

Con il Patrocinio di



2° Convegno Nazionale

IL TEAM INTERDISCIPLINARE NEL CARCINOMA DELLA PROSTATA

NEGRAR DI VALPOLICELLA 6-7 DICEMBRE 2019

Sala Perez - IRCCS Ospedale Sacro Cuore Don Calabria



Coordinatori: STEFANIA GORI - FILIPPO ALONGI - STEFANO CAVALLERI

Sabato 7 Dicembre

Quarta Sessione LA MALATTIA ORGANO-CONFINATA: IL CARCINOMA PROSTATICO AD ALTO RISCHIO

Moderatori **Giovanni Mandoliti, Francesco Massari**

08,30

08,45 Caso clinico **Carlo Messina**

08,50 *Confronto tra esperti:*

Urologo **Alessandro Antonelli**

Radioterapista **Fabio M...**

Oncologo **Maurizio Nicodemo**

09,30

Discussione

... per l'occasione sostituita da
Giovanni Pappagallo

G.L. Pappagallo: relazioni con l'Industria farmaceutica e potenziali conflitti di interesse (11.2019)

Azienda	Relazione	Patologia
Astellas	training, partecipazione advisory board	ca. prostata
AstraZeneca	partecipazione advisory board, valutazioni clinico-epidemiologiche	ca. polmone, ca. ovaio, ca. mammario, B-LLC
Clovis	partecipazione advisory board	ca. ovaio, ca. prostata
IPSEN	training, valutazioni clinico-epidemiologiche, partecipazione advisory board	ca. rene, epatocarcinoma
Janssen	partecipazione advisory board, valutazioni clinico-epidemiologiche	ca. prostata, depressione maggiore
MSD	valutazioni clinico-epidemiologiche	melanoma, ca. polmone, ca. vescica, VAP
Pierre Fabre	training, valutazioni clinico-epidemiologiche, partecipazione ad advisory board	ca. vescica, melanoma, ca. mammario
Pfizer	training, valutazioni clinico-epidemiologiche	ca. mammario, ca. rene, artrite reumatoide, m. cardiovascolari, amiloidosi
Roche	training, valutazioni clinico-epidemiologiche, partecipazione ad advisory board	ca. polmone, ca. mammella, ca. ovaio, sclerosi multipla, emofilia, linfomi, ACG
Servier	partecipazione advisory board, valutazioni clinico-epidemiologiche	ca. pancreas, ca. gastrico
Teva	training	emicrania

	High-Risk PC		Very High-Risk PC
	Localized	Non Localized	
EAU/ ESTRO/ESUR/SIOG Guidelines	PSA > 20 ng/ml <i>or</i> GS > 7 (ISUP Grade 4/5) <i>or</i> cT2c	any PSA <i>any</i> GS (<i>any</i> GS grade) cT3-4 <i>or</i> cN+	Not defined
AUA/ASTRO/SUO Guidelines	Localized PSA ≥ 20 ng/ml <i>or</i> GS > 7 (ISUP Grade 4/5) <i>or</i> ≥ cT3		Not defined
NCCN Guidelines	Localized PSA > 20 ng/ml <i>or</i> GS > 7 (ISUP Grade 4/5) <i>or</i> cT3a		Localized cT3b-cT4 <i>or</i> Primary Gleason pattern 5 <i>or</i> > 4 cores with GS > 7

EAU = European Association of Urology; **ESTRO** = European Society for Radiotherapy & Oncology; **SIOG** = International Society of Geriatric Oncology; **AUA** = American Urological Association; **ASTRO** = American Society for Radiation Oncology; **SUO** = Society of Urologic Oncology; **NCCN** = National Comprehensive Cancer Network. **PSA** = Prostate Specific Antigen; **GS** = Gleason score; **ISUP** = International Society of Urological Pathologists.

Recommendation	Strength rating
Radical Prostatectomy (RP)	
to patients with high-risk localised PCa and a life expectancy of > ten years only	
Extended pelvic lymph node dissection (ePLND)	
Perform an ePLND in high-risk disease.	Strong
Do not perform a frozen section of nodes during RP to decide whether to proceed with, or abandon, the procedure.	Strong
Radiotherapeutic treatment	
In patients with high-risk localised disease, with 76-78 Gy (two to three years).	
In patients with high-risk localised disease, (either high-dose rate or low-dose rate), (two to three years).	
Therapeutic options outside surgery and radiotherapy	
Do not offer either whole gland or focal therapy to high-risk patients.	Strong
Do not use ADT monotherapy in asymptomatic patients.	Strong

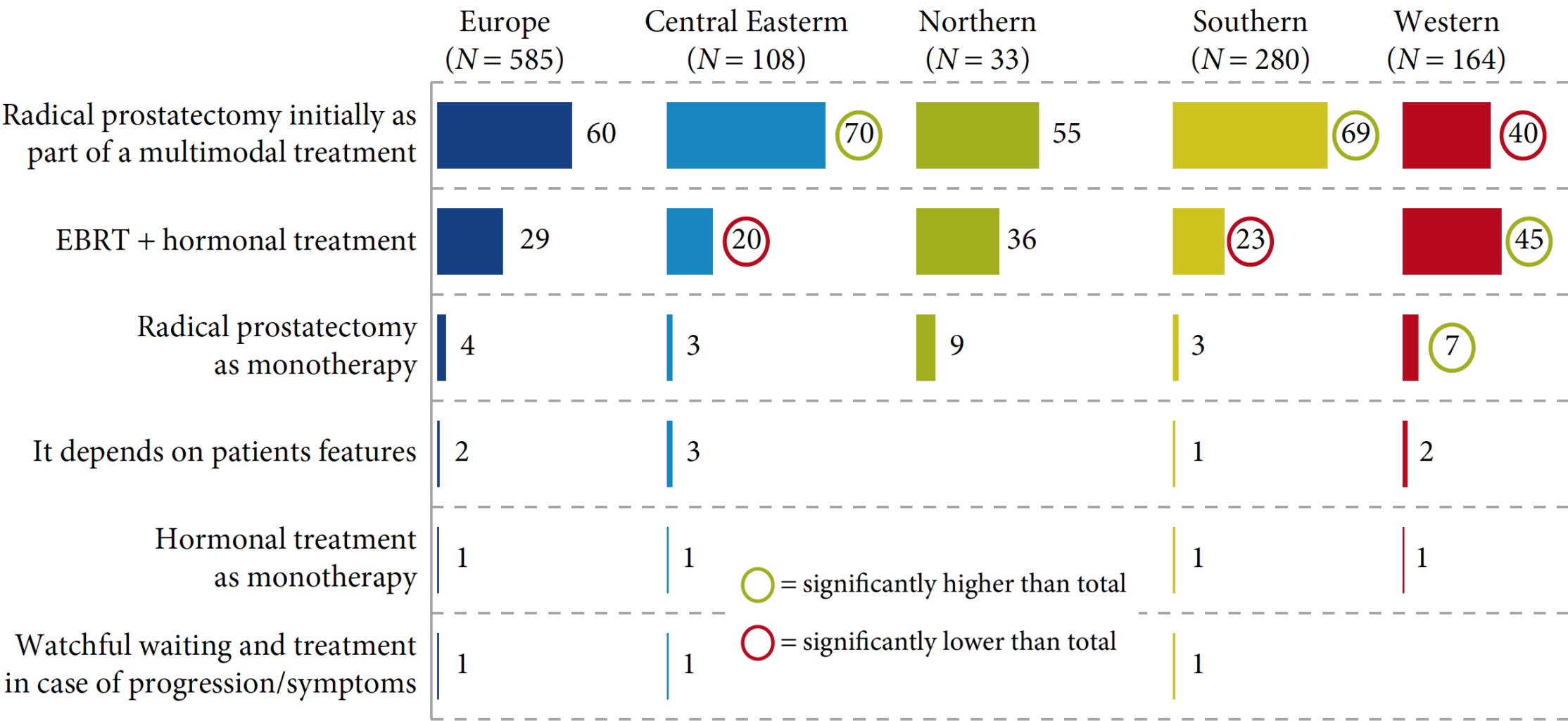
American Urological Association (AUA) / American Society for Radiation Oncology (ASTRO) / Society of Urologic Oncology (SUO)

