

Evidence-Based Prostate Cancer Risk Assessment and Diagnostic Algorithmic Tests

- I. Prostate cancer risk assessment and diagnostic algorithmic tests with sufficient evidence of clinical validity and utility are considered **medically necessary** when:
 - A. The member meets all of the following:
 1. The member has not had a prostate biopsy, **AND**
 2. The member has at least one of the following:
 - a) Prostate specific antigen (PSA) greater than 3 ng/ml, **OR**
 - b) A digital rectal exam (DRE) that is suspicious for cancer, **AND**
 3. The test is one of the following:
 - a) Prostate Health Index (PHI), **OR**
 - b) SelectMDx, **OR**
 - c) 4Kscore, **OR**
 - d) ExoDx Prostate Test, **OR**
 - e) MyProstateScore 2.0 (MPS2), **OR**
 - f) IsoPSA, **OR**
 - B. The member meets all of the following:
 1. The member has had a prostate biopsy, **AND**
 2. The result is one of the following:
 - a) Atypia, suspicious for cancer, **OR**
 - b) High-grade prostatic intraepithelial neoplasia (PIN), **OR**
 - c) Benign, **AND**

3. The test is one of the following:
 - a) Prostate Health Index (PHI), **OR**
 - b) 4Kscore, **OR**
 - c) ExoDx Prostate Test, **OR**
 - d) MyProstateScore 2.0 (MPS2), **OR**
 - e) IsoPSA, **OR**
 - f) ConfirmMDx, **OR**
 - g) PCA3.
- II. The use of prostate cancer risk assessment and diagnostic algorithmic tests with sufficient evidence of clinical validity and utility are considered **investigational** for all other indications where clinical validity and utility have not been demonstrated.

RATIONALE AND REFERENCES

Evidence-Based Prostate Cancer Risk Assessment and Diagnostic Algorithmic Tests

American Urological Association (AUA) and Society of Urologic Oncology (SUO)

The AUA/SUO published guidelines on the early detection of prostate cancer (2023). They state that clinicians and patients may use adjunctive urine or serum markers to inform the shared decision making process regarding prostate biopsy (initial and/or repeat biopsy). 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 (conditional recommendation, evidence level C) (p. 21-22, 24).

Of note, 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. For evidence level C, the balance

between benefits and risks is unclear but net benefit or net harm is comparable to other options.

Wei JT, Barocas D, Carlsson S, et al. Early Detection of Prostate Cancer: AUA/SUO Guideline Part I: Prostate Cancer Screening. J Urol. 2023;210(1):46-53. doi:10.1097/JU.0000000000003491

Wei JT, Barocas D, Carlsson S, et al. Early Detection of Prostate Cancer: AUA/SUO Guideline Part II: Considerations for a Prostate Biopsy. J Urol. 2023;210(1):54-63. doi:10.1097/JU.0000000000003492

National Comprehensive Cancer Network (NCCN): Prostate Cancer Early Detection (2.2025)

This guideline recommends consideration of biomarkers that improve the specificity of screening in patients considering biopsy after abnormal PSA and/or DRE. Specifically, NCCN recommends further evaluation for individuals with PSA “greater than 3 ng/ml and/or a very suspicious DRE” (p. PROSD-2). Biomarker testing is mentioned as part of this additional evaluation, and NCCN specifies the following tests as options for risk stratification: Prostate Health Index (PHI), SelectMDx, 4Kscore, ExoDx Prostate Test, MyProstateScore (MPS), and IsoPSA (p. PROSD-3 and PROSD-A).

On page PROSD-4, NCCN also recommends consideration of biomarker tests to improve specificity when considering a repeat biopsy for biopsy results showing the following: atypia, suspicious for cancer; high-grade prostatic intraepithelial neoplasia (PIN); benign. These tests include those listed above (except for SelectMDX) plus PCA3 and ConfirmMDX.

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer Early Detection 2.2025

https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf