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Prostate Cancer Screening

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INTRODUCTION

The U.S. Preventive Services Task Force (USPSTF) has dropped its opposition to routine prostate cancer (PCa) screening in favor of a shared decision-making process between men aged 55–69 years and their physicians. Screening for prostate cancer is controversial, but it shouldn't be. In the United States (U.S.), PCa is the third-leading cause of cancer death in men, with an estimated 161,360 new cases being diagnosed in 2017, and 26,730 projected cancer deaths.¹ PCa seldom produces symptoms until it is incurable, and currently-available methods cannot accurately distinguish between tumors that will progress so slowly that they will not produce symptoms and those that are likely to cause suffering or death. Therefore, with no known means of preventing PCa or for curing metastatic disease, the sole hope for reducing suffering and death from PCa is through early detection and appropriate and effective patient management.

THE PRE-PROSTATE-SPECIFIC ANTIGEN (PSA) SCREENING ERA

In the 6 decades before the PSA screening era, PCa death rates progressively increased, because more men lived long enough to succumb to PCa,¹ and most PCa patients were diagnosed with incurable disease. For those who did not die of other causes within 15 years, many died from PCa.

PSA as a First-Line Screening Test

Because of overlap in PSA levels in men with BPH, prostatitis, and PCa, it was believed that PSA could not be used for early detection of PCa. In 1991, Catalona et al showed that PSA could be used as a first-line screening test for PCa in men without suspicious DRE

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findings.² Subsequently, PSA testing was widely adopted, causing a spike in PCa incidence rates, as the inventory of previously undetectable PCa was unmasked. This led to the creation of a new clinical-stage classification (T1c), i.e., PCa with a normal DRE that has become the most common stage in practice.³

Randomized Clinical Trials of PSA Screening

Randomized clinical trials (RCTs) were launched to evaluate PSA screening. Of these, the Swedish Göteborg trial is the highest quality study. It is population-based, included younger men, used lower PSA cutoffs for biopsy, had the longest follow-up, and the lowest rate of contamination. Göteborg initially reported a 41% lower rate of advanced-stage PCa at diagnosis in the screening arm (66% lower in men actually screened) and a 44% lower PCa mortality rate (56% lower in men actually screened), despite 33% of patients being managed with active surveillance. The trial subsequently contributed 59% of its data from men in the core age group of the multinational European Randomized Study of Screening for Prostate Cancer (ERSPC)⁴ that reported a 21% lower PCa mortality rate in the screening arm (29% after adjustment for noncompliance with screening, and 38% for those with 10–11 years of follow-up).^{4–6}

Among the other RCTs of PSA screening,^{7,8} the U.S. Prostate, Lung, Colorectal, and Ovarian trial (PLCO) that reported no overall PCa mortality benefit from screening was non-informative on the benefits of screening *versus* no screening, because nearly 90% of PLCO controls had PSA testing before or during the trial.^{9–12} However, a recent statistical modeling re-analysis of ERSPC and PLCO by the Cancer Intervention and Surveillance Modeling Network of the National Cancer Institute (CISNET) estimated that screening in ERSPC produced a 25–31% reduction in PCa mortality *versus* a 27–32% reduction in PLCO.¹³

US Food and Drug Administration (FDA) Approval of PSA as an Aid to the Early Detection of PCa

In 1994, a pivotal study demonstrated that a 4.0 ng/mL PSA cutoff was effective in selecting patients for biopsy.¹⁴ For every 100 men tested, approximately 85 had PSA <4.0 ng/mL; the remaining 15 could then undergo prostate biopsy, of which 4–5 would be found to have PCa. The FDA approved PSA testing as an aid to early PCa detection using this cutoff; however, subsequent studies showed that many clinically-significant PCa are missed with a 4.0 PSA cutoff, especially in men with PSA levels in the 2.5–4.0 ng/mL range,^{15–17} in which cancers have more favorable features and progression-free survival rates.¹⁸

The probability of a PCa diagnosis increases with increasing serum PSA levels.^{2,19,20} The Prostate Cancer Prevention Trial (PCPT) demonstrated that 15% of men with a PSA level of 4.0 ng/mL and a normal DRE had PCa diagnosed (>20% with PSA of 2–4 ng/mL).¹⁶ Approximately 30–35% of men with PSA 4–10 ng/mL and >67% of men with PSA levels >10 ng/mL have PCa diagnosed.^{21,22} PSA levels correlate with the rate of change of PSA, the proportion of patients with high-grade tumors, the progression-free survival rate, and PCa mortality.²³ A caveat is that some poorly-differentiated and/or neuroendocrine PCa do

not produce much PSA, which reduces the value of PSA as a biomarker for these types of tumors.²⁴

THE PSA SCREENING ERA (1991–2008)

With the advent of PSA screening, there was a dramatic stage migration with most patients being diagnosed with curable disease. Thus, patients could elect treatment or observation, or they could opt not to have PSA testing and run the risk of later being diagnosed with incurable PCa.

