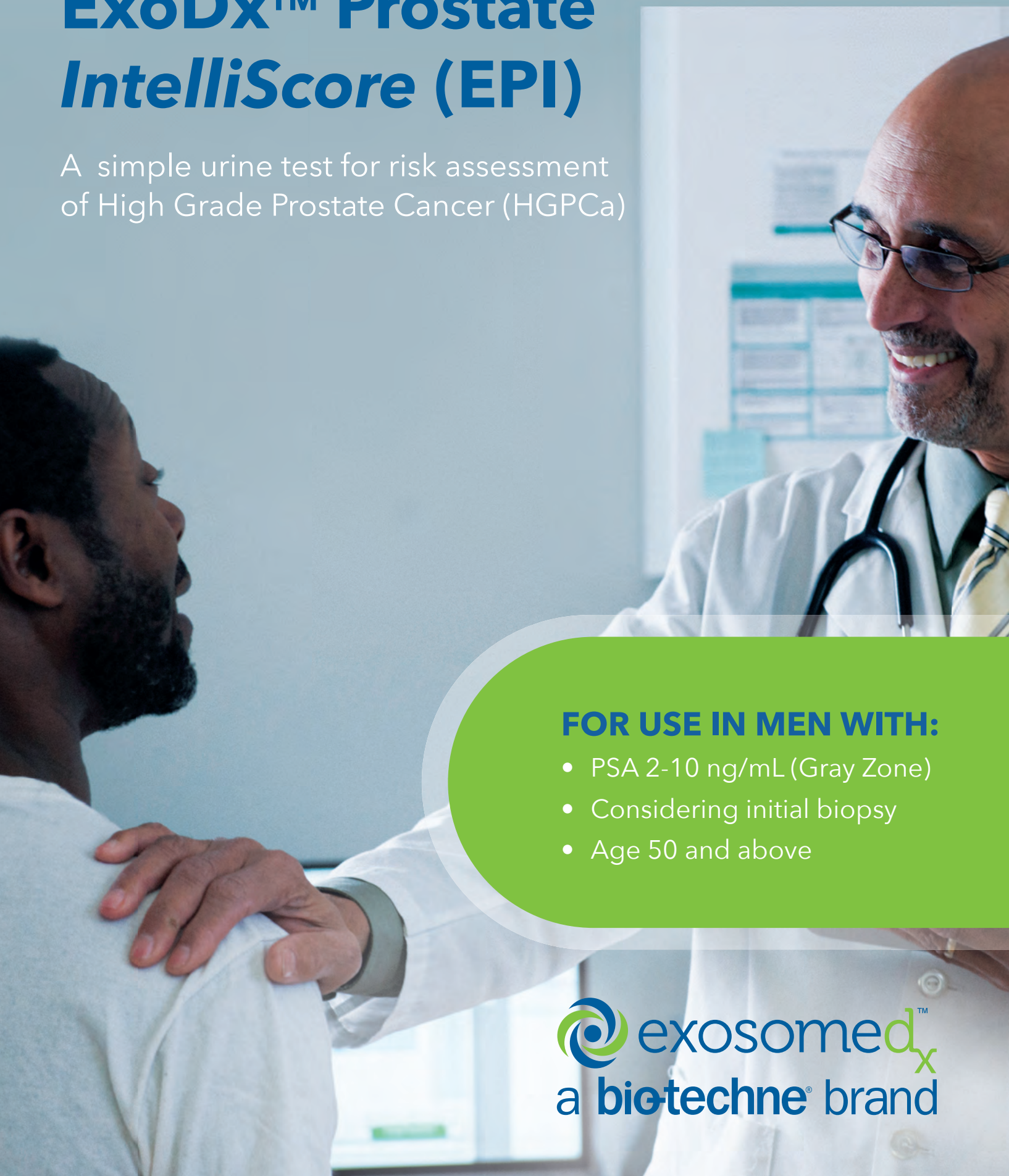
ExoDx™ Prostate *IntelliScore* (EPI)

A simple urine test for risk assessment of High Grade Prostate Cancer (HGPCa)



FOR USE IN MEN WITH:

