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University Medical Center Rotterdam



Pre-biopsy MRI for everyone? What if MRI negative?

Ivo Schoots, radiologist
Department Radiology & Nuclear Medicine, Rotterdam,
Department Radiology & Nuclear Medicine, Amsterdam, The Netherlands
EAU prostate cancer guidelines panel member, international PI-RADS steering committee

BAU – Oostende, 30 Nov 2019

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Disclosures

• Research Support/Agreement	None
• Employee	None
• Consultant	None
• Major Stockholder	None
• Speakers	None
• Honoraria	None
• Scientific Advisory Board	None

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Prebiopsy MRI for everyone?

- yes
- no

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Systematic biopsy in MRI-negative men?

- yes
- no

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Systematic biopsy in MRI-positive men?

- yes
- no


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Prostate MRI

It is just the **beginning** of a **new era!**

- its power and beauty
- its difficulties and limitations
- many challenges

1. diagnostic test
2. risk stratification tool
3. monitoring tool
4. tool for treatment planning & guid



What is new?



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EAU 2019: Recent Advances in Prostate Cancer: Real Game Changers? Multi-parametric Prostate MRI

Barcelona, Spain (UroToday.com) The use of multiparametric magnetic resonance imaging (mpMRI) of the prostate for cancer diagnosis has evolved significantly. Several years have shown that mpMRI provide actionable information for men.

Figure 1 – Results of important trials in biopsy naive patients, ISUP >=2 cancers:

	Cochrane meta-analysis	MRI-FIRST trial	4M trial
Targeted Biopsy	6.3% (4, 8-8.2)	7.6% (4, 6-11.6)	7.0% (ND)
Systematic Biopsy	4.3% (2.6-6.9)	5.2% (2.8-8.7)	5.0% (ND)
Overall prevalence	27.7% (23.7-32.6)	37.5% (31.4-43.8)	20% (ND)

www.urotoday.com | Prof. O. Rouviere, EAU 2019, representative EAU guideline panel Pca

2019 EAU-EANM-ESTRO-ESUR-SIOG PCa guideline

Recommendations for all men	Level of Evidence	Strength of rating
Do not use mpMRI as an initial screening tool	3	Strong
Adhere to PI-RADS guidelines for acquisition and interpretation of mpMRI	3	Strong
Recommendations in biopsy naive men		
Perform mpMRI before biopsy	1a	Weak
When mpMRI is positive (i.e., PI-RADS ≥3), combine systematic and targeted biopsy	2a	Strong
When mpMRI is negative (i.e., PI-RADS ≤2) and clinical suspicion of prostate cancer is low, omit biopsy based on shared decision making with the patient	2a	Weak
Recommendations in patients with prior negative biopsy		
Perform mpMRI before biopsy	1a	Strong
When mpMRI is positive (i.e., PI-RADS ≥3), perform targeted biopsy only	2a	Weak
When mpMRI is negative (i.e., PI-RADS ≤2) and clinical suspicion of prostate cancer is high, perform systematic biopsy based on shared decision making with the patient	2a	Weak

www.uroweb.org EAU guideline Pca 2019

2019 EAU-EANM-ESTRO-ESUR-SIOG PCa guideline


Recommendations for all men	Level of Evidence	Strength of rating
Do not use mpMRI as an initial screening tool	3	Strong
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Recommendations in biopsy naive men		
Perform mpMRI before biopsy	1a	Weak
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Recommendations in patients with prior negative biopsy		
Perform mpMRI before biopsy	1a	Strong
When mpMRI is positive (i.e., PI-RADS ≥3), perform targeted biopsy only	2a	Weak
When mpMRI is negative (i.e., PI-RADS ≤2) and clinical suspicion of prostate cancer is high, perform systematic biopsy based on shared decision making with the patient	2a	Weak

www.uroweb.org EAU guideline Pca 2019

Annotations:

- prebiopsy MRI in all men
- use different biopsy strategies in different patient populations
- considering risk profiles
- paradigm changes in prostate cancer diagnosis

What is the evidence?



