

# VALIDATION OF AN ACTIVE SURVEILLANCE THRESHOLD FOR THE CCP SCORE IN CONSERVATIVELY MANAGED MEN WITH LOCALIZED PROSTATE CANCER

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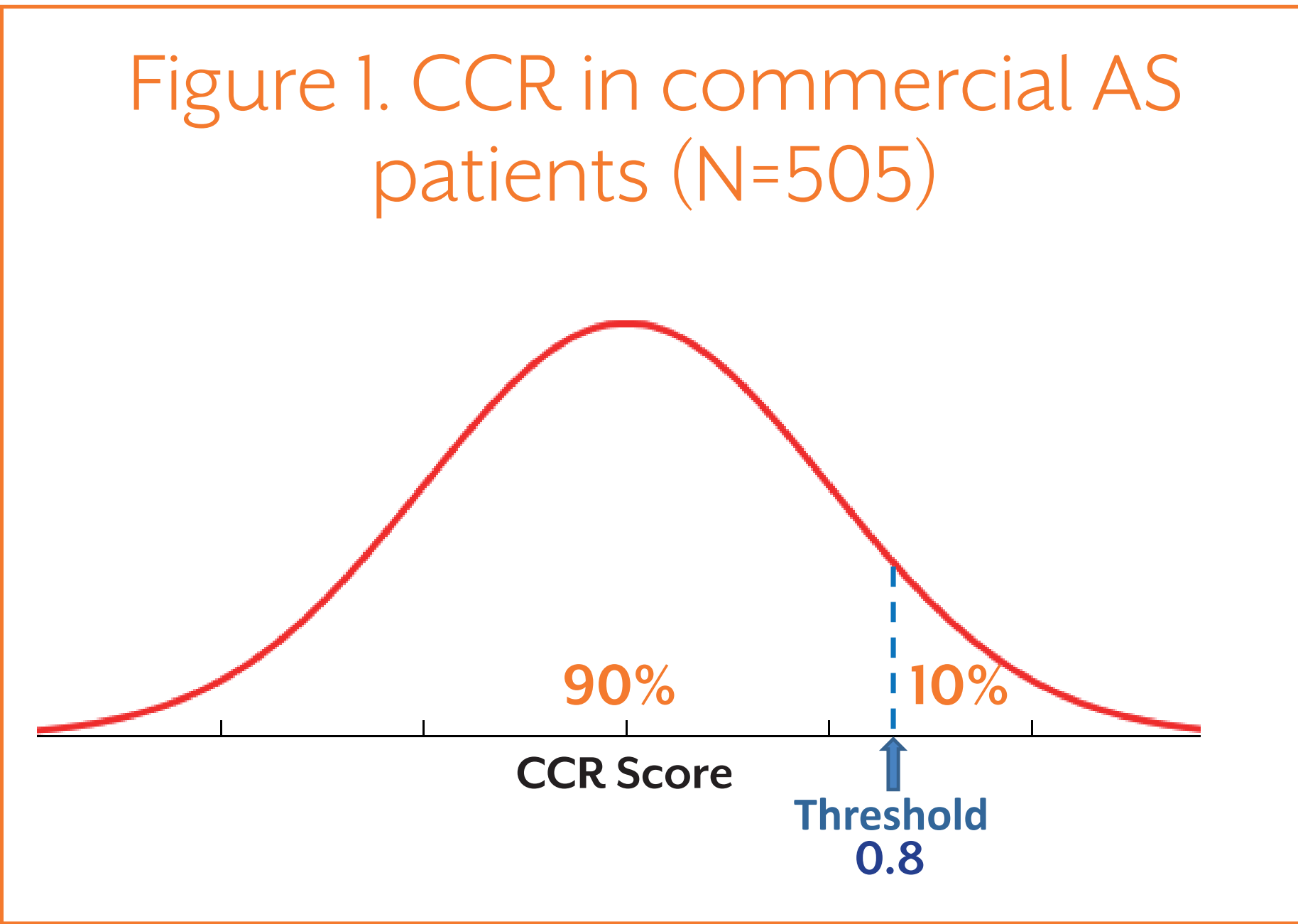
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## INTRODUCTION

- Active surveillance (AS) is an increasingly popular treatment modality for men with localized prostate cancer.
- However, better risk stratification is needed to appropriately select men for AS.
- The cell cycle progression (CCP) score, based on measuring the expression levels of CCP genes, has proven to be a robust predictor of prostate cancer outcomes in various clinical settings including in conservatively managed cohorts.<sup>1-6</sup>
- Here, we present a validation of an AS threshold for a predefined score that combines CCP with CAPRA (combined clinical CCP risk (CCR) score) for predicting prostate cancer mortality (PCM) in conservatively managed patients.

