Review Article

Prostate cancer screening—when to start and how to screen?

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Abstract: Prostate-specific antigen (PSA) screening reduces prostate cancer (PCa) mortality; however such screening may lead to harm in terms of overdiagnosis and overtreatment. Therefore, upfront shared decision making involving a discussion about pros and cons between a physician and a patient is crucial. Total PSA remains the most commonly used screening tool and is a strong predictor of future life-threatening PCa. Currently there is no strong consensus on the age at which to start PSA screening. Most guidelines recommend PSA screening to start no later than at age 55 and involve well-informed men in good health and a life expectancy of at least 10–15 years. Some suggest to start screening in early midlife for men with familial predisposition and men of African-American descent. Others suggest starting conversations at age 45 for all men. Re-screening intervals can be risk-stratified as guided by the man's age, general health and PSA-value; longer intervals for those at lower risk and shorter intervals for those at higher risk. Overdiagnosis and unnecessary biopsies can be reduced using reflex tests. Magnetic resonance imaging in the pre-diagnostic setting holds promise in pilot studies and large-scale prospective studies are ongoing.

Keywords: Prostate cancer (PCa); screening; baseline prostate-specific antigen

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Introduction

Currently, only two countries in the world—Lithuania and Kazakhstan—have an organized population-based screening program for prostate cancer (PCa) (1,2). Screening is still a controversial issue in most countries because there are both benefits and harms associated with such practice. Even experts and opinion leaders in the field disagree on who, when and how to best screen for PCa and interpret the evidence differently regarding the magnitude of prevention of PCa deaths and metastatic disease versus the risks of overdiagnosis and side-effects of treatment such as erectile dysfunction and urinary incontinence (3). For instance, an often cited estimate is that "there is a small but finite benefit from PCa screening in terms of PCa mortality—about 1 fewer PC death/1,000 men screened over 10 years" (4). This fails to address the time-to-event nature of the data (5). Computer simulation screening analysis have shown that the benefit increases with time, with 9 fewer deaths/1,000 men screened followed for their entire life span, i.e., closer to 1/100 rather than 1/1,000 (6). Although organized screening with the blood test prostate-specific antigen (PSA) has been shown to be more effective than opportunistic PSA-testing in terms of reducing PCa mortality (7), most guideline groups recommend against mass screening, as the benefits do not exceed the disadvantages with overdiagnosis and over-treatment. Therefore, shared, or

Table 1 Age to start shared decision making conversations about prostate-specific antigen (PSA) screening according to current guidelines

Guideline	Age (years)
NCCN, Melbourne Consensus	40–45
MSKCC	45
EAU-ESTRO-SIOG	50; 45 if family history or African-American
ASCO, ACS, ACP	50
AUA, USPSTF (draft)	55–69

informed, decision-making has been the trend in recent years, implying that the decision whether or not to be screened for PCa should be an individual one, after a discussion about the benefits and harms between the man and his health care provider (4,8). Simple decision support tools are available to facilitate such discussions (9). All experts agree that screening should take place only after shared decision making, and that increased use of active surveillance (monitoring) for low risk PCa is desirable (2,3). Risk-stratified screening algorithms have also become increasingly popular, with or without additional biomarkers added to the PSA-test to determine the need for biopsy (10). The objective of this article is to review the current literature regarding when to start PCa screening and how to screen.

Methods

Several known recommendations, as well as articles selected after searching PubMed, were included for this review. Several guidelines for PCa screening and "guideline to the guidelines" have been reported (11-15) (*Table 1*). All guidelines agree that any PCa screening ought to take place in the context of shared decision making. The United States Preventive Services Task Force (USPSTF) 2017 draft recommendation recommends shared decision making starting between the ages 55–69 (8). The American Cancer Society (ACS) and the American College of Physicians (ACP) recommend starting discussions about PSA testing at age 50 (16-18) and the American Society of Clinical Oncology (ASCO) recommends discussing the appropriateness of screening with men with a life expectancy >10 years (19).

