

Franco Berrino

IL CIBO DELL'UOMO

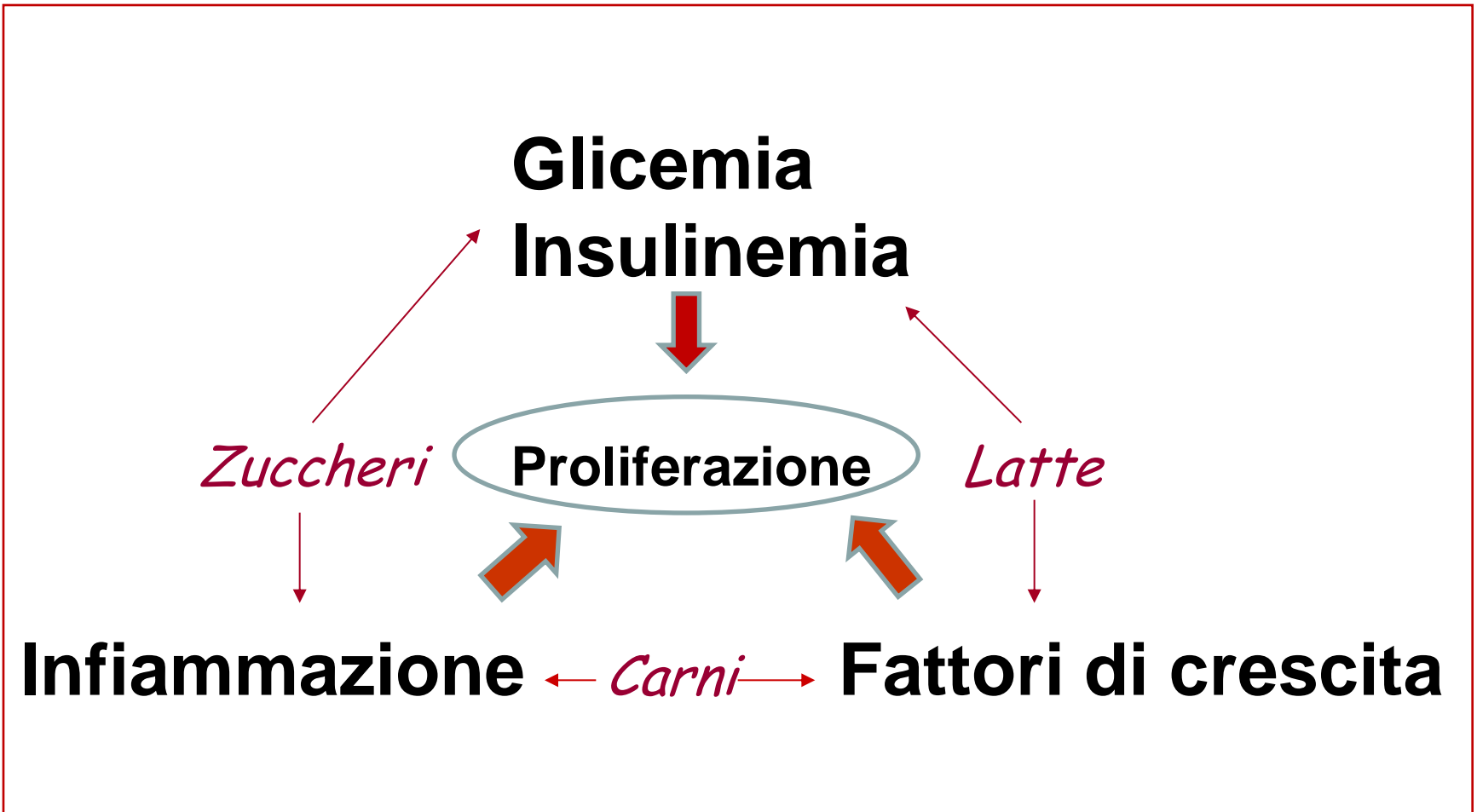
La via della salute
tra conoscenza scientifica
e antiche saggezze



FrancoAngeli/*Self-help*

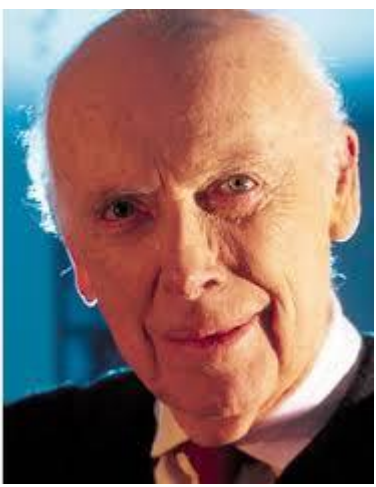
Per una dieta
adiuvante
le terapie
oncologiche

Fattori alimentari prognostici modificabili



**FATTORI
METABOLICI
ASSOCIATI
ALLA
PROGNOSI
DEI TUMORI**

	Obesità	Glicemia	Fattori di crescita	PCR
Testa e collo	--	+	+	+
Esofago (csc)	--			+
Stomaco		+	+	+
Colon	+	+	+	+
Fegato		+	--	+
Pancreas		+	+	+
Polmone	--	+	+	+
Sarcoma				+
Melanoma				+
Mammella	+	+	+	+
Ovaio		+	?	+
Endometri0	+			+
Cervice	+		+	
Prostata	+	+	+	+
Vescica	+	+		+
Rene	--	+		+
Cervello		+		+
Linfoma		+	+	+



Elementare, Watson 2013

DNA revealed the causes,
it may never reveal a cure

...we should focus far more on the wide range of
metabolic and oxidative vulnerabilities ... of cancer cells

Lawenda BD 2008 JNCI 100: 773

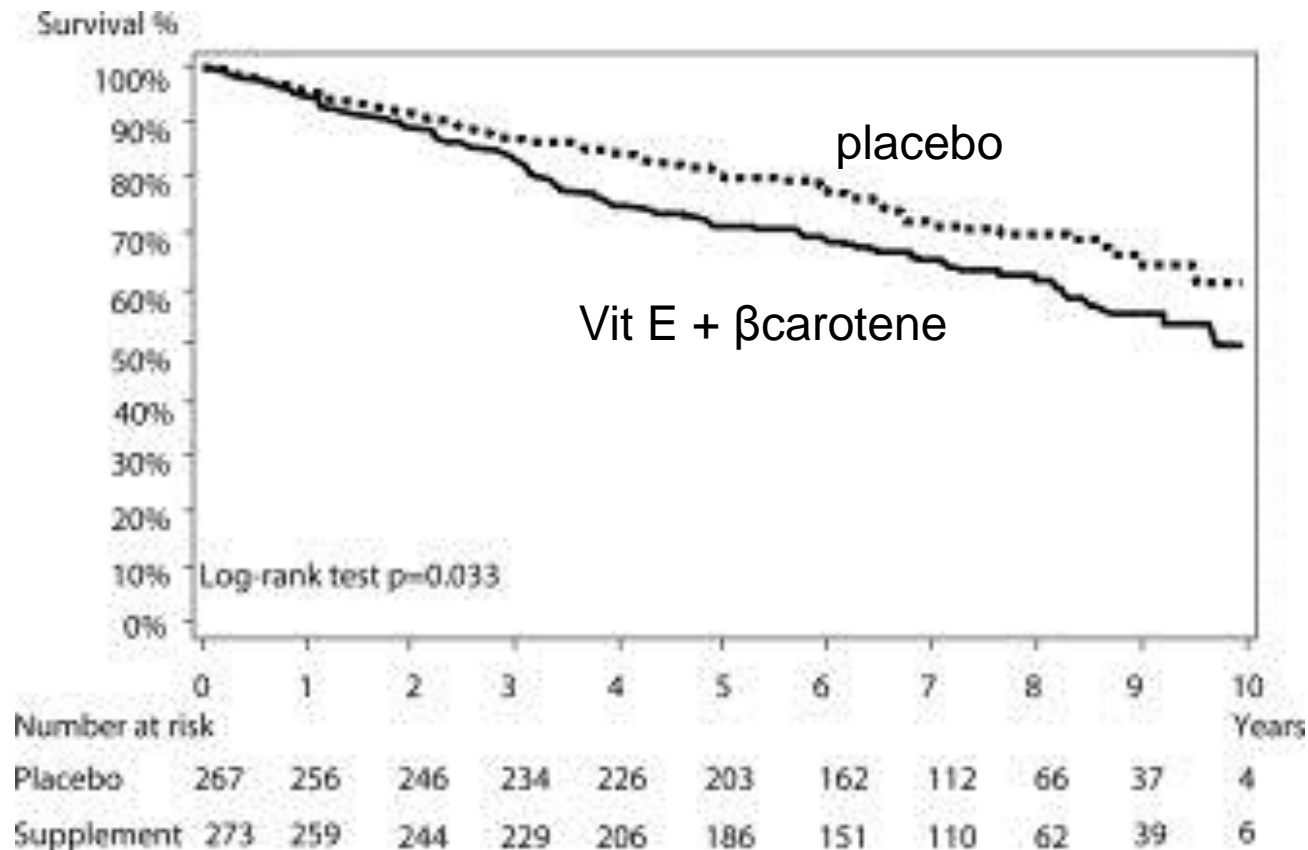
“... l’uso di supplementi antiossidanti durante la chemioterapia o la radioterapia dovrebbe essere scoraggiato perché potrebbe proteggere il tumore e ridurre la sopravvivenza”

D’Andrea GM 2005 CA Cancer J Clin 55:319

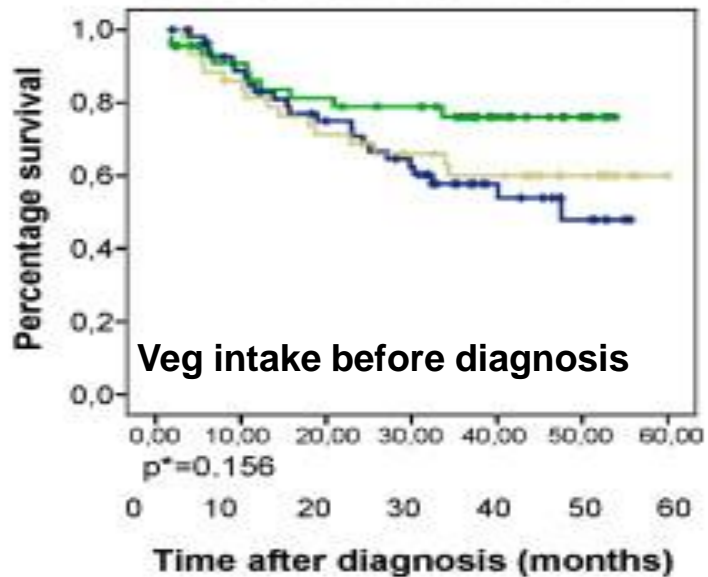
“I clinici dovrebbero consigliare ai pazienti di non usare supplementi antiossidanti durante la chemioterapia o la radioterapia”

Antioxidant vitamins supplementation and mortality

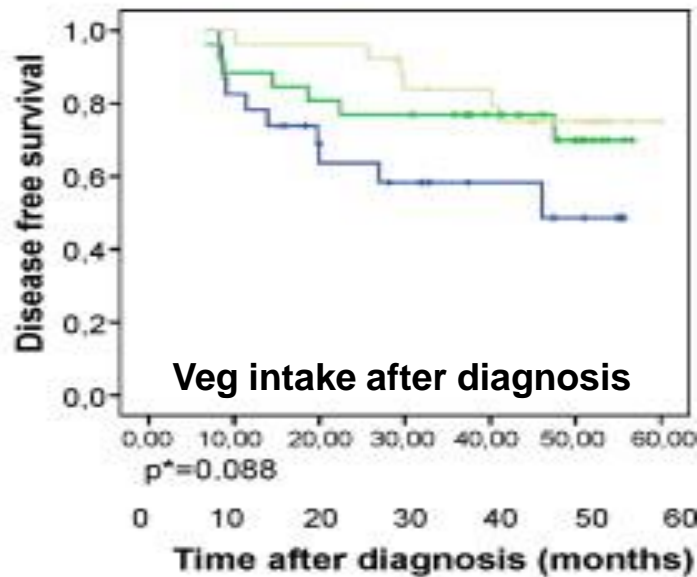
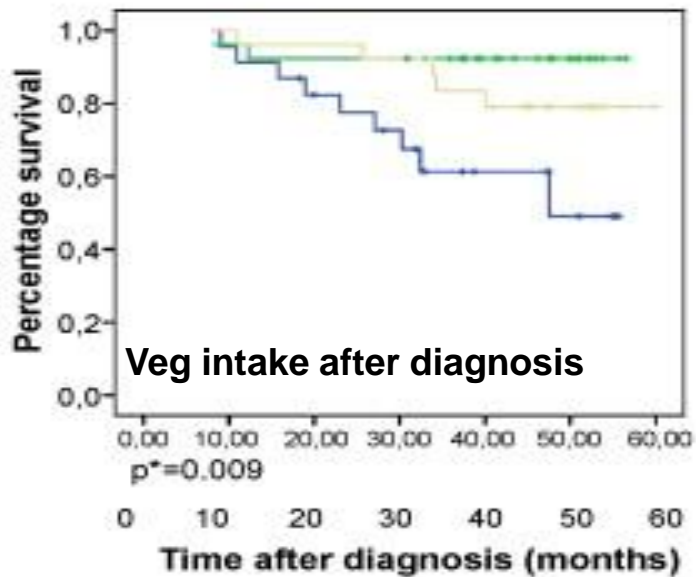
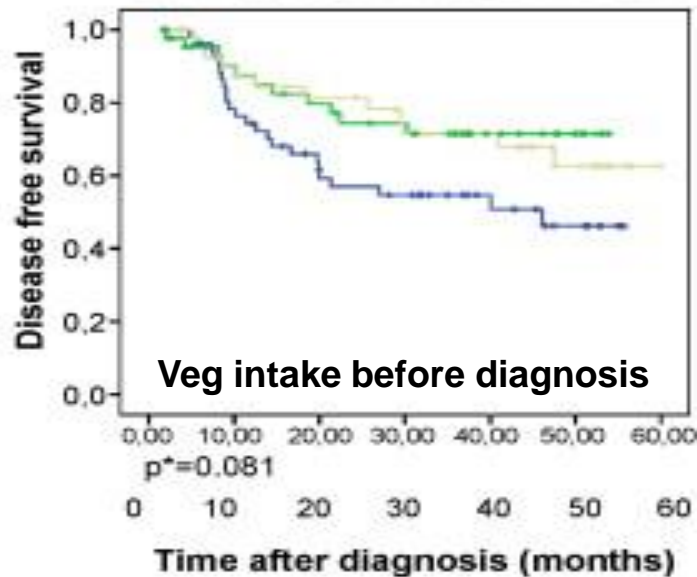
A randomized trial in head and neck cancer patients



ORAL CANCER MORTALITY



ORAL CANCER RECURRENCE



No. of servings per week:

- ≤4
- 5-7
- ≥8

Sandoval et al.
Int J Oral Max Surg
2009, 38:31

Lesperance ML 2002 BCRT 76:137

- 90 pazienti canadesi con CM trattate con **mega-dosi** di beta-carotene, vitamina C, niacina, selenio, coenzime Q10 e Zn
- Maggiore mortalità specifica

HR = 1.75 (95% CI = 0.83-2.69)

rispetto a un gruppo di controllo non trattato, appaiato per età e variabili prognostiche

Lipidome and antioxidants

- P Bougnoux 2000:

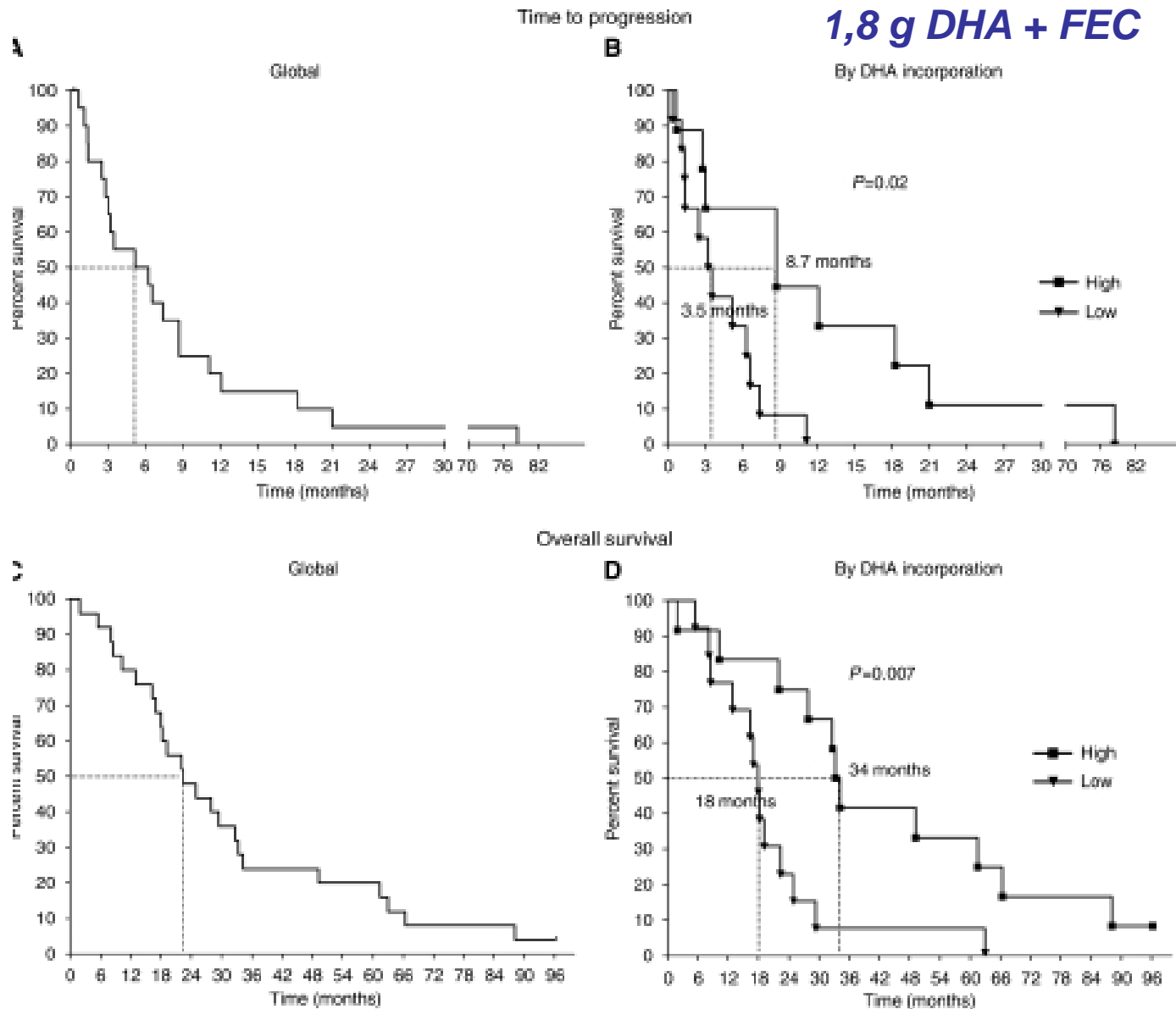
*NMU induced mammary tumours
+ high PUFA (DHA):*

Pro-oxidants reduce tumour growth

Anti-oxidants promote tumour growth

[Bougnoux P 2009 Br J Cancer 101:1978-85.](#)

Improving outcome of chemotherapy of metastatic breast cancer by docosahexaenoic acid: a phase II trial.



Glutathione

- Alcuni studi hanno mostrato che supplementi di glutathione riducono la tossicità di cisplatino e ciclofosfamide.
- La proprietà antiossidante del glutathione può però rendere le cellule tumorali resistenti alla chemioterapia.
- Un polimorfismo della *GSTP1* (*GSTP1* Ile105Val) che la rende sette volte più efficiente è associato a una minore sopravvivenza dei pazienti neoplastici.

Glutathione S-transferase P1 genetic polymorphism that generates an (105)Val in the GSTP1 protein and survival of patients with metastatic colorectal cancer.

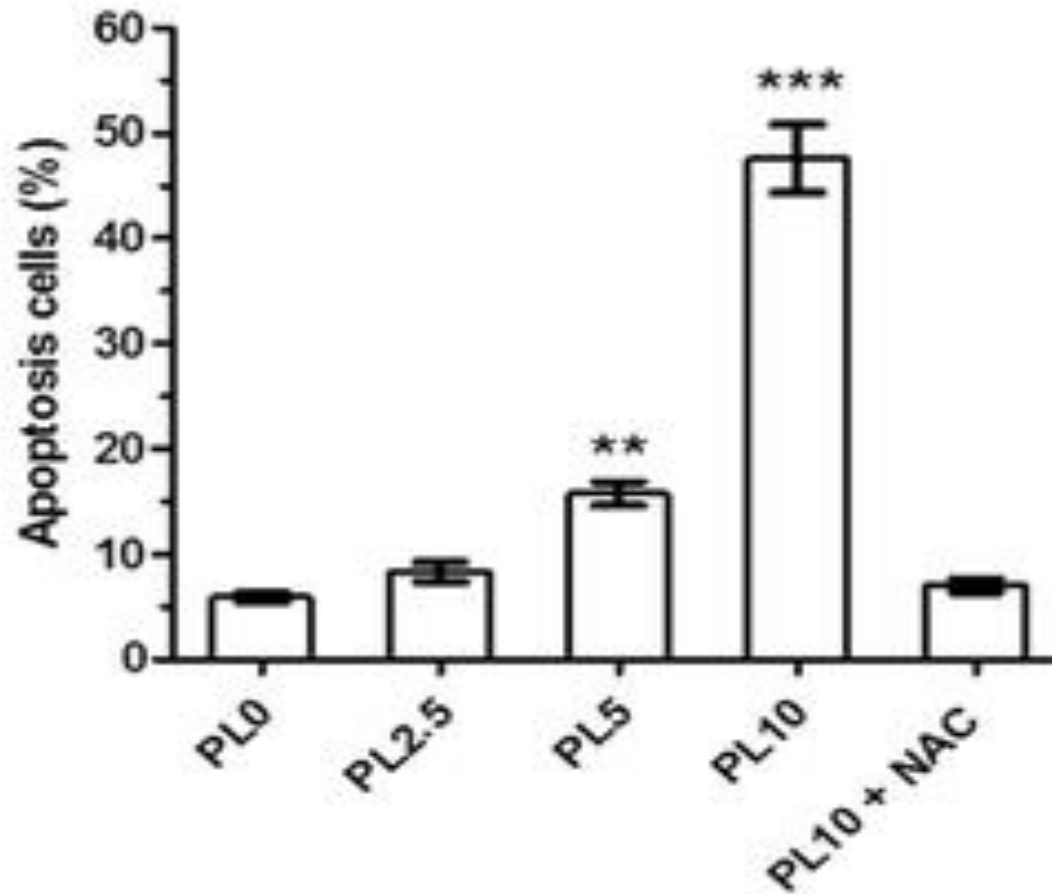
[Stoehlmacher J](#) 2002 [J Natl Cancer Inst.](#) 94:936.

- 107 previously treated patients received 5-FU/oxaliplatin combination chemotherapy.
- After adjustment for performance status and tumor site, the stratified RRs were
0.28 (95% CI = 0.07 to 1.10)
for patients with two (105)Val alleles and
0.64 (95% CI = 0.36 to 1.16)
for those with one (105)Val allele.

Alcune sostanze alimentari
hanno azione antitumorale
legandosi a siti attivi di sistemi
antiossidanti (as es. GST)
(**piperlongumina**)
o generando radicali liberi
interferendo con la
fosforilazione ossidativa
(**diindolimetano**)

d

KKU-055, PL-48 h



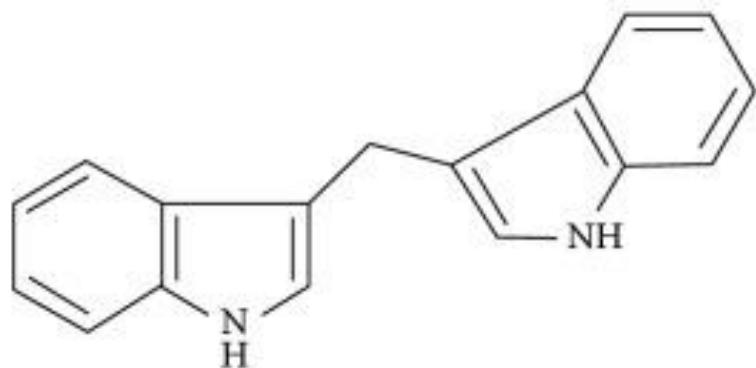
[Thongsom S](#) et al. 2017 [Apoptosis](#). Sep 14.

Piperlongumine induces G2/M phase arrest and apoptosis in cholangiocarcinoma cells through the ROS-JNK-ERK signaling pathway.

3,3'-Diindolylmethane: A Promising Sensitizer of γ -Irradiation.

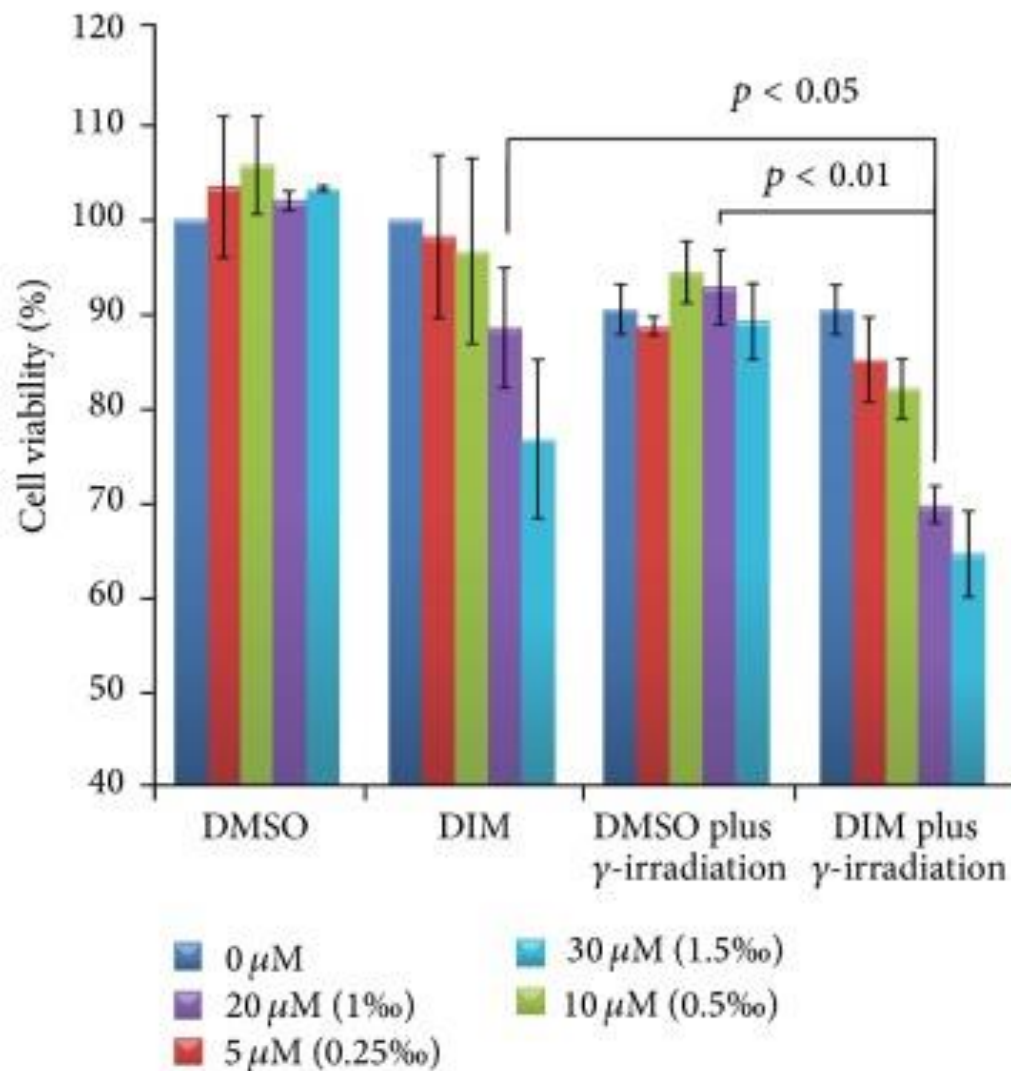
In MCF-7 cells

Wang W et al. 2015:
Biomed Res Int. 465105.



