



Prostate Cancer Screening & Diagnosis

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NEVADA CANCER CONTROL SUMMIT



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Disclosures

Employment	Funding Sources	Ownership or Investments	Leadership
Oncology Nevada	Boston Scientific Bionest TDG Health AstraZeneca	None	NRG Cervix/Vulva Subcommittee ABR Radiation Oncology Gynecologic Qualifying Committee ASTRO Gynecologic Committee

I have no relevant financial disclosures, and will not be discussing unlabeled/investigational uses

Goal

- To improve the quality of patient care, improve clinical efficiency, and reduce healthcare-related costs by reviewing the diagnostic workup for men with concern of prostate cancer.

Objectives

1. Prostate Anatomy & Function
2. Prostate Cancer Epidemiology
3. PSA Screening History & Evidence
4. Risks & Downsides of Screening
5. Screening Guidelines
6. Biomarkers
7. MRI in Risk Stratification
8. (A potential) Screening Algorithm

Thank you for coming!

***High-risk patients** may initiate screening at age 40 or 10 years prior to the youngest family members dx.

- Germline mutation
- Family hx
- Black

American Urological Association/
Society of Urologic Oncology Early
Detection of Prostate Cancer
Guideline (2023)



Shared decision making,
PSA obtained

Age 45 - 49*
Level B

PSA < 2.5 ng/mL

Resume screening at 50 q1,
q2-4 years

PSA ≥ 2.5 ng/mL

Confirmatory PSA, fPSA
4K/PHI/IsoPSA, MRI

Age 50 - 69
Level A

PSA ≥ 3.5 ng/mL

Confirmatory PSA, fPSA
4K/PHI/IsoPSA, MRI

PSA < 3.5 ng/mL

Continue PSA screening q1,
q2-4 years

Age ≥ 70
Level A

PSA ≥ 6.5 ng/mL
†Life expectancy ≥ 10 years

Confirmatory PSA, fPSA
4K/PHI/IsoPSA, MRI

PSA < 6.5 ng/mL
†Life expectancy ≥ 10 years

Continue PSA screening q1,
q2-4 years

†Life expectancy < 10 years
(age ≥ 77)

Discontinue screening

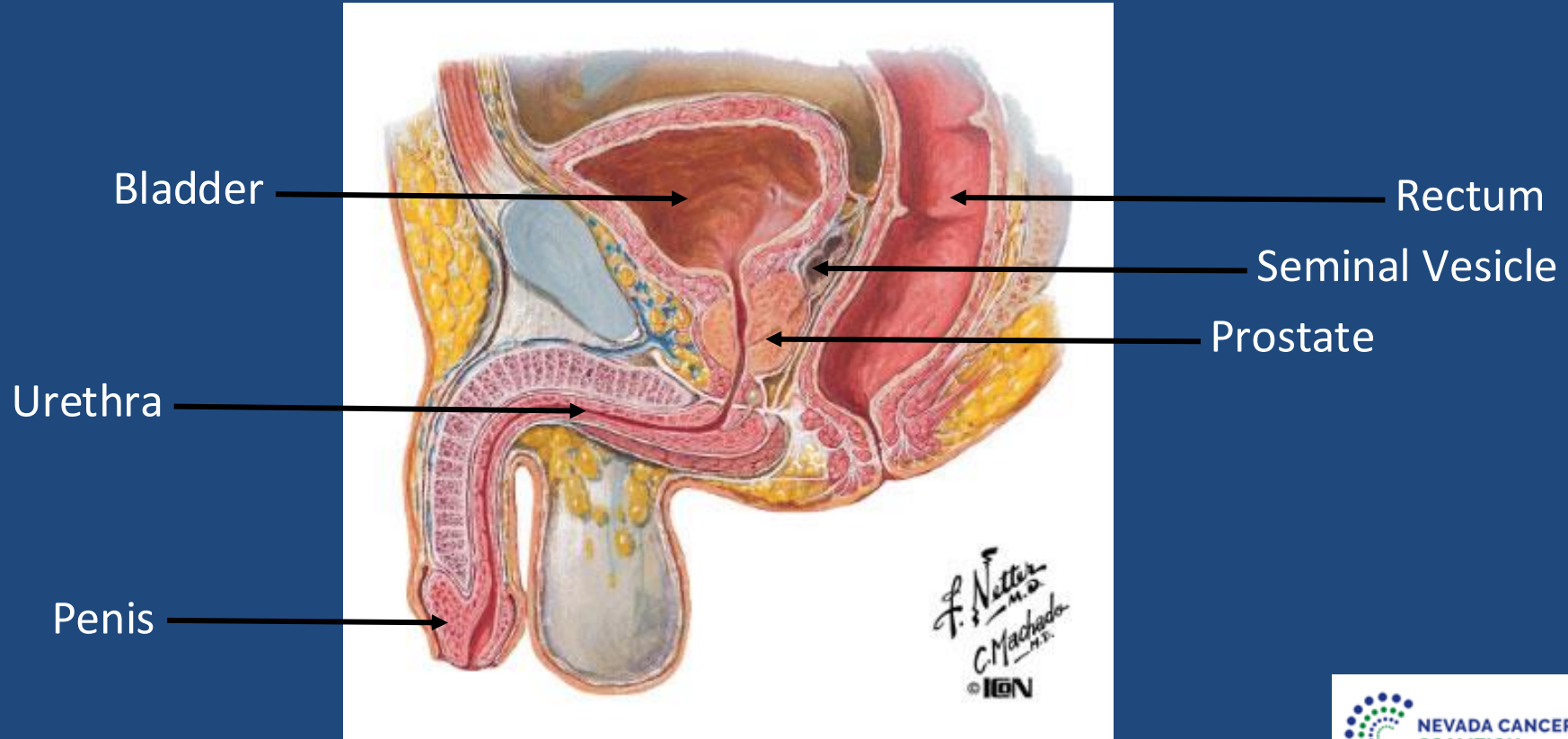
pCPT Prostate Cancer Risk Calculator

ACS, USPSTF, AUA, SUO

Adapted from the [AUA/SUO Early Detection of Prostate Cancer Screening Guideline](#)

†Life expectancy est. may be determined using the [Social Security Administration Life Tables](#), or other online calculators

What is the prostate?

