

## NCCN Guidelines® Insights

# Prostate Cancer Early Detection, Version 1.2014

## Featured Updates to the NCCN Guidelines

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### Abstract

The NCCN Guidelines for Prostate Cancer Early Detection provide recommendations for men choosing to participate in an early detection program for prostate cancer. These NCCN Guidelines Insights highlight notable recent updates. Overall, the 2014 update represents a more streamlined and concise set of recommendations. The panel stratified the age ranges at which initiating testing for prostate cancer should be considered. Indications for biopsy include both a cutpoint and the use of multiple risk variables in combination. In addition to other biomarkers of specificity, the Prostate Health Index has been included to aid biopsy decisions in certain men, given recent FDA approvals. (*J Natl Compr Canc Netw* 2014;12:1211–1219)

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**Learning Objectives:**

Upon completion of this activity, participants will be able to:

- Integrate into professional practice the updates to NCCN Guidelines for Prostate Cancer Early Detection
- Describe the rationale behind the decision-making process for developing the NCCN Guidelines for Prostate Cancer Early Detection

**Disclosure of Relevant Financial Relationships****Editor:**

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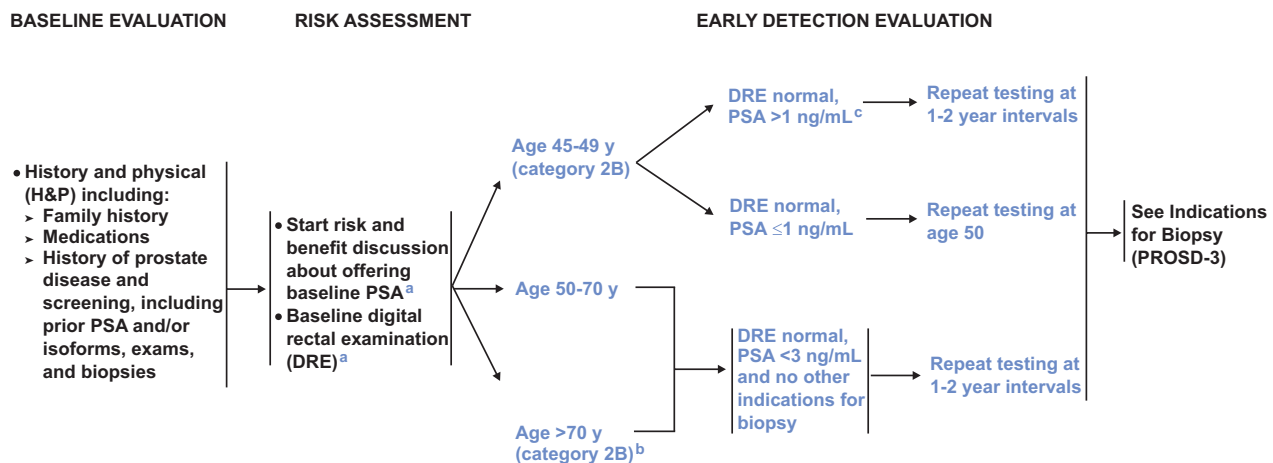
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<sup>a</sup>The best evidence supports the use of serum PSA for the early detection of prostate cancer. DRE should not be used as a stand-alone test, but should be performed in those with an elevated serum PSA. DRE should be considered as a baseline test in all patients as it may identify high-risk cancers associated with "normal" serum PSA values.

<sup>b</sup>Testing above the age of 70 years of age should be done with caution and only in very healthy men with little or no comorbidity as a large proportion may harbor cancer that would be unlikely to affect their life expectancy, and screening in this population would substantially increase rates of over-detection. However, a clinically significant number of men in this age group may present with high-risk cancers that pose a significant risk if left undetected until signs or symptoms develop. One could consider increasing the PSA threshold for biopsy in this group (i.e., >4 ng/mL). Very few men above the age of 75 years benefit from PSA testing. Finally, men at age 60 years with a serum PSA <1.0 ng/mL have a very low risk of metastases or death due to prostate cancer. Similarly, a cut point of 3.0 ng/mL at age 75 years has a similarly low risk of such outcomes.

