

# Voedingsonderzoek op een tweesprong: Voedingsstoffen of voedingsmiddelen

Daan Kromhout  
Division of Human Nutrition  
Wageningen University  
The Netherlands

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# Verwarrend voedingsonderzoek

Hoe verwarder de resultaten van het voedingsonderzoek er uitzien, hoe fanatieker de voedingsonderzoekers hierover discussiëren, des te nodiger is het om evidence-based onderzoek uit te voeren waarop de voedingsvoorlichting kan worden gebaseerd.

Vrij naar Hermann Hesse

THE BIG FEAT  
SURPRISE



THE BIG  
FAT  
SURPRISE

Why Butter, Meat & Cheese  
Belong in a Healthy Diet

NINA TEICHOLZ

NINA TEICHOLZ



JUNE 23, 2014

# TIME

## Eat Butter.

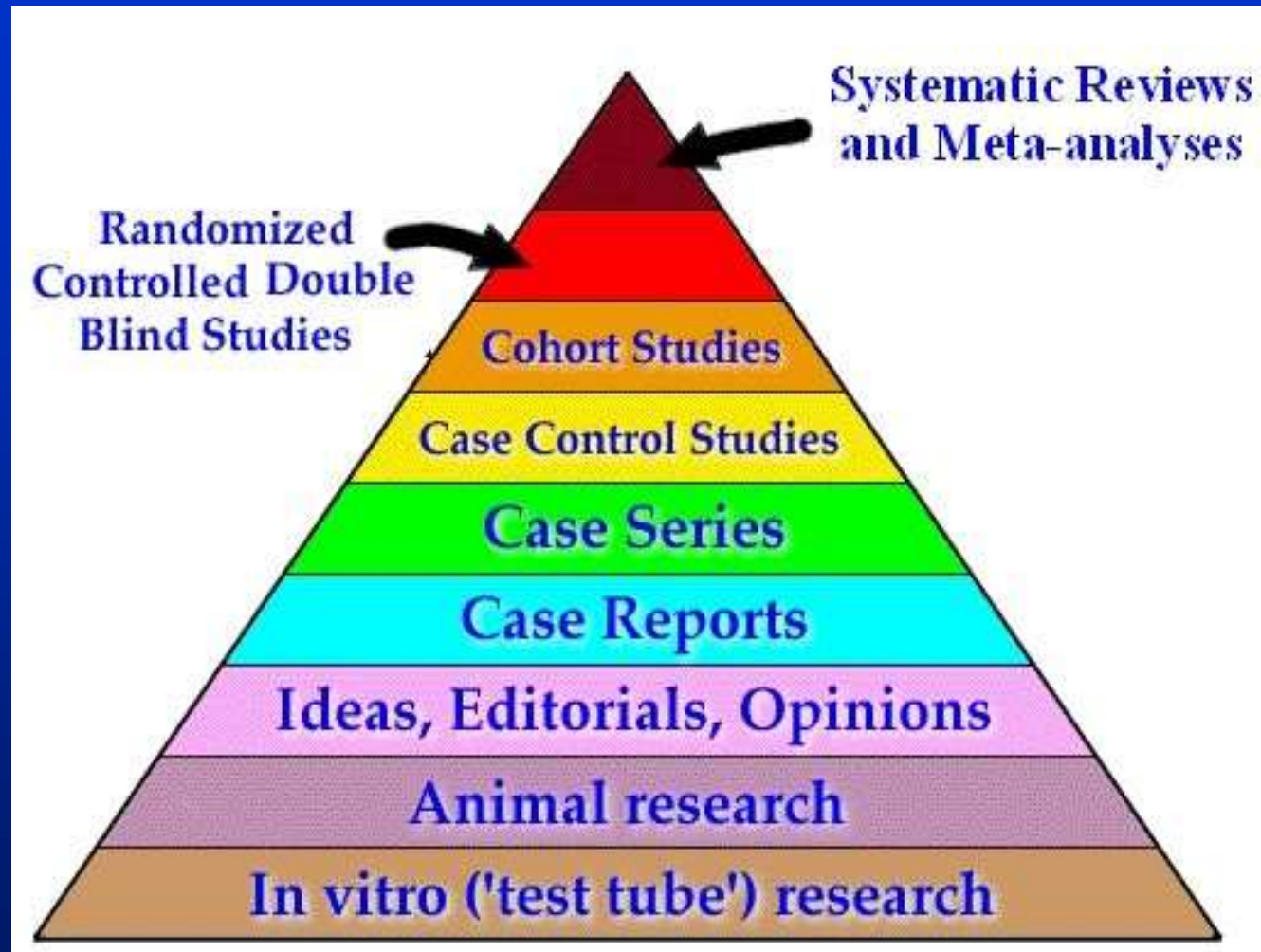
Scientists labeled fat the enemy. Why they were wrong

BY BRYAN WALSH



TIME.COM

# Strength of Evidence



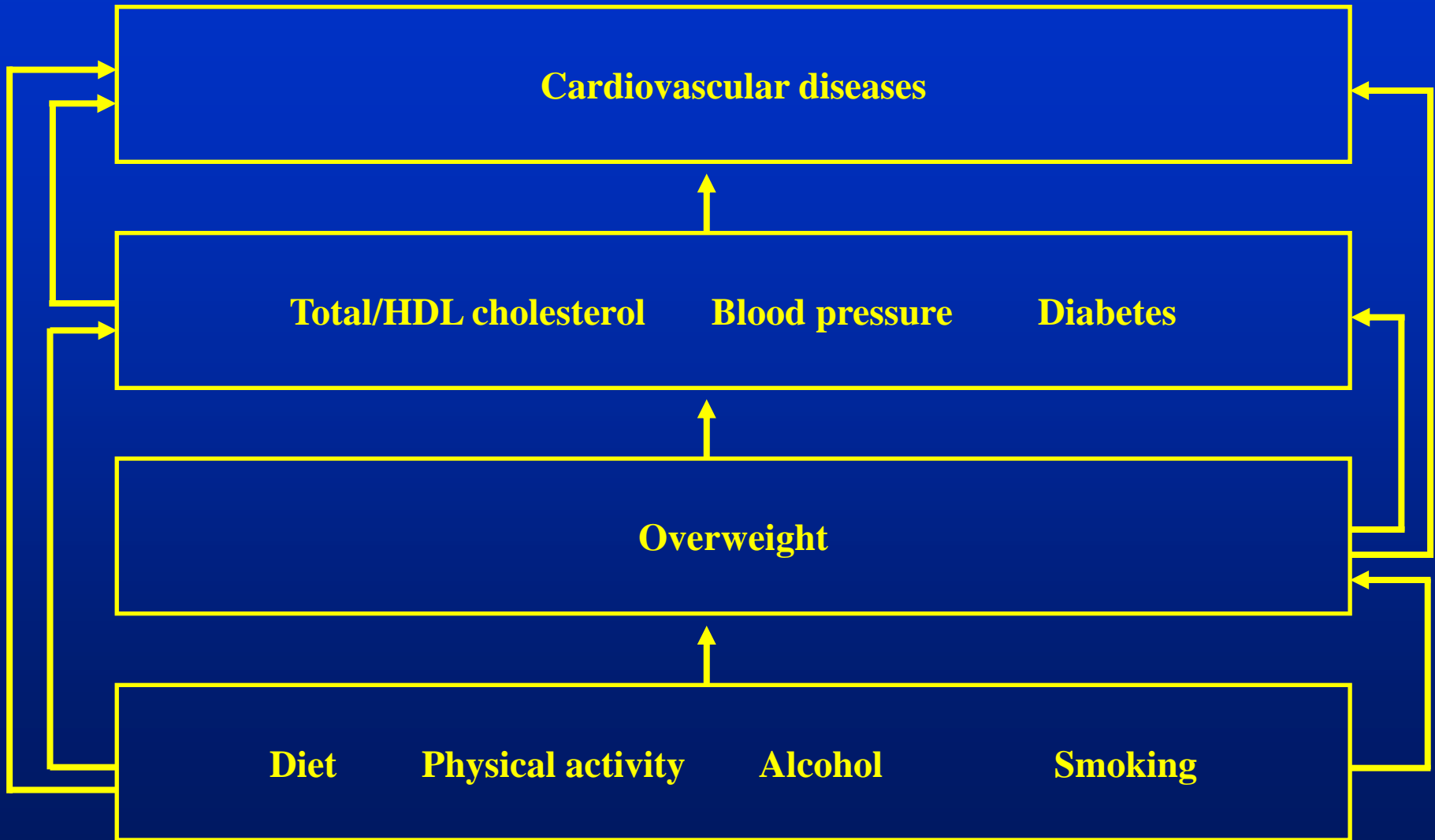
# Prospective studies

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	Experimental Randomized trials	Observational Cohort studies
Confounding	None	Residual
Evidence causality	Strong	Moderate
Number participants	Small	Large
Representativeness	Limited	Adequate
Endpoints	Risk factors	Disease
Study duration	Short	Long

