4Kscore®

A DIAGNOSTIC BLOOD TEST FOR DETECTING THE RISK OF
AGGRESSIVE PROSTATE CANCER

OPKO Health, Inc.

WHAT IS THE 4KSCORE TEST?

4Kscore Test incorporates measurements of four kallikrein biomarkers and clinical information of a man in a validated assessment algorithm to detect the risk of aggressive prostate cancer on prostate biopsy

Components | | Result

Total PSA
Free PSA
Proprietary to OPKO [Intact PSA
hK2
Prior Biopsy Status
Age
DRE (optional)

4Kscore® Algorithm

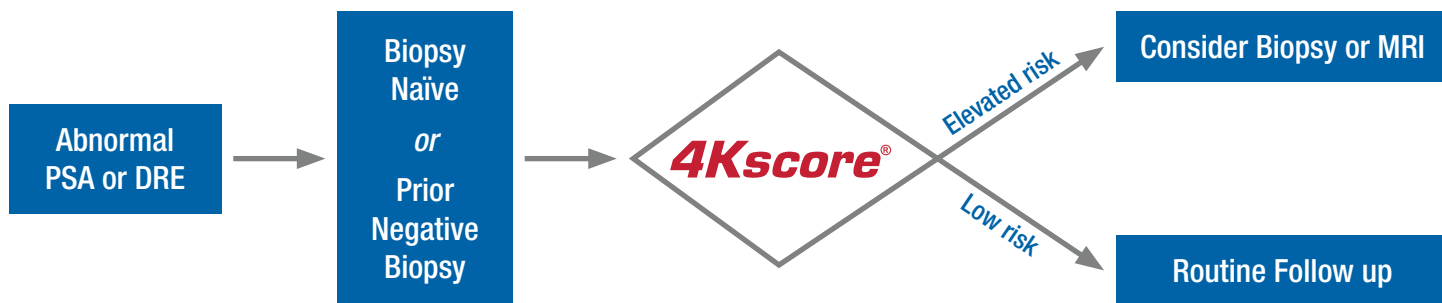Risk of aggressive prostate cancer (%)

- Assesses the risk of aggressive prostate cancer following an abnormal PSA or DRE
  - ➜ Provides the % risk of Gleason 7 or higher cancer if a prostate biopsy were performed
  - ➜ Avoids or delays unnecessary prostate biopsy
  - ➜ Prompts early intervention for men at elevated risk

WHY USE THE 4KSCORE TEST?

4Kscore Test determines the patient's risk for aggressive prostate cancer

- Two US based, prospective validation studies, including a 2017 study performed at Veterans Health Administration facilities involving a predominantly African American population, resulted in combined sensitivity of 94%, Negative Predictive Value (NPV) of 95% for the detection of Gleason 7 or higher (aggressive prostate cancer), with potential reduction of prostate biopsies of 32% when the 4Kscore Test at 7.5% cutoff was used. Both studies also demonstrated that the 4Kscore Test at 7.5% cutoff did not miss any Gleason 8 and higher on biopsy.[1,2]

- Two observational studies, using retrospective banked serum samples that were evaluated in over 4,000 subjects, show the long-term, 15-20 years prediction of prostate cancer metastasis and death in men with elevated PSA[3,4]