3,3'-Diindolylmethane (DIM)

(a)

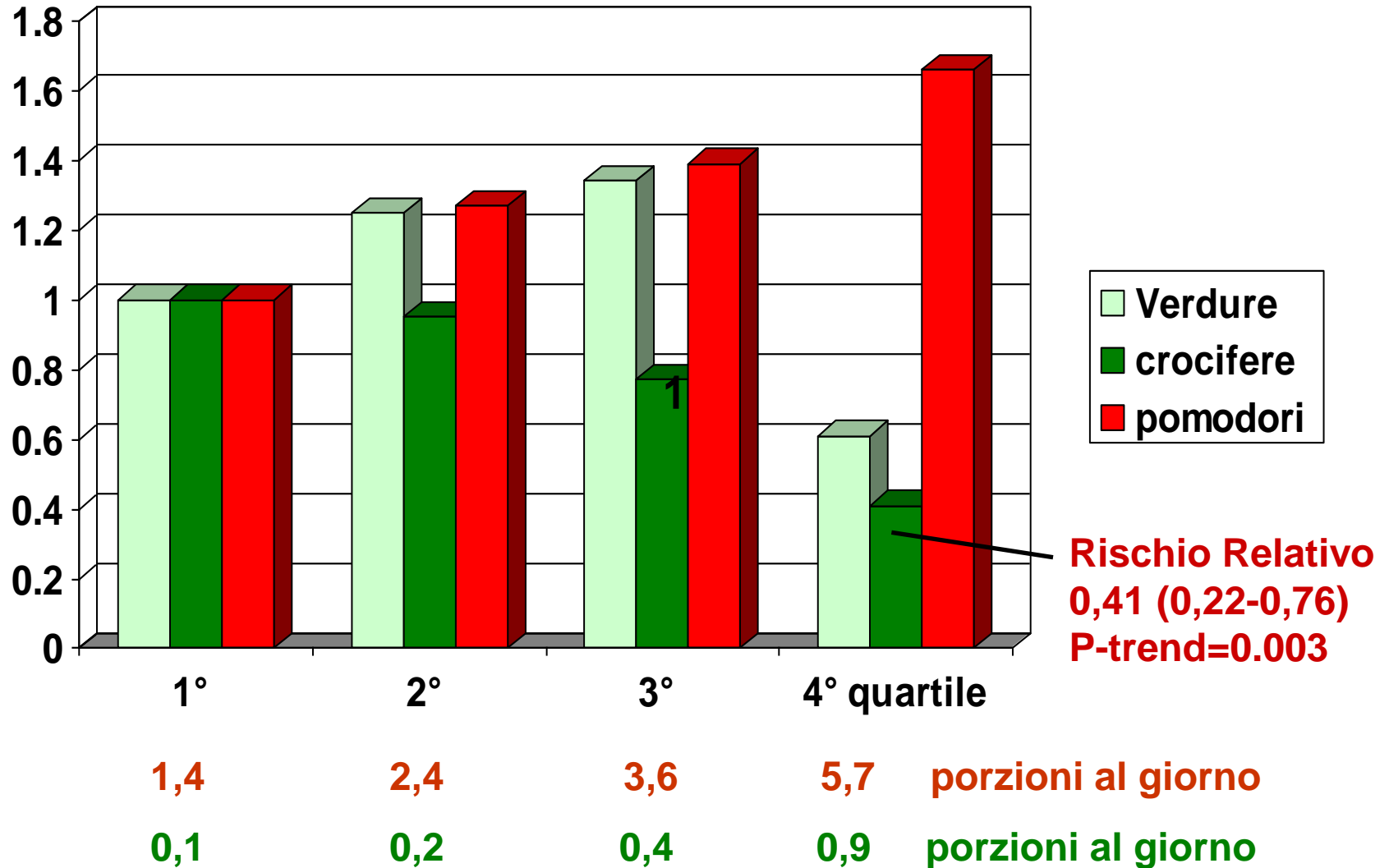


(b)

DIM plus γ -irradiation arrested the activity of G2/M phase cell cycle, increased intracellular ROS level, significantly suppressed PARP, and enhanced γ -irradiation-induced apoptosis, thereby inhibiting the proliferation of MCF-7 cells.

(Richman EL 2012 IJC 131:201)

Cancer of the Prostate Strategic Urologic Research Endeavor,
Rischio di progressione in 1560 casi non metastatici



Nessuna protezione da verdure diverse dalle crocifere

▪

**Fattori di crescita
IR, IGF-1R, EGFR**

DIGIUNO



AMPK



IRS



PI3K

AKT

PTEN



TSC



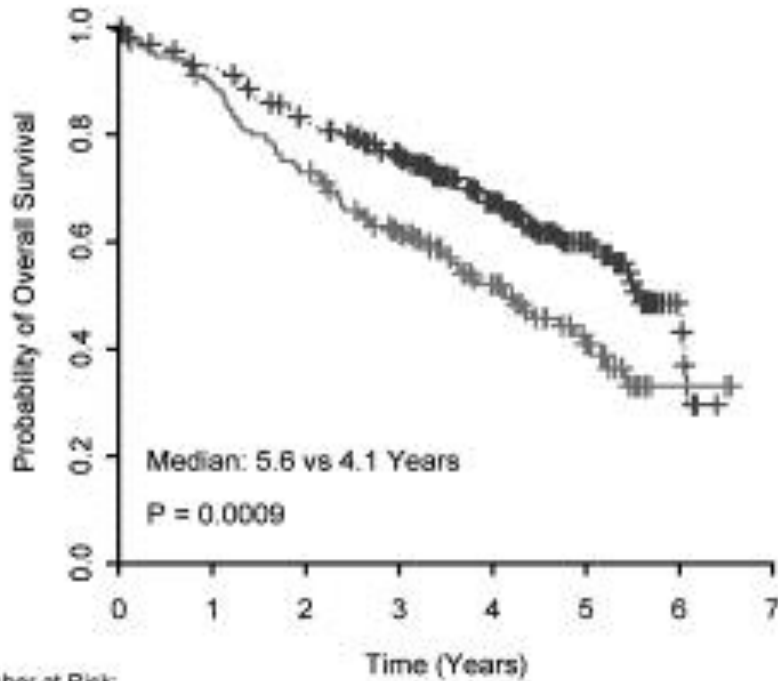
mTOR



HIF

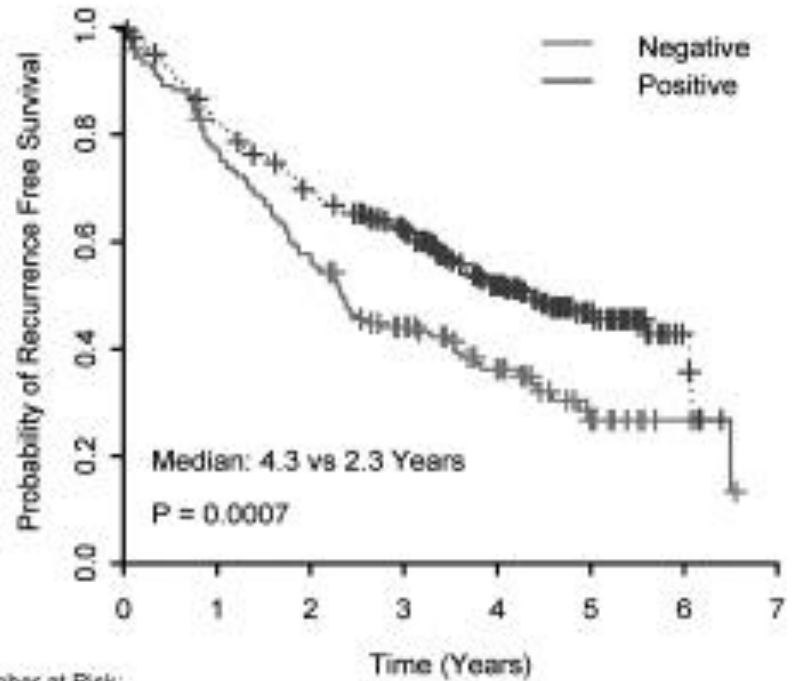
Fattori di crescita

A. Overall Survival



	0	1	2	3	4	5	6	7
Number at Risk:								
pAMPK positive	316	287	250	210	127	54	9	
pAMPK negative	147	129	105	79	47	23	3	

B. Recurrence Free Survival



	0	1	2	3	4	5	6	7
Number at Risk:								
pAMPK positive	316	255	211	170	95	38	6	
pAMPK negative	147	111	83	55	32	13	3	

High pAMPK expression levels are associated with increased survival in patients with NSCLC, William WN 2012 Ann Oncol 23:78

DIFFERENTIAL STRESS RESISTANCE TO SHORT TERM STARVATION

Lee C, Raffaghello L, Longo V, 2012 Drug Resist Updat 15:114

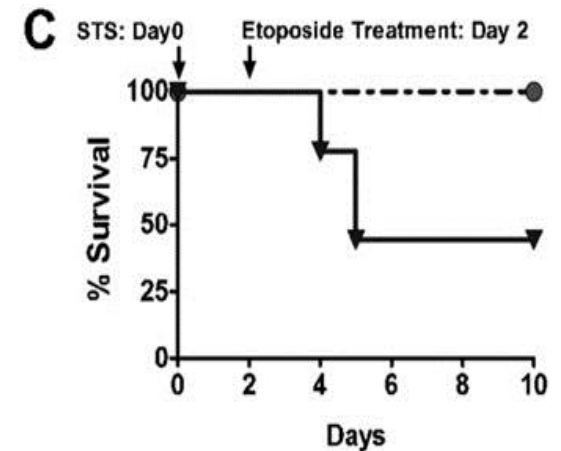
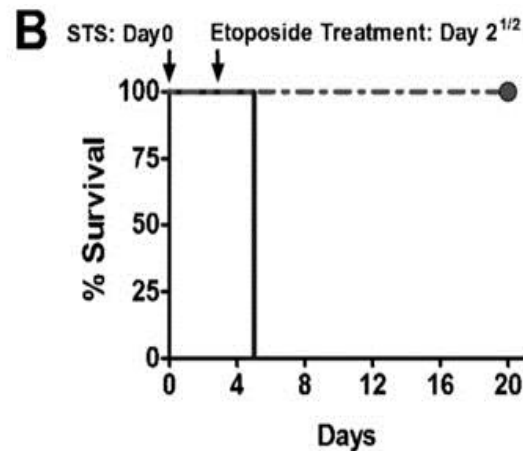
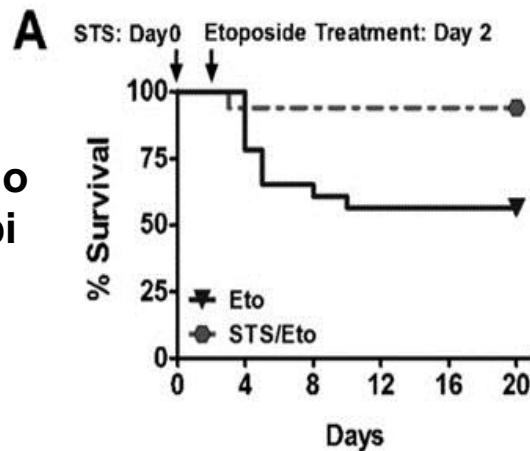
- **Brevi periodi di digiuno** scatenano meccanismi di protezione a vari tipi di stress, meccanismi altamente conservati: da batteri e lieviti a vermi, insetti, topi e primati
- Effetti in buona parte mediati dall'**inibizione di vie di segnale mitogene**, specie IGF-1 / PI3K / AKT, che sono invece spesso costitutivamente attivate nel cancro.

the remarkable changes in the levels of glucose, IGF-I, IGFBP-1 and in other proteins caused by fasting have the potential to improve the efficacy of chemotherapy against tumors by protecting normal cells and tissues and possibly by diminishing multidrug resistance in malignant cells.

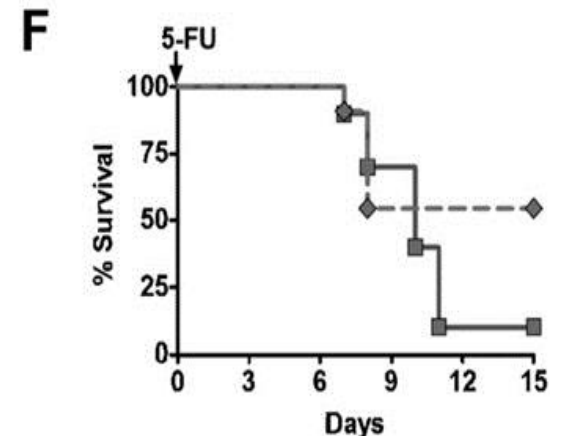
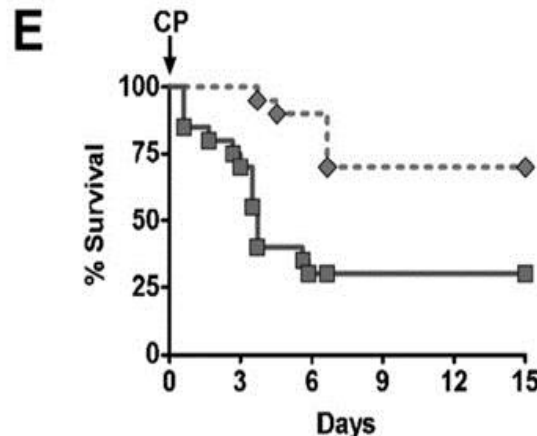
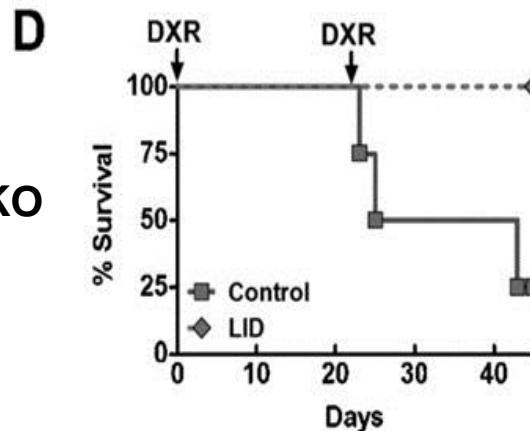
[Lee C1](#), [Raffaghello L](#), [Longo VD](#). [Drug Resist Updat](#). 2012;15:114-22.

Starvation, detoxification, and multidrug resistance in cancer therapy.

Digiuno
3 ceppi

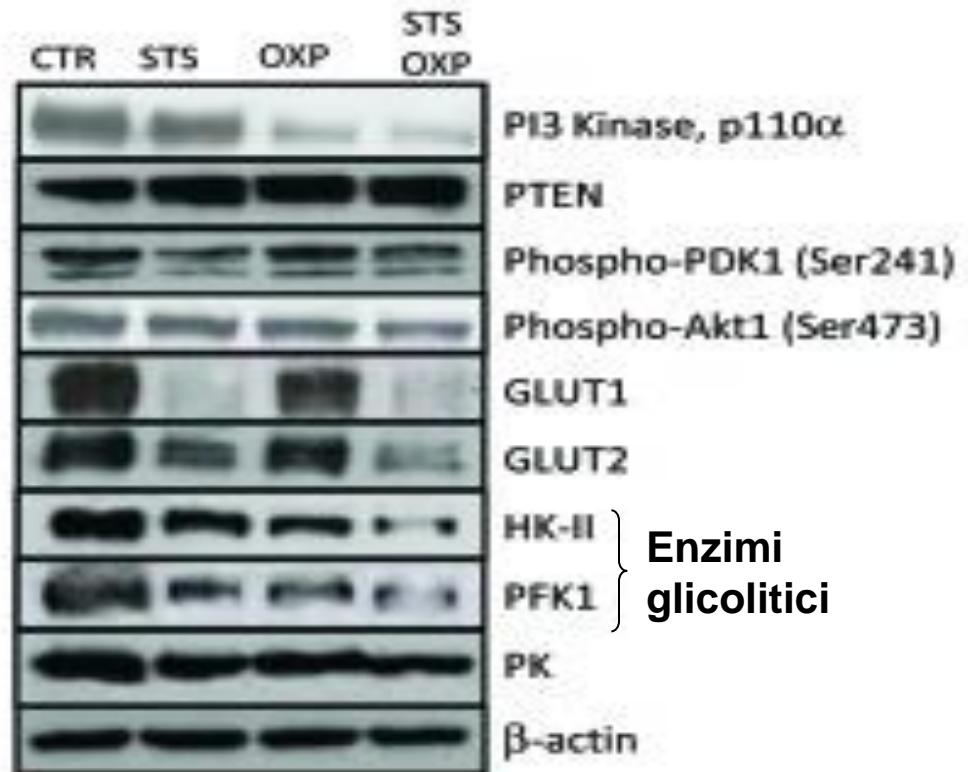


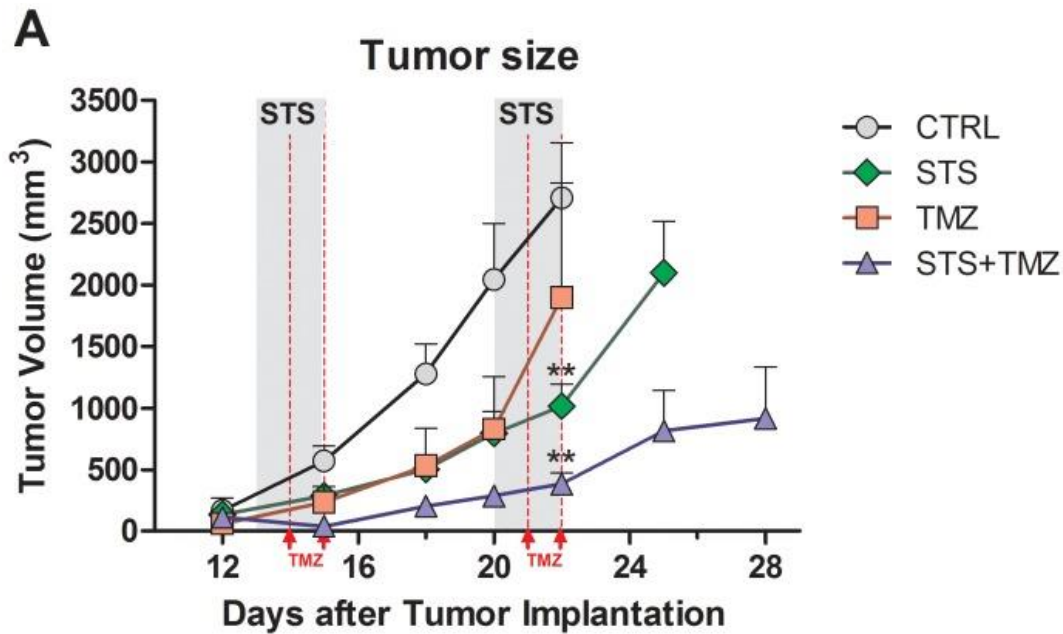
IGF-I KO



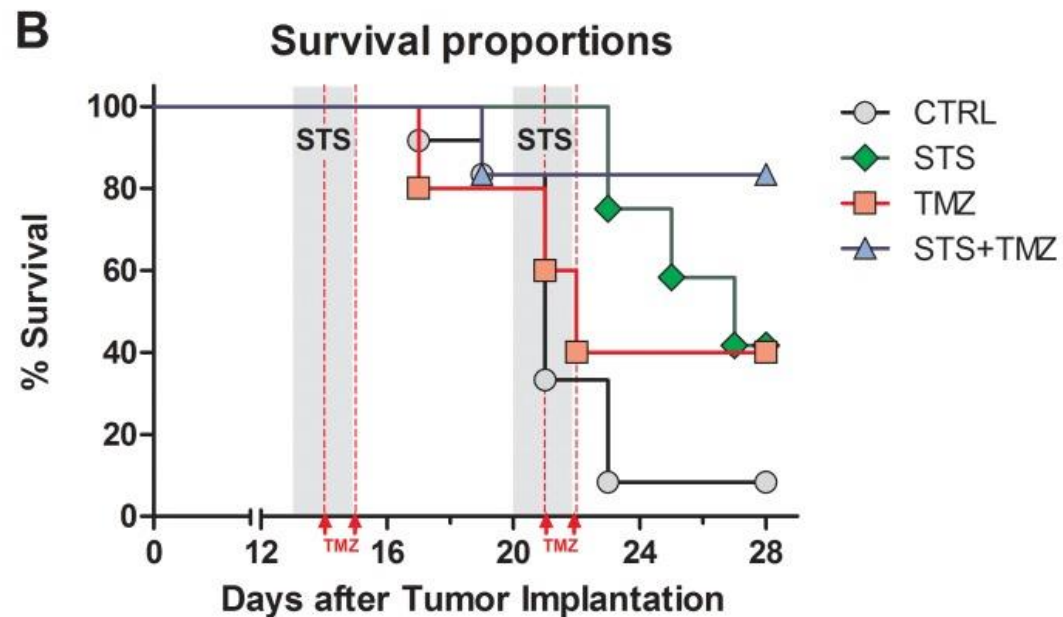
Brevi periodi di digiuno (STS) regolano l'attività di geni coinvolti in vie di segnale metaboliche e proliferative

[Bianchi G](#) ... [Longo VD](#). 2015 [Oncotarget](#). 6:11806

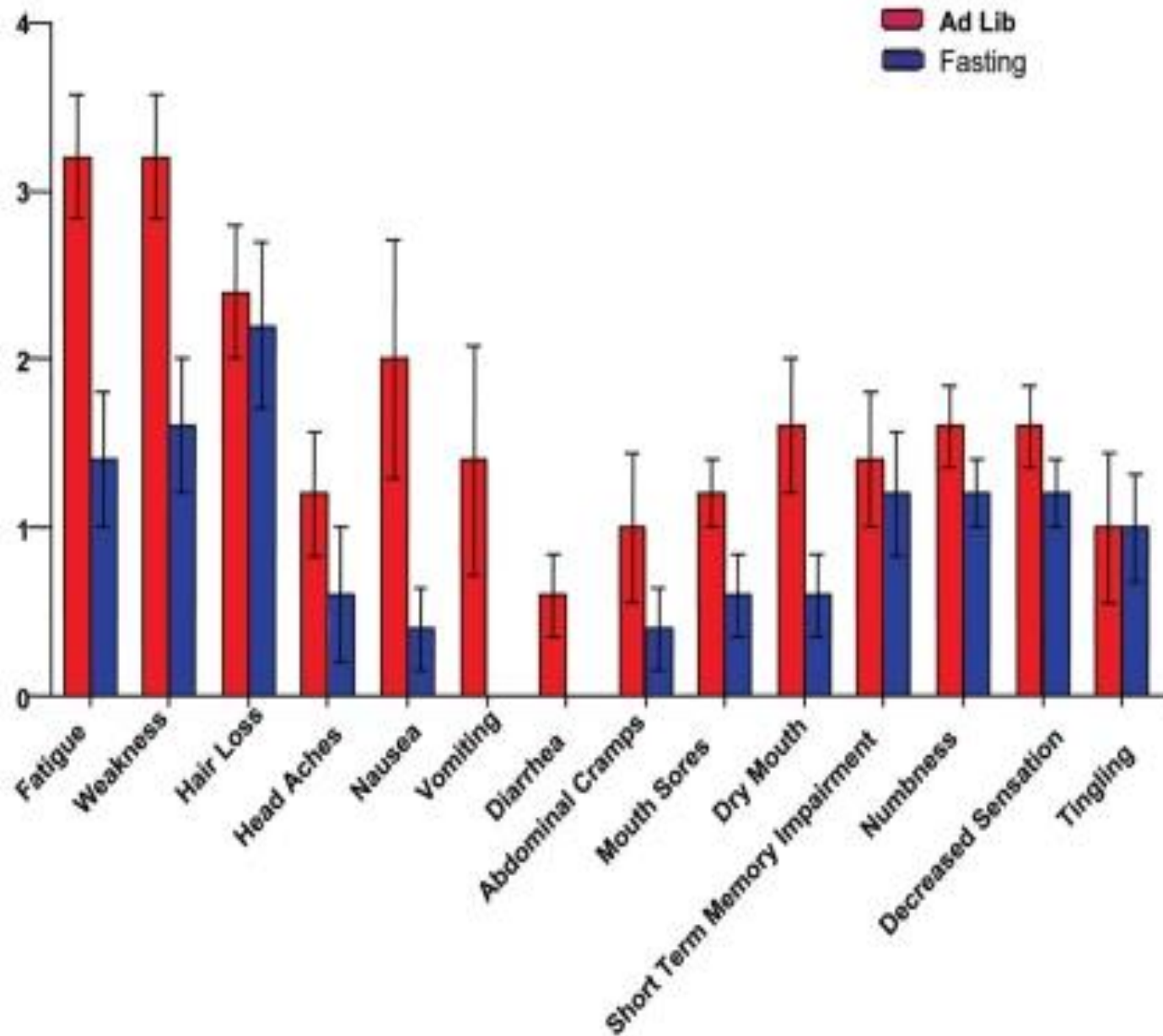




Enhanced Chemotherapy by Fasting in a murine GL26 Glioma Model



[PLoS One](https://doi.org/10.1371/journal.pone.0171103). 2012; 7: e44603.
Fasting Enhances the Response of Glioma to Chemo- and Radiotherapy
[Fernando Safdie](#) ...and [Valter D. Longo](#)¹



Safdie FM
 Fontana L
 Longo VD
 2009
 Aging 1:988

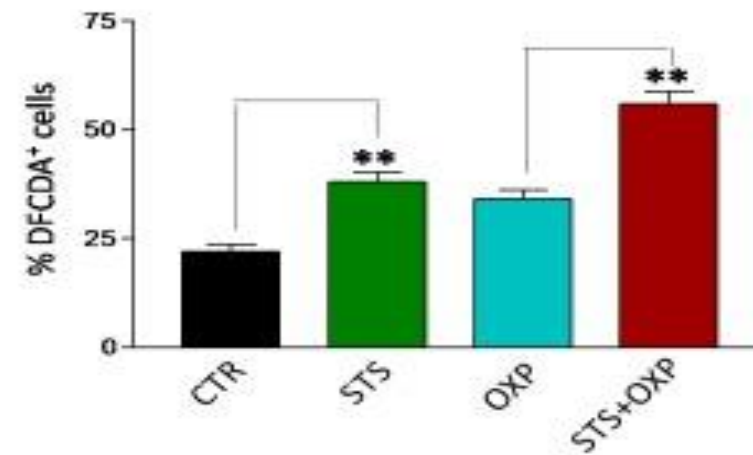
Patients self-reported side-effects after chemotherapy with and without fasting

L'augmentata attività della catena respiratoria mitocondriale con diminuita produzione di ATP suggerisce un'augmentata generazione di superossido causata dal *leakage* di elettroni, forse al complesso I e al III.

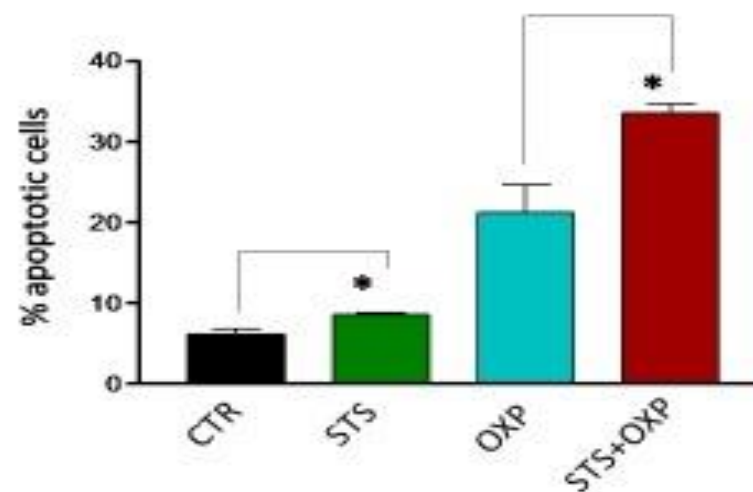
STS e OXP aumentano la generazione di ROS e STS+OXP la esacerba ulteriormente (Figura [A](#)),

Sono le alterazioni metaboliche verosimilmente responsabili degli effetti additivi di STS+OXP nello scatenare l'apoptosis in cellule CT26 (Figura [C](#)).

A



C



Dieta chetogenica (KD) e gliomi

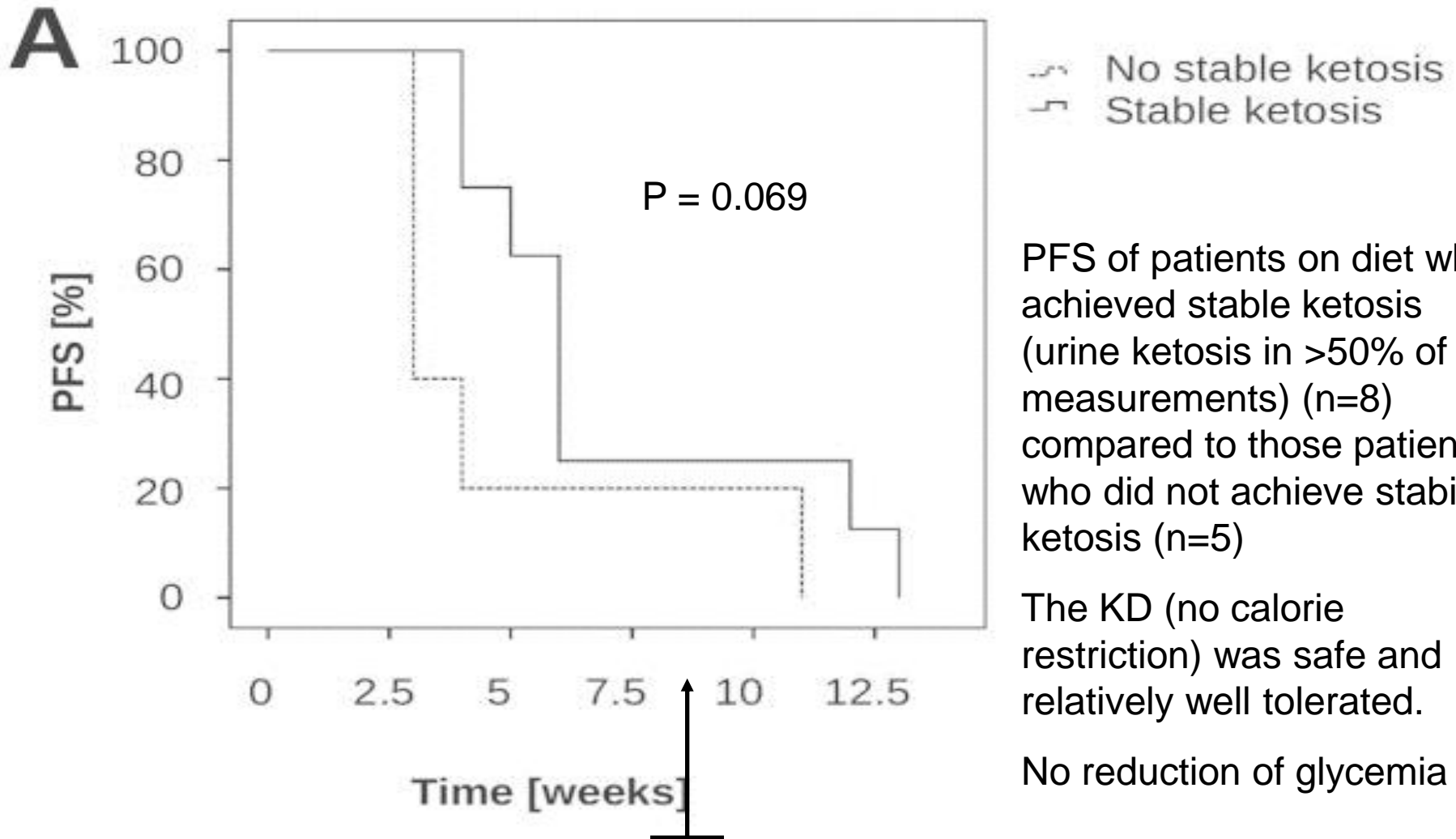
- [Nebeling 1995 J Am Coll Nutr 14:202:](#)
KD (60% grassi) x 1 anno: arresto della progressione in due bambine pretrattate con CT e RT
- [Zuccoli G 2010 Nutr Metab \(Lond\) 7: 33:](#)
regressione completa (PET e RMN) in paziente di 65 anni con GBM multicentrico associando CT e RT a KD 4:1 con 600 kcal/di per due mesi (perdita di peso:20%).
Recidiva dopo 10 mesi dall'interruzione della dieta, nuove CT, decesso dopo un anno

The ketogenic diet for the treatment of malignant glioma

[Eric C. Woolf](#), [Adrienne C. Scheck](#) 2015 [J Lipid Res](#). 56: 5.