Epidemiologic Impact of PSA Screening

Widespread PSA testing had a profound impact on the epidemiologic features of PCa.¹ In the U.S., the age-adjusted PCa mortality rate decreased by >53% during the PSA screening era²² resulting from an 80% decrease in the proportion of patients with metastases at diagnosis.^{1,25} CISNET estimated that 45–70% of this decrease was attributable directly to PSA screening.^{26,27} Benefits of PSA screening also are reflected in RCTs in which patients with clinically-localized PCa randomized to prompt prostatectomy fared better than those randomized to observation, including the ProtecT trial that exclusively enrolled men with screen-detected PCa.^{28–30}

Enhancements of PSA Tests to Increase Specificity

Because elevated PSA levels can be caused by conditions other than PCa, enhancements have been sought to increase the specificity of PSA testing:

PSA Velocity (PSAV) correlates with both PCa risk and aggressiveness^{31–36} but is confounded by BPH and by prostatitis, and its short-term utility is limited because of the time required to determine whether PSA increases persist.^{37,38} In men without PCa, PSA velocity increases by ~0.15 ng/mL/year *versus* ~0.35–0.40 ng/mL/year with PCa.^{32,34–36,39–41} The natural history of PSAV in PCa patients is that PSA increases by 2% per year prior to a change point when increases accelerate. After this, PSA increases by 15% in patients presenting with localized disease and 63% in those presenting with metastases. Usually, the change point occurs at PSA levels below 4.0 ng/mL, and the median age at the change point is 57 years old, occurring in the 40s in many patients.⁴¹ PSA velocities > 2.0 ng/mL/year not caused by prostatitis may reflect incurable PCa.^{34,42}

PSAV Risk Count quantifies the persistence of PSA increases over time, i.e., the number of times the PSAV increases by a specific amount, such as 0.2 or 0.4 ng/mL/year. Unless a long PSA history is available, PSAV risk count also is limited by the time required to obtain a valid result.^{33,43}

PSA Density (PSAD) (PSA ÷ prostate volume) measurements factor in the prostate size in relation to the serum PSA level, because an enlarged prostate produces higher serum PSA levels. PSAD is a valuable parameter to assess risk for clinically-significant PCa. A PSAD >0.10–0.15 ng/mL/cc indicates a high risk.

Age-Specific Median PSA Values help guide whether an individual's PSA value is elevated by comparing them to levels in his peer age group (Table 1). Baseline PSA levels in men in their 40s and 50s are the most powerful predictors of the risk for PCa metastases and death decades later^{44,45} -- even a more powerful than family history or African-American race.⁴⁶

The risk for aggressive PCa increases in men with PSA levels above the median for their age group, with more than half of PCa deaths occurring in men with PSA levels in the highest 25th percentile of their age-specific PSA reference range at age 40–55 years.^{52–54}

Free-to-Total PSA (%Free PSA) ($\text{free PSA} \div \text{total PSA} \times 100$) correlates with the probability of PCa and the presence of aggressive disease. If the F/T ratio is <10%, there is >50% probability that a biopsy would show PCa. In contrast, a ratio >25% is associated with <10% probability of PCa diagnosis.⁵⁵

Prostate Health Index (*phi*) This FDA-approved blood test measures total PSA, free PSA, and [-2]proPSA.^{56,57} These values are used in a mathematical model, $\text{phi} = [-2]\text{proPSA} \div \text{freePSA} \times \text{totalPSA}$). The output of the *phi* test is the probability that a biopsy would show PCa and also clinically-significant disease. A multivariable model including *phi* also has been developed to improve risk prediction.⁵⁸

The 4KScore blood test incorporates measurements of total PSA, free PSA, human kallikrein 2 (*hK2*), and intact PSA into a clinical model that combines these measurements with information about DRE and patient age to give statistical probabilities that a patient will have a high-grade tumor. 4KScore is commercially available but not FDA approved.^{59,60}