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Retrospective agreement / head-to-head studies

available at www.sciencedirect.com
journal homepage: www.europanurology.com

EAU European Association of Urology
Platinum Priority – Prostate Cancer
Editorial by XXX on pp. XXX–XXX

Urological Oncology

UROLOGIC ONCOLOGY
BJU International

Multicentre evaluation of magnetic resonance imaging supported transperineal prostate biopsy in biopsy-naïve men with suspicion of prostate cancer

M. Minhaj S. Lambros S. Baris Turkbey and Peter A. Nienke L. Hansen¹, Tristan Barrett^{1*}, Claudia Kesch¹, Lana Pepdjanovic², David Bonekamp³, Richard O'Sullivan^{4*}, Florian Distler⁵, Anne Warren^{6*}, Christina Samel⁷, Boris Hadaschik¹², Jeremy Grummet⁸ and Christof Kastner^{8*}

Prospective multicenter high-quality studies

MRI-FIRST

Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naïve men: a prospective, multicentre, paired comparison of MRI-FIRST versus standard biopsy

Head-to-head Comparison of Transrectal Ultrasound-guided Prostate Biopsy Versus Multiparametric Prostate Resonance Imaging with Subsequent Magnetic Resonance-guided Biopsy in Biopsy-naïve Men with Elevated Prostate-specific Antigen: A Large Prospective Multicenter Clinical Study

Platinum Priority – Prostate Cancer
Editorial by XXX on page xxx of this issue

Marlies van der Leest¹, Erik Cornel², Bas Israel³, Rianne Hendriks⁴, Anwar R. Pathani⁵, Martijn Hoogenboom⁶, Patrick Zamcenik⁷, Dirk Bakker⁸, Angèle Yanni Serkenti⁹, Jeroen Veltman¹⁰, Paul van den Hoof¹¹, Hans van der Leij¹², Inge van Oort¹³, Sjoerd Klaver¹⁴, Frans Debruyne¹⁵, Michel Seldous¹⁶, Geertje Hamming¹⁷, Marcoenka Bovers¹⁸, Christina Hübner-van de Kaa¹⁹, Jelle O. Barentsz²⁰

Randomized controlled study

MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

ORIGINAL ARTICLE

Prostate Cancer

Diagnostic Pathway with Imaging Versus Standard Prospective Study in Biopsy-naïve Men

V. Kasivisvanathan, A.S. Rannikko, M. Borghi, V. Panebianco, L.A. Mynderse, M.H. Vaarala, A. Briganti, L. Budius, G. Hellawell, R.G. Hindley, M.J. Roobol, S. Eggener, M. Ghei, A. Villers, F. Bladou, G.M. Villeirs, J. Virdi, S. Boxler, G. Robert, P.B. Singh, W. Venderink, B.A. Hadaschik, A. Ruffion, J.C. Hu, D. Margolis, S. Crouzet, L. Klotz, S.S. Taneja, P. Pinto, I. Gill, C. Allen, F. Giganti, A. Freeman, S. Morris, S. Punwani, N.R. Williams, C. Brew-Graves, J. Deeks, Y. Takwoingi, M. Emberton, and C.M. Moore, for the PRECISION Study Group Collaborators*

Systematic Reviews and Meta-analyses

Comparison of Magnetic Resonance Imaging-stratified Clinical Pathways and Systematic Transrectal Ultrasound-guided Biopsy Pathway for the Detection of Clinically Significant Prostate Cancer: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Comparison of Magnetic Resonance Imaging-stratified Clinical Pathways and Systematic Transrectal Ultrasound-guided Biopsy Pathway for the Detection of Clinically Significant Prostate Cancer: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Sungmin Woo¹, Chong Hyun Suh², James A. Eastham³, Michael J. Zelefsky⁴, Michael J. Morris⁵, Wissam Abida⁶, Howard I. Scher⁷, Robert Siddow⁸, Anton S. Becker⁹, Andreas G. Wibmer¹⁰, Hedvig Hricak¹¹, Hebert Alberto Vargas¹²

Cochrane Review

Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer (Review)

diagnostic test accuracy

accurate reference test

template mapping biopsies (>28)

>250 pages

> 3 years

extensive peer review

Prostate Magnetic Resonance Imaging, with or Without Magnetic Resonance Imaging-targeted Biopsy, and Systematic Biopsy for Detecting Prostate Cancer: A Cochrane Systematic Review and Meta-analysis

How good is the diagnostic test?

