Prostate Cancer Screening

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Disclosures

The following CME Planners do not have relevant financial relationships with ineligible companies in the past 24 months:

- Leilanie Mercurio, L.A. Care Provider Continuing Education (PCE) Program Manager, CME Planner.
- Bridget Freeley, Associate Director, State Partnerships, American Cancer Society, CME Planner.

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Commercial support was not received for this CME/CE activity.

Learning Objectives

At the completion of the activity, learners can:

1. Summarize updated prostate cancer screening guidelines.

2. Identify the three (3) main risk factors for prostate cancer.

3. Describe the various prostate cancer screening modalities.

4. List at least three (3) prostate cancer screening recommendations for high-risk patient subsets.

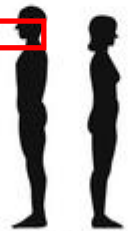
Epidemiology

Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	

Estimated Deaths

Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	

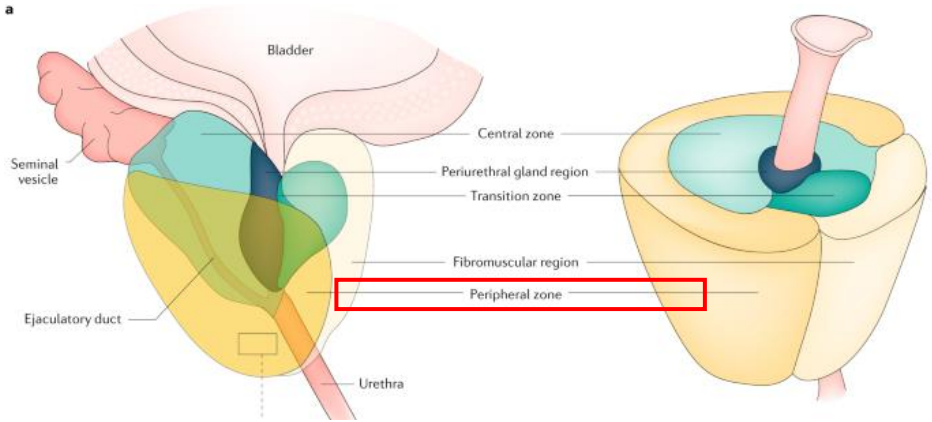


Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

Globally, prostate cancer constitutes the most common cancer diagnosis in men and the second leading cause of cancer death in men

Siegel RL, et al. CA Cancer J Clin. 2024;74(1):12-49
Sung H, et al. CA Cancer J Clin. 2021;71(3):209-249

Defining clinical features

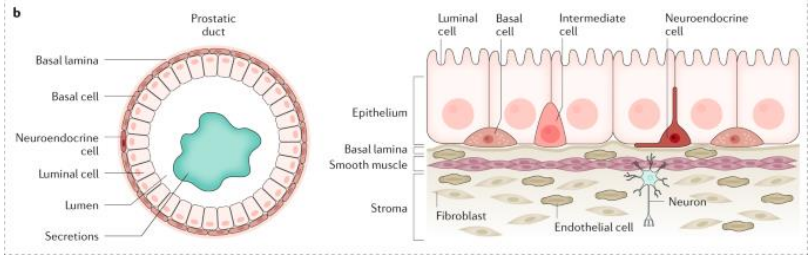


The prostate gland
- male reproductive accessory organ located beneath the bladder and surrounding the urethra
- main function is to contribute essential secretions to semen which formulate ejaculate and maintain sperm viability

Peripheral zone makes the largest contribution to normal prostate function in young adult men
- Nearly 80% of prostate tumors arise here

Rebello RJ, et al. Nat Rev Dis Primers. 2021;7(1):9

Prostate-Specific Antigen (PSA)



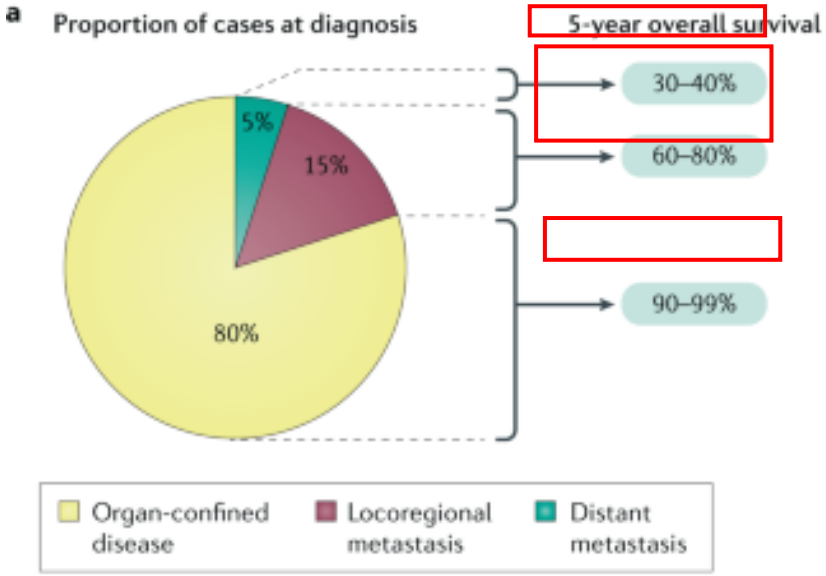
The normal prostate gland consists of ducts and acini comprised of a single layer of simple, columnar epithelium surrounded by a layer of basal epithelium (basement membrane) altogether embedded in stroma

Epithelial cells in normal and cancerous prostate express high levels of the androgen receptor (AR) and secrete **prostate-specific antigen (PSA),** which is transcriptionally activated by AR and commonly elevated in men with prostate cancer

Hallmark: Prostate cancer is a hormone-dependent and PSA is a key screening test

Rebello RJ, et al. Nat Rev Dis Primers. 2021;7(1):9

Disease Stages

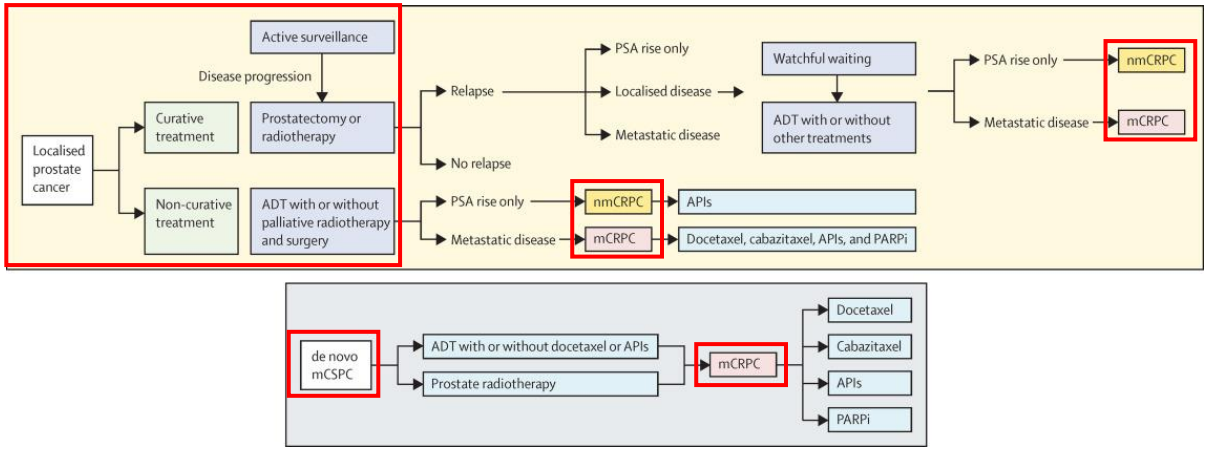


- Majority of cases diagnosed with localized disease

- Survival decreases with locoregional and distant metastatic disease

Rebello RJ, et al. Nat Rev Dis Primers. 2021;7(1):9

Treatment Overview



- Localized disease can have a varied course from indolent, slow growing to higher risk where disease relapse is expected following definitive treatment

Whether localized disease or de novo metastatic disease → evolution to more aggressive disease states is characterized by castration-sensitive to castration-resistant prostate cancer

Sandhu S, et al. Lancet. 2021;398(10305):1075-1090.

