Refining PSA Density Cut-Offs for Risk Stratification in Patients with PI-RADS 3 Lesions

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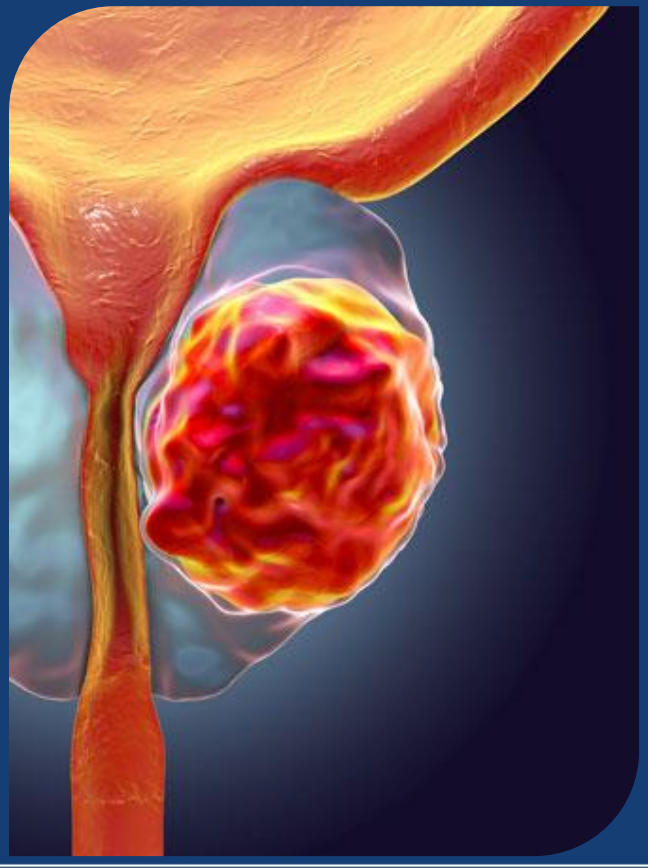

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11th Belgian Multidisciplinary Meeting on Urological Cancers

Conflicts of interest

I have no potential conflict of interest to report

Background

PI-RADS 3

PI-RADS

PI-RADS 1 = Very low - clinically significant cancer highly unlikely

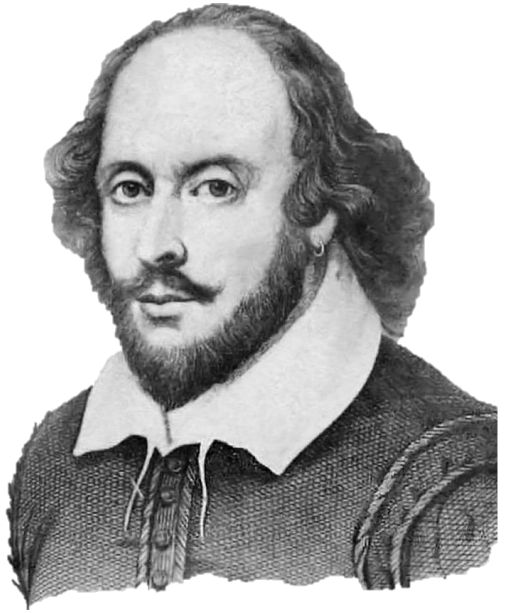
PI-RADS 2 = Low - clinically significant cancer unlikely

PI-RADS 3 = Intermediate - clinically significant cancer equivocal

PI-RADS 4 = High - clinically significant cancer likely

PI-RADS 5 = Very high - clinically significant cancer highly likely

To bx or not to bx, that is the question



Background

PI-RADS ≥3

45%

ISUP ≥2

PI-RADS 3

20%

ISUP ≥2

Real occurrence of csPCa following MRI-targeted biopsy in PI-RADS 3 lesions

≠ among different patient subgroups

4-29%

Purisko et al. 2020
Oerther et al. 2022
Schoots et al. 2018

Aim of the Study

To sub-stratify patients identified from a large European cohort of **patients** who underwent MRI-targeted and systematic biopsies for **PI-RADS 3** lesions and **to identify predictive factors of csPCa**