Clinically Localized Prostate Cancer

Table 4. Care Options for Localized Prostate Cancer by Level of Evidence and Strength of Recommendation ¹					
Evidence Level/ Recommendati on Strength	Prostate Cancer Severity/Aggressiveness				
	Low Risk		Intermediate Risk		
	Very Low Risk	Low Risk	Favorable	Unfavorable	
	Active Surveillance	NA	Radical Prostatectomy OR Radiotherapy ² with Androgen Deprivation Therapy	Radical Prostatectomy OR Radiotherapy ² with Androgen Deprivation Therapy	

Preferences in the management of high-risk prostate cancer among urologists in Europe: results of a web-based survey

BJU Int 2015; 115: 571-579

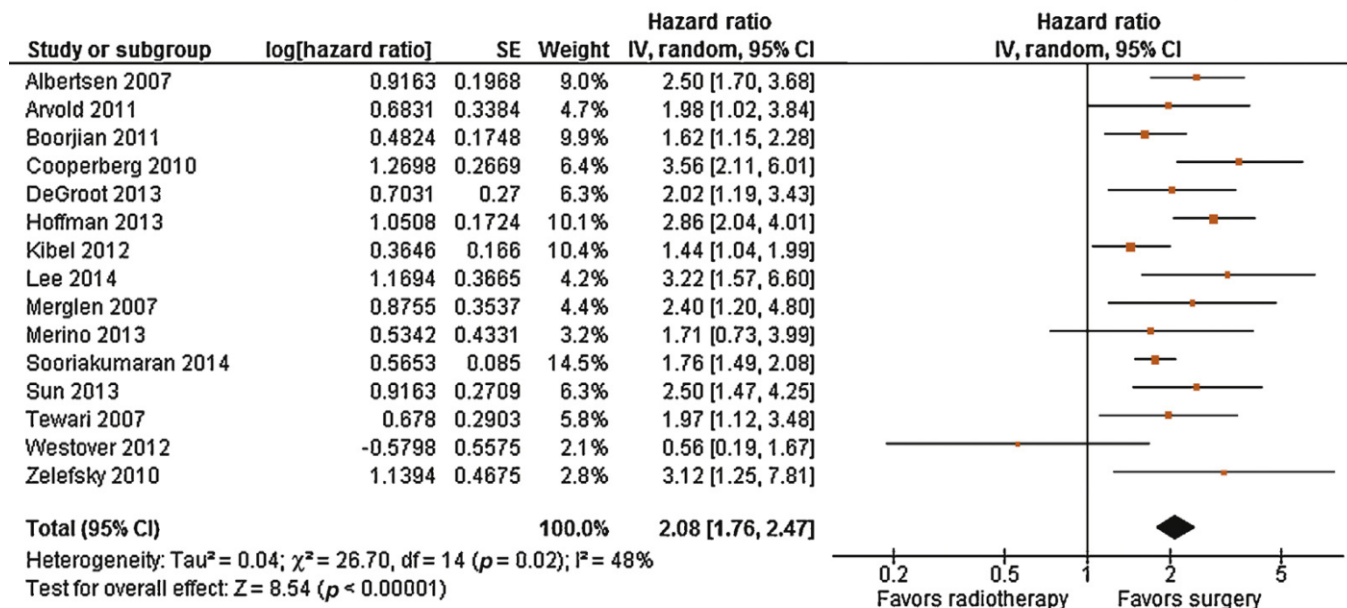
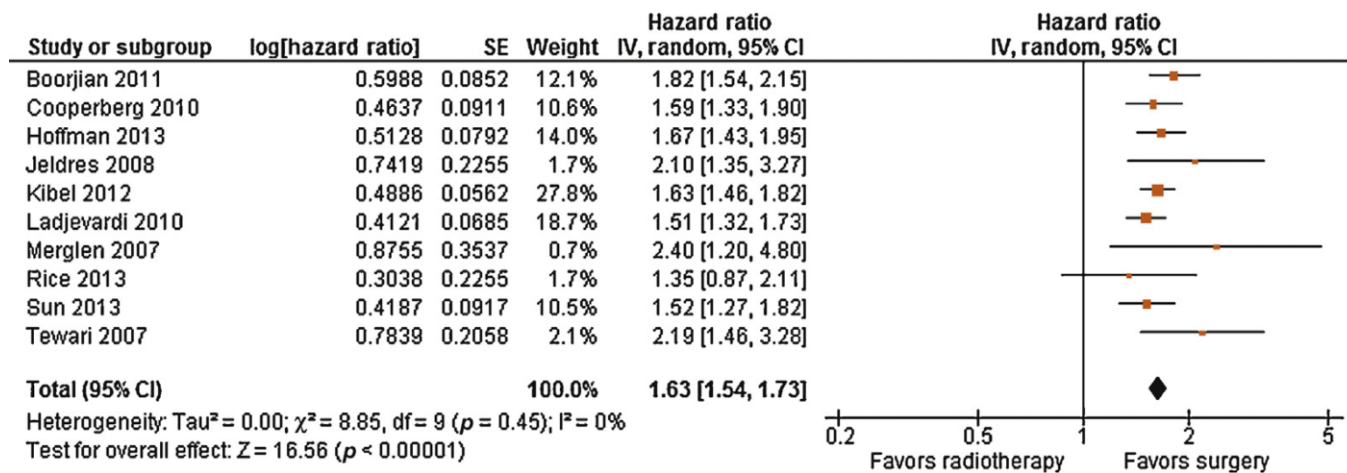


Surgery Versus Radiotherapy for Prostate Cancer: A Systematic Review and Meta-analysis

Christopher J.D. Wallis^{a,b,c}, Refik Saskin^{c,d}, Richard Choo^e, Sender Herschorn^{a,b}, Ronald T. Kodama^{a,b}, Raj Satkunasivam^{a,b}, Prakesh S. Shah^{c,f,g}, Cyril Danjoux^h, Robert K. Nam^{a,b,c,*}