- The medical community must be educated on the therapeutic value of metabolic alteration as an adjuvant therapy because the current dogma is to avoid weight loss in patients undergoing chemotherapy for fear of increased fatigue and further decline in overall patient health.
- Compliance can be made more difficult by the use of steroids (prescribed for peritumoral edema) that increase hunger and raise blood glucose levels.
- Sperimentazioni cliniche in corso (4:1 >>1:1).

ERGO: A pilot study of ketogenic diet in recurrent glioblastoma



PFS of patients on diet who achieved stable ketosis (urine ketosis in >50% of measurements) (n=8) compared to those patients who did not achieve stable ketosis (n=5)

The KD (no calorie restriction) was safe and relatively well tolerated.

No reduction of glycemia

Fattori alimentari prognostici modificabili

Glicemia
Insulinemia



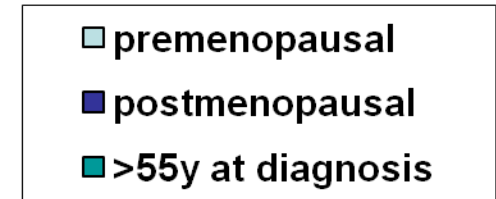
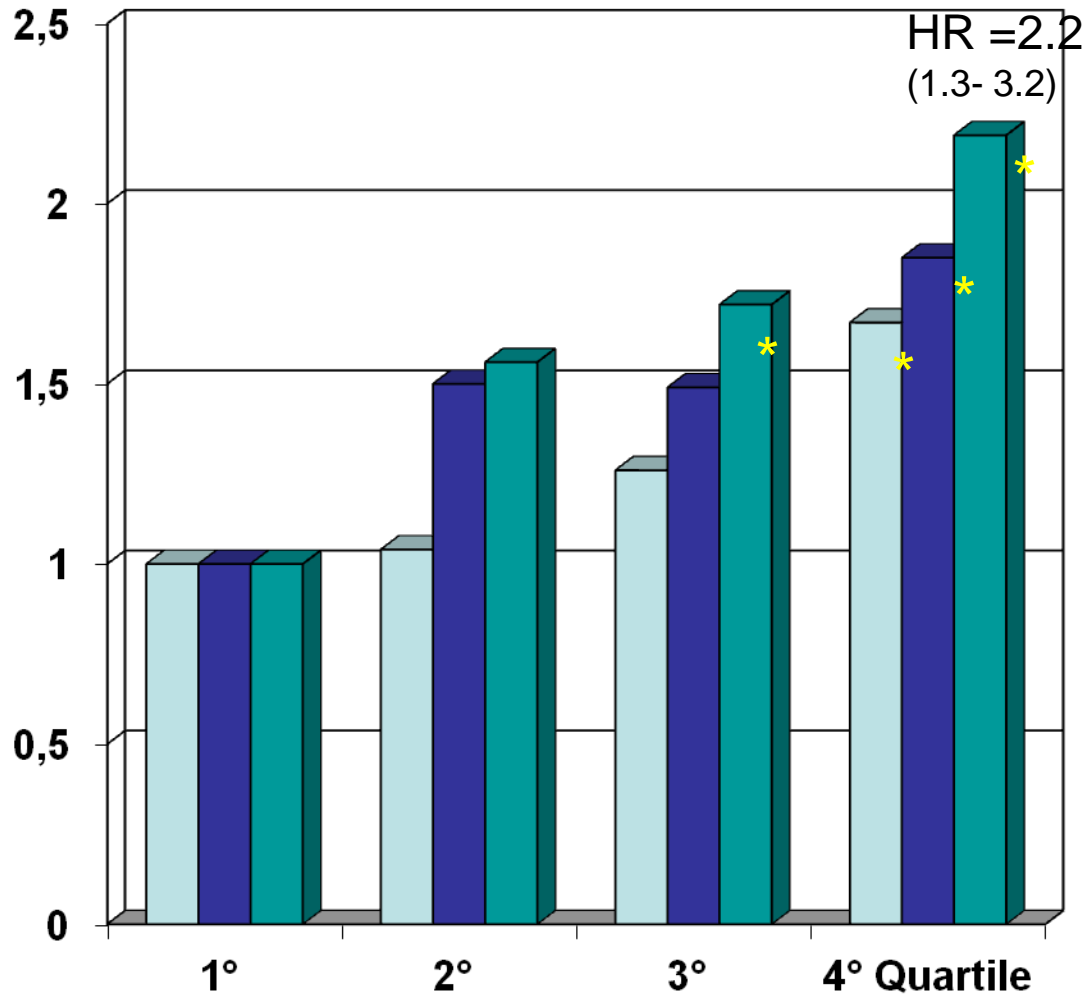
Proliferazione



Infiammazione



Fattori di crescita



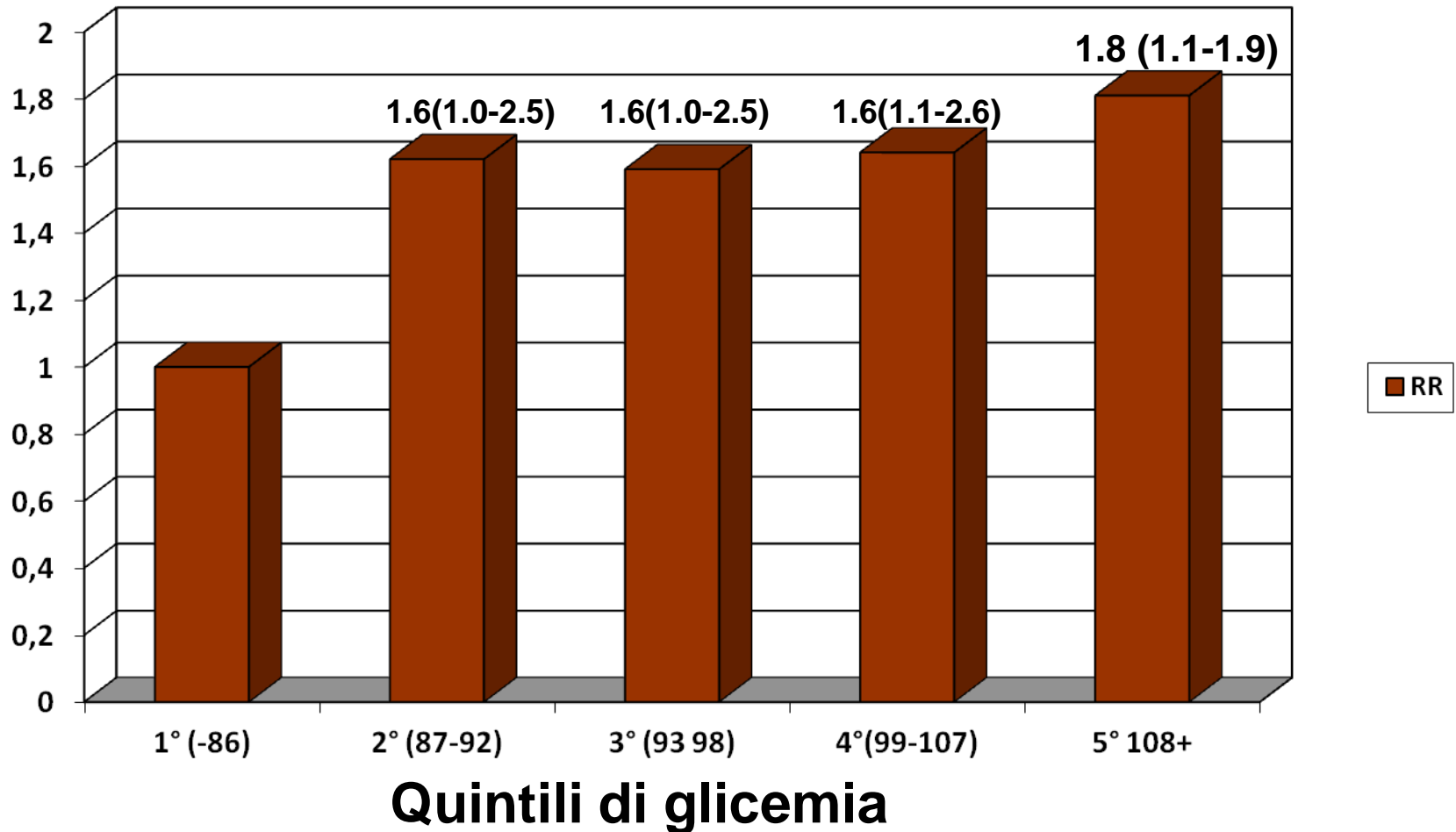
*P<0.05

Fully adjusted models

ORDET (Sieri, Berrino et al. 2011): 356 casi incidenti di cancro mammario
Rischio di cancro mammario in funzione della glicemia

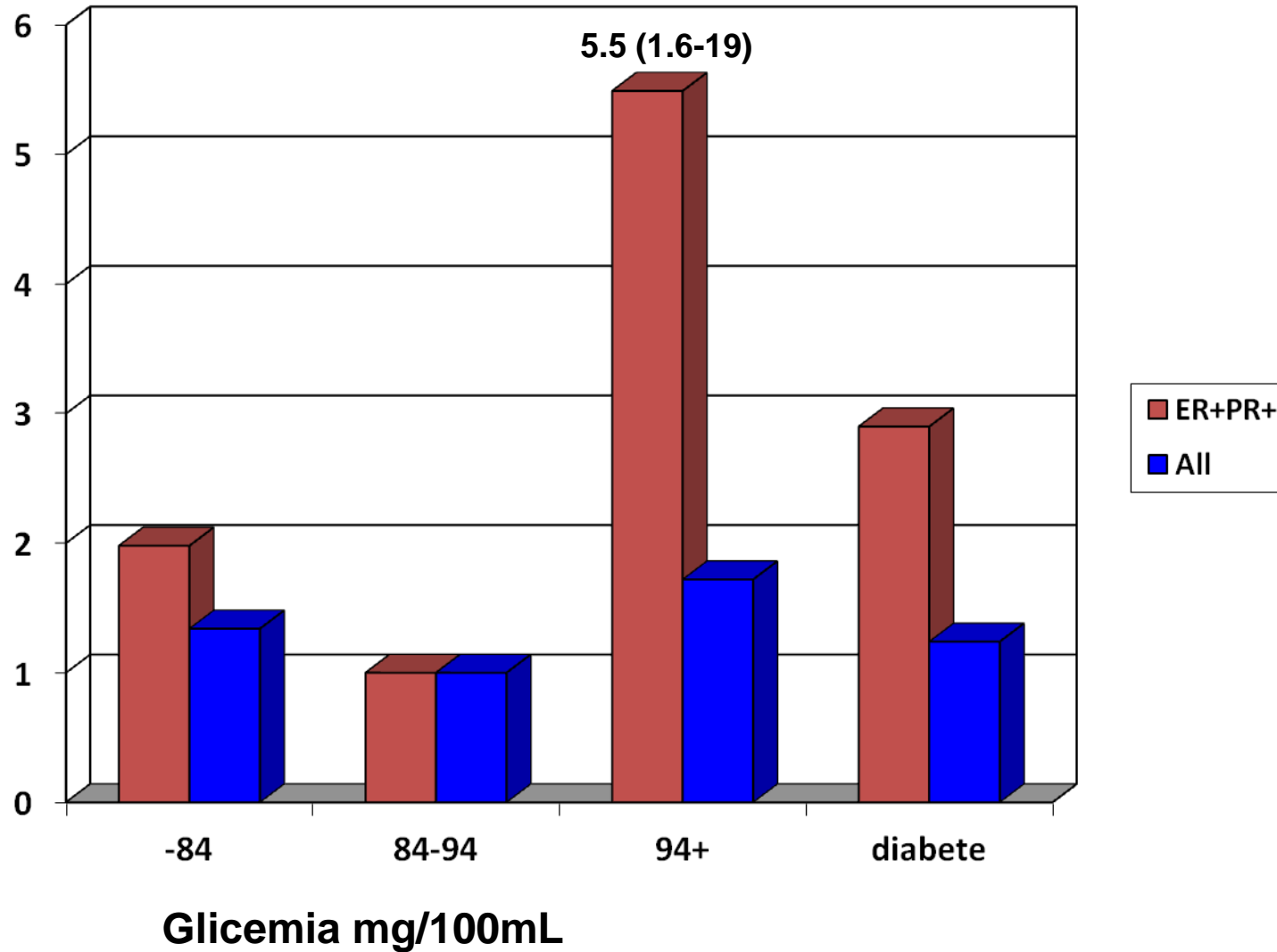
Rischio di recidiva del carcinoma mammario in funzione della concentrazione plasmatica di glucosio

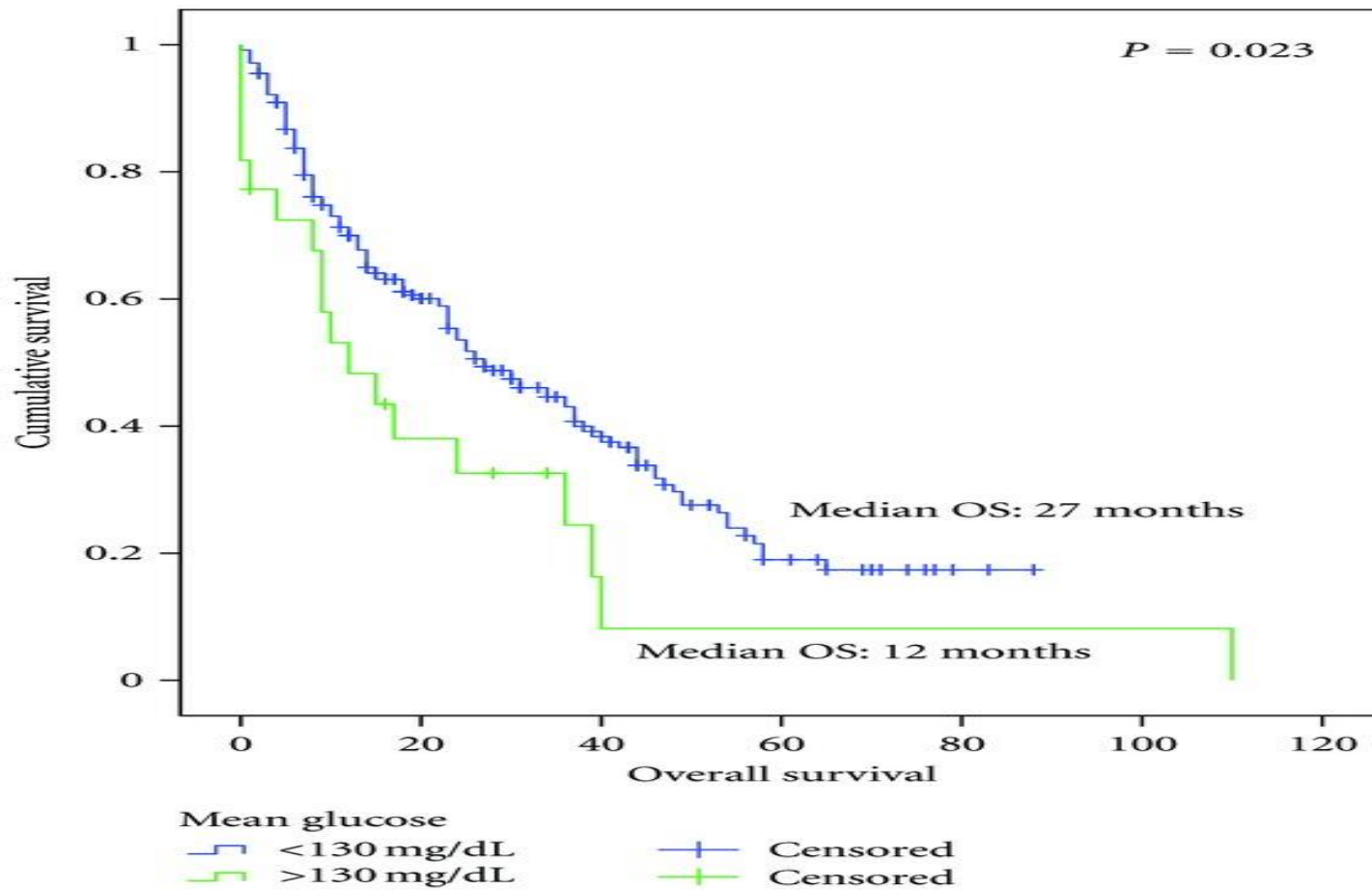
Contiero, Berrino 2013 BCRT (INT)



Rischio di recidiva del carcinoma mammario in funzione del livello di glicemia

(Minicozzi, Berrino, Sant 2013 Eur J Cancer)

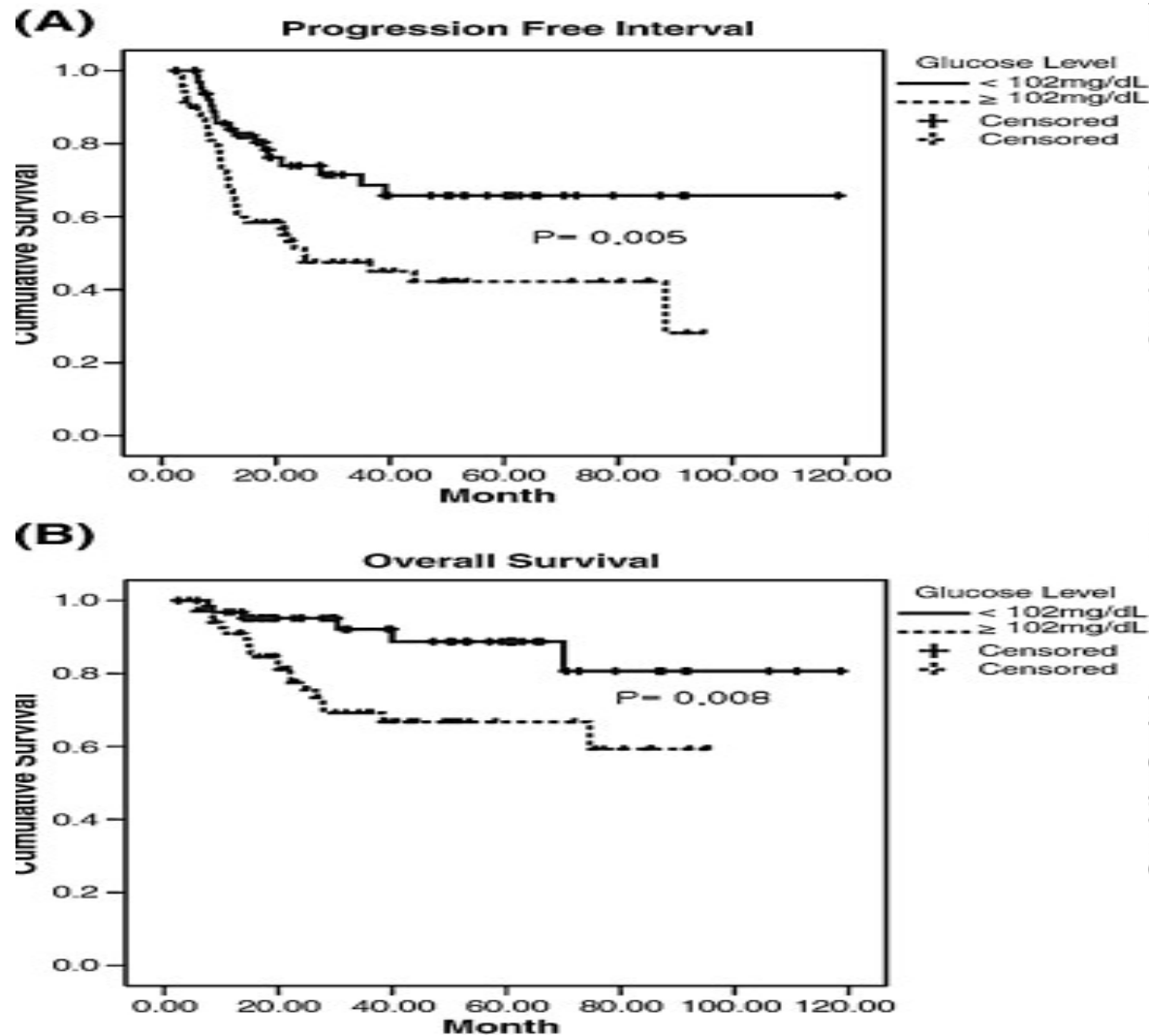




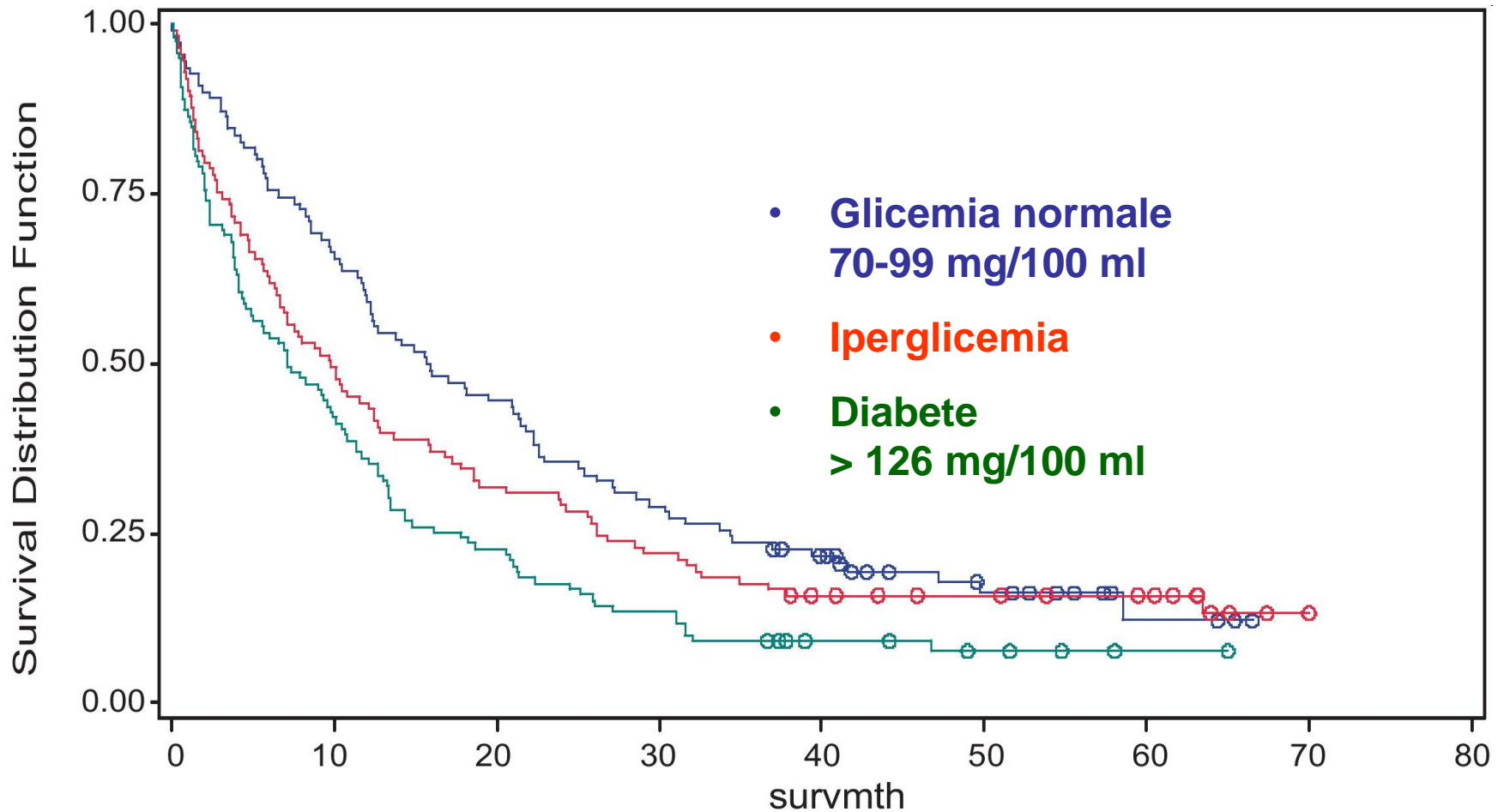
Overall survival since the diagnosis of advanced breast cancer according to mean glucose ≤ 130 ($n = 243$) versus glucose > 130 ($n = 22$).
 Villarreal-Garza C 2012 Exp Diabetes Res 2012:732027 (Mexico)

Glicemia e prognosi del carcinoma del collo dell'utero

Lee Y 2009 Gynecol Oncol 116:459



Glicemia e sopravvivenza dei tumori polmonari non a piccole cellule (Luo J 2012 Lung Cancer 76:242)



FRUIT & VEGETABLES AND SURVIVAL OF LUNG CANCER

Danish Prospective Health study

Rischi per consumi alti vs bassi

Vegetables 0.84 (0.59-1.21)

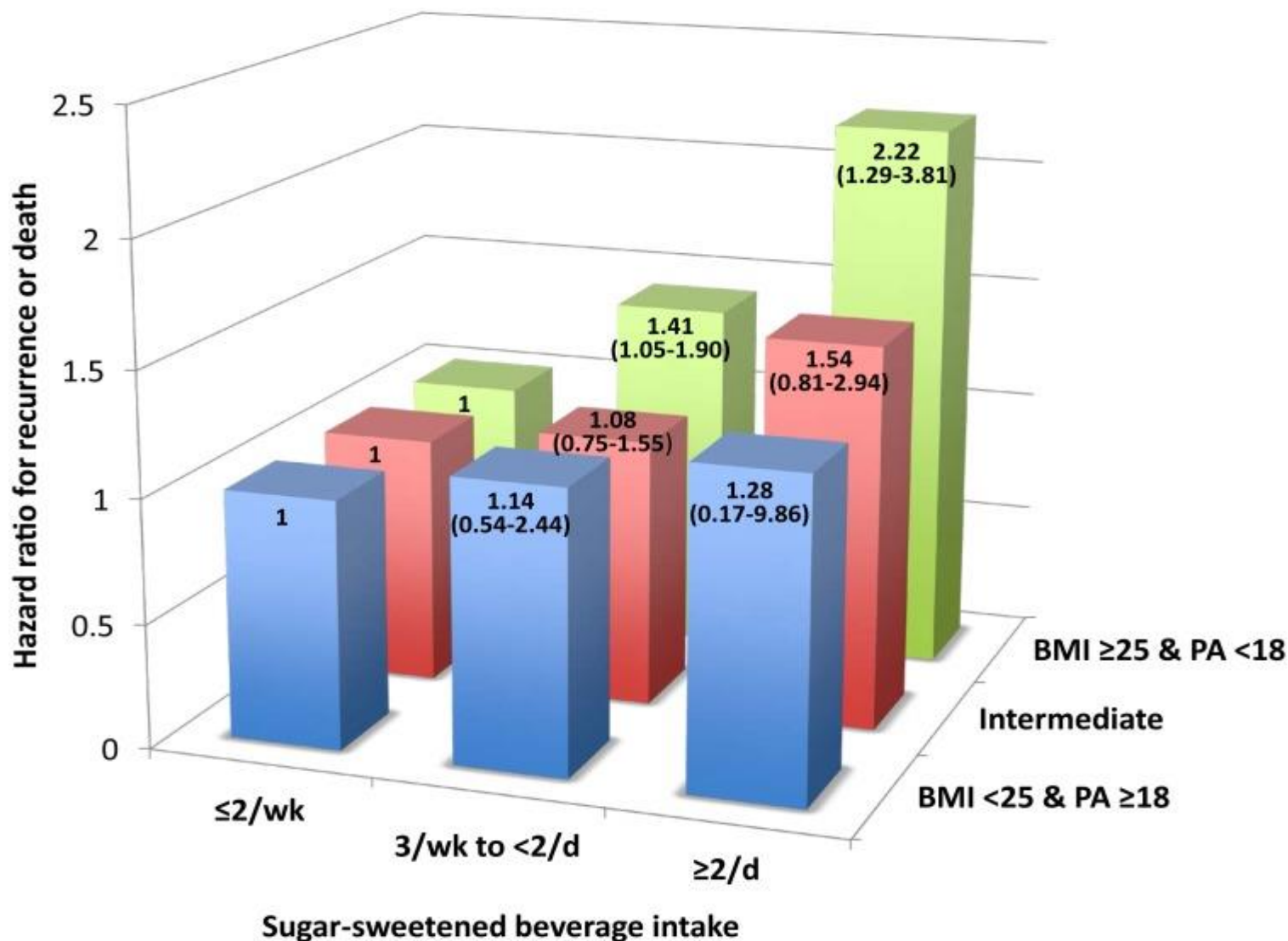
Fruit 0.81 (0.58-1.15)

Potatoes 1.51 (1.12-2.23)

