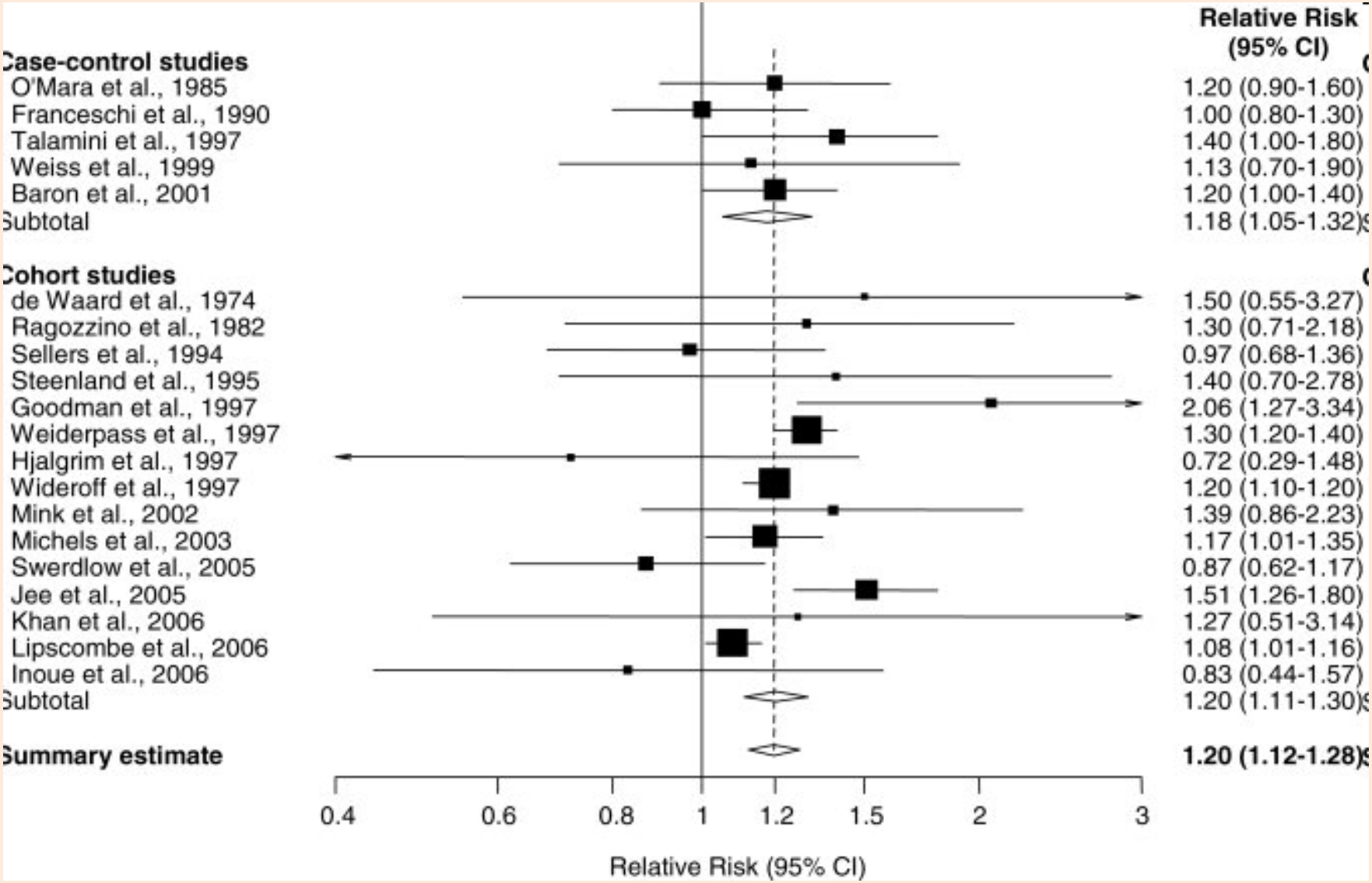
NAPOLI, 17-20 maggio 2017
XXI CONGRESSO NAZIONALE AMD

Simposio Diabete e cancro

Ruolo dell'alimentazione: epidemiologia e real life

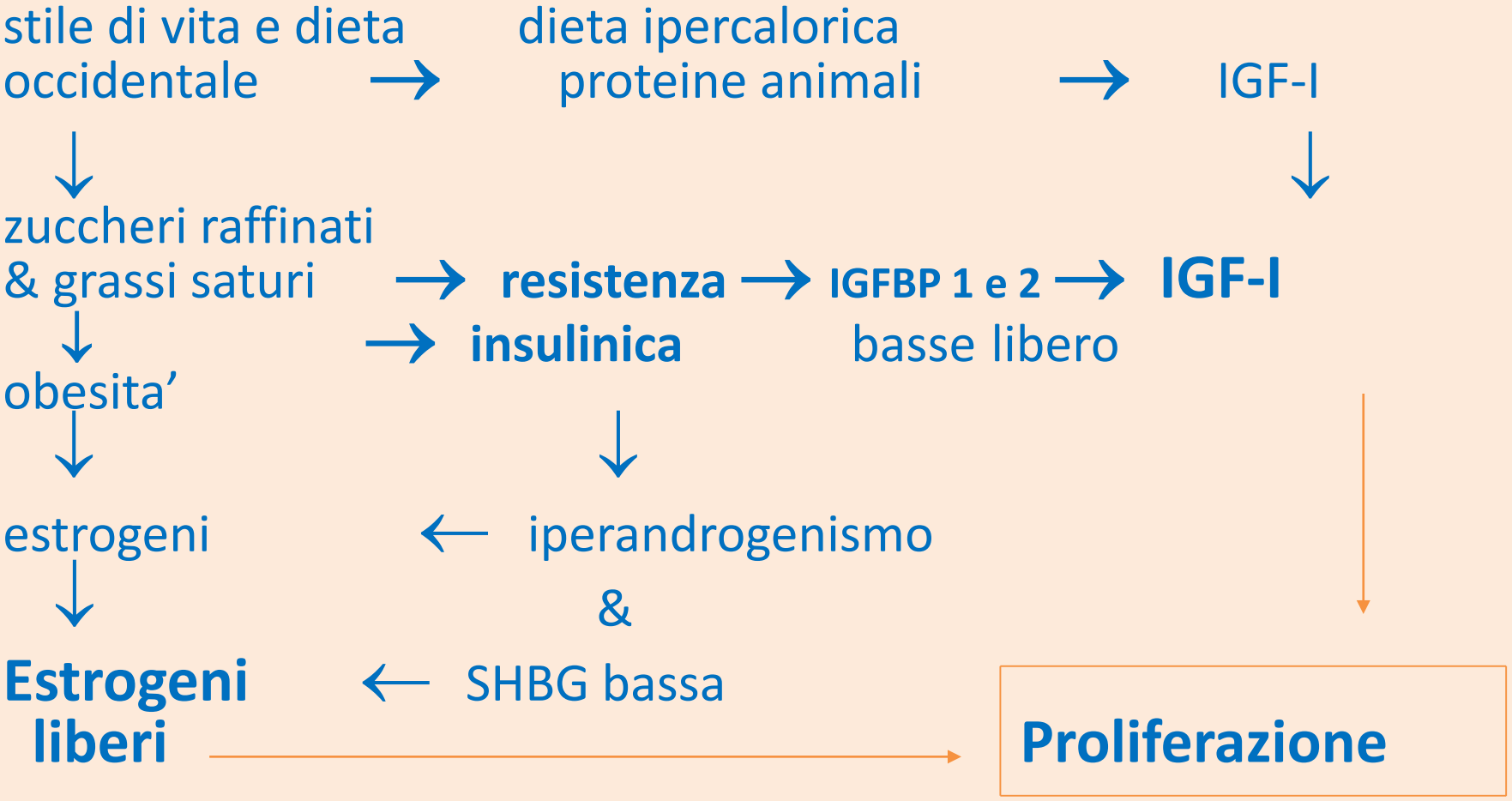
Salvatore Panico

Università Federico II Napoli

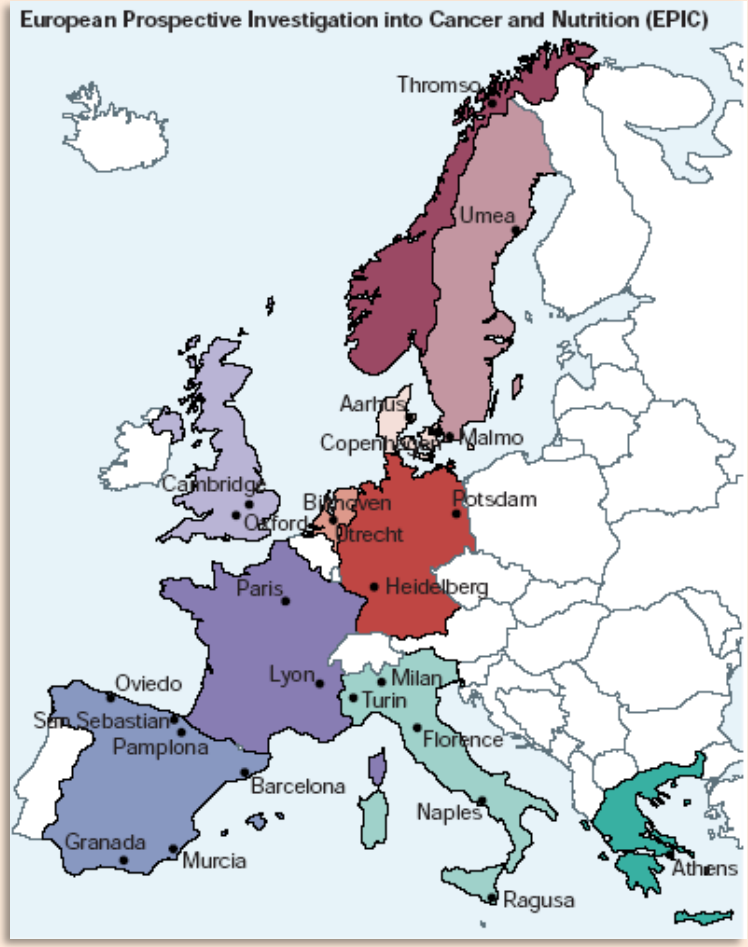


Diabete e cancro mammario. Larsson S, Wolk A 2007 int J Cancer 121:856

Meccanismi che legano la dieta e il rischio di carcinoma mammario



The *EPIC* Study



I.A.R.C
W.H.O

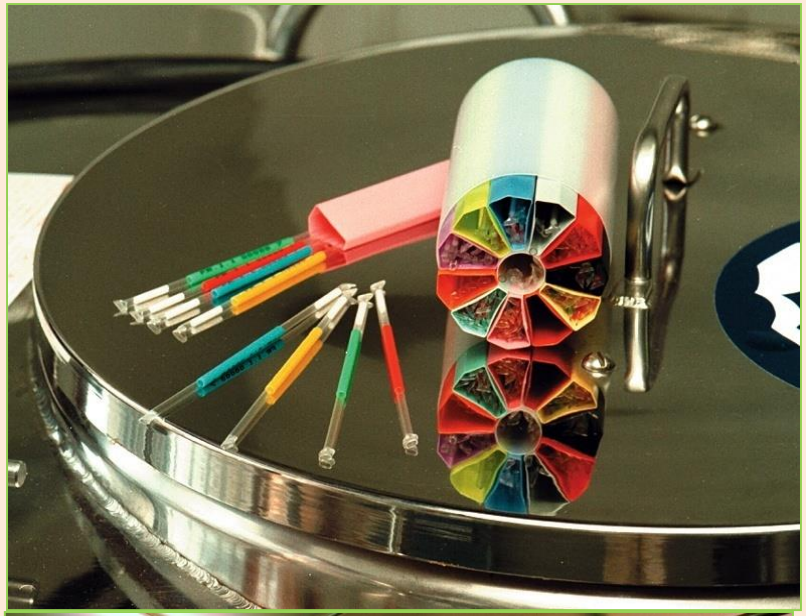
European Prospective Investigation into Cancer and Nutrition

Table 1 | **Sample numbers in the main EPIC-Europe cohort**

Country	Number of questionnaires	Number of blood samples collected	Individuals that developed cancer
Spain	41,440	39,579	1,560
Italy	47,749	47,725	1,609
United Kingdom	87,940	43,138	4,358
The Netherlands	40,072	36,318	1,814
France	72,996	20,725	5,180
Germany	53,094	50,679	2,011
Greece	28,572	28,500	337
Sweden	53,830	53,755	3,850
Denmark	57,054	56,131	2,965
Norway	37,231	9,197	511
Total	519,978	385,747	24,195

EPIC, European Prospective Investigation into Cancer and Nutrition. Sample numbers are from October 2003.

Banca biologica



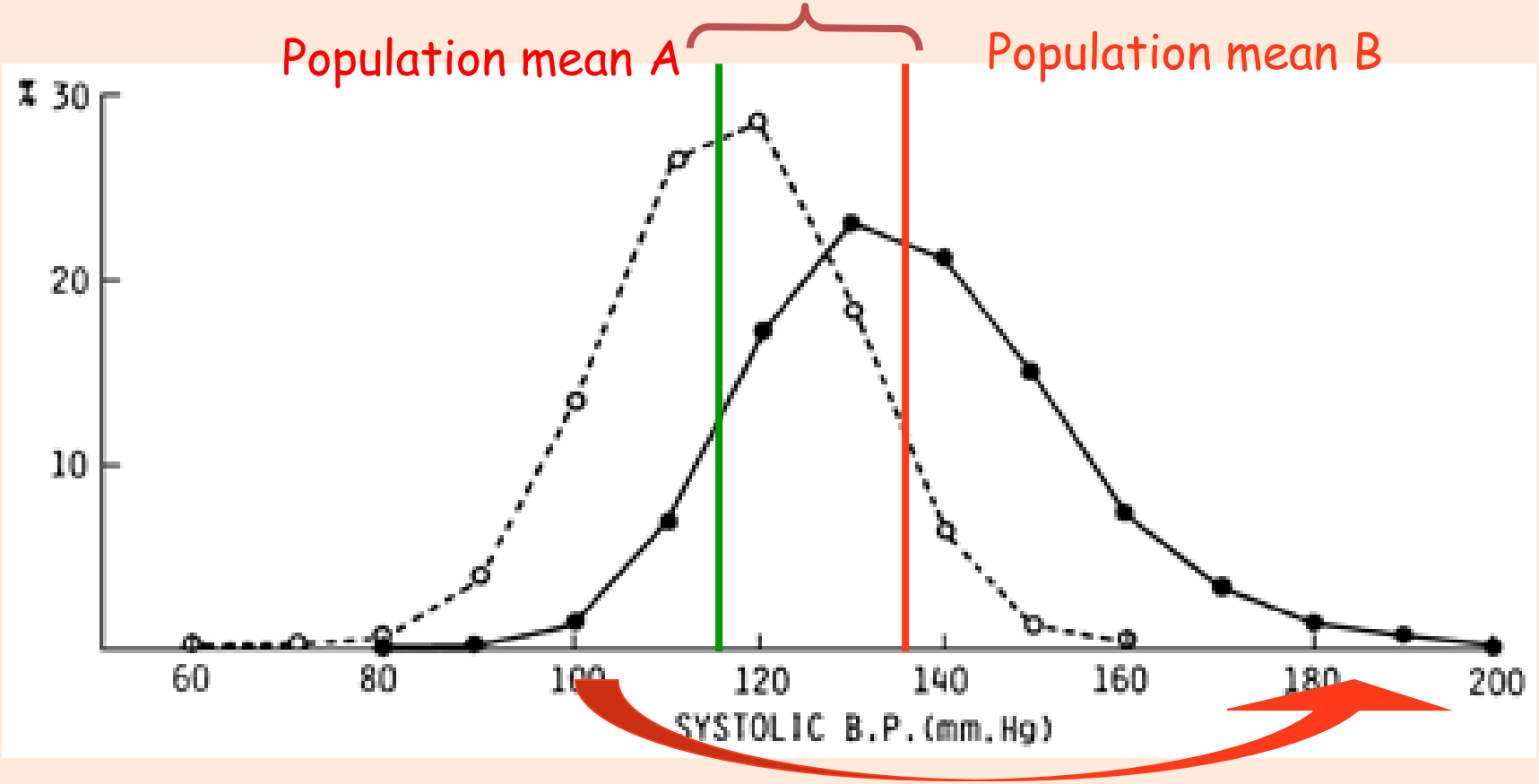
- 30 ml sangue venoso:
  - 20 ml citrato +10 ml secco
- 28 aliquote da 500 µl :
  - plasma 12 (red straws)
  - siero 8 (yellow straws)
  - leucociti 4 (blue straws)
  - globuli rossi 4 (green straws)

