Active Surveillance- Moving Forward

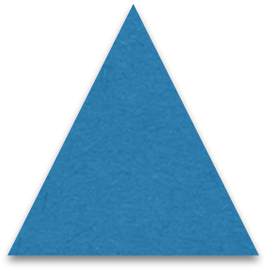
Declan Cahill

- Why Active surveillance?
- Why Gleason 3+3?
- What about adherence/drop out?
- MRI?

Active surveillance (1)

MDT
"All options"

Klotz
PIVOT
ProtecT



10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer

Freddie C. Hamdy, F.R.C.S.(Urol.), F.Med.Sci., Jenny L. Donovan, Ph.D., F.Med.Sci., J. Athene Lane, Ph.D., Malcolm Mason, M.D., F.R.C.R., Chris Metcalfe, Ph.D., Peter Holding, R.G.N., M.Sc., Michael Davis, M.Sc., Tim J. Peters, Ph.D., F.Med.Sci., Emma L. Turner, Ph.D., Richard M. Martin, Ph.D., Jon Oxley, M.D., F.R.C.Path., Mary Robinson, M.B., B.S., F.R.C.Path., John Staffurth, M.B., B.S., M.D., Eleanor Walsh, M.Sc., Prasad Bollina, M.B., B.S., F.R.C.S.(Urol.), James Catto, Ph.D., F.R.C.S.(Urol.), Andrew Doble, M.S., F.R.C.S.(Urol.), Alan Doherty, F.R.C.S.(Urol.), David Gillatt, M.S., F.R.C.S.(Urol.), Roger Kockelbergh, D.M., F.R.C.S.(Urol.), Howard Kynaston, M.D., F.R.C.S.(Urol.), Alan Paul, M.D., F.R.C.S.(Urol.), Philip Powell, M.D., F.R.C.S., Stephen Prescott, M.D., F.R.C.S.(Urol.), Derek J. Rosario, M.D., F.R.C.S.(Urol.), Edward Rowe, M.D., F.R.C.S.(Urol.), and David E. Neal, F.R.C.S., F.Med.Sci., for the ProtecT Study Group*

N Engl J Med 2016; 375:1415-1424 | October 13, 2016 | DOI: 10.1056/NEJMoa1606220

The NEW ENGLAND JOURNAL of MEDICINE

Radical Prostatectomy versus Observation for Localized Prostate Cancer

Timothy J. Wilt, M.D., M.P.H., Michael K. Brawer, M.D., Karen M. Jones, M.S., Michael J. Barry, M.D., William J. Aronson, M.D., Steven Fox, M.D., M.P.H., Jeffrey R. Gingrich, M.D., John T. Wei, M.D., Patricia Gilhooly, M.D., B. Mayer Grob, M.D., Imad Nsouli, M.D., Padmini Iyer, M.D., Ruben Cartagena, M.D., Glenn Snider, M.D., Claus Roehrborn, M.D., Ph.D., Roohollah Sharifi, M.D., William Blank, M.D., Parikshit Pandya, M.D., Gerald L. Andriole, M.D., Daniel Culkin, M.D., and Thomas Wheeler, M.D., for the Prostate Cancer Intervention versus Observation Trial (PIVOT) Study Group

N Engl J Med 2012; 367:203-213 | July 19, 2012 | DOI: 10.1056/NEJMoa1113162

The NEW ENGLAND JOURNAL of MEDICINE

Active surveillance (2)

- Avoids necessary radical treatments.
- Saves resources on managing functional shortcomings of treatment and treatment related complications
- Optimal surveillance protocol unclear
- PSA kinetics not great
- Repeat biopsies unacceptable to many (PROBE/ PRIAS)

Active surveillance (3)

- Needs chronic disease management strategies and research/tools
- MRI cheaper and more acceptable than biopsy- need to work out how. SPCG17-PCASTS
- Low risk/very low risk active surveillance
- Reduce need for clinic interaction but still get remunerated

Active Surveillance 2018

- Increasing confidence. USPSTF C v D in 2018
- John Hopkins. Overall, cancer specific, and metastasis free survival 69%, 99.9% and 99.4%at 15 yrs (Tosoian, J Clin Oncol 2015)
- Klotz 3+3 97% 15 yr actuarial CaP survival, 3+4 89%
- Occult high grade disease understood (1% progression v 25% misclassification)
- PSA kinetics flawed
- MP MRI- “Game changer”.

Klotz, Choo J Urol167:1664, 2002

Study	Year	Country	Patient No.	Median Age (years)	Follow up	Main finding
MSKCC (37)	2011	USA	238	64	5 years	5 year progression free survival 60%
John Hopkins (38)	2015	USA	1298	66	15 years	Cancer-specific, and metastasis-free survival rates - 99.9% (very low-risk group), and 99.4% (low-risk group) at 10 years and 99.9% (very low-risk), and 99.4% (low-risk group) at 15 years.
UCSF (39)	2015	USA	556	62	60 months (median)	5 year overall survival 98%. Treatment free survival 60%
PRIAS (40)	2013	Worldwide	2494	65.8	1.6 years (median)	21% of patients underwent active treatment
University of Miami (41)	2010	USA	230	64	44 months	14% of patients underwent active treatment. No patients progressed after treatment.
Royal Marsden (42)	2013	UK	471	66	5.7 years	31% of patients underwent active treatment. Overall survival rate 99% (2 years) and 96% (5 years)
ProtecT (43)	2016	UK	545	62	10 years	54.8% of patients underwent active treatment. Prostate cancer-specific survival 98.8% at 10 years
University of Toronto (44)	2015	Canada	993	67.8	6.4 years	Prostate cancer-specific disease free survival 98.1% (10 years) and 94.3% (15 years). 36.5% (10 years) and 45% (15 years) of patients underwent active treatment.
University of Copenhagen (45)	2015	Denmark	317	65	5 years	39.5% of patients underwent active treatment.
Australian (46)	2015	Australia	796	63	67 months (mean)	38% of men progressed to radical treatment. Median time to treatment 90 months. 15 year radical treatment free survival 42%. Prostate cancer specific metastasis free survival at 15 years
Goteborg (47)	2013	Sweden	439	65.4	6 years (median)	The prostate cancer-specific failure-free survival is 86.4% (10 years). Treatment free survival 45.4% (10 years)
Multi-institutional Canary PASS (48)	2016	USA	905	Not available	8.4 months (median)	19% of patients underwent active treatment. 68% of these due to disease reclassification and 32% without.

Mortality from CaP on AS very low. Transfer to treatment is high

Active Surveillance

Klotz

- 993 patients
- f/u 8.9 years
- 30 pts with mets, 15 died of CaP, 4 died other, 11 alive with mets
- 78% low risk
- 22% Gleason 7 or PSA >10
- 38% <70 yrs
- 1.5% CaP death
- 1.5% of cohort disadvantaged- developed mets rather that had them treatment early

Klotz, Choo J Urol167:1664, 2002

Active Surveillance

Klotz (contd)

- CaP mortality x4 in intermediate v low risk group
- All deaths in intermediates were Gleason 7 as opposed to PSA >10
- Gleason 3+4 11% mortality at projected 15 yrs
- Low risk 3% mortality

Yamamoto T, Klotz L. J Urol 2016 May;195(5):1409-14

- 22% Klotz series Intermediate risk = Gleason 3+4 or PSA >10
- 3.75 greater rate of CSM with initial surveillance
- Gleason score >>>>PSA

Achilles Heal of AS

- The Achilles heal of Active Surveillance is missing co-existent high risk, aggressive prostate cancer
- MRI and molecular biomarkers will lessen this risk

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Low hanging fruit

Easy pickings

= Gleason 3+3

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Van den Bergh et al Eur Urol 2009

- 616 screen detected CaP (ERSPC), sextant Bx
- PSA <10, PSAD <0.2, T1c/T2, 3+3, max 2 cores
- 10yr PCSS 100%
- 10yr OS 77%
- no strict protocol, urologist defined
- must be a mixed group with just sextant Bx diagnosis

PROTECT NEJM 2016

- The AS group were in between AS and WW
- Monitoring PSA not Bx

- 10 yr no difference in survival. Higher progression in AS arm- perhaps due to the 25% on AS with intermediate or high risk

Gleason 6
Is it cancer?

- A malignant neoplasm is an abnormal mass of tissue the growth of which exceeds that of normal tissue and continues in the same excessive manner after cessation of the stimulus that evoked the change. It may be locally invasive and or metastasize.

- So. Yes

Gleason 6

- 12,000 Gleason 6 cancers treated with RP with 20 year follow up (Eggener, J Urol 2011)
  - CaP mortality 0.2% at 20 years
    - Re-review of these cases showed higher grade
- 14,123 cases of pathologic Gleason 6 at RP (Ross, Am J Surg Path 2012)
  - 22 with positive nodes (obturator sampling)
  - All up graded on review

Gleason 6
Is it cancer?

- No expression of proliferative embryonic, neuronal, haemopoietic stem cells genes, EGF or EGFR

- Antigrowth signal insensitivity (Cyclin D2, CKDN1beta) expressed

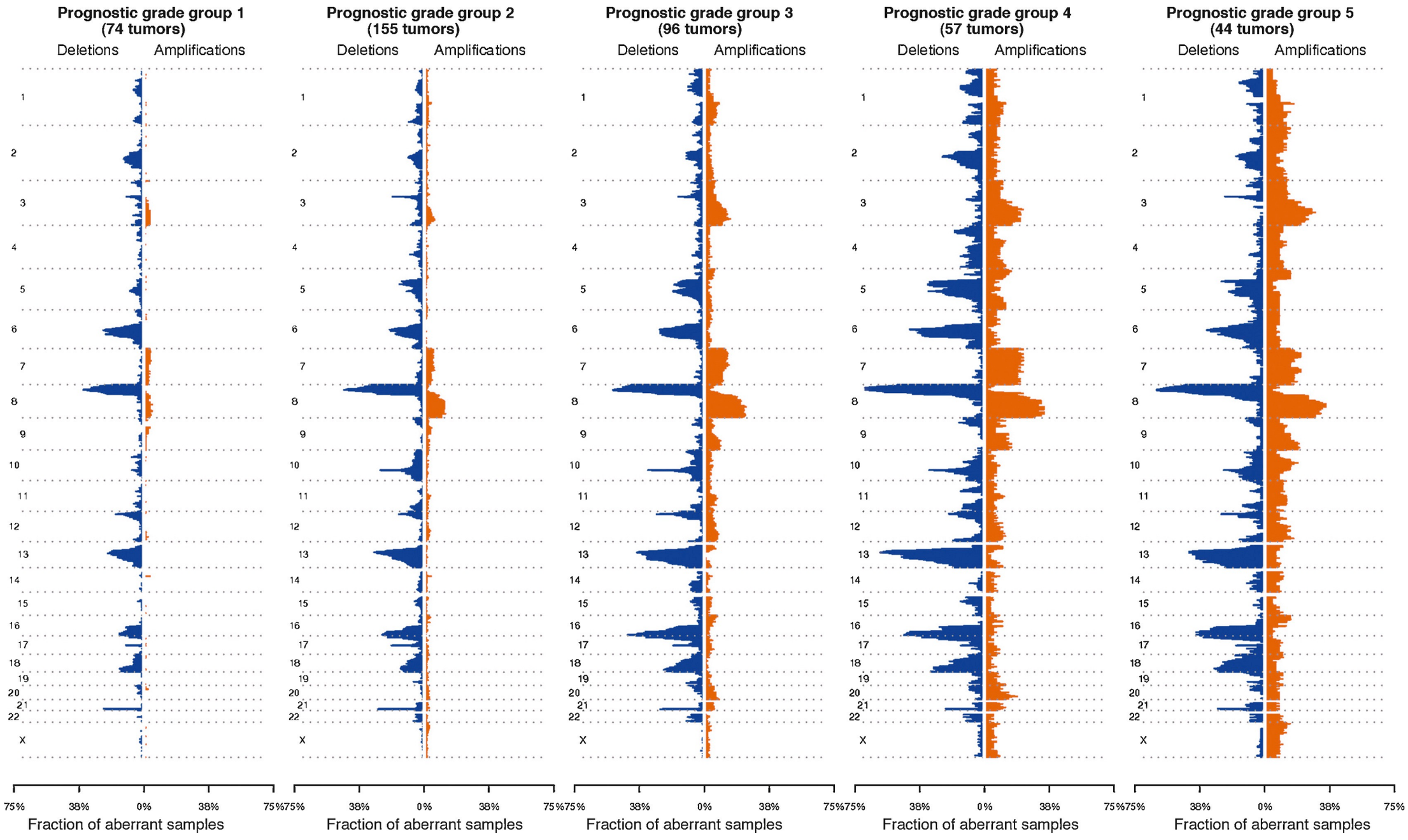
- Absence of senescence. TMPRSS2-ERG normal

