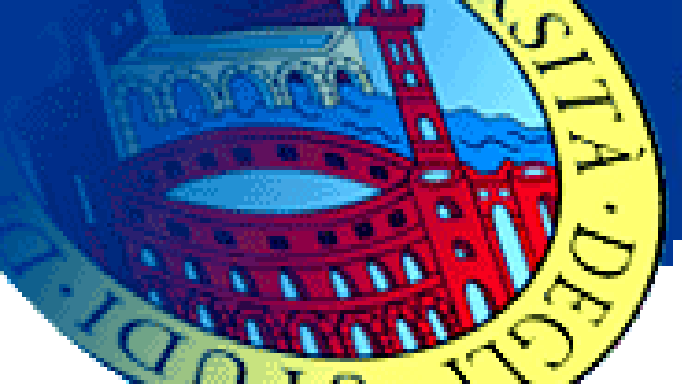


UNIVERSITÀ DEGLI STUDI DI VERONA

Healthy Aging
La nutrizione

Prof Mauro Zamboni

Clinica Geriatrica Università di Verona

58 Congresso Nazionale SIGG

27-30 Novembre,2013-Torino

In relazioni alle variabili estrinseche che influiscono sull'invecchiamento, forse nessuna è più importante della nutrizione

Lipschitz D.A., 2000

Longevity and Diet. Myth or pragmatism?

Christina Chrysohoou*, Christodoulos Stefanadis

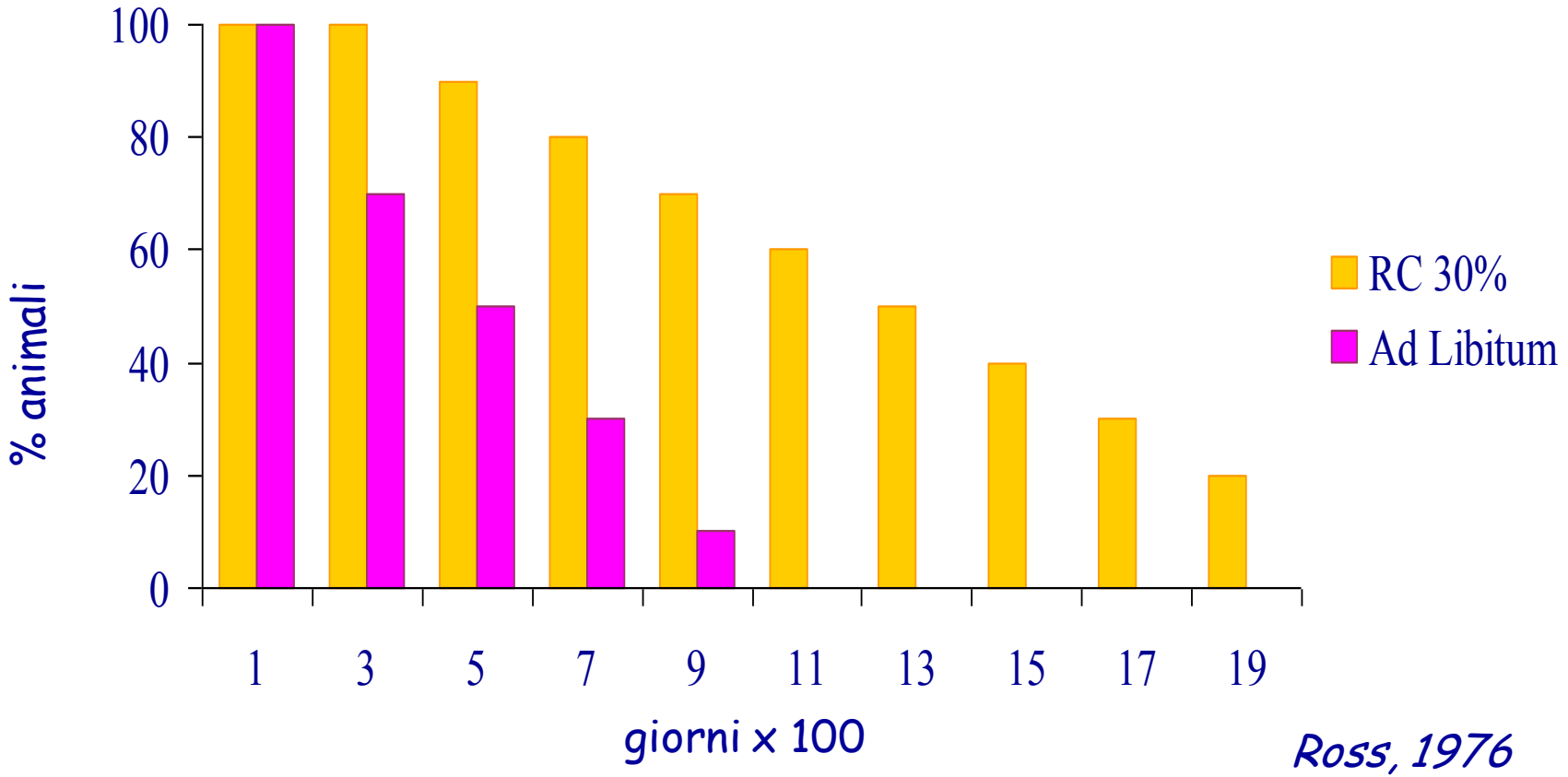
Maturitas, 2013

McCay C, Crowell M, Maynard L

The effect of retarted growth upon the lenght of life and upon the ultimate size

J Nutr, 10, 63-79, 1935

Restrizione Calorica e durata media della vita in roditori



Ross, 1976

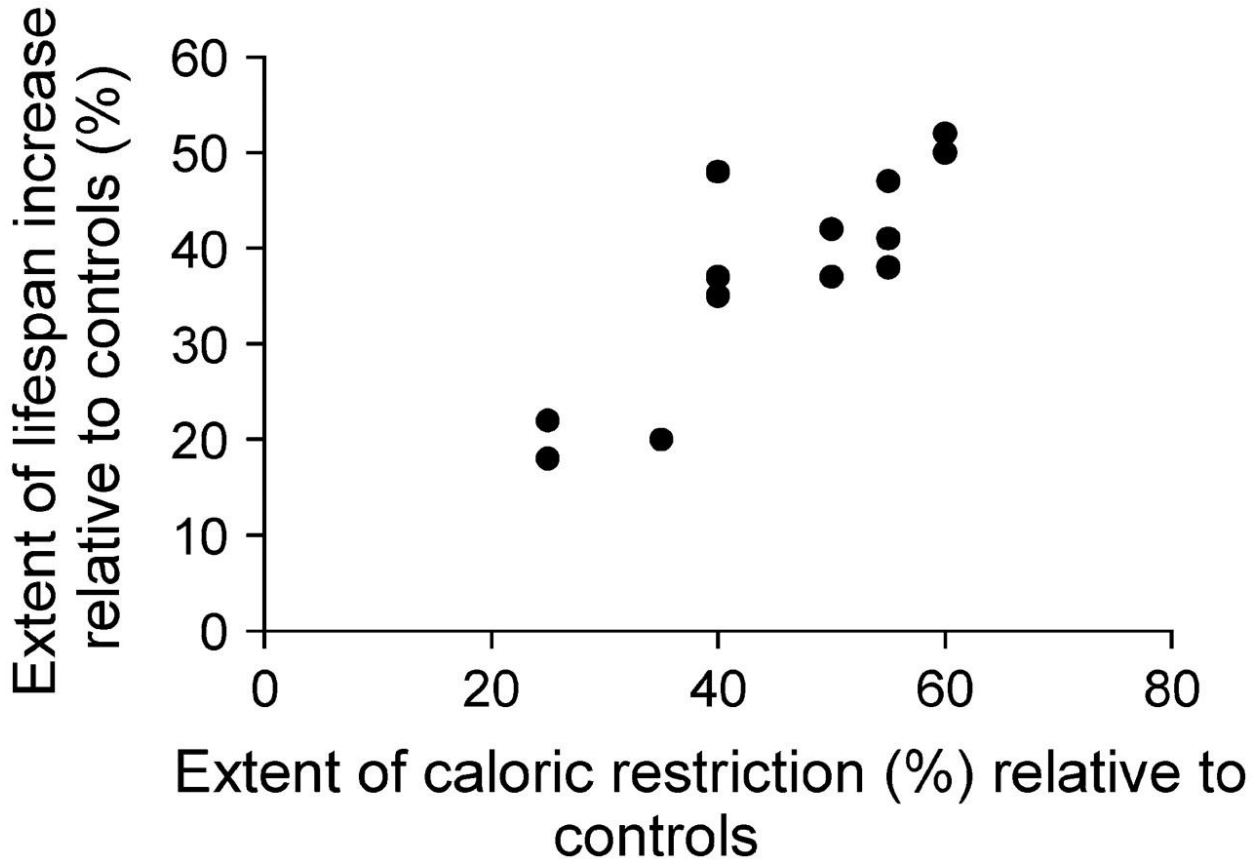
Restrizione Calorica e patologia organo-distrettuale dei roditori

	Glomerulosclerosi %	Artrosi %	Degenerazione miocardica %
Ad libitum	100	63	96
RC 30%	36	17	28
RC 50%	43	3	24

Ross, 1976

The benefits of CR (percentage increase in life over controls) in relation to the extent of restriction (percentage decrease in intake relative to controls), summarized across studies of both rats and mice

JN THE JOURNAL OF NUTRITION



Speakman, J. R. et al. J. Nutr. 2007;137:1078-1086

Winsconsin National Primate Research Center (WNPRC) Study

(30 % RC *versus* ad libitum: 20 years follow-up)

