guideline, is defined as PI-RADS 3 to 5 as supported by much of the literature. However, given the local variation and expertise in reading MRIs, some clinicians may opt to limit an abnormal MRI to PI-RADS 4 to 5.

This Guideline is intended for all patient populations with a prostate gland. For consistency purposes, this Guideline refers to these individuals as "people" or "patients" throughout this document.

METHODOLOGY

The systematic review utilized to inform this Guideline was conducted by an independent methodological consultant. Determination of the Guideline scope and review of the final systematic review to inform Guideline statements was conducted in conjunction with the Early Detection of Prostate Cancer Panel. In 2025, an independent methodologist conducted a search for studies published between November 2022 and December 2024 to capture new evidence published since the last update review. A second search that incorporated keywords for newly developed biomarkers was conducted in Ovid MEDLINE and Embase and identified studies published from January 2000 through December 2024 to align with the search inception date used in the original Guideline.

Panel Formation

The Panel was created in 2021 by the American Urological Association Education and Research, Inc. (AUAER). The Practice Guidelines Committee (PGC) of the AUA selected the Panel Chairs who in turn appointed the additional panel members with specific expertise in this area. The multidisciplinary panel includes representation from urology/urologic oncology, epidemiology, biostatistics, primary care, pathology, and radiology. The Panel additionally included patient representation. Funding of the Panel was provided by the AUA; panel members received no remuneration for their work.

The Early Detection of Prostate Cancer Amendment Panel was established in 2025 by the AUA to review new literature and provide updates herein.

Searches and Article Selection

A search was conducted for existing systematic reviews on October 11, 2021 and updated on November 21, 2022. Systematic reviews published as a component of practice Guidelines were also considered eligible for inclusion. An electronic search employing Ovid was used to systematically search the MEDLINE and Embase databases, as well as the Cochrane Library, for systematic reviews evaluating detection of prostate cancer.

When systematic reviews were not identified, or when identified reviews were incomplete, Ovid was used to systematically search MEDLINE and Embase databases for articles evaluating detection of prostate cancer utilizing the PICOTS elements. During PICOTS development, panel members submitted landmark studies addressing the KQs to the methodologist. These studies were defined as control articles and were compared with the literature search strategy output; the strategy was subsequently updated as necessary to capture all control articles. Databases were originally searched for studies published from January 1, 2000 through October 11, 2021 and subsequently updated to November 21, 2022. In addition to the MEDLINE and Embase database searches, reference lists of included systematic reviews and primary literature were scanned for potentially useful studies.

All hits from the Ovid literature search were input into a reference management software (EndNote X7), where duplicate citations were removed. Abstracts were reviewed by the methodologist to determine if each study addressed the KQs and met study design inclusion criteria. For all research questions, randomized controlled trials (RCTs), observational studies, modelling studies with theoretical cohorts, and case-control studies were considered for inclusion in the evidence base. For all KQs, studies had to enroll at least 30 patients per study arm. Case series, letters, editorials, *in vitro* studies, studies conducted in animal models, and studies not published in English were excluded from the evidence base *a priori*.

Full-text review was conducted on studies that passed the abstract screening phase. Studies were compared to the PICOTS criteria. Ten panel members were paired with the methodologist and completed duplicate full-text study selection of 10% of studies undergoing full-text review. The dual-review trained the methodologist, who then completed full-time review of the remaining studies.

In 2024, the methodologist conducted a literature search using Ovid MEDLINE and Embase for new evidence published between November 2022 and December 2024. A second search that incorporated keywords for newly developed markers was conducted in the same databases and identified studies published from January 2000 through December 2024 to align with the search inception date used in the original Guideline. The literature search returned 15,193 citations after deduplication. Following the study selection process outlined for the original Guideline and using the original PICOTS criteria, 40 new studies were added to the evidence base.

Titles and abstracts of studies identified by the search were reviewed in a two-stage process in Rayyan.[7] During the first stage, studies were reviewed to determine if they assessed early-detection of prostate cancer, and if they met the study selection criteria of prespecified study type. Studies not published in English were excluded from the evidence base. Allowable study types included systematic reviews, RCTs, observational studies, modeling studies with theoretical cohorts, and case-control studies. All other study types were excluded.

During the second stage of title and abstract review, abstracts were compared to the PICOTS criteria. Additionally, during the second stage of review, studies were assessed to determine if they could reaffirm or refute the original Guideline statements. In alignment with the Guideline, for all KQs, studies had to enroll at least 30 patients per study arm. Additionally, for studies reporting on detection rates of prostate cancer, at least 50 prostate cancers had to be detected for inclusion in the evidence base. This size limitation was waived for one of the KQs due to a paucity of studies.

Full-text review was conducted on studies that passed the title and abstract screen and flagged by the Panel to potentially change Guideline statements or inform new Guideline statements. Complete studies were compared to the PICOTS criteria. Those that met the PICOTS criteria and informed the proposed Guideline statement changes were included in the evidence base. Studies that did not inform the statements were defined as those with reported outcomes that did not affirm nor refute the proposed changes.

Data Abstraction

Data were extracted from all studies that passed full-text review by the methodologist.

Risk of Bias Assessment

Quality assessment for all retained studies was conducted. Using this method, studies deemed to be of low quality would not be excluded from the systematic review, but would be retained, and their methodological strengths and weaknesses were discussed where relevant. To evaluate the risk of bias within the identified studies, the Assessment of Multiple Systematic Reviews (AMSTAR),[8] tool was used for systematic reviews, the Cochrane Risk of Bias Tool[9] was used for randomized studies, a Risk of Bias in Non-Randomized Studies of Intervention (ROBINS-I)[10] was used for observational studies and modeling studies with theoretical cohorts, and Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2)[11] was used for diagnostic accuracy studies. Additional important quality features, such as comparison type, power of statistical analysis, and sources of funding were extracted for each study.

Data Synthesis

Meta-analysis was appropriate for studies informing four KQs and six outcomes using RevMan.[12] For all meta-analyses there was substantial heterogeneity in both the patient populations and the methodologies employed within the studies, making random-effects methods the most appropriate. Odds ratios for detection of clinically significant prostate cancer using MRI-targeted biopsy alone and fusion biopsy plus systematic biopsy were calculated based on raw data reported in studies and pooled using an inverse-variance method. For calculation of the number of avoided biopsies and missed clinically significant prostate cancer using various biomarkers in both biopsy naïve and repeat biopsy populations, prevalence and standard errors were extracted or calculated from reported raw data in studies and pooled using an inverse variance method. Finally, prevalence and standard errors for clinically significant prostate cancer detection using a PI-RADS score of 1 to 2, 3, 4, and 5 were calculated from raw data reported in studies and pooled using an inverse-variance method.[12] Due to the paucity of data using only PI-RADS version 2.1, pooled studies used version 1.0 through version 2.1.

Determination of Evidence Strength

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[13] system was used to determine the aggregate evidence quality for each outcome, or group of related outcomes, informing KQs. GRADE defines a body of evidence in relation to how confident Guideline developers can be that the estimate of effects as reported by that body of evidence, is correct. Evidence is categorized as high, moderate, low, and very low, and assessment is based on the aggregate risk of bias for the evidence base, plus limitations introduced as a consequence of inconsistency, indirectness, imprecision, and publication bias across the studies.[14] Additionally, certainty of evidence can be downgraded if confounding across the studies has resulted in the potential for the evidence base to overestimate the effect. Upgrading of evidence is possible if the body of evidence indicates a large effect or if confounding would suggest either spurious effects or would reduce the demonstrated effect.

The AUA employs a 3-tiered strength of evidence system to underpin evidence-based Guideline statements. **Table 1** summarizes the GRADE categories, definitions, and how these categories translate to the AUA strength of evidence categories. In short, high certainty by GRADE translates to AUA A-category strength of evidence, moderate to B, and both low and very low to C.

Table 1: Strength of Evidence Definitions

AUA Strength of Evidence Category	GRADE Certainty Rating	Definition
A	High	• Very confident that the true effect lies close to that of the estimate of the effect
B	Moderate	• Moderately confident in the effect estimate • The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
C	Low	• Confidence in the effect estimate is limited • The true effect may be substantially different from the estimate of the effect
	Very Low	• Very little confidence in the effect estimate • The true effect is likely to be substantially different from the estimate of effect

The AUA categorizes body of evidence strength as Grade A (e.g., well-conducted and highly-generalizable RCTs or exceptionally strong observational studies with consistent findings), Grade B (e.g., RCTs with some weaknesses of procedure or generalizability or moderately strong observational studies with consistent findings), or Grade C (e.g., RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes or observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data). By definition, Grade A evidence is evidence about which the Panel has a high level of certainty, Grade B evidence is evidence about which the Panel has a moderate level of certainty, and Grade C evidence is evidence about which the Panel has a low level of certainty.[15]

AUA Nomenclature: Linking Statement Type to Evidence Strength

The AUA nomenclature system explicitly links statement type to body of evidence strength, level of certainty, magnitude of benefit or risk/burdens, and the Panel's judgment regarding the balance between benefits and risks/burdens (**Table 2**). Strong Recommendations are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is substantial. Moderate Recommendations are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is moderate. Conditional Recommendations are non-directive statements used when the evidence indicates that there is no apparent net benefit or harm or when the balance between benefits and risks/burden is unclear. All three statement types may be supported by any body of evidence strength grade. Body of evidence strength Grade A in support of a Strong or Moderate

Recommendation indicates that the statement can be applied to most patients in most circumstances and future research is unlikely to change confidence. Body of evidence strength Grade B in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances, but better evidence could change confidence. Body of evidence strength Grade C in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances, but better evidence is likely to change confidence. Conditional Recommendations also can be supported by any evidence strength. When body of evidence strength is Grade A, the statement indicates that benefits and risks/burdens appear balanced, the best action depends on patient circumstances, and future research is unlikely to change confidence. When body of evidence strength Grade B is used, benefits and risks/burdens appear balanced, the best action also depends on individual patient circumstances and better evidence could change confidence. When body of evidence strength Grade C is used, there is uncertainty regarding the balance between benefits and risks/burdens, alternative strategies may be equally reasonable, and better evidence is likely to change confidence.

Where gaps in the evidence existed, the Panel provides guidance in the form of Clinical Principles or Expert Opinions with consensus achieved using a modified Delphi technique if differences in opinion emerged.[16] A Clinical Principle is a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature. Expert Opinion refers to a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment.

Peer Review and Document Approval

An integral part of the Guideline development process at the AUA is external peer review. The AUA conducted a comprehensive peer review process to ensure that the document was reviewed by experts who were knowledgeable in the area of early detection of prostate cancer. In addition to reviewers from the AUA PGC, Science and Quality Council (SQC), and Board of Directors (BOD), the document was reviewed by external content experts. Additionally, a call for reviewers was placed on the AUA website from October 10 to 24 of 2022 to allow any additional interested parties to request a copy of the document for review. The Guideline was also sent to the Urology Care Foundation and members of the AUA Patient Advocacy network to open the document further to the patient perspective. The draft Guideline document was distributed to 174 peer reviewers. All peer review comments were blinded and sent to the Panel for review. In total, 84 reviewers provided comments, including 69 external reviewers. At the end of the peer review process, a total of 770 comments were received. Following comment discussion, the Panel revised the draft as needed. Once finalized, the Guideline was submitted to the AUA PGC, SQC, and BOD for final approval as well as the Society of Urologic Oncology (SUO).

In 2025, as part of the amendment process, the AUA conducted a comprehensive peer review. A call for reviewers was issued from August 12 to August 29, 2025. On October 2, 2025 the draft Guideline document was distributed to a total of 88 peer reviewers, with 84 submitting comments. The Amendment Panel carefully reviewed and discussed all submitted comments, making revisions to the draft as necessary. Once finalized, the Guideline was submitted for approval to the PGC, SQC, and representatives from SUO. It was subsequently presented to the AUA BOD for final approval.

Table 2: AUA Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/Burden, and Body of Evidence Strength

Evidence Grade	Evidence Strength A (High Certainty)	Evidence Strength B (Moderate Certainty)	Evidence Strength C (Low Certainty)
Strong Recommendation (Net benefit or harm substantial)	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is substantial -Applies to most patients in most circumstances and future research is unlikely to change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is substantial -Applies to most patients in most circumstances but better evidence could change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) appears substantial -Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
Moderate Recommendation (Net benefit or harm moderate)	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is moderate -Applies to most patients in most circumstances and future research is unlikely to change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is moderate -Applies to most patients in most circumstances but better evidence could change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) appears moderate -Applies to most patients in most circumstances but better evidence is likely to change confidence
Conditional Recommendation (Net benefit or harm comparable to other options)	-Benefits = Risks/Burdens -Best action depends on individual patient circumstances -Future Research is unlikely to change confidence	-Benefits = Risks/Burdens -Best action appears to depend on individual patient circumstances -Better evidence could change confidence	-Balance between Benefits & Risks/Burdens unclear -Net benefit (or net harm) comparable to other options -Alternative strategies may be equally reasonable -Better evidence likely to change confidence
Clinical Principle	a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature		
Expert Opinion	a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence in the medical literature		

GUIDELINE STATEMENTS

PSA Screening

1. **Clinicians should engage in SDM with people for whom prostate cancer screening would be appropriate and proceed based on a person's values and preferences. (*Clinical Principle*)**

Prostate cancer screening is a preference-sensitive decision. For this reason, the Panel recommends clinicians engage in SDM with people considering prostate cancer screening so they can make an informed choice. The Panel discourages the practice of ordering a PSA test without informing the patient upfront, and likewise discourages the practice of failing to inform the patient of the availability of PSA screening, as appropriate.

SDM is considered state-of-the-art in patient counseling for preference-sensitive decisions.[17] This practice can be facilitated using a decision aid. A 2017 Cochrane systematic review and meta-analysis of 105 studies showed that people who view decision aids feel more knowledgeable, better informed, and clearer about their values.[18] A 2019 systematic review and meta-analysis of 19 RCTs evaluating decision aids specifically designed for the prostate cancer screening decision versus conventional care showed a small decrease in decisional conflict (moderate-quality evidence) and a small increase in knowledge (low-quality evidence). However, there was no association between clinician and patient discussion on prostate cancer screening or discussion on the type of screening to obtain.[19]

While SDM is strongly encouraged, the Panel acknowledges that downstream risks of screening of potential side-effects from curative treatment of screen-detected tumors are lower today with increased utilization of AS for low-risk disease. This is currently a practice endorsed by the AUA as a strong recommendation for patients with low-risk localized prostate cancer.[20]

A 2016 AUA White paper[17] recommends SDM which include four key elements:

1. Involvement of both the clinician and the patient in the decision-making process.
2. Sharing information by both the clinician and the patient.
3. Building consensus through the expression of preferences by both clinician and patient.
4. Agreement by both the clinician and patient on the decision to implement.

2. **When screening for prostate cancer, clinicians should use PSA as the first screening test. (*Strong Recommendation; Evidence Level: Grade A*)**

The PSA blood test remains the first-line screening test of choice based on randomized trials of PSA-based screening showing reductions in metastasis and prostate cancer death.[21, 22] At the time of this evidence review, very limited evidence has emerged regarding other candidates for first-line biomarkers or imaging.

Stockholm-3 (STHLM-3) has been evaluated as a first-line screening test for predicting the risk of GG2+ prostate cancers.

The STHLM-3 test is a multiplex test combining clinical variables (age, first-degree family history of prostate cancer, and previous biopsy), blood biomarkers (total PSA, free PSA, ratio of free to total PSA, human kallikrein 2 [hK2], macrophage inhibitory cytokine-1 [MIC-1], and microseminoprotein-beta [MSMB]), and a polygenic risk score (PRS). The STHLM-3 test has a higher predictive accuracy compared to PSA alone (area under the curve [AUC] 0.74 versus 0.56) and reduced unnecessary biopsies by 32%.[23] Using the STHLM-3 test and performing targeted plus systematic biopsies only in patients with MRI-suspicious lesions decreased overdetection and maintained the number of high-grade cancers found, as compared to systematic biopsy alone, in a screening-by-invitation trial.[24, 25] While this novel test appears promising, further validation in diverse populations to confirm these findings will be necessary to move forward into practice.

DRE should not be used as a first-line screening test prior to PSA or a replacement for PSA in otherwise asymptomatic patients. In symptomatic patients, DRE can be considered as a diagnostic tool rather than a screening test for cancer. It can be used as a complement to screening with PSA testing and is discussed in greater detail, including supportive references, under **Statement 8**.

3. **For people with a newly elevated PSA, clinicians should repeat the PSA prior to a secondary biomarker, imaging, or biopsy. (*Expert Opinion*)**

In people with a newly elevated PSA, it will return to a normal level in 25% to 40% upon retesting.[26] Among 1,686 biopsied patients in the STHLM-3 study with a PSA of 3 to 10 ng/mL, and 2 PSA tests 8 weeks apart, 283 (17%) subsequently had a PSA < 3 ng/mL. Given the clear evidence that PSA tests may normalize, it would be prudent to confirm a newly elevated PSA test before proceeding with further workup.[27]

The Panel also strongly supports the Choosing Wisely AUA initiative (https://www.choosingwisely.org/clinician-lists/american-urological-association-treating-elevated-psa-with-antibiotics/) that empiric antibiotics should not be utilized to treat an elevated PSA in an asymptomatic person.[28, 29] Neither DRE nor bicycle riding appreciably alters the PSA,[30, 31] and most controlled studies evaluating ejaculation suggest it either does not significantly impact or modestly increases (~10%) PSA.[32] The half-life of PSA is 2 to 3 days. A repeat PSA in a few months is recommended, though it can be shortened or lengthened depending on other clinical factors. Clinicians should also recognize that urinary tract infections and instrumentation (e.g., recent bladder catheterization, prostate biopsy or cystoscopy, urinary retention) cause transient increases in PSA. PSA elevations in these settings should be repeated after appropriate time periods to allow for PSA to reach baseline level.

The definition of an elevated PSA has changed over time. The commonly cited threshold of 4 ng/mL is based on very early studies that identify the highest levels typically observed among patients thought to be free of prostate cancer. Another cited threshold of 3 ng/mL is taken from the Finnish European Randomized Study of Screening for Prostate Cancer (ERSPC) trial of prostate cancer screening that showed a significant reduction in prostate cancer deaths among patients who entered the trial between ages 55 to 69 years and were referred to biopsy based on that threshold. The knowledge that PSA generally increases with age in people without prostate cancer has led to the consensus that the threshold above which a PSA level should be considered elevated should increase with age, and that the original threshold of 4 ng/mL is too high for people in their 40s and 50s and too low for people in their 70s and 80s who have a high risk of overdiagnosis. Most studies identifying age-varying thresholds specify threshold values of 2.5 ng/mL for people in their 40s, 3.5 ng/mL for people in their 50s, 4.5 ng/mL for people in their 60s, and 6.5 ng/mL for people in their 70s.[33-35] Typically, 5-alpha reductase inhibitors (5-ARIs) decrease PSA levels after at least 6 months of use, with some older studies suggesting serum PSA should be doubled for patients using 5-ARIs as an adjusted baseline.[36] However, PSA kinetics vary from patient to patient, with one trial suggesting only one-third of patients on 5-ARI therapy experience a 40% to 60% decline in PSA at one year.[37]

4. **Clinicians may begin prostate cancer screening and offer a baseline PSA test to people between ages 45 to 50 years. (*Conditional Recommendation; Evidence Level: Grade B*)**

For people at average risk of developing prostate cancer, there is no randomized evidence showing a benefit to initiation of routine screening for prostate cancer before 45 years of age. The randomized trials that demonstrate a benefit for prostate cancer screening (Goteborg-1[38] and ERSPC[21]) began at ages 50 and 55 years, respectively.

The earlier initiation of screening is supported by observational studies that have demonstrated a prognostic value of obtaining a baseline PSA in early midlife.[39, 40] A review of eight PSA studies in younger people have shown baseline PSA measurements were robust predictors of aggressive prostate cancer, metastasis, and disease-specific mortality many years later. Baseline PSA was a stronger predictor of prostate cancer risk than race and family history of prostate cancer. Median PSA levels ranged from ~0.4 to 0.7 ng/mL in patients in their 40s and from ~0.7 to 1 ng/mL in patients in their 50s.[39]

The prevalence of prostate cancer is low among patients aged 40 to 45 years. The modeling studies comparing various start ages have shown that lowering the screening start age to 40 to 45 years instead of 50 to 55 years slightly increased the probability of lives saved, but substantially increased the number of PSA tests.[33]

In the Malmö Preventive Project, the risk of prostate cancer metastases by 15 years' follow-up was low (0.6%) for patients with PSA in the highest percentile (≥ 1.3 ng/mL) at age 40 years of age. For patients aged 45 to 49 years with PSA below the median (0.68 ng/mL), the risk of prostate cancer metastasis within 25 years was 0.85%. Patients with PSA in the highest decile (≥ 1.6 ng/mL) at ages 45 to 49 years contributed to nearly half of prostate cancer deaths over the next 25 to 30 years.[40]

A randomized trial of risk-adapted screening for prostate cancer comparing patients starting at age 45 versus 50 years (the PROBASE trial) is currently ongoing, with 23,301 patients having participated in screening in the first round of the trial.[41] The participation rate was low (20%), and 35% with indication for biopsy refused to undergo the procedure. The prevalence of screen-detected prostate cancer in 45-year-old patients was very low (0.2%), and only 4 patients were diagnosed with aggressive prostate cancer GG3 or higher. Thus, the use of SDM is highly recommended given the uncertainty involved.

5. **Clinicians should offer prostate cancer screening beginning at age 40 to 45 years for people at increased risk of developing prostate cancer based on the following: Black race, germline mutations, strong family history of prostate cancer. (*Strong Recommendation; Evidence Level: Grade B*)**

If a person has risk factors associated with an increased risk of developing prostate cancer (including Black race, germline mutations, strong family history of prostate cancer), in particular if they have an increased risk of metastatic disease, an earlier age to begin screening may be appropriate in addition to a shorter re-screening interval.[42]

Black individuals have a disproportionate cancer burden and a two-fold higher risk of death from prostate cancer compared to White individuals.[43] A study using three models discovered that patients who self-identify as Black appear to have earlier age of onset and increased risk of metastases before clinical diagnosis.[44] This study found the risk of a Black patient developing fatal prostate cancer, if not diagnosed, reached the same level as that of the general population three to nine years earlier, informing the proposal that Black patients initiate screening approximately five to ten years prior to the recommendation for average-risk individuals.[44] This increased risk may be addressed by screening Black patients more frequently (e.g., annually), but the risk of overdiagnosis among older Black patients is considerably higher than the average-risk population, making SDM and personalized screening particularly important.

Empirical studies have shown patients with germline *BRCA1* and *BRCA2* variants have increased risks of both disease onset and progression.[45] The IMPACT study revealed a high positive predictive value (PPV) of PSA screening (with biopsy referral threshold 3 ng/mL) in these patients and a high frequency of clinically significant cancers,[46] particularly among *BRCA2* carriers.[47] The IMPACT study showed a stronger relationship (eight-fold increased risk) between *BRCA2* carriers and aggressive cancer for whom systematic PSA screening is indicated, while further study is needed to determine the role of screening among *BRCA1* mutation carriers.[47] Similarly, mutations in *ATM, MLH1, MSH2, MSH6, PMS2, HOXB13, NBS1,* and *CHEK2* need further study. In the IMPACT study, after one screening round, carriers of pathogenic variants in mismatch-repair genes *MSH2* and *MSH6* had a higher risk of prostate cancer compared with age-matched non-carrier controls, potentially supporting screening of these patients.[45] These patients may benefit from both earlier initiation of PSA screening and shorter intervals between screenings.

Although there is no standard definition of strong family history, several Guideline and consensus statements propose common criteria that include: 1) people with one brother or father or two or more male relatives with one of the following: a) diagnosed with prostate cancer at age < 60 years; b) any of whom died of prostate cancer; c) any of whom had metastatic prostate cancer. 2) family history of other cancers with two or more cancers in hereditary breast and ovarian cancer syndrome or Lynch syndrome spectrum.[48, 49]

Studies have consistently found elevated risk of prostate cancer in patients with a family history of prostate cancer[50-53] and also in patients with a family history of prostate and breast cancer.[54, 55] In some studies, the observed increase in risk may be partly due to detection bias associated with greater compliance to screening and biopsy[51] among patients with a known family history. Some studies have differentiated low- and high-risk prostate cancers associated with family history[52, 53] and have suggested focusing on the association between family history and high-risk cancer as more relevant for making screening recommendations. Patients with a strong family history (e.g., two or more first-degree relatives have a four-fold relative risk compared to those without a family history[50]) should ideally be genotyped to ascertain whether this is associated with a pathogenic variant (e.g., *BRCA1/2*, Lynch Syndrome, ATM, CHEK2) or one or more of a growing set of identified germline DNA damage-repair mutations found in patients with metastatic prostate cancer diagnoses.[56] In the absence of this information, patients with a strong family history may be screened earlier and/or more frequently, similar to those with detected germline pathogenic variants. Again, SDM is highly recommended given the uncertainty involved in the PSA screening setting.