- VEGF low, PTEN 36% v >90% in pattern 4

- Clinical metastasis/mortality very rare

Rubin et al Eur Urol 2016; 69(4):557-6

- Genomic alterations quantitatively not qualitatively different between grades



Achilles Heal of AS

- The Achilles heal of Active Surveillance is missing co-existent high risk, aggressive prostate cancer
- MRI and **molecular biomarkers will lessen this risk**

Genetic Biomarkers and risk

- pt with GG1 and favourable features
- 1-3% 15 yr probability of metastases
- Molecular diagnostic test with 90% accuracy
- So this gives a 3-4 fold risk of a false positive test

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Low hanging fruit

Easy pickings

= Gleason 3+3

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Reasons for poor AS uptake

- Urology team lack of confidence
- Patient lack of confidence
- Patient experience
- Poor patient education
- Experience and fear of AS failure
- Improving outcomes guidance- Case numbers. Surgeon and Center
- Minimally invasive therapies
- Referral base
- Private practice (remuneration, decision already made, flattery, fit men, good body habitus - complicated!)
- Less support for AS patients than treated patients with functional deficiencies.

Depression

•Cancer Research UK describes depression as an established response to a diagnosis of cancer, unrelated to stage or severity

•However, in PC the risk of moderate to severe depression (requiring treatment) has been reported as relatively low in comparison to other tumour groups, at 5% (Punnen et al BJUI 2013;112:E67-75).

AS Facilitators and Barriers

<u>Cancer characteristics</u>

- PSA, number of positive cores, Gleason Grade, tumour volume, stage

AS Facilitators and Barriers

Patient factors

- Age, comorbidity, years of education, fear of side effects, ethnicity, family history of prostate cancer, prostate biopsy fear.

AS Facilitators and Barriers

Family and Social Support

- Justifying decision to others difficult, pressure from family and friends,

AS Facilitators and Barriers

Healthcare Provider Level

- Specific clinician,clinician concerns about the burden of intensive monitoring, missing progression,

Adherence

- **Health literacy** is defined as an "individual's capacity to access, understand, communicate, evaluate, utilise, and make decisions based on health information". Therefore, provision and access to relevant information is a consistent theme in both increasing the uptake of and adherence to AS.

- Consistency of information
- Access to information
- Professional and peer support
- Multidisciplinary provider approach

MDT/Consistency

Patients receiving treatment-counselling from two or more specialist clinicians were twice as likely to opt for AS, than radical treatment (43% versus 22%). This was further confirmed and described during semi-structured interviews (Lyons et al American Journal of Mens Health 2017:11:63-72)

AS Facilitators and Barriers

Healthcare Organisation and Practice Level

- Imaging facilities, biopsy techniques, clinician expertise, public versus insured populations, Cancer diagnostic and treatment targets, National Guidelines

AS Uptake & Adherence

- Clinicians attitudes
- Family and social support
- Patient education

AS Uptake &Adherence

- International guidelines
- Multidisciplinary management strategy
- Psychological support
- Supportive self management
- Social media interventions
- Motivational interviewing

(Kinsella et al Eur Urol 2018 in press)

Patient adherence to Active Surveillance

GSTT AS Audit 2011:

Baseline drop out rate wit standard of care 32% at 12 months

Standard versus Group Seminar

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Group A = Standard care

- ✓ Access to a nurse specialist
- ✓ Written information on active surveillance

Group B = Standard care +

- ✓ Peer group educational seminar
  - ✓ Imaging
- ✓ Biopsy technique,
- ✓ Historical active surveillance co-hort's
- ✓ Diet and lifestyle advice

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Weakness of standard care

- Limited information
- No control over info delivered
- No peer support
- Limited hospital interaction

Strengths of group seminar

- Delivery of info through peer group education seminars
- Support of multidisciplinary team
- Space
- Staffing
- Support of primary care
- Cheaper

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Patient characteristics, pathology and outcome were compared 12 months post diagnosis using descriptive statistics (t-test, chi-square test, and fisher's exact test).

	Group A (N=127)	Group B (N=117)	P-value
Mean Age, years (SD)	62 (7)	63 (7)	0.405
Mean PSA, ng/mL (SD)	9.52 (7.05)	8.46 (5.24)	0.190
DRE			
Benign	44 (35)	45 (38)	0.513
T2	72 (57)	66 (56)	
T3	11 (9)	6 (5)	
Biopsy Gleason Grade			<0.001
3+3	39 (31)	109 (93)	
3+4	88 (69)	8 (7)	
Patients dropping out of Active surveillance			
3+3	14/39 (36)	13/109 (12)	0.001
3+4	18/88 (20)	0/8 (0)	0.345

Seminars significantly decreased the total number of men dropping out of active surveillance:

25% in group A
11% in group B

Despite more patients with 3+4 disease in group A, the p value was not statistically significant.

14/39 patients (36%).Gleason 3+3 (p = 0.001)
18/88 patients (20%) Gleason 3+4 (p = 0.345)

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Results at 5yrs:

Two groups of consecutive patients diagnosed with low to intermediate risk prostate cancer as defined by the D'Amico classification system (Jan 2011-Jan 2012).

All patients considering AS underwent:

1. transrectal prostate biopsy

2. transperineal prostate biopsy within 3 months of diagnosis

Multivariate logistic regression was used to examine drop-out rates due to :

1. seminar participation

2. disease progression.

TABLE 2	Group A No seminar	Group B Seminar	p-value
	N=135	N=120	
Characteristics at AS entry			
Mean Age (SD)	62.4 (6.8)	63.3 (7.4)	0.341
Mean PSA (SD)	9.2 (7.0)	8.6 (5.3)	0.422
Grade n (%)			
3+3	42 (31.1)	111 (92.5)	0.001
3+4	93 (68.9)	9 (7.5)	
DRE assessment n (%)			
Benign	47 (34.8)	46 (38.3)	0.559
T2	77 (57.0)	68 (56.7)	
T3	11 (8.2)	6 (5.0)	
Program outcomes n (%)			
At 1 year:			
Remained in AS program	101 (74.8)	107 (89.2)	0.003
Dropped out	34 (25.2)	13 (11.2)	
At 5 years:			
Remained in AS program	62 (45.9)	68 (56.7)	0.005
Dropped out due to disease progression	17 (12.6)	26 (21.7)	
Dropped out with no disease progression	56 (41.5)	26 (21.7)	

Conclusion:

A single educational seminar delivered to groups of men with low to intermediate risk prostate cancer results in an increase in adherence to Active Surveillance, even at 5 years

% of patients remaining on active surveillance at 5 years

= 56.7% (with intervention) versus 45. 9% (p=0.05)

% of patients dropping out of active surveillance (despite no evidence of PCa progression.

= 21.7% (with intervention) versus 41.5%

How to do AS?

Can we skip biopsies

- Patients get fatigue from tests
- Guidelines suggest confirmatory biopsy within 12 months and then biopsies every 1-4 yrs MRI NICE/ UK

How active is active surveillance? Intensity of follow up during AS for prostate cancer in USA. Loeb et al J Urol 196 (2016) 721-726

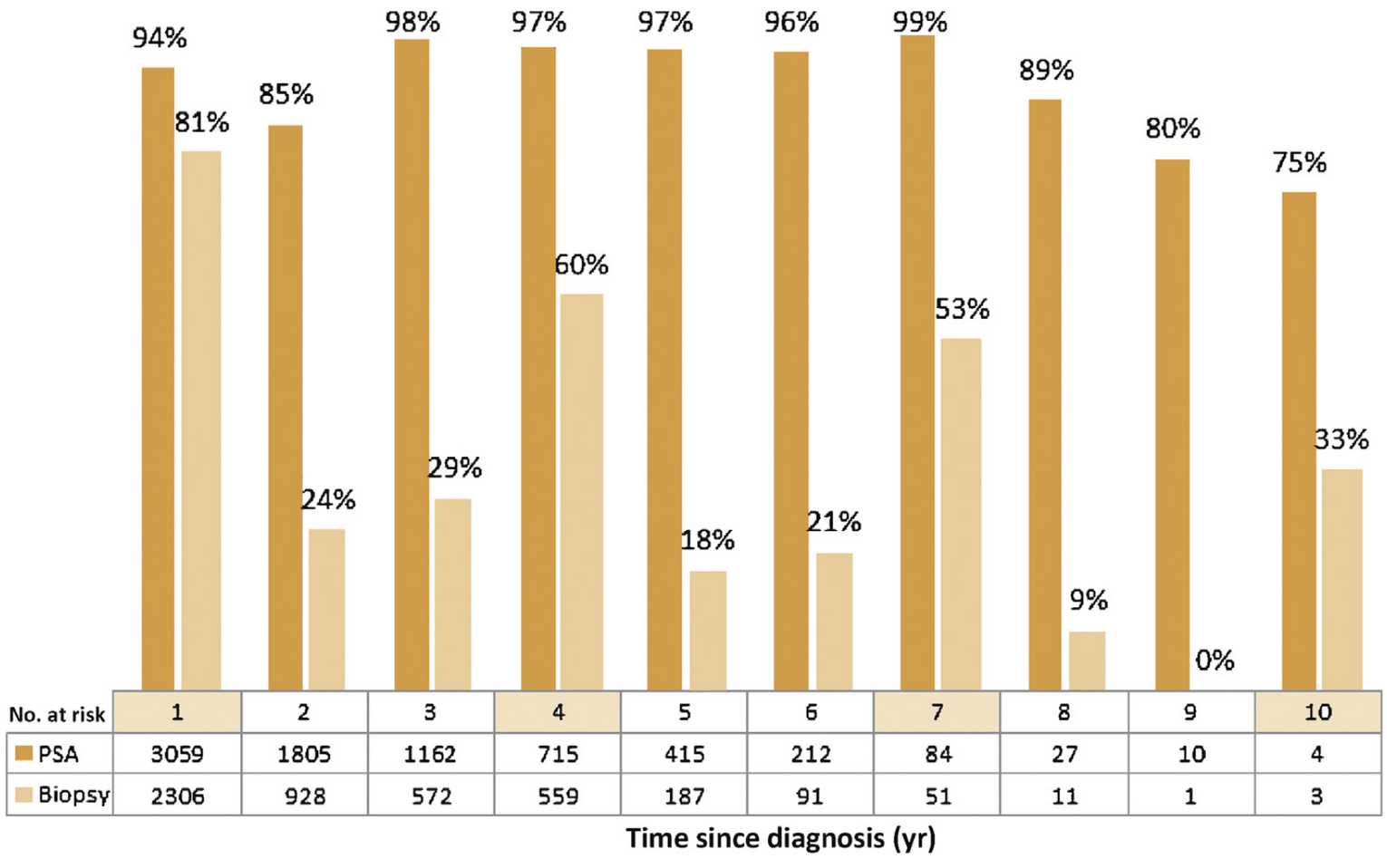
- PSA compliance good- 90%
- Biopsy compliance 10%
- Passive surveillance