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# Etiologic model for cardiovascular diseases



# Cholesterol hypothesis

Saturated fat



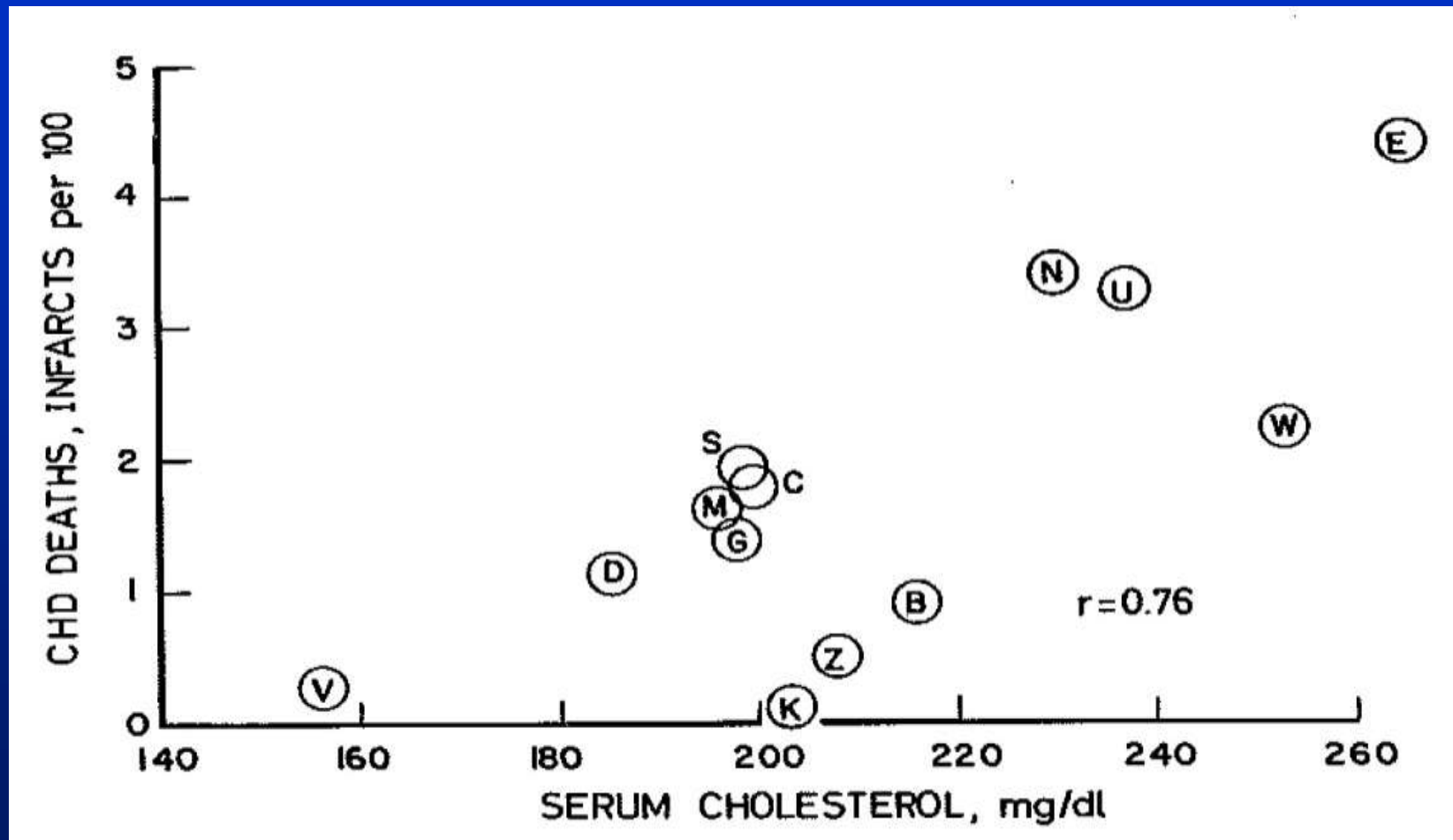
Serum cholesterol



Coronary heart disease

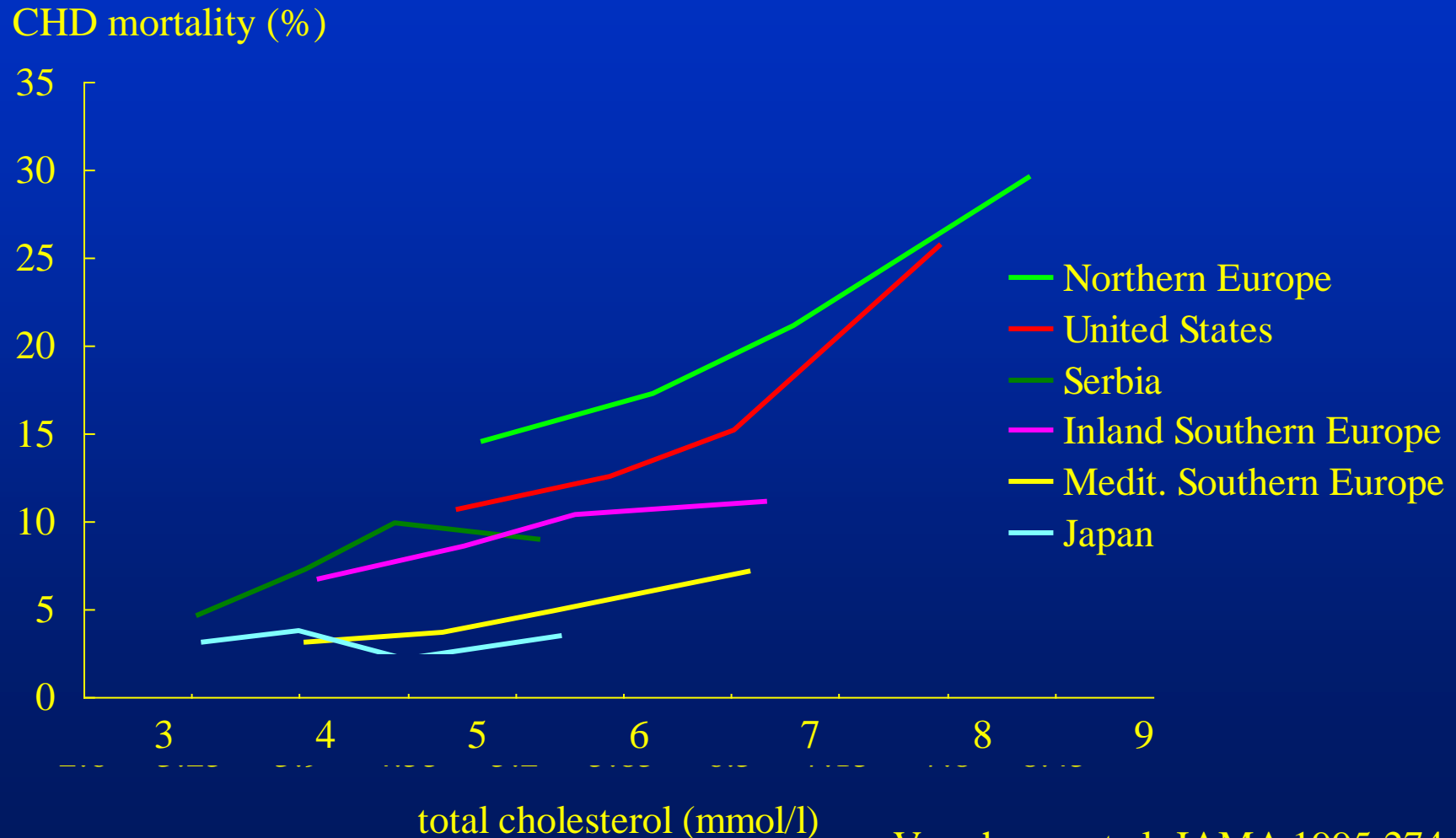


# Serum cholesterol and coronary heart disease in the Seven Countries Study

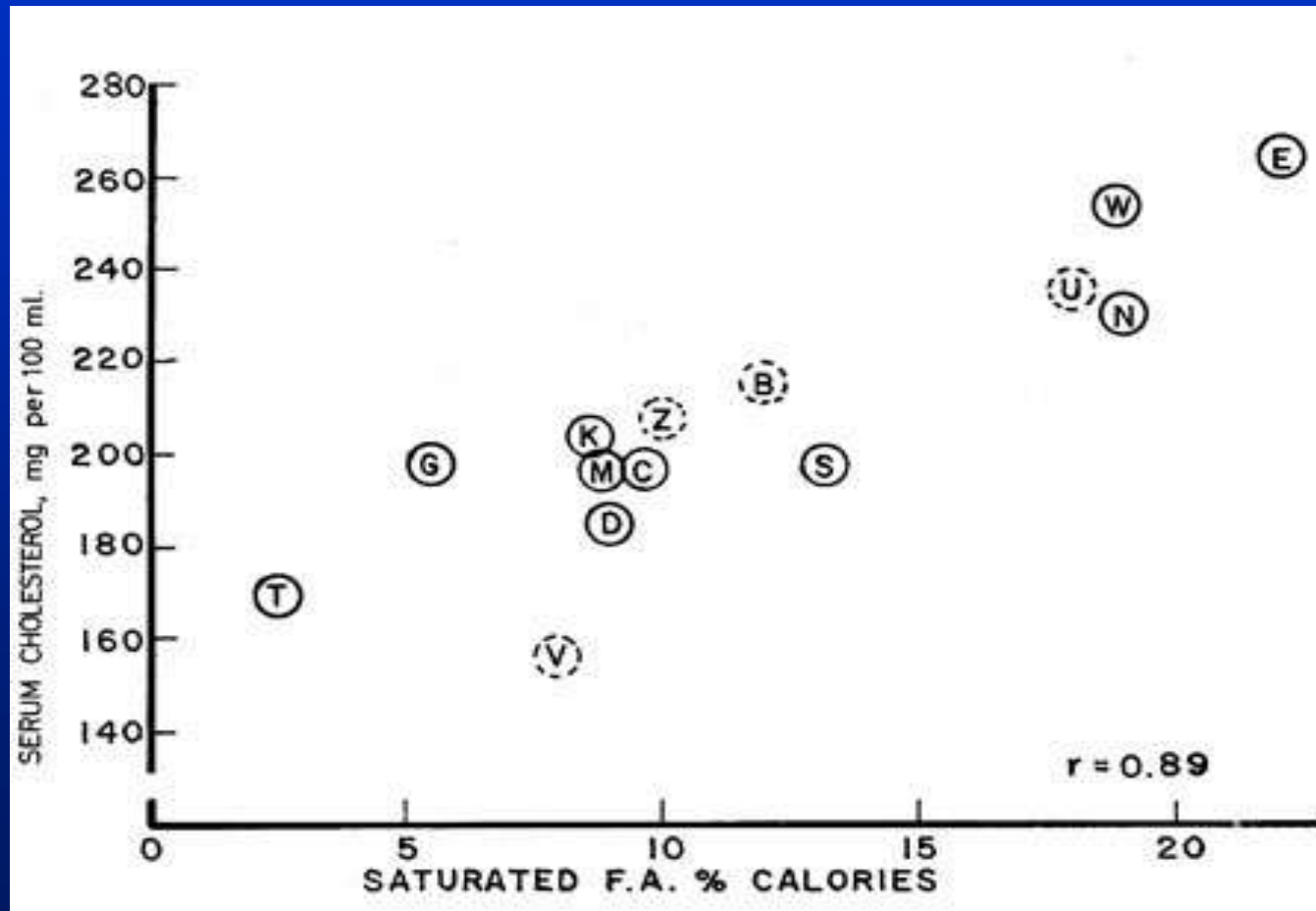