6. **Clinicians should offer regular prostate cancer screening every 2 to 4 years to people aged 50 to 69 years. (*Strong Recommendation; Evidence Level: Grade A*)**

Two RCTs, ERSPC[21] and the Goteborg population-based prostate cancer screening trial (Goteborg-1),[38] provide evidence that regular PSA screening every 2 to 4 years in patients aged 50 to 69 years reduces the risk of metastatic prostate cancer and prostate cancer mortality at 16 to 22 years, compared to no or opportunistic screening. The Goteborg-1 trial was designed separately from ERSPC with a separate power calculation and included patients 50 to 64 years of age.[57] Patients aged 55 to 69 years were later included in ERSPC.

The number needed to be screened (NNS, the inverse of the absolute risk reduction in prostate cancer mortality) and number needed to be diagnosed (NND, additional cases diagnosed) to prevent one death from prostate cancer depends on the screening protocol (including screening ages) and follow-up time (**Table 3**).

Table 3: Number Needed to Screen (NNS) and Additional Number Needed to Diagnose (NND) to Prevent One Death from Prostate Cancer by Study

Study	Screen Ages	Follow up time	Protocol	NNS	NND
ERSPC[21]	55-69	16 years	2-4 years Bx PSA > 3 ng/mL	570	18
ERSPC (2009)[58]	50-74	9 years	2-4 years Bx PSA > 3 ng/mL	1,410	48
Goteborg-1[38]	50-64	22 years	2 years Bx PSA 2.5-3 + ng/mL	221	9
ERSPC modeling study[59]	55-69	Lifetime horizon	Annual Bx PSA 3 + ng/mL 4 years	98 129	5 5
U.S. modeling study[33]	50-69	Lifetime horizon	2 years Bx PSA 4 + ng/mL Bx PSA 2.5 + ng/mL	 243 204	 3 4
(Abbreviations: Bx, biopsy; PSA, prostate-specific antigen)					

A study comparing patients 60 years of age who have been screened every 2 years in the Goteborg-1 trial, compared to unscreened patients 60 years of age in the Malmö Preventive Project, showed that continuing to screen patients with PSA ≥ 2 ng/mL at 60 years of age had a favorable net-benefit in terms of reducing risk of prostate cancer metastasis and mortality at 15 years. At 15 years, the NNS to prevent 1 death from prostate cancer was 23 and NND was 6.[60]

The U.S. Prostate Lung Colorectal and Ovarian (PLCO) cancer screening trial was unable to demonstrate a statistically significant difference in prostate cancer mortality at 17 years of follow-up between patients randomized to screening versus usual care.[61] However, the control group had a high degree of PSA testing (contamination) with more than 80% of patients receiving at least 1 PSA test during the trial.[62] In later years, patients in the control groups of ERSPC and Goteborg-1 have also been exposed to PSA testing. In PLCO, the cut-off for biopsy was higher than in ERSPC (4 versus 3 ng/mL), the proportion of patients with elevated PSAs that were biopsied was lower (34% versus over 90%) and screening stopped after 6 years. Taking differences in implementation into account, a modeling study aiming to reconcile PLCO and ERSPC showed PSA screening versus no screening can reduce prostate cancer mortality by approximately 30% at 11 to 13 years.[63]

A modeling study primarily based on ERSPC compared the benefits and harms of annual PSA screening of patients aged 55 to 69 years. Over a life-time horizon with a PSA threshold of 3 ng/mL, screening would lead to 9 fewer deaths from prostate cancer for every 1,000 screened. The NNS to prevent one death from prostate cancer over a lifetime horizon was 98, and the NND was 5. Overall, screening was offset by a 23% reduction in quality-adjusted life years from life years gained, mainly owing to long-term side-effects from treatment.[59] A U.S. model produced similarly low NND[33] in evaluation of screening between ages 50 and 69 years using a PSA threshold of 4 ng/mL, which had been standard practice in the U.S. Again, SDM is highly recommended given the uncertainty involved in the PSA screening setting.

7. **Clinicians may personalize the re-screening interval, or decide to discontinue screening, based on patient preference, age, PSA, prostate cancer risk, life expectancy, and general health following SDM. (*Conditional Recommendation; Evidence Level: Grade B*)**

The randomized trials (PLCO, Goteborg-1, ERSPC) screened patients aged 50 to 69 years every 1 to 4 years and demonstrated a reduction in prostate cancer mortality. However, increasing evidence from additional analyses of the randomized trials, observational studies, and modeling studies show the balance between benefits (reduction in metastatic prostate cancer and prostate cancer mortality) and harms (anxiety, false positives, overdiagnosis, side-effects from prostate biopsy) of screening can be modulated through personalized risk-stratified screening approaches.[33, 40, 60, 64-69]

Risk-stratified re-screening intervals and biopsy thresholds may be tailored for select patients

The re-screening interval can be 1 to 4 years for patients with PSA levels of 1 to 3 ng/mL between the ages of 45 to 70 years, while the re-screening interval can be prolonged for patients aged 45 to 70 years with a PSA < 1 ng/mL or those with a PSA below the age-specific median.[59, 64, 70] Studies have shown that patients in the age range of 40 to 59 years with a PSA below the age-specific median, without a strong family history of prostate cancer, and no known pathogenic germline mutation, have a very low risk of metastatic cancer or long-term prostate cancer mortality. In a case-control study conducted in Sweden (Malmö Preventive Project cohort),[40] among patients aged 40 to 55 years, the 15-year risk of metastasis for patients with PSA below the median at ages 45 to 49 years was 0.09%, and below the median at ages 51 to 55 years was 0.23%. In a U.S. case-control study (Physicians' Health Study cohort)[68] among patients 40 to 59 years, 82%, 71%, and 86% of lethal cases occurred in patients with PSA above the median at ages 40 to 49 years (median PSA 0.68 ng/mL), 50 to 54 years (median PSA 0.88 ng/mL), and 55 to 59 years (median PSA 0.96 ng/mL), respectively. Both studies suggest risk-stratified screening based on midlife PSA and should be considered in patients aged 45 to 59 years. However, they do not explicitly evaluate potential harm-benefit implications of any specific strategies. There were 2 models[71] used to examine the impact of lengthening the interval between PSA tests to 8 years from a baseline interval of 2 years for patients with a PSA < 1.0 ng/mL at 45 years of age. Compared with biennial screening from ages 45 to 69 years, this risk-stratified approach led to half the number of tests while preserving more than 95% of the lives saved.

Comparing 35 different screening strategies, a modeling study showed that PSA screening strategies using higher thresholds for biopsy referral for older patients, and screening patients with low PSA levels less frequently reduced the harms of screening (false positives, overdiagnoses) while saving the majority of lives with standard intervals (e.g., annual or biennial screening).[33]

Patients with low PSA

Amongst patients 60 years of age with a PSA < 1 ng/mL (age-specific median), the 25-year risk of metastases or death from prostate cancer in a largely *unscreened* population (Malmö Preventive Project) is extremely low (0.5% and 0.2%, respectively).[65] Although modeling data suggest a higher likelihood of death from prostate cancer if screening were discontinued in these patients (5% to 13.1% fewer lives saved compared with continuing screening to 69 years of age),[71] the absolute number of lives saved by continuing screening is small; therefore, it may be reasonable to significantly lengthen the re-screening interval or discontinue screening based on SDM provided there are no other risk factors, such as strong family history of prostate cancer.[60, 65, 71]

In comparison of regularly screened patients in the Goteborg-1 trial versus unscreened people 60 years of age in the Malmö Preventive Project with PSA < 2 ng/mL, continued screening every 2 years for 15 years found an increase in prostate cancer incidence (7.7%) without a decrease in prostate cancer mortality.[60] For patients with PSA ≥ 2 ng/mL, the reduction in cancer mortality for screened patients was large with 23 patients being screened (NNS) and 6 diagnosed (NND) to prevent 1 prostate cancer death at 15 years.[60] In long-term follow-up from ERSPC, the actuarial probability of clinically significant prostate cancer at 16 years was 1.2% to 1.5% for patients aged 55 to 69 years with baseline PSA < 1.0 ng/mL, while for those initially screened at age 60 to 61 years with baseline PSA < 2 ng/mL, further continuation of screening is unlikely to be beneficial after the age of 68 to 70 years if PSA is still < 2 ng/mL.[72]

Older patients

The decision to screen patients should be an SDM conversation predicated upon a person's prior PSA levels and general health. A flexible age to discontinue screening may be based on individualized decision-making to balance detection of aggressive cancers and overdiagnosis. This is particularly important in people between the ages of 70 to 80 years where there is a higher risk of competing mortality.[73, 74] Clinicians may discontinue or substantially lengthen the re-screening interval for patients 75 years of age or older if PSA is < 3 ng/mL. In the Baltimore Longitudinal Study of Aging, patients 75 years or older with a PSA < 3 ng/mL were unlikely to be diagnosed with aggressive prostate cancer, and no patients between the ages of 75 to 80 years with a PSA < 3 ng/mL died of prostate cancer during their remaining lifetime.[75] In ERSPC Rotterdam, patients aged 70 to 74 years who have previously undergone PSA-based screening without receiving a prostate cancer diagnosis had a cumulative incidence of prostate cancer-specific mortality of 0.54% (95% confidence interval [CI]: 0.40 to 0.70) in all patients, 0.11% (95% CI: 0.05 to 0.27) in patients with PSA < 2 ng/mL, and 0.85% (95% CI: 0.47 to 1.5) in patients with PSA 2 to 3 ng/mL, by age 85, suggesting that discontinuation of screening could be considered in patients with PSA < 3.0 ng/mL.[76]

A modeling study[77] found that discontinuing screening at ages 66 and 72 years for patients with severe and moderate comorbidity, respectively, resulted in similar harms and benefits compared to screening people with average health to 74 years of age.

Life expectancy

In select patients who are very healthy with an estimated life expectancy of at least ten years, ongoing screening every two to four years is reasonable following SDM as these patients are more likely to benefit from therapeutic interventions, if indicated. However, for patients with less than a ten-year estimated life expectancy, screening is not likely to provide a benefit in terms of disease-specific or overall mortality. The 95% CI around the relative risk (RR) of prostate cancer mortality between the screening and control groups in ERSPC for patients aged 70 to 74 years excluded any benefit (RR: 1.18; 95% CI: 0.81 to 1.7).[78] Furthermore, the evidence from randomized treatment trials comparing surgery, radiation, and monitoring has shown to have less benefit and more risk from curative treatment with increasing age.[79-82] The risk in overdiagnosis of prostate cancer increases with increasing age.[59, 74, 83, 84] Estimates of overdiagnosis also depend on the study population, design, and estimation methodology.[85] Empirical estimates of overdiagnosis based on excess incidence from randomized screening trials are generally biased and overstate the long-term overdiagnosis risk.[85]

Risk calculators have been developed to estimate a patient's life expectancy and can be informative during SDM. While a number of methods have been applied for estimating life expectancy, a simple approach is to use the social security life tables (https://www.ssa.gov/oact/STATS/table4c6.html). Based on current Social Security Administration (SSA) data, American patients older than 77 years of age have less than a 10-year life expectancy. The Michigan Urological Surgery Improvement Collaborative (MUSIC) has deployed a paper-based life expectancy tool that includes comorbidities (e.g., https://musicurology.com/wp-content/uploads/2022/02/Hawken_et_al-2017-BJU_International.pdf). Insurance companies are known to be particularly astute at estimating life expectancy and many have online calculators that include the use of tobacco, alcohol, physical activities, and comorbidities. For the purpose of estimating life expectancy, the use of these tools is likely more reliable than individual clinician judgment.[86]

The Panel notes most studies regarding baseline PSA have been conducted in populations of primarily White patients. The Southern Community Cohort Study (100% Black patients) showed that PSA levels in midlife were similar to those among White controls in prior studies and were strongly associated with risk of aggressive prostate cancer.[67]

Given the limitations in the range of evidence supporting screening intervals and for discontinuing screening, use of SDM is recommended to assist clinicians in tailoring the decision to each patient. The Agency of Healthcare Research and Quality (AHRQ) has developed a simple approach for SDM that addresses common clinician and patient level barriers called the SHARE approach.[87] This approach recommends clinicians to **Seek** the patient's participation, **Help** patients explore and compare options, **Assess** the patient's values and preferences, **Reach** a decision together with the patient, and **Evaluate** the patient's decision. The use of publicly available decision aids may be helpful in SDM, where available, and are updated to the most current level of evidence.

8. **Clinicians may use DRE alongside PSA to establish risk of clinically significant prostate cancer. (*Conditional Recommendation; Evidence Level: Grade C*)**

The primary screening modality recommended for the early detection of prostate cancer is a PSA blood test. Clinicians should not use DRE as the sole screening method in otherwise asymptomatic patients. This statement does not apply to symptomatic patients where a DRE could be considered a diagnostic exam.

There is insufficient evidence to support adding DRE to PSA-based prostate cancer screening. The PPV of DRE as a screening method to detect prostate cancer is low. In the PROBASE trial, DRE was not effective for early detection; the PPV of a suspicious DRE at 50 years of age was 0.87% (as compared to 4.9% among patients aged 55 to 59 years in PLCO); of the 57 participants with suspicious DRE, 37 were biopsied and only 2 had prostate cancer (both GG1).[41] A recent meta-analysis demonstrated that adding DRE to PSA screening did not significantly improve the PPV compared to PSA screening alone for detection of prostate cancer.[88] The study reported a pooled PPV of 0.21 (95% CI: 0.13 to 0.33) for DRE, which was similar to the PPV of PSA (0.22; 95% CI: 0.15 to 0.30; p=0.9), and no difference in PPV with the combination of DRE and PSA (PPV: 0.19; 95% CI: 0.13 to 0.26; p=0.5).[88]

For various reasons, clinicians may choose to complement PSA screening with DRE based on SDM; however, the evidence base for this practice is weak. In a U.S.-based cohort study, the risk for finding cancer among people with PSA < 4 ng/mL and abnormal DRE was only 3% but the addition of DRE was found to improve detection of higher-grade disease.[89] There are practical considerations for performing DRE in clinical practice, and it may not be acceptable to all patients as compared to a blood draw. Survey data suggest nearly a quarter of patients may forego prostate cancer screening when it includes up-front DRE with PSA testing.[90]

In contrast to a screening application, use of DRE subsequent to the screening encounter may be of value. It has been shown that the greatest utility of DRE in randomized trials is demonstrated in the workup of patients with an elevated PSA. For this reason, among patients with PSA ≥ 2 ng/mL, clinicians should strongly consider supplementary DRE to establish risk of clinically significant prostate cancer. In patients undergoing prostate biopsy for an elevated PSA during screening, abnormal DRE improves the PPV for any prostate cancer and GG2+ detection.[23, 91, 92] In ERSPC Rotterdam, the PPV of a suspicious DRE in conjunction with an elevated PSA level ≥ 3 ng/mL to detect prostate cancer was 48% compared to 22% in patients with a normal DRE. However, the impact of abnormal DRE on PPV became attenuated in the subsequent screening rounds.[91] In PLCO, the absolute difference in the risk of clinically significant prostate cancer at 10 years between patients with suspicious versus non-suspicious DRE was small for patients with PSA < 2 ng/mL (1.5% versus 0.7%), whereas the difference was modestly relevant for patients with PSAs 2 to 3 ng/mL (6.5% versus 3.5%) and clinically relevant for patients with PSA ≥ 3 ng/mL (23.0% versus 13.7%), all statistically significant increases.[93]

9. **For people undergoing prostate cancer screening, clinicians should not use PSA velocity as the sole indication for a secondary biomarker, imaging, or biopsy. (*Strong Recommendation; Evidence Level: Grade B*)**

With knowledge of a patient's age, PSA, DRE, percent free PSA, family history of prostate cancer, and presence of a previous biopsy, large-scale studies in Europe and the U.S. have shown the addition of PSA velocity at various thresholds does not add value in predicting the presence of clinically significant prostate cancer.[94, 95] Therefore, PSA velocity should not be used as sole indication for secondary biomarker, imaging, or a biopsy. Paradoxically, very high PSA velocity (> 3 ng/mL/year) is more closely associated with the presence of inflammation on biopsy rather than cancer.[96]

10. **Clinicians and patients may use validated risk calculators to inform the SDM process regarding prostate biopsy. (*Conditional Recommendation; Evidence Level: Grade B*)**

Contemporary evaluations of prostate cancer risk now typically include patient demographic factors, medical history, family history of prostate cancer, biomarkers, and imaging findings. Simple nomograms in tabular format are suboptimal in presenting risk for more than a few such factors; therefore, several groups have developed risk calculators based on actual patient data that allow patients and clinicians to simultaneously incorporate a larger number of these risk factors. It is beyond the scope of this Guideline to provide an exhaustive review of all published risk calculators, but several discussed by the Panel are listed below, noting that different risk calculators often use different risk factors.[97, 98]

One of the first risk calculators that was widely disseminated was based on the Prostate Cancer Prevention Trial (PCPT).[99] A number of additional datasets and risk factors have since been incorporated.[100] This risk calculator currently includes race, age, PSA, percent free PSA, family history of prostate cancer, DRE, prior biopsy, and urinary Prostate Cancer Antigen 3 [PCA3]. Chun is a comparable risk calculator that likewise includes age, PSA, DRE, prior biopsy, urinary PCA3, and prostate volume.[101] When compared, both of these risk calculators could be applied to estimate the risk of prostate cancer while also reducing the need for a prostate biopsy, although PCPT had higher AUC (0.84).[102] Several data driven risk calculators developed based on a clinical trial were developed in Europe.[103] The ERSPC online tool has several applications ranging from a risk calculator for patients who are interested in screening but have not had a PSA, to a risk calculator that includes age, PSA, DRE, prior biopsy, and prostate volume.[104] More recently, prostate MRI was added to this calculator. When DeNunzio et al. compared PCPT, ERSPC and the Chun risk calculators, they found that Chun outperformed the other 2 when the endpoint was high-grade prostate cancer, defined as GG > 3 (Gleason Score ≥ 4+3=7);[105] however, they only utilized the PSA-only version of the ERSPC risk calculator. In 2018, the Prostate Biopsy Collaborative Group (PBCG) published their calculator based on age, PSA, DRE, Black race, first-degree family history of prostate cancer, and prior negative biopsy.[106]

Table 4: Select Risk Calculators with Risk Factors and Risk Factors Evaluated

	PCPT V2 (https://riskcalc.org/PCPTRC/)	Chun (There is no publicly available online calculator for Chun)	ERSPC (https://www.prostatecancer-riskcalculator.com)	PBCG (https://riskcalc.org/PBCG/)
Race	x			x
Family history of prostate cancer	x			x
Age	x	x	x	x
PSA	x	x	x	x
Free PSA %	x	x		
DRE	x	x	x	x
Prior biopsy	x		x	x
Urinary PCA3	x	x		
TMPRSS2:ERG fusion	x			
Prostate volume		x	x	
Sampling density		x		
MRI – PI-RADS score			x	

Historically, clinicians have expressed concern that using risk calculators and nomograms are cumbersome and difficult to incorporate into practice; however, given the rise of Electronic Medical Records (EMR), and the use of computers in most clinical encounters, web-based risk calculators have become easily accessible for real-time clinical conversations. In the course of discussing prostate cancer risk, clinicians can easily enter pertinent risk information into their choice of risk calculator and produce estimates including likelihood of finding cancer, finding significant cancer, and often with graphics/icon arrays that aid in interpretation of individualized numerical risk data.

While these risk calculators provide estimates that facilitate clinician-patient discussion of detection risk, it should be kept in mind that these are population averages with potentially wide intervals in some subsets. Moreover, the data for a number of these, while extensive, may be based on historic screening and detection approaches (e.g., prior to widespread prostate MRI adoption). Furthermore, calibration of risk calculators may differ by subgroups. In one study, investigators compared PBCG with PCPT and concluded that PCPT performed better in minority groups.[97] One may also wish to use a U.S.-based risk calculator if this more closely resembles their practice population. Thus, clinicians need to incorporate their experience in the final refinement of risk estimates rather than solely relying on any of these risk calculator estimates as certainty.

11. When the risk of clinically significant prostate cancer is sufficiently low based on available clinical, laboratory, and imaging data, clinicians and patients may forgo near-term prostate biopsy. (*Clinical Principle*)

When assessing a patient's risk for prostate cancer, validated online calculators/nomograms may be used to incorporate multiple risk factors (e.g., PSA, family history of prostate cancer, race/ethnicity, age, DRE, percent free PSA, PSA density) to estimate risk of prostate cancer and risk of clinically significant prostate cancer.[107, 108] In many cases, the estimated risk for significant prostate cancer would be considered low as perceived by both the clinician and patient. Therefore, it would be reasonable to forgo a prostate biopsy in such instances following SDM, even where there may be some clinical features that indicate a risk for prostate cancer existing (e.g., mildly elevated PSA). If a decision is made after SDM to forgo a biopsy or additional testing, patients should be informed of their risk for underdiagnosing clinically significant prostate cancer and the need for future follow up screening, as appropriate.

Initial Biopsy

12. Clinicians should inform patients undergoing a prostate biopsy that there is a risk of identifying a cancer, with a sufficiently low risk of mortality, that could safely be monitored with AS rather than treated. (*Clinical Principle*)

A brief pre-biopsy discussion about pathologic findings warranting AS is expected to increase subsequent acceptance of AS by patients and lower rates of treatment. In a multicenter study of patients undergoing a prostate biopsy, GG1 prostate cancer was found in 44% and 61% of initial and repeat positive biopsies, respectively.[109] For low-risk prostate cancer, AS is the preferred management by the AUA and other international Guidelines.[20] However, a statewide registry from Michigan has documented overtreatment among patients with low-risk prostate cancer and less than a ten-year life expectancy.[110] The primary intent of screening and surveillance is to identify higher-grade cancers that may prompt definitive treatment.

13. Clinicians may use MRI prior to initial biopsy to increase the detection of GG2+ prostate cancer. (*Conditional Recommendation*; *Evidence Level: Grade A*)

Studies have demonstrated the clinical value of mpMRI and its use in guiding biopsy decision-making to increase the likelihood of detecting clinically significant prostate cancer while lowering detection of insignificant disease. While this is particularly true in patients with a prior negative prostate biopsy, more recent studies suggest that the mpMRI may have benefit in the screening setting.

The PRECISION trial (Prostate Evaluation for Clinically Important Disease: Sampling Using Image-guidance or Not?) was a randomized non-inferiority study that sought to compare the effectiveness of MRI-targeted versus systematic biopsy in detecting clinically significant prostate cancer in biopsy-naïve patients.[111] This 500-patient trial was performed at 25 centers in 11 countries, using 1.5T or 3T scanners, with or without an endorectal coil. There was no central reading of the MRI prior to biopsy, and biopsies were performed by transrectal or transperineal route, using a cognitive or ultrasound fusion technique. Hence, there was significant uncontrolled variability in reading of the MRI, method of biopsy, and fusion technique. Of patients who underwent an MRI, nearly 70% had a lesion targetable for biopsy (PI-RADS score ≥ 3). Clinically significant prostate cancer was detected in 38% of the patients undergoing mpMRI and 26% of patients undergoing systematic biopsy. Patients undergoing MRI-targeted biopsy also had fewer insignificant cancers detected (9% versus 22%). The agreement between a local and a central read for MRI was 78%, which was considered moderate.