28 aliquote x 300.000 soggetti =
8.4 milioni di aliquote,
Metà in ciascun centro EPIC,
metà alla IARC di Lione
Più: 12 x 110,000= 1.3 milioni in
Svezia e Danimarca

G. Rose's approaches:

"sick individuals and sick populations"

Average effect of environment and/or life style

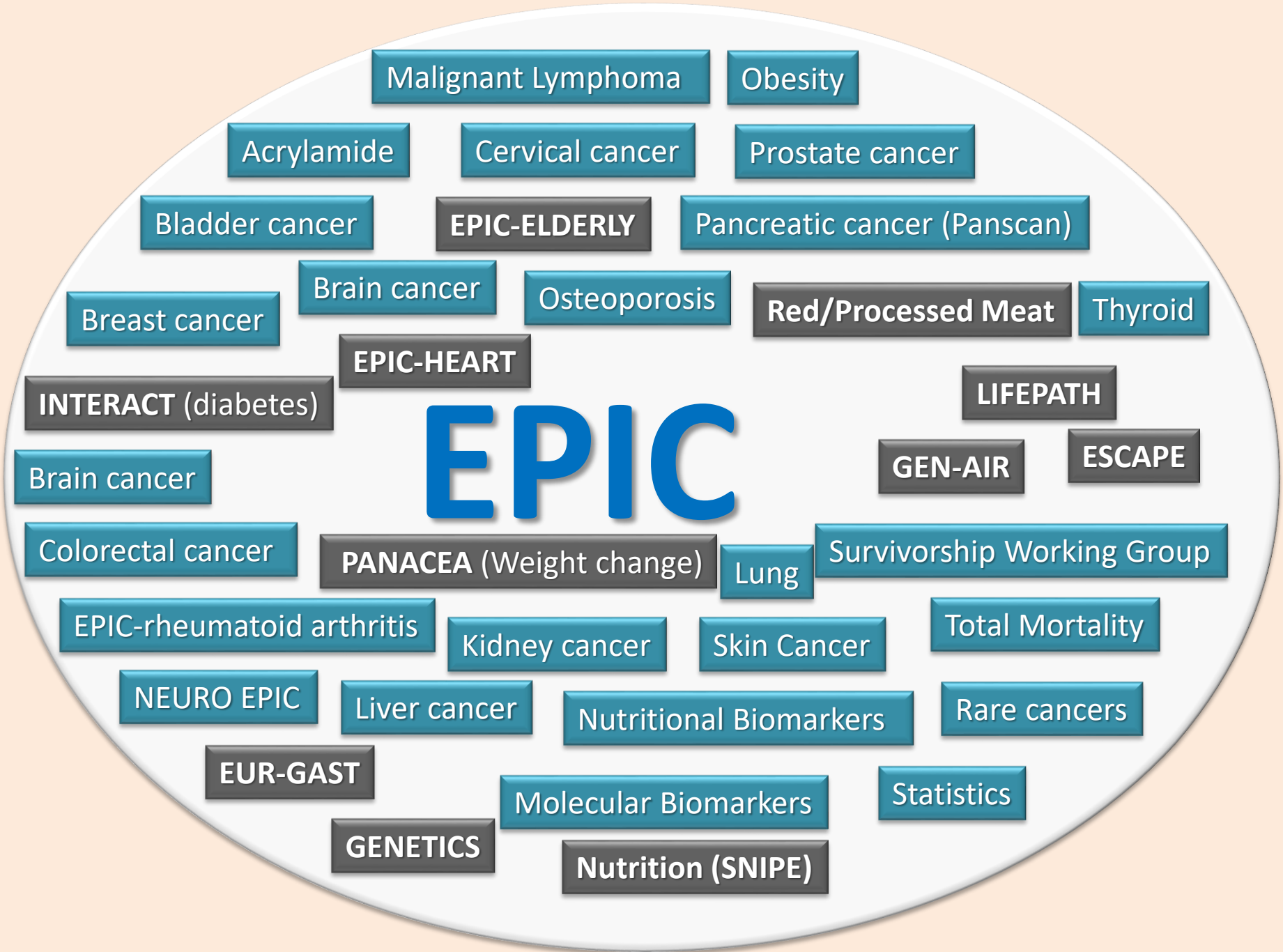


Combined effect of Genetic Susceptibility AND Life-Style

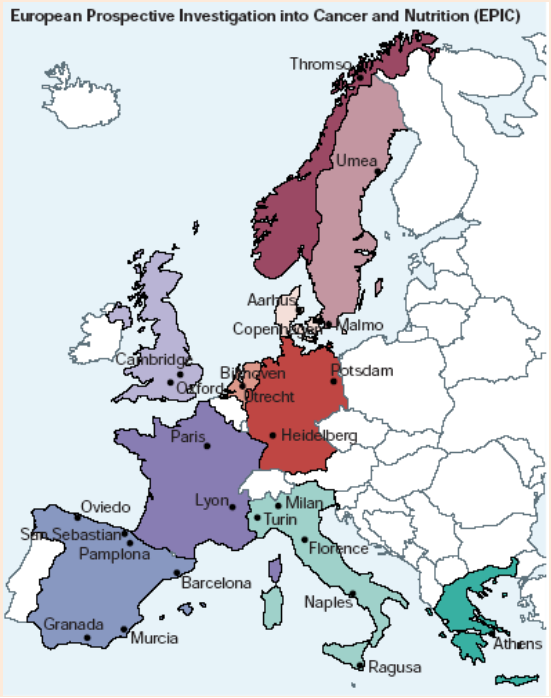
(Adapted from G.Rose, 1985)

Punti di forza di EPIC

- Grande dimensione
  - ➡ aumento della potenza dello studio
- Popolazioni diverse
  - ➡ grande variazione nell'incidenza delle malattie croniche
  - ➡ grande variazione nell'esposizione
- Questionari alimentari molto dettagliati per misurare localmente il consumo abituale
- Calibrazione dei dati dei questionari alimentari con un'intervista delle 24 ore
  - ➡ riduzione degli errori di misura
- Raccolta dei campioni di sangue
  - ➡ utilizzo di biomarker di esposizione
  - ➡ interazione tra fattori nutrizionali, ormonali e genetici

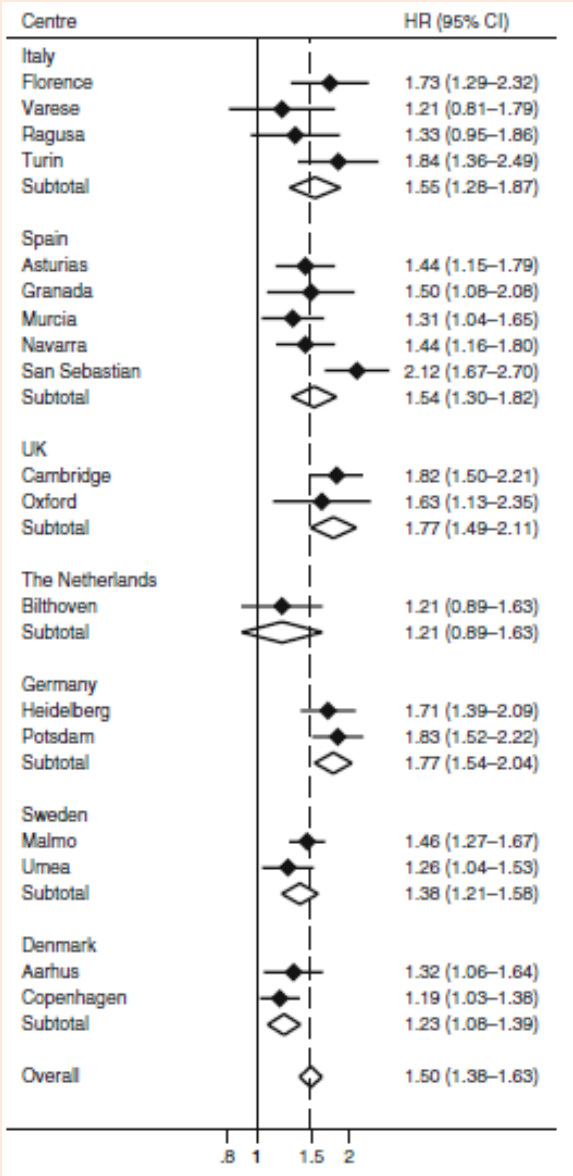

Malignant Lymphoma
Obesity
Acrylamide
Cervical cancer
Prostate cancer
Bladder cancer
EPIC-ELDERLY
Pancreatic cancer (Panscan)
Brain cancer
Osteoporosis
Breast cancer
Red/Processed Meat
Thyroid
EPIC-HEART
INTERACT (diabetes)
LIFEPATH
EPIC
Brain cancer
GEN-AIR
ESCAPE
Colorectal cancer
PANACEA (Weight change)
Lung
Survivorship Working Group
EPIC-rheumatoid arthritis
Kidney cancer
Skin Cancer
Total Mortality
NEURO EPIC
Liver cancer
Nutritional Biomarkers
Rare cancers
EUR-GAST
Molecular Biomarkers
Statistics
GENETICS
Nutrition (SNIPE)

InterAct

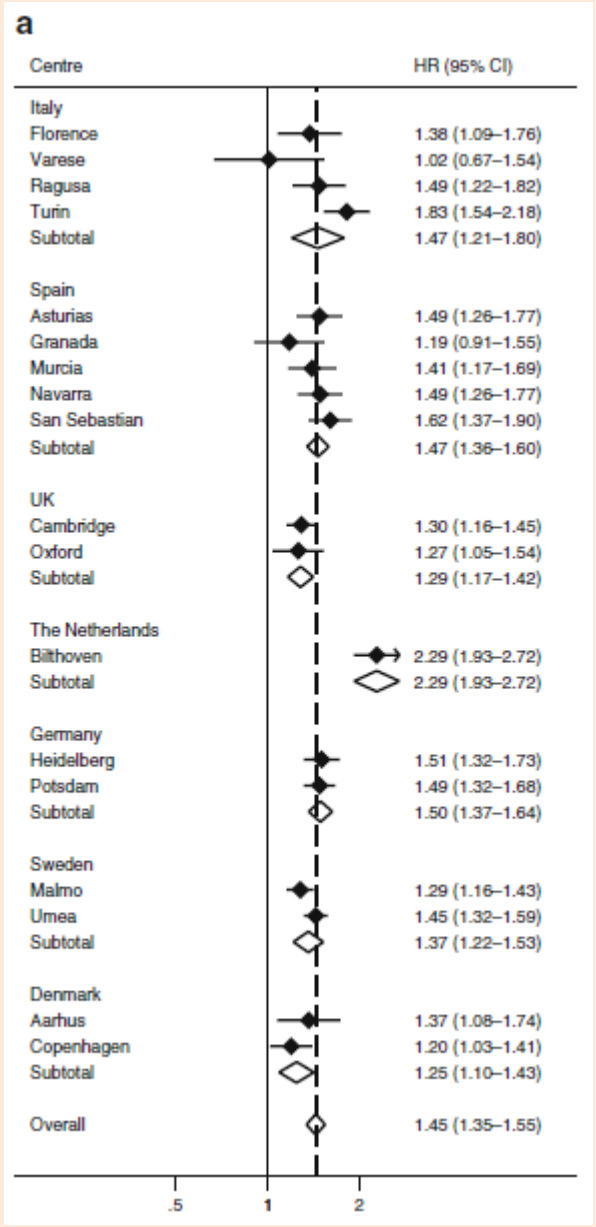


> An examination of the interaction of genetic and lifestyle factors on the incidence of type 2 diabetes

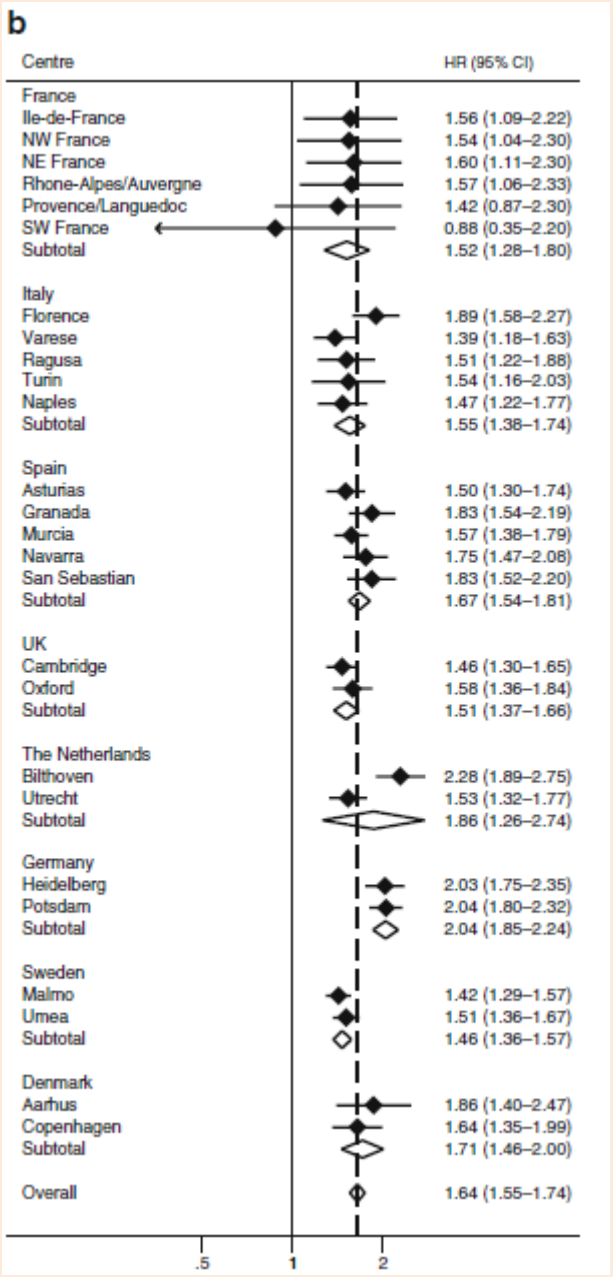
HRs for incident type 2 diabetes in men compared with women across InterAct centres and countries