- PSA 2-10 ng/mL (Gray Zone)
- Considering initial biopsy
- Age 50 and above

exosomedx™
a bio-techne® brand

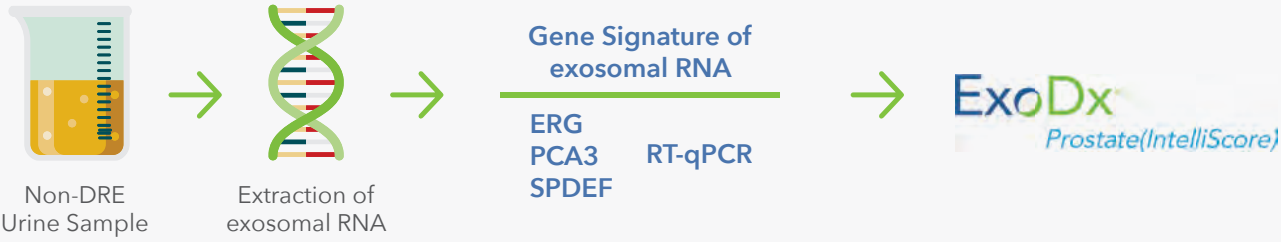
The *PRECISION* from a validated 3-gene Biomarker Algorithm (ERG, PCA3, SPDEF)

The intended use population is:

Men 50 years of age and older

Considering an initial prostate biopsy

PSA levels of 2-10 ng/mL



The 2019 NCCN guidelines include The EPI Test for early detection in men for both initial and repeat biopsy.*

The *PROMISE* of easy to interpret results

ExoDx *Prostate IntelliScore*	Result	Clinical decision
<15.6	Low Risk or Benign	Potentially avoid biopsy Continued Monitoring
>15.6	Higher Risk	Proceed to biopsy

*The test was developed as rule out test (91.3% negative predictive value and 92% sensitivity)

EXODx Prostate *IntelliScore* (EPI):
A simple urine test for risk assessment of High-Grade Prostate Cancer (HGPCa)

It is well known that prostate cancer is the 2nd leading cause of cancer in men with >1 million new cases and 300,000 deaths.[1]

The Unmet Clinical Need in Prostate Cancer:

Although Prostate Specific Antigen (PSA) screening is part of standard of care (SOC), its benefits have caused debate in recent years. The United States Preventive Services Task Force (USPSTF) changed its guidelines in 2018 advising men 55-69 years to make an informed choice and discuss with their doctor whether PSA screening is right for them, while recommending against screening for men over 70 years of age. This change in guidance came about after a review of published data of 1.9 million men on the use of PSA testing to screen for cancer based on the potential harms and benefits for PSA screening.

Limitations of PSA might include:

- Low sensitivity and specificity for prostate cancer
- PSA levels can be increased by benign prostatic hyperplasia (BPH) and prostatic inflammation or lower urinary tract infection
- When PSA results are in the "gray zone", other factors such as age, family history, ethnicity and digital rectal examination (DRE) factor into the shared decision-making discussion regarding prostate biopsy
- PSA cannot distinguish high grade from low grade cancer and is not prostate cancer specific

Importantly the increased detection of Prostate Cancer has led to over-treatment including potentially unnecessary biopsies.

When there is uncertainty about proceeding with a biopsy, The EPI Test may be a solution. Clinical studies show The EPI Test can help avoid 27% of biopsies[3] in patients with PSA levels in the gray zone (2-10 ng/mL). EPI results can be part of your best practices to send the right patient to the right intervention at the right time.

The *POWER* behind The EPI Test for prostate cancer

Introducing the first and only exosomal molecular test that relies on genomic information for risk assessment for HGPCa. This test was developed to assist physicians to reduce unnecessary biopsies* and can be used as a risk assessment tool to complement standard of care features in the biopsy decision making process.

The EPI Test allows for greater confidence to identify high grade prostate cancer (GS7 and above) in patients.