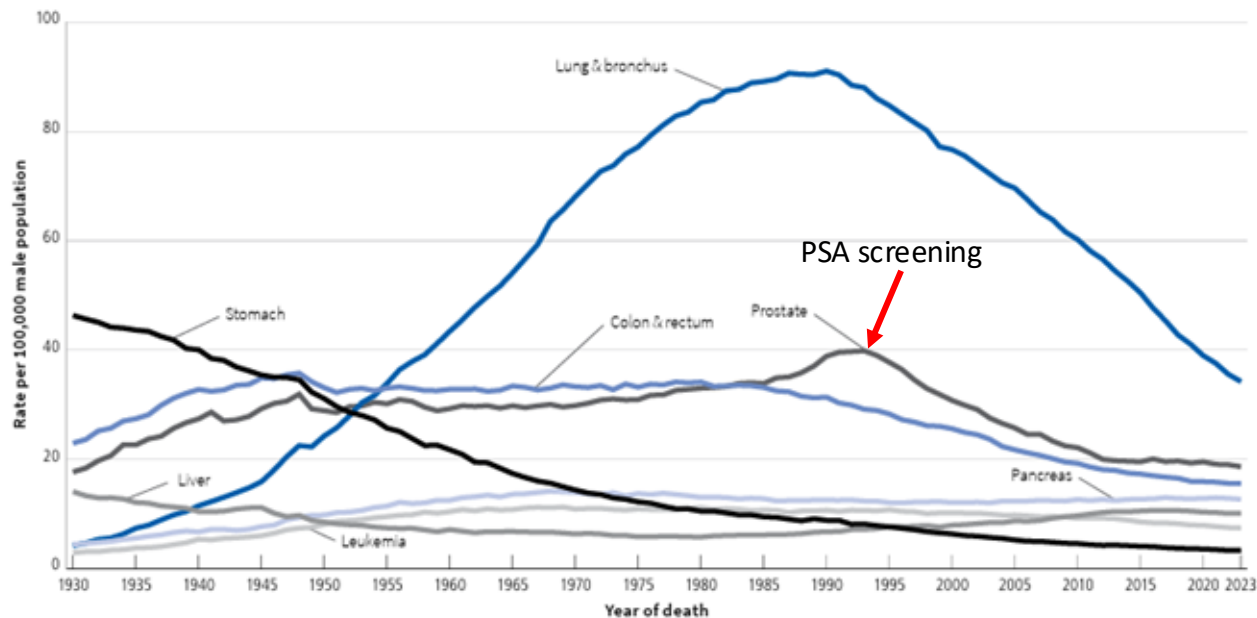


Lifetime Risk of Prostate Cancer

- 1 in 8 men will be diagnosed with PCa in their lifetime
- The incidence of prostate cancer is nearly 70% higher in black men than in white men
 - BRCA2, ATM, POLE, PREX2, FAT1, POLQ, LRP1B
 - Survival disparities are related to social determinants and lack of access

Mortality Trends in Cancer

Figure 1. Trends in Age-adjusted Cancer Death Rates by Site, Males, US, 1930-2023



Rates are age adjusted to the 2000 US standard population. Due to historical improvements in classification, lung & bronchus includes pleura, trachea, mediastinum, and other respiratory organs; colon & rectum includes small intestine; and liver includes intrahepatic bile duct, gallbladder, and other biliary sites.

Data source: US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2023, National Center for Health Statistics, Centers for Disease Control and Prevention.

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Risk of Prostate Cancer Death