EUROPEAN UROLOGY 70 (2016) 21–30

Warning!
Low to high risk patients

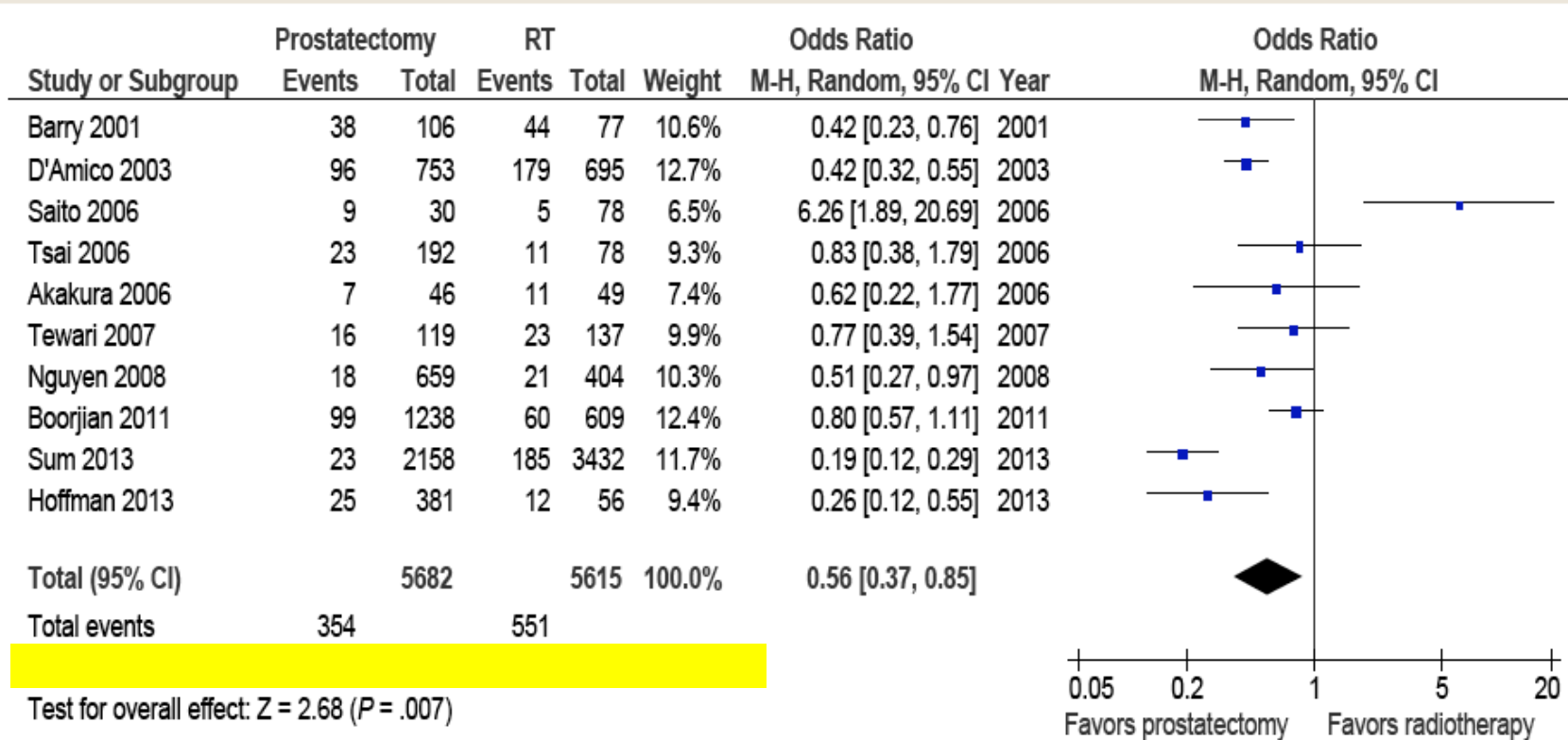


Radical Prostatectomy or Radiotherapy in High-Risk Prostate Cancer: A Systematic Review and Metaanalysis

Fausto Petrelli,¹ Ivano Vavassori,² Andrea Coinu,¹
Karen Borgonovo,¹ Enrico Sarti,³ Sandro Barni¹

Clinical Genitourinary Cancer, Vol. 12, No. 4, 215-24 © 2014 Elsevier Inc.

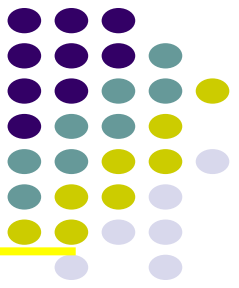
Figure 3 Metaanalysis of Prostate Cancer-Specific Mortality



What is Heterogeneity?

- Any kind of variability among studies in a systematic review may be termed heterogeneity.
- **I-squared (I^2)** $I^2 = \left(\frac{Q - df}{Q} \right) \times 100\%$, where Q is the chi-squared statistic and df is its degrees of freedom
 - ✓ describes the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance).
 - ✓ thresholds for the interpretation of I^2 :
 - 0% to 40%: might not be important;
 - 30% to 60%: may represent moderate heterogeneity;
 - **50% to 90%: may represent substantial heterogeneity;**
 - **75% to 100%: considerable heterogeneity.**

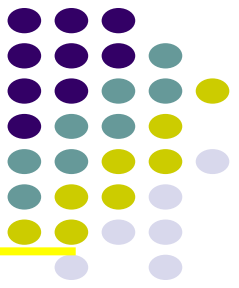
A Central Problem for Non-Experimental, Observational Studies



- One of the central problems for non-experimental, observational studies is to control, or somehow take account of the possible bias that occurs because **there is no random assignment** of units in a target population to treatments/exposures.

Any observed difference between the outcomes of study arms may be attributable to baseline differences rather than to a true treatment effect.

A Central Problem for Non-Experimental, Observational Studies



- One of the central problems for non- experimental, observational studies is to control, or somehow take account of the possible bias that occurs because **there is no random assignment** of units in a target population to treatments/exposures.
- **What can we do** to come closer to the goal of all epidemiological studies – an accurate estimation of the “true effect” of a treatment/ exposure in a target population?

Comparative Effectiveness Research in Oncology Methodology: Observational Data

Dawn L. Hershman and Jason D. Wright

J Clin Oncol 30:4215-4222. © 2012 by American Society of Clinical Oncology

Propensity Score Analysis

Propensity score analyses attempt to balance covariates between experimental groups. [REDACTED]

[REDACTED]

[REDACTED]

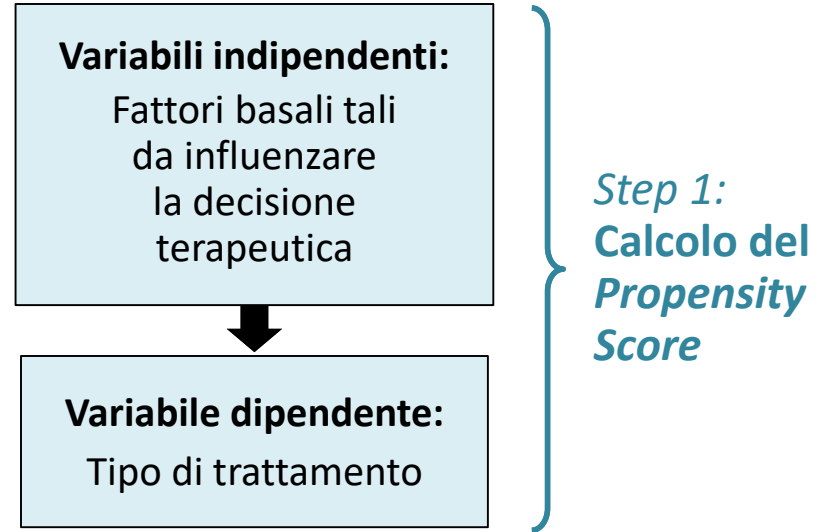
Le caratteristiche della coorte vengono usate per calcolare la probabilità di ricevere l'uno o l'altro dei trattamenti a confronto. Tale probabilità è il *propensity score*.