HRs for incident type 2 diabetes per 10 years of age in (a) men, and (b) women across InterAct centres and countries



men

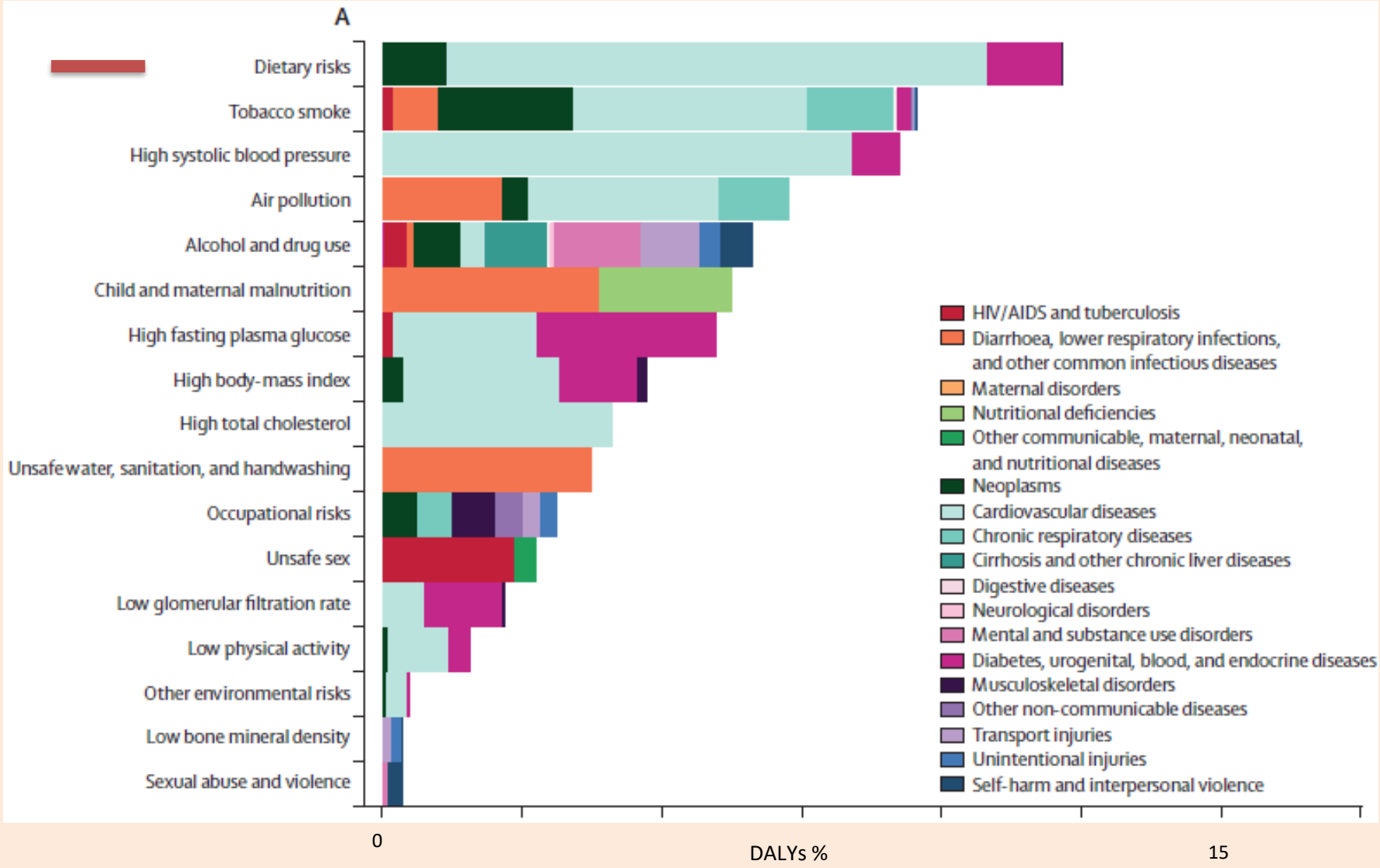


women

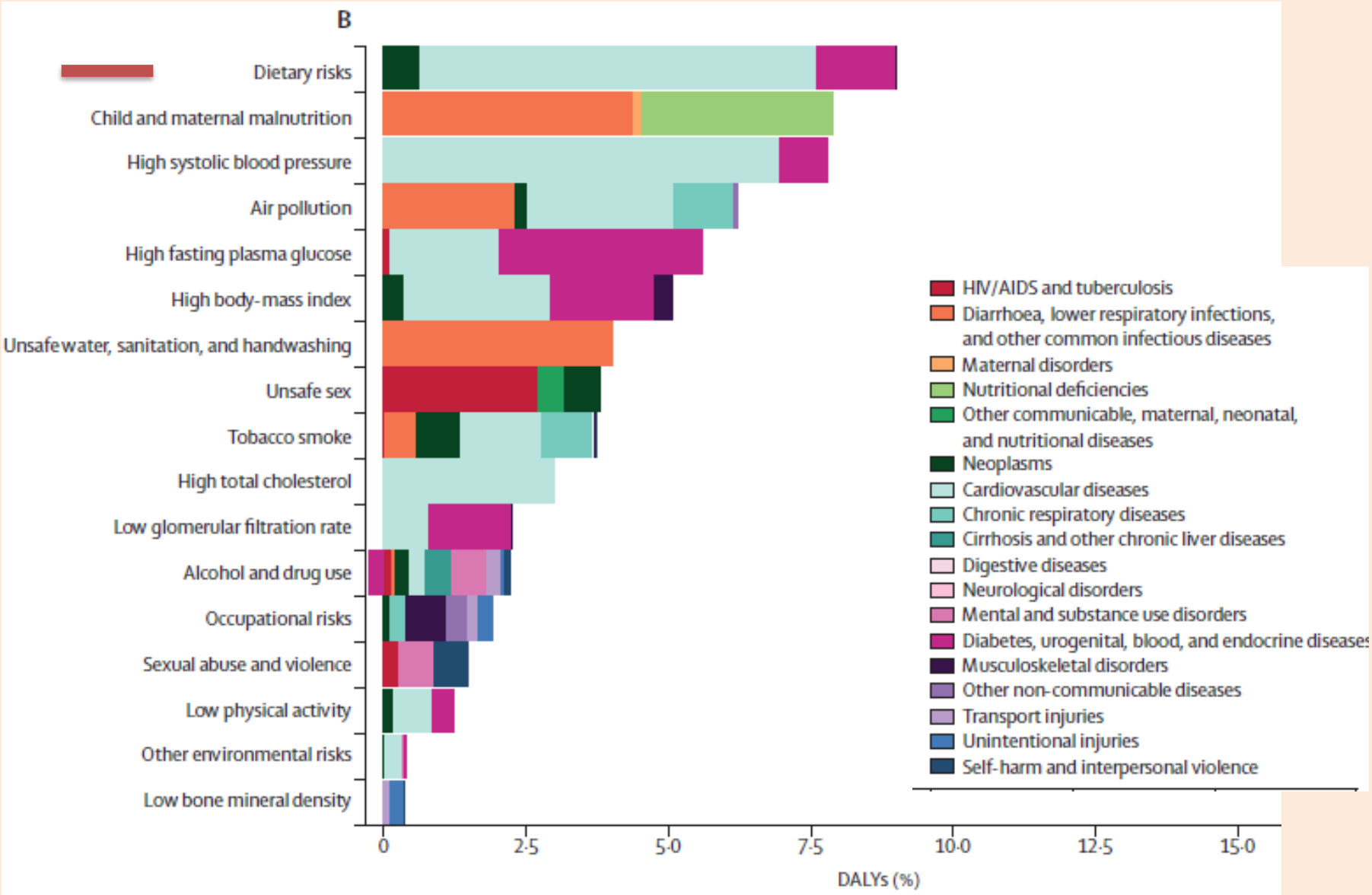
The Lancet, October 7°, 2016
Global Burden of Diseases

Il Global Burden of Disease è stato stimato attraverso il Disability-adjusted life years (DALYs) che misura la gravità globale di una malattia, espressa come il numero di anni persi a causa della malattia, per disabilità o per morte prematura.

The Lancet, October 7°, 2016
Global Burden of Diseases ITALY - MEN



The Lancet, October 7°, 2016
Global Burden of Diseases ITALY - WOMEN



30 April 2005

BMJ

BMJ VOLUME 330 30 APRIL 2005 bmj.com (Clinical research ed.) ISSN 0959-8138

A Mediterranean diet does prolong life

And can be modified to apply across Europe p991

Measuring NHS productivity by outcomes not activities p975
Treating staphylococcal infections p976
Radiotherapy for the future p979
Emergency endoscopy in the UK is inadequate p1000
Health inequalities continue to widen p1006

bmj.com

Indicatore Mediterraneo Modificato

- 9 componenti che danno punteggio 1 o 0
- Vegetali, legumi, frutta fresca e secca, prodotti caseari, cereali, pesce e rapporto monoinsaturi/saturi (modificato utilizzando i polinsaturi al posto dei saturi):

  punteggio=1 per consumo superiore alla mediana
- Carni rosse e processate: punteggio=1 per consumo inferiore alla mediana
- Mediane specifiche per genere
- Alcol: punteggio=1 per consumo tra 5-25 g/d (donne) o 10-50 g/d (uomini)
- Punteggio cumulativo da 0 a 9

Modificato dal Greek Mediterranean index. *Trichopoulou A, 2003, N Engl J Med*

Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study

Antonia Trichopoulou, Philippos Orfanos, Teresa Norat, Bas Bueno-de-Mesquita, Marga Ocké, Petra H Peeters, Yvonne T van der Schouw, Heiner Boeing, Kurt Hoffmann, Paolo Boffetta, Gabriele Nagel, Giovanna Masala, Vittorio Krogh, Salvatore Panico, Rosario Tumino, Paolo Vineis, Christina Bamia, Androniki Naska, Vassiliki Benetou, Pietro Ferrari, Nadia Slimani, Guillem Pera, Carmen Martinez-Garcia, Carmen Navarro, Miguel Rodriguez-Barranco, Miren Dorronsoro, Elizabeth Spencer, Timothy Key, Sheila Bingham, Kay-Tee Khaw, Emmanuelle Kesse, Francoise Clavel-Chapelon, Marie-Christine Boutron-Ruault, Goran Berglund, Elisabet Wirfalt, Goran Hallmans, Ingegerd Johansson, Anne Tjonneland, Anja Olsen, Kim Overvad, Heidi Hundborg, Elio Riboli, Dimitrios Trichopoulos

	n. deaths	2-unit increment	p-value for heterogeneity
Fixed effects	**4047**	**0.92(0.88-0.96)**	**0.328**
Random effects		**0.92(0.88-0.97)**	

8% di sopravvissuti in più per ogni incremento di 2 unità di punteggio

BMJ 2005 Apr 30;330(7498):991

Mediterranean dietary pattern and cancer risk in the EPIC cohort

E Couto[1,2], P Boffetta*[,1,3,4], P Lagiou[5], P Ferrari[6], G Buckland[7], K Overvad[8], CC Dahm[9], A Tjønneland[10], A Olsen[10], F Clavel-Chapelon[11,12], M-C Boutron-Ruault[11,12], V Cottet[11,12], D Trichopoulos[4,13,14], A Naska[5], V Benetou[5], R Kaaks[15], S Rohrmann[15], H Boeing[16], A von Ruesten[16], S Panico[17], V Pala[18], P Vineis[19,20], D Palli[21], R Tumino[22], A May[23], PH Peeters[23], HB Bueno-de-Mesquita[24,25], FL Büchner[24,26], E Lund[27], G Skeie[27], D Engeset[27], CA Gonzalez[7], C Navarro[28,29], L Rodríguez[30], M-J Sánchez[28,31], P Amiano[28,32], A Barricarte[28,33], G Hallmans[34], I Johansson[35], J Manjer[36], E Wirfärt[37], NE Allen[38], F Crowe[38], K-T Khaw[39], N Wareham[39], A Moskal[1], N Slimani[1], M Jenab[1], D Romaguera[19], T Mouw[19], T Norat[19], E Riboli[19] and A Trichopoulou[4,5]

Br J Cancer (2011) 104, 1493 – 1499

Table 3 Hazard ratios for all cancers associated with categories of the Mediterranean diet score

Score	Cohort members	Cases	HR[a] (95% CI)
Both sexes			
0–3	154 052	10 349	1.00
4	105 936	6849	0.96 (0.93–0.99)
5			0.92 (0.89–0.95)
6–9			0.93 (0.90–0.96)
			end = 0.00001
			1.00
4	30 770	2121	0.99 (0.93–1.04)
5	29 766	2049	0.97 (0.92–1.03)
6–9	38 908	2455	0.93 (0.88–0.99)
		P for trend = 0.02	
Women			
0–3	110 891	7305	1.00
4	75 166	4728	0.95 (0.91–0.98)
5	69 906	4176	0.90 (0.87–0.94)
6–9	79 910	4853	0.93 (0.89–0.96)
		P for trend = 0.0001	

8% di tumori in meno per punteggi medio alti

Mediterranean Diet and Type2Diabetes Risk in the European Prospective Investigation Into Cancer and Nutrition (EPIC) Study - INTERACT

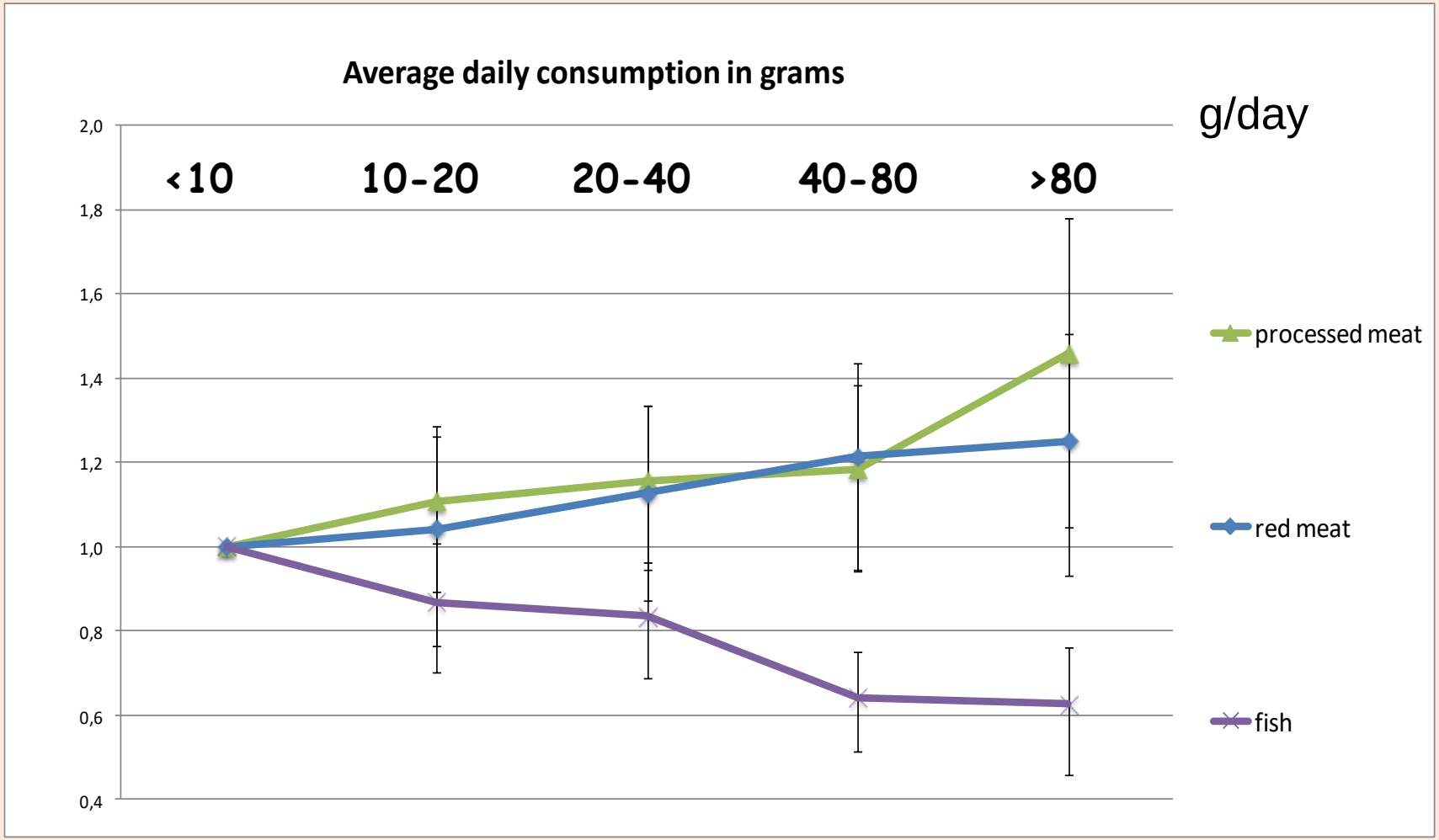
	Categories of rMED†						
	Low (3,879/3,902)		Medium (5,103/6,767)		High (4,380/7,392)		
	HR§	95% CI	HR§	95% CI	HR§	95% CI	*P* (trend)
Crude model	1.00	Referent	0.74	0.70–0.79	0.65	0.60–0.71	<0.001
Sex- and BMI-adjusted model	1.00	Referent	0.87	0.81–0.94	0.80	0.72–0.89	<0.001
Multiple adjusted model	1.00	Referent	0.93	0.86–1.01	0.88	0.79–0.97	0.013