- 4Kscore Test is included in the current US and European prostate cancer early detection guidelines[5,6]
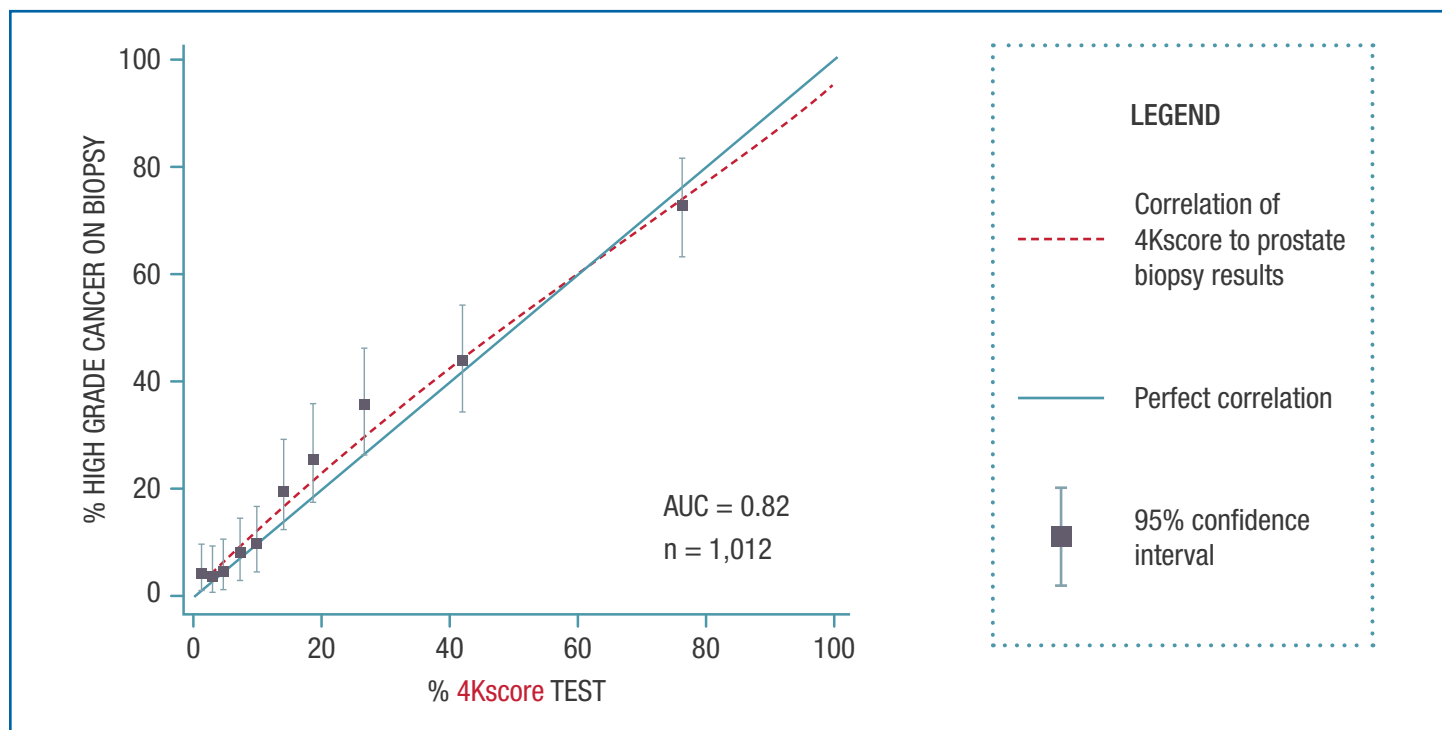
- Over 200,000 4Kscore tests have been performed in the US

WHEN TO USE THE 4KSCORE TEST?

```
Abnormal          Biopsy
PSA or DRE   →    Naïve      →    4Kscore®   ⟋ Elevated risk →  Consider Biopsy or MRI
                    or                        ⟍ Low risk      →  Routine Follow up
                  Prior
                  Negative
                  Biopsy
```

