Overdiagnosis

Making people sick in the pursuit of health

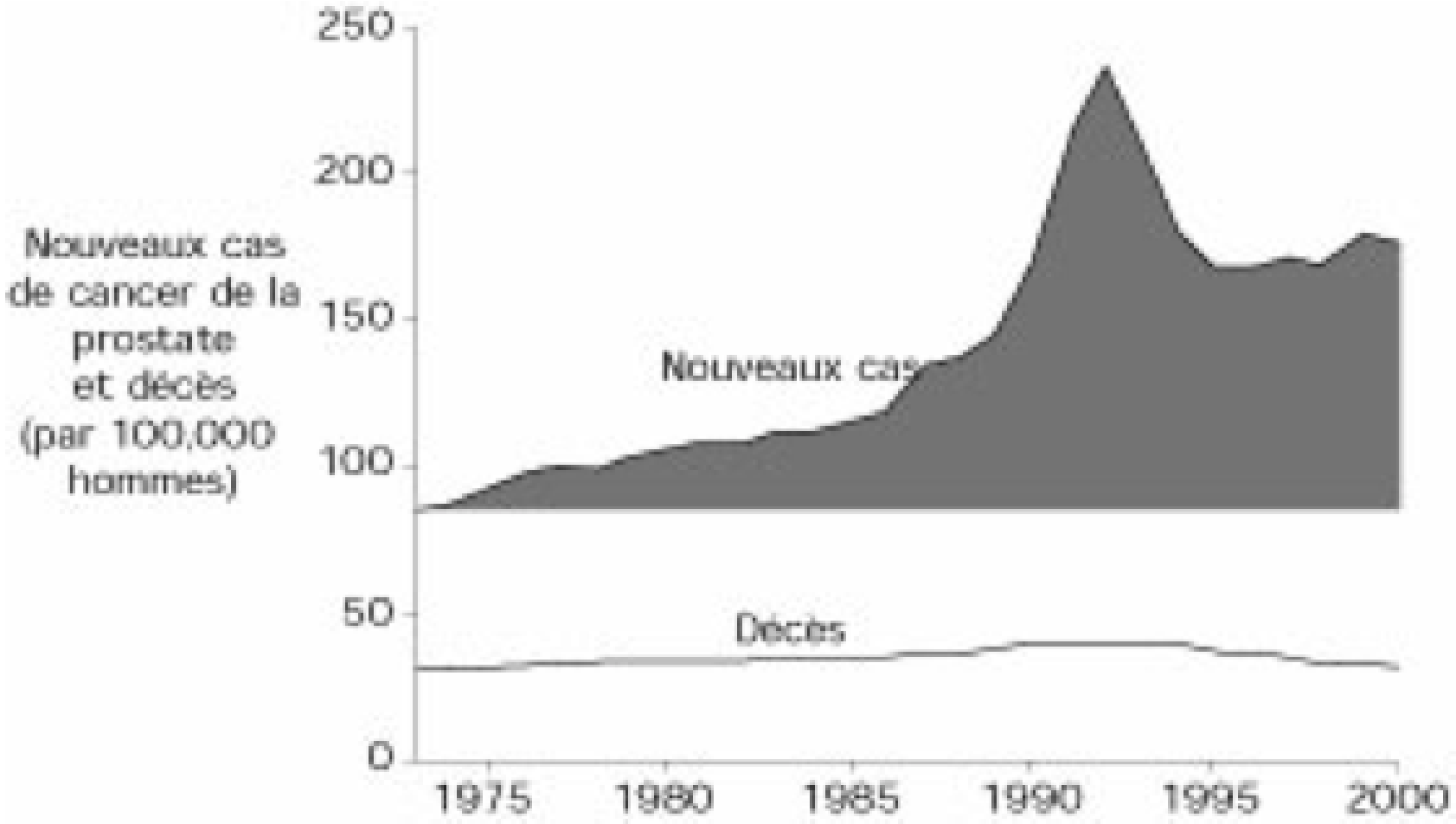
Drs Gilbert Welch, Lisa Schwartz, Steven Woloshin

Screening for prostate cancer

- « Screening for prostate cancer has become the poster child of overdiagnosis in cancer. »Welch, Schwartz and Woloshin.

- « A profit-driven public health disaster .» Prof. Ablin, discoverer of PSA

Prostate cancer overdiagnosis



Prostate cancer overdiagnosis

- 2.3 million US men diagnosed in the last quarter of XXth Century.
- Between 1 and 2 per thousand died in hospital following surgery.
- 17% required a second surgical intervention.
- 28% require to wear a diaper.
- More than half have become impotent.
- 33% of those treated with radiotherapy still have to put up with chronic diarrhea or imperative bm, 2 years after treatment.

Reservoir of overdiagnosis for prostate cancer: men killed in accidents and found to have prostate cancer

20-29 ans	8,6%
30-39	31%
40-49	40%
50-59	46%
60-69	68%
70-79	83%

Conclusion

- « All screening programmes do harm. »Angela Raffle and Muir Gray
- Some do good as well, at reasonable cost, in terms of human suffering and resources.
- Prostate cancer screening does not.

References

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Thank you

Fernand Turcotte, M.D., M.P.H., FRCPC
Université Laval.

Prostate Cancer Canada

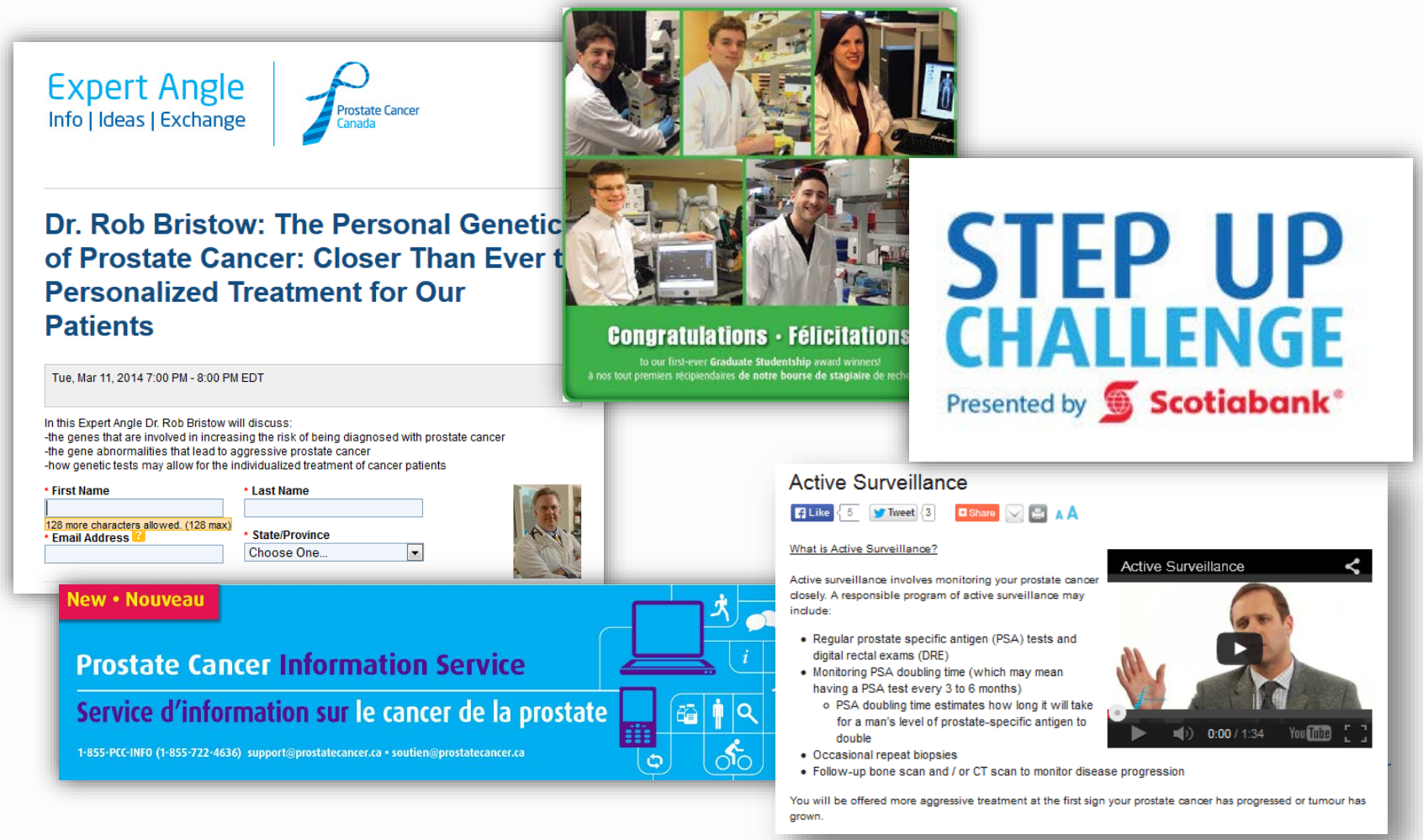
Presentation for

ARCC Conference 2015

Monday, May 25, 2015

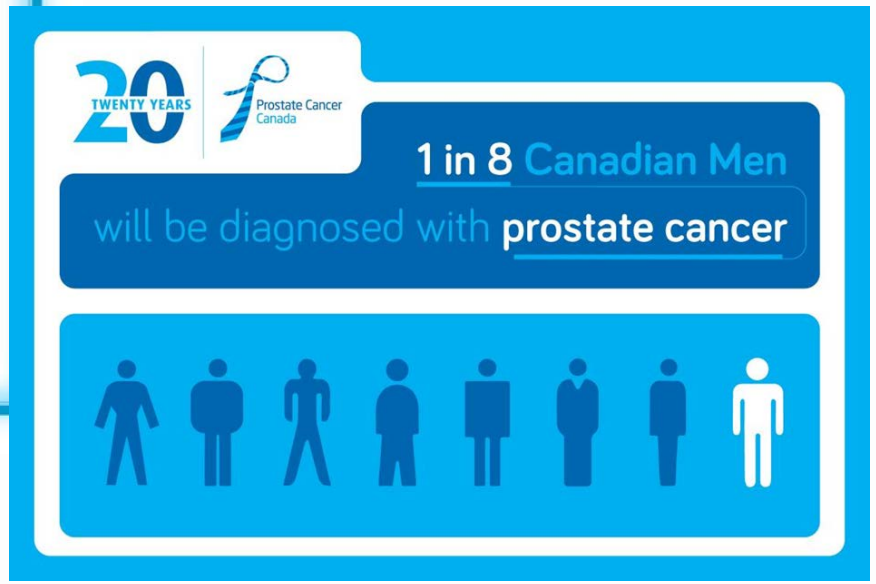
Rocco Rossi
President & CEO Prostate Cancer Canada
@roccorossiTO
rocco@prostatecancer.ca

Prostate Cancer Canada



Prostate Cancer Statistics

Prostate Cancer Canada



PSA Recommendations

- Conflicting views regarding screening using PSA test
  - No screening
    - US Task Force, Canadian Task Force
  - Establishing baseline
    - European Association of Urology, Melbourne Consensus
- All looking at same evidence but coming up with different recommendations

Prostate Cancer Canada

Prostate Cancer Screening RCTs

- Most credible prostate cancer screening trial (ERSPC) showed the longer you follow the cohort, the lower the number needed to screen and treat to save one life
- ERSPC screening trial shows substantial mortality reduction

ERSPC Follow up	# needed to screen	# needed to treat
9 years	1410	48
11 years	979	35
13 years	781	27

Early Detection

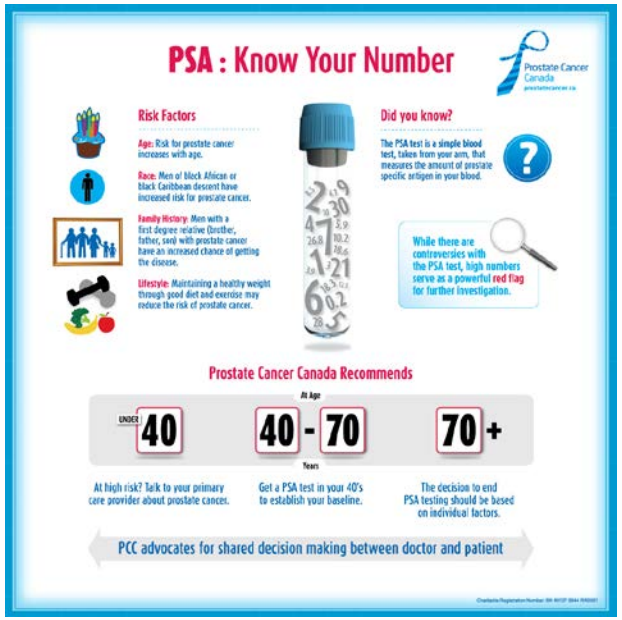
- Screening reduces the number of men dying from prostate cancer
- The cases of advanced (metastatic) prostate cancer would double, resulting in an estimated 13-20 percent increase in annual prostate cancer deaths
- Mortality from prostate cancer has dropped by 40% over the last 20 years

5-Year Relative Survival Rate by Stage at Time of Diagnosis*	
Stage	**5-year Relative Survival Rate**
Local	>90%
Metastatic	28%

*American Cancer Society. Survival Rates for Prostate Cancer. 2015.

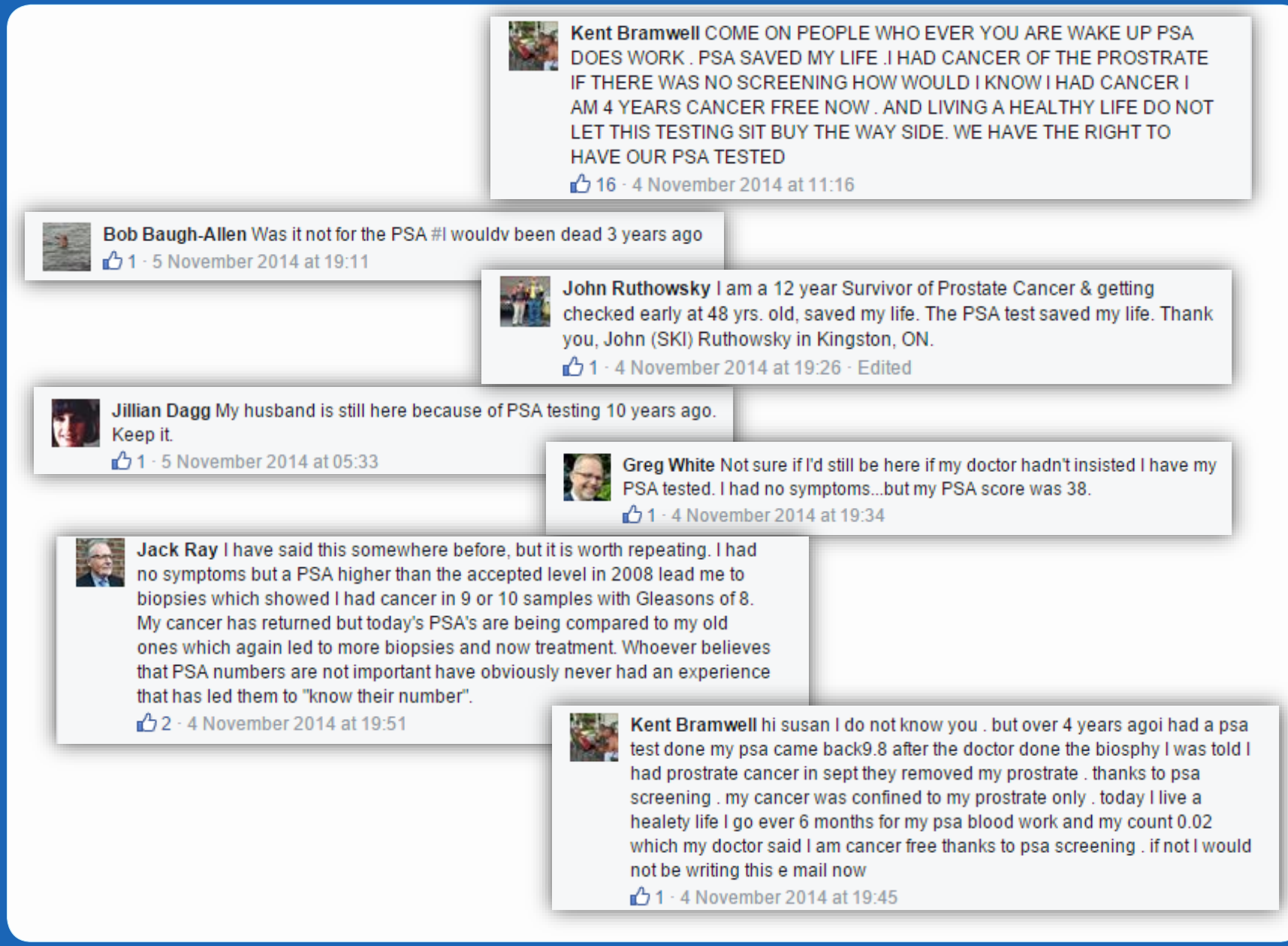
“Smart Screening”

