LifeLabs®

Elevated PSA Levels?

IsoPSA Testing Can Help Guide Next Steps

IsoPSA is a next-generation prostate cancer biomarker test designed for individuals who have elevated prostate-specific antigen (PSA) levels (≥ 4 ng/mL). The test supports clinical decision making by providing insight into whether elevated PSA is more likely to be related to prostate cancer or benign prostate conditions.

Elevated PSA Can Lack Clinical Clarity

While serum PSA testing remains a cornerstone of prostate cancer evaluation, total PSA lacks cancer specificity. Elevated PSA levels, which are often driven by benign conditions, such as benign prostatic hyperplasia, prostatitis, or inflammation, can lead to unnecessary imaging, biopsies, patient anxiety, and potential overtreatment. Traditional adjuncts, including %free PSA, offer incremental improvement but remain limited in reliably identifying clinically significant prostate cancer (csPCa).

IsoPSA Can Distinguish Cancer-Related PSA with Greater Certainty

By analyzing the structural isoforms of the PSA protein, rather than PSA concentration alone, IsoPSA helps clinicians determine whether an elevated PSA is more likely derived from malignant prostate cells rather than benign sources.

With high sensitivity and specificity 2-3 times that of traditional PSA tests[1,2], IsoPSA improves detection and has the ability to differentiate clinically significant prostate cancer from benign or less aggressive disease.

IsoPSA has been shown to be able to reduce up to 55% of unnecessary prostate biopsies[3] when used in conjunction with imaging, minimizing invasive procedures and meaningfully impacting patient care and quality of life.

IsoPSA can help:

- Support safer deferral of biopsy in low-risk patients
- Provide reassurance and give patients peace-of-mind
- Reduce false-positive results driven by benign PSA elevations
- Improve confidence in prostate cancer risk assessment
- Improve identification of clinically significant and high-grade prostate cancer
- Support personalized treatment decisions based on individual risk

Who is IsoPSA for?

IsoPSA is indicated for men over 50, with PSA levels ≥ 4 ng/mL. Its use in determining clinical next steps is especially valuable for medium-risk patients, with PSA levels between 4-10 ng/mL who are considering biopsy.

	IsoPSA	IsoPSA + MRI	PSA	%Free PSA	MRI Alone
AUC	0.783	0.83	0.672	0.724	0.76
Sensitivity	90-95%	93-94%	93%	95%	90-95%
Specificity	46-55%	75%	20%	14%	60%

Clinical Performance: Improved Specificity for Clinically Significant Prostate Cancer

IsoPSA demonstrates substantially higher specificity for clinically significant prostate cancer (csPCa) compared to standard PSA-based metrics:

- > 2× greater specificity than total PSA
- > 3× greater specificity than %free PSA

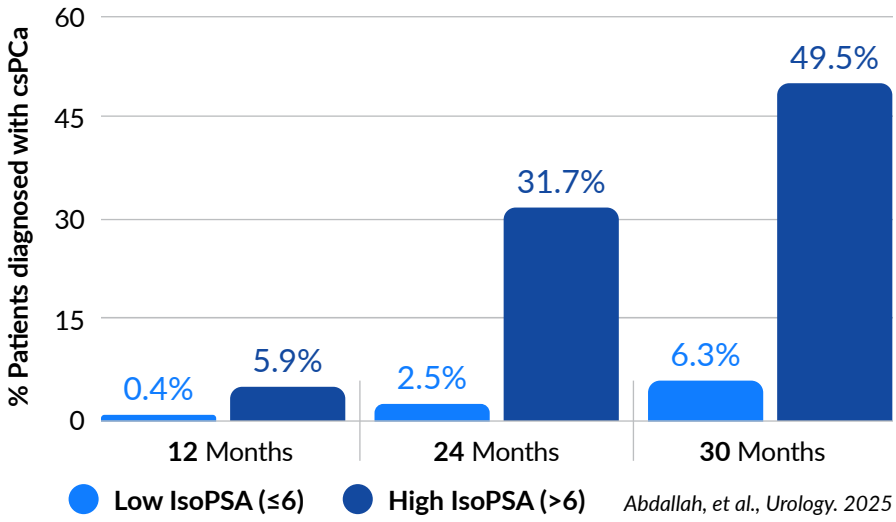
This improved specificity enables clinicians to more confidently distinguish patients who may benefit from biopsy from those who can safely defer invasive evaluation. Multiple studies report AUC values ranging from ~0.77 to 0.81 for high-grade prostate cancer detection, outperforming traditional concentration-based PSA measures[4,5].