For high vs low intake

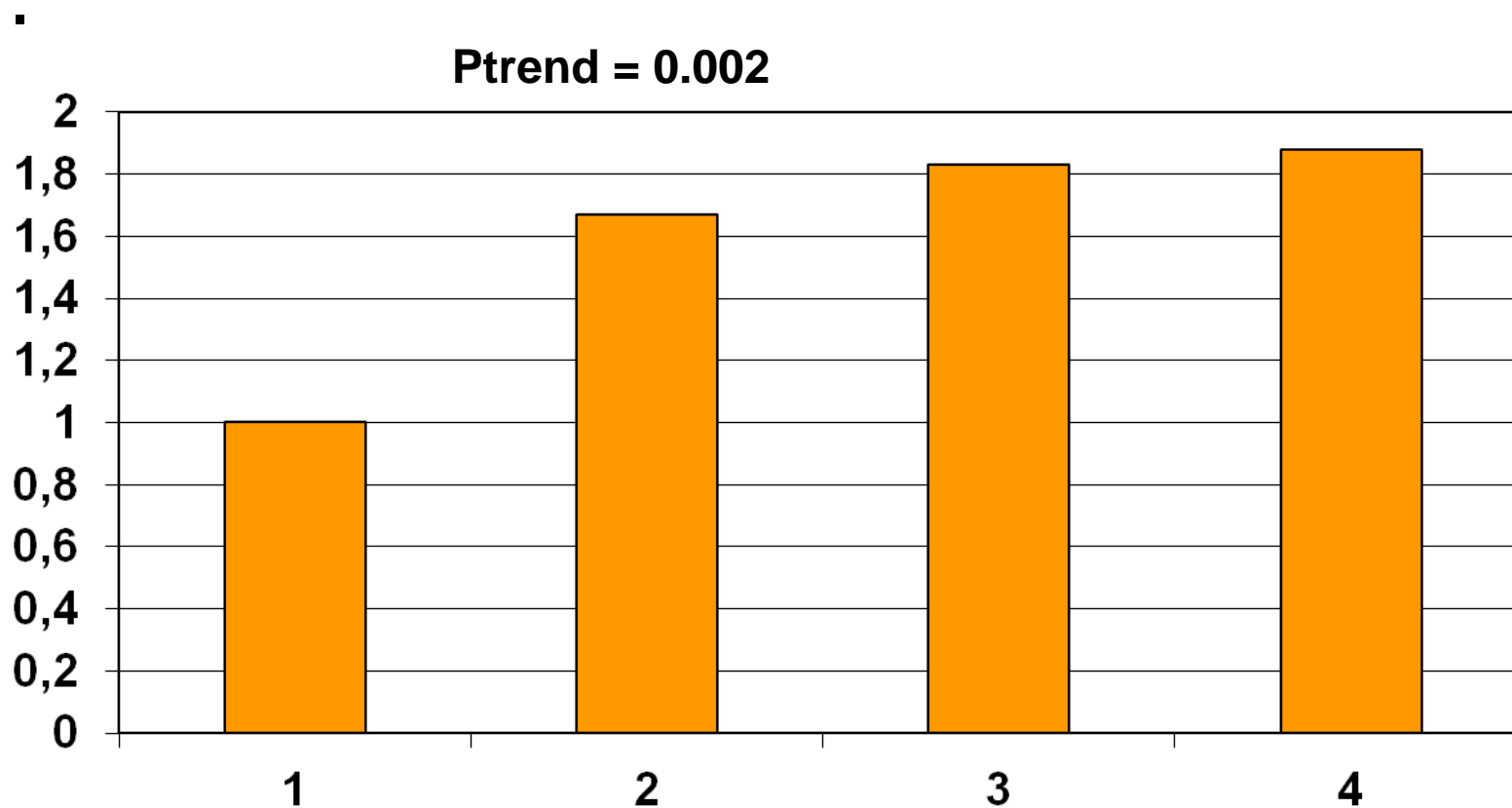
Cancro del colon nelle coorti di Harvard (Fuchs M 2014 PLoS)

Rischio di recidiva in funzione del consumo di *soft drink*



Bevande zuccherate e prognosi dei tumori delle alte vie aerodigestive

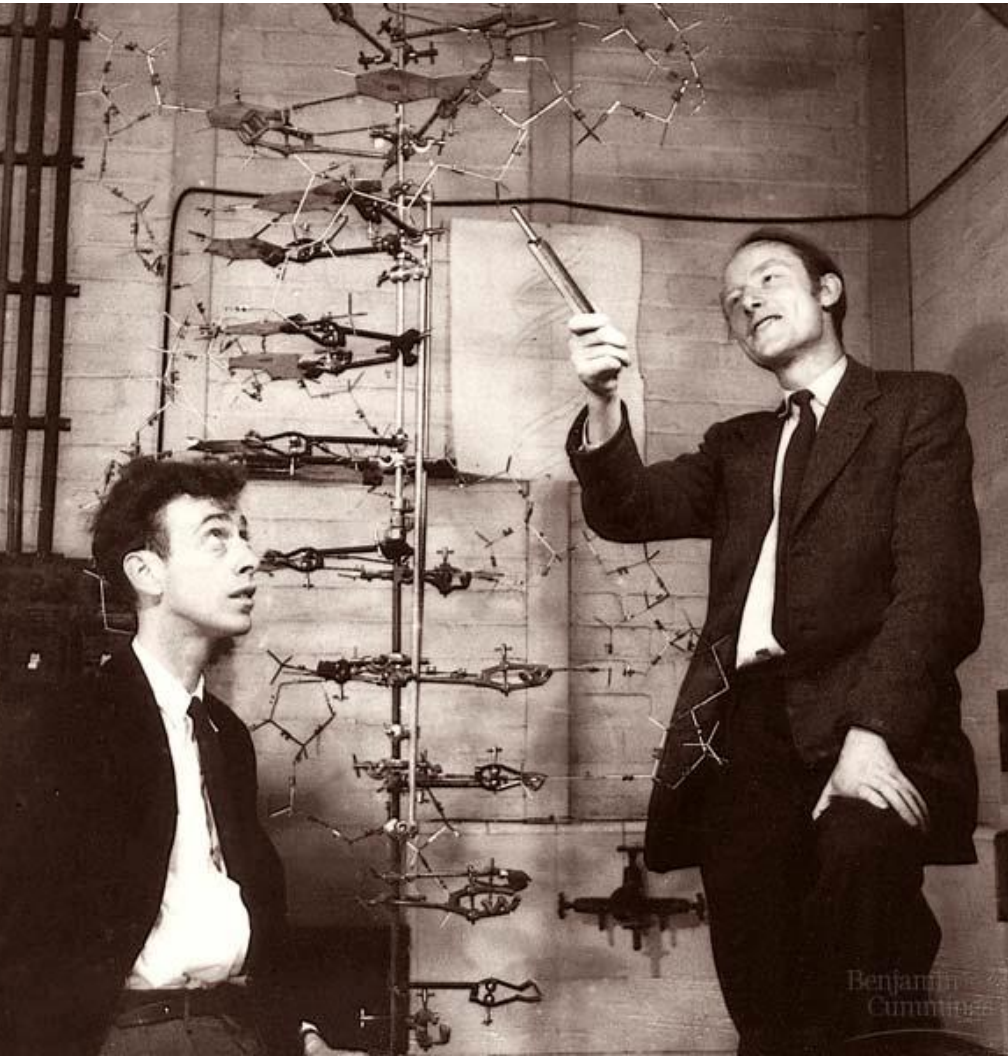
Miles FL 2016 CCC 27:1293 (UCLA)



Quartili di zucchero da soft drinks e succhi di frutta zuccherati

Elementare, Watson

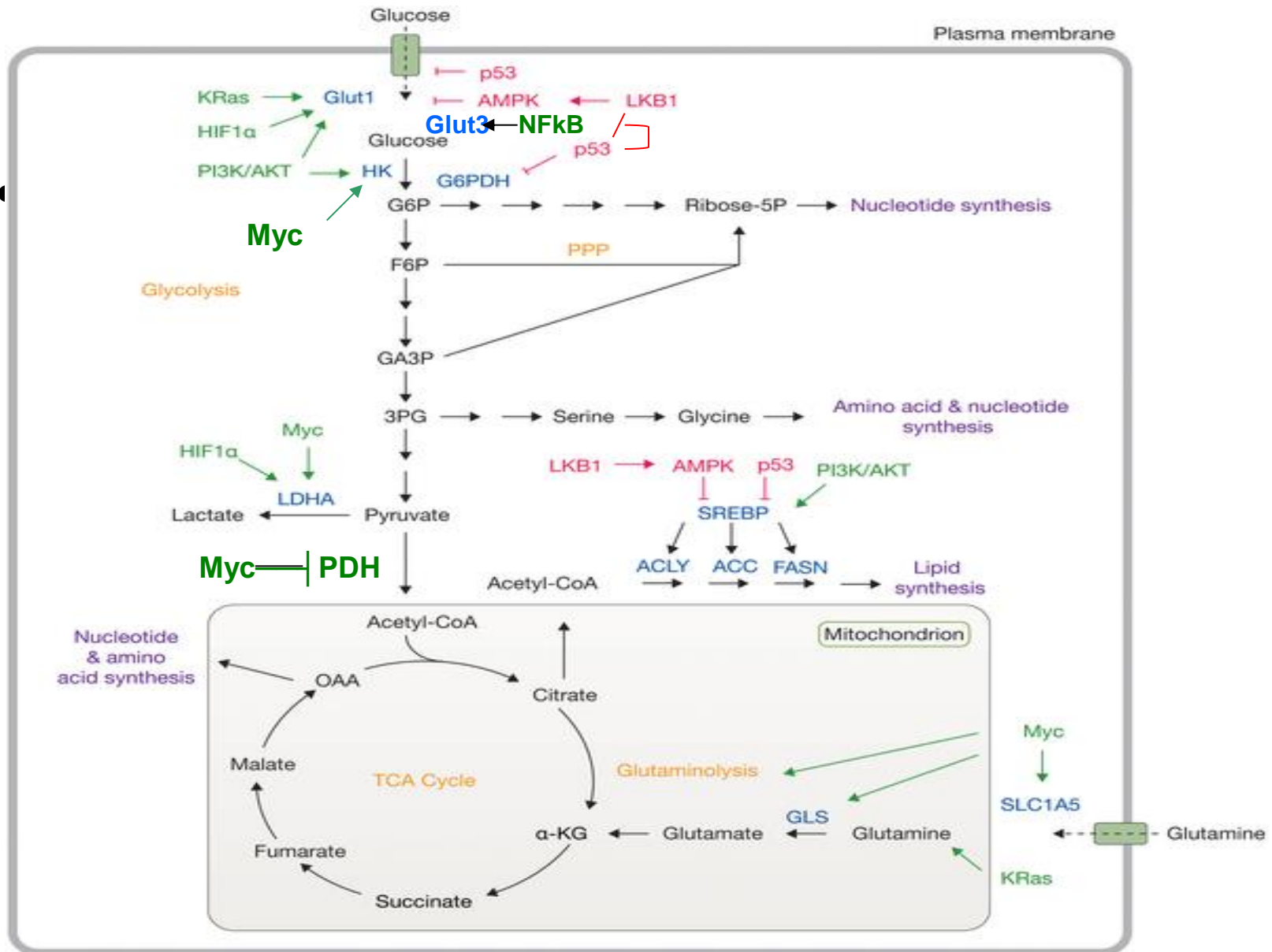
NOBEL 1962



NOBEL 1931

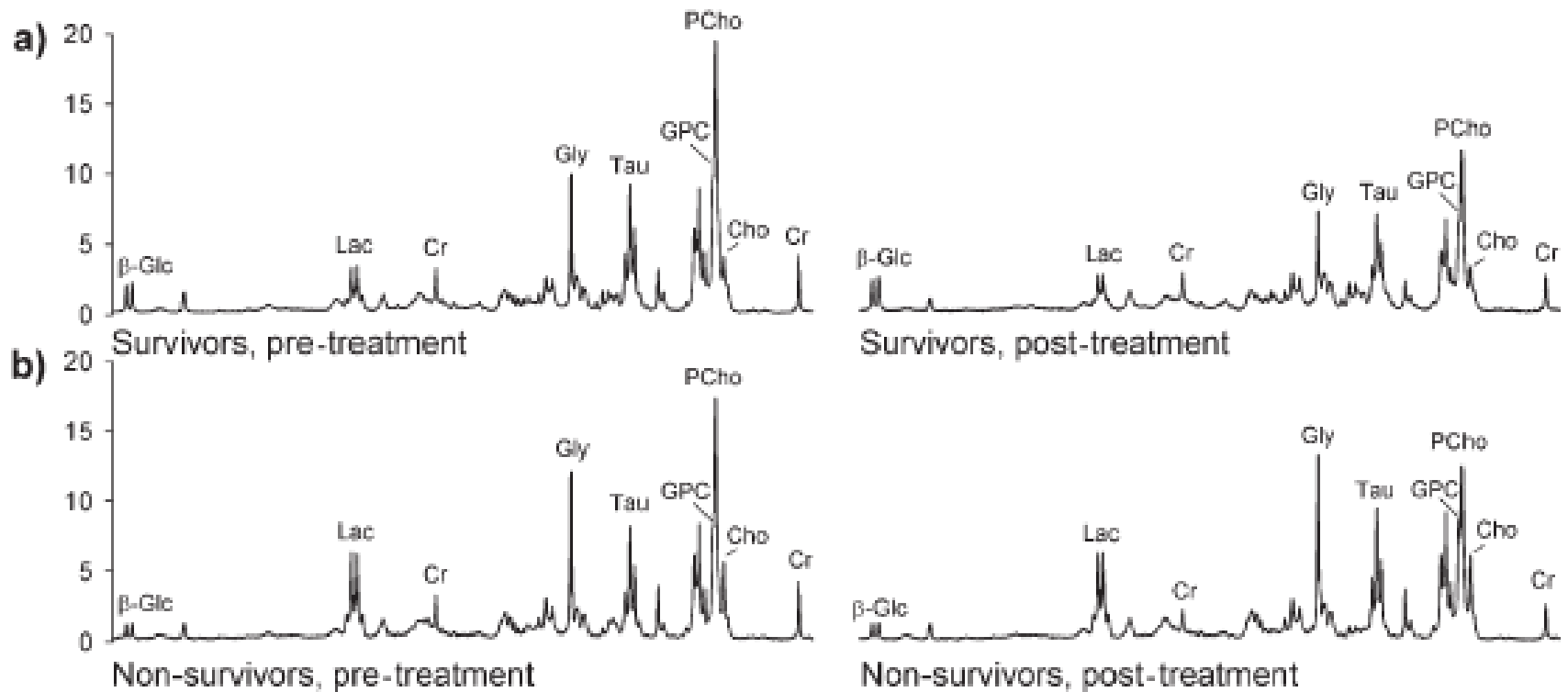


Boroughs LK DeBernardinis RJ 2015 Nat Cell Biol 17:351



Lattato

- Angiogenesi (via Monocarboxylate transporter MCT 1 > CXCL8 > migrazione delle cellule endoteliali)
- Angiogenesi (via sintesi di VEGF)
- Angiogenesi (via espressione di IL-8)
- Evasione dal sistema immunitario
- Stimolazione della motilità cellulare

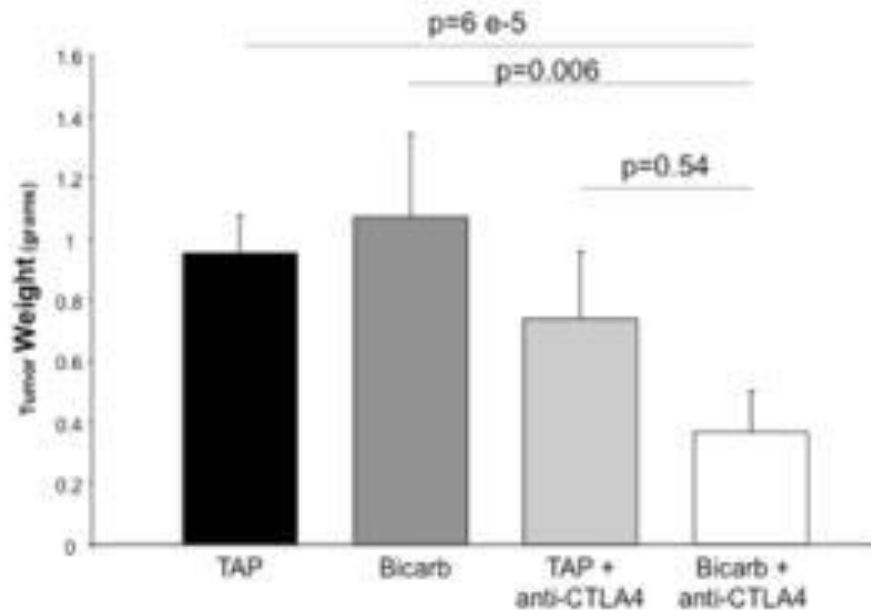


I tumori mammari a cattiva prognosi sono più ricchi di acido lattico

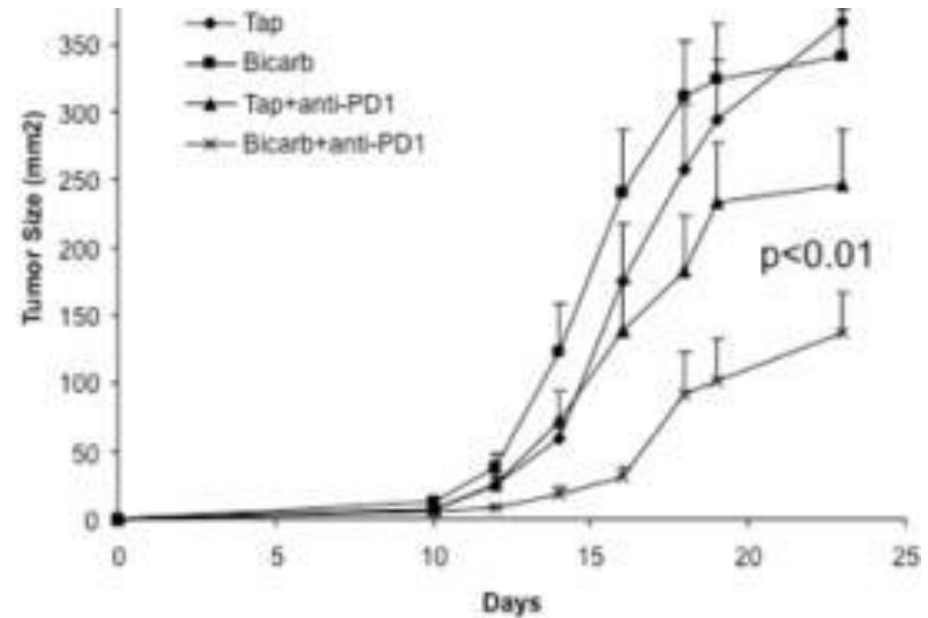
Cao MD 2012 [NMR Biomed.](#) 25:369 Predicting long-term survival and treatment response in breast cancer patients receiving neoadjuvant chemotherapy by MR metabolic profiling.

Buffer therapy enhances efficacy of anti-immune therapy in B16 melanoma

Pilon-Thomas S 2016 Cancer Res 76 1381



E

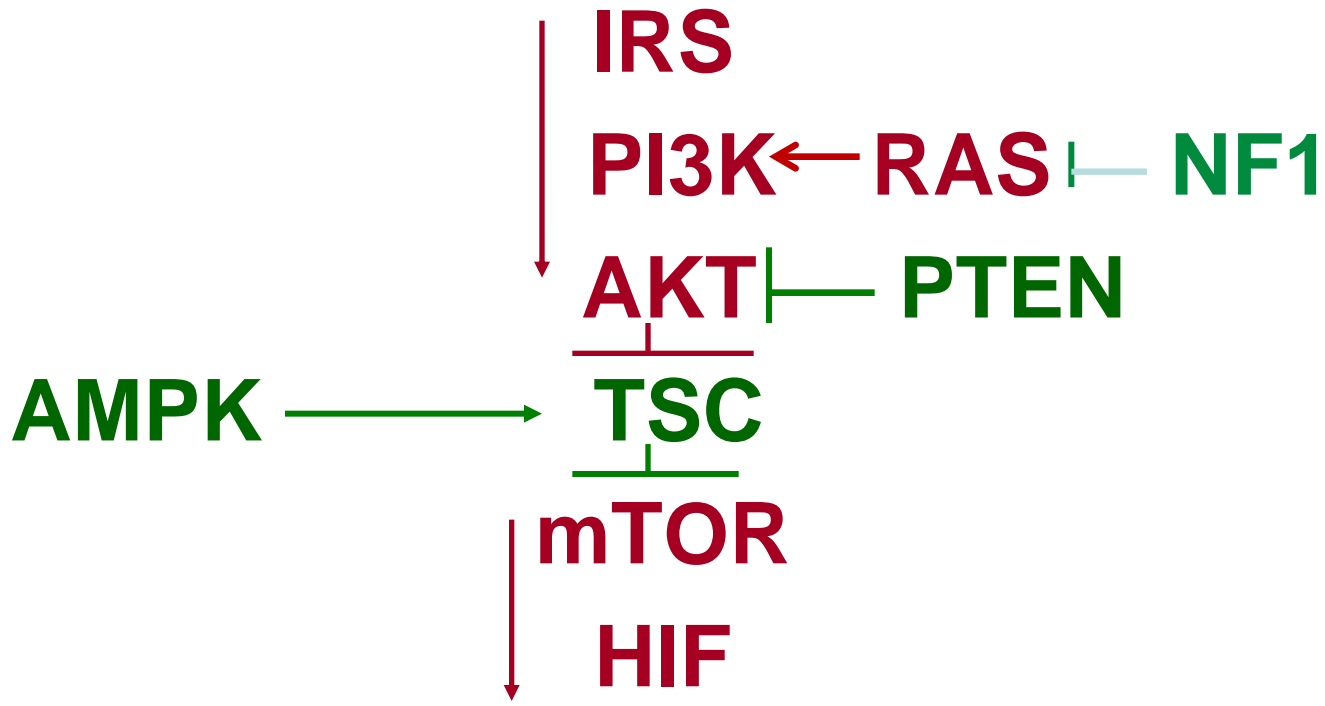


F

500

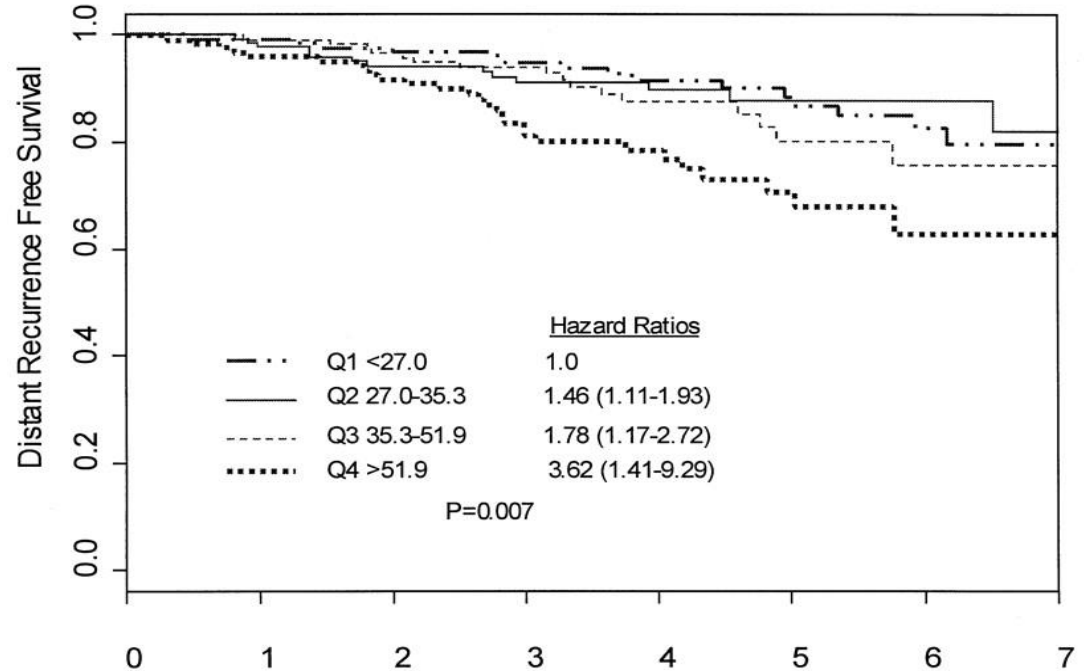
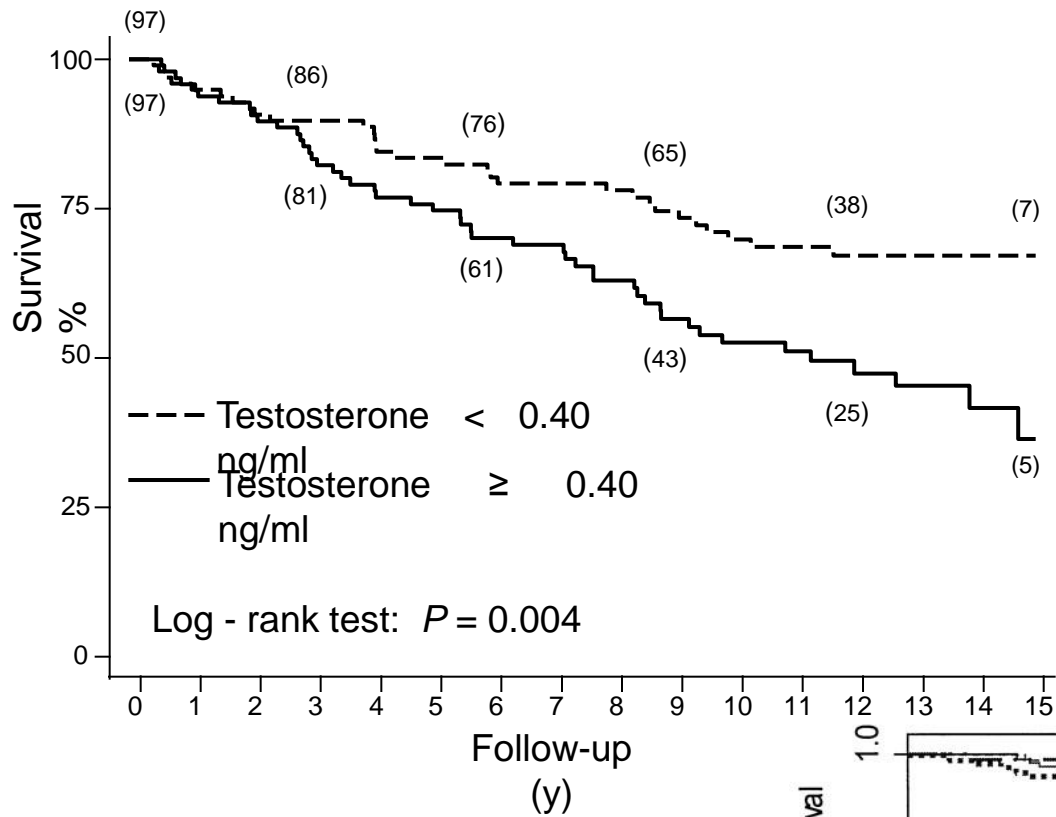
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Fattori di crescita
IR, IGF-1R, EGFR



Fattori di crescita

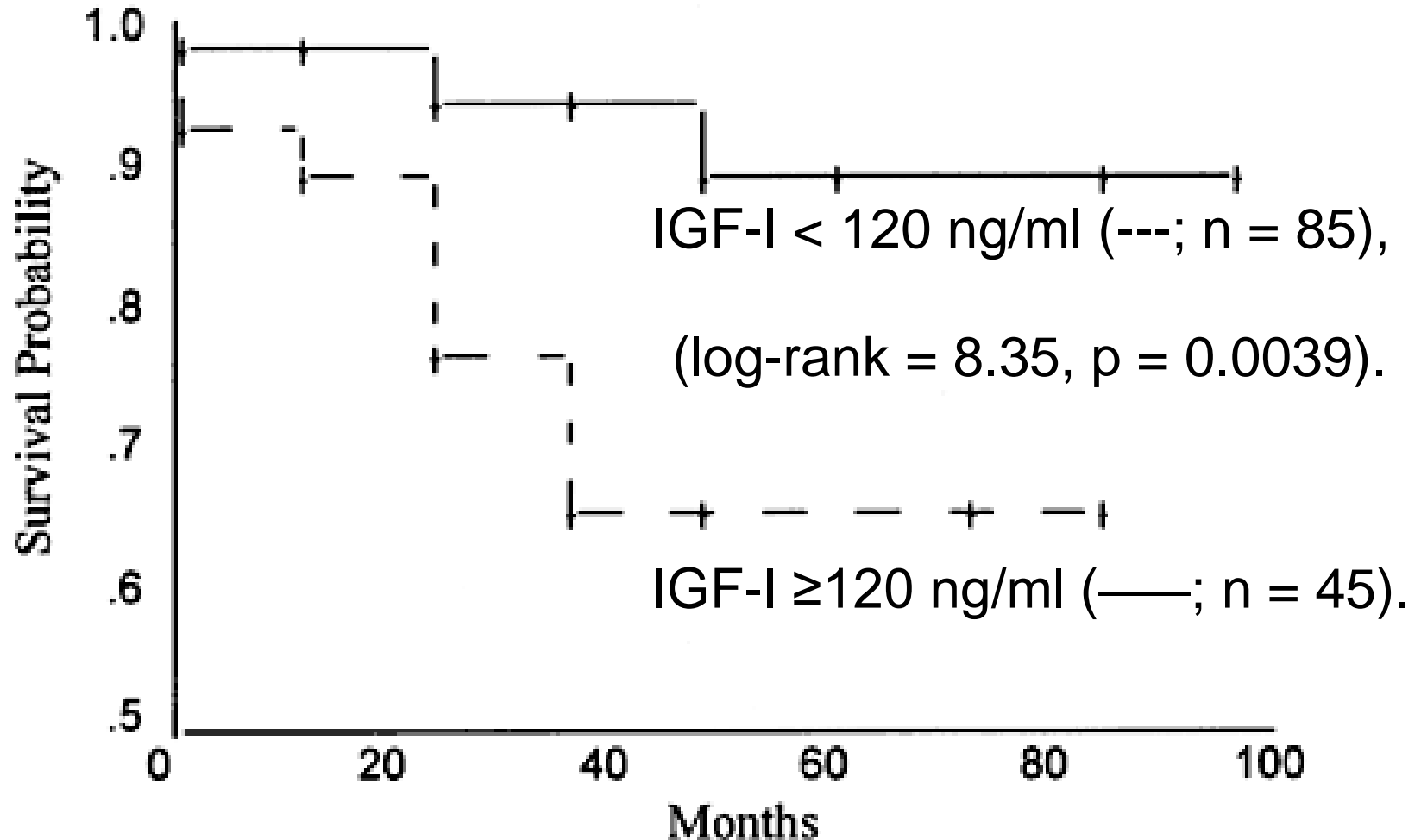
Micheli A JCO 2007 Testosterone



Goodwin P JCO 2002 Insulina

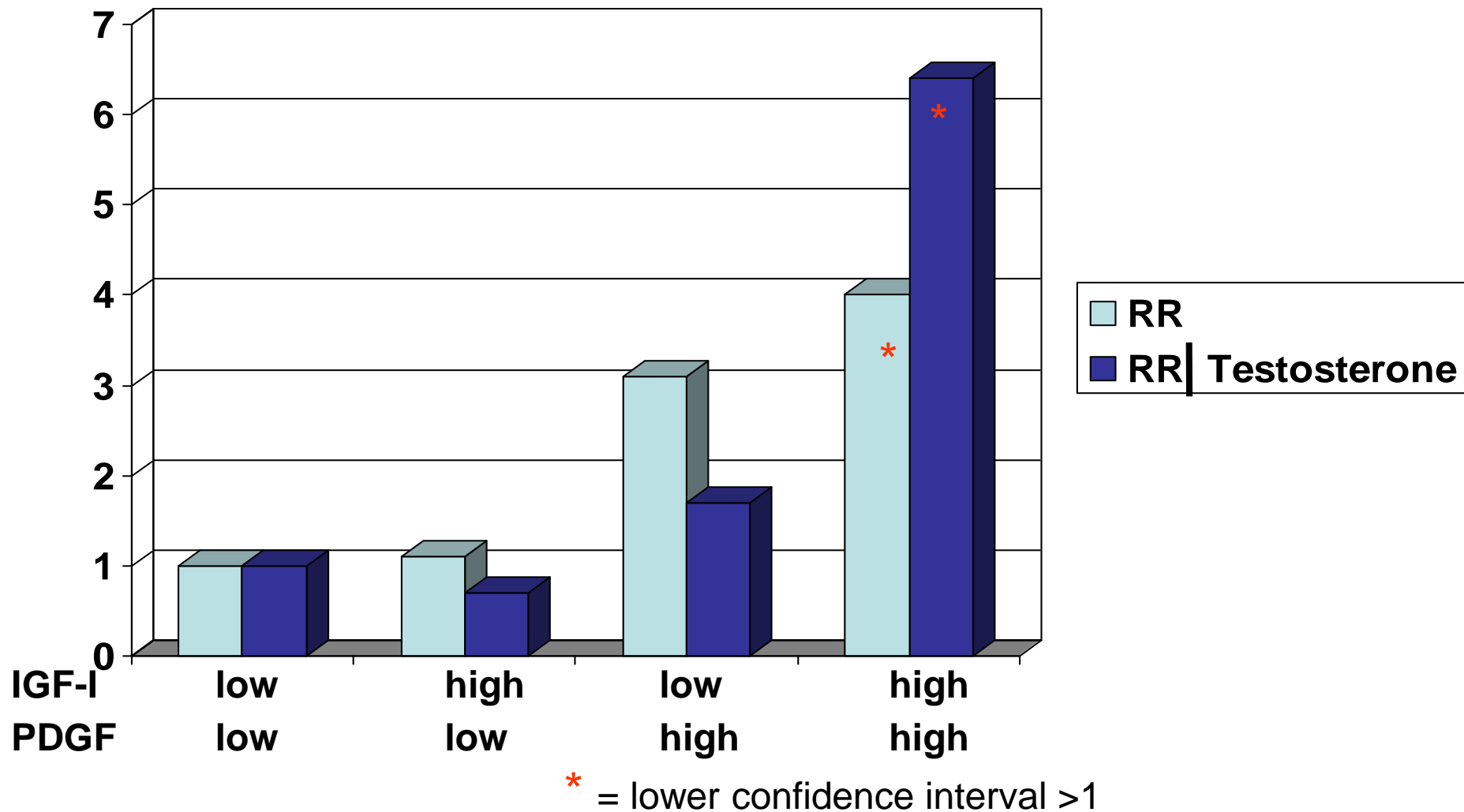
Prognosi del carcinoma mammario in funzione dei livelli sierici di IGF-I

