Vigile attesa, sorveglianza attiva, ormonoterapia esclusiva: a chi?

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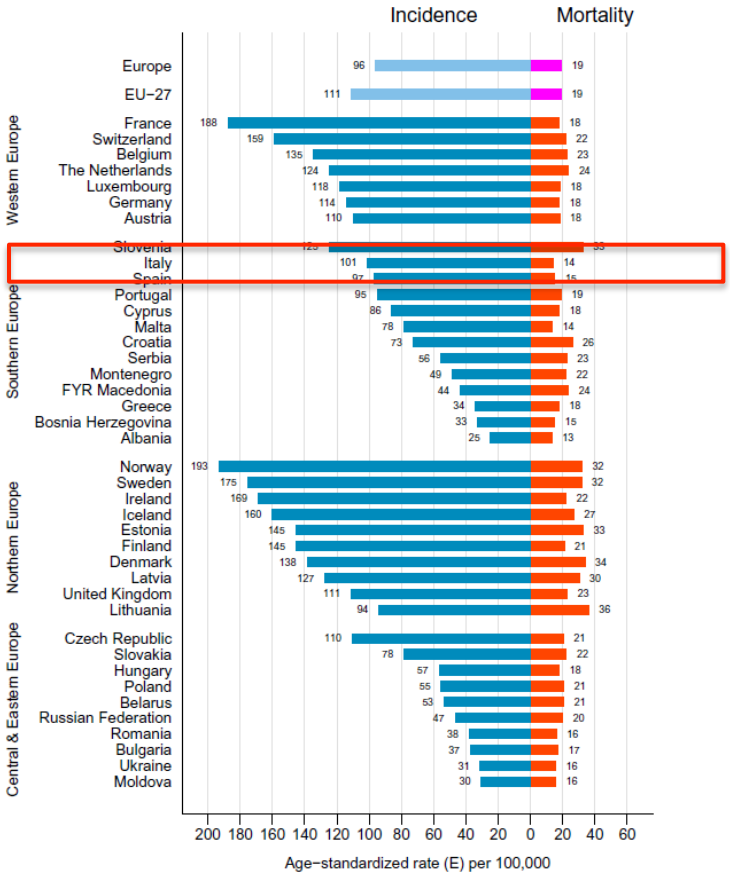
FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

PROSTATE CANCER PROGRAM

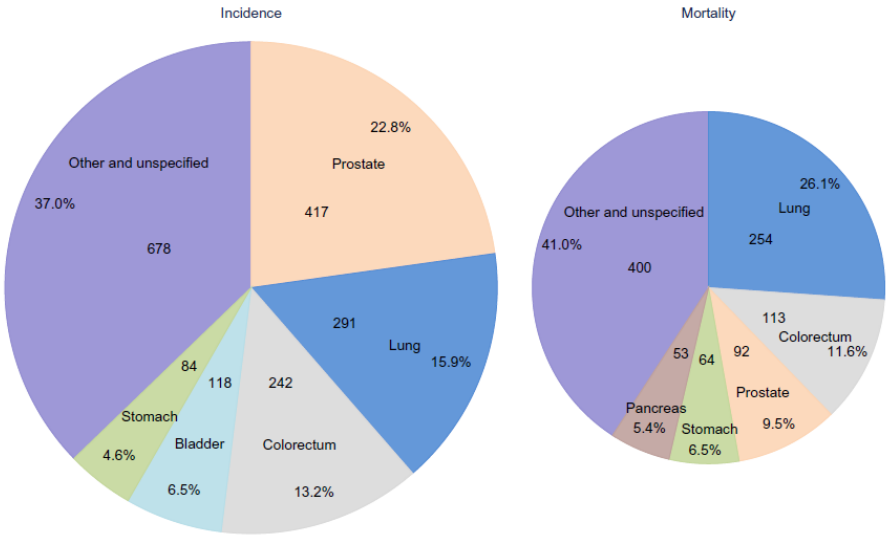
Tumore prostatico – le dimensioni del problema

Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012

J. Ferlay et al. European Journal of Cancer 2013



Age-standardised incidence and mortality rates by area and country in Europe 2012: prostate cancer.

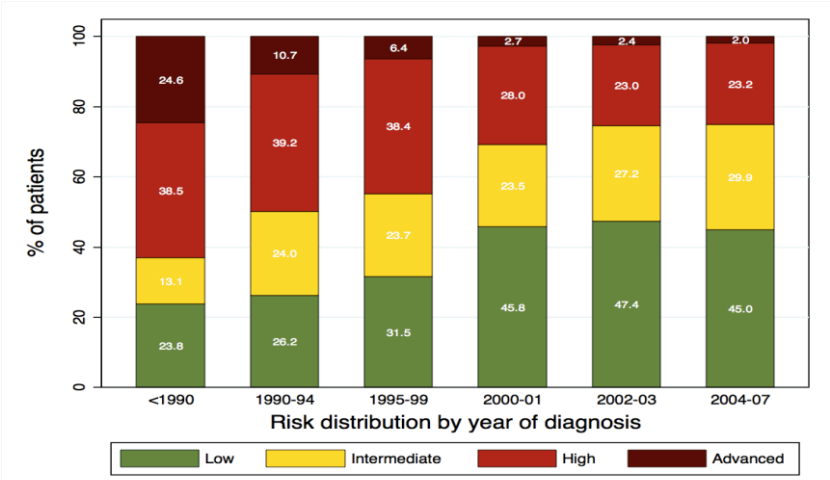


417,000 nuovi casi all'anno di tumore prostatico, con stimata riduzione della mortalità.

Tumore prostatico – le dimensioni del problema

Contemporary Trends in Low-Risk Prostate Cancer: Risk Assessment and Treatment

Cooperberg et al. J Urol, 2007



Risk class migration: aumento di diagnosi di pazienti in classe di rischio bassa.

Grade migration?

Penney Prostate cancer Foundation 18th annual meeting Abs67

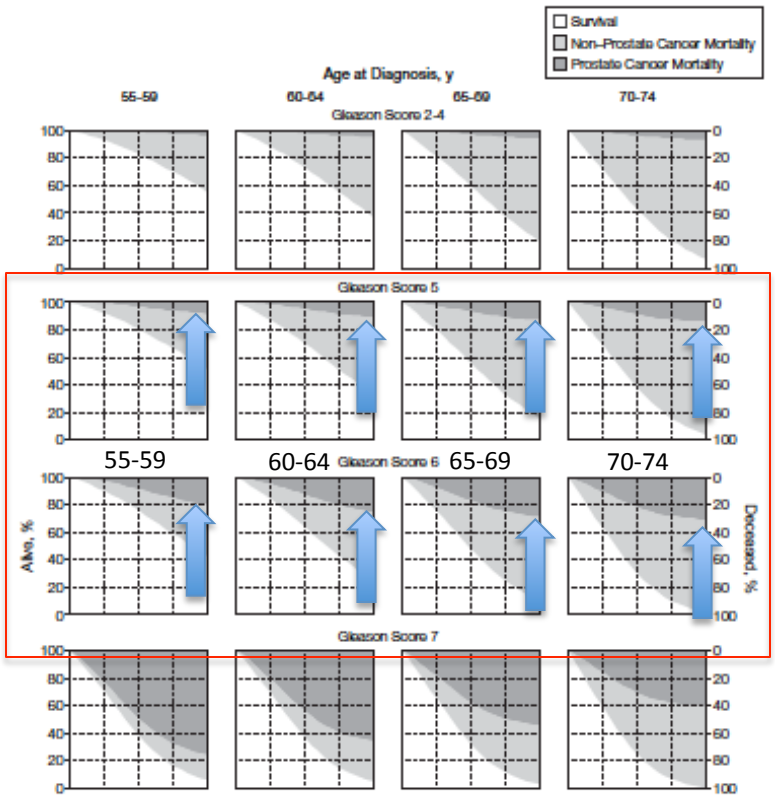
Conclusions

The dramatic shift in stage at diagnosis in the years after introduction of PSA screening was accompanied by a more modest shift to lower Gleason scores. On a population basis, these finding suggest that Gleason grade may be established early in the pathogenesis of prostate tumors. This finding has implications for our understanding of prognosis and of tumor progression.