# 25-year CHD mortality rates to serum cholesterol in the Seven Countries Study



# Saturated fat and serum cholesterol in the Seven Countries Study



# Effect of dietary fatty acids and cholesterol on serum cholesterol

$$\Delta TC = 1.35 ( 2 \Delta S - \Delta P ) + 1.5 \sqrt{\Delta Z}$$

TC = Total cholesterol (mg/dl)

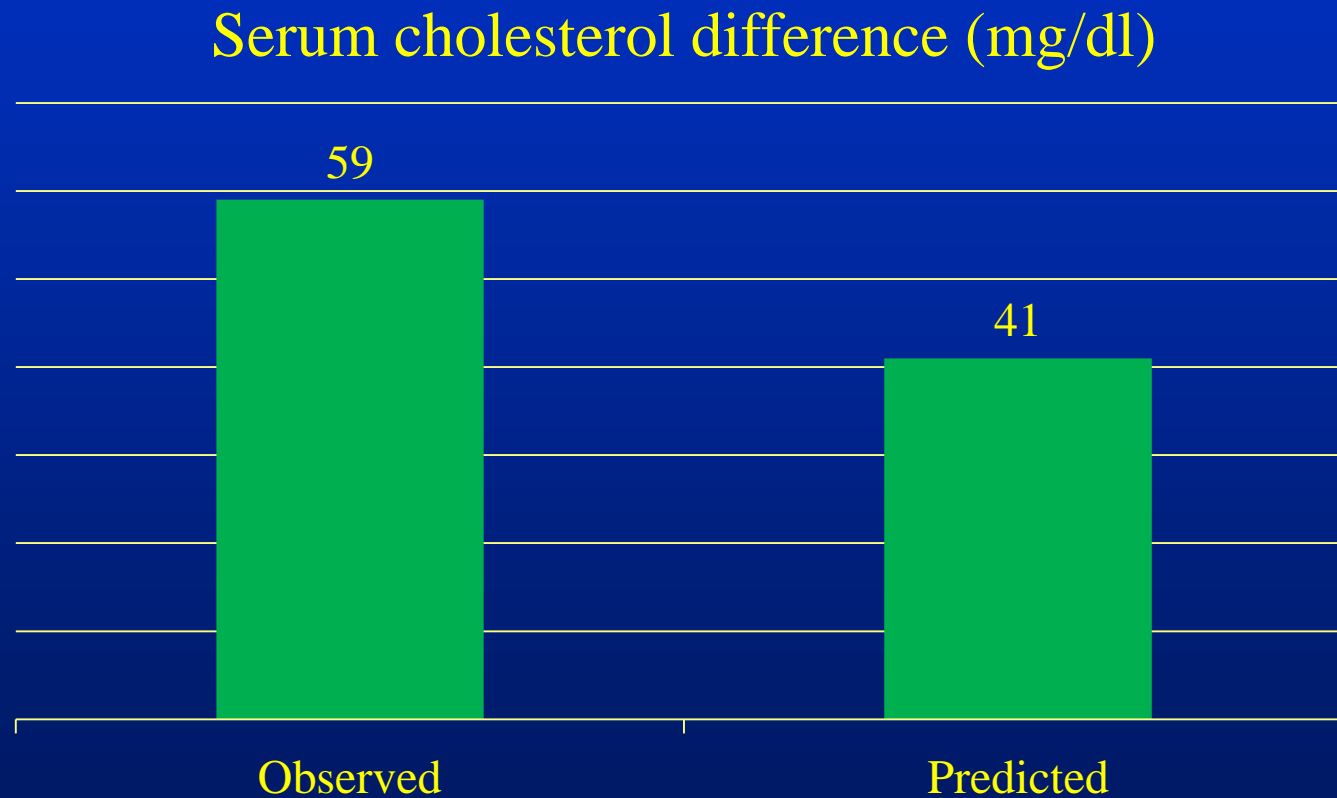
S = Saturated fat (% E)

P = Polyunsaturated fat (% E)

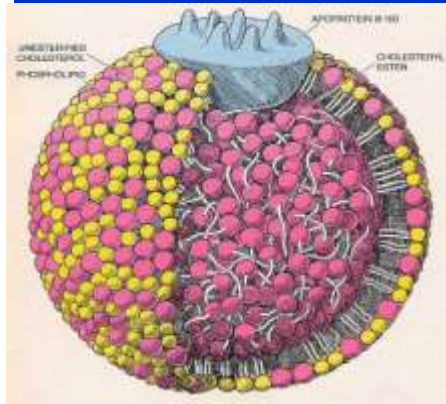
Z = Dietary cholesterol (mg/1000 kcal)

