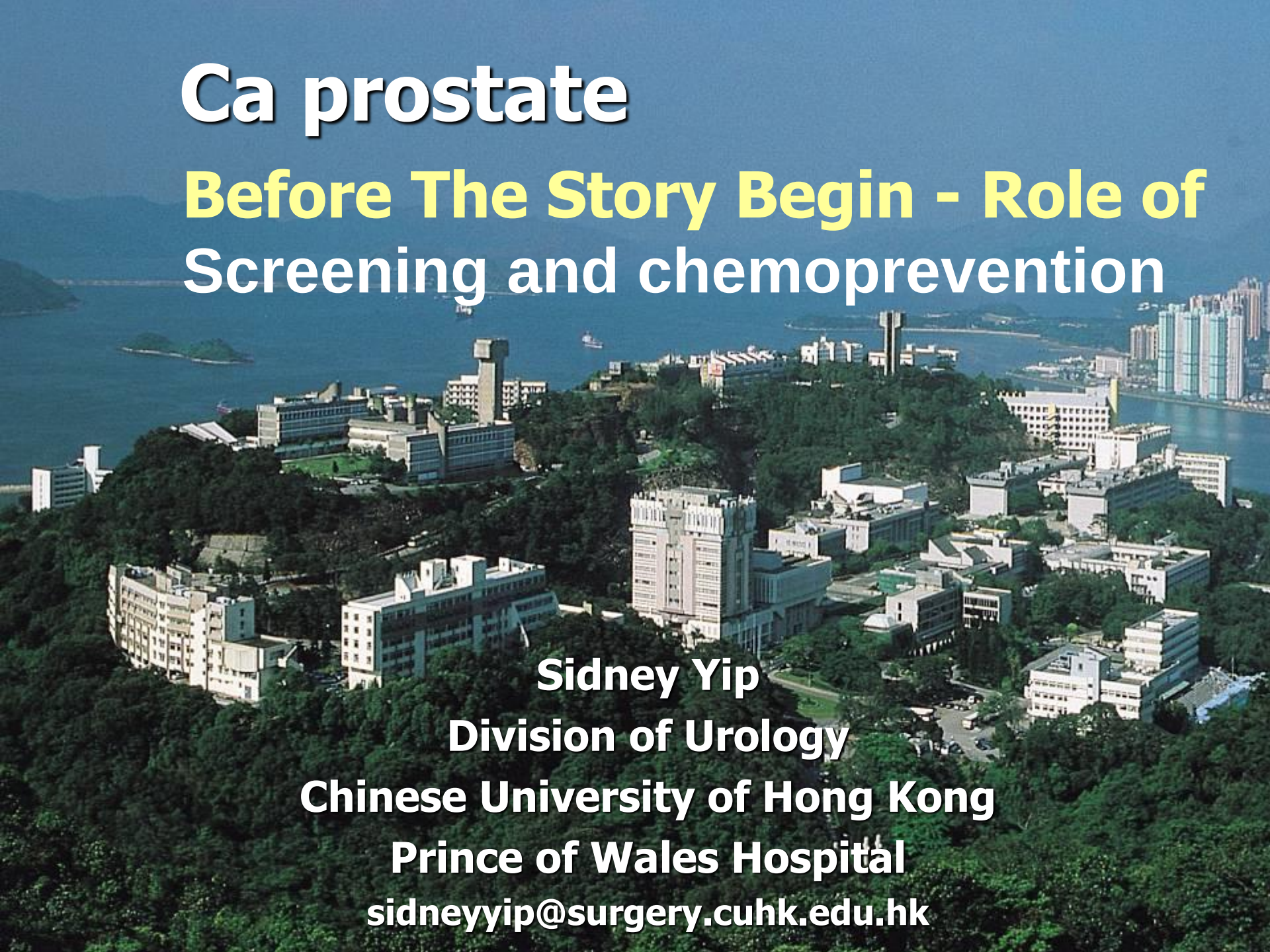
Ca prostate

Before The Story Begin - Role of Screening and chemoprevention



Sidney Yip

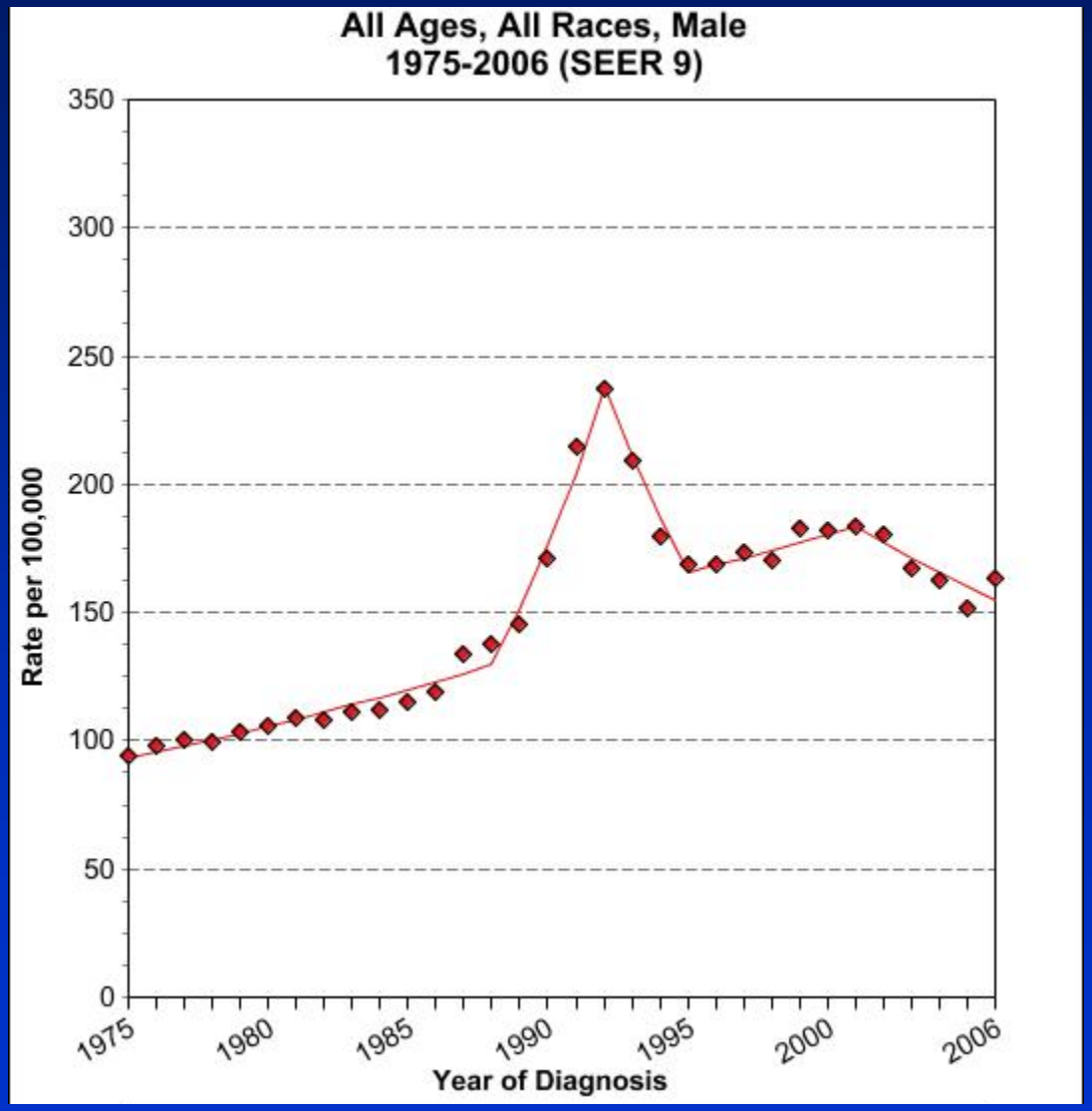
Division of Urology

Chinese University of Hong Kong

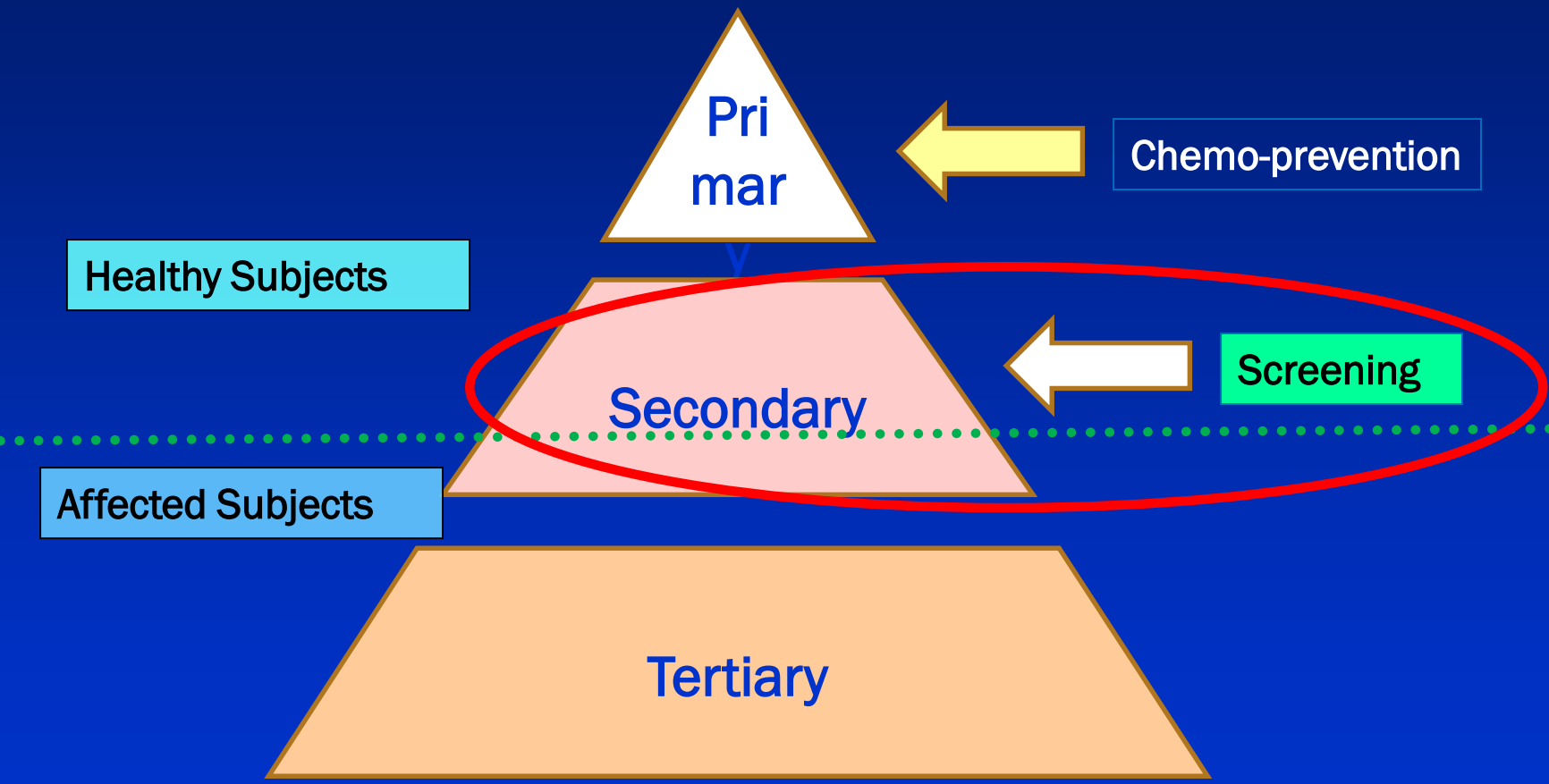
Prince of Wales Hospital

sidneyyip@surgery.cuhk.edu.hk