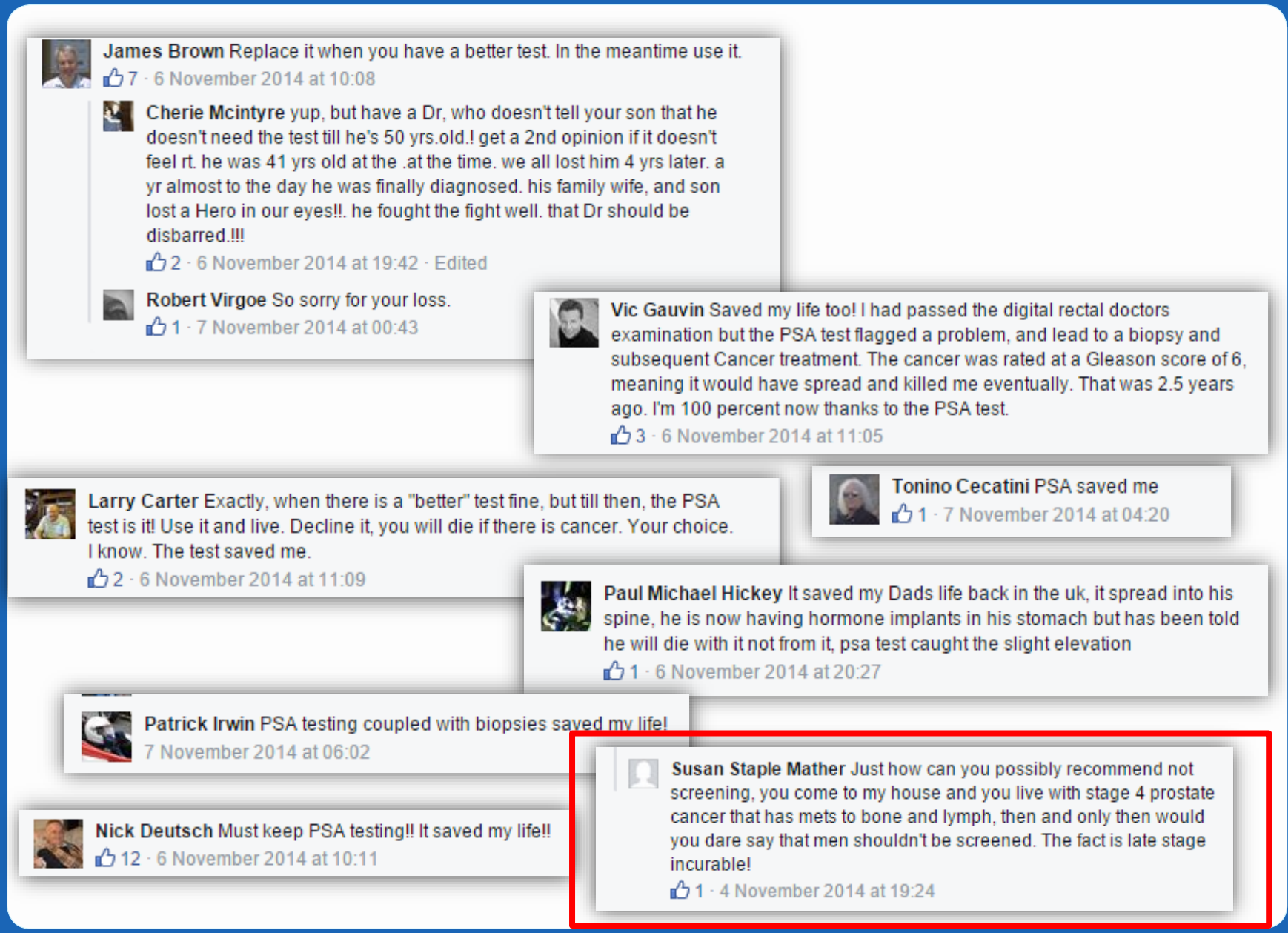
- Prostate Cancer Canada believes in “smart screening”
- Men are encouraged to be tested to establish a baseline number in their 40s with follow-up based on individual’s risk profile
- PSA test not perfect but is currently the best indicator that something may be wrong with the prostate
- While there are controversies with the PSA test, high numbers serve as a **red flag** for further investigation
- PSA test is only one part of the diagnostic process



Active Surveillance

- Early detection saves lives but cannot distinguish between low and high risk disease
  - Risk of over treatment
- One method to mitigate over treatment is to use Active Surveillance
- Not every case requires immediate treatment

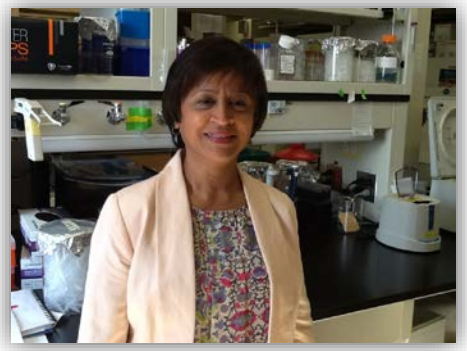

Kent Bramwell COME ON PEOPLE WHO EVER YOU ARE WAKE UP PSA DOES WORK . PSA SAVED MY LIFE .I HAD CANCER OF THE PROSTRATE IF THERE WAS NO SCREENING HOW WOULD I KNOW I HAD CANCER I AM 4 YEARS CANCER FREE NOW . AND LIVING A HEALTHY LIFE DO NOT LET THIS TESTING SIT BUY THE WAY SIDE. WE HAVE THE RIGHT TO HAVE OUR PSA TESTED
16 · 4 November 2014 at 11:16
Bob Baugh-Allen Was it not for the PSA #I wouldv been dead 3 years ago
1 · 5 November 2014 at 19:11
John Ruthowsky I am a 12 year Survivor of Prostate Cancer & getting checked early at 48 yrs. old, saved my life. The PSA test saved my life. Thank you, John (SKI) Ruthowsky in Kingston, ON.
1 · 4 November 2014 at 19:26 · Edited
Jillian Dagg My husband is still here because of PSA testing 10 years ago. Keep it.
1 · 5 November 2014 at 05:33
Greg White Not sure if I'd still be here if my doctor hadn't insisted I have my PSA tested. I had no symptoms...but my PSA score was 38.
1 · 4 November 2014 at 19:34
Jack Ray I have said this somewhere before, but it is worth repeating. I had no symptoms but a PSA higher than the accepted level in 2008 lead me to biopsies which showed I had cancer in 9 or 10 samples with Gleasons of 8. My cancer has returned but today's PSA's are being compared to my old ones which again led to more biopsies and now treatment. Whoever believes that PSA numbers are not important have obviously never had an experience that has led them to "know their number".
2 · 4 November 2014 at 19:51
Kent Bramwell hi susan I do not know you . but over 4 years agoi had a psa test done my psa came back9.8 after the doctor done the biosphy I was told I had prostrate cancer in sept they removed my prostrate . thanks to psa screening . my cancer was confined to my prostrate only . today I live a healety life I go ever 6 months for my psa blood work and my count 0.02 which my doctor said I am cancer free thanks to psa screening . if not I would not be writing this e mail now
1 · 4 November 2014 at 19:45


James Brown Replace it when you have a better test. In the meantime use it.
7 · 6 November 2014 at 10:08
Cherie Mcintyre yup, but have a Dr, who doesn't tell your son that he doesn't need the test till he's 50 yrs.old.! get a 2nd opinion if it doesn't feel rt. he was 41 yrs old at the .at the time. we all lost him 4 yrs later. a yr almost to the day he was finally diagnosed. his family wife, and son lost a Hero in our eyes!!. he fought the fight well. that Dr should be disbarred.!!!
2 · 6 November 2014 at 19:42 · Edited
Robert Virgoe So sorry for your loss.
1 · 7 November 2014 at 00:43
Vic Gauvin Saved my life too! I had passed the digital rectal doctors examination but the PSA test flagged a problem, and lead to a biopsy and subsequent Cancer treatment. The cancer was rated at a Gleason score of 6, meaning it would have spread and killed me eventually. That was 2.5 years ago. I'm 100 percent now thanks to the PSA test.
3 · 6 November 2014 at 11:05
Tonino Cecatini PSA saved me
1 · 7 November 2014 at 04:20
Larry Carter Exactly, when there is a "better" test fine, but till then, the PSA test is it! Use it and live. Decline it, you will die if there is cancer. Your choice. I know. The test saved me.
2 · 6 November 2014 at 11:09
Paul Michael Hickey It saved my Dads life back in the uk, it spread into his spine, he is now having hormone implants in his stomach but has been told he will die with it not from it, psa test caught the slight elevation
1 · 6 November 2014 at 20:27
Patrick Irwin PSA testing coupled with biopsies saved my life!
7 November 2014 at 06:02
Susan Staple Mather Just how can you possibly recommend not screening, you come to my house and you live with stage 4 prostate cancer that has mets to bone and lymph, then and only then would you dare say that men shouldn't be screened. The fact is late stage incurable!
1 · 4 November 2014 at 19:24
Nick Deutsch Must keep PSA testing!! It saved my life!!
12 · 6 November 2014 at 10:11

Funding New Research

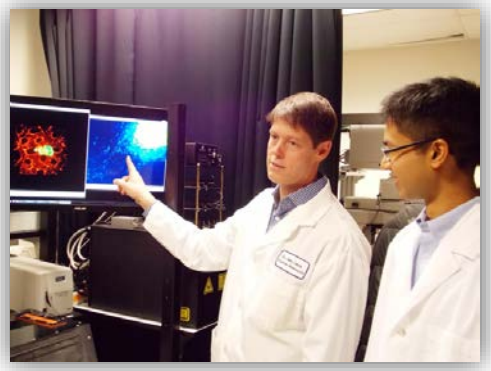
Prostate Cancer Canada

Distinguishing between aggressive and indolent prostate cancers



Dr. Bharati Bapat
Toronto, ON

Dr. Robert Day
Sherbrooke, QC



Dr. John Lewis
Edmonton, AB

MOVEMBER FOUNDATION

WEAR

PLAID

FOR

Dad

This
Father's Day Season,
Put on Something Plaid.

July 19TH, 2015

PORTEZ DU

CARREAUTÉ

POUR

papa

Cette année,
pendant la période de la fête des
Pères, portez un vêtement à carreaux.

19 Juin 2015

Thank you!

Prostate Cancer Canada

Clinical Solutions to the Over-Diagnosis and Treatment of Prostate Cancer

Andrew Loblaw
Professor
Department of Radiation Oncology
Institute of Health Policy, Management and Evaluation
University of Toronto

ARCC, Montreal
May 25 2015

University of Toronto

Sunnybrook
ODETTE CANCER CENTRE
A Cancer Care Ontario Partner

Objectives

- To review the data fueling the controversy of PSA screening
- To discuss current and future management strategies to improve outcomes and decrease cost

Faculty Disclosure Statement

Financial Disclosure (within 2 years)

Grants/Research Support:

- Sanofi, Paladin

Honoraria:

- Amgen, AstraZeneca, Elekta, GE, Janssen, Paladin, Sanofi

Advisory Boards:

- Amgen, Astellas, Janssen, Sanofi

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- TSRCC Radiation Oncology Associates, Sunnybrook International

Non-Financial Disclosure

Member of:

- Prostate Cure Foundation, Prostate Cancer Canada, CCO Program in Evidence-Based Care, ASCO Clinical Practice Guidelines Cmt

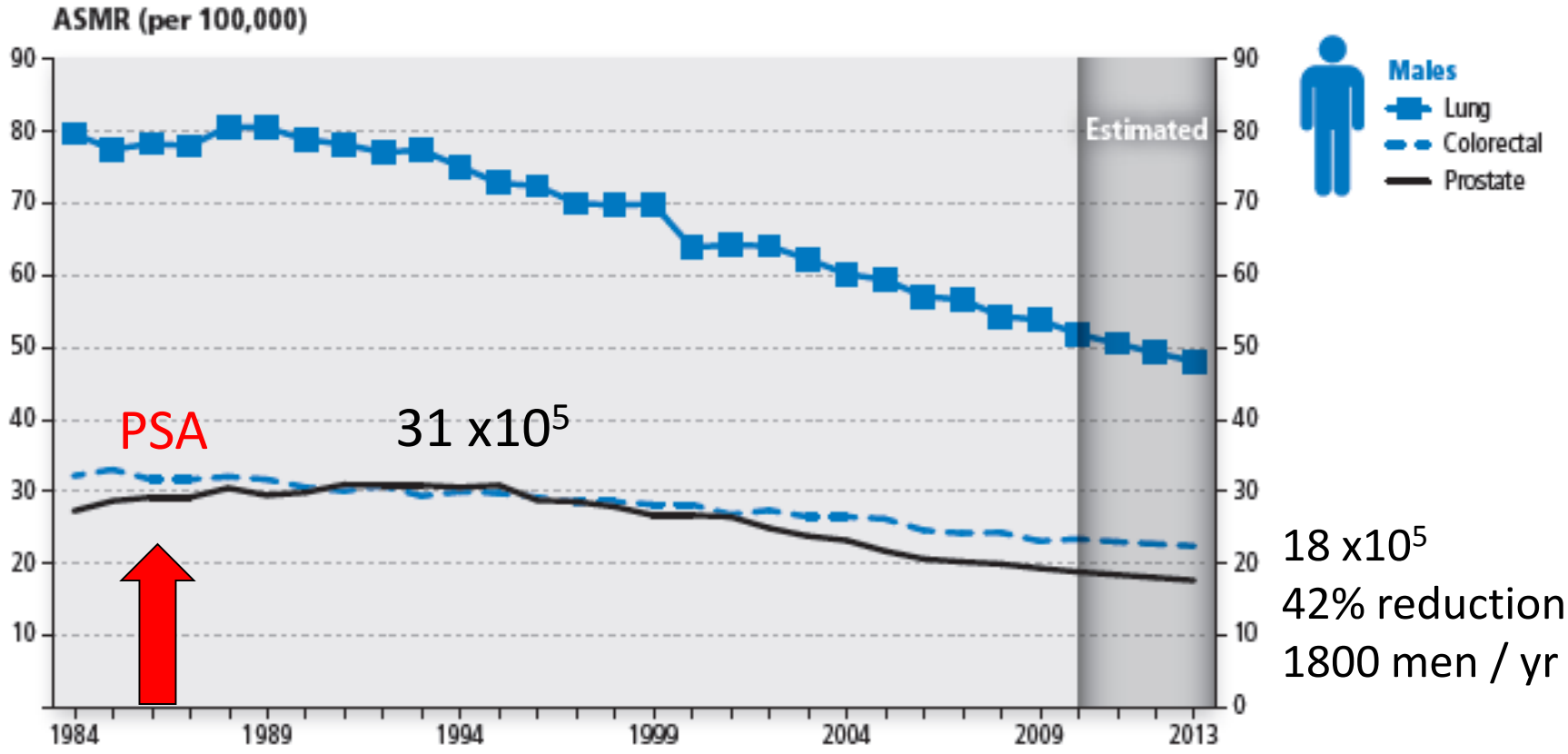
Plagiarism Disclosure

- I have presented some of these slides at previous talks

Screening for Prostate Cancer

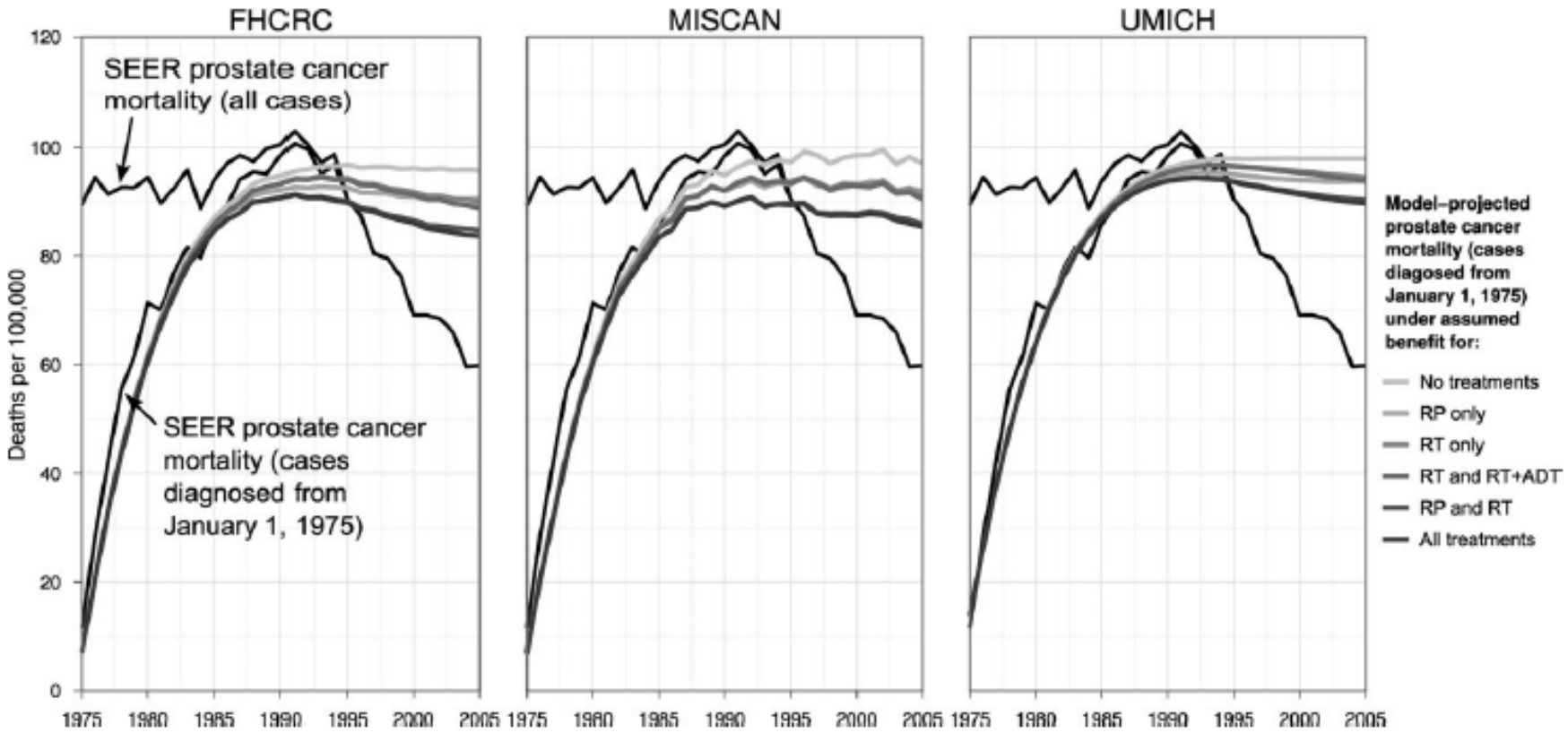
PC Mortality over 20 years

FIGURE 3.4 Age-standardized mortality rates (ASMR) for selected* cancers, males, Canada, 1984–2013