	Two-point increment in rMED‡ (11,994/15,049)		
	HR§	95% CI	*P*
Crude model	0.88	0.86–0.90	<0.001
Sex- and BMI-adjusted model	0.94	0.91–0.96	<0.001
Multiple adjusted model	0.96	0.94–0.99	0.002

Diabetes Care 34:1913–1918, 2011

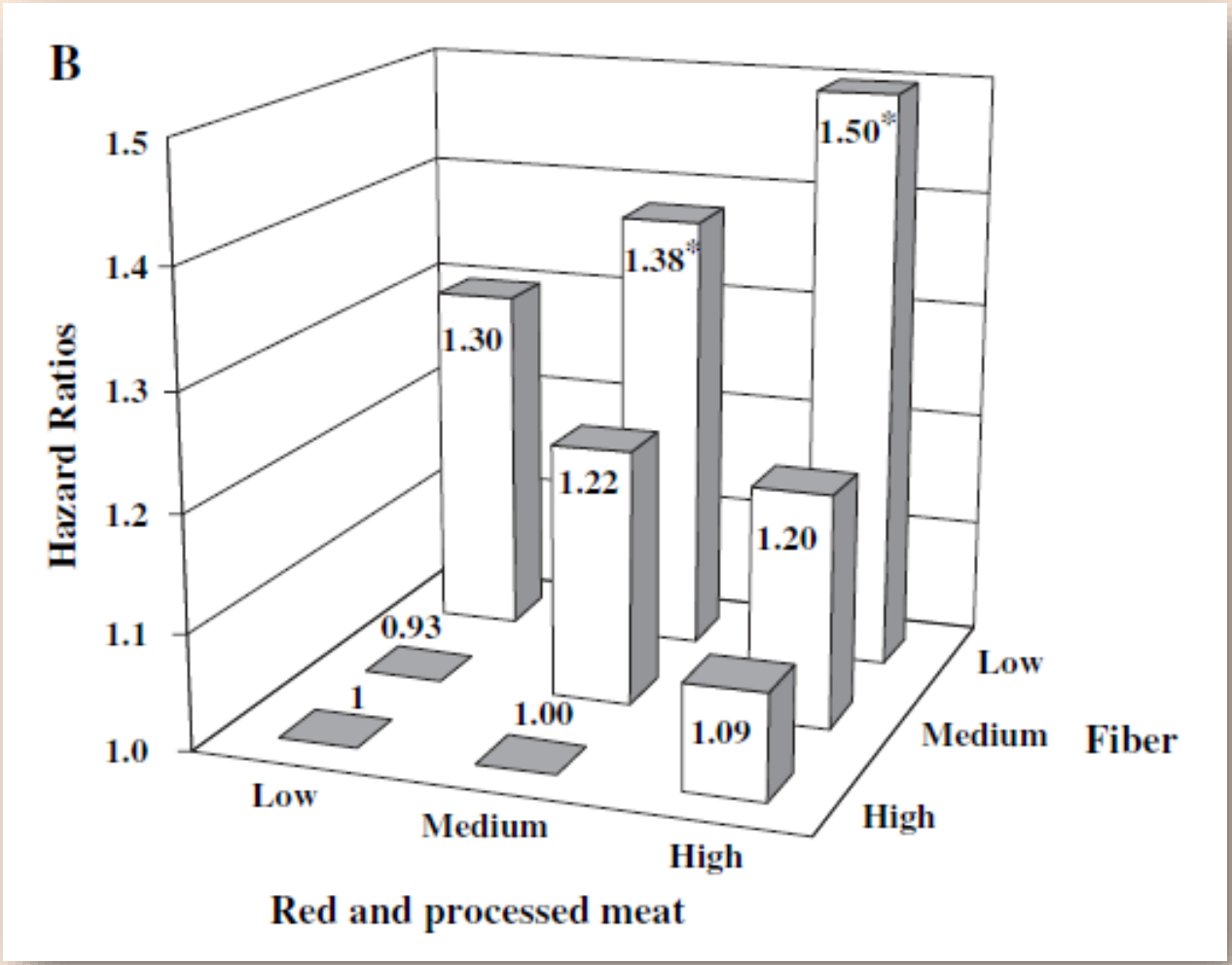
Meat, Fish, and Colorectal Cancer Risk: The European Prospective Investigation into Cancer and Nutrition

Norat T. et al. (JNCI, 2005)



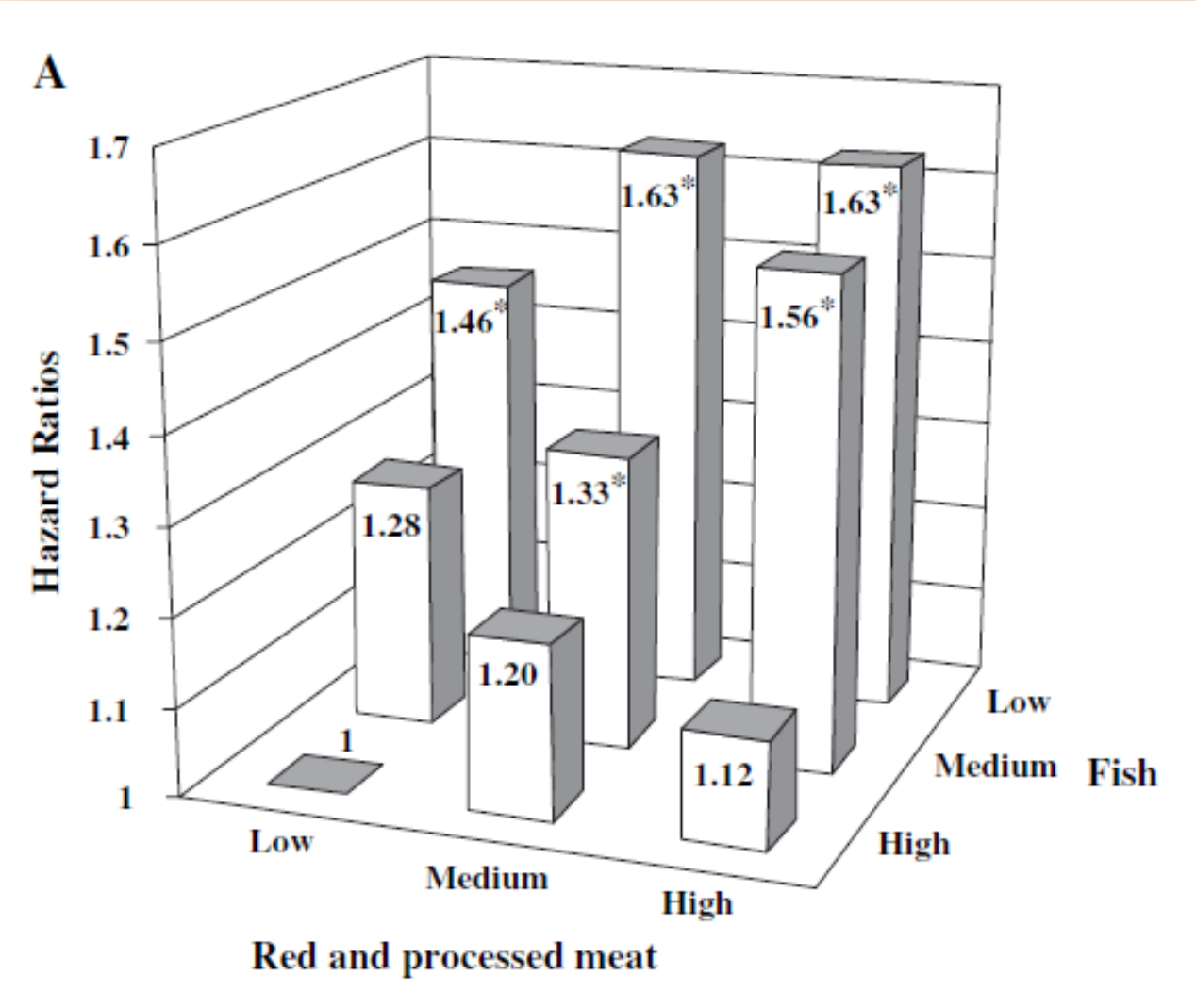
Statistical model adjusted for : energy, height, weight, physical activity, fiber, alcohol and tobacco

EPIC: colorectal cancer - Combined effect of consumption of red & processed meat and fiber



Norat T. et al. (JNCI, 2005)

EPIC: colorectal cancer - Combined effect of consumption of red & processed meat and fish

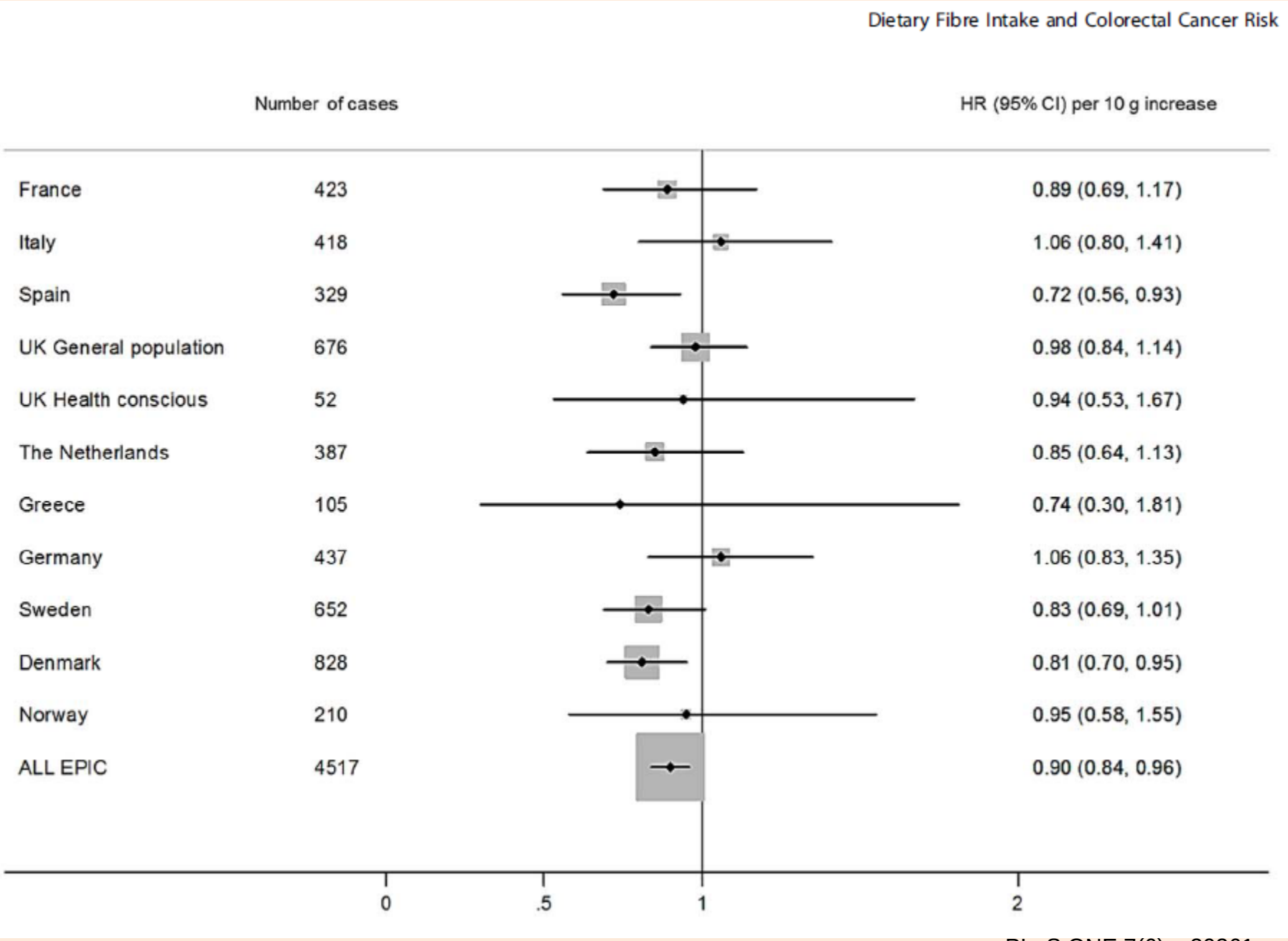


Norat T. et al. (JNCI, 2005)

Association between dietary meat consumption and incident type 2 diabetes: the EPIC-InterAct study

