# Panel Discussion on Pros and Cons of the AUA, NCCN, and EAU Screening Guidelines

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NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

# Prostate Cancer Early Detection

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European Association of Urology

Guidelines

## EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent

American Urological Association (AUA) Guideline

## EARLY DETECTION OF PROSTATE CANCER: AUA GUIDELINE

# Rules of engagement

- Assume healthy
- Assume asymptomatic
- Assume biopsy naïve

# Step 1: Develop a risk assessment

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- All three guidelines recommend increasing benefits and reducing harms of prostate ca screening by identifying at-risk individuals
  - Minimum requirements for risk-adapted strategy
    - Age
    - Race
    - Family history
      - Prostate cancer
      - High-risk germline mutations (BRCA1, BRCA2)
    - Prior history of screening

# Step 1: Develop a risk assessment

- Additional components of risk assessment
  - The baseline PSA
    - Definitions of high-risk based on initial baseline PSA
      - EAU: >1 at age 40; >2 at age 60
      - NCCN: Above median for age
        - > 0.5-0.7 for ages 40-49;
        - > 0.9-1.0 for age 50-59;
        - > 1.2-1.4 for ages 60-70
      - AUA: First PSA at age 50, stratify based on median of 0.9-1.0
        - Earlier baseline at age 40 prevents fewer than 1 prostate cancer death per 1,000

# Step 1: Develop a risk assessment

- At what age do recommend screening?
- What risk factors drive your decision to screen?
- What PSA level concerns you in a 50-year-old and how is management altered based on this threshold?
- Do you use any other tools?
  - PSAD, risk calculators, nomograms

# Step 2: Determine how frequently to screen

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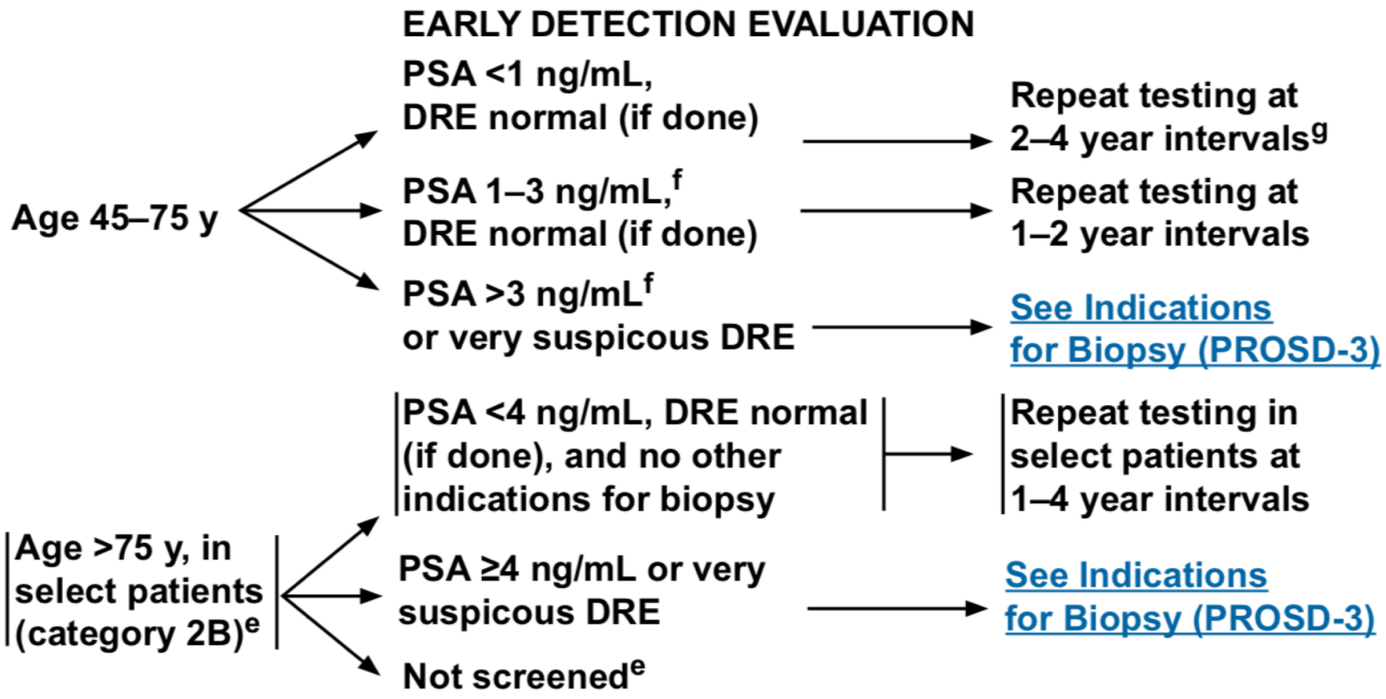
- Though the NCCN relies on PSA medians to develop an age based risk-adapted strategy for the baseline PSA, arbitrary PSA levels of 1-3 are used to determine frequency of screening