PC mortalità cancro specifica

20-Year Outcomes Following Conservative Management of Clinically Localized Prostate Cancer

Albertsen et al. JAMA 2005



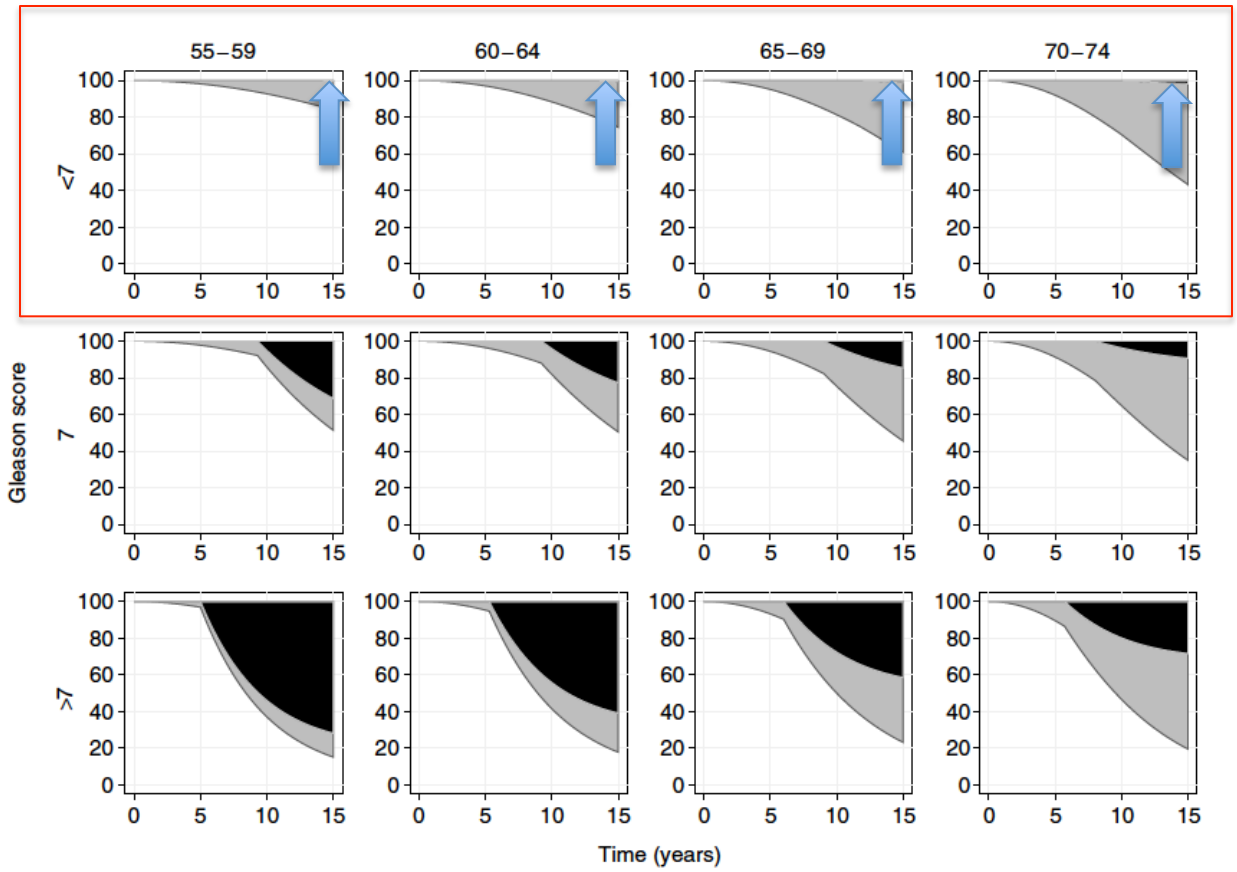
Results The prostate cancer mortality rate was 33 per 1000 person-years during the first 15 years of follow-up (95% confidence interval [CI], 28-38) and 18 per 1000 person-years after 15 years of follow-up (95% CI, 10-29). The mortality rates for these 2 follow-up periods were not statistically different, after adjusting for differences in tumor histology (rate ratio, 1.1; 95% CI, 0.6-1.9). Men with low-grade prostate cancers have a minimal risk of dying from prostate cancer during 20 years of follow-up (Gleason score of 2-4, 6 deaths per 1000 person-years; 95% CI, 2-11). Men with high-grade prostate cancers have a high probability of dying from prostate cancer within 10 years of diagnosis (Gleason score of 8-10, 121 deaths per 1000 person-years; 95% CI, 90-156). Men with Gleason score of 5 or 6 tumors have an intermediate risk of prostate cancer death.

Conclusion The annual mortality rate from prostate cancer appears to remain stable after 15 years from diagnosis, which does not support aggressive treatment for localized low-grade prostate cancer.

- ✓ Era pre-PSA
- ✓ Maggiore probabilità di avere malattia extracapsulare → i risultati possono sottostimare la sopravvivenza dei pazienti contemporanei.

PC: mortalità cancro specifica

A model of the natural history of screen-detected prostate cancer, and the effect of radical treatment on overall survival



Screen-detected PC: mortalità a 15 anni da 0 a 2% per GPS < 7

Death due to other causes

Death due to Pca

Parker et al. Brit J Canc 2006

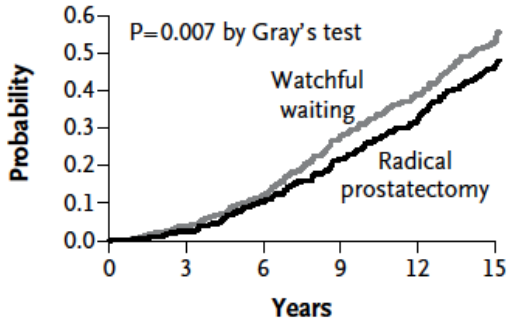
Prostatectomia vs Osservazione

Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

The NEW ENGLAND JOURNAL of MEDICINE

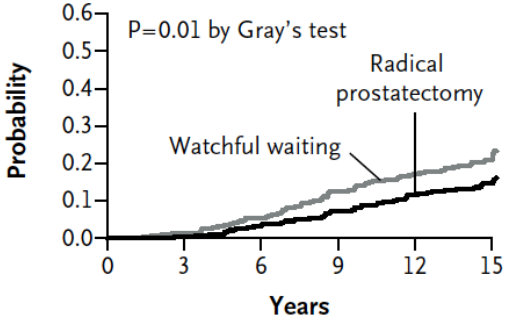
Bill-Axelson et al. 2011

A Death from Any Cause, Total Cohort



No. at Risk						
Radical prostatectomy	347	339	311	271	214	109
Watchful waiting	348	334	306	251	192	96

B Death from Prostate Cancer, Total Cohort



No. at Risk						
Radical prostatectomy	347	339	311	271	214	109
Watchful waiting	348	334	306	251	192	96

FU 15 yrs

CSM a 15 anni: 14,% in RP vs 20,7% in WW.

NNT 15 per prevenire una morte da neoplasia prostatica a 15 anni

Non screen-detected pts
WW ≠ AS
Non ripetizione delle biopsie
Non trattamento radicale differito
Solo 12% dei pazienti in stadio cT1c

Prostatectomia vs Osservazione

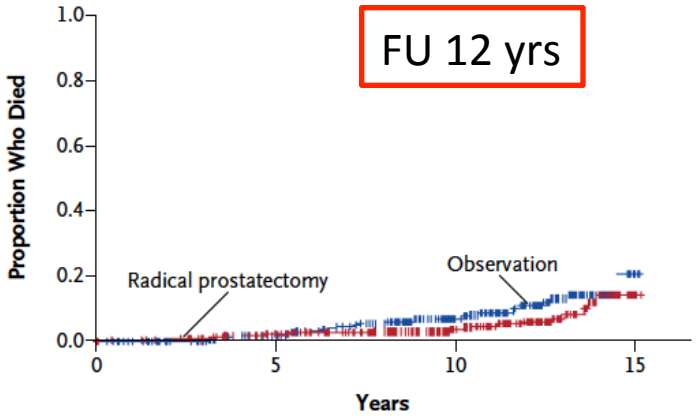
Radical Prostatectomy versus Observation for Localized Prostate Cancer

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

The NEW ENGLAND JOURNAL of MEDICINE

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

B Death from Prostate Cancer



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

FU 12 yrs

NNT ≈ 34.5

Chirurgia: riduzione della mortalità solo in malattia a rischio intermedio-alto e PSA > 10

CONCLUSIONS

Among men with localized prostate cancer detected during the early era of PSA testing, radical prostatectomy did not significantly reduce all-cause or prostate-cancer mortality, as compared with observation, through at least 12 years of follow-up. Absolute differences were less than 3 percentage points.

