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Multi-parametric MRI for all men at risk of prostate cancer

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Imperial College Healthcare NHS Trust

Chair, NCRI Prostate Clinical Studies Group

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Time to end blind biopsies and open our eyes

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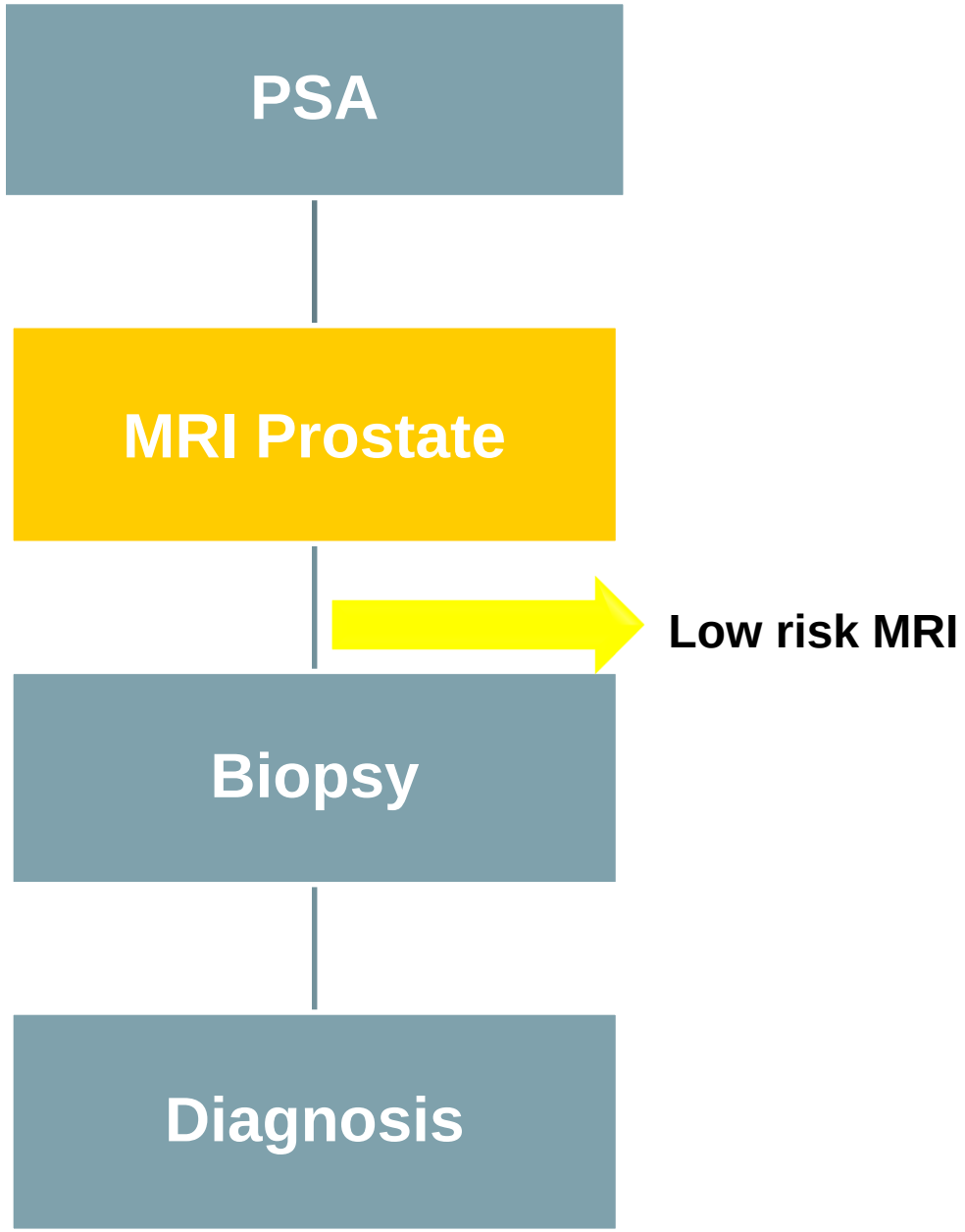
The new pathway