Keys et al. Metabolism 1965;14:776-87

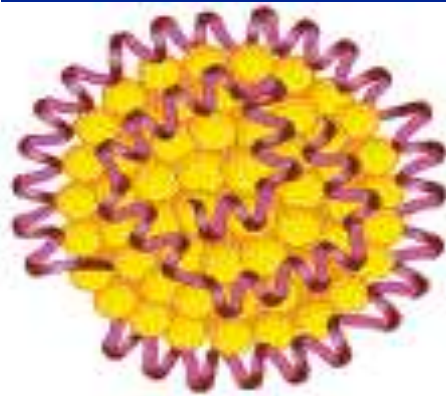
# Observed and predicted difference in average serum cholesterol level between Finland and Greece in 1960



# Bad and good cholesterol

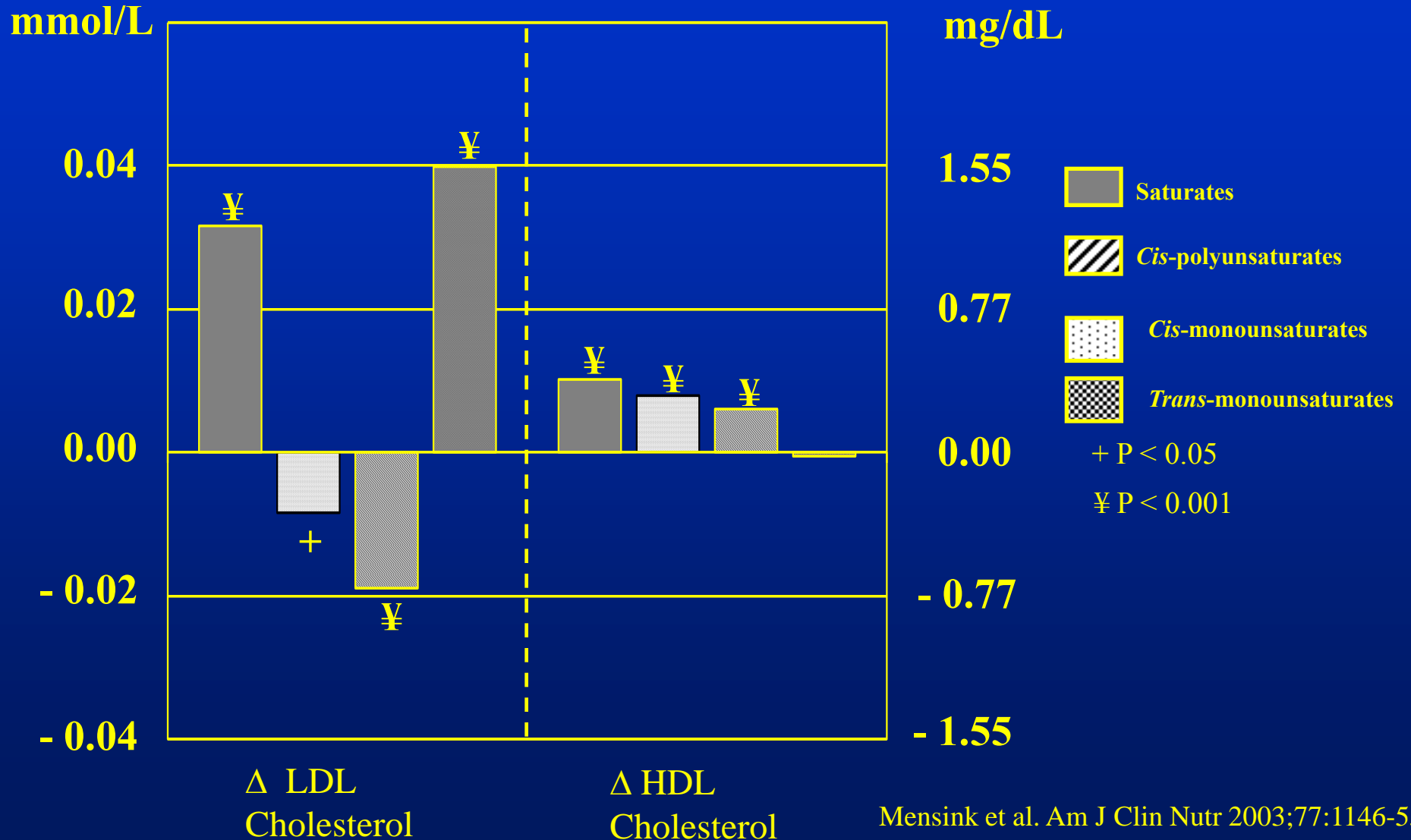


LDL deposits cholesterol in arteries. 50 to 80% of cholesterol in blood is LDL-cholesterol

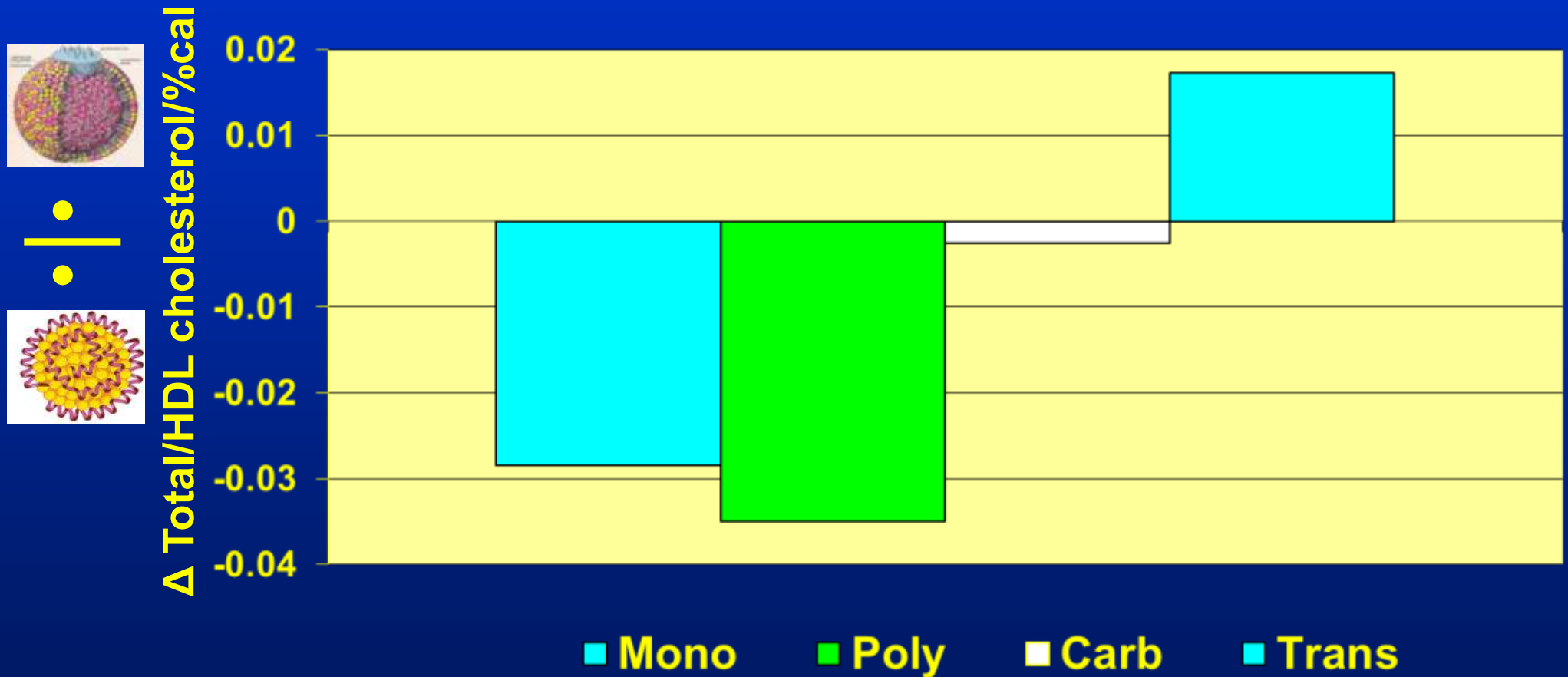


HDL takes up cholesterol from cells. 20-40% of cholesterol in blood is HDL-cholesterol

