IsoPSA® | Quest Diagnostics®

A more effective test to stratify patients with elevated PSA levels

Assesses structural isoforms of PSA correlated with malignancy

- Partitions PSA structural variants in a given sample to assess a patient's risk of prostate cancer
- Evaluates PSA structure (as opposed to concentration) to help identify or rule out high-grade prostate cancer

Clear results: single cutoff

An IsoPSA® Index below the risk threshold suggests a relatively low risk of high-grade prostate cancer (IsoPSA NPV: ~90%)

IsoPSA Result	Risk Threshold
5.0	>6.0

Easy to use, fewer restrictions

- IsoPSA can be used in patients being treated for benign prostatic hyperplasia (BPH) (ie, taking 5a-reductase inhibitors or alpha-blockers) and in patients with PSA levels from 4-100 ng/mL
- Unlike many other biomarkers, IsoPSA does NOT require other information (ie, patient demographics, additional clinical data) to derive a test result

Clinical validation and effectiveness[1]

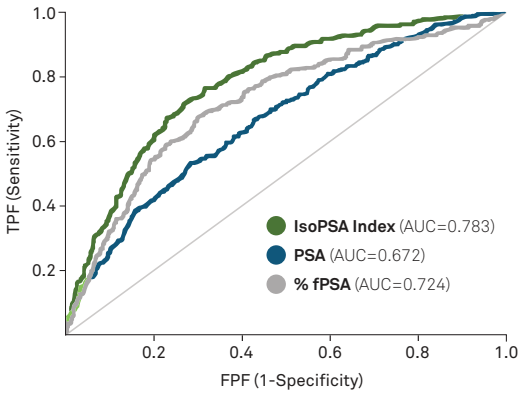
Proven accuracy in a large, multicenter, prospective study

- Among 888 patients scheduled for biopsy, IsoPSA demonstrated:
  - Improved accuracy for identifying high-grade prostate cancer (Gleason ≥7) vs PSA and % free PSA[1]
  - Significant improvement in AUC[1]
  - Significant improvement in specificity without a loss in sensitivity[1]
- IsoPSA is included in NCCN® Prostate Cancer Early Detection Guidelines

Clinical utility[2]

Stratifies patients with suspicious findings and reduces unnecessary biopsies by up to 55%

- IsoPSA may reduce overdiagnosis and overtreatment of slow-growing disease and thus reduce clinical risk
- IsoPSA allows for more efficient use of available biopsy capacity
  - Can better triage appropriate patients to biopsy, reduce biopsy backlogs, and increase biopsy yield (ie, more clinically relevant cancers detected per biopsy performed)



	IsoPSA Index	PSA	% free PSA
N	**888**	**112**	**112**
AUC (95% CI)	**0.783** (0.752-0.814)	**0.672** (0.639-0.706)	**0.724** (0.690-0.758)
Cutoff	**>6.0**	**>4.0**	**≤25%**
Sensitivity (95% CI)	**90.2%** (0.864-0.930)	**93.1%** (0.900-0.953)	**94.7%** (0.917-0.966)
Specificity (95% CI)	**45.5%** (0.414-0.496)	**20.2%** (0.174-0.232)	**13.7%** (0.111-0.166)
PPV (95% CI)	**47.7%** (0.457-0.498)	**36.1%** (0.351-0.372)	**38.2%** (0.372-0.392)
NPV (95% CI)	**89.3%** (0.856-0.922)	**85.8%** (0.801-0.900)	**82.0%** (0.736-0.882)

Test Cutoffs Used: IsoPSA Index: >6.0, PSA: > 4 ng/mL % free PSA: ≤ 25%
Cohorts Evaluated: IsoPSA: subjects with PSA ≤ 4 ng/mL(per indicated use), PSA: all subjects, % free PSA: subjects with PSAs ≤4 ng/mL

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Studies and clinical data

Clinical validation of IsoPSA, a single parameter, structure-focused assay for improved detection of prostate cancer: a prospective, multicenter study[1]

Authors include: Eric Klein, Alan Partin, Martin Dineen

Seminars in Urologic Oncology - September 2022

Abstract: IsoPSA is a novel structure-focused test that interrogates the prostate specific antigen isoform composition in blood. Routine use of IsoPSA could result in a substantial reduction of unnecessary biopsies and improve the risk-benefit ratio for prostate cancer early detection.

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[2]

Authors include: Jason Scovell, Eric Klein

Urology Practice - March 1, 2022

Abstract: In a real-world clinical setting, providers from diverse training backgrounds and practice settings readily adopted IsoPSA with substantial reductions in the rate of recommended prostate biopsies in patients with elevated PSA values (≥4 ng/ml). There was a high concordance between recommendation for or against prostate biopsy and the IsoPSA result.

Clinical validation of IsoPSA, a single parameter, structure based assay for improved detection of high grade prostate cancer[3]

Authors include: Mark Stovsky, Kannan Manickam

Journal of Urology - June 1, 2019

Abstract: Validation of the structure based IsoPSA assay demonstrated statistical concordance with previously reported results and verified its superior performance vs concentration based prostate specific antigen and the free-to-total prostate specific antigen ratio.

Elevated IsoPSA selects for clinically significant prostate cancer without a preference for any particular adverse histopathologic or radiographic feature[4]

Authors include: Tarik Benidir, Christopher Weight, Eric Klein

Journal of Urology - June 6, 2022

Abstract: Single center, retrospective review of patients who had undergone IsoPSA testing, prostate biopsy and RP at our institution from 2019-2021. Elevated IsoPSA is a diagnostic tool that can detect clinically significant prostate [cancer] at the time of biopsy.

Decision analysis model comparing cost of IsoPSA™ vs repeat biopsy for detection of clinically significant prostate cancer in men with previous negative findings on biopsy[5]

Authors include: Yair Lotan, Eric Klein

Urology Practice - January 1, 2021

Abstract: The use of IsoPSA to select patients for repeat biopsy reduced the number of biopsies needed by 34% and generated significant cost saving.

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[6]

Authors include: Eric Klein, Jason Hafron, Matthew Wagner

European Urology - April 7, 2017

Abstract: The structure-based IsoPSA assay outperformed concentration-based PSA measurement, and provided a net benefit against other protocols. Once validated, clinical use of IsoPSA could significantly reduce unnecessary biopsies while identifying patients needing treatment.

For more information about IsoPSA (test code 12061) contact your Quest Diagnostics representative or scan this code

1. Klein EA, Partin A, Lotan Y, et al. *Urol Oncol.* 2022;40(9):408.e9-408.e18. doi:10.1016/j.urolonc.2022.06.002
2. Scovell JM, Hettel D, Abouassaly R, et al. *Urol Pract.* 2022;(9)173-180. doi:10.1097/UPJ.0000000000000291
3. Stovsky M, Klein EA, Chait A, et al. *J Urol.* 2019;201(6):1115-1120. doi:10.1097/JU.0000000000000185
4. Benidir T, Hofman M, Lone Z, et al. *Urology.* 2022;168:150-155. doi:10.1016/j.urology.2022.05.029
5. Lotan Y, Stovsky M, Rochelle E, KLein E. *Urol Pract.* 2021;8(1):40-46. doi:10.1097/UPJ.0000000000000142
6. Klein EA, Chait A, Hafron JM, et al. *Eur Urol.* 2017;72(6):942-949. doi:10.1016/j.eururo.2017.03.025

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