- How good are **we** - radiologists ?
- How good are **we** - radiologists + urologists?

MRI

MRI-pathway

How good are we? (sens./PPV)

wolf in sheep's clothing

Schoots et al. 2017 Curr Opin Urol

How good are we? (spec./PPV)

sheep in wolf's clothing

Schoots et al. 2017 Curr Opin Urol

What is the evidence? underlying statistics - accuracy

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metrics for any diagnostic test

- discrimination** sensitivity / specificity
 - distinguish **men with** from **men without** prostate cancer
 - independent of **pre-test** probability
 - critical for the **implementation of MRI** into biopsy management
- prediction** positive / negative predictive value
 - estimate the **post-test** probability of prostate cancer
 - dependent on **pre-test** probability
 - critical for the **decision to (MRI-directed) biopsy**

policy makers radiologists

urologists radiologists patients

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Diagnostic test: 2x2 table

		Condition		prediction
		Yes	No	
Test outcome	+	(FP)	(FN)	positive predictive value
	-	(FN)	(FP)	negative predictive value
		sensitivity	specificity	

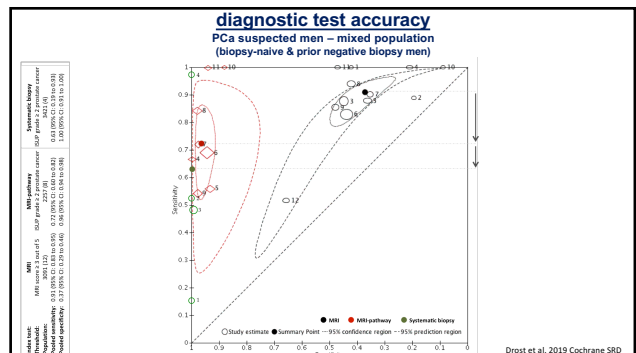
discrimination

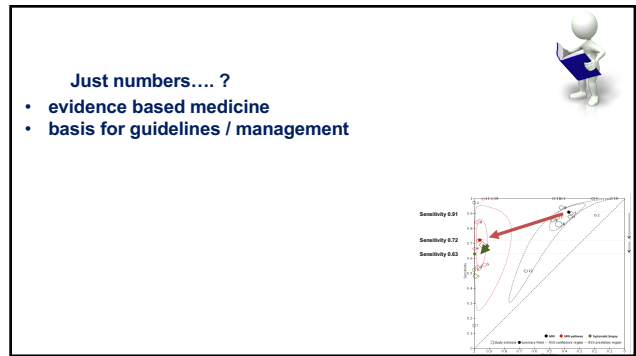
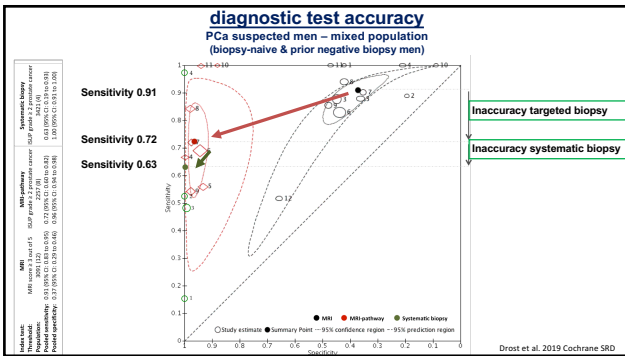
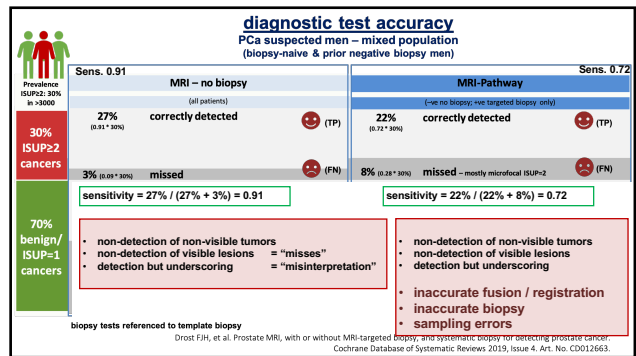
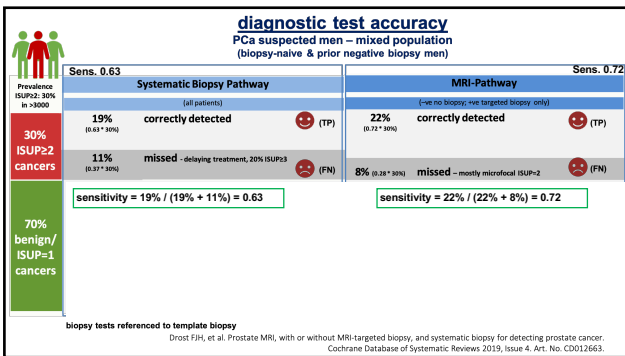
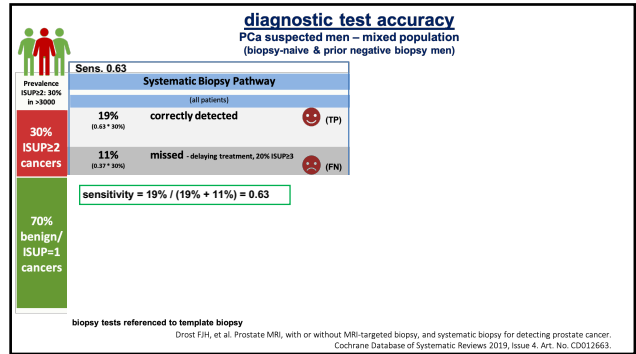