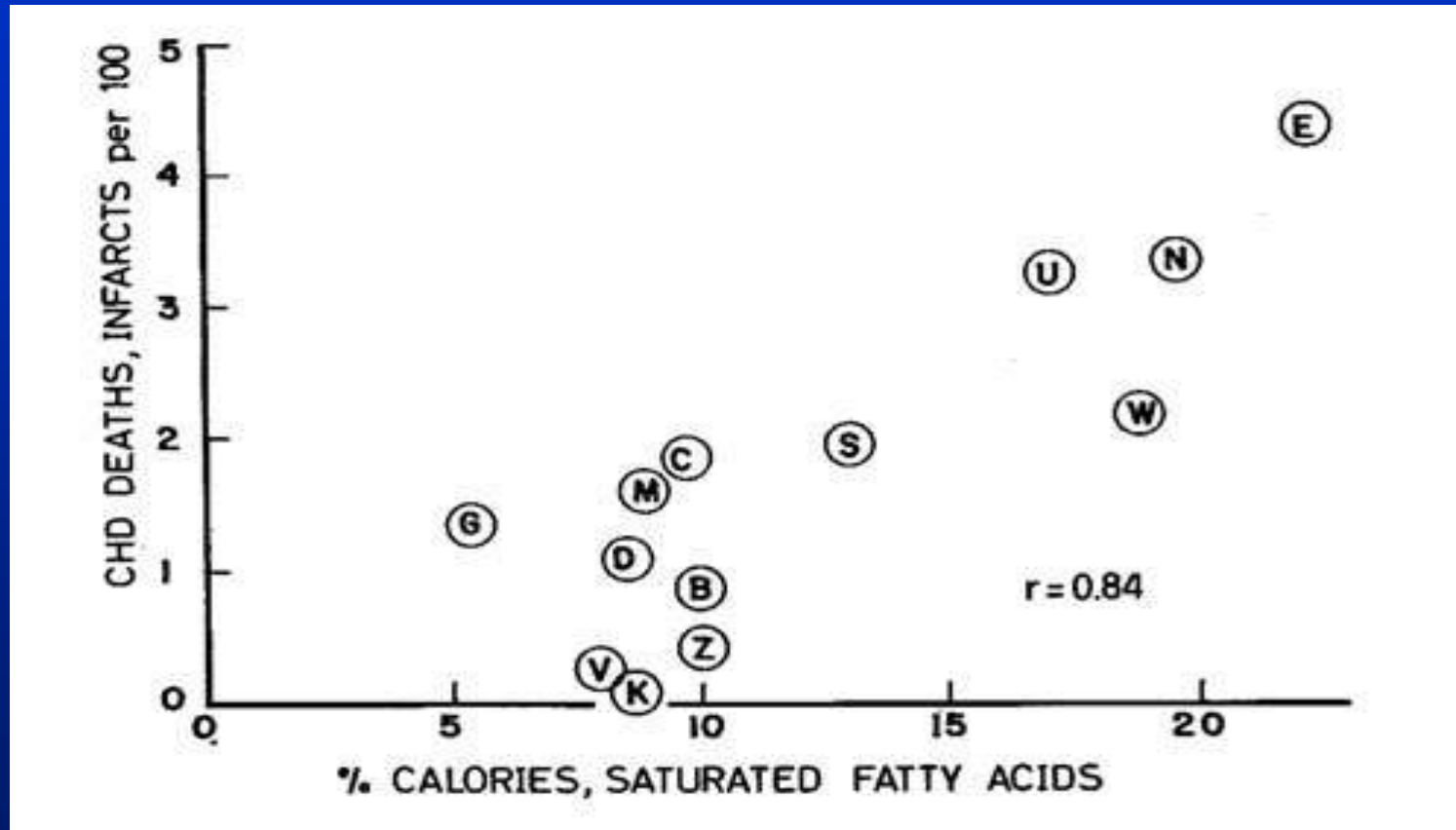
# Predicted changes ( $\Delta$ ) in LDL- and HDL cholesterol for carbohydrates (1% En) replaced by different fatty acids