# Step 2: Determine how frequently to screen

- The EAU Guidelines recommend annual or biannual screening based on initial PSA value and cutoffs of 1 for patients age 40 or 2 for patients age 60.

| | | |
|---|---|---|
| Offer PSA testing in men at elevated risk of having PCa:<br>• Men aged >50 yr<br>• Men aged >45 yr and a family history of PCa<br>• African American men aged >45 yr<br>• Men with a PSA level >1 ng/ml at age 40 yr<br>• Men with a PSA level >2 ng/ml at age 60 yr | 2b | A |
| Offer a risk-adapted strategy (based on initial PSA level), with follow-up intervals of 2 yr for those initially at risk:<br>• Men with a PSA level >1 ng/ml at age 40 yr<br>• Men with a PSA level >2 ng/ml at age 60 yr<br>Postpone follow-up to 8 yr in those not at risk. | 3 | C |

# Step 2: Determine how frequently to screen

Based on these data, the Panel believes that annual PSA screening as a routine should be discouraged for those who choose to be screened, that two year PSA intervals are a reasonable approach and will be unlikely to miss a curable prostate cancer in most men, and that for men over 60 with PSA levels below 1.0ng/mL, longer PSA screening intervals (e.g., of four years) could be considered. The reader is reminded that for men with a PSA below 3ng/mL at age 70 to 75 years, PSA screening could be safely discontinued if a man at this age is still being screened.[100]

The AUA guidelines recommends two-year screening frequency for basically all patients

# Step 2: Determine how frequently to screen

- What interval of screening do recommend in your practice?
- Describe challenges in screening intervals > 1 year, and how to avoid them?
- How does age impact your decisions?
- Do you age-adjust for PSA?
- Does PSAD impact decisions?

# Step 3: Determine who to biopsy

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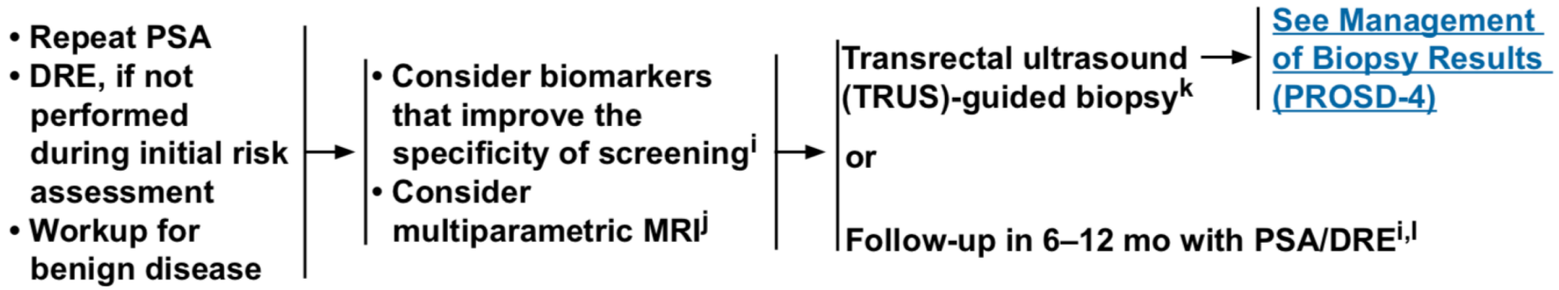
**Don’t treat an elevated PSA with antibiotics for patients not experiencing other symptoms.**