<sup>c</sup>The reported median PSA values for men aged 40-49 y range from 0.5-0.7 ng/mL, and the 75th percentile values range from 0.7-0.9 ng/mL. Therefore, the PSA value of 1.0 ng/mL selects for the upper range of PSA values. Men who have a PSA above the median for their age group are at a higher risk for prostate cancer and for the aggressive form of the disease. The higher above the median, the greater the risk.

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PROSD-2

### NCCN Categories of Evidence and Consensus

**Category 1:** Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

**Category 2A:** Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

**Category 2B:** Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

**Category 3:** Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

**All recommendations are category 2A unless otherwise noted.**

**Clinical trials:** NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

## Overview

Prostate cancer is the most commonly diagnosed cancer in American men.<sup>1</sup> Over the past 2 decades in the United States, death rates for prostate cancer have declined 45%, a reduction largely attributed to early detection and/or improved treatment.<sup>2</sup> Considerable stage migration has occurred over the years; approximately 80% of new diagnoses each year are localized disease.

The decision regarding whether to pursue early detection of prostate cancer using prostate-specific antigen (PSA) testing is complex. When, who, and how often to test remain major topics of debate. Although prostate cancer is a major cause of death and disability, many argue that the benefits of PSA testing are moderate at best and that PSA testing results in the identification of many men with indolent disease (overdetection), which is too often compounded by unnecessary treatment without benefit (overtreatment). In addition, PSA testing often produces false-positive results, which in turn may contribute to pa-

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## INDICATIONS FOR BIOPSY

DRE suspicious for cancer at any PSA level (category 2B)

PSA >3.0 ng/mL<sup>d</sup>

Excess risk based on multiple factors<sup>e</sup> (category 2B)

TRUS-guided biopsy

See Management of Biopsy Results (PROSD-4)

If TRUS-guided biopsy not performed follow up in 6-12 mo with PSA/DRE. Consider use of percent free PSA, PHI, and/or PCA3 in those with serum PSA between 3 ng/mL and 10 ng/mL<sup>f</sup>

Percent free PSA, PHI, or PCA3 in selected patients with serum PSA values between 3 ng/mL and 10 ng/mL<sup>f</sup>

**TRUS-GUIDED BIOPSY**  
Initial and Repeat  
**Extended-pattern biopsy (12 cores)**

- Number of cores:
  - > Sextant (6),
  - > Lateral peripheral zone (6), and
  - > Lesion-directed at palpable nodule or suspicious image
- Anteriorly directed biopsy is not supported in routine biopsy. However, the addition of a transition zone biopsy to an extended biopsy protocol may be considered in a repeat biopsy if PSA is persistently elevated.
- After 2 negative extended TRUS biopsies, prostate cancer is not commonly found at repeat biopsy. Additional imaging (MRI, T2 weighting, and diffusion weighting) may help identify regions of cancer missed on prior biopsies and should be considered in selected cases.
- For high-risk men with negative biopsies, consideration can be given to a saturation biopsy strategy (including transperineal techniques) and/or the use of multiparametric MRI followed by an appropriate biopsy technique based on the results.
- Local anesthesia can decrease pain/discomfort associated with prostate biopsy and should be offered to all patients.

<sup>d</sup>The level of PSA correlates with the risk of prostate cancer. The Prostate Cancer Prevention Trial (PCPT) demonstrated that 15% of men with a PSA level of  $\leq 4.0$  ng/mL and a normal DRE had prostate cancer diagnosed on end-of-study biopsies. Approximately 30% to 35% of men with serum PSA between 4 to 10 ng/mL will be found to have cancer. Total PSA levels >10 ng/mL confer a greater than 67% likelihood of prostate cancer.

<sup>e</sup>Many factors may influence and better inform decisions on biopsy including PSA kinetics and/or velocity. Alternatively, risk calculators could be used in those men similar to cohorts where risk calculators have been developed. These tools combine factors including age, family history, ethnicity, DRE, and PSA to aid in the decision of whom to biopsy. They have not been tested in randomized clinical trials and which cut-point of risk would be associated with a reduction in prostate cancer mortality remains unknown.

