Prostate Cancer Screening and Treatment of Localized Prostate Cancer

Akshay Sood, M.D.
Assistant Professor of Urologic Oncology
The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

The Ohio State University
Wexner Medical Center

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Epidemiology

1 in 8 men in the United States will be diagnosed with prostate cancer in their lifetime.

- PCa is the **second most common cancer** to occur in men, after skin cancer. In 2025, the American Cancer Society estimates 313,780 new cases.
- It is the **second most common cause of cancer-related** death in men, after lung cancer.

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Screening

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Guidelines – AUA

American Urological Association

Clinicians should engage in shared decision-making (SDM) with people for whom prostate cancer screening would be appropriate and proceed based on a person's values and preferences.	N/A
When screening for prostate cancer, clinicians should use PSA as the first screening test.	Strong
For people with a newly elevated PSA, clinicians should repeat the PSA prior to a secondary biomarker, imaging, or biopsy.	N/A
Clinicians may begin prostate cancer screening and offer a baseline PSA test to people between ages 45 to 50 years.	N/A
Clinicians should offer prostate cancer screening beginning at age 40 to 45 years for people at increased risk of developing prostate cancer based on the following factors: *Black ancestry, germline mutations, strong family history of prostate cancer.*	Strong

Clinicians should offer regular prostate cancer screening every 2 to 4 years to people aged 50 to 69 years.	Strong
Clinicians may personalize the re-screening interval, or decide to discontinue screening, based on patient preference, age, PSA, prostate cancer risk, life expectancy, and general health following SDM.	N/A
Clinicians may use digital rectal exam (DRE) alongside PSA to establish risk of clinically significant prostate cancer.	N/A
For people undergoing prostate cancer screening, clinicians should not use PSA velocity as the sole indication for a secondary biomarker, imaging, or biopsy.	Strong
Clinicians and patients may use validated risk calculators to inform the SDM process regarding prostate biopsy.	N/A
When the risk of clinically significant prostate cancer is sufficiently low based on available clinical, laboratory, and imaging data, clinicians and patients may forgo near-term prostate biopsy.	N/A

Wei et al. J Urol 2023

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What is PSA? Why is it elevated in PCa?

- PSA is a reproductive protein, which aids in seminal fluid liquefaction. Normally the serum concentration of PSA is low, but it can increase with infection, inflammation, trauma, and prostate cancer. Due to the association with prostate cancer, PSA can be used to screen men at risk.
- PSA elevation in prostate cancer results from the disruption of the glandular architecture and loss of the basal cell layer, resulting in leaching of the PSA into the bloodstream (loss of the basal cell layer is the histologic hallmark of prostate cancer).
  - In fact, prostate cancer cells make less PSA than do normal prostate cells and up to 15% of prostate cancers are diagnosed in men with “low PSA” levels (<4.0 ng/dL).

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Is PSA a bad test?

- No.
- We use it improperly.

Sensitivity and Specificity for Prostate Cancer and High-Grade Disease, by Cutpoints of Prostate-Specific Antigen (PSA) and by Age*

	Any Cancer (n = 1225) vs No Cancer (n = 4362)		Gleason Grade 7 (n = 250) vs Gleason Grade <7 or No Cancer (n = 5325)		Gleason Grade 8 ≥ (n = 57) vs Gleason Grade <8 or No Cancer (n = 5518)	
PSA, ng/mL	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
1.1	83.4	38.9	92.8	37.0	94.7	35.9
1.6	67.0	58.7	84.4	54.8	89.8	53.5
2.1	52.6	72.5	75.6	67.3	86.0	65.9
2.6	40.5	81.1	67.2	76.5	78.9	75.1
3.1	32.2	86.7	57.6	82.3	68.4	81.0
4.1	20.5	93.8	40.4	90.0	50.9	89.1
6.1	4.6	98.5	13.2	97.8	26.3	97.5
8.1	1.7	99.4	4.8	99.0	10.5	99.0
10.1	0.9	99.7	2.4	99.5	5.3	99.5

Note: This data is based on 6 core biopsy.

Current SN is about 80% and SP about 40%.