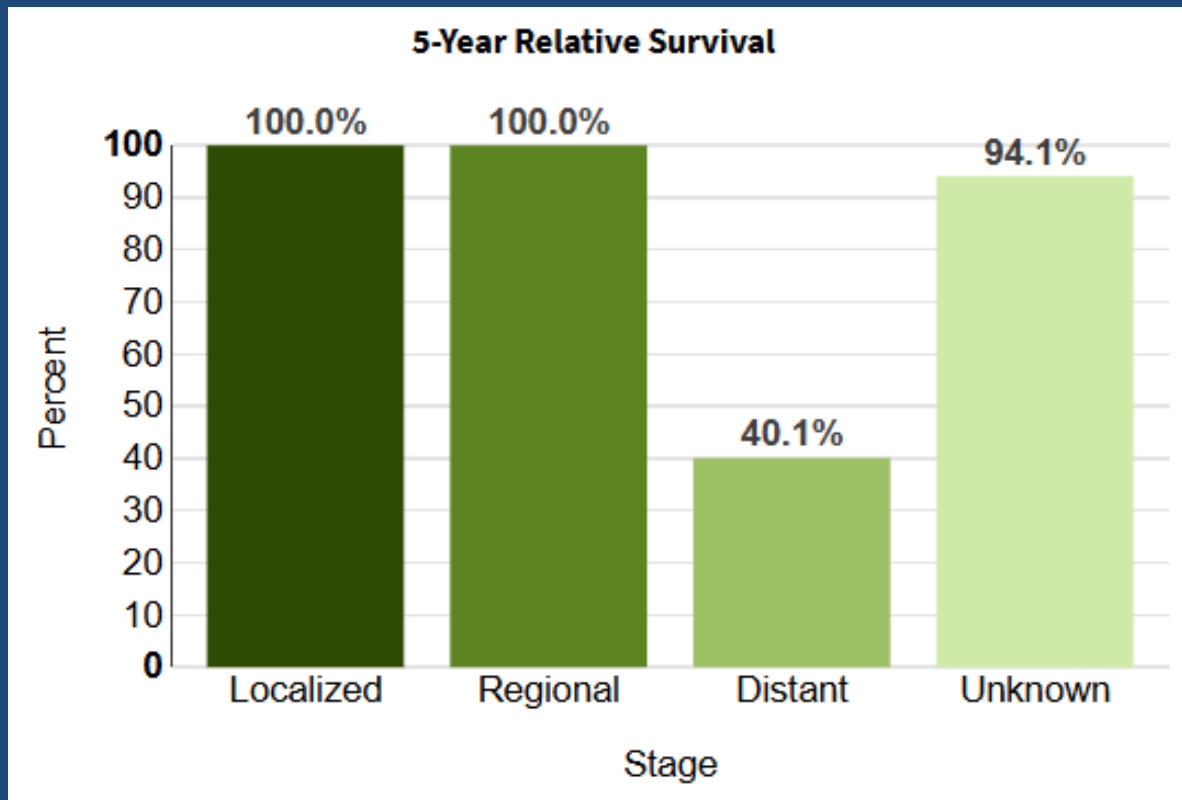


Figure 3. Leading Sites of New Cancer Cases and Deaths – 2026 Estimates

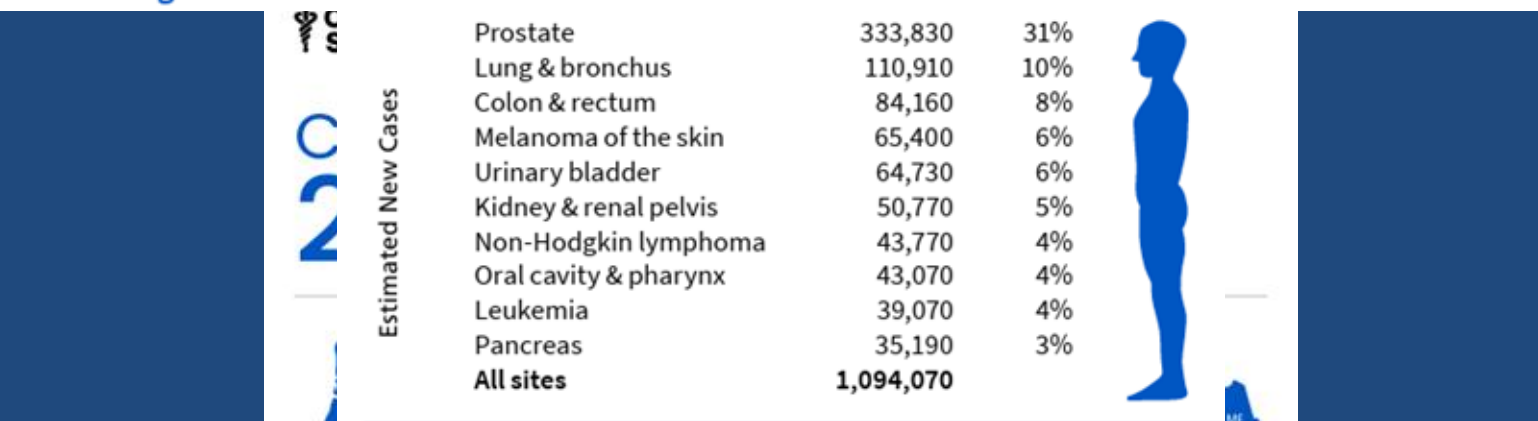
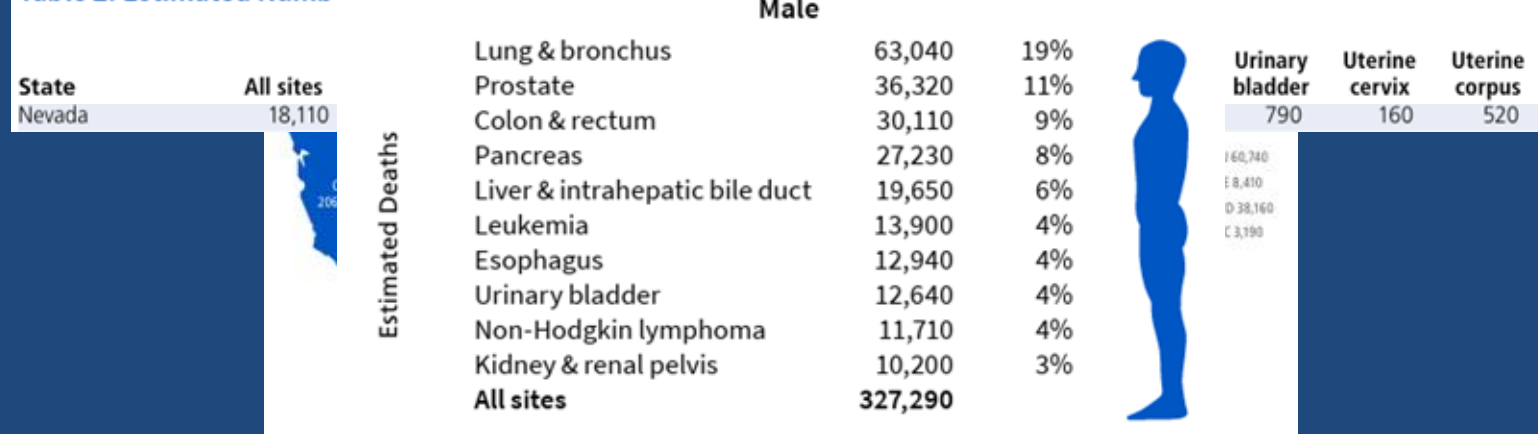


Table 2. Estimated Number of New Cancer Cases and Deaths – 2026 Estimates



Estimates are rounded to the nearest 10 and exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Rank is based on modeled estimates and may differ from observed data.