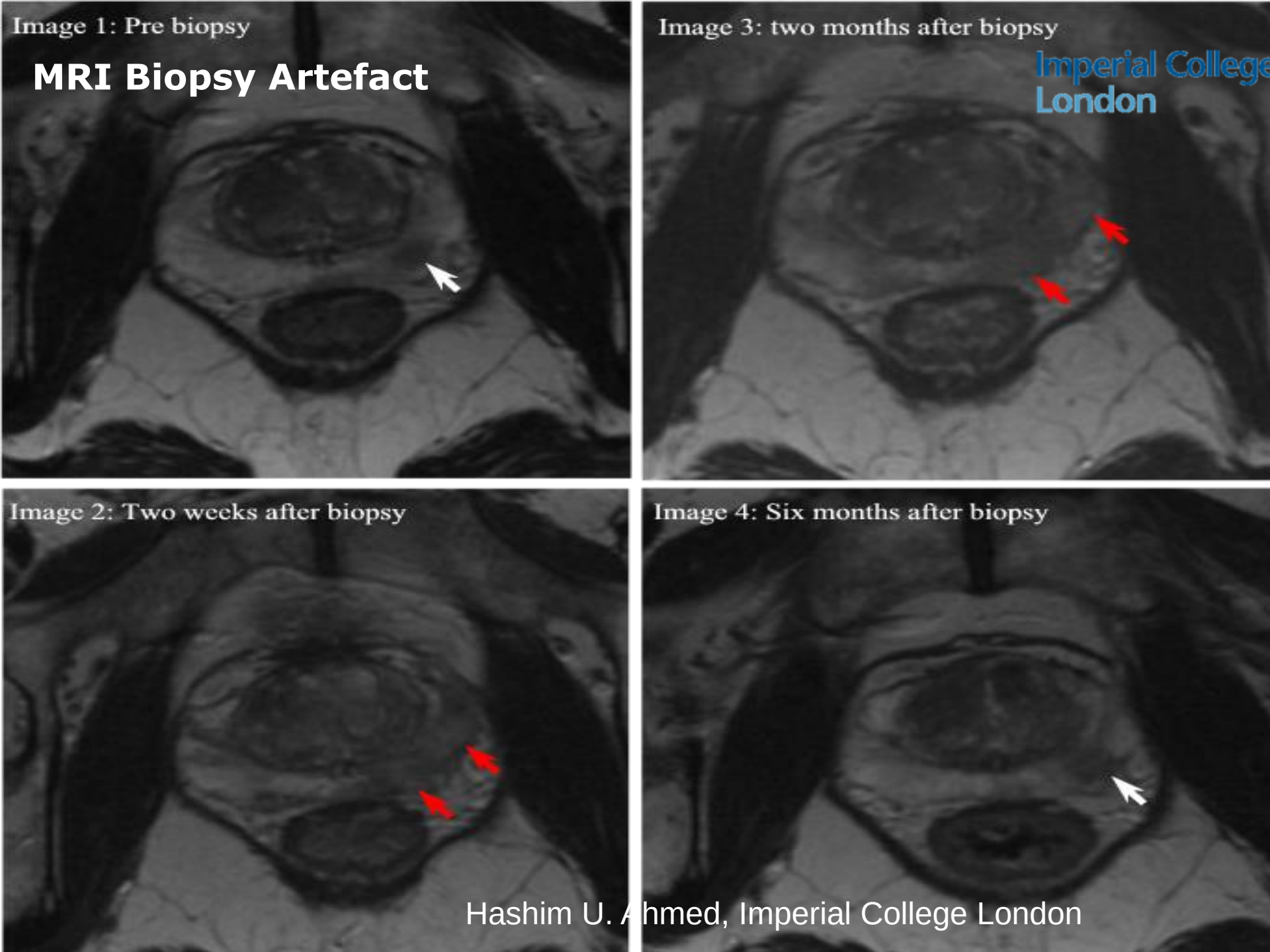


Image 1: Pre biopsy
MRI Biopsy Artefact
Image 3: two months after biopsy
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Image 2: Two weeks after biopsy
Image 4: Six months after biopsy
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PROMIS: Prostate MRI Imaging Study

THE LANCET

Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study

Hashim U Ahmed, Ahmed El-Shater Bosaily*, Louise C Brown*, Rhian Gabe, Richard Kaplan, Mahesh K Parmar, Yolanda Collaco-Moraes, Katie Ward, Richard G Hindley, Alex Freeman, Alex P Kirkham, Robert Oldroyd, Chris Parker, Mark Emberton, and the PROMIS study group†*

Presenter & Co-CI: Mr Hashim Ahmed
Chief Investigator: Prof Mark Emberton
Sponsored by University College London
Managed by MRC Clinical Trials Unit
Funded by UK NIHR HTA

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UK Department of Health Disclaimer: The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the health technology assessment program, NIHR, NHS or the Department of Health.

MRC Clinical Trials Unit | NHS National Institute for Health Research | UCL

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To assess the ability of Multi-Parametric prostate MRI prior to first biopsy to,

Identify men who can safely avoid unnecessary biopsy

Reduce over-diagnosis of clinically insignificant cancer

Improve the detection of clinically significant cancer

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- **11 centres**

- 1.5 Tesla, no endorectal coil
- Independent Quality Assurance and Quality Control of scans
- Compliant with international guidance

  T2W, Diffusion (ADC + b=1500), Dynamic gadolinium contrast

- LIKERT scoring 1 to 5:

