



# Grading and Risk Stratification in Prostate Cancer

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# وبینار تازه های درمانی سرطان پروستات

انجمن رادیوانکولوژی ایران شاخه اصفهان برگزار می کند

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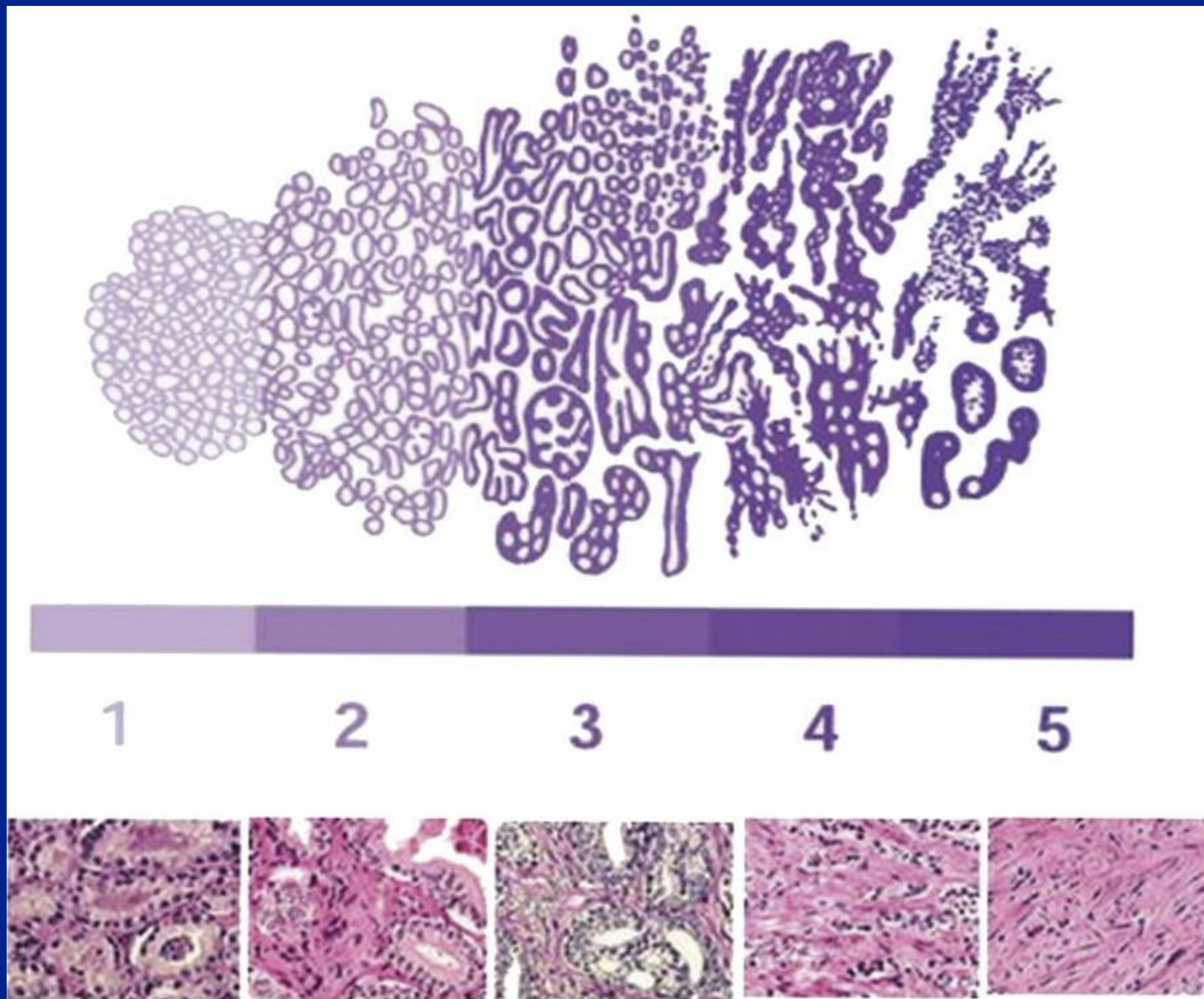


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# Prostate Cancer Grading







## Gleason Score

6

7

8

9

10



Gleason score	ISUP grade
2-6	1
7 (3+4)	2
7 (4+3)	3
8 (4+4 or 3+5 or 5+3)	4
9-10	5



## 5 year BCR free progression rate following RP:

- 96%
- 88%
- 63%
- 48%
- 26%

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# Risk Stratification



## Risk grouping systems

- (D'Amico, EAU, NICE, GUROC, AUA, NCCN, and CPG)