Thompson et al. JAMA 2005

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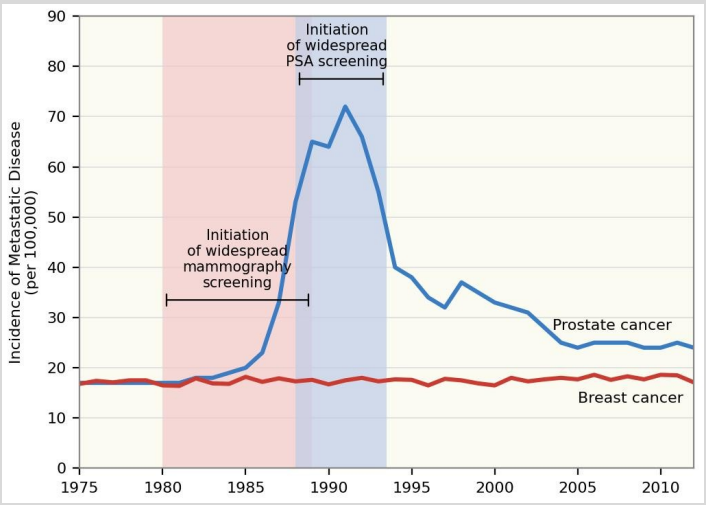
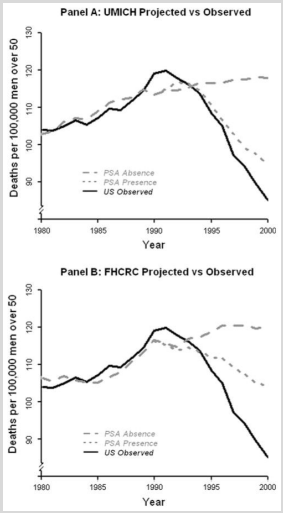
Is PSA screening bad?



Welch et al. NEJM 2015



Etzioni et al. Cancer Causes Control 2007

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Is PSA screening bad?

- PSA screening:
  - NNS: 221 (121 for mets)
  - NND: 10 (7 for mets)
  - USPSTF recommendation: Grade C
- Mammography:
  - NNS: 476 (age 60-69)
  - NNS: 1,250 (age 50-59)
  - NND: 10
  - USPSTF recommendation: Grade B
- Colonoscopy:
  - NNS: 489
  - USPSTF recommendation: Grade A

USPSTF. 2024

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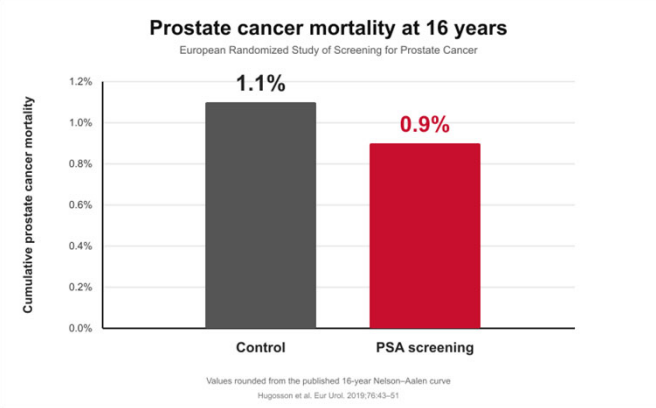
The ERSPC Study

- Age group: 55-69 yr
- Followed up until 2014 (maximum of 16 yr)
- RR 0.80 (95% CI 0.72-0.89, p<0.001) at 16 yr
- NNI for screening: 570
- NND: 18



Hugosson et al. Eur Urol 2019

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The ERSPC Study

Prostate cancer mortality at various lengths of follow-up				
	Years 1–9	Years 1–11	Years 1–13	Years 1–16
NNI (95% CI)	1947 (963–inf)	962 (598–2463)	742 (478–1650)	570 (380–1137)
NND	76	34	26	18

Hugosson et al. Eur Urol 2019

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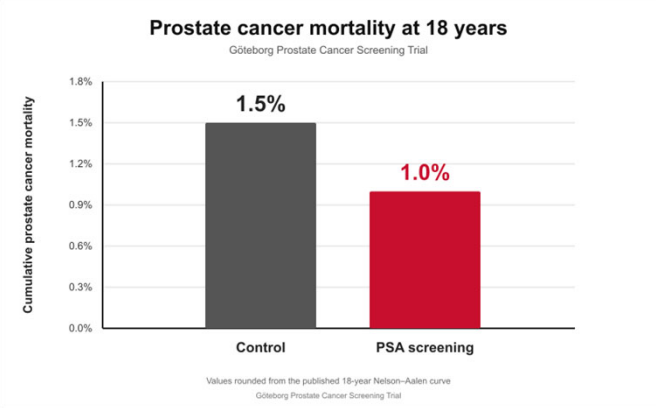
Göteborg Arm

- Age group: 50-64 yr
- Followed up until 2012 (maximum of 18 yr)
- RR 0.65 (95% CI 0.49-0.87, p<0.003) at 18 yr
- NNI for screening: 221
- NND: 10