Decreasing Mortality

- PSA screening widely implemented in 1991-92
 - USPSTF recommendations have shifted 3x
 - 1990's → for screening
 - 2012 → against screening
 - Screening ↓ 23.4%[†]
 - Biopsies ↓ 64.3%[†]
 - Prostate cancer detection ↓ 53.5%[†]
 - Metastases ↑ 36.9%[†] (NND 25)
 - 2018-2026 → individualized
- Improved diagnostic options
- Improved treatment options

Prostate Specific Antigen (PSA)

- Initially used to detect recurrence after prostate cancer treatment
- Can be elevated in BPH, prostatitis, UTI, sexual activity and ejaculation, exercise (cycling), urinary retention
- Total PSA (tPSA) $\frac{1}{2}$ -life is 2-3 days
- Free PSA (fPSA) $\frac{1}{2}$ -life is 90-120 minutes

Screening and Prostate-Cancer Mortality in a Randomized European Study

Table 2. Death from Prostate Cancer, According to the Age at Randomization.*

Age at Randomization	Screening Group		Control Group		Rate Ratio (95% CI)†
	No. of Deaths	Person-Yr (Death Rate per 1000 Person-Yr)	No. of Deaths	Person-Yr (Death Rate per 1000 Person-Yr)	
All subjects	261	737,397 (0.35)	363	878,547 (0.41)	0.85 (0.73–1.00)
Age group					
50–54 yr	6	55,241 (0.11)	4	53,734 (0.07)	1.47 (0.41–5.19)
55–59 yr	60	316,389 (0.19)	102	402,062 (0.25)	0.73 (0.53–1.00)
60–64 yr	76	191,542 (0.40)	95	221,113 (0.43)	0.94 (0.69–1.27)
65–69 yr	78	135,470 (0.58)	129	162,410 (0.79)	0.74 (0.56–0.99)
70–74 yr	41	38,755 (1.06)	33	39,228 (0.84)	1.26 (0.80–1.99)

* The result of the chi-square test for heterogeneity among subjects in the core age group (55 to 69 years) was 2.44 ($P=0.49$).

† Rate ratios were calculated with the use of Poisson regression and compare the rate of death from prostate cancer in the screening group with the rate in the control group.

PSA ~1x/4 yr
1° death from PCa

PCa 8.2% vs 4.8%

NNS 1410
NND 48

9 years of follow up

screening reduced
the rate of death
from prostate cancer
by 20%

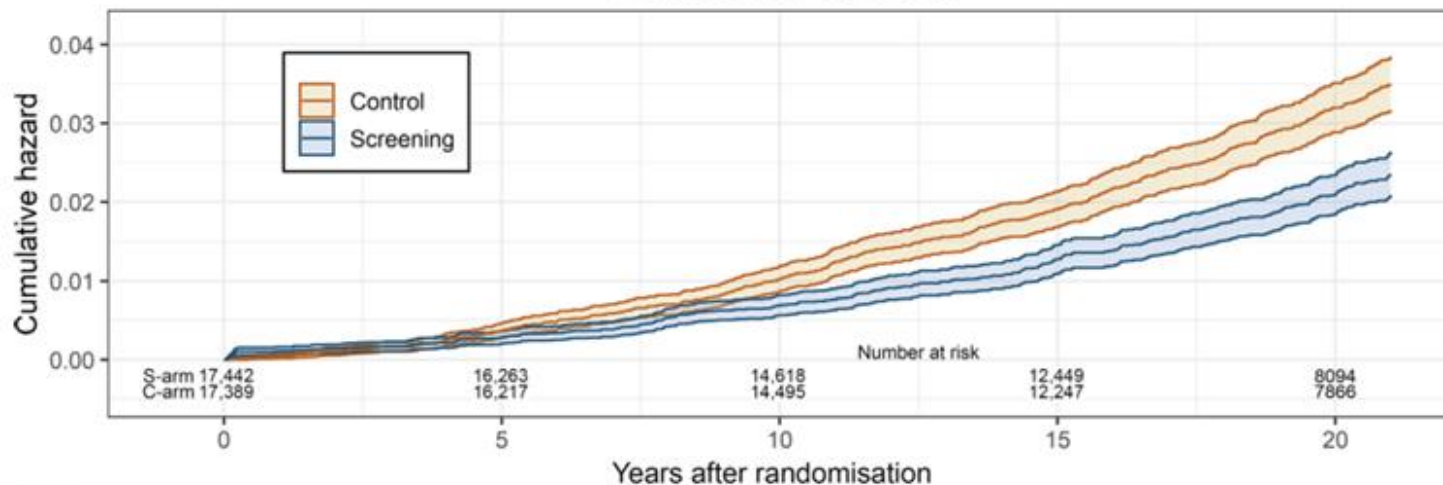
↑ risk of
overdiagnosis

A Detailed Evaluation of the Effect of Prostate-specific Antigen-based Screening on Morbidity and Mortality of Prostate Cancer: 21-year Follow-up Results of the Rotterdam Section of the European Randomised Study of Screening for Prostate Cancer