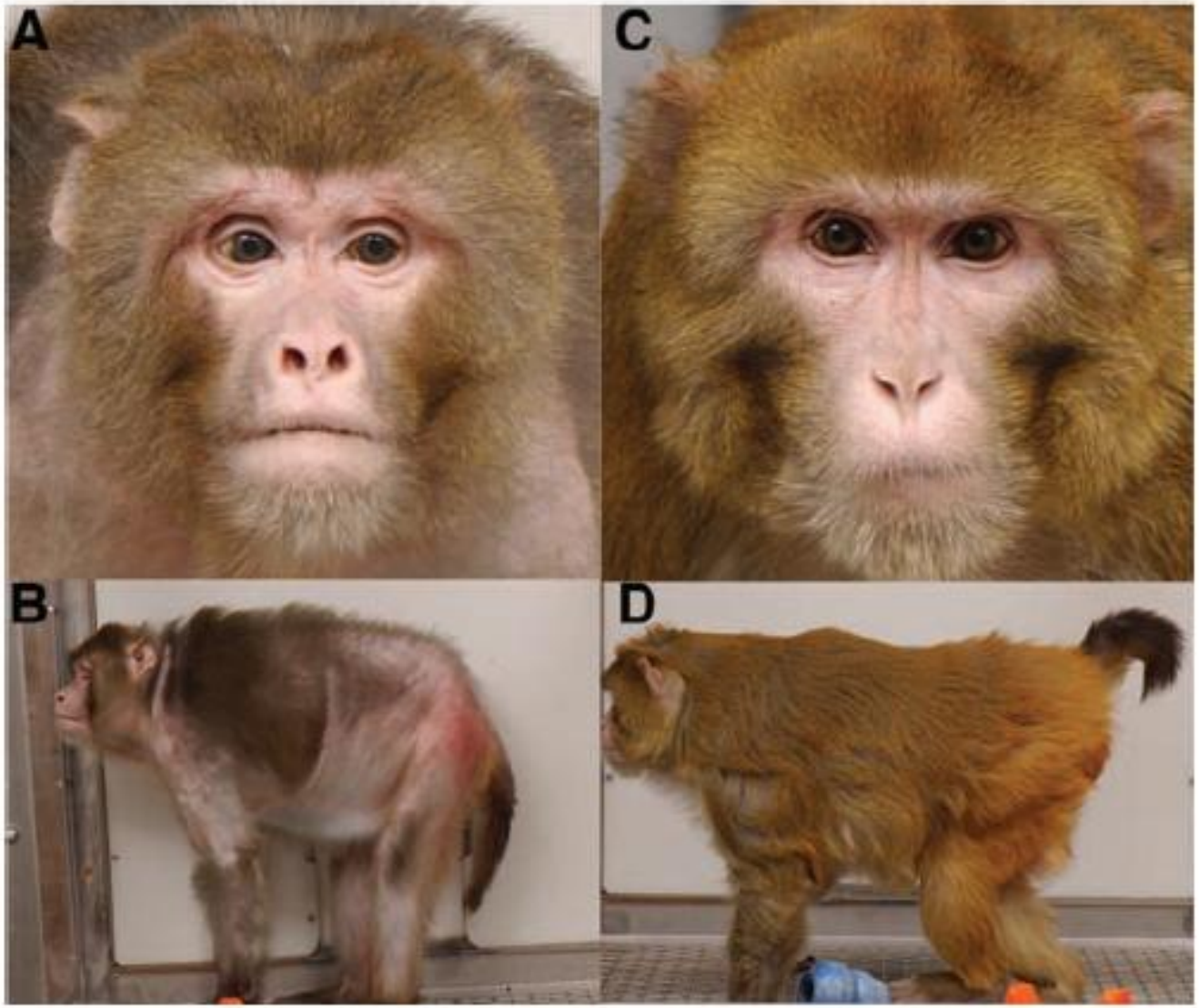


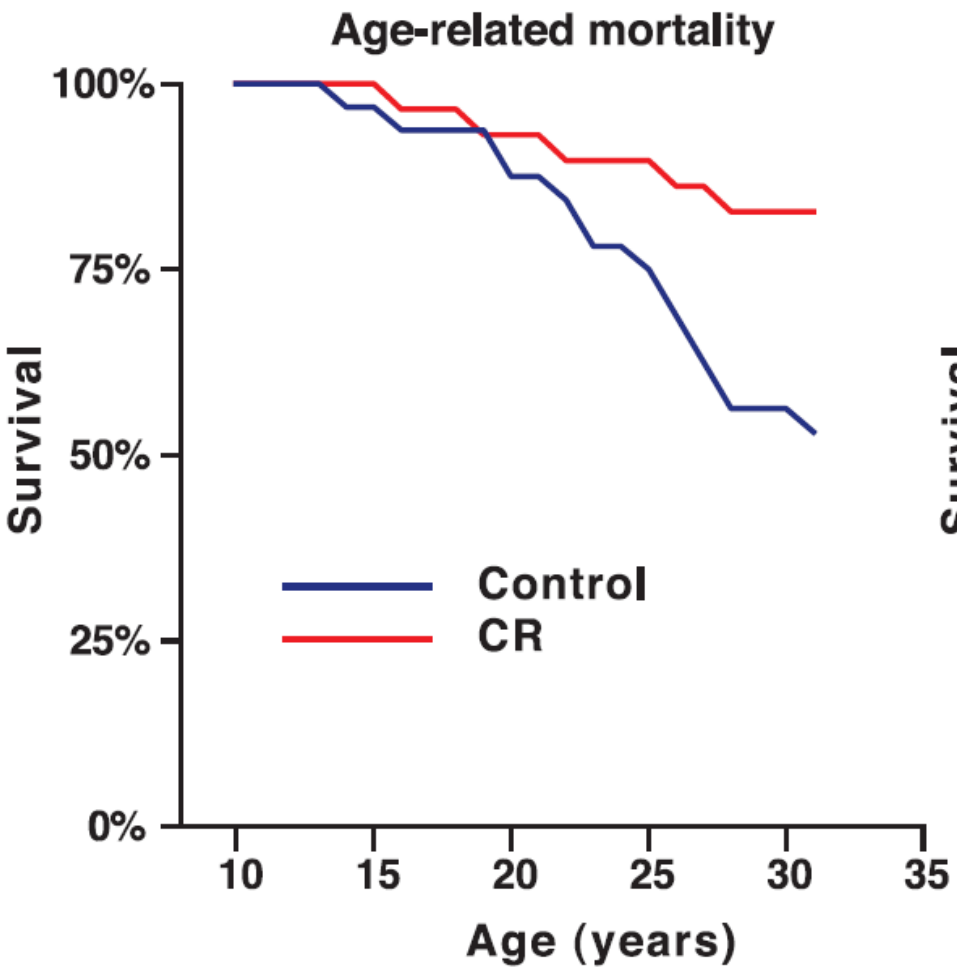
Fig. 1. Animal appearance in old age. (**A** and **B**) Photographs of a typical control animal at 27.6 years of age (about the average life span). (**C** and **D**) Photographs of an age-matched animal on CR.

7-14-year old
at the baseline

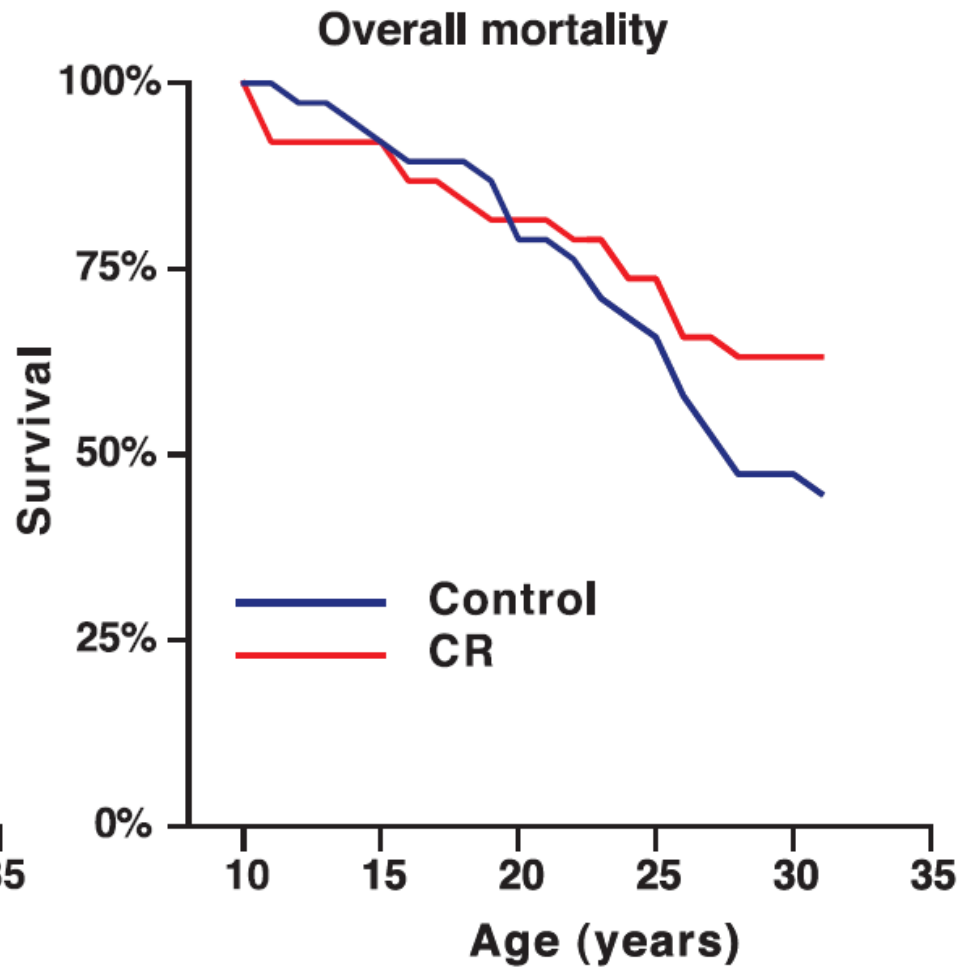
Vita media macaca mulata: 27 anni,
massima spettanza 40 anni