The MULTIPROS trial was a prospective, multicenter randomized study in the United Kingdom enrolling 413 biopsy-naïve patients with clinical suspicion for prostate cancer between 2015 and 2020. All participants underwent prebiopsy mpMRI, and those with suspicious lesions (PI-RADS ≥ 3) were randomized to systematic biopsy alone or combined MRI-targeted plus systematic biopsy. The study found that the combined approach significantly improved detection of clinically significant prostate cancer compared with systematic biopsy alone (adjusted odds ratio [aOR]: 1.79; 95% CI: 1.14 to 2.79; p=0.01). These results underscore that mpMRI guides lesion detection and augments biopsy strategy by increasing the yield of clinically significant cancers.[112]

Subsequent prospective trials in both initial diagnosis and screening settings provide evidence on outcomes among biopsy-naïve patients with negative MRI findings. In a follow-up report of the Göteborg-2 screening trial, a PSA+MRI strategy allowed those with negative MRI to avoid biopsy, leading to more than a 50% reduction in detection of clinically insignificant cancer without an excess of advanced or metastatic disease after a relatively short follow-up of 4 years. The relative risk of detecting clinically significant prostate cancer in the targeted biopsy group compared with the systematic biopsy group was modestly lower (RR: 0.84; 95% CI: 0.66 to 1.07) and not statistically significant.[113]

Similarly, the PROKOMB trial prospectively evaluated an MRI-informed biopsy strategy in biopsy-naïve patients with elevated PSA across multiple German centers. All participants underwent prebiopsy MRI; those with PI-RADS ≥ 3 lesions were recommended for targeted plus systematic biopsy, while those with negative MRI (PI-RADS 1 to 2) were advised to defer biopsy and instead undergo structured surveillance with serial PSA, DRE, and repeat MRI or biopsy only if risk indicators emerged. A total of 593 patients underwent mpMRI with 286 (48%) having negative MRI results, 261 (44%) avoiding biopsy initially, and 242 (41%) avoiding biopsy over 3 years. Of the 286 patients with a negative MRI, 25 (9%) underwent immediate biopsy with detection of 7 (28%) prostate cancers, of which 4 (57%) were GG2+. During three years of structured follow-up, an additional 44 (15%) patients from the negative-MRI group underwent biopsy, and clinically significant prostate cancer was detected in 7 (16%). No cases of metastatic disease were reported over a short monitoring period of 3 years.[114]

The PROBASE trial, a large German population-based, risk-adapted screening study, enrolled approximately 46,000 patients aged 45, who were randomized to immediate or delayed PSA testing as part of a long-term prostate cancer early-detection strategy. In the first screening round, of 186 participants with elevated PSA (≥3 ng/mL), 114 (61%) underwent mpMRI, followed by a combined targeted plus systematic biopsy if the PI-RADS score was ≥ 3. Among these 114 patients, 47 (41%) were diagnosed with prostate cancer, with 33 (29%) having clinically significant disease. For scans interpreted centrally by experienced reference radiologists, using PI-RADS ≥ 4 as the biopsy threshold yielded 79% sensitivity, 91% negative predictive value (NPV), and 85% accuracy for clinically significant cancer. In contrast, local MRI reads performed substantially worse using the same PI-RADS ≥4 threshold: only 55% sensitivity, 80% NPV, and 68% accuracy in identifying clinically significant prostate cancer. Furthermore, interobserver agreement between local and expert readings was moderate (κ=0.41), indicating only modest consistency in MRI interpretation across settings. These results emphasize that the oncologic safety of avoiding biopsy in patients with negative MRI (PI-RADS 1 to 2) depends heavily on high-quality imaging and expert interpretation.[115]

Prospective randomized studies that compared mpMRI driven biopsy to standard systematic biopsy in biopsy-naïve patients, used varying reference standards such as radical prostatectomy findings or saturation biopsy findings to assess the accuracy of mpMRI.[116] Some do not list a reference standard.[117] Data on patients with no MRI-detected, biopsy-eligible lesions, are also not provided but these patients could subsequently be diagnosed with prostate cancer including clinically significant prostate cancer. Different techniques have been utilized to perform MRI-guided biopsy, such as cognitive versus image-guided fusion. Patients in the MRI arm have also undergone standard systematic biopsies in addition to MRI-guided biopsy. In some studies, those with negative MRI results have crossed over to systematic biopsy.[116, 118] For instance, Hugosson et al. sought to examine the independent value of systematic biopsies in patients who had undergone an MRI following an elevated PSA. They found that avoidance of routine systematic biopsies and performing only MRI-directed biopsies reduced the detection of clinically insignificant cancers. However, all individuals in this study underwent an mpMRI, and it did not address the question of the need for routine MRI before biopsy. Patients with a PSA > 10 ng/mL and all patients with a diagnosis of cancer on MRI-guided biopsy were offered systematic biopsies as well. Performance of systematic biopsies did result in detection of clinically significant prostate cancer (including a Gleason 3+5) which was missed on MRI-guided biopsy in a small subset of people.[119]

Importantly, a Cochrane review on this topic pooled data from 18 studies that included biopsy-naïve patients and patients with prior negative prostate biopsy.[120]Analysis of the pooled data suggests the sensitivity of a pre-biopsy MRI is 0.91 (95% CI: 0.83 to 0.95), and specificity is 0.37 (95% CI: 0.29 to 0.46) for GG2+ prostate cancer. The pooled prostate cancer detection ratio for MRI prior to initial biopsy was 1.05 (95% CI: 0.95 to 1.16), which indicates prior MRI may have limited benefit in this setting. However, when considering patients who had undergone pre-biopsy MRI followed by a targeted and systematic biopsy compared to systematic biopsy alone, the pooled analysis found an additional 10 patients (out of 100 biopsied) would be diagnosed with clinically significant prostate cancer. The reference standard utilized for this analysis was detection of clinically significant cancer on template biopsy. The study found there to be significant heterogeneity in study conduct as well as high risk of bias in sample selection and reference standard. Hence, the study authors graded the evidence as low.

While it is reasonable to routinely obtain an mpMRI in biopsy-naïve patients, the dependance of the outcomes on image quality and expert interpretation tempers the enthusiasm for a stronger recommendation. Recognizing this challenge, multiple U.S. initiatives—particularly those led by the American College of Radiology (ACR)—have sought to enhance and standardize prostate MRI through structured quality-improvement collaboratives, education efforts, and accreditation programs that promote high-quality acquisition, interpretation, and reporting across diverse practices.[121] As in the PSA screening setting, the use of SDM is highly recommended given the uncertainty involved.

14. Radiologists should utilize PI-RADS in the reporting of mpMRI. (*Moderate Recommendation; Evidence Level: Grade C*)

Since the development of the first version of PI-RADS in 2012[122] with subsequent versions in 2015 (v2.0)[123] and 2019 (v2.1),[124] the system has been widely adopted and has standardized the reporting of mpMRI. Multiple studies have confirmed PI-RADS score, either on a per lesion or per patient basis, correlates with likelihood of detecting any cancer and GG2+ cancer. **Table 5** summarizes the detection prevalence for any prostate cancer and GG2+ prostate cancer based on the PI-RADS score when 23 studies[125-147] identified by the systematic review were pooled. Of the 23 studies, 10 reported on a per lesion analysis[126, 128, 129, 131, 133, 134, 137, 138, 142, 145] and 13 reported on a per patient analysis using an index lesion.[125, 127, 130, 132, 135, 136, 139-141, 143, 144, 146, 147] While PI-RADS v2.1 provides a structured system for lesion-based scoring approach and has contributed to the wider use of prostate MRI over the last decade, some of the required evaluation criteria remain subjective. As a result, reader variability remains a challenge,[145] especially for novice readers.[148] Reported measures of interobserver agreement for PI-RADS v2.1 include a weighted kappa value of 0.700 for a study with 5 radiologists of varying experience[149] and a Conger kappa value of 0.64 for a study with 6 radiologists of varying experience.[150] While interpretative variability remains a limitation, there is evidence that agreement is greater for PI-RADS v2.1 compared to v2.0 and also greater for more experienced readers.[151] Due to the paucity of data using PI-RADS version 2.1 specifically, pooled estimates in **Table 5** reflect PI-RADS version 1.0 through 2.1. Reader variability is only one of multiple factors that may influence performance differences between sites, including heterogeneity in patient selection, technical factors (e.g., MRI manufacturer and field strength, and use of an endorectal coil), method of prostate biopsy used for pathological correlation, and pathologist expertise and variability. Minimum training requirements to establish reader experience have been proposed and are under investigation.[152, 153] Continued evolution of training criteria and further iterative refinements of the PI-RADS should result in greater accuracy and reader agreement. In the interim, clinicians should interpret PI-RADS scores in the context of known local experience and expertise. This statement applies to both initial and repeat biopsy situations.

Table 5: Prevalence of Prostate Cancer Detection based on PI-RADS Score*

PI-RADS Score	Any Prostate Cancer (% (95%CI))	Clinically Significant Prostate Cancer (% (95%CI))
1 or 2	15% (95%CI: 8% to 22%)	7% (95%CI: 4% to 11%)
3	25% (95%CI: 22% to 29%)	11% (95%CI: 8% to 14%)
4	58% (95%CI: 53% to 63%)	37% (95%CI: 33% to 40%)
5	85% (95%CI: 80% to 90%)	70% (95%CI: 62% to 79%)

*Detection prevalence for both any prostate cancer and clinically significant prostate cancer based on the PI-RADS score when 23 identified studies were pooled using a random-effects inverse-variance method.[125-147] Due to the paucity of data using only PI-RADS version 2.1, pooled studies used version 1.0 through version 2.1.

15. For biopsy-naïve patients who have a suspicious lesion on MRI, clinicians should perform targeted biopsies of the suspicious lesion and may also perform a systematic template biopsy. (*Moderate Recommendation [targeted biopsies]/Conditional Recommendation [systematic template biopsy]; Evidence Level: Grade C)*

In the setting where a prostate MRI identifies a lesion suspicious for cancer (e.g., PI-RADS 3 to 5) among patients who are biopsy-naïve, clinicians will be confronted with a decision to proceed with targeted biopsies along with systematic biopsies, or to proceed with targeted biopsies alone. A number of observational studies have shown a higher detection of clinically significant prostate cancer when both targeted and systematic biopsies are combined.[128, 130, 154-159] In a study of 300 patients with either a PSA ≥ 4 ng/mL or an abnormal DRE, fusion biopsy detected 69%, systematic 12-core biopsy detected 80%, and combination of both yielded 87% of all GG2+ tumors.[155] These and other studies are further supported by a larger study that included a mix of biopsy-naïve patients and patients with prior biopsies. In this study of over 400 biopsy-naïve patients, a combination of targeted and systematic biopsies resulted in 9.9% greater detection of cancer than either approach alone.[160] Further, this study noted that the combination approach resulted in the lowest rate of surgical upgrading (3.5%) in a subset of patients who underwent prostatectomy.[160] It has been hypothesized that systematic biopsies may improve detection of GG2+ cancer in some cases by sampling the target when the targeted cores may have missed the target.[161, 162] Systematic biopsy alone detected 1.9% high-grade cancers (defined as GG3 or higher) that MRI-targeted biopsy failed to detect. In a post hoc analysis of this study, an expert genitourinary radiologist reviewed all the prostate MRIs and tracked the systematic and MRI targeted biopsy cores from these 41 patients. The registration targeting error during the MRI-ultrasound fusion biopsy accounted for 51% of the misses, with MRI invisible lesions or missed MRI lesions by radiology accounting for the remainder.[163] While not widely available, use of an in-bore biopsy approach eliminates the co-registration error but does not allow for systematic biopsy.[164] In contrast, Kim et al. found little difference in detection between the combined approach and targeted cores.[158] In reviewing the literature, the Panel found published studies have used a variety of fusion platforms, biopsy approaches, and systematic templates, making direct comparison prohibitive. In most cases an indication for a fusion biopsy was PI-RADS 3 to 5 findings on MRI. The tradeoff for finding more GG2+ cancer, with adding a systematic biopsy to the target only approach, is that more GG1 cancer will also be diagnosed. In recent publications, this rate has been reported between 1.2% and 5% GG1.[119, 160] Following the literature review window for these Guidelines, a randomized trial comparing targeted biopsy alone versus targeted plus systematic biopsies among patients with PI-RADS 3 to 5 findings on MRI was published.[119] This study demonstrated a 50% reduction in detection of GG1 cancers (absolute reduction from 1.2% to 0.6%), and a 27% reduction in findings of GG2+ cancers (absolute reduction from 1.1% to 0.8%), in the target-only arm. Although the decreased detection of GG2+ cancer detection was not statistically significant, (the study was not powered to detect this difference) it may well be clinically significant.[119] As in the PSA screening setting, use of SDM is highly recommended given the uncertainty involved.

16. For patients with both absence of suspicious findings on MRI and elevated risk for GG2+ prostate cancer, clinicians should proceed with a systematic biopsy. (*Moderate Recommendation; Evidence Level: Grade C*)

In a systematic review of 42 studies, the NPV of a "negative" MRI (defined as PI-RADS 1 to 2) to detect GG2+ prostate cancer among biopsy-naïve patients was 91%.[165] Thus, approximately 1 in 10 patients who have a negative prostate MRI may have GG2+ cancer on biopsy, although rates widely vary by study and the risk factors of the individual person. If the definition of a "negative" MRI was expanded to include PI-RADS 3, then NPV decreased to 87%.[165] Multiple factors contribute to risk calculation, including race, age, total PSA, PSA density, percent free PSA, and family history of prostate cancer, as used in available risk calculators. Therefore, patients with elevated risk for GG2+ prostate cancer and absence of findings on MRI should proceed with a systematic biopsy.

Among the factors to predict clinically significant prostate cancer in patients with negative (PI-RADS 1 to 2) or equivocal (PI-RADS 3) results, PSA density (i.e., serum PSA divided by gland volume) has been the most extensively investigated. Haj-Mirzaian et al. conducted a systematic review and meta-analysis of 72 studies including 36,366 patients to determine the optimal prostate biopsy decision-making strategy for avoiding unnecessary biopsies and minimizing the risk of missing clinically significant cancers by combining MRI PI-RADS scores and clinical data. In patients with negative MRI (PI-RADS 1 to 2), adding PSA density significantly improved the ability to exclude clinically significant prostate cancer. Using a PSA density threshold of 0.15 ng/mL/cc, biopsy could be avoided in up to 67% of patients with GG2+ prostate cancer while maintaining a 94% NPV. Similarly, in those with equivocal MRI (PI-RADS 3), using a PSA density threshold of 0.10 ng/mL/cc, biopsy could be avoided in up to 43% of patients while maintaining a 93% NPV. The strategy to forego biopsy in those with PI-RADS 3 or less and PSA density less than 0.10 ng/mL^2 or less than 0.15 ng/mL^2 would avoid 30% or 48% of unnecessary biopsies, respectively, while maintaining sensitivity of 97% or 95%, respectively. Across analyses, PSA density was consistently the strongest predictor of clinically significant disease in MRI-negative or equivocal cases, outperforming total PSA and other clinical factors. These findings suggest that incorporating PSA density could guide biopsy decisions in patients with negative or equivocal MRI findings, reducing unnecessary procedures.[166]

A systematic biopsy should include a minimum of 12 cores, distributed throughout the prostate, with thorough sampling of the peripheral zone. Various templates employing these principles exist for transrectal and transperineal approaches.[167-170] If a decision is made after SDM to omit a systematic biopsy, patients should be informed of their risk for underdiagnosing clinically significant prostate cancer.

17. Clinicians may use adjunctive urine or serum markers when further risk stratification would influence the decision regarding whether to proceed with biopsy. (*Conditional Recommendation*; *Evidence Level: Grade C*)

There are several blood and urine markers available alone or in combination to further risk stratify patients with a mildly elevated PSA, typically between 2.5 and 10 ng/mL. The intent is to improve upon the poor specificity of PSA and avoid the risks associated with unnecessary biopsies, including the risk of overdiagnosis of GG1 prostate cancer, in patients with a low probability of harboring GG2+ disease. Naturally, with avoidance of biopsies comes the risk of delaying the diagnosis of clinically significant prostate cancer ("false negatives"). Tests that report the likelihood of any prostate cancer, rather than reporting GG2+ prostate cancer are less valuable in terms of ameliorating overdiagnosis of low-grade prostate cancer.

Importantly, such biomarkers should not be used in situations in which, based on available clinical and laboratory data, the risk of GG2+ prostate cancer is so low or so high the result of adjunctive biomarkers would not influence the decision of whether to proceed with further testing (e.g., MRI and/or biopsy). For example, in patients with a prostate nodule, a PSA > 10 ng/mL, a strong family history of high-grade prostate cancer, or other significant risk factors, it is unlikely an adjunctive biomarker would change the decision to proceed with biopsy. In contrast, in a patient with a mildly elevated PSA, a very low PSA density (based on available imaging-based volume measurement), no other risk factors, and a desire to avoid biopsy, ongoing screening rather than further testing is preferable.

Perhaps the most widely available adjunctive test is percent free PSA. Lower percent free PSA is associated with greater likelihood of identifying prostate cancer on biopsy.[171-176] Additionally, it improves upon the prediction of GG2+, primarily in validation studies of multiplex tests that include percent free PSA. For example, in the study validating the use of the 4Kscore™, exclusion of percent free PSA from the model reduced the AUC from 0.821 (95% CI: 0.790 to 0.852) to 0.699 (95% CI: 0.664 to 0.735).[177] Similarly, percent free PSA improves prediction of GG2+ prostate cancer compared to total PSA (AUC 0.661 versus 0.551) in a study demonstrating the value of prostate health index (PHI)™.[178]

Numerous studies have shown that higher PSA density (serum PSA [ng/mL] divided by imaging measures of prostate volume [cc]) is associated with the risk of identifying clinically significant prostate cancer on biopsy.[179-181] Various thresholds have been proposed, with lower thresholds (e.g., PSA density ≥ 0.07) having higher sensitivity, but lower specificity, than higher thresholds (e.g., PSA density ≥ 0.15). Thus, PSA density is an important component of disease risk assessment when imaging is available for volume measurement. However, the Panel recognizes the continuous nature of risk associated with the spectrum of PSA density values and cautions against use of threshold values in isolation for management decision-making.

It is debatable which of the newer biomarkers (alone or in combination) is best, and comparative studies are sparse. A list of available tests for an initial biopsy cohort is summarized in **Table 6**. With this update, **Table 6** now includes additional references describing studies of previously included biomarkers for biopsy-naïve patients.[182] In general, the tests are calibrated such that avoiding biopsy in the setting of a sub-threshold test reduces biopsies by about one third, resulting in delayed detection or non-detection of 5% to 10% of clinically significant prostate cancers.[183] A meta-analysis of studies that met criteria for inclusion in the evidence base for this Guideline showed that use of secondary biomarkers would reduce the number of biopsies by 35% (95% CI: 26% to 44%; $p<0.0001$),[179, 184-195] and 9% (95% CI: 6% to 11%; $p<0.0001$)[179, 181, 184-189, 191-193, 196] of clinically significant prostate cancers would not be detected. A modeling study evaluating several of the tests in the reflex setting (to refer patients with PSA between 4 to 10 ng/mL to biopsy at pre-specified cutoffs) projected that if patients were screened annually the tests would minimally impact life years or quality-adjusted life years compared with all patients with PSA > 4 ng/mL undergoing biopsy.[197] Given their generally significant impact on biopsy reduction and their projected minimal impact on life expectancy, such tests may be of value among patients with modestly elevated PSA tests, especially in patients with a prior negative biopsy in whom PSA alone is not recommended as the sole trigger for re-biopsy. Considerations in selecting a test include test performance characteristics (such as NPV), availability, and familiarity. As in the PSA screening setting, the use of SDM is highly recommended given the uncertainty involved. This statement applies to both initial and repeat biopsy situations.

Table 6: Available Biomarker Assays

Test	Biomarker Component	Clinical Variable	Biopsy Population
Serum			
4Kscore[186, 194, 198-202]	PSA, fPSA, iPSA, hK2	Age, prior biopsy status, DRE (optional)	Initial biopsy[186, 194, 198, 200] Repeat biopsy[199] Mixed[201, 202]
IsoPSA[203-206]	All PSA isoforms	None	Mixed[203-206]
Proclarix[207-209]	THBS1, CTSD, PSA, fPSA	Age, prostate volume (optional)	Mixed[207-209]
PHI[179-181, 184, 194, 210-218]	p2PSA, fPSA, PSA	None	Initial biopsy[179-181, 184, 194, 213-216] Repeat biopsy[210-212] Mixed[217, 218]
STHLM-3[23, 219-221]	232 genetic polymorphisms (single nucleotide polymorphisms [SNPs]), PSA, fPSA, iPSA, hK2, MSMB, MIC1	Age, family history, previous biopsy, DRE (optional)	Initial biopsy[220] Mixed[23, 219, 221]
Urine			
PCA3[180, 185, 187, 196, 222-225]	PCA3	Some studies add age, PSA, prostate volume	Initial biopsy[180, 185, 187, 196, 222, 223] Repeat biopsy[224, 225]
SelectMDx[191, 226, 227]	HOXC6, DLX1 mRNA	Age, PSA, prostate volume, DRE	Initial biopsy[191, 226, 227]
TMPRSS2:ERG[223]	TMPRSS2:ERG	None	Initial biopsy[223]
ExoDx Prostate Intelliscore[192, 193, 195, 228-230]	PCA3, ERG, SPDEF mRNA	None	Initial biopsy[192, 193, 195, 229, 230] Repeat biopsy[228]
MyProstateScore 2.0 (MPS2)[182]	TMPRSS2:ERG, SCHLAP1, OR51E2, APOC1, PCAT14, CAMKK2, PCA3, NKAIN1,	Age, race, DRE, PSA, family history, previous biopsy	Initial biopsy[182] Repeat biopsy[182]

Test	Biomarker Component	Clinical Variable	Biopsy Population
	B3GNT6, TFF3, SPON2, PCGEM1, TRGV9, TMSB15A, ERG, KLK4, HOXC6, KLK3		Mixed[182]
MiR Sentinel[231]	Small non-coding RNAs	None	Mixed[231]
Tissue			
Confirm MDx[232, 233]	Hypermethylation of GSTP1, APC, RASSF1	None	Repeat biopsy[232, 233]
(Abbreviations: DRE, digital rectal exam; fPSA, free PSA; iPSA, intact PSA; mRNA, messenger ribonucleic acid; PSA, prostate-specific antigen; SNP, single nucleotide polymorphism.)			

In addition to the biomarkers in **Table 6**, PRSs that are based on SNPs measured in saliva or blood are genetic tests used to predict a person's risk of developing prostate cancer. Various combinations of SNPs have been mathematically integrated to produce several commercially available options. There is little evidence to mandate which SNP panel or PRS to use and where to threshold risk to create strata with different screening frequencies. The endpoint of the majority of studies on PRS has mainly focused on any detection of prostate cancer, not clinically significant, or metastatic/lethal prostate cancer. Few PRS scores have been shown to discriminate between aggressive and indolent prostate cancer risk.[234] Calculating a PRS based on genotypes of 66 known prostate cancer loci for 4,967 patients in the ERSPC, the rate of overdiagnosis (e.g., detection of GG1) of screen-detected cancers was 42%, with 58% of these found in the lower PRS risk group and 37% in those with higher PRS risk.[235] Adding SNPs to STHLM-3 added 1% to the AUC (from 0.75 to 0.76) for GG2+ (Gleason Score ≥ 7) after the clinical information and protein biomarkers.[219] The ongoing large-scale BARCODE-1 trial invited individuals to obtain prostate cancer screening using PRS and recently published the primary outcome. The participation rate was low (22%), which limits generalizability.[3, 236] Of over 40,000 patients invited, 6,393 participated and had a PRS calculated, of whom 745 (12%) were in the top 10% of PRS (i.e., elevated risk). Among those, about half (n=468) underwent an MRI and prostate biopsy, irrespective of PSA and 40% (187/468) had prostate cancer, half of which were considered clinically significant. However, whether PRS testing without PSA improves risk stratification of early detection strategies and favorably balances the risks of unnecessary biopsy, overdiagnosis and detection of clinically significant prostate cancer as compared to other currently available strategies, is unclear.[3] It is also important to note that PRS has largely been developed from European-ancestry genome-wide association studies, and their performance across other ancestries remains variable, underscoring the need for careful cross-ancestry calibration and multi-ancestry research. At present, PRS should not independently dictate prostate imaging or biopsy decisions outside of structured screening programs, as their clinical utility in isolation remains limited. Ongoing research efforts focus on the role of PRS in distinguishing aggressive versus indolent prostate cancers.

18. **For patients with a PSA > 50 ng/mL and no clinical concerns for infection or other cause for increased PSA (e.g., recent prostate instrumentation), clinicians may omit a prostate biopsy in cases where biopsy poses significant risk or where the need for prostate cancer treatment is urgent (e.g., impending spinal cord compression). (*Expert Opinion*)**

For patients with a PSA > 50 ng/mL and no evidence of inflammation, infection, recent instrumentation or catheterization, the likelihood of high-grade prostate cancer has been estimated to be as high as 98.5%.[237] Therefore, in situations where biopsy may be risky (e.g., anticoagulation, significant comorbidity, frailty) or delay urgent treatment (e.g., spinal cord compromise from metastases), immediate biopsy can be delayed or omitted. The extremely high risk of prostate cancer should be shared with the patient, and SDM should be used in the decision on whether to omit an immediate prostate biopsy. This recommendation does not exclude the potential to proceed with biopsy or other prostate cancer evaluation, if deemed clinically appropriate. In addition, it does not obviate the need for biopsy at a later time (e.g., required for treatment, insurance, genetic testing). Imaging to establish extent of disease or confirm metastasis may be helpful if an immediate biopsy is not performed.

