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EDITORIAL

The new American Cancer Society prostate cancer screening guideline and the case for risk-adapted screening

Prostate-specific antigen (PSA) may be among the most effective screening tests in the history of oncology, but historically it has not been used well: we screened men too late in life using inappropriately high thresholds, we overdiagnosed low-risk disease, and we both overtreated low-risk and undertreated high-risk cancers. Despite these problems, in the screening era, we drove down prostate cancer mortality rates by one half[1] and simultaneously reduced long-standing disparities[2]—gains threatened by the backlash against screening that peaked in 2012 with US Preventive Service Task Force (USPSTF) recommendation against any routine PSA testing.

In subsequent years, as we have learned better not just *whether* but *how* to screen for prostate cancer, the pendulum has swung back toward the center, and recent guideline updates reflect both a growing understanding of the complex evidence and a well-earned optimism with respect to PSA's potential.[3–5] The new American Cancer Society (ACS) guideline for the early detection of prostate cancer marks an important further evolution and welcome change in direction.[6] Drawing on randomized trials and high-quality cohorts with long-term follow-up, contemporary diagnostic approaches, and expressly commissioned modeling, the panel now recommends PSA screening every 2 years for average-risk men aged 50–69 years, with earlier screening for higher-risk groups—acknowledging that the benefits of screening now far outweigh its risks. The guideline also endorses confirmatory PSA testing, magnetic resonance imaging (MRI), and blood and urine biomarkers before biopsy, together with active surveillance for favorable-risk cancer, to reduce harms. These recommendations acknowledge how much evidence and clinical practice have changed in the last decade.

Perhaps the most consequential change is the movement away from requiring shared decision making (SDM) before screening. This is a courageous and correct step. To be clear, the guideline preserves the obligation to inform men about benefits and harms, yet encourages clinicians to recommend an intervention that has been judged beneficial. We reviewed the literature on SDM, modeled the expected utility from this practice, and observed little evidence that PSA screening is preference-sensitive.[7] Informing patients and obtaining consent remain essential but must be kept efficient and straightforward to be practical within the bounds of a periodic health examination visit.[8,9] The ACS has aligned the screening conversation with approaches used for other recommended preventive services.

The opportunity now is to implement PSA more effectively. Specifically, with a relatively low positive predictive value for clinically significant disease, PSA by itself is not a great test to identify men with prostate cancer, but it can be exceptionally good at identifying those men—the large majority of the population—who do *not* have clinically significant prostate cancer nor are at long-term risk for developing metastases or lethal disease. A low midlife PSA level can identify men whose risk of life-threatening prostate cancer will remain minimal for decades at least.[10–12] Crawford and colleagues proposed a practical primary care approach using a PSA level of 1.5 ng/mL to distinguish men suitable for infrequent retesting (5-year interval) from those who warrant further assessment.[13] The principle remains compelling: use an inexpensive first test with a low threshold defining an extremely good *negative* predictive value to determine who needs closer attention and who can safely undergo less testing.

Consistent with the ACS guideline, we would favor offering a baseline PSA test to essentially all healthy men beginning around ages 45–50 years but would argue that this first, baseline result should guide subsequent screening intensity. The ACS guideline explicitly declines to recommend this midlife baseline testing strategy, stating that the evidence remains insufficient that it improves prostate cancer mortality outcomes over the recommended strategy.[6] However, the purpose of optimal risk stratification is to preserve benefit while also reducing testing and downstream harms. Therefore, demonstrating more deaths prevented is not the only relevant standard.

In the Malmö Preventive Project, men with PSA <1.0 ng/mL—nearly 75% of the population—at ages 45–49 had a 15-year risk of metastasis of only 0.09%.[12] Among men aged 60 years with PSA <1.0 ng/mL, the estimated risk of lethal prostate cancer by age 85 years was as low as 0.2%, suggesting no further screening is needed for these men.[11] In the contemporary German PROBASE trial, men with baseline PSA <1.5 ng/mL at age 45 years had a prostate cancer detection rate over 5 years of only 0.13 per 1000 person-years, supporting *at least* a 5-year re-screening interval.[14] A uniform 2-year interval is simple, but simplicity alone does not establish that frequent retesting benefits men whose baseline risk, as defined by the first PSA test, is very low. This practice of *risk-adapted screening*, with re-screening intervals tailored to risk, is also endorsed

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by other guideline groups[3–5] and by the ongoing PRAISE-U Project, now implementing screening in several European countries.[15]