SCIENCE VOL 325 10 JULY 2009

WNPRC study: Survival curves



p=0.03 HR=3.0

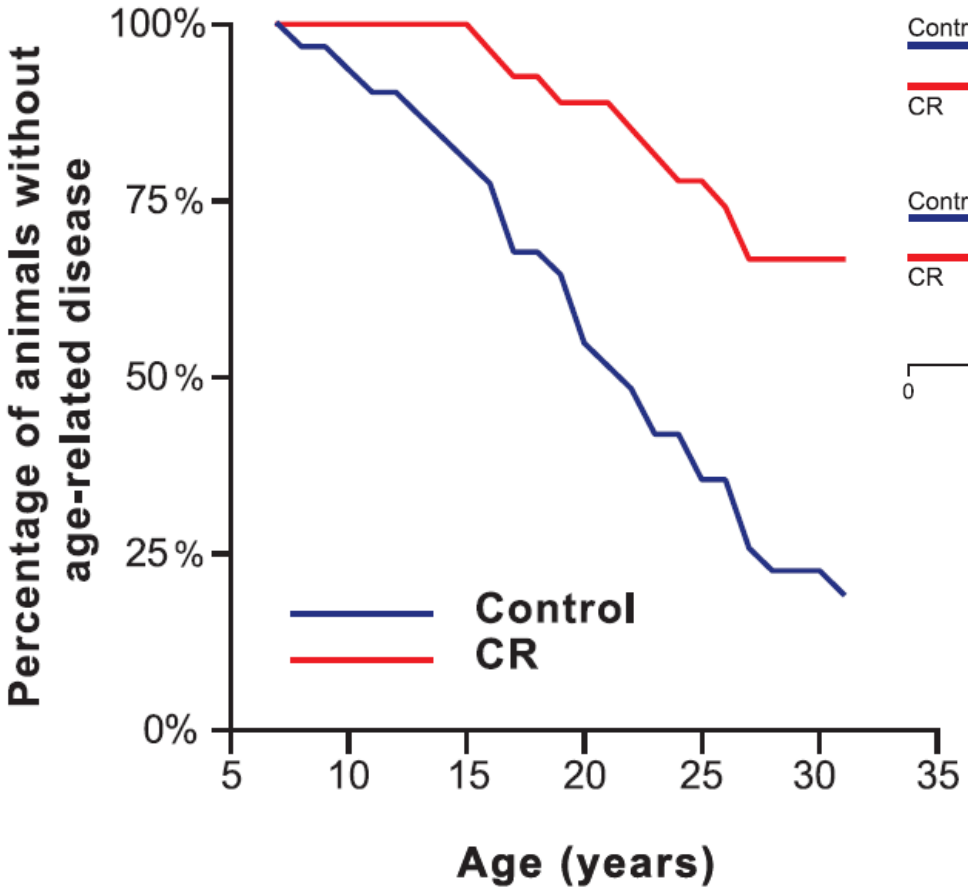


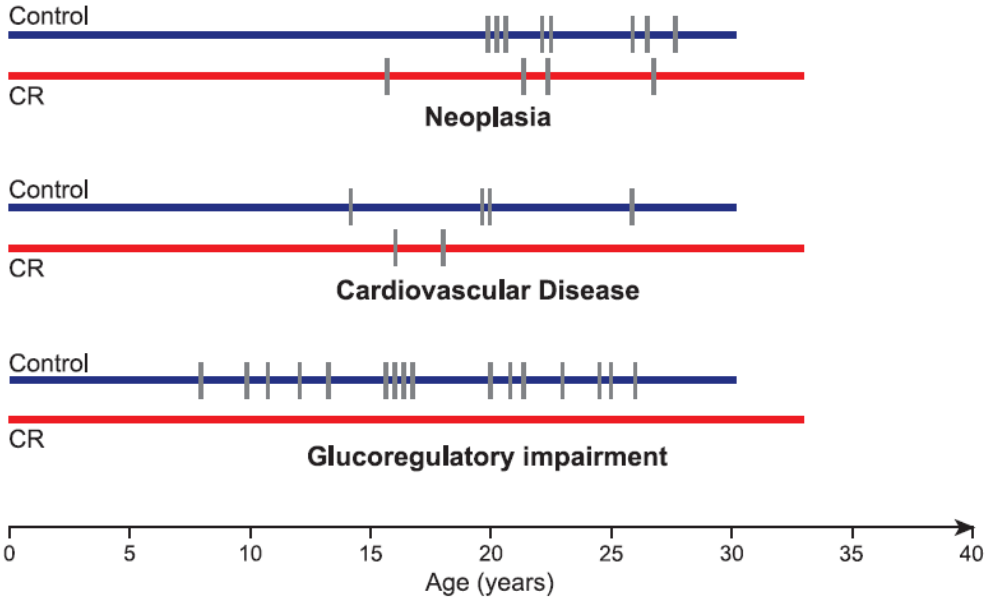
p=0.16

SCIENCE VOL 325 10 JULY 2009

WNPRC study

p=0.008 HR=2.9

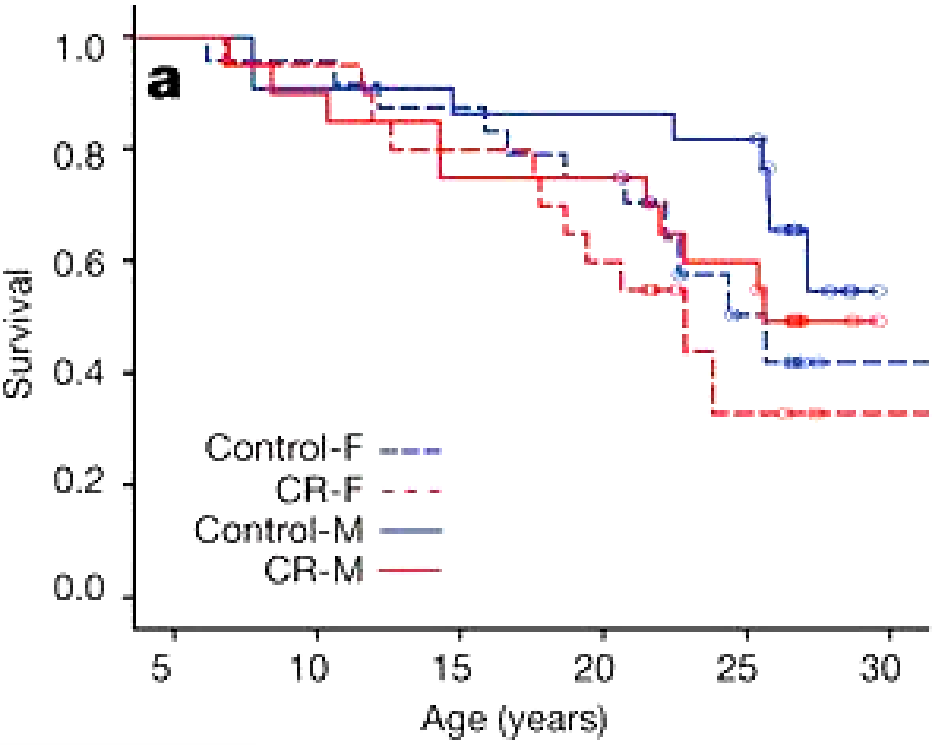




SCIENCE VOL 325 10 JULY 2009

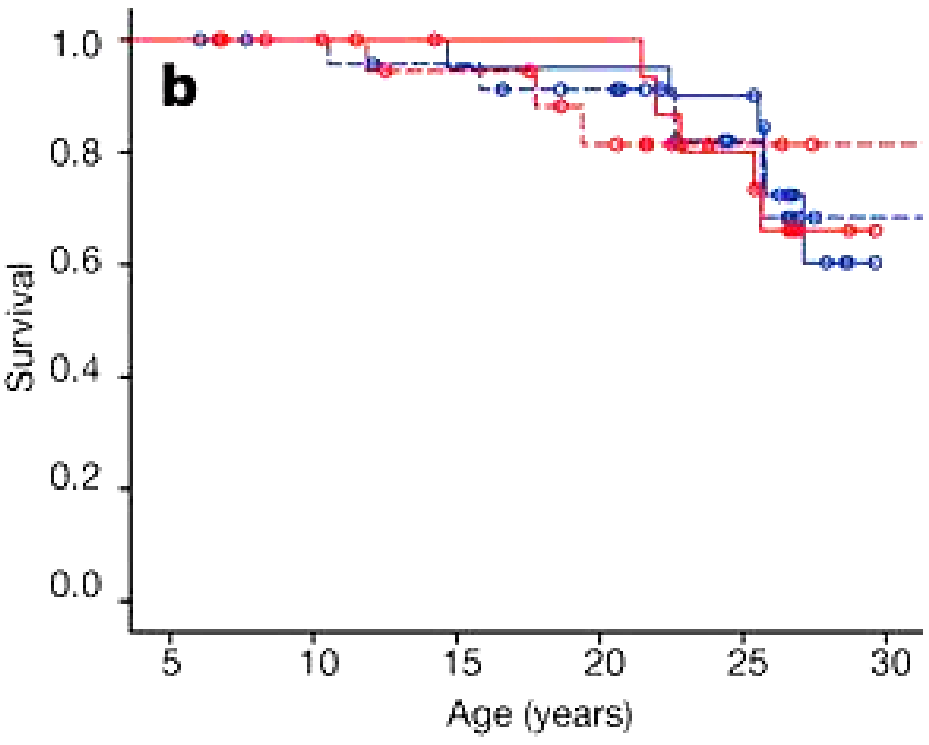
NIA study: Kaplan-Meier survival curves for young-onset monkeys (7-14 years)

all causes mortality



p=0.255

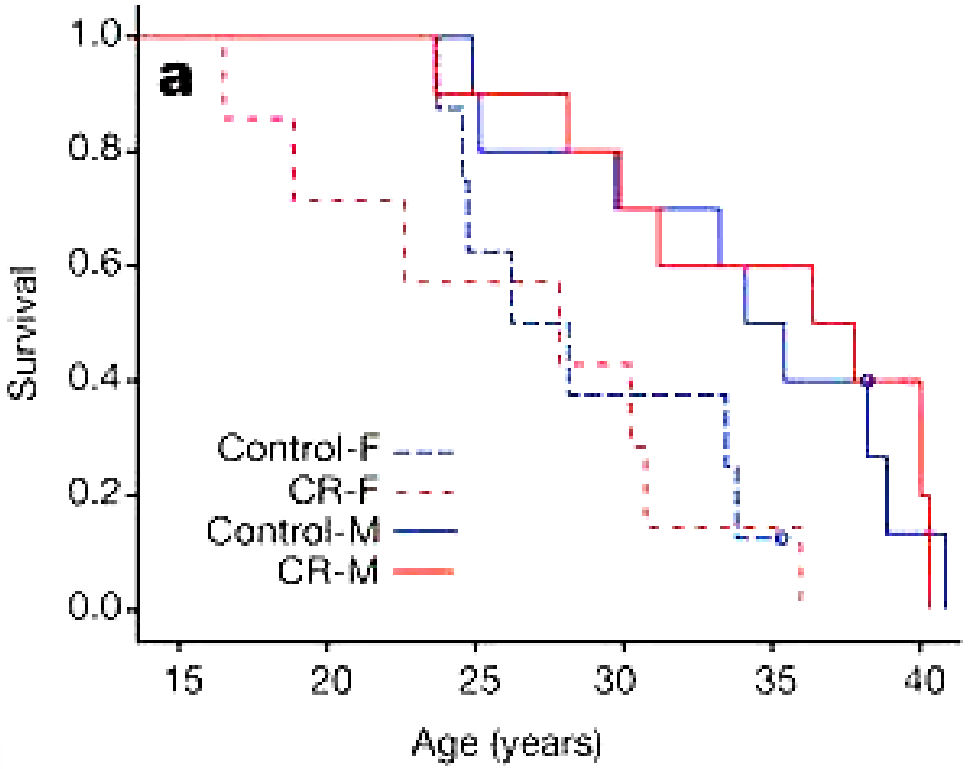
age-related mortality



p=0.975

Mattison JA et al., 2012

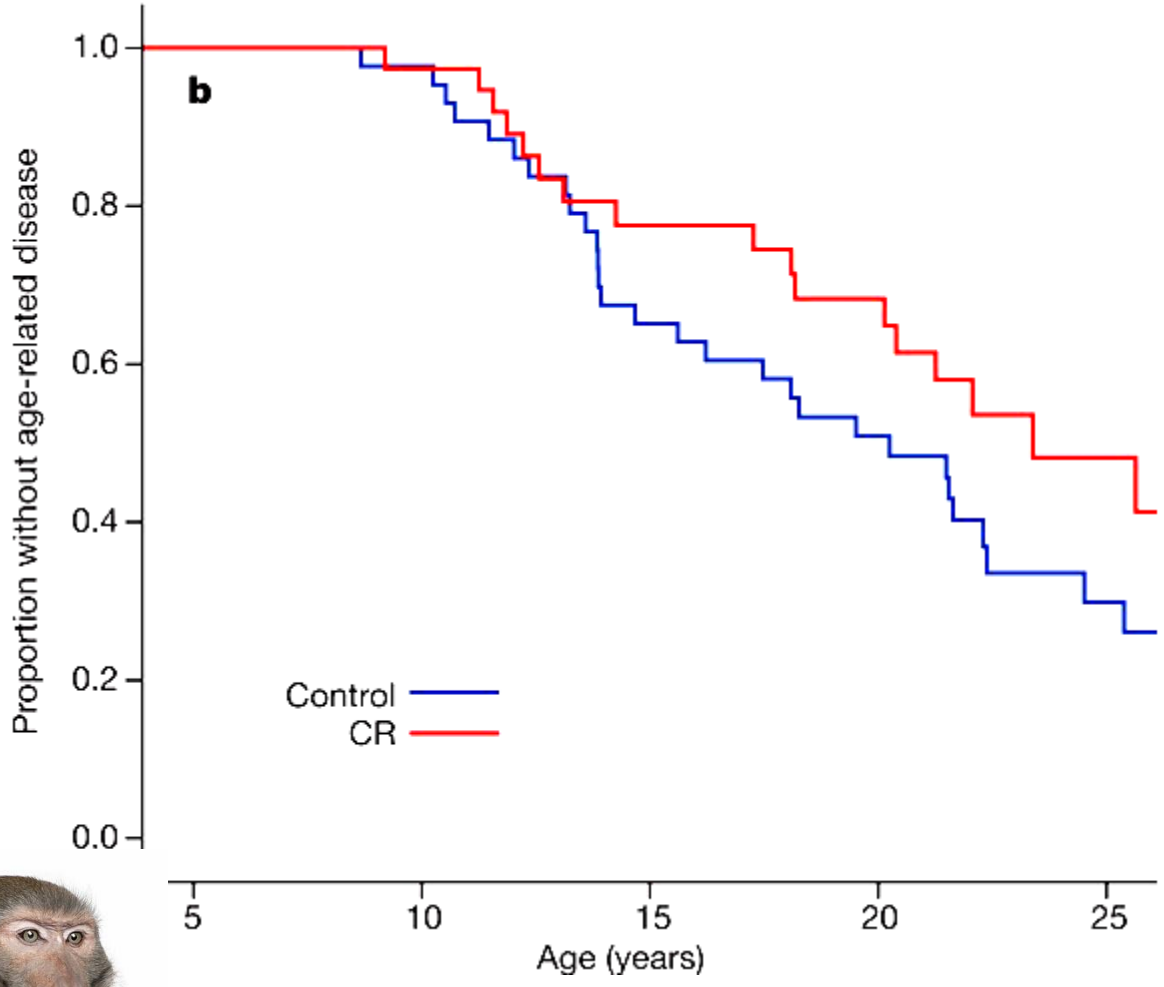
NIA study: Kaplan –Meier Survival Curves for old-onset monkeys (16-23 years)



The effect was **NOT** significant (**p= 0.934**) and sex was the only significant predictor (**p=0.003**)

Mattison JA et al., 2012

NIA study: Estimated proportions for the first occurrence of any age-related disease in each monkey from the young-onset



p = 0.06

Mattison JA et al., 2012

The Vallejo Study

Alternative day feeding in 120 non-obese men:
60 subjects **35% CR** *versus* 60 subjects **ad libitum**.

Post-hoc analyses indicated that **death rate tended to be lowered in the CR group and hospital admissions were reduced** in these individuals by approximately 50%
(123 days for CR vs. 219 days for Control).