  1=highly unlikely to harbour significant cancer

  …

  5=highly likely to harbour significant cancer

- Positive MP-MRI

  Score >/=3

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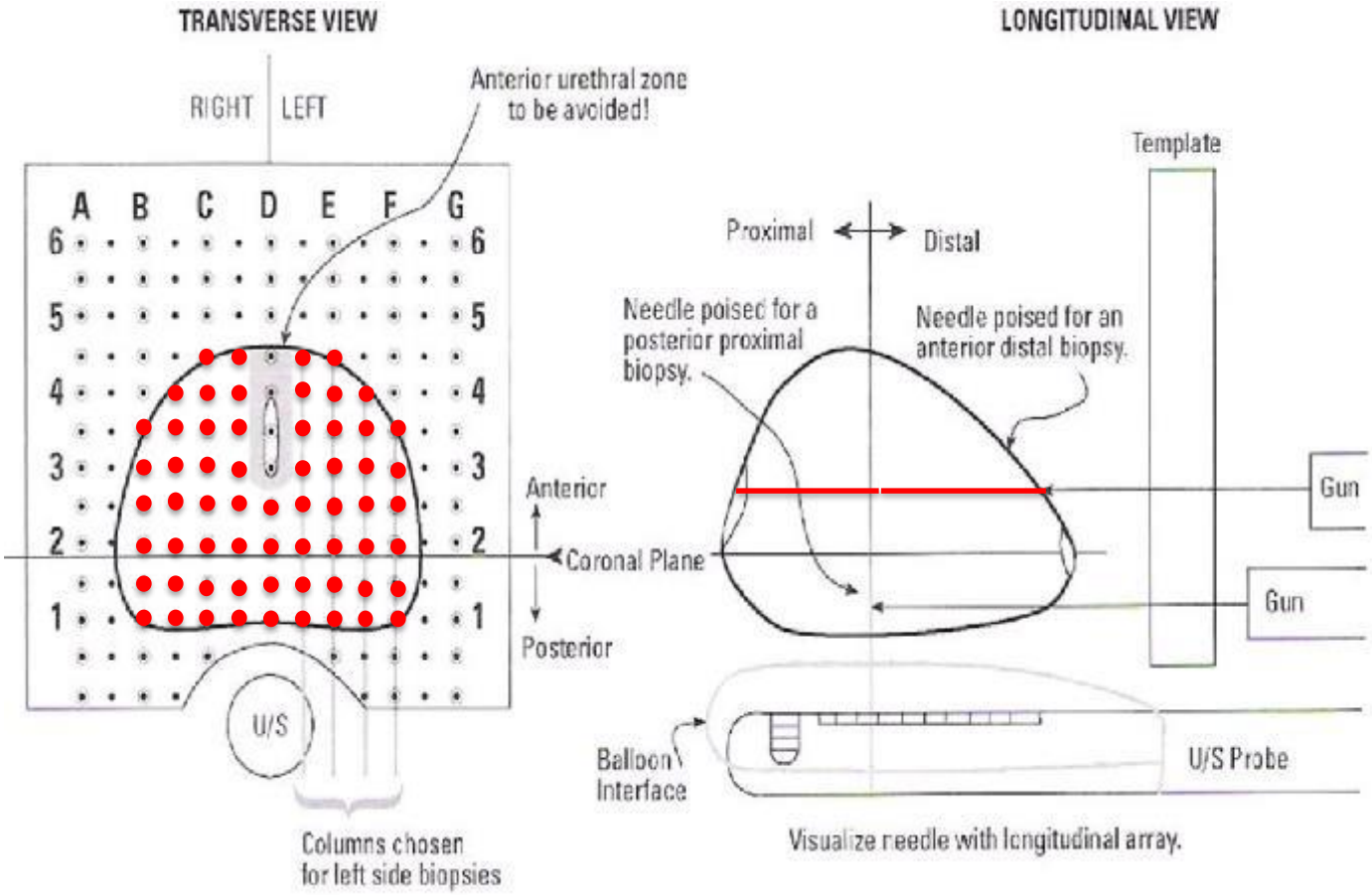
Template Prostate Mapping

Excellent diagnostic accuracy

Prostate biopsies every 5mm

Requires general anaesthetic



Barzell WE, Melamed MR. Urology. 2007;70(6 Suppl) 27-35.
Crawford ED et al. Prostate. 2013;73(7):778-87.

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Definition 1 Significant cancer Gleason 4+3 and/or Cancer length >/=6mm OF ANY GRADE

Test attribute	TRUS-biopsy	MP-MRI	Odds ratio* [95% CI]	*p-value*
Sensitivity	**48%**	**93%**	0.06 [0.02-0.12]	*p<0.0001*
Specificity	**96%**	**41%**	0.02 [0.003-0.05]	*p<0.0001*
PPV	**90%**	**51%**	8.2 [4.7-14.3]	*p<0.0001*
NPV	**74%**	**89%**	0.34 [0.21-0.55]	*p<0.0001*

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If MP-MRI were used as a triage test, what types of clinically significant cancers would be missed?

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Clinically significant cancers missed by TRUS-biopsy and MP-MRI

		TRUS-biopsy Total = 119	MP-MRI Total = 17
Number and cancer core length (mm)	Gleason 3+3	**7** (6-11mm)	**1** (8mm)
	Gleason 3+4	**99** (6-14mm)	**16** (6-12mm)
	Gleason >/=4+3	**13** (3-16mm)	**0**

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Is the PROMIS histological definition of clinically significant cancer correct?