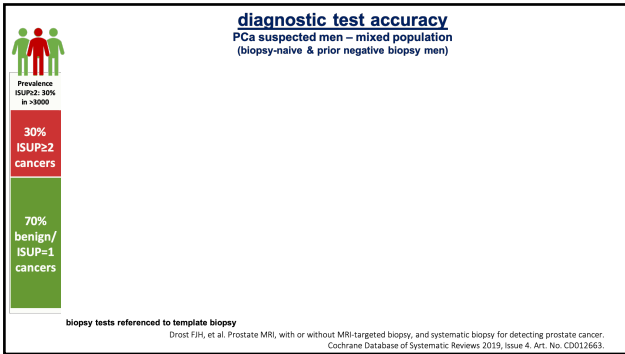
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- Diagnostic test accuracy analysis**
MRI (-pathway) vs. template biopsy (= reference standard)
- Agreement analysis**
MRI (-pathway) vs. systematic biopsy

Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer (Review)

Drost FJH, Osseas DF, Nieboer D, Steyerberg EW, Bangma CH, Roobol MJ, Schoots IG





Pre-biopsy MRI for everyone? ... yes!

Just numbers.... ?

- evidence based medicine
- basis for guidelines / management

MRI and MRI-pathway higher sensitivity

Recommendation 1: upfront MRI

Recommendations in biopsy naïve men
Perform mpMRI before biopsy

What to do

- targeted biopsy only?
- systematic + targeted biopsy?
- systematic biopsy only?

What to do in

- MRI-positive men?
- MRI-negative men?

What is the added value of a test?

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Coimbra

1. Diagnostic test accuracy analysis
MRI (-pathway) vs. template biopsy (= reference standard)

2. Agreement analysis
MRI-pathway vs. systematic biopsy

Cochrane Library
Cochrane Database of Systematic Reviews

Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer (Review)

Drost FJH, Ossen DF, Nieboer D, Stayerberg EW, Bangma CH, Roobol MJ, Schoots IG

Agreement analysis

1. which test performs **better**?
head-to-head: MRI-pathway or systematic biopsy?

but more important

2. what is the **overlap** between both tests?