Redman LM et al., 2008

Centenarians from Okinawa

From Age 65 expected Lifespan in Okinawa:
24.1 y for women, 18.5 for men
From Age 65 expected Lifespan in USA:
19.3 y for women, 16.2 for men

Low calorie diet reported in school children on Okinawa 40 years ago and later studies confirmed a 20% CR in adults

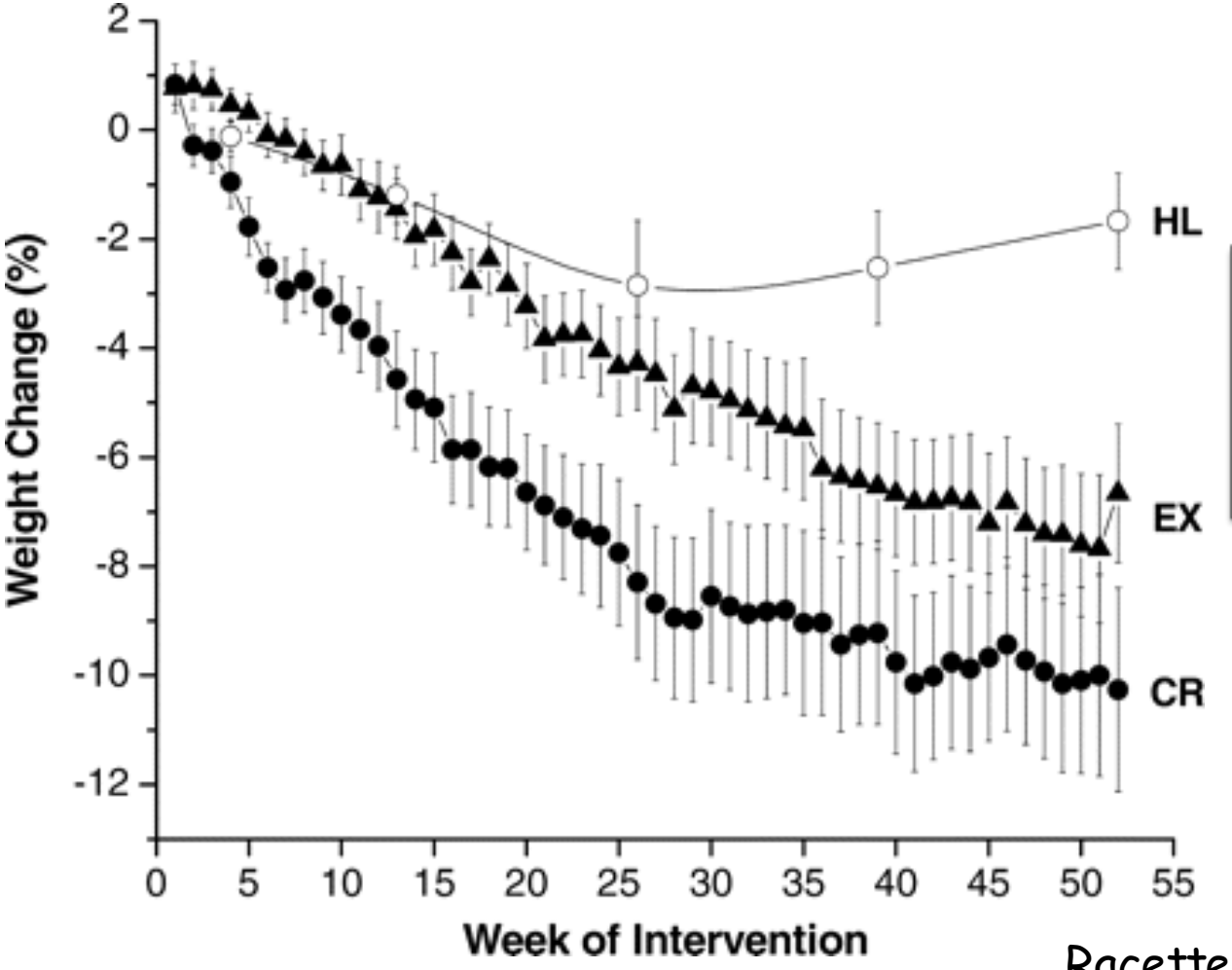
The diet, rich in green leafy vegetables, soy and some fish is similar with CR interventions providing adequate amounts of nutrients, essential vitamins and minerals

Redman LM et al., 2008

Effects of CR in humans: findings fron CALERIE study and CR Society Members

Body composition
Biomarkers of longevity
CVD risk factors
Metabolic adaptation
Endocrine function
Physiological and behavioral

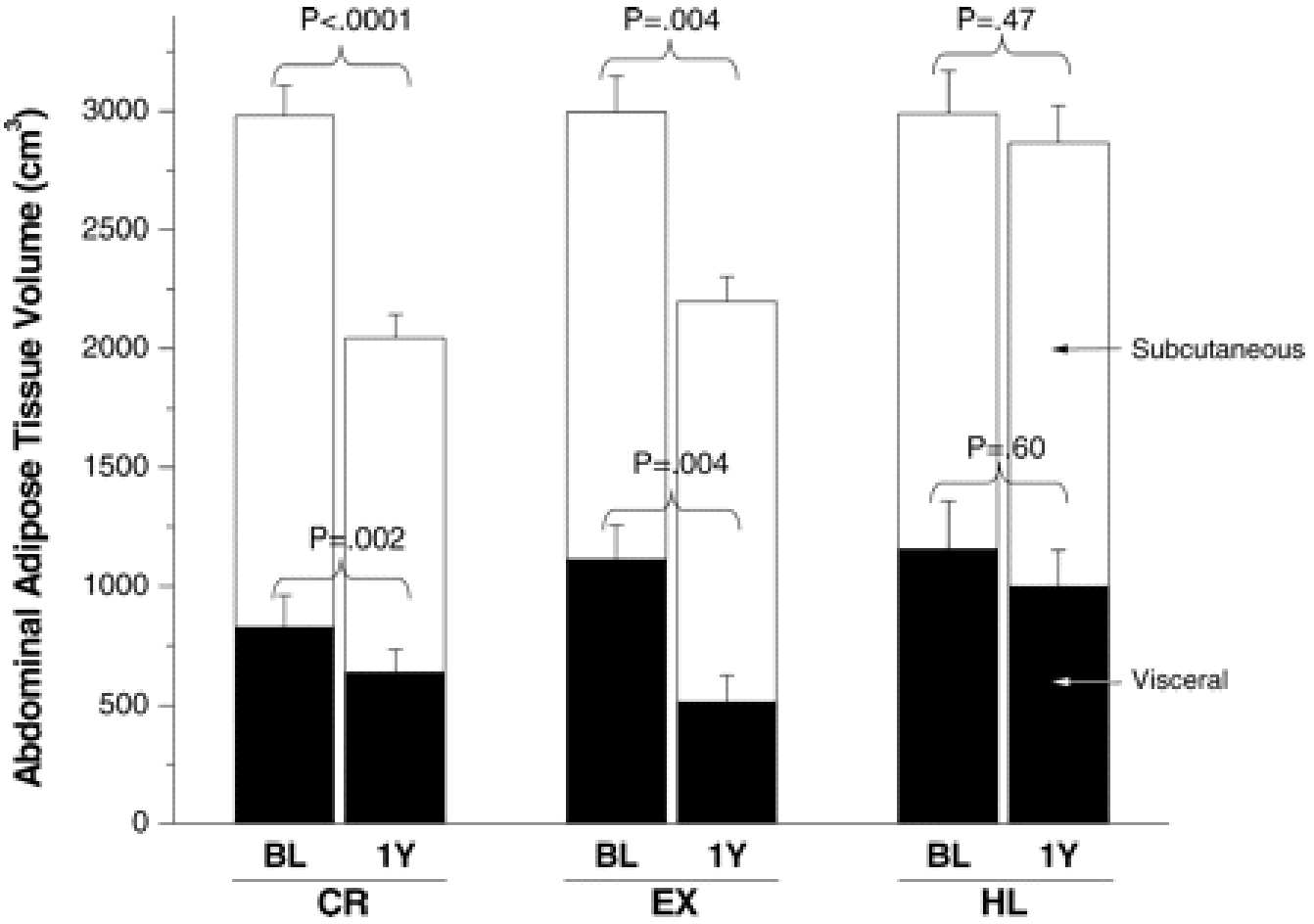
Body weight changes throughout the 1-year interventions
48 nonobese men and women aged 57 years
CALERIE study



randomly assigned to:
- 20% CR
- Ex to produce similar energy deficit
-Healthy Lifestyle (HL)

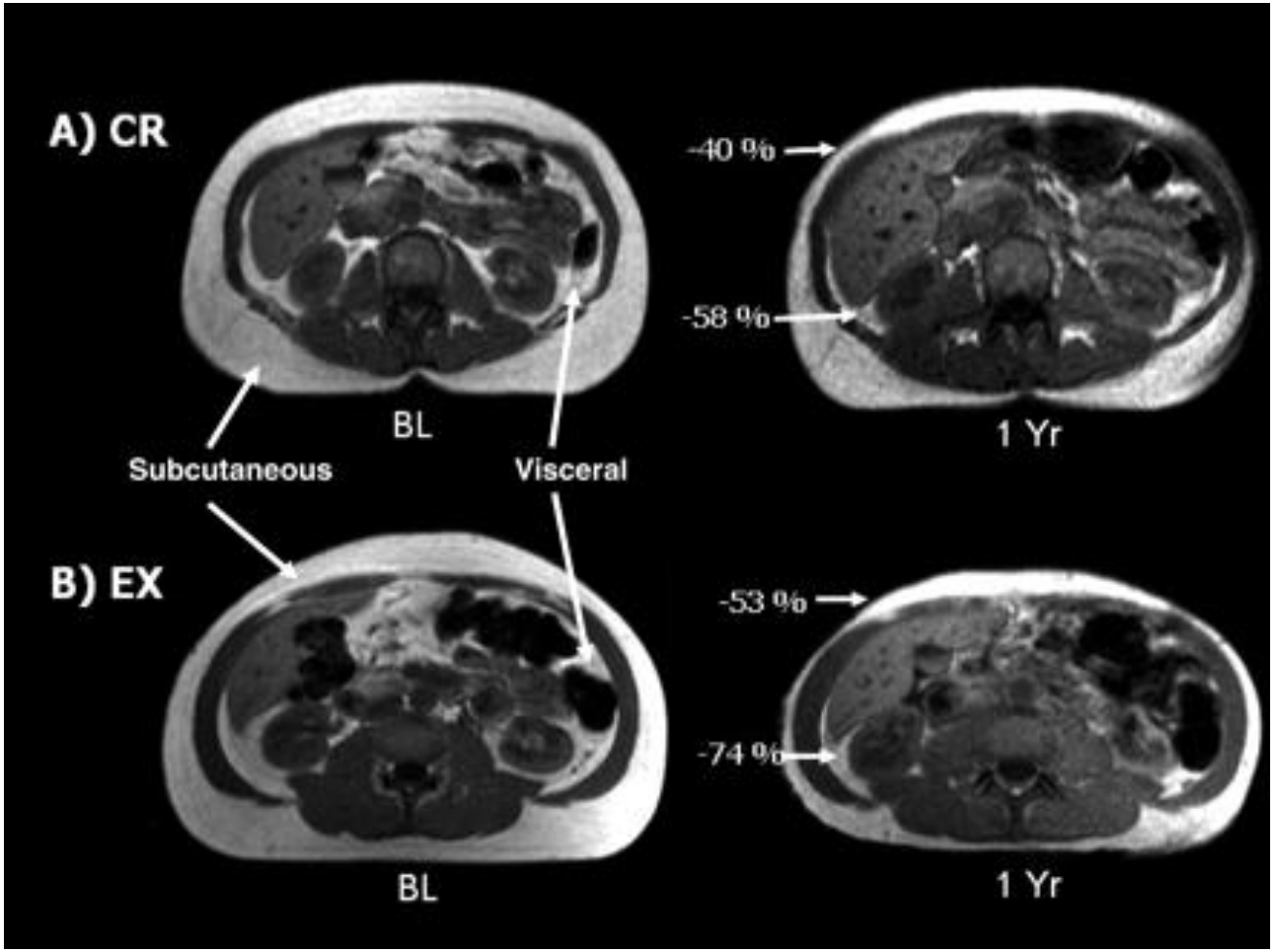
Racette SB et al, 2006

Visceral (black bars) and subcutaneous (white bars) abdominal adipose tissue
by MRI at baseline and after 1 year of intervention



Racette SB et al, 2006

Magnetic resonance images of the abdomen at baseline (BL) and after 1 year of caloric restriction