Overtreatment

Prostate-Cancer Mortality at 11 Years of Follow-up

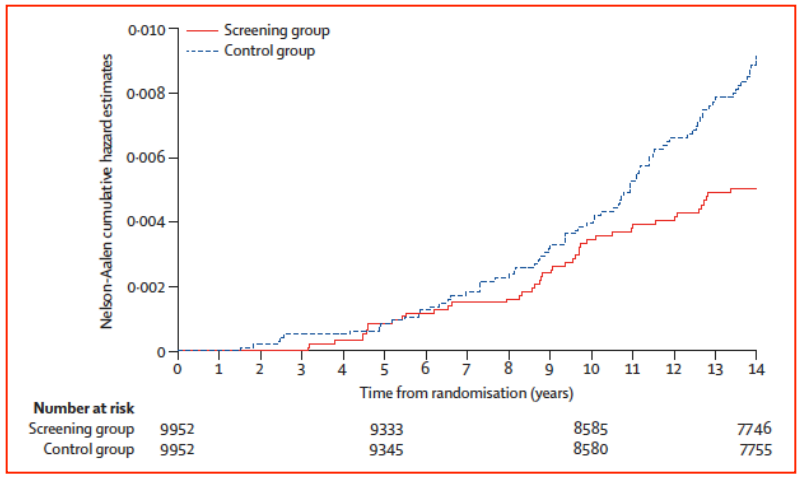
Schröder et al. NEJM 2012

Per prevenire una morte da neoplasia prostatica a 11 anni:

- **NNS 1055**
- **NNT 37**

Mortality results from the Göteborg randomised population-based prostate-cancer screening trial

Hugosson et al. Lancet 2010



FU 14 yrs

- **NNS 293**
- **NNT 12**

Sorveglianza attiva: razionale

Overdiagnosis

Diagnosi di una malattia *clinicamente insignificante*, che non causa morbidità o mortalità

⇩

Overtreatment

Trattamento di una neoplasia clinicamente insignificante

⇩

Sorveglianza Attiva

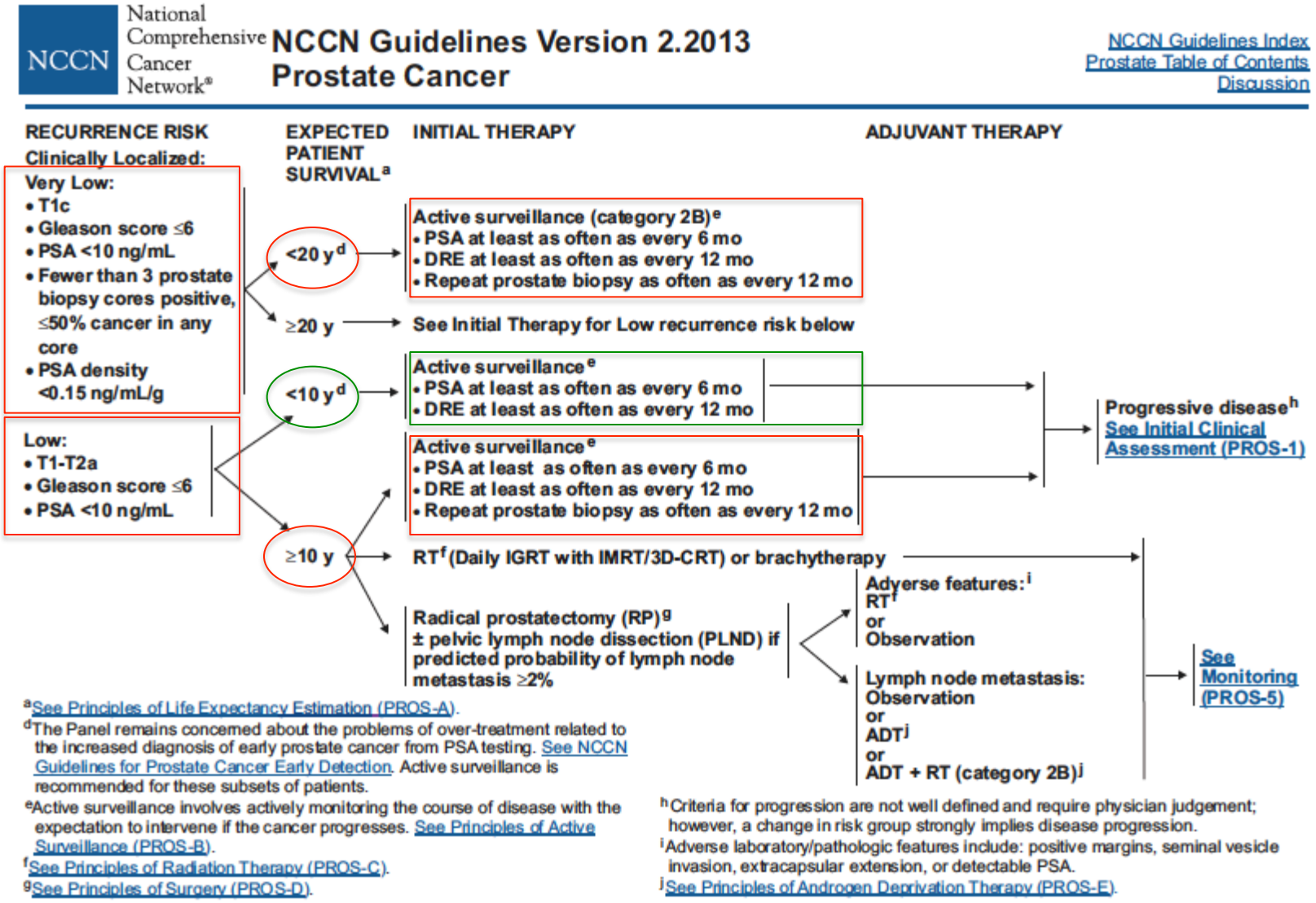
Riduzione dell'overtreatment dilazionando o addirittura evitando i trattamenti radicali ed i loro effetti collaterali mantenendo aperta una finestra di curabilità

