Prostate Cancer 101
GU Oncology Nursing Education

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Part 1

Introduction to Prostate Cancer
Pathophysiology, Epidemiology, Risk Factors, Screening, and Diagnosis

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Objectives

- Discuss the pathophysiology of Prostate Cancer
- Discuss the epidemiology of Prostate Cancer
- Identify the pros & cons of prostate cancer screening.
- Define the diagnostic process of prostate cancer.

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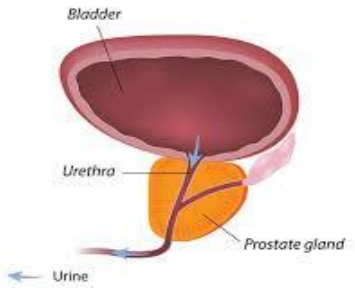
Definition

Prostate cancer is a disease in which malignant cells form in the prostate gland



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Physiology

- Partly glandular and muscular organ within lower pelvis
- Accessory reproductive gland
- Secretes alkaline fluid that forms a part of the ejaculate which aids in motility and nourishment of sperm
- 4 zones: peripheral (75%), central, transition, fibromuscular
- Average size 28-47 cc

Rebello, R.J., Oing, C., Knudsen, K.E. *et al.* Prostate cancer. *Nat Rev Dis Primers* **7**, 9 (2021)

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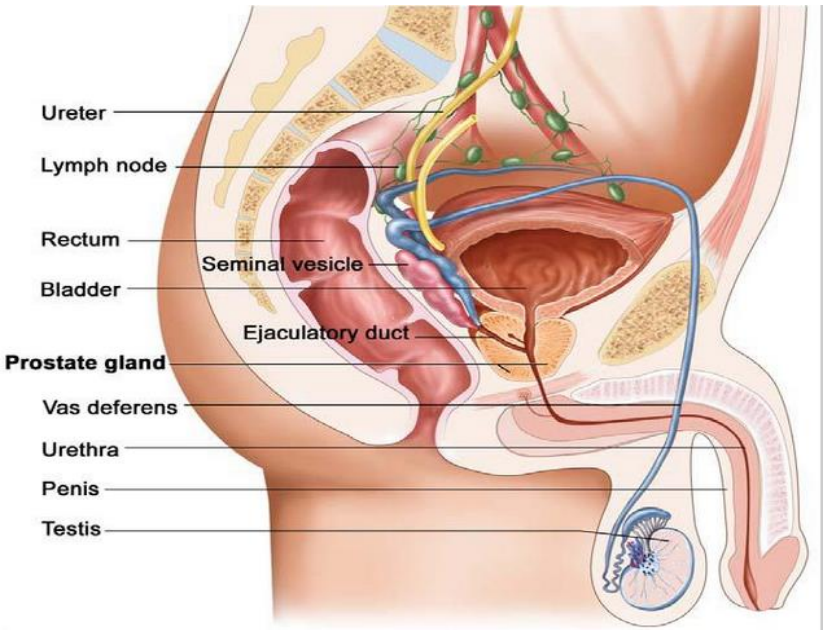

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Pathophysiology

- ~90% are adenocarcinomas
  - Remaining ~10% are primarily neuroendocrine
- Disseminated disease
  - Locally via lymphatic system
  - Hematologic
- Metastasis
  - Bone: Axial skeleton
  - Lymph nodes
  - Organs less common

Rebello, R.J., Oing, C., Knudsen, K.E. *et al.* Prostate cancer. *Nat Rev Dis Primers* **7**, 9 (2021)

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Epidemiology

- Most diagnosed non-cutaneous malignancy in men
- >3.1 million men living with prostate cancer
- Lifetime risk: 1 in 8 men
- 2nd leading cause of cancer death
- 1 in 41 die of prostate cancer
- 2023: 288,300 new; 34,700 deaths

American Cancer Society 2023

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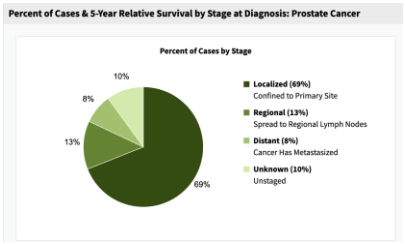
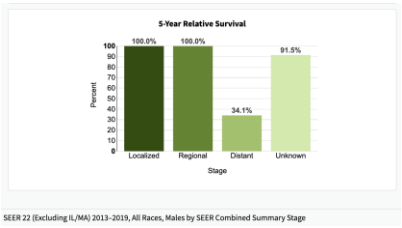
Epidemiology