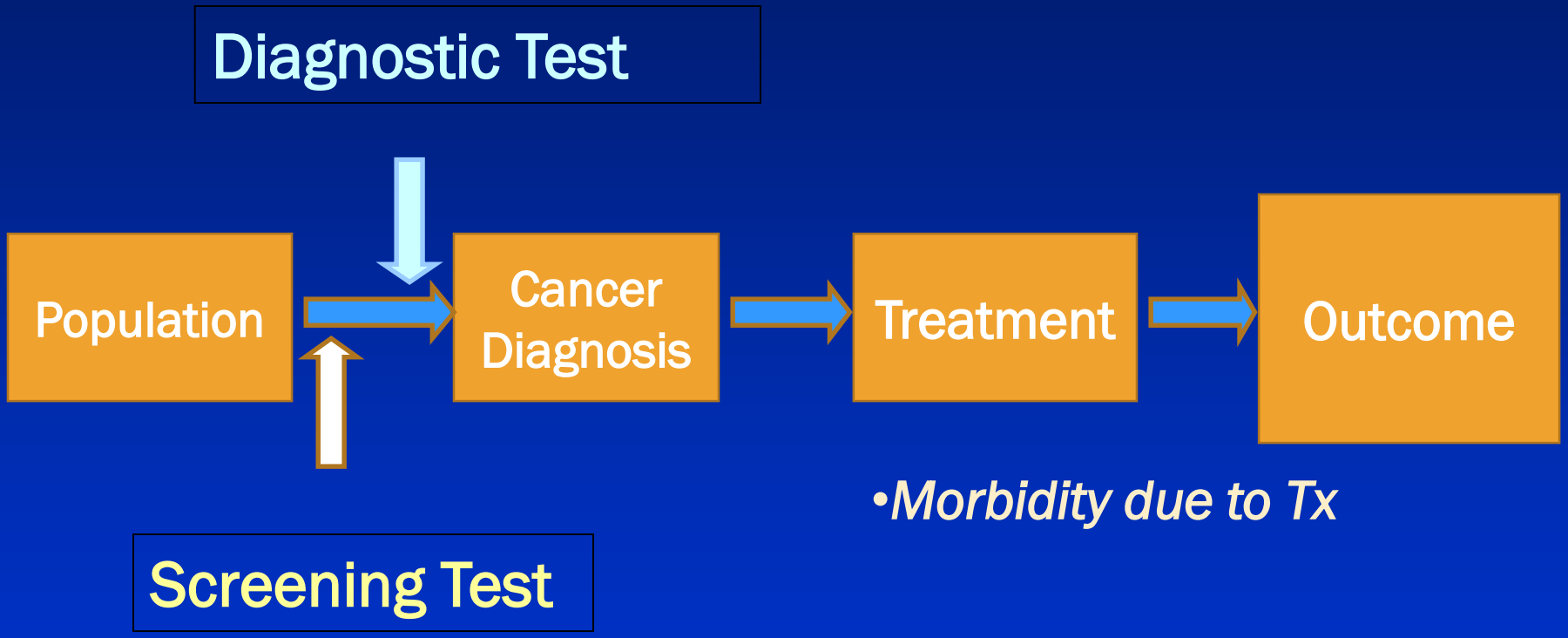
Ca Prostate age-adjusted SEER incidence



PREVENTION

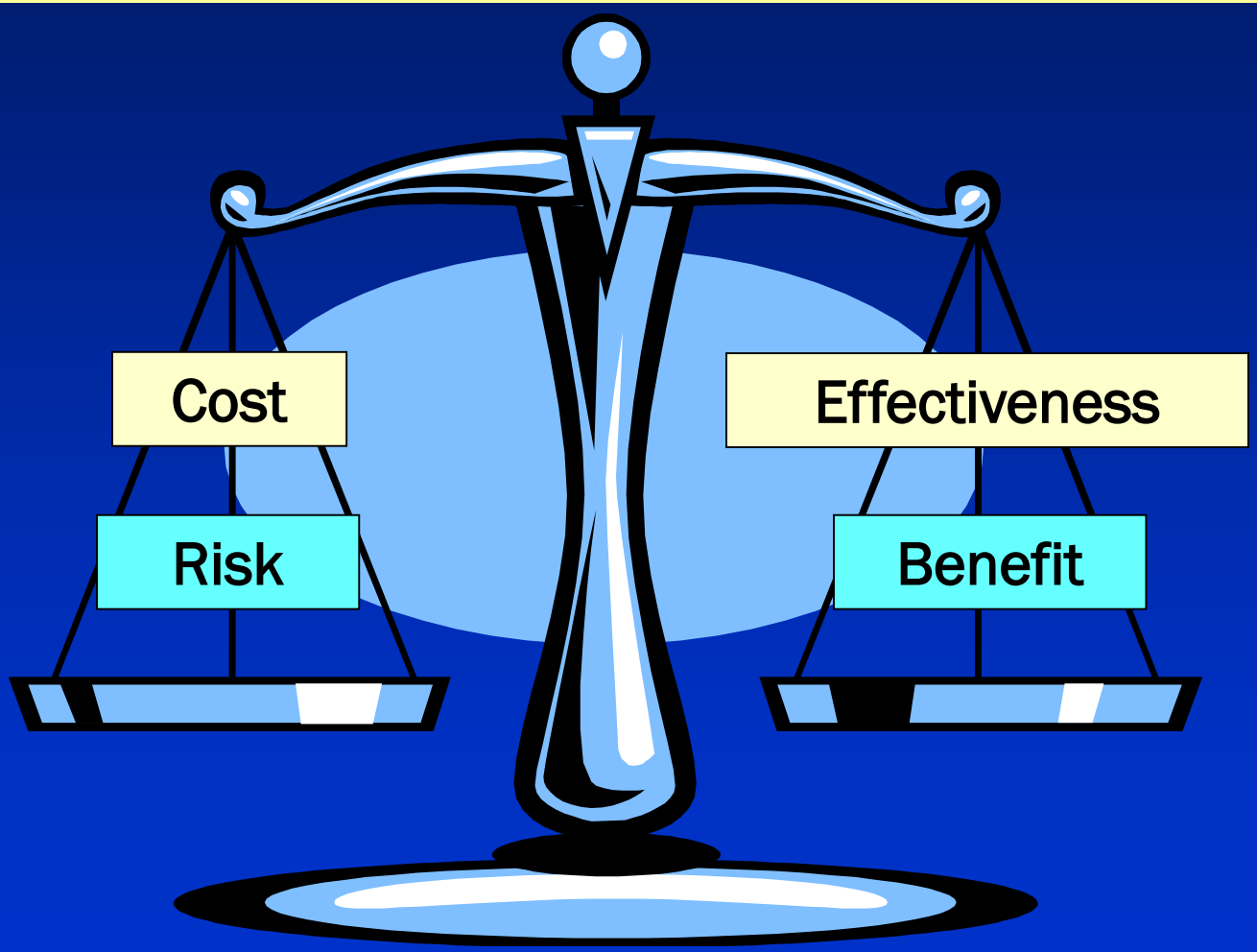

Pri
mar
Chemo-prevention
Healthy Subjects
Secondary
Screening
Affected Subjects
Tertiary

THE LOGISTIC



- *Morbidity due to Tx*

A MATTER OF BALANCE



Necessary to detect all cancers?