Concerns about PSA Screening

Screening for PCa has been challenged because of concerns about the risk of triggering unnecessary biopsies and the over-diagnosis and over-treatment of screen-detected, indolent tumors with possible untoward side effects.⁶¹

Politics of PSA Testing: The US Preventive Services Task Force (USPSTF)

Policymakers consider screening at the population level, while clinicians are trained to view PSA testing at the individual-patient level.⁶² Most physicians have little knowledge of the USPSTF, the processes under which it operates, or that reform of the process continues to be a legislative priority.^{63,64}

The USPSTF was created in 1984, as an advisory committee to Medicare. It consists of 16 volunteers serving 4-year terms and is funded from the Agency for Health Research and Quality. Its mission is to evaluate the benefits and harms of health services and make recommendations for primary care physicians. The USPSTF panel is composed of internists, pediatricians, family physicians, obstetricians, gynecologists, and nurses, but no urologists, radiation oncologists or medical oncologists.⁶¹ It is allowed to select the studies it deems most relevant to review and typically weighs RCTs most heavily.⁶²

Functionally, the USPSTF reviews the specialty-care literature and translates it into the context of primary care practice, scoring the services in terms of merit as either A, B, C, D, or I (incomplete information). A “D” score means there is a moderate-to-high certainty that the intervention has no net benefit or that harms outweigh benefits. Under its charter, the USPSTF initially functioned solely as an advisory panel to physicians and patients and deliberately excluded any specialty stakeholders. Thus, physicians and patients were free to evaluate USPSTF recommendations and decide how best to incorporate them into clinical practice.

The USPSTF’s authority was broadened under the Medicare Improvements for Patients and Providers Act (MIPPA 2008) that changed the way Medicare conducted business. MIPPA created a National Coverage Determination process that was still under Medicare’s control but was significantly influenced by the USPSTF. Under MIPPA, a USPSTF recommendation of “A” or “B” permitted Medicare to expand its coverage of a service without the action of Congress, based on the advisory capacity of the USPSTF. This was a pivotal change, because all other entities that advise other government agencies are governed by a completely different set of rules.

The USPSTF’s role was further expanded under the Affordable Care Act (ACA) that transformed the role of the USPSTF from an advisory capacity to a funding mandate. Under ACA, if the USPSTF issued an “A” or “B” recommendation, Medicare would have to cover it and would be permitted to deny coverage for services that had a “D” rating. Furthermore, if the USPSTF simply opted not to review a service and did not issue a recommendation, the Secretary of Health and Human Services or Medicare would be permitted to deny coverage. This transformed the USPSTF from an agency that merely advised physicians and patients to one that now advised Medicare and could set mandatory payment policy. This is problematic, since the USPSTF was not chartered as an agency that would advise the government, it is exempt from all of the important regulations that govern entities that do advise government agencies.

In 2008, the USPSTF issued a Grade D recommendation against screening men >75 years old⁶⁵ despite the fact that RCT data to support this recommendation was limited. One year later, after the first reports of the ESRPC and PLCO trials,^{4,9} the USPSTF began a new evidence review, 1 year ahead of schedule.⁶² Giving prostate cancer screening a grade “C” recommendation would have required physicians to counsel men. Instead, the Task Force gave a grade “D” recommendation, concluding that the harms outweigh the benefits.⁶¹ Grade “D” reduced access to PSA testing because, under the ACA, grades “A” and “B” get full coverage by Medicare with no co-payment; whereas, grade “D” does not have to be covered and, if it is, beneficiaries must make co-payment.⁶²

2008–2017: THE PSA PROHIBITION ERA

In the aftermath of the USPSTF’s 2008 and 2012 grade “D” recommendations, PSA testing declined in the U.S. by 25–30%,⁶⁶ significantly reducing overall PCa incidence rates and precluding early PCa detection in many patients.^{67–71} Beginning with the 2008 recommendation, in men over age 75, there has been a reversal of the favorable tumor stage

migration, and since 2011, among men 75 years old, there has been a significant increase in the proportion and the absolute number of men presenting with metastases at the time of diagnosis with a similar trend in younger men.⁶⁷ CISNET has projected that if screening had been completely phased out in 2012, as recommended by the USPSTF, the number of cases of distant-stage disease would return to the pre-PSA screening era levels by the year 2025.⁷² Empirically, in the Göteborg screening trial, 9 years after the termination of PSA testing, the incidence of potentially lethal cancers was the same as that of non-screened men.^{73,74}

Criticisms of USPSTF Analysis

The USPSTF overstepped its mandate by superimposing the harms of treatment upon those of testing and diagnosis.^{75–80} The USPSTF placed screening in a context that would be applied across the population, which underestimates benefits and overestimates harms with reasonable use in appropriate candidates. It incorrectly assumed that every man with abnormal screening results would undergo biopsy and that all men diagnosed with PCa would undergo definitive treatment.