National Cancer Institute; Surveillance, Epidemiology, and End Results Program

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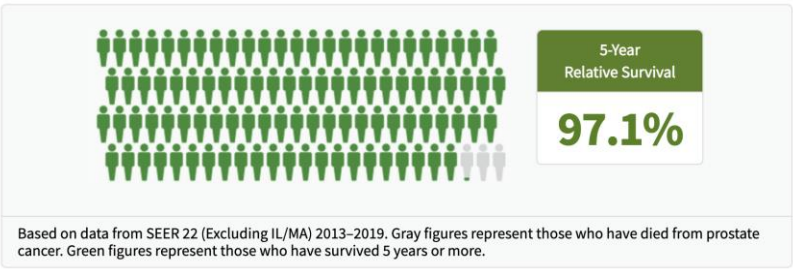
Relative Survival



Percent surviving 5 years:
97.1%

National Cancer Institute; Surveillance, Epidemiology, and End Results Program

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Risk Factors

- Age
  - 60% dx at ≥ 65 years old
- Race
  - AA men highest incidence & mortality
  - Complex socioeconomic disparities
    - Access, quality of care, comorbidities, health insurance, income
    - Less screening
    - More aggressive stage
    - Less likely to receive aggressive tx
- Family History
  - Men with a 1st degree relative dx with prostate CA have a twofold risk
  - Familial Prostate Cancer (FPC)
    - Clustering within families
    - 10-20% have family hx
  - Hereditary Prostate Cancer (HPC)
    - FPC subtype

Berenguer, C.V.; Pereira, F.; Câmara, J.S.; Pereira, J.A.M. Underlying Features of Prostate Cancer—Statistics, Risk Factors, and Emerging Methods for Its Diagnosis. *Curr. Oncol.* **2023**, *30*, 2300-2321

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Risk Factors

- Diet/supplements
  - Extensively studied
  - Dietary calcium, micronutrients, cooked meat, phytoestrogens, vitamins A,D,E, selenium
  - Above have been hypothesized to increase risk, ***no conclusive data exist***
- Others
  - BMI, inactivity, chemical exposure, STIs, vasectomy
  - ***Little/no evidence***

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Prevention

- Prostate Cancer Prevention Trial (PCPT)
  - Arm 1: finasteride daily
  - Arm 2: Placebo
  - N= 18,882, 7 years
  - Pbx at end if PSA >4 or abnormal DRE
  - 24.8% reduction in PRCA, but more likely to have more aggressive cancer
  - True incidence of high-grade prca not reduced
- Reduction by Dutasteride of Prostate Cancer Events (REDUCE)
  - Arm 1: dutasteride daily
  - Arm 2: placebo
  - 4 year follow up
  - 27% reduction in PRCA
  - No reduction in more aggressive grades
- Neither approved for prevention

Thompson IM, Goodman PJ, Tangen CM, et al. The influence of finasteride on the development of prostate cancer. N Engl J Med 2003;349:215-224

Gomella LG. Chemoprevention using dutasteride: the REDUCE trial. Curr Opin Urol. 2005 Jan;15(1):29-32

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Prevention

- The European Prospective Investigation into Cancer and Nutrition (EPIC) trial
  - Prospective cohort
  - 500k, 10 countries, 14 cancers
  - 130,544 men, 1,104 prostate ca
  - 27 studies using EPIC data have been published
  - Review has not found association for prca risk with fruit/veggie consumption
  - Limitation = recall data from food diaries
- Selenium and Vitamin E Prevention Trial (SELECT)
  - N = 35,533
  - Placebo, daily Vit E, daily selenium, or daily Vit E + selenium
  - Median 7 yr follow up
  - No reduction in prca incidence
- HOPE trial
  - Placebo v daily Vit E
- Physicians Health Study II
  - Placebo, daily Vit E, daily Vit C, daily Vit E + C

Neither showed reduction in incidence

Riboli E, et al. European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. Public Health Nutr. 2002 Dec;5(6B):1113-24.

Klein EA, et al Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA. 2011 Oct 12;306(14):1549-56.