- **Large discrepancy between autopsy rate of cancer and clinical disease**

TIGER

PUSSY CAT

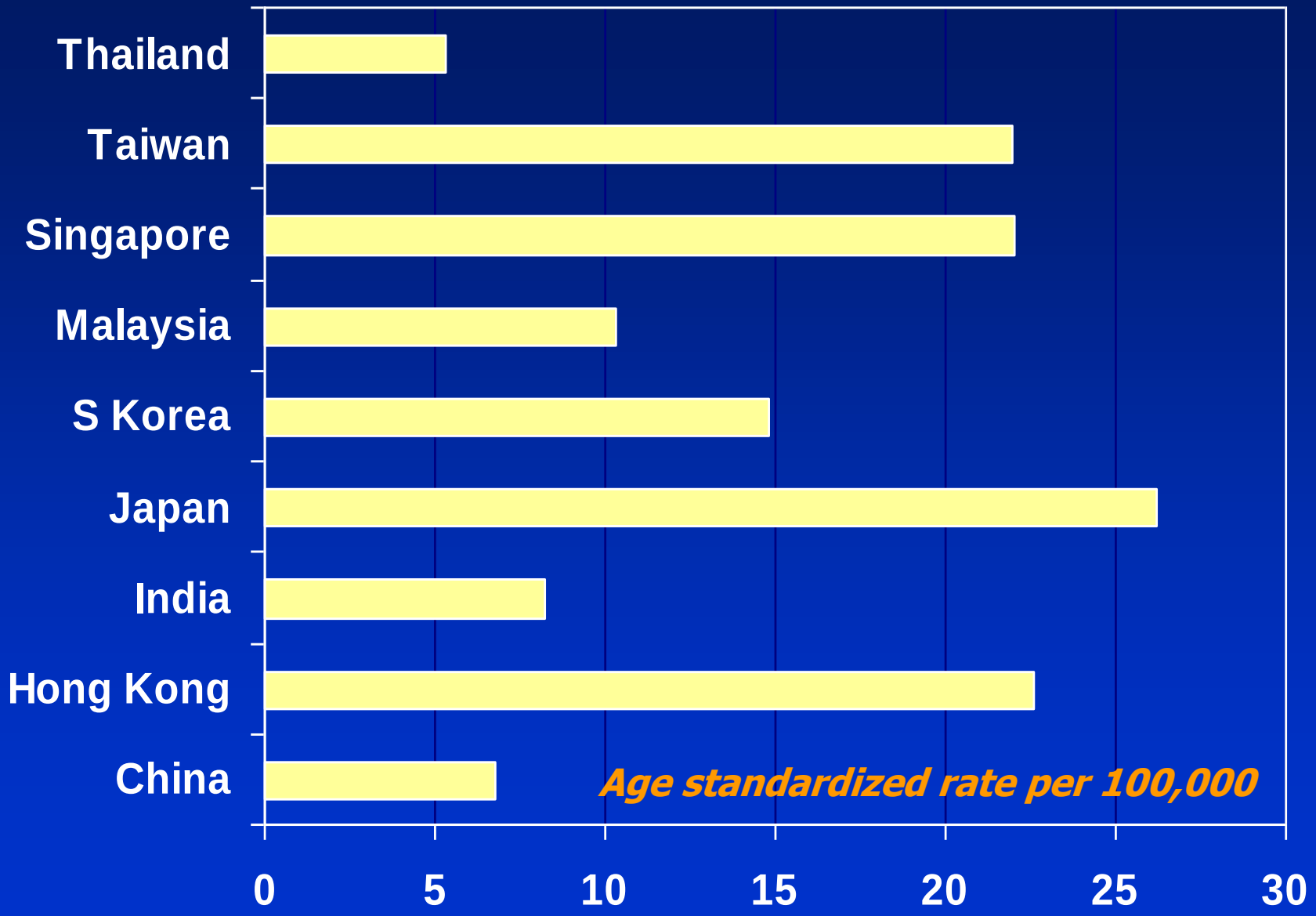
The more biopsies, the more likely to detect insignificant cancers

Desirable not to detect clinically insignificant cancers

Diagnosis and Treatment bring more harm than good

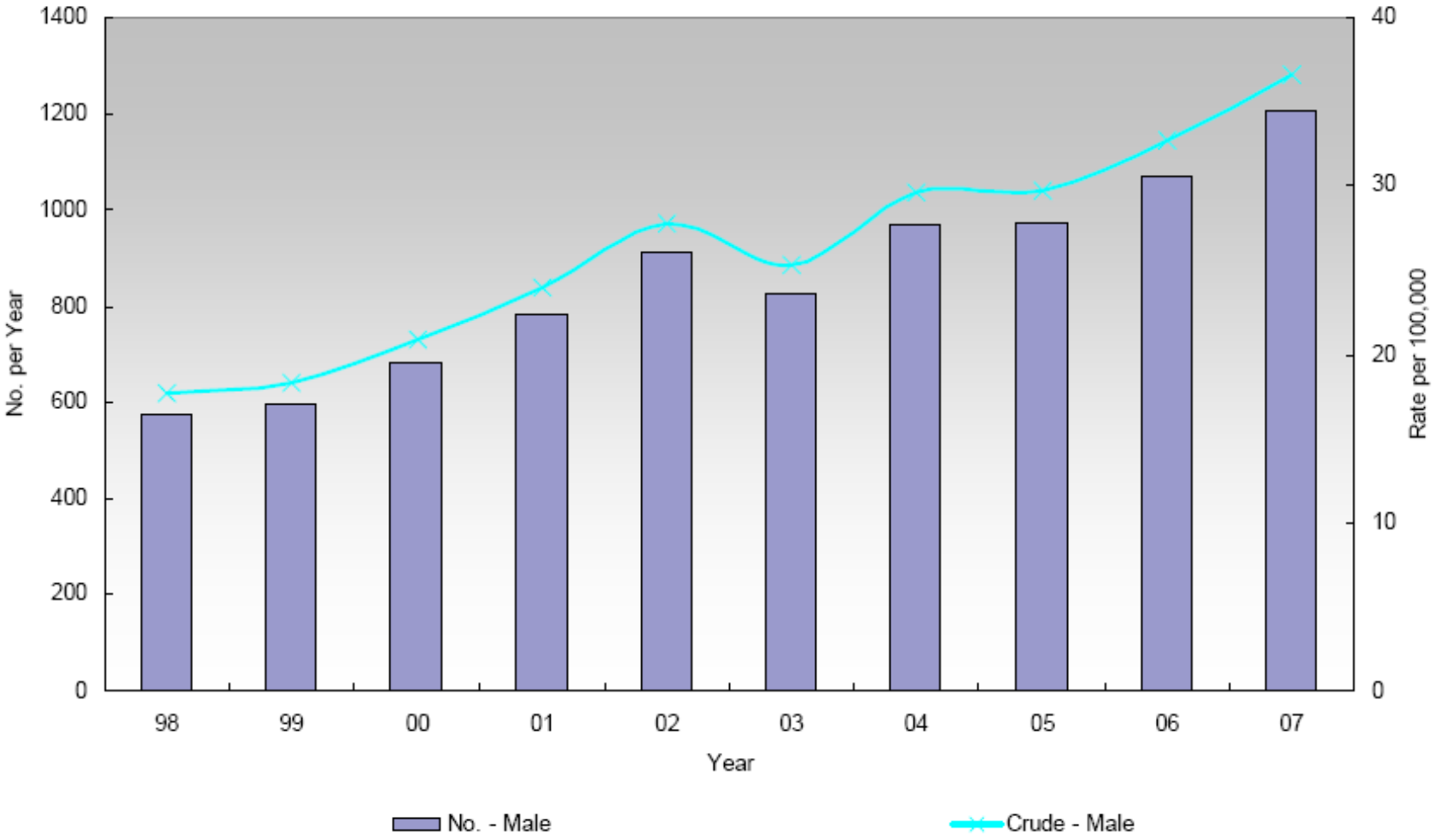
Ca Prostate – increased detection through PSA testing

Incidence in Asia Countries



Yip Current Opinion Urology 2009

Incidence Trend 1998-2007



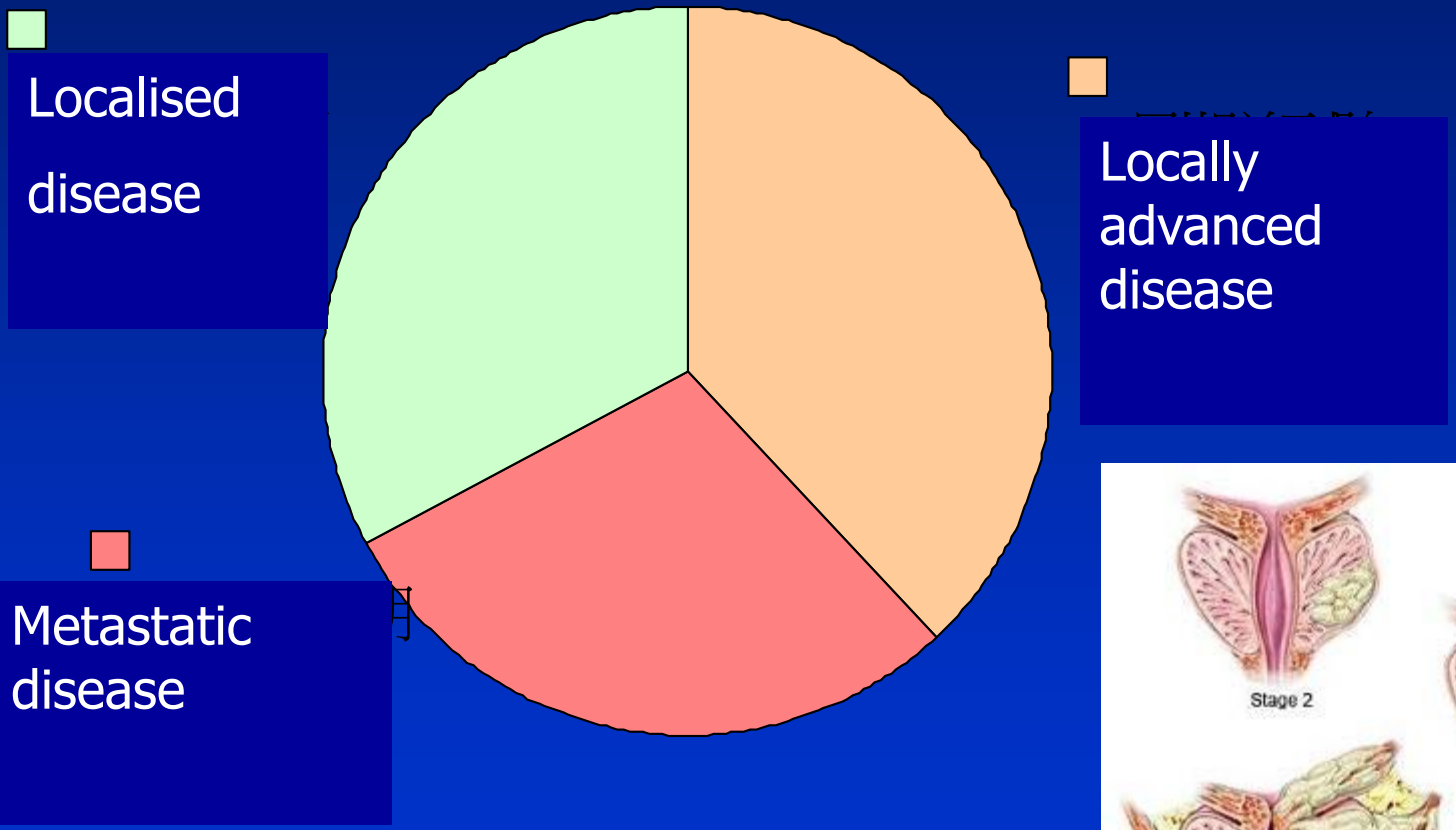
Incidence & Mortality Data *2007*

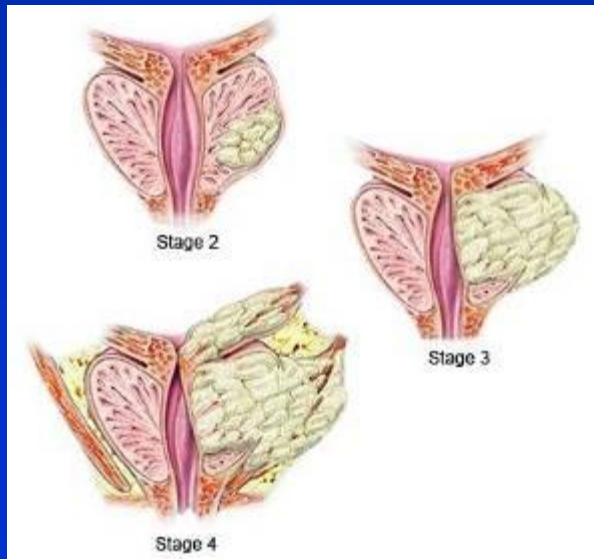
	New Case	Death
Number of cases registered	1,205	296
Rank	4	5
Relative Frequency (%)	9.2	3.9
Median age (years)	73	79
Crude Rate	36.7	9
Age-standardized rate (World)*	24.5	5.9
Cumulative life-time risk (0-74 yrs)	1 in 39	1 in 277