Longitudinal data demonstrates that a single IsoPSA result can accurately predict csPCa risk for up to 30 months, with low IsoPSA indices associated with a very low subsequent risk of csPCa[6,8].

A single result accurately predicts csPCa over 2.5 years

IsoPSA Index ≤ 6
Demonstrated low risk of csPCa, providing confidence to defer biopsy or extend intervals between biopsies.

IsoPSA Index > 6
Nearly 50% develop csPCa within 2.5 years (30 months), indicating closer monitoring and follow-up is warranted.



Abdallah, et al., Urology. 2025

Methodology & Results

IsoPSA is performed on a blood sample and reported as a numerical score that reflects prostate cancer risk. Results should be interpreted by a healthcare provider in conjunction with PSA levels, clinical findings, imaging, and patient history.

Results may be available online through MyCareCompass and integrated healthcare provider Electronic Medical Records (EMRs).

IsoPSA Index	Risk Output Category	Suggested Interpretation
≤ 6.00	**Low**	**The patient's score falls in the Low-Risk category, associated with a decreased likelihood** of high-grade prostate cancer if a biopsy were performed. The clinician should consider obtaining mpMRI results to reduce the risk of missing high-grade prostate cancer (Grade Group ≥ 2; Gleason score ≥ 7).
6.00-10.00	**Medium**	**The patient's score falls in the Medium Risk category, associated with no change in likelihood** of high-grade prostate cancer if a biopsy were performed.
> 10.00	**High**	**The patient's score falls in the High-Risk category, associated with an increased likelihood** of high-grade prostate cancer if a biopsy were performed.

IsoPSA is used as an aid in the detection of high-grade prostate cancer (Gleason ≥ 7). In a ClevelandDx study of 575 patients with no prior mpMRI undergoing biopsy, IsoPSA had a sensitivity of 96% and a specificity of 62% for detecting high-grade cancer on biopsy (Disease prevalence = 37%).

Low Risk

IsoPSA Index	NPV
≤ 6	92%

Medium and High Risk

IsoPSA Index	PPV
>6	44%
>10	54%

As with all laboratory tests, results near the threshold should be interpreted with caution and in the context of other clinical risk indicators and risk assessments.

Risk Assessment Combined with MRI

- Combination of isoPSA with MRI (PI-RADS scores) provides meaningful predicted probabilities for likelihood of detecting csPCa at biopsy
- This technique benefits from a reassuringly low probability of clinically-significant prostate cancer when PI-RADS 1-3 is found in conjunction with a low (≤6) isoPSA index
- Biopsy may be confidently avoided if both MRI and isoPSA results are low (green highlight)

Clinically-significant prostate cancer (csPCA) risk (%)		IsoPSA index	
		≤6	>6
		Avoid biopsy	Consider biopsy
PI-RADs	1-2	2%	15%
	3	4.5%	16%
		Proceed with biopsy	
	4-5	19%	49%

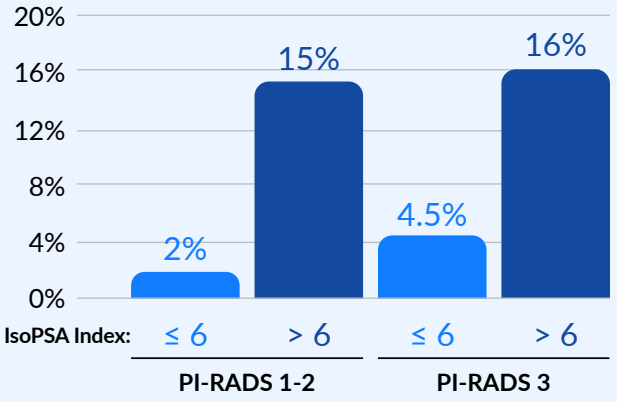
Prostate cancer risk based on MRI + IsoPSA combination testing results[7]

IsoPSA improves the interpretation of PI-RADS scores.[7]

IsoPSA can help:

- Clarify equivocal MRI (PI-RADS 3) to better triage patients
- Identify risk of MRI-invisible csPCa in PI-RADS 1-2 results

Additionally, IsoPSA results can refine the biopsy decision-making process when MRI is not an option.