An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies

Peter C. Austin

All measured baseline covariates, all baseline covariates that are associated with treatment assignment, all covariates that affect the outcome (i.e., the potential confounders), and all covariates that affect both treatment assignment and the outcome (i.e., the true confounders).

Propensity Score adjustment

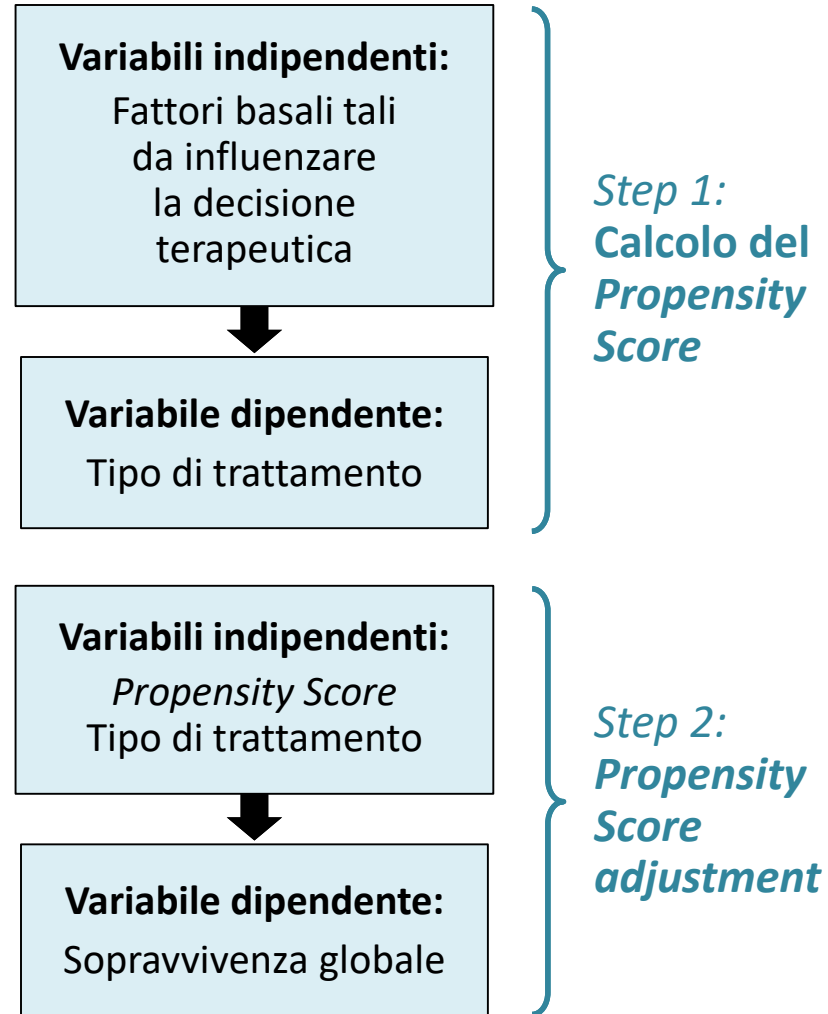


An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies

Peter C. Austin

All measured baseline covariates, all baseline covariates that are associated with treatment assignment, all covariates that affect the outcome (i.e., the potential confounders), and all covariates that affect both treatment assignment and the outcome (i.e., the true confounders).

Propensity Score adjustment



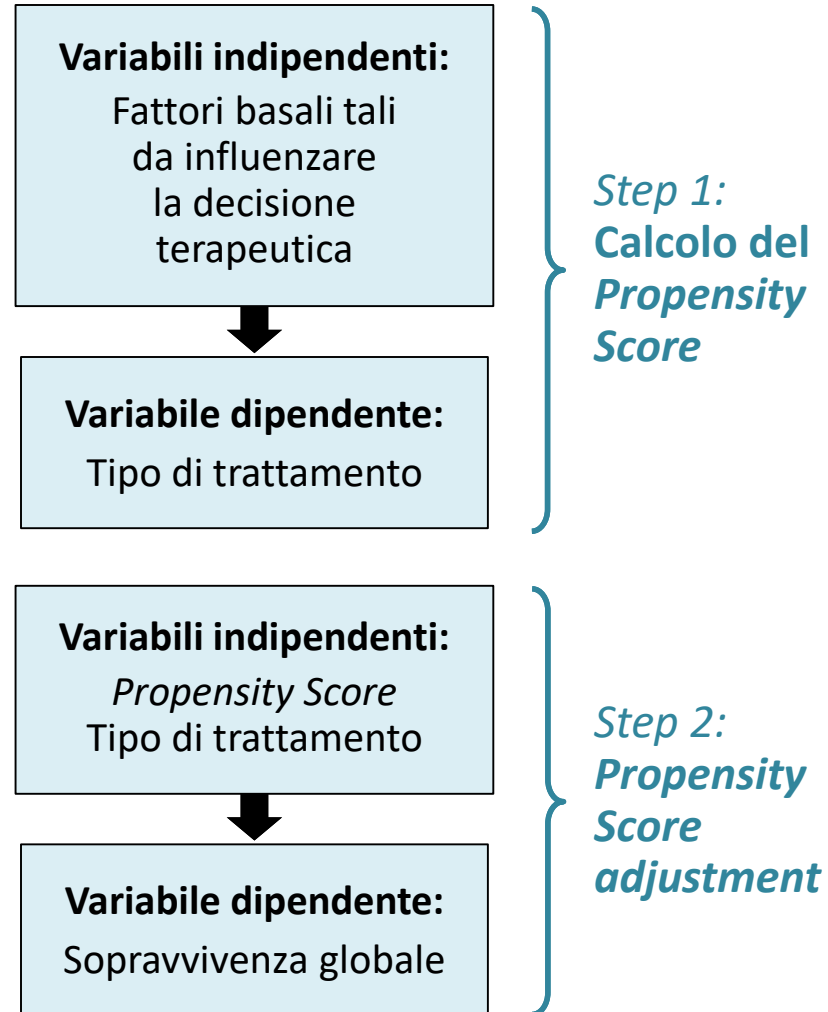
Visione ottimistica:

Il *Propensity Score adjustment* rimuove fino al 90% del bias di selezione

Visione realistica:

Non risolve il problema dei fattori di confondimento non disponibili o non noti; il rischio di *bias* di selezione non può quindi essere mai del tutto escluso.