Patients and Methods

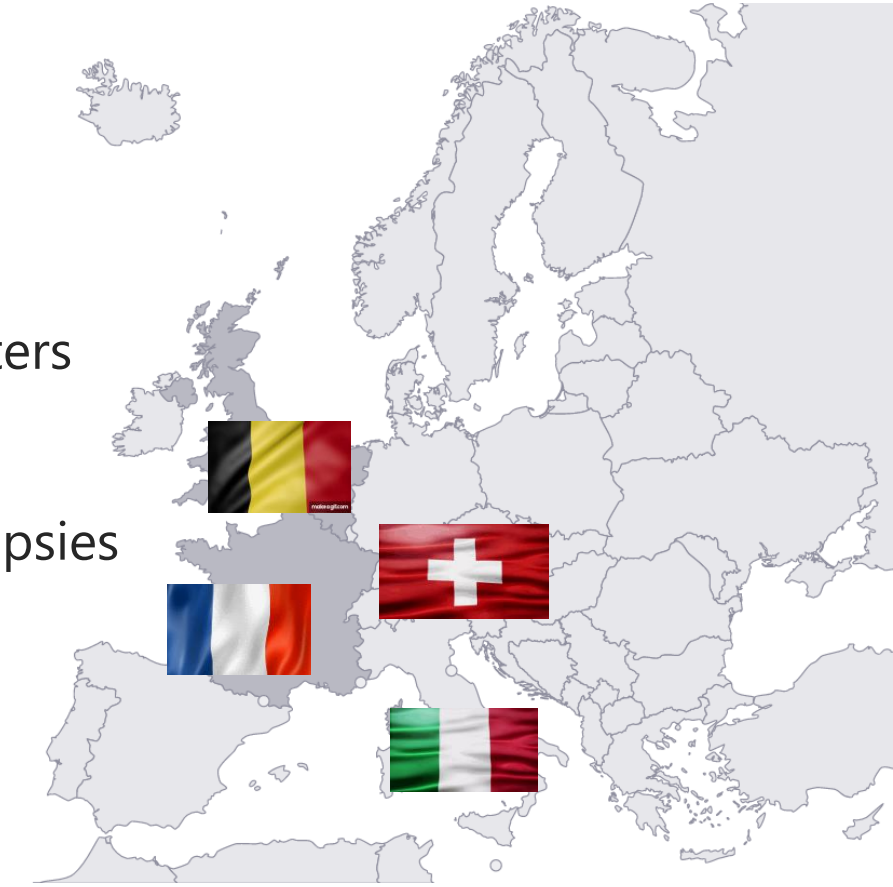
Population

4841 patients

11 European tertiary referral centers

MRI-targeted and systematic biopsies

January 2016 – April 2023



Patients and Methods

MRI and biopsy procedures

All prebiopsy MRI were performed within **6 months before biopsy**, following the ESUR guidelines and scored using the **PI-RADS version 2.1**

Dedicated Genitourinary Radiologist

Dedicated Urologist

Dedicated Uropathologist

KOELIS® system allowing elastic **MRI-3D ultrasound images fusion**

Patients and Methods

Selection criteria

PI-RADS 3 lesions

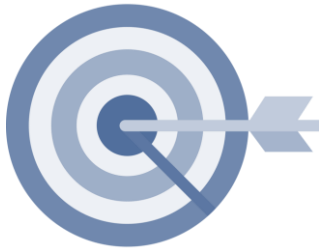
Exclusion criteria:

Missing information on clinical, radiological and biopsy data

Patients and Methods

Data collected

- Age
- PSA
- Clinical stage at DRE
- Prostate volume
- PSA density (PSAd)
- Maximum MRI lesion diameter
- Localization of lesion
- Previous biopsy status
- Biopsy approach
- Number of cores taken



Primary Outcome

The identification of <u>covariates</u> significantly associated with a risk of <u>csPCa</u> defined as an <u>ISUP grade group ≥2</u> on MRI-targeted and systematic biopsies