Repeat Biopsy

19. **Clinicians should communicate with patients following biopsy to review biopsy results, reassess risk of undetected or future development of GG2+ disease, and mutually decide whether to discontinue screening, continue screening, or perform adjunctive testing for early reassessment of risk. (*Clinical Principle*)**

20. **Clinicians should not discontinue prostate cancer screening based solely on a negative prostate biopsy. (*Strong Recommendation; Evidence Level: Grade C*)**

21. **After a negative biopsy, clinicians should not solely use a PSA threshold to decide whether to repeat the biopsy. (*Strong Recommendation; Evidence Level: Grade B*)**

22. **If the clinician and patient decide to continue screening after a negative biopsy, clinicians should re-evaluate the patient within the normal screening interval (two to four years) or sooner, depending on risk of clinically significant prostate cancer and life expectancy. (*Clinical Principle*)**

23. **At the time of re-evaluation after negative biopsy, clinicians should use a risk assessment tool that incorporates the protective effect of prior negative biopsy. (*Strong Recommendation; Evidence Level: Grade B*)**

Following a prostate biopsy, clinicians should not only share biopsy results with patients but also make recommendations for further follow-up. Routine management after a negative biopsy would be resumption of screening. The time frame for next evaluation should mirror the standard screening interval, such that a patient should be re-evaluated within two to four years or sooner, typically with a PSA (**see Statement 6**).

While negative prostate biopsy significantly lowers the probability of subsequently identifying GG2+ prostate cancer, the protective effect of a negative biopsy likely subsides over time since prior biopsy. Patients with a prior negative biopsy remain at risk for undetected or subsequent development of GG2+ disease. The systematic review performed for this Guideline, has shown that 5% to 25% of patients who undergo a subsequent biopsy in the short term are diagnosed with GG2+ disease.[238-246] Additionally, over a 20-year time horizon, the risk of prostate cancer mortality ranges from 1.4% to 5.2%.[247, 248] Therefore, a negative biopsy alone should not be used to justify discontinuation of prostate cancer screening.

PSA level alone should not be used to decide whether to repeat the prostate biopsy in patients with a previous negative biopsy.[106] While PSA does factor into risk calculation, it should not be used exclusively to justify repeat biopsy, especially if the original biopsy was prompted by an elevated PSA, because this can result in repeated unnecessary biopsies. If concern remains elevated for GG2+ based on PSA density, previous MRI findings, or other factors, the clinician and patient may consider adjunctive testing (blood, urine, or tissue tests), or MRI (if not previously performed) to further risk stratify the patient and guide further management.

The likelihood of identifying GG2+ disease on subsequent biopsy has been associated with a few factors, including age, Black race, total PSA, percent free PSA,[107] PSA density,[249] abnormal DRE findings, presence of germline mutations, pathology findings on prior biopsy (e.g., AIP), results of available adjunctive testing, number of cores taken at initial biopsy, MRI findings, planned method of subsequent biopsy (e.g., number of cores, saturation, template mapping),[238-246] and family history.[106] Previous biopsy reduces the risk of identifying GG2+ disease on subsequent biopsy and should be considered in decisions about further management.[106]

Given the multiple factors involved in computing the risk of GG2+ disease, the Panel recommends use of a risk calculator (**see Statement 10**) that incorporates standard factors, with or without additional factors.[106, 107, 249, 250] (**see Table 4**)

For example, in a patient with a low risk of GG2+ disease based on risk calculation, the clinician and patient may decide to discontinue further prostate cancer screening (**see Statement 7**). Although, in a standard/high-risk patient, the clinician and patient may resume interval screening with or without adjunctive testing and/or repeat biopsy. As in the PSA screening setting, the use of SDM is highly recommended given the uncertainty involved.

24. After a negative initial biopsy in patients with low probability for harboring GG2+ prostate cancer, clinicians should not reflexively perform biomarker testing. (*Clinical Principle*)

The goal of early detection is to identify patients at high risk for harboring GG2+ prostate cancer. While biomarkers may improve the capacity to identify patients at risk for high-grade disease, these tests generally provide the probability of disease or high-grade disease as discussed previously (**see Statement 17**). In patients with a negative biopsy, with low probability for GG2+ disease, it is unlikely that additional biomarker tests will be informative. For example, a low PSA density (≤ 0.10 ng/mL^2) at the time of initial prostate biopsy is associated with a low likelihood of harboring GG2+, including in the setting of negative or equivocal mpMRI.[251, 252] It is unlikely a biomarker test will provide any additional clinically actionable information in this scenario. Thus, clinicians should not implement reflex biomarker testing without prior consideration to the utility of the test or how the information gathered will impact the decision to undergo repeat biopsy.

25. After a negative biopsy, clinicians may use blood-, urine-, or tissue-based biomarkers selectively for further risk stratification if results are likely to influence the decision regarding repeat biopsy or otherwise substantively change the patient's management. (*Conditional Recommendation; Evidence Level: Grade C*)

Blood-, urine-, or tissue-based biomarkers may provide additional information for risk stratification in patients with a prior negative biopsy and with ongoing suspicion for GG2+ prostate cancer. Several blood-, urine-, and tissue-based biomarkers have been developed and reported in several studies with varying performance characteristics. These tests generally present percentage risk of biopsy-detectable disease (and/or GG2+), and it is up to the clinician and patient to decide on the threshold for proceeding with a biopsy with consideration given to the performance metrics of the test. For example, the proportion of GG2+ prostate cancer missed by 4Kscore at ≥ 10%, 15%, and 20% threshold were 5%, 16%, and 16%, respectively, which might impact a patient's decision to pursue a repeat prostate biopsy.[199] In another example, a validation study showed that using a threshold of 40 for MPS would result in 95% NPV and avoid 67% of biopsies among those considering repeat prostate biopsy.[253] The MPS2 urine-based biomarker may help avoid half of biopsies while maintaining 95% sensitivity for GG2 cancer detection.[182] Additionally, there is significant heterogeneity in the outcomes reported for these biomarkers. For example, ConfirmMDx, the only tissue-based biomarker assessing epigenetic changes in *GSTP1, APC, RASSF1* in negative biopsy tissue was developed in the MATLOC study[254] and validated in the DOCUMENT[255] study to detect any prostate cancer and not specifically for GG2+ disease. Moreover, how to integrate the use of these tests with mpMRI in prostate cancer early detection paradigms is yet to be studied comprehensively.[211, 212, 256] In a study, combining mpMRI with PHI improved the NPV of mpMRI from 78% to 95% and AUC from 0.64 to 0.75 for detecting GG2+ cancer.[211] In a recent study, MPS was shown to be significantly associated with GG2+ cancer across all PI-RADS scores inclusive of PI-RADS 3 lesions.[256] Pending future prospective validation studies, biomarkers may augment mpMRI for identifying patients for prostate biopsy especially in patients with negative or equivocal mpMRI findings but with ongoing suspicion for GG2+ cancer. It is imperative clinicians are familiar with biomarkers, understand what information or data each test provides, and consider whether additional information will impact management decisions before ordering a test. As in the PSA screening setting, the use of SDM is highly recommended given the uncertainty involved.

26. In patients with focal (one core) HGPIN on biopsy, clinicians should not perform immediate repeat biopsy. (*Moderate Recommendation; Evidence Level: Grade C*)

The risk of cancer detection following a diagnosis of HGPIN has evolved. Early reports that utilized less than 12-core systematic sampling often found a high risk of undetected prostate cancer.[257, 258] However, contemporary studies indicate a 20% to 30% risk of any cancer detected (not just high-grade) in subsequent biopsies,[246, 259-265] which is the same risk following an initial benign biopsy. Even when repeat biopsy is performed, the risk of GG2+ carcinoma is relatively low (~10%).[259, 261, 262, 264, 265] As such, immediate repeat biopsy is not recommended for patients with a diagnosis of focal HGPIN on initial biopsy.[266] Nonetheless, routine follow-up is warranted, which may include mpMRI and/or additional biomarkers (**see Statements 25 and 30**). Patients with a diagnosis of HGPIN in the setting of other biopsy cores showing invasive prostate cancer should be managed in accordance with the definitive carcinoma component.

27. In patients with multifocal HGPIN, clinicians may proceed with additional risk evaluation, guided by PSA/DRE and mpMRI findings. (*Expert Opinion*)

Relatively few studies on the risk of prostate cancer following an initial diagnosis of HGPIN have focused on multifocal HGPIN (e.g., HGPIN in ≥ 2 cores). Older reports suggest a higher risk of cancer detection for multifocal HGPIN (approximately 30% to 45%), compared to isolated HGPIN.[246, 259, 267] However, these studies lacked repeat biopsy with mpMRI and did not specify the detection of clinically significant prostate cancer. More recent data with repeat biopsy done with mpMRI guidance demonstrate that in approximately 25% of patients with previous multifocal HGPIN, serum PSA and/or DRE are normalized after the non-cancer bearing prostate biopsy.[268] The risk of GG2+ detection in repeat biopsies of patients with multifocal HGPIN is approximately 30%, which is not higher than in those without this finding.[268] In patients with persistent prostate cancer suspicion, the risk of detecting clinically significant prostate cancer in repeat prostate biopsies, based on PSA and DRE, is independent of the previous finding of HGPIN. Thus, a recommendation to repeat a prostate biopsy after HGPIN should be based on PSA and DRE evolution, and mpMRI findings. Due to a lack of data stating otherwise, repeat prostate biopsy should not be recommended solely because of a previous diagnosis of HGPIN, even if multifocal. As in the PSA screening setting, the use of SDM is highly recommended given the uncertainty involved.

28. In patients with ASAP, clinicians should perform additional testing, which may include repeat biopsy. (*Moderate Recommendation; Evidence Level: Grade C*)

In routine pathology reports, ASAP is synonymous with a small focus (or foci) of atypical glands suspicious, but not definitive, for a diagnosis of carcinoma.[269-271] An ASAP finding alone on needle biopsy is associated with a 30% to 50% risk of prostate cancer detection on repeat biopsy,[246, 258, 262, 266, 269-276] with approximately 10% to 20% of these being GG2+.[258, 274-276] A recent meta-analysis reported that following a diagnosis of ASAP on initial biopsy, the pooled incidence rate of GG2+ cancer detection on repeat biopsy was 12%.[277] MRI guidance was rarely used for the initial biopsy for many patients in this study. Nevertheless, based on this study, the previous Expert Opinion can now be considered a Moderate Recommendation, and now includes repeat biopsy among options for repeat testing. Less information is available on the risk of prostate cancer detection following an ASAP diagnosis in patients for whom MRI-targeted biopsy was included in the initial biopsy. Given these risks, additional testing should be considered following an ASAP diagnosis, which may include repeat systematic needle biopsy with consideration of mpMRI +/- targeted biopsy, PSA, as well as urine-, serum-, or tissue-based biomarkers (**see Statements 25 and 30**). Evidence is limited regarding the optimal tests to use in this setting. Regarding repeat testing, including biopsy, there is limited evidence on optimal timing following an ASAP diagnosis. Patients with a diagnosis of ASAP in the setting of other biopsy cores showing invasive prostate cancer should be managed in accordance with the definitive carcinoma component.

29. In patients with AIP, clinicians should perform additional testing. (*Expert Opinion*)

AIP describes lesions with greater architectural complexity and/or cytologic atypia than would be expected in HGPIN but lacking definitive criteria for the diagnosis of intraductal carcinoma (IDC-P).[278-282] AIP encompasses many of the lesions formerly designated cribriform HGPIN, exhibiting loose cribriform architecture with moderate cytologic atypia, but lacking marked pleomorphism or necrosis.[278, 279] AIP, like IDC-P, is usually seen in the context of GG2+ cancer, but uncommonly, may be seen as a sole finding on biopsy or in association with GG1 cancer only. Although there are no prospective studies or those with extended follow-up, available data suggest a close association with unsampled IDC-P[280, 282] and similar adverse pathologic characteristics as IDC-P in patients who went onto radical prostatectomy.[281, 282] Given these associations, a diagnosis of AIP as either the sole finding or together with GG1 cancer only warrants additional testing, which may include early repeat systematic needle biopsy or MRI +/- targeted biopsy. The timing of additional testing should be based on reassessment of risk and SDM. Patients with a diagnosis of AIP in the setting of other biopsy cores showing clinically significant prostate cancer should be managed in accordance with the definitive carcinoma component. As in the PSA screening setting, the use of SDM is highly recommended given the uncertainty involved.

30. In patients undergoing repeat biopsy with no prior prostate MRI, clinicians should obtain a prostate MRI prior to biopsy. (*Strong Recommendation; Evidence Level: Grade C*)

Repeat biopsy is generally performed when there remains ongoing concern for GG2+ prostate cancer. One role for an MRI is to evaluate for suspicious lesions for targeted biopsy that may have been missed on a prior biopsy. In patients with a prior negative systematic biopsy, MRI will show a suspicious target (variably defined) in 36% to 90% of patients and a biopsy directed to the target will be positive in 37% to 66% of patients,[283-287] and positive for GG2+ cancer in 21% to 60% of patients.[284, 286, 287] In patients with a prior biopsy showing only GG1 disease, MRI will show a suspicious target (variably defined) in 33% to 51% of patients and a biopsy directed to the target will be positive for GG2+ disease in 49% to 90% of patients.[156, 287-289] Given the substantial rates of suspicious target identification and PPV for GG2+ disease in the repeat biopsy setting, an mpMRI is recommended if there was no prior imaging.

31. In patients with indications for a repeat biopsy who do not have a suspicious lesion on MRI, clinicians may proceed with a systematic biopsy. (*Conditional Recommendation; Evidence Level: Grade B*)

Repeat biopsy should be used judiciously after an initial negative biopsy, as repeat biopsy detects fewer and less lethal cancers. Medicare data show 38% of patients with an initial negative biopsy of the prostate undergo a repeat biopsy within 5 years, and the percentage of positive biopsies falls from 34% for the first biopsy to 25% for the second.[290] Nevertheless, many patients have indications for repeat biopsy. Factors that may identify patients likely to have clinically significant prostate cancer after a negative biopsy and a negative MRI include a PSA density > 0.15 ng/mL,[291] a PHI density value > 0.44,[292] or a PSA velocity of 0.27 ng/mL/year or greater.[293] MRI can be an important factor in the decision to perform a repeat biopsy, although a meta-analysis of 29 eligible studies with 8,503 participants[294] suggested mpMRI misses 13% of all cancers. Thus, if a patient has sufficient risk of GG2+ cancer with a negative prostate MRI, clinicians may proceed with systematic biopsy.

32. In patients undergoing repeat biopsy and who have a suspicious lesion on MRI, clinicians should perform targeted biopsies of the suspicious lesion and may also perform a systematic template biopsy. (*Moderate Recommendation [targeted biopsies]/Conditional Recommendation [systematic template biopsy]; Evidence Level: Grade C)*

In the repeat biopsy setting with targeted and systematic biopsy, the frequency of cancer found in systematic biopsy samples range from 5% to 10% across multiple studies.[160, 295, 296] While these results suggest a combined biopsy with systematic and targeted cores optimizes cancer yield, such an approach entails obtaining a larger number of cores, which may increase patient discomfort and other biopsy-associated complications,[297, 298] and the apparent incremental yield of off-target biopsy samples may be influenced by the sampling error associated with software image registration at targeted biopsy.[299] Ultimately, the decision to perform systematic sampling in addition to target sampling should be based on an integrated evaluation of MRI factors such as quality and confidence in target presence and clinical factors such as PSA, technique of initial biopsy, and time since prior systematic biopsy.

Biopsy Technique

33. Clinicians may use software registration of MRI and ultrasound images during fusion biopsy, when available. (*Expert Opinion*)

Targeted prostate biopsy of a visible lesion on mpMRI can be performed using software-based registration of mpMRI images and real-time ultrasound or cognitive registration. Other than in 1 RCT[300] where software-based registration demonstrated better cancer detection rate (CDR) compared with cognitive registration (33.3% versus 19.0%; p=0.016), both approaches have been shown to have similar CDR in multiple studies,[301-304] inclusive of an RCT showing no difference in CDR of software-based versus cognitive fusion or in-bore MRI targeted biopsy.[305] Nonetheless, use of software registration facilitates the fusion of multiple MRI and ultrasound images in two to three planes, allowing for the creation of a composite image that provides a more comprehensive view of the target lesion. Thus, clinicians with relevant training and experience may use software-based registration of mpMRI and ultrasound images during fusion biopsy, when available, especially for small MRI lesions. There are drawbacks, however, to implementing software-based fusion biopsy program. There are technical issues (e.g., software bugs, system crashes), operator error, and unusual anatomy (e.g., large prostates, previous transurethral resections of the prostate). Thus, the ability to perform cognitive fusion techniques using anatomic fiducial markers such as intraprostatic cysts may augment software-based fusion approaches in some cases such as to minimize the risk of misregistration. Clinicians who adopt the cognitive fusion technique exclusively should undergo advanced training in MRI interpretation to optimize cancer detection.

34. Clinicians should obtain at least two needle biopsy cores per target in patients with suspicious prostate lesion(s) on MRI. (*Moderate Recommendation; Evidence Level: Grade C*)

The optimal number of biopsy cores per MRI target may differ based on multiple factors including patient characteristics (e.g., age, PSA, biopsy naïve versus prior biopsy), target characteristics (e.g., size, location, PI-RADS classification), and biopsy approach/technique (e.g., software fusion versus cognitive fusion, transrectal versus transperineal).[306] In general, higher number of biopsy cores per target improves the CDR at the potential expense of increased complication rate and time.[307] However, the incremental value in cancer detection is diminished after obtaining more than three cores per target.[307, 308] In patients with a suspicious prostate lesion(s) by MRI, at least two needle cores per target provides the most reproducible and accurate CDR. For prostate cancer risk group stratification, all cores from the same MRI target should be considered as a single core.[309]

35. Clinicians may use either a transrectal or transperineal biopsy route when performing a biopsy. (*Conditional Recommendation; Evidence Level: Grade B*)

In patients with a suspicion for GG2+ prostate cancer who are undergoing biopsy, the CDRs associated with transrectal versus transperineal biopsy route are not significantly different.[168, 310] Prior data from case series suggested that transperineal biopsy may detect anterior and apical cancers at a higher rate or yield longer cancer core length and percentage of core involvement.[311-313] However, 2 subsequent meta-analyses, 1 of 11 retrospective series[311] and another of 3 randomized controlled studies[314] do not suggest a difference in the overall detection rates of clinically significant prostate cancer between the transperineal or transrectal biopsy approaches. Data from the pre- and post-MRI guided biopsy era suggest that similarity in cancer detection rates is consistent regardless of the use of MRI imaging.[315] In the PERFECT trial, Ploussard et al. found that transrectal biopsies may have a higher rate of detection for peripheral zone cancers, while transperineal biopsies may be better at detecting anterior zone cancers.[316] The most recently reported randomized trial on this topic, the TRANSLATE study, fell outside the search range for the updated search conducted in 2024.[317] Data from the TRANSLATE suggest that the study was powered to demonstrate a difference of 10% in detection rate of Gleason GG2+ prostate cancer between those undergoing local anesthetic transperineal prostate biopsy (LATP) versus transrectal ultrasound (TRUS) guided biopsies. The actual difference detected was 6%. Almost all the differences between the groups favoring LATP biopsy was from a higher level of detection of GG2 cancer (52.8% versus 45.7%) with no differences between groups for detection of GG3+ prostate cancer. There was no difference in overall complication rates between the groups including infection requiring hospital admission. Local pain was higher among those undergoing LATP. All patients undergoing TRUS biopsy received antibiotic prophylaxis compared to only 11% in the LATP group. Per prespecified subgroup analysis, lesion site did not seem to affect detection rates, and the only significant variable was prostate volume with detection rate by LATP being higher in those with prostate volume < 50 cc. Prior meta-analyses and retrospective reviews of single center data suggest a lower risk of infections with the transperineal approach; however, these data are not entirely substantiated by recently reported RCTs (0.8% to 2.6% versus 0% to 2.7%; transperineal versus TRUS biopsies, respectively) including the recently reported TRANSLATE study (<1% versus 2%; transperineal versus TRUS biopsies, respectively).[316-320] One has to acknowledge, however, that the usage of antibiotic prophylaxis is significantly lower to none in those undergoing transperineal biopsies.

The three RCTs comparing transperineal and transrectal prostate biopsy had different primary endpoints and trial designs. The PREVENT trial[320] and the PROBE-PC trial[318, 319] were superiority trials aiming to demonstrate a difference in infectious complication rates of 0.4% versus 5% or 0.8% versus 4%, respectively, in the two trials, between the transperineal and the transrectal biopsy arms.[318, 320] The PERFECT trial was a non-inferiority trial aimed at demonstrating equivalence in detection of clinically significant prostate cancer between transperineal and transrectal biopsy arms.[316] It is noted that two of the three (PREVENT and PERFECT trials) and many of the recent studies on this subject have used patients exclusively undergoing MRI-guided prostate biopsies.[314] Antibiotic regimen also varied between the two trials aimed at demonstrating differences in infection rates (PREVENT and PROBE-PC trials).[314] In the PREVENT trial, patients undergoing transperineal biopsy did not receive any antibiotics, whereas those undergoing transrectal biopsy received prophylactic antibiotics based on prebiopsy rectal swab culture. In the PROBE-PC study, those undergoing transperineal biopsy received prophylactic antibiotics based on surgeon assessment of high risk (4/367 patients) while all patients undergoing transrectal biopsy received either 1 day of oral antibiotics or a combination of oral antibiotics and intramuscular antibiotics. The incidence of infection was not statistically significantly different between the two arms in any of the three randomized trials. It is also unclear if the administration of routine prophylactic antibiotics versus rectal swab directed antibiotics significantly impacts the occurrence of infectious complications.[321, 322] There was one episode of sepsis in the PERFECT trial in the transrectal biopsy arm. The overall incidence of infectious complications of any kind was approximately 2% in either the transperineal or transrectal biopsy group.[314] Some cohort studies do indicate a higher rate of urinary tract infections even with antibiotic prophylaxis in the transrectal biopsy patients.[323] It is to be noted that the other potential complication of urinary retention was not statistically different between the transrectal or transperineal biopsy groups; rectal bleeding was more common among those undergoing transrectal biopsies, as was the incidence of prolonged hematospermia. Pain, particularly persistent pain, was more common among those undergoing transperineal biopsy versus transrectal biopsy.[320, 324, 325] Use of transperineal biopsies may have specific value in patients who have experienced infectious complications with a prior biopsy, are at higher risk for biopsy-related infection, or have anterior lesions that may not be as easily accessible transrectally. There are multiple RCTs listed in clinicaltrials.gov that address these and other questions (https://clinicaltrials.gov/ct2/show/NCT04815876, https://clinicaltrials.gov/ct2/show/NCT05179694, https://clinicaltrials.gov/study/NCT05763355) and the results are pending.

Given the concern surrounding the rising rate of sepsis and antibiotic resistance, using transperineal biopsy to mitigate these concerns is a reasonable approach and is gaining traction. The lack of definitive results supporting the superiority of the transperineal biopsy approach either for clinically significant cancer detection or for reduction of infection rates render it difficult to exclusively emphasize the transperineal approach over the transrectal approach at this time. The transperineal approach requires specific equipment such as a biplanar linear side firing probe, precise delivery of local anesthetic, training in localization and other accessories which can facilitate the procedure. On the other hand, use of transrectal approach may be appropriate in certain situations (e.g., patient preference/comfort, patient cannot be placed into the lithotomy position, clinician training/experience or lack of appropriate equipment for the transperineal approach). Moreover, use of adjunctive measures (e.g., rectal swab cultures, augmented antibiotic approaches) to reduce sepsis for a transrectal biopsy approach have also been shown to reduce sepsis and have been effective in the randomized trials as well as in several retrospective studies, with lower than expected cases of infection complications including sepsis.[326]

FUTURE DIRECTIONS

Screening and diagnosis of prostate cancer remain intensely debated topics with major implications for individual and population health. There continue to be many unanswered questions that can prompt future research, preferably in the form of clinical trials and modeling studies to enhance and optimize patient care. Future trials will hopefully prioritize inclusion of historically underrepresented populations.

SDM regarding whether to screen, how frequently, and when to proceed to secondary testing (e.g., imaging or biomarkers) or biopsy is critically important. However, clinicians tend to discuss potential benefits of screening far more frequently than potential harms.[327] There is an unmet need for decision aids in multiple languages for persons at various levels of health literacy which clearly and comprehensively inform the patient of potential benefits and harms.