Propensity Score adjustment



Radical Prostatectomy, External Beam Radiotherapy,
or External Beam Radiotherapy With Brachytherapy Boost
and Disease Progression and Mortality in Patients
With Gleason Score 9-10 Prostate Cancer

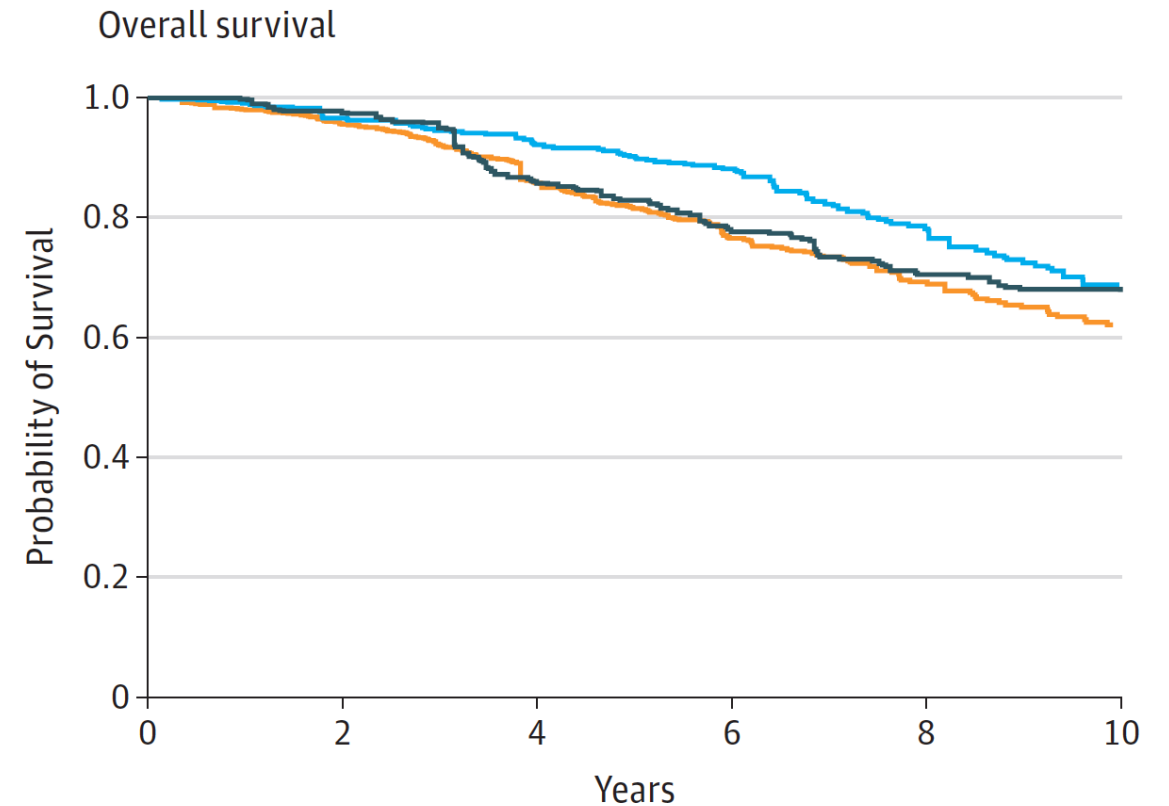
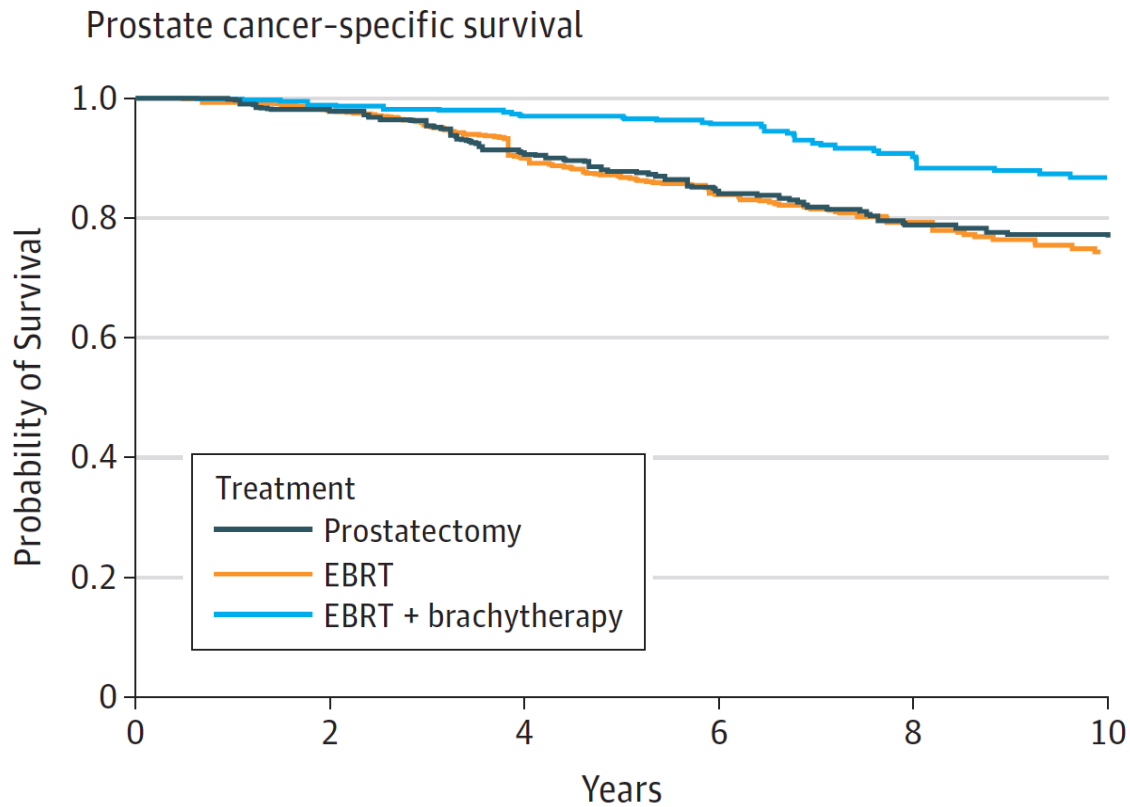
JAMA. 2018;319(9):896-905. doi:[10.1001/jama.2018.0587](https://doi.org/10.1001/jama.2018.0587)

Cox proportional hazards and Fine-Gray competing risks regression models with propensity scores included as covariates to control for confounding were used to evaluate distant metastasis, prostate cancer–specific mortality, and overall survival outcomes between treatment groups

	Unadjusted, No. (%)			P Value ^a		Propensity Score Adjusted	
	Prostatectomy (n=639)	EBRT (n=734)	EBRT+BT (n=436)	EBRT vs Prostatectomy	EBRT+BT vs Prostatectomy	EBRT vs Prostatectomy	EBRT+BT vs Prostatectomy
Clinical Characteristics							
Age, mean (median) [range], y	61.0 (61.2) [39-77.1]	67.7 (68) [39.7-98]	67.5 (68.0) [48-83]	< .001	<.001	63.78	64.35

Radical Prostatectomy, External Beam Radiotherapy, or External Beam Radiotherapy With Brachytherapy Boost and Disease Progression and Mortality in Patients With Gleason Score 9-10 Prostate Cancer

JAMA. 2018;319(9):896-905. doi:[10.1001/jama.2018.0587](https://doi.org/10.1001/jama.2018.0587)



Brachytherapy-Based Radiotherapy and Radical Prostatectomy Are Associated With Similar Survival in High-Risk Localized Prostate Cancer

Ronald D. Ennis, Liangyuan Hu, Shannon N. Ryemon, Joyce Lin, and Madhu Mazumdar

J Clin Oncol 36:1192-1198. © 2018 by American Society of Clinical Oncology

The inverse probability of treatment weighting (IPTW) was used to adjust for covariable imbalance. The propensity score, probability of receiving the actual treatment, was estimated by a multinomial logistic regression model.