Compliance rates with PRIAS Protocol and disease reclassification in non-compliers Borkhorst et al Eur Urol 68 (2015) 814-821

- PSA compliance is good - 90%
- Biopsy compliance is poor- 30%
- This is study cohort so better than real life

Can we avoid a protocol Bx in -ve MRI AS patient? Bokhorst et al Eur Urol 68 (2015) 814-82

- Men don't want protocol biopsy and urologists not convinced.



No. at risk	1	2	3	4	5	6	7	8	9	10
PSA	3059	1805	1162	715	415	212	84	27	10	4
Biopsy	2306	928	572	559	187	91	51	11	1	3

Time since diagnosis (yr)

Fig. 2 – Percentage complying with prostate-specific antigen (PSA) testing and prostate biopsies among men on active surveillance per year (standard repeat biopsies are highlighted).

Need to relax AS protcols

- AS is currently done according to strict protocols, with safe inclusion criteria

- Compliance to AS protocols is poor (PRIAS, PROBE)

- Screening causes significant lead time during which AS is a waste of time and gets men fed up of protocol before they are actually at any risk

- Need relaxed protocols to ensure longterm compliance after the first year confirming stage and grade

- Use MRI and molecular testing to identify the 10% of men that might progress.

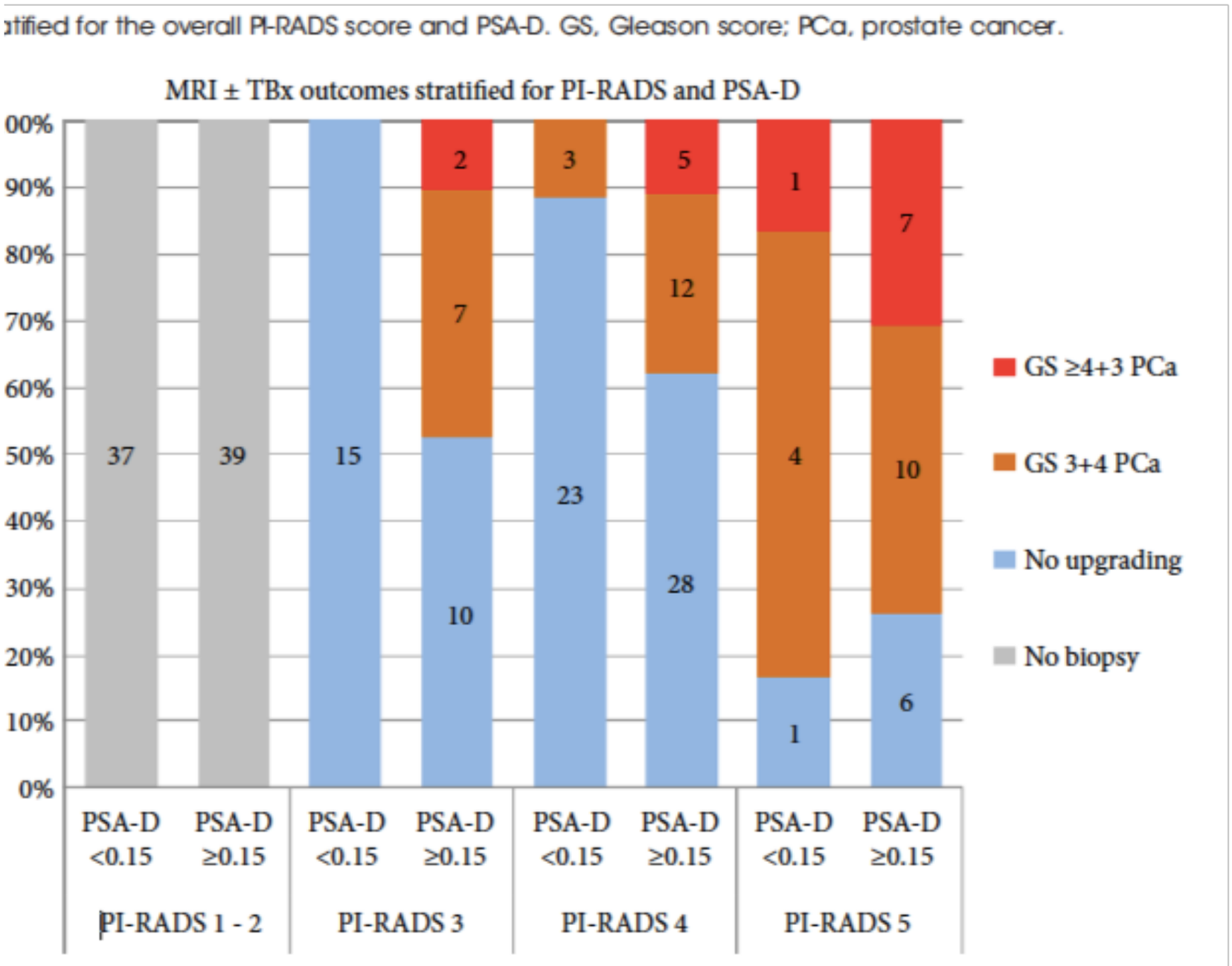
Ideal AS Test

- Men who need immediate treatment
- Men who would never benefit from treatment
- Men who may benefit from treatment at some point in the future

Role of MRI

- Reduce misclassification
- Data mostly in favour of MRI
- High NPV
- MRI very user dependant
- MRI role at diagnosis is clear. Less clear in AS

Risk stratification based on MRI and PSAD may reduce unnecessary follow up biopsy procedures in men on AS. Alberts et al BJU Int 2017 120:511-519



The efficacy of MP MRI and MRI Targeted Bx in risk classification of patients with CaP on AS. Recable et al JUrol 2016 196 374-381

- 1000 MRI and systematic bx- 35% reclassified and nothing missed

- Bx only PI-RADS 5, 5% of men, Reclassify 5%. Miss a lot.

- If biopsy PI-RADS 3-5, only Bx 66% of men. Reclassify 31%. Miss little

- Perhaps consider biopsies to men with an adverse PSAD

Active Surveillance

- Do consider all Gleason 3+3 for AS
- Some Gleason 3+4
- Use MRI to assist with AS
- Educate men. Support AS

Active Surveillance- Moving Forward

Declan Cahill

Gleason 6
Is it cancer?

- Linear versus bifurcated model of cancer

- Proliferative growth leads to BPH, LGPIN and Gleason 3

- Dysplastic growth leads to HGPIN, Gleason 4/5

A prospective comparison of MRI-US fused Targeted biopsy versus systematic ultrasound guided biopsy for detecting clinically significant prostate cancer in patients on AS. Da Rosa et al Journal of Magnetic resonance imaging 2015 41:220-225

- 100% NPV for clinically significant disease with negative MRI in men on AS

Serial MRI

- Reporting MRI in men on AS for CaP. The PRECISE Recommendations. A report of a European School of Oncology Task Force. Eur Urol 2016

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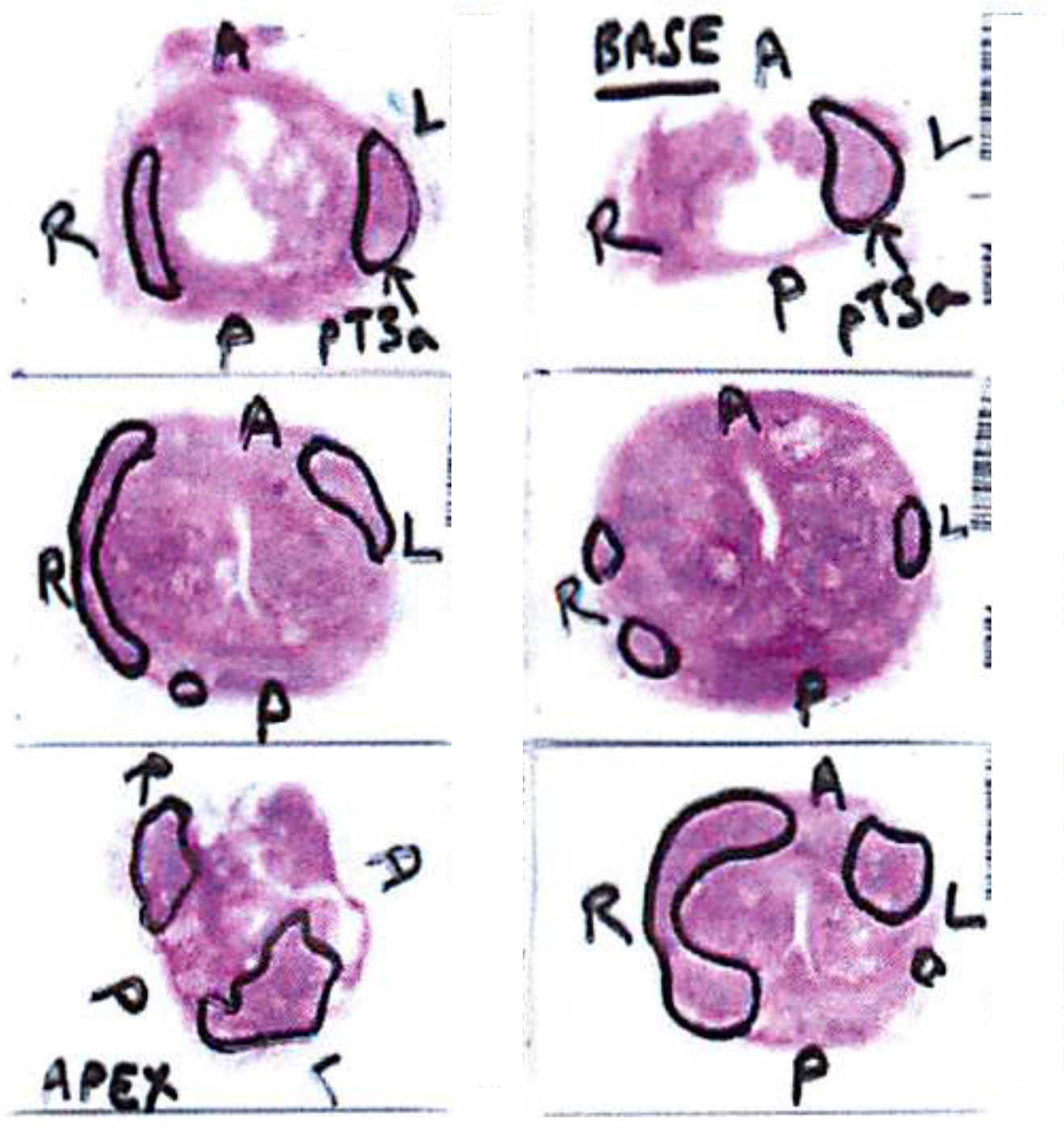