<sup>f</sup>Biomarkers that improve the specificity of detection are not recommended as first-line screening tests, but are reserved, for the most part, in selecting those who have undergone at least one negative biopsy for a repeat biopsy. However, there may be some patients who meet either PSA or DRE standards for biopsy, but for whom the patients and/or the physician wish to further define the probability of cancer before undergoing biopsy. A PHI >35, percent free PSA <10% and/or PCA3 score >35 are strongly suspicious for prostate cancer.

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PROSD-3

tient anxiety and potential complications associated with unnecessary biopsies.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Prostate Cancer Early Detection were developed for the treatment of men who have elected to participate in an early detection program for prostate cancer after being informed of the risks and benefits of testing. The guidelines provide a set of sequential recommendations on screening and subsequent workup for maximizing the detection of the subset of prostate cancers that are potentially curable and, if left undetected, represent a risk to the patient. These NCCN Guidelines Insights highlight important revisions to the guideline.

The reduction in prostate cancer mortality must be balanced against the adverse effects of treatment, emphasizing the importance of selective treatment of men with prostate cancer identified by screening, such that many men can be managed on active surveillance.<sup>3</sup> Hence the panel emphasizes that these guidelines should

be linked to the NCCN Guidelines for Prostate Cancer, which explicitly recommend active surveillance for appropriate candidates (to view the complete version of the guidelines, visit NCCN.org). Early detection strategies that do not recognize the importance of refined and selective treatment may result in harm. Lastly, these recommendations are most relevant for Caucasian men, who constitute most of the men enrolled in screening trials. Application to other ethnic groups should be made with caution. Clearly, much research on the benefits and risk of screening in other ethnic groups is needed.

### Population-Based Screening Studies

Although many trials have been cited with regard to PSA testing, 2 studies are most relevant because of their topicality and randomized design. Unfortunately, these trials did not address the potential benefit of screening in men with high-risk factors, including African Ameri-

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can men. Also, many men in these studies underwent sextant prostate biopsies rather than extended core biopsies, which is the standard diagnostic technique currently used.

### European Randomized Study of Screening for Prostate Cancer

The European Randomized Study of Screening for Prostate Cancer (ERSPC) enrolled approximately 182,000 men between the ages of 50 and 74 years in 7 European countries, randomly assigned to either a group that was offered PSA screening at an average of once every 4 years or a control group that did not receive such screening.<sup>4,5</sup> During a median follow-up of 11 years, the cumulative incidence of prostate cancer was 7.4% in the screening group versus 5.1% in the control group. The rate ratio for death from prostate cancer were 0.79 for the screening arm compared with the control arm (95% CI, 0.68–0.91;  $P=.001$ ). Over the long term, the number needed to screen and the additional number needed to treat to prevent 1 death from prostate cancer were 200 and 5, respectively.<sup>3,6</sup> Modeling the ERSPC data, Heijnsdijk et al<sup>3</sup> estimated the number needed to screen was 98 and number needed to treat was 5 to save 1 life.

The Göteborg randomized population-based prostate cancer screening trial was initiated in Sweden before and independently of the ERSPC, but some of its patients were reported as part of the ERSPC.<sup>7</sup> The Göteborg study randomized 20,000 men, aged 50 to 64 years, to either a screening group invited for PSA testing every 2 years or a control group not invited for testing. In men randomized to screening, 76% attended at least 1 test. PSA testing in the general population was very low at the beginning (3%) but increased over time.

During a median follow-up of 14 years, the cumulative prostate cancer incidence was 12.7% in the screening group and 8.2% in the control group (hazard ratio, 1.64; 95% CI, 1.50–1.80;  $P<.0001$ ). The rate ratio for death from prostate cancer was 0.56 (95% CI, 0.39–0.82;  $P=.002$ ) in the screening group compared with the control group. Overall, 293 men needed to be screened and 12 needed to be diagnosed to prevent 1 prostate cancer death at 14 years. Notably, a cause-specific survival benefit was observed despite the fact that not all cancers were immediately treated. A total of 45% of men were assigned to active surveillance and 32% were managed with it. This suggests that early detection combined with selective treatment based on risk can lower mortality rates without uniform treatment of all cancers.