As for the suggested screening algorithms, we narrowed this review down to guidelines describing more detailed risk-stratified approaches to PSA-screening—the current trend in the academic urologic oncology community to improve the balance between benefits and harms. To this end, we included select guidelines currently available in Europe and the U.S.: the European Association of Urology (EAU)-European Society for Radiotherapy & Oncology (ESTRO)-International Society of Geriatric Oncology (SIOG) Guidelines on Prostate Cancer (20), the National Comprehensive Cancer Center (NCCN) Guidelines Prostate Cancer Early Detection Guideline (10), the Memorial Sloan Kettering Cancer Center (MSKCC) Recommendations for Prostate Cancer Screening and the American Urological Association (AUA) Guideline (21), as well as articles published in the last 5 years from the PubMed search. When searching PubMed, Medical Subject Heading (MeSH) terms such as "Prostatic Neoplasms", "Mass Screening", "Risk Factors", "Age Factors", etc., were used, supplemented by relevant keywords to include in-process citations and PubMed articles not indexed for Medline. Publication types such as Case Reports, Letter and Editorial were excluded from the search. A total of 43 full-text articles were selected for the final review. These were categorized into one of five categories: age to start, risk factors, PSA, magnetic resonance imaging (MRI) and other screening alternatives.

Results

Does screening reduce PC mortality?

The European Randomized Study of Screening for Prostate Cancer (ERSPC) is the world's largest randomized controlled trial (RCT) on PSA-screening including 162,388 men aged 55–69 years in 8 European countries (22). The 13-year follow-up report showed that PSA-screening every 2–4 years reduces PC mortality by 21%. The reduction in PCa mortality was even larger—44% at 14 years—in the Göteborg trial where 20,000 men ages 50–64 were randomized to biennial PSA-screening or a control group (7,23). The U.S. Prostate Lung Colorectal and Ovarian (PLCO) cancer screening trial randomized 76,685 men aged 55–74 years but did not show any difference in PCa mortality between the screening and control arm (24). The reason for this was high pre-screening rates in both arms and a high contamination rate in the control arm; i.e., the two arms were subjected to almost the same amount of screening (25). However,

with these discrepancies accounted for, both the ERSPC and PLCO trials provide compatible evidence that PSA screening reduces PC mortality (26). There is also compelling evidence from observational data. In the U.S., where the PSA test was introduced as a screening tool in the early 90's, the age-adjusted death rate from PCa dropped 51% between 1993 to 2014 (27).

When to start PCa screening

Age

There is no consensus regarding the age at which to initiate PSA-testing (*Table 1*). Most guidelines recommend that discussions about PSA screening start around ages 45–55 (10,20,21) with well-informed men in good health and a life expectancy of at least 10–15 years. The core age group in the ERSPC trial started screening between ages 55–69. The AUA guideline supports starting screening at age 55 based on the ERSPC trial and because of the risk of overdiagnosis (and overtreatment) in younger men, but also acknowledge that men at higher risk for PCa can start before 55.

Men in the Göteborg trial started screening between ages 50–64. A recent analysis comparing screened men in Göteborg, Sweden, to unscreened men in Malmö, Sweden, showed that regular screening starting at 50–54 could reduce PCa mortality by 17% at 17 years (28). The EAU Guideline recommends to start at age 50 for most men, except in men with a family history of PCa or African American men for whom the recommendation is to start at age 45 (20). The NCCN and MSKCC Guidelines support testing beginning at age 45 after shared decision-making (10,29). Indirect support for starting PSA screening no later than age 55 also comes from an Australian study of 598 prostate biopsies and 723 prostatectomy matched subjects, in which the rates of high-risk PCa (and insignificant PC) were similar between men ≤55 years and men >55 years (30). A sub study from the Göteborg screening trial, in which men were screened every 2 years between ages 50–70 investigated the effect of age at start and the number of screening occasions on the risk of PCa diagnosis, by following the age cohorts over time (e.g., starting at age 52 resulted in 9 screens and starting at 60 resulted in 5 screens). The study showed that starting screening at an earlier age advanced the time of PCa diagnosis but did not increase the risk of being diagnosed, suggesting that starting early does not increase the risk of overdiagnosis, whereas the age for stopping screening does (31). A study from Johns Hopkins showed that older men (75+) who underwent radiotherapy for PCa and who had no history of PSA testing presented with worse disease (more high-risk and high-grade PC) than men who were previously screened (32). Weight *et al.* (33) suggest that there is no advantage in starting screening at age 40 instead of 50. They compared screening in a younger group of men, aged 40–49, with men in their 50s and found greater risk of undergoing a biopsy and receiving the diagnosis of low-risk PCa (HR 2.4, 95% CI: 1.7–3.3 and HR 2.2, 95% CI: 1.12–4.0 respectively) for the younger group. The authors did not find any difference in PCa deaths between the groups, however, follow-up longer than the 17 years in the study is likely necessary to detect any difference in PCa mortality between groups. Another limitation of the study was the rather small sample size.