VadgamaJV 1999 Oncology 57:330



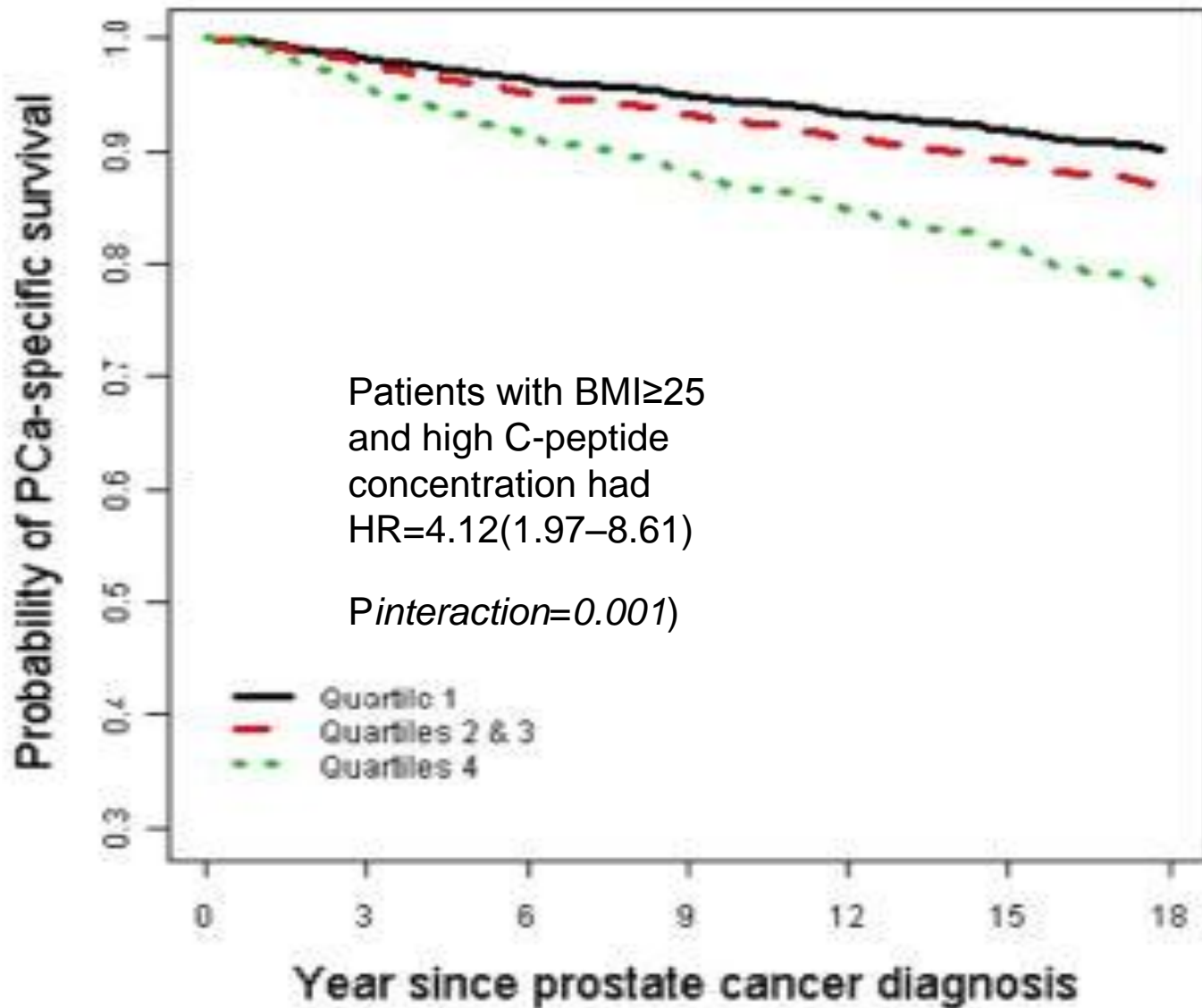
DIANA-2: Breast cancer recurrence risk by serum levels of PDGF and IGF-I

Pasanisi et al. 2008 CEBP 17:1719



D.

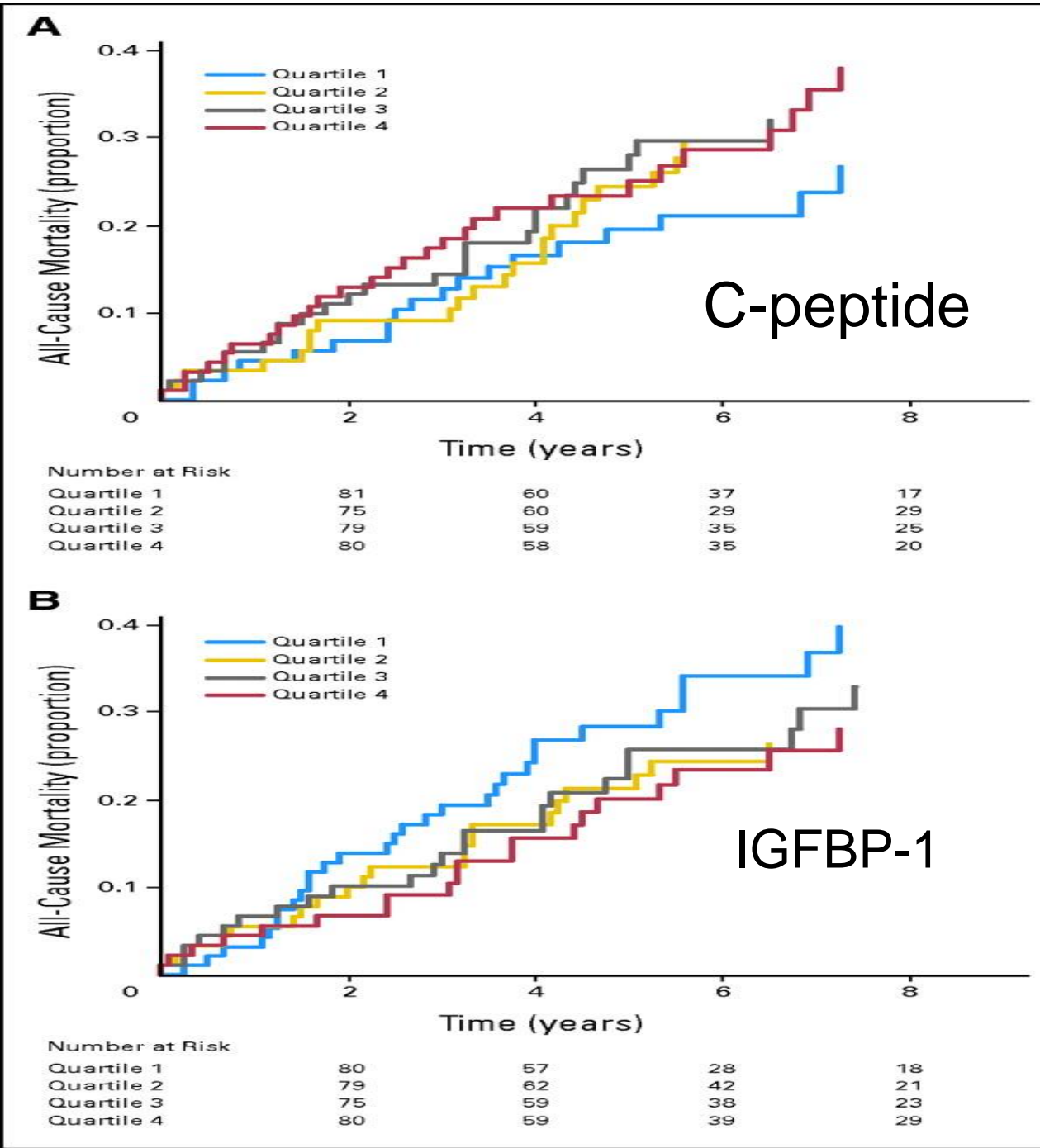
Baseline plasma C-peptide levels



Ma J et al. 2008 Lancet Oncol 9:1039

281 prostate cancer deaths /2546 patients

Mortalità cumulativa dei pazienti con cancro del colon in funzione della concentrazione di
(A) C-peptide &
(B) IGFBP-1



Wolpin, Meyerhardt et al.
JCO 2009, 27:176

Schirripa M 2017 Int J Cancer 141:383

Chang CF 2013 Ann Surg Oncol 20:2446

Muendlein A 2013 J Cancer Res Clin Oncol 139:491

Un raro SNP rs2946834
del gene IGF-I è associato a
cattiva prognosi dei tumori di
colon, prostata e mammella

LUNG CANCER

Fu S-I 2013 J Huazhong Univ Sci Technol 33 (2)

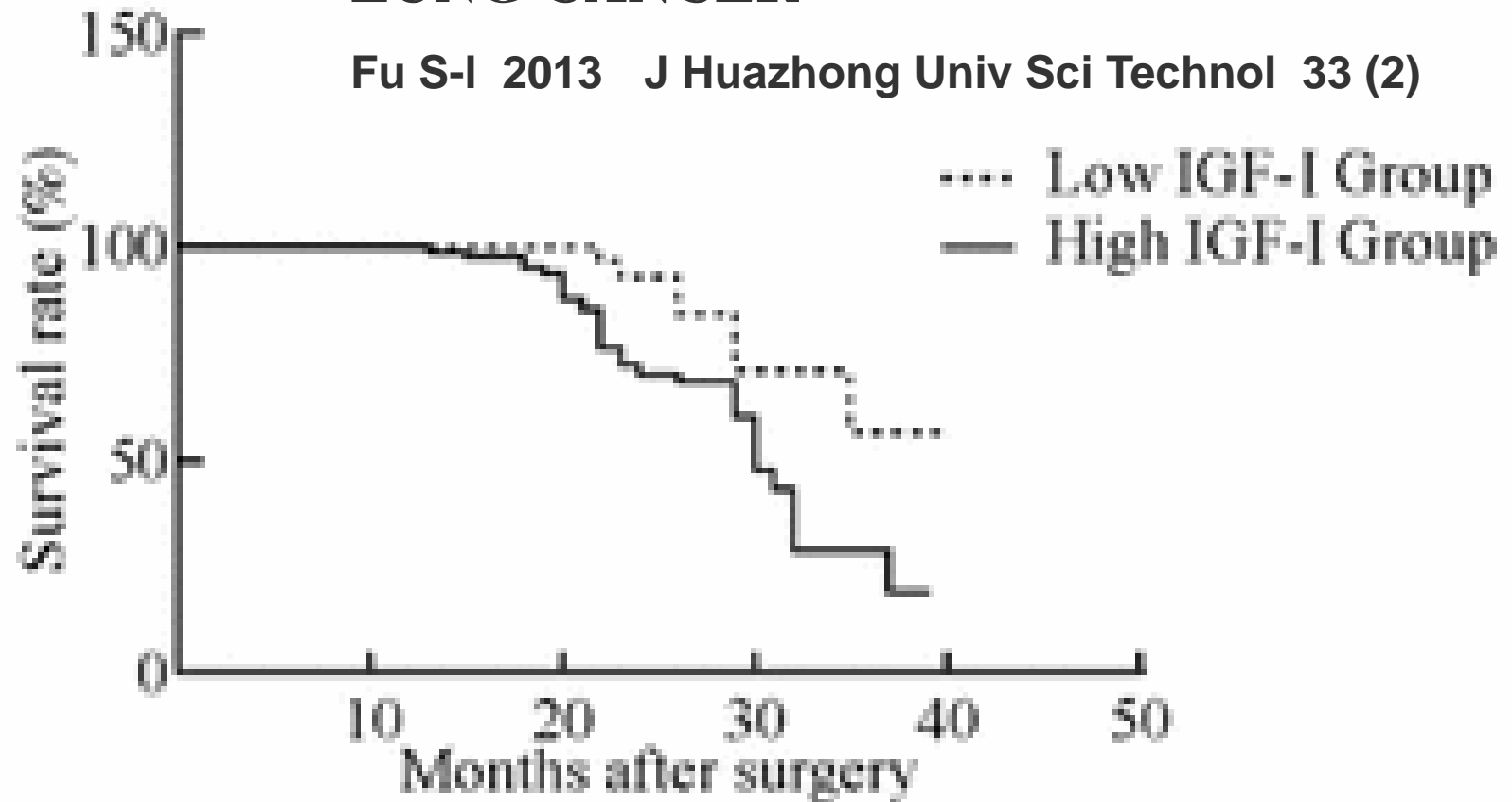
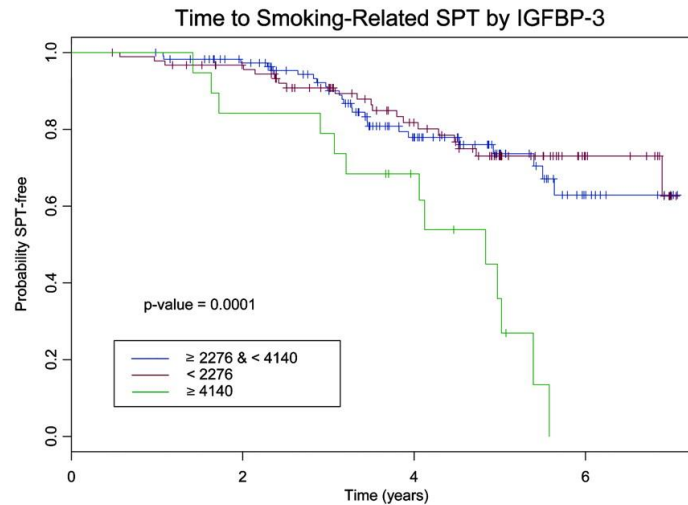
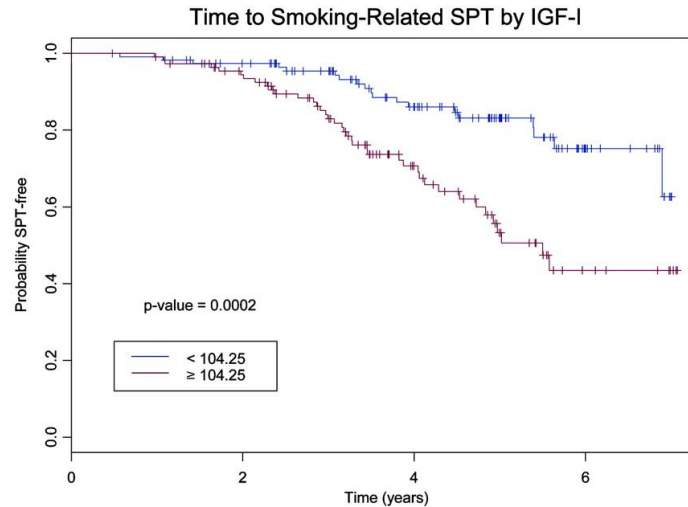


Fig. 2 Prognostic significance of high and low levels of preoperative IGF- I concentration
Kaplan-Meier analysis revealed that the survival rate of patients with high levels of serum IGF- I was significantly lower ($P=0.0171$).

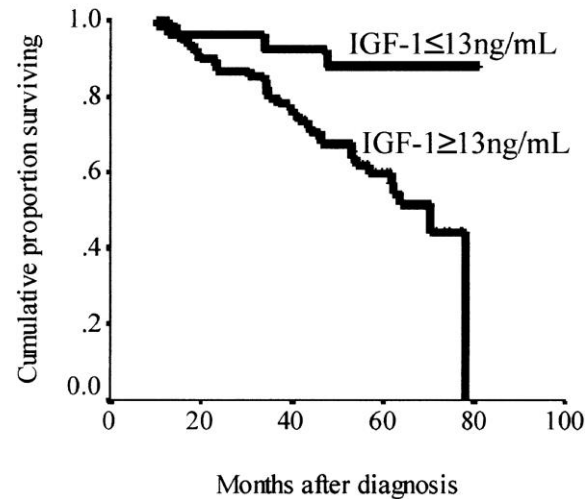
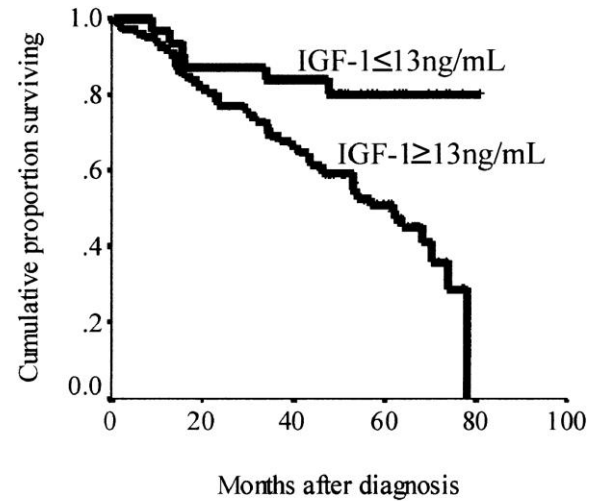
Head and neck Second Primary Tumor-free survival curves: by IGF-I and IGFBP-3.



Xifeng Wu et al. Clin Cancer Res 2004;10:3988-3995

Kaplan-Meier survival plots for patients with MM. The curves are separated by IGF-1 levels: “low” IGF-1 (25th percentile, < 13 nM) compared to remaining patients (IGF-1 ≥ 13 nM).

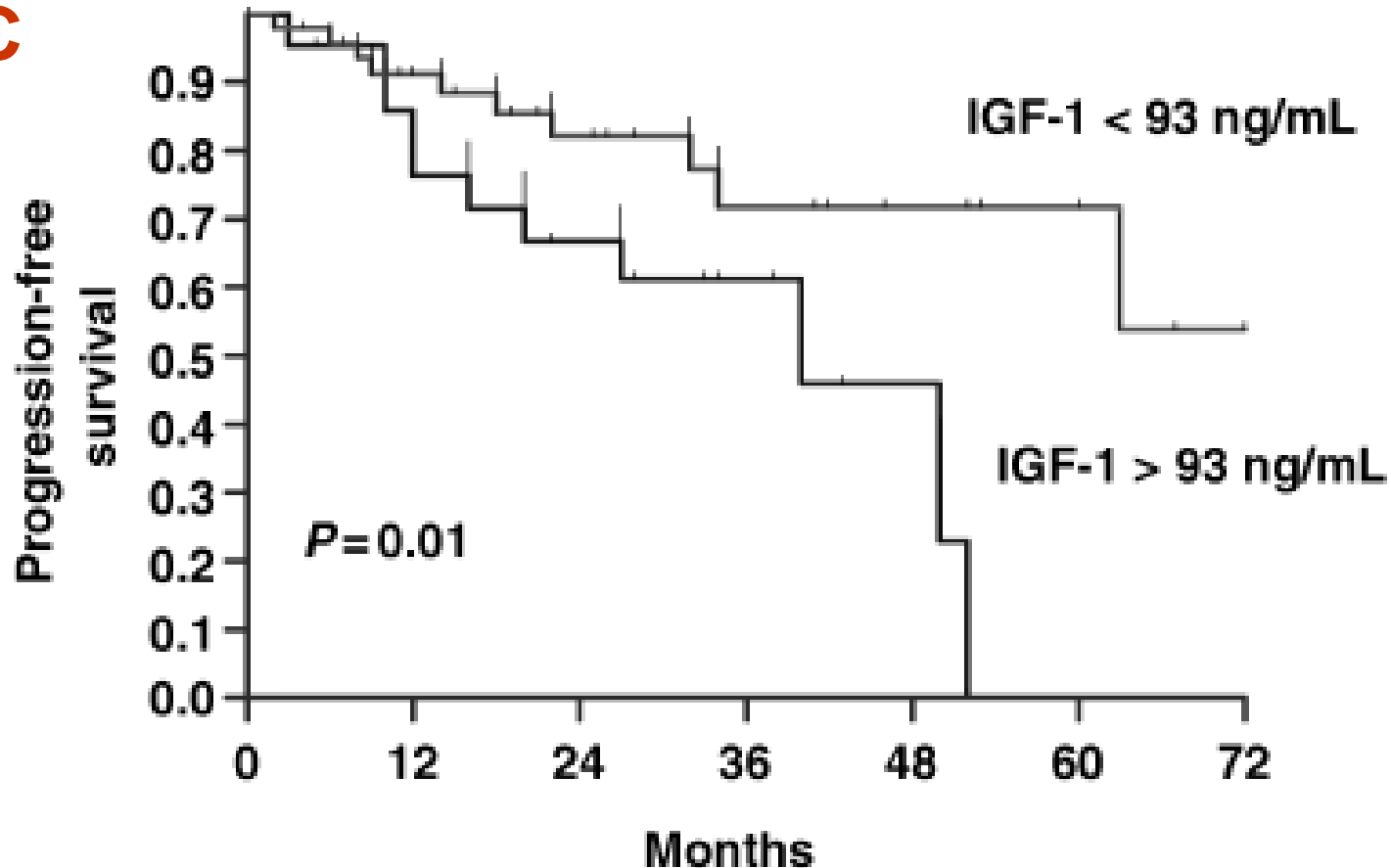
MIELOMA MULTIPLO



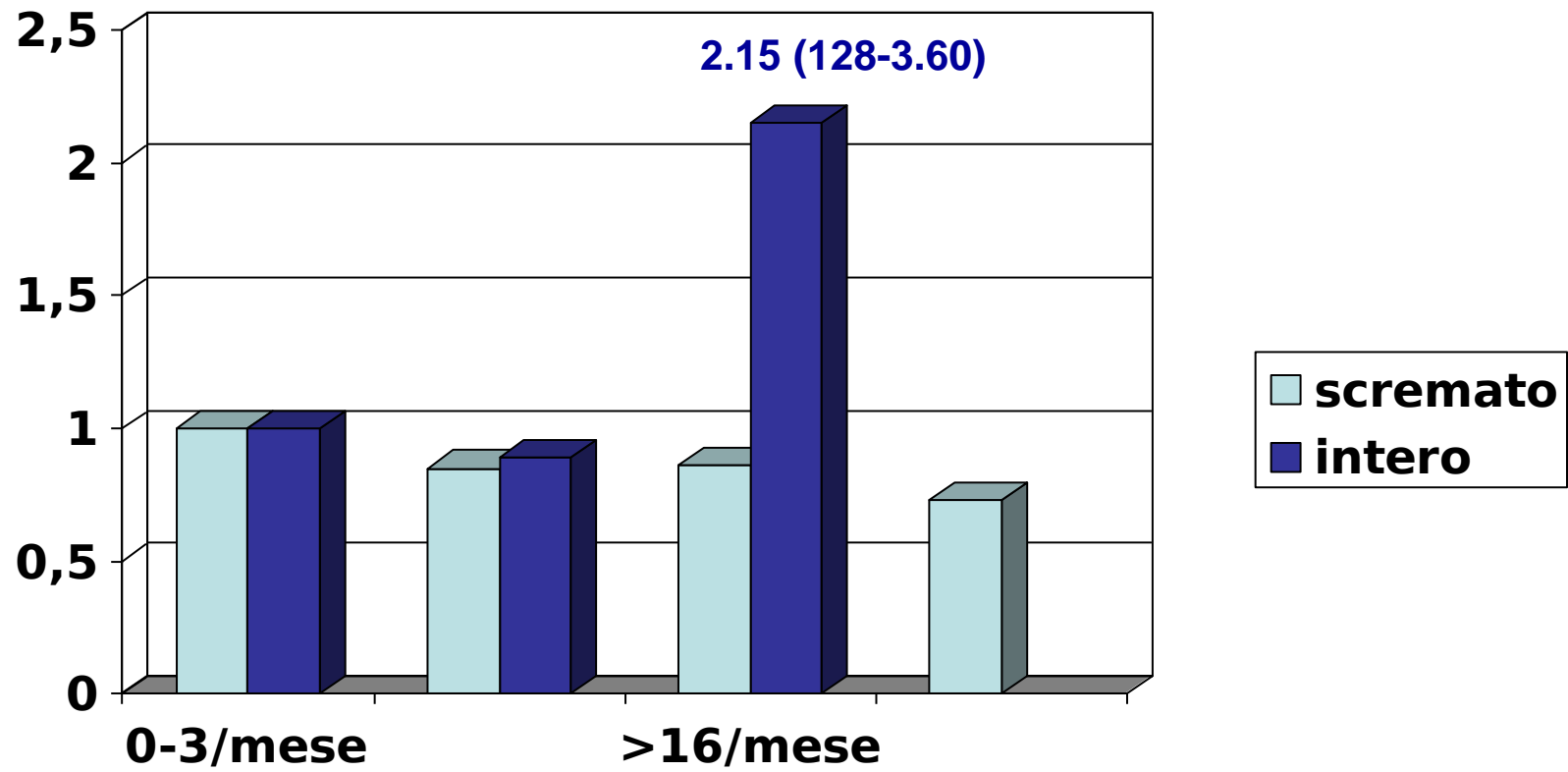
Therese Standal et al. Blood 2002;100:3925-3929

Serum insulin-like growth factor is not elevated in patients with early B-cell chronic lymphocytic leukemia but is still a prognostic factor for disease progression