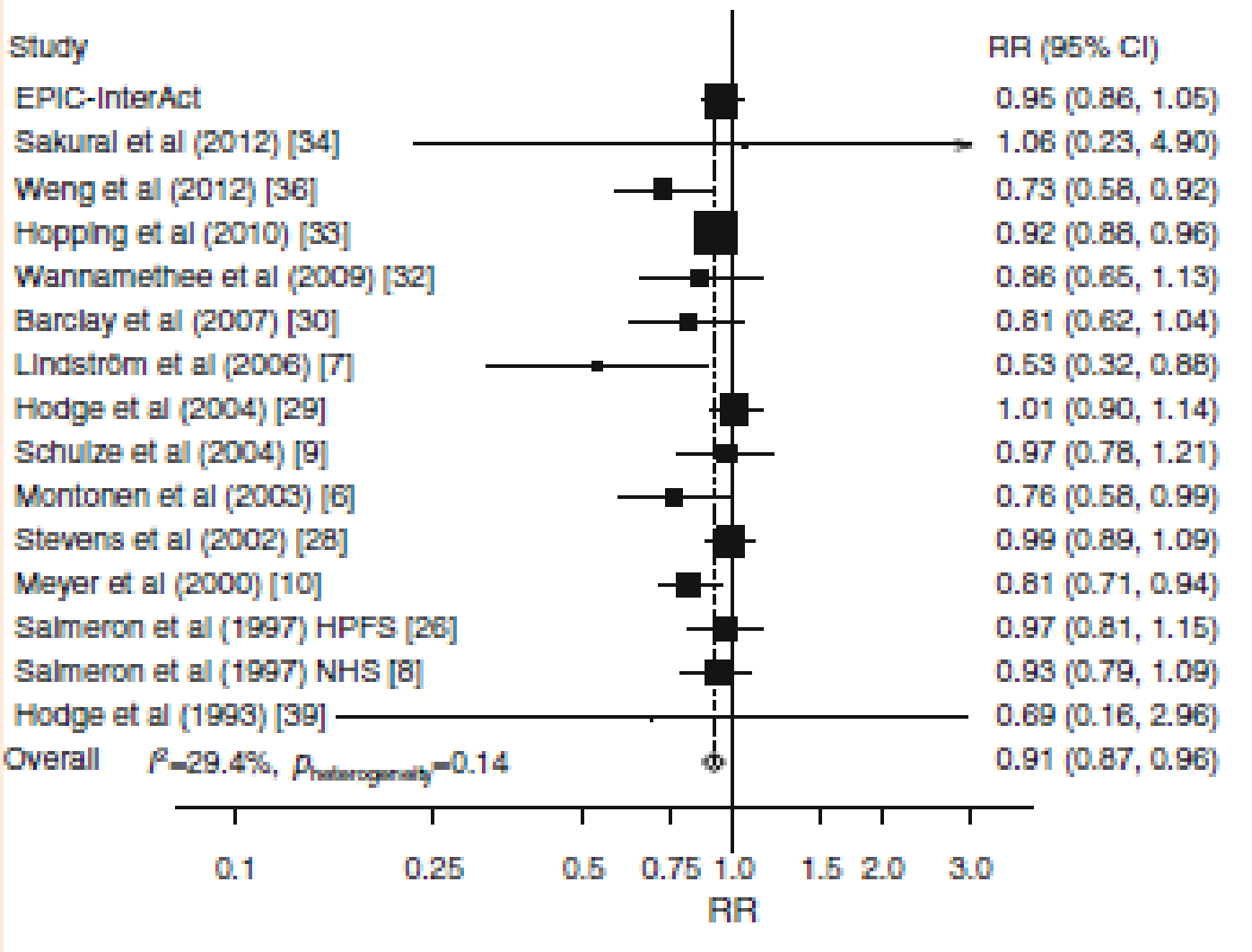
Daily consumption	No. of cases	Basic model[a]		Multivariate model 1[b]		Multivariate model 2[c]	
		HR	CI	HR	CI	HR	CI
Total meat							
Q1 (m=61.6, w=38.3)	1,970	1.00		1.00		1.00	
Q2 (m=99.3, w=66.9)	2,070	1.16	1.06, 1.26	1.15	1.05, 1.25	1.01	0.91, 1.11
Q3 (m=129.7, w=90.0)	2,441	1.44	1.32, 1.57	1.39	1.27, 1.52	1.17	1.06, 1.30
Q4 (m=164.4, w=114.1)	2,347	1.50	1.37, 1.64	1.45	1.32, 1.59	1.19	1.07, 1.32
Q5 (m=228.1, w=155.4)	2,731	1.97	1.78, 2.16	1.82	1.65, 2.01	1.27	1.13, 1.42
p value for linear trend		<0.0001		<0.0001		<0.0001	
50 g increments		1.21	1.18, 1.24	1.18	1.15, 1.22	1.08	1.05, 1.12
Red meat							
Q1 (m=11.2, w=7.1)	2,061	1.00		1.00		1.00	
Q2 (m=30.8, w=20.4)	2,233	1.16	1.07, 1.27	1.16	1.06, 1.26	0.99	0.89, 1.11
Q3 (m=51.0, w=34.8)	2,285	1.26	1.16, 1.38	1.24	1.13, 1.36	1.10	1.00, 1.22
Q4 (m=76.3, w=52.1)	2,437	1.40	1.27, 1.53	1.33	1.21, 1.46	1.16	1.05, 1.29
Q5 (m=116.8, w=80.7)	2,543	1.57	1.42, 1.73	1.50	1.36, 1.56	1.20	1.07, 1.35
p value for linear trend		<0.0001		<0.0001		<0.0001	
50 g increments		1.20	1.15, 1.25	1.18	1.13, 1.23	1.08	1.03, 1.13
Processed meat							
Q1 (m=9.1, w=4.3)	2,015	1.00		1.00		1.00	
Q2 (m=23.2, w=13.2)	2,190	1.13	1.04, 1.22	1.13	1.04, 1.23	1.08	0.98, 1.19
Q3 (m=36.9, w=21.6)	2,275	1.20	1.10, 1.30	1.18	1.08, 1.28	1.03	0.94, 1.14
Q4 (m=55.7, w=34.4)	2,447	1.36	1.25, 1.48	1.31	1.20, 1.43	1.14	1.04, 1.26
Q5 (m=93.5, w=60.5)	2,632	1.61	1.47, 1.76	1.51	1.37, 1.65	1.16	1.04, 1.31
p value for linear trend		<0.0001		<0.0001		0.006	
50 g increments		1.30	1.23, 1.36	1.24	1.18, 1.31	1.12	1.05, 1.19
Red and processed meat							
Q1 (m=38.4, w=22.3)	1,991	1.00		1.00		1.00	
Q2 (m=71.0, w=45.4)	2,112	1.15	1.05, 1.25	1.11	1.01, 1.21	0.97	0.88, 1.08
Q3 (m=97.4, w=63.6)	2,328	1.34	1.23, 1.46	1.28	1.17, 1.40	1.08	0.97, 1.20
Q4 (m=129.0, w=85.3)	2,410	1.47	1.34, 1.61	1.39	1.26, 1.52	1.18	1.06, 1.31
Q5 (m=182.3, w=120.4)	2,718	1.84	1.67, 2.02	1.70	1.54, 1.88	1.18	1.04, 1.33
p value for linear trend		<0.0001		<0.0001		<0.0001	
50 g increments		1.23	1.1, 1.27	1.20	1.16, 1.24	1.09	1.05, 1.13

Diabetologia (2013) 56:47–59



PLoS ONE 7(6): e39361.

Dietary fibre and incidence of type 2 diabetes: a meta-analysis of prospective studies



Diabetologia (2015) 58:1394–1408

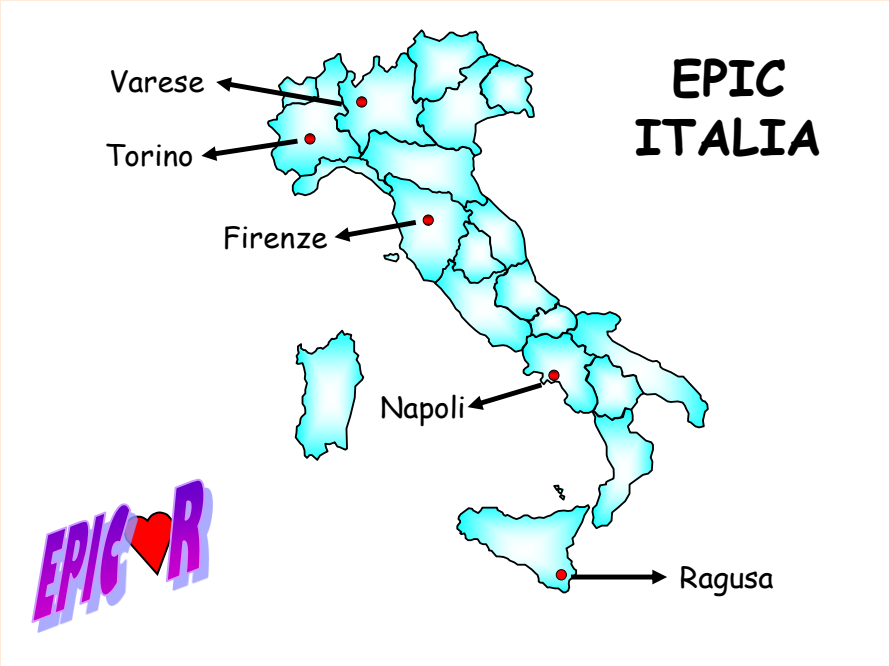
Fruit and vegetables consumption and breast cancer risk: the EPIC Italy study

Breast Cancer Res Treat (2012)

Giovanna Masala · Melania Assedi · Benedetta Bendinelli · Ilaria Ermini · Sabina Sieri · Sara Grioni · Carlotta Sacerdote · Fulvio Ricceri · Salvatore Panico · Amalia Mattiello · Rosario Tumino · Maria Concetta Giurdanella · Franco Berrino · Calogero Saieva · Domenico Palli

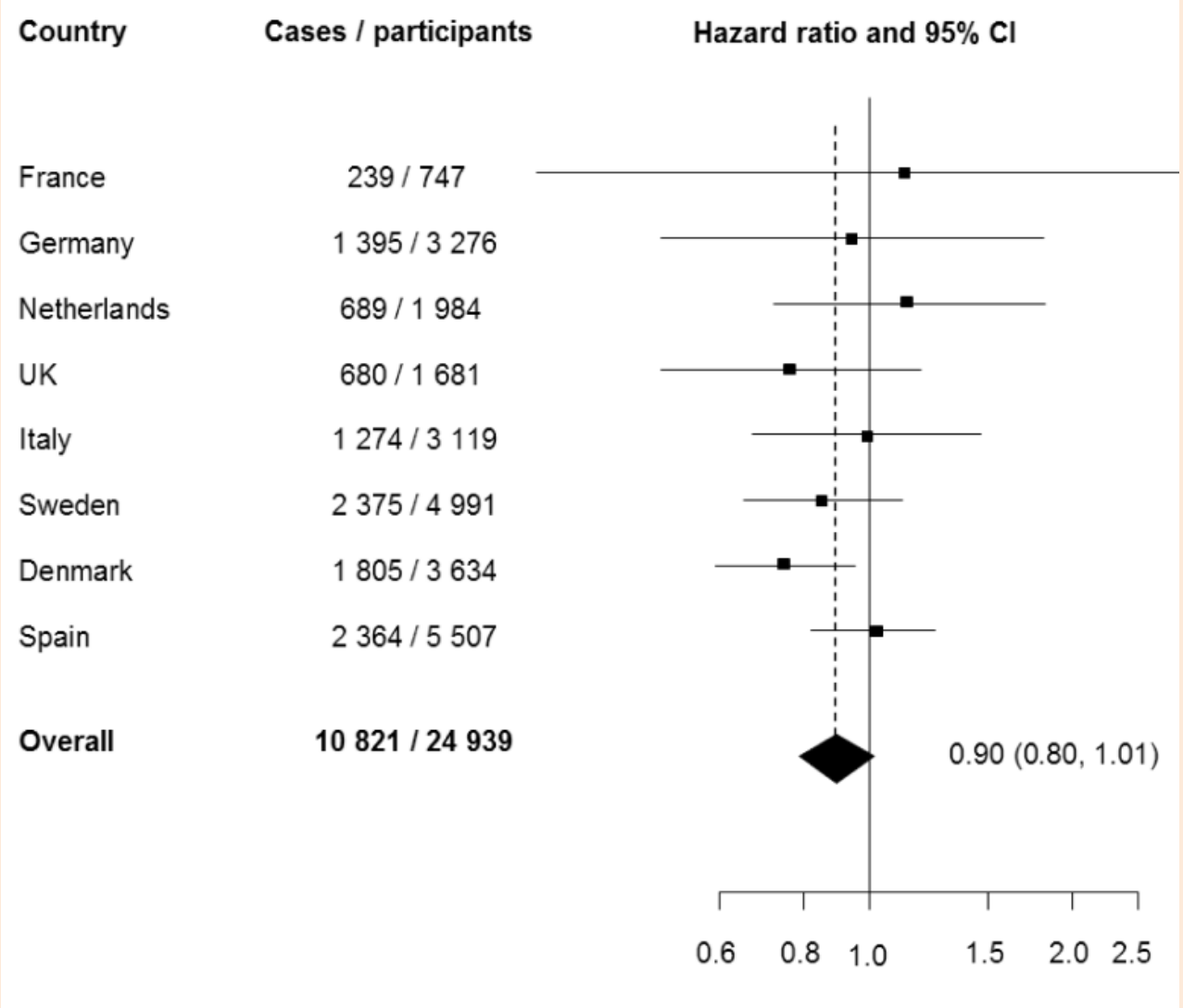
Table 3 Quintiles of consumption of vegetables (overall and specific sub-groups) in relation to breast cancer risk

		Range (g/day)	cases	HR (95% CI)[a]	HR (95% CI)[b]
Vegetables (all types)	I	<107.8	259	1.00	1.00
	II	107.8–151.9	215	0.83 (0.69–0.99)	0.81 (0.67–0.97)
	III	151.9–197.9	240	0.96 (0.81–1.15)	0.93 (0.78–1.12)
	IV	197.9–264.8	195	0.82 (0.67–0.99)	0.78 (0.64–0.96)
	V	>264.8	163	0.69 (0.56–0.85)	0.65 (0.53–0.81)
	P trend			0.0007	0.003
Leafy vegetables all types	I	<15.3	247	1.00	1.00
	II	15.3–24.9	252	1.01 (0.84–1.20)	1.01 (0.85–1.21)
	III	24.9–37.6	201	0.82 (0.68–0.99)	0.83 (0.68–1.00)
	IV	37.7-56.9	199	0.84 (0.69–1.01)	0.83 (0.65–1.01)
	V	>56.9	173	0.70 (0.57–0.85)	0.70 (0.57–0.86)
	P trend			< 0.0001	0.0001
Leafy vegetables raw	I	<5.6	210	1.00	1.00
	II	5.6–11.3	224	0.99 (0.82–1.20)	1.01 (0.83–1.22)
	III	11.3–17.7	242	0.96 (0.80–1.17)	0.97 (0.80–1.18)
	IV	17.7–31.8	199	0.87 (0.71–1.07)	0.87 (0.71–1.06)
	V	>31.8	197	0.79 (0.64–0.96)	0.79 (0.64–0.97)
	P trend			0.005	0.005
Leafy vegetables: cooked	I	<5.1	263	1.00	1.00
	II	5.1–9.8	235	0.88 (0.74–1.05)	0.89 (0.75–1.06)
	III	9.8–15.1	203	0.80 (0.66–0.96)	0.81 (0.67–0.98)
	IV	15.1–24.8	197	0.83 (0.69–1.01)	0.84 (0.69–1.02)
	V	>24.8	174	0.76 (0.62–0.93)	0.77 (0.63–0.95)
	P trend			0.018	0.03