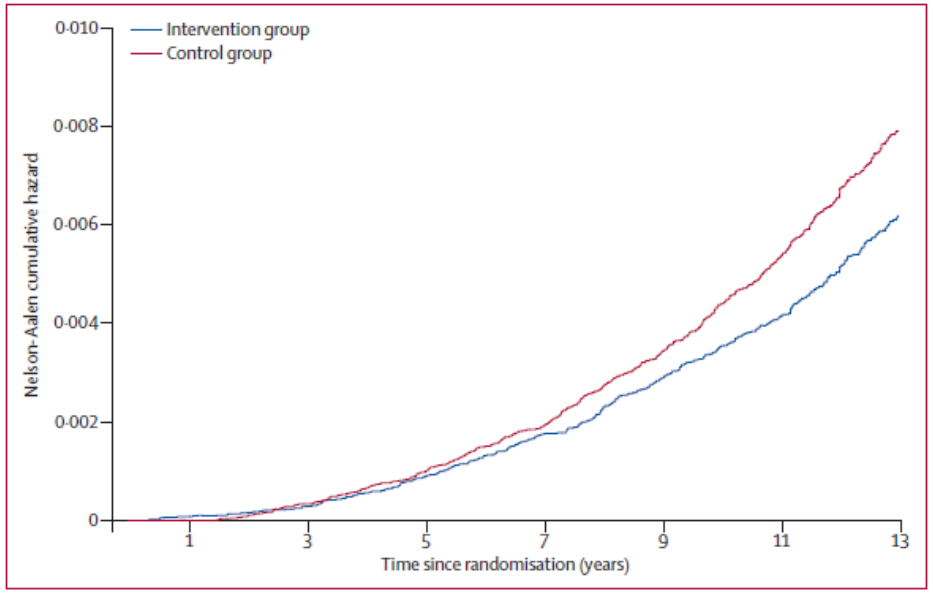
Canadian Cancer Society Stats 2013

Treatment Effect on Mortality



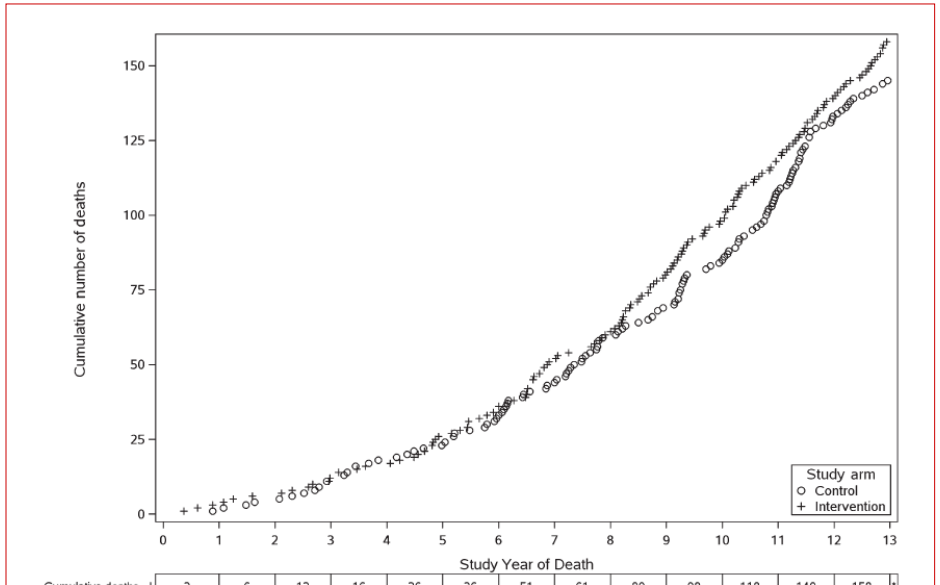
treatment explained only 16% to 23% of the mortality decline by 2005. **CONCLUSIONS:** Changes in primary treatment explained a minority of the observed decline in prostate cancer mortality. The remainder of the decline probably was because of other interventions, such as prostate-specific antigen screening and advances in the treatment of recurrent and progressive disease. ***Cancer***

Etzioni R et al., Cancer 2012



ERSPC

Schroder F et al. Lancet epub Aug 7 2014
182,160 men 50-74y
162,388 men 55-69y
CSS HR (ITT) 0.79 (95% CI: 0.69-0.91) at 13y
CSS HR (eff) 0.73 (95% CI 0.61-0.88)
NNS 781
NNT 27
No diff in OS (only 10% power)
MFS HR 0.33

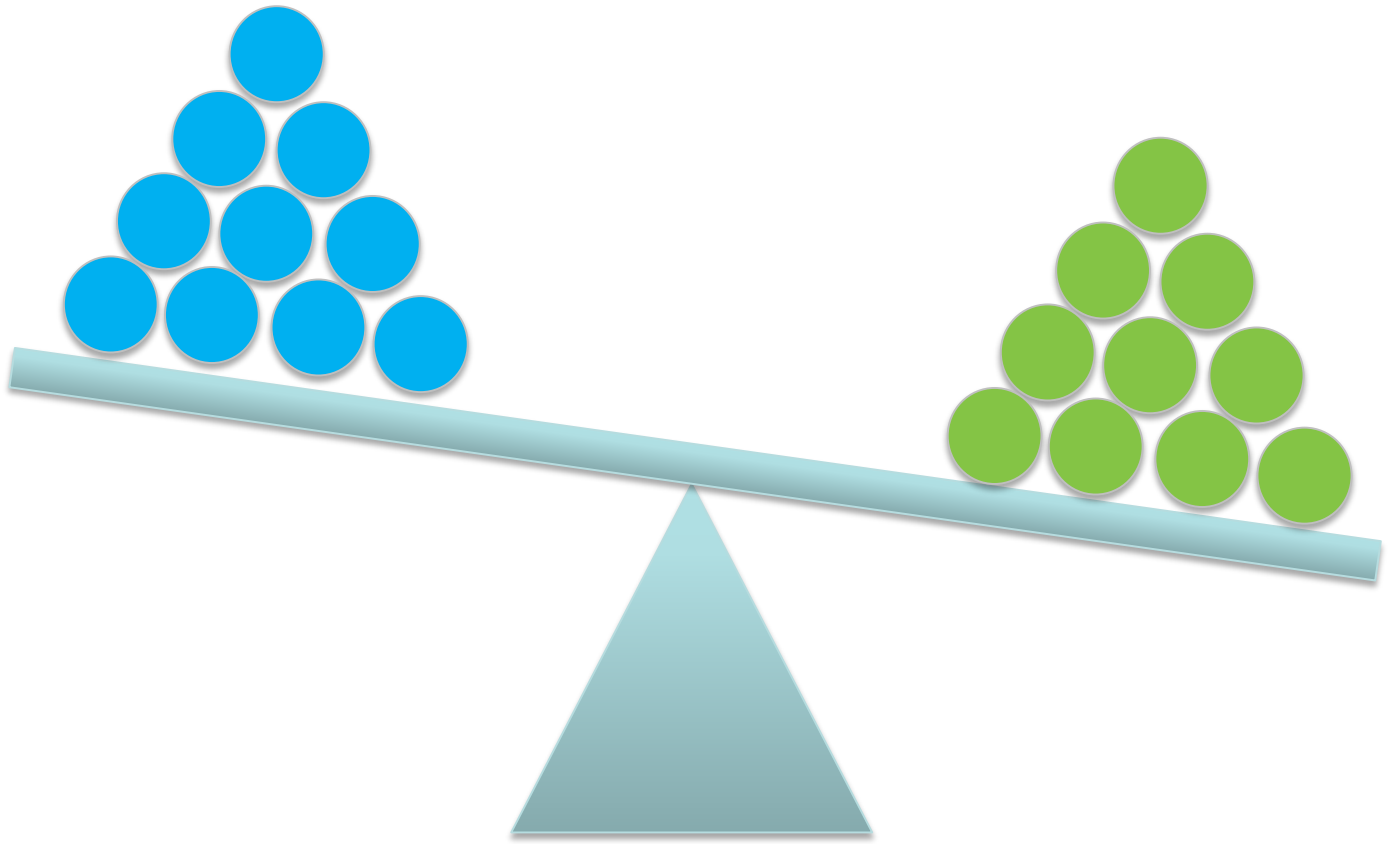


Cumulative deaths - I	3	6	12	16	26	36	51	61	80	98	118	140	158
Cumulative PY - I	38217	76112	113629	150725	187382	223541	259118	294052	328048	359768	387164	409535	426977
Cumulative deaths - C	1	4	11	18	23	33	44	59	69	85	108	133	145
Cumulative PY - C	38223	76132	113635	150689	187278	223329	258811	293631	327455	358904	386109	408262	425439

PLCO

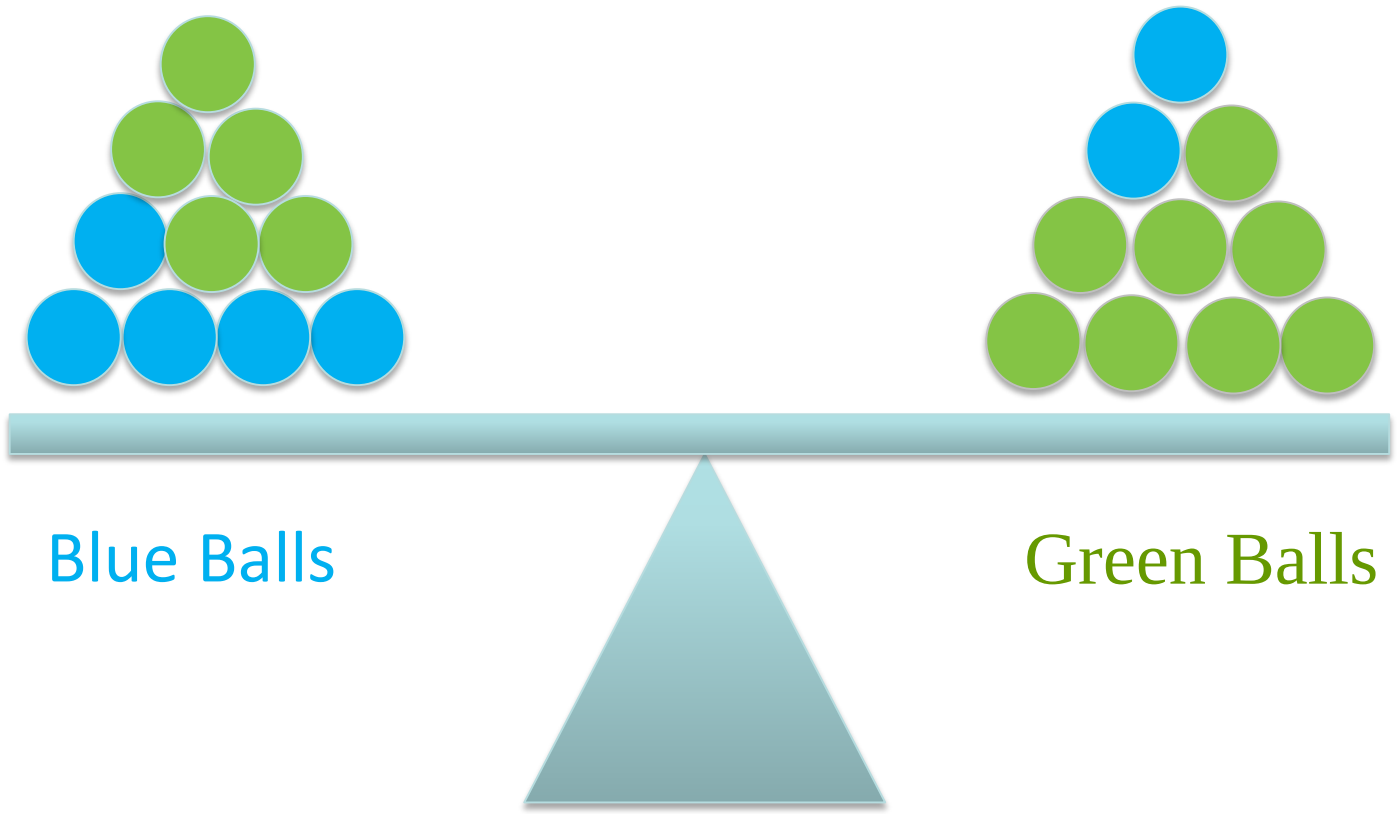
Andriole GA et al. JNCI 104(2), 2012
76,685 men 55-74y
HR (ITT) 1.09 (95% CI: 0.87-1.36) at 13y
Non-compliance control 52%
Non-compliance screen 20%

Which Weigh More?



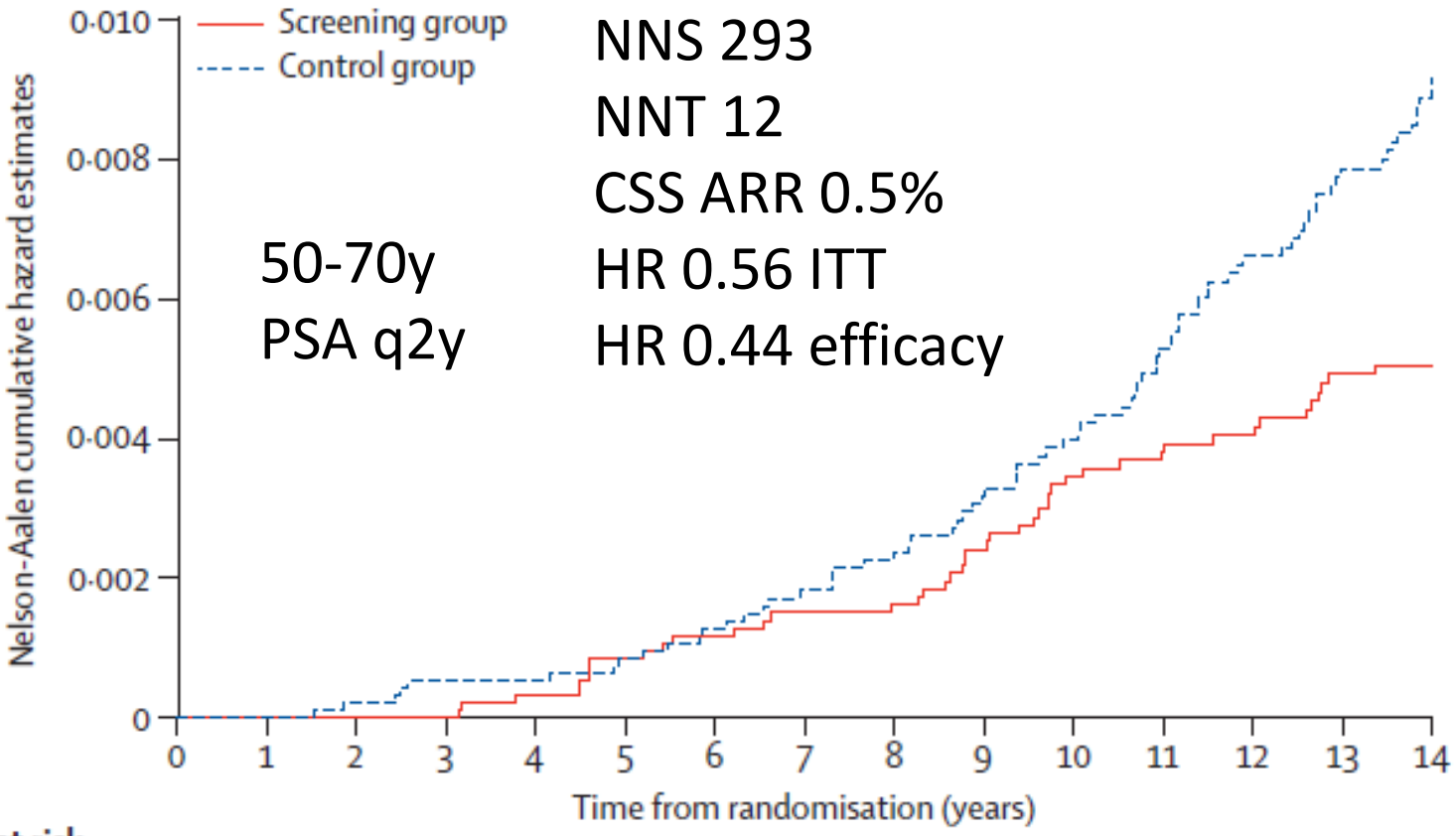
Conclusion: Green balls weigh more

Which Weigh More?



Conclusion: Green balls weigh the same?

PSA Screening – Real Effect?



50-70y
PSA q2y

NNS 293
NNT 12
CSS ARR 0.5%
HR 0.56 ITT
HR 0.44 efficacy

Number at risk				
Screening group	9952	9333	8585	7746
Control group	9952	9345	8580	7755

Hugosson J et al., Lancet 2010

Cdn Task Force 2014

Box 2: Summary of recommendations for clinicians and policy-makers

The recommendations apply to all men without a previous diagnosis of prostate cancer.