Hugosson et al. Scan J Urol 2018

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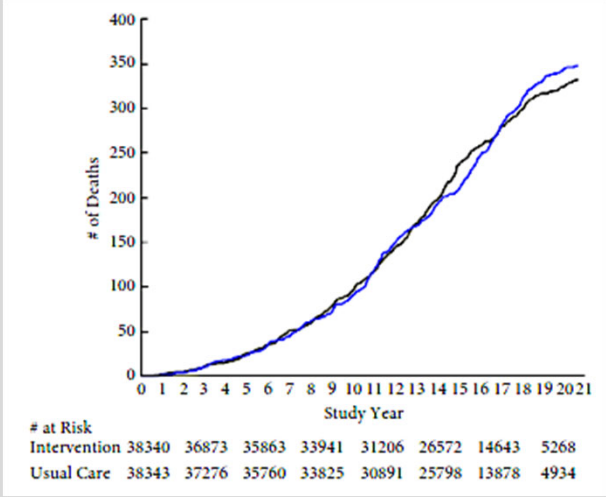
The PLCO Trial

- Age group: 55-74 yr
- Follow up 16.9 yr
- RR 0.93 (95% CI 0.81-1.08, p=0.38)



Pinksky et al. BJUI 2019

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The PLCO Trial

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

Shoag et al. NEJM 2016

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Work-Up

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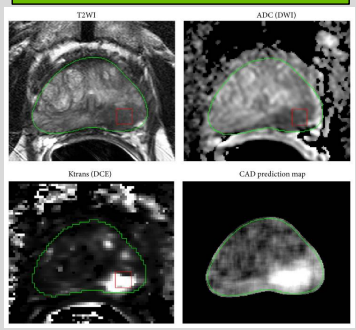
Clinical Work-Up

Elevated PSA (>4 ng/mL) → Refer to a urologic oncologist → Repeat PSA, DRE

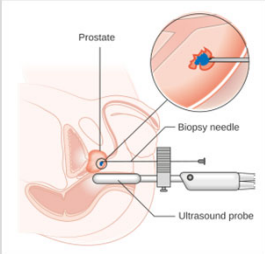
Still elevated/abnormal DRE → Multiparametric MRI



Suspicious lesion on mp-MRI (PI-RADS ≥ 3)

4K score
PHI
ExoDx
SelectMDx

MRI-US fusion transperineal biopsy



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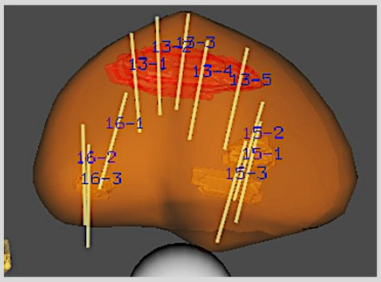
mp-MRI

Pre-biopsy test of choice, recommended by the AUA and SUO guidelines.

1. "Radiomic Biomarker"

	≥GG2	GG1
PI-RADS 1-2	6.0%	14.0%
PI-RADS 3	14.5%	8.0%
PI-RADS 4	48.5%	21.0%
PI-RADS 5	72.2%	12.0%

2. "Anatomic Guidance"



Remember, a negative mp-MRI, does not preclude the need for BX!
- Shared decision making as 14% can still harbor PCa (AUC 0.86).

Wikimedia Foundation, Inc. Ahmed et al. Lancet 2012.

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Biomarkers

Could guide decision making about prostate biopsy but none are guideline recommended.

Biomarker	Components	Source of Specimen	Indication	Clinical Variables in the Test	DRE Dependent	AUC
PHI	p2PSA, fPSA, tPSA	Blood	Biopsy naïve or repeat biopsy	None	No	0.82
4Kscore	tPSA, fPSA, iPSA, hk2	Blood	Biopsy naïve or repeat biopsy	Age, prior biopsy, DRE	No	0.82
ExoDx Prostate Intelliscore (EPI)	PCA3, ERG, SPDEFF	Urine	Biopsy naïve or repeat biopsy	PSA, age, family history	No	0.74
SelectMDx	HOX6 and DLX1	Urine	Biopsy naïve or repeat biopsy	PSA, PSA density, prior biopsy, family history	Yes	0.82