## Risk scores

- (CAPRA)

## Nomograms

- (MSKCC)





# End Point

Biochemical Recurrence

Progression free survival

Capra

Cancer specific death

The CPG system

MSKCC nomogram



# D'Amico Risk Classification

Risk group	Parameters
Low risk	PSA $\leq$ 10 ng/mL and Gleason score 6 (Gleason grade group I) and cT category 1c, 2a
Intermediate risk	PSA $>$ 10 to $\leq$ 20 ng/mL or Gleason score 7 (Gleason grade groups II and III) or cT category 2b
High risk	PSA $>$ 20 ng/mL or Gleason score $\geq$ 8 (Gleason grade groups IV and V) or cT category 2c

System	Very low risk	Low risk	Intermediate risk		High risk	Very high risk
			Favorable	Unfavorable		
D'Amico		PSA $\leq$ 10 and GS $\leq$ 6 and cT1c-2a	PSA >10-20 or GS 7 or cT2b		PSA > 20 or GS 8-10 or cT2c	
EAU		PSA <10 and GS $\leq$ 6 (ISUP 1) and cT1c-2a	PSA 10-20 or GS 7 (ISUP 2-3) or cT2b		PSA > 20 or GS >7 (ISUP 4-5) or cT2c	
NICE		PSA <10 and GS $\leq$ 6 and cT1-2a	PSA 10-20 or GS 7 or cT2b		PSA > 20 or GS 8-10 or $\geq$ cT2c	
GUROC		PSA $\leq$ 10 and GS $\leq$ 6 and cT1-2a	PSA $\leq$ 20 and GS $\leq$ 7 and cT1-2 not otherwise low-risk		PSA > 20 or GS 8-10 or $\geq$ cT3a	
AUA	PSA <10 and ISUP 1 and cT1-2a and <34% positive cores and 0 cores with >50% cancer and PSAD <0.15	PSA <10 and ISUP 1 and cT1-2a	PSA 10-<20 or ISUP 2-3 or cT2b-2c		PSA $\geq$ 20 or ISUP 4-5 or $\geq$ cT3	
AUA_i	PSA <10 and ISUP 1 and cT1-2a and <34% positive cores and no cores with >50% cancer and PSAD <0.15	PSA <10 and ISUP 1 and cT1-2a	ISUP 1 and PSA 10-<20 or ISUP 2 and PSA <10	ISUP 2 and (PSA 10-<20 or cT2b-2c) or ISUP 3 and PSA <20	PSA $\geq$ 20 or ISUP 4-5 or $\geq$ cT3	
NCCN	PSA <10 and GS $\leq$ 6 (ISUP 1) and cT1c and <3 positive cores and $\leq$ 50% cancer in each core and PSAD <0.15	PSA <10 and GS $\leq$ 6 (ISUP 1) and cT1-2a	PSA 10-20 or GS 3+4 (ISUP 2) or cT2b-2c and <50% positive cores	PSA 10-20 or GS 3+4/4+3 (ISUP 2-3) or cT2b-2c	PSA > 20 or GS 4+4/4+5 (ISUP 4-5) or cT3a	GG1 5 or >4 cores with GS8-10 (ISUP 4-5) or cT3b-4
CPG		PSA <10 and GS 6 (ISUP 1) and cT1-T2	PSA 10-20 or GS 3+4 (ISUP 2) and cT1-T2	PSA 10-20 and GS 3+4 (ISUP 2) and cT1-T2 or GS 4+3 (ISUP 3) and cT1-T2	PSA > 20 or GS 8 (ISUP 4) or cT3	More than one of PSA > 20, GS 8 (ISUP 4), cT3 or GS 9-10 (ISUP 5) or cT4



# EAU/ESMO

Definition			
Low-risk	Intermediate-risk	High-risk	
PSA < 10 ng/mL and GS < 7 (ISUP grade 1) and cT1-2a	PSA 10-20 ng/mL or GS 7 (ISUP grade 2/3) or cT2b	PSA > 20 ng/mL or GS > 7 (ISUP grade 4/5) or cT2c	any PSA any GS (any ISUP grade) cT3-4 or cN+
Localised			Locally advanced