Risk Factors (established)

- Age (>85% of cases >60 years of age
- Race (African or Caribbean descent, two-fold higher relative risk of prostate cancer than White men)
- Family history (having first-degree relative with prostate cancer → two-fold increased risk of prostate cancer)
  - Germline BRCA2 and HOXB13 → 7-8-fold and 3-fold increased relative risk, respectively

Attard G, et al. Lancet. 2016;387(10013):70-82
Rebello RJ, et al. Nat Rev Dis Primers. 2021;7(1):9

Risk Factors (less established/controversial)

- Smoking/ – association w/more aggressive prostate cancer
- Obesity/metabolic syndrome/lack of exercise - association w/more aggressive prostate cancer
- Agent Orange exposure – independent risk factor
- Diet and lifestyle – multiple links to prostate cancer for intake of fried food, daily consumption of meat, sugar-sweetened beverages although these have been relatively weak associations according to meta-analyses. Conflicting results for alcohol
- Occupational exposures – firefighters (potential)
- Ejaculation frequency – correlated w/decreased prostate cancer risk
- Vasectomy – disproven largely
- Prostatitis – no definitive risk for prostate cancer

Gandaglia G, et al. Eur Urol Oncol. 2021;4(6):877-892

Why screen?

- European Randomized study of Screening for Prostate Cancer (ERSPC)
- 1991-2003, men between the ages of 55-69 years randomized 1:1 across 8 European centers to screening vs. control groups
  - Annual PSA testing for 4 years
  - PSA ≥ 3.0 ng/mL was positive
    - Referred for prostate biopsy if +
  - Prostate cancer-specific mortality = primary endpoint

Schröder FH, et al. Lancet. 2014;384(9959):2027-35.
Schröder FH, et al. N Engl J Med. 2012;366(11):981-90

European Randomized Study of Screening for Prostate Cancer (ERSPC)

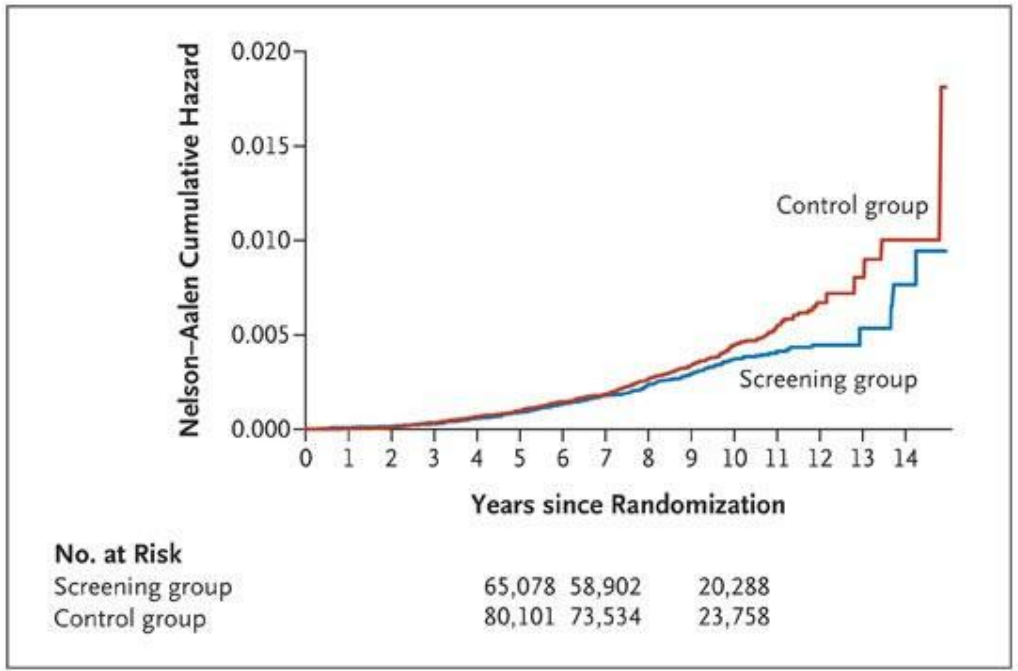
Table 1. Numbers of Subjects and Results of Screening, According to Study Center.*

Variable	The Netherlands	Belgium	Sweden	Finland	Italy	Spain	Switzerland	Total
	November 1993–March 2000	June 1991–December 2003	June 1991–December 2003	January 1996–January 1999	October 1996–October 2000	February 1996–June 1999	September 1998–August 2003	June 1991–December 2003
Total no. of subjects	34,833	8562	11,852	80,379	14,517	2197	9903	162,243
Screening group — no. (%)	17,443 (50.1)	4307 (50.3)	5,901 (49.9)	31,970 (39.8)	7,265 (50.0)	1056 (48.1)	4948 (50.0)	72,890 (44.9)
Control group — no. (%)	17,390 (49.9)	4255 (49.7)	5,951 (50.1)	48,409 (60.2)	7,252 (50.0)	1141 (51.9)	4955 (50.0)	89,353 (55.1)
Age at randomization — yr								
All subjects								
Mean	61.9	63.0	59.8	59.6	62.2	61.0	61.6	60.8
Median	61.7	63.0	59.7	58.7	61.8	60.4	61.1	60.1
Screening group								
Mean	61.9	63.0	59.8	59.6	62.2	60.5	61.6	60.9
Median	61.7	63.0	59.7	58.7	61.7	59.7	61.0	60.3
Control group								
Mean	62.0	63.0	59.8	59.6	62.2	61.4	61.7	60.7
Median	61.7	63.1	59.7	58.7	61.9	61.1	61.2	59.9
First round of screening — no. (%)	16,502 (94.6)	3795 (88.1)	3,649 (61.8)	20,796 (65.0)	4,961 (68.3)	1056 (100)	4721 (95.4)	55,480 (76.1)
Screening interval — yr	4	4–7	2	4	4	4	4	NA
Screened at least once — no. (%)	16,502 (94.6)	3876 (90.0)	4,466 (75.7)	23,008 (71.8)	5,075 (78.1)	1056 (100)	4746 (95.8)	59,923 (82.2)
No. of screening tests performed	34,526	6042	14,848	48,900	11,377	1846	8923	126,462
Positive PSA tests — no. (%)	7,707 (22.3)	984 (16.3)	2,751 (18.5)	5,528 (11.3)	1,287 (11.1)	334 (18.2)	1848 (20.7)	20,457 (16.2)
Biopsies — no. (%)	6,929 (89.9)	728 (74.0)	2,382 (86.6)	4,991 (90.3)	828 (65.4)	263 (74.3)	1422 (77.0)	17,543 (85.8)
Prostate cancers								
Total detected in screening group — no. (%)	1,736 (10.0)	363 (8.4)	697 (11.8)	2,493 (7.8)	280 (3.9)	68 (6.4)	353 (7.1)	5,990 (8.2)
Detected during screening — no.	1,521	182	550	1,477	180	60	265	4,235
Detected outside of screening protocol — no.	215	181	147	1,016	100	8	88	1,755
Positive predictive value of screening — %†	22.0	25.0	23.1	29.6	21.7	22.8	18.6	24.1
Total detected in control group — no. (%)	685 (3.9)	252 (5.9)	421 (7.1)	2,632 (5.4)	133 (1.8)	24 (2.1)	160 (3.2)	4,307 (4.8)

* The results are for the predefined core age group for this study, which included men between the ages of 55 and 69 years. The dates that are listed for each country are the periods in which subjects underwent randomization. NA denotes not applicable, and PSA prostate-specific antigen.
† The positive predictive value of biopsy was calculated as the number of screen-detected cancers divided by the number of biopsies.