Several explanations are possible for the more favorable results of the Göteborg trial compared with the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial (discussed later) and ERSPC. First, the patients were younger and less likely to have incurable prostate cancer at first screening; second, there was less contamination of the control arm; third, a lower PSA threshold was used for recommending biopsy; and finally, men were screened more frequently than in ERSPC and for a longer period than in PLCO. However, the Göteborg trial results should not be interpreted as belonging to an independent confirmatory study, because more than half of the patients were included in the main analysis of ERSPC.

### PLCO Trial

The PLCO trial randomized 76,685 men aged 55 to 74 years at 10 US study centers to annual PSA testing for 6 years and digital rectal examination (DRE) for 4 years or usual care.<sup>8</sup> After 13 years of follow-up, the incidence rate ratio for the screening arm compared with the control arm was 1.12 (95% CI, 1.07–1.17). The investigators did not find a statistically significant difference between the disease-specific mortality rates of the screening and control groups (relative risk, 1.09; 95% CI, 0.87–1.36). Because of the high rate of prescreening and the high contamination rate of 40% to 52% each year in the control group (ie, 74% in the usual care arm were screened at least once), the trial cannot be described as a trial of screening, but rather a comparison of different approaches to screening (ie, opportunistic vs systematic). The estimated mean number of screening PSA tests (DREs) in the control arm was 2.7 (1.1), compared with 5.0 (3.5) in the screened arm. Virtually the same percentage of men in the control and screening arms was screened during the study. In addition, the biopsy rate for patients with elevated serum PSA values was relatively low compared with rates in the European trials. However, it did show that yearly screening may be of limited value compared with less frequent testing.<sup>9</sup>

In a subset analysis reported by Crawford et al,<sup>10</sup> a 44% decrease in the risk of prostate cancer–specific death was observed in men with no or minimal comorbidity assigned to screening compared with controls, and the numbers needed to screen and treat to prevent 1 death were 723 and 5, respectively. This benefit was not found among men with 1 or more significant comorbidities. These results suggest that screening is more useful among men in good health because of the lack of a competing cause for mortality. However, some in-

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investigators argue that major methodological errors are inherent in such an analysis.<sup>11</sup>

### Ages to Initiate and Stop Testing

Controversy exists surrounding the ideal age at which to begin testing for prostate cancer. Recent randomized clinical trials (RCTs) looking at the impact of screening on prostate cancer mortality have focused primarily on men aged 55 to 69 years. The ERSPC and the Göteborg trial reported decreased disease-specific mortality in men aged 55 to 69 and 50 to 64 years, respectively.<sup>4,5,7</sup> These results support baseline PSA testing in men aged 50 to 55 years, with the strongest evidence supporting testing at age 55 years. Many recommend earlier testing based on risk, including ethnicity (African American men), family history, and *BRCA* mutations.

Because younger men were not included in these screening studies, baseline testing at an earlier age has not been evaluated in RCTs. However, observational evidence suggests that baseline testing of men in their 40s and early 50s may have value for future risk stratification, although some would describe it as marginal.<sup>12</sup> A study by Lilja et al<sup>13</sup> assessed blood collected from 21,277 men in Sweden aged 33 to 50 years who were followed until 2006. Among the 1312 cases of prostate cancer and 3728 controls without prostate cancer, these investigators reported that a single PSA test before age 50 years predicted subsequent prostate cancer up to 30 years later, with a robust area under the curve (AUC) of 0.72 (0.75 for advanced prostate cancer). This suggests that one could perform early, baseline testing and then determine the frequency of testing based on risk.

A recent report based on the same cohort clarified associations of age with long-term risk for metastases.<sup>14</sup> In this study, the risk of prostate cancer death was strongly correlated with baseline PSA level in men aged 45 to 49 years and 51 to 55 years; 44% of the deaths in the analytic cohort occurred in men in the highest tenth of the distribution of PSA level, suggesting that there may be a strong rationale for baseline testing in men younger than 55 years. Although many advocate earlier testing only in men thought to be at higher risk because of family history or ethnicity, as noted previously, a baseline serum PSA level is a stronger predictor of the future risk of the disease compared with either of these risk factors.