For populations at higher risk of being diagnosed with prostate cancer, such as those with a concerning family history of prostate cancer, Black race, genetic risk, or elevated baseline PSA, a targeted and perhaps more intensive screening warrants further investigation and is the focus of ongoing clinical trials (e.g., NCT04472338, NCT05129605). Additionally, investigation of novel approaches is strongly encouraged which may have operating characteristics which outperform currently available tools. Conversely, to minimize overdetection rates, people with a very low likelihood of clinically significant prostate cancer may benefit from less intensive or discontinuation of screening.

Although emerging data exist, a far more comprehensive understanding is required of the impact of race and ethnicity on the operating characteristics of PSA, secondary biomarkers, and prostate imaging. It is also essential to recognize many people undergoing screening are of mixed (or unknown) race and ethnicity. Since dramatic disparities exist regarding access and affordability of certain diagnostic or imaging modalities, efforts should be made by clinicians, payors, and health care systems to bridge this gap.

For non-binary patients or transgender women there is a lack of data on prostate cancer screening preferences, if and when to initiate, the accuracy of biomarkers (e.g., PSA, secondary biomarkers, MRI), potential psychological consequences, impact of gender-affirming hormonal therapy, and priorities regarding management options.[328] Considerably more effort and research are required.

While there are a plethora of serum, urine, tissue, and imaging biomarkers to assess the likelihood of high-grade prostate cancer, there is little knowledge on comparative effectiveness, how they may complement or supplement each other, and how various stepwise algorithms perform. Considerable research is required to achieve the goal of a highly effective, practical, scalable, and widely available approach.

While this update extensively reviewed emerging data surrounding MRI imaging of the prostate, other imaging technologies, such as micro-ultrasound, have shown similar promise in the detection of clinically significant prostate cancer in patients with elevated PSA.[329] Furthermore, no imaging technique has been shown to impact meaningful long-term outcomes such as cancer-specific mortality. Even with growing clinical experience with mpMRI and fusion biopsies, there remain some cases concerning GG2+ cancer where the targeted biopsy either did not detect cancer or only detected GG1 disease. While this may be due to false positive mpMRI reading, it is also possible that the lesion was under-sampled (e.g., small target in a difficult to access location), and the use of perilesional + lesion-only biopsies is being investigated in retrospective data. On a practical level, the impact of interobserver variability and reliance on high-quality imaging and expert interpretation have been highlighted by recent studies. As such, the future directions in the imaging domain will focus on evolving MRI protocols, such as biparametric MRI, and the use of computer-aided and artificial intelligence-enhanced interpretation of MRI-acquired prostate anatomic and radiomic imaging.[121, 330]

ABBREVIATIONS

95%CI	95% confidence interval
5-ARI	5-alpha reductase inhibitor
ACR	American College of Radiology
AHRQ	Agency of Healthcare Research and Quality
AIP	Atypical intraductal proliferation
AMSTAR	Assessment of Multiple Systematic Reviews
aOR	adjusted odds ratio
AS	Active surveillance
ASAP	Atypical small acinar proliferation
AUA	American Urological Association
AUAER	American Urological Association Education and Research, Inc.
AUC	Area under the curve
BOD	Board of Directors
CDR	Cancer detection rate
DRE	Digital rectal exam
EMR	Electronic medical records
ERSPC	European Randomized Study of Screening for Prostate Cancer
GG	Grade Group
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HGPIN	High-grade prostatic intraepithelial neoplasia
hK2	Human kallikrein 2
IDC-P	Intraductal carcinoma of prostate
LATP	Local anesthetic transperineal prostate biopsy
MIC-1	Macrophage inhibitory cytokine-1
mpMRI	multi-parametric magnetic resonance imaging
MPS	MyProstateScore
MRI	Magnetic resonance imaging
MSMB	Microseminoprotein-beta
MUSIC	Michigan Urological Surgery Improvement Collaborative
NND	Number needed to diagnose
NNS	Number needed to screen
NPV	Negative predictive value
PBCG	Prostate biopsy collaborative group
PCA3	Prostate Cancer Antigen 3
PCPT	Prostate cancer prevention trial
PGC	Practice Guidelines Committee
PHI	Prostate health index
PICOTS	Populations, interventions, comparators, outcomes, timing, and settings
PI-RADS	Prostate Imaging Reporting & Data System
PLCO	The Prostate, Lung, Colorectal and Ovarian
PPV	Positive predictive value
PRS	Polygenic risk score
PSA	Prostate-specific antigen
QUADAS- 2	Quality Assessment of Diagnostic Accuracy Studies-2
RCT	Randomized controlled trial
ROBINS-I	Risk of Bias in Non-Randomized Studies of Intervention
ROC	Receiver operating characteristic curve
RR	Relative risk
SDM	Shared decision-making
SNP	Single nucleotide polymorphism
SQC	Science and Quality Council
SSA	Social security administration
STHLM-3	Stockholm-3
SUO	Society of Urologic Oncology
TRUS	Transrectal ultrasound
U.S.	United States

EARLY DETECTION OF PROSTATE CANCER PANEL, CONSULTANTS, AND STAFF

Panel 2023

John T. Wei, MD, MS (Chair)
University of Michigan
Ann Arbor, MI

Daniel W. Lin, MD (Vice Chair)
University of Washington
Seattle, WA

Badrinath R. Konety, MD (PGC Rep)
Allina Health
Minneapolis, MN

Merel G. Nissenberg, JD (Patient Advocate)
Los Angeles, CA

Daniel Barocas, MD
Vanderbilt University
Nashville, TN

Sigrid Carlsson, MD, PhD, MPH
Memorial Sloan Kettering Cancer Center
New York, NY

Fergus Coakley, MD
Oregon Health & Science University
Portland, OR

Scott Eggener, MD
University of Chicago
Chicago, IL

Ruth Etzioni, PhD
Fred Hutchinson Cancer Center
Seattle, WA

Samson W. Fine, MD
Memorial Sloan Kettering Cancer Center
New York, NY

Misop Han, MD
Johns Hopkins University
Baltimore, MD

Martin Miner, MD
Brown University
Providence, RI

Kelvin Moses, MD, PhD
Vanderbilt University
Nashville, TN

Peter A. Pinto, MD
National Institutes of Health
Bethesda, MD

Simpa S. Salami, MD, MPH
University of Michigan
Ann Arbor, MI

Ian M. Thompson, MD
CHRISTUS Health
San Antonio, TX

Panel 2026 (Update)

Daniel W. Lin, MD (Chair)
University of Washington
Seattle, WA

Sigrid Carlsson, MD, PhD, MPH
German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ)
Heidelberg, GERMANY

Christopher P. Filson, MD, MS
Kaiser Permanente Los Angeles Medical Center
Los Angeles, CA

Badrinath R. Konety, MD
Allina Health
Minneapolis, MN

Andrei S. Purysko, MD
Cleveland Clinic
Cleveland, OH

Consultant 2023 and 2026
Lesley Souter, PhD

Staff 2023
Erin Kirkby, MS
Sennett K. Kim
Brooke Bixler, MPH
Leila Rahimi, MHS
Chelsi Matthews

Staff 2026
Sennett Kim
Erin Kirkby, MS
Leila Rahimi, MHS
Lauren J. Pak, MHS, MS

CONFLICT OF INTEREST DISCLOSURES 2023

All panel members completed COI disclosures. Disclosures listed include both topic– and non -topic-related relationships. Panel members not listed below have nothing to disclose.

Consultant/Advisor: Daniel Barocas, lantheus, Pacific Edge Diagnostics, Optum Health, Astellas; **Sigrid Carlsson**, Prevent Cancer Foundation, Prostate Cancer Foundation; **Scott Eggener**, Profound Medical, Insightec, CellVax, MetasTx; **Badrinath Konety**, Asieris, Inc.; **Daniel Lin**, Astellas, Janssen; **Martin Miner**, Acerus, Halozyme; **Ian Thompson**, MagForce, Harvard University

Scientific Study or Trial: **Scott Eggener**, Candel; **Misop Han**, NIH; **Daniel Lin**, NIH/NCI, MDxHealth, MagForce USA; **Ian Thompson**, NIH/NCI

Meeting Participant/Lecturer: Scott Eggener, Janssen, Francis Medical

Owner: Fergus Coakley, OmnEcoil Instruments, Inc.

Investment Interest: **Badrinath Konety**, Astrin Biosciences, Styx Biotechnology

Health Publishing: **Sigrid Carlsson**, Studentlitteratur AB, British Journal of Urology International, Journal of Sexual Medicine; **Scott Eggener**, ASCO

Leadership Position: **Ian Thompson**, SWOG, H-E-B

Other: **Sigrid Carlsson**, NIH/NCI, NCCN; **Misop Han**, Eigen; **Peter Pinto**, Philips/In Vivo, Inc.; **John Wei**, NCI

CONFLICT OF INTEREST DISCLOSURES 2026

All panel members completed COI disclosures. Disclosures listed include both topic– and non -topic-related relationships. Panel members not listed below have nothing to disclose.

Consultant/Advisor: Badrinath Konety, Asieris Inc., Abbott Inc., Valar Labs; **Daniel Lin,** Astellas, Janssen

Scientific Study or Trial: **Daniel Lin,** NIH/NCI; **Andrei Purysko,** Profound Medical, Lantheus, Blue Earth Diagnostics, Siemens Healthineers

Health Publishing: **Sigrid Carlsson,** Studentlitteratur AB, British Journal of Urology International (BJUI); **Badrinath Konety**, Bladder Cancer, Translational Andrology Urology

Leadership Position: **Badrinath Konety,** Society of Urologic Oncology, Idaho College of Osteopathic Medicine

Other: Badrinath Konety, Astrin Biosciences, Styx Biotechnology, American College of Surgeons, American Society of Clinical Oncology

PEER REVIEWERS 2023

We are grateful to the persons listed below who contributed to the Guideline by providing comments during the peer review process. Their reviews do not necessarily imply endorsement of the Guideline.

AUA (Board of Directors, Science and Quality Council, Practice Guidelines Committee, Journal of Urology)
Gregory Auffenberg, MD
Erin Bird, MD
Stephen Boorjian, MD
Benjamin Breyer, MD
Sam Chang, MD
John D. Denstedt, MD
David Ginsberg, MD
Kathleen Kobashi, MD
Suzanne Merrill, MD
Edward Messing, MD
David F. Penson, MD
Hassan Razvi, MD
Angela Smith, MD
Thomas F. Stringer, MD
Mark Tyson, MD
Thomas Richards, MD

External Reviewers (Non-AUA Affiliates)
Matt Cooperberg, MD
Jonathan Epstein, MD
Chris Filson, MD
Jennifer Gordetsky, MD
Justin Robert Gregg, MD
Cary Gross, MD
Brian Helfand, MD
Richard Hoffman, MD
Steve Hyman
Dan Joyce, MD

Jeff Karnes, MD
Eric Klein, MD
Michael Liss, MD
Brock O'Neil, MD
Sanoj Punnen, MD
Kristen Scarpato, MD
Preston Sprenkle, MD
Jeff Tosoian, MD
Alexandre Zlotta, MD

Public Commenters (Via public notice on AUA website)
Laurent Boccon-Gibod, MD
Marty Chakoian
Stacy J. Childs, MD
Franklin Chu, MD
Elward Crawford, MD
Daoud Dajani, MD
Richard Davis
Ved Desai, MD
Vidal Despradel, MD
Robert Dusenka, MD
Sam Haywood, MD
Christine Ibilibor, MD
Sumit Isharwal, MD
Kazuto Ito, MD
Guram Karazanashvili, MD
Evan Kovac, MD
Brian Lane, MD
Aaron Laviana, MD
Stephen Leslie, MD
Stephen Lieberman, MD
Jen-Jane Liu, MD
Amy Luckenbaugh, MD
Roy Mano, MD
Tobias Maurer, MD
Shelby Moneer
Reza Nabavizadeh, MD
Ben Nathanson
Flavio Ordones, MD
William Parker, MD
Mark Perloe, MD
Maniyur Raghavendran, MD
Weranja Ranasinghe, MD
Keyan Salari, MD
James Schraidt
Mihir Shah, MD
Kirill Shiranov, MD
Jonathan Shoag, MD
Nirmish Singla, MD
George Southiere, MD
Massimiliano Spaliviero, MD
Michael Stencel, DO
Hendrik Van Poppel, MD
Chris Wambi, MD
John Ward, MD
Kara Watts, MD
Howard Wolinsky
Paul Yurkanin, MD
Stephen Zappala, MD
JJ Zhang, MD

PEER REVIEWERS 2026

We are grateful to the persons listed below who contributed to the Guideline by providing comments during the peer review process. Their reviews do not necessarily imply endorsement of the Guideline.

AUA (Board of Directors, Science and Quality Council, Practice Guidelines Committee, Journal of Urology)
Erin T. Bird, MD
Stephen A. Boorjian, MD
Arthur L. Burnett, II, MD
Sam S. Chang, MD
David A. Ginsberg, MD
Andrew M. Harris, MD
Daniel Joyce, MD
Damara L. Kaplan, MD
Ronald P. Kaufman Jr., MD
Tobias S. Kohler, MD
Stephen Kraus, MD
Janet B. Kukreja, MD
Gary E. Lemack, MD
Jennifer U. Miles-Thomas, MD
Stephen Y. Nakada, MD
Matthew E. Nielsen, MD
Sima P. Porten, MD
Christopher Porter, MD
Sarah Psutka, MD
Angela B. Smith, MD
Mary Westerman, MD

External Reviewers (Non-AUA Affiliates)
Daniel Barocas, MD
Brian Chapin, MD
Fergus Coakley, MD
Matt Cooperberg, MD
Adam Feldman, MD
Michael Leapman, MD
Martin Miner, MD
Merel Nissenberg, JD
Yaw Nyame, MD
William Parker, MD
Ian Thompson, MD
Quoc Trinh, MD

John Wei, MD
Antonio Westphalen, MD

Public Commenters (Via public notice on AUA website)
Peter Albers, MD
Indraneel Banerjee, MD
Courtney Bugler
Jaime Cajigas, MD
Marty Chakoian
Steve Chung, MD
Niall Corcoran
Mike Crosby, MSc, CDR USN ret
Danny Darlington, MD
Richard Davis
Daben Dawam, MD
Robert Dusenka, MD, PhD
Chad Ellimoottil, MD
Andreas Forsvall, MD
Huber Diaz Fuentes, PhD
Xiong Guo-bing, MD
Motaz Hassan, MD
Paul Hatcher, MD
Emily Huang, MD
Sumit Isharwal, MD
Alex Qinyang Liu, MBBS
John Ludlow, MD
Davide Maffei, MD
Pankaj Maheshwari, MBBS
Abdul Wasay Mahmood, MBBS
Sumit Mandal, MBBS
Ali Manson, MPH
Raymundo A. Munoz, MD
Athanasios Papatsoris, MD
Jae Young Park, MD
Nicola Pavan, MD, PhD
Kevin Pelletier, MPAS
Maniyur Raghavendran, MD
Juan Gómez Rivas, MD
Keyan Salari, MD
Juan Felipe Alarcon Salvador, MD
Rafael Sanchez-Salas, MD
James A. Schraidt, JD
Yoshitake Sekine, MD
Mohammed Shahait, MBBS
Kirill Shiranov, MD
Maria Chiara Sighinolfi, MD
Petros Sountoulides, MD
Mark Stovsky, MD
Richard C. Sylvester
Thiago Iorio Tagliari, MD
Rajesh Venkataraman, PhD
Brian Wodlinger, PhD
Howard Wolinsky

DISCLAIMER

This document was written by the Early Detection of Prostate Cancer Panel of the American Urological Association Education and Research, Inc., which was created in 2021. The Practice Guidelines Committee (PGC) of the AUA selected the Panel Chair. Panel members were selected by the Panel and PGC Chair.

Membership of the panel included specialists with specific expertise on this disorder. The mission of the panel was to develop recommendations that are analysis-based or consensus-based, depending on panel processes and available data, for optimal clinical practices in the early detection of prostate cancer setting.

Funding of the panel was provided by the AUA. Panel members received no remuneration for their work. Each member of the panel provides an ongoing conflict of interest disclosure to the AUA.

While these Guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated. As medical knowledge expands and technology advances, the Guidelines will change. Today these evidence-based Guideline statements represent not absolute mandates but provisional proposals for treatment under the specific conditions described in each document. For all these reasons, the Guidelines do not pre-empt physician judgment in individual cases.

Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Conformance with any clinical Guideline does not guarantee a successful outcome. The Guideline text may include information or recommendations about certain drug uses ("off label") that are not approved by the Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to carefully follow all available prescribing information about indications, contraindications, precautions and warnings. These Guideline and best practice statements are not intended to provide legal advice about use and misuse of these substances.

Although Guidelines are intended to encourage best practices and potentially encompass available technologies with sufficient data as of close of the literature review, they are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies or management, including those that are FDA-approved, which may immediately come to represent accepted clinical practices.

For this reason, the AUA does not regard technologies or management that are too new to be addressed by this Guideline as necessarily experimental or investigational.

REFERENCES

1. Siegel RL, Kratzer TB, Wagle NS et al: Cancer statistics, 2026. CA: A Cancer Journal for Clinicians 2026; **76:** e70043
2. Wang L, Lu B, He M et al: Prostate cancer incidence and mortality: Global status and temporal trends in 89 countries from 2000 to 2019. Front Public Health 2022; **10:** 811044
3. McHugh JK, Bancroft EK, Saunders E et al: Assessment of a polygenic risk score in screening for prostate cancer. N Engl J Med 2025; **392:** 1406
4. Conti DV, Darst BF, Moss LC et al: Trans-ancestry genome-wide association meta-analysis of prostate cancer identifies new susceptibility loci and informs genetic risk prediction. Nat Genet 2021; **53:** 65
5. Eggener SE, Scardino PT, Walsh PC et al: Predicting 15-year prostate cancer specific mortality after radical prostatectomy. J Urol 2011; **185:** 869
6. Mahal BA, Berman RA, Taplin ME and Huang FW: Prostate cancer-specific mortality across gleason scores in black vs nonblack men. Jama 2018; **320:** 2479
7. Ouzzani M, Hammady H, Fedorowicz Z and Elmagarmid A: Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016; **5:** 210
8. Shea BJ, Grimshaw JM, Wells GA et al: Development of amstar: A measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol 2007; **7:** 10
9. Higgins JP, Altman DG, Gotzsche PC et al: The cochrane collaboration's tool for assessing risk of bias in randomised trials. Bmj 2011; **343:** d5928
10. Sterne JA, Hernan MA, Reeves BC et al: Robins-i: A tool for assessing risk of bias in non-randomised studies of interventions. Bmj 2016; **355:** i4919
11. Whiting PF, Rutjes AW, Westwood ME et al: Quadas-2: A revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011; **155:** 529
12. The Nordic Cochrane Centre: Review manager (revman), Version 5.3 ed. Copenhagen: The Chochrane Collaboration 2014
13. Guyatt G, Oxman AD, Akl EA et al: Grade guidelines: 1. Introduction-grade evidence profiles and summary of findings tables. J Clin Epidemiol 2011; **64:** 383
14. Balshem H, Helfand M, Schünemann HJ et al: Grade guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011; **64:** 401
15. Faraday M, Hubbard H, Kosiak B and Dmochowski R: Staying at the cutting edge: A review and analysis of evidence reporting and grading; the recommendations of the american urological association. BJU Int 2009; **104:** 294
16. Hsu C-C and Sandford B: The delphi technique: Making sense of consensus. Practical Assessment, Research and Evaluation 2007; **12**
17. Makarov DV, Chrouser K, Gore JL et al: Aua white paper on implementation of shared decision making into urological practice. Urology Practice 2016; **3:** 355
18. Stacey D, Legare F, Lewis K et al: Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev 2017; **4:** CD001431
19. Riikonen JM, Guyatt GH, Kilpelainen TP et al: Decision aids for prostate cancer screening choice: A systematic review and meta-analysis. JAMA Intern Med 2019; **179:** 1072

20. Eastham JA, Boorjian SA and Kirkby E: Clinically localized prostate cancer: Aua/astro guideline. J Urol 2022; **208:** 505
21. Hugosson J, Roobol MJ, Mansson M et al: A 16-yr follow-up of the european randomized study of screening for prostate cancer. Eur Urol 2019; **76:** 43
22. Hugosson J, Godtman RA, Carlsson SV et al: Eighteen-year follow-up of the goteborg randomized population-based prostate cancer screening trial: Effect of sociodemographic variables on participation, prostate cancer incidence and mortality. Scand J Urol 2018; **52:** 27
23. Gronberg H, Adolfsson J, Aly M et al: Prostate cancer screening in men aged 50-69 years (sthlm3): A prospective population-based diagnostic study. Lancet Oncol 2015; **16:** 1667
24. Nordstrom T, Discacciati A, Bergman M et al: 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
25. Eklund M, Jaderling F, Discacciati A et al: Mri-targeted or standard biopsy in prostate cancer screening. New England Journal of Medicine 2021; **385:** 908
26. Eastham JA, Riedel E, Scardino PT et al: Variation of serum prostate-specific antigen levels: An evaluation of year-to-year fluctuations. JAMA 2003; **289:** 2695
27. Nordström T, Adolfsson J, Grönberg H and Eklund M: Repeat prostate-specific antigen tests before prostate biopsy decisions. J Natl Cancer Inst 2016; **108:** djw165
28. Eggener SE, Large MC, Gerber GS et al: Empiric antibiotics for an elevated prostate-specific antigen (psa) level: A randomised, prospective, controlled multi-institutional trial. BJU Int 2013; **112:** 925
29. Greiman A, Shah J, Bhavsar R et al: Six weeks of fluoroquinolone antibiotic therapy for patients with elevated serum prostate-specific antigen is not clinically beneficial: A randomized controlled clinical trial. Urology 2016; **90:** 32
30. Crawford ED, Schutz MJ, Clejan S et al: The effect of digital rectal examination on prostate-specific antigen levels. JAMA 1992; **267:** 2227
31. Jiandani D, Randhawa A, Brown RE et al: The effect of bicycling on psa levels: A systematic review and meta-analysis. Prostate Cancer Prostatic Dis 2015; **18:** 208
32. Tarhan F, Demir K, Orcun A and Madenci OC: Effect of ejaculation on serum prostate-specific antigen concentration. Int Braz J Urol 2016; **42:** 472
33. Gulati R, Gore JL and Etzioni R: Comparative effectiveness of alternative prostate-specific antigen--based prostate cancer screening strategies: Model estimates of potential benefits and harms. Annals of Internal Medicine 2013; **158:** 145
34. Oesterling JE, Jacobsen SJ, Chute CG et al: Serum prostate-specific antigen in a community-based population of healthy men. Establishment of age-specific reference ranges. Jama 1993; **270:** 860
35. Partin AW, Criley SR, Subong EN et al: Standard versus age-specific prostate specific antigen reference ranges among men with clinically localized prostate cancer: A pathological analysis. J Urol 1996; **155:** 1336
36. Guess HA, Gormley GJ, Stoner E and Oesterling JE: The effect of finasteride on prostate specific antigen: Review of available data. J Urol 1996; **155:** 3
37. Brawer MK, Lin DW, Williford WO et al: Effect of finasteride and/or terazosin on serum psa: Results of va cooperative study #359. Prostate 1999; **39:** 234
38. Franlund M, Mansson M, Godtman RA et al: Results from 22 years of followup in the goteborg randomized population-based prostate cancer screening trial. J Urol 2022; **208:** 292
39. Loeb S, Carter HB, Catalona WJ et al: Baseline prostate-specific antigen testing at a young age. Eur Urol 2012; **61:** 1
40. Vickers AJ, Ulmert D, Sjoberg DD et al: Strategy for detection of prostate cancer based on relation between prostate specific antigen at age 40-55 and long term risk of metastasis: Case-control study. BMJ 2013; **346:** f2023
41. 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
42. Gulati R, Cheng HH, Lange PH et al: Screening men at increased risk for prostate cancer diagnosis: Model estimates of benefits and harms. Cancer Epidemiology, Biomarkers & Prevention 2017; **26:** 222
43. Giaquinto AN, Miller KD, Tossas KY et al: Cancer statistics for african american/black people 2022. CA Cancer J Clin 2022; **72:** 202
44. Tsodikov A, Gulati R, de Carvalho TM et al: Is prostate cancer different in black men? Answers from 3 natural history models. Cancer 2017; **123:** 2312