Overdiagnosis and overtreatment are inherent in all cancer screening. From statistical modeling studies, overdiagnosis of PCa with screening has been estimated to be 17–66%. The true extent cannot be determined for individual patients and can only be roughly estimated in populations using excess cases diagnosed in the screening arm of a RCT as a proxy measure.⁸¹ However, using incidence data from RCT produces inflated results, because the excess incidence in the screened arm, the typical proxy for overdiagnosis, consists of a mixture of overdiagnosed cases and true life-threatening cases, but because it is not possible to distinguish between them, they all get counted as overdiagnosed cases. Thus, empirical results of RCT do not accurately inform about the benefits of screening *versus* no screening, overdiagnosis, or the number of PCa that must be detected to save one life,⁸² and early trial data especially exaggerates overdiagnosis. It is likely that the current estimates based on incidence data from the PLCO and ERSPC trials are too high.

RCTs conducted over a short time period do not reveal accurate estimates of the absolute benefits of screening over a lifetime. There is a delay from the start of a RCT until a screening-induced mortality reduction can be attained, and early data underestimates benefits and exaggerates harms.⁸³

Unlike mortality rates that are affected by both early detection and better treatment, the frequency of metastases at diagnosis is determined only by early detection.⁸⁴ The USPSTF 2012 analysis failed to consider preventing suffering and treatment of metastatic disease. Avoiding metastases shifts the balance of harms and benefits. Also, many men in the RCTs who died of PCa were diagnosed with metastases on their first screening visit. Better results are achieved over the long-term with longitudinal screening. In ERSPC, the rate of metastases was lower across all sites.^{85,86} In an intent-to-screen analysis, there was a 50% reduction in metastases at diagnosis and a 30% reduction of metastases during 12 years of follow-up (42% for men who were actually screened).^{6,86} The initial incidence of metastases was 22% lower in the screening arm of PLCO; however, PLCO did not report on the cumulative incidence of metastases.⁸⁴

The most important criticism of the USPSTF methodology is its heavy weighting of PLCO results in which it was only later revealed that nearly 90% of controls had PSA testing before or during the trial. In arriving at its grade D recommendation, the USPSTF relied on the incorrectly-reported ~50% rate of PSA testing in the control arm in the 2009 PLCO report,

“...approximately 50% of men in the control group received at least 1 PSA test during the study”⁹

In contrast, in a 2016 independent evaluation of the PLCO data, Shoag, et al reported,

“... the proportion of control participants who reported having undergone at least 1 PSA test before or during the trial was close to 90%.”⁸⁷

PLCO co-authors published a re-evaluation of PSA testing in the control group in 2010 in a publication that received little public notice.^{10,11} Their most recent report cites an 86% rate of PSA testing in the control arm *versus* 99% in the intervention arm and asserts that 46% of controls underwent *yearly* testing during the screening phase as compared with 84% in the screening arm. They concede that PLCO is not informative on the benefits of screening *versus* no screening but maintain that it is a trial demonstrating no advantage of organized screening over opportunistic screening.¹²

Shoag et al responded that before their independent review of PLCO data, guideline panels had not recognized the high rate of contamination when formulating policy recommendations (e.g., the 2010 PLCO paper was not cited in the USPSTF’s announcement of its grade D recommendation).⁶¹

Gulati and Albertsen editorialized that the PLCO trial may have reached a saturation point for screening in both arms, beyond which more frequent screening could not produce more benefits.⁸⁸ They suggested that certain methods of organized screening could, in fact, be superior to certain methods of opportunistic screening. In this regard, Arnsrud-Godtman reported on opportunistic and organized screening in the Göteborg trial, in which organized screening produced a 42% reduction in PCa mortality over opportunistic screening.⁸⁹