- For men aged less than 55 years, we recommend not screening for prostate cancer with the prostate-specific antigen (PSA) test. (*Strong recommendation; low-quality evidence.*)
- For men aged 55–69 years, we recommend not screening for prostate cancer with the PSA test. (*Weak recommendation; moderate-quality evidence.*)
- For men 70 years of age and older, we recommend not screening for prostate cancer with the PSA test. (*Strong recommendation; low-quality evidence.*)

Most common advice?
Shared decision-making for men 50-70y

Table 3: Summary of recommendations for PSA screening for prostate cancer from Canada and elsewhere

Organization	Age at initiation of PSA screening	Screening interval	Age at discontinuation of PSA screening
Canadian Task Force on Preventive Health Care (current)	Routine PSA screening not recommended		
Canadian Task Force on the Periodic Health Examination (1994)[11]	Routine PSA screening not recommended as part of periodic health examination		
US Preventive Services Task Force (2012)[8]	PSA screening not recommended; applies to men of all ages		
Canadian Urological Association (2011)[54]	• Average risk: offer at age 50 yr to men with life expectancy ≥ 10 yr • Increased risk (e.g., family history of prostate cancer, African descent): offer at 40 yr • Offer baseline PSA test at age 40–49 yr to establish future risk of prostate cancer	Not specified	75 yr
Canadian Cancer Society (2014)[55]	Men aged > 50 yr should talk with their doctor about whether they should be tested for prostate cancer	Not specified	Not specified
American Cancer Society (2012)[56]	Average risk: discussion at age 50 yr Increased risk: discussion at age 40 or 45 yr, depending on extent of risk	PSA < 2.5 ng/mL: 2 yr PSA ≥ 2.5 ng/mL: annual	Life expectancy < 10 yr
National Cancer Institute (2012)[22]	Insufficient evidence to determine whether screening with PSA or digital rectal examination reduces prostate cancer mortality		
National Health Service (2013)[57]	No organized screening program; informed-choice program = men concerned about the risk of prostate cancer receive clear and balanced information about the advantages and disadvantages of PSA testing and cancer treatment		
Prostate Cancer Canada (2013)[58]	• Offer baseline PSA test at age 40–49 yr • Men aged > 40 yr should talk with their doctor about early detection • Men at high risk should talk with their primary care provider before age 40 yr about prostate cancer	Not specified	≥ 70 yr; decision should be based on individual factors (not specified)
American Urological Association (2013)[59]	• Routine screening not recommended for men aged 40–54 yr at average risk • Shared decision-making recommended for men aged 55–69 yr; decision to proceed based on patient's values and preferences	≥ 2 yr	≥ 70 yr or life expectancy < 10–15 yr
American College of Physicians (2013)[60]	Men aged 50–69 yr: clinicians should discuss the limited benefits and substantial harms of screening for prostate cancer; they should not screen for prostate cancer with the PSA test in patients who do not express a clear preference for screening	Not specified	≥ 70 yr or life expectancy < 10–15 yr
Cancer Council Australia, Australian Health Ministers' Advisory Council (2010)[61]	PSA test not suitable for population screening		

Note: PSA = prostate-specific antigen.

Why the Confusion?

1. Early diagnosis too harmful
   - Diagnostic process has harms
   - Diagnosis = Treatment for all patients
2. For those needing treatment, treatments not effective enough
3. (Too expensive?)

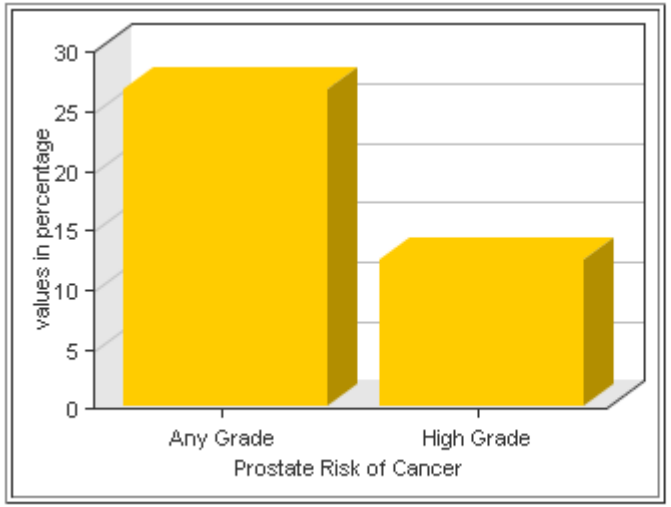
Smart Diagnosis

Risk Adapted

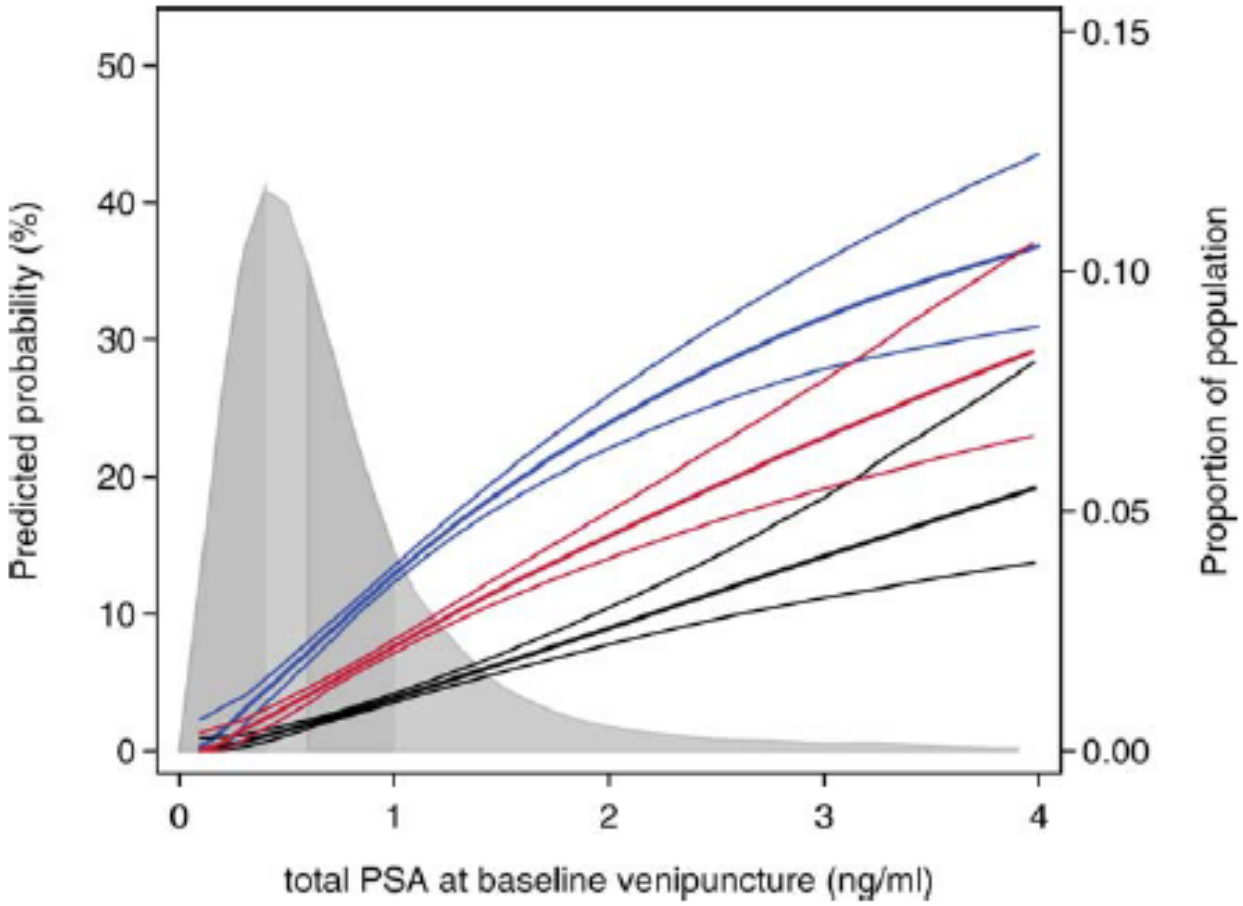
Results

Age:	55
IPSS(Urinary voiding Symptom score):	10
PSA:	2.5
FTPSA (Free:total PSA ratio):	.15
Ethnic Background:	Caucasian
Family history of prostate cancer:	No
Abnormal DRE(by Doctor):	No

Probability Of Any Grade Cancer is: 26.8%
Probability Of High Grade Cancer is: 12.4% (Gleason Score 7 or more)



Long-Term Risk of PCa Ages 44-50y

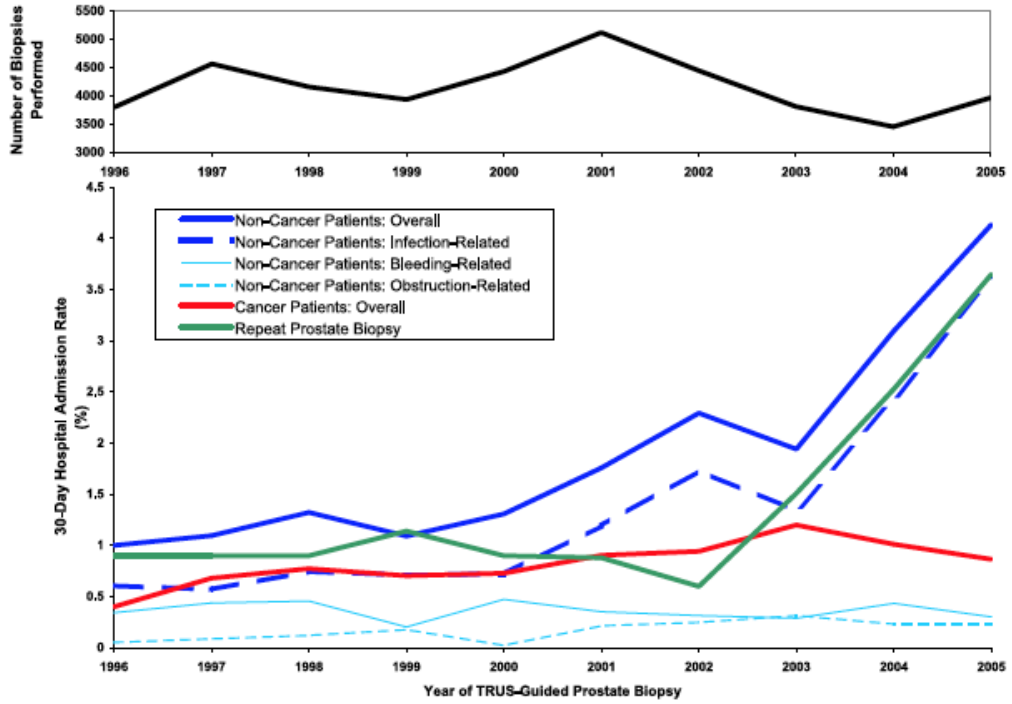


Any Cancer
Palpable Cancer
Advanced Cancer

Lilja H et al., Cancer 2011

Need to consider harms of biopsy

N=41,682



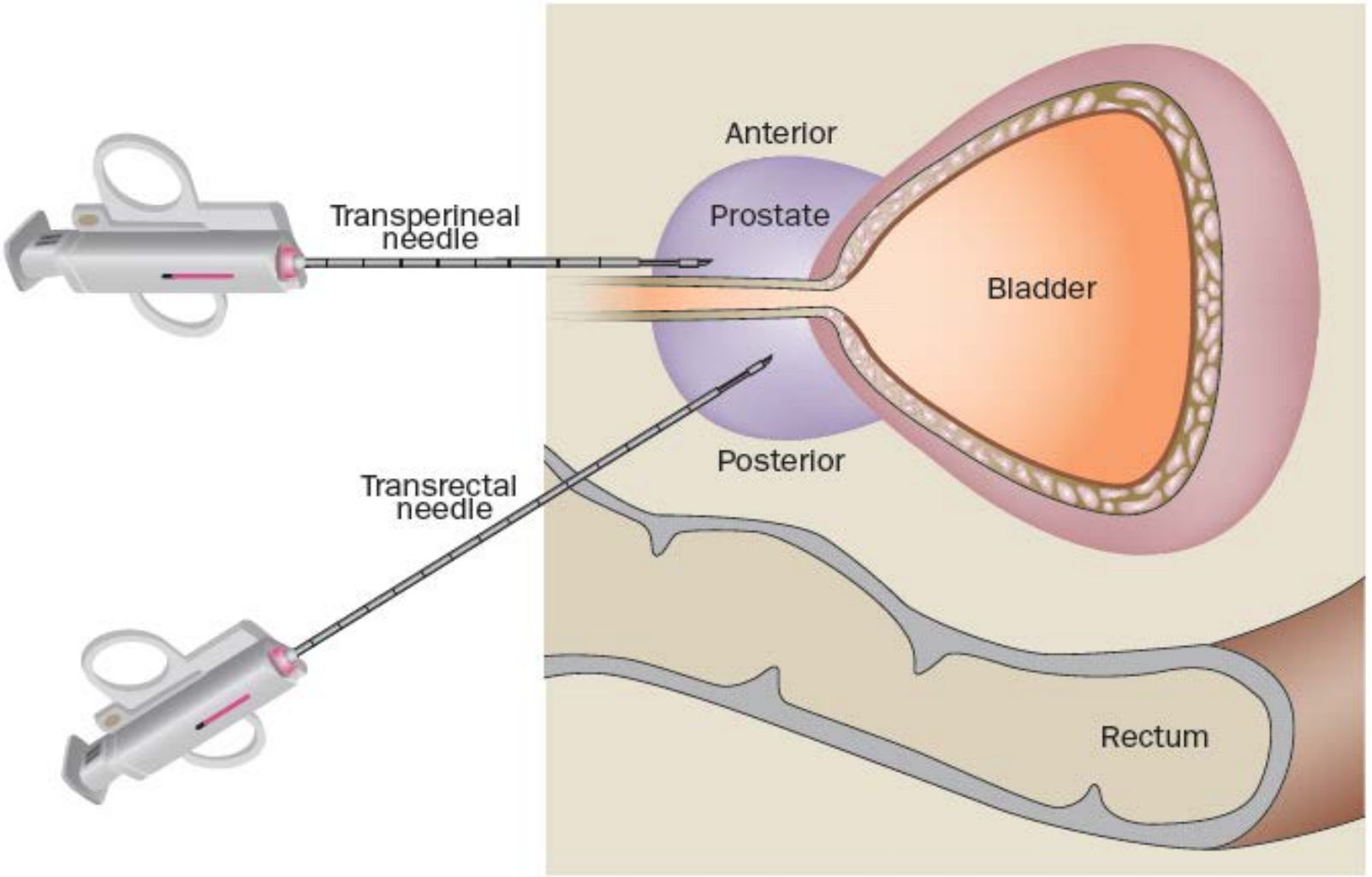
Confirmed from:

SEER:
Loeb et al, J Urol, 186(5): 1830-4, 2011

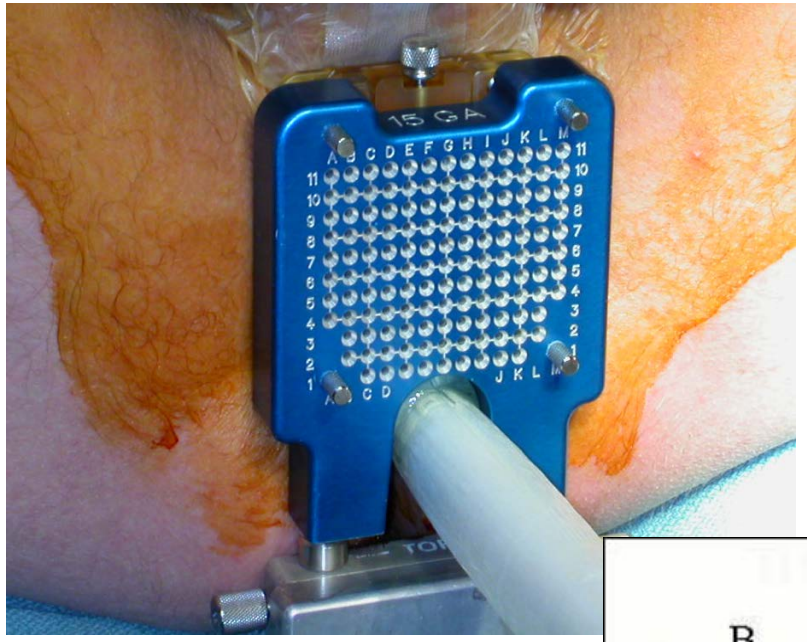
ERSPC:
Loeb et al, Eur Urol, 61(6): 1110-4, 2012

Nam et al, J Urol,183(3):963-8, 2010

TP vs TRUS Bx

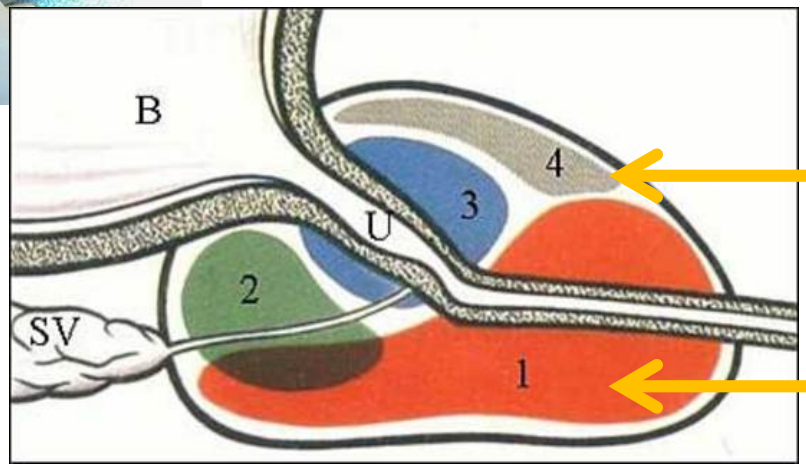

Anterior
Prostate
Bladder
Transperineal needle
Posterior
Transrectal needle
Rectum

Transperineal Biopsy



vs. TRUS bx:

- more ant tumors: 16 v 12%, p=0.046
- R1 rate: 69 v 34% for ant tumors
- smaller size: 1.4 v 2.1cm, p=0.03
- lower pT3 rate: 13 vs 28%, p=0.03



Hossak T et al., J Urol 2012

Complications after TP Bx

Table 2 Systematic literature review of re-admission for sepsis after TP biopsy.