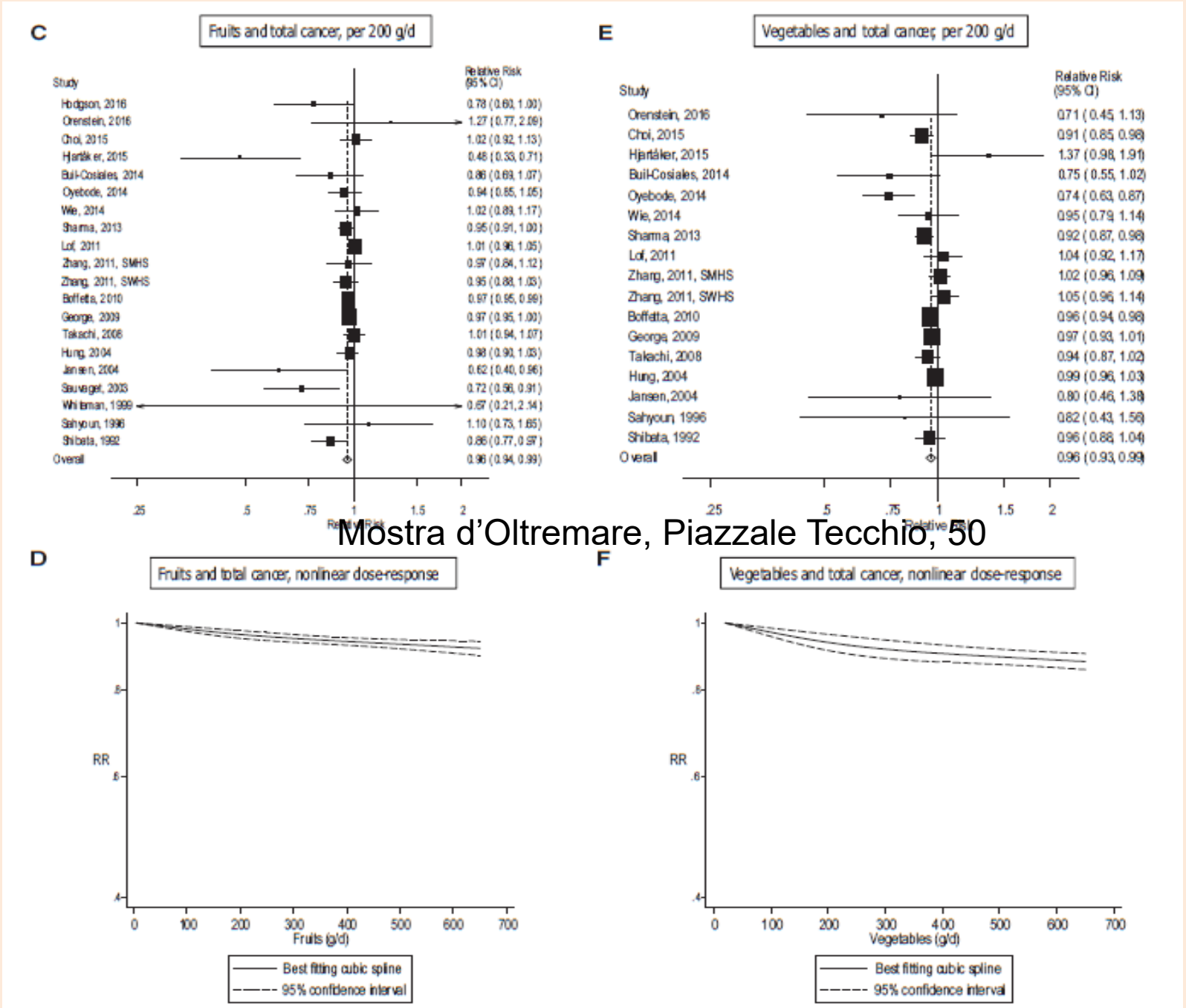
Italy	Men	Women	Total
Torino	6,047	4,557	10,604
Varese	2,557	9,526	12,083
Firenze	3,514	10,083	13,597
Napoli	-	5,062	5,062
Ragusa	3,053	3,350	6,403
Total	15,171	32,578	47,749

Fruit and vegetable intake and type 2 diabetes: EPIC-InterAct prospective study and meta-analysis



Hazard ratio of type 2 diabetes comparing the highest with the lowest quartile of estimated total fruit and vegetable intake across countries: EPIC-InterAct study

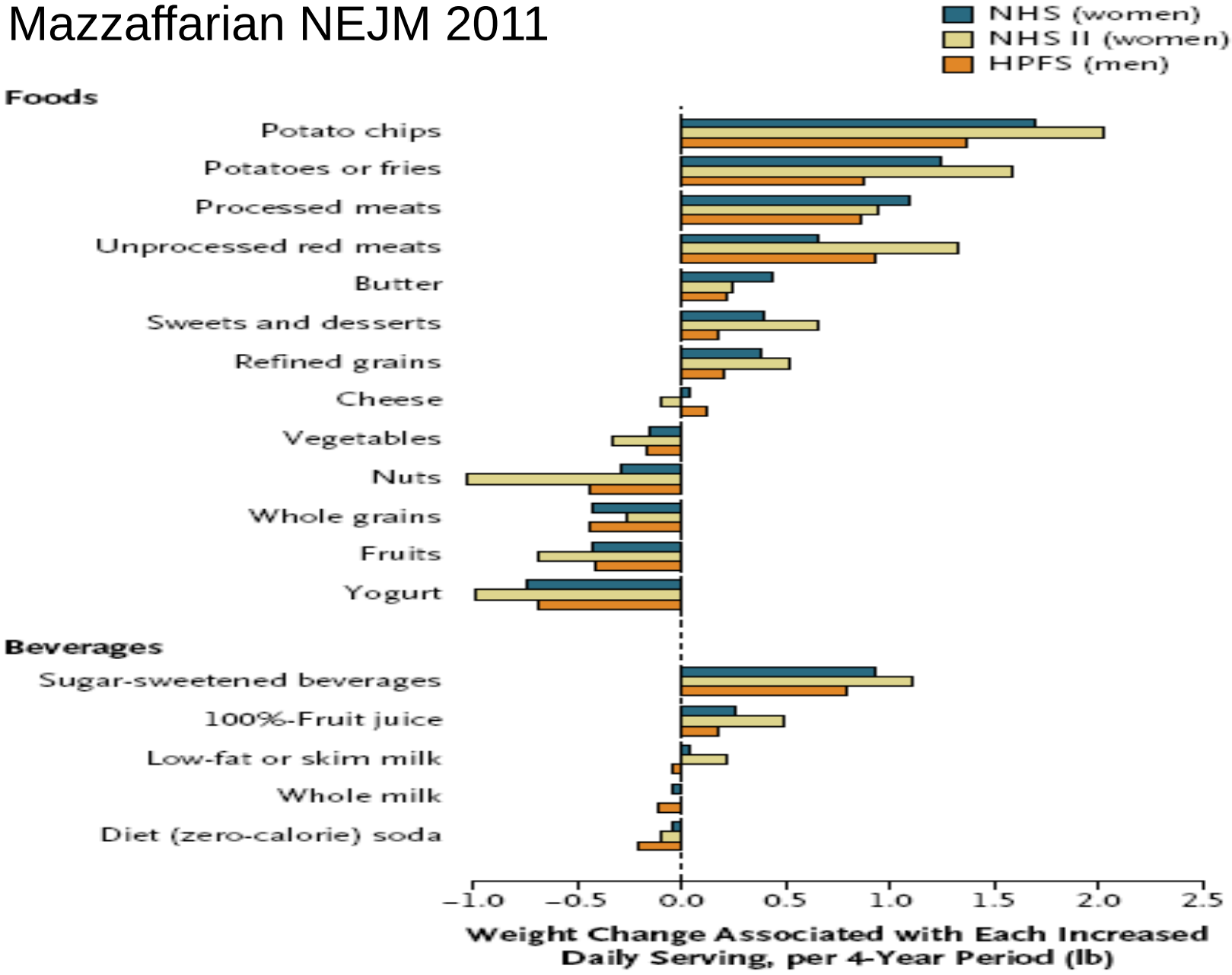
Eur J Clin Nutr. 2012 October ; 66(10): 1082–1092



Mostra d'Oltremare, Piazzale Tecchio, 50

International Journal of Epidemiology, 2017, 1–28

Mazzaffarian NEJM 2011

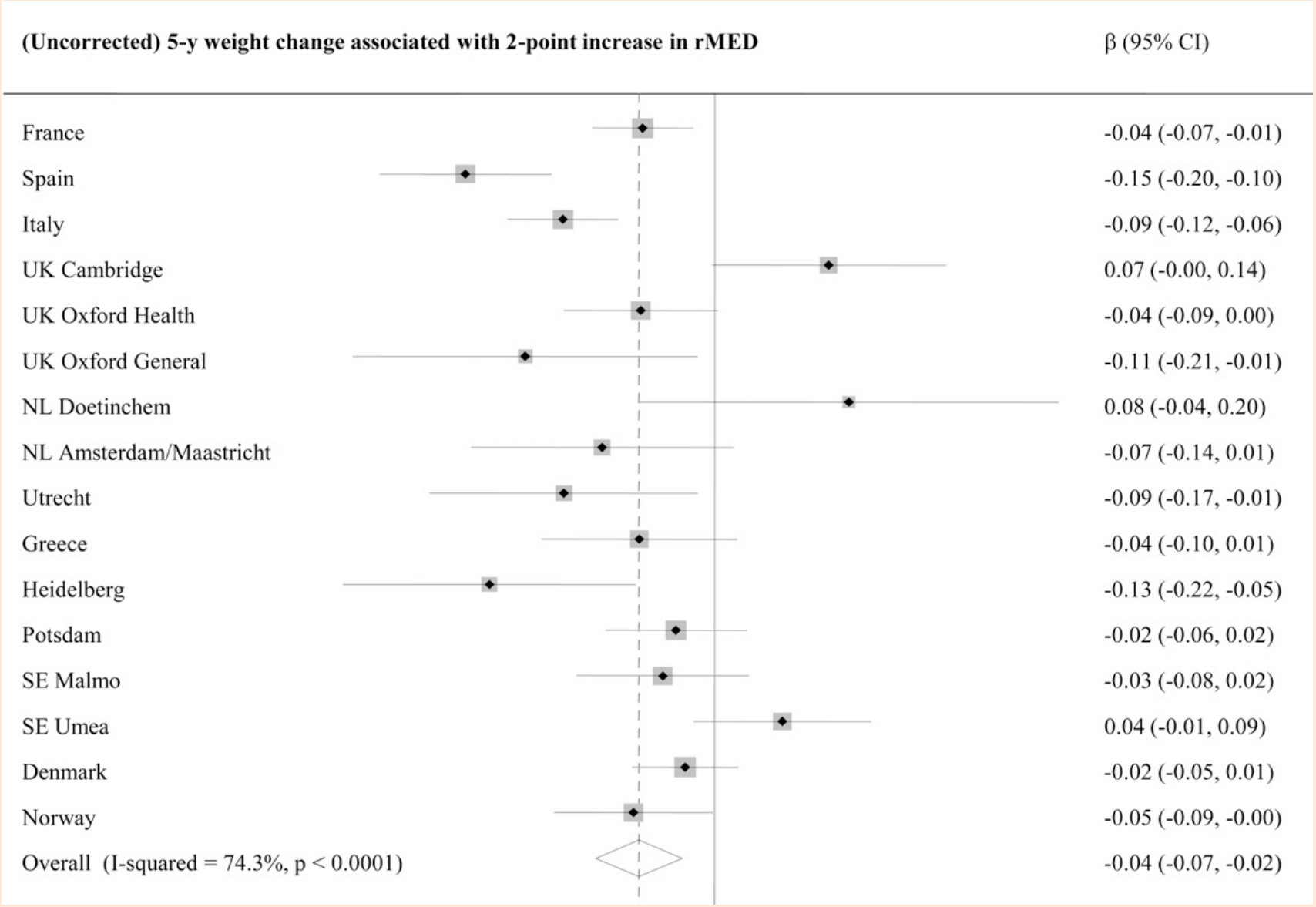


Consumption of sweet beverages and type 2 diabetes incidence in European adults: results from EPIC-InterAct

Variable and model	<1 glass[a]/ month HR	1–4 glasses[a]/ month HR[b] (95% CI)	>1–6 glasses[a]/ week HR[b] (95% CI)	≥1 glass[a]/ day HR[b] (95% CI)	*p* for trend
Total soft drinks[c] (median intake, g/day)	(0.0)	(20.0)	(95.1)	(413.1)	
No. cases	5,794	1,604	2,987	1,299	
Crude model	1.00 (ref)	1.21 (1.07, 1.36)	1.30 (1.18, 1.43)	1.78 (1.55, 2.04)	<0.0001
Adjusted model	1.00 (ref)	1.21 (1.07, 1.37)	1.26 (1.13, 1.42)	1.58 (1.35, 1.84)	<0.0001
Adjusted model+EI	1.00 (ref)	1.21 (1.07, 1.37)	1.27 (1.12, 1.43)	1.59 (1.35, 1.88)	<0.0001
Adjusted model+EI+BMI	1.00 (ref)	1.17 (0.97, 1.42)	1.11 (0.98, 1.26)	1.21 (1.05, 1.41)	0.0005
Sugar-sweetened soft drinks[d] (median intake, g/day)	(0.0)	(19.3)	(94.3)	(425.7)	
No. cases	3,948	964	1,599	605	
Crude model	1.00 (ref)	1.14 (0.97, 1.35)	1.16 (1.05, 1.28)	1.68 (1.40, 2.02)	<0.0001
Adjusted model	1.00 (ref)	1.13 (0.97, 1.31)	1.04 (0.94, 1.15)	1.39 (1.16, 1.67)	<0.0001
Adjusted model+EI	1.00 (ref)	1.12 (0.96, 1.31)	1.04 (0.94, 1.15)	1.39 (1.15, 1.69)	0.001
Adjusted model+EI+BMI	1.00 (ref)	1.19 (0.91, 1.56)	1.07 (0.94, 1.21)	1.29 (1.02, 1.63)	0.013

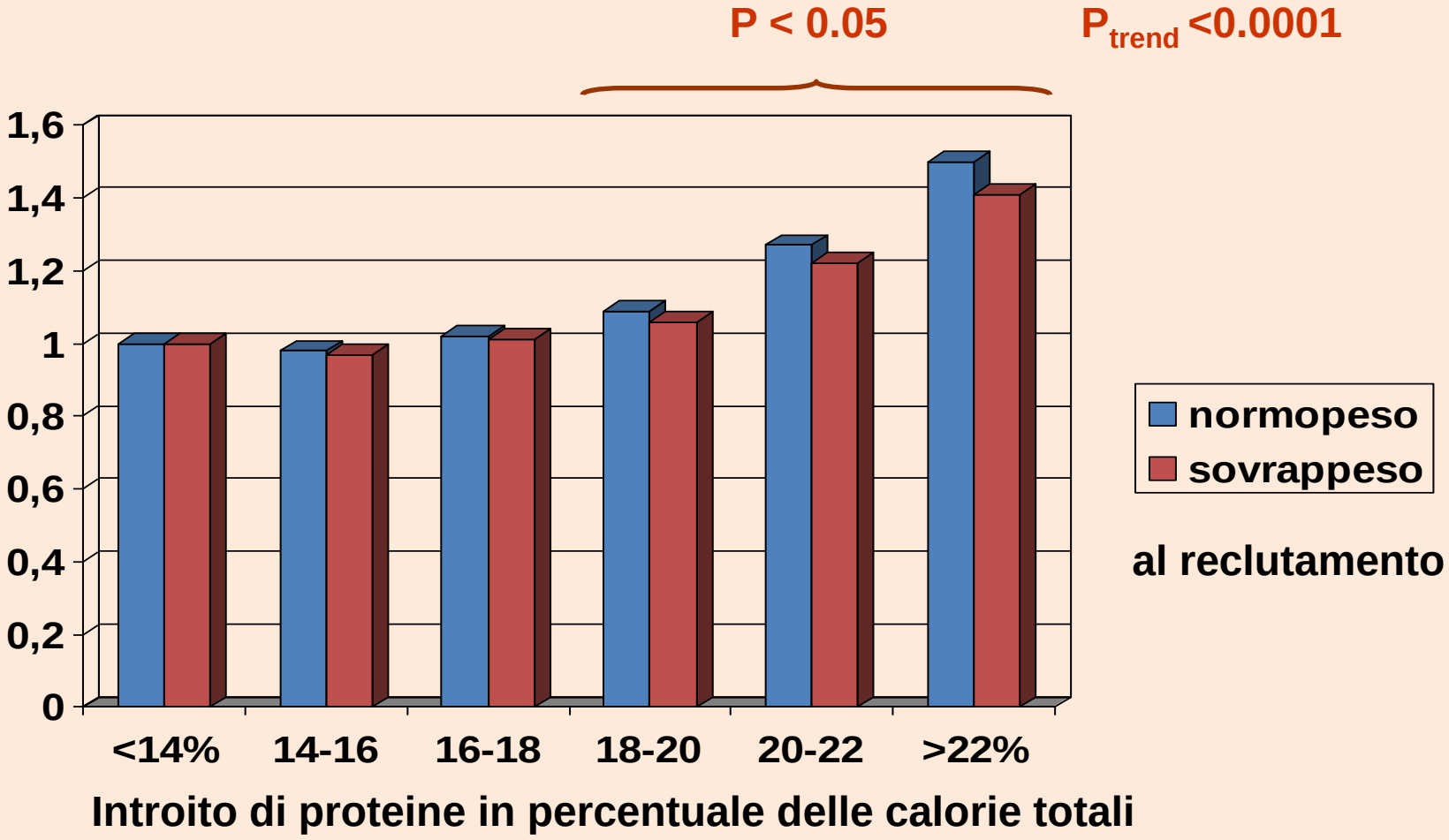
Diabetologia (2013) 56:1520–1530

Mediterranean dietary patterns and prospective weight change in participants of the EPIC-PANACEA project