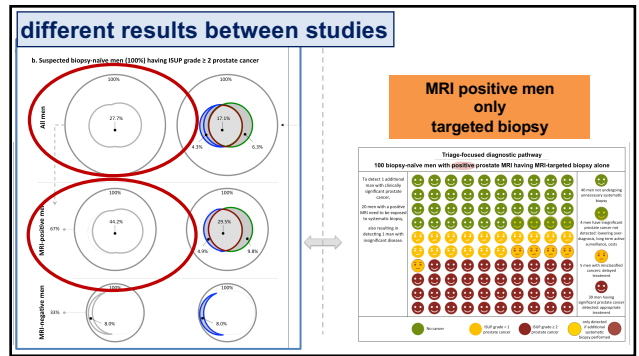
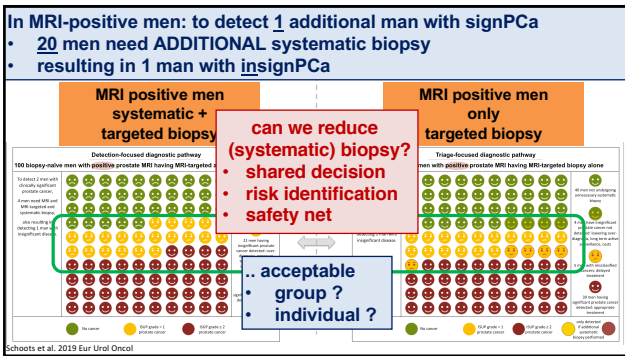
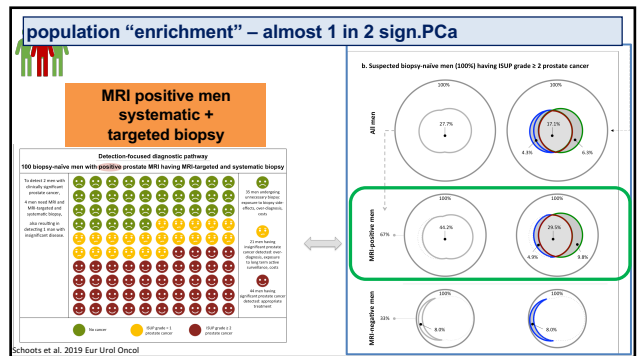
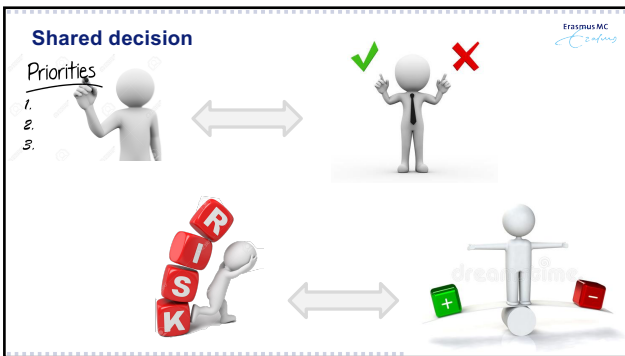
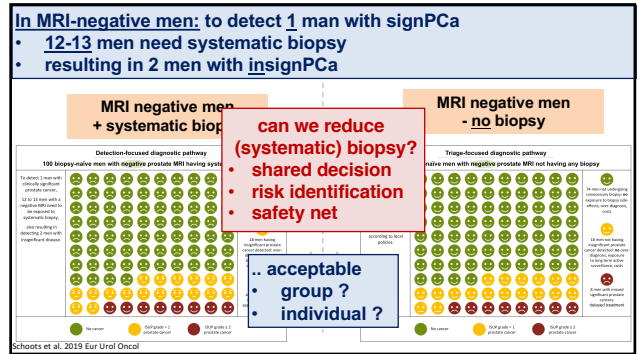
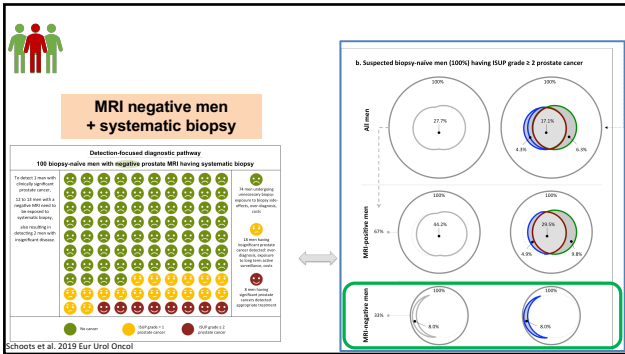
is critical for **decision** to perform