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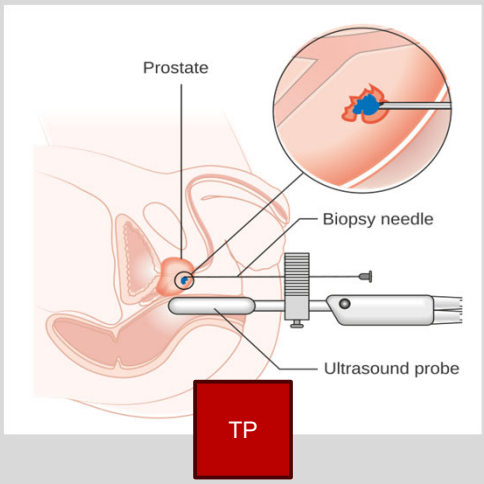
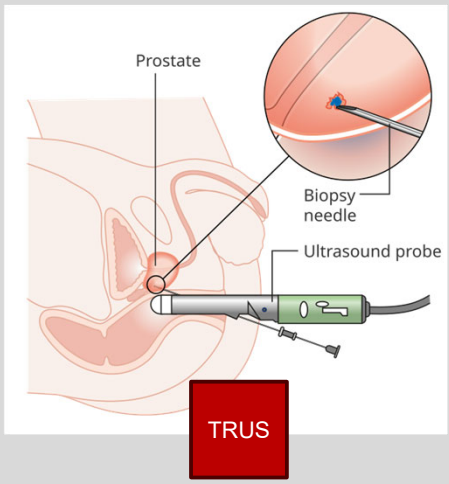
Prostate Biopsy

Transperineal vs transrectal approaches (MRI-guided fusion).





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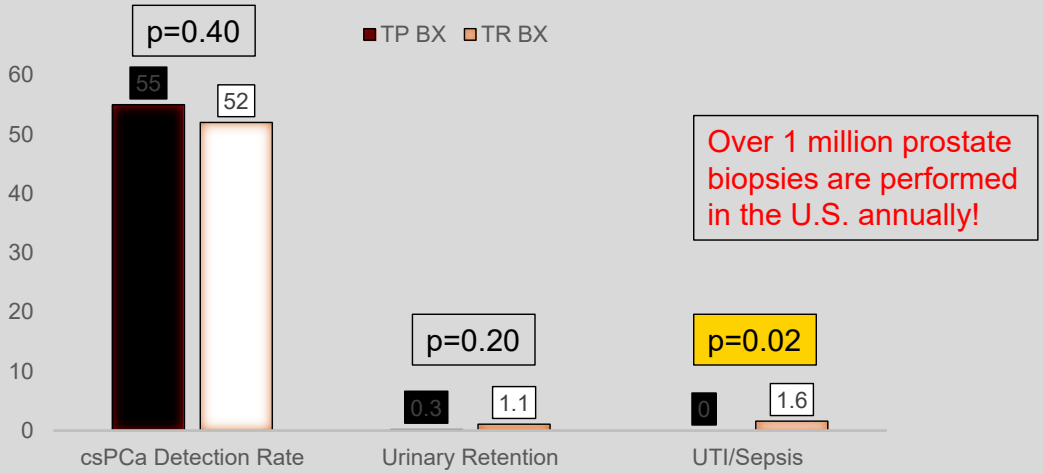
Prostate Biopsy

PREVENT Randomized Clinical Trial.



Over 1 million prostate biopsies are performed in the U.S. annually!

Hu et al. JAMA Onc 2024.

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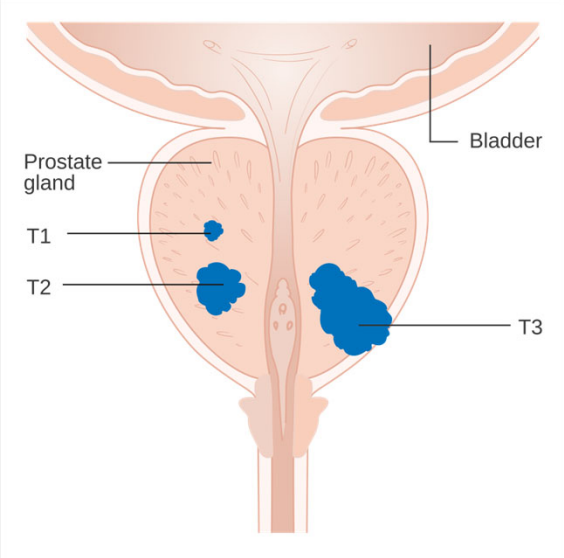
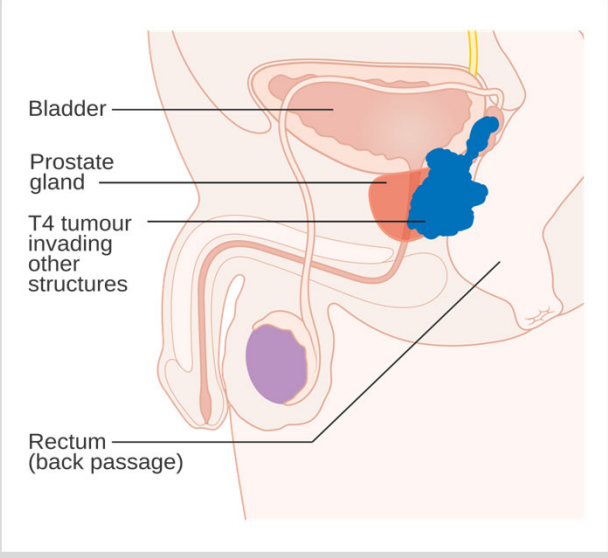
T Stage





