The ExoDx™ Prostate Test

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

Introducing the first exosomal molecular test that relies on genomic information to provide risk assessment for HGPCa. The ExoDx Prostate Intelliscore Test (also referred to as the EPI Test) was developed to assist physicians in making the shared physician-patient decision for prostate biopsy, and can be used to complement standard of care features in the biopsy decision process.

When there is uncertainty about proceeding with a biopsy, the ExoDx Prostate Test may be a solution. The ExoDx Prostate Test can be part of your best practices to send the right patient to the right intervention at the right time.
**ExoDx Prostate Test At A Glance**

**Who’s the test for?**
- Men 50 years of age or older
- Considering an initial or repeat biopsy
- PSA levels of 2–10 ng/mL

**How does it work?**
1. **Non-DRE First Catch Urine Sample**
2. **Extraction of Exosomal RNA**
3. **Gene Signature of Exosomal RNA**
   - ERG
   - PCA3
   - SPDEF
4. **ExoDx Score**

**What does the test score mean?**
- **ExoDx below cut point:** Low risk of HGPCa
- **ExoDx above cut point:** Higher risk of HGPCa

**Cut Point:** 15.6

**Shared Decision-Making**
- Potentially avoid biopsy, continued monitoring
- Consider mpMRI or proceed to biopsy

*ExoDx Prostate Test score is based on a non-linear value of 0 to 100, with the cut point at 15.6*

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*The NCCN guidelines have included the ExoDx Prostate test since 2019 for early detection of HGPCa 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 for ≥ GG2).

Interpreting the ExoDx™ Prostate Test Score

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.

Likelihood of Finding HGPCa on Biopsy in Intended Use Population

Figure 1: As the ExoDx Prostate Test score increases the likelihood of finding HGPCa on prostate biopsy increases.

The ExoDx Prostate Test Performed the Same in Two Prospective Validation Studies Published in Top-Tier Peer-Reviewed Journals Over 1,000 Patients

Figure 2: This chart represents the 519 patients from the validation study published in JAMA Oncology in 2016 who were candidates for initial biopsy, and who had the ExoDx Prostate Test performed and subsequently underwent the biopsy procedure. All patients were in the intended use population (50 years of age or older, and PSA 2–10 ng/mL).

Key Points:
- Every patient in this data set is in the intended use population (PSA 2–10 ng/mL, presenting for initial biopsy, and 50 years and above).
- The ExoDx Prostate Test provides a risk assessment that’s independent of PSA level or other clinical factors.

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.

Other clinical information should be considered when interpreting the results.
ExoDx™ Prostate Test

Key Points:
• The ExoDx Prostate test accurately classified patients that were unlikely to require biopsy (GG1/Gleason 6) or benign tissue with a score of 15.6 or less. Note the density of blue below the cut point.
• The ExoDx Prostate test accurately classified patients that were likely to require biopsy (≥GG2/Gleason (3+4)) with a score of 15.6 or higher. Note the density of yellow and red above the cut point.
• Every patient in this data set is in the intended use population (PSA 2–10 ng/mL, presenting for initial biopsy, and 50 years and above).
• The ExoDx Prostate Test provides a risk assessment that’s independent of PSA level or other clinical factors.
Enhance Compliance with the ExoDx™ Prostate Test

Clinical Utility Data

Title:
Clinical Utility of the exosome based ExoDx Prostate 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 clinical utility trial with a blinded control arm for a prostate cancer marker in the early-detection setting (Level 1 Evidence).

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

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

Access the Full Clinical Utility Publication
Elevated PSA Levels (2-10 ng/mL)

More Compliance to Proceed to Biopsy
72% of patients proceeded to biopsy based on physician recommendation when the cut-point was above 15.6 vs. 39% in the Standard of Care Control Arm.

ExoDx Prostate Test (Score ≤15.6)

92% of patients complied with physician recommendation to defer biopsy when the ExoDx Prostate Test result was low-risk.

ExoDx Prostate Test (Score >15.6)

30% More high-grade prostate cancer (HGPCa) was detected vs. the Standard of Care Control Arm.

85% More Compliance Amongst Patients Complying with Initial Biopsy

Shared Decision Between Physician and Patient.
Patients and physicians were either shown their ExoDx™ Prostate Test result or not given the information. The ExoDx Prostate Test has a cut off of 15.6, above the cut point having a higher risk of high-grade prostate cancer.
**Complementary Testing with The ExoDx™ Prostate Test and MRI**

The NCCN, AUA, and EAU guidelines call for mpMRI utilization in multiple places in the prostate cancer management pathway. All risk assessment tools like mpMRI have strengths and limitations. mpMRI limitations include well-known dependencies on reader expertise and therefore variable interpretation, tumor size, multifocality, tissue architecture, process standardization, availability and insurance coverage disparity, and, of course, cost. Patient management is best informed when complementary risk assessment methods are appropriately combined to mitigate the limitations of each approach.

The ExoDx Prostate Test Advantages
- Test independent of PSA and other clinical features
- Objective score
- Complementary to MRI

Figure 3: Potential clinical strategies for combining the ExoDx Prostate Test and multiparametric magnetic resonance imaging (mpMRI). Using the ExoDx Test either before or after mpMRI are possible approaches for layered risk assessment and more informed decision-making.11,12,13

Get More Info in the Full White Paper: The ExoDx Prostate Test & MRI - A Complementary Approach
At-Home Collection Available

Available now as an At-Home Collection Kit, ordering can be initiated through a HIPAA-compliant online form signed by a patient’s physician, then sent directly to the patient’s home for comfortable and convenient self-collection. FedEx will pick up the specimen from their home and overnight it directly to our ExosomeDx Laboratory where a result is provided to the ordering physician within 3-5 days of sample receipt.