# Effect on total/HDL cholesterol ratio of replacing saturated by unsaturated fatty acids or carbohydrates

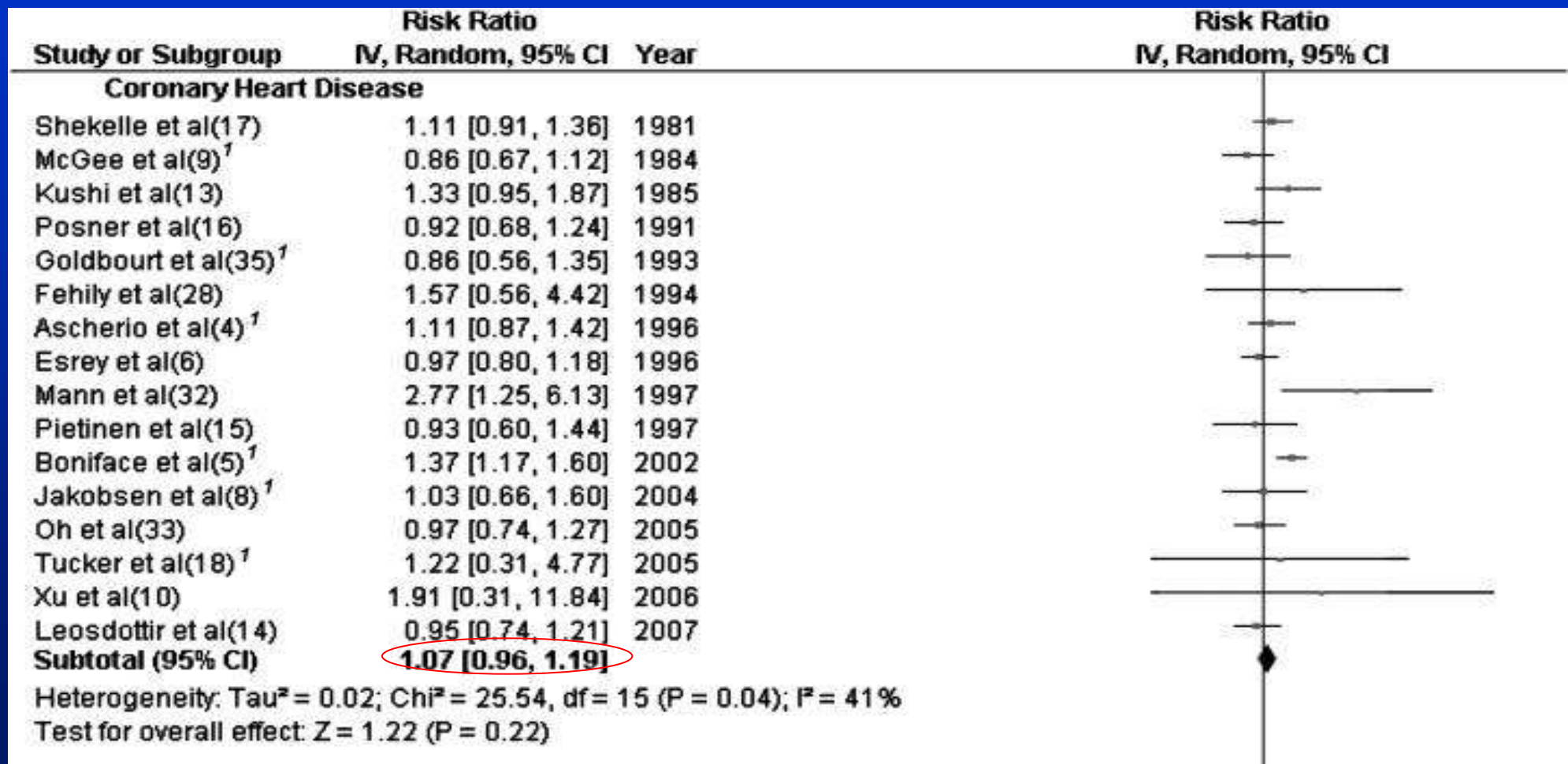


# Saturated fat and coronary heart disease in the Seven Countries Study

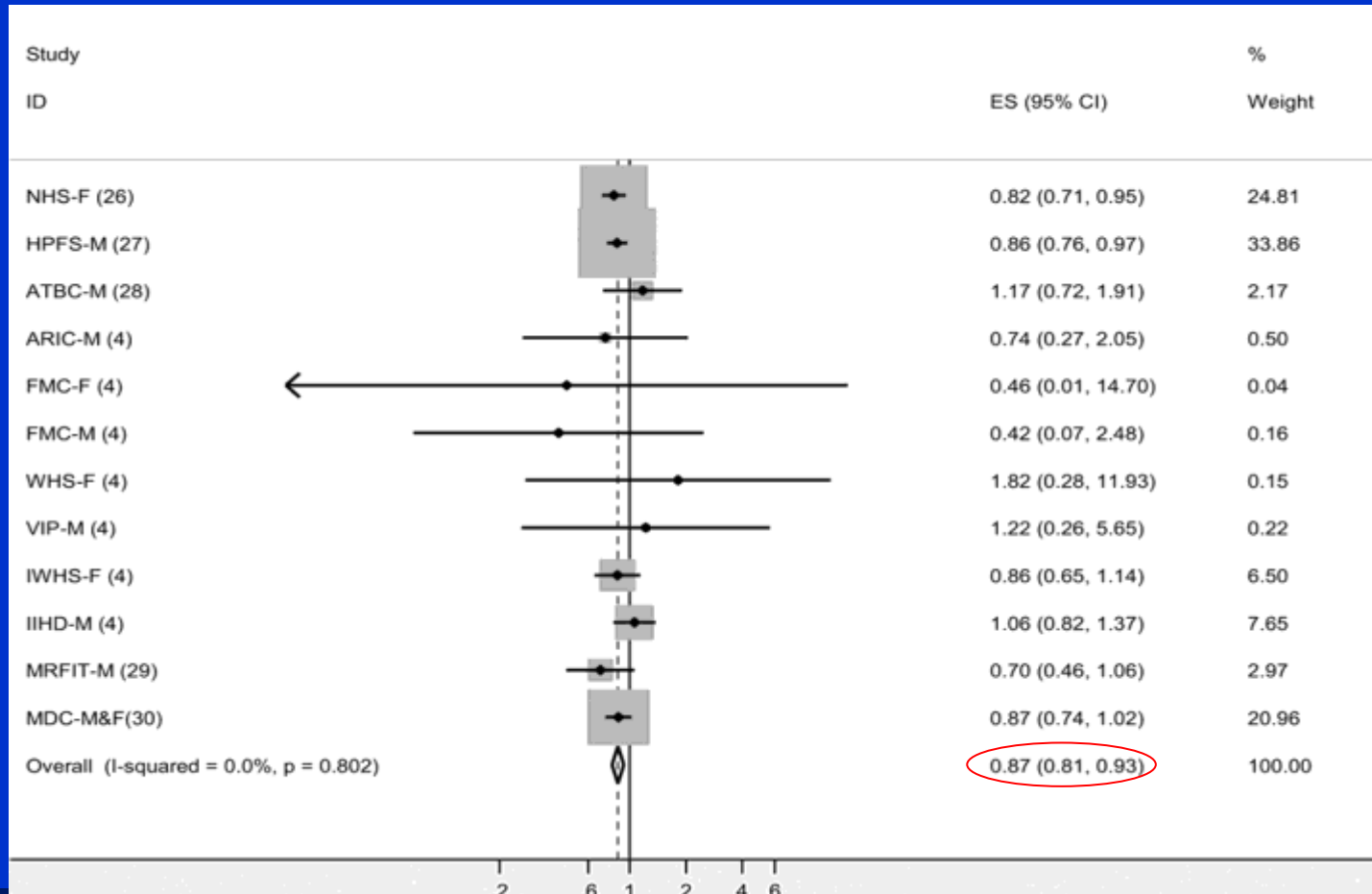




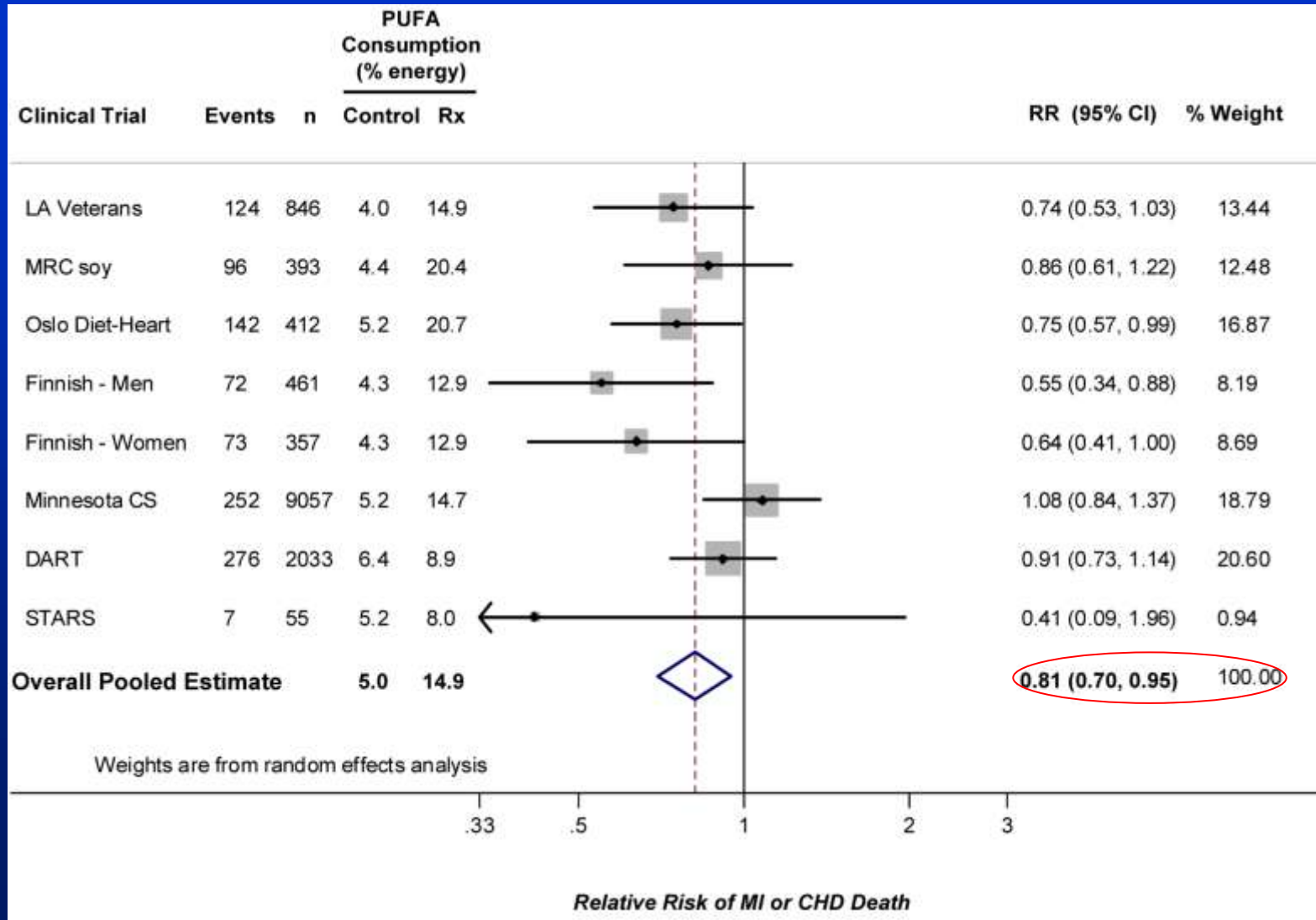
# Meta-analysis of saturated fat intake and coronary heart disease



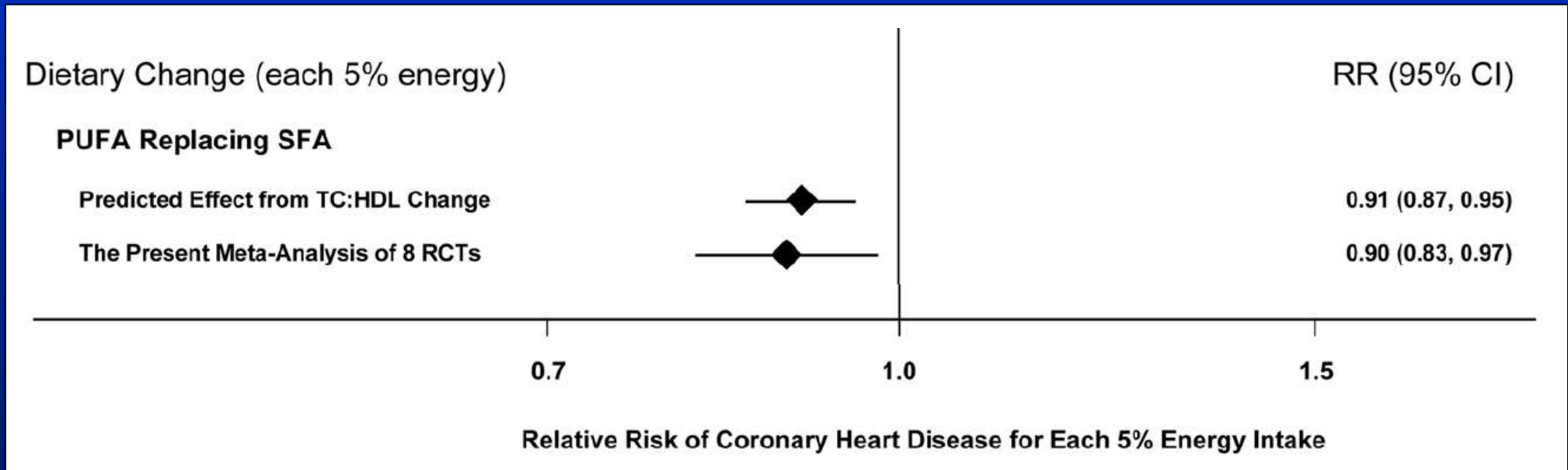
# Dose-response meta-analysis of substituting 5%E dietary linoleic acid for 5%E saturated fat and CHD events