A recent analysis of the U.S. PLCO trial specifically studied characteristics of 151 men who died from PCa within 13 years of follow-up and were randomized to the screening arm. The authors found that more than half of these men were never screened and they were also older at study start than the average participant (66 *vs.* 62 years) (34).

Critical for balancing the benefits and harms of screening, particularly the risk of overdiagnosis, is the age to stop screening—which is covered in another article in this issue of *TAU* (35). For instance, stopping screening at age 70 can reduce overdiagnosis by 42% (36).

Risk factors

Men with family history of PCa and Afro-American race have increased risk of PCa (15,37,38). According to SEER data, the U.S. incidence of PCa among black men is 60% higher than in white men; the PCa mortality rate is also 2–3 times higher (39). As pointed out by Grill *et al.*, taking a detailed family history is inexpensive and also family history is an independent predictor of PCa among other commonly considered risk factors (40). The likelihood of PCa diagnosis is increased by 2.1- to 2.5-fold in men with a first degree relative who had PCa diagnosed before the age of 60 (40,41). However, men with family history of PCa are at risk of low-grade PCa diagnosis with screening, similar to all men screened (42). In a study of 461 PCa patients treated with radical prostatectomy, Raheem *et al.* found no increased risk of aggressive PCa or biochemical recurrence among patients with first-degree relatives who died of PCa compared to those without family history (43).

However, whether screening should start sooner for these men remains an issue for debate. While both the NCCN and MSKCC screening guidelines (10,29) acknowledge

the above-mentioned groups of men as high-risk groups, however they consider data on screening in diverse and high-risk populations as lacking since PCa screening has mainly been studied in Caucasian men. Of the two major screening trials, one, ERSPC, reported no information on race or family history, and the other one, PLCO, had enrolled approximately 4.4% African-Americans and 6.9% men had a positive family history. The guidelines mentioned above (NCCN and MSKCC) instead stress that the PSA value at age 45 is a stronger risk factor for long-term PCa death than both family history and race (44) suggesting no differential screening guidelines but start age 45 for most (10,29). However, there may be synergistic effects between a positive family history and elevated PSA. Some call for separate PCa screening guidelines for African-American men as there are differences between African-Americans and Caucasians in terms of PCa incidence, clinical course and outcomes, PSA levels and social barriers (45). In a retrospective analysis, Verges et al investigated the relationship of baseline PSA and risk of future PCa and its variance by race. Black men were more likely to be diagnosed with PCa (OR 1.62, P<0.0001) despite that the median baseline PSA was similar between black and white men. The risk was particularly high among black men younger than 70 years (46).

The EAU guidelines recommend starting PSA testing earlier, from 45 years, for men with a family history of PCa or African American men (20). The AUA guidelines recommend against routine screening for men below 55 years unless they are at higher risk; positive family history or African-American race (21). They advocate individualized and well-informed discussion regarding the uncertainty of benefit and the associated harms of screening, pointing out that a strong family history (two or more first degree relatives and/or PCa in multiple generations and/or early onset of PCa <60 years in relatives) is associated with an increased risk of disease and should be taken into account when discussing the potential benefit and harm.

Albright and colleagues analyzed data from 600,000 men in the population-based SEER registry with information on family history and found that the relative risks of lethal PCa varied with the number of affected first-degree relatives [RR 2.5 (95% CI: 2.3–2.7) if 1 relative and 5.3 (95% CI: 2.1–10.9) if 3+ relatives] (47).

Several germline single nucleotide polymorphisms (SNPs) have been associated with PCa risk (48). It has been suggested that SNPs can play a role in targeted screening (49,50). The ongoing PROFILE study will investigate the probability of detecting PCa with biopsy in men with family history by combining SNP profiling with clinical variables (51). With data from 4,528 men in the Prostate Cancer Prevention Trial (PCPT), Chen *et al.* developed a genetic risk score based on 29 PCa risk-associated SNPs and found that more high-grade PCa cases could be identified if family history was supplemented by the genetic risk score (52). Turner and colleagues carried out a randomized trial of 700 men aged 40–49 years randomized to counseling men regarding screening based on family history *vs.* family history plus a SNP-based genetic risk score. At 3 years of follow-up, the authors found no increases in anxiety or PSA screening utilization (neither overuse, nor underuse), rather suggesting a more targeted use of PSA screening in high risk men, without negative effects on quality-of-life (53).