Study	Journal/year of publication	Number of patients	Patient admissions for sepsis, *n* (%)	Antibiotic prophylaxis	Number of cores
Pepe et al. [7]	*Urology*/2013	3000	0	Levofloxacin	12–24
Vyas et al. [8]	*BJU Int*/2013	634	0	Amikacin	24–38
Symons et al. [9]	*BJU Int*/2013	409	1	Norfloxacin/gentamicin	22
Kuru et al. [10]	*J Urol*/2013	347	0	N/A	N/A
Ekweune et al. [11]	*BJU Int*/2013	270	1	Gentamicin/metronidazole	28
Dimmen et al. [12]	*BJU Int*/2012	69	1	Nil	N/A
Pal et al. [13]	*BJU Int*/2012	40	0	Coamoxiclav/gentamicin	36
Suzuki et al. [14]	*Int J Urol*/2009	539	0	Levofloxacin	14
Kubo et al. [15]	*Int J Urol*/2009	45	0	Levofloxacin	14
Merrick et al. [16]	*BJU Int*/2008	129	0	Not specified	24
Hara et al. [17]	*Urology*/2008	126	0	Levofloxacin	12
Li et al. [18]	*Urology*/2007	303	0	N/A	24
Yamamoto et al. [19]	*Int J Clin Oncol*/2005	300	1	Sublactam/cephalexin/ levofloxacin	12
Pinkstaff et al. [20]	*Urology*/2005	210	0	Fluoroquinolone	21
Miller et al. [21]	*ANZ J Surg*/2005	81	1	Nil	6
Emiliozzi et al. [22]	*Urology*/2003	107	0	Quinolone	6
Total		6609	5 (0.076)		

N/A, not available.

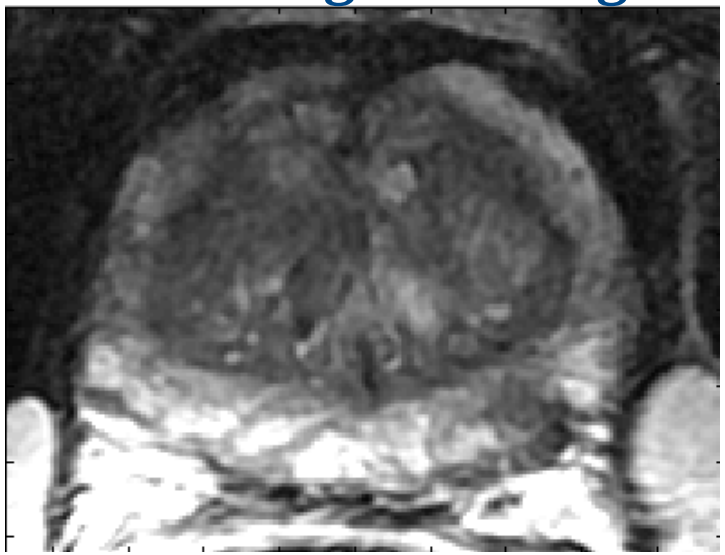
0.076% sepsis risk

>50x lower risk than TRUSbx

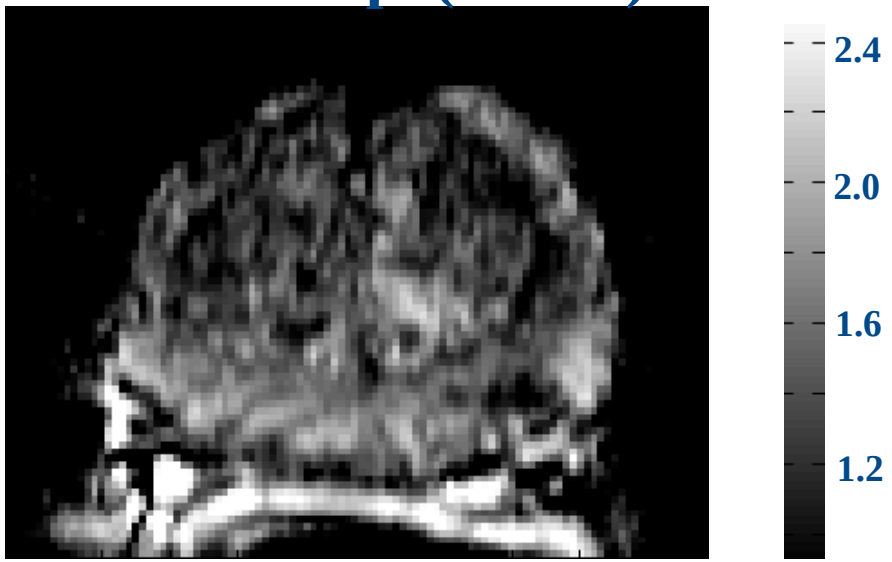
Chang DTS et al., Nat Rev Urol 2013

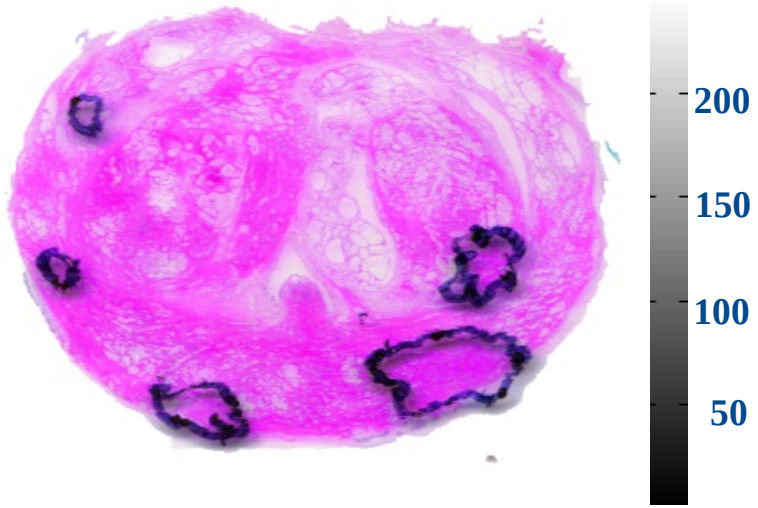
Smart Biopsies:
The Value of MRI

T2-weighted image

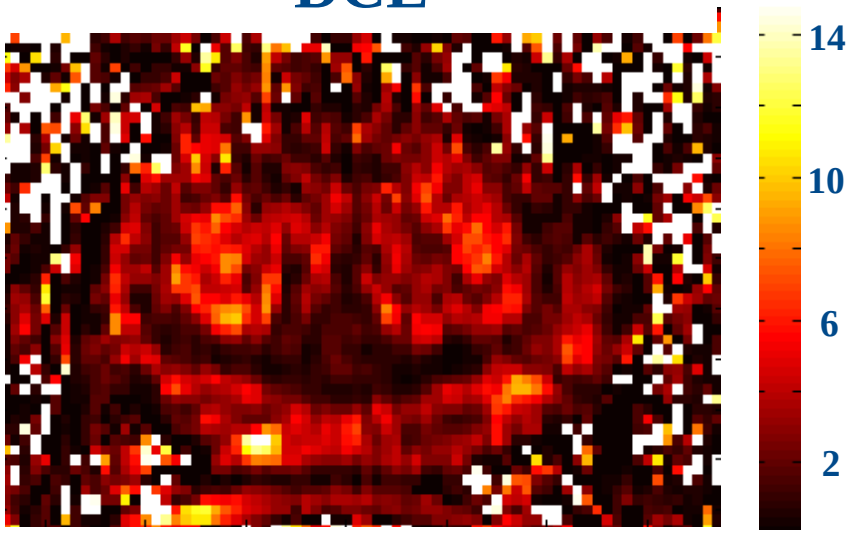


ADC map (mm^2/s)



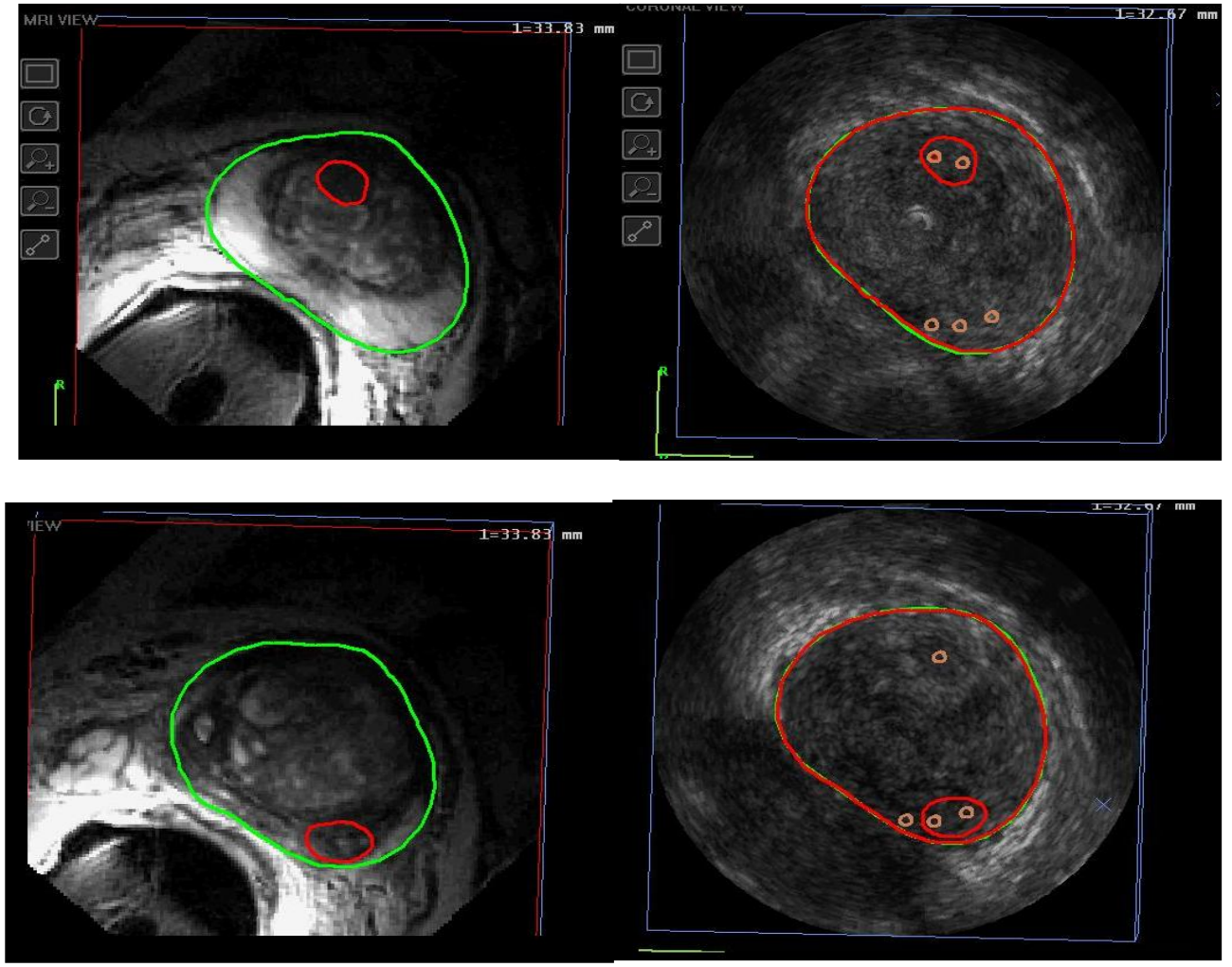


DCE



3D US/MRI Registration for Biopsy

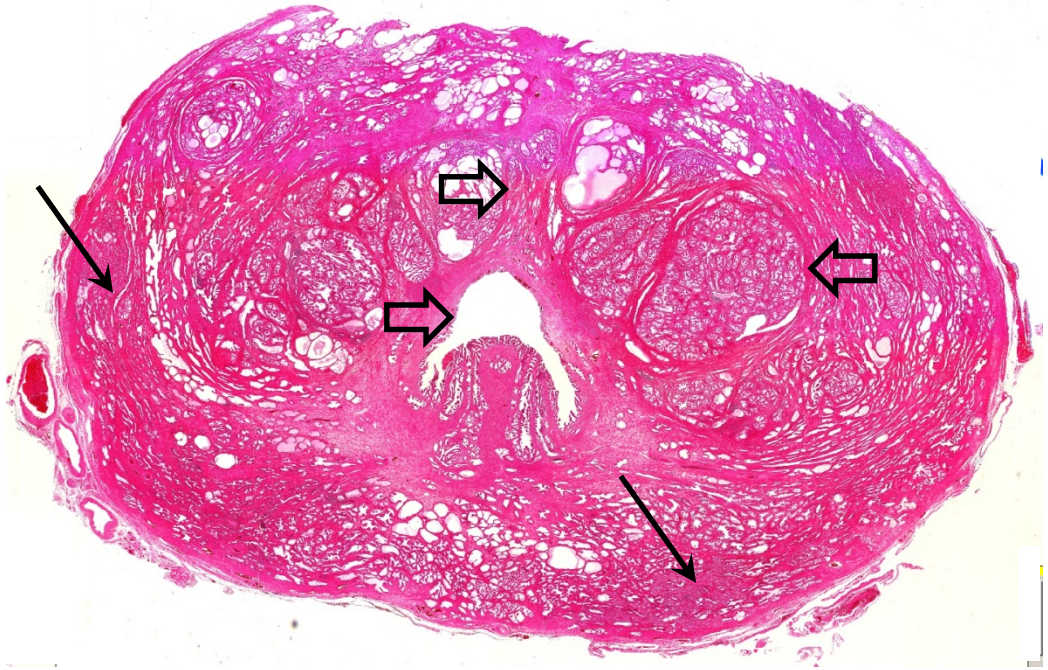
MRI

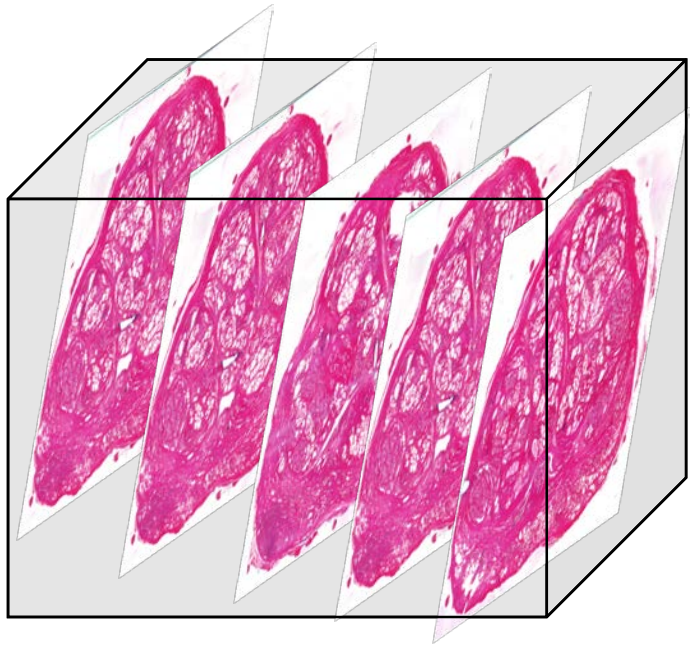


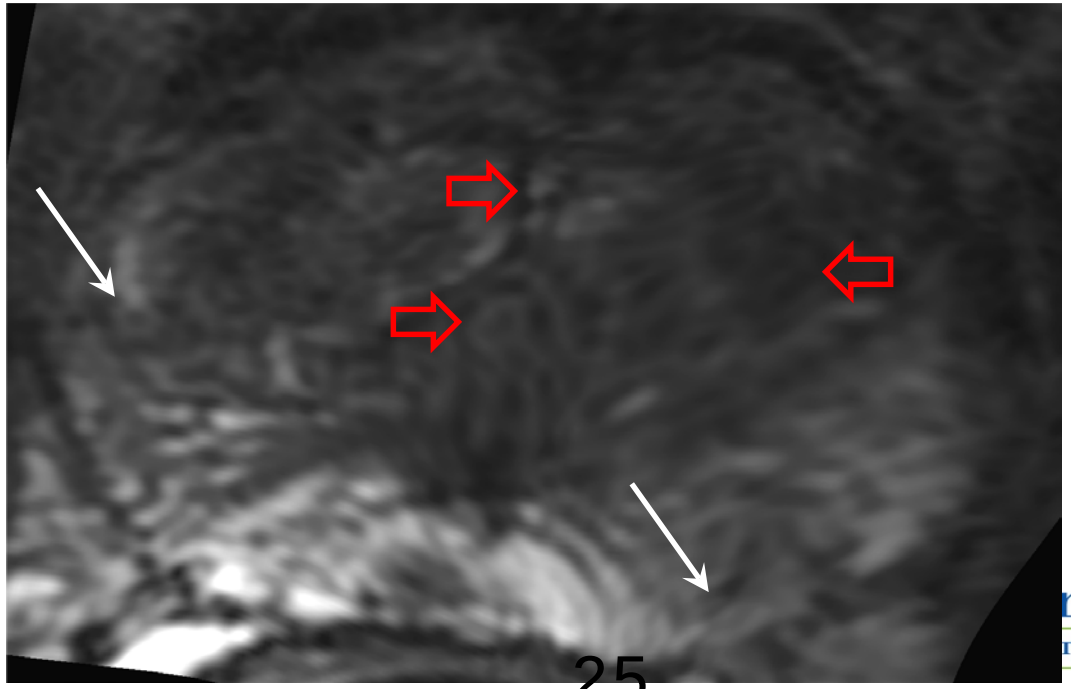
US

Pathology/MRI Registration

- Generate 3D histology image
- Non-rigid registration of 3D MRI to 3D US







MAST vs TRUS bx (Bx Naïve)

a.