How the IsoPSA Assay Works

The IsoPSA assay uses an innovative biochemical approach that evaluates the structural isoforms of PSA proteins in the patient's blood sample. Cancer-associated PSA proteins differ in their folding and molecular conformation compared to PSA produced by benign prostate tissue. IsoPSA detects and quantifies these structural differences, allowing for more accurate risk assessment.

By focusing on protein isoforms rather than PSA concentration alone, IsoPSA improves diagnostic performance and reduces the false-positive rates seen with conventional PSA testing.

Order IsoPSA for Your Patients:

1. Sign and complete the IsoPSA requisition form (available at LifeLabs.com/IsoPSA) or write "IsoPSA" in the *Other* section of the standard provincial requisition form.
2. Patient brings the completed requisition form to a LifeLabs location to complete their blood draw.
3. Results are sent directly to the ordering healthcare provider after about two weeks from receipt of sample.

Learn More About LifeLabs Cancer Tests
lifelabs.com/oncology

References: 1. Klein EA, Chait A, Hafron JM, Kernen KM, Manickam K, Stephenson AJ, Wagner M, Zhu H, Kestranek A, Zaslavsky B, Stovsky M. 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. European Urology. 2017;72(6):942–949. doi:10.1016/j.eururo.2017.03.025 | **2.** Stovsky M, Klein EA, Chait A, Manickam K, Stephenson AJ, Wagner M, Dineen M, Lotan Y, Partin A, Baniel J, Kestranek A, Zaslavsky B. Clinical validation of IsoPSA™, a single-parameter, structure-based assay for improved detection of high-grade prostate cancer. The Journal of Urology. 2019;202(4):732–739. doi:10.1097/JU.0000000000000185 | **3.** Scovell JM, Hettel D, Abouassaly R, Almassi N, Berglund R, Breaux T, Weight C, Isac W, Zampini A, Stark E, Rochelle R, Kestranek A, Stovsky M, Klein EA. IsoPSA® reduces provider recommendations for biopsy and magnetic resonance imaging in men with total prostate-specific antigen ≥4 ng/mL: a real-world observational clinical utility study. Urology Practice. 2022;9(2):174–180. doi:10.1097/UPJ.0000000000000291 | **4.** Jain P, Ganatra N, Pasnoor DS, Battar A, Vashi R, Nimmala S, Desai R, Jain A. IsoPSA in prostate cancer: a systematic review of diagnostic, prognostic, and economic implications. Journal of Clinical Oncology. 2025;43(16_suppl):e17166. doi:10.1200/JCO.2025.43.16_suppl.e17166. | **5.** Cleveland Diagnostics, Inc. IsoPSA® for clinicians: improved risk stratification for clinically significant prostate cancer. IsoPSA. 2026. Accessed April 29, 2026. https://www.IsoPSA.com/for-clinicians/ | **6.** Sava J. Long-term data validates IsoPSA for prostate cancer risk stratification. Targeted Oncology. 2025. Published July 3, 2025. Accessed April 29, 2026. https://www.targetedonc.com/view/long-term-data-validates-IsoPSA-for-prostate-cancer-risk-stratification | **7.** Benidir T, Lone Z, Wood A, Abdallah N, Campbell R, Bajic P, Purysko A, Nguyen JK, Kaouk J, Haber GP, Eltemamy M, Stein R, Haywood S, Klein EA, Almassi N, Campbell SC, Abouassaly R, Weight CJ. Using IsoPSA with prostate imaging reporting and data system score may help refine biopsy decision making in patients with elevated PSA. Urology. 2023;176:115–120. doi:10.1016/j.urology.2023.03.014. | **8.** Abdallah N, Campbell RA, Benidir T, Wood A, Lone Z, Zhang A, Ergun O, Curry C, Michael P, Liao R, Chavali JS, Pieretti A, McKenney J, Purysko A, Haywood S, Schwen Z, Olivares R, Kaouk J, Abouassaly R, Klein EA, Weight CJ. Low baseline IsoPSA index is associated with a prolonged low risk of clinically significant prostate cancer diagnosis in men with an elevated PSA. Urology. 2025;201:69–75. doi:10.1016/j.urology.2025.01.019.