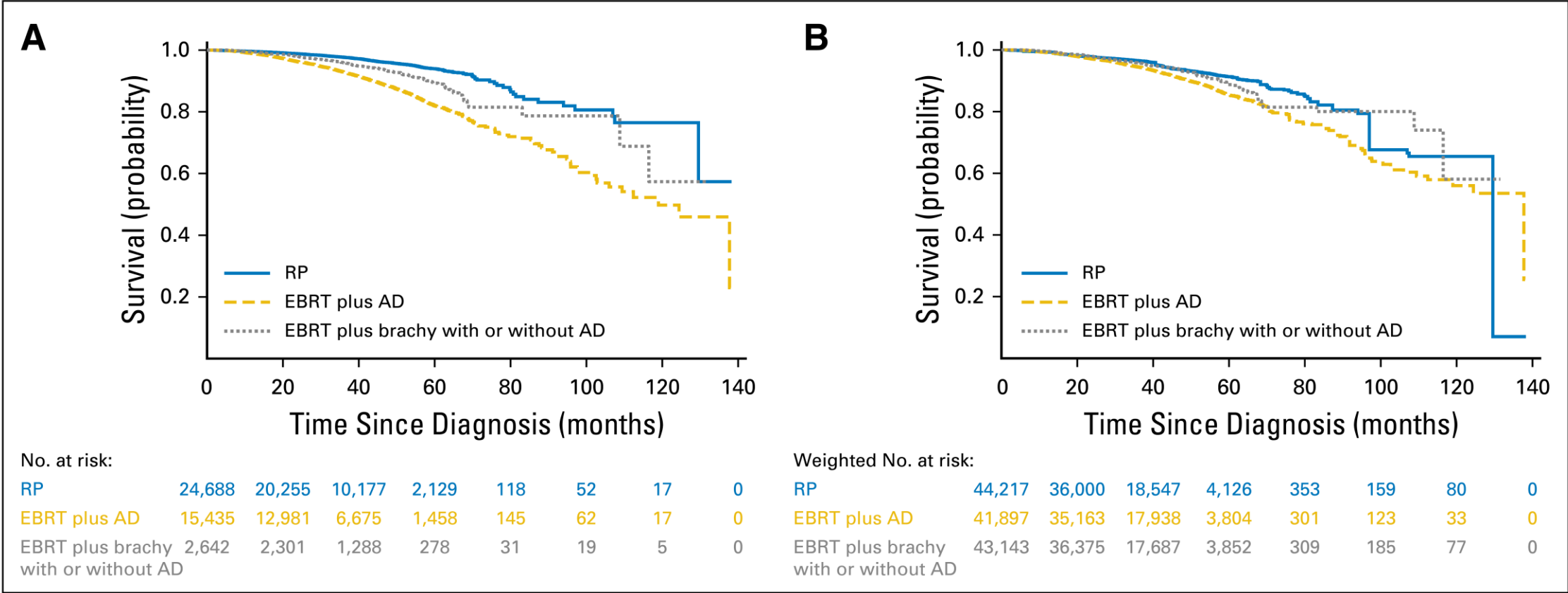


Fig 1. (A) Unweighted versus (B) inverse probability of treatment weighting–adjusted Kaplan-Meier curves stratified by the three treatments.

JAMA Oncol. 2019;5(2):213-220.

Surgery vs Radiotherapy in the Management of Biopsy Gleason Score 9-10 Prostate Cancer and the Risk of Mortality

Derya Tilki, MD; Ming-Hui Chen, PhD; Jing Wu, PhD; Hartwig Huland, MD; Markus Graefen, MD, PhD; Michelle Braccioforte, MPH; Brian J. Moran, MD; Anthony V. D'Amico, MD, PhD

Question Can treatment with radical prostatectomy, adjuvant external beam radiotherapy, and androgen deprivation therapy (termed *MaxRP*) or external beam radiotherapy, brachytherapy, and androgen deprivation therapy (termed *MaxRT*) in men with Gleason score 9-10 prostate cancer provide similar survival outcomes?

Clinical Characteristic	Without PS Adjustment			With PS Adjustment		
	RP-Containing Therapy (n = 559)	MaxRT (n = 80)	P Value ^a	RP-Containing Therapy (n = 559)	MaxRT (n = 80)	P Value ^b
PSA level, median (IQR), ng/mL	12.75 (8.00-25.00)	10.55 (6.58-18.38)	.07 ^c	13.16 (7.67-24.56)	12.18 (7.28-23.44)	.48 ^c
Biopsy Gleason score, No. (%)						
4 + 5	461 (82.5)	57 (71.3)	.001	450 (80.5)	67 (83.8)	.91
5 + 4	95 (17.0)	18 (22.5)		103 (18.4)	12 (15.0)	
5 + 5	3 (0.5)	5 (6.3)		6 (1.1)	1 (1.3)	
Biopsy AJCC tumor category, No. (%)						
T3,4	21 (3.8)	33 (41.3)	<.001	42 (7.5)	7 (8.8)	.33
T2	265 (47.4)	32 (40.0)		265 (47.4)	37 (46.3)	
T1c	273 (48.8)	15 (18.8)		252 (45.1)	36 (45.0)	
Age at diagnosis, y, No. (%)						
>70	145 (25.9)	40 (50.0)	<.001	161 (28.8)	21 (26.3)	.74
≤70	414 (74.1)	40 (50.0)		398 (71.2)	59 (73.8)	