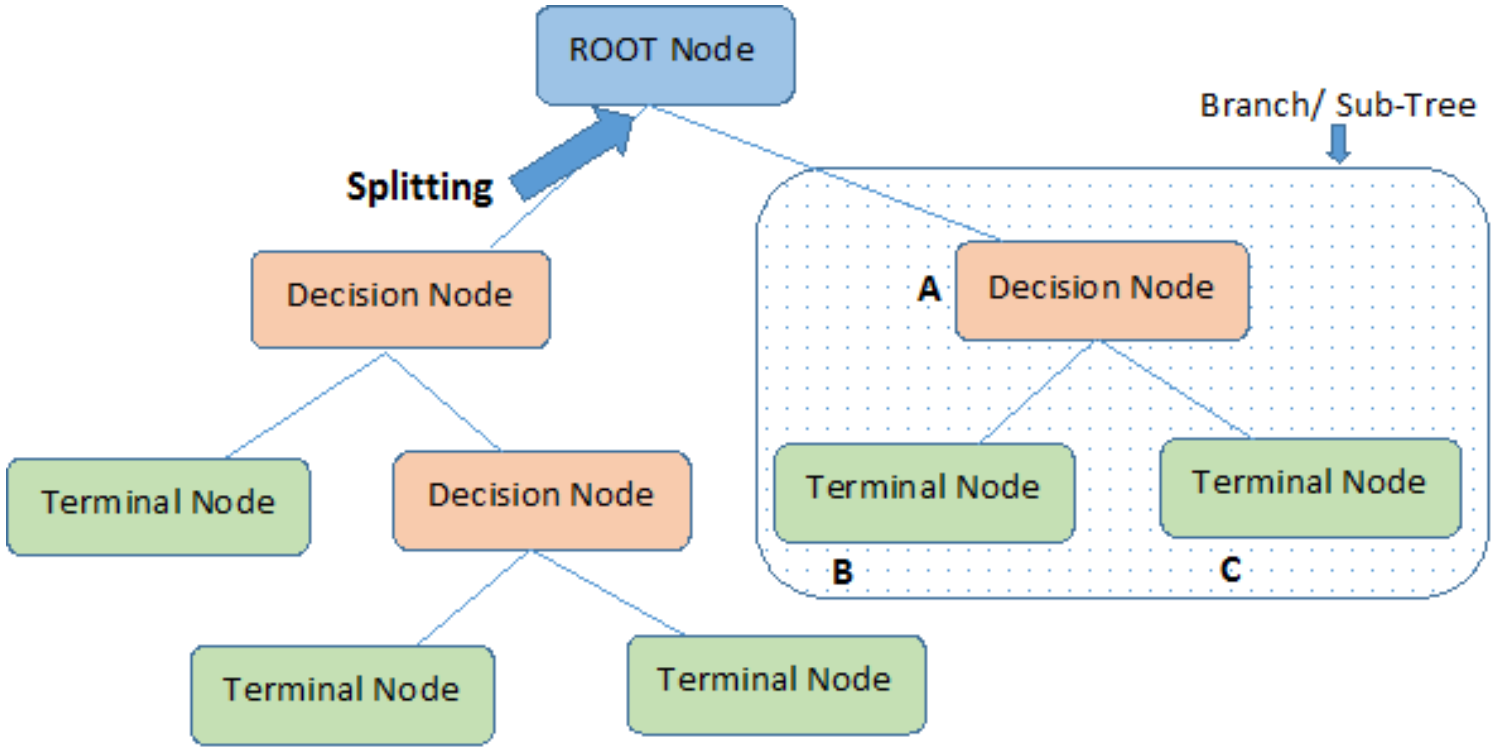
Patients and Methods

Statistical analysis

- **Descriptive statistics**
- **Multivariable logistic regression analysis**
  - ***Three models***:
    - Clinical
    - Clinical + Radiological
    - Clinical + Radiological + Previous biopsy status
  - ***Model evaluation according to TRIPOD recommendations***
    - AUC for discrimination
    - Internal validation by bootstrap
    - Calibration plots and DCA for assessment

Patients and Methods

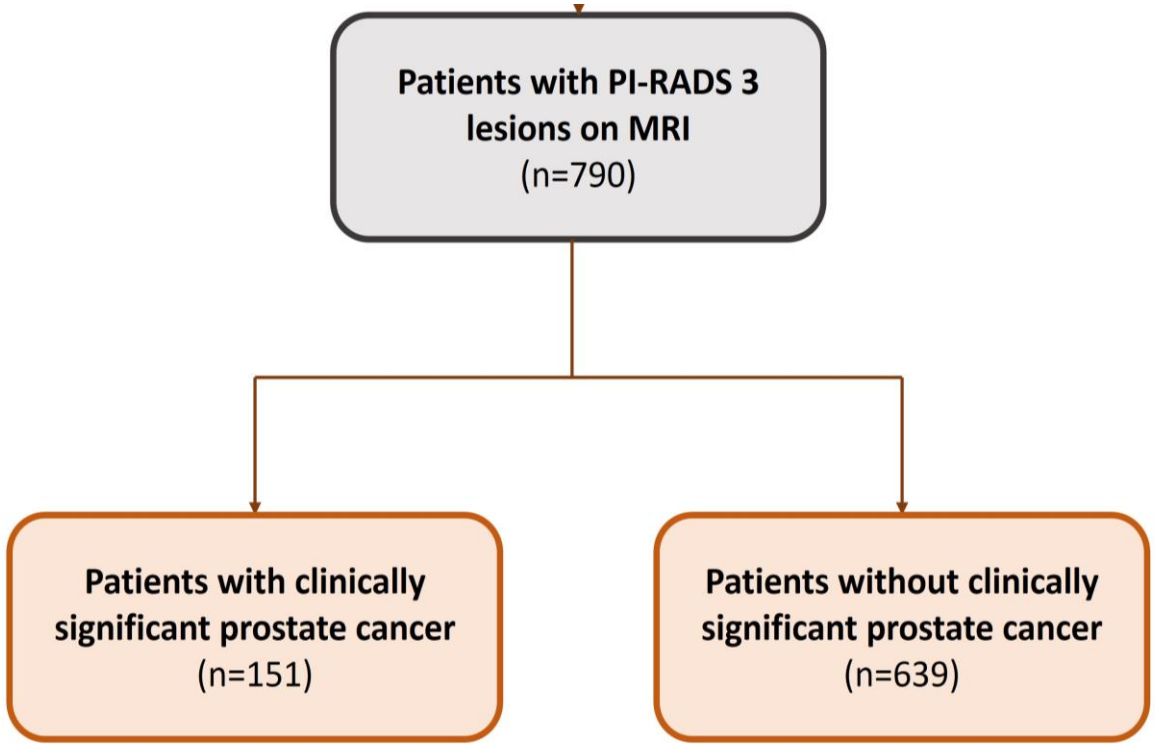
CHAID Analysis



Dependent **covariables** found to be **significant** on the logistic regression analysis were then **selected for further exploration using** a Chi-squared Automatic Interaction Detection (**CHAID**) analysis