Sorveglianza Attiva vs Watchful Waiting

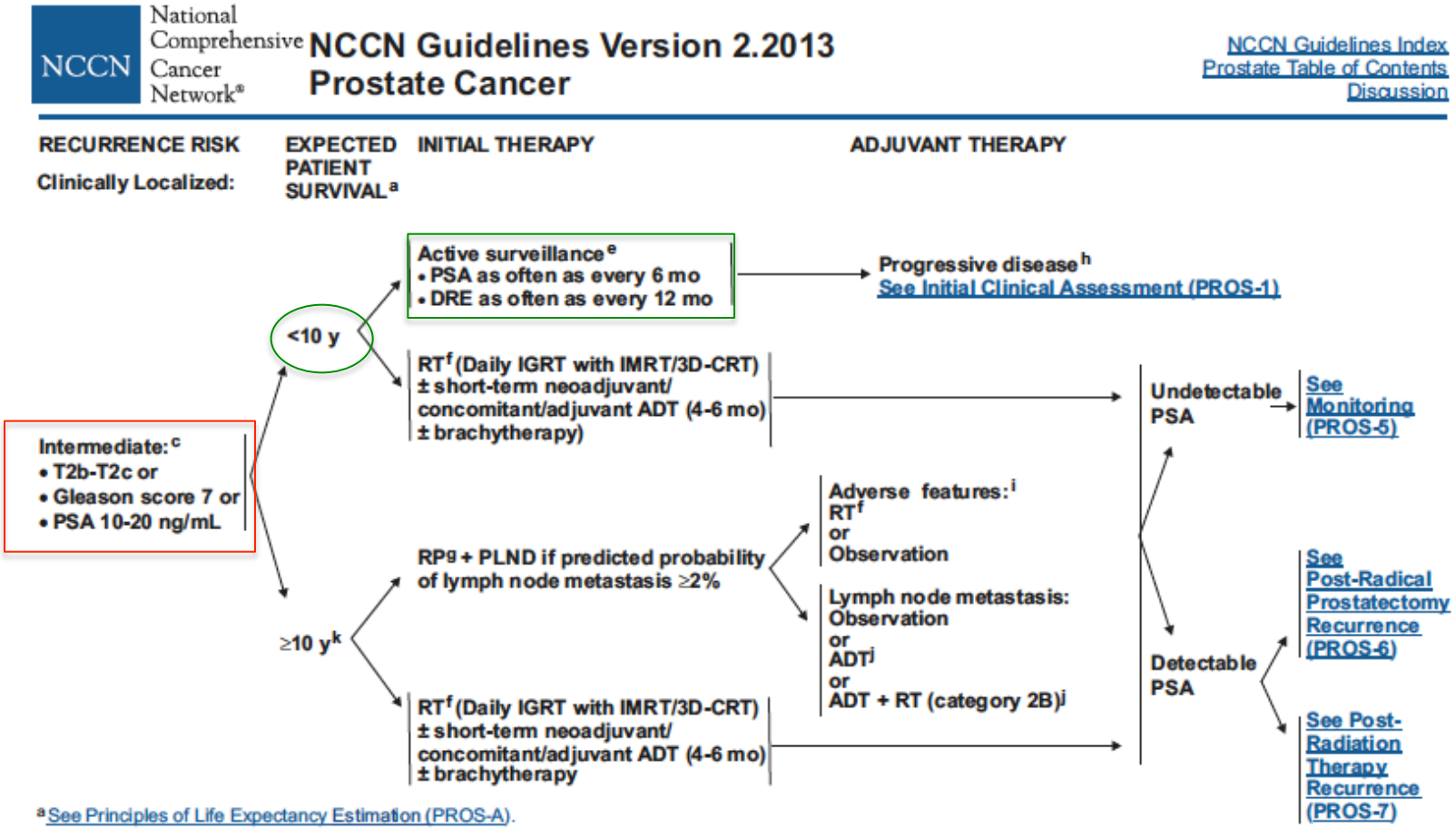
	Active Surveillance	Watchful Waiting
* Aim	To individualize strategy according to the biologic behavior of cancer	To avoid radical treatments and related side effects
Patient characteristics	Fit for radical treatments Age < 80	Life expectancy < 15 years Age > 70
*Disease characteristics	e. g. PRIAS: cT1-2a; GPS ≤ 3+3; PSA ≤ 10 ng/ml, pos cores <3	Any T stage and any PSA; GPS ≤ 7
*Monitoring	e. g. PRIAS: PSA: systematic Re-biopsies: systematic	PSA: unimportant No re-biopsy
*Indications for Treatment	Short PSA DT Upgrading/upsizing PSA > 10-20 ng/ml	Symptomatic progression
Treatment Timing	Early	Delayed
*Treatment Intent	Radical	Palliative

Modified from C. Parker et al, Lancet Oncol, 2004

Malattia clinicamente localizzata: indicazioni



Malattia clinicamente localizzata: indicazioni



[a] See Principles of Life Expectancy Estimation (PROS-A).
[c] Patients with multiple adverse factors may be shifted into the next highest risk group.
[e] Active surveillance involves actively monitoring the course of disease with the expectation to intervene if the cancer progresses. See Principles of Active Surveillance (PROS-B).
[f] See Principles of Radiation Therapy (PROS-C).
[g] See Principles of Surgery (PROS-D).
[h] Criteria for progression are not well defined and require physician judgement; however, a change in risk group strongly implies disease progression.
[i] Adverse laboratory/pathologic features include: positive margins, seminal vesicle invasion, extracapsular extension, or detectable PSA.
[j] See Principles of Androgen Deprivation Therapy (PROS-E).
[k] Active surveillance of intermediate and high-risk clinically localized cancers is not recommended in patients with a life expectancy >10 years (category 1).

Sorveglianza Attiva: selezione dei pazienti

Insignificant Prostate Cancer and Active Surveillance: From Definition to Clinical Implications

Patrick J. Bastian [a,], Ballentine H. Carter [d], Anders Bjartell [c], Michael Seitz [a], Peter Stanislaus [a], Francesco Montorsi [e], Christian G. Stief [a], Fritz Schröder [b]*

2009

Study	Definition
Epstein et al [5] and Bastian et al [18]	Clinical stage T1c PSA density <0.15 ng/ml No Gleason pattern 4 or 5 <3 positive cores <50% cancer per core
D'Amico et al [22]	PSA level ≤10 ng/ml No Gleason pattern 4 or 5 Clinical stage T2a or lower
Dall'Era et al [13]	PSA level ≤10 ng/ml No Gleason pattern 4 or 5 Clinical stage T2a or lower PSA density <0.15 ng/ml <33% positive cores
Patel et al [74]	Clinical stage T3 or lower Gleason sum ≤7
Soloway et al [47]	Clinical stage T2 or lower PSA level <15 ng/ml No Gleason pattern 4 or 5 <50% cancer per two positive cores
Van den Bergh et al [72] (PRIAS)	Clinical stage T1c–T2b No Gleason pattern 4 or 5 PSA density <0.20 ng/ml PSA level <10 ng/ml Fewer than three positive cores
Van As et al [38]	Clinical stage T1–T2a Gleason sum ≤7 (3 + 4) PSA level <15 ng/ml <50% of biopsy cores positive
Dall'Era et al [14] (commonly used criteria)	Gleason sum 6 No Gleason pattern 4 or 5 PSA level <10 ng/ml and stable PSA kinetics ≤50% single core involvement ≤33% positive cores

PSA = prostate-specific antigen; PRIAS = Prostate Cancer Research International: Active Surveillance.

Protocolli attivi in INT

PRIAS

- ✓ Stadio cT1c-T2a
- ✓ GPS 3+3=6 (< 3 core positivi)
- ✓ iPSA < 10 ng/ml
- ✓ PSAD < 0,20

SAINT

- ✓ Stadio cT1c-T2a
- ✓ GPS 3+3=6 (< 25% dei campioni)
- ✓ iPSA < 10 ng/ml
- ✓ < 50% interessamento dei core

Sorveglianza attiva: monitoraggio e criteri di uscita

- **<u>Follow-up:</u>**

➢ Biopsia prostatica confermatoria a 6-12 mesi.

- Ripetizione della biopsia a cadenze programmate (es. 12 mesi JHU, 36 mesi PRIAS)

➢ PSA

➢ DRE

- **<u>Criteri di uscita dalla sorveglianza attiva</u>**

➢ Bioptici: upgrading

upsizing (> 3 core bioptici positivi)

➢ PSA > 10 ng/ml→"there is no clear justification…"

(Adamy (MSKKC) J Urol 2011)

➢ PSA DT < 3yrs →"significantly associated to disease reclassification" (Bull M. et al. Eur Urol ,2011)

"PSADT≤ 3 yrs as a flag for higher-risk disease"(Klotz L. et al. Curr Urol Rep, 2012)

➢ Progressione clinica di malattia

Sorveglianza attiva: finestra di curabilità

Platinum Priority – Review – Prostate Cancer

Editorial by XXX on pp. x–y of this issue

Timing of Curative Treatment for Prostate Cancer: A Systematic Review

Roderick C.N. van den Bergh [a,b,], Peter C. Albertsen [c], Chris H. Bangma [d], Stephen J. Freedland [e], Markus Graefen [f], Andrew Vickers [g], Henk G. van der Poel [b]*

ahead of print

Review comprendente 17 studi retrospettivi e non randomizzati (34517 pts)

Conclusioni:

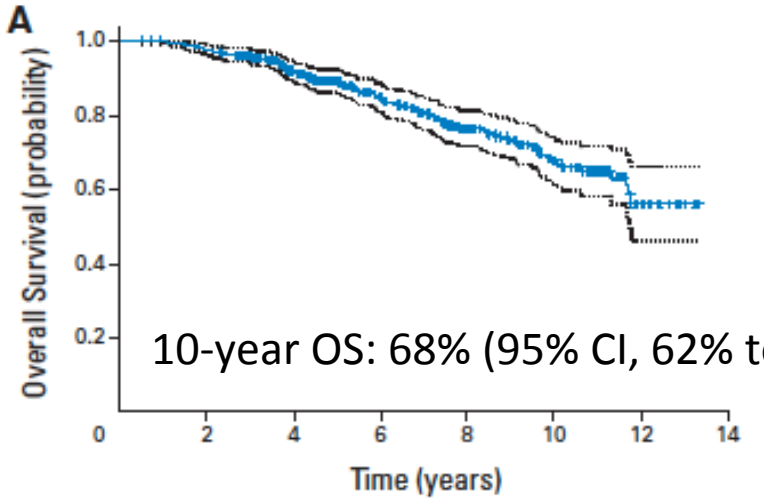
- ✓ Il dilazionamento del trattamento di mesi o anni non sembra impattare sull'outcome dei pazienti con neoplasia prostatica in classe di rischio bassa
- ✓ Dati limitati suggeriscono che il dilazionamento del trattamento può avere un impatto nei pazienti affetti da un tumore non in bassa classe di rischio
- ✓ Necessità di biopsia confermatoria per individuare quei pazienti affetti da malattia aggressiva inizialmente misconosciuta.

Sorveglianza attiva: outcome

Clinical Results of Long-Term Follow-Up of a Large, Active Surveillance Cohort With Localized Prostate Cancer

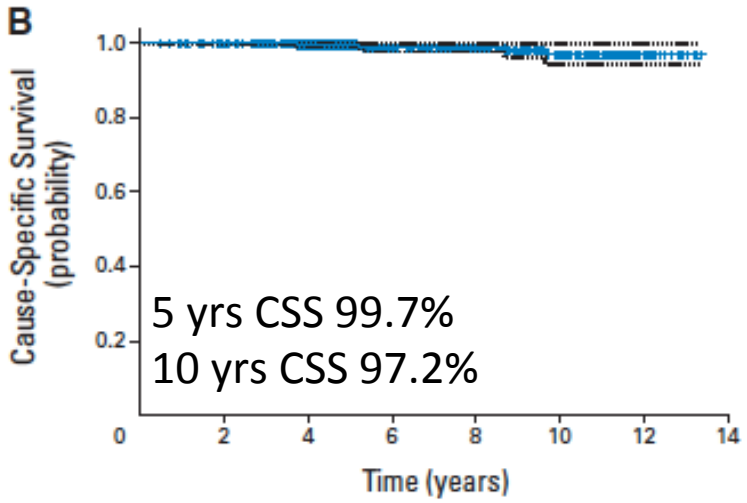
Laurence Klotz, Liying Zhang, Adam Lam, Robert Nam, Alexandre Mamedov, and Andrew Loblaw

JOURNAL OF CLINICAL ONCOLOGY 2010

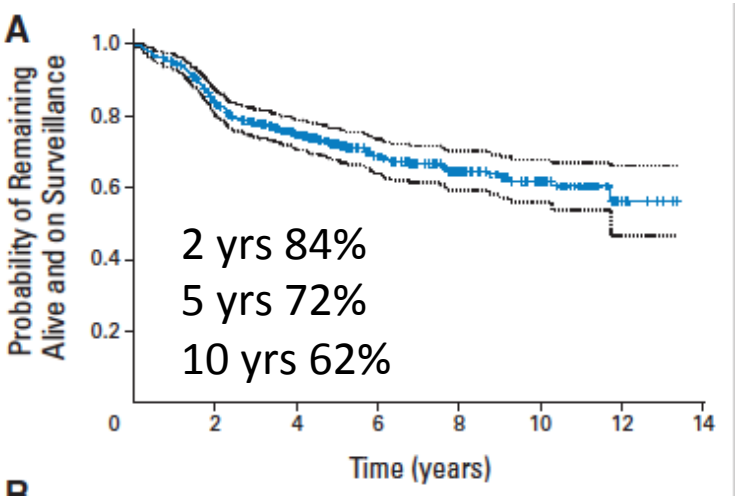


10-year OS: 68% (95% CI, 62% to 74%)

450 pazienti
Età media 70,3 anni
FU medio 6,8 yrs
17% pts GPS 3+4
12% pts PSA ≥ 10 ng/ml



5 yrs CSS 99.7%
10 yrs CSS 97.2%



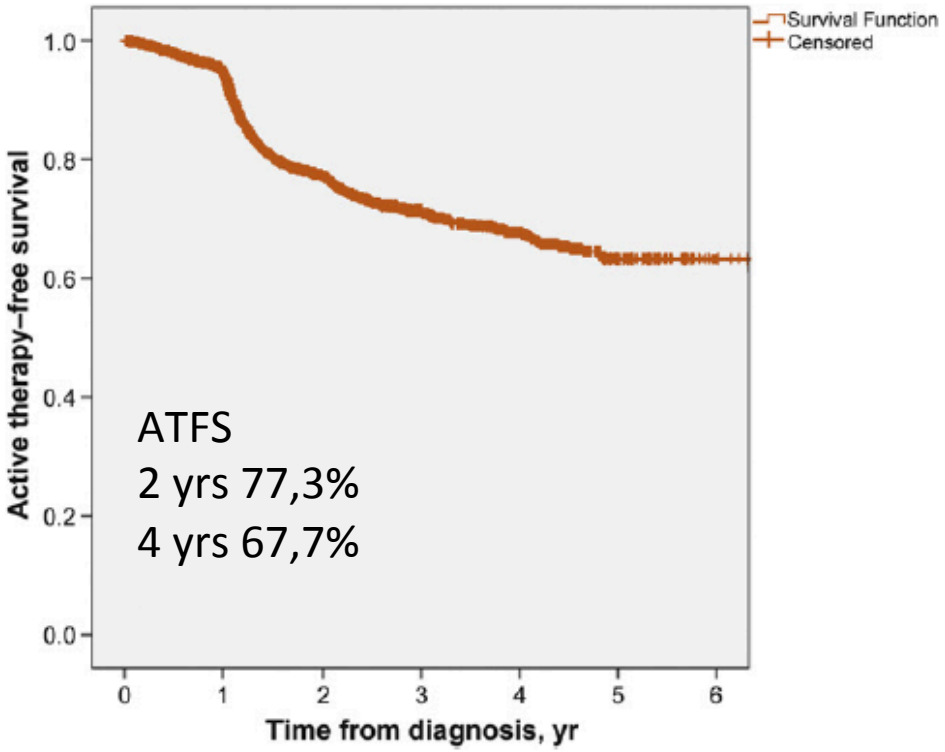
2 yrs 84%
5 yrs 72%
10 yrs 62%

Sorveglianza attiva: outcome

Active Surveillance for Low-Risk Prostate Cancer Worldwide: The PRIAS Study

Meelan Bul[a,], Xiaoye Zhu[a], Riccardo Valdagni[b], Tom Pickles[c], Yoshiyuki Kakehi[d], Antti Rannikko[e], Anders Bjartell[f], Deric K. van der Schoot[g], Erik B. Cornel[h], Giario N. Conti[i], Egbert R. Boevé[j], Frédéric Staerman[k], Jenneke J. Vis-Maters[l], Henk Vergunst[m], Joris J. Jaspars[n], Petra Strölin[o], Erik van Muilekom[p], Fritz H. Schröder[a], Chris H. Bangma[a], Monique J. Roobol[a]*

2013



2494 pts; FU medio 1,6 yrs

Predittori di riclassificazione alla prima rebiopsia:

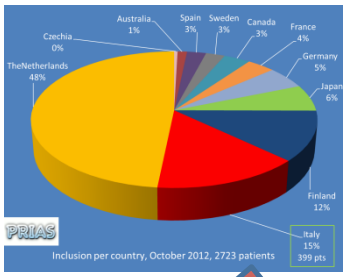
- ✓ PSADT (<3yrs)
- ✓ 2 core positivi alla precedente biopsia
- ✓ PSAD