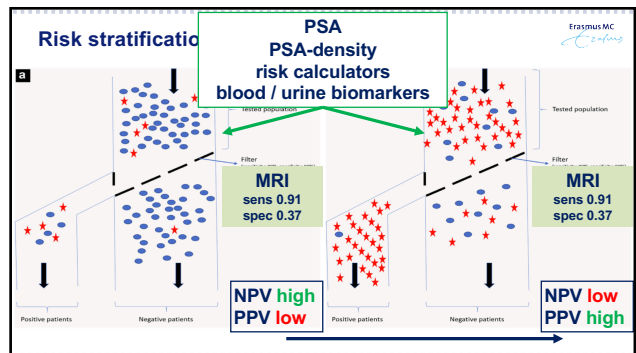
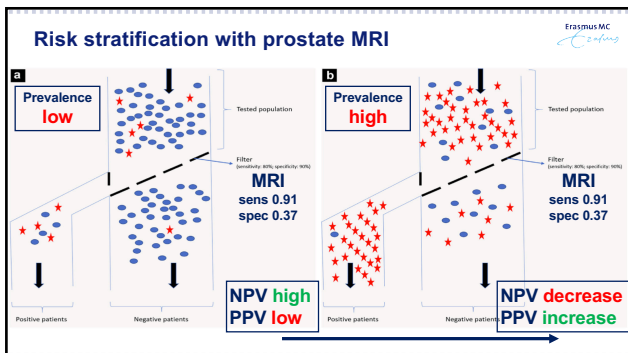
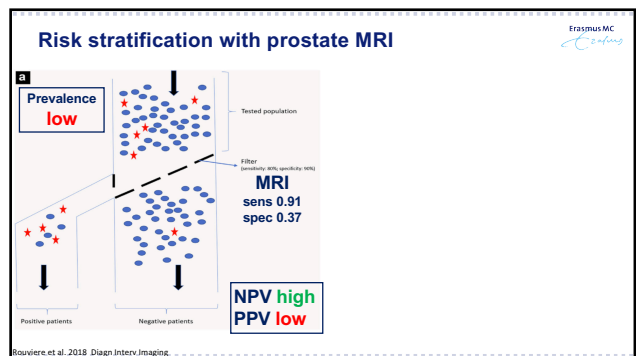
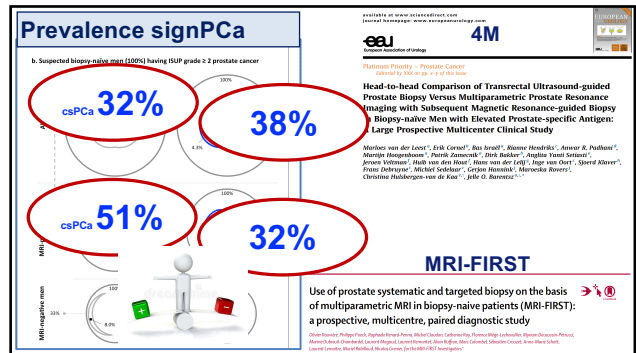
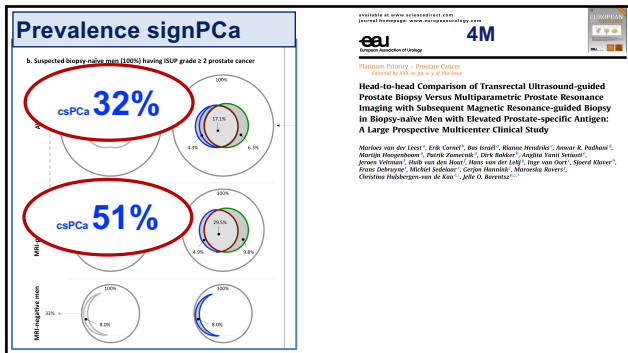
- MRI-targeted biopsy only
- systematic biopsy only
- both MRI-targeted and systematic biopsy