Patient management should be based on clinical judgment. Other clinical information (health status, medical history, family history of prostate cancer, PSA history, etc.), along with the 4Kscore Test result, should be considered in the shared decision making process.
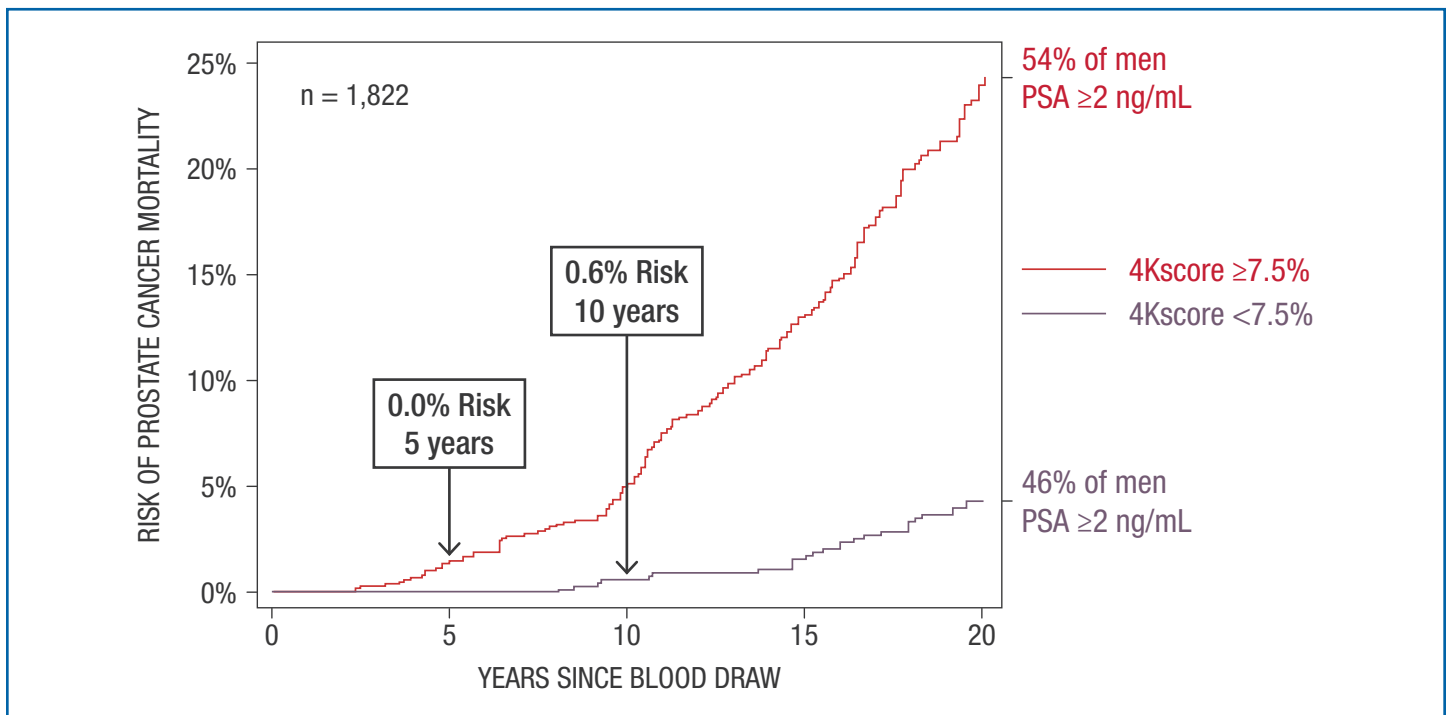
4Kscore Accuracy

Near-perfect calibration of 4Kscore risk assessments for aggressive prostate cancer and prostate biopsy results[1]

AUC = 0.82
n = 1,012

LEGEND

- - - - Correlation of 4Kscore to prostate biopsy results

——— Perfect correlation

▪ 95% confidence interval

4Kscore Predictive Value

The 4Kscore Test can stratify men and predict distant prostate cancer mortality[3]

Age enrolled 60–73, with a PSA of 2ng/ml at baseline would have 1.7% and 13% risks of death in 15 years, due to prostate cancer in the 4Kscore <7.5% and 4Kscore ≥7.5% respectively.[3]

4KSCORE TEST IS NOT INDICATED IN MEN WITH:

- Previous diagnosis of prostate cancer
- Digital Rectal Exam (DRE) performed within 96 hours before blood draw
- Use of 5-alpha reductase medication within previous 6 months
- Prostate procedure within the last 6 months

REFERENCES

1. Parekh et al. A multi-institutional prospective trial in the USA confirms that the 4Kscore accurately identifies men with high-grade prostate cancer. Eur Urol. 2015;68(3):464-470.
2. Punnen et al. A multi-institutional prospective trial confirms noninvasive blood test maintains predictive value in African American men. J Urol. 2018;199(6);1459-1463.
3. Sjoberg et al. Twenty-year risk of prostate cancer death by midlife prostate-specific antigen and a panel of four kallikrein markers in a large population-based cohort of healthy men. Eur Urol. 2018;73(6):941-948.
4. Stattin et al. Improving the Specificity of Screening for Lethal Prostate cancer using prostate-specific antigen and a panel of kallikrein markers: a nested case-control study. Eur Urol. 2015;68(2):207-213.
5. National Comprehensive Cancer Network (NCCN). Prostate Cancer Early Detection (Version 1.2019). https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf
6. European Association of Urology (EAU). Guidelines on Prostate Cancer (Version 3.2016). https://uroweb.org/wp-content/uploads/EAU-Guidelines-Prostate-Cancer-2016.pdf