Although Lynch syndrome is associated with a 2- to 5-fold increase in risk for PCa (54), there are currently no specific screening recommendations for men with Lynch syndrome in any of the major guidelines. BRCA2 mutations have similarly been associated with a 2- to 6-fold increase risk for PCa (55,56). Men with BRCA2 mutations have a high PCa mortality despite PSA testing (57). BRCA2 mutations are associated with early onset and poor prognosis of PCa (58,59). The NCCN guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian (60) recommend that men with BRCA1/2 mutations start PCa screening at age 40. However, due to insufficient data, this practice is currently not supported by the panel for the NCCN guidelines on PCa early detection v2.2017 (10). There are ongoing screening studies in genetically higher-risk cohorts, such as carriers of germ-line mutations in BRCA1/2 and Lynch syndrome, that will investigate the clinical utility of these genetic variants as there are suggestions that these patients benefit from screening and earlier diagnosis and treatment (61,62).

Mutations in the tumor suppressor gene HOXB13 is associated with increased risk of PCa (63). In a study in a Swedish population, the relative risk of PCa was 3.4-fold higher in carriers of this mutation compared to matched cases (64). In their review on screening for familial and hereditary PC, Lynch et al propose that PSA testing could be supplemented by testing alleles, such as BRCA2 and HOXB13, in families with unfavorable family cancer history, and encourages that genomic sequencing protocols be included in future population studies (65).

Gulati *et al.* addressed the lack of guidelines for PSA screening in subgroups with higher risks (BRCA1/2

carriers) and analyzed these subgroups further in computer simulation models, finding that more lives could indeed be saved by screening these subgroups compared to average risk groups, but also found that more intensive screening did not necessarily improve the balance between benefits and harm of screening (66). Muhlberger *et al.* found contradictory findings using a decision-analytic model, and suggested that PCa screening should take into account age, individual quality-of-life preferences and familiar predisposition as that optimized the benefit-harm balance, whereas screening men with average PCa risk yielded life expectancy gains but potential losses in quality-adjusted life expectancy (67).

How to screen

Total PSA

Total PSA measured in serum or plasma has been the mainstay as a screening tool for PCa since its introduction in the late 1980's to the early-mid 1990's (68,69) The evidence is growing regarding the value of the "baseline" PSA measured in midlife for risk-stratification of future screening intensity, as shown by several large population-based observational studies (e.g., Malmö Preventive Project, Malmö Diet and Cancer, Västerbotten Intervention Project, the Baltimore Longitudinal Study of Aging, the Physician's Health Study) (28,70-72). Recently, one of the first baseline PSA cohort studies, The Olmsted Study, reported 17-year follow-up data from the population of 1,052 men who were screened biennially with PSA, DRE and TRUS starting between the ages 40–49 and were compared to men who began screening in their 50's. The younger cohort was more likely to undergo prostate biopsy (HR 2.4, 95% CI: 1.8–3.3) and be diagnosed with PCa (HR 2.2, 95% CI: 1.1–4.0), however, longer follow-up is needed to determine the effect of PCa mortality (33). The prospective German study PROBASE, starting screening at 45 is currently under way (73).

Taken together, these studies support starting screening in midlife and stratifying risk based on PSA in midlife to tailor further re-screening intervals to risk of future metastasis and/or PCa death with more frequent screening if higher risk and less frequent screening if lower risk. These studies, together with data from the randomized trials, have helped inform the screening algorithms outlined by the NCCN, EAU and MSKCC guidelines (10,20,29). For example, the MSKCC guideline recommends starting at age 45 and considering biopsy if the PSA ≥3 ng/mL. If the PSA is ≥1 but <3 ng/mL, the guideline suggest returning for PSA testing every 2–4 years. If the PSA <1 ng/mL, returning for PSA testing at 6–10 years (29).

For over two decades, a PSA cut-off of ≥4 ng/mL was used to recommend biopsy. However, the Prostate Cancer Prevention Trial (PCPT) in 2004, in which all men had an end-of-study biopsy regardless of PSA-level, changed this paradigm. PCa was found in 15% of men with PSA <4.0 ng/mL, and of which 15% were Gleason score 7 or higher. Many cancers were found in the PSA-range 3–4 ng/mL. After this trial, PSA is no longer seen as a dichotomous marker ("normal" *vs.* "elevated") but as a continuum of risk.