# NCCN

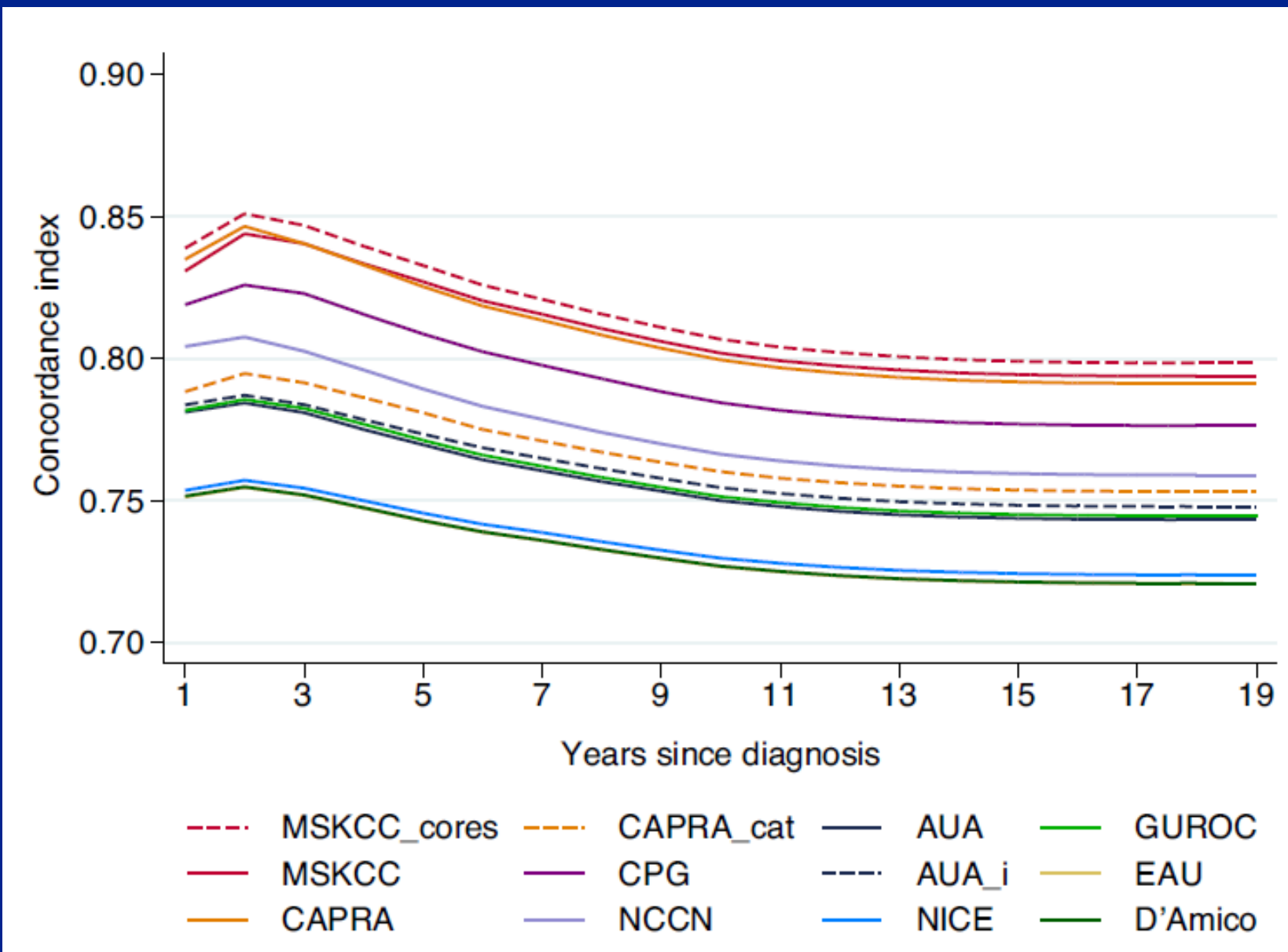
Very low <sup>e</sup>	Has all of the following: <ul style="list-style-type: none"> <li>• cT1c</li> <li>• Grade Group 1</li> <li>• PSA &lt;10 ng/mL</li> <li>• Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core</li> <li>• PSA density &lt;0.15 ng/mL/g</li> </ul>		
Low <sup>e</sup>	Has all of the following but does not qualify for very low risk: <ul style="list-style-type: none"> <li>• cT1–cT2a</li> <li>• Grade Group 1</li> <li>• PSA &lt;10 ng/mL</li> </ul>		
Intermediate <sup>e</sup>	Has all of the following: <ul style="list-style-type: none"> <li>• No high-risk group features</li> <li>• No very-high-risk group features</li> <li>• Has one or more intermediate risk factors (IRFs):             <ul style="list-style-type: none"> <li>▶ cT2b–cT2c</li> <li>▶ Grade Group 2 or 3</li> <li>▶ PSA 10–20 ng/mL</li> </ul> </li> </ul>	Favorable intermediate	Has all of the following: <ul style="list-style-type: none"> <li>• 1 IRF</li> <li>• Grade Group 1 or 2</li> <li>• &lt;50% biopsy cores positive (eg, &lt;6 of 12 cores)<sup>f</sup></li> </ul>
		Unfavorable intermediate	Has one or more of the following: <ul style="list-style-type: none"> <li>• 2 or 3 IRFs</li> <li>• Grade Group 3</li> <li>• ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)<sup>f</sup></li> </ul>
High	Has no very-high-risk features and has exactly one high-risk feature: <ul style="list-style-type: none"> <li>• cT3a OR</li> <li>• Grade Group 4 or Grade Group 5 OR</li> <li>• PSA &gt;20 ng/mL</li> </ul>		
Very high	Has at least one of the following: <ul style="list-style-type: none"> <li>• cT3b–cT4</li> <li>• Primary Gleason pattern 5</li> <li>• 2 or 3 high-risk features</li> <li>• &gt;4 cores with Grade Group 4 or 5</li> </ul>		