	TRUSGB pathway	MRGB pathway	Difference, %
Biopsy, no. of men	223	142	−36.3
Biopsy cores, no.	2672	417	−84.4
Low-risk PCa	47	6	−87.2
Intermediate/high-risk PCa	79	93	17.7

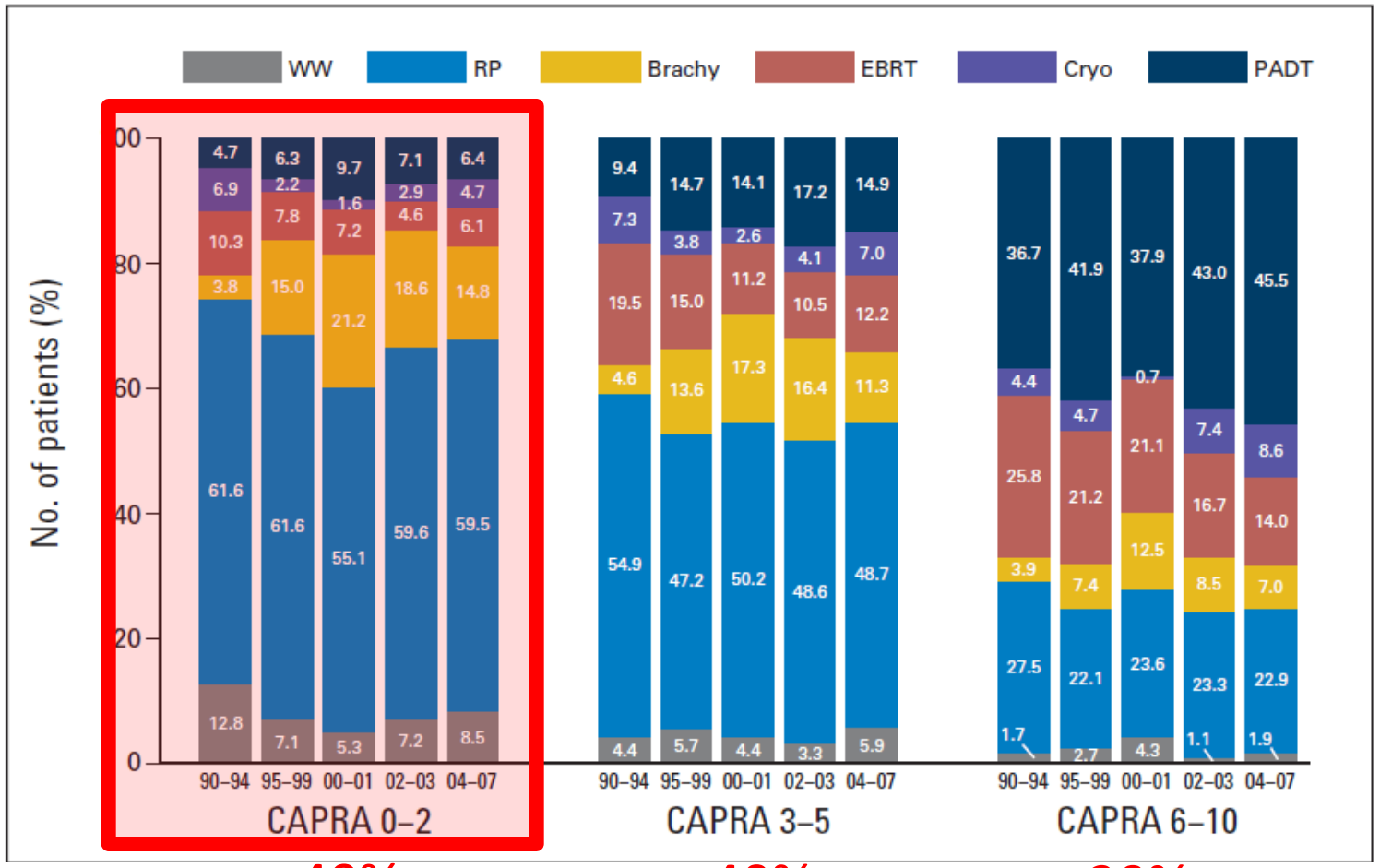
Table 5 – Statistical performance characteristics of transrectal ultrasound–guided biopsy and magnetic resonance–guided biopsy

Parameter	Estimate	95% confidence interval
Sensitivity: MRGB	0.9234	0.878–0.953
Sensitivity: TRUSGB	0.7044	0.639–0.762
Specificity: MRGB	0.9691	0.934–0.986
Specificity: TRUSGB	0.9364	0.894–0.963
PPV: MRGB	0.9232	0.878–0.953
PPV: TRUSGB	0.9321	0.889–0.960
NPV: MRGB	0.9691	0.934–0.987
NPV: TRUSGB	0.719	0.654–0.776
LR(+): MRGB	12.908	
LR(+): TRUSGB	5.4	
LR(−): MRGB	0.126	
LR(−): TRUSGB	0.293	

LR = likelihood ratio; MRGB = magnetic resonance–guided biopsy; NPV = negative predictive value; PPV = positive predictive value; TRUSGB = transrectal ultrasound–guided biopsy.

Pokorny MR, Eur Urol 2014

Risk Stratification and Management



40% 40% 20%

Risk group														
Low	397	9.2	2,449	56.8	691	16.0	315	7.3	132	3.1	330	7.6	4,314	36.3
Intermediate	209	4.8	2,283	52.9	581	13.5	530	12.3	194	4.5	515	11.9	4,312	36.3
High	58	3.2	576	32.2	135	7.5	324	18.1	109	6.1	588	32.8	1,790	15.1
Unknown	146	9.9	623	42.2	176	11.9	213	14.4	39	2.6	279	18.9	1,476	12.4

Cooperberg M et al., JCO 2010

Walt Witmore:

Where cure is possible, is it necessary?

Where necessary, is it possible?

Smart Management

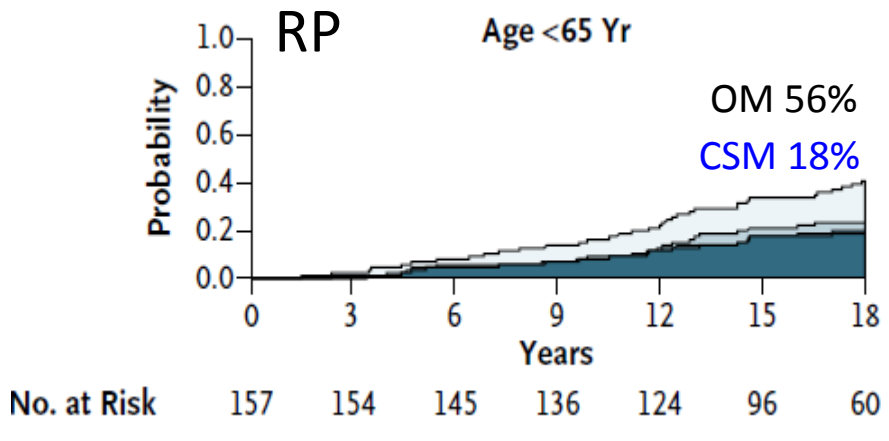
Active Surveillance for Low Risk

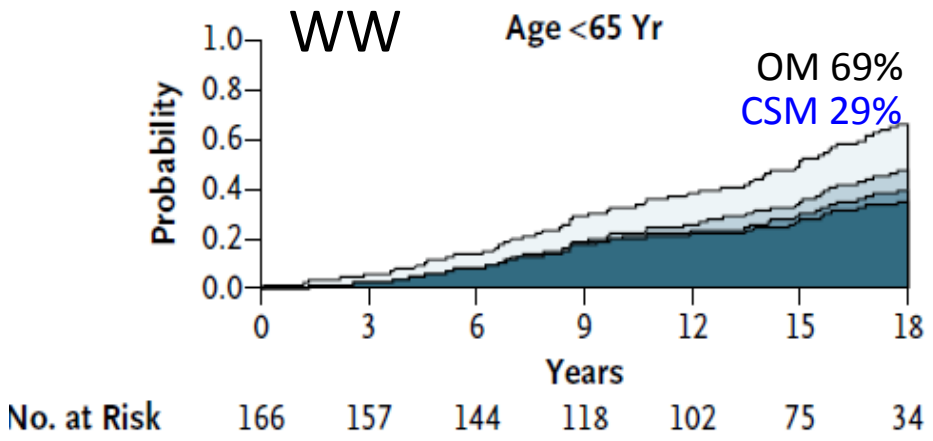
ORIGINAL ARTICLE

Radical Prostatectomy or Watchful Waiting in Early Prostate Cancer

Anna Bill-Axelson, M.D., Ph.D., Lars Holmberg, M.D., Ph.D., Hans Garmo, Ph.D., Jennifer R. Rider, Sc.D., Kimmo Taari, M.D., Ph.D., Christer Busch, M.D., Ph.D., Stig Nordling, M.D., Ph.D., Michael Häggman, M.D., Ph.D., Swen-Olof Andersson, M.D., Ph.D., Anders Spångberg, M.D., Ph.D., Ove Andrén, M.D., Ph.D., Juni Palmgren, Ph.D., Gunnar Steineck, M.D., Ph.D., Hans-Olov Adami, M.D., Ph.D., and Jan-Erik Johansson, M.D., Ph.D.

N ENGL J MED 370;10 NEJM.ORG MARCH 6, 2014





12% T1c, mPSA 13

The NEW ENGLAND JOURNAL of MEDICINE

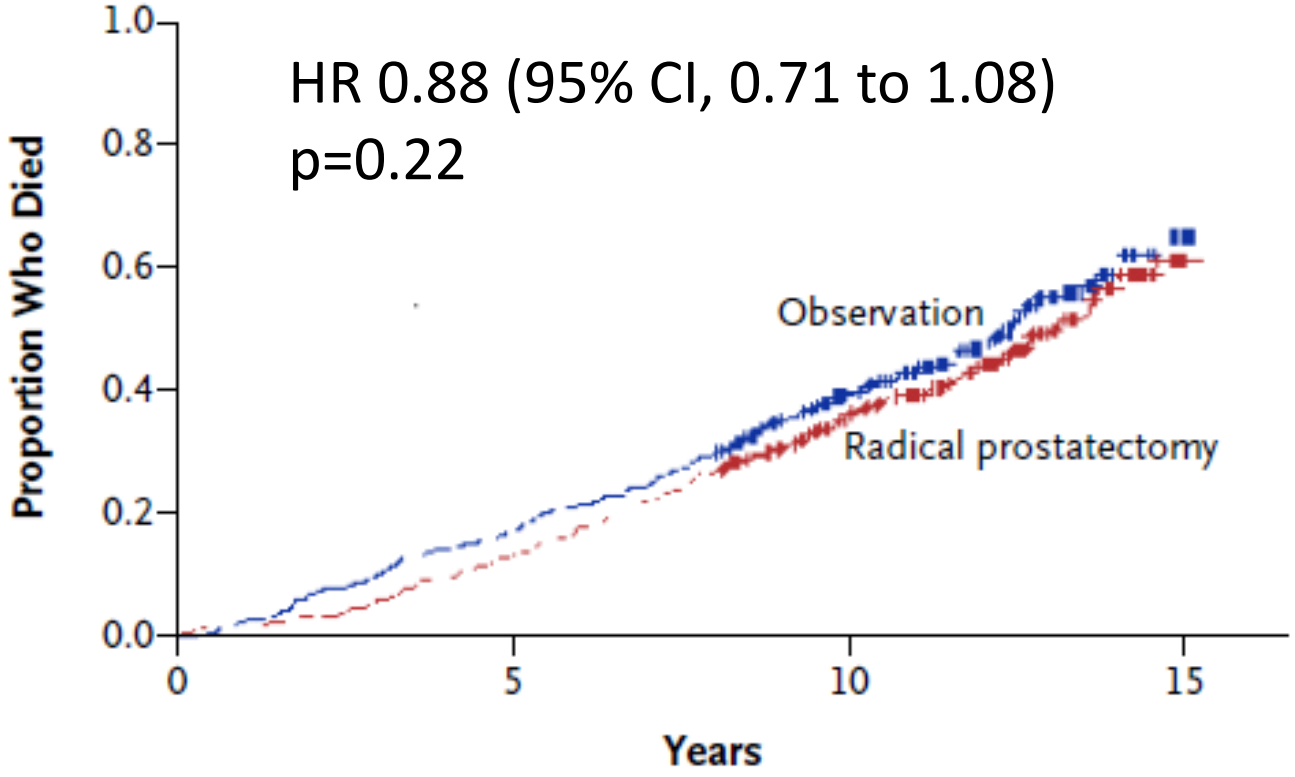
ESTABLISHED IN 1812 JULY 19, 2012 VOL. 367 NO. 3

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

Overall Survival

A Death from Any Cause

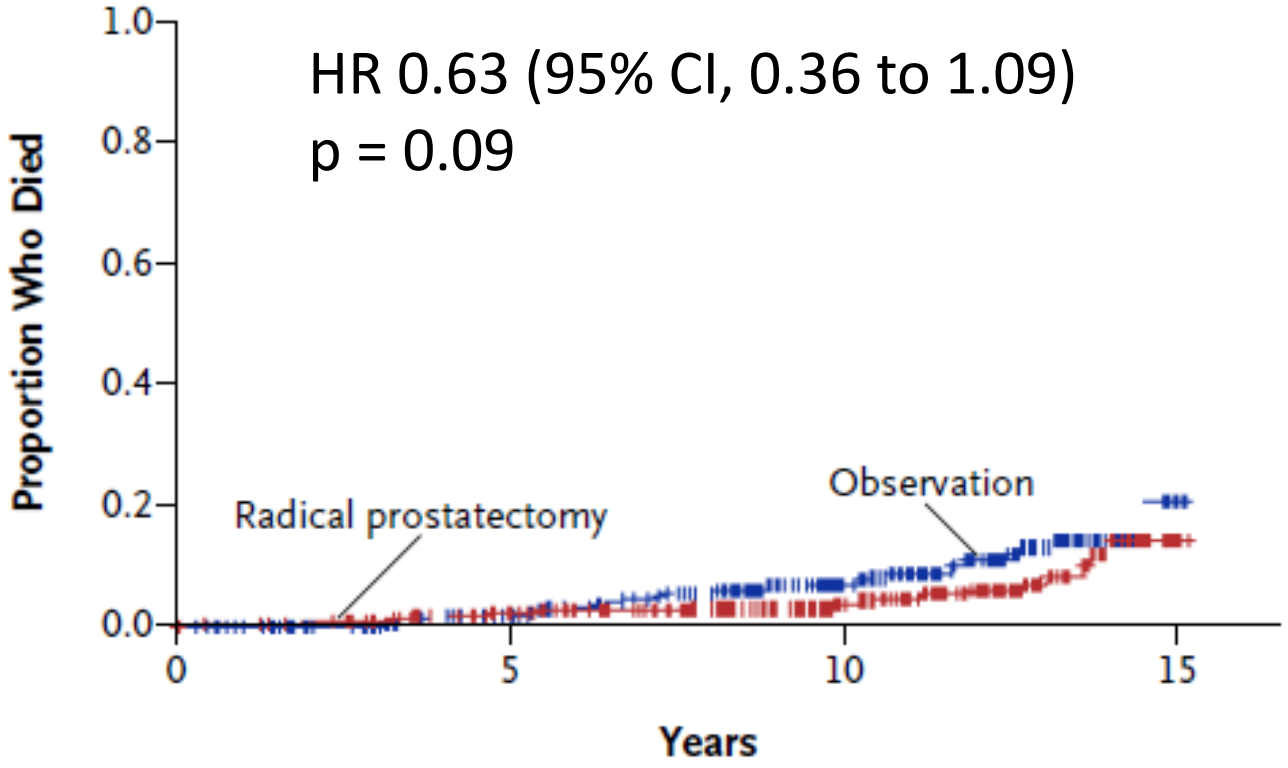


HR 0.88 (95% CI, 0.71 to 1.08)
p=0.22

No. at Risk									
Observation	367	341	315	288	258	176	106	26	0
Radical prostatectomy	364	352	329	300	267	187	126	36	0

Cause-Specific Survival

B Death from Prostate Cancer

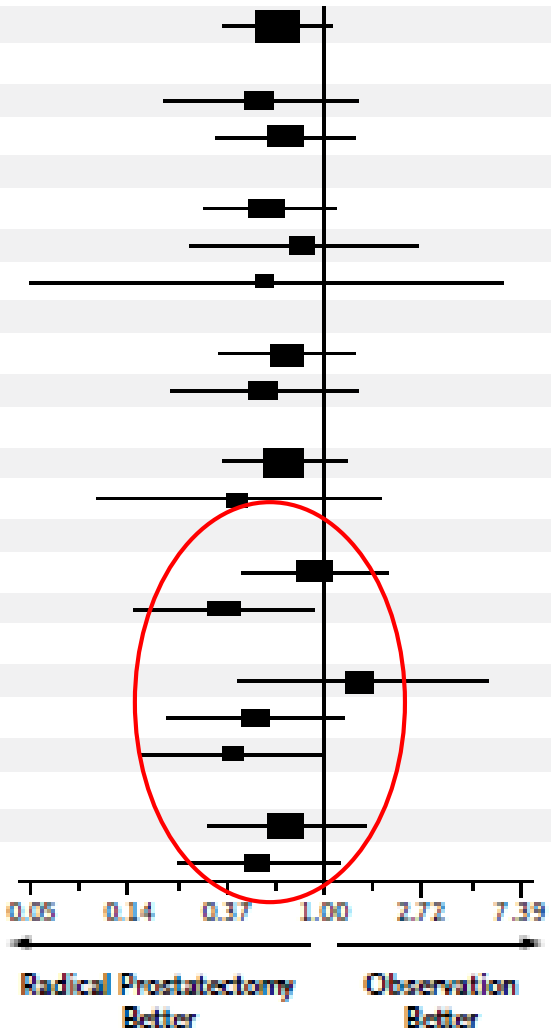


HR 0.63 (95% CI, 0.36 to 1.09)
p = 0.09

No. at Risk									
Observation	367	341	315	288	258	176	106	26	0
Radical prostatectomy	364	352	329	300	267	187	126	36	0