Results

Patients' Characteristics



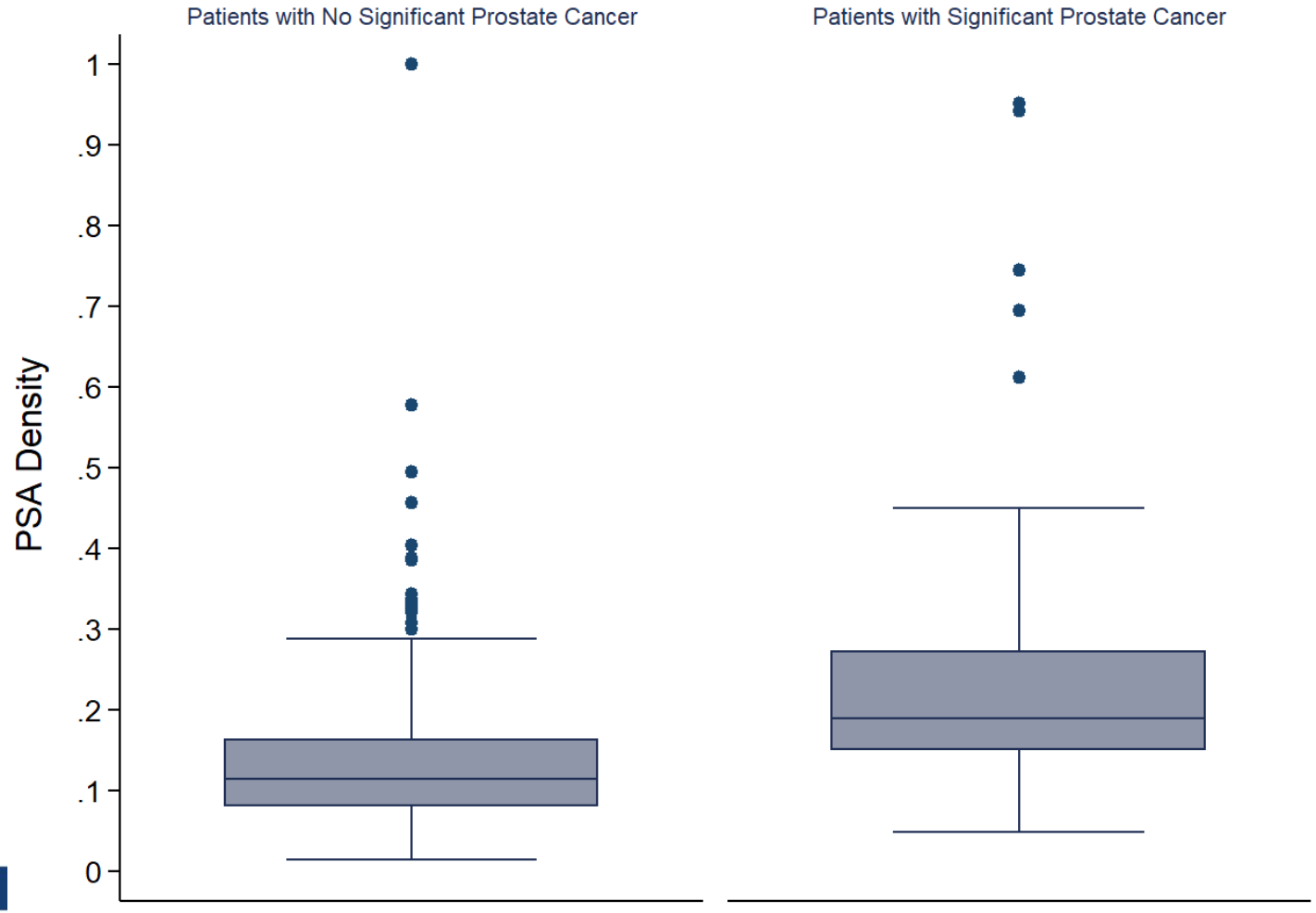
Variable		Whole population (n=790)	Clinically Significant Cancer (n=151)	No Clinically Significant Cancer (n=639)
Age, year (IQR)		65 (60-70)	68 (63-72)	65 (59-69)
Positive digital rectal exam, n(%)		85 (11%)	24 (16%)	61 (10%)
PSA density, ng/ml/cc (IQR)		0.13 (0.09 - 0.18)	0.19 (0.15-0.28)	0.11 (0.08 - 0.16)
Previous negative biopsy, n(%)		184 (23%)	27 (18%)	157 (25%)
Number of biopsy cores	Targeted	3 (3-4)	3 (3-4)	3 (3-4)
	Systematic	9 (7-12)	12 (12-13)	9 (7-12)
Highest ISUP GG on MRI-targeted biopsy, n(%)	No PCa	554 (72%)	38 (25%)	528 (85%)
	1	110 (14%)	9 (6%)	96 (15%)
	2	53 (7%)	57 (38%)	0 (0%)
	3	32 (4%)	27 (18%)	0 (0%)
	4	11 (1%)	13 (9%)	0 (0%)
	5	7 (1%)	6 (4%)	0 (0%)
Highest ISUP GG overall, n(%)	0	480 (61%)	0 (0%)	480 (75%)
	1	159 (20%)	0 (0%)	159 (25%)
	2	80 (10%)	80 (53%)	0 (0%)
	3	42 (5%)	42 (28%)	0 (0%)
	4	19 (2%)	4 (13%)	0 (0%)
	5	9 (1%)	5 (6%)	0 (0%)

Results

PSA density

Median PSAd :

- **0.19** ng/ml/cc (0.15-0.28) in patients with **csPCa**
- **0.11** ng/ml/cc (0.08-0.16) in patients with **non csPCa**