Psychological Effects

Most quality-of-life studies of PSA screening have revealed significant early excess bother from urinary, sexual, and bowel dysfunction with active treatment and excess anxiety associated with conservative management; however, after longer-term follow-up, global quality of life and sense of wellbeing are not significantly different between screened and non-screened men. These studies reflect substantial declines in sexual and urinary function in untreated men in their 60s–80s.^{28,90–94} The ESRPC’s quality-of-life adjustment study reported the total benefit was 73 life-years gained per 1000 men screened (mean 8.4 years per death avoided). The net benefit had to be reduced by 23% due to risks and harms, but there was still 56 life-years gained per 1000 men screened.⁹⁰

EPILOG: 2017 CISNET RE-ANALYSIS OF PLCO AND ERSPC DATA

In 2017, CISNET published a statistical modeling study examining the conflicting ERSPC and PLCO results by focusing on differences in implementation of screening between the trials. In an intent-to-treat analyses, they calculated a continuous score reflecting how much earlier participants in the screening arm were diagnosed relative to a non-screened population from the pre-PSA era, called the “mean lead time.” They found the greater the mean lead time, the greater the reduction in mortality. They reported that screening produced a significant 25–31% reduction in PCa mortality in ERSPC and a 27–32% reduction in PLCO. Thus, correcting for the implementation of screening, both trials showed that PSA screening saves lives.¹³

2017 – THE FUTURE: PSA SCREENING RENAISSANCE

USPSTF Backs Away from Total Ban on PSA Testing

In May, 2017, the Task Force backed away from its grade “D” recommendation and issued a draft recommendation that clinicians inform men aged 55 to 69 years about the potential benefits and harms of PSA screening. However, the new draft recommendation maintains the grade “D” score for men younger than 55 and older than 69 years, even though PSA screening has not been adequately tested in RCTs in men < 55 years or > 70 years. Therefore, there is insufficient evidence to recommend for or against early detection in men in these younger and older age groups. The limited evidence from the Göteborg trial that included screening of men at age 50 suggests that screening is beneficial in this age group. Thus, the new USPSTF draft recommendation excludes baseline screening in men in their 40s for assessment for future risk for metastatic or lethal PCa.

The Task Force’s 2017 draft also lacks a recommendation for more intensive screening in high-risk men, such as men with a family history of PCa or for men of African ancestry, for which there is compelling evidence of greater risk for PCa morbidity and mortality and thus potentially greater potential for screening benefits.^{95,96} In the PLCO trial, men with a positive family history had a 56% higher PCa detection rate and a 51% higher PCa mortality rate. In the screening arm, there was a trend ($P=0.06$) toward a 50% lower PCa mortality rate that was not statistically significant, owing to the small sample size.⁹⁷ Similarly, evidence suggests possible increased benefits from earlier and more frequent PSA testing in African-American men.^{95,98,99}

The USPSTF stated that, while it is possible that screening may offer greater benefits for African-American men, currently no direct evidence demonstrates whether this is true. However, it is well documented that African-American men present with more advanced disease and have shorter progression-free survival following treatment.^{95,96,99} African-American men are more likely to have longer time intervals between screenings; thus, more frequent screening may reduce their risk of advanced-stage disease.^{95,98} A natural history modeling study reported that African-American men have more preclinical and progressive PCa and are more likely to develop PCa at a younger age and more likely to progress to a metastases or higher stage or grade before clinical diagnosis. This suggests that African-American men should consider beginning screening earlier and/or more frequently.⁹⁵

The Burden of PCa in the Future

It has been estimated that, with changing age demographics, the number of PCa deaths in the U.S. will increase 3-fold in the mid-2000s^{100–102}. PCa diagnosed in older men is more frequently aggressive, and nearly half of U.S. PCa deaths occur in men diagnosed after the age of 74 years, despite men in this age group comprising only about one-fourth of PCa patients.¹⁰³ Thus, in the future, even with reinstitution of widespread PSA testing, more men will live long enough to succumb to PCa, and there will be more total PCa deaths. It is sobering to consider that without PSA testing, the death rate would be more than twice as high.⁸⁴

Author's Recommendations for PSA Testing

The controversy over PSA screening has not ended despite unequivocal evidence that it saves lives. Although the USPSTF's 2017 draft recommendation is a step in the right direction, there is more progress to be made with respect to: (1) baseline testing in men in their 40s to assess future risk for life-threatening disease, (2) earlier testing of high-risk men, such as African-Americans and men with a family history whose risk of metastatic and lethal PCa is greater, and (3) testing healthy men 70 who are also at higher risk for life-threatening PCa.¹⁰⁴