CSS Forest Plot

Subgroup	Observation	Radical Prostatectomy	Hazard Ratio (95% CI)	P Value for Interaction
	no. of events/total no.			
Overall	31/367	21/364	0.63 (0.36–1.09)	
Age				0.63
<65 yr	12/131	6/122	0.52 (0.20–1.39)	
≥65 yr	19/236	15/242	0.68 (0.34–1.33)	
Race				0.76
White	22/220	15/232	0.57 (0.30–1.10)	
Black	7/121	5/111	0.80 (0.25–2.54)	
Other	2/26	1/21	0.56 (0.05–6.17)	
Charlson score				0.63
0	19/220	14/224	0.69 (0.34–1.37)	
≥1	12/147	7/140	0.54 (0.21–1.38)	
Performance score				0.57
0	25/310	18/312	0.67 (0.37–1.23)	
1–4	6/57	3/52	0.41 (0.10–1.71)	
PSA				0.11
≤10	15/241	14/238	0.92 (0.44–1.91)	
>10	16/125	7/126	0.36 (0.15–0.89)	
Risk				0.11
Low	4/148	6/148	1.48 (0.42–5.24)	
Intermediate	13/120	6/129	0.50 (0.21–1.21)	
High	14/80	7/77	0.40 (0.16–1.00)	
Gleason score				0.57
<7	15/261	11/254	0.68 (0.31–1.49)	
≥7	15/86	10/98	0.51 (0.23–1.14)	



VOLUME 33 · NUMBER 3 · JANUARY 20 2015

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Long-Term Follow-Up of a Large Active Surveillance Cohort of Patients With Prostate Cancer

Laurence Klotz, Danny Vesprini, Perakaa Sethukavalan, Vibhuti Jethava, Liying Zhang, Suneil Jain, Toshihiro Yamamoto, Alexandre Mamedov, and Andrew Loblaw

See accompanying editorial on page 238

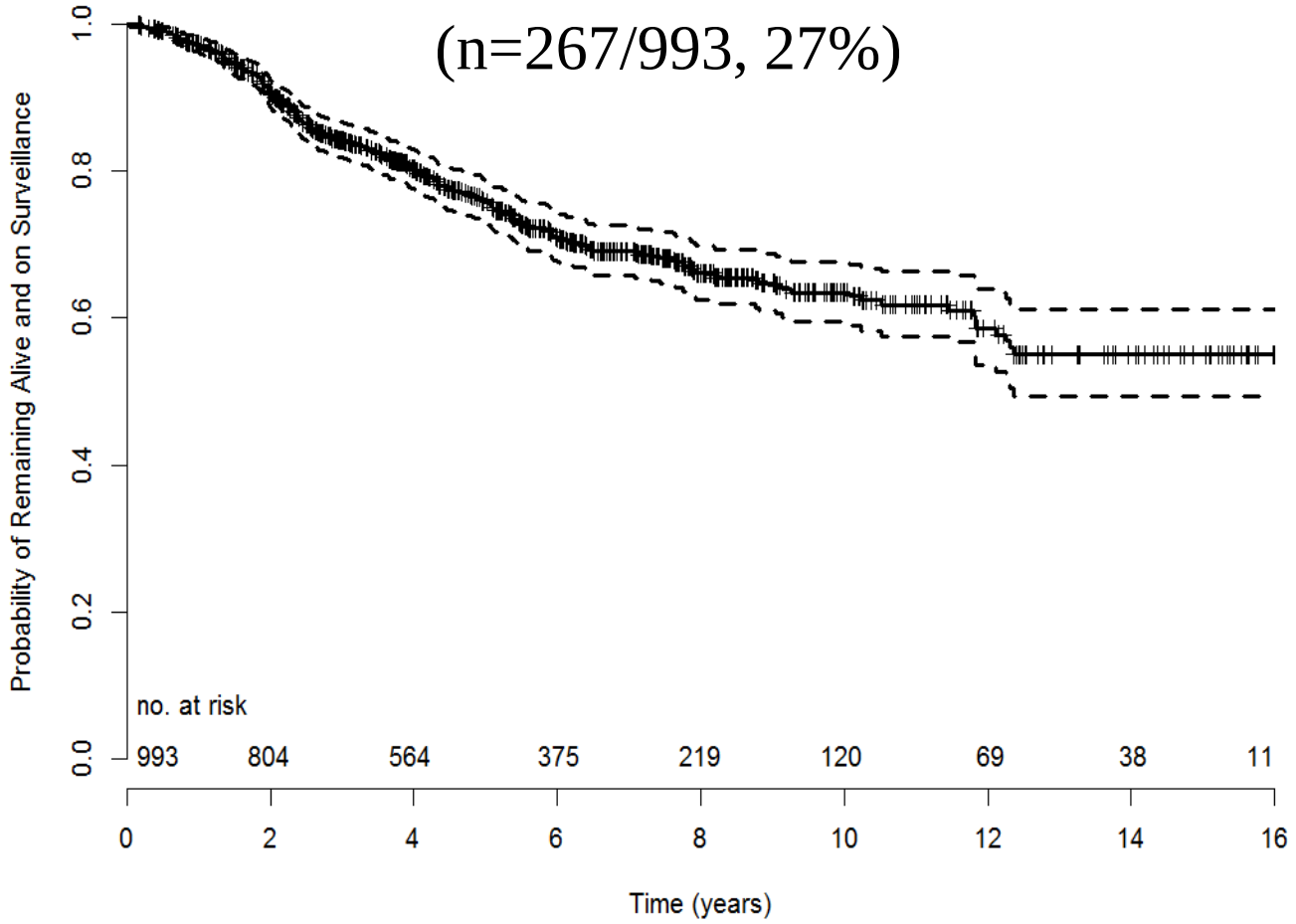
Table 1. Baseline Gleason score and PSA of Patients

	Patients by PSA														Patients by Age			
	0 to 2.5 ng/mL		> 2.5 to 5 ng/mL		> 5 to 10 ng/mL		> 10 to 15 ng/mL		> 15 ng/mL		Unknown		Total		< 70 Years		≥ 70 Years	
Gleason Score	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
≤ 6	124*	89	267*	90	349*	82	62	70	15	71	20	80	837	84	536	90	301	75
7	13	9	21	7	64	15	25	27	5	23	4	16	132	13	45	8	87	22
Not available	3	2	9	3	9	2	1	1	1	5	1	4	24	24	14	2	10	3
Total	140		297		422		88		21		25		993		595		398	

Abbreviation: PSA, prostate-specific antigen.
*Low-risk group.

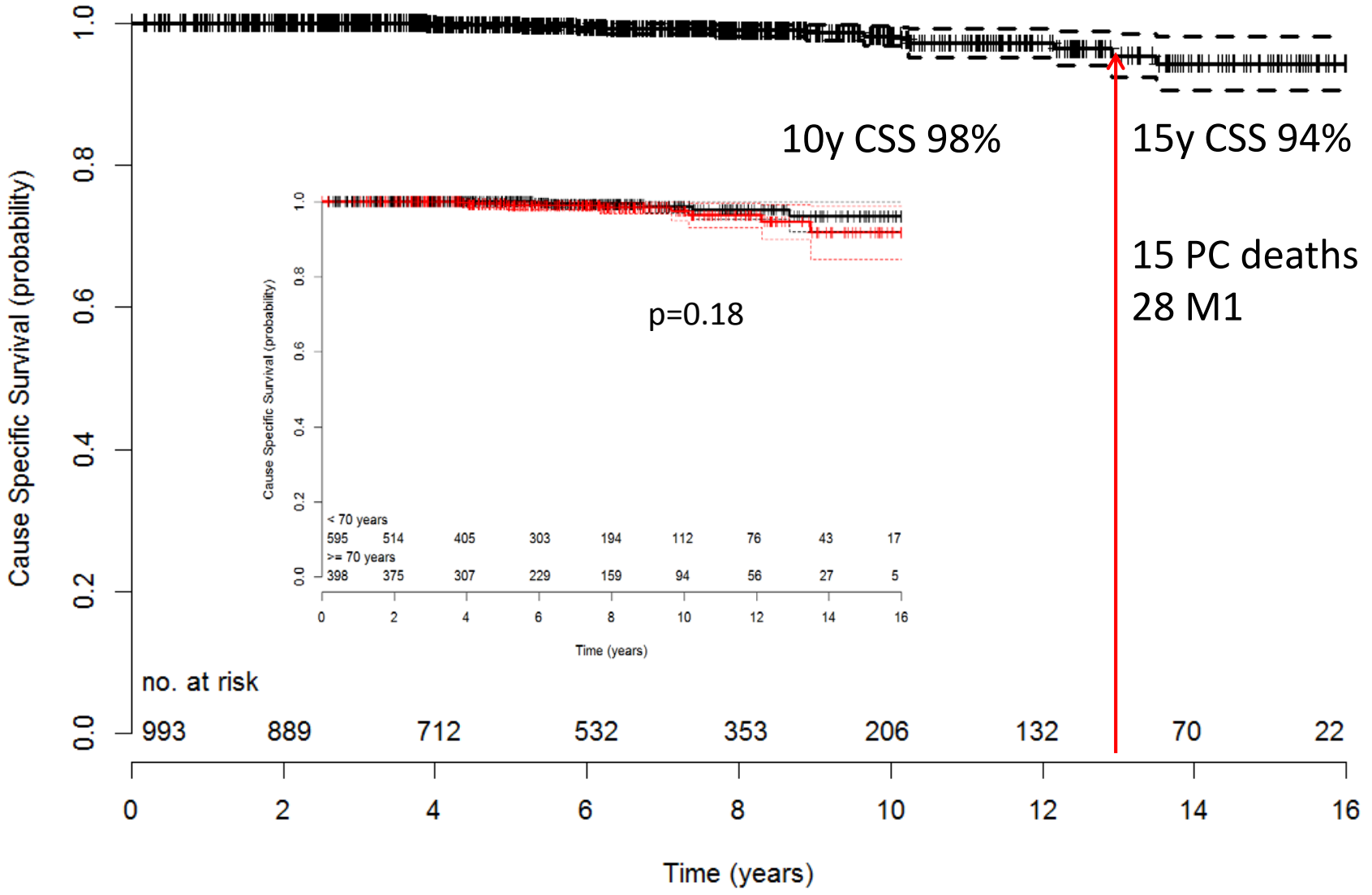
75% low risk, mFU 6.4y (0.5 – 20.2y)

Chance of Discontinuing Surveillance



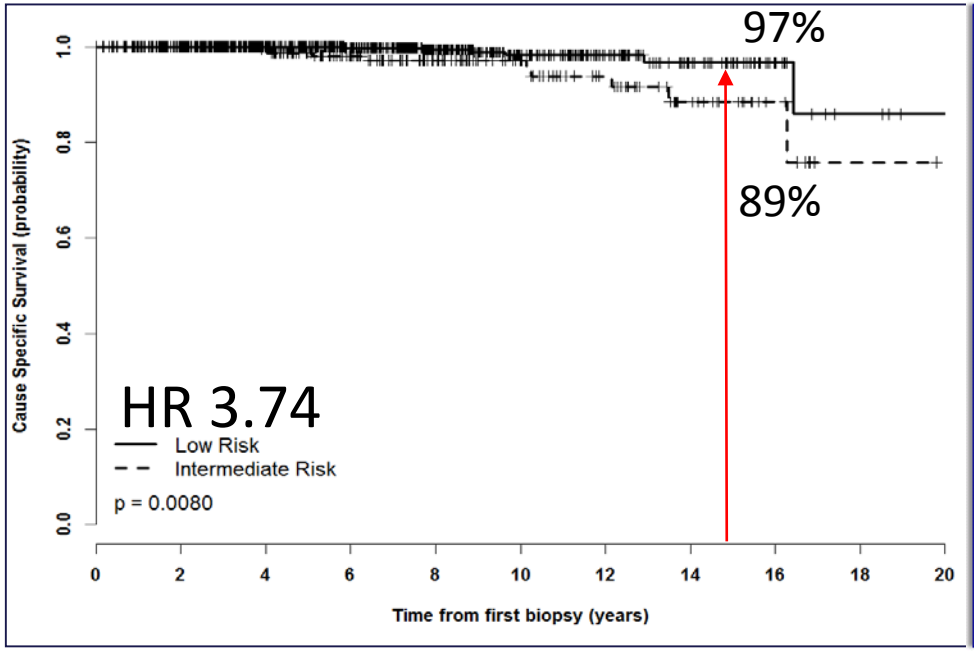
Klotz L et al., JCO 2014

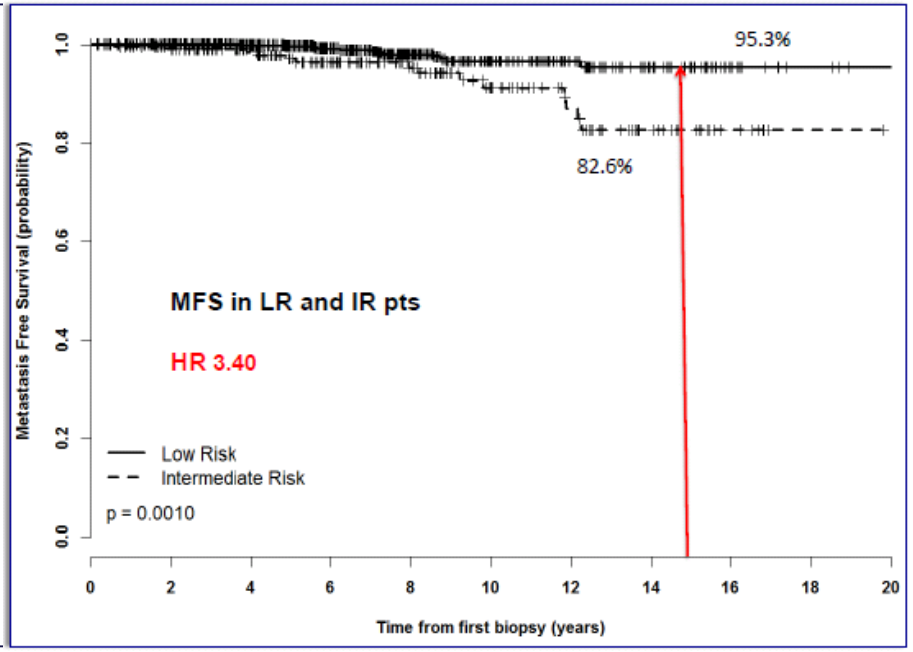
CSS Active Surveillance N=993



Low- vs Int Risk

n = 708 v 218





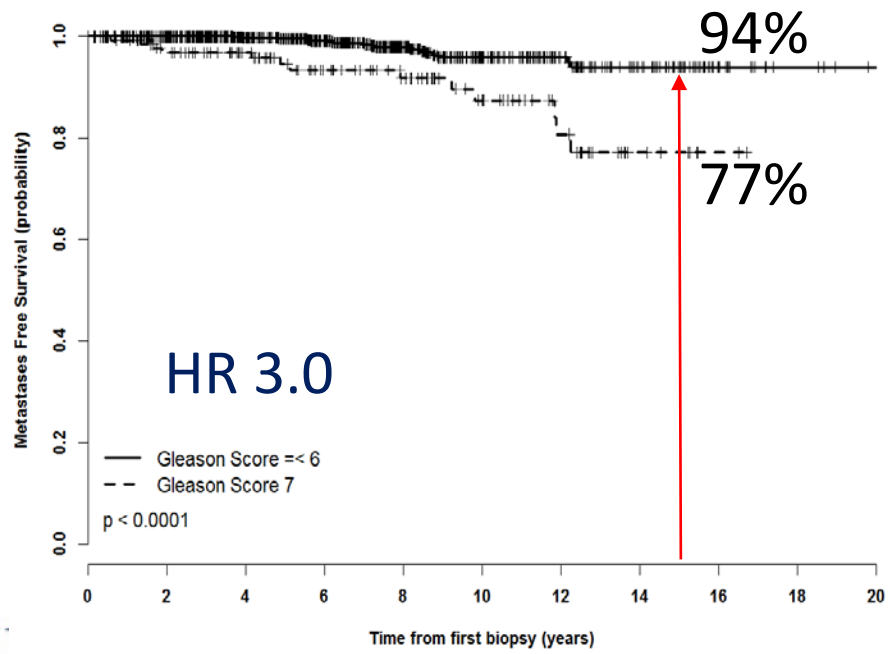
Cause Specific Survival

Metastases Free Survival

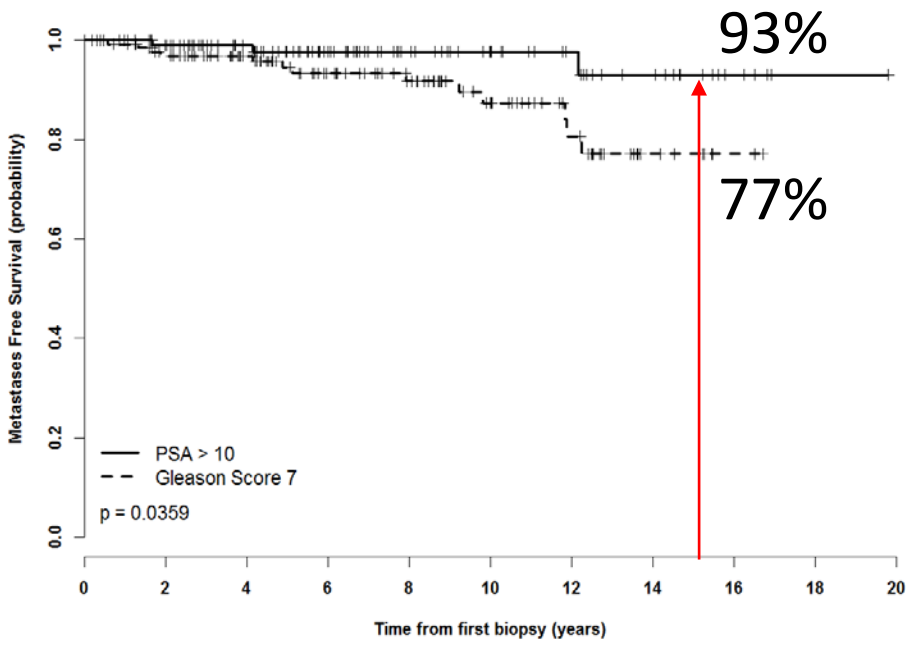
Multivariate Analysis

Predictive factors	p-value	HR (95% CI)
PSA DT (≤3 years vs >3 years)	0.0062	3.7 (1.4, 9.4)
Gleason 7 vs ≤ 6	0.0181	3.0 (1.2, 7.3)