Cancer Research UK, CC BY-SA 4.0

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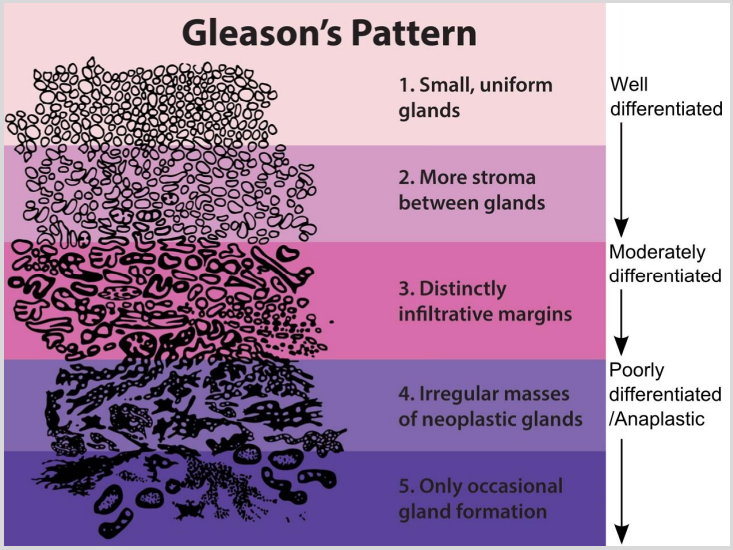
Gleason Scoring and Grade Group



GG1: 3+3

GG2: 3+4

GG3: 4+3

GG4: 4+4

GG5: 4+5, 5+4, 5+5

Morphology & Grade. ICD-O-3 Morphology Codes, National Institutes of Health.

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Risk Stratification

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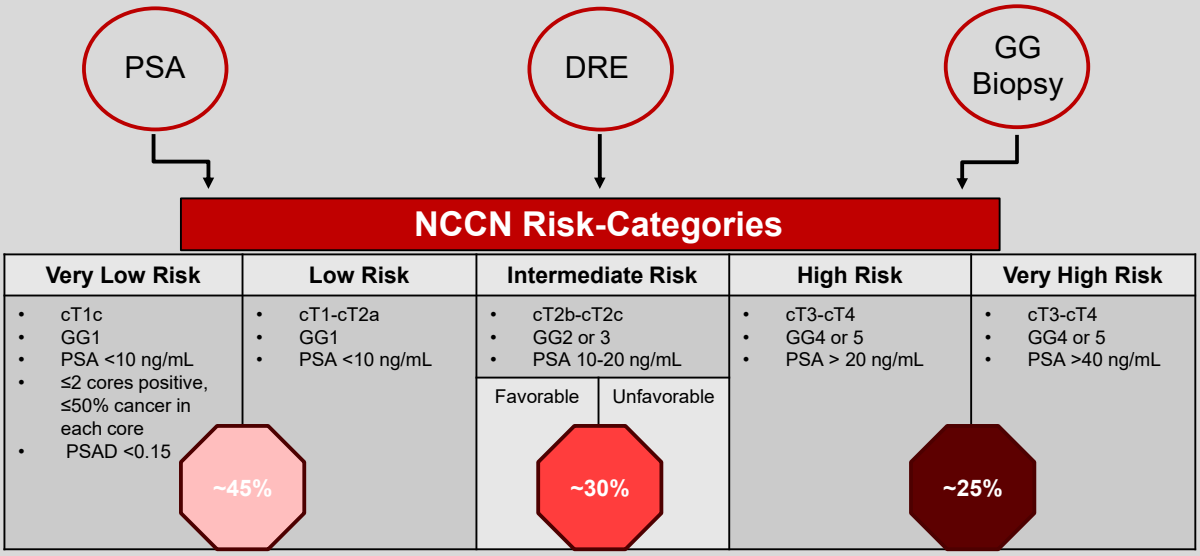
NCCN Risk-Categories



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Goals of Treatment

Optimize oncologic control and maximize quality-of-life.