61 yrs, 3+3, PSA 6.7, T1c, (Brother CaP PSA 25, 3+4)
RARP 3+4, 6 ml, T3a (BN Invasion), PSA <0.04

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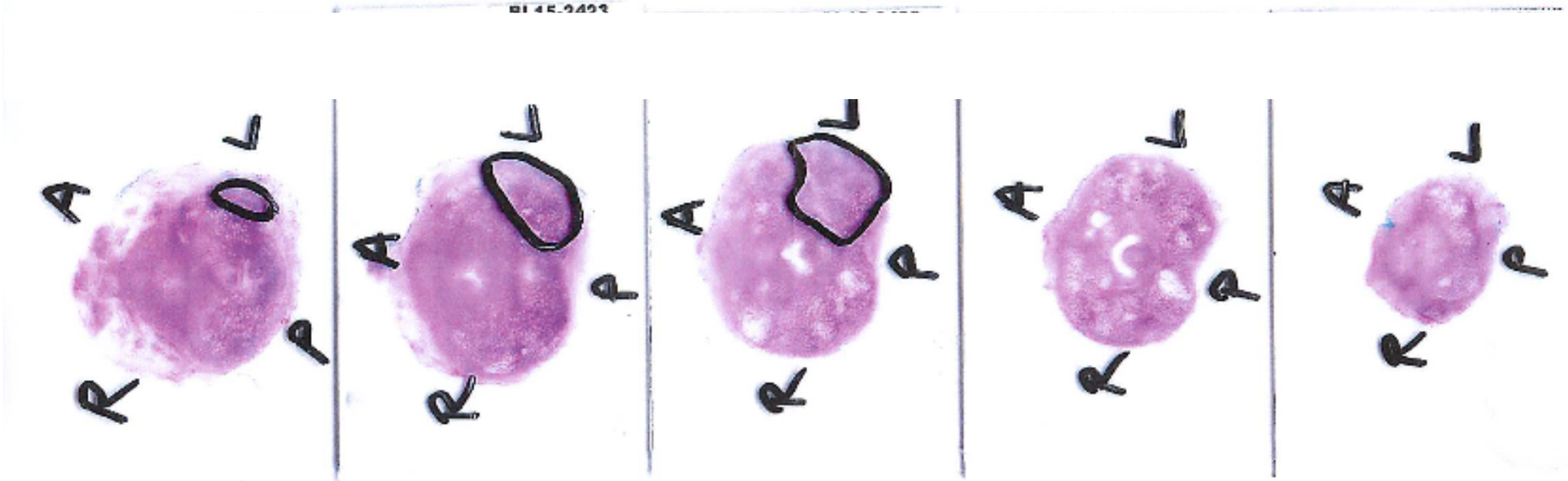

54 yrs, PSA 3.4, 3+3, T2 left base, RARP 2 cc of tumour, 3+4

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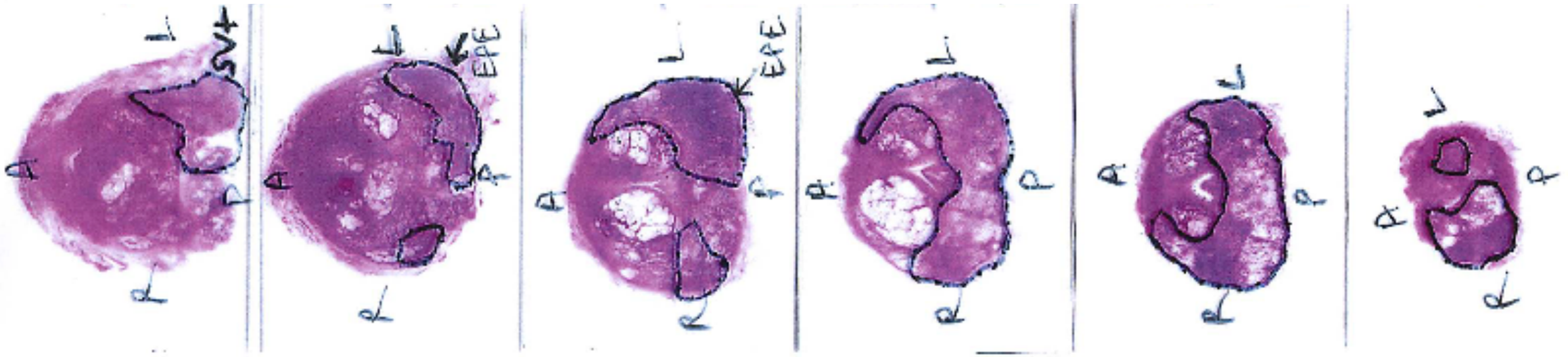

50 yrs, PSA 14, cT2, 4+3. RARP 8 cc 4+3, EPE, T3b, N0, PSA undetectable

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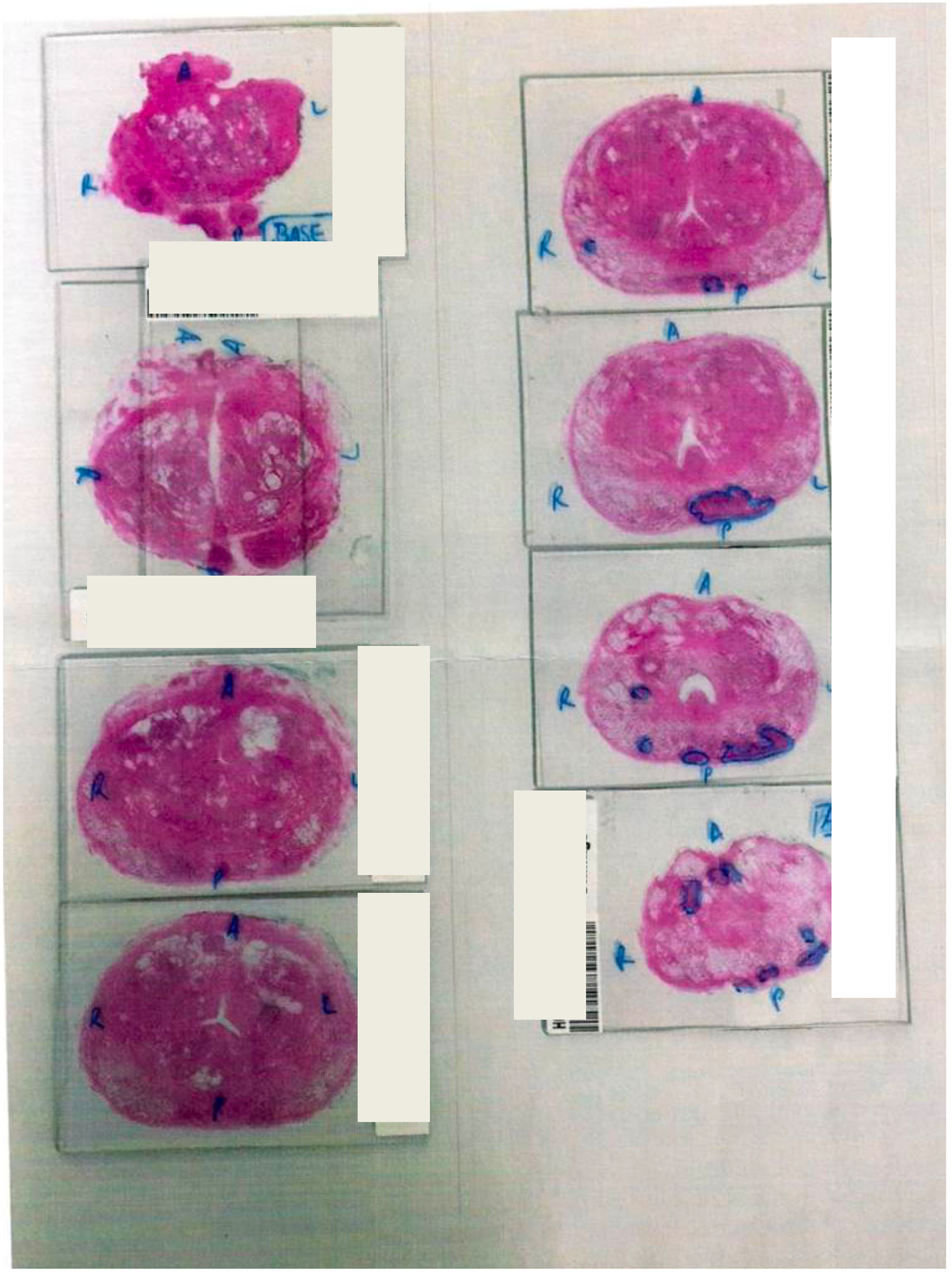

PSA 6, 70cc, Fit sexually active, 1 core 3+3, RP strongly recommended elsewhere.
TP Bx low volume 4+3
Pt choice RARP.
T2 4+3, SM –ve
PSA 0.2 at 7 months

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Meaningless?