UCL Definition 1

Gleason >/=4+3 and/or

Cancer core length >/=6mm

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Over the last decade, our threshold for clinical significance has been rising…

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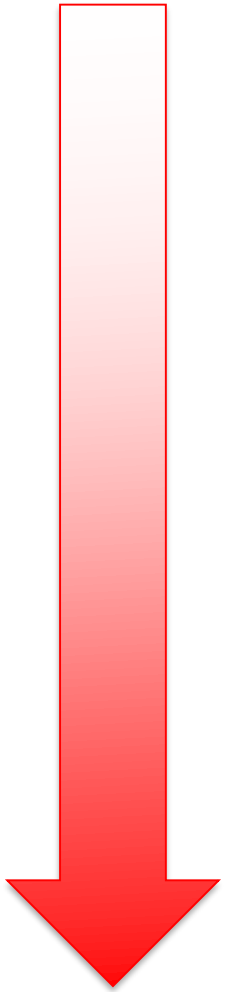
On radical prostatectomy - Tumour Volume



0.2ml (Epstein)	**(>/=4mm)**
0.5ml (Stamey)	**(>/=6mm)**
0.5ml for any grade (EPSRC)	**(>/=6mm)**
1.3ml for Gleason 6 (EPSRC)	**(>/=10mm)**

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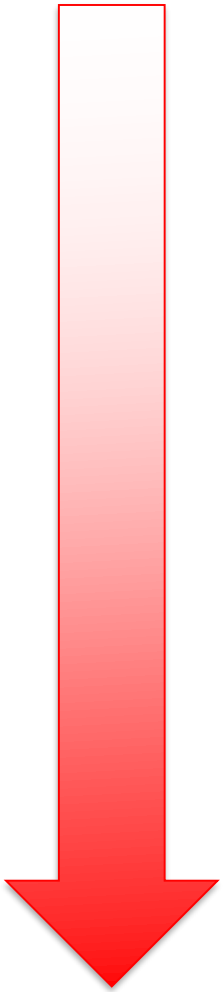
On biopsy - Length of cancer



2mm (Epstein)

3mm (Stamey)

6mm (UCL)

8mm (Swedish Cancer Registry)

10mm (NICE)

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Is it legitimate to not biopsy men with a non-suspicious mp-MRI?

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If one is really serious about overcoming the ***1 in 10 miss rate of MP-MRI*** for clinically significant prostate cancer, then you should not be applying a ***systematic TRUS biopsy that has a 1 in 3 miss rate***

You should do a template mapping biopsy…

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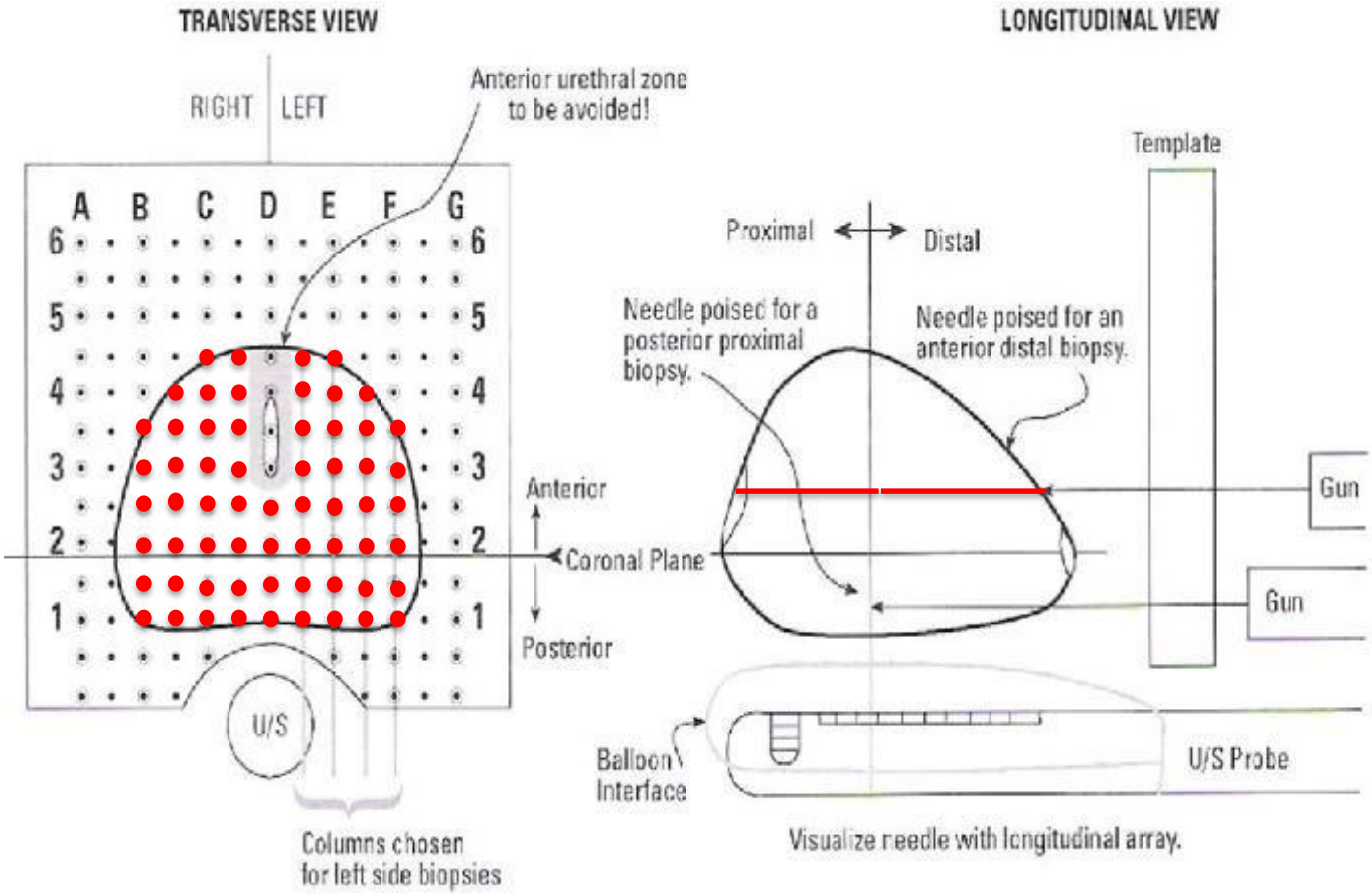
Template Prostate Mapping!!