Predittori di uscita alla rebiopsia:

- ✓ PSAD
- ✓ Numero di core positivi (2 vs 1)

Sorveglianza Attiva – INT (454 pts)

PRIAS



Da Marzo 2005

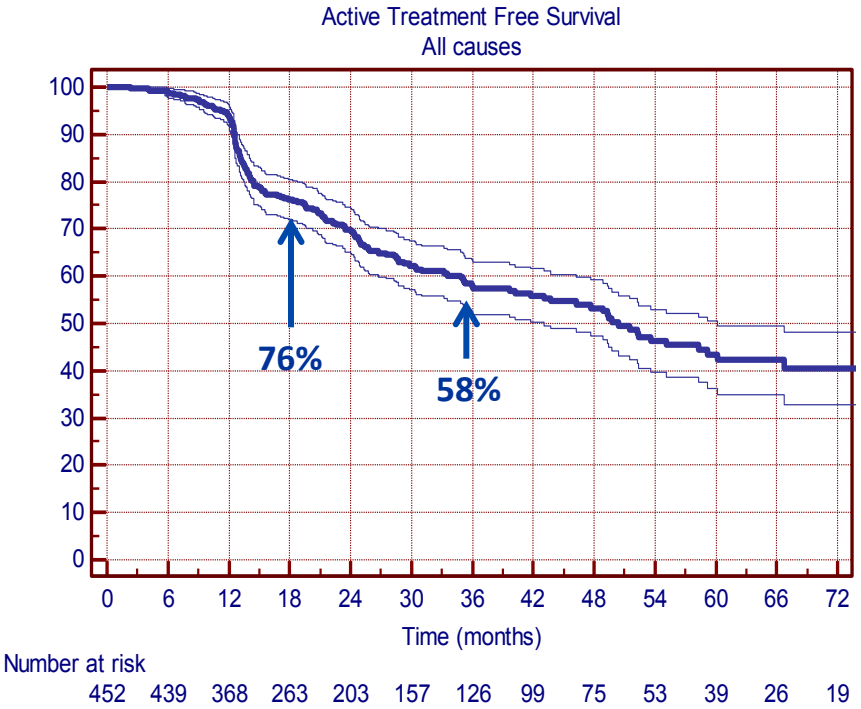
Sorveglianza attiva INT : 167 pts

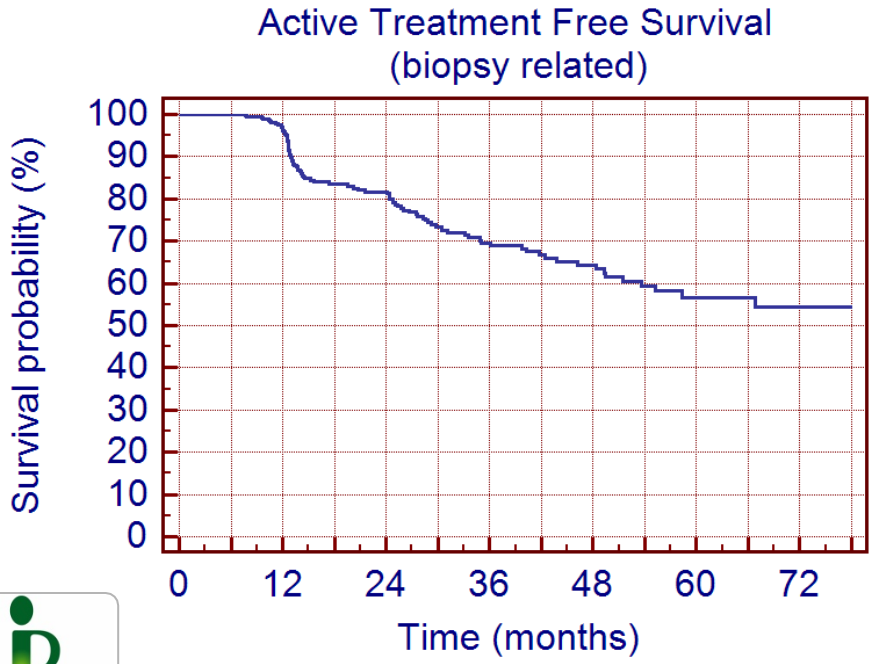
Settembre 2007 – Febbraio 2013

PRIAS: 287 pts

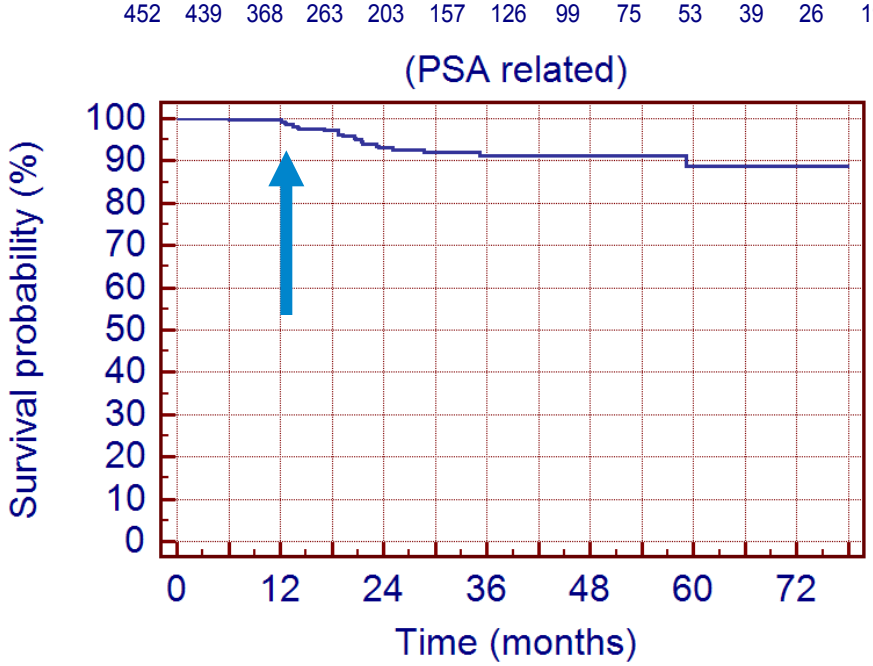
Ancillary studies:

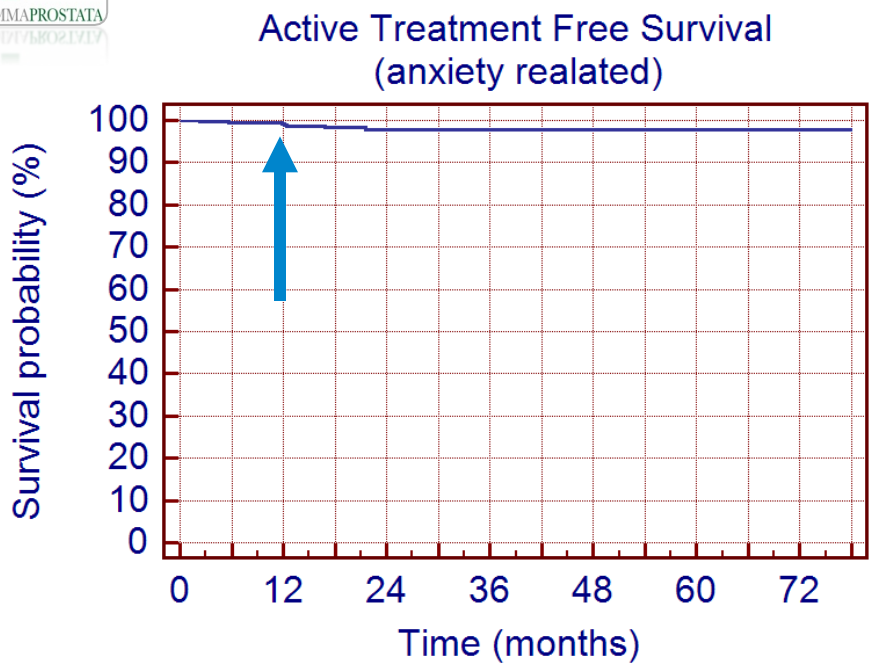
- ✓ PROCABIO (biomarkers): 169 pts
- ✓ Hormonal/genetic characterization: 160 pts
- ✓ Quality of Life: 286 pts