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TRUSBx followed by TPBX- Guy's cohort

177 pts with Gleason 3+3 prostate cancer

69% confirmed Gleason 3+3

23% Gleason 3+4

12% 4+3/4+4/4+5

2/3 v 1/3

2/3 v 1/3

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38 pts had intermediate risk disease on TRUSBx

23 (61%) had intermediate disease confirmed

9 (24%) had in fact low risk disease

6 (16%) had high risk disease (2=4+4, 4=4+5)

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83/177 have had a second biopsy

2 x 4+3
1 x 4+4

3.6% grade progression in those rebiopsied

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A single TPBx does not compromise erectile function at 6 months

- 278 underwent a TPbx as stratification for active surveillance
- 24-38 cores

	IIEF-5
Pre biopsy	20.2
1 month post TPBx	10.4
3 month post TPBx	19.6
6 months post TPBx	20.4

EAU 2014

2nd TPBx and ED

- Sept 2009-Sept 2010 64 pts 2nd TPBx within 24 months of initial TPBx
- 24-38 cores
- 63 yrs, Mean PSA 9, 89%T2
- Benign 30%, 3+3 36%, 3+4 25%, 4+3/4/5 9%

•5/64 (8%) clot retention, 4/5 infected (no clot retention after 1st Bx)

•3/39 (8%) of those with normal erectile function pre Bx has significant persistent ED after 2nd Bx

TPBx as part of Active Surveillance does not compromise RARP

- 88 pts with TPBx pre RARP matched to 88 pts with TRBx pre RARP

	TPBx	TRBx	
n	88	88	
T stage		↑ T Stage	0.005
Op time (mins)	139	129	ns
Blood loss	340	260	ns
T2 +ve margins	5%	7%	ns
8wk pad free	66%	66%	ns
12m pad free	95%	92%	ns

Cost

	4 cases TPBx	6 cases TPBx	6 cases TRBX
Salary	£192/£125	£192/£125	£192/£125
Income	£1412	£2119	£2119
DSU Theatre cost	£1750	£1750	£48
Disposables	£544	£816	£180
Income	- £1032	-£597	+£1741

How to decide???

	Transrectal Bx	TPBx
Diagnosis		✔
Infection		✔
Active Surveillance		✔
Cost	✔	
Service provision	✔	

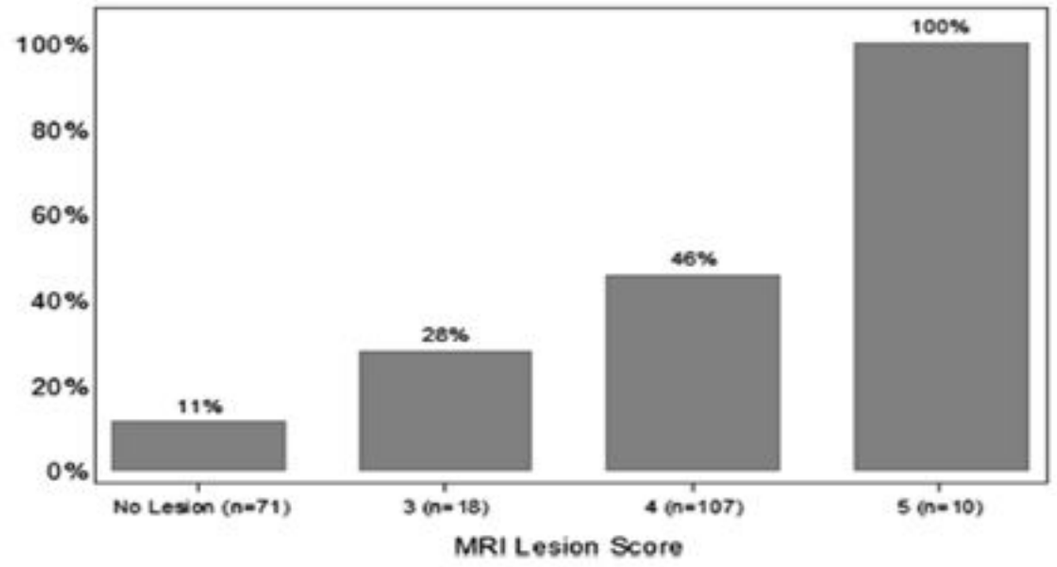
Alberts et al Eur Urol 2017

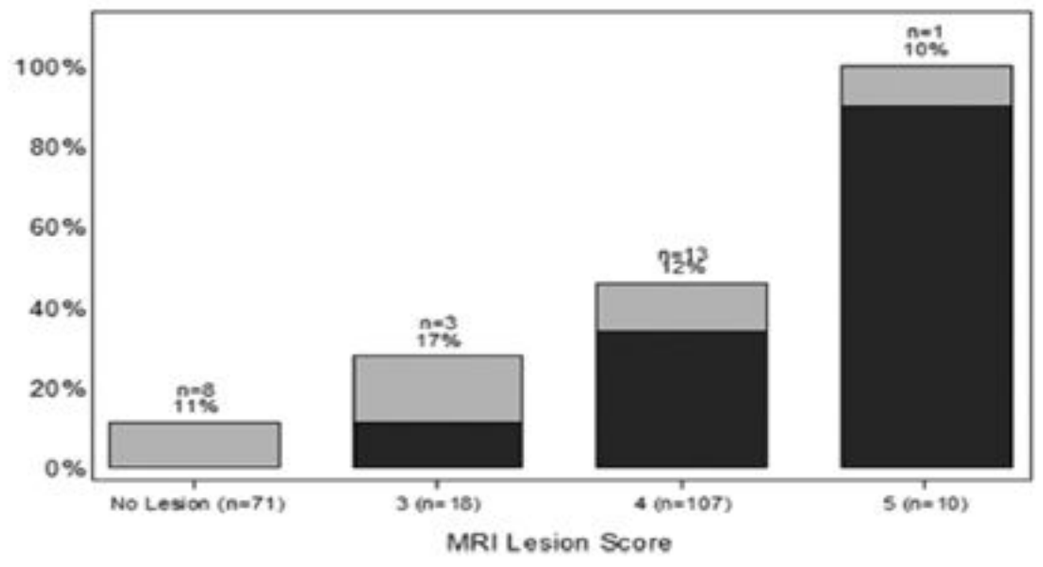
- Risk stratification before MRI and biopsy can avoid up to 68% of Gleason 3+3

- Considerable reduction in the detection of GS 3+3 CaP with MRI and TgBx

The Efficacy of Multiparametric Magnetic Resonance Imaging and Magnetic Resonance Imaging Targeted Biopsy in Risk Classification for Patients with Prostate Cancer on Active Surveillance

Pedro Recabal, Melissa Assel, Daniel D. Sjoberg, Daniel Lee, Vincent P. Laudone, Karim Touijer, James A. Eastham, Hebert A. Vargas, Jonathan Coleman and Behfar Ehdaie*





- 206 men on AS for 3+3
- 135 +ve MRI
- 73 had higher grade cancer detected
- Risk increases with MRI score

Recabal et al J Urol 2016 196 374-381

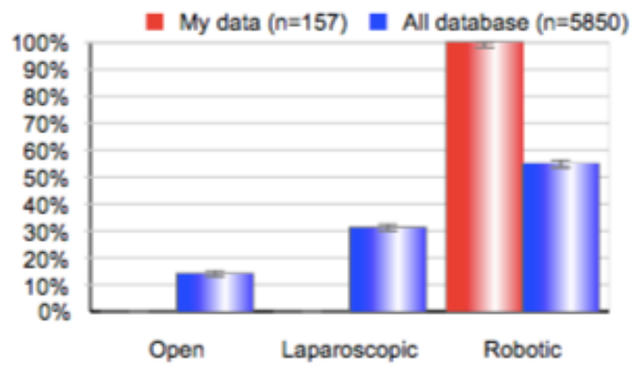
THE ROYAL MARSDEN

BAUS Data and Audit System

Log out

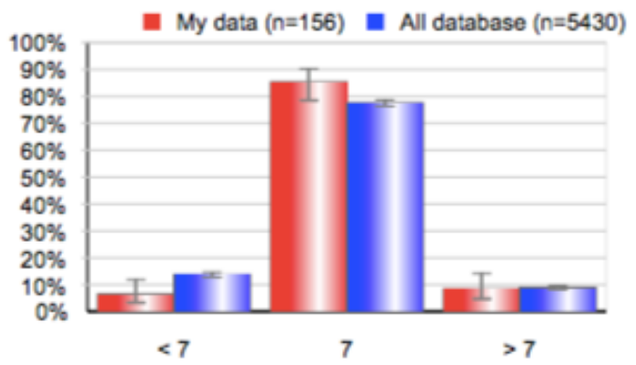
Radical Prostatectomy dashboard
All my data
Period between 01 January 2014 and 31 December 2014

Technique used

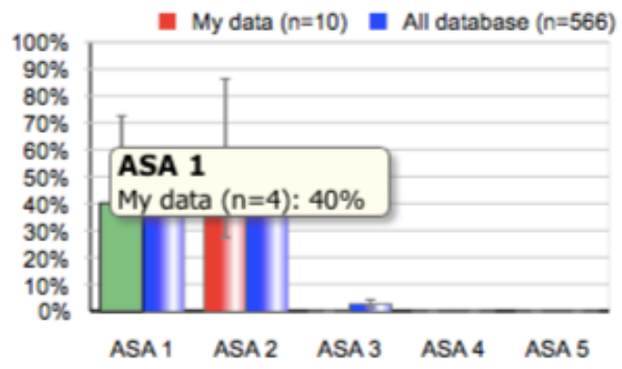


Biopsy Gleason Sum Score

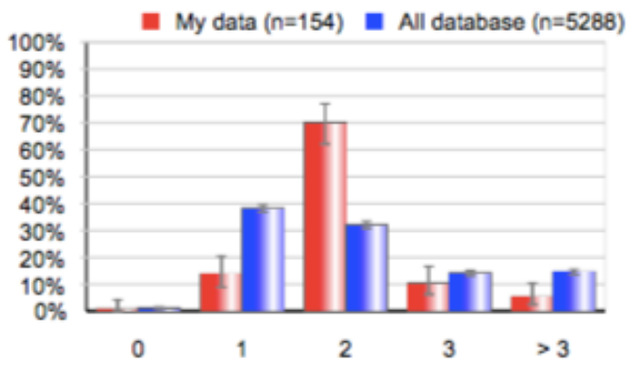
Surgical Specimen Gleason Sum Score



Pre-operative ASA Grade



Post-operative stay



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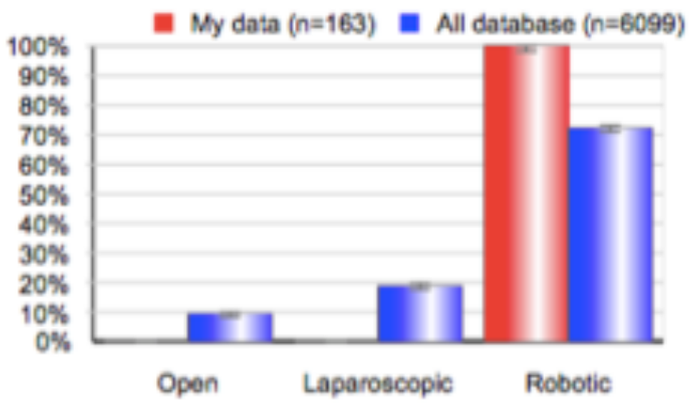
BAUS Data and Audit System

Log out

Radical Prostatectomy dashboard
All my data
Period between 01 January 2015 and 31 December 2015