- Tested in >26,000 patients
- Cut-point prospectively validated in 1,022 men
- Test algorithm independent of PSA and SOC
- Complementary tool to clinical information
- Publications in top-tier peer-reviewed journals: JAMA Oncology & European Urology
- Simple urine test that can be collected any time of the day
- No DRE required prior to testing

*"Unnecessary biopsies" is defined as negative for prostate cancer or Gleason 6

EPI score ranges are proportional to increased percent likelihood for HGPCa

Likelihood of finding HGPCa on biopsy in intended use population[3,4]

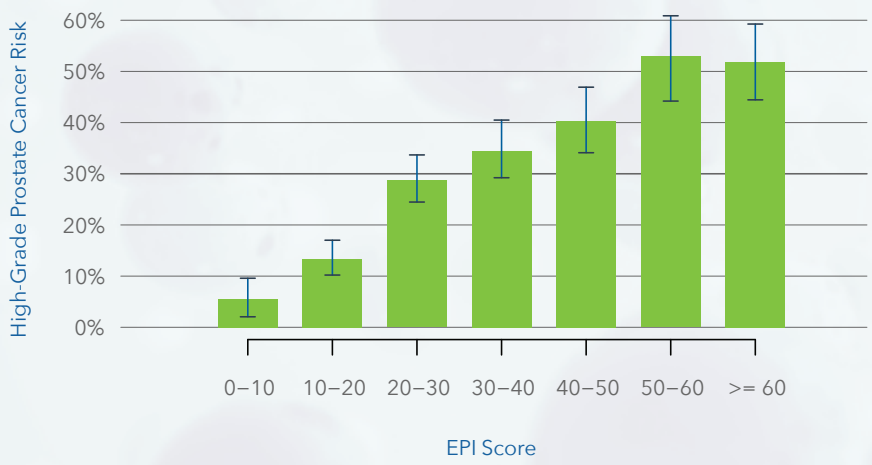
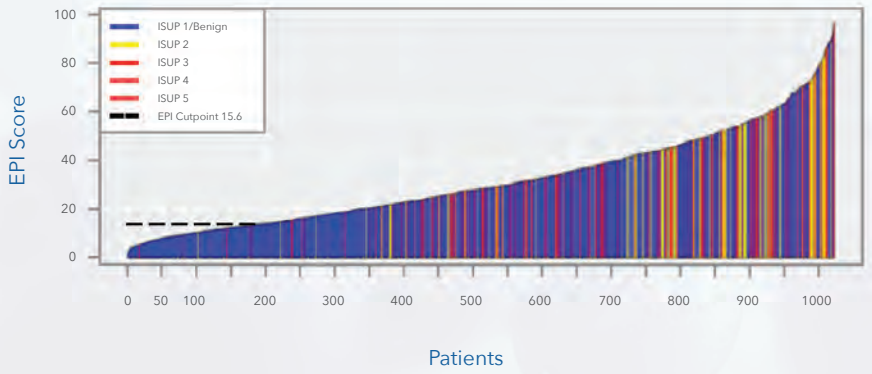


Figure 1

Key Points:

- Every patient in this data is in the intended use population (PSA 2-10ng/mL, presenting with initial biopsy, and 50 years and above)
- Consider age group relative to EPI score and Risk when interpreting results

The EPI Test performed the same in two prospective validation studies published in top-tier peer-reviewed journals in over 1000 patients[3,4]



This chart represents >1000 patients who were candidates for initial biopsy. All patients were in the intended use population (50 years of age or older, and PSA 2-10ng/mL).

Figure 2

Key Points:

- EPI was able to accurately classify patients that were not likely to need a biopsy (Gleason 6/ISUP1) with a score of 15.6 or less. Note the density of blue below the cut point (indicating ISUP1/benign)
- EPI was able to accurately classify patients that were more likely to need a biopsy (Gleason 7/GG2) with a score of 15.6. Note the high density of yellow and red color above the cut point, indicating Gleason 7 and above (indicating higher grade group and need for biopsy)
- ISUP 1/benign: Gleason 6
  ISUP 2: Gleason 7/(3+4)
  ISUP 3: Gleason 7/(4+3)

These charts represent pooled analysis of two prospective validation studies with over 1000 subjects (JAMA Oncology 2016 and European Urology 2018)

FAQs: Understanding the test

The EPI Test for prostate cancer

ExoDx Prostate (*IntelliScore*) – common name, "The EPI Test"