LLC



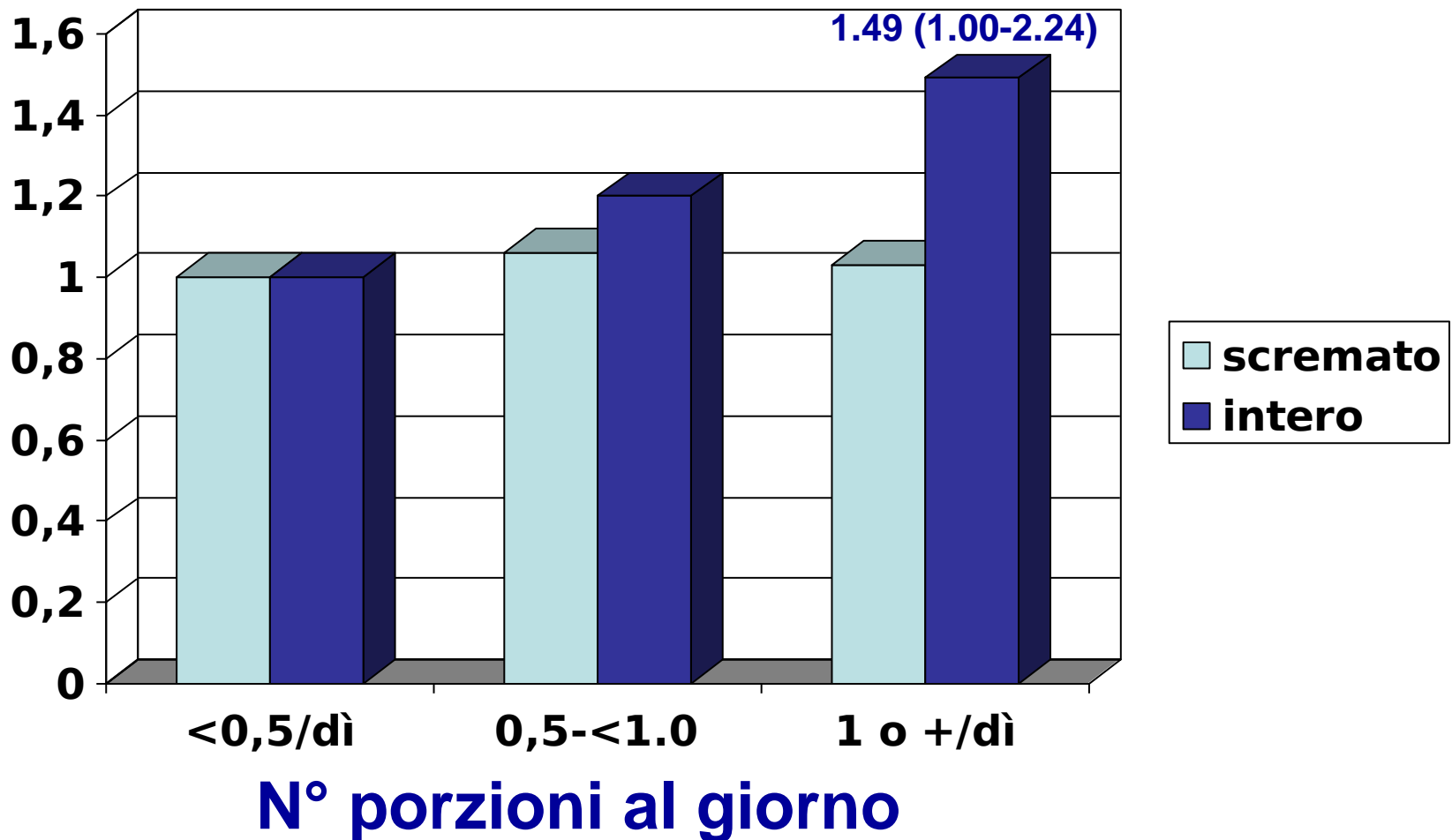
Letalità del cancro prostatico nei pazienti che consumano latte (PetterssonA, Giovannucci E 2012 CEBP 21:428, nessuna relazione con grassi saturi totali)

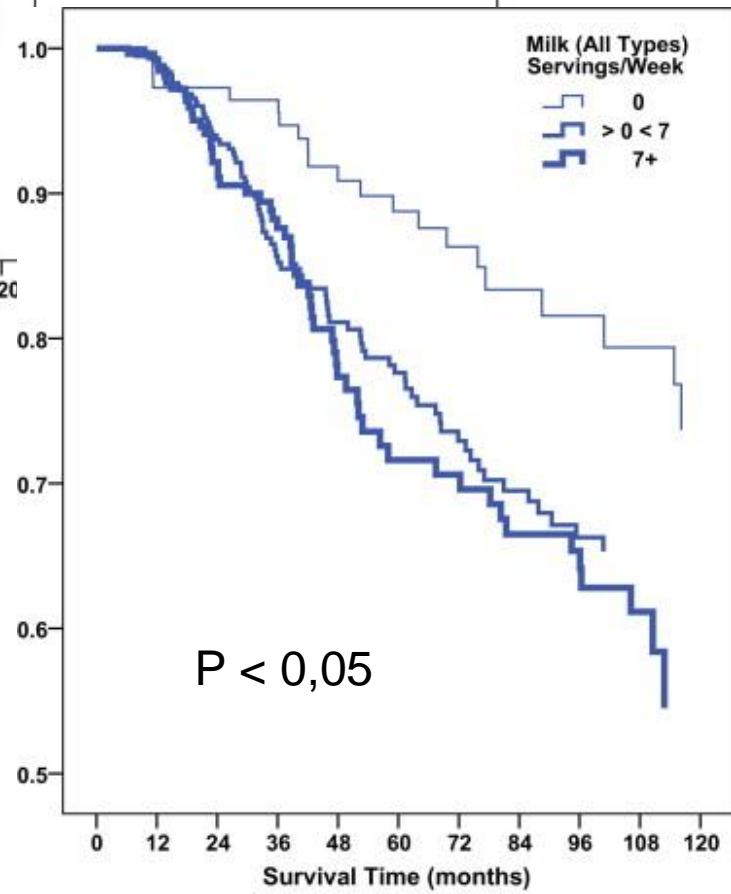
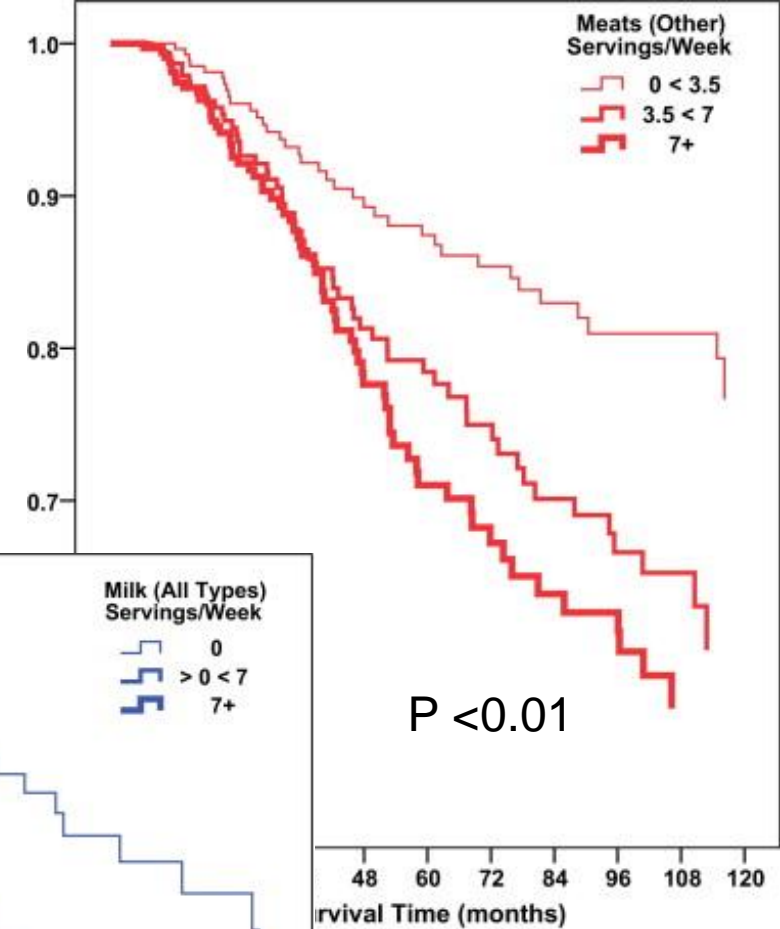
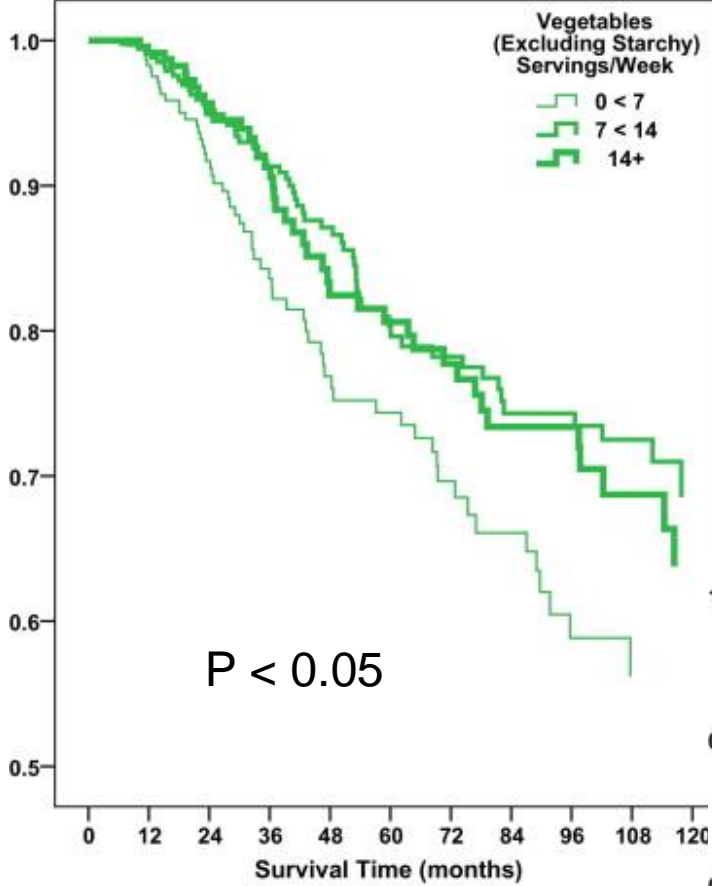


N° porzioni al giorno

Letalità del cancro mammario nelle pazienti che consumano latte

(Kroenke C
2013 JNCI 105:16, nessuna relazione con
grassi saturi totali)





Prediagnostic food pattern and survival from ovarian cancer

Dolecek 2010
JADA 110:369

Tumors: wounds that do not heal

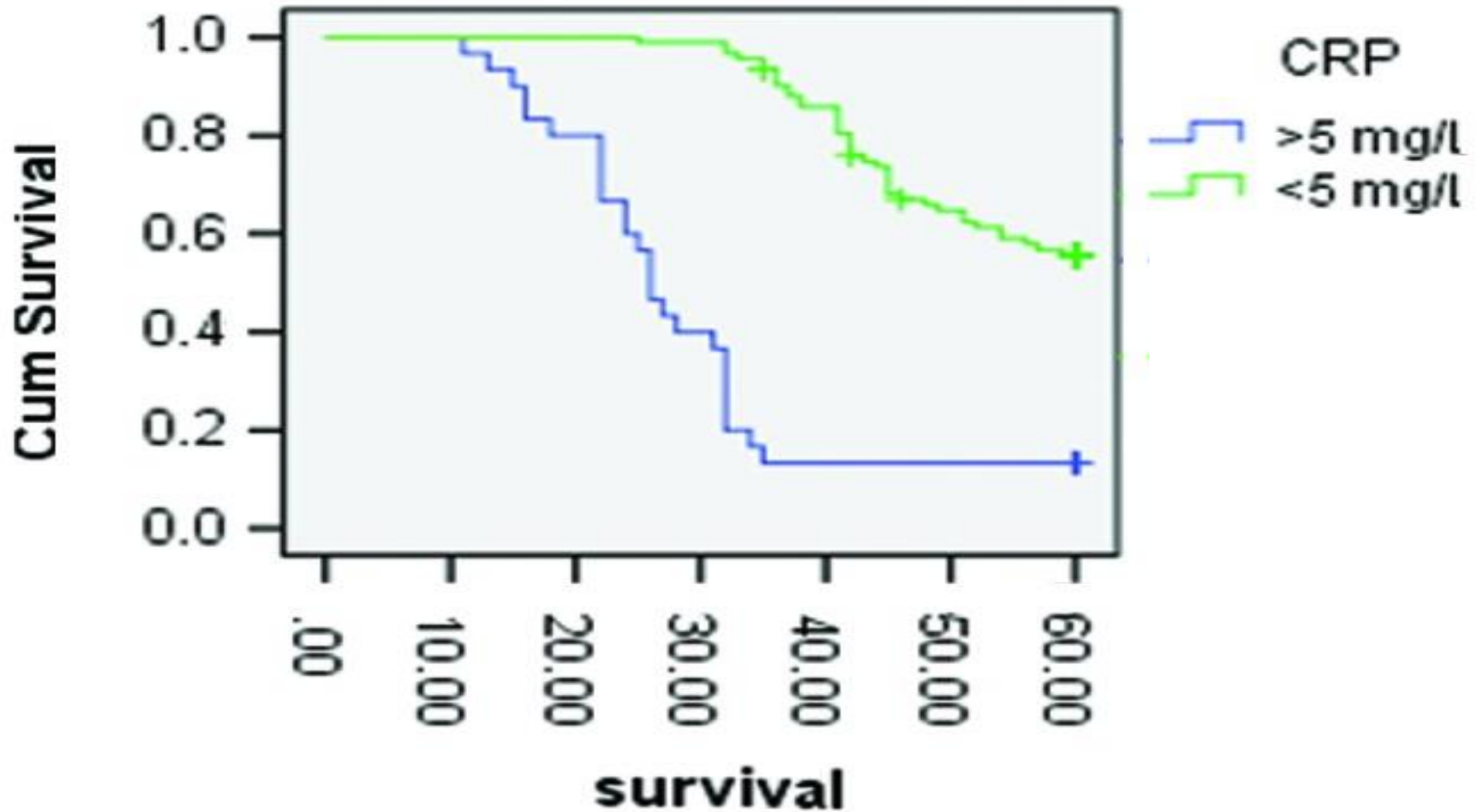
Dvorak HF 1986 NEJM 315:1650

Cancer as an overhealing wound

Schäfer M & Werner S 2008 Nat Rev Mol Cell Biol 9:628

- Per acquisire i caratteri tumorali una cellula deve riattivare i programmi normalmente attivi durante la vita embrionale e durante la guarigione delle ferite:
 - proliferazione
 - migrazione / invasione
 - angiogenesi
 - soppressione dell'inibizione da contatto
- senza però riattivare i programmi morfogenetici differenzianti (vedi resistenza al cancro di coda e arti di anfibi)

Lin M 2013 Exp Ther Med 6:1369
Colorectal cancer survival



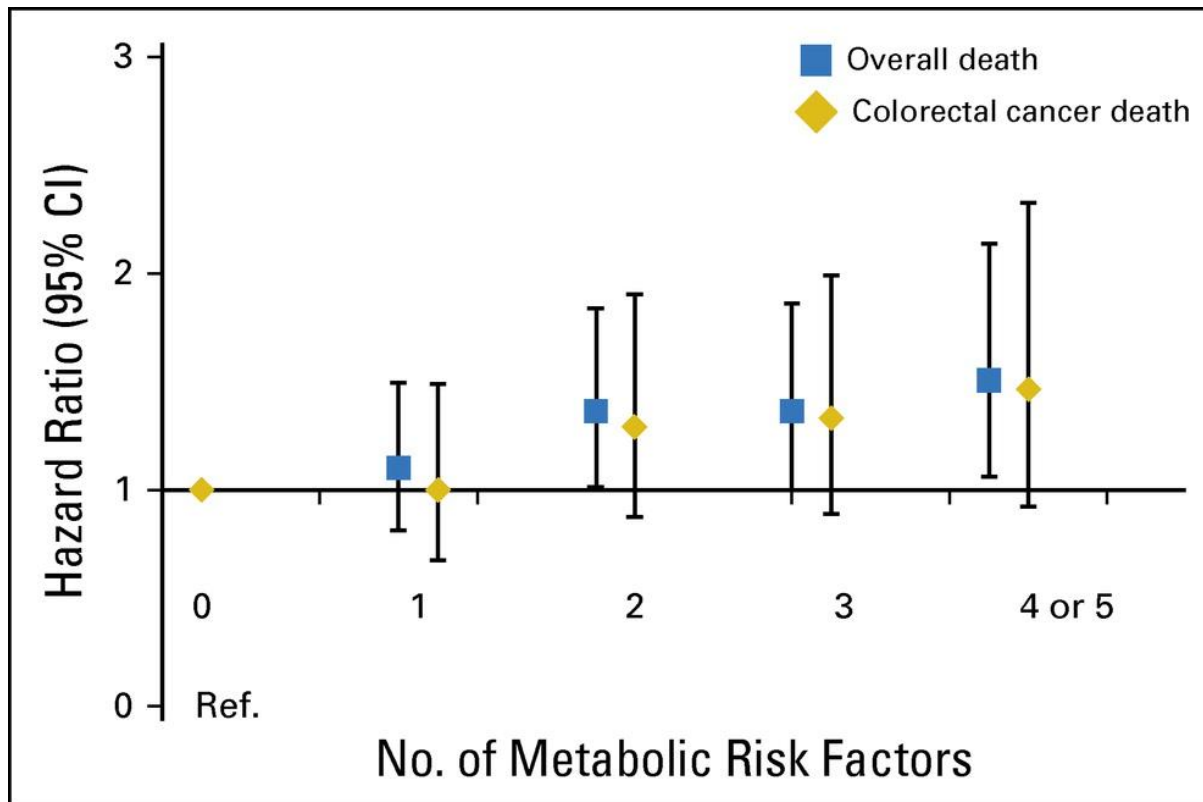
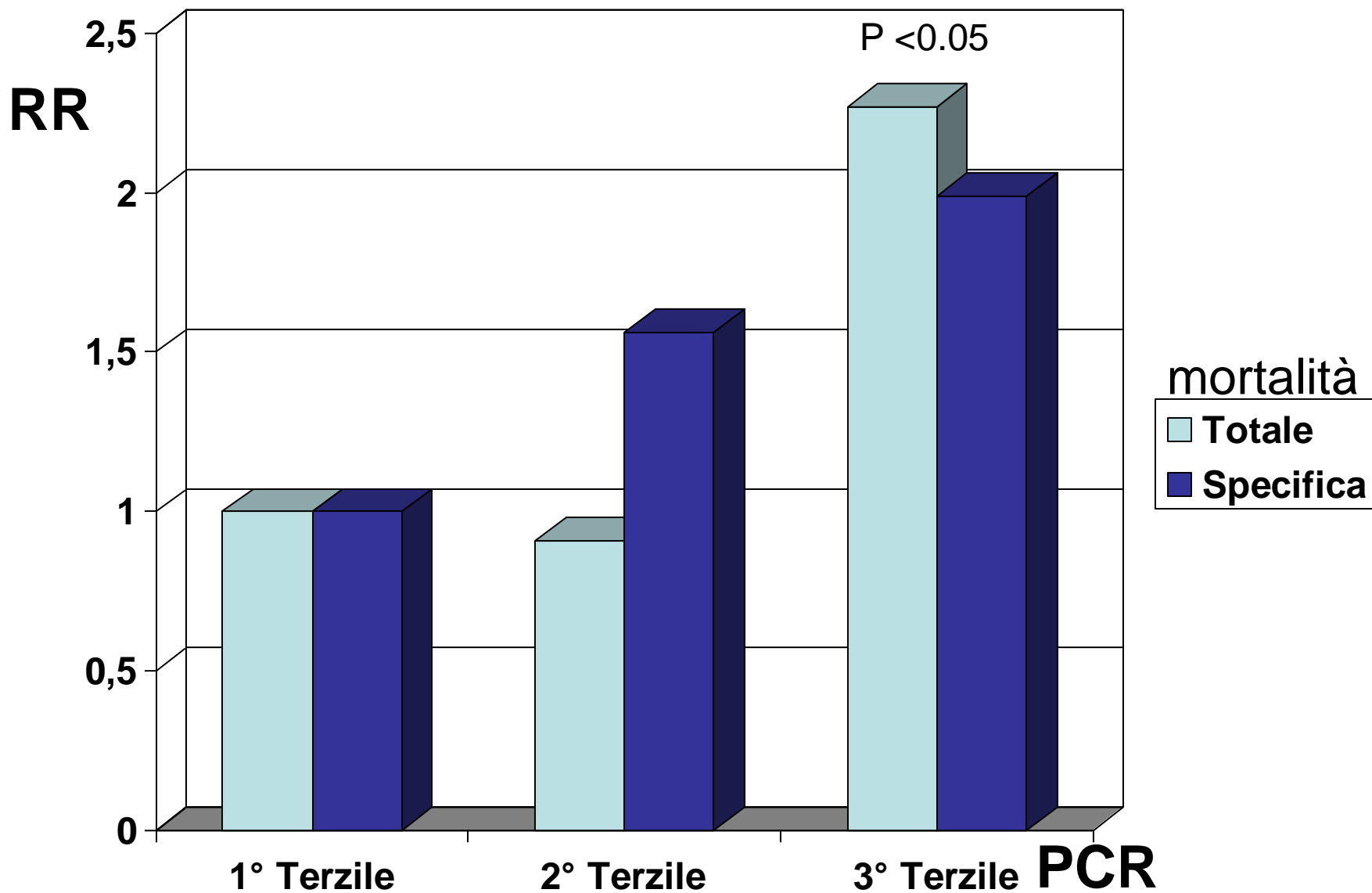


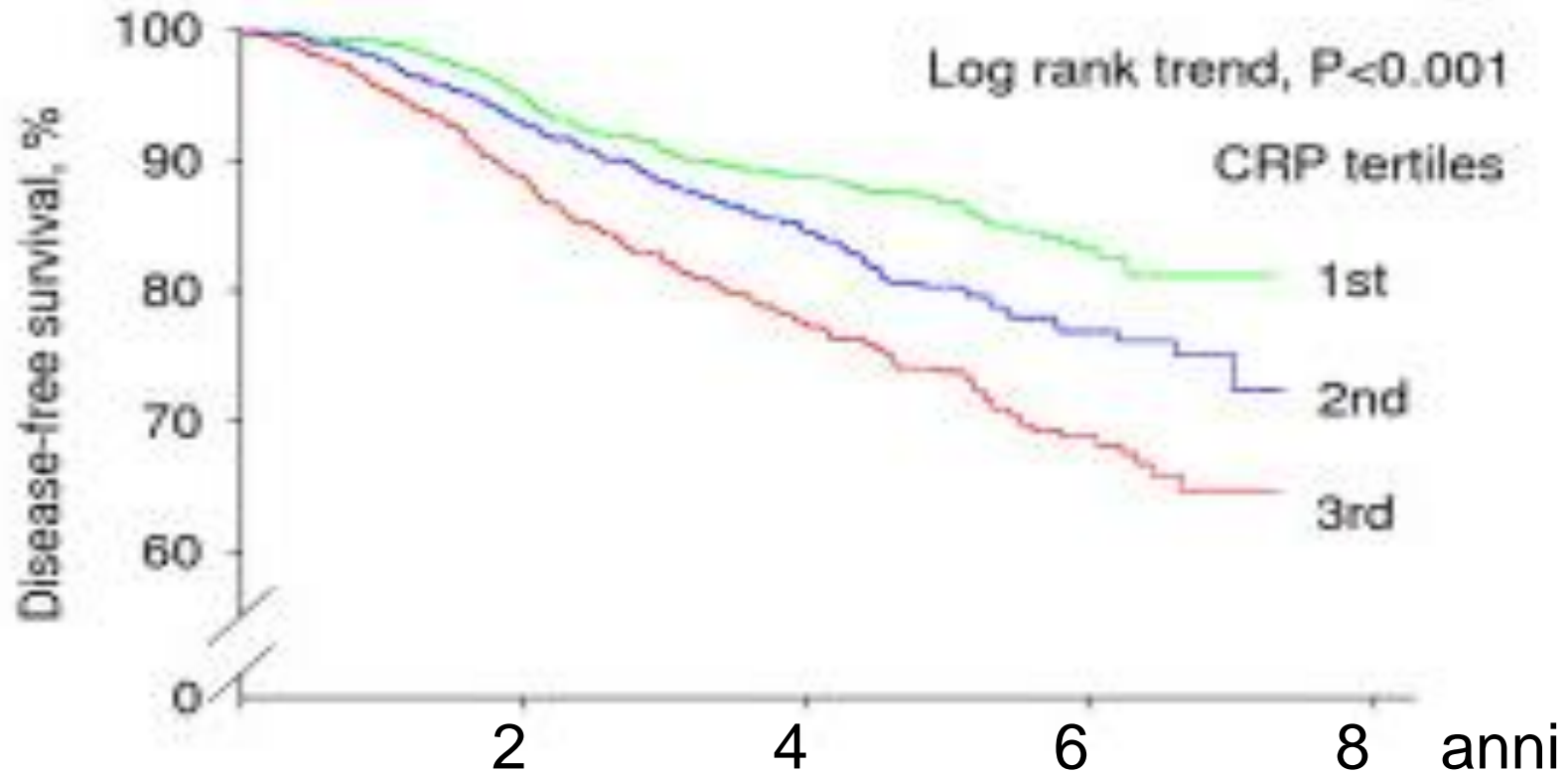
Fig 3. Degree of metabolic dysregulation at diagnosis and overall and colorectal cancer (CRC)–specific survival ($n = 2,446$). Each additional metabolic syndrome component present at diagnosis increased hazard of death by 11% (hazard ratio [HR], 1.11; 95% CI, 1.03 to 1.19; $P = .01$) for overall survival and 14% (HR, 1.14; 95% CI, 1.01 to 1.23; $P = .03$) for CRC-related survival. Cox regression models adjusted for age at diagnosis, sex, race/ethnicity, smoking history, tumor site, stage and grade, chemotherapy and/or radiation, sex-specific tertile of muscle tissue, and body mass index category at diagnosis. Number of risk factors indicates the number of abnormal metabolic syndrome components present at diagnosis (ie, high glucose, high blood pressure, low HDL, high triglyceride level, and/or visceral adiposity). The reference group had 0 metabolic risk factors ($n = 344$; total deaths = 63; CRC deaths = 40). Risk factor = 1 ($n = 562$; total deaths = 131; CRC deaths = 68); risk factor = 2 ($n = 643$; total deaths = 169; CRC deaths = 88); risk factor = 3 ($n = 570$; total deaths = 147; CRC deaths = 80); risk factor = 4 or 5 ($n = 327$; total deaths = 91; CRC deaths = 49).



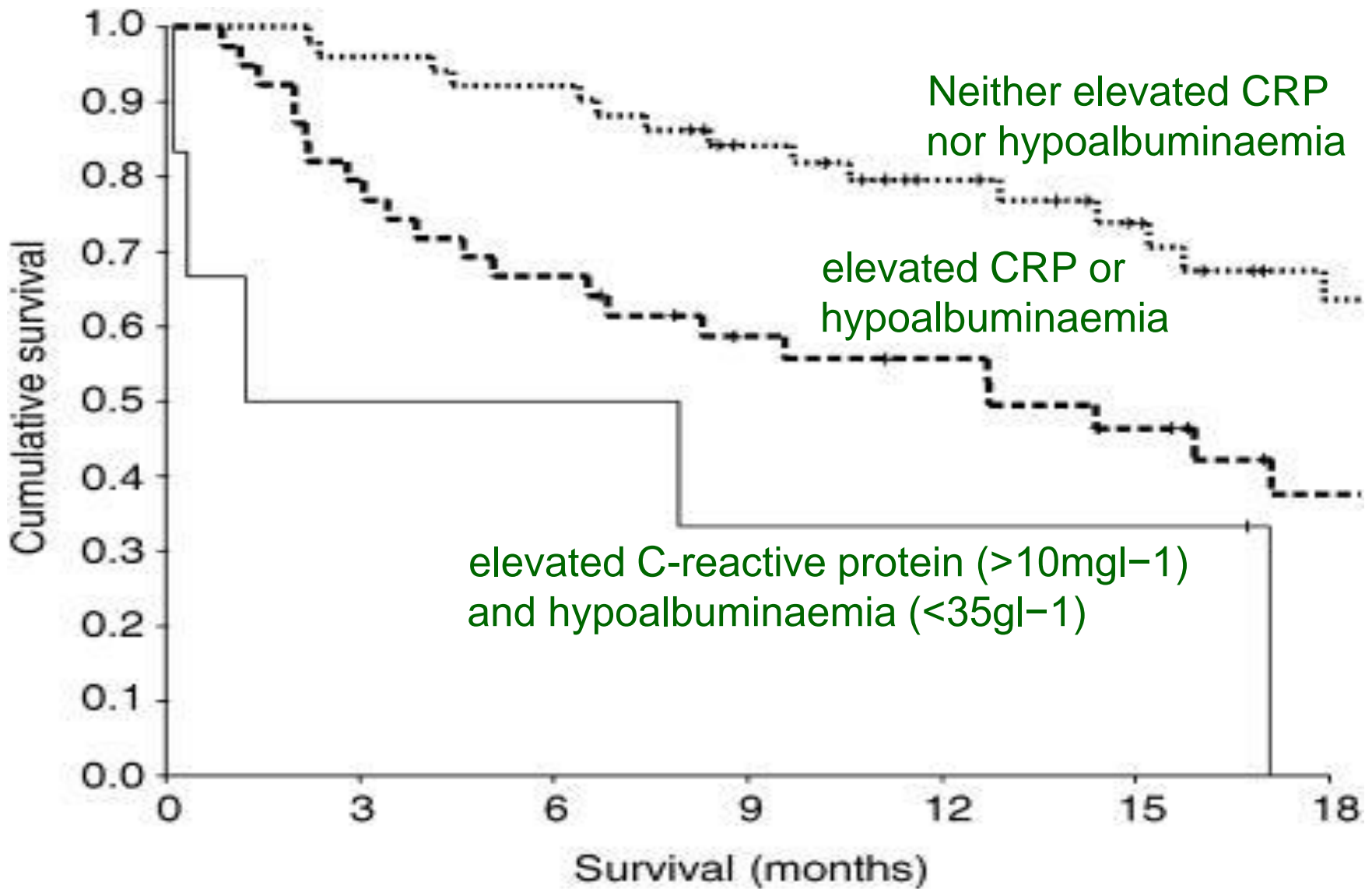
Stato infiammatorio e prognosi dei tumori della mammella
 (734 pazienti seguite per 7 anni, Pierce 2009 JCO 21:3437)