54 year old woman
body weight loss
12 kg

60 year old woman
body weight loss
16 kg

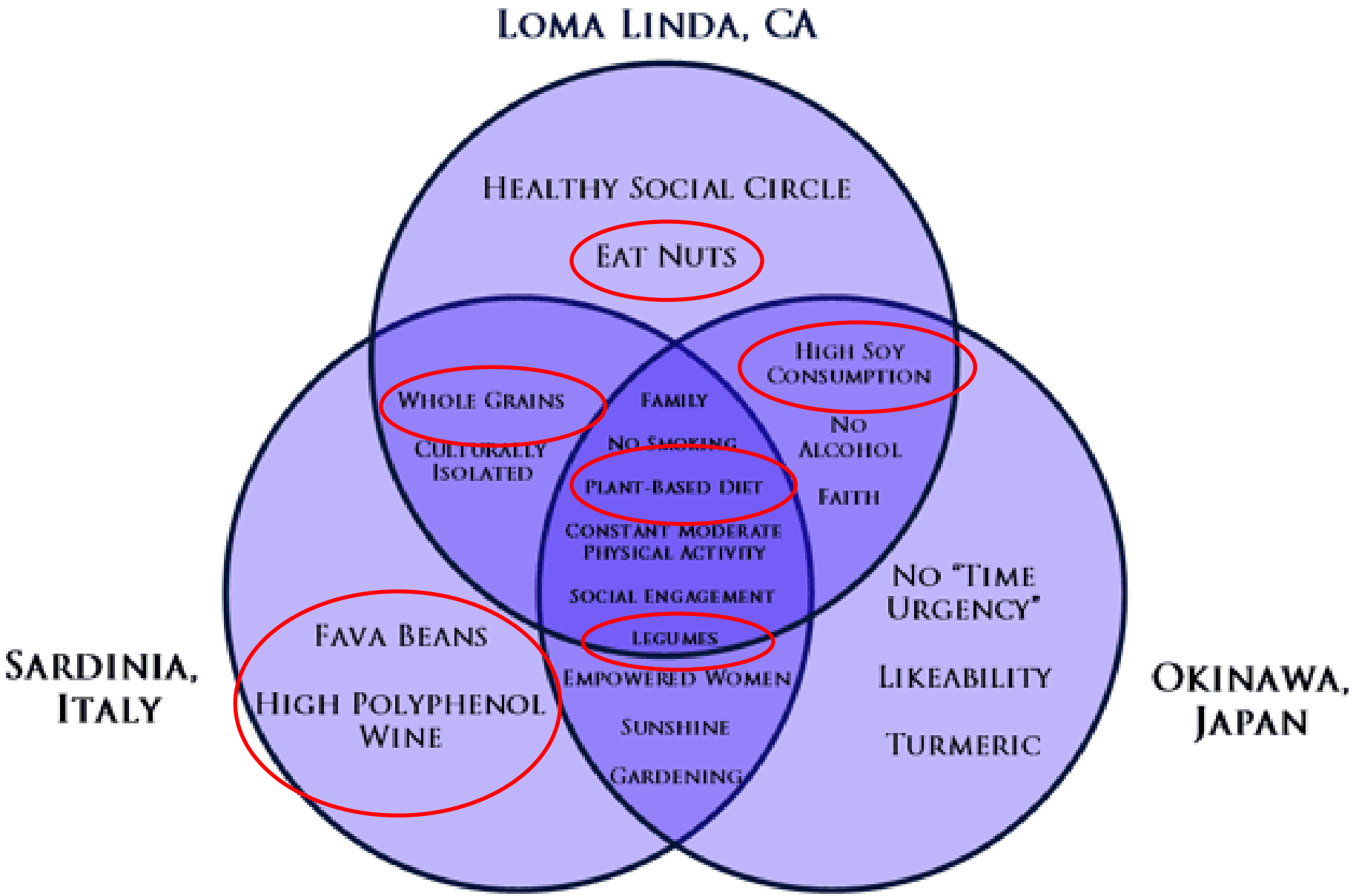
Racette SB et al, 2006

CR is the only known intervention that can slow primary aging and has protective effect against secondary aging.

However it is challenge for most individuals to practice CR in a obesogenic environment so conductive to overfeeding

Redman L et al, 2008

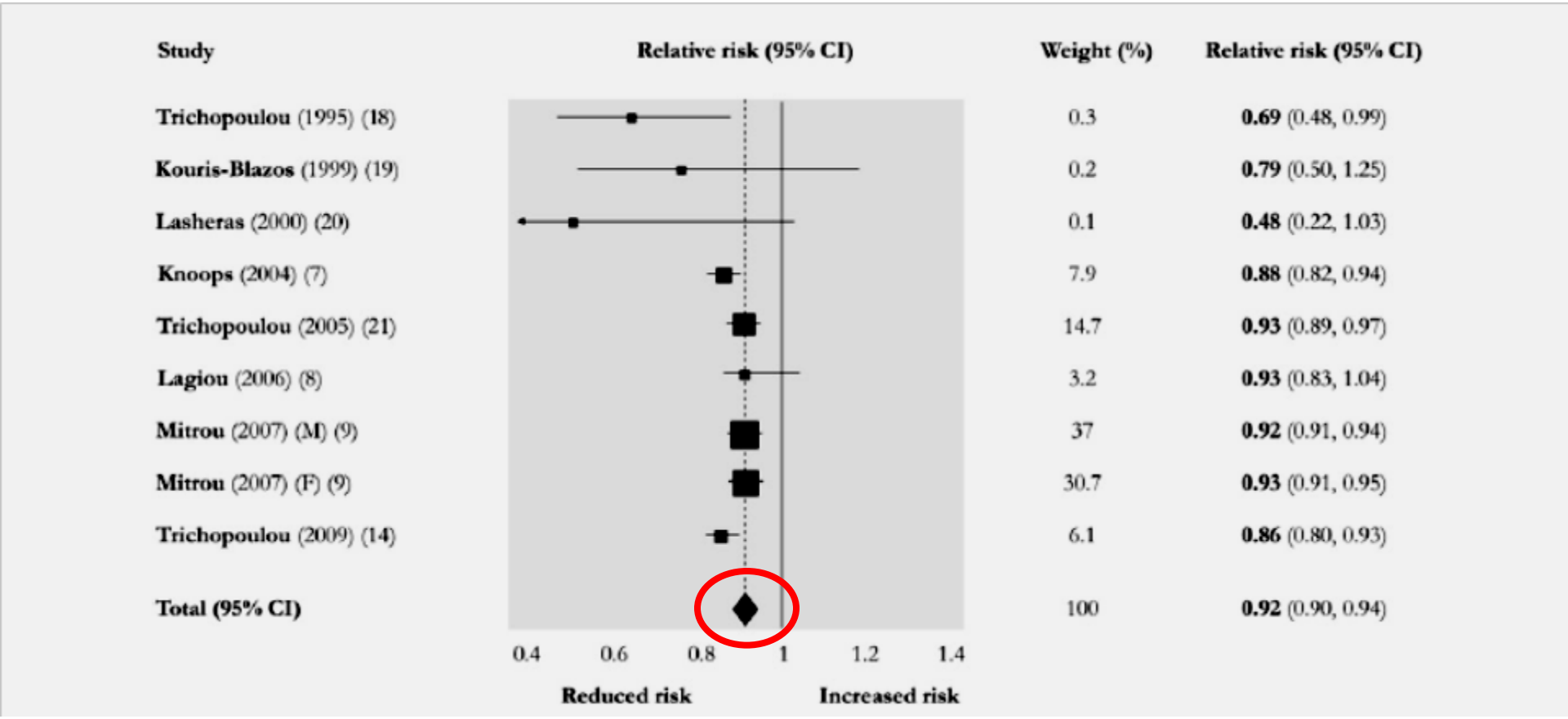
LOMA LINDA
CALIFORNIA
SARDINIA
ITALY
ICARIA
GREECE
OKINAWA
JAPAN
NICOYA
COSTA RICA
BLUE ZONES
LONGEVITY HOTSPOTS
BLUE ZONE LIFE LESSONS
MOVE NATURALLY
RIGHT TRIBE
RIGHT OUTLOOK
EAT WISELY



"Live Longer, Better: Longevity Secrets", Quest Network, 2006.

2 point increase adherences to the Mediterranean diet determines a decrease risk of the overall mortality rate

Meta-analisi of 9 studies, 514.118 subjects, 4-20 years follow-up; no evidence of statistical heterogeneity across studies

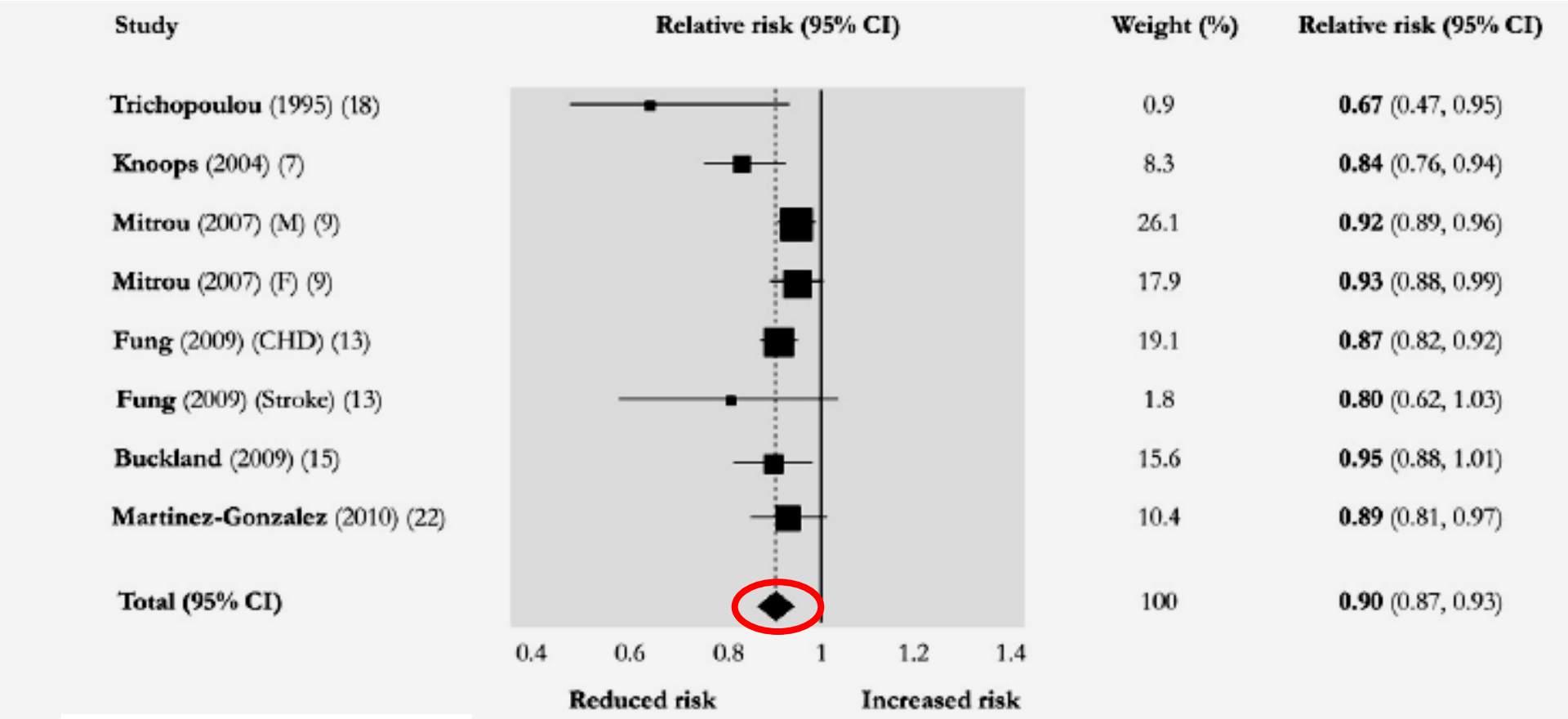


The American Journal of CLINICAL NUTRITION

Sofi et al., 2012

2-point increase of adherence to the Mediterranean diet is associated with a reduced risk of mortality from and incidence of CVD

Meta-analisi of 8 studies, 534.064 subjects, 4-20 years follow-up; no evidence of statistical heterogeneity across studies