# CPG

Cambridge Prognostic Group (CPG) classification			
CPG	Criteria	10-year risk of dying from prostate cancer without treatment* (%)	10-year risk of dying from prostate cancer with treatment* (%)
1	Gleason score 6 (grade group 1) AND PSA < 10 ng/ml AND stages T1-T2	4.2	1.2
2	Gleason score 3 + 4 = 7 (grade group 2) OR PSA 10-20 ng/ml AND stages T1-T2	4.7	2.3
3	Gleason score 3 + 4 = 7 (grade group 2) AND PSA 10-20 ng/ml AND stages T1-T2 OR Gleason score 4 + 3 = 7 (grade group 3) AND stages T1-T2	15.1	3.2
4	One of the following: Gleason score 8 (grade group 4) OR PSA > 20 ng/ml OR stage T3	N/A**	5.8
5	Any combination of Gleason score 8 (grade group 4), PSA > 20 ng/ml or stage T3 OR Gleason score 9-10 (grade group 5) OR stage T4	N/A**	13.7





MSKCC nomogram (c-index: 0.81, 95% CI: 0.80– 0.81)

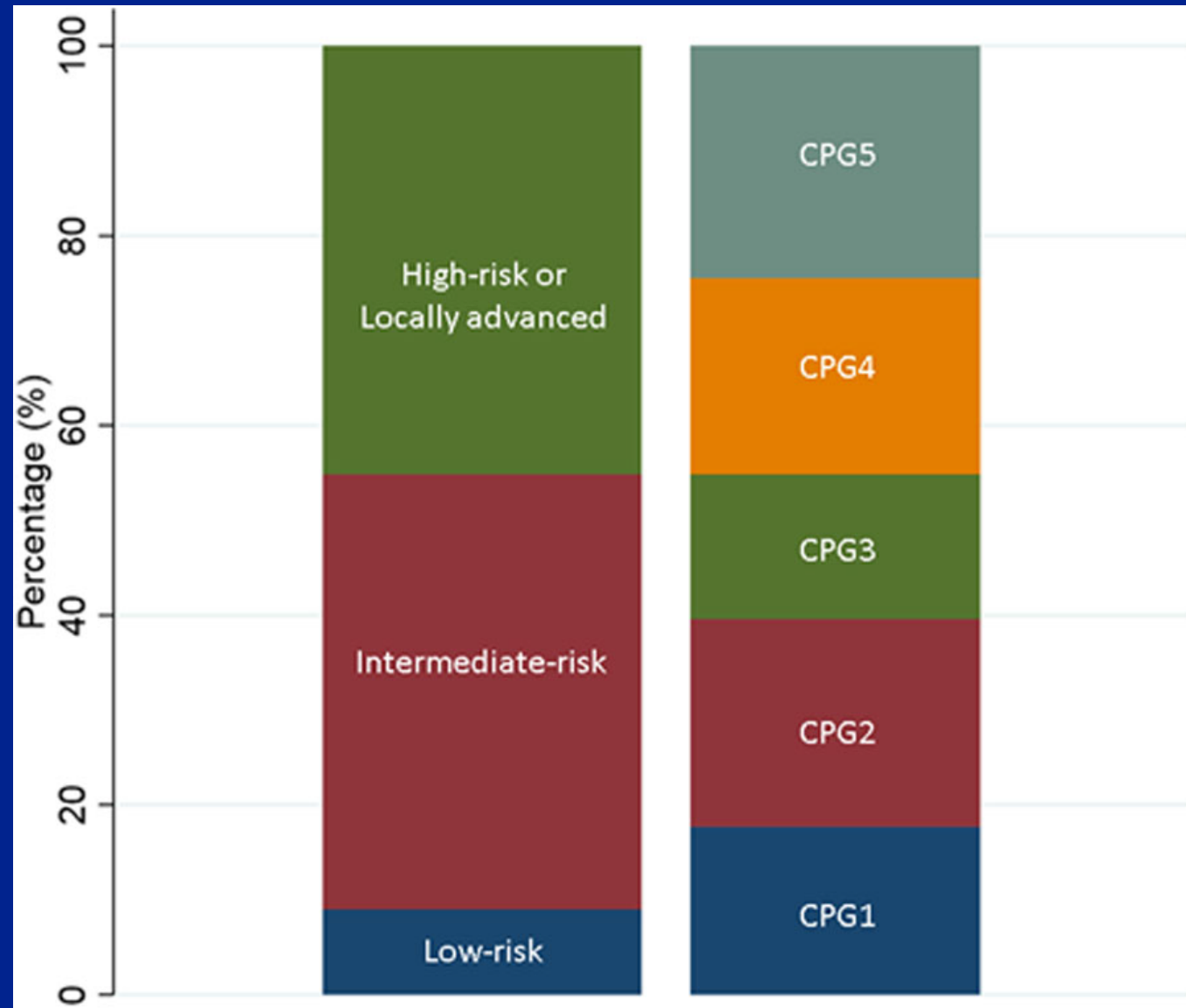
CAPRA score (c-index: 0.80, 95% CI: 0.79– 0.81)