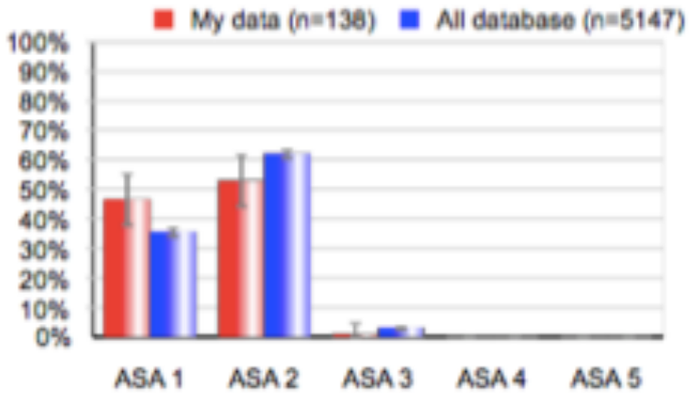
Technique used



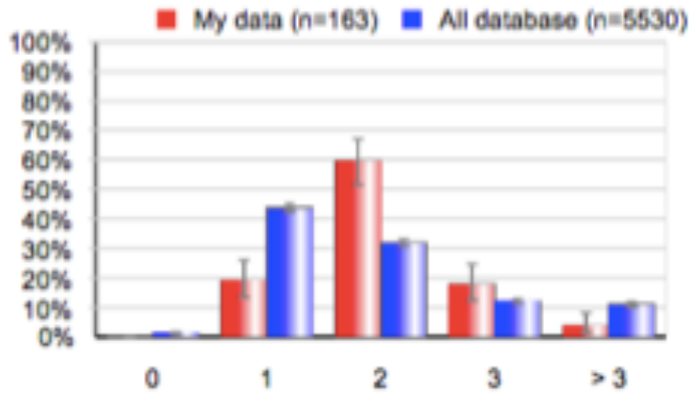
Biopsy Gleason Sum Score

Surgical Specimen Gleason Sum Score

Pre-operative ASA Grade



Post-operative stay



DC 3+3 RARP 2014

- "No 3+3 in 2014"

DC 3+3 RARP 2014

- "No 3+3 in 2014"

- 1st 3+3 case 23/1/2014 !!!!

3+3 in 2014

- 21/157 (13%) cases Bx 3+3
- 4/21 PSA >10, T3a
- 8/21 (38%) Private- overall 22% of cases private
- Other reasons Volume, MRI, LUTS, patient experience

- 4/21 (19%) +ve SM versus 14.8% in whole cohort
- 3/21 (14%) T3a, 2 established, 2 focal
- 3/21 (14%) 4+3 or ductal

- All PSA undetectable

3+3 in 2015

- 8/150 (5%) cases Bx 3+3
- 2/8 (25%) PSA >10, T3a
- 4/8(50%) Private
- Other reasons Volume, MRI, LUTS, patient drive

- 0/8 +ve SM versus 13% in whole cohort
- 3/8 (38%) T3a,
- All primary pattern 3
- One urethral stricture, one awful pelvic haematoma

3+3 in 2016

- 18/147 (12%) cases Bx 3+3
- 1/18 PSA >10
- 5/18(28%) Private
- Other reasons Volume, MRI, LUTS, patient drive

- 1/18 +ve SM
- 6/18 (33%) T3a,
- All primary pattern 3
- One significant positive margin, one awful post op sepsis/Coamox liver reaction/depression

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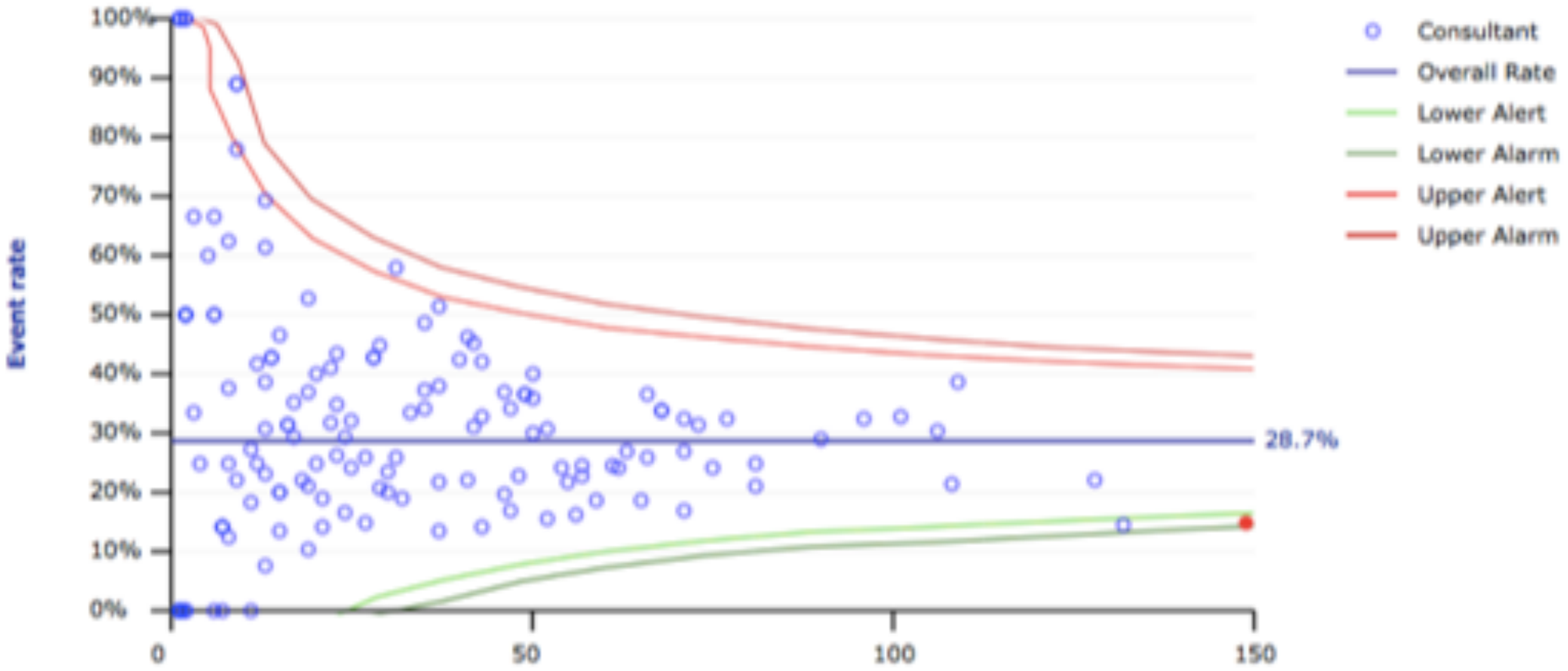
Funnel Plot - Positive Margin Rate (PROS) for Mr D J P Cahill (@ 14 June 2015)



Funnel Plot Setup Details

Selected outcomes: Positive margins <3 mm length, Positive margins >=3 mm length, Positive margins length unknown

Time Period: Jan 1st 2014 to Dec 31st 2014

Recorded number of patients with this outcome = 22 out of a total of 149

Observed rate = 14.8% *versus* the Overall rate = 28.7%

○ 1 and 2 σ ○ 2 and 3 σ ○ 3 and 4 σ ○ 4 and 5 σ ○ 90% and 95% ○ 95% and 99% ○ 99% and 99.9% ◉ 99.9% and 99.99%

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- 01412750285 esure
- 4004174006 reference
-

Biomarkers

- Who to biopsy?- PSA, PCA3, PHI, TMPRSS2-Erg, hK2, SKHLM-3

- Who to watch or treat? Oncotype Dx, Polaris, Promark, Decipher

- But now MPMRI

AS- Urology perspective

a)
PSA < 10

≤ T2

Gleason 3+3

b)
? 3+4, low volume 4+3- Possibly

a) >>>>>>>>>>>>>>>>>>>b)

AS- Pt Perspective

a)
Patients pushing surveillance

Almost any disease spec

b)
Doctors pushing surveillance

≤ T2
3+3
PSA 10ng/ml

NICE Guidelines

•Offer active surveillance as an option to men with low-risk localised prostate cancer for whom radical prostatectomy or radical radiotherapy is suitable. **(new 2014)**

•Consider active surveillance for men with intermediate-risk localised prostate cancer who do not wish to have immediate radical prostatectomy or radical radiotherapy. **[new 2014]**

•Do not offer active surveillance to men with high-risk localised prostate cancer. **[2014]**

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EUROPEAN UROLOGY

Systematic Review and Meta-analysis of Factors Determining Change to Radical Treatment in Active Surveillance for Localized Prostate Cancer

Andrew J. Simpkin [a,*], *Kate Tilling* [a,†], *Richard M. Martin* [a,b], *J. Athene Lane* [a], *Freddie C. Hamdy* [c], *Lars Holmberg* [d], *David E. Neal* [e], *Chris Metcalfe* [a,†], *Jenny L. Donovan* [a,†]

[a] *School of Social and Community Medicine, University of Bristol, Bristol, UK;* [b] *NIHR Bristol Nutrition Biomedical Research Unit, University of Bristol, Bristol, UK;* [c] *Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK;* [d] *Guy's Hospital, London, UK;* [e] *Cancer Research UK, Cambridge Research Institute, Cambridge, UK*