Excellent diagnostic accuracy

Prostate biopsies every 5mm

Requires general anaesthetic



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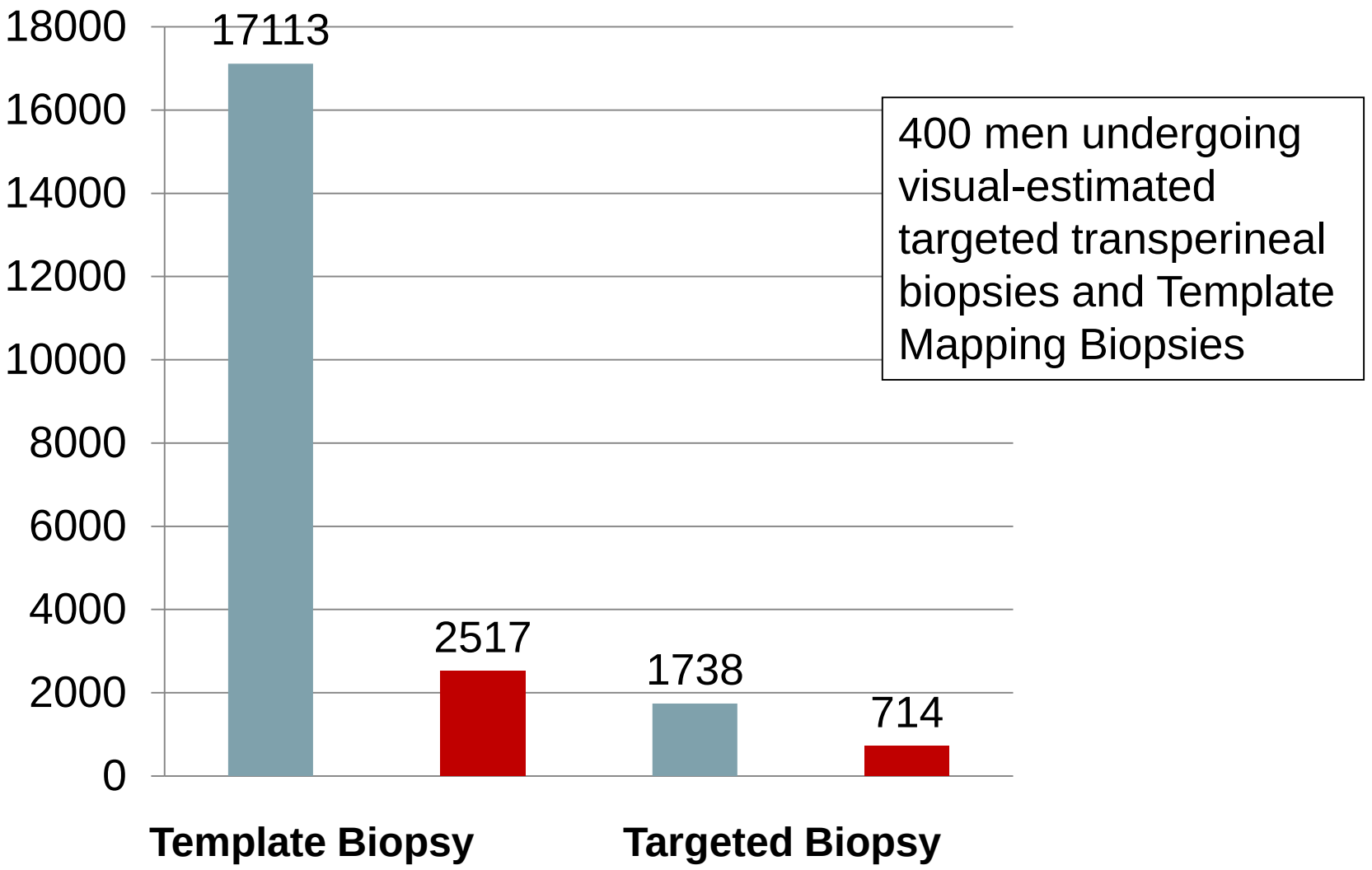
Total cores taken v Cores positive for any cancer