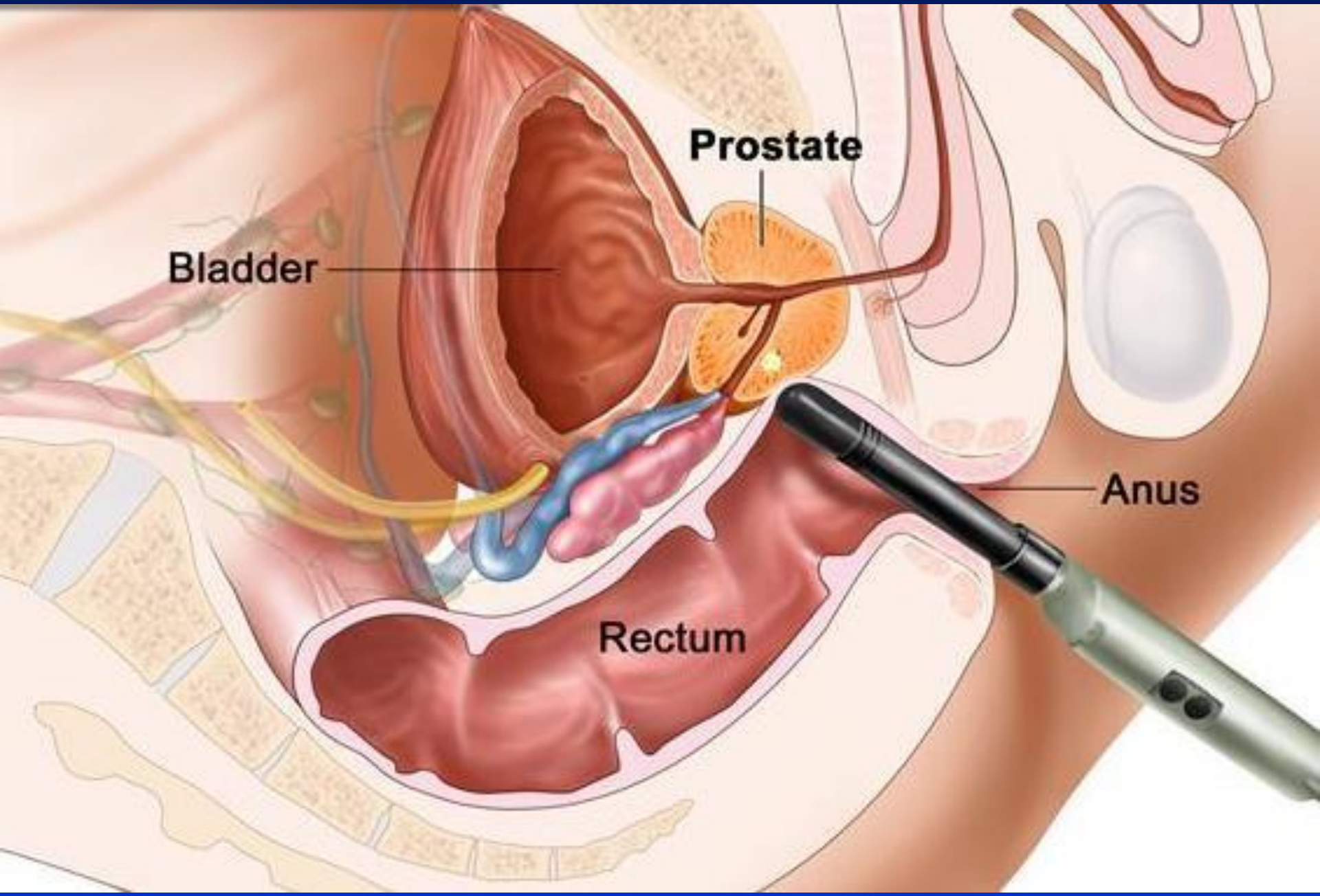
•The age-standardized rate (World) is calculated based on the world standard population published in the 1997-99 World Health Statistics Annual, WHO.
•All rates are expressed per 100,000.

Ca prostate 2005-2007 in PWH

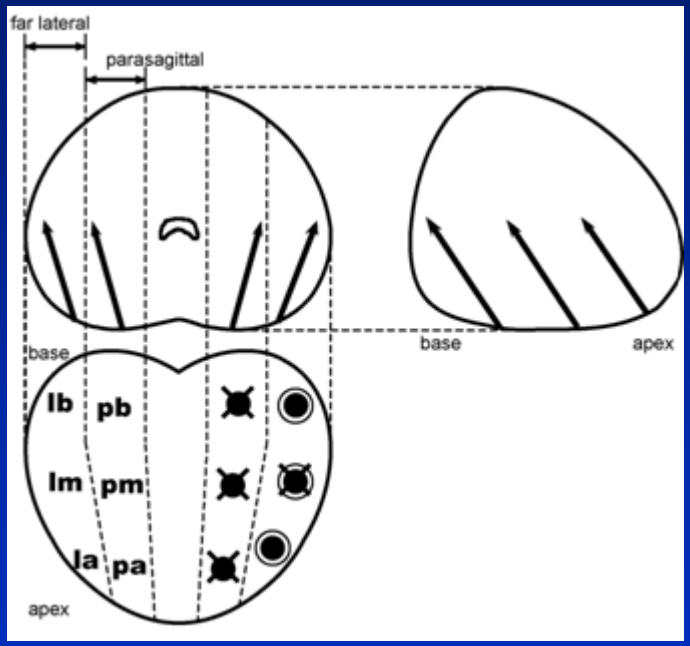
Disease stage at 1st presentation






Prostate
Bladder
Anus
Rectum

Biopsy policy



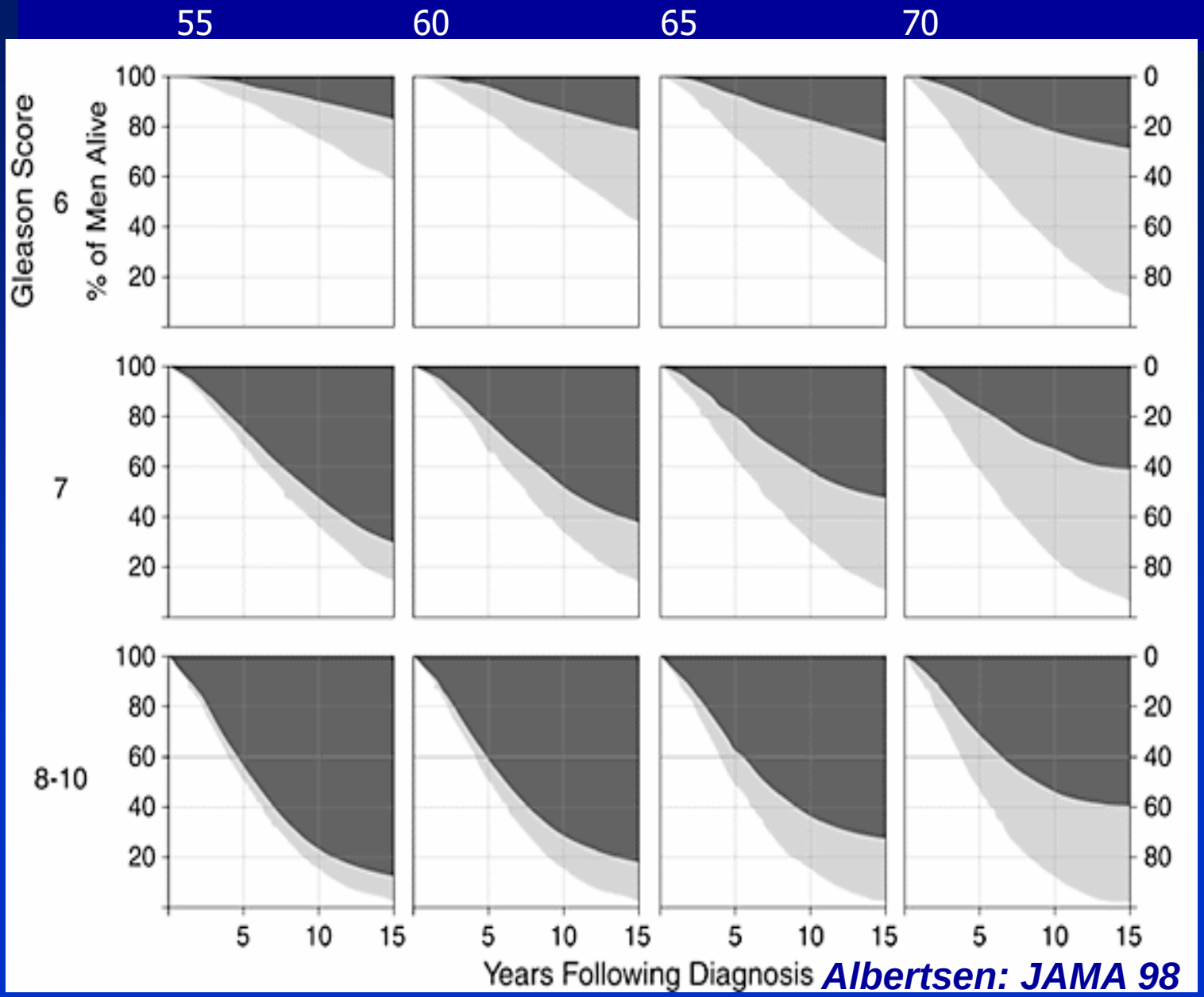
- ***Standard 10 core biopsy***

  Ng, Yip Asian J Surg 01

- ***2 biopsies negative, low risk***

  Djavan J Urol 01

Age at diagnosis

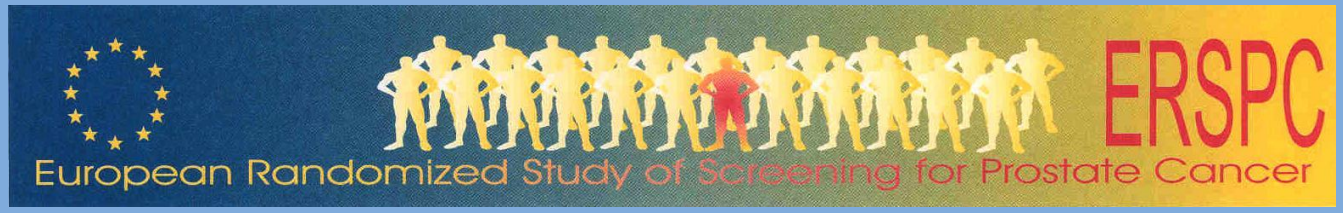


CAP SUITABLE FOR SCREENING?

