Stockholm3: Prostate Cancer Risk Score Technical Brief

Specimen Type	Whole blood
Specimen Volume	10 mL
Collection	Collect 2 x 6mL whole blood EDTA lavender top tubes
Minimum Volume	8 mL
Handling	**Store and ship AMBIENT (room temperature), with temperature insulated gel pack** **To arrive at laboratory within 48 hours of collection**
Rejection Criteria	Specimens received frozen. Specimens outside of listed stability. Samples submitted without two unique identifiers and date of collection.
Stability	48 hours ambient pre-processing
Methodology	ECLIA, ELISA, PCR (SNP panel)
Reference Range	Stockholm3 Risk Score 1-10 (Non-elevated risk) Stockholm3 Risk Score ≥11 (Elevated risk) Stockholm3 is a blood-based test that risk stratifies men for ISUP Grade Group 2 or higher prostate cancer. Indications for use are: (1) PSA: 1.5-20 ng/ml, (2) age: 40-80 years, and (3) no prior diagnosis of prostate cancer.
Turnaround Time	Up to 10 business days.
CPT Code	(CPT PLA:) 0495U (effective October 1st 2024)

Clinical Significance	Prostate cancer is the most common non-cutaneous cancer in men. Although prostate cancer testing with prostate specific antigen (PSA) testing leads to decreased mortality, it also results in many men undergoing unnecessary diagnostic procedures, while others have cancers missed by conventional PSA thresholds. Stockholm3 is a multivariate model that includes clinical variables (age, first-degree family history of prostate cancer, and prior negative biopsy history), blood biomarkers (total PSA, free PSA, GDF15 (Growth/Differentiation Factor 15), PSP94 (Prostate Secretory Protein 94), and KLK2 (Kallikrein 2), and a germline genetic score based on single-nucleotide polymorphisms (SNPs). Stockholm3 predicts detection of clinically significant cancer (Grade Group ≥2) improving the performance of prostate cancer testing when used as a reflex test to PSA in the range of 1.5-20 ng/mL. Evidence shows use of Stockholm3 improved clinically significant cancer detection, resulting in reduction in unnecessary MRI and unnecessary biopsies, lower over detection of indolent cancers and overall decreased healthcare costs. Stockholm3 intended use is for men aged 40-80 years with PSA 1.5 - 20 ng/ml and no prior evidence of prostate cancer. Stockholm3 was originally developed in prospective, population-based trials in Sweden. Clinical utility studies using Stockholm3 at a PSA reflex of 1.5 ng/ml have been shown to increase clinically significant cancer (Grade Group ≥2) detection suggested to be driven by the ability to detect cancers between PSA 1.5-3 ng/ml. Stockholm3 has been evaluated in the US clinical trial setting and showed equivalent performance to the European-based trials.
Principle	Stockholm3 utilizes a proprietary algorithm based on clinical data, protein markers (tPSA, fPSA, GDF15, PSP94, and KLK2), and genetic markers (SNP panel) to generate a risk score that indicates risk of aggressive prostate cancer. Specifically, EDTA whole blood is centrifuged for plasma. This plasma is used to perform immunoassay protein measurement of tPSA, fPSA, GDF15, PSP94, and KLK2. EDTA whole blood is also utilized to extract germline DNA which is then used for PCR analysis of single nucleotide polymorphisms known to be associated with prostate cancer risk. SNP risk and reference alleles are used to generate a quantitative polygenic risk score. Protein measurements, the polygenic risk score, and clinical data (age, first degree family history of prostate cancer, prior negative prostate biopsy) are used in an algorithm to generate a Stockholm3 risk score, with a Stockholm3 risk score ≥11 deemed to indicate an elevated risk of clinically relevant prostate cancer.