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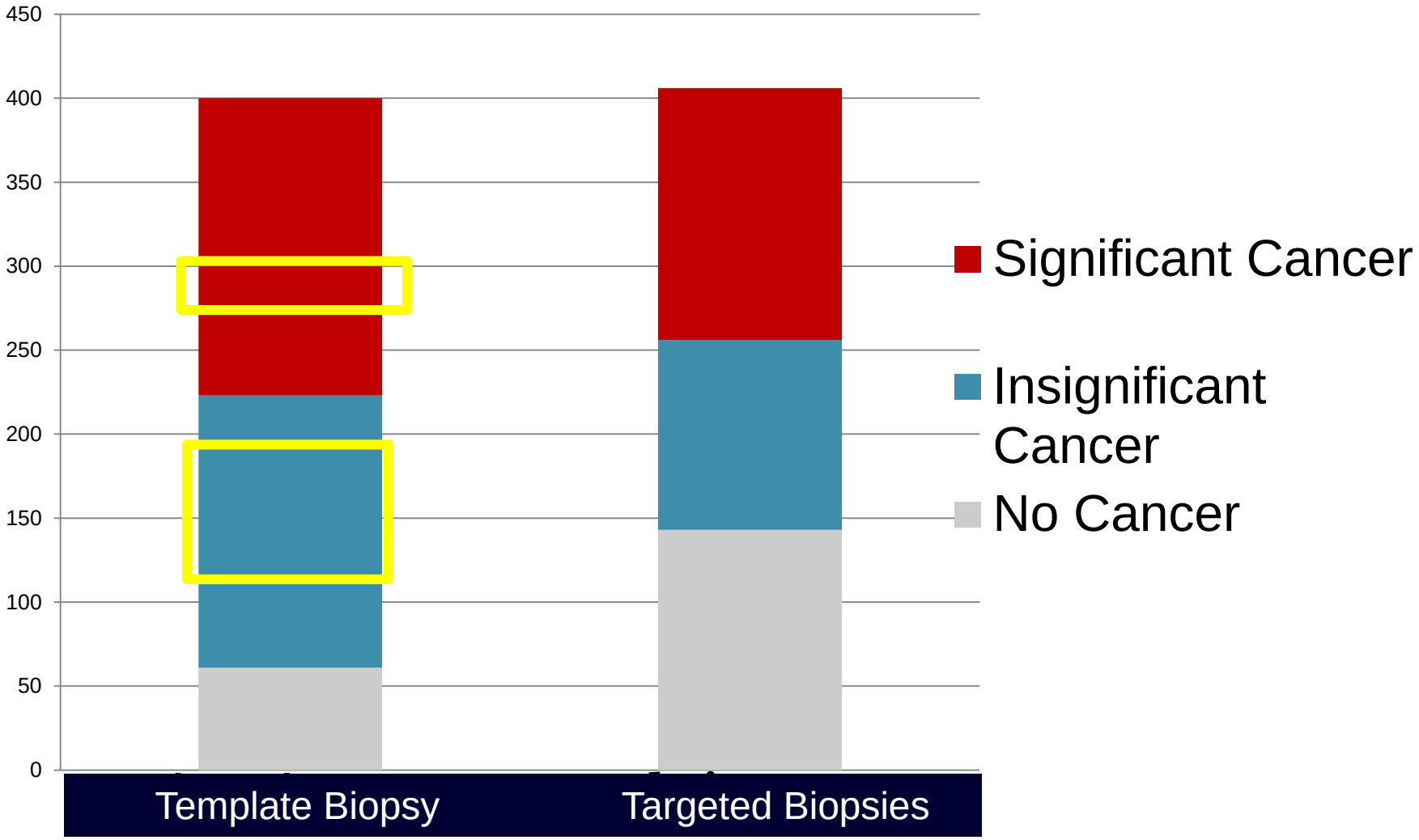
Balance between under-detection and over-diagnosis…



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However, transperineal GA Mapping biopsies in all is an unsustainable strategy

Would cost an additional £1BN / year in Europe

Impact on healthcare systems would be disastrous

Such a strategy is clearly **NOT** the way forward

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We use tests and diagnostic strategies that always miss some disease

US National Cancer Institute states for mammography

“6% to 46% of women with invasive cancer will have negative mammograms”

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Detection rate of Gleason 7 cancer on <u>TRUS Biopsy</u> when MP-MRI is Negative

Panebianco et al, 2016	0%
Wysock et al, 2016	0%
Lu et al, 2017	2.6%
Siddiqui et al, 2015	7%
Itatani et al, 2014	10.4
Pokorny et al, 2015	11.1%
Filson et al, 2016	16%

PSA density </=0.12, Gleason 7 detection goes down to 0% to 5%

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Looking at MRIs is like predicting the weather

No one remembers the huge numbers of times we get it right

Everyone remembers the big misses...

Everyone forgets how bad it was before MRI...

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Can MRI targeted biopsies detect clinically significant cancer?