European Urology 67 (2015) 993-1005

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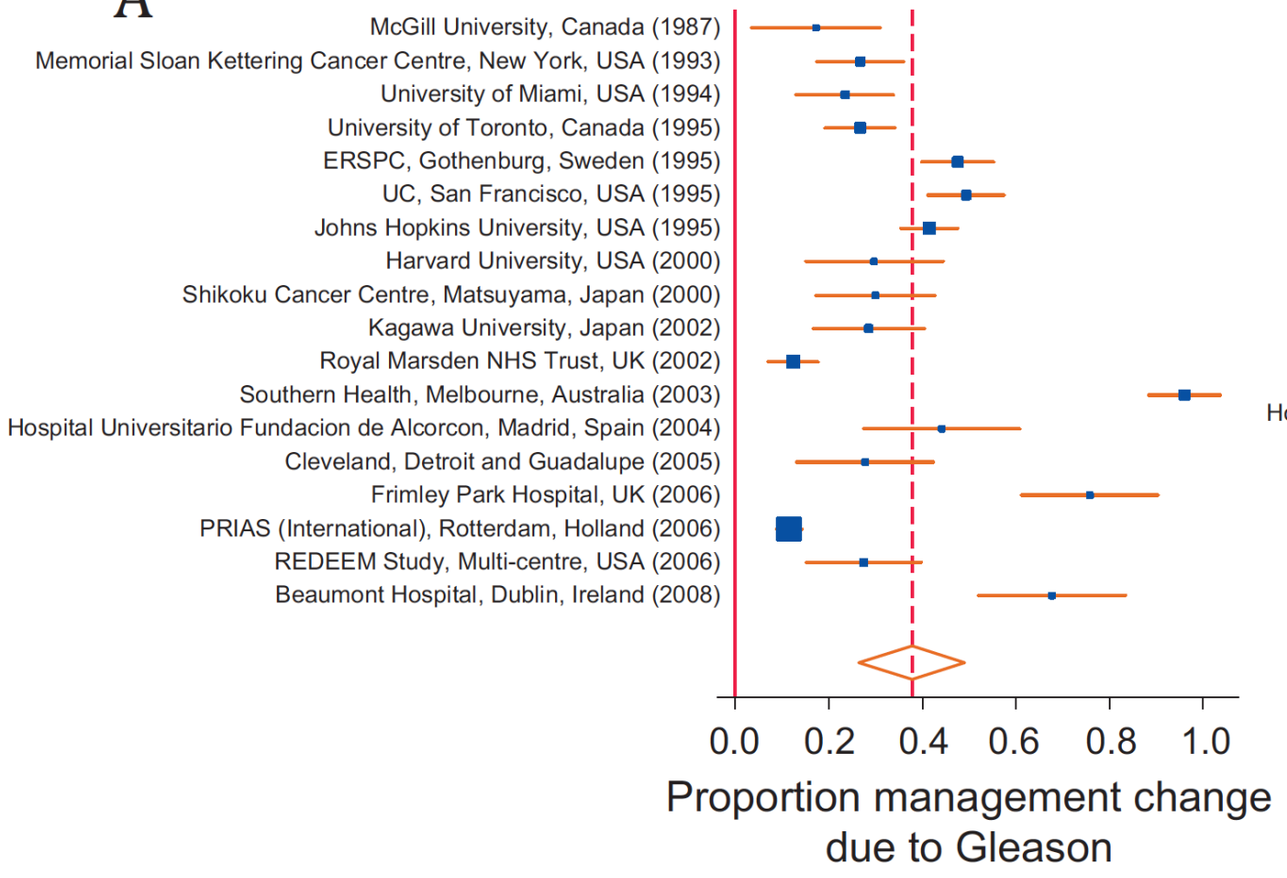
A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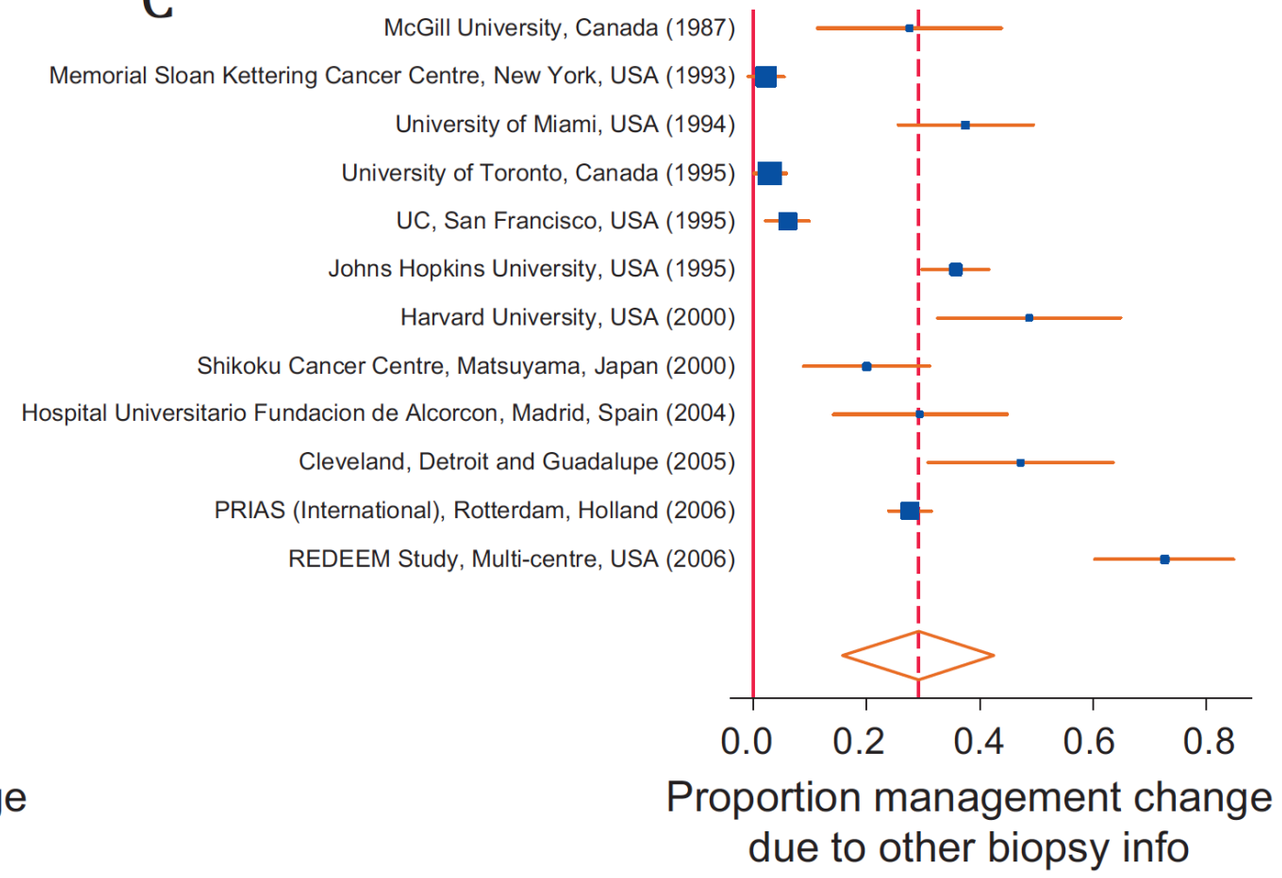
ERSPC, Gothenburg, Sweden (1995)
UC, San Francisco, USA (1995)
Johns Hopkins University, USA (1995)
Harvard University, USA (2000)
Shikoku Cancer Centre, Matsuyama, Japan (2000)
Kagawa University, Japan (2002)
Royal Marsden NHS Trust, UK (2002)
Southern Health, Melbourne, Australia (2003)
Hospital Universitario Fundacion de Alcorcon, Madrid, Spain (2004)
Cleveland, Detroit and Guadalupe (2005)
Frimley Park Hospital, UK (2006)
PRIAS (International), Rotterdam, Holland (2006)
REDEEM Study, Multi-centre, USA (2006)
Beaumont Hospital, Dublin, Ireland (2008)
0.0
0.2
0.4
0.6
0.8
1.0
Proportion management change due to Gleason

C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Harvard University, USA (2000)
Shikoku Cancer Centre, Matsuyama, Japan (2000)
Hospital Universitario Fundacion de Alcorcon, Madrid, Spain (2004)
Cleveland, Detroit and Guadalupe (2005)
PRIAS (International), Rotterdam, Holland (2006)
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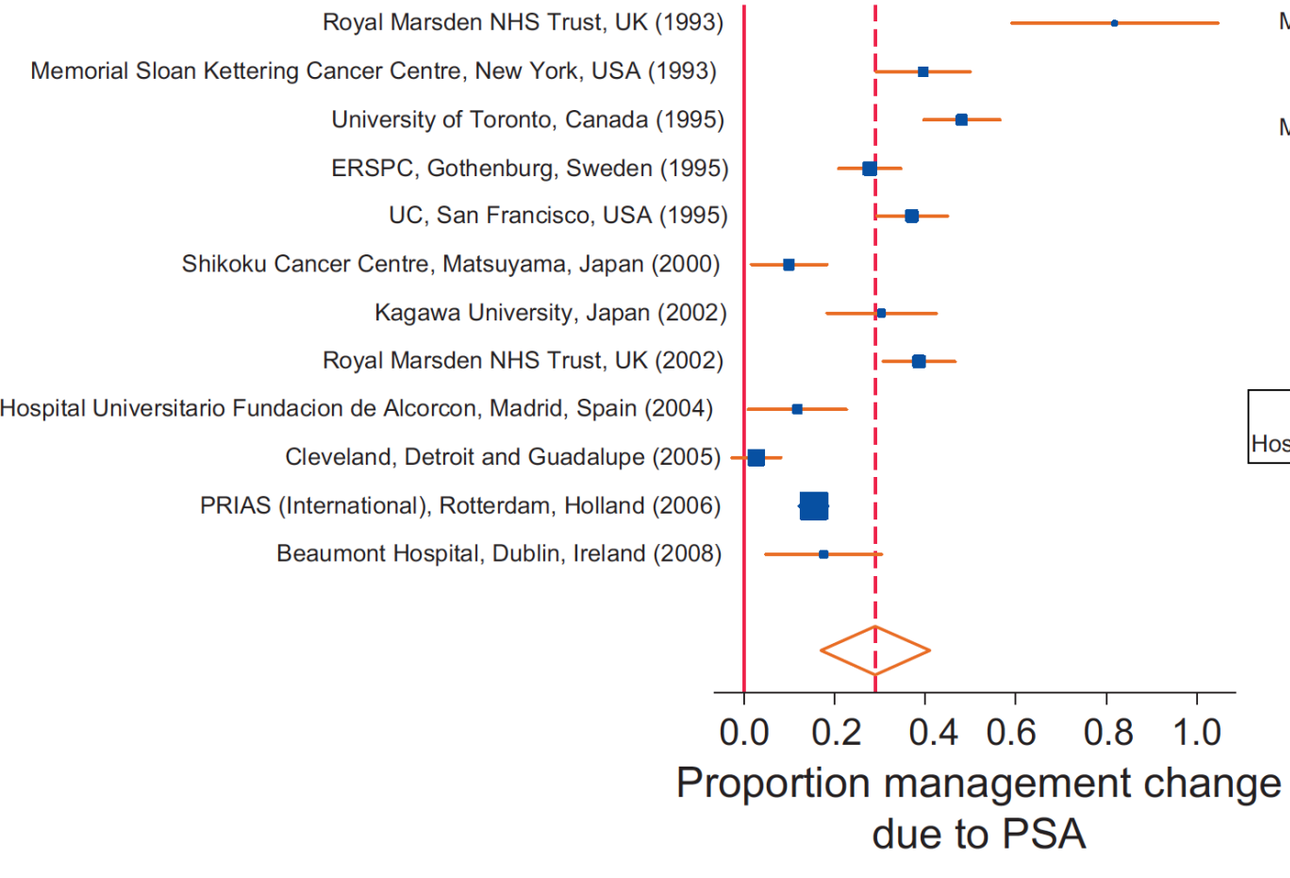
0.0
0.2
0.4
0.6
0.8
Proportion management change due to other biopsy info