- CaP highly prevalent
  - Usually indolent
  - Sometimes deadly
  - Issue of over Dx and Tx
- Long natural course
  - Window for Screening and Tx
  - Issue of lead-time
- Availability of effective Tx ?
  - Balance between risk and benefit

Prostate Cancer Screening: Evidence for Efficacy and Screening in Elderly Men

Fritz H. Schröder, MD
Professor of Urology, Erasmus University Medical Centre, Rotterdam, The Netherlands



European Association of Urology

Methods - ERSPC

Main end point: PCa mortality, screened versus control

Age: 50-74; core group 55-69 (population-based; N = 162.387)

Screening interval:

- 4 years (87%)
- 2 years (13%)

Sextant (lateral) biopsy recommended for PSA ≥3.0 ng/ml

Results – Recruitment and screen detection (core age group)

Screening arm: 72.890 men

Control arm: 89.353 men

20.437 (16.2%) positive tests, 17.543 (85.8%) biopsied, PPV 24.1%

Screening arm: 5.990 PCa (8.2%), 214 PCa deaths

Control arm: 4.307 PCa (4.8%), 326 PCa deaths

Follow-up: mean 8.8 years, median 9 years

PCa mortality

ITS analysis: 20% fewer men die of PCa in the screening arm (P=0.04)

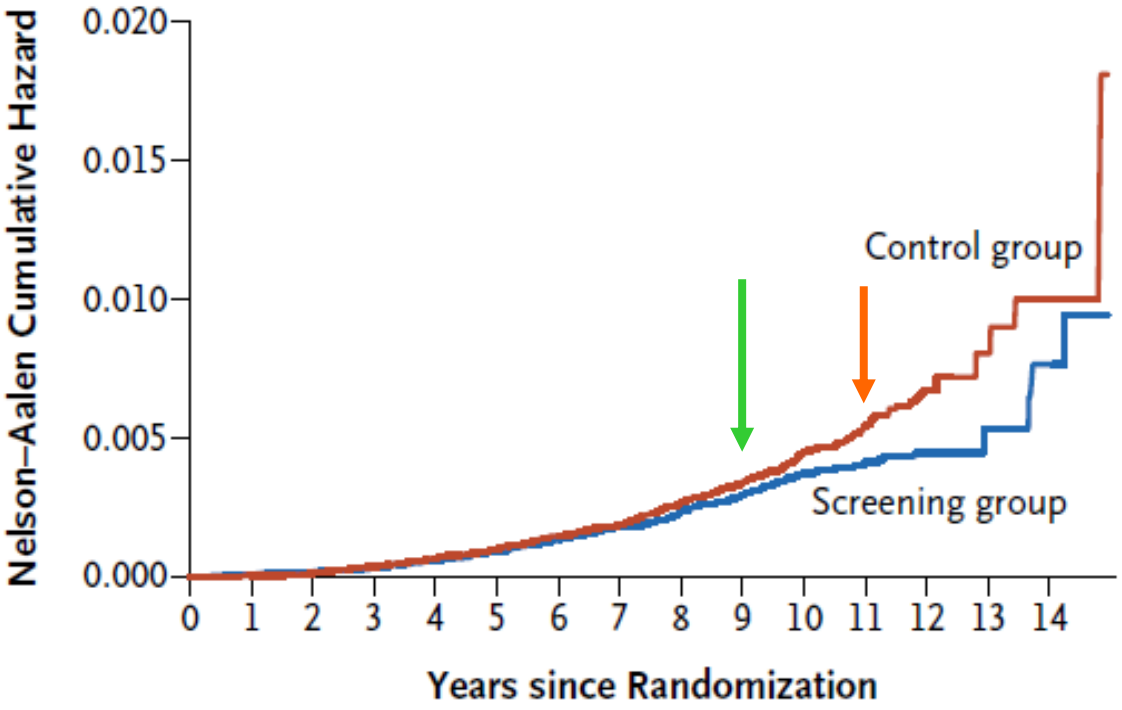
Adjustment for non-compliance, 27% fewer PCa deaths in men actually screened

Absolute risk reduction: 7 per 10.000 screened men

NNS: 1.410, NNT: 48 in excess of control group

European Association of Urology

Cumulative risk of death from PCa



No. at Risk	5 years	7 years	10 years
Screening group	65,078	58,902	20,288
Control group	80,101	73,534	23,758

European Association of Urology

Schröder et al. NEJM 2009

Conclusions

Significant reduction of 20% in the relative risk of PCa death for men aged 55-69 (ITS analysis)

In men actually screened the relative risk reduction is 27%

The trend seen in the mortality curves suggests larger effects with longer follow-up

Healthcare providers will struggle with the high rate of overdiagnosis and NNT (48)

European Association of Urology

The Prostate, Lung, Colon, Ovary Cancer Screening Trial (PLCO) (Andriole et al, NEJM 2009)

RCT of screening versus 'general care' control group

N = 76.693 men age 55-74

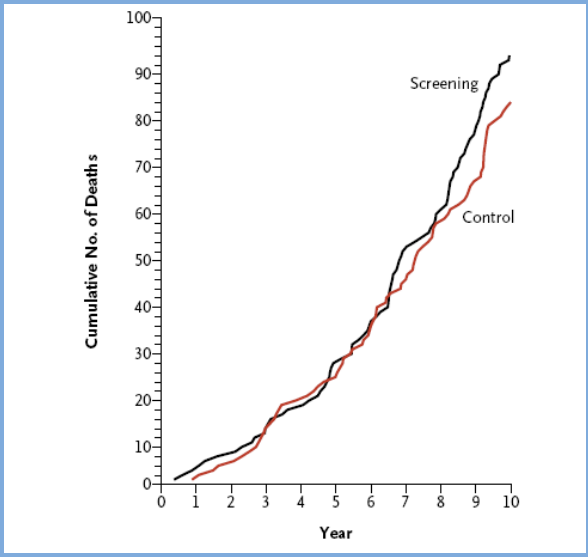
PSA testing yearly for 6 years, DRE year 1-4

Biopsy for PSA > 4.0 ng/ml or abnormal DRE

Average 7 year follow-up

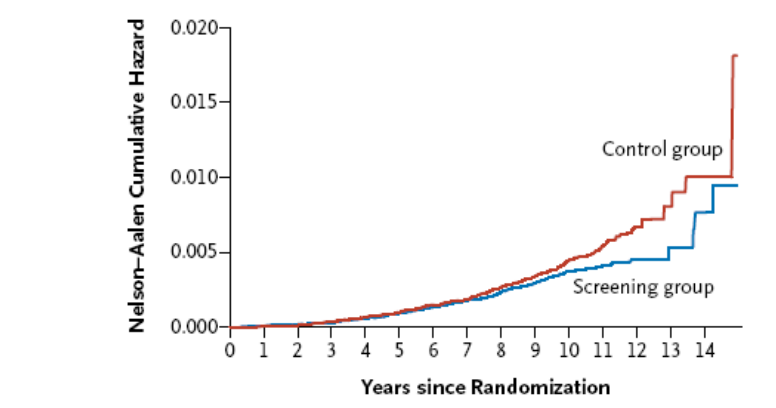
Prostate cancer screening: PLCO versus ERSPC

No benefit of screening



PLCO Study

Risk reduction of 20%



ERSPC

European Association of Urology

PLCO Cancer screening trial and ERSPC results differ – why?

Testing in 44% of men prior to randomization decreased numbers of events

Low rates of Pca deaths in both arms: screened vs. Control, 2.0 vs 1.7/10.000 person-years in PLCO trial, and 3.3 vs 4.3 in ERSPC

PLCO does not contribute to determine the value of screening

WHAT SHOULD WE DO?

- Should we catch all the fish (CaP) by liberal screening (population-based) ?
- Are we catching the right fish?

THE FUTURE

- PSA
  - Not cancer specific
  - Limited in sensitivity and specificity as an screening test
- ?Role for PCA3

PSA cut-off	Sensitivity	Specificity
1.1 ng/ml	83.4%	38.9%
2.1 ng/ml	52.6%	72.5%
3.1 ng/ml	32.2%	86.7%
4.1 ng/ml	20.5%	93.8%

Data from PCPT

What advice can be given to men who wish to be screened?