## METHODS

- We determined the CCR score distribution in 505 men who were tested in our clinical laboratory and, based on their clinical characteristics only, might typically be considered for AS.
  - The training cohort consisted of men with:
    - Gleason score  $\leq 3+4$
    - PSA  $< 10$  ng/ml
    - $< 25\%$  cores positive
    - Clinical stage  $\leq T2a$ .
- A threshold CCR score of 0.80 was selected such that 90% of the men in the training cohort had scores below the threshold.
- The performance characteristics of the threshold were then evaluated in two independent cohorts of conservatively managed men (TAPG1 [N= 180] and TAPG2 [N=585]).
- As reported previously, the CCP score was a strong prognostic indicator in both cohorts.<sup>2,6</sup>
- Survival data were censored at 10 years.



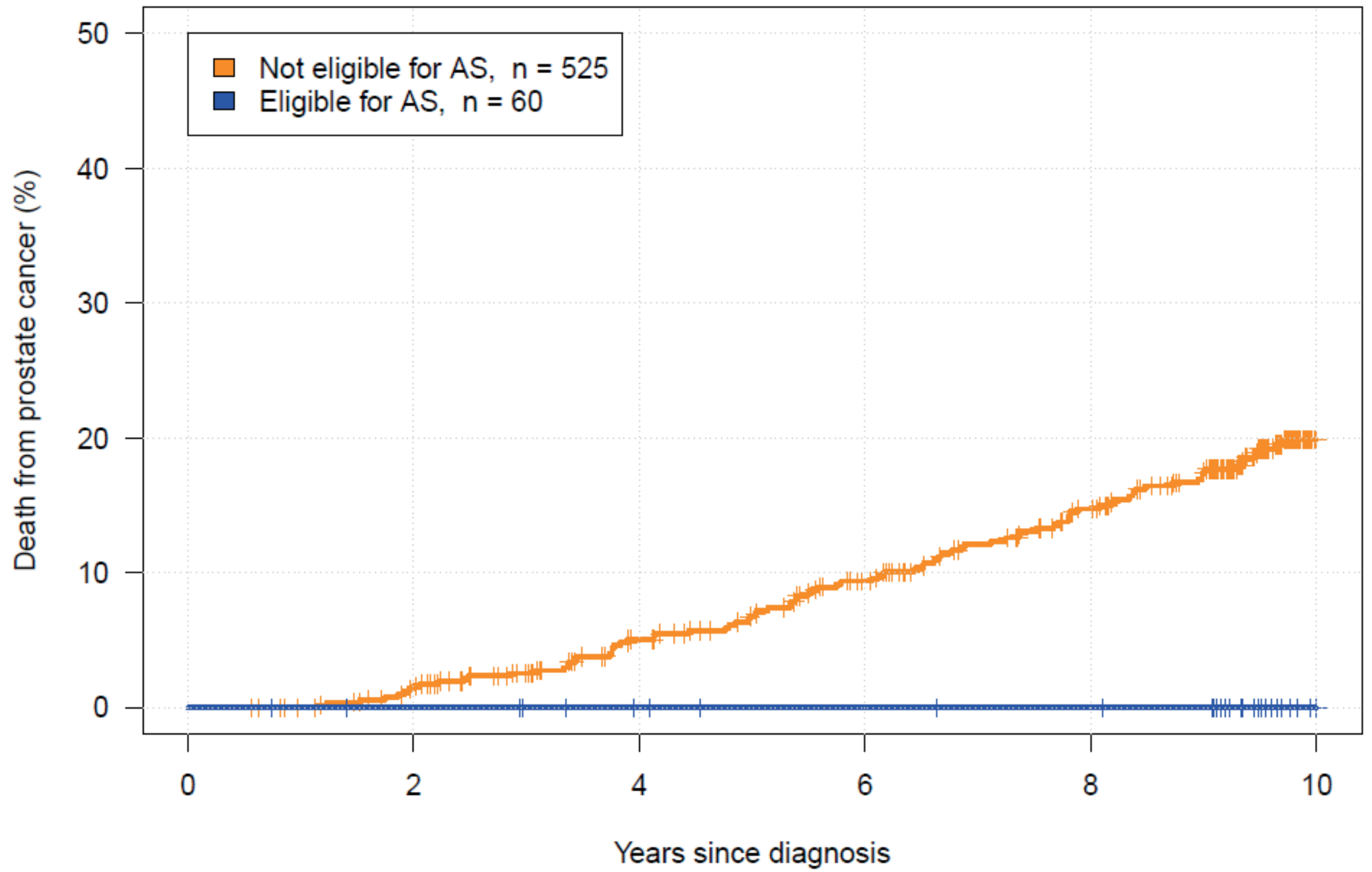
## RESULTS

- The primary pre-planned analysis called for evaluating the CCR threshold on TAPG2.
  - There were 60 men (of 585) below the threshold in the validation cohort and the threshold validated, dichotomizing the cohort into high and low risk groups (log rank P-value = 0.0008).
- For the combined cohort (TAPG1 and TAPG2), the average risk was 2.6% for men below the threshold and 21.4% for men above the threshold.
  - There were no prostate cancer deaths in patients below the threshold (Table 1).