CPG (c-index: 0.78, 95% CI: 0.78–0.79)

D'Amico and D'Amico-derived systems performed similarly  
(C-index: 0.73–0.77).



Very low <sup>e</sup>	Has all of the following: <ul style="list-style-type: none"> <li>• cT1c</li> <li>• Grade Group 1</li> <li>• PSA &lt;10 ng/mL</li> <li>• Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core</li> <li>• PSA density &lt;0.15 ng/mL/g</li> </ul>		
Low <sup>e</sup>	Has all of the following but does not qualify for very low risk: <ul style="list-style-type: none"> <li>• cT1–cT2a</li> <li>• Grade Group 1</li> <li>• PSA &lt;10 ng/mL</li> </ul>		
Intermediate <sup>e</sup>	Has all of the following: <ul style="list-style-type: none"> <li>• No high-risk group features</li> <li>• No very-high-risk group features</li> <li>• Has one or more intermediate risk factors (IRFs):             <ul style="list-style-type: none"> <li>▶ cT2b–cT2c</li> <li>▶ Grade Group 2 or 3</li> <li>▶ PSA 10–20 ng/mL</li> </ul> </li> </ul>	Favorable intermediate	Has all of the following: <ul style="list-style-type: none"> <li>• 1 IRF</li> <li>• Grade Group 1 or 2</li> <li>• &lt;50% biopsy cores positive (eg, &lt;6 of 12 cores)<sup>f</sup></li> </ul>
		Unfavorable intermediate	Has one or more of the following: <ul style="list-style-type: none"> <li>• 2 or 3 IRFs</li> <li>• Grade Group 3</li> <li>• ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)<sup>f</sup></li> </ul>
High	Has no very-high-risk features and has exactly one high-risk feature: <ul style="list-style-type: none"> <li>• cT3a OR</li> <li>• Grade Group 4 or Grade Group 5 OR</li> <li>• PSA &gt;20 ng/mL</li> </ul>		
Very high	Has at least one of the following: <ul style="list-style-type: none"> <li>• cT3b–cT4</li> <li>• Primary Gleason pattern 5</li> <li>• 2 or 3 high-risk features</li> <li>• &gt;4 cores with Grade Group 4 or 5</li> </ul>		







Discrimination does not necessarily improve by simply subdividing the standard risk groups

**NCCN:**

very low and low (C-index at 10 yr: 0.76 vs 0.76)

favorable and unfavorable risk (C-index at 10 yr: 0.76 vs 0.77)

very high and high risk (C-index at 10 yr: 0.75 vs 0.76)



# Conclusion

Use nomograms for individual **counseling**

Use risk groups in choosing **treatment** option

**Genetic tests** may incorporate into future tools

- Decipher
- Oncotype Dx
- Prolaris