Ivo I. de Vos^{1,*}, Annick Meertens¹, Renée Hogenhout, Sebastiaan Remmers, Monique J. Roobol, on behalf of the ERSPC Rotterdam Study Group

Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, The Netherlands

A Metastatic PCa overall



PSA screening for men aged 55-69
PCSM ↓ 27%

for all men (55-74)
PCSM ↓ 17%

there was no statistical difference in PCSM for men ≥ 70

PLCO

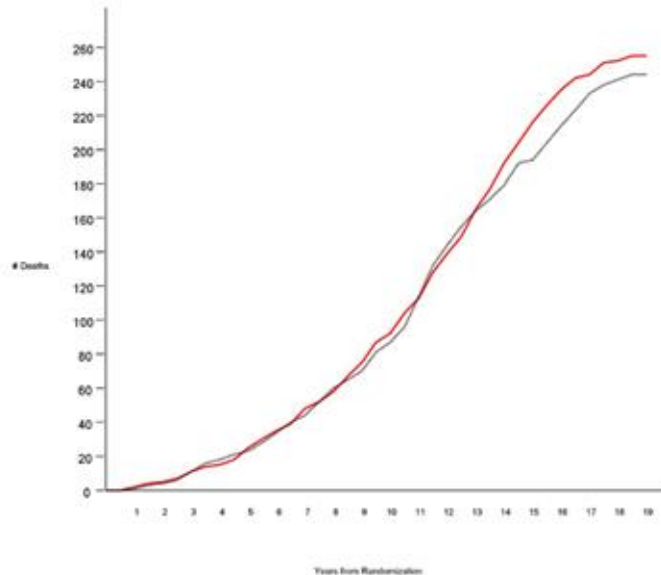
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ORIGINAL ARTICLE

Mortality Results from a Randomized Prostate-Cancer Screening Trial

TABLE 1. Demographics of the Prostate, Lung, Colorectal, and Ovarian Trial Population

Characteristic	Intervention Arm (n = 38,340)	Control Arm (n = 38,343)
Age, No. (%)		
55-59 y	12,387 (32.3)	12,372 (32.3)
60-64 y	12,012 (31.3)	12,015 (31.3)
65-69 y	8877 (23.2)	8885 (23.2)
70-74 y	5064 (13.2)	5071 (13.2)
Family history of prostate cancer, No. (%)	2737 (7.5)	2589 (7.3)
PSA test within past 3 y, No. (%)		
Once	13,252 (38.8)	13,135 (39.5)
More than once	3588 (10.5)	3760 (11.3)



Risks of PSA Screening

- False positive
- Overdetection (treatment not required)
- Overtreatment (treatment not needed, harm)
- Cancer stigma
- Anxiety/psychological stress
- Cost
 - Cancer patients 2.5x ↑ in bankruptcy

US Preventive Services Task Force

Figure 2. Clinical Summary: Screening for Prostate Cancer

Population	Men aged 55 to 69 y	Men 70 y and older
Recommendation	The decision to be screened for prostate cancer should be an individual one. Grade: C	Do not screen for prostate cancer. Grade: D
	SELECTIVE	AGAINST

Informed Decision Making	Before deciding whether to be screened, men aged 55 to 69 years should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. However, many men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and erectile dysfunction. Harms are greater for men 70 years and older. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening and should not routinely screen men 70 years and older.
Risk Assessment	Older age, African American race, and family history of prostate cancer are the most important risk factors for prostate cancer.
Screening Tests	Screening for prostate cancer begins with a test that measures the amount of prostate-specific antigen (PSA) protein in the blood. An elevated PSA level may be caused by prostate cancer but can also be caused by other conditions, including an enlarged prostate (benign prostatic hyperplasia) and inflammation of the prostate (prostatitis). Some men without prostate cancer may therefore have false-positive results. Men with a positive PSA test result may undergo a transrectal ultrasound-guided core-needle biopsy of the prostate to diagnose prostate cancer.
Treatments	The 3 most common treatment options for men with screen-detected, localized prostate cancer are surgical removal of the prostate gland (radical prostatectomy), radiation therapy (external-beam radiation therapy, proton beam therapy, or brachytherapy), and active surveillance.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to <https://www.uspreventiveservicestaskforce.org>.