It had previously been suggested that a course of antibiotics might lead to a decrease in an initially raised PSA and reduce the need for prostate biopsy; however, there is a lack of clinical studies to show that antibiotics actually decrease PSA levels. It should also be noted that a decrease in PSA does not indicate an absence of prostate cancer. There is no information available on the implications of deferring a biopsy following a decrease in PSA.

# Step 3: Determine who to biopsy

- The NCCN guidelines have incorporated the use of biomarkers and mp-MRI into their recommendations for enhanced pre-biopsy risk assessment



# Step 3: Determine who to biopsy

- The AUA guidelines consider biomarkers to be “secondary tests” and do not yet mention the utility of mp-MRI for refining assessment of risk in biopsy-naïve patients undergoing screening

Much effort has been invested in the discovery of methods for improving the ability of PSA to predict the presence of prostate cancer. At this point, the use of DRE, PSA derivatives (PSA density and age specific reference ranges) and PSA kinetics (velocity and doubling time), PSA molecular forms (percent free PSA and proPSA), novel urinary markers (PCA3), and prostate imaging should be considered secondary tests (not primary screening tests) with potential utility for determining the need for a prostate biopsy, but with unproven benefit as primary screening tests. The Panel recognizes that these tests can be used as adjuncts for informing decisions about the need for a prostate biopsy –or repeat biopsy- after PSA screening, but emphasizes the lack of evidence that these tests will increase the ratio of benefit to harm. Further, risk calculators that include multiple variables (in addition to

# Step 3: Determine who to biopsy

- Similarly, the EAU guidelines mention free/total PSA, PHI, and 4K but do not yet incorporate mp-MRI into their guidelines

The free-to-total PSA ratio stratifies the risk of PCa in men with 4–10 ng/ml total PSA and a previous negative biopsy but may be affected by several preanalytical and clinical factors (eg, instability of free PSA at 4 °C and room temperature, variable assay characteristics, and large concomitant benign prostatic hyperplasia [BPH]). Novel assays for risk stratification measuring a panel of kallikreins including the Prostate Health Index test and the four-kallikrein score test are intended to reduce the number of unnecessary biopsies in men with a PSA between 2 and 10 ng/ml. Prospective multicentre studies demonstrated that both tests outperformed free-to-total PSA for PCa detection [23,24]. A formal comparison of these new tests is lacking.

#MRI First
@UroWeb

# Recommendations EAU 2019

In Press: Rouviere et al.
Lancet Oncology 2018

| Recommendations in *biopsy naïve patients* | LE | Strength rating |
|---|---|---|
| Perform mpMRI before prostate biopsy. | 1a | Strong |
| When mpMRI is positive (i.e., PI-RADS ≥3), perform the combination of targeted biopsy and systematic biopsy | 2a | Weak |
| When mpMRI is negative (i.e., PI-RADS ≤2) AND the patient has low-risk of clinically-significant disease based on risk calculator or biomarker results, consider not to perform systematic biopsies | 2a | Weak |

| Recommendations in *patients with prior negative biopsy* | LE | Strength rating |
|---|---|---|
| Perform mpMRI before prostate biopsy. | 1a | Strong |
| When mpMRI is positive (i.e., PI-RADS ≥3), perform only targeted biopsy | 2a | Weak |
| When mpMRI is negative (i.e., PI-RADS ≤2), do not perform systematic biopsy, unless the patient has high-risk of clinically-significant disease based on risk calculator or biomarker results | 2a | Weak |

# Step 3: Determine who to biopsy

- What biomarkers are most useful and why?
- Should MRI of the prostate should be obtained prior to biopsy?
  - PROMIS, PRESCION
- If MRI is negative, do you still biopsy?
- Do you do fusion biopsy?
- Biopsy strategy: random vs. target?
- Are biomarkers alone sufficient?
- What to do when biomarkers are discordant with MRI?