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Prevention: Takeaways

- No nutritional supplements recommended for prevention of prostate cancer
- Counsel patients to avoid costly supplements for prostate cancer prevention
- Risk/benefit with 5 ARI
  - Not to be used for prevention
  - FDA approved for BPH
  - Counsel re: data
- Healthy lifestyle (diet, exercise, avoiding tobacco, minimal alcohol) good for overall health

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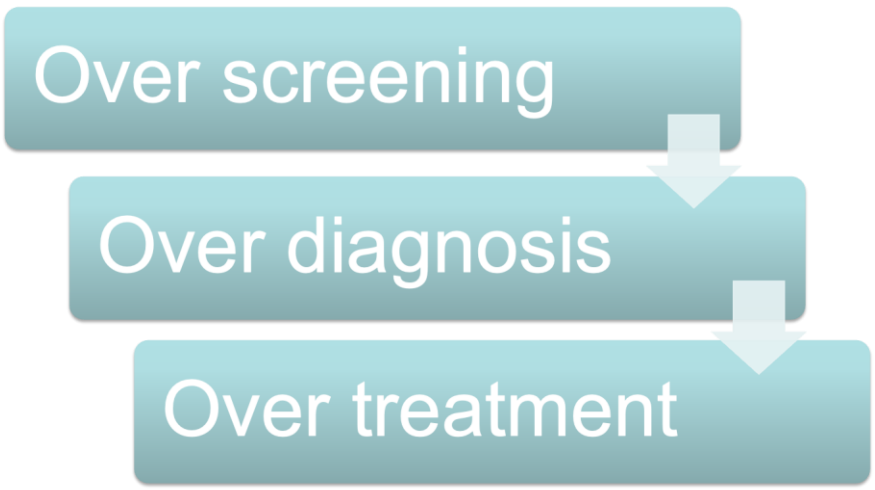
Screening



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Screening

- Prostate exam via digital rectal exam (DRE)
- Blood test called prostate specific antigen (PSA)
  - Protease found in prostate luminal cells
  - Hormone dependent
  - Adoption for screening in later 1980s

Dunn MW. Prostate Cancer Screening. Semin Oncol Nurs. 2017 May;33(2):156-164.

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Prostate Specific Antigen

Age	Caucasian	African-American	Asian-American
40-49	0-2.5	0-2.0	0-2.0
50-59	0-3.5	0-4.0	0-3.0
60-69	0-4.5	0-4.5	0-4.0
70-79	0-6.5	0-5.5	0-5.0

DeAntoni EP, et al. Age- and race-specific reference ranges for prostate-specific antigen from a large community-based study. Urology. 1996 Aug;48(2):234-9

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Prostate Specific Antigen

- PSA elevation
  - Infection
  - Lab error
  - Inflammation
  - Retention
  - BPH
  - Instrumentation
  - Age
  - Abnormal cells
  - Prostate cancer
- PSA decrease
  - 5 ARI
  - ADT
  - Prostatectomy
  - XRT
  - Lab error
- No robust data
  - Ejaculating
  - Bike riding
  - Rectal exam

Thompson IM, et al. Prevalence of prostate cancer among men with a prostate-specific antigen level < or =4.0 ng per milliliter. *New England Journal of Medicine* 2004; 350(22):2239–2246

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Screening

- The only consensus is that men should be presented with benefits vs. risks
- AUA: Early Detection of Prostate Cancer, 2013 update: Yes
- ACS: Yes
- USPSTF: 2012 Update: No
  2018 Update: Yes

Carter HB, et al: Early detection of prostate cancer: AUA Guideline. J Urol 2013; **190:** 419

Smith RA,, et al. Cancer screening in the United States, 2018: A review of current American Cancer Society guidelines and current issues in cancer screening. *CA Cancer J Clin*. 2018;68(4):297-316
Moyer V et al. Ann Intern Med. 2012;157:120-134.
Grossman et al. JAMA. 2018;319(18):1901-1913.

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But wait!

2016 analysis of the surveys used in the PLCO trial found that nearly 90% of men in the control arm (i.e. not supposed to get PSA testing) got cumulative PSA testing during the time of the study, resulting in a much higher degree of contamination than initially reported

Grossman et al. JAMA. 2018;319(18):1901-1913.

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Updated USPSTF recs

Recommendation Summary

Population	Recommendation	Grade (What's This?)
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

Grossman et al. JAMA. 2018;319(18):1901-1913.

