Test Specific Guidelines

SelectMDx

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Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

Procedure addressed by this guideline	Procedure code
SelectMDx	0339U

What Is SelectMDx?

Definition

SelectMDx is a proprietary, non-invasive urine test that is designed to identify an individual's risk of prostate cancer without the need for a biopsy.

Prostate cancer is the most common cancer among men, with over 200,000 new cases identified each year in the United States.[1,2] The median age at diagnosis is 66 years.[3] Older men are more likely to be affected than younger men, and African American men have higher rates compared to men of other ethnic backgrounds.[3]

Screening programs for prostate cancer allow for its early detection. Screening is typically performed by prostate-specific antigen (PSA) test and digital rectal examination (DRE).[2,4]

Diagnosis is confirmed by prostate biopsy.[5-8] Biopsy is typically performed by collection of approximately 12 needle biopsy cores.[7]

Initial biopsies only detect 65-77% of prostate cancers, and repeat biopsies are frequently performed.[9,10] The false negative rate of biopsy may be as high as 25%.[11]

Test Information

SelectMDx is a urine based assay that measures mRNA levels of DLX1 and HOXC6 to determine an individual's risk of prostate cancer. KLK3 expression is used as an internal reference.[12]

Higher levels of DLX1 and HOXC6 are associated with an increased risk of prostate cancer.

This test is performed on first-void urine samples in patients post-digital rectal exam. Individuals with a high risk score on SelectMDx may benefit from a biopsy and/or MRI.[12]

Individuals with a low risk score on this test may be able to avoid a biopsy.[12]

Guidelines and Evidence

American Urological Association

The American Urological Association issued a Guideline Statement (AUA, 2018) that stated:[13]

"While the benefits of PSA-based prostate cancer screening have been evaluated in randomized-controlled trials, the literature supporting the efficacy of digital rectal exam (DRE), PSA derivatives and isoforms (e.g. free PSA, -2proPSA, prostate health index, hK2, PSA velocity or PSA doubling time) and novel urinary markers and biomarkers (e.g. PCA3) for screening with the goal of reducing prostate cancer mortality provide limited evidence to draw conclusions."

European Association of Urology

The European Association of Urology (EAU, 2021) guidelines for prostate cancer stated the following in regards to SelectMDx:[14]

"In men with an elevated risk of PCa with a prior negative biopsy, additional information may be gained by the Progensa-PCA3 and SelectMDX DRE urine tests, the serum 4Kscore and PHI tests or a tissue-based epigenetic test (ConfirmMDx). The role of PHI, Progensa PCA3, and SelectMDX in deciding whether to take a repeat biopsy in men who had a previous negative biopsy is uncertain and probably not cost-effective."

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2022) stated the following regarding the use of SelectMDx:[7]

"Biomarkers that improve specificity of detection are not, as yet, mandated as first-line screening tests in conjunction with serum PSA."

"The probability of high-grade cancer (Gleason score ≥ 3+4, Grade Group 2 or higher) may be further defined utilizing the Prostate Health Index (PHI), SelectMDx, 4Kscore, ExoDx Prostate Test, MyProstateScore (MPS), and IsoPSA. Extent of validation of these tests across diverse populations is variable. It is not yet known how such tests could be applied in optimal combination with MRI."

"Overall the panel believes that SelectMDx score is potentially informative in patients who have never undergone biopsy, and it can therefore be considered in such individuals."

Selected Relevant Publications

Overall, the evidence base for SelectMDx consists of studies describing the development and initial clinical validation, studies evaluating the diagnostic performance characteristics of SelectMDx, and studies comparing SelectMDx performance with mpMRI, PCA3, 4Kscore, or ERSPC RC4 results.[15-28] Though the initial results are encouraging, there is an overall paucity of sufficient evidence currently available in the peer-reviewed literature to evaluate the clinical validity and clinical utility of this test.

Across the evidence, SelectMDx cutoffs were variable making it difficult to draw conclusions about test performance. The studies were also hampered by several other limitations including: small sample sizes, retrospective study designs, limited follow-up times, and wide or unreported confidence intervals. Clinical utility studies are lacking. It is unclear if use of SelectMDx results in changes to clinical decision-making that ultimately lead to improved patient-relevant health outcomes. Additional well-designed trials in large, independent patient populations and with sufficient follow-ups are needed.

Criteria

This test is considered investigational and/or experimental.

Investigational and experimental (I&E) molecular and genomic (MolGen) tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact, which typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), and/or performs better than an existing standard of care medical management option. Such tests are also not generally accepted as standard of care in the evaluation or management of a particular condition.

In the case of MolGen testing, FDA clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight and FDA clearance often does not assess clinical utility.

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