Hashim U. Ahmed, Imperial College London

EUROPEAN UROLOGY 68 (2015) 8–19

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

European Association of Urology

Platinum Priority – Collaborative Review – Prostate Cancer
Editorial by Stacy Loeb on pp. 20–21 of this issue

Detection of Clinically Significant Prostate Cancer Using Magnetic Resonance Imaging–Ultrasound Fusion Targeted Biopsy: A Systematic Review

Massimo Valerio[a,b,c,*,†], *Ian Donaldson*[a,b,†], *Mark Emberton*[a,b], *Behfar Ehdaie*[d], *Boris A. Hadaschik*[e], *Leonard S. Marks*[f], *Pierre Mozer*[g,h], *Ardeshir R. Rastinehad*[i], *Hashim U. Ahmed*[a,b]

MRI-US fusion targeted biopsies compared to standard biopsy

- Detects more clinically significant cancers 33.3% vs. 23.6%

- Using fewer cores 9.2 vs. 37.1

- Lower detection rate of all cancer 50.5% vs. 43.4%

- Detects 9.1% clinically significant cancers missed by standard biopsy

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EUROPEAN UROLOGY 68 (2015) 438–450

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

European Association of Urology

Review – Prostate Cancer

Magnetic Resonance Imaging–targeted Biopsy May Enhance the Diagnostic Accuracy of Significant Prostate Cancer Detection Compared to Standard Transrectal Ultrasound-guided Biopsy: A Systematic Review and Meta-analysis

Ivo G. Schoots [a,], Monique J. Roobol [b], Daan Nieboer [c], Chris H. Bangma [b], Ewout W. Steyerberg [c], M.G. Myriam Hunink [a,d,e]*

MRI-Targeted biopsy compared to TRUS Biopsy was better for clinically significant tumour

SEN 0.91 vs. 0.76

MRI-targeted biopsy detected fewer insignificant prostate cancer

SEN 0.44 vs. 0.83

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Imperial - before and after introduction of mpMRI

Number men biopsied
100% versus 59%

Detection of pure Gleason 6
1.7% vs. 12.3%, p < 0.05

	Standard TRUS pathway	Triage mp-MRI Pathway	P value
UCL/Ahmed definition 1	12.2%	24.1%	≤ 0.05
UCL/Ahmed definition 2	24.7%	32.7%	≤ 0.05
Any length of Gleason >/=3+4	22.8%	31%	≤ 0.05
Any length of Gleason >/=4+3	5.7%	15.5%	≤ 0.05

Hashim U. Ahmed, Imperial College London

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Is mp-MRI before all first biopsies cost-effective?

Hashim U. Ahmed, Imperial College London

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ELSEVIER

CrossMark

UROLOGIC ONCOLOGY

Urologic Oncology: Seminars and Original Investigations 34 (2016) 119.e1–119.e9

Original article

Cost-effectiveness of multiparametric magnetic resonance imaging and targeted biopsy in diagnosing prostate cancer

Yannick Cerantola[a,b,1], Alice Dragomir[a,1], Simon Tanguay[a], Franck Bladou[a], Armen Aprikian[a], Wassim Kassouf[a,2,*]

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Received 30 May 2015; received in revised form 31 August 2015; accepted 9 September 2015

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Table 3
Incremental cost and QALY (TRUSGB vs. MRGB) summary table (Canadian dollars)

Variable and variations	Incremental cost (10 years)	Incremental QALY (10 years)	TRUSGB vs. MRGB	Incremental cost (15 years)	Incremental QALY (15 years)	TRUSGB vs. MRGB	Incremental cost (20 years)	Incremental QALY (20 years)	TRUSGB vs. MRGB
Base case	−$956	0.086	Dominated	−$1,616	0.134	Dominated	−$2,187	0.168	Dominated
20%	−$775	0.095	Dominated	−$1,628	0.127	Dominated	−$2,049	0.149	Dominated
25%	−$934	0.091	Dominated	−$1,449	0.167	Dominated	−$2,099	0.181	Dominated
Variation of probability of recurrence in intermediate-high-risk group									
2.9%	−$951	0.094	Dominated	−$1,297	0.114	Dominated	−$2,100	0.191	Dominated
5.3%	−$1,091	0.111	Dominated	−$1,917	0.133	Dominated	−$1,752	0.183	Dominated
6.5%	−$1,193	0.089	Dominated	−$1,179	0.144	Dominated	−$2,191	0.166	Dominated
7.7%	−$652	0.081	Dominated	−$1,462	0.146	Dominated	−$1,988	0.158	Dominated
Variation of utilities									
0.95; 0.95; 0.81; 0.48	−$914	0.067	Dominated	−$1,697	0.101	Dominated	−$1,927	0.107	Dominated
0.89; 0.89; 0.75; 0.42	−$990	0.114	Dominated	−$1,451	0.184	Dominated	−$2,087	0.191	Dominated
0.85; 0.85; 0.7; 0.4	−$962	0.156	Dominated	−$1,996	0.252	Dominated	−$1,568	0.275	Dominated

[a]Sensitivity analyses: (1) a discount rate of 0%, 3%, and 10%; (2) a variation of AS rate in both TRUSGB and MRGTB between 10% and 25%; (3) a variation of yearly probability of recurrence in intermediate-high-risk group between 2.9% [34] and 7.7% [35]; (4) different utilities; and (5) a variation of treatments distribution and associated costs (data not shown).

Incorporation of MRI and MRI-targeted biopsy in PCa diagnosis and management represents a cost-effective measure at 5, 10, 15, and 20 years after initial diagnosis.

