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

![Flowchart of the process](image)

The **PROMISE** of easy to interpret results

<table>
<thead>
<tr>
<th>ExoDx Prostate IntelliScore</th>
<th>Result</th>
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</tr>
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<tbody>
<tr>
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*The test was developed as a rule-out test (91.3% negative predictive value and 92% sensitivity)

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**Experience the power of exosome technology**

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<tr>
<th>Strength of the Test</th>
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**ExoDx™ Prostate IntelliScore (EPI)**

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

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**FOR USE IN MEN WITH:**

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

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**References**


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

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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

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It is becoming clear that prostate cancer is the second leading cause of cancer in men with ~17 million new cases and 300,000 deaths.*

The Unmet Clinical Need in Prostate Cancer: Although Prostate-Specific Antigen (PSA) screening is part of standard of care (SOC), its benefits have received debate in recent years. The United States Preventive Services Task Force (USPSTF) changed its guidelines in 2019 removing men age 75 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 ~1.5 million men over the age of 50 years 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 prostate 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 algorithm regarding positive.
• 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 is an exosomal molecular test that relies on genomic information for risk assessment for prostate cancer.

ExoDx Prostate IntelliScore (EPI): Introducing the first and only exosomal molecular test that relies on genomic information to assess patients for high grade prostate cancer.

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

The Test and 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.

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 making process.

The EPI Test performed the same in two prospective validation studies published in top-tier peer-reviewed journals in over 1000 patients**

The EPI Test comes back at “Higher Risk” but a biopsy result come 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 see below the 15.6 cut-off 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 say how often we can rule out a negative outcome in this case. The EPI Test, as an NPV of 91% means we are 91% certain that the patient will not need a biopsy or at a cut point of 15.6.

What is the specificity of The EPI Test?

Specificity of The EPI Test is 93%. The sensitivity measure for proportion of actual false and above that can be identified.

What is the cut-point used to determine high risk or lower risk?

The EPI Test has been validated using cut point of 15.6 to determine when patients are at lower risk for grade prostate cancer, defined as Gleason 3+3 or Grade Group 1.

Does The EPI Test distinguish between GS6 and GS7 and higher prostate cancer?

Yes. The EPI Test is optimized as a rule out tool to distinguish high grade prostate cancer (defined as Gleason 7 and above) from lower grade prostate cancer.

The prostate biomarkers we are looking for have the highest concentration in the “First Catch” urine sample which is the first catch and discard additional urine that would dilute the concentration in the “First Catch” urine sample which is the first catch and discard additional urine that would dilute the concentration in the “First Catch” urine sample.

Key Points:

• EPI score is an intuitive design to distinguish high grade prostate cancer (defined as Gleason 7 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.

<table>
<thead>
<tr>
<th>EPI Score</th>
<th>Likelihood of finding HGPCA on biopsy in intended use population*</th>
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FAqs: Understanding the test
ExoDx Prostate (IntelliScore) – common name, “The EPI Test”

What is the sensitivity of The EPI Test?

The sensitivity of The EPI Test is 89%. The sensitivity measures for proportion of actual true and above that can be identified.

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.

What are the RNA biomarkers analyzed?

PCA3, ERG and SPDEF

What is the cut-point used to determine high risk vs. lower risk?

ExoDx collection cup that we provide allows us to capture this First Catch and discard additional urine that would dilute the sample.

What is EPI?

The ExoDx Prostate IntelliScore (EPI) is an exosomal molecular test that relies on genomic information for risk assessment for high grade prostate cancer (HGPCA).

What is the optimal cut-point used to distinguish high grade prostate cancer (defined as Gleason 7 and above) from low grade prostate cancer? (indicating higher grade prostate cancer)

ISUP 1/low risk: Gleason 2/3
ISUP 2/low/intermediate risk: Gleason 4/3
ISUP 3/intermediate risk: Gleason 7/(4+3)
ISUP 4/high risk: Gleason 7/(3+4)
ISUP 5/high risk: Gleason 7 and above

Figure 1

Figure 2

*The cut-point for The EPI Test was used in >26,000 patients

**These charts represent pooled analysis of two prospective validation studies with over 1000 subjects (JAMA Oncology & European Urology 2018).
The EPI Test may be a solution. Clinical studies show The EPI Test has led to over-treatment including potentially unnecessary biopsies.

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.

PSA levels can be increased by benign prostatic hyperplasia (BPH) and prostatic inflammation or lower urinary tract infection.

When there is uncertainty about proceeding with a biopsy, The EPI Test can help avoid 27% of biopsies in patients with PSA levels in the gray zone (1.0-19.9 ng/mL). EPI results can be used to sort your patients into one of two groups: those who might benefit from an intervention and those who might not.

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 removing men 75 years of age or older from the age group for screening.
- PSA was recommended for men up to 75 years of age.
- The change in guidance came about after a review of published data of 1.9 million men on the use of PSA testing in 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.

The EPI Test for prostate cancer

The EPI Test has been validated using a cut point of 15.6 to determine when a patient is at risk for high grade prostate cancer. The EPI Test was able to accurately classify patients that were most likely to need a biopsy and patients that were not likely to need a biopsy with a score of 15.6.

The sensitivity of the EPI Test was 83%, meaning that 83% of patients with prostate cancer were identified as positive. The EPI Test was able to accurately classify patients that were most likely to need a biopsy and patients that were not likely to need a biopsy with a score of 15.6.

The EPI Test was the same in two prospective validation studies published in top-tier peer-reviewed journals in over 1000 patients.