45. Bancroft EK, Page EC, Brook MN et al: A prospective prostate cancer screening programme for men with pathogenic variants in mismatch repair genes (impact): Initial results from an international prospective study. Lancet Oncol 2021; **22:** 1618
46. Mitra AV, Bancroft EK, Barbachano Y et al: Targeted prostate cancer screening in men with mutations in brca1 and brca2 detects aggressive prostate cancer: Preliminary analysis of the results of the impact study. BJU International 2011; **107:** 28
47. Page EC, Bancroft EK, Brook MN et al: Interim results from the impact study: Evidence for prostate-specific antigen screening in brca2 mutation carriers. European Urology 2019; **76:** 831
48. Schaeffer EM, Srinivas S, Adra N et al: Nccn guidelines® insights: Prostate cancer, version 1.2023. J Natl Compr Canc Netw 2022; **20:** 1288
49. Giri VN, Knudsen KE, Kelly WK et al: Role of genetic testing for inherited prostate cancer risk: Philadelphia prostate cancer consensus conference 2017. J Clin Oncol 2018; **36:** 414
50. Albright F, Stephenson RA, Agarwal N et al: Prostate cancer risk prediction based on complete prostate cancer family history. Prostate 2015; **75:** 390
51. Tangen CM, Goodman PJ, Till C et al: Biases in recommendations for and acceptance of prostate biopsy significantly affect assessment of prostate cancer risk factors: Results from two large randomized clinical trials. J Clin Oncol 2016; **34:** 4338
52. Clements MB, Vertosick EA, Guerrios-Rivera L et al: Defining the impact of family history on detection of high-grade prostate cancer in a large multi-institutional cohort. Eur Urol 2022; **82:** 163
53. Bratt O, Drevin L, Akre O et al: Family history and probability of prostate cancer, differentiated by risk category: A nationwide population-based study. J Natl Cancer Inst 2016; **108:** djw110
54. Barber L, Gerke T, Markt SC et al: Family history of breast or prostate cancer and prostate cancer risk. Clin Cancer Res 2018; **24:** 5910
55. Thomas JA, 2nd, Gerber L, Moreira DM et al: Prostate cancer risk in men with prostate and breast cancer family history: Results from the reduce study (r1). J Intern Med 2012; **272:** 85
56. Pritchard CC, Mateo J, Walsh MF et al: Inherited DNA-repair gene mutations in men with metastatic prostate cancer. N Engl J Med 2016; **375:** 443
57. Hugosson J, Carlsson S, Aus G et al: Mortality results from the goteborg randomised population-based prostate-cancer screening trial. Lancet Oncol 2010; **11:** 725
58. Schroder FH, Hugosson J, Roobol MJ et al: Screening and prostate-cancer mortality in a randomized european study. New England Journal of Medicine 2009; **360:** 1320
59. Heijnsdijk EA, Wever EM, Auvinen A et al: Quality-of-life effects of prostate-specific antigen screening. N Engl J Med 2012; **367:** 595
60. Carlsson S, Assel M, Sjoberg D et al: Influence of blood prostate specific antigen levels at age 60 on benefits and harms of prostate cancer screening: Population based cohort study. BMJ 2014; **348:** g2296
61. Pinsky PF, Miller E, Prorok P et al: Extended follow-up for prostate cancer incidence and mortality among participants in the prostate, lung, colorectal and ovarian randomized cancer screening trial. BJU Int 2019; **123:** 854
62. Shoag JE, Mittal S and Hu JC: Reevaluating psa testing rates in the plco trial. N Engl J Med 2016; **374:** 1795
63. 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
64. Roobol MJ, Roobol DW and Schroder FH: Is additional testing necessary in men with prostate-specific antigen levels of 1.0 ng/ml or less in a population-based screening setting? (erspc, section rotterdam). Urology 2005; **65:** 343
65. Vickers AJ, Cronin AM, Bjork T et al: Prostate specific antigen concentration at age 60 and death or metastasis from prostate cancer: Case-control study. BMJ 2010; **341:** c4521
66. Vertosick EA, Haggstrom C, Sjoberg DD et al: Prespecified 4-kallikrein marker model at age 50 or 60 for early detection of lethal prostate cancer in a large population based cohort of asymptomatic men followed for 20 years. J Urol 2020; **204:** 281
67. Preston MA, Gerke T, Carlsson SV et al: Baseline prostate-specific antigen level in midlife and aggressive prostate cancer in black men. Eur Urol 2019; **75:** 399
68. Preston MA, Batista JL, Wilson KM et al: Baseline prostate-specific antigen levels in midlife predict lethal prostate cancer. J Clin Oncol 2016; **34:** 2705
69. Kovac E, Carlsson SV, Lilja H et al: Association of baseline prostate-specific antigen level with long-term diagnosis of clinically significant prostate cancer among patients aged 55 to 60 years: A secondary analysis of a

cohort in the prostate, lung, colorectal, and ovarian (plco) cancer screening trial. JAMA Netw Open 2020; **3:** e1919284
70. Ross KS, Carter HB, Pearson JD and Guess HA: Comparative efficiency of prostate-specific antigen screening strategies for prostate cancer detection. JAMA 2000; **284:** 1399
71. Heijnsdijk EAM, Gulati R, Tsodikov A et al: Lifetime benefits and harms of prostate-specific antigen-based risk-stratified screening for prostate cancer. Journal of the National Cancer Institute 2020; **112:** 1013
72. Remmers S, Bangma CH, Godtman RA et al: Relationship between baseline prostate-specific antigen on cancer detection and prostate cancer death: Long-term follow-up from the european randomized study of screening for prostate cancer. Eur Urol 2023; **84:** 503
73. Grenabo Bergdahl A, Holmberg E, Moss S and Hugosson J: Incidence of prostate cancer after termination of screening in a population-based randomised screening trial. European Urology 2013; **64:** 703
74. Godtman RA, Kollberg KS, Pihl CG et al: The association between age, prostate cancer risk, and higher gleason score in a long-term screening program: Results from the goteborg-1 prostate cancer screening trial. Eur Urol 2022; **82:** 311
75. Schaeffer EM, Carter HB, Kettermann A et al: Prostate specific antigen testing among the elderly--when to stop? Journal of Urology 2009; **181:** 1606
76. de V, II, Remmers S, Hogenhout R and Roobol MJ: Prostate cancer mortality among elderly men after discontinuing organised screening: Long-term results from the european randomized study of screening for prostate cancer rotterdam. Eur Urol 2024; **85:** 74
77. Lansdorp-Vogelaar I, Gulati R, Mariotto AB et al: Personalizing age of cancer screening cessation based on comorbid conditions: Model estimates of harms and benefits. Ann Intern Med 2014; **161:** 104
78. Schroder FH, Hugosson J, Roobol MJ et al: Prostate-cancer mortality at 11 years of follow-up. New England Journal of Medicine 2012; **366:** 981
79. Bill-Axelson A, Holmberg L, Garmo H et al: Radical prostatectomy or watchful waiting in early prostate cancer. N Engl J Med 2014; **370:** 932
80. Vickers A, Bennette C, Steineck G et al: Individualized estimation of the benefit of radical prostatectomy from the scandinavian prostate cancer group randomized trial. Eur Urol 2012; **62:** 204
81. Hamdy FC, Donovan JL, Lane JA et al: 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. N Engl J Med 2016; **375:** 1415
82. Wilt TJ, Vo TN, Langsetmo L et al: Radical prostatectomy or observation for clinically localized prostate cancer: Extended follow-up of the prostate cancer intervention versus observation trial (pivot). Eur Urol 2020; **77:** 713
83. Sakr WA, Grignon DJ, Crissman JD et al: High grade prostatic intraepithelial neoplasia (hgpin) and prostatic adenocarcinoma between the ages of 20-69: An autopsy study of 249 cases. In Vivo 1994; **8:** 439
84. Vickers AJ, Sjoberg DD, Ulmert D et al: Empirical estimates of prostate cancer overdiagnosis by age and prostate-specific antigen. BMC Med 2014; **12:** 26
85. Gulati R, Feuer EJ and Etzioni R: Conditions for valid empirical estimates of cancer overdiagnosis in randomized trials and population studies. Am J Epidemiol 2016; **184:** 140
86. Wilson JR, Clarke MG, Ewings P et al: The assessment of patient life-expectancy: How accurate are urologists and oncologists? BJU Int 2005; **95:** 794
87. Makarov D, A F, J F et al: Implementation of shared decision making into urological practice, 2022
88. Matsukawa A, Yanagisawa T, Bekku K et al: Comparing the performance of digital rectal examination and prostate-specific antigen as a screening test for prostate cancer: A systematic review and meta-analysis. Eur Urol Oncol 2024; **7:** 697
89. Thompson IM, Tangen CM, Goodman PJ et al: Finasteride improves the sensitivity of digital rectal examination for prostate cancer detection. J Urol 2007; **177:** 1749
90. Nagler HM, Gerber EW, Homel P et al: Digital rectal examination is barrier to population-based prostate cancer screening. Urology 2005; **65:** 1137
91. Gosselaar C, Roobol MJ, Roemeling S and Schroder FH: The role of the digital rectal examination in subsequent screening visits in the european randomized study of screening for prostate cancer (erspc), rotterdam. European Urology 2008; **54:** 581
92. Luboldt HJ, Bex A, Swoboda A et al: Early detection of prostate cancer in germany: A study using digital rectal examination and 4.0 ng/ml prostate-specific antigen as cutoff. European Urology 2001; **39:** 131
93. Halpern JA, Oromendia C, Shoag JE et al: Use of digital rectal examination as an adjunct to prostate specific antigen in the detection of clinically significant prostate cancer. J Urol 2018; **199:** 947
94. Vickers AJ, Till C, Tangen CM et al: An empirical evaluation of guidelines on prostate-specific antigen velocity in prostate cancer detection. Journal of the National Cancer Institute 2011; **103:** 462

95. Vickers AJ, Wolters T, Savage CJ et al: Prostate-specific antigen velocity for early detection of prostate cancer: Result from a large, representative, population-based cohort. European Urology 2009; **56:** 753
96. Eggener SE, Yossepowitch O, Roehl KA et al: Relationship of prostate-specific antigen velocity to histologic findings in a prostate cancer screening program. Urology 2008; **71:** 1016
97. Carbunaru S, Nettey OS, Gogana P et al: A comparative effectiveness analysis of the pbcg vs. Pcpt risks calculators in a multi-ethnic cohort. BMC Urol 2019; **19:** 121
98. Breza J, Subin F, Bernadic M et al: The use of european randomized study of screening for prostate cancer calculator as a diagnostic tool for prostate biopsy indication. Bratisl Lek Listy 2019; **120:** 331
99. Thompson IM, Ankerst DP, Chi C et al: Assessing prostate cancer risk: Results from the prostate cancer prevention trial. J Natl Cancer Inst 2006; **98:** 529
100. Ankerst DP, Goros M, Tomlins SA et al: Incorporation of urinary prostate cancer antigen 3 and tmprss2:Erg into prostate cancer prevention trial risk calculator. Eur Urol Focus 2019; **5:** 54
101. Chun FK, Briganti A, Graefen M et al: Development and external validation of an extended 10-core biopsy nomogram. Eur Urol 2007; **52:** 436
102. Perdonà S, Cavadas V, Di Lorenzo G et al: Prostate cancer detection in the "grey area" of prostate-specific antigen below 10 ng/ml: Head-to-head comparison of the updated pcpt calculator and chun's nomogram, two risk estimators incorporating prostate cancer antigen 3. Eur Urol 2011; **59:** 81
103. Kranse R, Roobol M and Schröder FH: A graphical device to represent the outcomes of a logistic regression analysis. Prostate 2008; **68:** 1674
104. Roobol MJ, Schröder FH, Hugosson J et al: Importance of prostate volume in the european randomised study of screening for prostate cancer (erspc) risk calculators: Results from the prostate biopsy collaborative group. World J Urol 2012; **30:** 149
105. De Nunzio C, Lombardo R, Tema G et al: External validation of chun, pcpt, erspc, kawakami, and karakiewicz nomograms in the prediction of prostate cancer: A single center cohort-study. Urol Oncol 2018; **36:** 364.e1
106. Ankerst DP, Straubinger J, Selig K et al: A contemporary prostate biopsy risk calculator based on multiple heterogeneous cohorts. Eur Urol 2018; **74:** 197
107. Ankerst DP, Hoefler J, Bock S et al: Prostate cancer prevention trial risk calculator 2.0 for the prediction of low- vs high-grade prostate cancer. Urology 2014; **83:** 1362
108. Fenton JJ, Weyrich MS, Durbin S et al: U.S. Preventive services task force evidence syntheses, formerly systematic evidence reviews. In: Prostate-specific antigen-based screening for prostate cancer: A systematic evidence review for the u.S. Preventive services task force. Rockville (MD): Agency for Healthcare Research and Quality (US), 2018
109. Wei JT, Feng Z, Partin AW et al: Can urinary pca3 supplement psa in the early detection of prostate cancer? Journal of Clinical Oncology 2014; **32:** 4066
110. Singhal U, Tosoian JJ, Qi J et al: Overtreatment and underutilization of watchful waiting in men with limited life expectancy: An analysis of the michigan urological surgery improvement collaborative registry. Urology 2020; **145:** 190
111. Kasivisvanathan V, Rannikko AS, Borghi M et al: Mri-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018; **378:** 1767
112. Wei C, Szewczyk-Bieda M, Bates AS et al: Multicenter randomized trial assessing mri and image-guided biopsy for suspected prostate cancer: The multipros study. Radiology 2023; **308:** e221428
113. 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
114. Hamm CA, Asbach P, Pöhlmann A et al: Oncological safety of mri-informed biopsy decision-making in men with suspected prostate cancer. JAMA Oncol 2025; **11:** 145
115. 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
116. Panebianco V, Barchetti F, Sciarra A et al: Multiparametric magnetic resonance imaging vs. Standard care in men being evaluated for prostate cancer: A randomized study. Urol Oncol 2015; **33:** 17 e1
117. Tonttila PP, Lantto J, Pääkkö E et al: Prebiopsy multiparametric magnetic resonance imaging for prostate cancer diagnosis in biopsy-naive men with suspected prostate cancer based on elevated prostate-specific antigen values: Results from a randomized prospective blinded controlled trial. Eur Urol 2016; **69:** 419
118. Porpiglia F, Manfredi M, Mele F et al: Diagnostic pathway with multiparametric magnetic resonance imaging versus standard pathway: Results from a randomized prospective study in biopsy-naive patients with suspected prostate cancer. Eur Urol 2017; **72:** 282

119. Hugosson J, Månsson M, Wallström J et al: Prostate cancer screening with psa and mri followed by targeted biopsy only. N Engl J Med 2022; **387:** 2126
120. Drost FH, Osses DF, Nieboer D et al: Prostate mri, with or without mri-targeted biopsy, and systematic biopsy for detecting prostate cancer. Cochrane Database of Systematic Reviews 2019; **4:** CD012663
121. Purysko AS, Tempany C, Macura KJ et al: American college of radiology initiatives on prostate magnetic resonance imaging quality. Eur J Radiol 2023; **165:** 110937
122. Barentsz JO, Richenberg J, Clements R et al: Esur prostate mr guidelines 2012. Eur Radiol 2012; **22:** 746
123. Weinreb JC, Barentsz JO, Choyke PL et al: Pi-rads prostate imaging - reporting and data system: 2015, version 2. Eur Urol 2016; **69:** 16
124. 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
125. Ahdoot M, Lebastchi AH, Long L et al: Using prostate imaging-reporting and data system (pi-rads) scores to select an optimal prostate biopsy method: A secondary analysis of the trio study. European Urology Oncology 2021; **10:** 10
126. Barkovich EJ, Shankar PR and Westphalen AC: A systematic review of the existing prostate imaging reporting and data system version 2 (pi-radsv2) literature and subset meta-analysis of pi-radsv2 categories stratified by gleason scores. AJR American Journal of Roentgenology 2019; **212:** 847
127. Benndorf M, Waibel L, Kronig M et al: Peripheral zone lesions of intermediary risk in multiparametric prostate mri: Frequency and validation of the pi-radsv2 risk stratification algorithm based on focal contrast enhancement. European Journal of Radiology 2018; **99:** 62
128. Borkowetz A, Hadaschik B, Platzek I et al: Prospective comparison of transperineal magnetic resonance imaging/ultrasonography fusion biopsy and transrectal systematic biopsy in biopsy-naive patients. BJU International 2018; **121:** 53
129. Chen Y, Ruan M, Zhou B et al: Cutoff values of prostate imaging reporting and data system version 2.1 score in men with prostate-specific antigen level 4 to 10 ng/ml: Importance of lesion location. Clinical Genitourinary Cancer 2021; **19:** 288
130. Cheng Y, Qi F, Liang L et al: Use of prostate systematic and targeted biopsy on the basis of bi-parametric magnetic resonance imaging in biopsy-naive patients. Journal of Investigative Surgery 2020; **35:** 92
131. Daun M, Fardin S, Ushinsky A et al: Pi-rads version 2 is an excellent screening tool for clinically significant prostate cancer as designated by the validated international society of urological pathology criteria: A retrospective analysis. Current Problems in Diagnostic Radiology 2020; **49:** 407
132. Hofbauer SL, Maxeiner A, Kittner B et al: Validation of prostate imaging reporting and data system version 2 for the detection of prostate cancer. Journal of Urology 2018; **200:** 767
133. John S, Cooper S, Breau RH et al: Multiparametric magnetic resonance imaging-transrectal ultrasound-guided cognitive fusion biopsy of the prostate: Clinically significant cancer detection rates stratified by the prostate imaging and data reporting system version 2 assessment categories. Canadian Urological Association Journal 2018; **12:** 401
134. Jordan EJ, Fiske C, Zagoria RJ and Westphalen AC: Evaluating the performance of pi-rads v2 in the non-academic setting. Abdominal Radiology 2017; **42:** 2725
135. Kim M, Ryu H, Lee HJ et al: Who can safely evade a magnetic resonance imaging fusion-targeted biopsy (mriftb) for prostate imaging reporting and data system (pi-rads) 3 lesion? World Journal of Urology 2021; **39:** 1463
136. Lee CU, Choi J, Sung SH et al: The role of prostate combination biopsy consisting of targeted and additional systematic biopsy. Journal of Clinical Medicine 2021; **10:** 4804
137. Lim C, Abreu-Gomez J, Leblond MA et al: When to biopsy prostate imaging and data reporting system version 2 (pi-radsv2) assessment category 3 lesions? Use of clinical and imaging variables to predict cancer diagnosis at targeted biopsy. Canadian Urological Association Journal 2020; **15:** 115
138. Mathur S, O'Malley ME, Ghai S et al: Correlation of 3t multiparametric prostate mri using prostate imaging reporting and data system (pirads) version 2 with biopsy as reference standard. Abdominal Radiology 2019; **44:** 252
139. Osses DF, van Asten JJ, Kieft GJ and Tijsterman JD: Prostate cancer detection rates of magnetic resonance imaging-guided prostate biopsy related to prostate imaging reporting and data system score. World Journal of Urology 2017; **35:** 207
140. Park BK and Park SY: New biopsy techniques and imaging features of transrectal ultrasound for targeting pi-rads 4 and 5 lesions. Journal of Clinical Medicine 2020; **9:** 15

141. Ryoo H, Kang MY, Sung HH et al: Detection of prostate cancer using prostate imaging reporting and data system score and prostate-specific antigen density in biopsy-naive and prior biopsy-negative patients. Prostate International 2020; **8:** 125
142. Sathianathen NJ, Konety BR, Soubra A et al: Which scores need a core? An evaluation of mr-targeted biopsy yield by pirads score across different biopsy indications. Prostate Cancer & Prostatic Diseases 2018; **21:** 573
143. Sokhi HK, Padhani AR, Patel S and Pope A: Diagnostic yields in patients with suspected prostate cancer undergoing mri as the first-line investigation in routine practice. Clinical Radiology 2020; **75:** 950
144. Syed JS, Nguyen KA, Nawaf CB et al: Prostate zonal anatomy correlates with the detection of prostate cancer on multiparametric magnetic resonance imaging/ultrasound fusion-targeted biopsy in patients with a solitary pi-rads v2-scored lesion. Urologic Oncology 2017; **35:** 542.e19
145. 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
146. Abdul Raheem R, Razzaq A, Beraud V et al: Can a prostate biopsy be safely deferred on pi-rads 1,2 or 3 lesions seen on pre-biopsy mp-mri? Arab Journal of Urology 2022; **21:** 10
147. Nowier A, Mazhar H, Salah R and Shabayek M: Performance of multi-parametric magnetic resonance imaging through pirads scoring system in biopsy naive patients with suspicious prostate cancer. Arab Journal of Urology Print 2022; **20:** 121
148. Rosenkrantz AB, Ayoola A, Hoffman D et al: The learning curve in prostate mri interpretation: Self-directed learning versus continual reader feedback. AJR Am J Roentgenol 2017; **208:** W92
149. Wei CG, Zhang YY, Pan P et al: Diagnostic accuracy and interobserver agreement of pi-rads version 2 and version 2.1 for the detection of transition zone prostate cancers. AJR Am J Roentgenol 2021; **216:** 1247
150. Bhayana R, O'Shea A, Anderson MA et al: Pi-rads versions 2 and 2.1: Interobserver agreement and diagnostic performance in peripheral and transition zone lesions among six radiologists. AJR Am J Roentgenol 2021; **217:** 141
151. Annamalai A, Fustok JN, Beltran-Perez J et al: Interobserver agreement and accuracy in interpreting mpmri of the prostate: A systematic review. Curr Urol Rep 2022; **23:** 1
152. de Rooij M, Israel 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
153. Li JL, Phillips D, Towfighi S et al: Second-opinion reads in prostate mri: Added value of subspecialty interpretation and review at multidisciplinary rounds. Abdom Radiol (NY) 2022; **47:** 827
154. Al Hussein Al Awamlh B, Marks LS, Sonn GA et al: Multicenter analysis of clinical and mri characteristics associated with detecting clinically significant prostate cancer in pi-rads (v2.0) category 3 lesions. Urologic Oncology 2020; **38:** 637.e9
155. Cata E, Andras I, Ferro M et al: Systematic sampling during mri-us fusion prostate biopsy can overcome errors of targeting-prospective single center experience after 300 cases in first biopsy setting. Translational Andrology & Urology 2020; **9:** 2510
156. Filson CP, Natarajan S, Margolis DJ et al: Prostate cancer detection with magnetic resonance-ultrasound fusion biopsy: The role of systematic and targeted biopsies. Cancer 2016; **122:** 884
157. Fujii S, Hayashi T, Honda Y et al: Magnetic resonance imaging/transrectal ultrasonography fusion targeted prostate biopsy finds more significant prostate cancer in biopsy-naive japanese men compared with the standard biopsy. International Journal of Urology 2020; **27:** 140
158. Kim YJ, Huh JS and Park KK: Effectiveness of bi-parametric mr/us fusion biopsy for detecting clinically significant prostate cancer in prostate biopsy naive men. Yonsei Medical Journal 2019; **60:** 346
159. Maxeiner A, Kittner B, Blobel C et al: Primary magnetic resonance imaging/ultrasonography fusion-guided biopsy of the prostate. BJU International 2018; **122:** 211
160. Ahdoot M, Wilbur AR, Reese SE et al: Mri-targeted, systematic, and combined biopsy for prostate cancer diagnosis. New England Journal of Medicine 2020; **382:** 917
161. Coker MA, Glaser ZA, Gordetsky JB et al: Targets missed: Predictors of mri-targeted biopsy failing to accurately localize prostate cancer found on systematic biopsy. Prostate Cancer Prostatic Dis 2018; **21:** 549
162. Brisbane WG, Priester AM, Ballon J et al: Targeted prostate biopsy: Umbra, penumbra, and value of perilesional sampling. Eur Urol 2022; **82:** 303
163. Williams C, Ahdoot M, Daneshvar MA et al: Why does magnetic resonance imaging-targeted biopsy miss clinically significant cancer? J Urol 2022; **207:** 95