If a man asks his physician whether or not he should have a PSA test, the physician should encourage appropriate testing. Moreover, men in their 40s should be informed that baseline PSA testing in their 40s is the best way to assess their risk for subsequent life-threatening PCa, as those in the top 10% PSA levels for their age group account for almost half of all PCa deaths up to 30 years later, and those with levels above 1.0 ng/mL clearly warrant more careful monitoring. Healthy men in their 70s should not be discouraged from being tested if their life expectancy is 10 years. Life expectancy at age 70 years in the U.S is > 15 years; therefore, some older men will benefit from early detection and treatment of a potentially aggressive tumor.^{105,106}

In interpreting PSA testing results, age-specific PSA cutoffs should be used to help determine whether an individual has an elevated PSA level, and testing intervals should not exceed 1 to 2 years, as less frequent PSA testing limits the ability to detect aggressive cancers that have the shortest preclinical phases. Some authors have recommended increasing the PSA trigger for recommending a biopsy of men >69 years to 10 ng/mL. However, higher thresholds for biopsy are less likely to detect aggressive cancers that produce less PSA while they are in a curable stage. Deferring or discontinuing screening in men with a low baseline PSA also may critically delay the diagnosis of aggressive PCa.

Prostate Cancer Screening Renaissance

The USPSTF recommendation against all screening was patently wrong and has engendered cynicism about USPSTF procedures. Its recommendations have created a generation of primary care physicians that rejects PSA testing. The release of the USPSTF's 2017 draft recommendation is a first step in acknowledging to the medical community that the benefits of PSA screening outweigh the harms, and physicians and patients should now accept the

truth and the value of the practical application of PSA testing, which will reduce the suffering and death from PCa.

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KEY POINTS

- Prostate cancer (PCa) screening is controversial. PSA-based screening has effected a dramatic stage shift from mostly incurable to mostly curable disease along with a >53% reduction in the U.S. PCa mortality rate; however, concerns have arisen about overdiagnosis and treatment of screen-detected indolent tumors.
- Randomized clinical trials of varying quality and much of their misinterpreted data have created confusion about the benefits *versus* harms of screening, leading to flawed recommendations in 2008 and 2012 against PSA screening by the US Preventive Services Task Force (USPSTF).
- In the aftermath of the USPSTF recommendations, the widespread rejection of screening by many primary care physicians has had far-reaching consequences, most notably, a reversion to more PCa cases being high-grade and advanced at diagnosis.
- A 2017 statistical modeling re-analysis the large European (ERSPC) and U.S. (PLCO) screening trials by the Cancer Intervention and Surveillance Modeling Network of the National Cancer Institute revealed that screening in ERSPC produced a 25–31% reduction in PCa mortality vs. a 27–32% reduction in PLCO.
- The USPSTF has now issued a revised draft recommendation, suggesting shared decision making for screening healthy men 55–69 years of age.
- Further consideration is needed for more intensive screening in men with high-risk factors, such as African ancestry and/or a strong family history of PCa, as well as for healthy men aged 70 years.

SYNOPSIS

PSA-based prostate cancer (PCa) screening has produced a dramatic stage shift at diagnosis from mostly incurable to mostly curable disease that provides men an opportunity for early detection and curative treatment of potentially lethal PCa and has reduced the U.S. PCa mortality rate by 53%. Concerns about overdiagnosis and treatment of screen-detected indolent tumors combined with misinterpretation of clinical trial data led to a recommendation against PSA screening by the US Preventive Services Task Force (USPSTF), resulting in a reversion to more high-grade, advanced disease at diagnosis. In 2017, a statistical modeling re-analysis of the large screening trials by the Cancer Intervention and Surveillance Modeling Network of the National Cancer Institute revealed that screening in ERSPC produced a 25–31% reduction in PCa mortality versus a 27–32% reduction in PLCO.

- The USPSTF has now dropped its total opposition to PCa screening with a draft recommendation for shared decision making for patients aged 55 to 69 years old.
- Further consideration is needed for more intensive screening in men with high-risk factors, such as African ancestry and/or a strong family history of PCa, as well as for healthy men age 70 years. When correctly interpreted, the data are clear: PSA screening significantly reduces suffering and death from PCa.

Table 1

Median PSA by Age *

Age (Years)	PSA (ng/mL)
30–39	0.5
40–49	0.7
50–59	0.9
60–69	1.3
70–79	1.7
80–89	2.1

* Median values are from the author's PSA studies from approximately 30,000 subjects; they are consistent with other reports.^{39,47–51}