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European Association of Urology

Platinum Priority – Prostate Cancer

Editorial by Mark Emberton on pp. 437–438 of this issue

Cost-effectiveness of Magnetic Resonance (MR) Imaging and MR-guided Targeted Biopsy Versus Systematic Transrectal Ultrasound–Guided Biopsy in Diagnosing Prostate Cancer: A Modelling Study from a Health Care Perspective

Maarten de Rooij [a,b,], Simone Crienen [a], J. Alfred Witjes [c], Jelle O. Barentsz [b], Maroeska M. Rovers [a,d], Janneke P.C. Grutters [a,d]*

[a] *Department of Operating Rooms, Radboud University Medical Center, Nijmegen, The Netherlands;* [b] *Department of Radiology, Radboud University Medical Center, Nijmegen, The Netherlands;* [c] *Department of Urology, Radboud University Medical Center, Nijmegen, The Netherlands;* [d] *Department for Health Evidence, Radboud University Medical Center, Nijmegen, The Netherlands*

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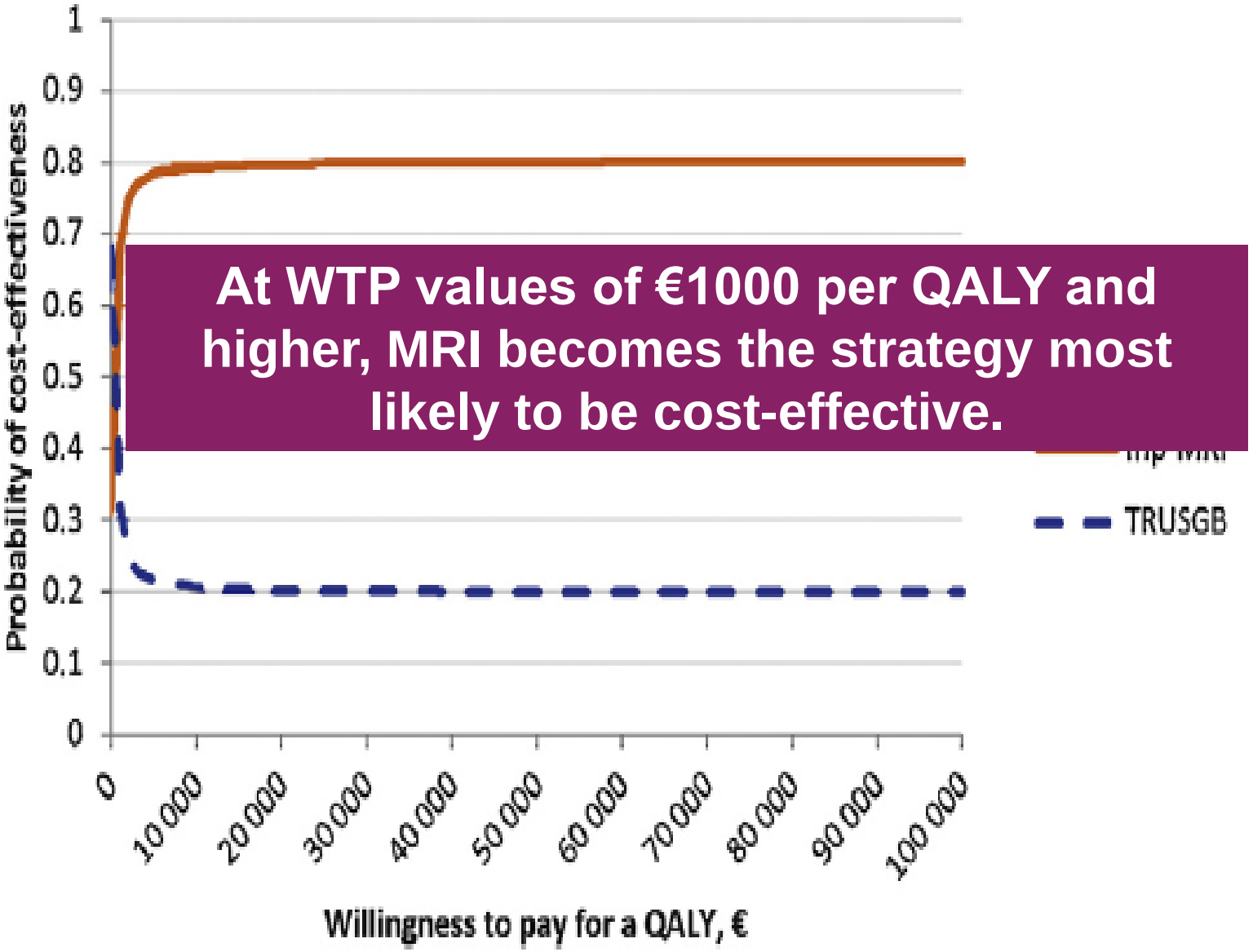

At WTP values of €1000 per QALY and higher, MRI becomes the strategy most likely to be cost-effective.

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PROMIS Cost-Effectiveness Analysis

Improved health outcomes
Cost-effective

	Clinically significant cancers	Costs of testing	QALYS	Costs	ICER
TRUS biopsy	0.52 (0.45-0.61)	£742 (£727-£757)	8.49 (8.19-8.80)	£4603 (£4174-£5044)	-
MP-MRI pre-biopsy, biopsy only score 3-5	0.82 (0.75-0.87)	£687 (£657-£719)	8.65 (8.35-8.95)	£5027 (£4609-£5512)	£2,730

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In conclusion...

Looking at MRIs is like predicting the weather

No one remembers the huge numbers of times we get it right

Everyone remembers the big misses...

Everyone forgets how bad it was before MRI...