A baseline PSA test provides an opportunity to reduce subsequent testing for the majority of men. Approximately three quarters of men in midlife have PSA levels <1.5 ng/mL and can be reassured that their risk is low without further immediate workup. Subsequent testing can be deferred for several years or discontinued according to PSA level, age, and overall health. For the smaller group with higher PSA, further risk assessment can determine who needs closer follow-up or early workup. Although proposed strategies targeting screening efforts to those with high risk based on race, genetics, family history, or other factors have garnered a good deal of excitement,[16] no parameter has approached baseline/midlife PSA levels of <1.0 or 1.5 ng/mL as a determinant of lifetime risk. Thus the value of optimized screening lies *both* in identifying potentially lethal disease *and* in identifying men who can safely undergo *less* screening to reduce downstream testing, biopsies, overdiagnosis, and overtreatment.

The other half of risk-adapted screening is a sufficiently low threshold for further evaluation. The ACS specifies a PSA level of 3.0 ng/mL for men aged 45–69 years.[6] This is more sensitive than the outdated 4.0 ng/mL threshold, but it remains too high to serve as the trigger in midlife. Even 2.5 ng/mL can provide false reassurance in younger men. In the Malmö Preventive Project, 44% of subsequent prostate cancer deaths occurred among men whose PSA at ages 45–49 years was in the highest decile, defined as 1.6 ng/mL.[12] Therefore, a PSA level near 2 ng/mL in a healthy man in his 40s or 50s should prompt attention and further workup rather than automatic reassurance simply because it falls within a laboratory reference range. In the Göteborg-2 trial, 47% of clinically significant prostate cancers were identified in the PSA 1.8–3.0 ng/mL interval.[17]

Crucially, *further workup* need not mean biopsy—and, in fact, only in rare cases today should a biopsy immediately follow a PSA test. PSA is only the first step; after confirming an unexpected elevation with repeat testing, clinicians should use an appropriately validated risk calculator, PSA density, urine or serum biomarker, and/or high-quality MRI to refine the risk of clinically significant cancer.

The distinction matters because the thresholds of 3 or 4 ng/mL still maintained in the new ACS guideline were developed when an elevated PSA led directly to sextant or other systematic, non-image-guided biopsy. Randomized evidence demonstrates that MRI-based or biomarker-based screening pathways can substantially reduce overdiagnosis of low-grade prostate cancer,[18,19] which we are progressively relegating to an incidentaloma perhaps unworthy of a *cancer* designation,[20] although some clinically significant cancers may of course be diagnosed later.[18,21] MRI quality and interpretation remain important, and biomarkers are not interchangeable. Future modeling should directly compare lower thresholds for secondary assessment combined with longer intervals for men with low baseline PSA.

Publication of the new guideline alone will not ensure adoption. Primary care clinicians who order most screening tests face competing preventive priorities and receive recommendations from several organizations. Earlier survey evidence identified the USPSTF as by far the most influential on physicians' practices.[22] The ACS recommendation may help change practice, but oncology specialists cannot assume that its message will reach every consultation or resolve uncertainty about what follows an abnormal result. Urologists, medical oncologists, and other clinicians caring for patients who have prostate cancer should work directly with primary care colleagues to agree on practical pathways: who receives a baseline test, when to repeat it, which results warrant referral, and who arranges secondary testing. Referral advice should explain why a PSA level below the conventional laboratory cutoff may still matter in midlife. Shared protocols also need to ensure access to risk calculators, PSA density, biomarkers, and/or MRI and reliable follow-up, so that recommending screening does not leave patients navigating an incomplete diagnostic process.

Specialists must also uphold the principles of modern screening by prioritizing risk assessment before biopsy and recommending active surveillance for men with favorable-risk prostate cancer. Although uptake has reached 90% in equal-access systems such as Veterans Affairs, substantial variation persists across the United States.[23,24]

In 2026, the question is no longer whether we should screen men for prostate cancer but how to optimize screening protocols. The ACS has provided a stronger foundation for screening and joins other organizations in embracing the promise of modern early detection. The ACS has also committed to a *living guideline* to be updated as new evidence emerges, which could offer an opportunity to incorporate less frequent screening for men with lower baseline PSA thresholds and closer follow-up for those at higher risk. We fervently hope the USPSTF will follow suit with their update, which is expected to be forthcoming soon. Our responsibility is to translate guidelines into care that recognizes concerning midlife PSA levels earlier, diagnoses low-risk disease less often, and directs intervention only toward the real cancers that threaten life.

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