Rather than the one-size-fits-all, more personalized and risk-stratified strategies have been proposed. Recently, some groups have suggested to perform further risk assessment already at PSA values >1.0 ng/mL, as suggested by Brawley *et al.* (74) or having discussions and performing clinical workup including considerations of additional biomarkers and/or urology referral for men above >1.5 ng/mL, as suggested by Crawford *et al.* (75), as men below these cut-points have low risk for significant PC. Simple cut-offs for urology referral would facilitate the work of primary care physicians, however, whether these approaches would be clinically feasible is not known, in terms of number of referrals and resources needed. Moreover, the number of men needed to screen and biopsy to find one high-grade cancer and prevent PCa mortality with these approaches are not known.

Several studies and guidelines also emphasize repeating the PSA before biopsy, due to commonly observed fluctuations in this measurement (29,76-78).

MRI

Due to its ability to help detect, localize and characterize PC, multiparametric (mp)MRI plays an important role in a wide array of areas regarding PCa diagnosis, risk stratification, staging and treatment planning (79). In recent years, mpMRI has become increasingly utilized also in the *pre*-diagnostic setting, i.e., before prostate biopsy. EAU guidelines cite a recent systematic review, where prostate MRI in the pre-diagnostic setting had a negative predictive value (NPV) ranging from 63% to 98% and a positive predictive value (PPV) ranging from 34% to 68%, respectively (80). Because we have yet to see studies with consistently high NPV in excluding PCa on biopsy (81)—especially in the community setting—it is still too early to make recommendations on the routine use of pre-biopsy mpMRI in biopsy-naïve patients. A recent systematic review showed that the accuracy of mpMRI is highly

variable depending on the setting and that sharpened risk stratification before mpMRI can help improve the accuracy of prebiopsy mpMRI (81). Several recent studies (82-86) have shown higher detection rate of clinically significant PCa when using targeted biopsies compared to systematic biopsies, mainly in the repeat biopsy setting (87), however, there are several contradictory studies (88-90). The EAU guideline recommends MRI before repeat biopsy, which should consist of both targeted and systematic biopsies, if the clinical suspicion of PCa persists despite negative biopsies (20). Moreover, the MRI rating system PI-RADS v.2 has been shown to have low specificity (91,92) and a moderate inter-reader reproducibility (92-95).

The NCCN guideline panel shares a similar opinion as the EAU; that current data has not convincingly—and consistently—shown that MRI can improve detection for clinically significant PCa in the initial biopsy setting (10). The AUA guideline also agrees that the current data supports the use of MRI in patients with previous negative biopsy and with persistent suspicion of PC, but not in other settings such as screening (96).

Up to recently, there were no prospective studies on MRI in the biopsy-naïve setting until Ahmed and colleagues reported the PROMIS study (97), which suggests that mpMRI can be used as a triage test before first prostate biopsy to avoid unnecessary biopsies, reduce over-diagnosis of clinically insignificant PCa and improve detection of clinically significant cancer (96). MRI was more accurate than transrectal ultrasound (TRUS)-biopsy in terms of both sensitivity; 93% *vs.* 48%, and NPV; 89% *vs.* 74%. There are several ongoing trials that will elucidate the role of MRI as a screening tool, such as the Göteborg-2 trial which is a large population-based randomized clinical screening trial with PSA and MRI. This trial was preceded by a pilot study within the 10th round of the Göteborg-1 trial which assessed the role of MRI in screening by investigating three different screening strategies; the two strategies that included MRI and PSA (with different thresholds) had significantly higher sensitivity than the strategy with only PSA (98). This pilot included 384 both biopsy-naïve men and men with previous biopsy. A separate pilot study from Toronto included 47 biopsy-naïve men who underwent MRI and systematic biopsies, as well as targeted biopsies if the MRI showed a suspicious lesion (99). MRI performed better than PSA in predicting PCa (OR 2.7 *vs.* 1.1). PRECISION is another ongoing trial; a multicenter RCT that investigates whether MRI-targeted biopsy is non-inferior to standard TRUS-guided biopsy for the diagnosis of clinically significant PCa in men without prior biopsy (100).