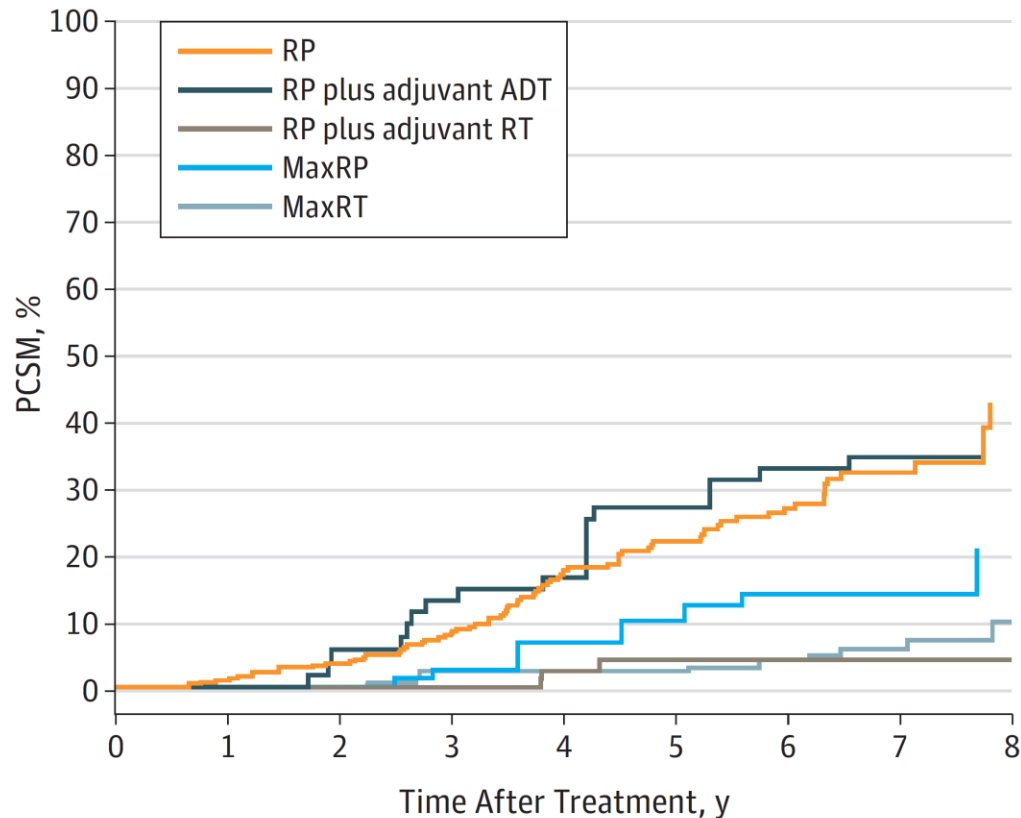
JAMA Oncol. 2019;5(2):213-220.

Surgery vs Radiotherapy in the Management of Biopsy Gleason Score 9-10 Prostate Cancer and the Risk of Mortality

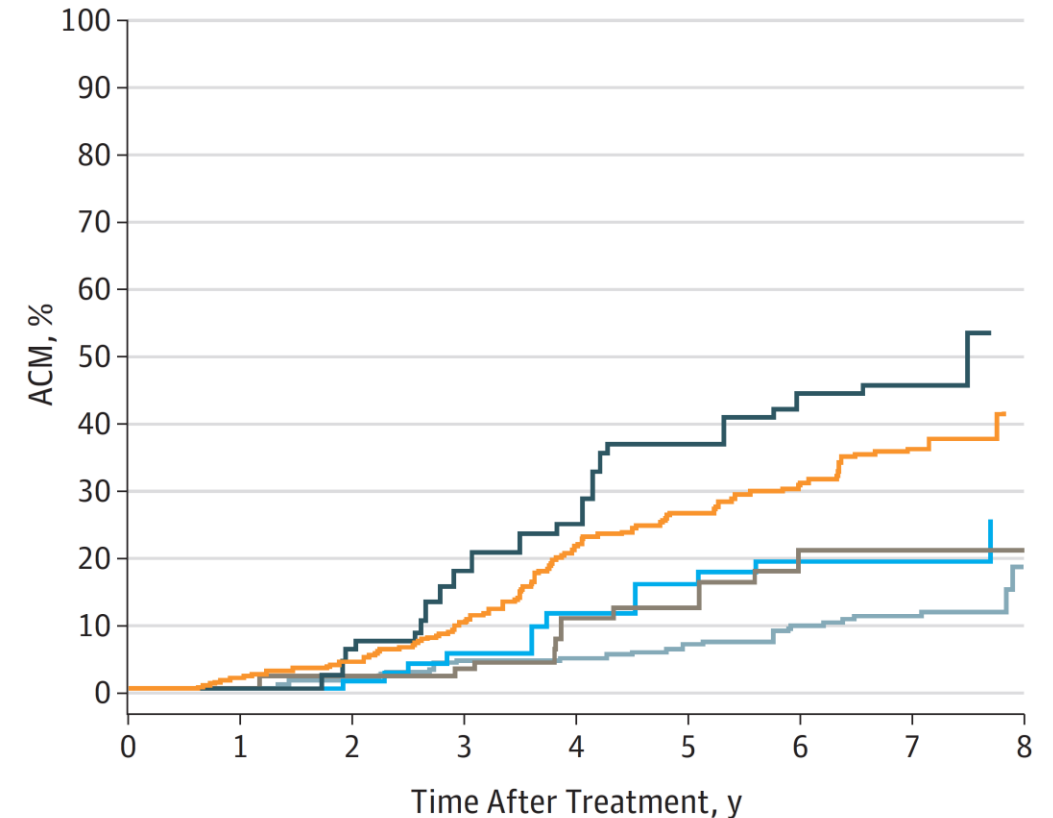
Derya Tilki, MD; Ming-Hui Chen, PhD; Jing Wu, PhD; Hartwig Huland, MD; Markus Graefen, MD, PhD; Michelle Braccioforte, MPH; Brian J. Moran, MD; Anthony V. D'Amico, MD, PhD

Question Can treatment with radical prostatectomy, adjuvant external beam radiotherapy, and androgen deprivation therapy (termed *MaxRP*) or external beam radiotherapy, brachytherapy, and androgen deprivation therapy (termed *MaxRT*) in men with Gleason score 9-10 prostate cancer provide similar survival outcomes?