Most panel members favored baseline, informed testing beginning at ages 45 to 50 years (although some

felt that testing at age 40 years was most appropriate), annual to biannual follow-up in those above the 75th percentile for age-specific PSA level ( $\geq 1.0$  ng/mL), and retesting at age 50 years in those below this level.<sup>15</sup> Median PSA levels for men aged 40 to 49 and 50 to 59 years are 0.7 ng/mL and 0.9 ng/mL, respectively.<sup>16,17</sup>

### Testing in Elderly Men

Because the previously cited RCTs (ESRPC, PLCO, and Göteborg) observed benefits to testing only in men aged up to 70 years, several panel members favored stopping testing at age 70 years. However, other data would suggest a benefit to screening beyond 70 years. A study of 4561 men who underwent radical prostatectomy found that men older than 70 years were more likely to have a higher grade and stage of disease and worse survival compared with their younger counterparts.<sup>18</sup> Others have published similar findings.<sup>19</sup>

To assess the appropriate ages for discontinuing screening, a microsimulation model<sup>6</sup> predicted that decreasing the stopping age from 74 to 69 years would lead to a 27% relative reduction in the probability of life saved, but an almost 50% reduction in the probability of overdiagnosis. It also assessed a strategy of screening men up to age 74 years while simultaneously increasing the PSA threshold for biopsy with increasing age. Compared with using a uniform cutoff of 4.0 ng/mL, this strategy reduced the rate of overdiagnosis by one-third while only slightly altering lives saved. Any strategy that reduces overdiagnosis will have some impact on prostate cancer mortality rates. The goal of refined testing beyond age 70 years is to maximize the reduction in overdiagnosis and minimize the impact on cancer-specific mortality.

Total PSA at certain ages may predict future risk. Vickers et al<sup>20</sup> examined the relationship between baseline PSA level at age 60 years and the future risk of prostate cancer death or metastases, and found that those with a PSA level below the median ( $< 1$  ng/mL) were unlikely to develop clinically significant prostate cancer (0.5% risk of metastases and 0.2% risk of prostate cancer death). Similarly, in a study of 849 men in the Baltimore Longitudinal Study of Aging, no men aged 75 to 80 years with a PSA level less than 3.0 ng/mL died of prostate cancer.<sup>21</sup> Moreover, the time to death or diagnosis of aggressive prostate cancer was longer in men with a PSA level less than 3.0 ng/mL than in those with a PSA level greater than 3.0 ng/mL, suggesting that men aged 75 years or older with a PSA level less than 3.0 ng/mL are unlikely to die or experience aggressive

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prostate cancer throughout their remaining life and may safely discontinue screening.

In summary, one strategy to reduce overdiagnosis in the older population would be to discontinue screening at age 69 years; a second would be to continue screening up to age 74 years but increase the PSA threshold for biopsy among men aged 70 to 74 years; and a third would be to discontinue screening at age 75 years for men with a PSA level less than 3.0 ng/mL. Obviously, only men who have a life expectancy beyond 10 years should be screened at any age.

### NCCN Recommendations

The panel uniformly recommends that baseline PSA testing be offered to healthy, well-informed men aged 50 to 70 years (see PROSD-2, page 1213). Most panelists believed that baseline testing should be available to men aged 45 to 49 years. The category 2B designation for this age group reflects the nonuniform consensus.

The panel recommends that PSA testing be individualized after age 70 years and that indication for biopsy be carefully evaluated (see PROSD-2, page 1213). This is also a category 2B recommendation because of nonuniform consensus. Testing in those older than 70 years should be performed with caution and only in very healthy men with little or no comorbidity, because a large proportion may harbor cancer that would be unlikely to affect their life expectancy, and routine screening in this population would substantially increase rates of overdiagnosis. Alternately, some panel members pointed out that a clinically significant number of men in this age group may (>70 years) present with high-risk cancers that pose a clinically significant risk if left undetected until signs or symptoms develop. One could therefore consider increasing the PSA threshold for biopsy in this group to reduce overdiagnosis. The panel agreed that very few men older than 75 years benefit from PSA testing.