The At-Home Collection Kit provides greater accessibility for patients while seamlessly integrating with in-office procedures. At-home sample collection is an important benefit of the ExoDx™ Prostate Test, and others include:

- ExoDx Prostate Test ordered for >100,000 patients
- Cut point prospectively validated in 1,022 men
- Test independent of PSA and other clinical factors
- 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 sample collection

**New!** At-Home Collection Kit available for use in the comfort of home. More and more urologists and patients are taking advantage of this convenient option.
**ExoCARES**

The **ExoDx™ Prostate Test**, is a simple, non-invasive urine test that can help you and your doctor determine the need for a prostate biopsy. The ExoDx Prostate Test provides actionable information that aids the prostate biopsy decision for men in the PSA ‘gray zone’ of 2-10 ng/mL, and is not dependent on PSA or other clinical risk factors.

**The Three Pillars of ExoCARES**

**Covered by Medicare**
Traditional Medicare covers the ExoDx Prostate Test for most patients in the intended use population. Most Medicare Advantage plans cover The ExoDx Prostate Test.

**Supported by Guidelines**
The ExoDx Prostate Test is included in the NCCN guidelines and is covered by major insurance plans throughout the US. It is also covered through all VA Medical Centers.

**Covered by the Patient Advocacy Team**
For patients whose insurance does not cover the ExoDx Prostate Test, our Patient Advocacy Team will auto-enroll you in The ExoCARES Program which will provide services that may reduce out-of-pocket costs.

Find Out More on the ExoCARES Program
The Insurance Process by ExoCARES

1. **Submit a Claim**
   A claim is submitted to your insurer.

2. **Receive an EOB**
   Receive an Explanation of Benefits (EOB) from your insurer. This is not a bill.

3. **Payment Covered by your insurance**
   In many cases insurance will pay for the complete cost of your test.

4. **ExoCARES Coverage & Appeal**
   In the event your insurance company does not pay, we may appeal on your behalf.

5. **Personalized Consultation**
   If, after appeal, there is no insurance coverage, an ExoCARES Representative will contact you to review options. One call will be made, please call back.
### Frequently Asked Questions

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<th>Question</th>
<th>Answer</th>
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| **Is this covered by insurance?**                                        | Depending on your specific circumstances, trained professionals at Exosome Diagnostics can help you with your journey to ensure the ExoDx™ Prostate Test is:  
  • Covered by your insurance when possible  
  • Covered by a VA Medical Center and the Government Services Award if applicable  
  • Covered by the ExoCARES (Comprehensive Assistance and Resources from Exosome Support) Program, which provides personalized payment options  
  • Supported each step along your journey by the Patient Advocacy Team                                                                                                                        |
<p>| <strong>The EPI Test came back at “Higher Risk” but a biopsy result came back negative. How should I interpret this result?</strong>          | 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. |
| <strong>What is the Negative Predictive Value (NPV)?</strong>                        | 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% and 97%, at a cut point of 15.6, for HGPCa defined as ≥GG2 and ≥GG3, respectively. In the repeat biopsy population, the NPV is 92%, at a cut point of 15.6, for HGPCa defined as ≥GG2. |
| <strong>What is the sensitivity of The EPI Test?</strong>                            | 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.                                                                 |
| <strong>What is the cut point used to determine high risk vs. lower risk?</strong>    | 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 having high-grade prostate cancer. |</p>
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<tr>
<th>Question</th>
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<tr>
<td><strong>Does The EPI Test distinguish between GS6 and GS7 and higher prostate cancer?</strong></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 higher risk of finding high-grade prostate cancer upon biopsy. 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>
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<td><strong>Is the score a percentage of risk?</strong></td>
<td>Published data demonstrates that an increased EPI score increases the risk of finding HGPCa upon biopsy. Below the cut point of 15.6 the NPV of 91.3% for HGPCa (≥GG2) applies. As the score goes up the risk increases. For example, an EPI score of 50 in this data set was associated with roughly a 50% +/-10% risk of finding HGPCa upon biopsy. EPI Test scores of 60 or higher are not demonstrated to have higher risk of finding HGPCa upon biopsy than a score of 50 (see Figure 1). The risk should be considered within the context of other clinical parameters.</td>
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<td><strong>Why do I need to use your collection cup?</strong></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>
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<td><strong>Which RNA biomarkers are analyzed?</strong></td>
<td>PCA3, ERG and SPDEF.</td>
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<td><strong>What should I do if the patient voided 30 minutes ago?</strong></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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Experience the Power of Exosomes

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<tr>
<th>Strength of the Test*</th>
<th>ExoDX™</th>
<th>Select MDx²</th>
<th>PHI³⁻⁹</th>
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*Selected list of biomarkers.
References


3. Tutrone, R et al. Clinical utility of the exosome based ExoDx Prostate(IntelliScore) EPI test in men presenting for initial Biopsy with a PSA 2-10 ng/mL, Prostate Cancer and Prostatic Dis. 2020.