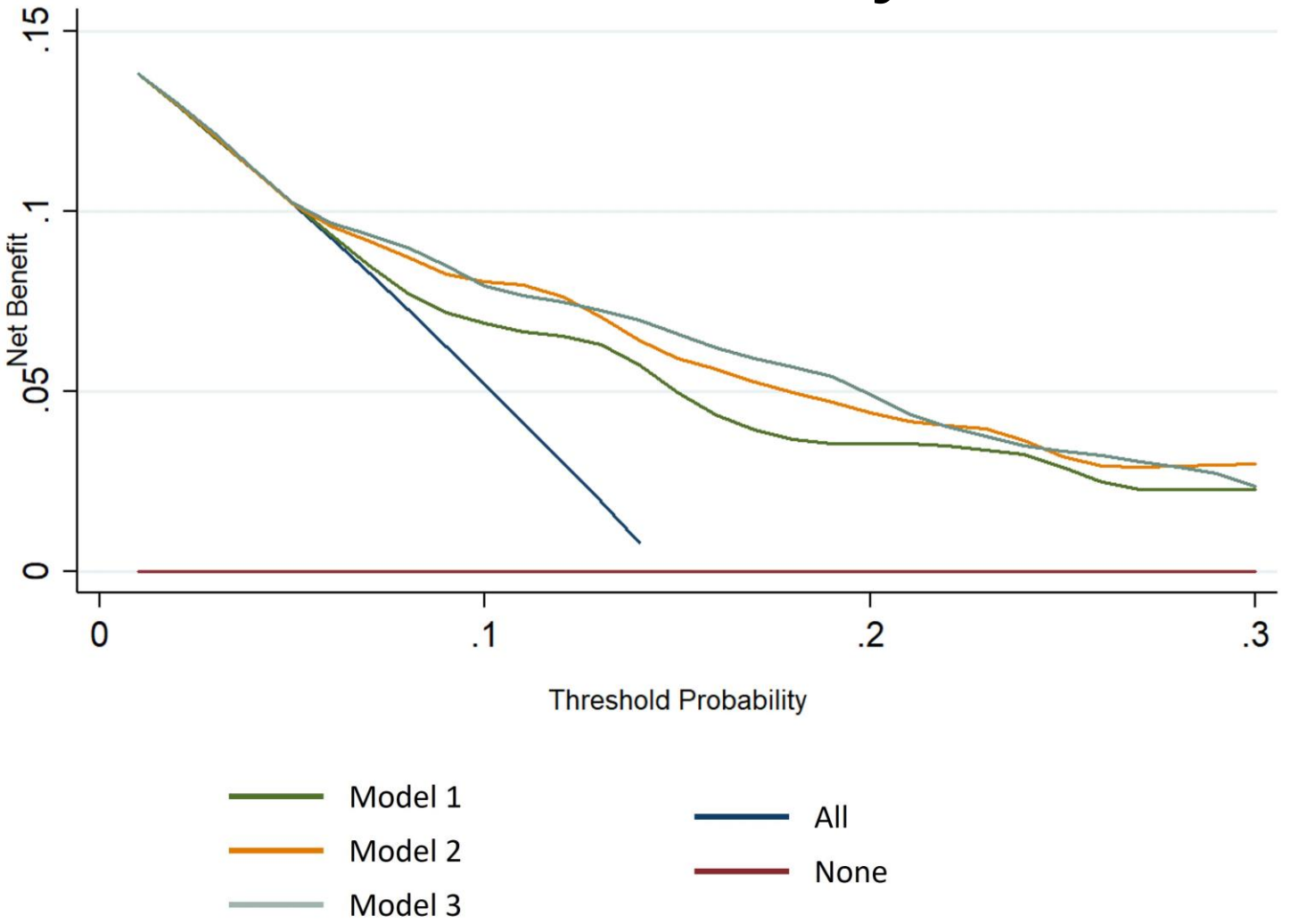
Results

Multivariable logistic regression

			Model 1		Model 2		Model 3	
			OR [95%CI]	p-value	OR [95%CI]	p-value	OR [95%CI]	p-value
Clinical parameters	PSA density		83 [10-699]	<0.001	1,434 [60-34,049]	<0.001	1,643 [2,717-41,997]	<0.001
	Age		1.0 [0.9-1.1]	0.05	1.1 [1.0-1.1]	0.02	1.1 [1.0-1.1]	0.01
	Digital rectal exam status		2.2 [0.8-6.2]	0.07	2.2 [0.8-6.3]	0.13	2.1 [0.7-5.9]	0.17
MRI parameters	Index lesion diameter		-	-	0.9 [0.8-1.0]	0.212	0.9 [0.9-1.0]	0.19
	Index lesion localization	Anterior	-	-	ref	ref	ref	ref
		Mid	-	-	2.0 [0.7-5.7]	0.18	2.3 [0.8-6.6]	0.12
		Posterior	-	-	1.8 [0.7-4.4]	0.2	1.8 [0.7-4.5]	0.19
	Previous biopsy status		-	-	-	-	0.6 [0.3-1.4]	0.21
Area Under the Curve (AUC) [95%CI]			0.77 [0.74-0.79]		0.78 [0.75-0.79]		0.79 [0.76-0.81]	