Sopravvivenza libera da malattia in funzione dei livelli plasmatici di PRC

B. Disease-free survival after a breast cancer diagnosis



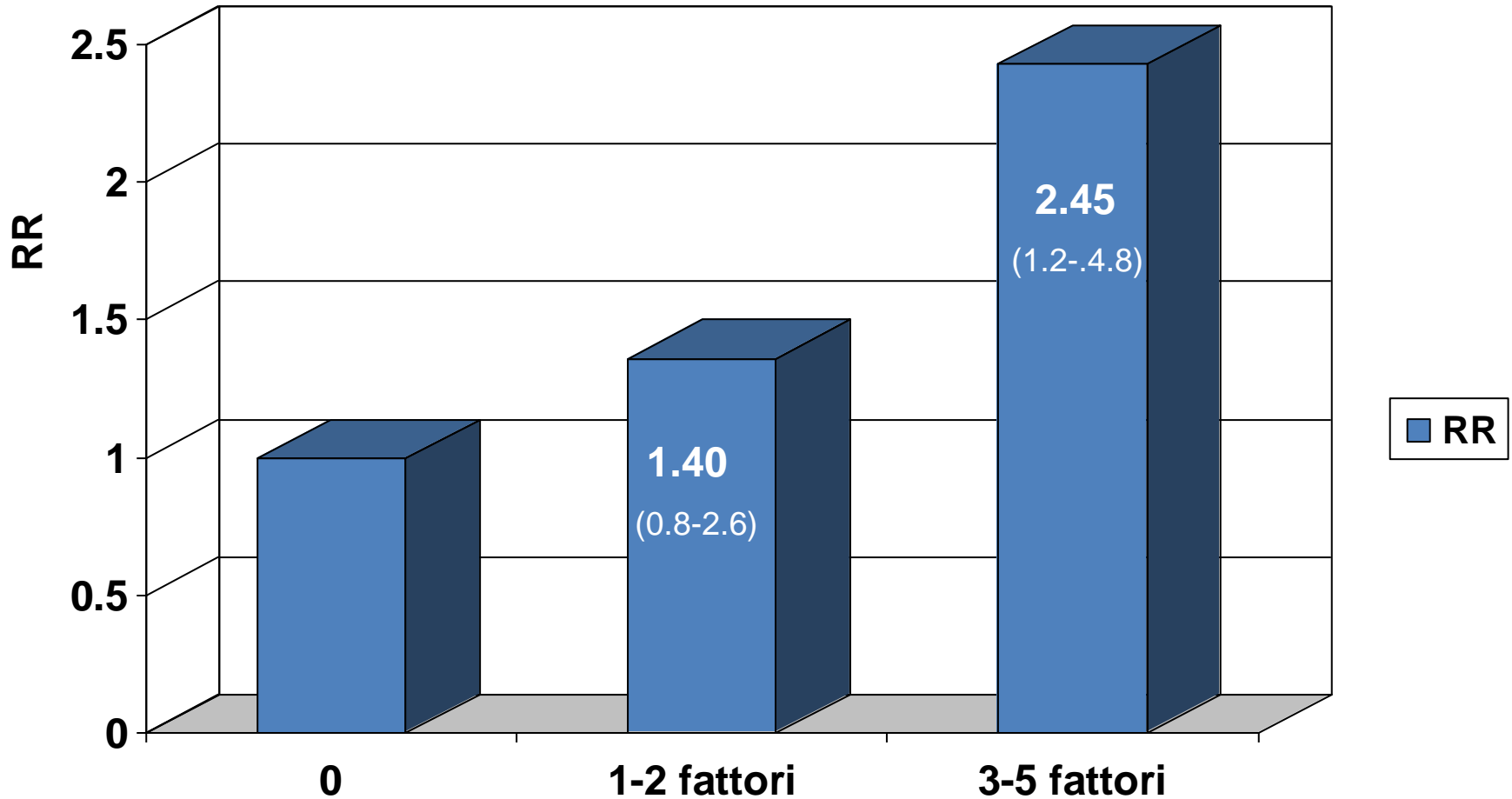
Allin 2011 BCR 13: R55



Inflammation and prognosis of metastatic breast cancer
 Al Murri et al 2006 BJC 94:227

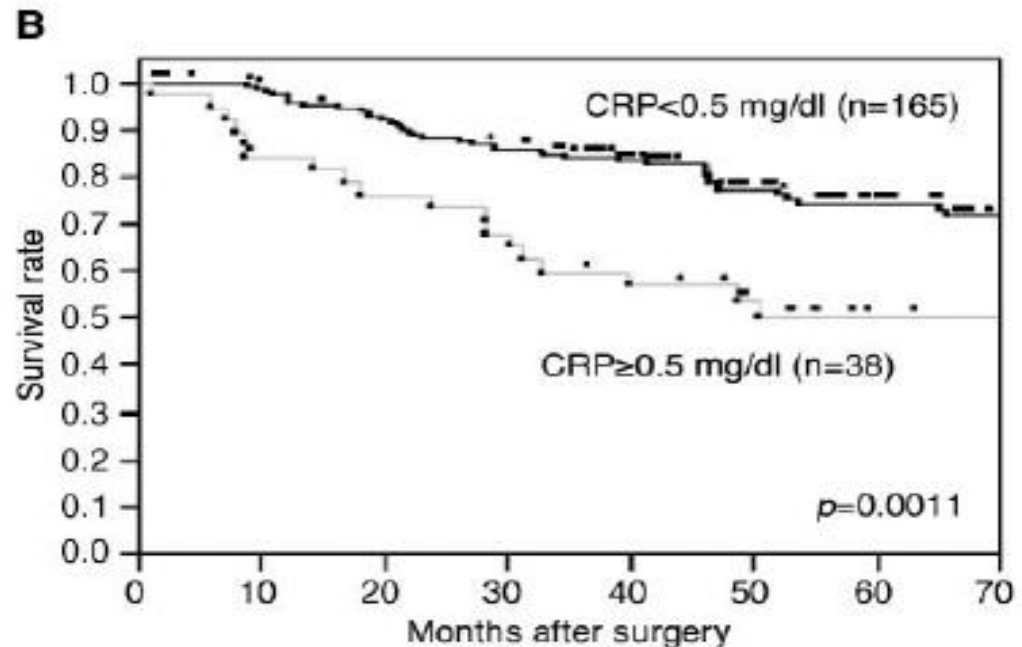
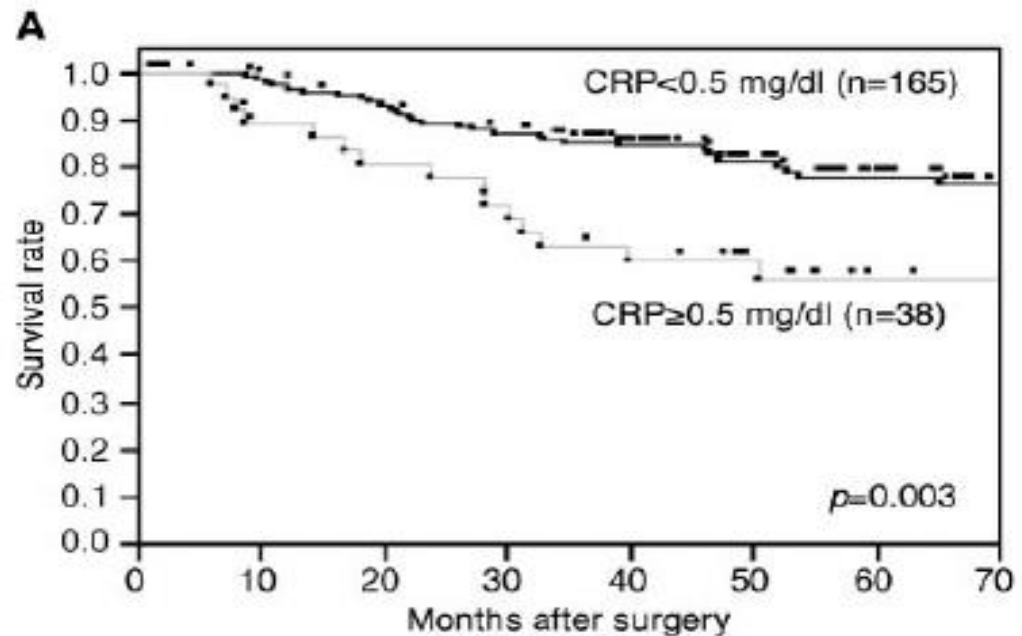
DIANA-5: METASTASI A DISTANZA IN FUNZIONE DEL NUMERO DI FATTORI DI SINDROME METABOLICA

RR aggiustati per età educazione, stadio e espressione di ER



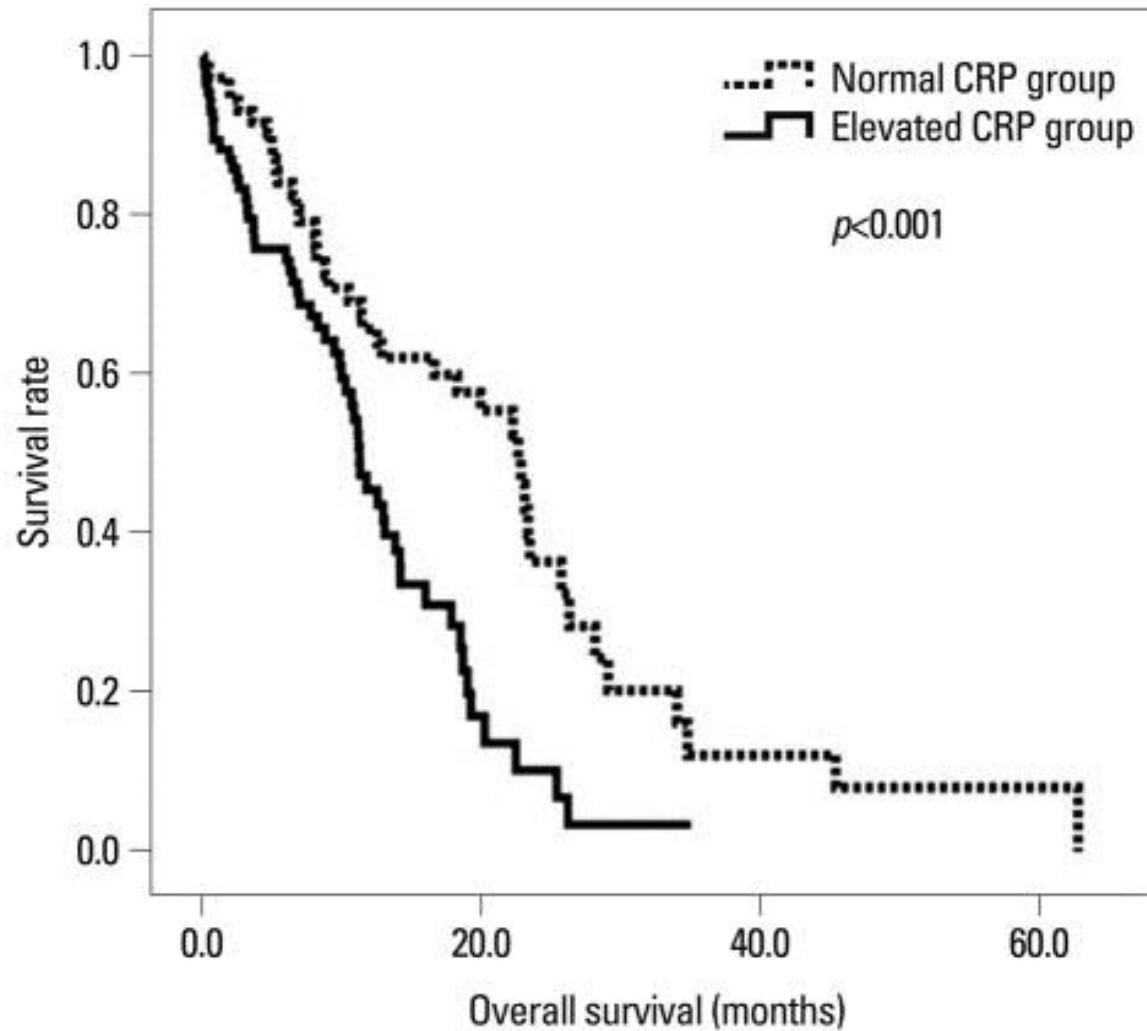
[Hara M 2007](#)
[Anticancer Res.](#)
27:3001

Sopravvivenza dei
pazienti con carcinoma
non a piccole cellule
del polmone



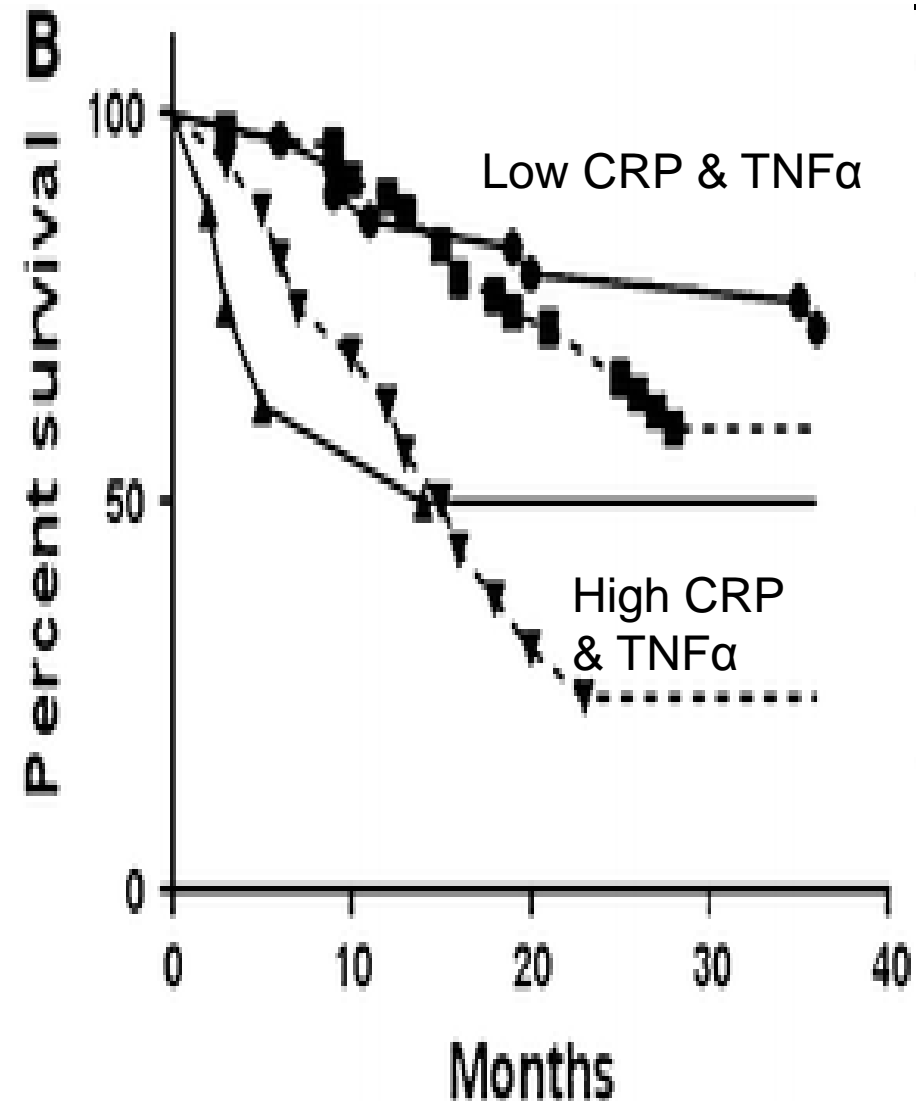
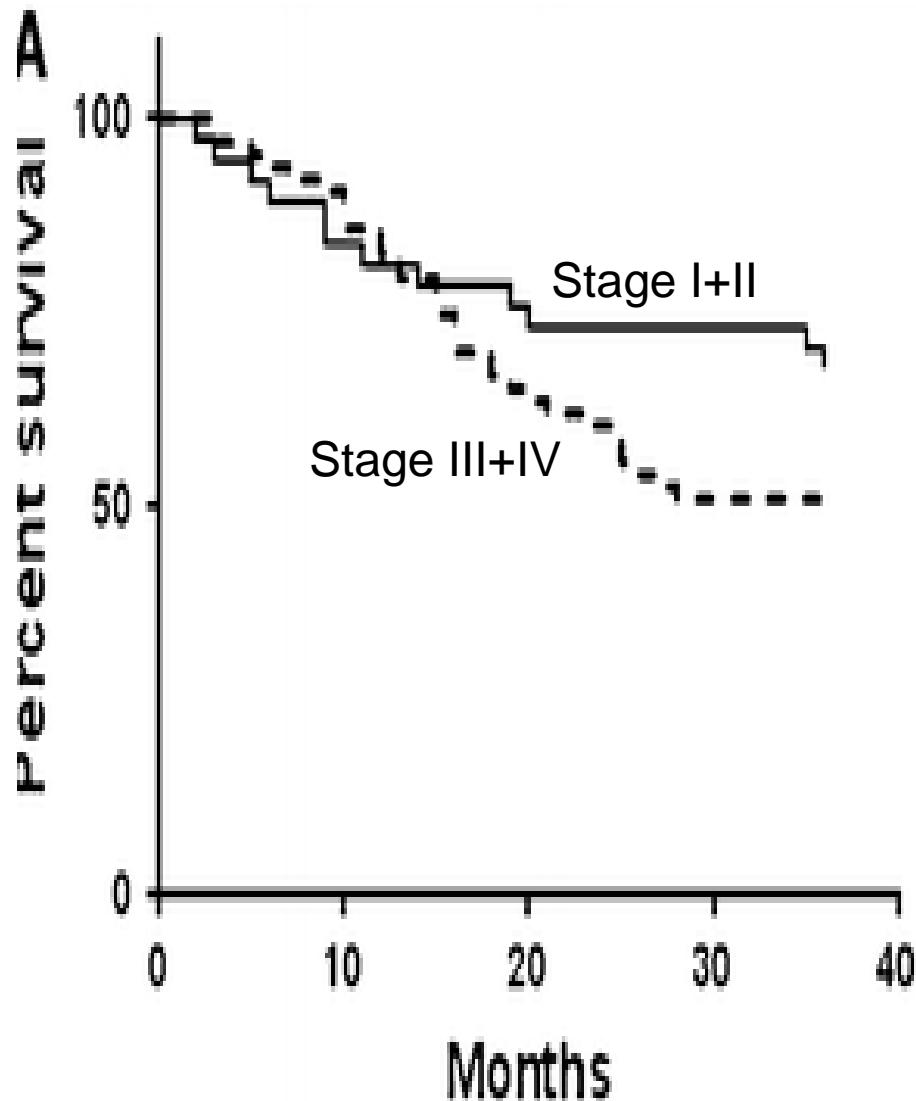
CRP and small cell lung cancer survival

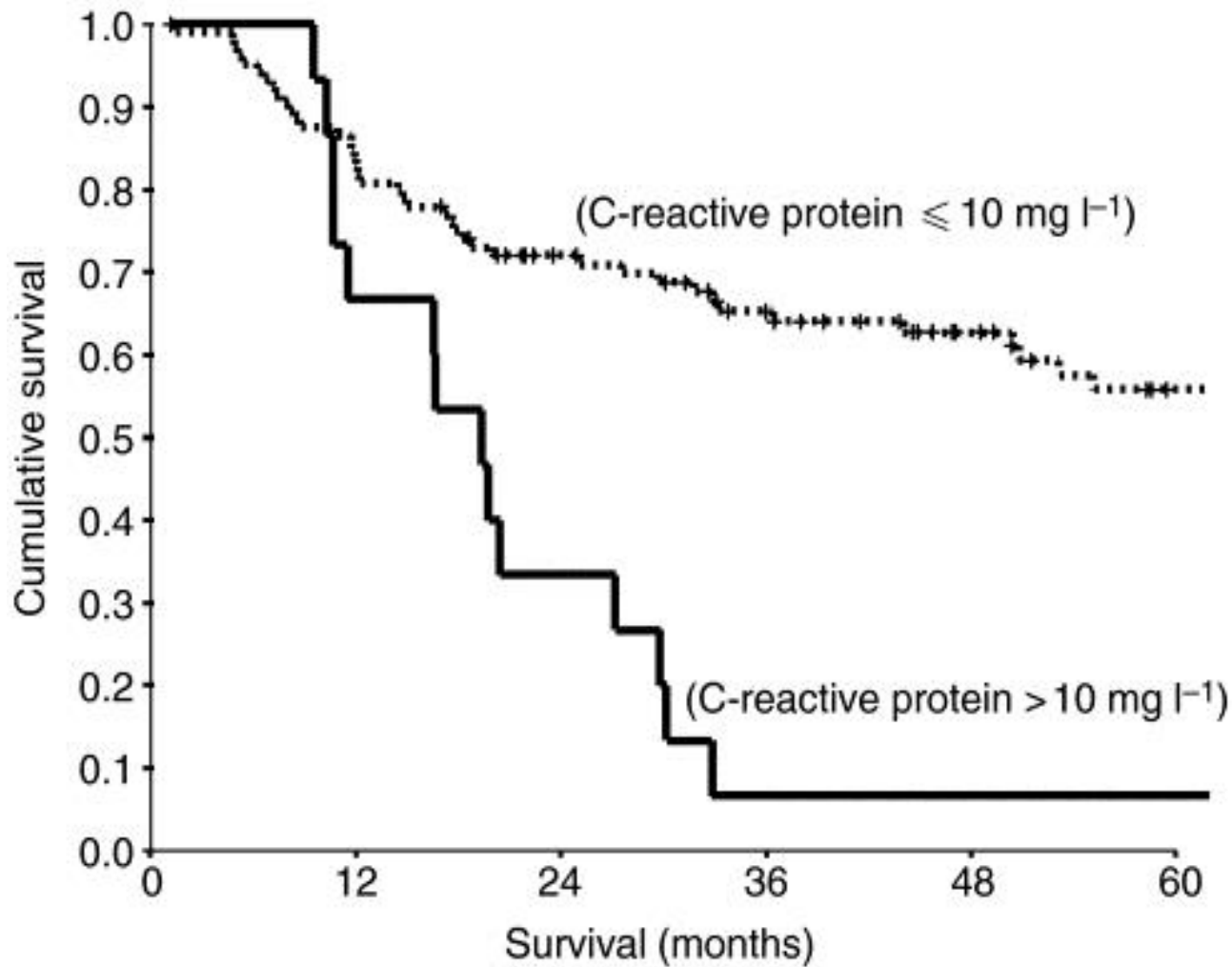
Hong S, Yonsei Med J. 2012,53:111



PlasmaTNF- α and CRP as biomarker for survival in head and neck squamous cell carcinoma

(Bengt-Åke Andersson 2014 JI Cancer Res Clinl Oncol 140:515)



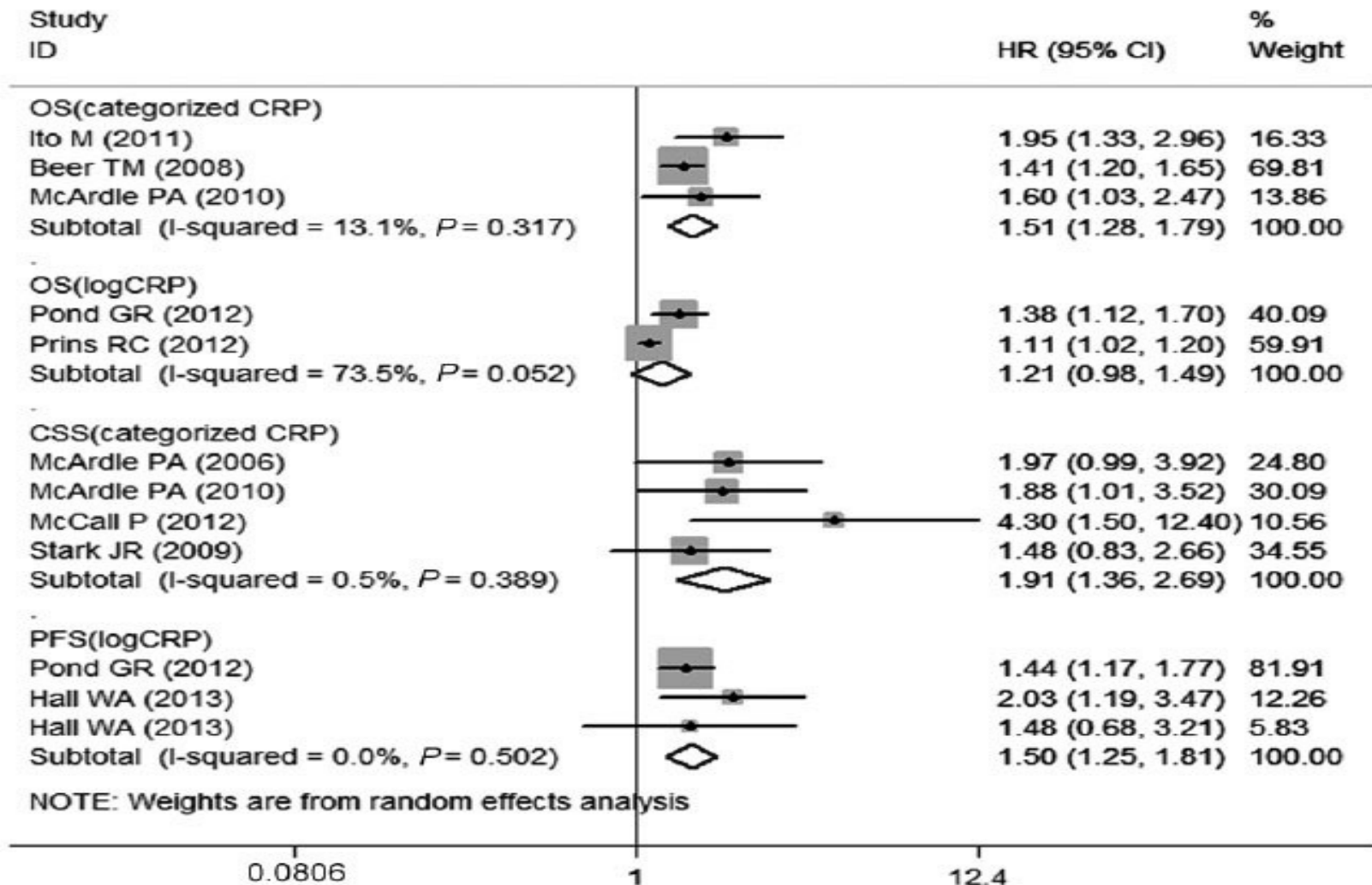


An elevated C-reactive protein concentration, prior to surgery, predicts poor cancer-specific survival in patients undergoing resection for gastro-oesophageal cancer.

Crumlev AB 2006 [Br J Cancer](#). 94:1568

Prostate cancer survival: hazard ratios for high CRP levels vs low levels.

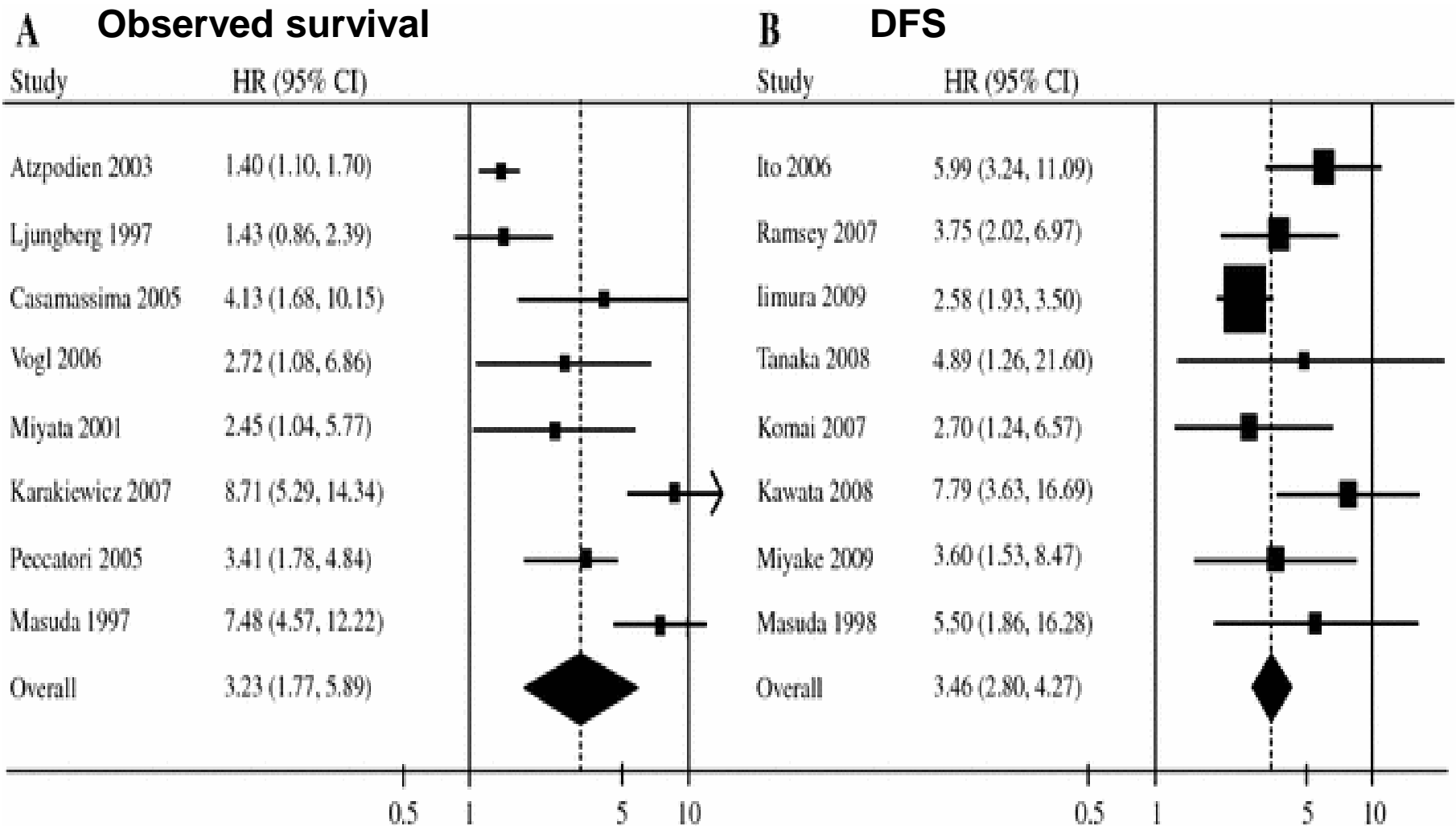
(Liu 2014 Asian J Androl 16:1)



Prognostic role of systemic inflammatory response in renal cell carcinoma

Wu Y et al 2011 [J](#)

[Cancer Res Clin Oncol.](#) 137:887.