Message has changed dramatically

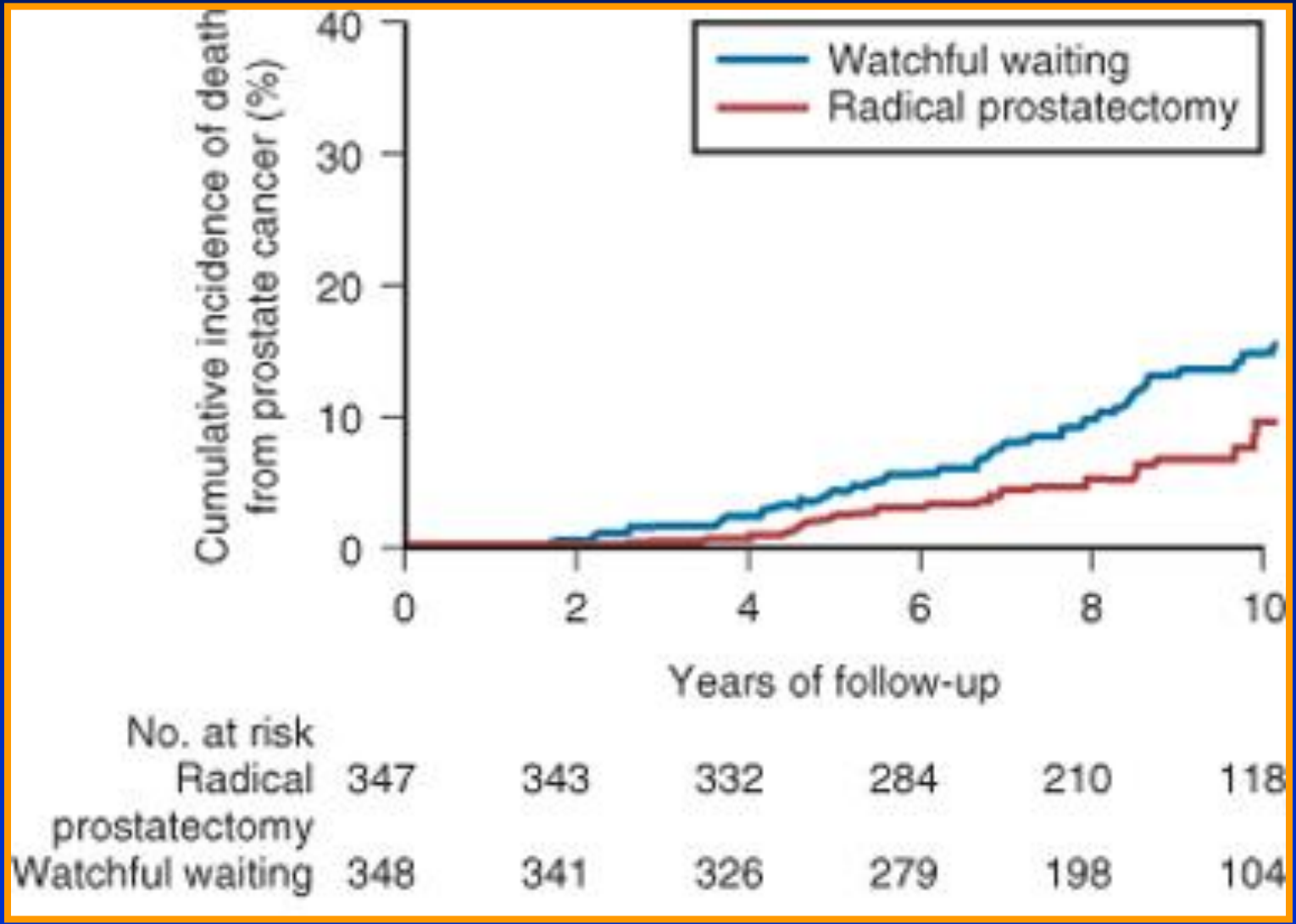
If you do have Pca, early detection decreases the chance of dying

The downside remains: there is a high chance of being diagnosed and treated for disease which otherwise may not harm you

However, if you are diagnosed with 'indolent' disease, treatment can be avoided at least for some time