Results

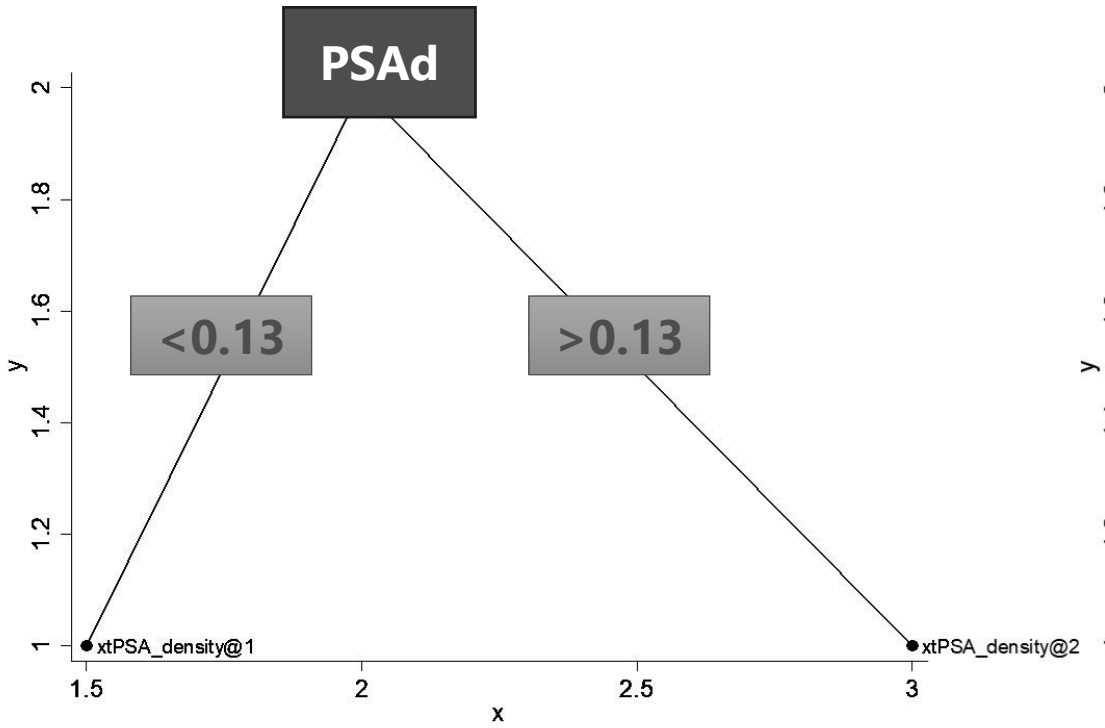
Decision curve analyses

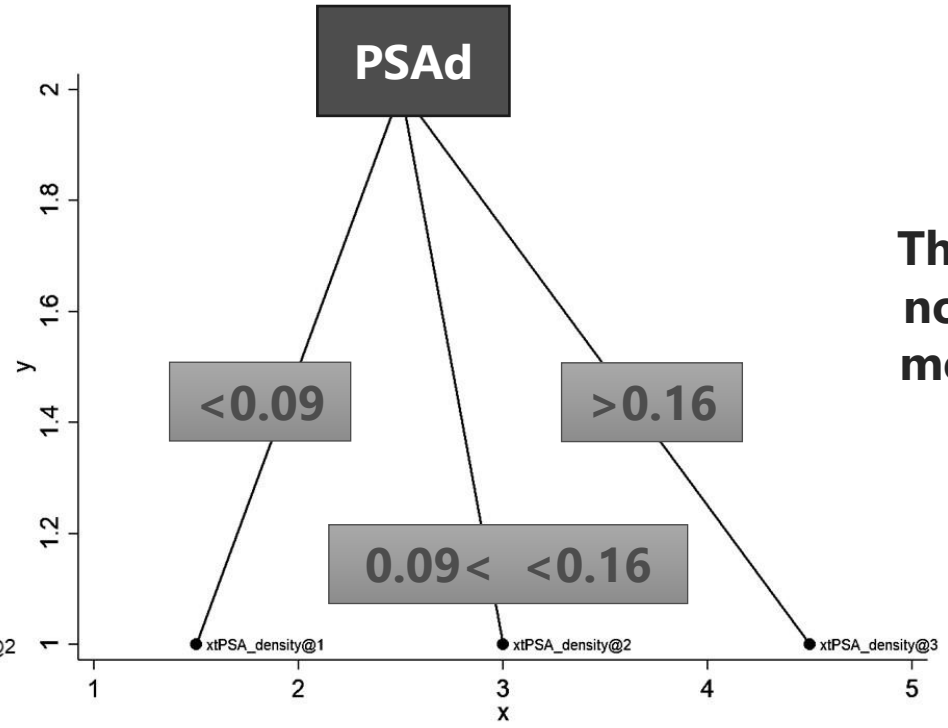


Results

CHAID analysis

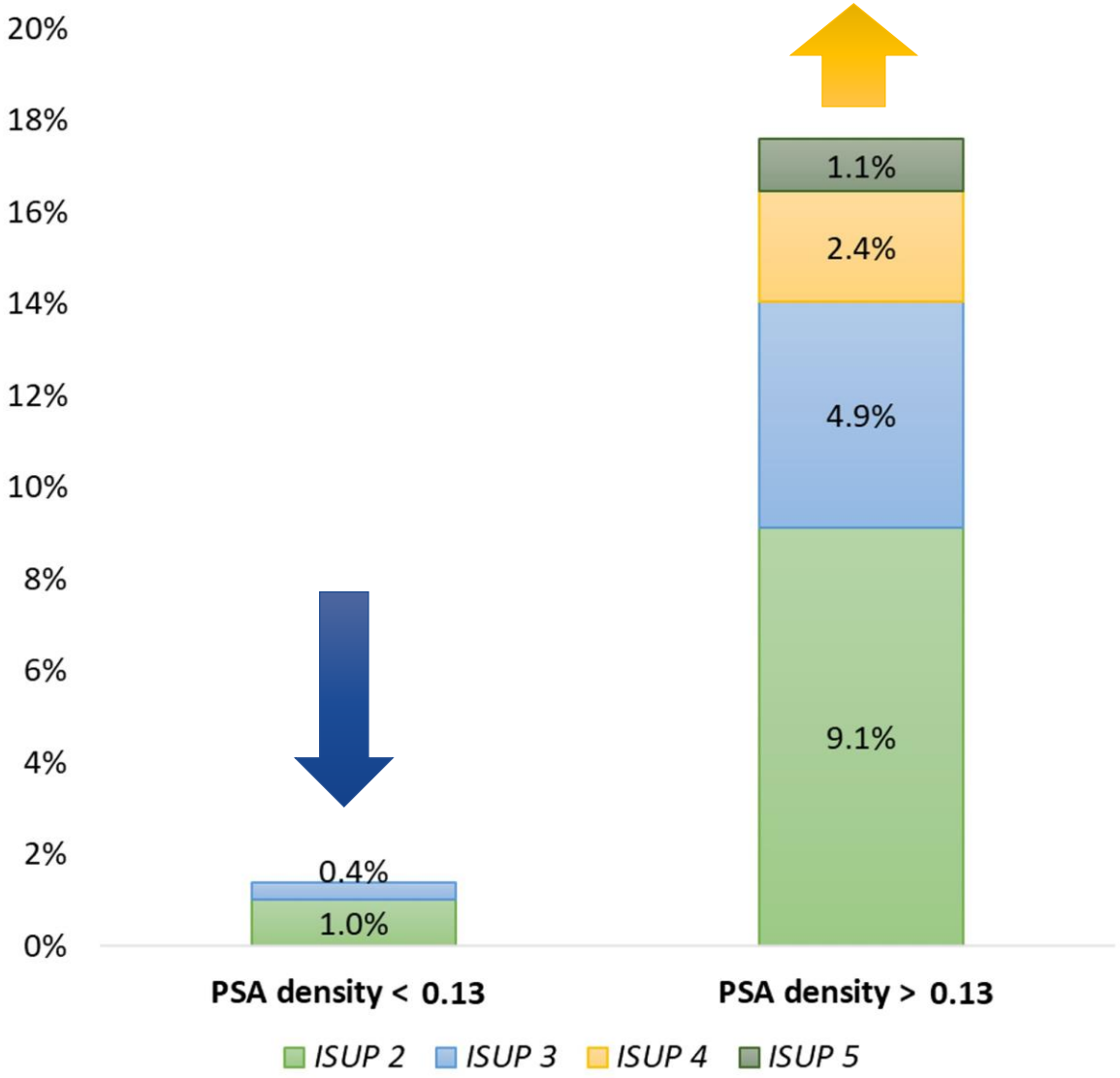
Two-nodes model

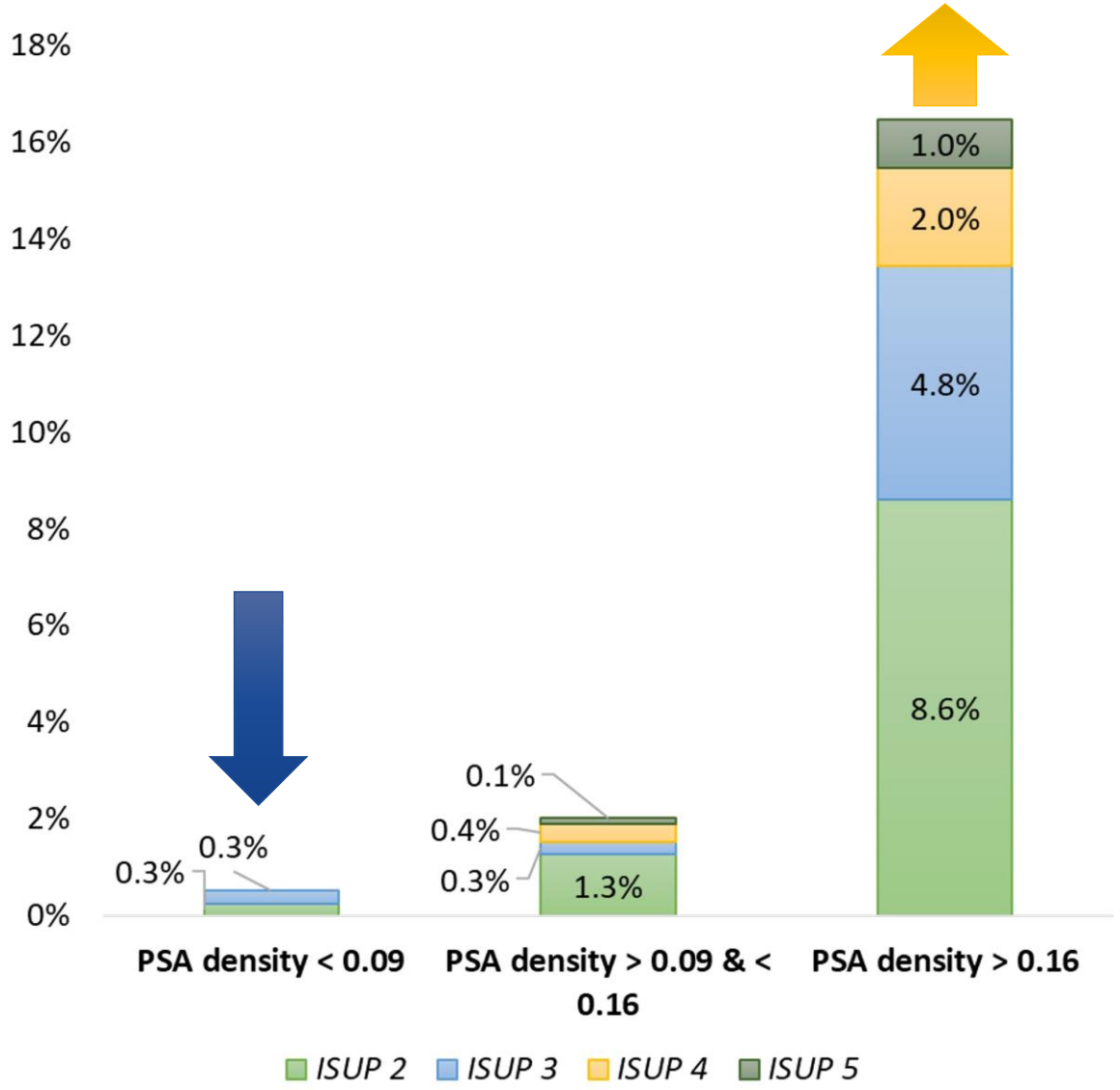




Three-nodes model

PSAd as the sole significant factor influencing the decision tree


20%
18%
16%
14%
12%
10%
8%
6%
4%
2%
0%
0.4%
1.0%
1.1%
2.4%
4.9%
9.1%
PSA density < 0.13
PSA density > 0.13
ISUP 2
ISUP 3
ISUP 4
ISUP 5


18%
16%
14%
12%
10%
8%
6%
4%
2%
0%
0.3%
0.3%
0.1%
0.4%
0.3%
1.3%
1.0%