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The great debate

- Can we justify mass public screenings to detect prostate cancer?
- Several randomized controlled clinical trials serve as basis for screening recommendations, but not much clarity re: screening and impact on mortality
- Financial: Does cost spent on screening prolong life or prevent unnecessary death?
- Clinically significant and insignificant

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MRI

- Multiparametric prostate MRI- diffusion weighted imaging + dynamic contrasted-enhanced MRI
- Does not:
  - Have an evidence-based role in stand-alone screening for prostate cancer (yet)
  - Replace prostate biopsy for diagnosis
  - Definitively diagnose prostate cancer; still need tissue
  - Get paid for by all insurance carriers
- Does have a role in:
  - Further characterizing unusual clinical pictures
  - Helping explain persistently elevated PSA with prior negative biopsy
  - Part of active surveillance
  - Abnormal PSA with no prior biopsy (no consensus, yet)
  - Staging

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MRI: PRECISION

- MRI (with or without targeted bx) or standard TRUS bx for men w/ suspicion of prostate cancer
- N = 500 (had not undergone previous bx)
- In MRI group, 28% had neg MRI so did not have bx
- In MRI group, clinically significant cancer dx in 38%
- In TRUS bx group, clinically significant cancer dx in 26%

- The use of risk assessment w/ MRI before bx and MRI-targeted bx was superior to TRUS bx in men at clinical risk for prostate cancer

Kasivisvanathan, V et al, *NEJM 2018*

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MRI

PI-RADS: Prostate Imaging Reporting and Data System

- Grade 1-5

Score	Meaning	Meaning
Score 1	Not suspicious	Highly unlikely to contain a clinically significant lesion
Score 2	Not very suspicious	Unlikely to contain a clinically significant lesion
Score 3	Ambiguous	Impossible to offer an opinion as to whether or not it contains a clinically significant lesion
Score 4	Suspicious	Likely to contain a clinically significant lesion
Score 5	Very suspicious	Highly likely to contain a clinically significant lesion

3: 15%

4: 40%

5: 80-90%

Scott R, et al. PI-RADS v2.1: What has changed and how to report. SA J Radiol. 2021 Jun 1;25(1):2062

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MRI: Future

- Consensus on use for patients with abnormal PSA and no prior biopsy
- Consensus on foregoing standard biopsy if MRI is negative
- Should men with positive MRI only get targeted biopsy?
- Continued integration into pre and post-diagnosis management

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Other tools

- Biomarkers
  - Who to biopsy
    - PHI, 4K, Select MDx
  - Who to rebiopsy
    - PCA3, Confirm MDx
  - Surveillance v intervention
    - Oncotype, Prolaris, Decipher, Promark

Where these will be useful is still yet to be determined

Farha MW, et al.. Biomarkers for prostate cancer detection and risk stratification. Ther Adv Urol. 2022 Jun 14;14

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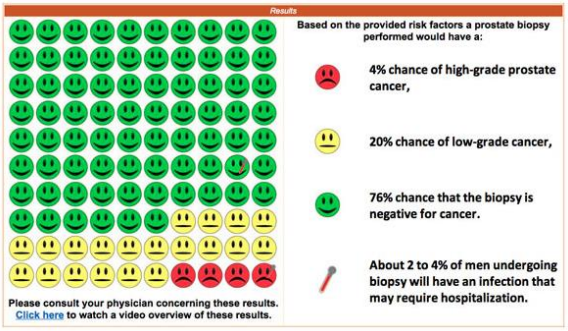
Other tools

- Prostate Cancer Prevention Trial Risk Calculator
  - Myprostatecancerrisk.com
  - Race, age, PSA, family hx, DRE, prior biopsy



Ankerst DP, et al. Prostate Cancer Prevention Trial risk calculator 2.0 for the prediction of low- vs high-grade prostate cancer. Urology. 2014 Jun;83(6):1362-7

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Clinical Presentation

- Usually, asymptomatic
- Lower urinary tract symptoms (LUTS)
- Bony pain
  - Hips, Back, Pelvis
- Bladder outlet obstruction/Renal failure
- Spinal cord compression

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Diagnosis

Transrectal Biopsy

- Cognitive (12 cores)
- Fusion (cognitive + targeted)
- Local anesthetic
- Prep: Antibiotic, enema, cease blood thinners
- Risks: Pain, infection, bleeding
- Pros: Not as painful

Transperineal Biopsy

- Cognitive (12 cores)
- Fusion (cognitive + targets)
- Local anesthetic (or GA)
- Prep: Cease blood thinners
- Risks: Pain, bleeding
- Pros: Decreased risk of sepsis

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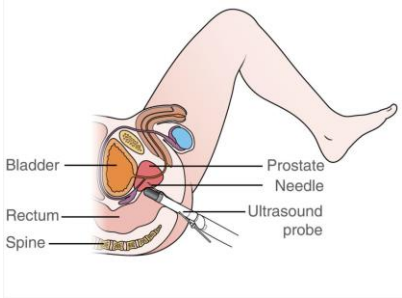
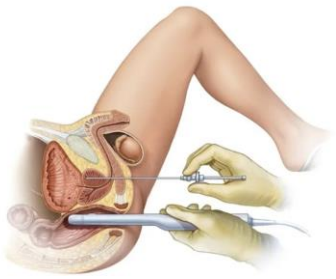
Diagnosis