Schröder FH, et al. Lancet. 2014;384(9959):2027-35.
Schröder FH, et al. N Engl J Med. 2012;366(11):981-90

ERSPC



Average follow-up of 8.8 years

- Relative reduction of 20% in the rate of death w/screening vs. control
- To prevent 1 prostate-cancer death, 1410 men would have to be screened, and an additional 48 men would have to be treated
- Those who had biopsy for PSA+, 13,308 (75.9%) had a false positive result

Schröder FH, et al. Lancet. 2014;384(9959):2027-35.
Schröder FH, et al. N Engl J Med. 2012;366(11):981-90

Prostate, Lung, Colorectal, and Ovarian (PLCO)

- **Prostate, Lung, Colorectal, and Ovarian (PLCO)** Cancer Screening Trial
  - 1993-2001, men and women between the ages of 55-74 years were enrolled at 10 study centers across the United States
  - Annual PSA testing for 6 years and annual digital rectal examination for 4 years
  - PSA ≥ 4.0 ng/mL was positive
    - DRE positive if nodularity or induration of the prostate or if suspicious for cancer w/other criteria, including asymmetry
    - Advised to seek diagnostic evaluation for + screens
  - Cancer-specific mortality = primary endpoint

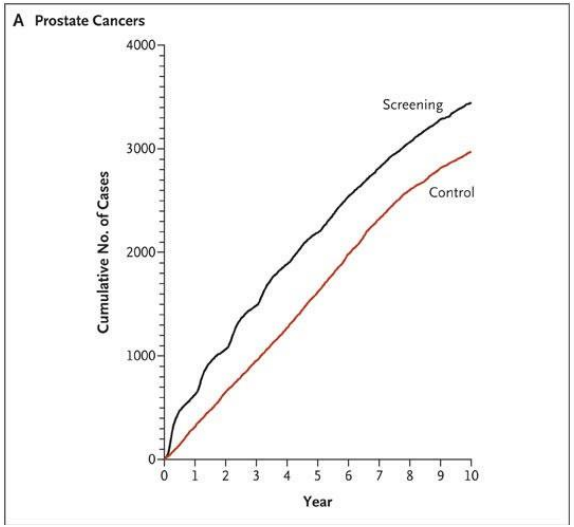
Andriole GL, et al. N Engl J Med. 2009;360:1310-1319

PLCO

Table 1. Characteristics of the Subjects at Baseline.*

Variable	Screening Group (N=38,343)	Control Group (N=38,350)
	percent	
Age		
55–59 yr	32.3	32.3
60–64 yr	31.3	31.3
65–69 yr	23.2	23.2
70–74 yr	13.2	13.2
Race or ethnic group†		
Non-Hispanic white	86.2	83.8
Non-Hispanic black	4.5	4.3
Hispanic	2.1	2.1
Asian	4.0	3.9
Other	0.8	0.9
Missing data	2.4	5.0
Enlarged prostate or benign prostatic hyperplasia	21.4	20.5
Previous prostate biopsy	4.3	4.3
Family history of prostate cancer	7.1	6.7
PSA test within past 3 yr		
Once	34.6	34.3
Two or more times	9.4	9.8
Digital rectal examination within past 3 yr		
Once	32.8	31.9
Two or more times	22.2	22.0

* PSA denotes prostate-specific antigen.
† Race or ethnic group was self-reported.



10 years of follow-up
- 3452 (screening) vs 2974 (control, rate ratio, 1.17; 95% CI, 1.11 to 1.22)

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Andriole GL, et al. N Engl J Med. 2009;360:1310-1319

PLCO

Table 2. Tumor Stage, Histopathological Type, and Gleason Score for All Prostate Cancers at 10 Years, According to Method of Detection and Time of Diagnosis.*

Variable	Screening Group						Control Group
	According to Method of Detection					All Subjects (N=3452)	All Subjects (N=2974)
	Never Screened (N=154)	After Screening (N=875)	Outside of Screening Protocol (N=374)	Screen Detected at Baseline (N=549)	Screen Detected at Yr 1–Yr 5 (N=1500)		
	number (percent)						
Clinical stage							
I	1 (0.6)	5 (0.6)	8 (2.1)	2 (0.4)	2 (0.1)	18 (0.5)	15 (0.5)
II	138 (89.6)	838 (95.8)	347 (92.8)	516 (94.0)	1458 (97.2)	3297 (95.5)	2790 (93.8)
III	5 (3.2)	7 (0.8)	3 (0.8)	12 (2.2)	22 (1.5)	49 (1.4)	56 (1.9)
IV	10 (6.5)	20 (2.3)	9 (2.4)	19 (3.5)	15 (1.0)	73 (2.1)	79 (2.7)
Unknown	0	5 (0.6)	7 (1.9)	0	3 (0.2)	15 (0.4)	34 (1.1)
Histopathological type							
Adenocarcinoma							
Any	144 (93.5)	824 (94.2)	346 (92.5)	511 (93.1)	1375 (91.7)	3200 (92.7)	2802 (94.2)
Acinar	9 (5.8)	48 (5.5)	25 (6.7)	36 (6.6)	124 (8.3)	242 (7.0)	158 (5.3)
Other	1 (0.6)	3 (0.3)	3 (0.8)	2 (0.4)	1 (0.1)	10 (0.3)	14 (0.5)
Gleason score on biopsy†							
2–4	11 (7.1)	1.7 (1.9)	36 (9.6)	64 (11.7)	94 (6.3)	222 (6.4)	137 (4.6)
5–6	78 (50.6)	500 (57.1)	228 (61.0)	278 (50.6)	963 (64.2)	2047 (59.3)	1656 (55.7)
7	39 (25.3)	252 (28.8)	74 (19.8)	132 (24.0)	318 (21.2)	815 (23.6)	779 (26.2)
8–10	16 (10.4)	95 (10.9)	25 (6.7)	55 (10.0)	98 (6.5)	289 (8.4)	341 (11.5)
Unknown	10 (6.5)	11 (1.3)	11 (2.9)	20 (3.6)	27 (1.8)	79 (2.3)	61 (2.1)

* Subjects with available data for tumor staging but not for nodal status or the presence or absence of metastasis were classified as having stage II disease. Percentages may not total 100 because of rounding.
† The Gleason score ranges from 2 to 10, with higher scores indicating more aggressive disease.

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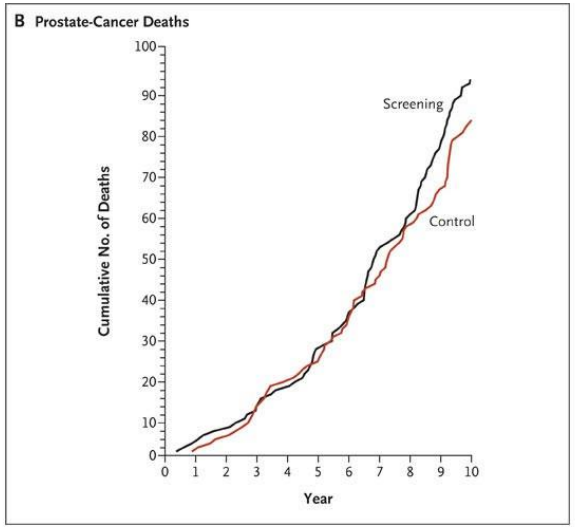
Andriole GL, et al. N Engl J Med. 2009;360:1310-1319

PLCO



At 10 yr follow-up (67% completed screening phase)
- Prostate cancer deaths 92 (screening) vs 82 (control, rate ratio, 1.11; 95% CI, 0.83 to 1.50)