# Meta-analysis of RCTs evaluating effects on CHD of replacing SAFA by PUFA



# Effects on CHD incidence of replacing SAFA by PUFA



# Effect of duration on CHD of replacing SAFA by PUFA

Duration	RR	95% CI
< 4.25 years	0.91	0.76 - 1.10
> 4.25 years	0.73	0.61 - 0.87

Mozaffarian et al. PLoS Med 2010;7:e1000252

# Effect replacement of 10%E SAFA by PUFA on fatal endpoints

Mortality	RR	95%CI
Coronary heart disease	0.80	0.65 – 0.98
All-causes	0.98	0.98 – 1.08

Mozaffarian et al. PLoS Med 2010;7:e1000252

# Effects of statins and fatty acids on blood lipids and hard endpoints in RCTs

Effect parameter	Statins	Fatty acids
	Change (%)	
Total cholesterol	-20	-13
LDL cholesterol	-28	
HDL cholesterol	+5	
Triglycerides	-13	
Major coronary events	-31	-20
All cause mortality	-21	- 2

LaRosa et al. JAMA 1999;282:2340-6  
Mozaffarian et al. PLoS Med 2010;7:e1000252

# Adjusted hazard ratios (95%CIs) of CVD to different sources of saturated fat

Source of saturated fat	5g/d	For each 5% of energy	P-value
Total	0.86	0.71 (0.56-0.89)	<0.01
Dairy	0.79	0.62 (0.47-0.82)	<0.01
Meat	1.26	1.48 (0.98-2.23)	0.06
Butter	0.87	0.83 (0.50-1.37)	0.47



# Examples of a priori defined dietary indices

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Dietary guidelines

Recommended diets

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Healthy Diet Indicator, WHO

Mediterranean diet

Nutrient Adequacy Ratio, USA

DASH diet

Healthy Eating Index, USA

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# Criteria Healthy Diet Indicator based on WHO guidelines 1990

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Nutrients (%En)		Nutrients/foods (g/day)	
Saturated fatty acids	<10	Cholesterol (a)	<300
Poly-unsaturated fatty acids	3-7	Dietary fibre	27-40
Protein	10-15	Fruits and vegs	>400
Complex carbohydrates	50-70	Legumes, nuts, seeds	>30
Mono and disaccharides	<10		

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a=(mg/day)

Huijbregts et al. BMJ 1997;315:13-7

# Adjusted Relative Risk for 20-year all-cause mortality to Healthy Diet Indicator

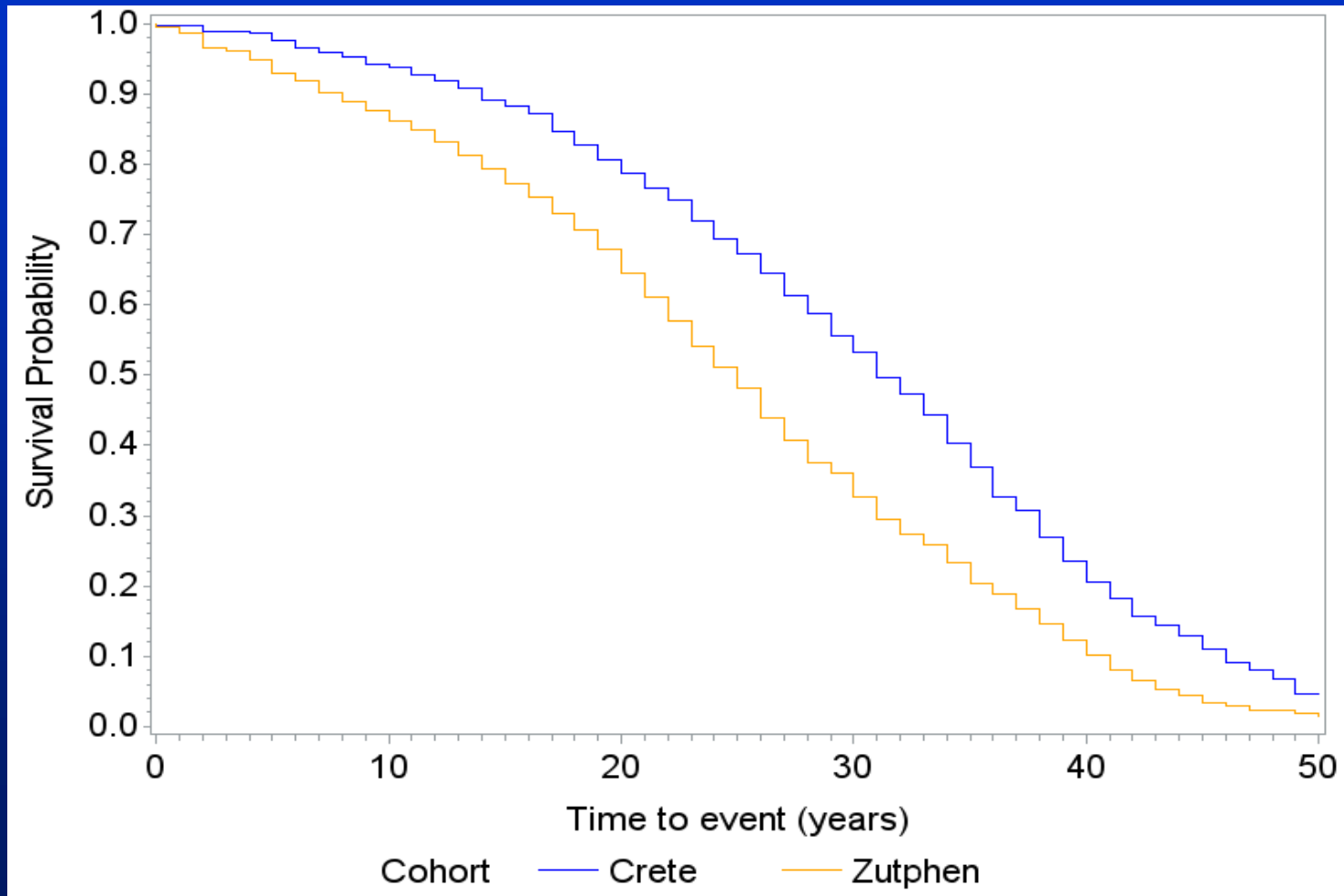
Country	Low	Medium	High
Finland	1.00	0.97	0.90
Netherlands	1.00	0.91	0.75
Italy	1.00	1.04	0.89
Pooled	1.00	0.99	0.87
(95% CI)		(0.87-1.11)	(0.77-0.98)