Pooled analysis of two prospective validation studies with over 1000 subjects (JAMA Oncology 2016 and European Urology 2018)

Figure 1
- Likelihood of finding HGPCa on biopsy in intended use population.
- EPI score range.
- Key Points:
  - EPI was able to accurately classify patients that were most likely to need a biopsy (defined as Gleason 6/ISUP 1 with a score of 15.6).
  - EPI was able to accurately classify patients that were most likely to need a biopsy with a score of 15.6.
  - EPI score of 15.6 or less was associated with high risk of HGPCa.
  - EPI score of 15.6 or less was associated with high risk of HGPCa (indicating higher grade prostate cancer).
  - EPI score of 15.6 or less was associated with high risk of HGPCa (indicating higher grade prostate cancer).

Figure 2
- Likelihood of finding HGPCa in the intended use population.
- EPI score range.
- Key Points:
  - EPI was able to accurately classify patients that were most likely to need a biopsy (defined as Gleason 6/ISUP 1 with a score of 15.6).
  - EPI was able to accurately classify patients that were most likely to need a biopsy with a score of 15.6.
  - EPI score of 15.6 or less was associated with high risk of HGPCa.
  - EPI score of 15.6 or less was associated with high risk of HGPCa (indicating higher grade prostate cancer).

FAQs: Understanding the test

What is the Negative Predictive Value (NPV)?
- Negative Predictive Value is a statistical measure that says how often the test is negative when an outcome is negative. In the case of The EPI Test, an NPV of 97% means we are 97% certain that the patient will not need a biopsy at or out of cut point.

What is the sensitivity of The EPI Test?
- Sensitivity is defined as the proportion of actual GS7 and above that are correctly identified as positive.

What is the cut point used to determine high risk or low risk?
- The EPI Test has been validated using a cut point of 15.6.

Does the EPI Test distinguish between GS6 and GS7 and higher prostate cancer?
- Yes, The EPI Test is optimised as a rule to distinguish high grade prostate cancer (defined as Gleason 7 and above) from low grade prostate cancer.

The prostate biomarkers we are looking for have the highest density of blue below the EPI score of 15.6 (indicating higher grade prostate cancer). The risk should be considered within the context of other patient parameters.

The purpose of the EPI test is to rule out patients who don’t need a biopsy. If you see below the 15.6 cut point, the chance of finding HGPCa is illustrated in Figure 1.

The EPI Test can help avoid 27% of biopsies in patients with PSA levels in the gray zone (1.0-19.9 ng/mL). EPI results can be used to sort your patients into one of two groups: those who might benefit from an intervention and those who might not.

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Introducing the first and only non-invasive 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 care features in the biopsy decision-making process.

The EPI Test allows for greater confidence to identify high grade prostate cancer (G7 and above) in patients.

Tested in >24,000 patients

Cut-off point prospectively validated in 1,022 men

Test algorithm is independent of PSA and SOC

Complementary tool to clinical information

Publications in top-tier peer-reviewed journals, JAMA Oncology and European Urology

Simple urine test that can be collected any time of the day

No DRE required prior to testing

The EPI Test performed similarly to two prospective validation studies published in top-tier peer-reviewed journals in over 1000 patients

**Key Points:**
- EPI was able to accurately classify patients that were more likely to need a biopsy (sensitivity of 93.5%) using the identity of a blue color band only (ISUP 5).
- EPI was able to accurately classify patients that were more likely to receive no biopsy (specificity of 77%) using a score of 15.6. Note: The specificity decreases at higher ISUP grades (indicating higher grade groups are more likely to biopsy).
- EPI score ranges are proportional to increased percent likelihood for HGPCa (see Figure 1).

**EPI score ranges are proportional to increased percent likelihood for HGPCa**

*Note: Sensitivity is defined as the ability of the test to correctly identify patients that are more likely to receive no biopsy. Specificity is defined as the ability of the test to correctly identify patients that are more likely to need a biopsy.*

**Figure 1:**
- **Likelihood of finding HGPCa on biopsy in intended use population**
- **EPI score ranges are proportional to increased percent likelihood for HGPCa**
- **Key Points:**
  - Every patient in the study is in the intended use population (PSA 2-10 ng/mL).
  - ISUP 1/2 are in the gray zone and do not need a biopsy.
  - ISUP 3/4/5 are in the high risk zone and need a biopsy.
  - ISUP 6/7/8 are in the very high risk zone and need a biopsy.

**Figure 2:**
- **EPI score ranges are proportional to increased percent likelihood for HGPCa**
- **Key Points:**
  - EPI was able to accurately classify patients that were more likely to need a biopsy (sensitivity of 93.5%) using the identity of a blue color band only (ISUP 5).
  - EPI was able to accurately classify patients that were more likely to receive no biopsy (specificity of 77%) using a score of 15.6. Note: The specificity decreases at higher ISUP grades (indicating higher grade groups are more likely to biopsy).

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**The EPI Test for prostate cancer**

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**What is the Negative Predictive Value (NPV)?**

Negative Predictive Value is a statistical measure that gives us the probability that the test result is negative and the patient does not have the disease. In the case of The EPI Test, an NPV of 91% means we are 91% certain that the patient will not need a biopsy if we are not at or out of cut point.

**What is the sensitivity of The EPI Test?**

The sensitivity of The EPI Test is 92%. The sensitivity measures the proportion of actual G7 and above that are correctly identified as positive.

**What is the cut-point used to determine high risk or low 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. Patients below the cut-point of 15.6 are associated with low risk of high grade prostate cancer. Patients above the cut-point of 15.6 are associated with high risk of high grade prostate cancer (Reference Figure 1 to see the likelihood of finding HGPCa in the intended use population).

**What 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 0 is lower than not demonstrated to be higher than a score of 0.

**What 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 vital 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?**

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