A PCSM



B ACM

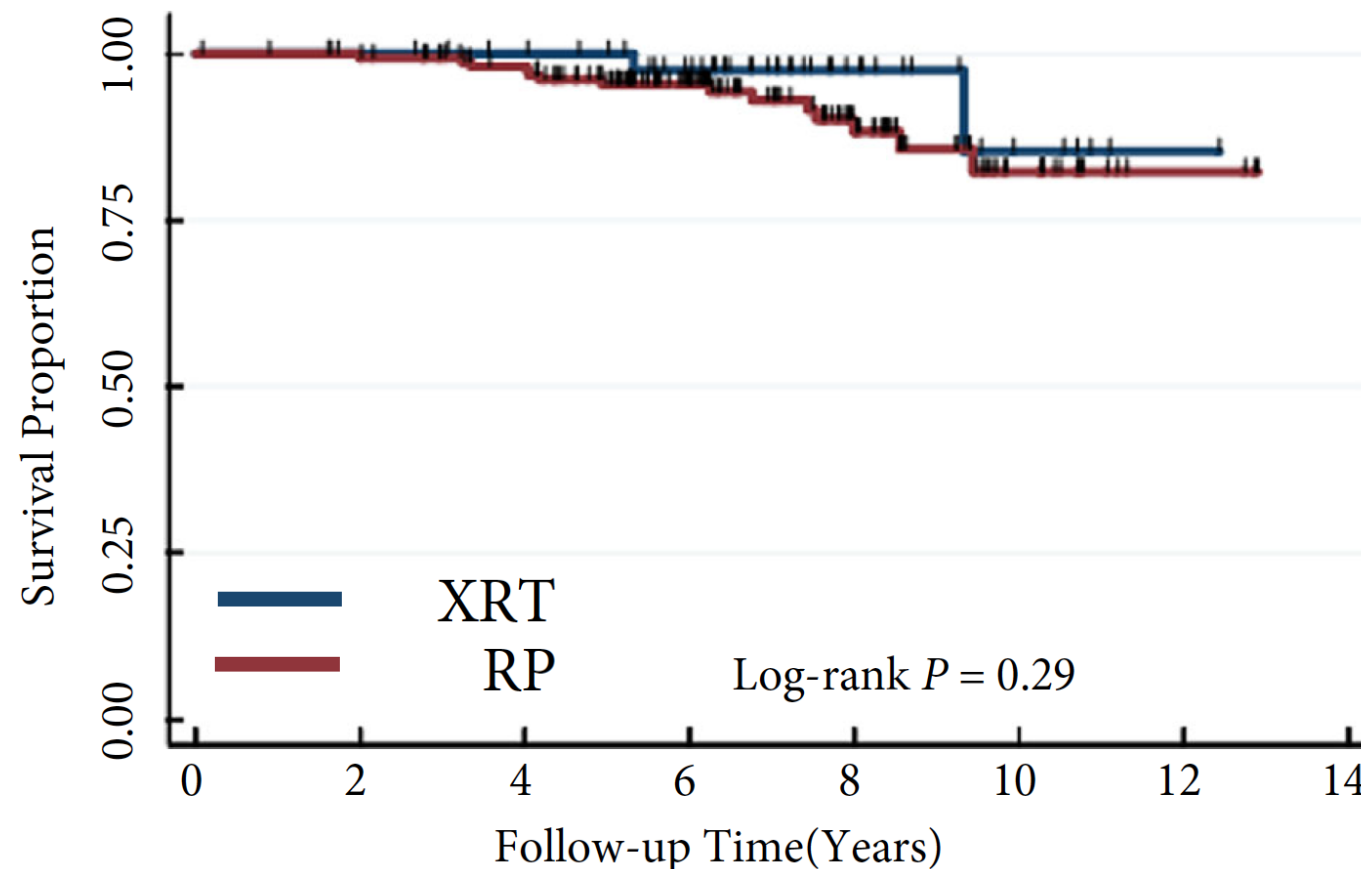


Radical prostatectomy or radiotherapy for high- and very high-risk prostate cancer: a multidisciplinary prostate cancer clinic experience of patients eligible for either treatment

Chad A. Reichard^{*} , Karen E. Hoffman[†], Chad Tang[†], Stephen B. Williams[‡] , Pamela K. Allen[†], Mary F. Achim^{*}, Deborah A. Kuban[†] and Brian F. Chapin^{*}

BJU Int 2019; **124**: 811–819

Propensity score matching was performed utilising nearest neighbour matching. Treatment effects adjusted for included: race, year of diagnosis, age at diagnosis, Gleason score, and baseline PSA level.



Surgery Versus Radiation for High-risk Prostate Cancer: The Fight Continues. But Is It Time To Call a Draw and Reach Consensus?

Prasanna Sooriakumaran^{a,b,}, Nicola Pavan^{a,c}, Peter N. Wiklund^{d,e}, Mack Roach 3rd^f*

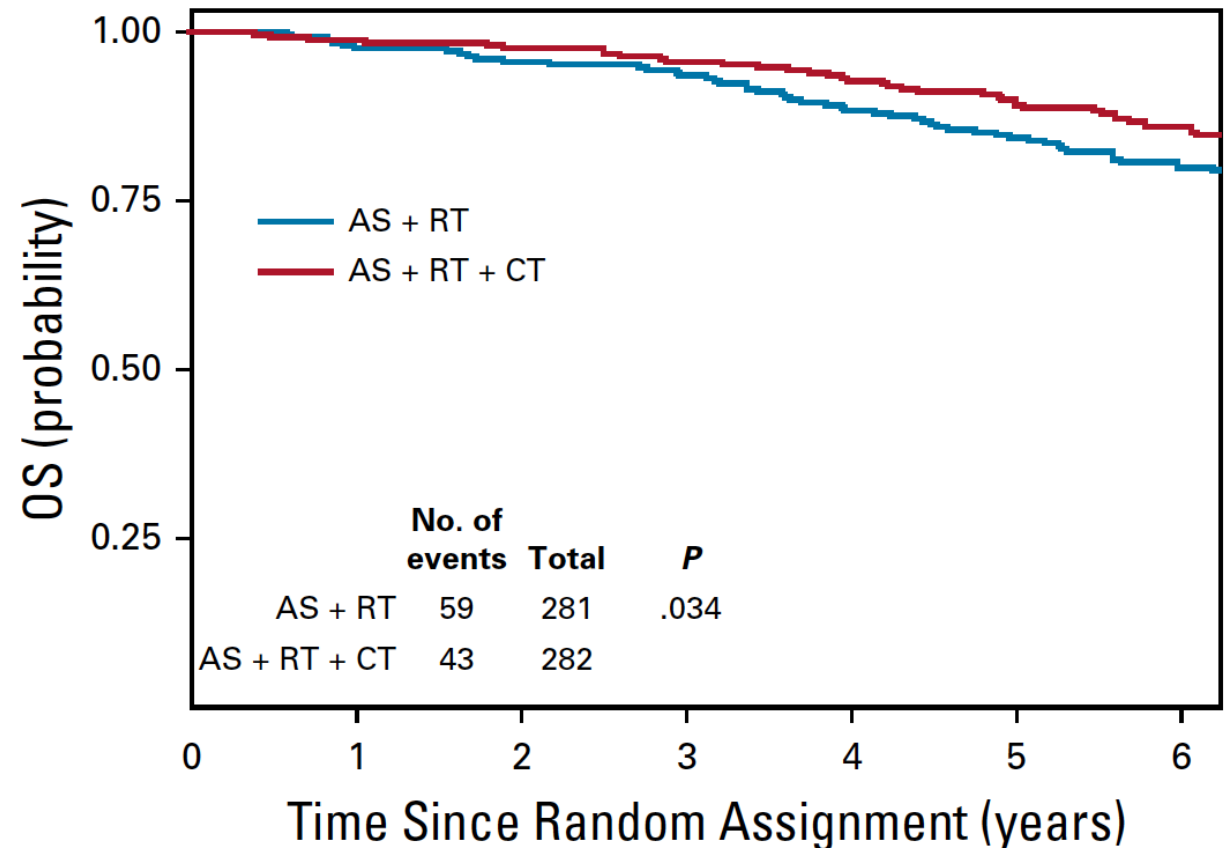
As it stands, the surgical management of HRPC is a multimodal one where patients should expect the use of adjuvant therapies such as radiation or ADT.

Given the lack of level 1 evidence, it is important to discuss the pros and cons of each treatment option (RP vs EBRT+BT+ADT vs. EBRT+ADT) in a multidisciplinary setting.

Effect of Chemotherapy With Docetaxel With Androgen Suppression and Radiotherapy for Localized High-Risk Prostate Cancer: The Randomized Phase III NRG Oncology RT0G 0521 Trial

J Clin Oncol 37:1159-1168. © 2019 by American Society of Clinical Oncology

PURPOSE Radiotherapy (RT) plus long-term androgen suppression (AS) are a standard treatment option for patients with high-risk localized prostate cancer. We hypothesized that docetaxel chemotherapy (CT) could improve overall survival (OS) and clinical outcomes among patients with high-risk prostate cancer.



editorial

Multidisciplinary Care in High-Risk Prostate Cancer Is the New Standard of Care

Rahul R. Parikh, MD¹ and Biren Saraiya, MD¹

SIURO



Società Italiana di Uro-Oncologia
Italian Society of Uro-Oncology

[Home](#)