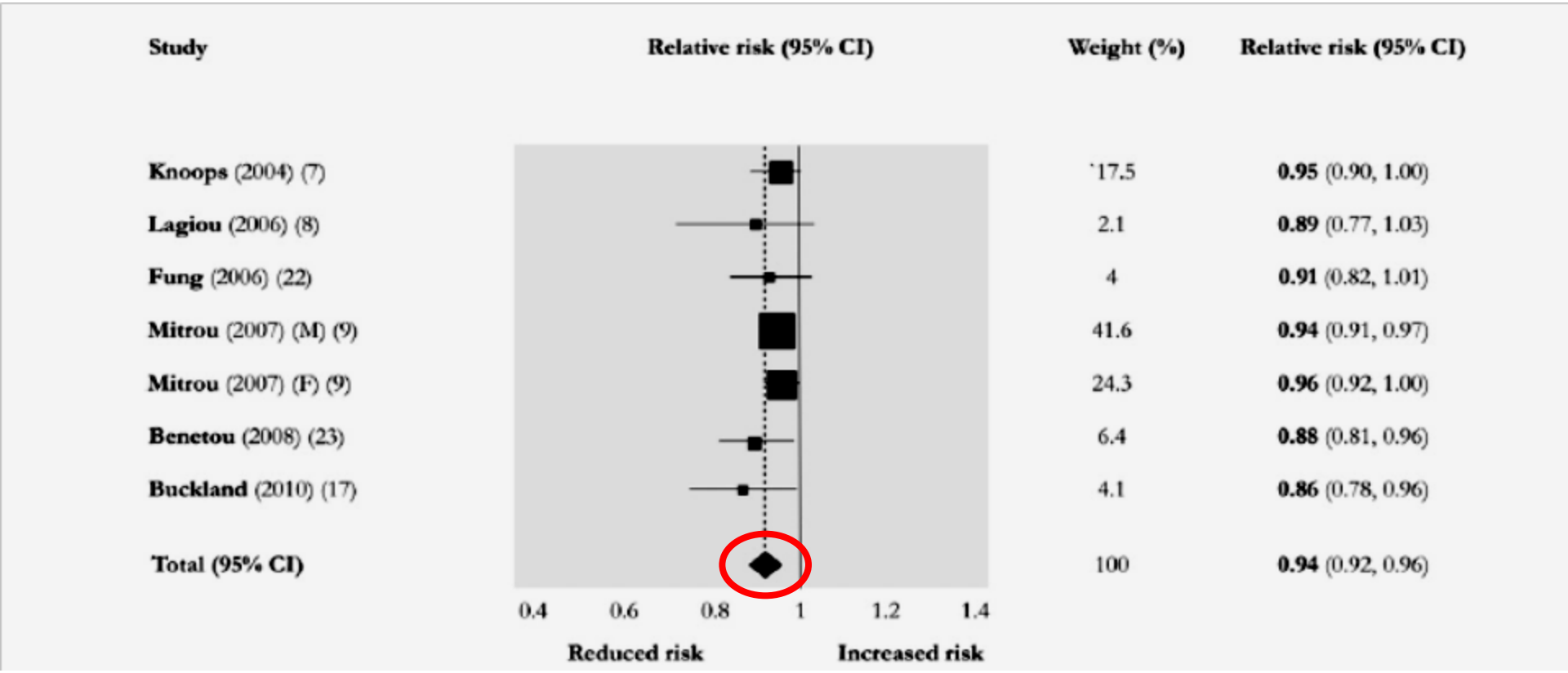


The American Journal of CLINICAL NUTRITION

Sofi et al., 2012

2-point increase of adherence to the Mediterranean diet is associated with a reduced risk of mortality from and incidence of cancer disease

Meta-analisi of 7 studies, 1.006.410 subjects, 4-20 years follow-up; no evidence of statistical heterogeneity across studies

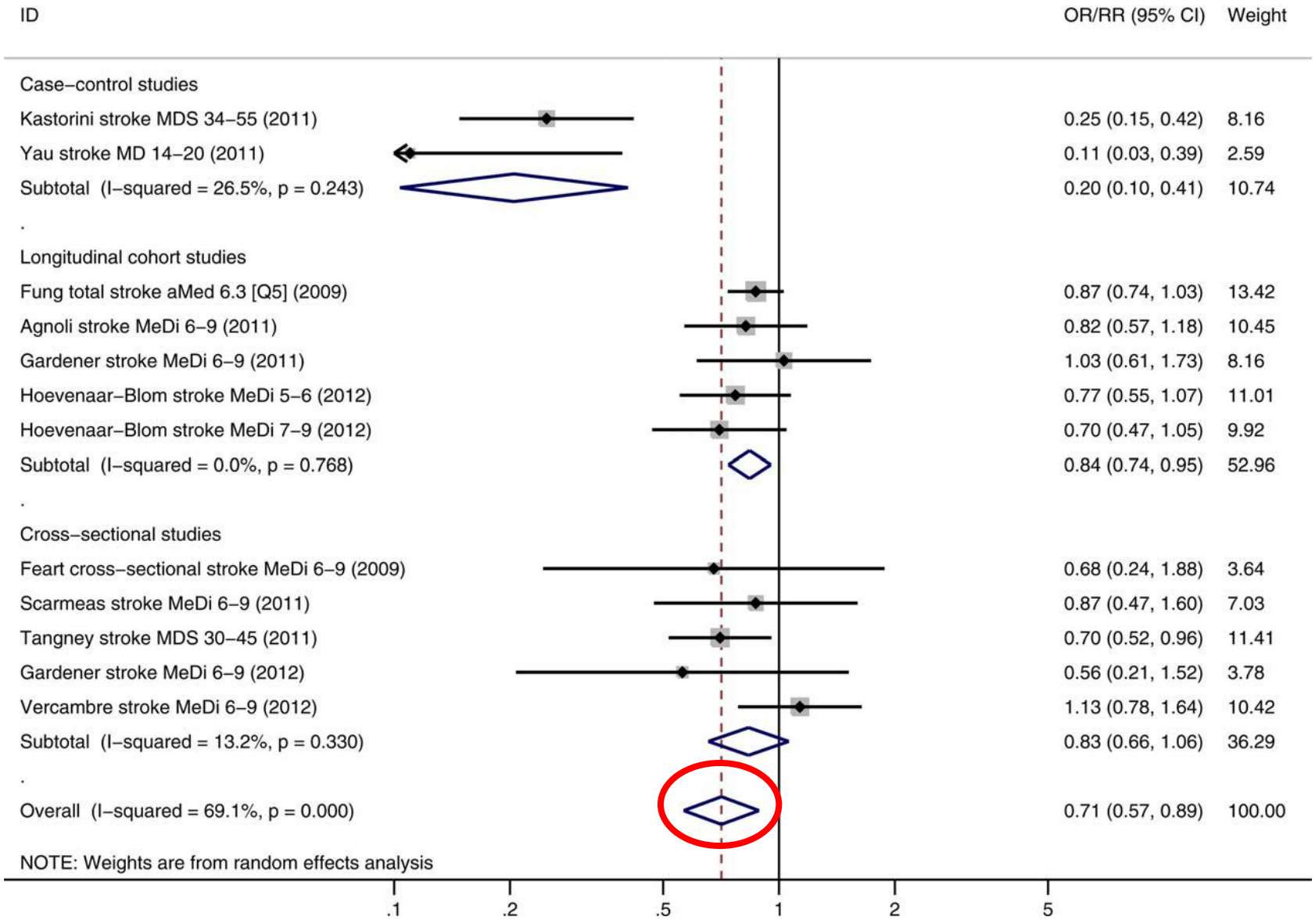


The American Journal of CLINICAL NUTRITION

Sofi et al., 2012

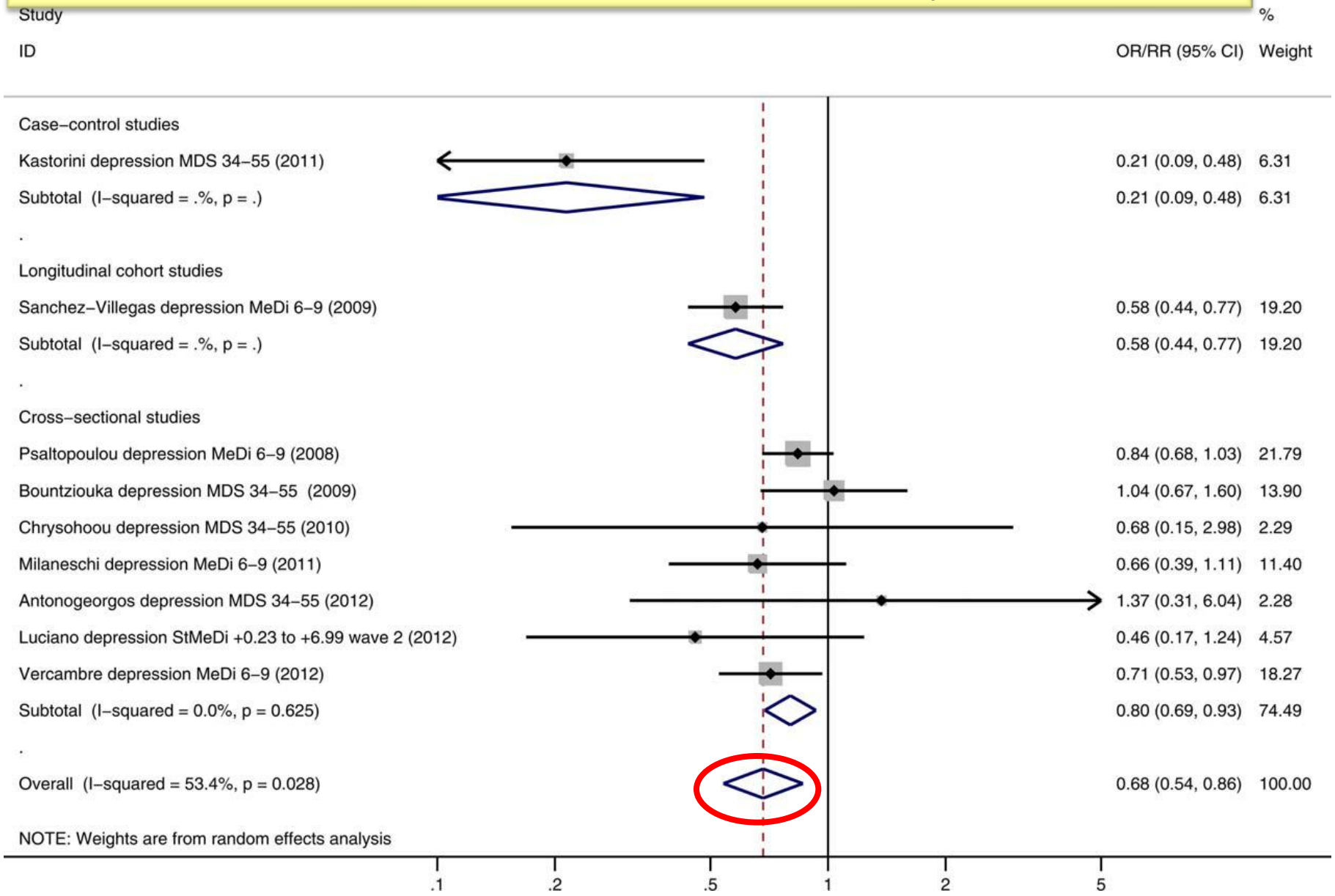
High adherence to Mediterranean diet decreased **stroke risk**

Meta-analysis of 11 studies (162.685 subjects)