# Step 4: Determine when to stop screening

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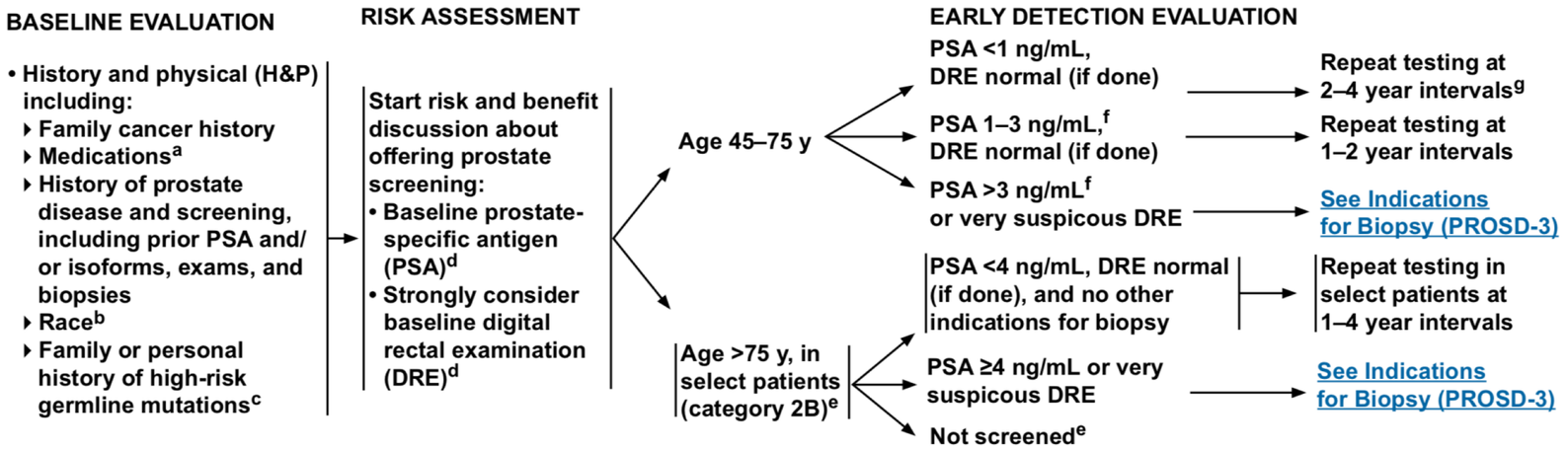
- The NCCN guidelines again utilize an arbitrary age based cutoff of 75 around a PSA of 4 to determine optimal time to stop screening



# Step 4: Determine when to stop screening

- Guideline statement #5 from the AUA Guidelines specifically establishes age 70 as a distinct cutoff for cessation of prostate cancer screening (earlier if life expectancy <10-15 years).

**Age 70+**

**Guideline Statement 5.**

**The Panel does not recommend routine PSA screening in men over age 70 years or any man with less than a 10 to 15 year life expectancy. (Recommendation; Evidence Strength Grade C)**

# Step 4: Determine when to stop screening

- The EAU guidelines do not explicitly state an age at which prostate cancer screening should be stopped, only that performance status and life expectancy should be taken into account in the decision to continue or stop screening.

| | | |
|---|---|---|
| Decide on the age at which early diagnosis of PCa should be stopped based on life expectancy and performance status; men who have a life expectancy <15 yr are unlikely to benefit. | 3 | A |

# Step 4: Determine when to stop screening

- At what age do recommend to stop screening?
- When do you stop screening older patients with and elevated PSA?