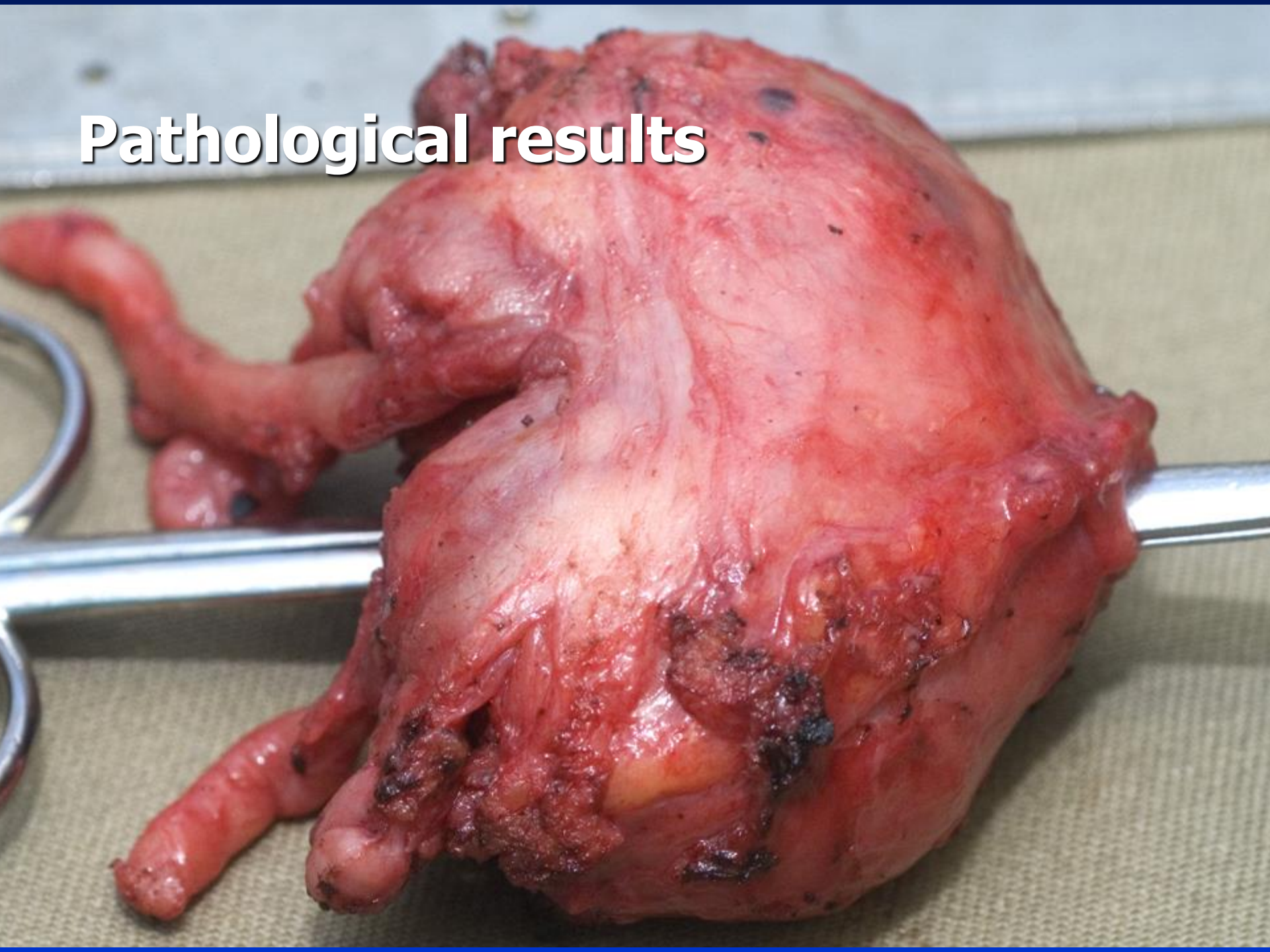
European Association of Urology

Ca P: surgery & watchful waiting



Bill-Axelson A et al. N Engl J Med 2005;352:1977-1984

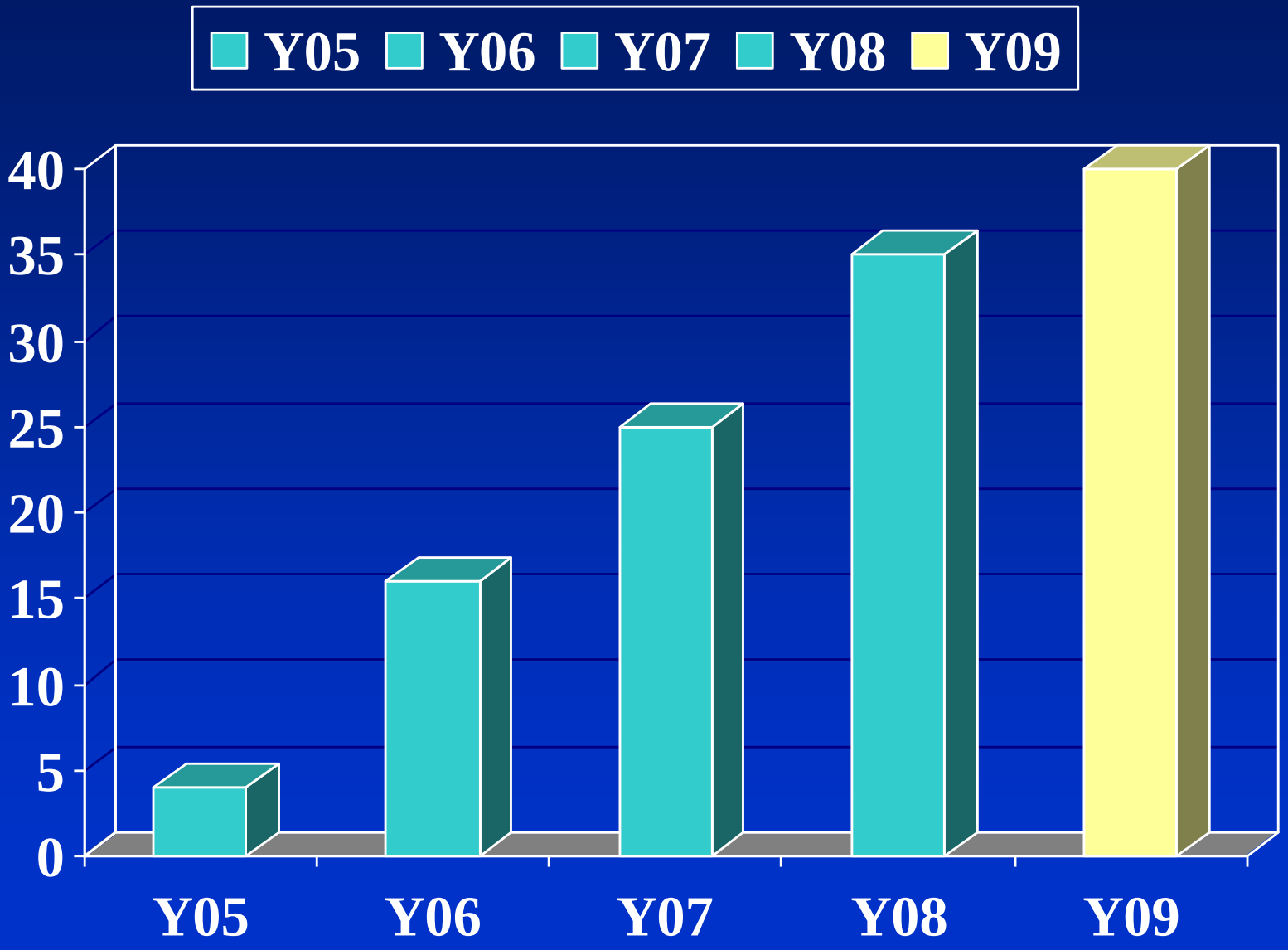
Pathological results



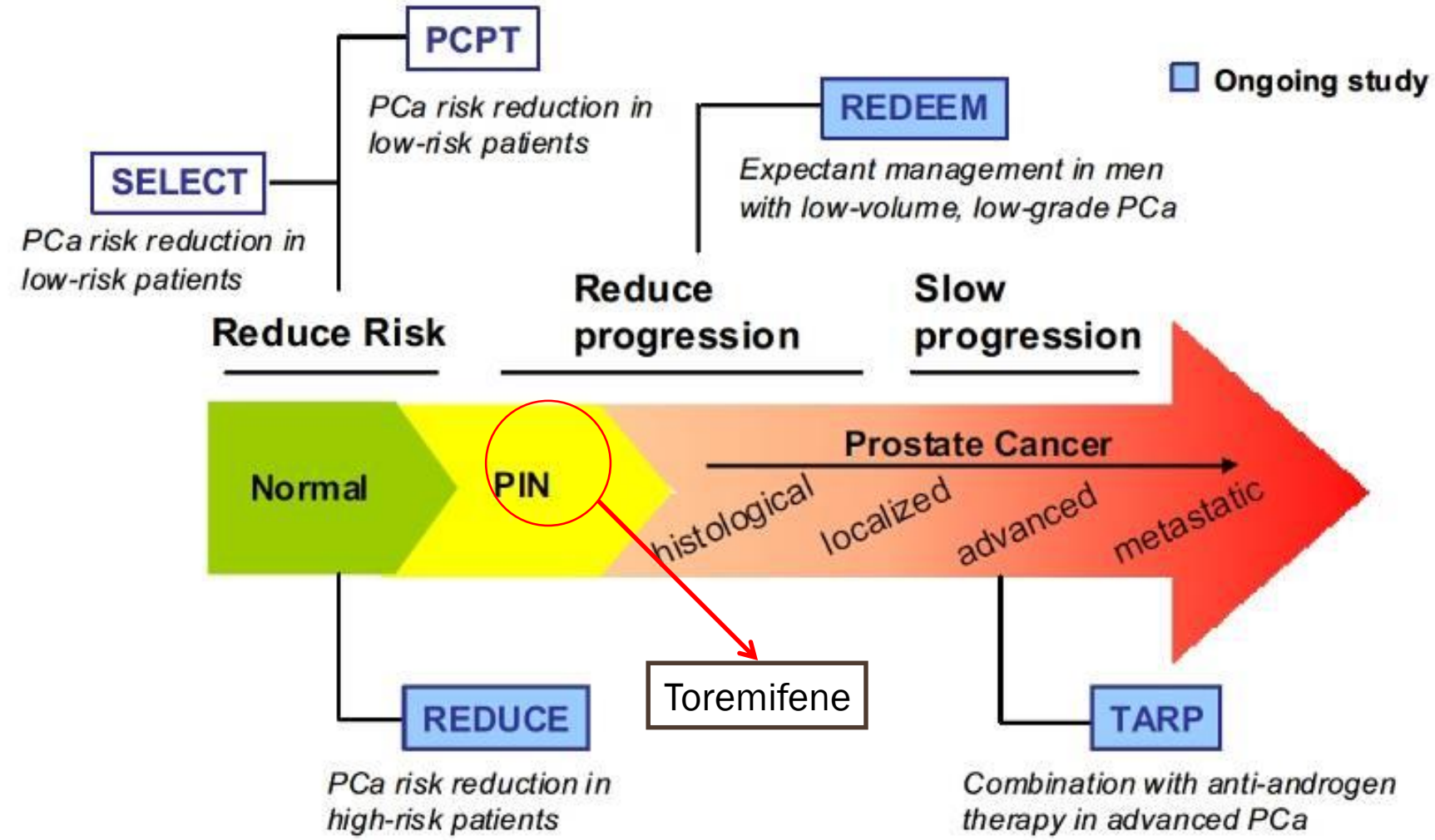
2nd donation: da Vinci S HD since Feb 08


Robotic prostatectomy
Initial 100 cases
transfusion
7.4 %
Major complications
4%
Catheter time (days)
8.4
Hospital stay (days)
2.9
Sim & Yip Int J Urol 2006

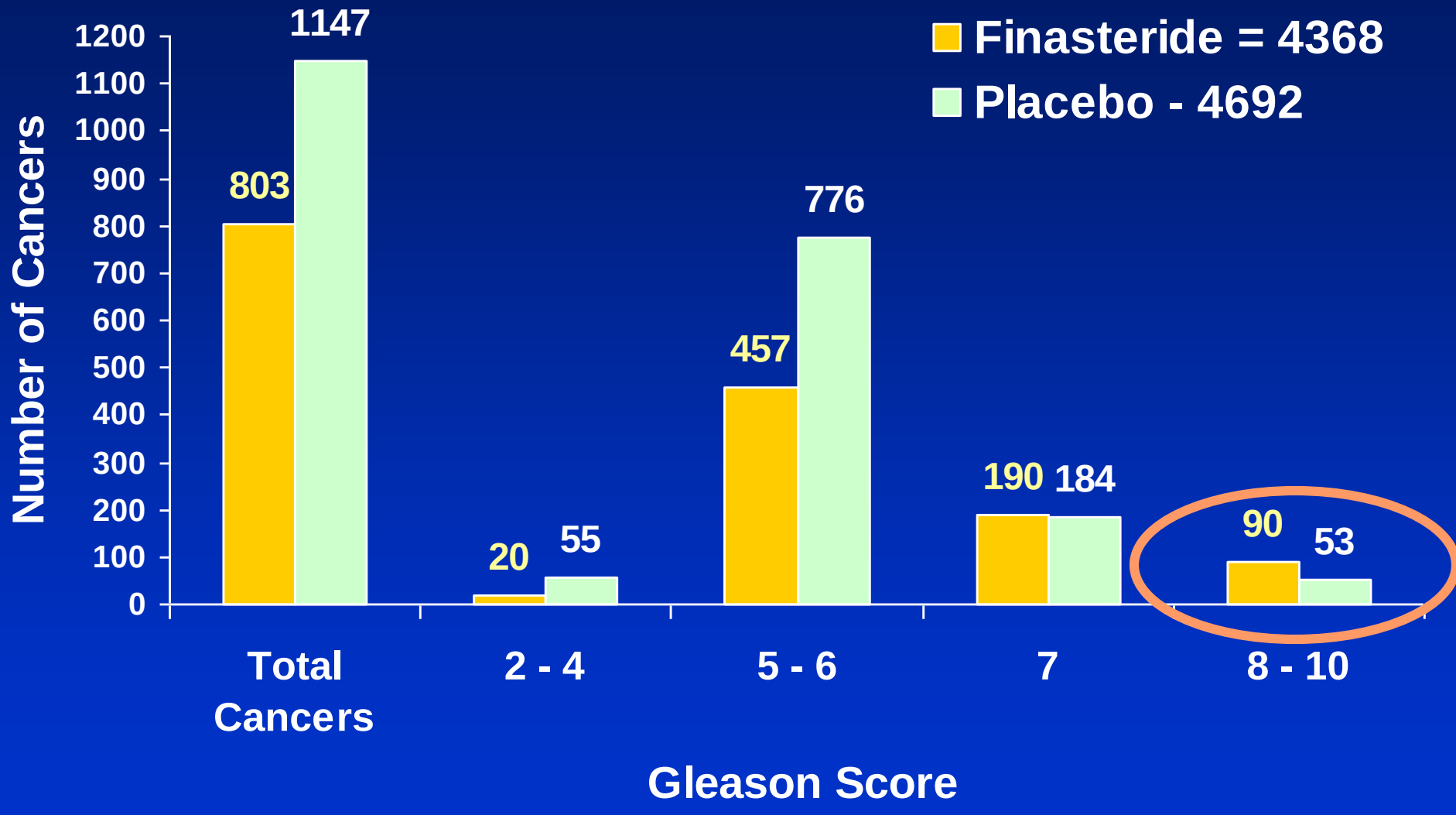
Trend of RRP in PWH



CHEMOPREVENTION



PCPT Gleason Scores



Thompson I. NEJM 2003;349:215

Higher Gleason ≥7 PCa in PCPT:

Result of ascertainment problem?

- Lower prostate volume favours detection of high grade PCa[1]
- More upgrading at RP in placebo group[2,3]
- Incidence does not increase over time
- Finasteride impact on PSA promotes detection of high grade cancers[4]