The EPI Test came back at "Higher Risk" but a biopsy result came back negative. How should I interpret this result?	The purpose of the EPI test is to rule out patients who don't need a biopsy. If you are below the 15.6 cut-point, the chance of finding HGPCa is illustrated in Figure 1.
What is the Negative Predictive Value (NPV)?	Negative Predictive Value is a statistical measure that says how confident we are about a negative outcome. In the case of The EPI Test, an NPV of 91% means we are 91% certain that the patient will not have HGPCa at a cut point of 15.6 or less.
What is the sensitivity of The EPI Test?	The sensitivity of The EPI Test is 92%. The sensitivity measures the proportion of actual GS7 and above that are correctly identified as positive
What is the cut-point used to determine high risk vs. lower risk?	The EPI Test has been validated using a cut point of 15.6 to determine when patients are at lower risk for high grade prostate cancer, defined as Gleason 7(3+4) or Grade Group 2 or higher. Patients with an EPI score below this cut point have a very low risk (9%) of not having high grade prostate cancer.
Does The EPI Test distinguish between GS6 and GS7 and higher prostate cancer?	Yes. The EPI Test is optimized as a rule out test to distinguish high grade prostate cancer (defined as GS7 and above) from low grade prostate cancer. Patients above the cut-point of 15.6 are associated with high risk of high grade prostate cancer. Patients below the cut-point of 15.6 are associated with lower risk of high grade prostate cancer. Reference Figure 1 to see the likelihood of finding HGPCa in the intended use population.
Is the score a percentage of risk?	Recent data presented at ASCO GU 2019 clearly demonstrated that the EPI score is proportional to increased risk of HGPCa. For example, an EPI score of 50 is associated with a 50% risk for HGPCa (see Figure 1). The risk should be considered within the context of other patient parameters. A score of 60 or higher is not demonstrated to have higher risk than a score of 50.
Why do I need to use your collection cup?	The prostate biomarkers we are looking for have the highest concentration in the "First Catch" urine sample which is the first 20 mLs of the void and is mostly from the prostate. Using the ExoDx collection cup that we provide allows us to capture this first catch and discard additional urine that would dilute the sample.
Which RNA biomarkers are analyzed?	PCA3, ERG and SPDEF
What should I do if the patient voided 30 minutes ago?	Please have the patient wait one full hour before providing a new sample. The EPI Test is most accurate when there is sufficient signal in the urine sample, which occurs with the First Catch.

Experience the power of exosome technology

Strength of the Test	ExoDX	Select MDx[5]	PHI[6,7]	4K[8]
Based on proprietary algorithm	●	●	●	●
Risk assessment for Prostate Cancer	●	●	●	●
Non-invasive urine test	●	●	○	○
Genomic marker test	●	●	○	○
PSA excluded from algorithm	●	○	○	○
Standard of Care (SOC) parameters / clinical risk factors are excluded from algorithm	●	○	●	○
No DRE required	●	○	○	○

1. Ferlay, J et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015. **2.** USPSTF Final Recommendation Statement Prostate Cancer Screening: wwwuspreventiveservicestaskforce.org, 2018. **3.** McKiernan J, Donovan M, et al. A Novel Urine Exosome Gene Expression Assay to Predict High-grade Prostate Cancer at Initial Biopsy. *JAMA Oncology*, July 2016. **4.** McKiernan J., and Donovan, M. et al., A Prospective Adaptive Utility Trial to Validate Performance of a Novel Urine Exosome Gene Expression Assay to Predict Exosome Gene High-grade Prostate Cancer in Patients with Prostate-specific antigen 2-10ng/ml at Initial Biopsy, *Eur Urol*, 2018. **5.** Haese A. et al. Multicenter Optimization and Validation of a 2-Gene mRNA urine test for Detection of Clinically Significant Prostate Cancer before Initial Prostate Biopsy. *J Urol*. 2019. **6.** Loeb S. and Catalona, W. The Prostate Health Index: a new test for the detection of prostate cancer. *Ther Adv Urol*. 2014. **7.** Beckman Coulter PMA Approval letter, https://www.accessdata.fda.gov/cdrh_docs/pdf9/P090026A.pdf, 2012. **8.** Punnen, S. et al. Finding the Wolf in Sheep's Clothing: The 4kscore Is a Novel Blood Test That Can Accurately Identify the Risk of Aggressive Prostate Cancer. *Rev Urol*. 2015.

This test was evaluated and its performance characteristics determined by Exosome Diagnostics, Inc. Exosome Diagnostics is certified under the Clinical Laboratory Improvement Amendments (CLIA) Act of 1988 as qualified to perform high complexity clinical testing. CLIA number – 22D2093470

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