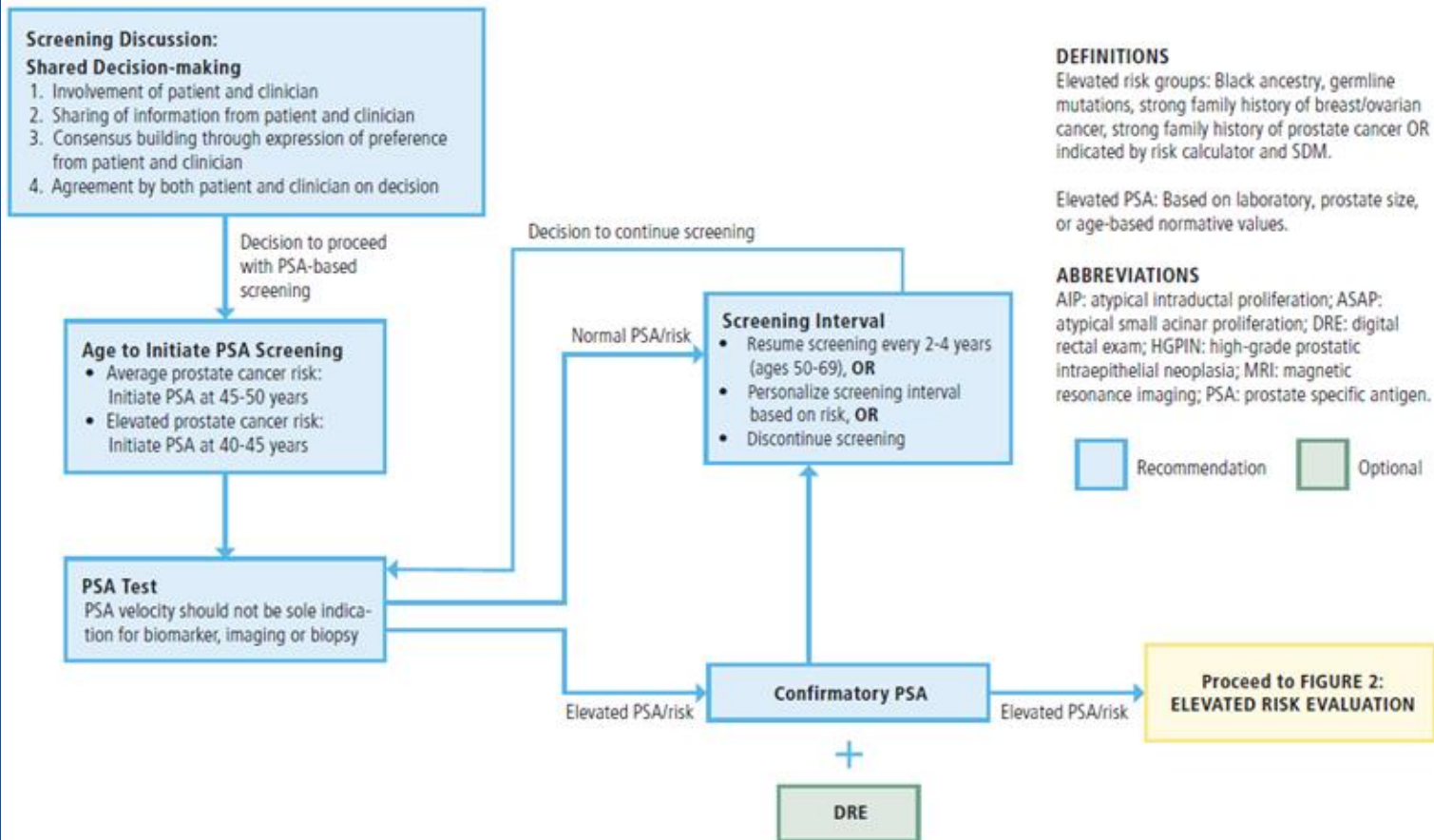
Screening for Prostate Cancer US Preventive Services Task Force Recommendation Statement JAMA 2018

American Cancer Society Recommendations

- Shared decision making
- Begin at age 50 if life expectancy ≥ 10 years
- Begin at age 40-45 if at high risk (family history, genetic mutation, black)
- Screen with **PSA + DRE**
- If PSA < 2.5 ng/mL, retest every 2 years
- If PSA ≥ 2.5 ng/mL, retest annually

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. DRE can be considered as a baseline test in addition to serum PSA in all patients, but has its greatest usefulness in those with elevated PSA. Consider referral for biopsy or further testing if DRE is suspicious for cancer at any PSA level. Halpern JA, et al. J Urol 2018;199:947-953; Arsov C, et al. Int J Cancer 2022;150:1861-1869; Matsukawa A, et al. Eur Urol Oncol 2024;7:697-704.

FIGURE 1: INITIAL SCREENING FOR PROSTATE CANCER



Digital Rectal Examination

- DRE was performed in primary care clinics on 3225 symptomatic

TBL: DRE is a poor screening tool. It misses roughly 7 out of 10 prostate cancers and an abnormal finding only confirms cancer about half the time.

- Specificity 90.7%
- PPV 42.3%
- NPV 84.2%

What is PSA?

- Serine protease
- Found exclusively in the epithelial cells of the prostate
- Important in reproductive physiology
- Role in lysing clot in ejaculate

Free PSA

INTERPRETIVE INFORMATION

INTERPRETIVE TABLE: Probability of prostatic carcinoma based on percent of free PSA in men with total PSA OF 4.00-10.00 ng/mL and negative digital rectal examination:

Free PSA (%)	Patient Age		
	50-59 years (%)	60-69 years (%)	>=70 years (%)
→ ≤10	49	58	65
→ 11-18	27	34	41
→ 19-25	18	24	30
→ ≥26	9	12	16

Concern for PCa
Indeterminate
Usually BPH

INTERPRETIVE TABLE: Sensitivity and specificity for prostate carcinoma, men of all age groups, no prior stratification by total PSA:

Free PSA cutoff (Less than %)	Sensitivity (%)	Specificity (%)
23	86	30
25	93	20
27	96	14

(Ref: Catalona WJ et al. JAMA; 277: 1452-1455. Chen YT et al. Urology; 47:518-524. Thiel RP et al. Urology; 48:45-50.)

PCPT Risk Calculator

RACE
AGE
tPSA
FHx
± DRE
± Biopsy
% fPSA

Characteristics

Race
Caucasian

Age
66

PSA [ng/ml]
6.5

Family History of Prostate Cancer
No

Digital rectal examination
Not performed or not sure

Prior biopsy
Never had a prior biopsy

☒ Percent free PSA available?

