



# Effective Health Care

## Prostate Cancer Screening (using PCA3)

### Nomination Summary Document

#### Results of Topic Selection Process & Next Steps

- Prostate cancer screening (using PCA3) will go forward for refinement as a systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the refinement phase.
- When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to <http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/>.

#### Topic Description

**Nominator:** Government agency

**Nomination Summary:** The nominator questions whether screening among the general adult male population for elevated PCA3 (also known as DD3) gene expression can identify those at risk for prostate cancer who may be candidates for prostate biopsy and reduce morbidity and mortality. The nominator has an interest in comparing results of screening with PCA3 with results of traditional prostate specific antigen (PSA) screening and with a no screening regimen.

#### **Staff-Generated PICO**

**Population(s):** Males over the age of 50 (or at age 40 if baseline is sought), males with positive family history for prostate; African American males

**Intervention(s):** PCA3 measurement in urine

**Comparator(s):** No screening or screening using total PSA without PCA3

**Outcome(s):** Intermediate outcomes – diagnostic accuracy for detection of tumor; adverse events of testing and diagnostic work up (biopsies); Health outcomes – morbidity and mortality

**Key Questions from Nominator:**

1. Does use of PCA3 mRNA expression analysis in:
  - I. adult men to identify those at risk for prostate cancer who may be candidates for prostate biopsy
  - or
  - II. adult men with previous normal biopsy following elevated PSA levels to determine need for repeat biopsy vs. conservative follow up
  - or
  - III. adult men with a positive prostate biopsy to assist in management decisions

(active surveillance vs. active treatment)

lead to improvements in health outcomes compared to a no-testing strategy, or are test results useful in medical, personal, or public health decision-making?

(*overarching question*)

2. What is the *analytic validity* (sensitivity, specificity, reproducibility, reliability) of tests designed to measure PCA3 mRNA expression?
  - a. Transcription-mediated amplification of PCA3 and PSA mRNA in urine sample
  - b. Do measures of AV vary by assay design, method of sample collection, etc.?
3. What is the *clinical validity* (sensitivity, specificity, positive predictive value, negative predictive value) of the PCA3 assay?
  - a. How well does the PCA3 assay predict the presence or absence of prostate cancer?
    - i. How does sensitivity and specificity vary by score (ratio of PCA3/PSA mRNA) cut-off?
  - b. How well does the PCA3 assay differentiate between clinically significant and clinically insignificant prostate cancers?
  - c. What is the improvement in sensitivity or specificity of the PCA3 assay in detecting prostate cancer beyond that of PSA (and DRE)?
  - d. How well does the PCA3 assay predict the aggressiveness of prostate cancer?
  - e. How do these issues vary as a function of PSA result and biopsy status?
4. Does use of the PCA3 assay lead to improved health outcomes when compared with or in addition to use of standard screening and management practices? (*clinical utility*)
  - a. Does use of the PCA3 assay influence decisions on whether to proceed to prostate biopsy?
    - i. Reduction in unnecessary *initial* biopsies resulting from false positive PSA results
    - ii. Reduction in unnecessary *repeat* biopsies in men with previous elevated PSA and  $\geq 1$  negative biopsy
  - b. Does use of the PCA3 assay influence treatment decisions in men with positive biopsies?
    - i. Avoidance of unnecessary treatment in men with clinically insignificant prostate cancer
    - ii. Initiation of treatment in men with a high probability of clinically significant prostate cancer
  - c. Do changes in screening and management for prostate cancer resulting from use of PCA3 assays lead to a reduction in cancer-related morbidity or mortality?
  - d. What is the cost-effectiveness of using PCA3 assays to guide screening and management for prostate cancer compared to current practice?
5. What are the potential harms of testing or subsequent management options associated with use of the PCA3 assay for prostate cancer diagnosis and management decisions?
  - a. Errors in test assay leading to inaccurate results.
  - b. Potential for clinically significant prostate cancers to be missed in individuals presumed to be at "low risk" based on PCA3 score (false-negatives).
  - c. Potential for unnecessary and costly screening and management of individuals

- presumed to be at “high risk” of clinically significant prostate cancer as a result of PCA3 score (false positives).
- d. Potential for morbidity related to altered screening/management (e.g., biopsy, repeat biopsy, adjuvant therapy, surgery) on the basis of PCA3 score.
  - e. Potential for social, economic, or psychological harm associated with use of PCA3 assay for prostate cancer diagnosis and management.

## Considerations

- The topic meets all EHC Program selection criteria. (For more information, see <http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/>.)
- The burden of prostate cancer is significant. Virtually all males reaching the age of 50 will need to make informed decisions about prostate cancer screening, and some will go on to have additional diagnostic testing. Having a tool with enhanced diagnostic specificity that improves diagnostic testing may partially reduce the uncertainty that plagues this decision-making process. While there are currently several guidelines addressing total PSA testing and prostate cancer screening, none to date focus on use of PCA3. This test is already being marketed and there is a critical need for an understanding of how this marker compares to current practices for screening, diagnosis, and management decisions. Therefore, this topic will move forward as a new systematic review by the EHC Program.