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Risk Stratified Treatment

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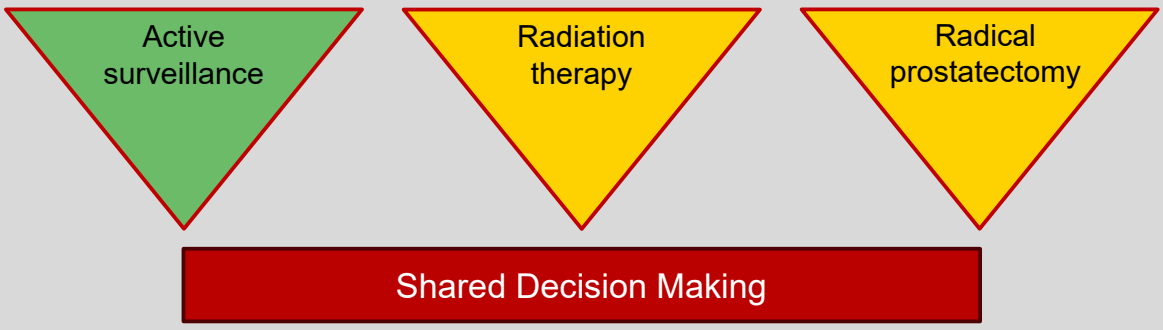
Management of VLR and LR PCa

VLR: Watchful waiting vs active surveillance, based on 10-year life expectancy.
LR: Current options include



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Active Surveillance

- Repeat PSA 6-monthly.
- Repeat confirmatory biopsy within 1 year, may use mp-MRI to guide decision.
- May consider genomic testing.

When do you change management?

- Patient decision
- Grade reclassification
- ↑ tumor volume

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Active Surveillance

- Safe approach with over 2 decades of data.

Cohort	Toronto[5,7,8]	Johns Hopkins[4,9-11]	UCSF		Canary PASS[14]	Cooley/Catalona Meta-Dataset[6]	PRIAS[15]
			Initial Cohort[12]	Newer Cohort[13]			
No. patients	993	1298	321	810	2155	6775	5302
Median age (y)	68	66	63	62	63	64	66
Core involvement and risk groups	% of cohort with ≤2 positive cores, 69 25% IR (D'Amico criteria)	Median # positive cores, 1	Mean % positive cores, 20.3%	Not available	Median % positive cores, 12.5% 17% NCCN IR/HR	% of cohort with ≤2 positive cores, 77.6	% of cohort with ≤2 positive cores, 99
Median follow-up (months)	77	60	43	60	86	80	120
Conversion to treatment*	36.5% (10-y)	50% (10-y)	24% (3-y)	40% (5-y)	49% (10-y)	33% (6.7-y)	52% (5-y) 73% (10-y)
Systemic progression Lymph node involvement and/or metastasis	3.1% (1.8% distant metastases; 1.3% positive lymph nodes) 6.6% systemic progression in IR group	0.15% distant metastases 0.08% positive lymph nodes	0% distant metastases 0.2% positive lymph nodes	0.1%	0.5% distant metastases 0.5% positive lymph nodes	0.4%	0.2%
Cancer-specific survival	98% (10-y)	99.9% (10-y)	100% (5-y)	100% (5-y)	99.9% (10-y)	99.8% (6.7-y)	>99% (10-y)
Overall survival	80% (10-y)	93% (10-y)	98% (10-y)	98% (5-y)	94.3% (10-y)	—	—

At 10-yrs: **~60%** remain free of radical treatment.

NCCN Guidelines 2025.

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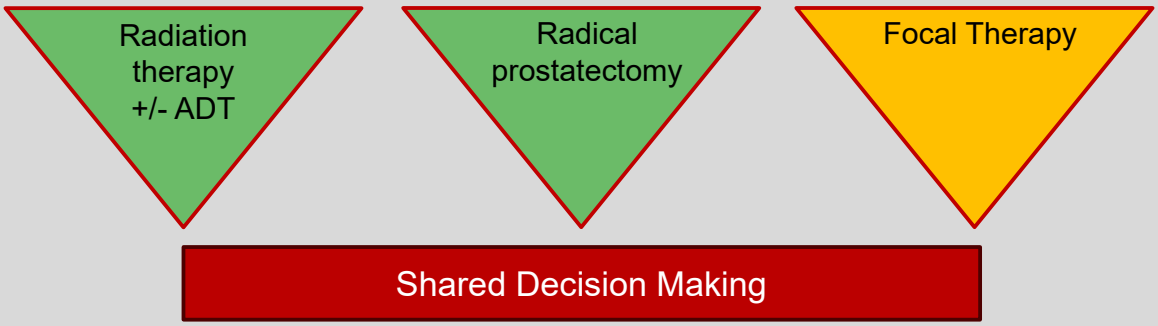
Management of Fav or Unfav-IR PCa

F-IR: RT alone vs RARP vs focal therapy (as part of a trial only).
UF-IR: RT w ADT (6 months) vs RARP.