Other alternatives

There are currently no alternative first-line screening tests, such as total-PSA, but several markers exist that are intended to be used as reflex markers [e.g., free-to-total (F/T) PSA, Prostate Health Index (PHI), 4Kscore, PCA3] in men with indications for biopsy (e.g., elevated PSA, positive DRE etc.). The NCCN guideline recommends consideration of F/T PSA, PHI or 4Kscore before *initial* biopsy (10). The same tests, or the urine test PCA3, are recommended also before *repeat* biopsy. The PCA3 test has been studies in multiple studies and has been shown to be useful mainly for *repeat* biopsy. This is because of the rather high risk (13%) of high-grade disease among men with low PCA3 values at initial biopsy (101). These reflex markers have been shown to improve the specificity of PSA and help reduce the number of unnecessary biopsies (10,15,76,102,103). The PHI and 4Kscore are widely used tests and both have been validated in multiple studies in thousands of patients including prospective multicenter validation studies (104-106). For instance, and a study done in over 600 men with abnormal PSA and/or DRE in routine U.S. care reduced 65% of biopsies with the use of the 4Kscore (107). In a prospective multicenter study of nearly 900 men with PSA 2–10 ng/mL, use of the PHI test with a cut-off of 25 for biopsy reduced about 40% of unnecessary biopsies (105). However, a recent study showed that while the clinical use of PHI indeed reduced biopsies among men with PSA 4–10 ng/mL, the risk of high grade cancer in men not biopsied in the PHI group was estimated to be about 1 in 3, far too many missed cancers for acceptable clinical use (101).

The most common cause of a PSA-elevation is a large prostate gland (benign prostatic hyperplasia, BPH). Because of this, PSA density is an adjunct that can help discriminate PCa from BPH (108). It is calculated as the PSA value (ng/mL) divided by prostate volume (cc) measured by TRUS. A lower PSA density implies a higher probability of BPH. Using a PSA density cut-off of >0.15 ng/mL/cc to recommend biopsy can reduce unnecessary biopsies, however, with the caveat that TRUS volume measurement can be user dependent and the sensitivity of this cut-off is insufficient, missing 31% of cancers among men with PSA 4–10 ng/mL in one study (10,109).

PSA velocity has no place in the decision-making regarding biopsy after screening as argued by Vickers *et al.* (110).

The STHLM3-test (a combination of several biomarkers,

clinical information and genetic polymorphisms) has been proposed as a first-line test (74,111). The study invited nearly 150,000 men aged 50–69 to STHLM3 testing compared to PSA alone. The predictive accuracy (AUC) was higher for the STHLM3 test for high-grade PCa (Gleason Score 7 or higher) compared to PSA alone and reduced the number of unnecessary biopsies by 32% (95% CI: 23–39) (74,111). However, the cost-effectiveness of using the test for screening is not known and the marginal added value of each of the individual components of the STHLM3 test remain to be understood (112,113).

A new urine exosome assay (ExoDx Prostate IntelliScore) was recently validated by McKiernan *et al.*, showing a reduction of 27% of biopsies at the cost of missing 8% PCa Gleason Score 7 or higher (114). However, this test has yet only been evaluated in a single study.

Multivariable approaches to reduce the number of biopsies have long been proposed through the use of risk calculators, e.g., the ERSPC or PCPT risk calculators, which combine clinical information with PSA into predicted risk of high-grade PCa on biopsy (17). MRI has been proposed to be used in combination with PSA and/or other biomarkers or risk calculators to further stratify risk and is currently being studied. In a retrospective study of 1,159 men who underwent MRI before targeted and systematic transperineal biopsies, Radtke and colleagues proposed a risk model for risk of PCa based on age, clinical parameters (PSA, prostate volume, DRE) and PI-RADS v.1. score. The risk model's performance characteristic (AUC 0.81) was superior to commonly used risk calculators and PIRADS v.1. alone to discriminate between the presence and absence of clinically significant PCa (115).

Conclusions

Urologists agree on the fact that PSA screening reduces PCa mortality. Total PSA is still currently the preferred screening tool and a powerful marker of future risk of metastasis (AUC 0.86) and PCa death (116,117). Yet, there is no consensus on the age to start PSA screening, due to insufficient data. The different guidelines recommend starting at ages 45, 50 and 55. Discussions between a patient and a physician on the pros and cons of screening and shared decision-making are crucial.

There is strong consensus regarding which men are at increased risk for PC; men with family history of PCa and African-American race/men, but there is no consensus regarding the screening practices for these men; EAU, MSKCC and NCCN recommend PSA testing at the age of 45 for these men and AUA strongly recommends shared decision-making after discussion concerning the impact of the individual man's risk.

International guidelines do not currently recommend mpMRI before initial biopsy decision, but considerations in patients with persistently rising PSA and previous negative biopsies. While there are promising pilot studies, current data is still insufficient to support a role for MRI in biopsy decision making in the screening context because studies have not shown consistently high NPVs. Future, larger-scale prospective studies are around the corner (87,98).

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Footnote

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