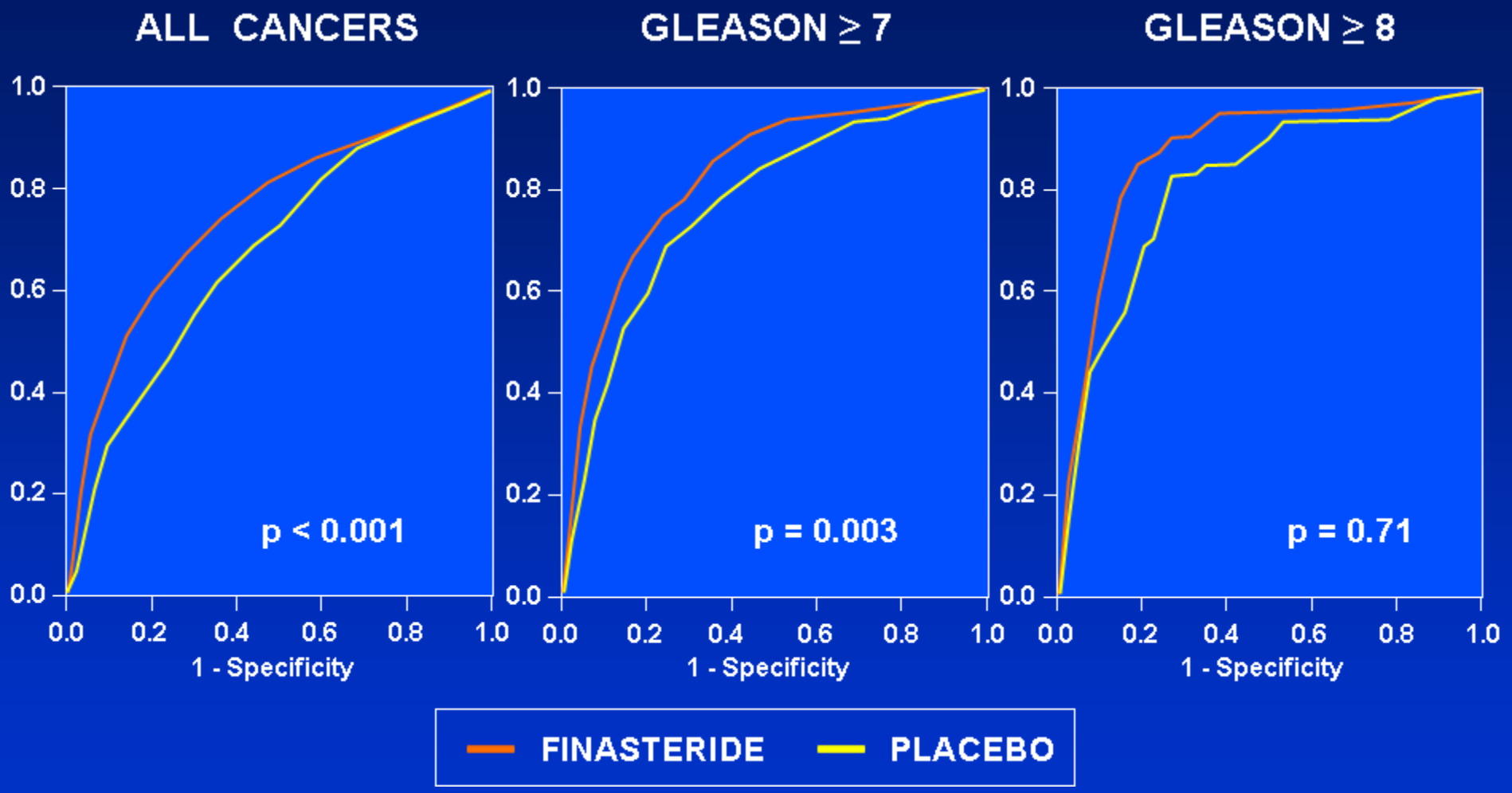
1) Cohen, J.NCI 99:1366, 2007

2) Lucia, J.NCI 99:1375, 2007

3) Kulkarni, J.UROL. 175:419, 2007

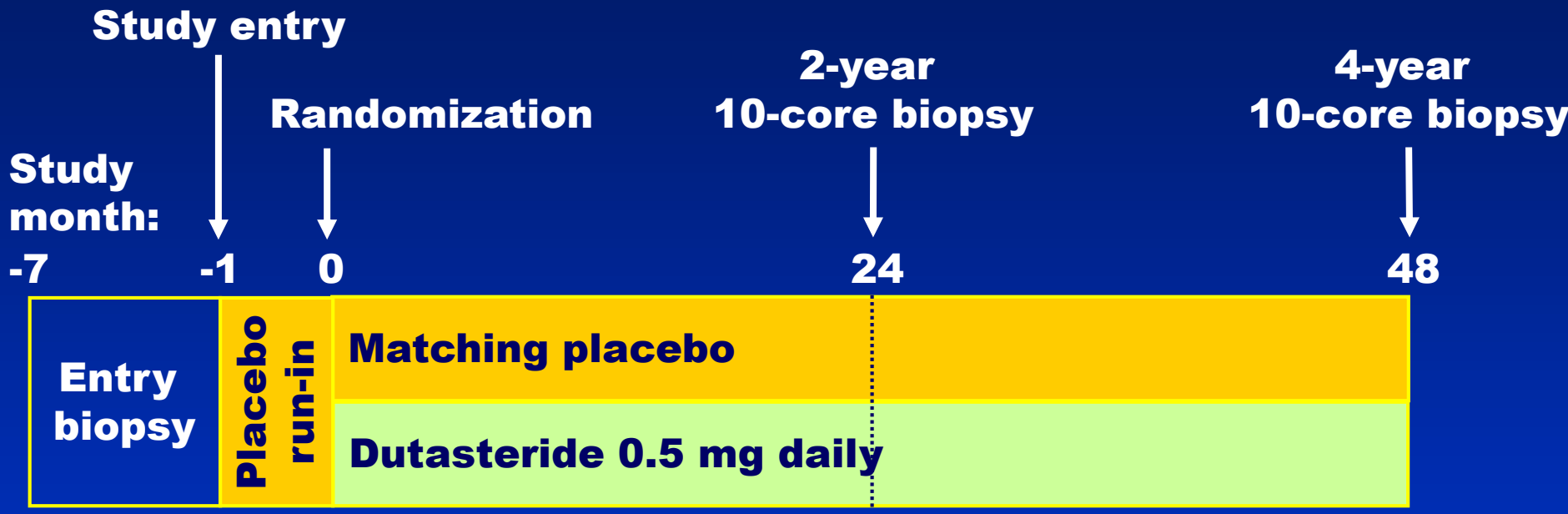
4) Thompson, J.NCI 98:1128, 2006

PSA Performance in PCPT



Thompson, JNCI 98:1128, 2006

REDUCE: Study design



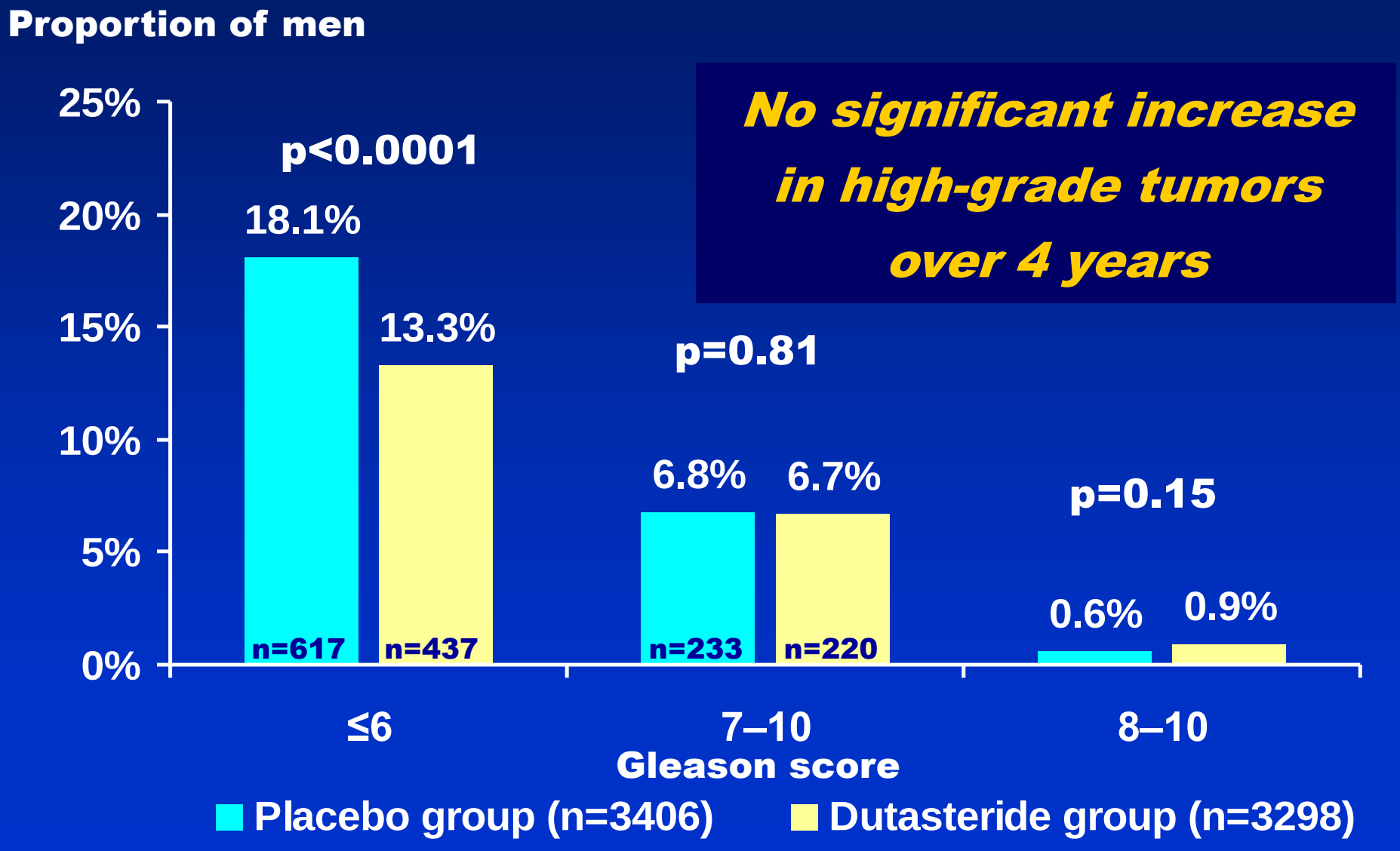
- Age 50-75 yrs, PSA 2.5–10 ng/mL (> 3.0 if age ≥60)
- Negative biopsy (6–12 cores) within 6/12
- Prostate volume ≤80 cc

Andriole J Urol 2004

PCPT & REDUCE

	PCPT[1]	REDUCE[2]
Study drug **5AR isozyme inhibition** **Study duration**	Finasteride Type 2 7 years	Dutasteride Types 1 and 2 4 years
No. of subjects	18,882	~8000
Age	≥55	≥50
Baseline biopsies	No	Yes (1 neg. bx.)
Follow-up biopsies	7 years	2 and 4 years
PSA entry criteria	<3.0	2.5–10.0
Location	USA only	International

REDUCE: Gleason distribution



No significant increase in high-grade tumors over 4 years

Two lingering questions

1. Are the tumors that are prevented 'significant' or, are they only a result of the end of study biopsies?
2. Uncertainty regarding the impact on high grade cancer.

5ARI studies: Conclusions

- Enhanced utility of PSA as a diagnostic test for prostate cancer (all tumors and Gleason 7–10)
- Significant beneficial effects on BPH outcomes
- Next Step: Identify optimal population for risk reduction

Ca P screening & chemoprevention

- Seemingly conflicting results from US and Europe large scale screening studies
- Possible to reconcile by referring to methodology
- High number to treat to reduce mortality
- Shortfalls of earlier cancer prevention trial potentially addressed by latest study
- Chemo-prevention ? may be considered at least for high risk group with previous negative biopsy