Similar findings at extended 15 yr follow-up

- No benefit to organized screening vs opportunistic screening

Andriole GL, et al. N Engl J Med. 2009;360:1310-1319
Pinsky, PF et al. Cancer. 2017;123(4):592-599

Cluster Randomized Trial of PSA Testing for Prostate Cancer (CAP)

- Cluster Randomized Trial of PSA Testing for Prostate Cancer
- 2001-2009, 419,582 men between the ages of 50-69 years across 573 primary care practices in UK enrolled
  - Invitation to attend a PSA testing clinic and receive a single PSA test vs. no screen (control)
  - Single PSA ≥ 3.0 ng/mL was positive
    - Prostate biopsy if PSA+
  - Prostate cancer-specific mortality = primary endpoint

Martin RM, et al. Cancer. JAMA. 2018;319(9):883-895

CAP

Table 1. Baseline Individual and Primary Care Practice Level Characteristics[a]

Characteristics	Intervention Group	Control Group
Individual		
No. of men	189 386	219 439
Age, median (IQR), y	58.5 (54.3-63.5)	58.6 (54.3-63.5)
Index of Multiple Deprivation, median (IQR)[b]		
England	17.5 (10.1-33.2)	16.9 (9.8-32.4)
Wales	17.6 (9.2-29.5)	13.7 (7.1-29.0)
Live in urban area, No. (%)	163 751 (86)	189 707 (86)
Primary Care Practice		
No. of practices	271	302
No. of individuals per practice, median (IQR)	6300 (4150-9107)	6300 (3793-9000)
Located in urban area, No. (%)	244 (90)	267 (88)
Multiple partners within practice, No. (%)	242 (89)	267 (88)
Quality and Outcomes Framework[c]		
No. of practices in England	224	266
Percentage of total points achieved, median (IQR)[d]	98.9 (97.4-99.6)	99.0 (97.4-99.7)
Index of Multiple Deprivation[b]		
No. of practices in England	231	271
Median (IQR)	21.8 (12.7-44.1)	23.6 (13.3-46.7)
No. of practices in Wales	40	31
Median (IQR)	18.8 (11.9-22.9)	20.1 (7.6-34.5)
Prevalence across practices, mean (SD), %[e]		
All types of cancer	0.6 (0.3)	0.5 (0.2)
Diabetes	3.6 (1.0)	3.7 (1.0)
Obesity	8.0 (2.8)	7.8 (2.8)
Coronary heart disease	4.1 (1.4)	3.9 (1.3)

Abbreviation: IQR, interquartile range (25th to 75th percentile).

[a] Adapted from Turner et al.[14]

[b] A measure of relative deprivation for small areas; a higher score indicates more deprivation (range, 0-100). English and Welsh scores are not directly comparable; therefore, they are reported separately.

[c] A system for the performance management and payment of primary care clinicians based on the quality of their care.

[d] Based on data from 2007 and 2008.

[e] Calculated as (No. of individuals registered with a health condition at each practice/total No. of individuals registered at each practice) × 100.

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Martin RM, et al. Cancer. JAMA. 2018;319(9):883-895

CAP

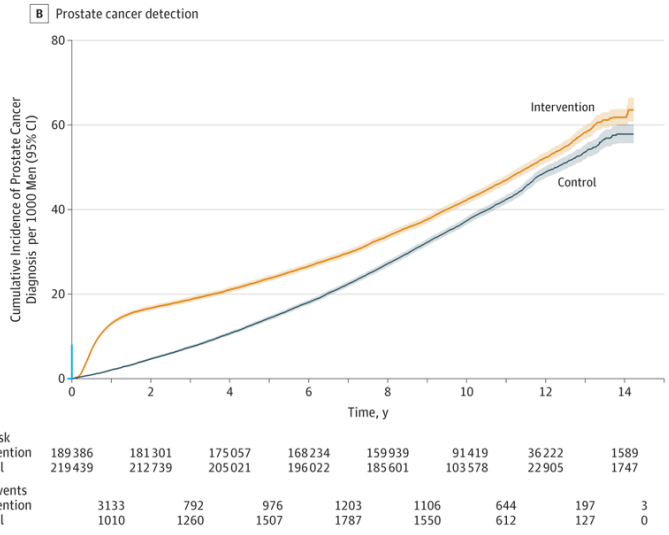

Table 3. Characteristics of Prostate Cancer Cases at Diagnosis

	Intervention Group			Control Group	Between-Group Difference
	Total (n = 189 386)	Attended PSA Clinic (n = 75 707)	Did Not Attend PSA Clinic (n = 113 679)	(n = 219 439)	(95% CI)
Prostate cancer, No. (%)	8054 (4.3)	4687 (6.2)	3367 (3.0)	7853 (3.6)	
Person-years of follow-up[a]	1 808 031	750 573	1 057 458	2 063 912	
Incidence rate per 1000 person-years	4.45 (4.36 to 4.55)	6.24 (6.07 to 6.43)	3.18 (3.08 to 3.29)	3.80 (3.72 to 3.89)	0.65 (0.52 to 0.78)[b]
Age, median (IQR), y	66.3 (62.1 to 70.0)	65.3 (61.2 to 69.0)	67.9 (63.7 to 71.5)	67.7 (63.6 to 71.6)	−1.37 (−1.56 to −1.19)[c]
Time from randomization to diagnosis, median (IQR), y	4.3 (0.8 to 7.9)	1.2 (0.5 to 7.0)	6.2 (3.4 to 8.7)	6.2 (3.6 to 8.4)	−1.49 (−1.61 to −1.37)[c]
Gleason grade recorded, No./total (%)	7276/8054 (90.3)	4388/4687 (93.6)	2888/3367 (85.8)	6899/7853 (87.9)	
≤6	3263/189 386 (1.7)	2297/75 707 (3.0)	966/113 679 (0.8)	2440/219 439 (1.1)	6.11 (5.38 to 6.84)[d]
7	2710/189 386 (1.4)	1526/75 707 (2.0)	1184/113 679 (1.0)	2823/219 439 (1.3)	1.44 (0.73 to 2.16)[d]
≥8	1303/189 386 (0.7)	565/75 707 (0.7)	738/113 679 (0.6)	1636/219 439 (0.7)	−0.58 (−1.09 to −0.06)[d]
Cancer stage recorded, No./total (%)	7197/8054 (89.4)	4299/4687 (91.7)	2898/3367 (86.1)	7009/7853 (89.3)	
T1 or T2	4938/189 386 (2.6)	3308/75 707 (4.4)	1630/113 679 (1.4)	4192/219 439 (1.9)	6.97 (6.05 to 7.89)[d]
T3	1329/189 386 (0.7)	690/75 707 (0.9)	639/113 679 (0.6)	1540/219 439 (0.7)	0 (−0.51 to 0.51)[d]
T4, N1, or M1	930/189 386 (0.5)	301/75 707 (0.4)	629/113 679 (0.6)	1277/219 439 (0.6)	−0.91 (−1.36 to −0.46)[d]

Abbreviations: IQR, interquartile range (25th to 75th percentile); PSA, prostate-specific antigen.

[a] Person-years of follow-up were calculated as the time until diagnosis, death, or censoring. These figures are lower than those in Table 2 because they exclude person-years after diagnosis.

[b] Difference in incidence rate.

[c] Difference in medians calculated using the generalized Hodges-Lehmann method.[28]

[d] Difference per 1000 men.