Percent free PSA
11

☐ PCA3 available?

☐ T2-ERG available?

Calculate Risk

Result More Information

Risk of prostate cancer if biopsy were to be performed

Based on the provided risk factors a prostate biopsy performed would have a:

- 18% chance of high-grade prostate cancer,
- 38% chance of low-grade cancer,
- 44% chance that the biopsy is negative for cancer.

About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.

If you are Caucasian, click [here](#) for a new update to the PCPTRC that incorporates detailed family history into a risk of prostate cancer calculation.

If you are Caucasian, click [here](#) for a research calculator that allows the incorporation of up to five single-nucleotide polymorphisms (SNP).

Make a Gift to Support Prostate Cancer Research

Risk Category	Percentage	Visual Count (Faces)
High-grade prostate cancer	18%	9
Low-grade cancer	38%	18
Biopsy negative for cancer	44%	23

Risk Stratification

- Prostate biomarkers
 - 4K, ~\$395
 - Prostate Health Index, ~\$170
 - IsoPSA, ~\$450

4K Score

- Integrates results of total PSA, free PSA, intact PSA, Human Kallikrein 2 (hK2), age, prior biopsy status, and DRE (if available) to predict biopsy Gleason ≥ 7
- AUC = 0.80
- Affected by DRE for 96 hours, 5 α -reductase medications, BPH procedure for 6 months

4K Score

Age-stratified PSA

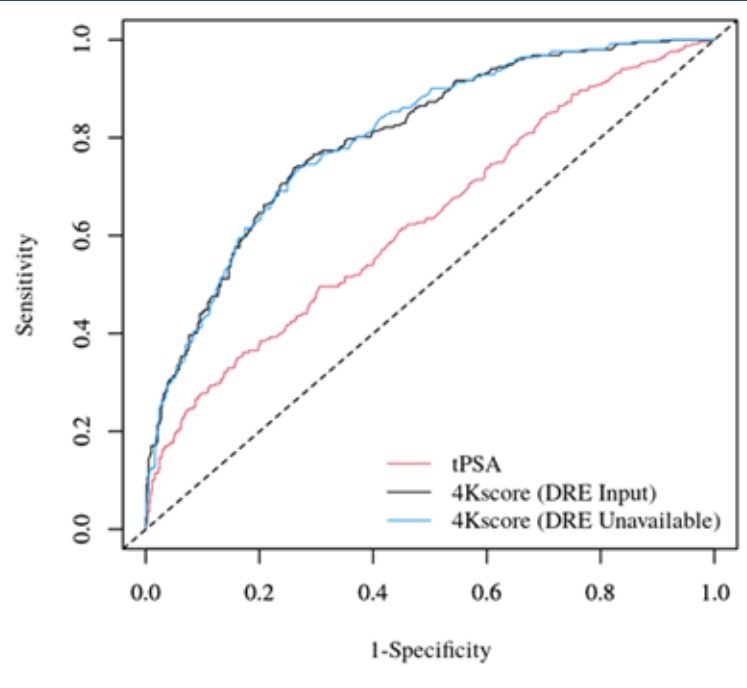
45-54 years old: total PSA ≥ 2 ng/mL

55-75 years old: total PSA ≥ 3 ng/mL

≥ 76 years old: total PSA ≥ 4 ng/mL

OR

Suspicious nodule on DRE,
regardless of whether PSA is elevated



- **Cut-point of 5.0**, the detection of Gleason ≥ 7 :
- Sensitivity of 96.9% and Negative Predictive Value of 95.9% with DRE
- Sensitivity 97.6% and NPV of 96.4% w/o DRE

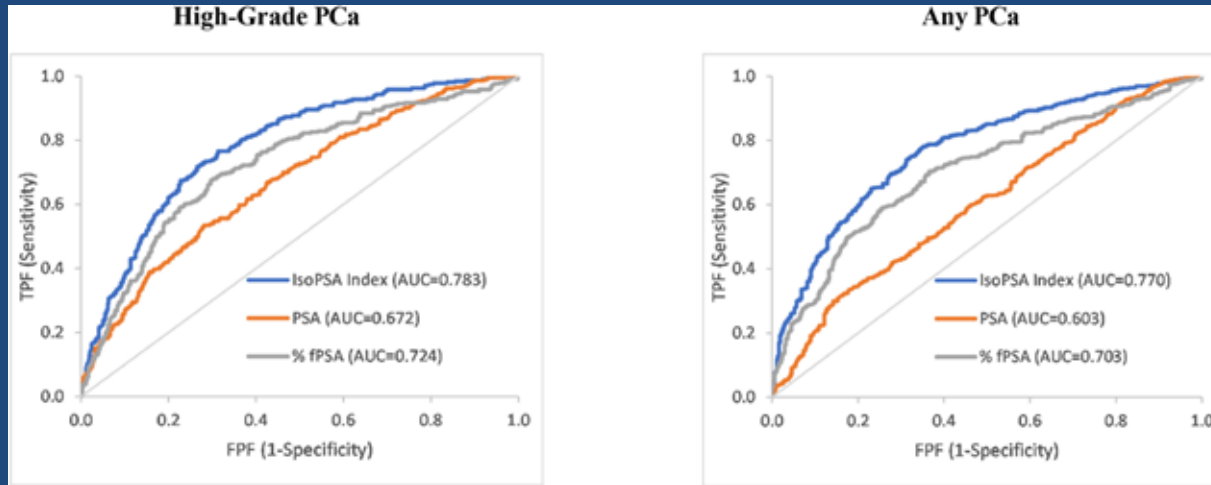
Prostate Health Index

Table 1. Probability of Prostate Cancer Based on phi Results Between 4 and 10 ng/mL¹

phi Range*	Probability of Cancer	95% Confidence Interval
0-26.9	9.8%	5.2%-15.4%
27.0-35.9	16.8%	11.3%-22.2%
36.0-54.9	33.3%	26.8%-39.9%
55.0+	50.1%	39.8%-61.0%