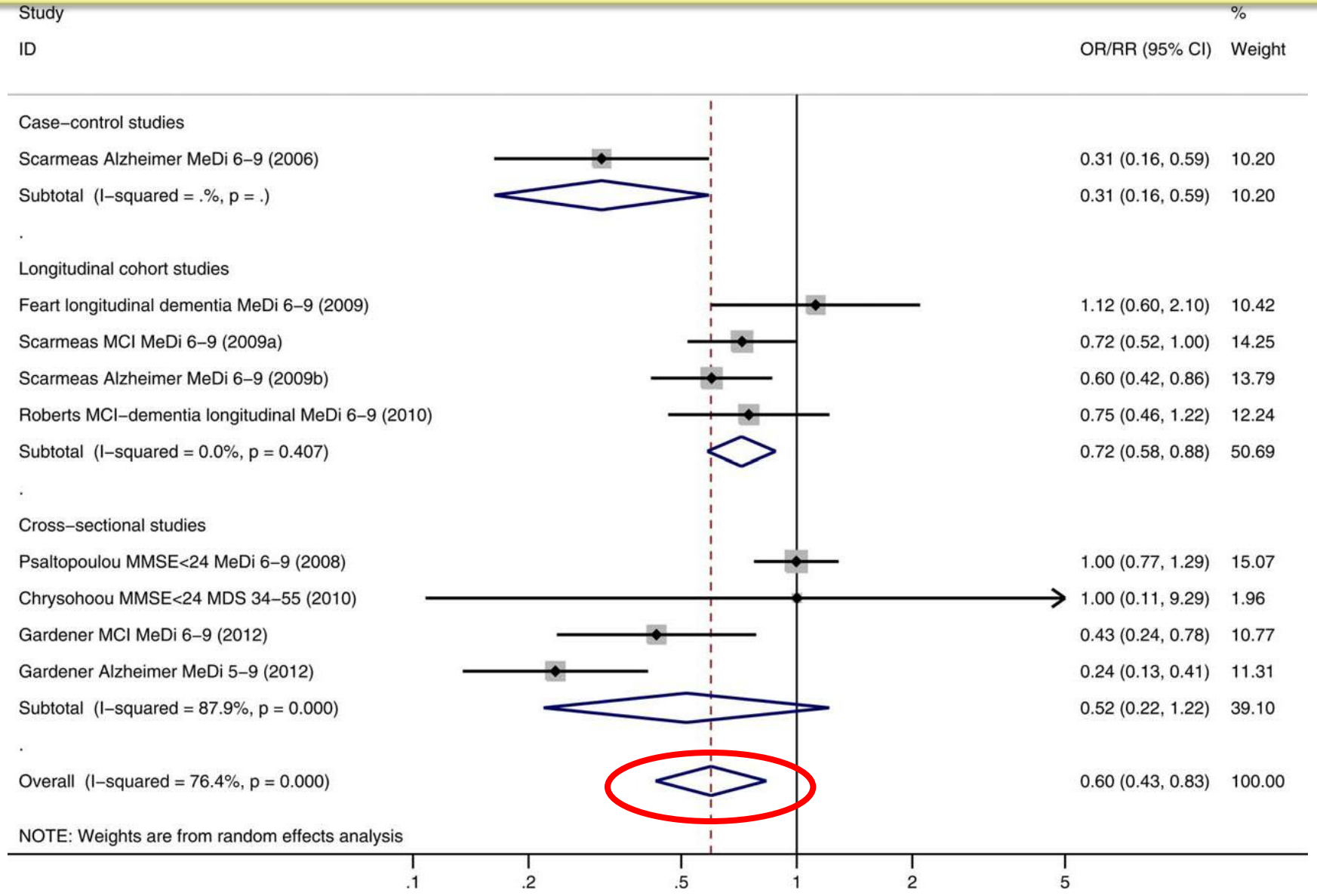
Psaltopoulou et al., 2013

High adherence to Mediterranean diet and depression risk
Meta-analysis of 9 studies (17 175 subjects)



Psaltopoulou et al., 2013

High adherence to Mediterranean diet and cognitive impairment risk
Meta-analysis of 11 studies (10 273 subjects)



Psaltopoulou et al., 2013

Better diet (AHEI or Med Diet) quality at MIDLIFE seems strongly associated to greater health and well-being in persons surviving to older age

Nurses Health Study, 10 670 women average age 59 years, 15 years follow-up, 4 health domains: no major chronic disease, impairments in cognitive or physical function, or mental health.

Variable	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	*P* Value for Trend
AHEI-2010 score						
Median score (IQR)	38.1 (34.9–40.3)	45.1 (43.7–46.5)	50.4 (49.2–51.9)	56.2 (54.6–57.7)	64.3 (61.6–68.3)	
Healthy ager, *n*	181	169	233	290	298	
Age-adjusted OR (95% CI)	Reference	0.94 (0.75–1.17)	1.34 (1.10–1.65)	1.74 (1.43–2.12)	1.80 (1.48–2.19)	<0.001
Multivariable-adjusted OR (95% CI)†	Reference	0.87 (0.70–1.09)	1.20 (0.97–1.48)	1.37 (1.12–1.69)	1.34 (1.09–1.66)	<0.001
A-MeDi score						
Median score (IQR)	2.0 (1.5–2.5)	3.0 (3.0–3.5)	4.0 (4.0–4.5)	5.0 (5.0–5.5)	6.5 (6.0–7.0)	
Healthy ager, *n*	176	218	248	240	289	
Age-adjusted OR (95% CI)	Reference	1.30 (1.05–1.60)	1.30 (1.06–1.59)	1.35 (1.10–1.66)	1.61 (1.32–1.97)	<0.001
Multivariable-adjusted OR (95% CI)†	Reference	1.25 (1.01–1.55)	1.24 (1.00–1.53)	1.28 (1.03–1.60)	1.46 (1.17–1.83)	0.002

ls ratio.

parated/divorced); median annual (quintiles of metabolic-equivalent -14, 15–24, or ≥25 cigarettes/d); high blood pressure (yes/no); and

Implication

The potential benefits of healthy eating include living to older ages without major functional impairment.

—*The Editors*

Annals of Internal Medicine

Samieri et al, 2013

Healthy-diet (AHEI) is inverserly associated with non-CV mortality, while Western-diet subjects had lower odds for ideal aging (higher odds foe CV and non-CV death)

Whitehall II study 5350 adults (51,3 years), 16 years follow-up.

THE AMERICAN JOURNAL of MEDICINE®

Aging Outcome at Follow-up

Dietary Pattern at Baseline	Ideal Aging OR	95% CI	P Value	Nonfatal CVD OR	95% CI	P Value	CVD Death OR	95% CI	P Value	Non-CVD Death OR	95% CI	P-Value
Healthy-foods diet												
Model 1												
Tertile 1	1	Ref								1	Ref	
Tertile 2	1.28	0.90-							.04	0.70	0.54-0.90	.005
Tertile 3	1.19	0.82-							.05	0.61	0.47-0.80	<.0001
Effect per 1 SD	1.08	0.94-							.10	0.76	0.68-0.84	<.0001
Model 2												
Tertile 1	1	Ref								1	Ref	
Tertile 2	1.20	0.85-							.15	0.77	0.59-1.00	.04
Tertile 3	1.08	0.75-							.25	0.85	0.65-1.12	.25
Effect per 1 SD	1.04	0.90-							.46	0.90	0.79-1.01	.07
Western-type diet												
Model 1												
Tertile 1	1	Ref								1	Ref	
Tertile 2	0.94	0.67-							.12	0.90	0.68-1.18	.44
Tertile 3	0.52	0.33-							.07	1.23	0.87-1.72	.24
Effect per 1 SD	0.73	0.58-							.003	1.36	1.14-1.61	<.0001
Model 2												
Tertile 1	1	Ref								1	Ref	
Tertile 2	0.96	0.68-							.21	0.83	0.63-1.10	.19
Tertile 3	0.58	0.36-							.29	0.99	0.70-1.38	.94
Effect per 1 SD	0.81	0.64-							.05	1.15	0.96-1.37	.12

CLINICAL SIGNIFICANCE

- Data from British adults suggest that avoidance of a diet comprising fried and sweet food, processed and red meat, refined grains, and high-fat dairy products is associated with a higher chance of achieving older ages disease-free and highly functional.
- Adherence to dietary recommendations provided by the Alternative Healthy Eating Index is associated with reduced risk of premature death.

Akbaraly et al., 2012

beyond midlife ?

The effect of CR expressed relative to the same effect when initiated at weaning as a function of the proportion of expected lifespan that had elapsed when restriction was initiated

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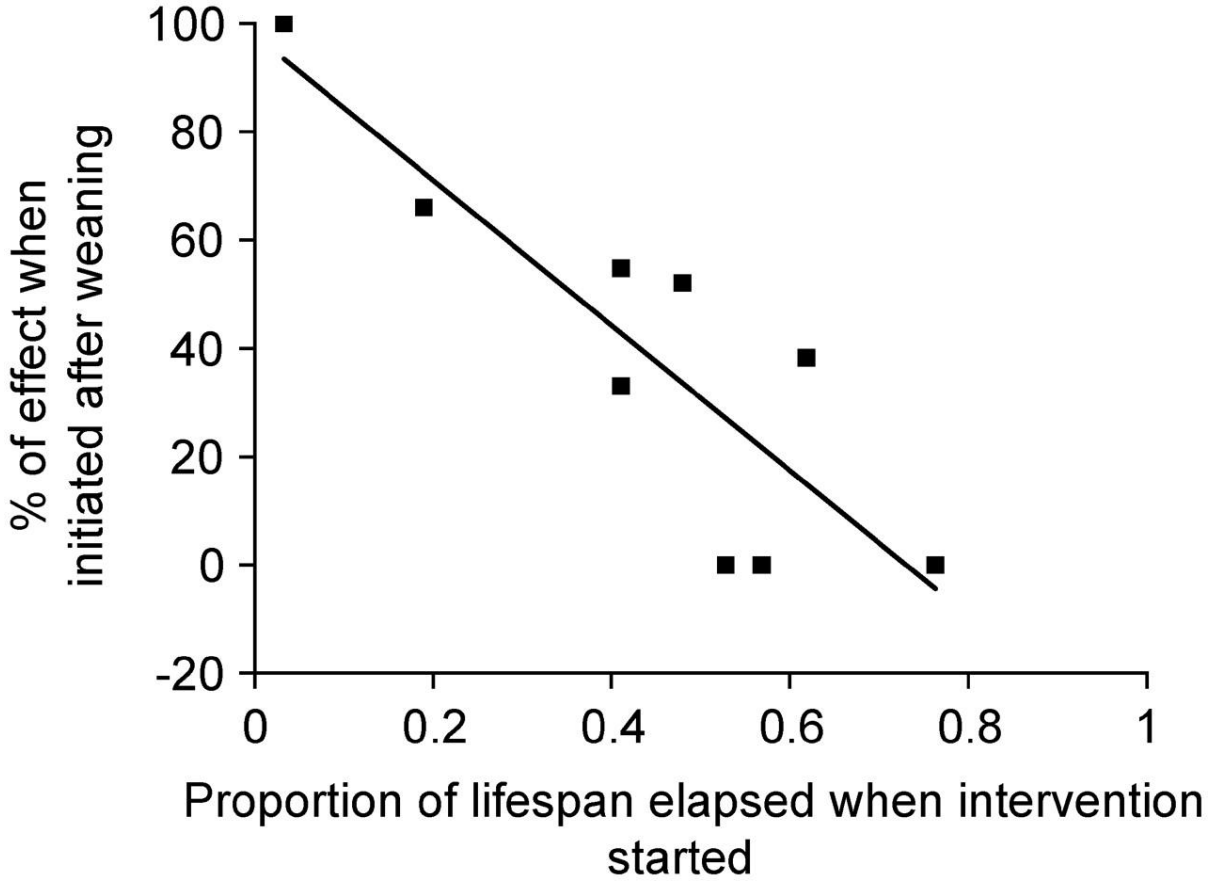

Speakman, J. R. et al. J. Nutr. 2007;137:1078-1086

Modeled benefits (years of life extension) of CR in humans at 2 different levels (15% and 30% CR below control) in relation to the age at which restriction is initiated

Percentage of life at onset	Age at onset, *y*	Time on restriction, *y*	Benefit, *y* Degree of restriction	
			15%	30%
20	15.6	62.4	5.6	11.2
30	23.4	54.6	4.7	9.4
40	31.2	46.8	3.3	6.5
50	39	39	2.4	4.8
60	46.8	31.2	1.4	2.8
70	54.6	23.4	0.25	0.3
80	62.4	15.6	0	0