B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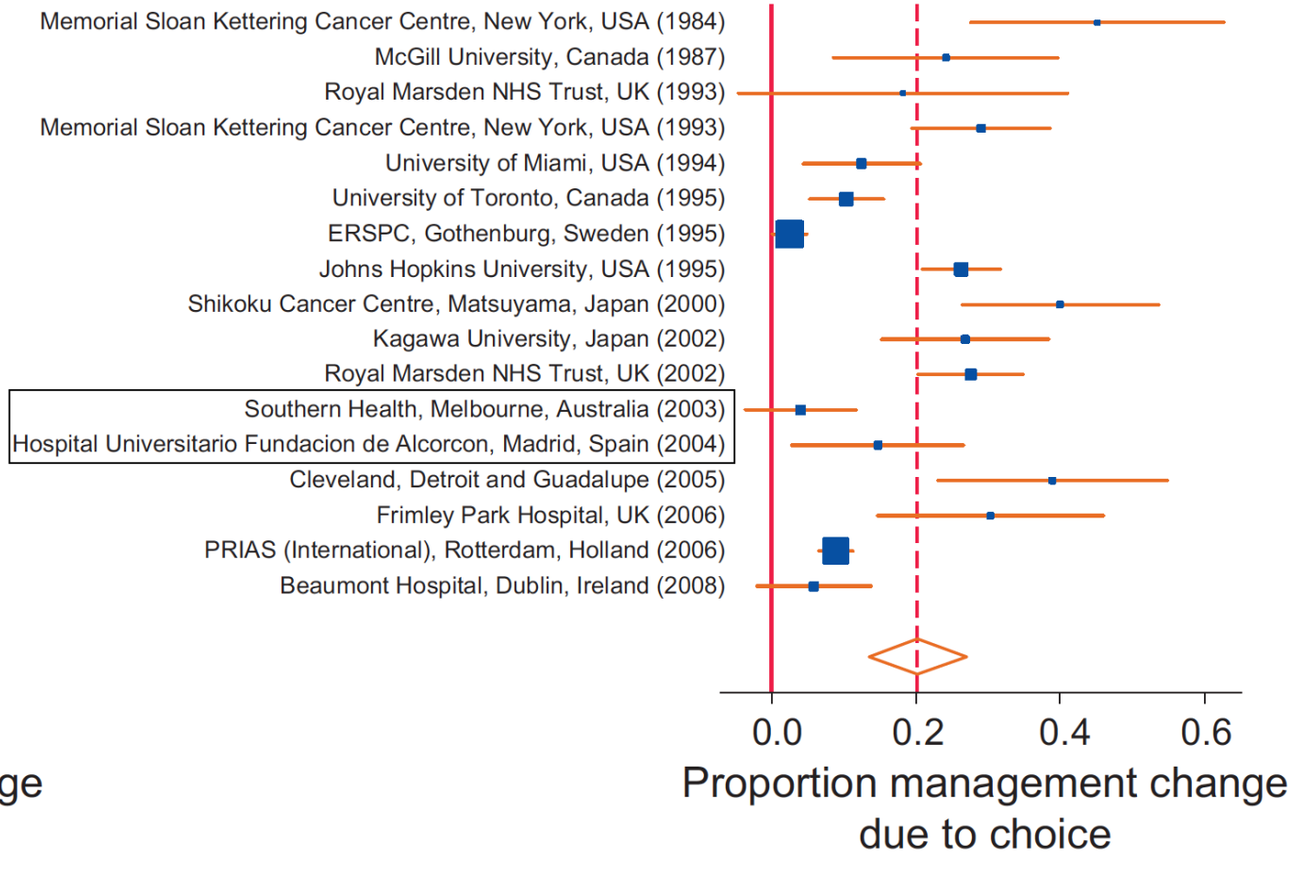
0.0
0.2
0.4
0.6
0.8
1.0
Proportion management change due to PSA

D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Cleveland, Detroit and Guadalupe (2005)
Frimley Park Hospital, UK (2006)
PRIAS (International), Rotterdam, Holland (2006)
Beaumont Hospital, Dublin, Ireland (2008)
0.0
0.2
0.4
0.6
Proportion management change due to choice

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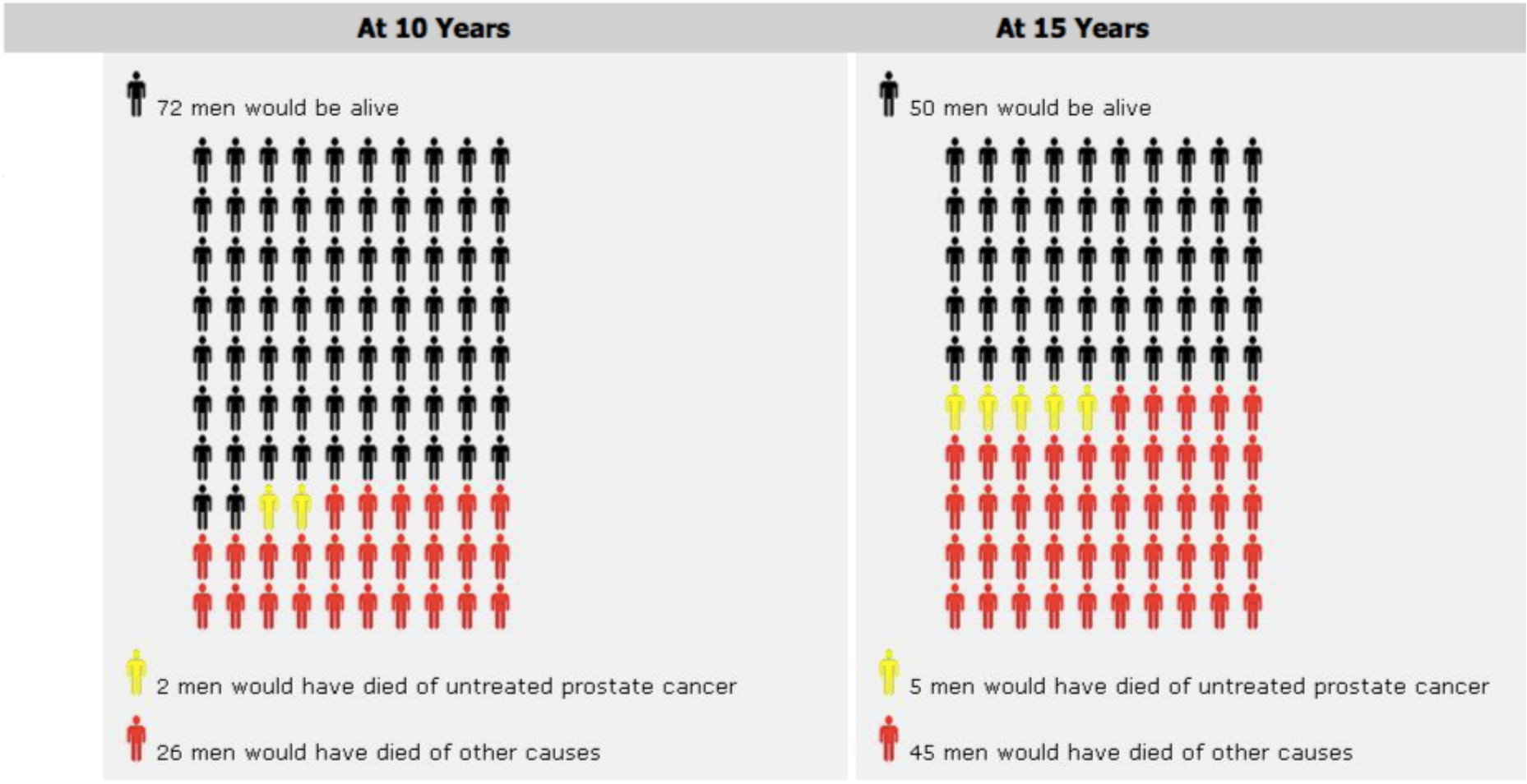
nomograms.org



The graph above has taken account the following information that you have reported:

Health Conditions: Asthma.

Prostate Cancer Characteristics

Age: 68.

T Stage: T2A.

Gleason Grade: 6.

PSA: 7.

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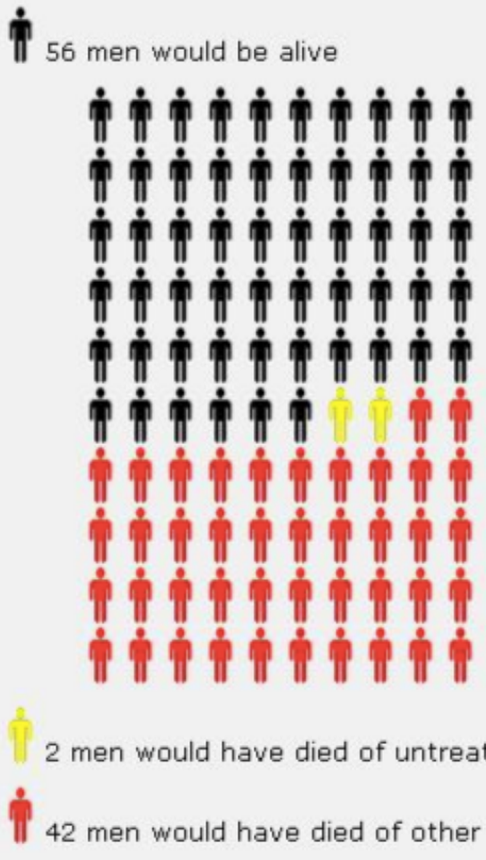
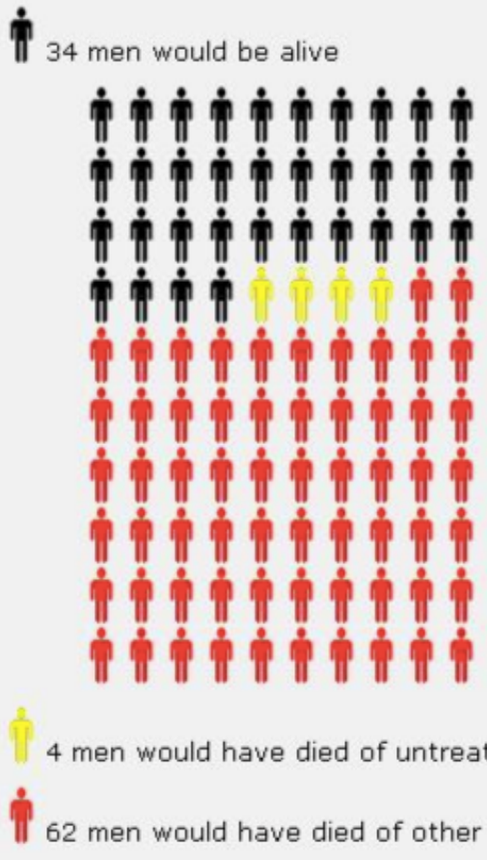
At 10 Years	At 15 Years
	
56 men would be alive	34 men would be alive
2 men would have died of untreated prostate cancer	4 men would have died of untreated prostate cancer
42 men would have died of other causes	62 men would have died of other causes

The graph above has taken account the following information that you have reported:

Health Conditions: Asthma; Smoked more than 100 cigarettes.

Prostate Cancer Characteristics

Age: 68.

T Stage: T2A.

Gleason Grade: 6.

PSA: 7.

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Pre PSA non treatment studies, T1a prostate cancers

- Johansson et al, Albertson et al, Rider et al
- Excellent 10-20 yr survival. Little room for improvement from biopsies.