IsoPSA

- Blood based, partitions isoforms of PSA linked to cancer
- May reduce unnecessary biopsies by 43%



Stovksy J Urol 2019, Klein Uro Oncol 2022

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 10, 2018

VOL. 378 NO. 19

Men with suspicion of prostate cancer MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

RESULTS

A total of 500 men underwent randomization. In the MRI-targeted biopsy group, 71 of 252 men (28%) had MRI results that were not suggestive of prostate cancer, so they did not undergo biopsy. Clinically significant cancer was detected in 95 men (38%) in the MRI-targeted biopsy group, as compared with 64 of 248 (26%) in the standard-biopsy group (adjusted difference, 12 percentage points; 95% confidence interval [CI], 4 to 20; $P=0.005$). MRI, with or without targeted biopsy, was noninferior to standard biopsy, and the 95% confidence interval indicated the superiority of this strategy over standard biopsy. Fewer men in the MRI-targeted biopsy group than in the standard-biopsy group received a diagnosis of clinically insignificant cancer (adjusted difference, -13 percentage points; 95% CI, -19 to -7; $P<0.001$).

MRI improved the detection of clinically significant prostate cancer by 12%

IsoPSA + MRI

	IsoPSA Low (≤ 6) vs High	PI-RADS SCORE	Prostate Cancer Risk
AS	Low	1-2	4.2%
	Low	3	4.6%
BIOPSY	Low	≥ 4	22%
	High	1-2	8.2%
	High	3	16%
	High	≥ 4	48%

(Possible) Screening Algorithm

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Age ≥ 70
Level A

PSA ≥ 6.5 ng/mL
†Life expectancy ≥ 10 years

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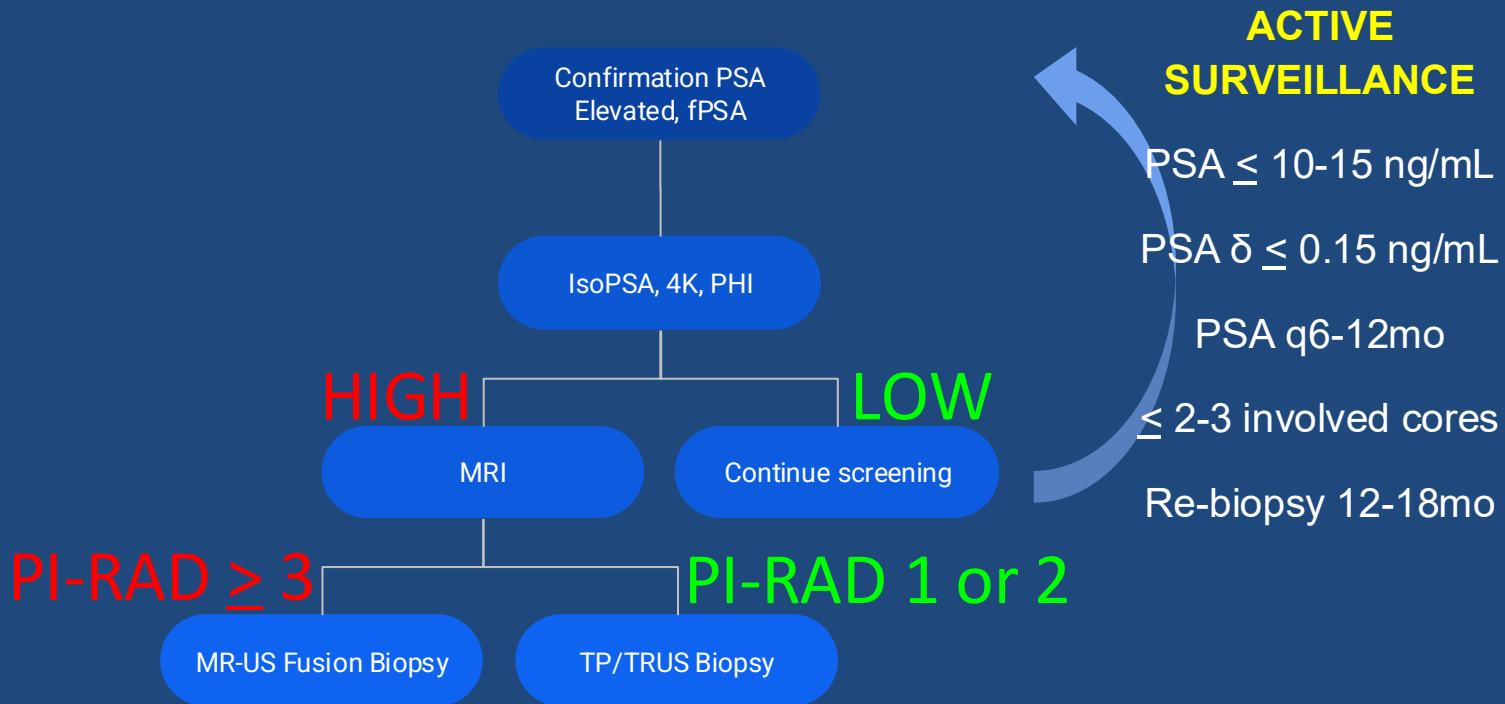
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Something Must Be Done





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