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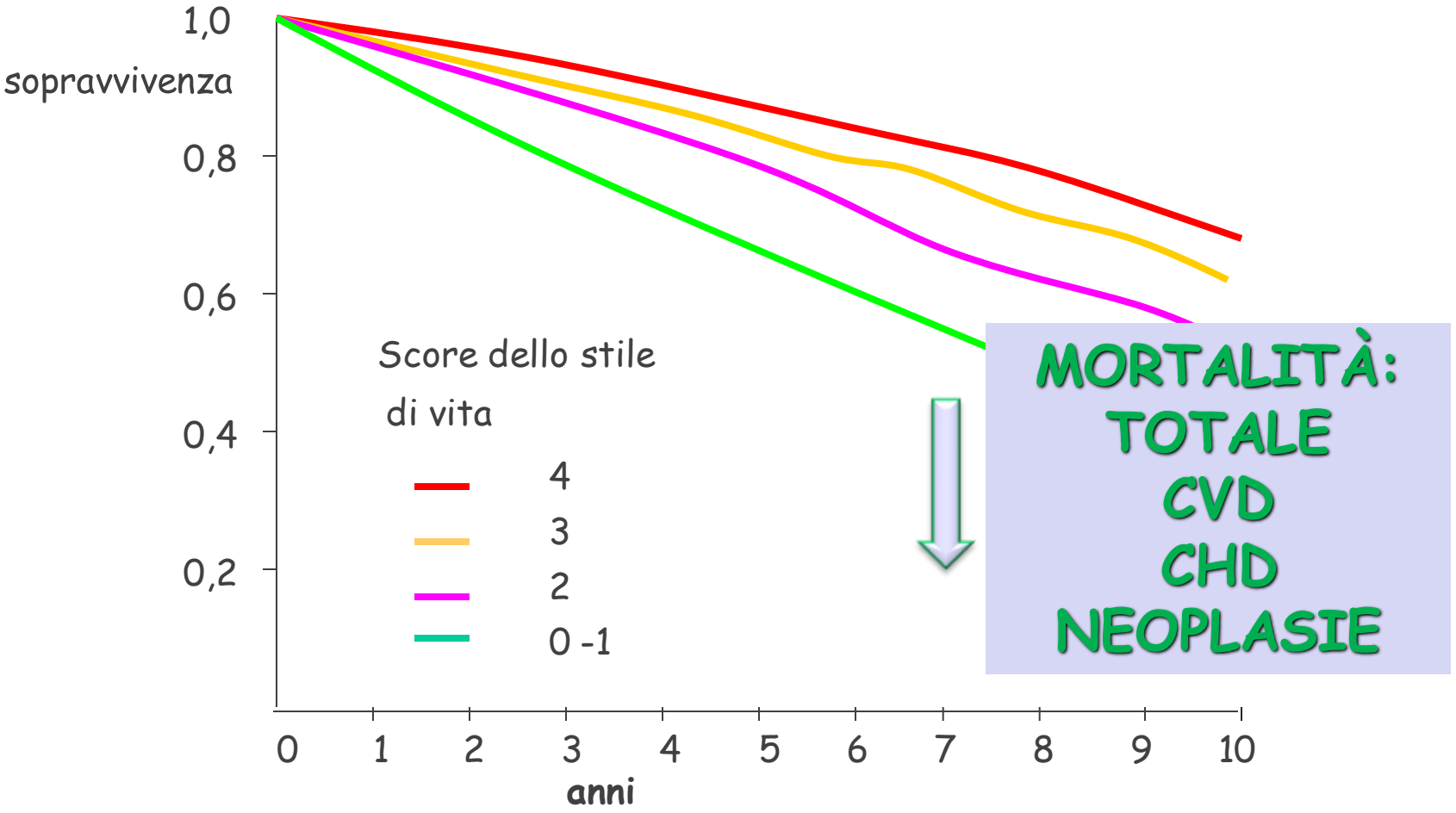
Speakman, J. R. et al. J. Nutr. 2007;137:1078-1086

The Healthy Aging Study: 1507 maschi e 832 donne con età compresa tra 70- 90 anni 10 anni di follow-up



Elementi dello stile di vita sano: dieta mediterranea, attività fisica, non fumo, moderato consumo di alcool

JAMA

Knoops KT et al, 2004

MODIFIED MEDITERRANEAN DIET AND SURVIVAL: EPIC-ELDERLY PROSPECTIVE COHORT STUDY

Design: Multicentre, prospective cohort study

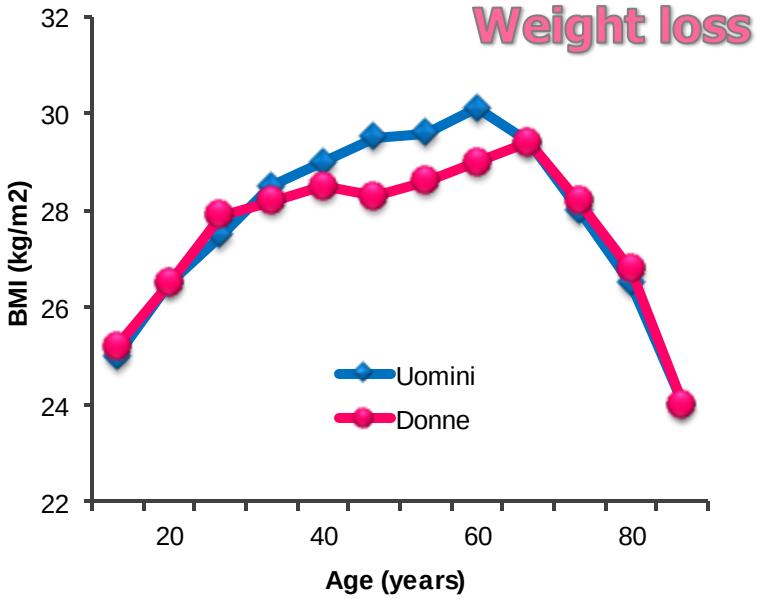
Setting: Nine European Countries (Denmark, France, Germany, Greece, Italy, the Netherlands, Spain, Sweden, United Kingdom)

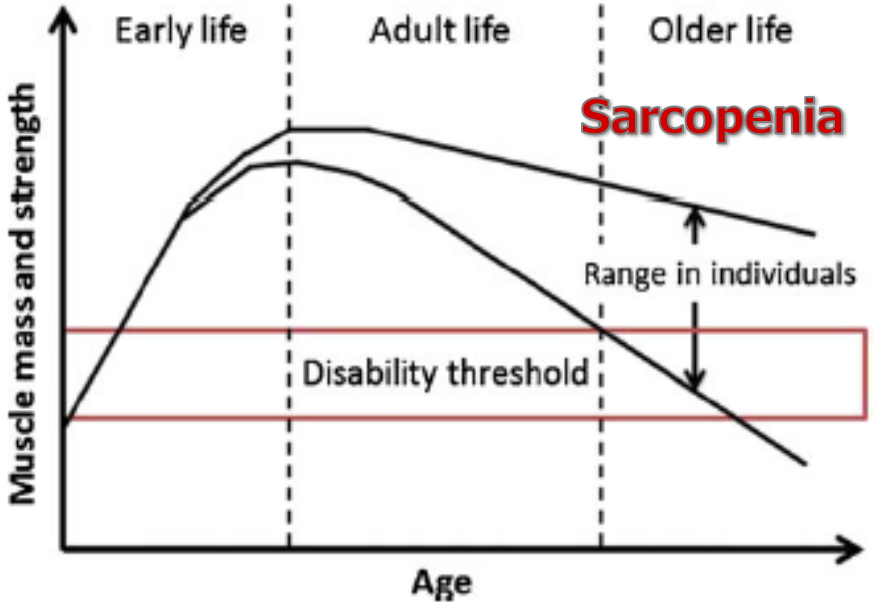
Participants: 74607 men and women; age > 60
without CHD, stroke, cancer at the enrolment
complete information about dietary intake and potentially confounding variables

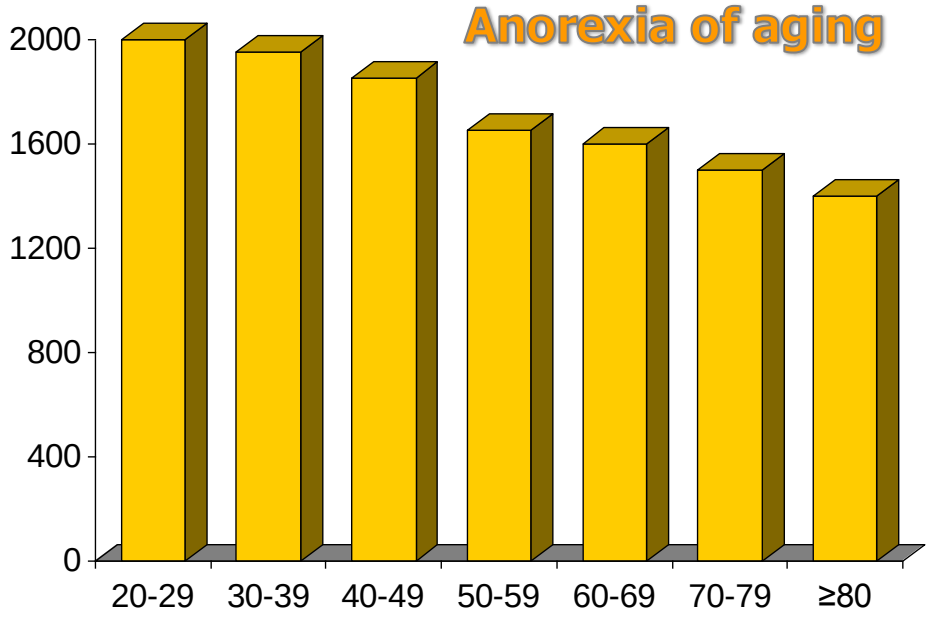
Main outcome measures: Adherence to a modified Mediterranean diet (scoring system on a 10 point scale)
Death from any cause by time of occurrence (Cox regression)

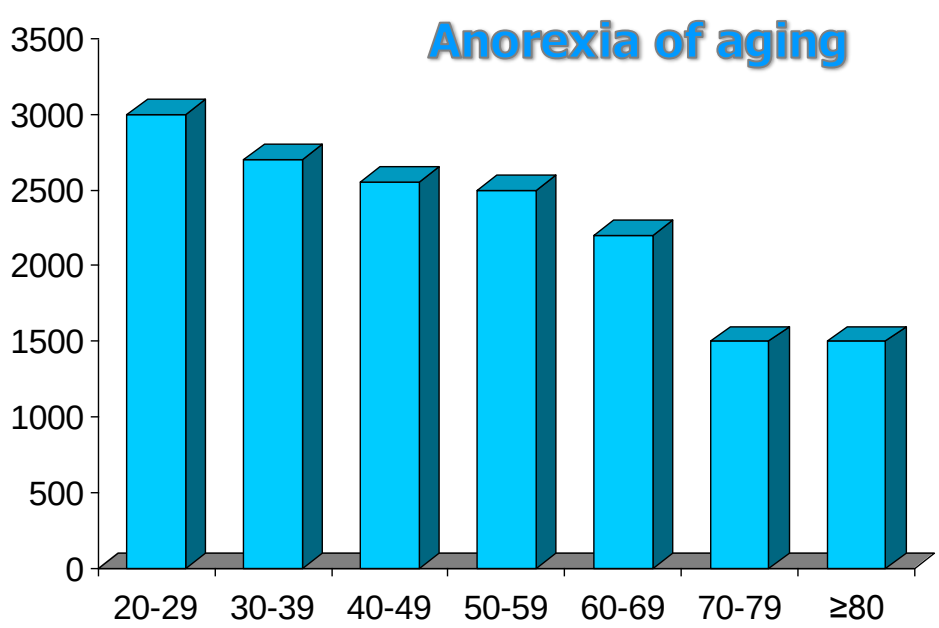
Results: **Qualitative aspects of diet predict overall death rate and hence survival**
A dietary pattern that resembles that of Mediterranean is associated with lower overall death rate
Polyunsaturated lipids are an acceptable substitute when monounsaturated lipids are not readily available

A Trichopoulou et al, BMJ 2005;330;991-997


Weight loss
32
30
28
26
24
22
BMI (kg/m2)
20
40
60
80
Age (years)
Uomini
Donne

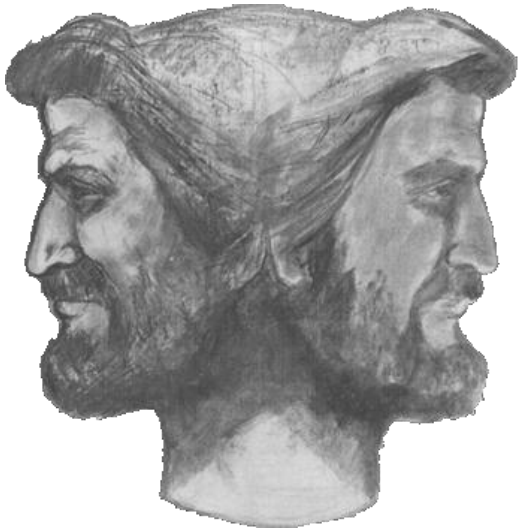

Early life
Adult life
Older life
Sarcopenia
Muscle mass and strength
Range in individuals
Disability threshold
Age


Anorexia of aging
2000
1600
1200
800
400
0
20-29
30-39
40-49
50-59
60-69
70-79
≥80


Anorexia of aging
3500
3000
2500
2000
1500
1000
500
0
20-29
30-39
40-49
50-59
60-69
70-79
≥80

Among young-middle healthy → **Nutrition** to prevent disease

Among old at risk → **Nutrition** to stabilize disease prevent disability prevent progression of disability



Nutrizione **Invecchiamento**