164. Prince M, Foster BR, Kaempf A et al: In-bore versus fusion mri-targeted prostate biopsy of pi-rads category 4 or 5 lesions: A retrospective comparative analysis using propensity score weighting. AJR Am J Roentgenol 2021; **217:** 1123
165. Sathianathen NJ, Omer A, Harriss E et al: Negative predictive value of multiparametric magnetic resonance imaging in the detection of clinically significant prostate cancer in the prostate imaging reporting and data system era: A systematic review and meta-analysis. European Urology 2020; **78:** 402
166. Haj-Mirzaian A, Burk KS, Lacson R et al: Magnetic resonance imaging, clinical, and biopsy findings in suspected prostate cancer: A systematic review and meta-analysis. JAMA Netw Open 2024; **7:** e244258
167. Eichler K, Hempel S, Wilby J et al: Diagnostic value of systematic biopsy methods in the investigation of prostate cancer: A systematic review. J Urol 2006; **175:** 1605
168. Ristau BT, Allaway M, Cendo D et al: Free-hand transperineal prostate biopsy provides acceptable cancer detection and minimizes risk of infection: Evolving experience with a 10-sector template. Urol Oncol 2018; **36:** 528.e15
169. Ukimura O, Coleman JA, de la Taille A et al: Contemporary role of systematic prostate biopsies: Indications, techniques, and implications for patient care. Eur Urol 2013; **63:** 214
170. Presti JC, Jr., O'Dowd GJ, Miller MC et al: Extended peripheral zone biopsy schemes increase cancer detection rates and minimize variance in prostate specific antigen and age related cancer rates: Results of a community multi-practice study. J Urol 2003; **169:** 125
171. Catalona WJ, Partin AW, Slawin KM et al: Use of the percentage of free prostate-specific antigen to enhance differentiation of prostate cancer from benign prostatic disease: A prospective multicenter clinical trial. JAMA 1998; **279:** 1542
172. Roddam AW, Duffy MJ, Hamdy FC et al: Use of prostate-specific antigen (psa) isoforms for the detection of prostate cancer in men with a psa level of 2-10 ng/ml: Systematic review and meta-analysis. Eur Urol 2005; **48:** 386
173. Lee R, Localio AR, Armstrong K et al: A meta-analysis of the performance characteristics of the free prostate-specific antigen test. Urology 2006; **67:** 762
174. Catalona WJ, Southwick PC, Slawin KM et al: Comparison of percent free psa, psa density, and age-specific psa cutoffs for prostate cancer detection and staging. Urology 2000; **56:** 255
175. Bruzzese D, Mazzarella C, Ferro M et al: Prostate health index vs percent free prostate-specific antigen for prostate cancer detection in men with "gray" prostate-specific antigen levels at first biopsy: Systematic review and meta-analysis. Transl Res 2014; **164:** 444
176. Finne P, Auvinen A, Maattanen L et al: Diagnostic value of free prostate-specific antigen among men with a prostate-specific antigen level of <3.0 microg per liter. European Urology 2008; **54:** 362
177. Parekh DJ, Punnen S, Sjoberg DD et al: A multi-institutional prospective trial in the USA confirms that the 4kscore accurately identifies men with high-grade prostate cancer. European Urology 2015; **68:** 464
178. Loeb S, Sanda MG, Broyles DL et al: The prostate health index selectively identifies clinically significant prostate cancer. Journal of Urology 2015; **193:** 1163
179. Morote J, Celma A, Planas J et al: Diagnostic accuracy of prostate health index to identify aggressive prostate cancer. An institutional validation study. Actas Urologicas Espanolas 2016; **40:** 378
180. Seisen T, Roupret M, Brault D et al: Accuracy of the prostate health index versus the urinary prostate cancer antigen 3 score to predict overall and significant prostate cancer at initial biopsy. Prostate 2015; **75:** 103
181. Kim L, Boxall N, George A et al: Clinical utility and cost modelling of the phi test to triage referrals into image-based diagnostic services for suspected prostate cancer: The prim (phi to refine mri) study. BMC Medicine 2020; **18:** 95
182. Tosoian JJ, Zhang Y, Xiao L et al: Development and validation of an 18-gene urine test for high-grade prostate cancer. JAMA Oncology 2024; **10:** 726
183. Eyrich NW, Morgan TM and Tosoian JJ: Biomarkers for detection of clinically significant prostate cancer: Contemporary clinical data and future directions. Transl Androl Urol 2021; **10:** 3091
184. de la Calle C, Patil D, Wei JT et al: Multicenter evaluation of the prostate health index to detect aggressive prostate cancer in biopsy naive men. Journal of Urology 2015; **194:** 65
185. de la Taille A, Irani J, Graefen M et al: Clinical evaluation of the pca3 assay in guiding initial biopsy decisions. Journal of Urology 2011; **185:** 2119
186. Falagario UG, Martini A, Wajswol E et al: Avoiding unnecessary magnetic resonance imaging (mri) and biopsies: Negative and positive predictive value of mri according to prostate-specific antigen density, 4kscore and risk calculators. European Urology Oncology 2020; **3:** 700

187. Hansen J, Auprich M, Ahyai SA et al: Initial prostate biopsy: Development and internal validation of a biopsy-specific nomogram based on the prostate cancer antigen 3 assay. European Urology 2013; **63:** 201
188. Hendriks RJ, van der Leest MMG, Israel B et al: Clinical use of the selectmdx urinary-biomarker test with or without mpmri in prostate cancer diagnosis: A prospective, multicenter study in biopsy-naive men. Prostate Cancer & Prostatic Diseases 2021; **3:** 03
189. Lazzeri M, Haese A, de la Taille A et al: Serum isoform [-2]propsa derivatives significantly improve prediction of prostate cancer at initial biopsy in a total psa range of 2-10 ng/ml: A multicentric european study. Eur Urol 2013; **63:** 986
190. Lebastchi AH, Russell CM, Niknafs YS et al: Impact of the myprostatescore (mps) test on the clinical decision to undergo prostate biopsy: Results from a contemporary academic practice. Urology 2020; **145:** 204
191. Lendinez-Cano G, Ojeda-Claro AV, Gomez-Gomez E et al: Prospective study of diagnostic accuracy in the detection of high-grade prostate cancer in biopsy-naive patients with clinical suspicion of prostate cancer who underwent the select mdx test. Prostate 2021; **81:** 857
192. McKiernan J, Donovan MJ, Margolis E et al: A prospective adaptive utility trial to validate performance of a novel urine exosome gene expression assay to predict high-grade prostate cancer in patients with prostate-specific antigen 2-10ng/ml at initial biopsy. European Urology 2018; **74:** 731
193. McKiernan J, Donovan MJ, O'Neill V et al: A novel urine exosome gene expression assay to predict high-grade prostate cancer at initial biopsy. JAMA Oncology 2016; **2:** 882
194. Nordstrom T, Vickers A, Assel M et al: Comparison between the four-kallikrein panel and prostate health index for predicting prostate cancer. European Urology 2015; **68:** 139
195. Tutrone R, Donovan MJ, Torkler P et al: Clinical utility of the exosome based exodx prostate(intelliscore) epi test in men presenting for initial biopsy with a psa 2-10 ng/ml. Prostate Cancer & Prostatic Diseases 2020; **23:** 607
196. Rubio-Briones J, Borque A, Esteban LM et al: Optimizing the clinical utility of pca3 to diagnose prostate cancer in initial prostate biopsy. BMC Cancer 2015; **15:** 633
197. Jiao B, Gulati R, Hendrix N et al: Economic evaluation of urine-based or magnetic resonance imaging reflex tests in men with intermediate prostate-specific antigen levels in the united states. Value Health 2021; **24:** 1111
198. Benchikh A, Savage C, Cronin A et al: A panel of kallikrein markers can predict outcome of prostate biopsy following clinical work-up: An independent validation study from the european randomized study of prostate cancer screening, france. BMC Cancer 2010; **10:** 635
199. Gupta A, Roobol MJ, Savage CJ et al: A four-kallikrein panel for the prediction of repeat prostate biopsy: Data from the european randomized study of prostate cancer screening in rotterdam, netherlands. British Journal of Cancer 2010; **103:** 708
200. Josefsson A, Mansson M, Kohestani K et al: Performance of 4kscore as a reflex test to prostate-specific antigen in the goteborg-2 prostate cancer screening trial. European Urology 2024; **86:** 223
201. de Almeida SR, Jr., Thomas J, Mason MM et al: Optimum threshold of the 4kscore for biopsy in men with negative or indeterminate multiparametric magnetic resonance imaging. BJUI Compass 2023; **4:** 591
202. Thomas J, Atluri S, Zucker I et al: A multi-institutional study of 1,111 men with 4k score, multiparametric magnetic resonance imaging, and prostate biopsy. Urologic Oncology 2023; **41:** 430.e9
203. Stovsky M, Klein EA, Chait A et al: Clinical validation of isopsa™, a single parameter, structure based assay for improved detection of high grade prostate cancer. J Urol 2019; **201:** 1115
204. Benidir T, Lone Z, Wood A et al: Using isopsa with prostate imaging reporting and data system score may help refine biopsy decision making in patients with elevated psa. Urology 2023; **176:** 115
205. Klein EA, Chait A, Hafron JM et al: The single-parameter, structure-based isopsa assay demonstrates improved diagnostic accuracy for detection of any prostate cancer and high-grade prostate cancer compared to a concentration-based assay of total prostate-specific antigen: A preliminary report. Eur Urol 2017; **72:** 942
206. Klein EA, Partin A, Lotan Y et al: Clinical validation of isopsa, a single parameter, structure-focused assay for improved detection of prostate cancer: A prospective, multicenter study. Urol Oncol 2022; **40:** 408.e9
207. Steuber T, Heidegger I, Kafka M et al: Propose: A real-life prospective study of proclarix, a novel blood-based test to support challenging biopsy decision-making in prostate cancer. Eur Urol Oncol 2022; **5:** 321
208. Kaufmann B, Fischer S, Athanasiou A et al: Evaluation of proclarix in the diagnostic work-up of prostate cancer. BJUI Compass 2024; **5:** 297
209. Morote J, Pye H, Campistol M et al: Accurate diagnosis of prostate cancer by combining proclarix with magnetic resonance imaging. BJU International 2023; **132:** 188
210. Lazzeri M, Briganti A, Scattoni V et al: Serum index test %[-2]propsa and prostate health index are more accurate than prostate specific antigen and %fpsa in predicting a positive repeat prostate biopsy. Journal of Urology 2012; **188:** 1137

211. Gnanapragasam VJ, Burling K, George A et al: The prostate health index adds predictive value to multi-parametric mri in detecting significant prostate cancers in a repeat biopsy population. Scientific Reports 2016; **6:** 35364
212. Porpiglia F, Russo F, Manfredi M et al: The roles of multiparametric magnetic resonance imaging, pca3 and prostate health index-which is the best predictor of prostate cancer after a negative biopsy? Journal of Urology 2014; **192:** 60
213. Zhou Y, Fu Q, Shao Z et al: The function of prostate health index in detecting clinically significant prostate cancer in the pi-rads 3 population: A multicenter prospective study. World Journal of Urology 2023; **41:** 455
214. Zhu M, Fu Q, Zang Y et al: Different diagnostic strategies combining prostate health index and magnetic resonance imaging for predicting prostate cancer: A multicentre study. Urologic Oncology 2024; **42:** 159.e17
215. Chiu PK, Lam TY, Ng CF et al: The combined role of mri prostate and prostate health index in improving detection of significant prostate cancer in a screening population of chinese men. Asian Journal of Andrology 2023; **25:** 674
216. Boo Y, Chung JH, Kang M et al: Comparison of prostate-specific antigen and its density and prostate health index and its density for detection of prostate cancer. Biomedicines 2023; **11:** 06
217. Chiu PK, Leow JJ, Chiang CH et al: Prostate health index density outperforms prostate-specific antigen density in the diagnosis of clinically significant prostate cancer in equivocal magnetic resonance imaging of the prostate: A multicenter evaluation. Journal of Urology 2023; **210:** 88
218. Chiu PK, Liu AQ, Lau SY et al: A 2-year prospective evaluation of the prostate health index in guiding biopsy decisions in a large cohort. BJU International 2024; **4:** 04
219. Strom P, Nordstrom T, Aly M et al: The stockholm-3 model for prostate cancer detection: Algorithm update, biomarker contribution, and reflex test potential. European Urology 2018; **74:** 204
220. Bjornebo L, Discacciati A, Falagario U et al: Biomarker vs mri-enhanced strategies for prostate cancer screening: The sthlm3-mri randomized clinical trial. JAMA Network Open 2024; **7:** e247131
221. Elyan A, Saba K, Sigle A et al: Prospective multicenter validation of the stockholm3 test in a central european cohort. European Urology Focus 2023; **7:** 07
222. Chevli KK, Duff M, Walter P et al: Urinary pca3 as a predictor of prostate cancer in a cohort of 3,073 men undergoing initial prostate biopsy. Journal of Urology 2014; **191:** 1743
223. Sanda MG, Feng Z, Howard DH et al: Association between combined tmprss2:Erg and pca3 rna urinary testing and detection of aggressive prostate cancer. JAMA Oncology 2017; **3:** 1085
224. Haese A, de la Taille A, van Poppel H et al: Clinical utility of the pca3 urine assay in european men scheduled for repeat biopsy. European Urology 2008; **54:** 1081
225. Gittelman MC, Hertzman B, Bailen J et al: Pca3 molecular urine test as a predictor of repeat prostate biopsy outcome in men with previous negative biopsies: A prospective multicenter clinical study. Journal of Urology 2013; **190:** 64
226. Haese A, Trooskens G, Steyaert S et al: Multicenter optimization and validation of a 2-gene mrna urine test for detection of clinically significant prostate cancer before initial prostate biopsy. Journal of Urology 2019; **202:** 256
227. Wagaskar VG, Levy M, Ratnani P et al: A selectmdx/magnetic resonance imaging-based nomogram to diagnose prostate cancer. Cancer Reports 2023; **6:** e1668
228. McKiernan J, Noerholm M, Tadigotla V et al: A urine-based exosomal gene expression test stratifies risk of high-grade prostate cancer in men with prior negative prostate biopsy undergoing repeat biopsy. BMC Urology 2020; **20:** 138
229. Tutrone R, Lowentritt B, Neuman B et al: Exodx prostate test as a predictor of outcomes of high-grade prostate cancer - an interim analysis. Prostate Cancer & Prostatic Diseases 2023; **26:** 596
230. Sultan MI, Huynh LM, Kamil S et al: Utility of noninvasive biomarker testing and mri to predict a prostate cancer diagnosis. International Urology & Nephrology 2024; **56:** 539
231. Wang WW, Sorokin I, Aleksic I et al: Expression of small noncoding rnas in urinary exosomes classifies prostate cancer into indolent and aggressive disease. J Urol 2020; **204:** 466
232. Van Neste L, Partin AW, Stewart GD et al: Risk score predicts high-grade prostate cancer in DNA-methylation positive, histopathologically negative biopsies. Prostate 2016; **76:** 1078
233. Waterhouse RL, Jr., Van Neste L, Moses KA et al: Evaluation of an epigenetic assay for predicting repeat prostate biopsy outcome in african american men. Urology 2019; **128:** 62
234. Huynh-Le MP, Fan CC, Karunamuni R et al: Polygenic hazard score is associated with prostate cancer in multi-ethnic populations. Nat Commun 2021; **12:** 1236
235. Pashayan N, Pharoah PD, Schleutker J et al: Reducing overdiagnosis by polygenic risk-stratified screening: Findings from the finnish section of the erspc. British Journal of Cancer 2015; **113:** 1086

236. Benafif S, Ni Raghallaigh H, McGrowder E et al: The barcode1 pilot: A feasibility study of using germline single nucleotide polymorphisms to target prostate cancer screening. BJU Int 2021; **129:** 325
237. Gerstenbluth RE, Seftel AD, Hampel N et al: The accuracy of the increased prostate specific antigen level (greater than or equal to 20 ng./ml.) in predicting prostate cancer: Is biopsy always required? Journal of Urology 2002; **168:** 1990
238. Abraham NE, Mendhiratta N and Taneja SS: Patterns of repeat prostate biopsy in contemporary clinical practice. Journal of Urology 2015; **193:** 1178
239. Bittner N, Merrick GS, Butler WM et al: Incidence and pathological features of prostate cancer detected on transperineal template guided mapping biopsy after negative transrectal ultrasound guided biopsy. Journal of Urology 2013; **190:** 509
240. Giulianelli R, Brunori S, Gentile BC et al: Saturation biopsy technique increase the capacity to diagnose adenocarcinoma of prostate in patients with psa < 10 ng/ml, after a first negative biopsy. Archivio Italiano di Urologia, Andrologia 2011; **83:** 154
241. Nam RK, Toi A, Trachtenberg J et al: Variation in patterns of practice in diagnosing screen-detected prostate cancer. BJU International 2004; **94:** 1239
242. Ploussard G, Nicolaiew N, Marchand C et al: Risk of repeat biopsy and prostate cancer detection after an initial extended negative biopsy: Longitudinal follow-up from a prospective trial. BJU International 2013; **111:** 988
243. Thompson IM, Tangen CM, Ankerst DP et al: The performance of prostate specific antigen for predicting prostate cancer is maintained after a prior negative prostate biopsy. J Urol 2008; **180:** 544
244. Cucchiara V, Cooperberg MR, Dall'Era M et al: Genomic markers in prostate cancer decision making. Eur Urol 2018; **73:** 572
245. Foley RW, Maweni RM, Gorman L et al: European randomised study of screening for prostate cancer (erspc) risk calculators significantly outperform the prostate cancer prevention trial (pcpt) 2.0 in the prediction of prostate cancer: A multi-institutional study. BJU International 2016; **1:** 706
246. Kim TS, Ko KJ, Shin SJ et al: Multiple cores of high grade prostatic intraepithelial neoplasia and any core of atypia on first biopsy are significant predictor for cancer detection at a repeat biopsy. Korean Journal of Urology 2015; **56:** 796
247. Palmstedt E, Mansson M, Franlund M et al: Long-term outcomes for men in a prostate screening trial with an initial benign prostate biopsy: A population-based cohort. Eur Urol Oncol 2019; **2:** 716
248. Klemann N, Roder MA, Helgstrand JT et al: Risk of prostate cancer diagnosis and mortality in men with a benign initial transrectal ultrasound-guided biopsy set: A population-based study. Lancet Oncol 2017; **18:** 221
249. Roobol MJ, Steyerberg EW, Kranse R et al: A risk-based strategy improves prostate-specific antigen-driven detection of prostate cancer. Eur Urol 2010; **57:** 79
250. Nam RK, Satkunavisam R, Chin JL et al: Next-generation prostate cancer risk calculator for primary care physicians. Can Urol Assoc J 2018; **12:** E64
251. Nordstrom T, Akre O, Aly M et al: Prostate-specific antigen (psa) density in the diagnostic algorithm of prostate cancer. Prostate Cancer & Prostatic Diseases 2018; **21:** 57
252. Hansen NL, Barrett T, Koo B et al: The influence of prostate-specific antigen density on positive and negative predictive values of multiparametric magnetic resonance imaging to detect gleason score 7-10 prostate cancer in a repeat biopsy setting. BJU International 2017; **119:** 724
253. Tosoian JJ, Sessine MS, Trock BJ et al: Myprostatescore in men considering repeat biopsy: Validation of a simple testing approach. Prostate Cancer & Prostatic Diseases 2023; **26:** 563
254. Stewart GD, Van Neste L, Delvenne P et al: Clinical utility of an epigenetic assay to detect occult prostate cancer in histopathologically negative biopsies: Results of the matloc study. Journal of Urology 2013; **189:** 1110
255. Partin AW, Van Neste L, Klein EA et al: Clinical validation of an epigenetic assay to predict negative histopathological results in repeat prostate biopsies. J Urol 2014; **192:** 1081
256. Tosoian JJ, Singhal U, Davenport MS et al: Urinary myprostatescore (mps) to rule out clinically-significant cancer in men with equivocal (pi-rads 3) multiparametric mri: Addressing an unmet clinical need. Urology 2022; **164:** 184
257. Herawi M, Kahane H, Cavallo C and Epstein JI: Risk of prostate cancer on first re-biopsy within 1 year following a diagnosis of high grade prostatic intraepithelial neoplasia is related to the number of cores sampled. J Urol 2006; **175:** 121
258. Tosoian JJ, Alam R, Ball MW et al: Managing high-grade prostatic intraepithelial neoplasia (hgpin) and atypical glands on prostate biopsy. Nat Rev Urol 2018; **15:** 55
259. Bishara T, Ramnani DM and Epstein JI: High-grade prostatic intraepithelial neoplasia on needle biopsy: Risk of cancer on repeat biopsy related to number of involved cores and morphologic pattern. American Journal of Surgical Pathology 2004; **28:** 629

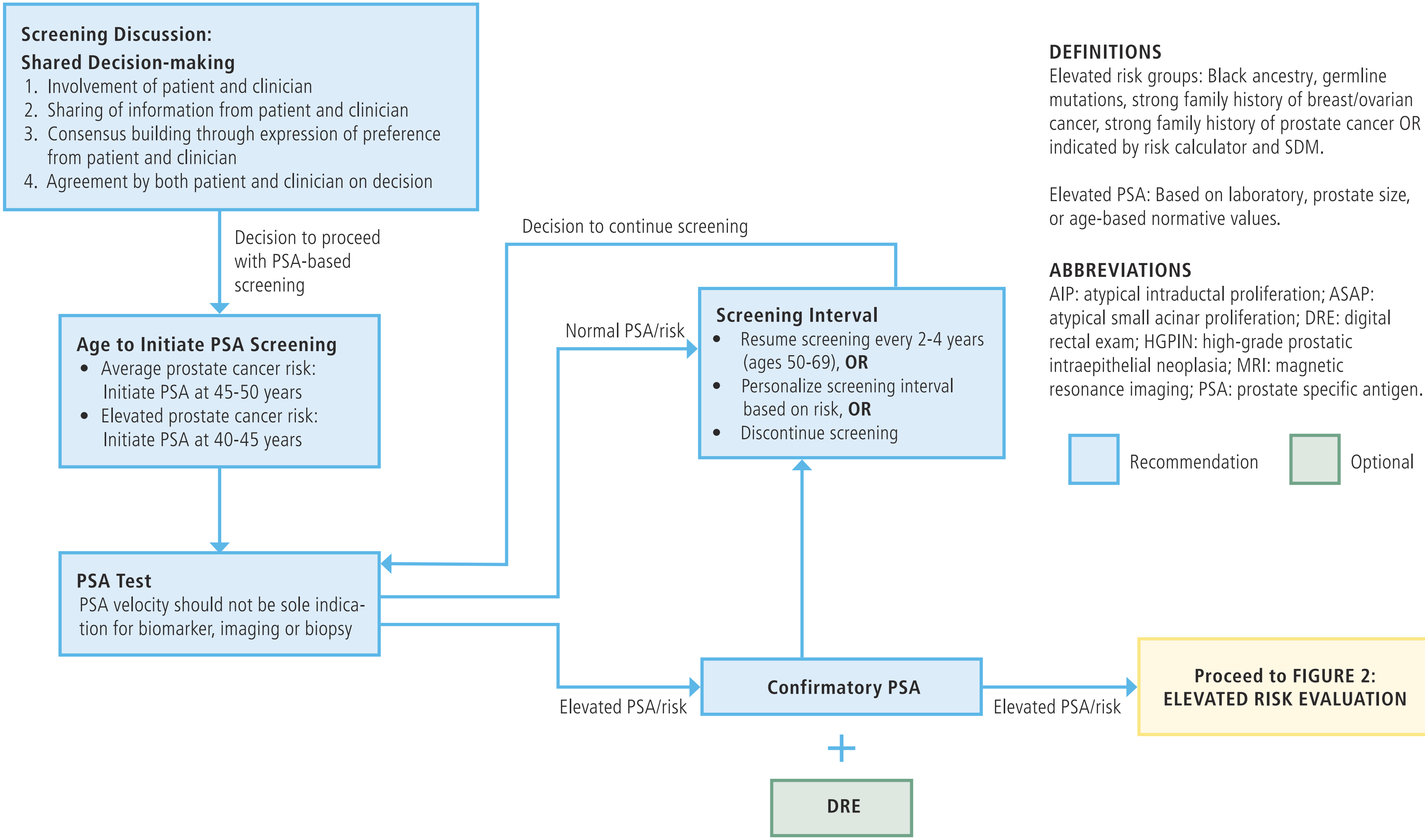
260. Godoy G, Huang GJ, Patel T and Taneja SS: Long-term follow-up of men with isolated high-grade prostatic intra-epithelial neoplasia followed by serial delayed interval biopsy. Urology 2011; **77:** 669
261. Patel P, Nayak JG, Biljetina Z et al: Prostate cancer after initial high-grade prostatic intraepithelial neoplasia and benign prostate biopsy. Canadian Journal of Urology 2015; **22:** 8056
262. Wiener S, Haddock P, Cusano J et al: Incidence of clinically significant prostate cancer after a diagnosis of atypical small acinar proliferation, high-grade prostatic intraepithelial neoplasia, or benign tissue. Urology 2017; **110:** 161
263. Girasole CR, Cookson MS, Putzi MJ et al: Significance of atypical and suspicious small acinar proliferations, and high grade prostatic intraepithelial neoplasia on prostate biopsy: Implications for cancer detection and biopsy strategy. Journal of Urology 2006; **175:** 929
264. Tan PH, Tan HW, Tan Y et al: Is high-grade prostatic intraepithelial neoplasia on needle biopsy different in an asian population: A clinicopathologic study performed in singapore. Urology 2006; **68:** 800
265. Akhavan A, Keith JD, Bastacky SI et al: The proportion of cores with high-grade prostatic intraepithelial neoplasia on extended-pattern needle biopsy is significantly associated with prostate cancer on site-directed repeat biopsy. BJU Int 2007; **99:** 765
266. Oderda M, Rosazza M, Agnello M et al: Natural history of widespread high grade prostatic intraepithelial neoplasia and atypical small acinar proliferation: Should we rebiopsy them all? Scandinavian Journal of Urology 2021; **55:** 129
267. Netto GJ and Epstein JI: Widespread high-grade prostatic intraepithelial neoplasia on prostatic needle biopsy: A significant likelihood of subsequently diagnosed adenocarcinoma. Am J Surg Pathol 2006; **30:** 1184
268. Morote J, Schwartzmann I, Celma A et al: The current recommendation for the management of isolated high-grade prostatic intraepithelial neoplasia. BJU International 2021; **10:** 10
269. Iczkowski KA, Bassler TJ, Schwob VS et al: Diagnosis of "suspicious for malignancy" in prostate biopsies: Predictive value for cancer. Urology 1998; **51:** 749
270. Iczkowski KA, Chen HM, Yang XJ and Beach RA: Prostate cancer diagnosed after initial biopsy with atypical small acinar proliferation suspicious for malignancy is similar to cancer found on initial biopsy. Urology 2002; **60:** 851
271. Schlesinger C, Bostwick DG and Iczkowski KA: High-grade prostatic intraepithelial neoplasia and atypical small acinar proliferation: Predictive value for cancer in current practice. Am J Surg Pathol 2005; **29:** 1201
272. Epstein JI and Herawi M: Prostate needle biopsies containing prostatic intraepithelial neoplasia or atypical foci suspicious for carcinoma: Implications for patient care. J Urol 2006; **175:** 820
273. Koca O, Caliskan S, Ozturk MI et al: Significance of atypical small acinar proliferation and high-grade prostatic intraepithelial neoplasia in prostate biopsy. Korean Journal of Urology 2011; **52:** 736
274. Leone A, Gershman B, Rotker K et al: Atypical small acinar proliferation (asap): Is a repeat biopsy necessary asap? A multi-institutional review. Prostate Cancer & Prostatic Diseases 2016; **19:** 68
275. Warlick C, Feia K, Tomasini J et al: Rate of gleason 7 or higher prostate cancer on repeat biopsy after a diagnosis of atypical small acinar proliferation. Prostate Cancer & Prostatic Diseases 2015; **18:** 255
276. Dorin RP, Wiener S, Harris CD and Wagner JR: Prostate atypia: Does repeat biopsy detect clinically significant prostate cancer? Prostate 2015; **75:** 673
277. Ji WT, Jin XF and Wang Y: The rate of clinically significant prostate cancer on repeat biopsy after a diagnosis of atypical small acinar proliferation: A systematic review and meta-analysis. Oncology 2024; **102:** 631
278. Shah RB, Magi-Galluzzi C, Han B and Zhou M: Atypical cribriform lesions of the prostate: Relationship to prostatic carcinoma and implication for diagnosis in prostate biopsies. Am J Surg Pathol 2010; **34:** 470
279. Shah RB and Zhou M: Atypical cribriform lesions of the prostate: Clinical significance, differential diagnosis and current concept of intraductal carcinoma of the prostate. Adv Anat Pathol 2012; **19:** 270
280. Shah RB, Yoon J, Liu G and Tian W: Atypical intraductal proliferation and intraductal carcinoma of the prostate on core needle biopsy: A comparative clinicopathological and molecular study with a proposal to expand the morphological spectrum of intraductal carcinoma. Histopathology 2017; **71:** 693
281. Hickman RA, Yu H, Li J et al: Atypical intraductal cribriform proliferations of the prostate exhibit similar molecular and clinicopathologic characteristics as intraductal carcinoma of the prostate. Am J Surg Pathol 2017; **41:** 550
282. Shah RB, Nguyen JK, Przybycin CG et al: Atypical intraductal proliferation detected in prostate needle biopsy is a marker of unsampled intraductal carcinoma and other adverse pathological features: A prospective clinicopathological study of 62 cases with emphasis on pathological outcomes. Histopathology 2019; **75(3):** 346
283. Hoeks CM, Schouten MG, Bomers JG et al: Three-tesla magnetic resonance-guided prostate biopsy in men with increased prostate-specific antigen and repeated, negative, random, systematic, transrectal ultrasound biopsies: Detection of clinically significant prostate cancers. European Urology 2012; **62:** 902