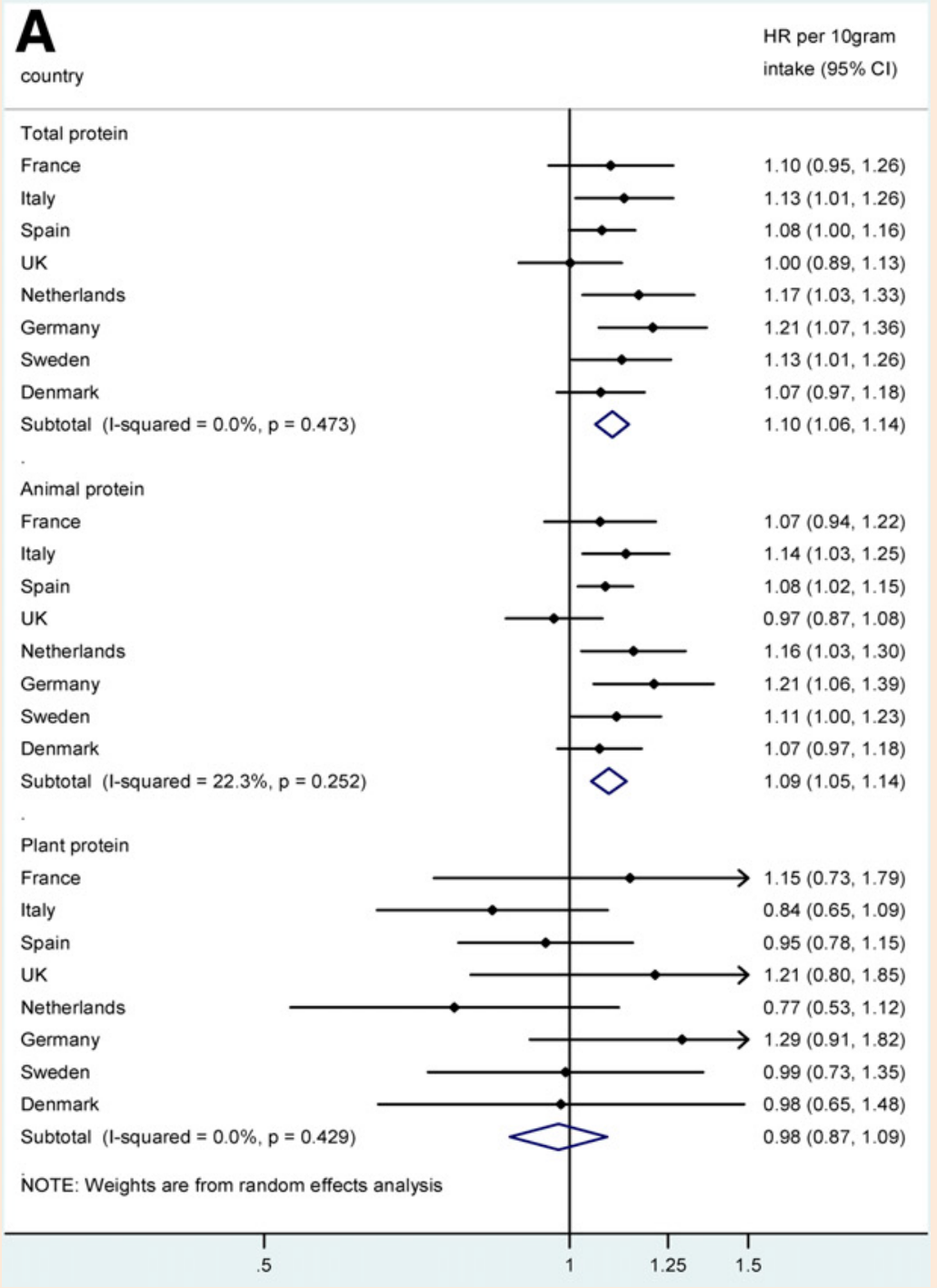


Am J Clin Nutr 2010;92:912–21.

EPIC: rischio di diventare sovrappeso (per i normopeso) od obesi (per i sovrappeso) in funzione del consumo proteico (*Vergnaud 2012*)



Dietary Protein Intake and Incidence of Type 2 Diabetes in Europe: The EPIC-InterAct Case-Cohort Study (WOMEN)



Breast – Cox regression results
EPIC Italy

	Unadjusted*			Adjusted*		
Breast	HR	LCL	UCL	HR	LCL	UCL
NCEP/ATPIII	1.60	1.15	2.23	1.68	1.17	2.40
Harmonized	1.60	1.19	2.16	1.75	1.28	2.40
Tertile	1.52	1.13	2.05	1.60	1.15	2.21

Unadjusted: stratified by centre and age-class
Adjusted: education, smoke, Med Ind, Alcool, PALS, # childrens, age at menarche

Panico S, Chiodini P, Mattiello A. (in preparation)

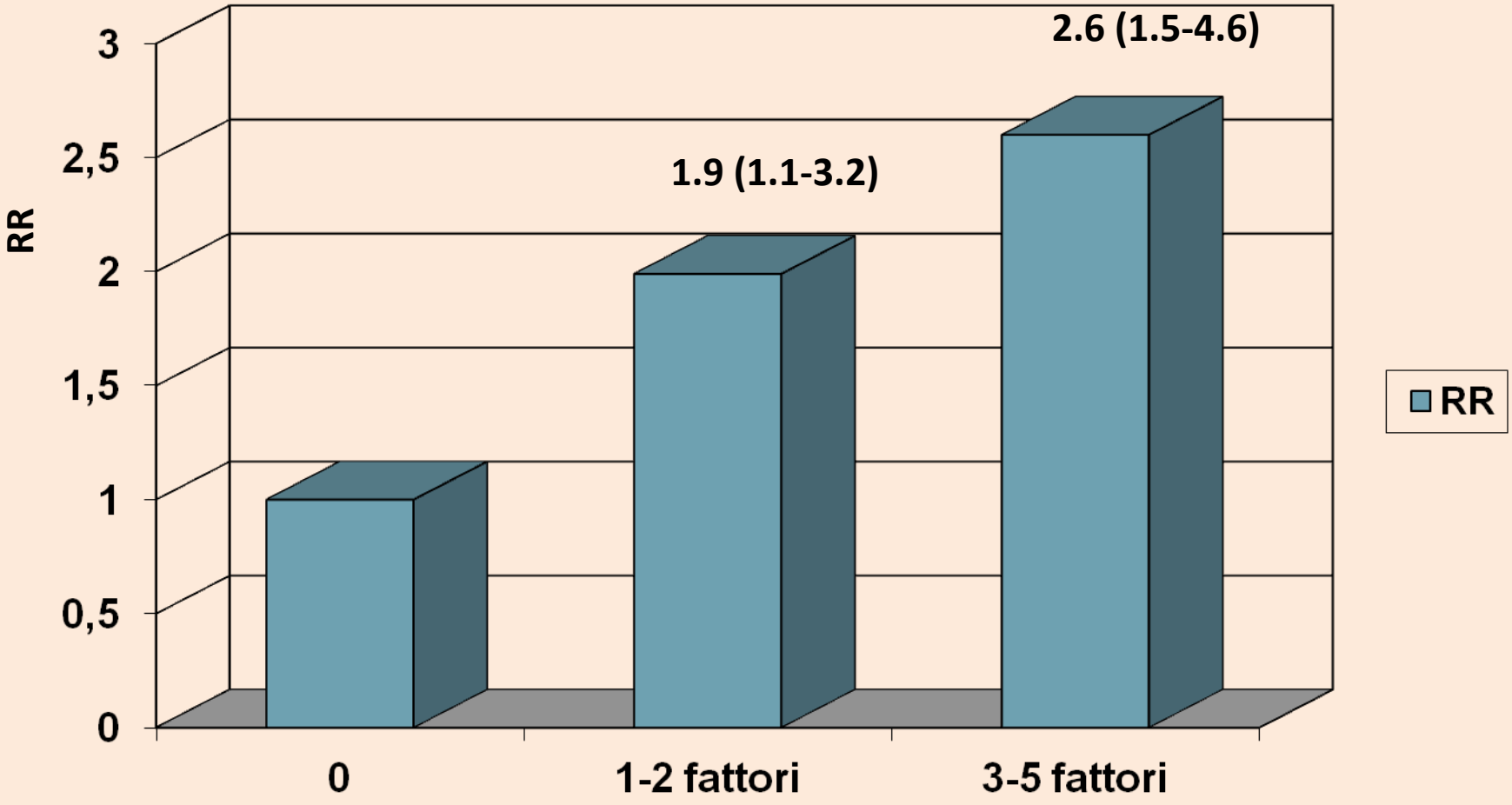
Colon – Cox regression results
EPIC Italy

	Unadjusted*			Adjusted*		
Men	HR	LCL	UCL	HR	LCL	UCL
NCEP/ATPIII	1.97	1.06	3.64	2.10	1.12	3.95
Harmonized	1.75	1.02	2.99	1.81	0.99	3.34
Tertile	1.82	1.07	3.09	1.89	1.09	3.29
Women						
NCEP/ATPIII	1.49	0.91	2.45	1.60	0.95	2.70
Harmonized	1.70	1.08	2.67	1.83	1.14	2.93
Tertile	1.88	1.19	2.96	2.15	1.30	3.56

Unadjusted: stratified by centre and age-class
Adjusted: education, smoke, Med Ind, Alcool, PALS, (menopausal status)

Panico S, Chiodini P, Mattiello A. (in preparation)

Breast cancer risk according to the number of components of the metabolic syndrome
ORDET STUDY – EPIC Varese (post-menopause)



Agnoli C, Berrino F, Krogh V, Panico S et al. NMCD, 2009

Metabolic syndrome and colorectal cancer in EPIC

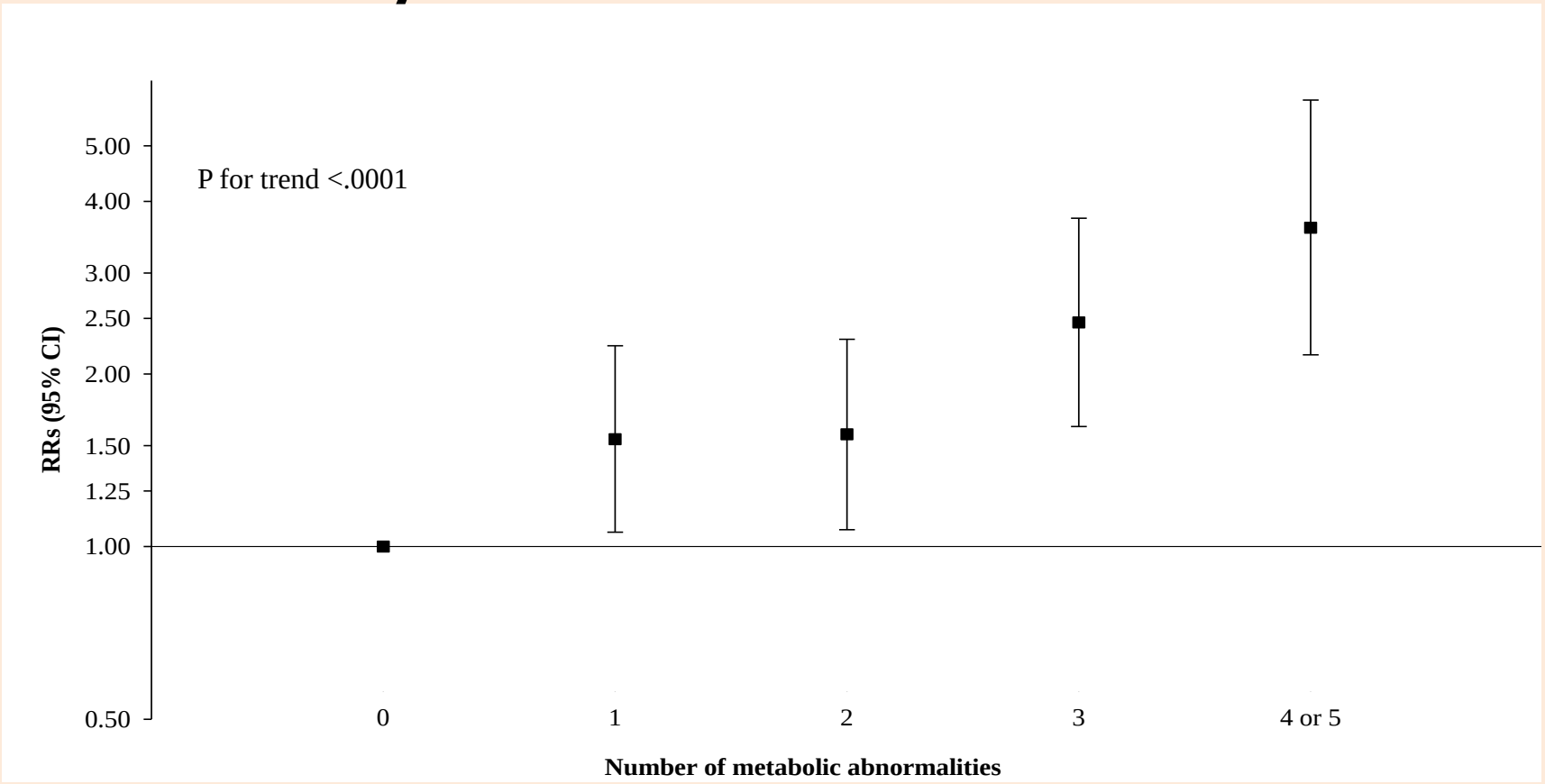


Figure 2a: Multivariable-adjusted relative risks (95%CI) for **colon cancer** for presence of increasing number of individual MetS components