Gleason ≤6 (45%)
Gleason 7 (37%) vs. 23% (PLCO)
Gleason ≥8 (18%) vs. 8.4% (PLCO)
- Higher grades due to 1-time PSA testing

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Martin RM, et al. Cancer. JAMA. 2018;319(9):883-895

CAP

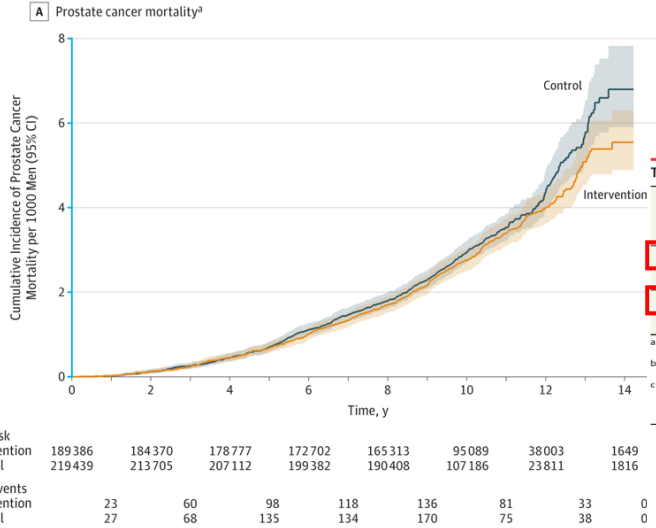

Table 2. Prostate Cancer-Specific and All-Cause Mortality in the Single Prostate-Specific Antigen (PSA) Testing Intervention Group vs Standard Practice (Control)

	Intervention Group (n = 189 386)[a]		Control Group (n = 219 439)[b]						
	No. of Deaths	Rate/1000 Person-Years (95% CI)	No. of Deaths	Rate/1000 Person-Years (95% CI)	Rate Difference/1000 Person-Years (95% CI)	Rate Ratio (95% CI)[c]	*P* Value	Rate Ratio (95% CI)[d]	*P* Value
Primary Outcome: Prostate Cancer Mortality[e]									
Intention-to-screen cohort	549	0.30 (0.27 to 0.32)	647	0.31 (0.29 to 0.33)	−0.013 (−0.047 to 0.022)	0.96 (0.85 to 1.08)	.50	0.93 (0.67 to 1.29)	.66
Secondary Outcome: All-Cause Mortality									
Intention-to-screen cohort	25 459	13.74 (13.57 to 13.91)	28 306	13.51 (13.35 to 13.67)	0.229 (−0.001 to 0.460)	0.99 (0.94 to 1.03)	.49	1.07 (0.93 to 1.23)	.35

[a] There were 1 853 167 person-years, calculated as the time until death or censoring.

[b] There were 2 095 405 person-years, calculated as the time until death or censoring.

[c] Likelihood ratio test of the null hypothesis (ie, no difference in prostate cancer mortality between the groups) adjusted for randomization cluster and age stratum.

[d] Analysis to obtain the causal effect of screening among those attending the PSA testing clinic using a generalized method of moments estimator with random allocation as an instrumental variable.

[e] Defined as definite, probable, or intervention-related prostate cancer death as determined by an independent cause of death committee.

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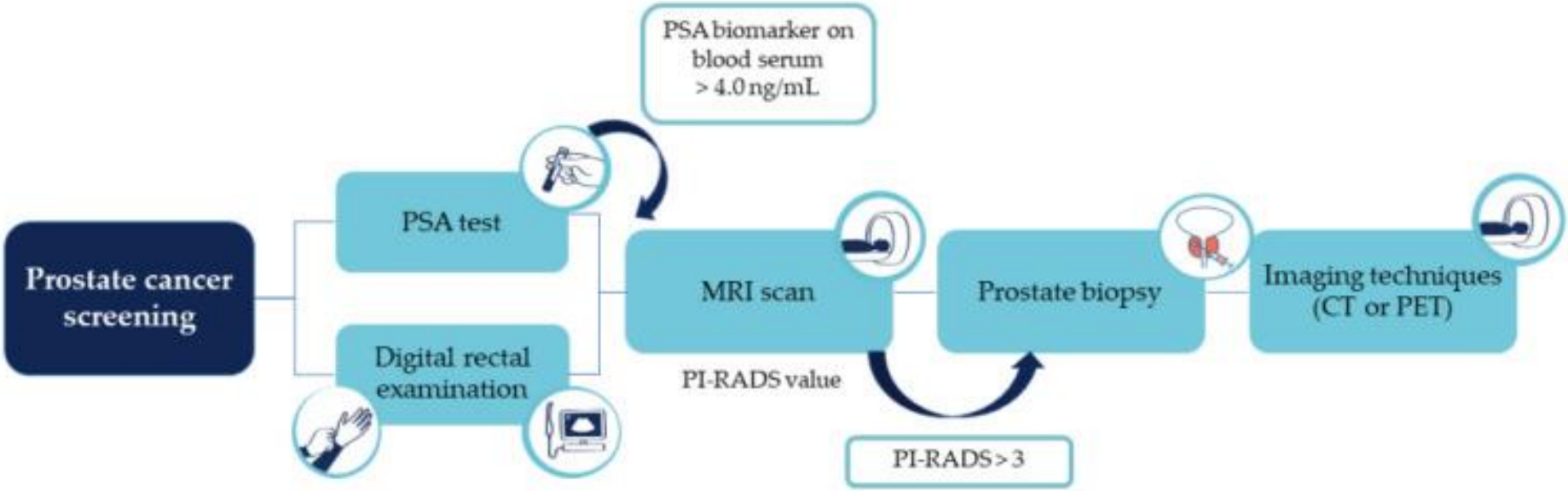
Martin RM, et al. Cancer. JAMA. 2018;319(9):883-895

How do we screen?



Berenguer CV, et al. Curr Oncol. 2023 Feb; 30(2): 2300–2321
US Preventive Services Task Force, et al. JAMA. 2018;319(18):1901-1913

USPSTF 2018

Recommendation Summary

Population	Recommendation	Grade
Men aged 55 to 69 years	For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)-based screening for prostate cancer should be an individual one. Before deciding whether to be screened, men 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. 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.	C
Men 70 years and older	The USPSTF recommends against PSA-based screening for prostate cancer in men 70 years and older.	D

Clinician Summary

Expand All

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.	Do not screen for prostate cancer. Grade: D

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US Preventive Services Task Force, et al. JAMA. 2018;319(18):1901-1913

Initial Test

- USPSTF, NCCN, and AUA recommend PSA as the first screening test
- What's positive?
  - 3 ng/mL-4 ng/mL historical positives
  - Age-varying thresholds: 2.5 ng/mL for people in their 40s, 3.5 ng/mL for in 50s, 4.5 ng/mL in 60s, and 6.5 ng/mL in 70s
- Newly elevated PSA → repeat the PSA
  - Can return to normal in 25%-40% upon retesting
  - In those w/PSA 3-10 ng/mL, 2 PSA tests 8 weeks apart (17% returned to <3 ng/mL)
- Normal – interval testing 2-4 years in normal risk, 1-2 years in high-risk

Prostate Cancer Early Detection. NCCN Guidelines Version 2.2024. 2024; https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf
US Preventive Services Task Force, et al. JAMA. 2018;319(18):1901-1913
Wei JT, et al. J Urol. 2023;210(1):46-53