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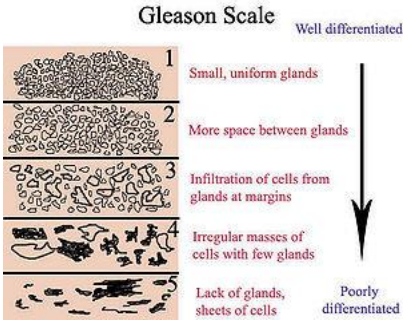
Diagnosis

- The Gleason Scoring System
  - Assigns a grade to the 2 largest areas in each biopsy
  - Ex: Gleason 4+3=7: Pattern 4 most abundant, Pattern 3 2nd most



Gleason, D.F. (1966) Classification of Prostatic Carcinomas. Cancer Chemotherapy Reports, 50, 125-128

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Diagnosis: New grading system

Grade	Gleason	Characteristics
1	≤6	Individual discrete well-formed glands
2	3+4 = 7	Predom well-formed glands w/ a lesser component of poorly formed/fused glands
3	4+3 = 7	Predom poorly formed/fused glands w/ a lesser component of well-formed glands
4	8	Only poorly formed or predom well-formed w/ lesser comp lacking glands or predom lacking glands w/ lesser comp well-formed
5	9-10	Lacks gland formation

Epstein JI, et al A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score. Eur Urol. 2016 Mar;69(3):428-35

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Staging

- Variables: PSA, DRE, pathology, imaging
- Clinical (PSA, DRE, imaging) v. Pathologic
- Risk Categories: Very low-very high risk
- AJCC Prostate Cancer Staging
- Imaging depends on risk category

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Group	T	N	M	PSA	Gleason
I	T1a-c	N0	M0	PSA <10	Gleason ≤6
	T2a	N0	M0	PSA <10	Gleason ≤ 6
	T1-2a	N0	M0	PSA X	Gleason X
IIA	T1a-c	N0	M0	PSA <20	Gleason 7
	T1a-c	N0	M0	PSA ≥10<20	Gleason ≤ 6
	T2a	N0	M0	PSA≥10<20	Gleason ≤ 6
	T2a	N0	M0	PSA <20	Gleason 7
	T2b	N0	M0	PSA <20	Gleason ≤ 7
	T2b	N0	M0	PSA X	Gleason X
IIB	T2c	N0	M0	Any PSA	Any Gleason
	T1-2	N0	M0	PSA ≥ 20	Any Gleason
	T1-2	N0	M0	Any PSA	Gleason ≥ 8
III	T3a-b	N0	M0	Any PSA	Any Gleason
IV	T4	N0	M0	Any PSA	Any Gleason
	Any T	N1	M0	Any PSA	Any Gleason
	Any T	Any N	M1	Any PSA	Any Gleason

American Cancer Society

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INITIAL RISK STRATIFICATION AND STAGING WORKUP FOR CLINICALLY LOCALIZED DISEASE[e]

Risk Group	Clinical/Pathologic Features See Staging (ST-1)			Additional Evaluation[h,i]	Initial Therapy
Very low[f]	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/mL • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core[g] • PSA density <0.15 ng/mL/g			• Confirmatory testing can be used to assess the appropriateness of active surveillance (See PROS-F 2 of 5)	See PROS-3
Low[f]	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL			• Confirmatory testing can be used to assess the appropriateness of active surveillance (See PROS-F 2 of 5)	See PROS-4
Intermediate[f]	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): ▸ cT2b–cT2c ▸ Grade Group 2 or 3 ▸ PSA 10–20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)[g]	• Confirmatory testing can be used to assess the appropriateness of active surveillance (See PROS-F 2 of 5)	See PROS-5
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)[g]	Bone and soft tissue imaging[j,k] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-6
High	Has no very-high-risk features and has exactly one high-risk feature: • cT3a OR • Grade Group 4 or Grade Group 5 OR • PSA >20 ng/mL			Bone and soft tissue imaging[j,k] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7
Very high	Has at least one of the following: • cT3b–cT4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • >4 cores with Grade Group 4 or 5			Bone and soft tissue imaging[j,k] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7

National Comprehensive Cancer Network

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Part 1 Takeaways

- Prostate cancer is very common
- Black men and men with a family history have higher risk
- No one way to prevent prostate cancer
- Screening involves shared decision making
- More precise tools are needed for screening
- After diagnosis, several factors help determine staging, which will then guide treatment recommendations
- Patient education along the way is essential

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