NCCN panel members uniformly discouraged PSA testing in men unlikely to benefit from prostate cancer diagnosis based on age and/or comorbidity.

### Frequency of Testing

A recent comparison of 2 centers in the ERSPC trial studied the impact of different screening intervals on the diagnosis of cancers in men aged 55 to 64 years.<sup>22</sup> The Göteborg arm randomized 4202 men to screening every 2 years, whereas the Rotterdam arm randomized 13,301 men to screening every 4 years, with a similar

follow-up of 11 to 12 years. Compared with screening every 4 years, a significant 43% reduction was seen in the diagnosis of advanced prostate cancer (clinical stage  $\geq$ T3a, N1, or M1; PSA level  $>$ 20 ng/mL; Gleason score  $\geq$ 8 at biopsy) for screening every 2 years. However, a 46% increase in the diagnosis of low-risk prostate cancer (clinical stage T1c, Gleason score  $<$ 6, and PSA level  $<$ 10 ng/mL at biopsy) was seen with screening every 2 years.

A study using microsimulation models of prostate cancer incidence and mortality predicted that a strategy using biennial screening intervals in men with average PSA levels and longer screening intervals (every 5 years) for those with low PSA levels (below median for age by decade) would be associated with a 2.27% risk of prostate cancer–related death compared with 2.86% with no screening.<sup>6</sup> In addition, compared with annual screening and using a biopsy threshold of 4.0 ng/mL, the biennial strategy also projected a relatively lower overdiagnosis rate of 2.4% (vs 3.3% for annual screening), a 59% reduction in total tests, and a 50% reduction in false-positive results.

These data therefore suggest that screening every 2 years may provide comparable survival to annual screening while allowing modest reductions in overdiagnosis and significant reductions in unnecessary testing. However, panel members did not uniformly agree on the recommendation for biannual screening. Some pointed out the logistical impracticality in testing every 2 years, because many men receive PSA testing during their annual checkup.

### NCCN Recommendations

The panel recommends PSA testing every 1 to 2 years (see PROSD-2, page 1213). For men aged 45 to 49 years with serum PSA values of 1 ng/mL or less, additional testing may be deferred until age 50 years. For men with PSA levels exceeding 1.0 ng/mL, testing should be repeated at 1- to 2-year intervals.

### Indications for Biopsy

The previously cited RCTs used PSA thresholds to prompt a biopsy. PSA cutpoints for biopsy varied somewhat among centers and trials over time. Although a serum PSA level of 2.5 ng/mL has been used by many, a level of 3.0 ng/mL is supported by the trials and would more robustly limit the risk of overdiagnosis. However, some panel members did not recommend limiting the option of biopsy to pre-

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specified PSA thresholds, noting that many other factors (eg, age, ethnicity, family history, PSA kinetics) should also inform the decision to perform a biopsy.

Several panel members also noted that risk calculators could be used in appropriately selected men. These calculators have been developed to estimate an individual's risk for biopsy-detectable prostate cancer using multiple clinical factors. Common risk calculators are the Sunnybrook nomogram-based risk calculator, ERSPC risk calculator, and Prostate Cancer Prevention Trial risk calculator.<sup>23–26</sup> These online tools combine clinical variables, including age, family history, ethnicity, DRE results, and PSA level, to estimate both the risk of biopsy-detectable prostate cancer and the risk of biopsy-detectable high-grade prostate cancer. Such information potentially allows for more informed decision-making.<sup>27</sup> However, these calculators have not been assessed in RCTs. Moreover, a specific cutpoint expressed as the probability of biopsy-detectable prostate cancer associated with a reduction in prostate cancer mortality remains to be elucidated.