2.0%
4.8%
8.6%
PSA density < 0.09
PSA density > 0.09 & < 0.16
PSA density > 0.16
ISUP 2
ISUP 3
ISUP 4
ISUP 5

Update of the PSA density cut-off to consider in the era of MRI-targeted biopsies when tackling PI-RADS 3 lesions

- **Largest multi-institutional European study** published to date aimed at defining the association between parameters of patients with PI-RADS 3 lesions and the presence of csPCa.

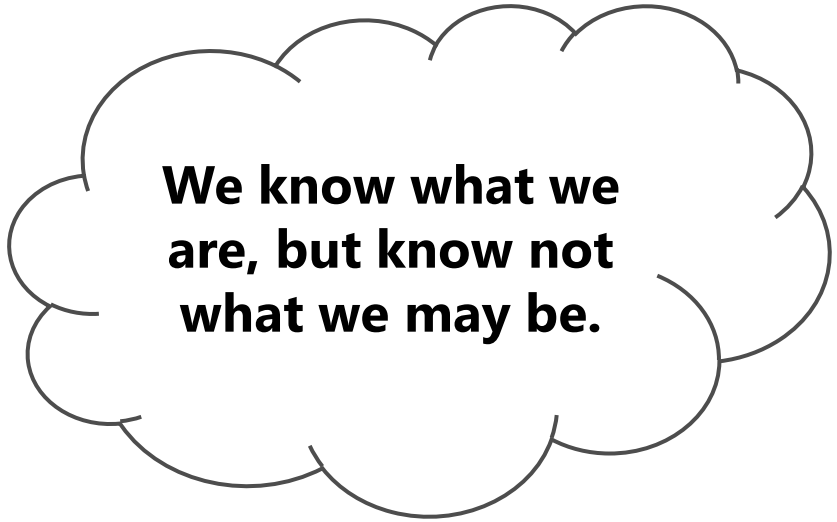
- **PSAd emerged as the only statistically significant factor** influencing the construction of the decision tree, with a cut-off of 0.13 in the two-nodes model and 0.09-0.16 in the three-nodes model.

- This nuanced strategy may lead to ***more precise and informed decision-making***, potentially **sparing certain patients from an unnecessary invasive procedure**.

Conclusion

For individuals with PI-RADS 3 lesions and a PSAd below 0.13, especially below 0.09, prostate biopsy could be omitted, in order to avoid overdiagnosis of non-csPCa.

Thank you for your attention



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