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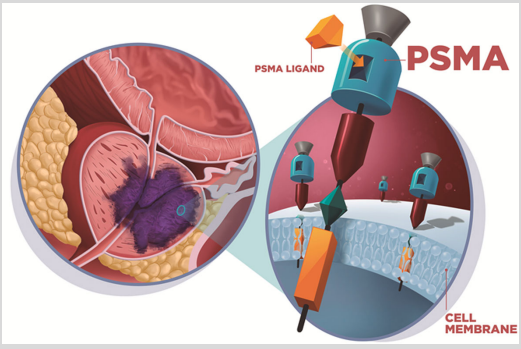
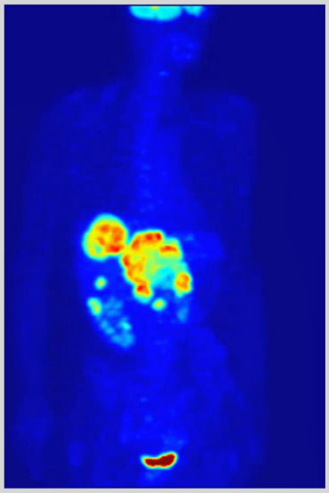
PSMA PET Scan For TNM Staging





Wikimedia Foundation, Inc.

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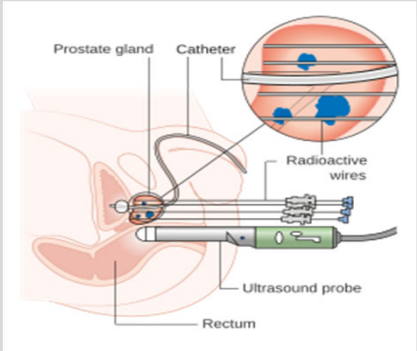
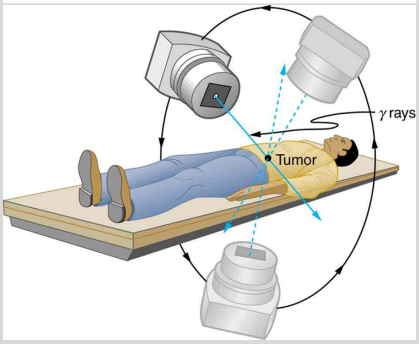
Radiation Therapy

- RT when used as definitive therapy can be through:

- Brachytherapy (BT)
  OR
- External beam radiotherapy (EBRT)





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Radical Prostatectomy

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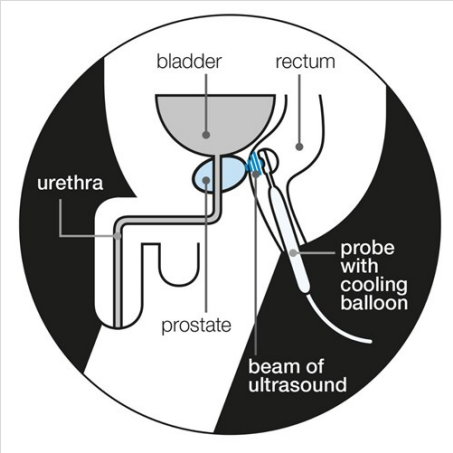
Focal Therapy

- Treating the “index lesion”.
- By performing “organ-sparing” treatment, the side-effects of treatment are considerably lessened.
- ~100% continent at 12-months.
- ~85% potent at 12-months.



