The 4Kscore®
A Precision Test for Risk of Aggressive Prostate Cancer

Reduce Unnecessary Invasive Procedures And Healthcare Costs
Abnormal PSA leads to over 1 million prostate biopsies each year

- **Low yield:** 75% of biopsies show no cancer or indolent cancer\(^1\)
- **Unnecessary surgical removal of prostate:** 66% of indolent cancers on biopsy are confirmed indolent when the prostate is removed\(^2,3\)
- **Adverse events:** 4.1% hospitalization rate: bleeding, infections, septicemia\(^4\) and with therapeutic interventions - complications of surgical removal or radiation

Impact of USPSTF Recommendations
Reducing PSA Utilization

Second leading cause of cancer death in men – 26,000 in 2016

- Results of contemporary reductions in screening: More Metastatic/Lethal disease²⁻⁵

\[ \text{Incidence of Metastatic Disease (per 100,000)} \]

- PSA Not Widespread
- Widespread PSA Screening

Presenting NCCN risk group relative to number diagnosed in 2004

- Low Risk
- Intermediate Risk
- High Risk
- Very High Risk
- Metastatic
- Total

Year of Diagnosis


1. Welch HG et al NEJM 2015
### 4Kscore

**A follow up test to identify risk for high grade, aggressive prostate cancer**

#### Components

<table>
<thead>
<tr>
<th>Aggressive cancer</th>
<th>Total PSA</th>
<th>Free PSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>Intact PSA</td>
<td>hK2</td>
</tr>
<tr>
<td></td>
<td>+ Age, DRE, and prior biopsy status</td>
<td></td>
</tr>
</tbody>
</table>

#### Results

4Kscore algorithm specifically provides % risk of having high grade prostate cancer on prostate biopsy.

- Commercial- CLIA certified laboratory developed test
- Designed to identify aggressive prostate cancer- Gleason ≥7 from Gleason 6 or no cancer
- OPKO - Intact PSA and hK2 associated with poorly differentiated prostate cancer

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4Kscore Cost Savings

- 4Kscore Medicare Price: $602.10
- Loaded Cost of Biopsy: Over $2,100
  - Cost of prostate biopsy
  - Around 4.1% hospitalization rate including septicemia
  - Associated MRI (including mpMRI-Biopsy)
  - Post biopsy consultation/second opinion
  - Molecular confirmatory tests
  - Treatment and complications costs for indolent cancer
- After referral for biopsy - using a low risk 4Kscore (< 7.5%) cutoff for biopsy decisions
  - $1,500 in savings per patient considered for prostate biopsy
4Kscore Predicts Aggressive Prostate Cancer

Validated in a prospective, blinded, multicentre US study of 1012 men using current prostate cancer protocols

4Kscore predicts biopsy results

Legend:
- Dashed line: Actual percentage of aggressive prostate cancer detected by biopsy
- Solid line with confidence interval: Predicted by 4Kscore Test
- Perfect correlation

**4Kscore** Categorizes Long Term Risk of Developing Distant Metastasis

Men who have a low risk 4Kscore test are at low risk for distant metastasis within 15-20 years.

<table>
<thead>
<tr>
<th>Age 50 PSA ≥ 2 ng/mL</th>
<th>10 yr</th>
<th>15 yr</th>
<th>20 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>4Kscore &lt; 7.5%</td>
<td>0.26%</td>
<td>0.90%</td>
<td>1.25%</td>
</tr>
<tr>
<td>4Kscore &gt; 7.5%</td>
<td>2.40%</td>
<td>8.25%</td>
<td>10.68%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age 60 PSA ≥ 3 ng/mL</th>
<th>10 yr</th>
<th>15 yr</th>
<th>20 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>4Kscore &lt; 7.5%</td>
<td>0.18%</td>
<td>0.99%</td>
<td>1.82%</td>
</tr>
<tr>
<td>4Kscore &gt; 7.5%</td>
<td>5.62%</td>
<td>9.85%</td>
<td>16.36%</td>
</tr>
</tbody>
</table>

4Kscore Substantially Reduces Biopsy Rate in Low Risk Patients

- 611 subjects with suspicion of prostate cancer seen by 35 urologists
- Overall biopsy reduction rate = 65%
- 542 (89%) of the biopsy decisions were impacted by the 4Kscore. In this group:
  - 95% of 4Kscore low risk group did not receive prostate biopsy
  - 9% of 4Kscore high risk group did not receive a prostate biopsy

**Low Risk** 4Kscore < 7.5%

**Intermediate Risk** 4Kscore 7.5-19.9%

**High Risk** 4Kscore ≥ 20%

Konety et al. Rev. in Urol. 2015
National Clinical Guidelines Include 4Kscore

“…for whom the patient and/or the physician wish to further define the probability of high grade cancer”

4Kscore in Clinical Practice

• Reduces uncertainty by providing an accurate risk percentage for aggressive prostate cancer
• Excellent calibration with prostate biopsy results
• Predicts risk of distant metastasis for up to 20 years
• Included in National Clinical Guidelines
• Influences physician/patient decision making in 88% of cases
• Reduces prostate biopsies by up to 65%
• Reduces complications and pain from unnecessary prostate biopsies and potential unnecessary treatment
• Reduces cost of unnecessary procedures
4Kscore Hurdles

• Paradigm shift
  – Continue screening of men to find aggressive prostate cancer early
  – Avoid immediate biopsy in all men with a suspicious PSA
    • Reduce complications from unnecessary procedures
    • Reduce healthcare cost

• Provide a continuous risk score with risk categories
  – Reduce uncertainty in physician-patient shared decision making
    – Provide actionable, accurate, and easily interpretable results

• Acceptance amongst payors and providers