### Combinations of Biomarkers

The search continues for an optimal test that can accurately identify clinically significant prostate cancer. Because of the limitations of PSA testing, several PSA derivatives and other tests have been studied in the effort to improve specificity of prostate cancer detection and aid biopsy decisions. Examples include assessment of PSA velocity,<sup>28</sup> percent free PSA,<sup>29</sup> and prostate cancer antigen 3.<sup>30</sup>

Recent research has begun to focus on combining biomarkers to enhance their performance. The Prostate Health Index (PHI) is a combination of existing markers (total PSA, free PSA, and pro-PSA).<sup>31–33</sup> This scoring system was assessed in a multicenter study and potentially doubles the sensitivity of total or free PSA analysis for cancer detection in patients with serum PSA concentrations between 2 and 10 ng/dL.<sup>34</sup> In addition, the PHI correlates with cancer grade. The PHI was approved by the FDA in 2012 for use in individuals with serum PSA values between 4 and 10 ng/mL. Another test combination, the 4-kallikrein panel, also seems to have value.<sup>35</sup> Note that these tests are designed as “reflex tests”; that is, tests to be ordered to inform biopsy decisions when PSA level is elevated. They are not intended for use as a “first-line” screening tool.

### NCCN Recommendations

Indications for biopsy have been significantly simplified in the latest version of the NCCN Guidelines and include both a PSA cutpoint and use of multiple factors (see PROSD-3, page 1214). The panel uniformly recommends that transrectal ultrasound (TRUS)–guided biopsy be considered in patients with a serum PSA level greater than 3.0 ng/mL. A suspicious DRE result, regardless of PSA level, is another indication for biopsy. This is a category 2B recommendation, because many panel members felt that DRE should not be used as a stand-alone test but rather should be performed in men with an elevated serum PSA level. All panel members agreed that a decision to perform a biopsy should not be based on a PSA cutpoint alone, but should incorporate other important clinical variables, including repeat PSA testing, age, health status, and patient preference. Some panel members also argued that additional factors, including family history, PSA kinetics, and ethnicity, should play a role in biopsy decision-making. Use of these factors to determine whether the patient should undergo biopsy is a category 2B recommendation.

If a biopsy is not performed for the conditions that suggest a high risk of prostate cancer, the patient should be reevaluated in 6 to 12 months. Consideration may be given to biomarkers that improve specificity such as percent free PSA, PHI, and PCA3 in select patients with PSA levels between 3 and 10 ng/mL, although these biomarkers are indicated more strongly in the consideration of a repeat biopsy after an initially benign result.

### Conclusions

Important updates to the detection of prostate cancer in the NCCN Guidelines for Prostate Cancer Early Detection are highlighted in these NCCN Guidelines Insights (to view the complete version of the guidelines, visit [NCCN.org](http://NCCN.org)). The NCCN Guidelines are updated at least annually and more often when new high-quality clinical data become available in the interim. The most up-to-date version of these continuously evolving guidelines is available online at [NCCN.org](http://NCCN.org). The recommendations in the NCCN Guidelines are based on evidence from available clinical data and expert consensus of the NCCN panel. Independent medical judgment is required to apply these guidelines to individual patients to optimize care. The physician and patient have the responsibility to jointly explore and select the most appropriate option from among the available alternatives.



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To participate in this journal CE activity: 1) review the learning objectives and author disclosures; 2) study the education content; 3) take the posttest with a 66% minimum passing score and complete the evaluation at <http://education.nccn.org/node/53069>; and 4) view/print certificate. After reading the article, you should be able to answer the following multiple-

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### Posttest Questions

1. In a clinical practice setting where annual examinations are routinely performed on men, which of the following cases would least likely benefit from an early detection program for prostate cancer?
  - a. 47-year-old man with baseline PSA level of 2.4 ng/mL
  - b. 62-year-old man of African American descent
  - c. 75-year-old man in the highest health quartile with no comorbidities
  - d. 17-year-old man with poor renal function from type 2 diabetes
2. True or False: TRUS-guided biopsy is appropriate in patients with a serum PSA level > 3.0 ng/mL.
3. Which of the following tests may improve the specificity of prostate cancer detection and aid in biopsy decisions?
  - a. PSA velocity
  - b. Percent-free PSA
  - c. Prostate Health Index
  - d. All of the above