284. Arsov C, Rabenalt R, Blondin D et al: Prospective randomized trial comparing magnetic resonance imaging (mri)-guided in-bore biopsy to mri-ultrasound fusion and transrectal ultrasound-guided prostate biopsy in patients with prior negative biopsies. European Urology 2015; **68:** 713
285. Hambrock T, Somford DM, Hoeks C et al: Magnetic resonance imaging guided prostate biopsy in men with repeat negative biopsies and increased prostate specific antigen. Journal of Urology 2010; **183:** 520
286. Sonn GA, Chang E, Natarajan S et al: Value of targeted prostate biopsy using magnetic resonance-ultrasound fusion in men with prior negative biopsy and elevated prostate-specific antigen. European Urology 2014; **65:** 809
287. Meermeier NP, Foster BR, Liu JJ et al: Impact of direct mri-guided biopsy of the prostate on clinical management. AJR American Journal of Roentgenology 2019; **213:** 371
288. Da Rosa MR, Milot L, Sugar L et al: A prospective comparison of mri-us fused targeted biopsy versus systematic ultrasound-guided biopsy for detecting clinically significant prostate cancer in patients on active surveillance. J Magn Reson Imaging 2015; **41:** 220
289. Elkjær MC, Andersen MH, Høyer S et al: Prostate cancer: In-bore magnetic resonance guided biopsies at active surveillance inclusion improve selection of patients for active treatment. Acta Radiol 2018; **59:** 619
290. Welch HG, Fisher ES, Gottlieb DJ and Barry MJ: Detection of prostate cancer via biopsy in the medicare-seer population during the psa era. Journal of the National Cancer Institute 2007; **99:** 1395
291. Distler FA, Radtke JP, Bonekamp D et al: The value of psa density in combination with pi-rads for the accuracy of prostate cancer prediction. J Urol 2017; **198:** 575
292. Druskin SC, Tosoian JJ, Young A et al: Combining prostate health index density, magnetic resonance imaging and prior negative biopsy status to improve the detection of clinically significant prostate cancer. BJU International 2018; **121:** 619
293. Kamal O, Comerford J, Foster BR et al: Intermediate-term oncological outcomes after a negative endorectal coil multiparametric mri of the prostate in patients without biopsy proven prostate cancer. Clinical Imaging 2022; **92:** 112
294. Zhen L, Liu X, Yegang C et al: Accuracy of multiparametric magnetic resonance imaging for diagnosing prostate cancer: A systematic review and meta-analysis. BMC Cancer 2019; **19:** 1244
295. Patel N, Cricco-Lizza E, Kasabwala K et al: The role of systematic and targeted biopsies in light of overlap on magnetic resonance imaging ultrasound fusion biopsy. European Urology Oncology 2018; **1:** 263
296. Salami SS, Ben-Levi E, Yaskiv O et al: In patients with a previous negative prostate biopsy and a suspicious lesion on magnetic resonance imaging, is a 12-core biopsy still necessary in addition to a targeted biopsy? BJU International 2015; **115:** 562
297. Loeb S, Carter HB, Berndt SI et al: Is repeat prostate biopsy associated with a greater risk of hospitalization? Data from seer-medicare. Journal of Urology 2013; **189:** 867
298. Fujita K, Landis P, McNeil BK and Pavlovich CP: Serial prostate biopsies are associated with an increased risk of erectile dysfunction in men with prostate cancer on active surveillance. J Urol 2009; **182:** 2664
299. Hale GR, Czarniecki M, Cheng A et al: Comparison of elastic and rigid registration during magnetic resonance imaging/ultrasound fusion-guided prostate biopsy: A multi-operator phantom study. J Urol 2018; **200:** 1114
300. Izadpanahi MH, Elahian A, Gholipour F et al: Diagnostic yield of fusion magnetic resonance-guided prostate biopsy versus cognitive-guided biopsy in biopsy-naive patients: A head-to-head randomized controlled trial. Prostate Cancer & Prostatic Diseases 2021; **27:** 27
301. Watts KL, Frechette L, Muller B et al: Systematic review and meta-analysis comparing cognitive vs. Image-guided fusion prostate biopsy for the detection of prostate cancer. Urologic Oncology 2020; **38:** 734.e19
302. Hamid S, Donaldson IA, Hu Y et al: The smarttarget biopsy trial: A prospective, within-person randomised, blinded trial comparing the accuracy of visual-registration and magnetic resonance imaging/ultrasound image-fusion targeted biopsies for prostate cancer risk stratification. European Urology 2019; **75:** 733
303. Liang L, Cheng Y, Qi F et al: A comparative study of prostate cancer detection rate between transperineal cog-tb and transperineal fus-tb in patients with psa <=20 ng/ml. Journal of Endourology 2020; **34:** 1008
304. Dai Z, Liu Y, Huangfu Z et al: Magnetic resonance imaging (mri)-targeted biopsy in patients with prostate-specific antigen (psa) levels <20 ng/ml: A single-center study in northeastern china. Medical Science Monitor 2021; **27:** e930234
305. Wegelin O, Exterkate L, van der Leest M et al: The future trial: A multicenter randomised controlled trial on target biopsy techniques based on magnetic resonance imaging in the diagnosis of prostate cancer in patients with prior negative biopsies. European Urology 2019; **75:** 582
306. Sonmez G, Demirtas T, Tombul ST et al: What is the ideal number of biopsy cores per lesion in targeted prostate biopsy? Prostate International 2020; **8:** 112

307. Subramanian N, Recchimuzzi DZ, Xi Y et al: Impact of the number of cores on the prostate cancer detection rate in men undergoing in-bore magnetic resonance imaging-guided targeted biopsies. J Comput Assist Tomogr 2021; **45:** 203
308. Tu X, Lin T, Cai D et al: The optimal core number and site for mri-targeted biopsy of prostate? A systematic review and pooled analysis. Minerva Urologica e Nefrologica 2020; **72:** 144
309. Eastham JA, Auffenberg GB, Barocas DA et al: Clinically localized prostate cancer: Aua/astro guideline, part i: Introduction, risk assessment, staging, and risk-based management. J Urol 2022; **208:** 10
310. Scott S, Samaratunga H, Chabert C et al: Is transperineal prostate biopsy more accurate than transrectal biopsy in determining final gleason score and clinical risk category? A comparative analysis. BJU Int 2015; **116 Suppl 3:** 26
311. Uleri A, Baboudjian M, Tedde A et al: Is there an impact of transperineal versus transrectal magnetic resonance imaging-targeted biopsy in clinically significant prostate cancer detection rate? A systematic review and meta-analysis. Eur Urol Oncol 2023; **6:** 621
312. Diamand R, Guenzel K, Mjaess G et al: Transperineal or transrectal magnetic resonance imaging-targeted biopsy for prostate cancer detection. Eur Urol Focus 2024; **10:** 805
313. Kaneko M, Medina LG, Lenon MSL et al: Transperineal vs transrectal magnetic resonance and ultrasound image fusion prostate biopsy: A pair-matched comparison. Sci Rep 2023; **13:** 13457
314. Zattoni F, Rajwa P, Miszczyk M et al: Transperineal versus transrectal magnetic resonance imaging-targeted prostate biopsy: A systematic review and meta-analysis of prospective studies. Eur Urol Oncol 2024; **7:** 1303
315. Hara R, Jo Y, Fujii T et al: Optimal approach for prostate cancer detection as initial biopsy: Prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy. Urology 2008; **71:** 191
316. Ploussard G, Barret E, Fiard G et al: Transperineal versus transrectal magnetic resonance imaging-targeted biopsies for prostate cancer diagnosis: Final results of the randomized perfect trial (ccafu-pr1). Eur Urol Oncol 2024; **7:** 1080
317. Bryant RJ, Marian IR, Williams R et al: Local anaesthetic transperineal biopsy versus transrectal prostate biopsy in prostate cancer detection (translate): A multicentre, randomised, controlled trial. Lancet Oncol 2025; **26:** 583
318. Mian BM, Feustel PJ, Aziz A et al: Complications following transrectal and transperineal prostate biopsy: Results of the probe-pc randomized clinical trial. J Urol 2024; **211:** 205
319. Mian BM, Feustel PJ, Aziz A et al: Clinically significant prostate cancer detection following transrectal and transperineal biopsy: Results of the prostate biopsy efficacy and complications randomized clinical trial. J Urol 2024; **212:** 21
320. Hu JC, Assel M, Allaf ME et al: Transperineal versus transrectal magnetic resonance imaging-targeted and systematic prostate biopsy to prevent infectious complications: The prevent randomized trial. Eur Urol 2024; **86:** 61
321. Berg S, Tully KH, Hoffmann V et al: Assessment of complications after transperineal and transrectal prostate biopsy using a risk-stratified pathway identifying patients at risk for post-biopsy infections. Scand J Urol 2023; **57:** 41
322. Berquin C, Perletti G, Develtere D et al: Transperineal vs. Transrectal prostate biopsies under local anesthesia: A prospective cohort study on patient tolerability and complication rates. Urol Oncol 2023; **41:** 388.e17
323. Hogenhout R, Remmers S, van Leenders G and Roobol MJ: The transition from transrectal to transperineal prostate biopsy without antibiotic prophylaxis: Cancer detection rates and complication rates. Prostate Cancer Prostatic Dis 2023; **26:** 581
324. Meyer AR, Mamawala M, Winoker JS et al: Transperineal prostate biopsy improves the detection of clinically significant prostate cancer among men on active surveillance. J Urol 2021; **205:** 1069
325. Roberts MJ, Bennett HY, Harris PN et al: Prostate biopsy-related infection: A systematic review of risk factors, prevention strategies, and management approaches. Urology 2017; **104:** 11
326. Womble PR, Linsell SM, Gao Y et al: A statewide intervention to reduce hospitalizations after prostate biopsy. J Urol 2015; **194:** 403
327. Drazer MW, Prasad SM, Huo D et al: National trends in prostate cancer screening among older american men with limited 9-year life expectancies: Evidence of an increased need for shared decision making. Cancer 2014; **120:** 1491
328. Nik-Ahd F, Jarjour A, Figueiredo J et al: Prostate-specific antigen screening in transgender patients. Eur Urol 2023; **83:** 48
329. Kinnaird A, Luger F, Cash H et al: Microultrasonography-guided vs mri-guided biopsy for prostate cancer diagnosis: The optimum randomized clinical trial. Jama 2025; **333:** 1679

330. Ng A, Asif A, Agarwal R et al: Biparametric vs multiparametric mri for prostate cancer diagnosis: The prime diagnostic clinical trial. Jama 2025; **334:** 1170

FIGURE 1: INITIAL SCREENING FOR PROSTATE CANCER



DEFINITIONS

Elevated risk groups: Black ancestry, germline mutations, strong family history of breast/ovarian cancer, strong family history of prostate cancer OR indicated by risk calculator and SDM.

Elevated PSA: Based on laboratory, prostate size, or age-based normative values.

ABBREVIATIONS

AIP: atypical intraductal proliferation; ASAP: atypical small acinar proliferation; DRE: digital rectal exam; HGPIN: high-grade prostatic intraepithelial neoplasia; MRI: magnetic resonance imaging; PSA: prostate specific antigen.

FIGURE 2: ELEVATED RISK EVALUATION

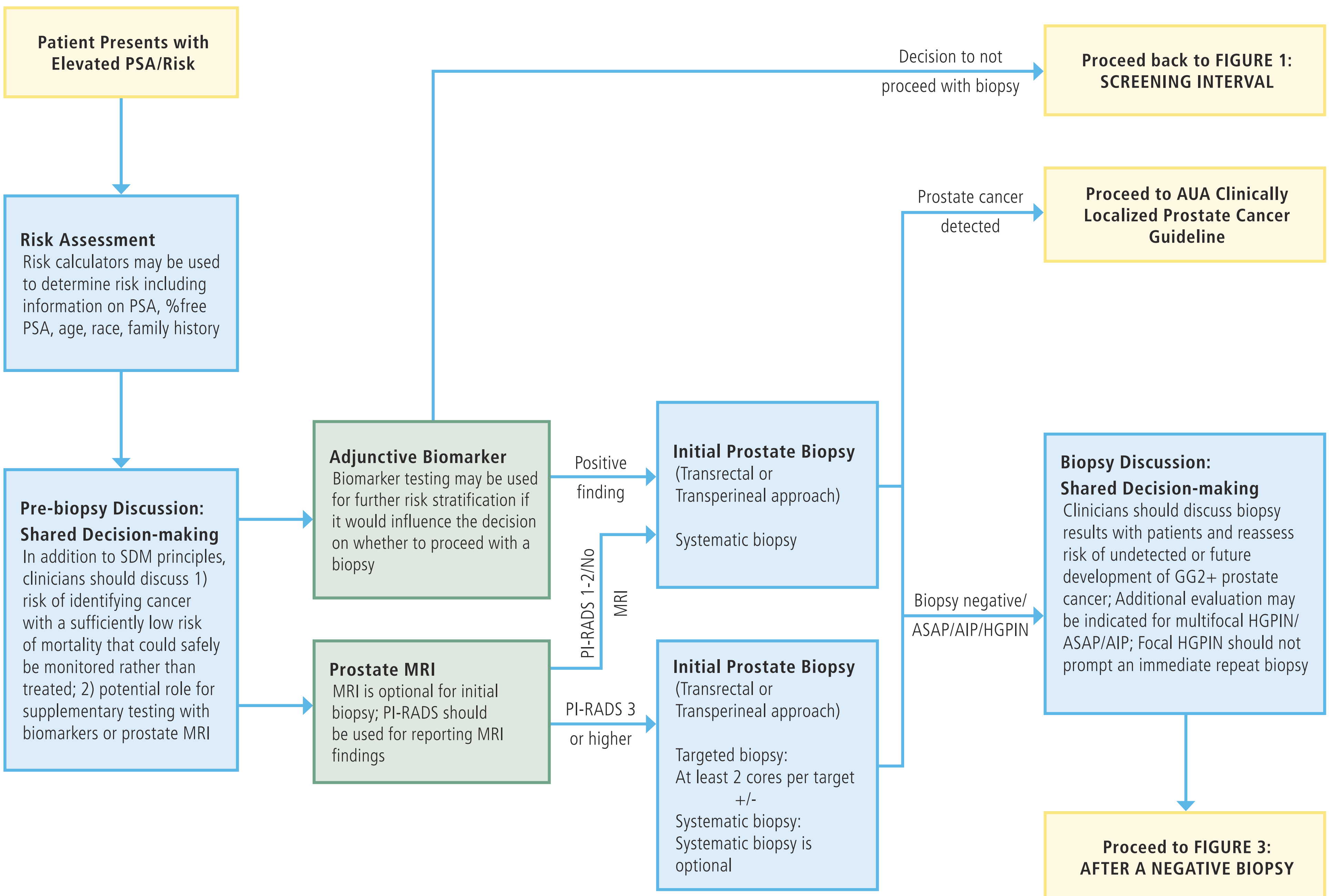
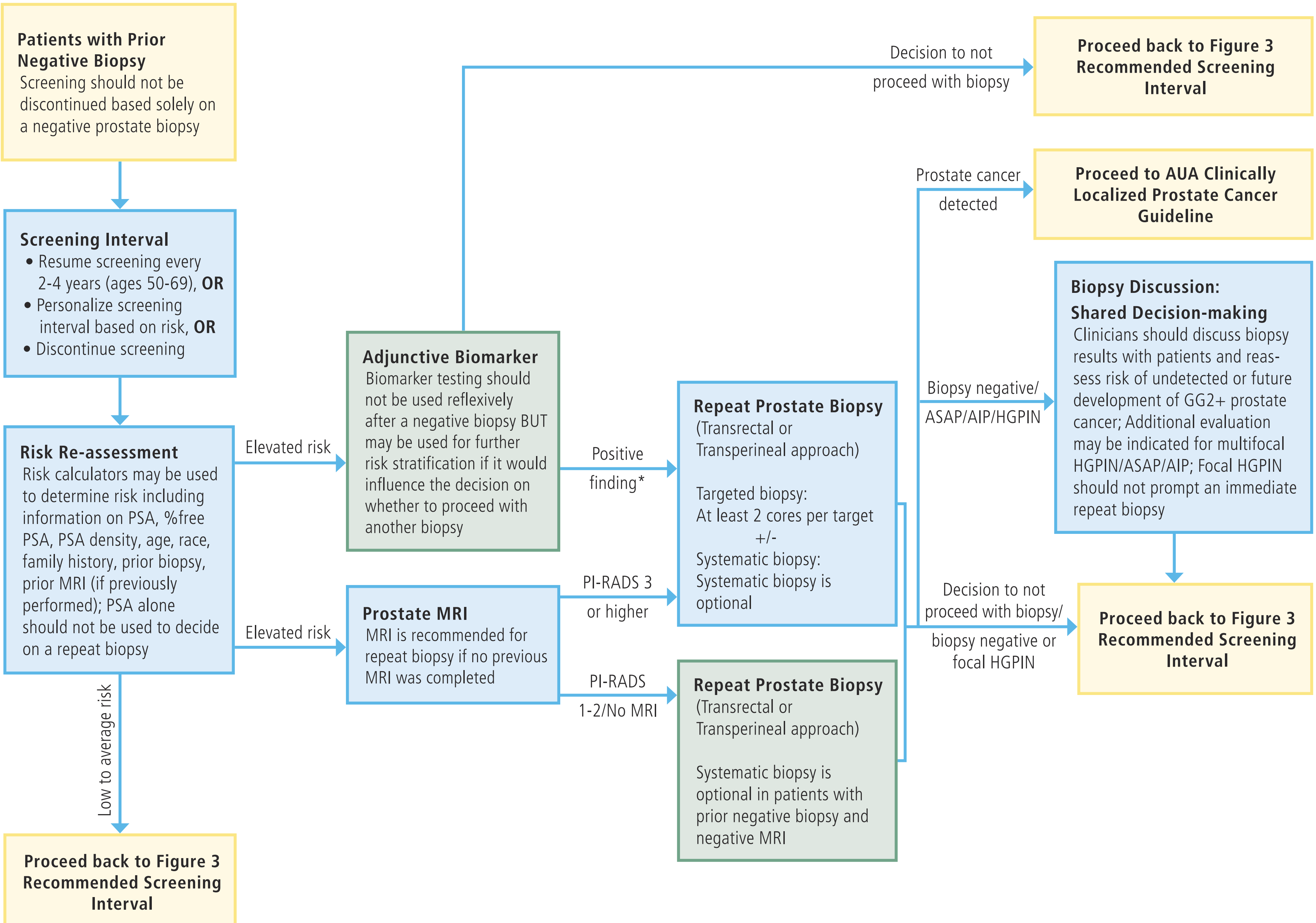


FIGURE 3: AFTER A NEGATIVE BIOPSY



 2023 AUA/SUO Early Detection of Prostate Cancer Algorithm *= if adjunctive biomarker is positive but MRI only shows PI-RADS 1 to 2, then should proceed with systematic biopsy.

Guideline Amendment Summary

Early Detection of Prostate Cancer: AUA/SUO Guideline (2026)

Published 2023; Amended 2026

The changes below constitute updates made in the 2026 Amendment:

Section	Document Update
Methodology	Updated to include 2026 amendment process
Introduction	Updated the following sections: "Panel Formation" "Searches and Articles Selection" "Peer Review and Document Approval"
Background	• Updated prostate cancer statistics • Included citations for polygenic risk scores
Statement #2	Statement remains unchanged Supporting text updated
Statement #3	Statement remains unchanged Supporting text updated
Statement #7	Statement remains unchanged Supporting text updated
Statement #8	Statement remains unchanged Supporting text updated

Section	Document Update
Statement #13	Statement grade has changed from Evidence Level Grade B to an A Supporting text has been updated
Statement #14	Statement remains unchanged Supporting text updated
Statement #16	Statement remains unchanged Supporting text updated
Statement #17	Statement remains unchanged Supporting text updated
Table 6	Table 6 on available biomarker assays has been updated
Statement #25	Statement remains unchanged Supporting text updated
Statement #28	Statement has changed to include “which may include repeat biopsy” Statement was previously an Expert Opinion and is now a Moderate Recommendation with an Evidence Level Grade C Supporting text updated
Statement #29	Statement remains unchanged First paragraph of supporting text was moved to Statement #28
Statement #35	Statement grade has changed from Evidence Level Grade C to a B Supporting text updated

Section	Document Update
Future Directions	Text has been updated to include: • Ongoing clinical trials • Evolving MRI protocols and the use of artificial intelligence
References	The reference list was updated to reflect document additions and deletions

Note: Additional editorial changes were made throughout the Guideline to align with current AUA Guideline criteria and for consistency purposes. These additional changes were not substantial and were not content-related.