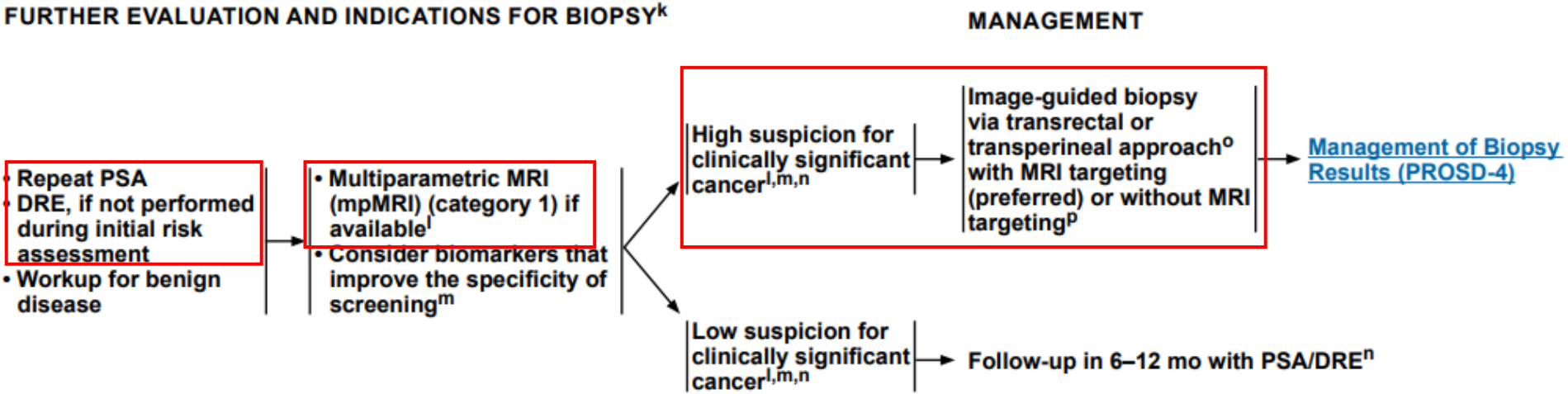
PSA Caveats

- Non-cancer causes of PSA elevation
  - DRE (test PSA 3 days after DRE)
  - Recent instrumentation, ejaculation, or trauma
  - Infection (e.g., prostatitis)
  - 5α-reductase inhibitors (5-ARIs) finasteride and dutasteride, which are medicines commonly used to treat benign prostatic hyperplasia (BPH) typically lead to an approximate 50% decrease in serum PSA levels within 6 to 12 months of initiating therapy

- Free and Total PSA (if total <10 ng/mL, low free PSA can suggest higher prostate cancer risk (risk >50% if free PSA% <10%, risk <10% if free PSA% >25%)
  - PSA velocity not a good indicator of malignancy, PSA density (total PSA/prostate volume [width x length x height x 0.5]) >0.15 suspicious

Jain MA, et al. StatPearls. 2023;https://www.ncbi.nlm.nih.gov/books/NBK556081/
Wei JT, et al. J Urol. 2023;210(1):46-53

Next Testing Modalities



Approx 30-35% w/serum PSA between 4-10 ng/mL will have prostate cancer

- Total PSA levels >10 ng/mL >67% likelihood of prostate cancer

Prostate Cancer Early Detection. NCCN Guidelines Version 2.2024. 2024; https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf

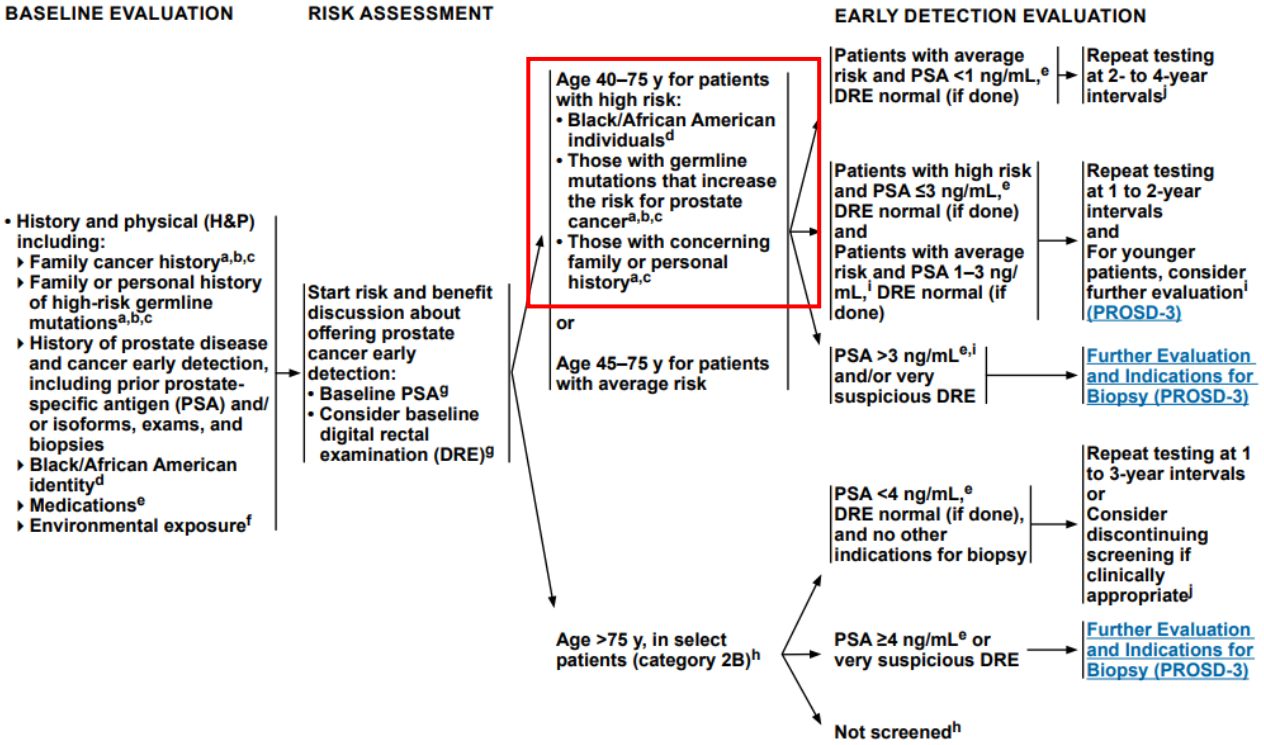
About Digital Rectal Exam (DREs)…

- Low sensitivity (51%) and specificity (59%)
  - Detects palpable abnormalities in the posterior and lateral aspects of the prostate gland
  - 1/3 of prostate cancers detected by DRE alone are advanced vs. <10% by PSA screening
  - T1c prostate cancers, majority of screen-detected cancers, are nonpalpable

Most guidelines do not suggest DRE for screening (at most as an adjunct)

Jain MA, et al. StatPearls. 2023;https://www.ncbi.nlm.nih.gov/books/NBK556081/
Wei JT, et al. J Urol. 2023;210(1):46-53

High-Risk Patients



Garraway IP, et al. NEJM Evid. 2024;3(5):EVIDoa2300289.
Hereditary Cancer Testing Criteria. NCCN Guidelines Version 3.2024. 2024; https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf
Wei JT, et al. J Urol. 2023;210(1):46-53

High-Risk Patients

TESTING CRITERIA FOR PROSTATE CANCER SUSCEPTIBILITY GENES
(Specifically *ATM, BRCA1, BRCA2, CHEK2,* and *HOXB13*[z]) (GENE-A)[a,aa,bb]

Testing is clinically indicated in the following scenarios:

- See General Tumor Criteria on CRIT-1.
- Personal history of prostate cancer with specific features:
  - By tumor characteristics (any age)
    - Metastatic[p]
    - Histology
      - high- or very-high-risk group (see Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer)
  - By family history and ancestry
    - ≥1 close blood relative[o] with:
      - breast cancer at age ≤50 y
      - triple-negative breast cancer at any age
      - male breast cancer at any age
      - ovarian cancer at any age
      - pancreatic cancer at any age
      - metastatic,[p] high-, or very-high-risk group (see Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer) at any age
    - ≥3 close blood relatives[o] with prostate cancer (any grade) and/or breast cancer on the same side of the family including the patient with prostate cancer
    - Ashkenazi Jewish ancestry
- Family history of cancer
  - An affected (not meeting testing criteria listed above) or unaffected individual with a first-degree blood relative meeting any of the criteria listed above (except unaffected individuals whose relatives meet criteria only for systemic therapy decision-making)[q]