Table 1. Patients meeting AS threshold in both cohorts.

	# Patients Meeting AS Threshold (# Prostate Cancer Deaths)		
	TAPG1	TAPG2	TAPG1 and TAPG2
AS = No (CCR > 0.8)	178 (33)	525 (87)	703 (120)
AS = Yes (CCR $\leq 0.8$ )	2 (0)	60 (0)	62 (0)

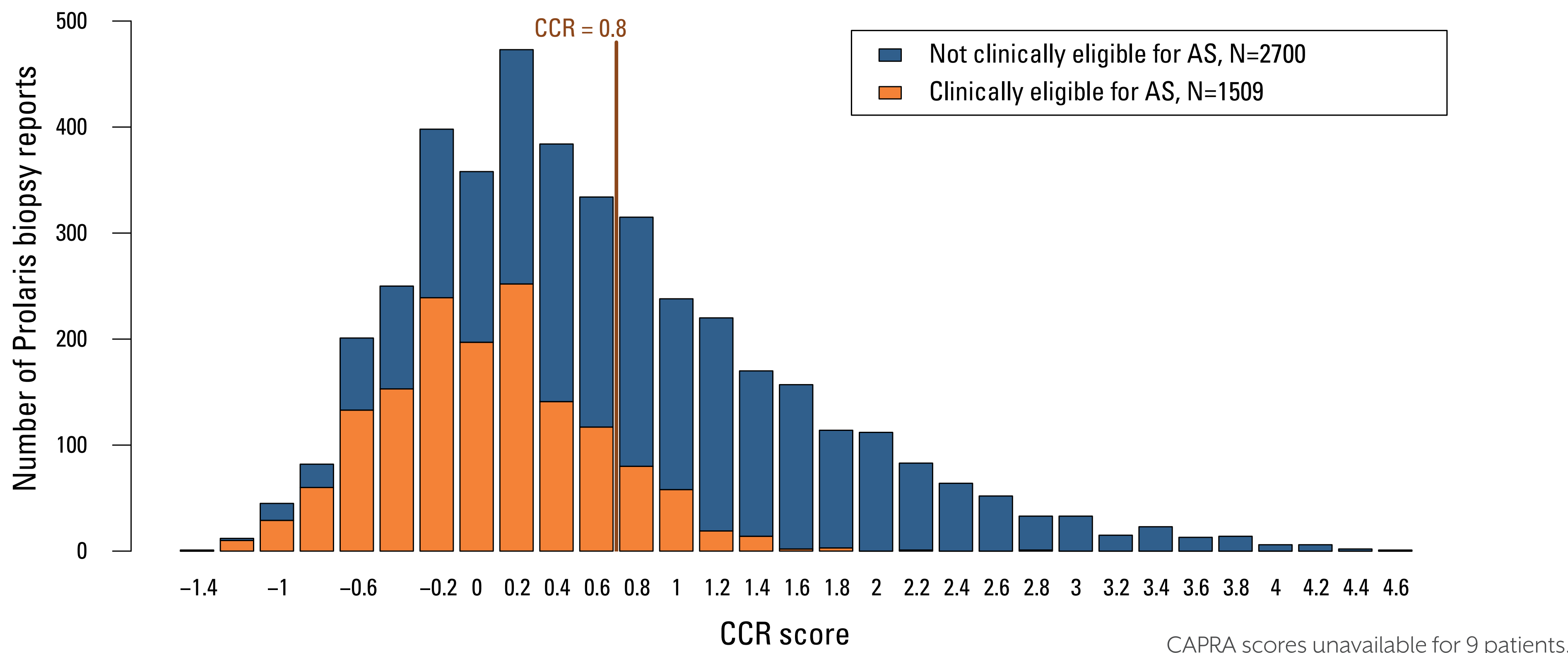
Figure 2. AS thresholds dichotomize patients by CCR score into significantly different groups. The criteria for AS is CCR  $\leq 0.8$ .



## RESULTS

- For the combined cohort (TAPG1 and TAPG2), the 10-year risk of PCM at the threshold was 3.2%.
- We have also evaluated this threshold in a commercially-tested cohort (N=4218) (Figure 3).
  - Thirty-six percent of patients would qualify for AS on clinical parameters alone. In contrast, 60% of patients fall below the AS threshold when CCP score is included in determining risk.

Figure 3. Application of AS threshold to modern clinical samples.



## CONCLUSIONS

- For patients considering deferred treatment, the CCR score provides significant prognostic information at disease diagnosis.
- The CCR risk threshold presented here is 'typical' for patients considering AS patients in the U.S., and it can be used to guide patient selection for AS based on an integrated view of risk assessment.

## REFERENCES

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