Cancer Prev Res (Phila). 2011 Jun 22. Epub ahead of print

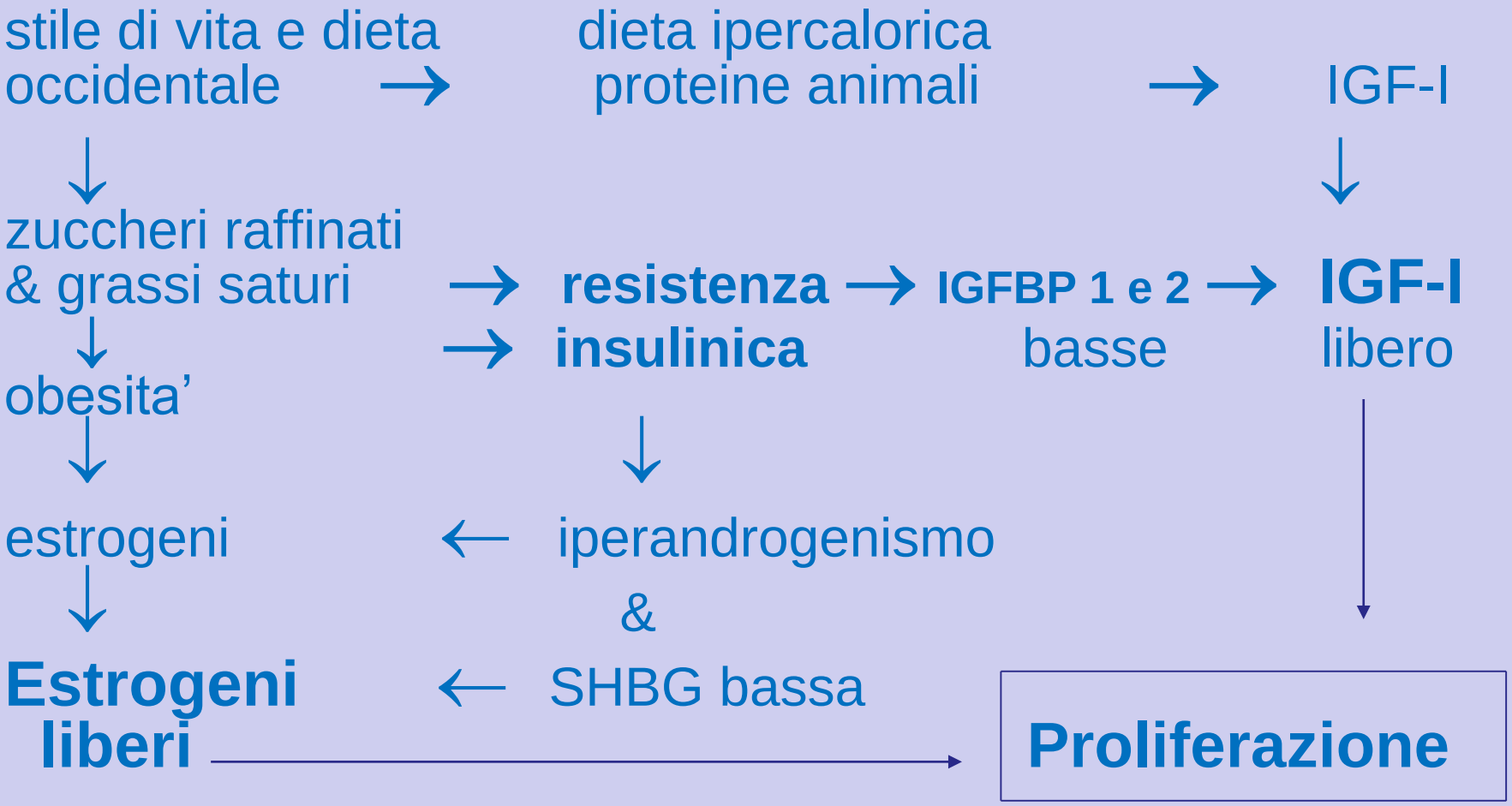
Un nuovo concetto si afferma grazie all'epidemiologia nutrizionale del cancro:

La carcinogenesi metabolica

DIANA (DIeta e ANdrogeni)

sperimentazione preventiva controllata per valutare l'efficacia di un cambiamento dello stile di vita per prevenire o ritardare lo sviluppo di recidive e metastasi nelle donne operate di carcinoma mammario

Meccanismi che legano la dieta e il rischio di carcinoma mammario



DIANA-1: effetti di 4,5 mesi di dieta

	Cambia mento%	P		Cambia mento%	P
SHBG	+ 25.2	0.0001	glicemia	-5.7	0.026
Testosterone	-18.3	0.0040	Area glicemica	+4.8	0.85
Estradiolo	-18.0	0.1300	GH	+54.2	0.22
Testosterone libero	-28.6	<0.0001	GHBP	+29.1	0.002
Estradiolo libero	-23.4	0.0500	IGF-1	-5.9	0.64
Insulina	-10.4	0.1400	IGFBP-1	+12.2	0.015
Area insulinica	-7.7	0.0404	IGFBP-2	+30.4	0.0004
C-Peptide	-19.1	0.03	IGFBP-3	-4.5	0.21

Metabolic syndrome and breast cancer prognosis

Franco Berrino · Anna Villarini · Adele Traina · Bernardo Bonanni · Salvatore Panico · Maria Piera Mano · Angelica Mercandino · Rocco Galasso · Maggiorino Barbero · Milena Simeoni · Maria Chiara Bassi · Elena Consolaro · Harriet Johansson · Maurizio Zarcone · Eleonora Bruno · Giuliana Gargano · Elisabetta Venturelli · Patrizia Pasanisi

Metabolic syndrome		
0 components	42	1
1–2 components	77	1.39 (0.91–2.14)
3+ components	45	**2.17 (1.31–3.60)**
Analysis restricted to distant metastases		
No Metabolic syndrome	22	**1**
1–2 components	40	1.40 (0.76–2.55)
3+ components	27	**2.45 (1.24–4.82)**

Adjusted by age, education, stage at diagnosis, and ER expression

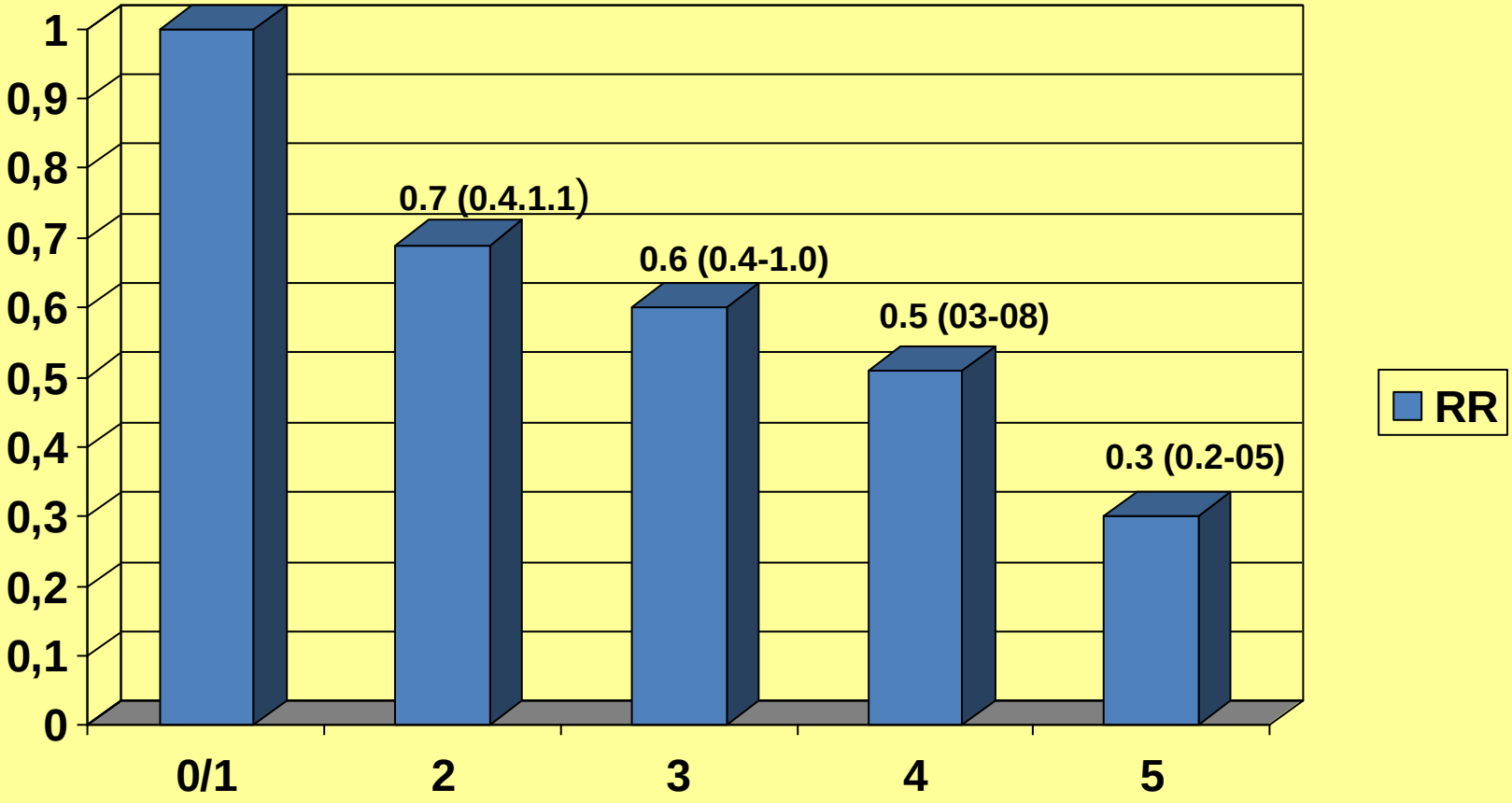
Breast Cancer Res Treat (2014) 147:159–165

WCRF 2014: Istruzioni nutrizionali per la prevenzione del cancro e delle sue recidive

http://www.wcrf.org/int/research-we-fund/our-cancer-prevention-recommendations

- **Mantenersi snelli per tutta la vita**
- **Praticare quotidianamente esercizio fisico**
- **Limitare cibi ad alta densità calorica ed evitare bevande zuccherate**
- **Basare l'alimentazione quotidiana prevalentemente su cibi di provenienza vegetale con un'ampia varietà di cereali non raffinati, legumi, verdure e frutta**
- **Limitare in consumo di carni rosse ed evitare il consumo di carni conservate**
- **Limitare il consumo di bevande alcoliche**
- **Limitare il consumo di sale e cibi conservati sotto sale, ed evitare cereali e legumi conservati in ambienti umidi**
- **Meglio non usare integratori alimentari**
- **Allattare i figli**

Sindrome metabolica: diminuzione del rischio in funzione dell'aderenza alle raccomandazioni del WCRF



DIANA-5: stime basate sul questionario di 24h consegnato al reclutamento su attività fisica, bevande zuccherate, cibi vegetali non raffinati, carni, alcol.

DIANA-1: effetti di 4,5 mesi di dieta

	Cambia mento%	P		Cambia mento%	P
SHBG	+ 25.2	0.0001	glicemia	-5.7	0.026
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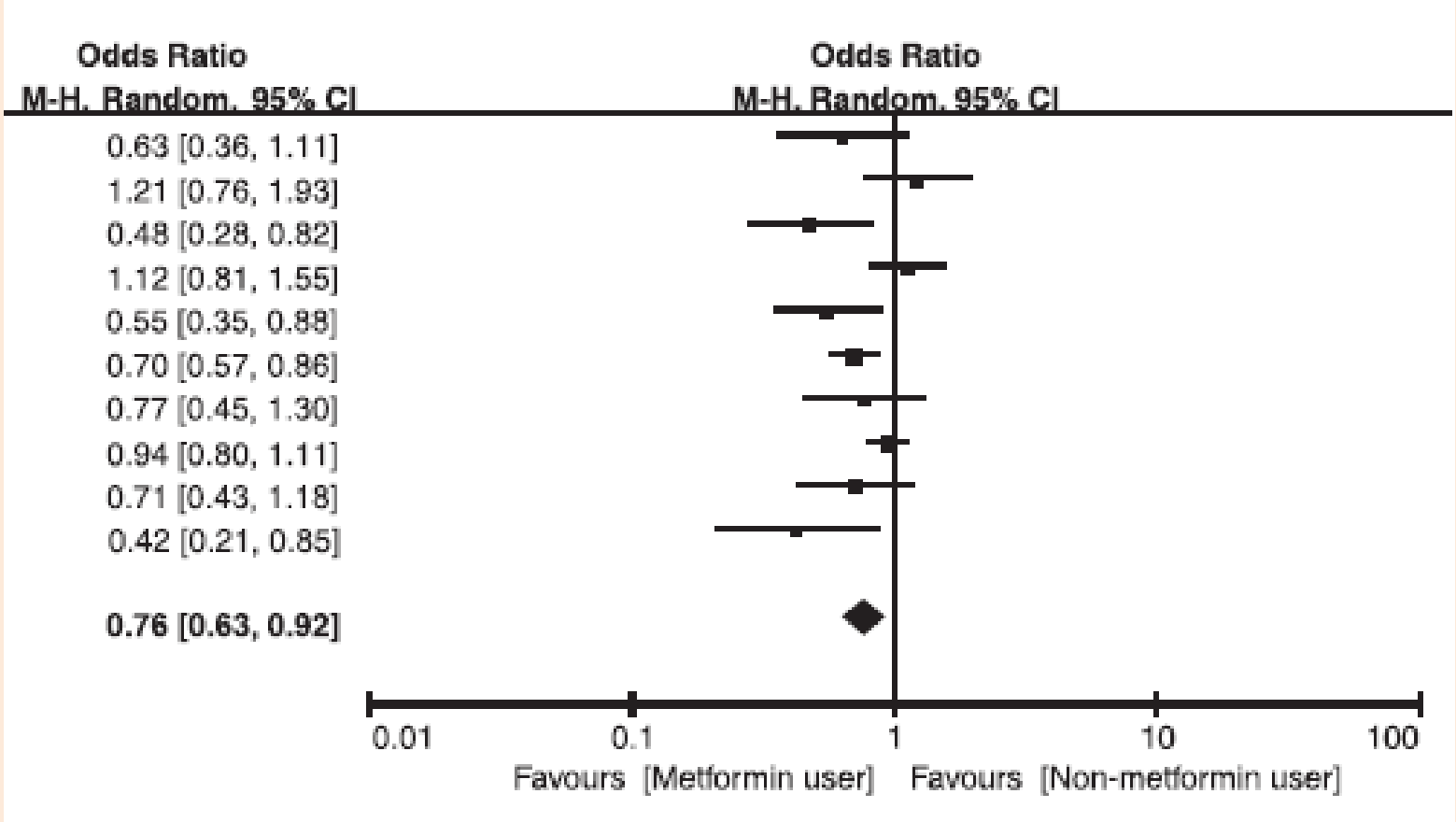
Estradiolo libero	-23.4	0.0500	IGF-1	-5.9	0.64
Insulina	-10.4	0.1400	IGFBP-1	+12.2	0.015
Area insulinica	-7.7	0.0404	IGFBP-2	+30.4	0.0004
C-Peptide	-19.1	0.03	IGFBP-3	-4.5	0.21

% change of breast cancer risk factors in two randomised studies

	Berrino 2001, DIANA-1 **MEDITERRASIAN DIET** 104 healthy women	Campagnoli 2012: **METFORMIN 1500mg** 108 breast cancer patient
SHBG	**+ 25**	**+ 14**
Testosterone	**– 18**	**– 25**
Free-test	**– 29**	**– 29**
Estradiol	**– 18**	**– 38**
Insulin	**– 10**	**– 25**
IGF-I	**– 6**	**– 6**

Metformin use and the risk of colorectal adenoma: A systematic review and meta-analysis



Journal of Gastroenterology and Hepatology 32 (2017) 957–965

Metformin and lung cancer risk in patients with type 2 diabetes mellitus

Subgroup analyses estimating hazard ratios for lung cancer for ever versus never users of metformin

Model	*n*/*N* in ever users	*n*/*N* in never users	HR	95% CI	*P* value
Age <65 years	1001 / 174601	105 / 7958	0.503	(0.403-0.628)	<0.0001
Age ≥65 years	1364 / 105558	126 / 7456	0.734	(0.611-0.880)	0.0009
Men	1541 / 150517	133 / 8819	0.649	(0.544-0.775)	<0.0001
Women	824 / 129642	78 / 6595	0.507	(0.402-0.639)	<0.0001
Follow-up duration <5 years	2014 / 102702	184 / 6200	0.557	(0.479-0.647)	<0.0001

Oncotarget, Advance Publications *April 12, 2017*

Gene-Lifestyle Interaction and Type 2 Diabetes: The EPIC InterAct Case-Cohort Study

Conclusions: The relative effect of a T2D genetic risk score is greater in younger and leaner participants. However, this subgroup is at low absolute risk and would not be a logical target for preventive interventions. The high absolute risk associated with obesity at any level of genetic risk highlights the importance of universal rather than targeted approaches to lifestyle intervention.

PLoS Med 2014;11(5): e1001647