Testing *may be* considered in the following scenario:

- Personal history of prostate cancer with intermediate-risk prostate cancer with intraductal/cribriform histology (see Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer) at any age

Family history of prostate cancer (diagnosed before age <60, metastatic disease, died from prostate cancer)

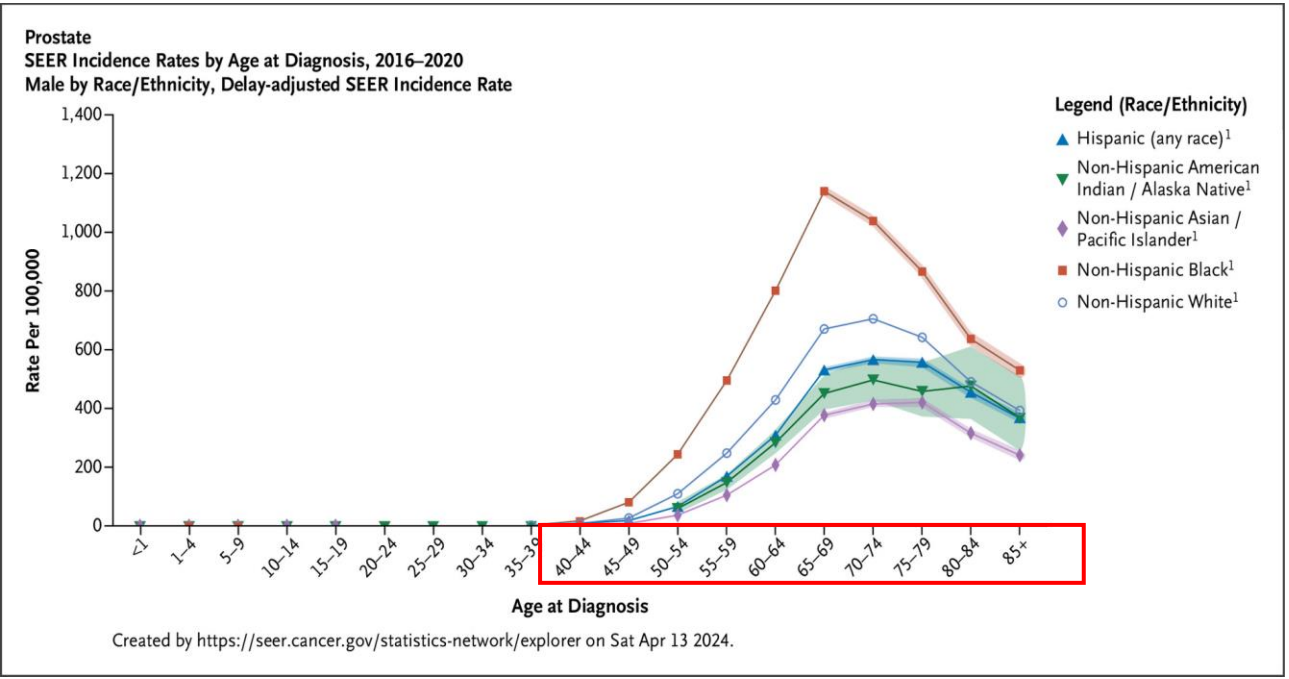
- Agent Orange exposure
- Ashkenazi Jewish ancestry

Annual PSA screenings should start as early as age 40 years

- Until significant cancer is found
- Patient changes mind about screening
- Develops medical comorbidities that limit life expectancy <10 years

Garraway IP, et al. NEJM Evid. 2024;3(5):EVIDoa2300289.
Hereditary Cancer Testing Criteria. NCCN Guidelines Version 3.2024. 2024; https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf
Wei JT, et al. J Urol. 2023;210(1):46-53

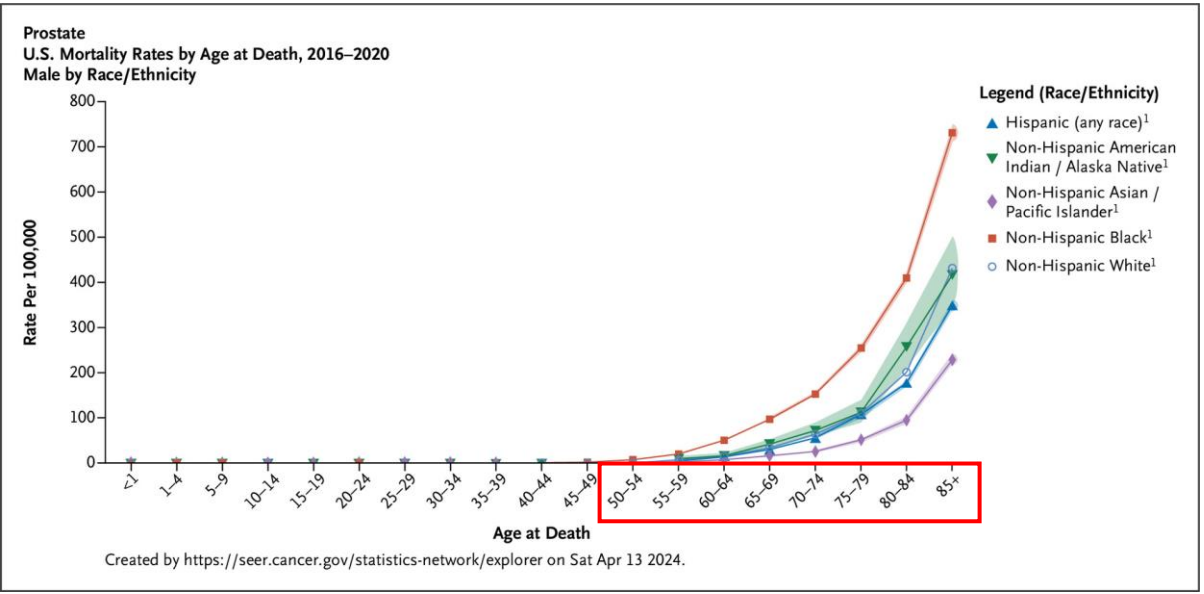
Racial Disparities in Prostate Cancer



Prostate cancer incidence disproportionately highest among Black men compared to all other racial groups, and in all age groups at diagnosis

Garraway IP, et al. NEJM Evid. 2024;3(5):EVIDoa2300289.