PROSTATE CANCER UK

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Focal Therapy

Oncological Outcomes after Focal Therapy

Study	Year	Cohort	HIFU Template	Post-HIFU Biopsy				Oncological Outcomes			
				Biopsy Cohort	Biopsy Indication	Time to Biopsy	Biopsy Template (Treated-area only or Whole-gland)	Residual Cancer, Any	Residual Cancer, GS>7	Secondary Treatment Rate[a]	Radical Treatment Rate
Abreu	2020	100	HG	58 (58%)	Protocol or Clinically Indicated[b]	6-12 m	Whole Gland	32 of 58 (55.2%)	18 of 58 (31.0%)	17 of 89 (19.1%)	8 of 89 (9.0%)
Mortezavi	2019	75	F	68 (90.6%)	Protocol	6 m	Whole Gland	38 of 68 (55.9%)	28 of 68 (41.2%)	12 of 68 (17.6%)	6 of 68 (8.8%)
Bass	2018	150	PG	87 (58.0%)	Protocol	15 m[c]	Whole Gland	61 of 87 (70.1%)	37 of 87 (42.5%)	37 of 150 (24.7%)	20 of 150 (13.3%)
Rischmann	2017	111	HG	101 (90.9%)	Protocol	1 y	Whole Gland	33 of 101 (32.7%)	12 of 101[d] (11.9%)	18 of 101 (17.8%)	15 of 101[d] (14.6%)
Van Velthoven	2016	50	HG w/wo TURP	8 (16.0%)	Phoenix BCF	NA	Whole Gland	6 of 8 (75%)	6 of 8 (75%)	NA	NA
Feijoo	2016	67	HG w/wo TURP	67 (100%)	Protocol	<1 y	Whole Gland	17 of 67 (25.4%)	NA	NA	NA
Ahmed	2015	56	F	52 (92.8%)	Protocol	6 m	Treated or mp-MRI Suspicious Lesions	22 of 52 (42.3%)	10 of 52 (19.2%)	4 of 52 (7.8%)	2 of 52 (3.8%)
Shoji	2015	45	HG[e]	45 (100%)	Protocol	6 m	Limited Whole Gland[f]	4 of 45 (9.0%)	NA	3 of 45 (6.7%)	1/45 (2.2%)
Ghai[g]	2015	4	F	4 (100%)	Protocol	6 m	Whole Gland	4 of 4 (100%)	0	0	0
Ahmed	2012	41	F	39 (95.1%)	Protocol	6 m	Treated or mp-MRI Suspicious lesions	9 of 39 (23.1%)	3 of 39 (7.7%)	4 of 39 (10.3%)	0
Ahmed	2011	20	HG	19 (95.0%)	Protocol	6 m	Treated or mp-MRI Suspicious lesions	2 of 19 (10.5%)	0	1 of 19 (5.3%)	0
El Fegoun	2011	12	HG	12 (100%)	Protocol or Rising PSA	1 y	Limited Whole Gland[f]	1 of 12 (8.3%)	0	5 of 12 (41.6%)	4 of 12 (33.3%)

Sood et al. Eur Urol 2024.

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Management of Fav or Unfav-IR PCa

- Surgery
  - Oncological efficacy (90+% at 15-yrs)
  - Long-term urinary continence (98%)
  - ED recovery (50%)
  - Invasive
  - Down-time
- Radiation
  - Oncological efficacy (85+% at 15-yrs)
  - Long-term urinary continence (98%)
  - ED recovery (75%)
  - Bowel side-effects
  - Second primary cancers
  - Effects of ADT
  - Non-Invasive

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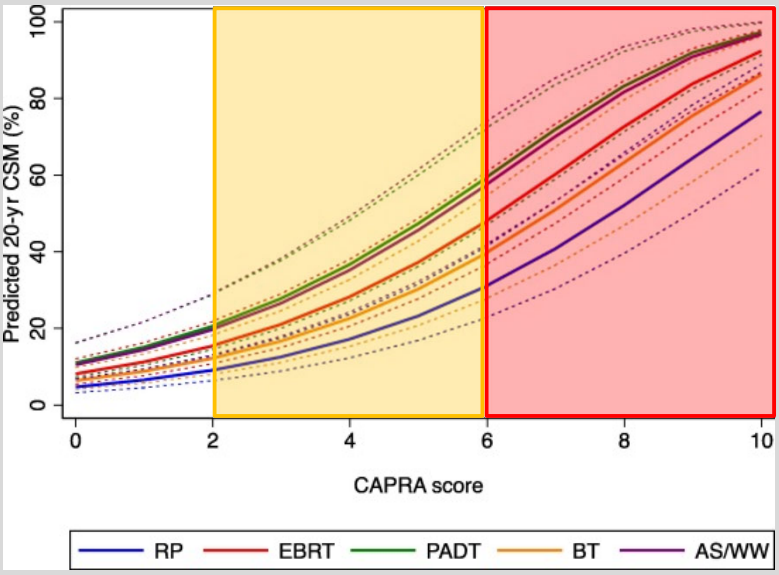
Management of Fav or Unfav-IR PCa



Herlemann et al. Eur Urol 2024.

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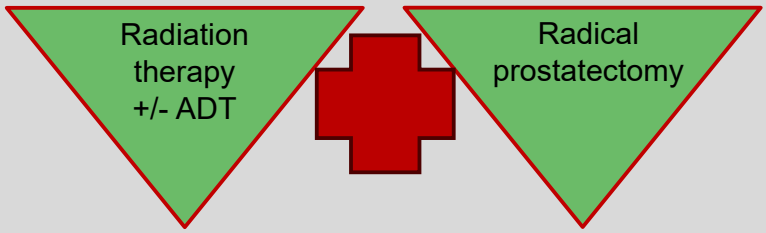
Management of HR and VHR PCa

Multimodal treatment is the rule.



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Summary

Treatment for localized prostate cancer is highly successful.

Management is highly individualized and multidisciplinary in the modern era.

Ongoing research efforts in this space are directed towards better risk-stratification to allow precision guided medicine with evolving use of biomarkers, imaging, and newer surgical, focal, and radiotherapy techniques.

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