ExoDx™ Prostate IntelliScore (EPI)
A simple urine test for risk assessment of high-grade prostate cancer (HGPCa)

FOR USE IN MEN WHO:
- Have PSA 2-10 ng/mL (Gray Zone)
- Are considering an initial or prior negative biopsy
- Are age 50 and above
Introducing the first and only exosomal molecular test that relies on genomic information to provide risk assessment for HGPCa.

The EPI 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 process.

The 2019 NCCN guidelines include the ExoDx Prostate test (EPI) for early detection in men for both initial and prior negative biopsy.*

*The test was developed as a rule-out test (91.3% negative predictive value and 92% sensitivity in the initial biopsy cohort).
The ExoDx™ Prostate Test

The right patient, the right intervention, at the right time

Prostate cancer is the second leading cause of cancer in men, with over 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.² 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 enlargement (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 prostatic biopsy
- PSA cannot distinguish high-grade from low-grade cancer and is not prostate cancer-specific

Importantly, increased detection of prostate cancer has led to potentially unnecessary biopsies and overtreatment. The EPI Test allows for greater confidence to identify high-grade prostate cancer (GS7 and above) in patients.

- Tested in >50,000 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 and Prostate Cancer and Prostatic Diseases
- Simple urine test that can be collected any time of the day
- No DRE required prior to testing
- New! At-Home Collection Kit available for patients as a convenient option in the comfort of home

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 unnecessary biopsies⁴ 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.
Clinical utility data

**Title:**
Clinical utility of the exosome based ExoDx Prostate (IntelliScore) EPI test in men presenting for initial biopsy with a PSA 2–10 ng/mL (Tutrone et al, May 2020, Prostate Cancer and Prostatic Diseases).

**Study design:**
The ExoDx Prostate Test was studied in a real-world clinical setting that included 72 urologists, 24 sites and more than 1,000 patients. The study is the first-ever prospective, multi-center, randomized prostate biomarker trial with a blinded control arm conducted in a clinical utility setting.

**Key findings:**
When implementing the ExoDx Prostate Test in a real-world clinical setting, patients demonstrated improved compliance with the physician’s recommendation to defer prostate biopsy when the test score was below the cut point of 15.6, and proceed to biopsy when the test score was above 15.6.³

- **92%** of patients complied to physician recommendation to defer biopsy due to the EPI test based on the physician-patient shared decision.
- **72%** of patients complied to physician recommendation to proceed to biopsy due to the EPI test based on the physician-patient shared decision making, compared to only 39% in the SOC control arm.
- **30%** more cases of clinically significant or high-grade prostate cancer were detected by physicians due to increased compliance, compared to the standard of care control arm.

Urologists use the EPI score in a real-world clinical setting to inform the **right intervention**, with the **right patient**, at the **right time**.
1 458 subjects received EPI test results
2 93 were low risk (<15.6)
3 63% were recommended to defer their biopsy (Bx)
4 This was a 92% compliance rate to MD recommendation
5 72% complied with physician recommendation to go to biopsy compared to the standard of care (SOC) arm (39%). See Supplemental Table S2 – “Clinical Utility Paper” for SOC arm outcomes.

The ExoDx Prostate Test was a moment of clarity for me. *It may have saved my life.*

— Major League Baseball All-Star, Iron Man and Hall of Famer
CAL RIPKEN, Jr.

Read about Cal’s journey: exosomedx.com/FightLikeCal
Scores from the ExoDx Prostate Test range from 0 to 100, with the cut point at 15.6. Score ranges are proportional to increased likelihood for HGPCa.

**Figure 1:** Likelihood of finding HGPCa on biopsy in intended use population\(^4\,^5\)

**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 and other standard of care factors when interpreting the results

**Figure 2:** The EPI Test performed the same in two prospective validation studies published in top-tier peer-reviewed journals over 1,000 patients\(^4\,^5\)

**Key Points:**
- EPI was able to accurately classify patients that were not likely to need a biopsy (Gleason 6/GG1) 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)

This chart represents >1,000 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).
<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>The EPI Test came back at “Higher Risk” but a biopsy result came back</td>
<td>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, you have a very low (9%) chance of finding high-grade cancer upon biopsy. The chance of finding high-grade cancer upon a biopsy is illustrated in Figure 1.</td>
</tr>
<tr>
<td>negative. How should I interpret this result?</td>
<td></td>
</tr>
<tr>
<td>What is the Negative Predictive Value (NPV)?</td>
<td>Negative Predictive Value is a statistical measure that says how confident we are about a negative outcome. In the initial biopsy population, the NPV is 91%, at a cut point of 15.6. In the repeat biopsy population, the NPV is 92%, at a cut point of 15.6.</td>
</tr>
<tr>
<td>What is the sensitivity of The EPI Test?</td>
<td>The sensitivity of The EPI Test is 92% in the initial biopsy population, and the sensitivity of The EPI Test is 82% in the repeat biopsy population. The sensitivity measures the proportion of actual GS7 and above that are correctly identified as positive.</td>
</tr>
<tr>
<td>What is the cut-point used to determine high risk vs. lower risk?</td>
<td>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.</td>
</tr>
<tr>
<td>Does The EPI Test distinguish between GS6 and GS7 and higher prostate</td>
<td>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.</td>
</tr>
<tr>
<td>cancer?</td>
<td></td>
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<tr>
<td>Is the score a percentage of risk?</td>
<td>Recent data presented at ASCO GU 2019 clearly demonstrated that the EPI score is proportional to increased risk of finding HPGC upon biopsy. For example, an EPI score of 50 is associated with a 50% risk of finding HGPC upon biopsy (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 of finding HPGC upon biopsy than a score of 50.</td>
</tr>
<tr>
<td>Why do I need to use your collection cup?</td>
<td>The prostate biomarkers we are looking for have the highest concentration in the “first catch” urine sample, which is the first 15 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.</td>
</tr>
<tr>
<td>Which RNA biomarkers are analyzed?</td>
<td>PCA3, ERG and SPDEF.</td>
</tr>
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<td>What should I do if the patient voided 30 minutes ago?</td>
<td>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. We also offer an At-Home Collection kit that can be sent directly to the patient’s home for later collection.</td>
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</tbody>
</table>
### Experience the power of exosomes

<table>
<thead>
<tr>
<th>Strength of the Test</th>
<th>ExoDX</th>
<th>Select MDx</th>
<th>PHI&lt;sup&gt;8,9&lt;/sup&gt;</th>
<th>4K&lt;sup&gt;10&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>Based on proprietary algorithm</td>
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<td>●</td>
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<td>Risk assessment for Prostate Cancer</td>
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<td>Non-invasive urine test</td>
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<td>Genomic marker test</td>
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<tr>
<td>PSA excluded from algorithm</td>
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<tr>
<td>Standard of Care (SOC) parameters / clinical risk factors are excluded from algorithm</td>
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<tr>
<td>No DRE required</td>
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<td>At-Home Collection Kit</td>
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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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