Racial Disparities in Prostate Cancer

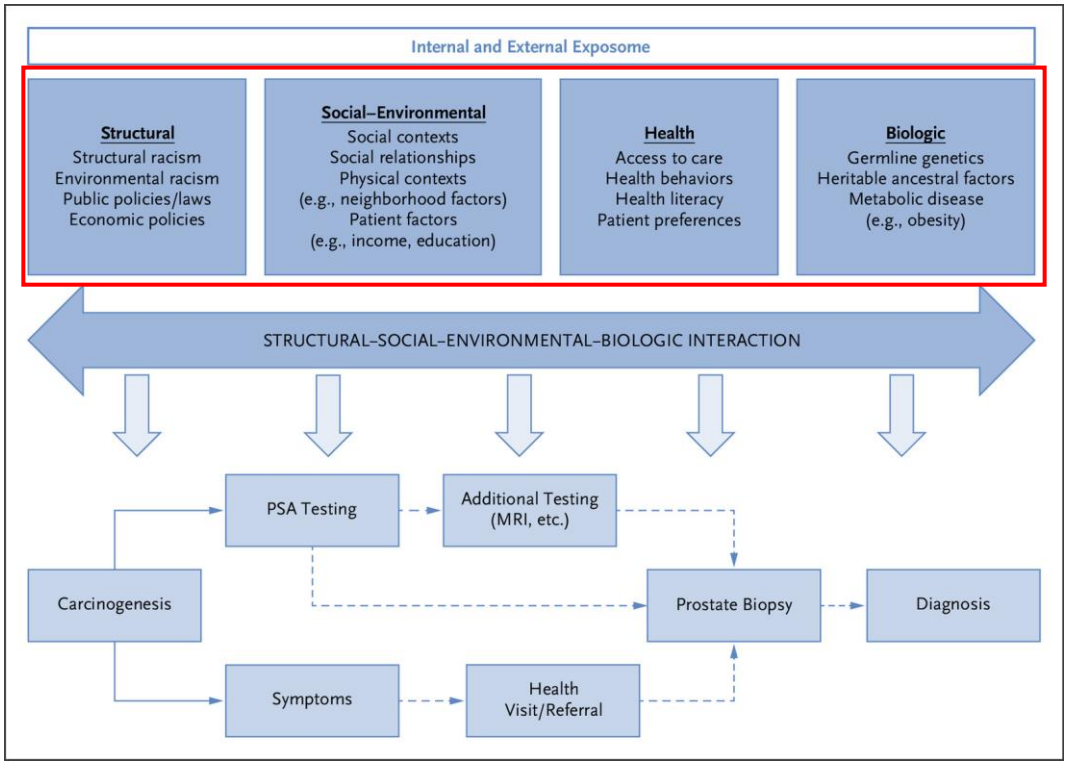


Black men are 2-4 times more likely to die from prostate cancer than other racial and ethnic groups

Cedars Sinai

Garraway IP, et al. NEJM Evid. 2024;3(5):EVIDoa2300289.

Racial Disparities in Prostate Cancer



Garraway IP, et al. NEJM Evid. 2024;3(5):EVIDoa2300289.

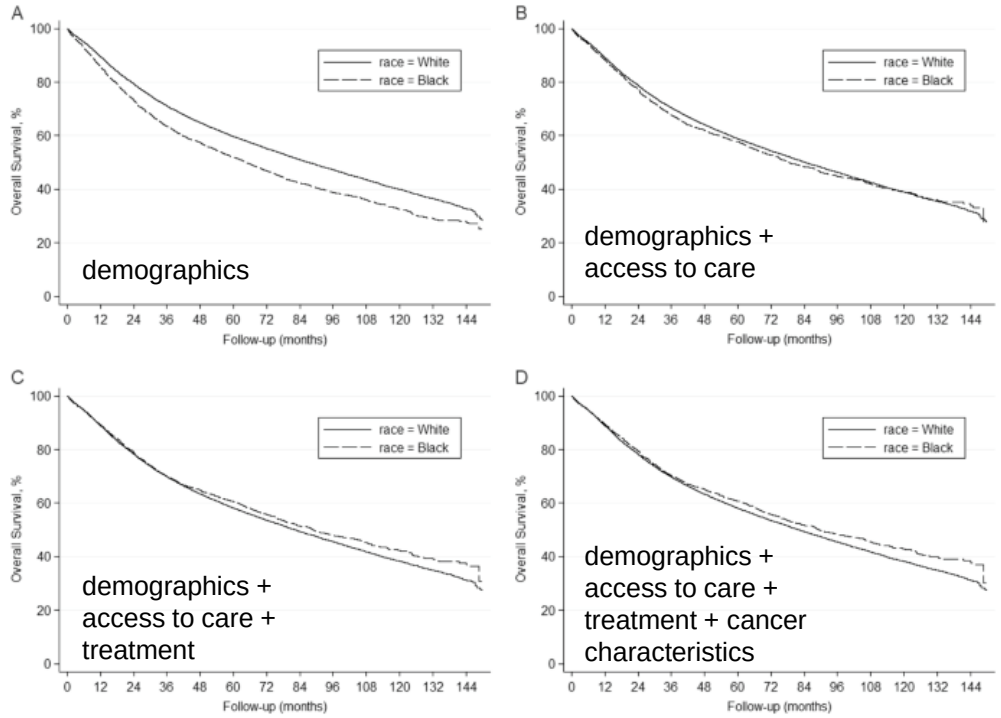
High Risk Screening in Black Men

Table 1. Prostate Cancer Foundation 2023 Guideline Statements for Prostate Cancer Screening in Black Men in the United States.*

No.	Key Questions	Prostate Cancer Foundation Recommendations
1	Should Black men be screened for prostate cancer?	Yes. Since Black men are at high risk for prostate cancer, the benefits of screening generally outweigh the risks.
2	What should Black men know about how screening for prostate cancer is conducted?	Prostate-specific antigen (PSA) is a blood test that should be considered first-line for prostate cancer screening. Some providers may recommend an optional digital rectal exam (DRE) in addition to the PSA test.
3	What information should Black men obtain to make an informed decision about PSA screening and early detection of prostate cancer?	Decisions about PSA testing depend on individual preferences. Black men should engage in shared decision-making with their health care providers and other trusted sources of information to learn about the pros and cons of screening.
4	At what age should Black men obtain their first PSA test and how often should they be screened for prostate cancer?	For Black men who elect screening, a baseline PSA test should be done between ages 40–45. Depending on the PSA value and the individual's health status, annual PSA screening should be strongly considered.
5	At what age should Black men consider stopping PSA screening?	Black men over age 70 who have been undergoing prostate cancer screening should talk with their health care provider about whether to continue PSA testing and make an informed decision based on their age, life expectancy, health status, family history, and prior PSA levels.
6	How should family history and genetic risk be taken into consideration when screening Black men for prostate cancer?	Black men with an even higher risk of prostate cancer due to a strong family history and/or known carriers of high-risk genetic variants should consider initiating annual PSA screening as early as age 40.

Garraway IP, et al. NEJM Evid. 2024;3(5):EVIDoa2300289.

Racial Disparities in Prostate Cancer



access-related factors account for 84.7% of excess risk of death among Black men vs 4.7% from cancer-related factors

Krimphove MJ, et al. Prostate Cancer Prostatic Dis. 2019;22(1):125-136.

Summary

- Population-based prostate cancer screening not yet ready
- Prostate cancer screening should be individualized (shared-decision making)
- Initial best test is serum PSA
  - Repeat test for an initially elevated test for confirmation
  - If elevated after confirmation, MRI prostate and prostate biopsy
- Average risk patient, screen age 55-69 (though may start as early as 45), interval 2-4 year testing

Summary

- High-risk patients
  - Black/African/Caribbean ancestry
  - Germline/hereditary mutations
  - Strong family history of cancer
  - Ashkenazi Jewish
  - Agent Orange exposure
    - Screen as early as age 40, annual PSA screening

- Racial disparities exist in prostate cancer
  - Biological drivers
  - Social determinants (e.g., access to care)

FAQs

1. What are the 2018 United States Preventive Services Task Force (USPSTF) recommendations for prostate cancer screening?
   a. Screen men from age 55 to 69; refrain from screening in men aged 70 years or older
   b. Screen all average-risk individuals age 40 to 75
   c. Screen all high-risk men aged 55 to 69; selectively offer screening up until age 70

FAQs

2. The following is not a risk factor for prostate cancer for which men require earlier screening?

a) Black/African-American race
b) Germline mutations that increase risk of prostate cancer
c) Family or personal cancer history
d) Low Vitamin D levels

FAQs

3. If shared-decision making between provider and patient occurs and prostate cancer early detection is to be pursued, what is the recommended initial screening test?
   a) Digital rectal examination
   b) PSA
   c) MRI
   d) Prostate biopsy

FAQs

4. Which of the following can lead to elevated PSA?
   a) Infection
   b) Recent instrumentation or trauma
   c) Ejaculation
   d) Medications such as finasteride and dutasteride
   e) All of the above

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Thank You!

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