Active Treatment Free Survival
All causes
100
90
80
70
60
50
40
30
20
10
0
76%
58%
0 6 12 18 24 30 36 42 48 54 60 66 72
Time (months)
Number at risk
452 439 368 263 203 157 126 99 75 53 39 26 19


Active Treatment Free Survival
(biopsy related)
Survival probability (%)
100
90
80
70
60
50
40
30
20
10
0
0 12 24 36 48 60 72
Time (months)


PROGRAMMAPROSTATA


(PSA related)
Survival probability (%)
100
90
80
70
60
50
40
30
20
10
0
0 12 24 36 48 60 72
Time (months)


Active Treatment Free Survival
(anxiety realated)
Survival probability (%)
100
90
80
70
60
50
40
30
20
10
0
0 12 24 36 48 60 72
Time (months)

Sorveglianza attiva: outcome

Author		Median FU (mos)	Pts still on AS (%)
Roemeling (Netherland	2006	41	71% 5-ys
Dall'Era (San Francisco)	2008	43	76%
Stattin (Sweden)	2010	120	nr
Klotz (Toronto)	2010	82	62% 10-yr
Soloway (Miami)	2010	44	73%
Adamy (MSKCC)	2011	22	65%
Tosoian (JHU)	2011	32	66%
Ischia (PRIAS Australia)	2012	nr	62% 5-yr
Bul (PRIAS)	2012	19	68% 4-yr
Valdagni (unpub, 2013)	2013	37	58% 3-yr
Thomsen (Danmark)	2013	41	60% 5-yr
Godman (Sweden)	2013	72	63% 6-yr
Selvadurai (Royal Marsden)	2013	68	70% 5-yr

Courtesy dott. Valdagni

Cancer Specific Survival (CSS)

		N of pts	median age / f-up (mos)	CSS (%)
Roemeling (Netherland)	2006	278	70 / 41	**100 - 8yr**
Khatami (Sweden)	2007	270	64 / 63	100
Dall'Era	2008	321	63 / 43	100
Van As	2008	326	67 / 22	100
Eggener	2009	262	64 / 29	100
Klotz (Toronto)	2010	450	70 / 82	**97.2 - 10yr**
Soloway (Miami)	2010	230	63 / 44	100
Adamy (MSKCC)	2011	238	64 / 22	100
Tosoian (JHU)	2011	769	66 / 32	100
Valdagni (INT-Mi, unpub)	2012	423	66 / 36	100
Ischia (PRIAS Australia)	2012	154	63/nas	100
Bul (PRIAS,accepted EuUrol,) 2012		2454	66 / 19	100

Courtesy dott. Valdagni

20 yrs-PCa Mortality

Prostate Cancer Mortality following Active Surveillance versus Immediate Radical Prostatectomy

Jing Xia[1], Bruce J. Trock[4], Matthew R. Cooperberg[6], Roman Gulati[1], Steven B. Zeliadt[2], John L. Gore[3], Daniel W. Lin[3], Peter R. Carroll[6], H. Ballentine Carter[5], and Ruth Etzioni[1]

Clinical Cancer Research

Projection based on CAPSURE and J. Hopkins database (5202 pts)

Results: The model projected that 2.8% of men on active surveillance and 1.6% of men with immediate radical prostatectomy would die of their disease in 20 years. Corresponding lifetime estimates were 3.4% for active surveillance and 2.0% for immediate radical prostatectomy. The average projected increase in life expectancy associated with immediate radical prostatectomy was 1.8 months. On average, the model projected that men on active surveillance would remain free of treatment for an additional 6.4 years relative to men treated immediately.

Conclusions: Active surveillance is likely to produce a very modest decline in prostate cancer-specific survival among men diagnosed with low-risk prostate cancer but could lead to significant benefits in terms of quality of life. *Clin Cancer Res; 18(19); 5471–8. ©2012 AACR.*

At 20 yrs: 36% of patients still on AS

Qualità di vita

Predictors of Health-related Quality of Life and Adjustment to Prostate Cancer During Active Surveillance

Bellardita et al. 2012

Bassa HRQoL:

- ✓ Mancanza di partner
- ✓ Stato mentale alterato
- ✓ Breve lasso di tempo tra diagnosi ed ingresso in sorveglianza attiva

Alta HRQoL:

- ✓ Presenza di un partner
- ✓ Influenza di più medici sulla scelta della sorveglianza attiva
- ✓ Biopsia diagnostica con > 18 core

Reason for choosing active surveillance	%
"I trusted what the physicians told me."	74
"To avoid side effects of the therapies and maintain my quality of life"	72
"I trust this cancer centre."	58
"You can always go back; it is a reversible option."	47
"Medical checks are frequent."	28
"I am comforted and satisfied with participating in a protocol."	13
"I found scientific papers about AS."	10
"I trusted what other people told me."	9
"I do not trust active therapies."	1

- Positive adjustment to cancer (anxiety due to the presence of an untreated cancer and to the idea of disease progression is low and decreases over time)
- Patients report very high level of physical, social and emotional wellbeing

Bellardita et al, unpublished, 2012

Uscite dalla sorveglianza attiva per ansia

Uscite dalla sorveglianza attiva		Ansia
van den Bergh et al.	2009	1.6% (8/500)
Eggener et al.	2009	5.3% (14/262)
Bellardita et al. (INT PRIAS)	2013	2% (6/293)
Valdagni et al (SAINT1-2 and PRIAS)	2013	1.2% (7/454)

Courtesy dott. Valdagni

Approccio multidisciplinare

Multidisciplinary Care and Pursuit of Active Surveillance in Low-Risk Prostate Cancer

JOURNAL OF CLINICAL ONCOLOGY

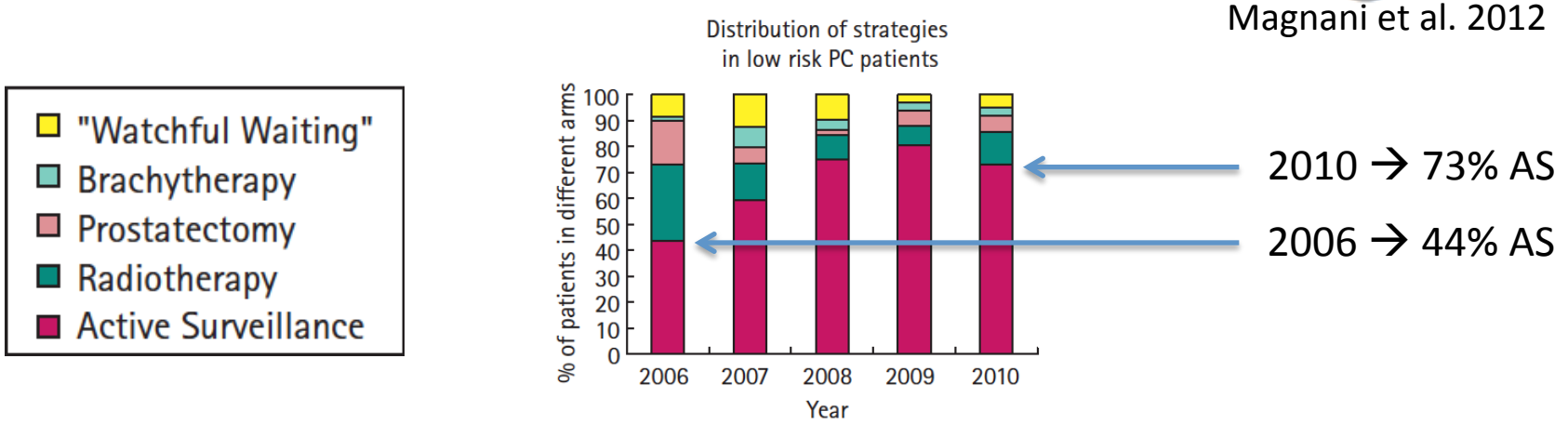
Aizer et al. 2012

"Crude rates of selection of active surveillance in patients seen at a multidisciplinary clinic were double that of patients seen by individual practitioners (43% v 22%), whereas the proportion of men treated with prostatectomy or radiation decreased by approximately 30% (P<.001)"