Baseline Gleason 7 vs ≤ 6



Baseline PSA >10 vs GS 7 in Intermediate risk group



University of

nnybrook
TE CANCER CENTRE
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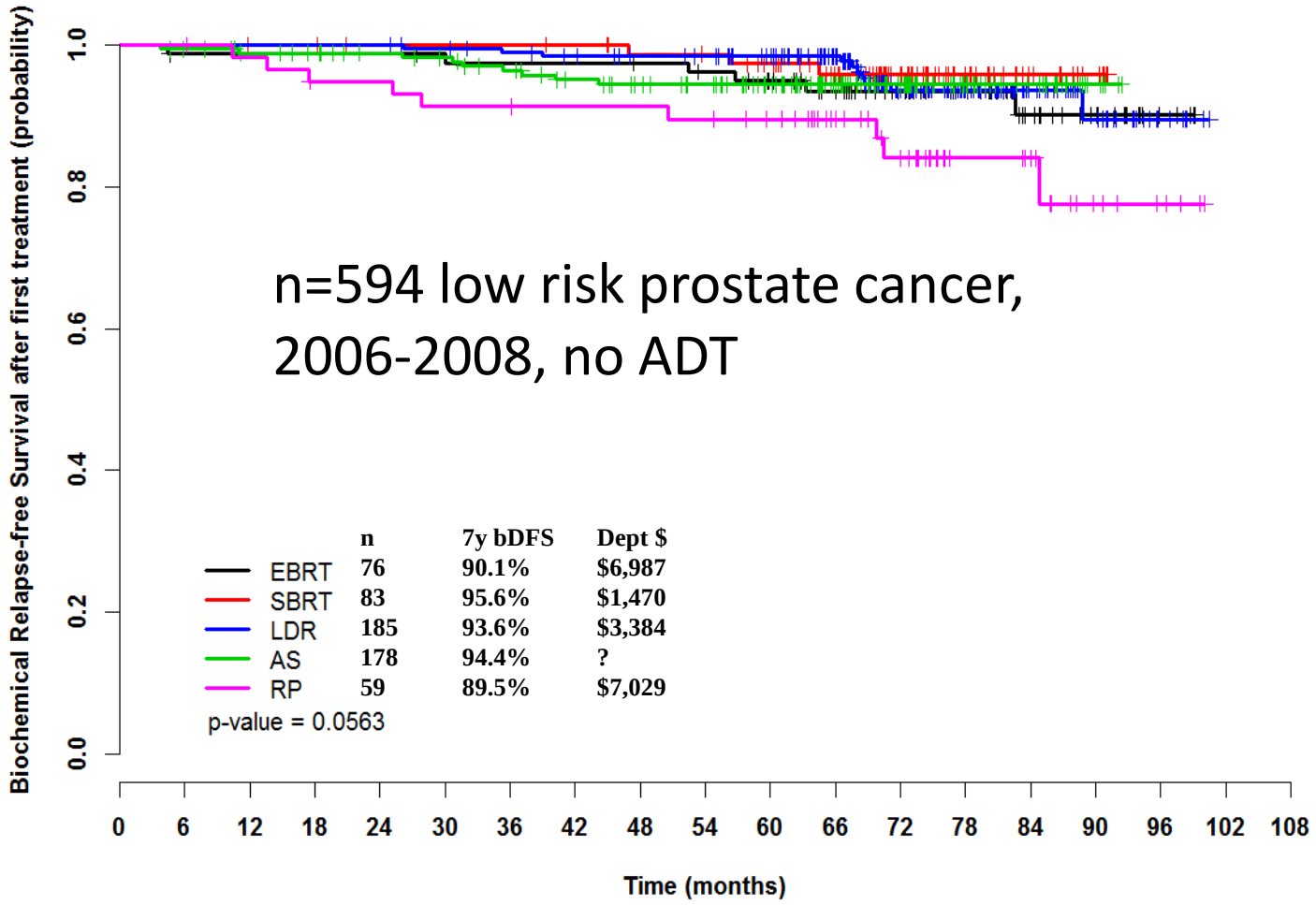
How Does AS compare to Active Treatment for Low Risk Pr Ca?

bDFS stratified by Treatment Modality



Musurunu BH et al., JCO 33(Suppl 7); 2015 (abstr 178)

System Savings with AS

Table 4: Total cost for active surveillance and immediate treatment and possible cost savings corresponding to an annual cohort of 12 750 patients with prostate cancer stratified by patients' treatment status

Treatment status	% (no.) of patients	Mean cost per patient, $		Total cost, $		Cost difference, $	
		Active surveillance	Immediate treatment	Active surveillance	Immediate treatment	Per patient	Total
First year and 5-year follow-up							
Patients requiring treatment	25.5 (3 247)	16 257	13 735	52 786 479	44 597 545	2 522	8 188 934*
Patients not requiring treatment	74.5 (9 503)	2 753	13 735	26 161 759	130 523 705	–10 982	–104 361 946†
Total	100.0 (12 750)	6 200	13 735	79 050 000	175 121 250	–7 535	–96 071 250‡
First year and 10-year follow-up							
Patients requiring treatment	30.8 (3 922)	25 552	18 407	100 214 944	72 192 254	7 145	28 022 690*
Patients not requiring treatment	69.2 (8 828)	3 959	18 407	34 950 052	162 496 996	–14 448	–127 546 944†
Total	100.0 (12 750)	10 600	18 407	135 150 000	234 689 250	–7 807	–99 539 250‡

*Additional cost attributable to delayed treatment.
†Cost savings attributable to active surveillance.
‡Total cost savings obtained through active surveillance.

$100,000,000 per year!

University of Toronto

Dragomar A, Cury FL, Aprikian AJ. CMAJ Open 2(2):e60-68; 2014

Sunnybrook ODETTE CANCER CENTRE
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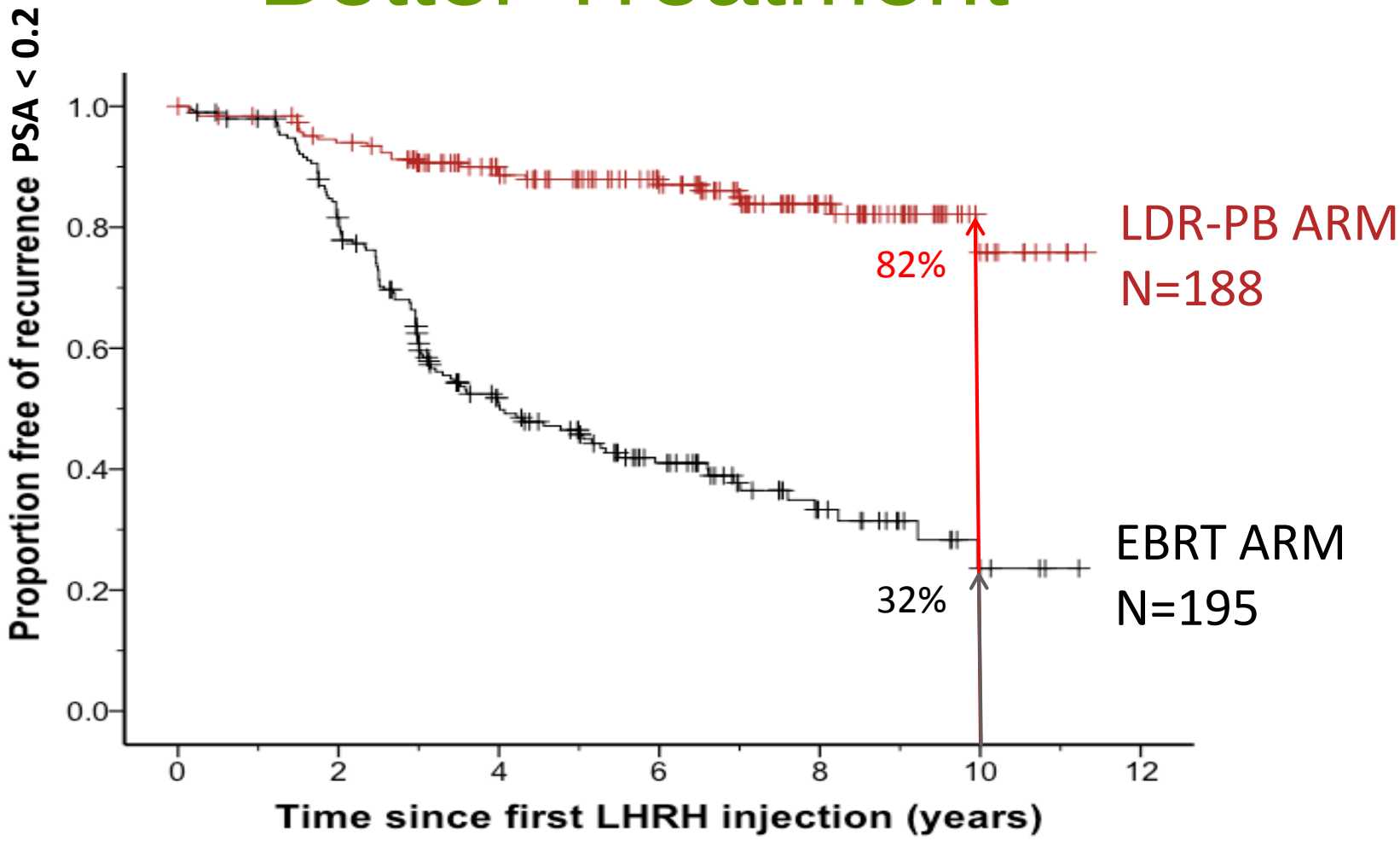
Better Treatment



Morris WJ et al., GU Symp 2015

RP for High Risk Disease

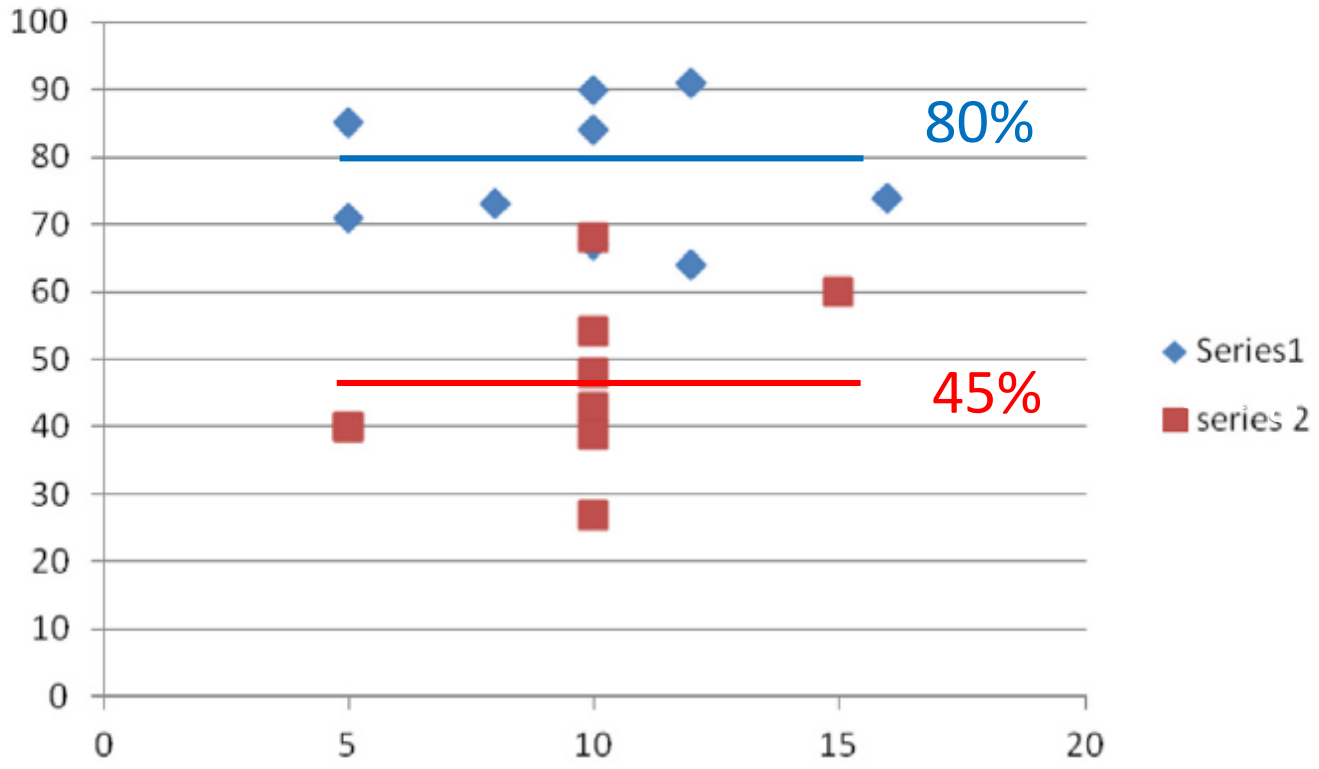
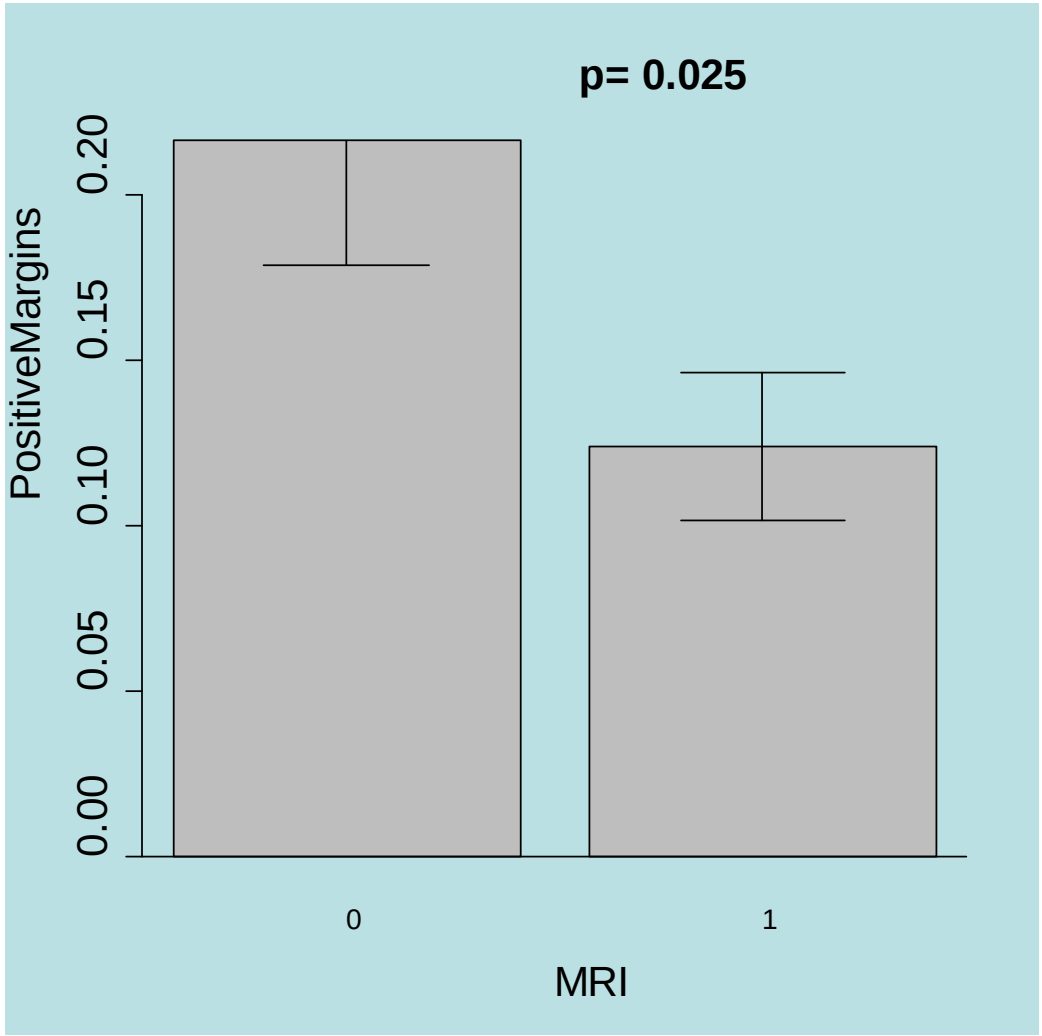


Fig. 2. Comparison of biochemical disease-free rates for high-risk prostate cancer. Series 1: Brachytherapy-based treatment; Series 2: radical prostatectomy.

Crook J et al., Brachy 2014

MRI Reduces Overall Surgical Positive Margin Rate



N=104
1.5 T ERC
27% change in
surgical approach

Margolis et al. Radiology, 2012

Conclusions

- Screening for prostate cancer reduces risk of metastases and dying of prostate cancer
- Diagnostic harms can be reduced by risk adaption, use of MR and TP biopsies
- Treatment harms can be reduced by using active surveillance for low risk patients
- High risk patients should be treated with most effective / cost-effective treatments up front