Per tener bassa la concentrazione di citochine infiammatorie ridurre cibo animale (eccetto pesce), zucchero e cibi ad alto IG

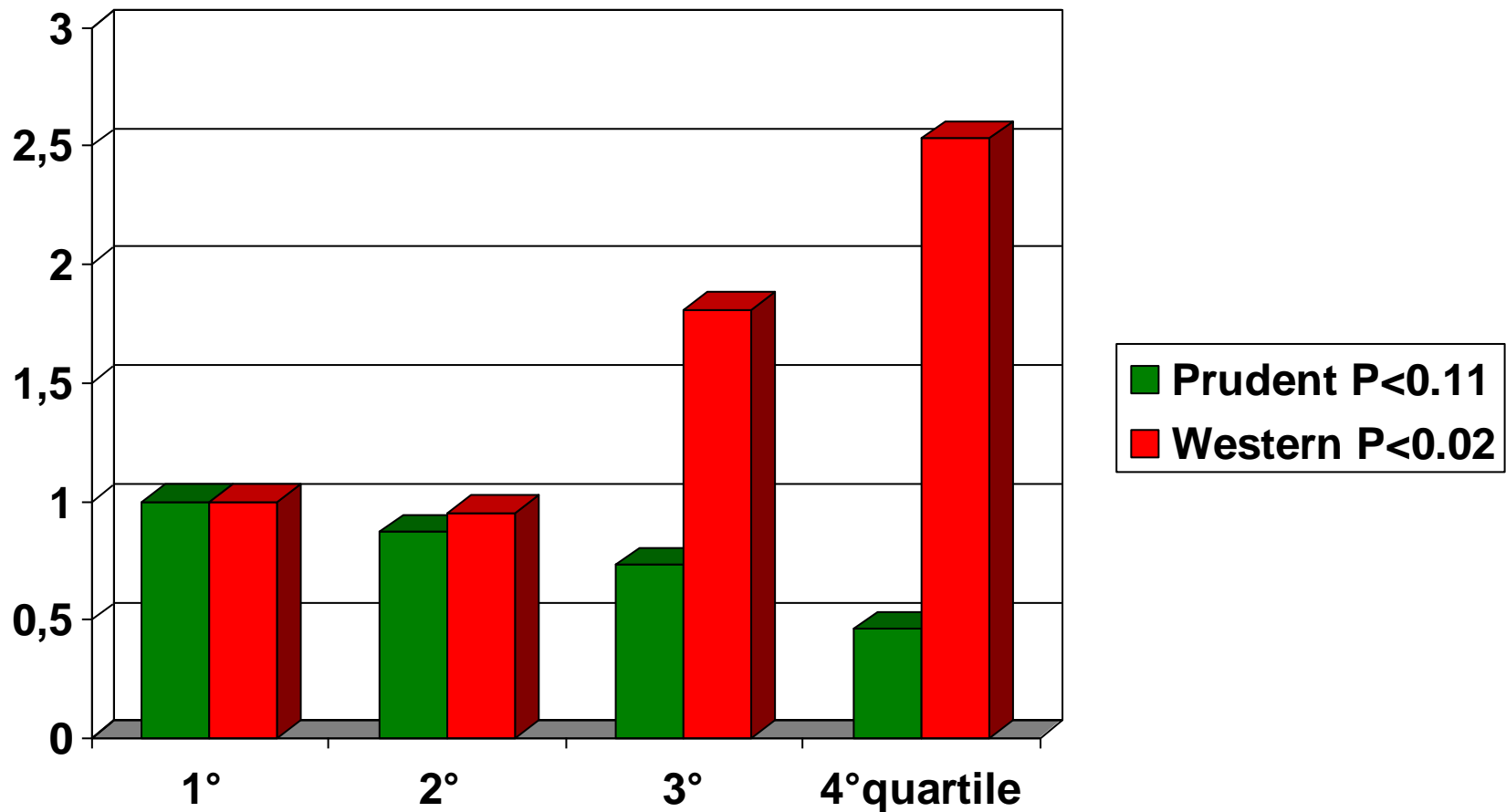
Carne[1], particolarmente carni lavorate, sale[2], grassi idrogenati[3], cibi ad alto indice glicemico[4], stile alimentare occidentale[5]

Dieta Mediterranea[6], frutta e verdura[7], cereali integrali[8], legumi[9], fibre vegetali[10], pesce[11] riso integrale[12], orzo[13], olio extra-vergine di oliva[14], cipolle[15], mele[16], uvetta[17], crucifere[18], tè verde[19], curcuma[20], zenzero[21] , cioccolato nero[22].

- [1] Montonen J 2013 [Eur J Nutr.](#) 52:337.
- [2] [Yilmaz R](#), 2012 [Eur J Clin Nutr.](#) 66:1214.
- [3] Mozaffarian D 2004 [Am J Clin Nutr](#) 79:606.
- [4] [Levitan EB](#), [Metabolism.](#) 2008;57:437. [Liu S](#), [Am J Clin Nutr.](#) 2002;75:492; [Neuhouser ML](#) 2012 [J Nutr.](#) 142:369.
- [5] [5] [Nettleton JA](#) 2006 [Am J Clin Nutr.](#)83:1369; [Esmailzadeh A](#), 2007 [J Nutr](#),137:992.
- Lucas M 2014 [Brain Behav Immun](#) 36:46; [Schulze MB](#) 2005 [Am J Clin Nutr](#) 82:675.
- [6] [Esposito K](#) 2004 [JAMA](#) 292:1440; [Ahluwalia N](#) 2013 [Diabetes & Metab](#) 39:99.
- [7] [Lopez-Garcia E](#) 2004 [Am. J. Clin. Nutr.](#) 80:1029; [Esmailzadeh A](#) 2007 [J. Nutr.](#)137:992; [Gao X](#) 2004 [J Nutr](#) 134:913; [Watzl B](#) 2005 [AJCN](#) 82:1052.
- [8] Montonen J 2013 [Eur J Nutr.](#) 52:337; [de Mello VD](#) 2011 [Diabetologia.](#) 54:2755.
- [9] [Esmailzadeh A](#), 2012 [J Nutr.](#) 142:334.
- [10] [Villaseñor A](#), 2011 [Breast Cancer Res Treat.](#) 129:485.
- [11] [Reinders I](#) 2012 [Eur J Clin Nutr.](#) 66:736.
- [12] [Wang Q](#) 2007 [Asia Pac J Clin Nutr. Suppl](#) 1:295; [Cai H](#) 2005 [Mol Cancer Ther](#) 4:1287.
- [13] [Kanauchi O](#) 1998 [Gastroenterol](#) 33:179.
- [14] [Fitò M](#) 2008 [Eur J Clin Nutr](#) 62:570; [Kostantinidou V](#) 2013 [Mol Nutr Food res](#) 57:772.
- [15] [Shaik YB](#) [J 2006 Biol Regul Homeost Agents](#) 20:47.
- [16] [Denis MC](#) 2013 [PLoS One](#) 8:e53725.
- [17] [Kaliora AC](#) 2008 [Nutr Cancer](#) 60:792.
- [18] [Xu C](#) 2005, [Oncogene](#) 24:4486.
- [19] [Yang F](#) [J Nutr](#) 1998 128:2334.
- [20] [Brennan P](#) 1998 [Biochem Pharmacol](#) 55:965.
- [21] [Chung SV](#) 2009 [J Med Food](#) 12:345.
- [22] [di Giuseppe R](#) 2008 [J Nutr](#) 138: 1939.

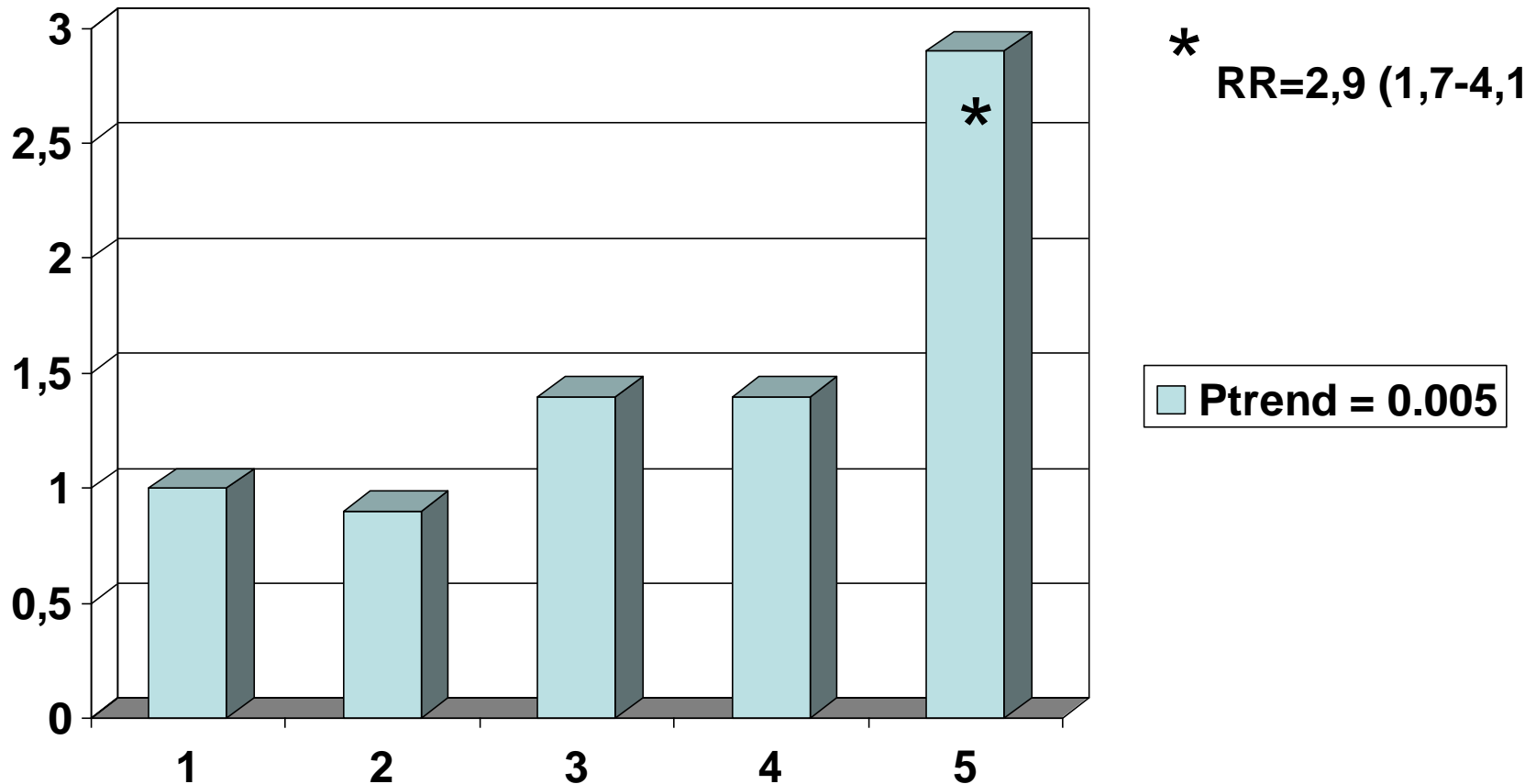
Stile alimentare dopo la diagnosi e mortalità specifica in pazienti con cancro prostatico non metastatico

Yang M (PHS I&II) 2015 Cancer Prev Res 8:545



Rischio di recidiva nei pazienti operati di cancro del colon localmente avanzato

Aggiustato x sesso, età, T, N, perforazione, ostruzione, stato generale, braccio di trattamento, cambiamento di peso, attività fisica e calorie (Meyerhardt 2007)



Intensità di pattern alimentare "occidentale"

Correlazioni con:

Pattern 'prudente'

• Altre verdure	0.72
• Verdure a foglia	0.71
• Verdure verdi	0.67
• Crocifere	0.65
• Legumi	0.56
• Frutta	0.55
• Condimenti leggeri	0.48
• Pomodoro	0.46
• Pesce	0.46
• Aglio	0.39
• Pollo	0.37
• Succo di frutta	0.35
• Cereali integrali	0.32

Pattern 'occidentale'

• Formaggi grassi	0.67
• Formaggi magri	0.64
• Cereali raffinati	0.60
• Carni rosse	0.53
• Dolci	0.53
• Condimenti grassi	0.51
• Margarina	0.50
• Carni conservate	0.45
• Patate	0.45
• Maionese	0.35
• Patate fritte	0.37
• Pomodoro	0.36
• Salatini	0.36
• Burro	0.33

Dieta e prognosi del melanoma

Gould Rothberg BE 2014 Cancer Epidemiol 38:599

Frutta quotidiana

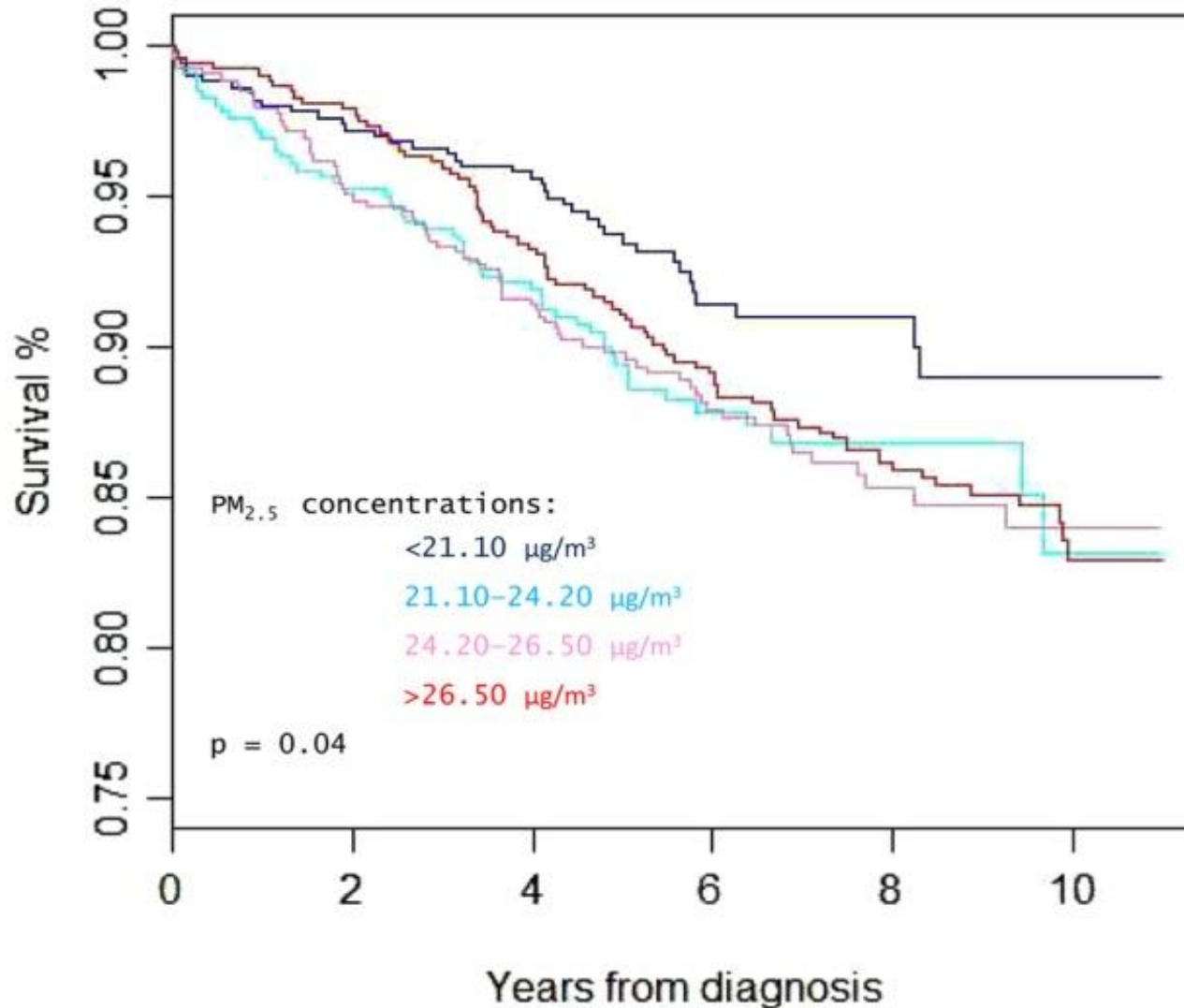
HR = 0.54 (0.34-0.86)

Carne rossa settimanale

HR = 1.84 (1.02-3.30)

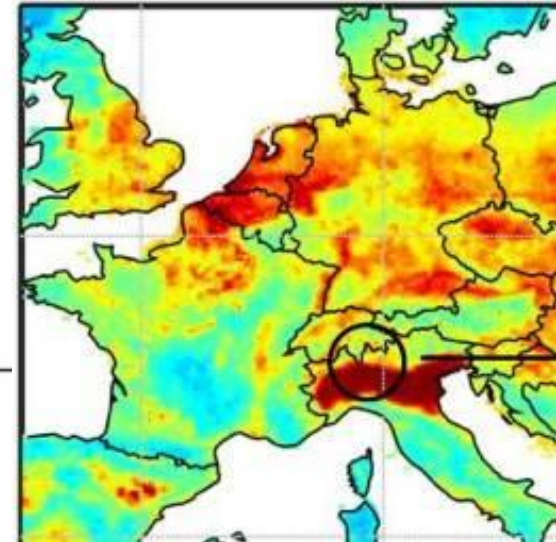
Tagliabue G ...Contiero P 2016 [BMJ Open](#) 6: e012580

Atmospheric fine particulate matter and breast cancer survival



Individual PM_{2.5} exposures were assessed from satellite data.

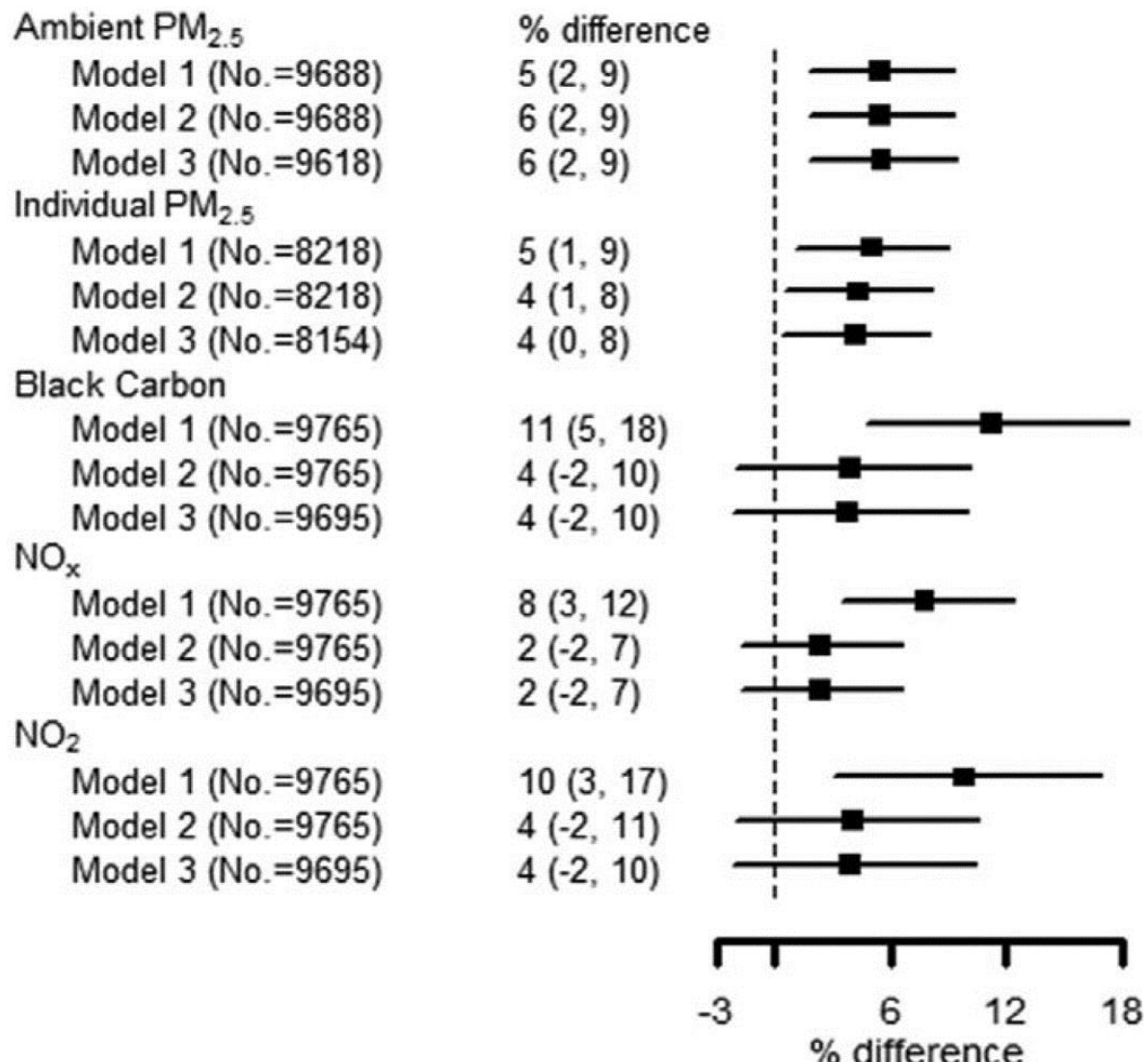
Grade, stage, age at diagnosis, period of diagnosis and participation in BC screening were potential confounders.



Associations between IL-6 and annual average concentrations of air pollutants, per 5 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$, $0.7 \cdot 10^{-6} \text{ m}^{-1}$ increases in black carbon, 40 ppb increase in NO_x , and 17 ppb increase in NO_2 .

Model 1 is adjusted for age, race/ethnicity, gender, exam, and site. Model 2 is adjusted for the covariates in Model 1 as well as for education, employment, income, neighborhood SES, recent infection, second-hand smoke exposure, smoking status, alcohol consumption, physical activity, BMI, waist-hip ratio, and splines for calendar time. Model 3 is adjusted for the covariates in Model 2 as well as for hypertension, diabetes, and anti-inflammatory medications.

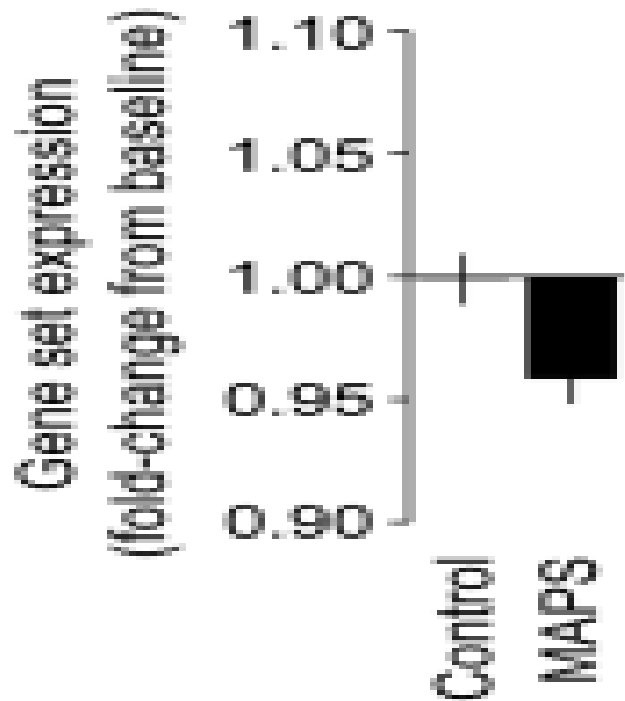
Multi-Ethnic Study of Atherosclerosis (MESA) Hajat A [2015](#)
Epidemiology: [26:310](#)



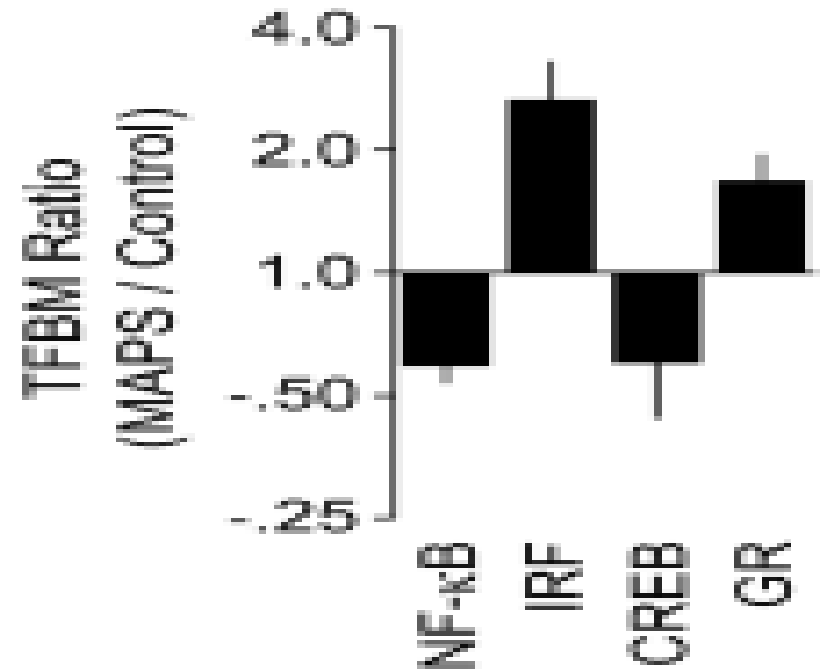
Mindful Awareness Practice meditation for younger breast cancer survivors:

A randomized controlled trial Bower JE
2015 Cancer 121:1231

A. Pro-inflammatory genes



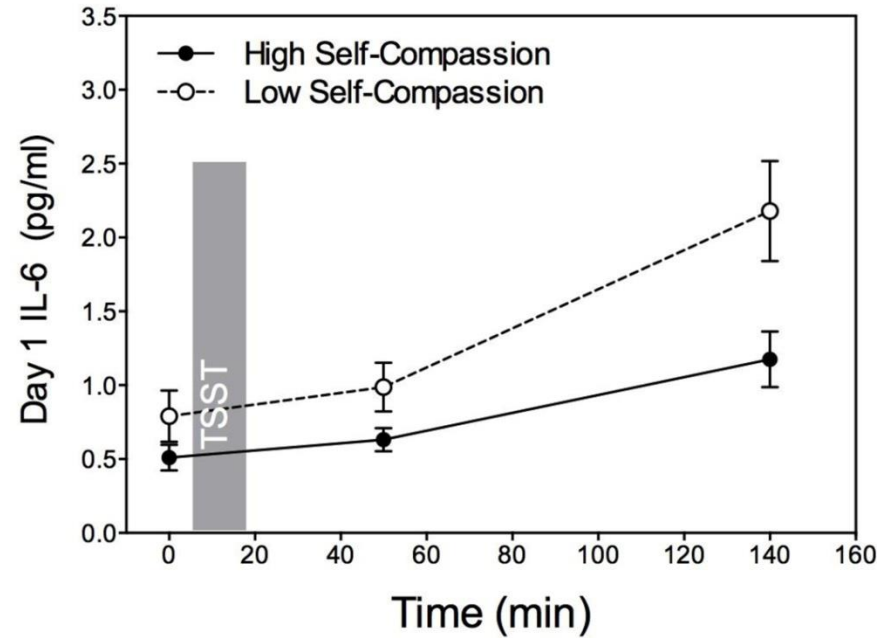
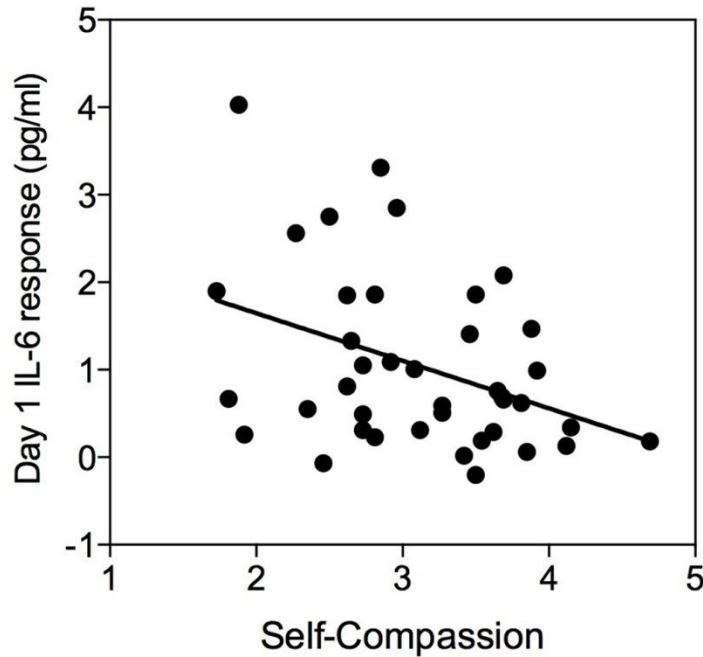
B. Transcription factors



empatia



■



Self-compassion reduces IL-6 response to acute psychosocial stress

Breines JG et al. 2014 Brain Behav Immun 37:109

La Grande Via

- La via del cibo
- La via del movimento
- La via della meditazione

www.lagrandevia.it

	Obesità	Glicemia	Fattori di crescita	PCR	
FATTORI METABOLICI ASSOCIATI ALLA PROGNOSE DEI TUMORI	Testa e collo	--	+	+	+
	Esofago (csc)	--			+
	Stomaco		+	+	+
	Colon	+	+	+	+
	Fegato		+	--	+
	Pancreas		+	+	+
	Polmone	--	+	+	+
	Sarcoma				+
	Melanoma				+
	Mammella	+	+	+	+
	Ovaio		+	?	+
	Endometrio	+			+
	Cervice	+		+	
	Prostata	+	+	+	+
	Vescica	+	+		+
	Rene	--	+		+
	Cervello		+		+
	Linfoma		+	+	+

ECAC: Il Codice Europeo Contro il Cancro 2014

Raccomandazioni mutuuate dal WCRF

- 1 Manteneate un peso corporeo sano**
- 2 Fate quotidianamente esercizio fisico.**
- 3 Consumate abbondantemente cereali integrali, legumi, verdure e frutta.**
- 4 Limitate i cibi ipercalorici (ricchi di zucchero e grassi) e Evitate le bevande zuccherate.**
- 5 Limitate le carni rosse e Evitate le carni conservate.**
- 6 Limitate i cibi ricchi di sale.**
- 7 Limitate il consumo di bevande alcoliche**
- 8 Per le donne: Allattare al seno.**

Sopravvivenza
relativa a 5 anni

EUROCORE
2000-2007
Lancet oncology