The 6-year attendance of a multidisciplinary prostate cancer clinic in Italy: incidence of management changes

BJUI BJU INTERNATIONAL

Magnani et al. 2012

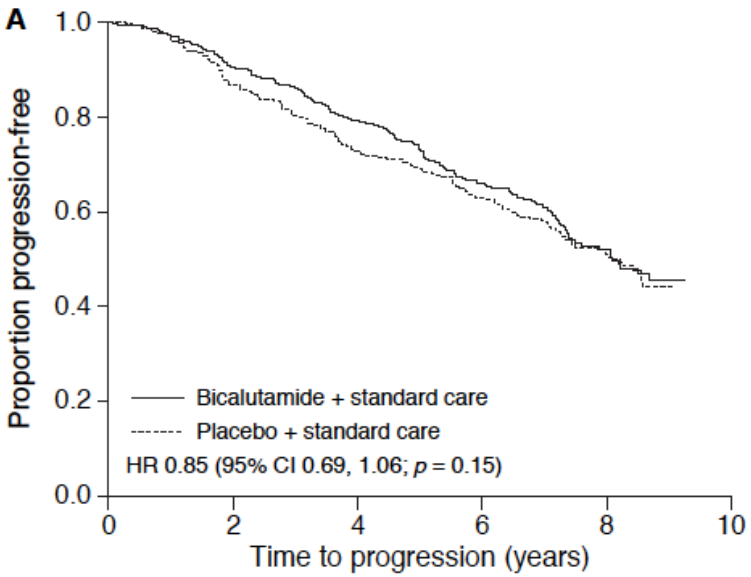


Ormonoterapia esclusiva ?

Ormonoterapia esclusiva – a chi?

Bicalutamide 150 mg in addition to standard care for patients with early non-metastatic prostate cancer: updated results from the Scandinavian Prostate Cancer Period Group-6 Study after a median follow-up period of 7.1 years

Iversen et al. Scan J Urol Nephr 2006



" In patients with localized disease who would have otherwise undergone watchful waiting (n=631), bicalutamide showed **a trend towards an increased risk of dying compared with those undergoing watchful waiting alone**"

Antiandrogen monotherapy in patients with localized or locally advanced prostate cancer: final results from the bicalutamide Early Prostate Cancer programme at a median follow-up of 9.7 years

Iversen et al. BJUI 2010

"A similarlack of efficacy was reported for other antiandrogens, including nilutamide 150 mg and flutamide 250 mg in patients with localized disease, suggesting that **antiandrogen therapy might be an inappropriate treatment for patients with localized prostate cancer**"

Ormonoterapia esclusiva – a chi?

Survival Following Primary Androgen Deprivation Therapy Among Men With Localized Prostate Cancer

Lu-Yao G et al. JAMA, 2008

Objective To evaluate the association between PADT and survival in elderly men with localized prostate cancer.

Results Among patients with localized prostate cancer (median age, 77 years), 7867 (41%) received PADT, and 11 404 were treated with conservative management, not including PADT. During the follow-up period, there were 1560 prostate cancer deaths and 11 045 deaths from all causes. Primary androgen deprivation therapy was associated with lower 10-year prostate cancer–specific survival (80.1% vs 82.6%; hazard ratio [HR], 1.17; 95% confidence interval [CI], 1.03-1.33) and no increase in 10-year overall survival (30.2% vs 30.3%; HR, 1.00; 95% CI, 0.96-1.05) compared with conservative management. However, in a prespecified subset analysis, PADT use in men with poorly differentiated cancer was associated with improved prostate cancer–specific survival (59.8% vs 54.3%; HR, 0.84; 95% CI, 0.70-1.00; $P=.049$) but not overall survival (17.3% vs 15.3%; HR, 0.92; 95% CI, 0.84-1.01).

Conclusion Primary androgen deprivation therapy is not associated with improved survival among the majority of elderly men with localized prostate cancer when compared with conservative management.

Ormonoterapia esclusiva – a chi?

Does Primary Androgen-Deprivation Therapy Delay the Receipt of Secondary Cancer Therapy for Localized Prostate Cancer?

Grace L. Lu-Yao [a,b,c,], Peter C. Albertsen [d], Hui Li [b], Dirk F. Moore [c,e], Weichung Shih [c,e], Yong Lin [c,e], Robert S. DiPaola [a,b,c], Siu-Long Yao [a,b]*

2012

Background: Despite evidence that shows no survival advantage, many older patients receive primary androgen-deprivation therapy (PADT) shortly after the diagnosis of localized prostate cancer (PCa).
Objective: This study evaluates whether the early use of PADT affects the subsequent receipt of additional palliative cancer treatments such as chemotherapy, palliative radiation therapy, or intervention for spinal cord compression or bladder outlet obstruction.

Conclusions: Early treatment of low-risk, localized PCa with PADT does not delay the receipt of subsequent palliative therapies and is associated with an increased use of chemotherapy.

Ormonoterapia esclusiva – a chi?

European Association of Urology

Guidelines on

Prostate Cancer

UPDATE MARCH 2013

Stage	Treatment	Comment	GR
T1a	Watchful waiting	Standard treatment for Gleason score ≤ 6 and 7 adenocarcinomas and < 10-year life expectancy.	B
	Active surveillance	In patients with > 10-year life expectancy, re-staging with TRUS and biopsy is recommended.	B
	Radical prostatectomy	Optional in younger patients with a long life expectancy, especially for Gleason score ≥ 7 adenocarcinomas.	B
	Radiotherapy	Optional in younger patients with a long life expectancy, in particular in poorly differentiated tumours. Higher complication risks after TURP, especially with interstitial radiation.	B
	Hormonal	Not an option.	A
	Combination	Not an option.	C
T1b-T2b	Active surveillance	Treatment option in patients with cT1c-cT2a, PSA < 10 ng/mL, biopsy Gleason score ≤ 6, ≤ 2 biopsies positive, ≤ 50% cancer involvement of each biopsy.	B
		Patients with a life expectancy < 10 years.	
		Patients with a life expectancy > 10 years once they are informed about the lack of survival data beyond 10 years.	
		Patients who do not accept treatment-related complications.	
T1a-T2c	Radical prostatectomy	Optional in patients with pT1a PCa. Standard treatment for patients with a life expectancy > 10 years who accept treatment-related complications.	A
	Radiotherapy	Patients with a life expectancy > 10 years who accept treatment-related complications.	B
		Patients with contraindications for surgery.	
		Unfit patients with 5-10 years of life expectancy and poorly differentiated tumours (combination therapy is recommended; see below).	
	Brachytherapy	Low-dose rate brachytherapy can be considered for low risk PCa patients with a prostate volume ≤ 50 mL and an IPSS ≤ 12.	B
	Hormonal	Symptomatic patients, who need palliation of symptoms, unfit for curative treatment.	C
		Anti-androgens are associated with a poorer outcome compared to 'active surveillance' and are not recommended.	A
	Combination	For high-risk patients, neoadjuvant hormonal treatment and concomitant hormonal therapy plus radiotherapy results in increased overall survival.	A

Conclusioni – Sorveglianza attiva, vigile attesa, ormonoterapia esclusiva: a chi?

- ✓ **Sorveglianza attiva:**
- Proposta alternativa in pazienti fit per trattamenti attivi (chirurgia o radioterapia)
- Pazienti in bassa classe di rischio attentamente selezionati
- Complianti con la necessità di effettuare controlli clinici, di PSA e re-biopsie a cadenze predefinite.
- Adeguata aspettativa di vita
- ✓ **Vigile attesa:**
- Pazienti in classe di rischio bassa/intermedia
- Unfit per comorbidità a trattamenti attivi o con breve aspettativa di vita
- ✓ **Ormonoterapia esclusiva:**
- Non indicazione elettiva in questa tipologia di pazienti

GRAZIE PER L’ATTENZIONE!