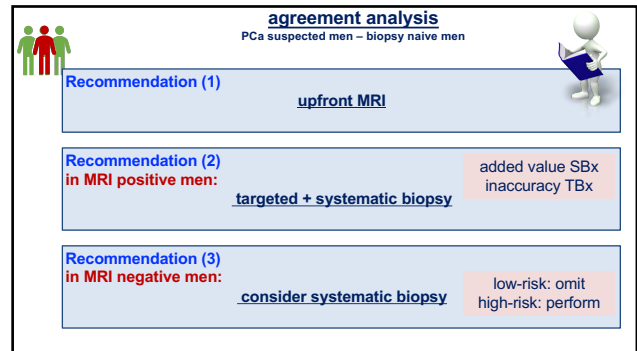
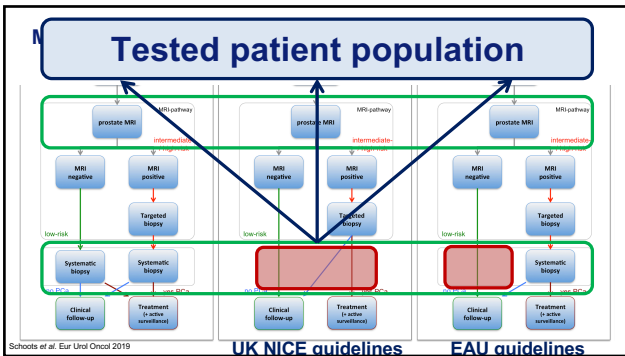
a. Detected ISUP grade ≥ 2 prostate cancer in suspected biopsy-naïve men

b. Suspected biopsy-naïve men (100%) having ISUP grade ≥ 2 prostate cancer

Schoots et al. 2019 Eur Urol Oncol







2019 EAU-EANM-ESTRO-ESUR-SIOG PCa guideline Erasmus MC

Recommendations for all men
Do not use mpMRI as an initial screening tool
Adhere to PI-RADS guidelines for acquisition and interpretation

Recommendations in biopsy naive men
Perform mpMRI before biopsy

When mpMRI is positive (i.e., PI-RADS ≥3), combine systematic and targeted biopsy	1a	Weak
When mpMRI is positive (i.e., PI-RADS ≥3) and clinical suspicion of prostate cancer is low, omit biopsy based on shared decision making with the patient	2a	Strong
When mpMRI is negative (i.e., PI-RADS ≤2) and clinical suspicion of prostate cancer is low, omit biopsy based on shared decision making with the patient	2a	Weak

prebiopsy MRI in all men
use different biopsy strategies
in different patient populations
considering different risk profile

changing paradigm in prostate cancer diagnosis

www.uroweb.org EAU guideline PCa 2019

- Important!** Erasmus MC
- (non)specialized PCa units must have **knowledge of**
 - their **patient population**
 - the (estimated) **prevalence** of signPCa
 - their **performance** of prostate MRI and MRI-pathway
 - with also **balance** between MRI-negative / positive men
 - before** considering
 - omitting** systematic biopsies in MRI-negative men
 - omitting** systematic biopsies in MRI-positive men
- prostate MRI



Prebiopsy MRI for everyone?

- yes
- no

Systematic biopsy in MRI-negative men?

- yes
- no

Systematic biopsy in MRI-positive men?

- yes
- no

Does MRI equal MRI-pathway?

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diagnostic test accuracy
 PCa suspected men – mixed population
 (biopsy-naïve & prior negative biopsy men)

	Sens. 0.91 (0.81* 30%)	Spec. 0.37	Spec. 0.96	Sens. 0.72 (0.72* 30%)
30% ISUP≥2 cancers	27% (0.81* 30%) correctly detected (TP)			22% (0.72* 30%) correctly detected (TP)
	3% (0.09* 30%) missed (FN)			8% (0.24* 30%) missed – mostly microfocal ISUP=2 (FN)
70% benign ISUP=1 cancer	26% (0.57* 70%) correctly identified (TN) potentially unnecessary, imposing patient burden, procedure complications & over-diagnosis impacts			67% (0.96* 70%) correctly identified (TN) as negative for cancer after negative MRI so avoiding biopsy harms
	44% (0.61* 70%) incorrectly identified (FP) imposing patient burden, procedure complications & over-diagnosis impacts			3% need biopsy to confirm no cancer (FP)

biopsy tests referenced to template biopsy
 Drost FJH, et al. Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. Cochrane Database of Systematic Reviews 2019, Issue 4. Art. No. CD012663.

What different strategies?

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