Huijbregts et al. BMJ 1997;315:13-7

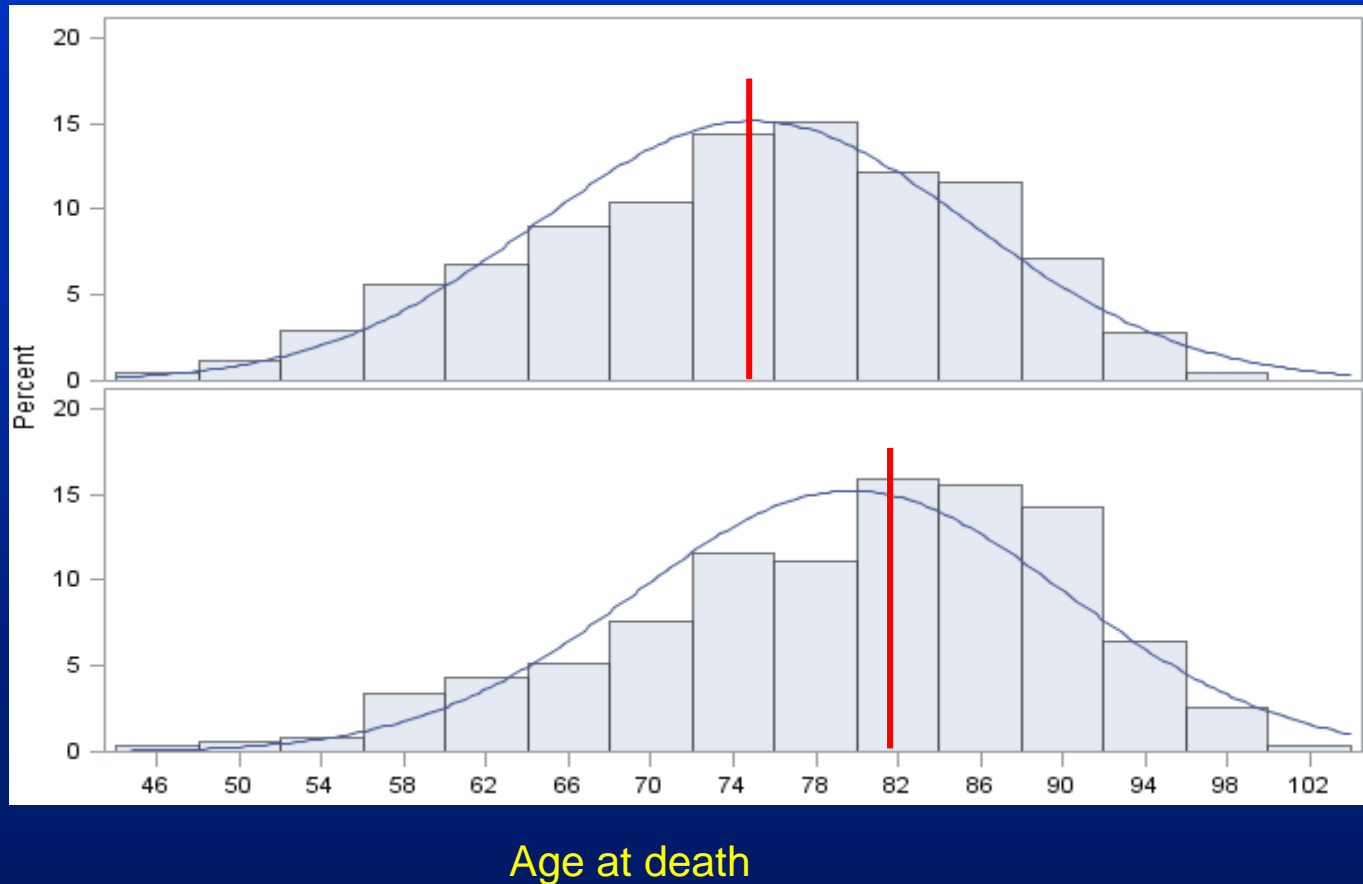




# Survival probability of all-cause mortality in Crete and Zutphen



# Age at death distributions of Zutphen and Crete after 50 years of follow-up



Zutphen

Median=75.9

Crete

Median=81.6

# Vital status and causes of death in Crete and Zutphen after 50 years of follow-up

Vital status Causes of death	Crete		Zutphen	
	Number	%	Number	%
Alive	32	4.7	15	1.7
Deceased	654	95.3	863	98.3
CHD	105	16.1	236	27.3
Stroke	100	15.3	69	8.0
Heart failure	71	7.8	51	4.5
Lung cancer	32	4.9	105	12.2

CHD = Coronary Heart Disease



The *traditional* Mediterranean diet is plant-food based with olive oil as principle source of fat



# Mediterranean diet score

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Cereals

MUFA to SAFA ratio

Fruits

Fish

Vegetables/potatoes

Meat and poultry

Legumes/nuts/seeds

Dairy products

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Adapted from Trichopoulou et al. BMJ 2005;330:991-8

# Individual food groups and 10-year mortality (The HALE project)

Food group	HR (95% CI)
Grains (g/d)	0.84 (0.77-0.92)
Fruit (g/d)	0.86 (0.78-0.94)
Vegetables/potatoes (g/d)	0.99 (0.90-1.09)
Legumes/nuts/seeds (g/d)	0.95 (0.86-1.04)
MUFA/SAFA ratio	0.89 (0.81-1.00)
Fish (g/d)	0.89 (0.82-0.97)
Meat/poultry (g/d)	0.97 (0.87-1.09)
Milk/milk products (g/d)	1.10 (1.00-1.21)

# Relative risk of 10-year mortality to Mediterranean Diet Score (The HALE project)

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Cause of death	Relative risk	95%CI
All-causes	0.77	0.68-0.88
Coronary heart disease	0.61	0.43-0.88
Cardiovascular diseases	0.71	0.58-0.88
Cancer	0.90	0.70-1.17

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Knoops et al. JAMA 2004;292:1433-9

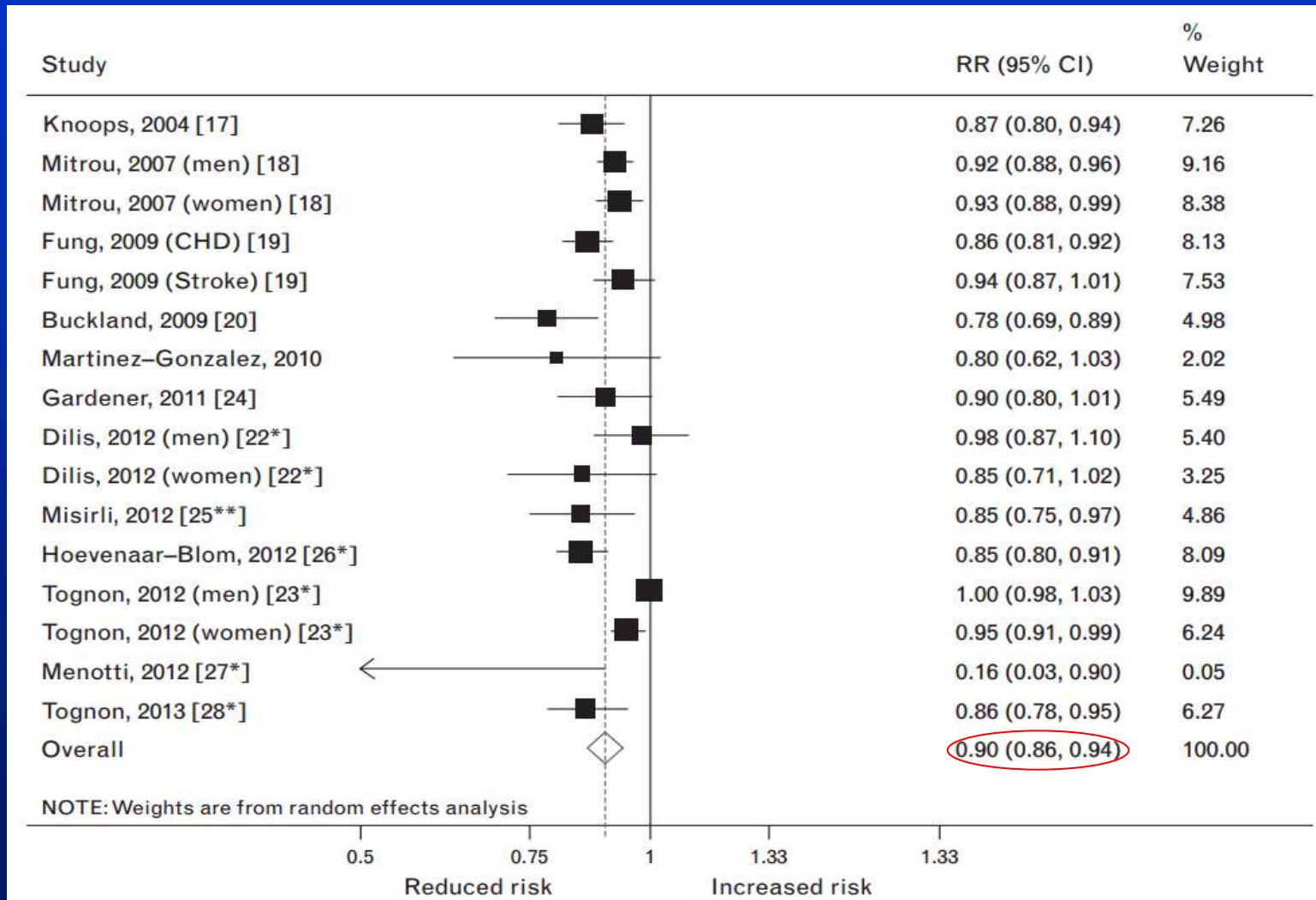
# Should alcohol be in or excluded from the Mediterranean Diet Score (MDS)? (The HALE project)

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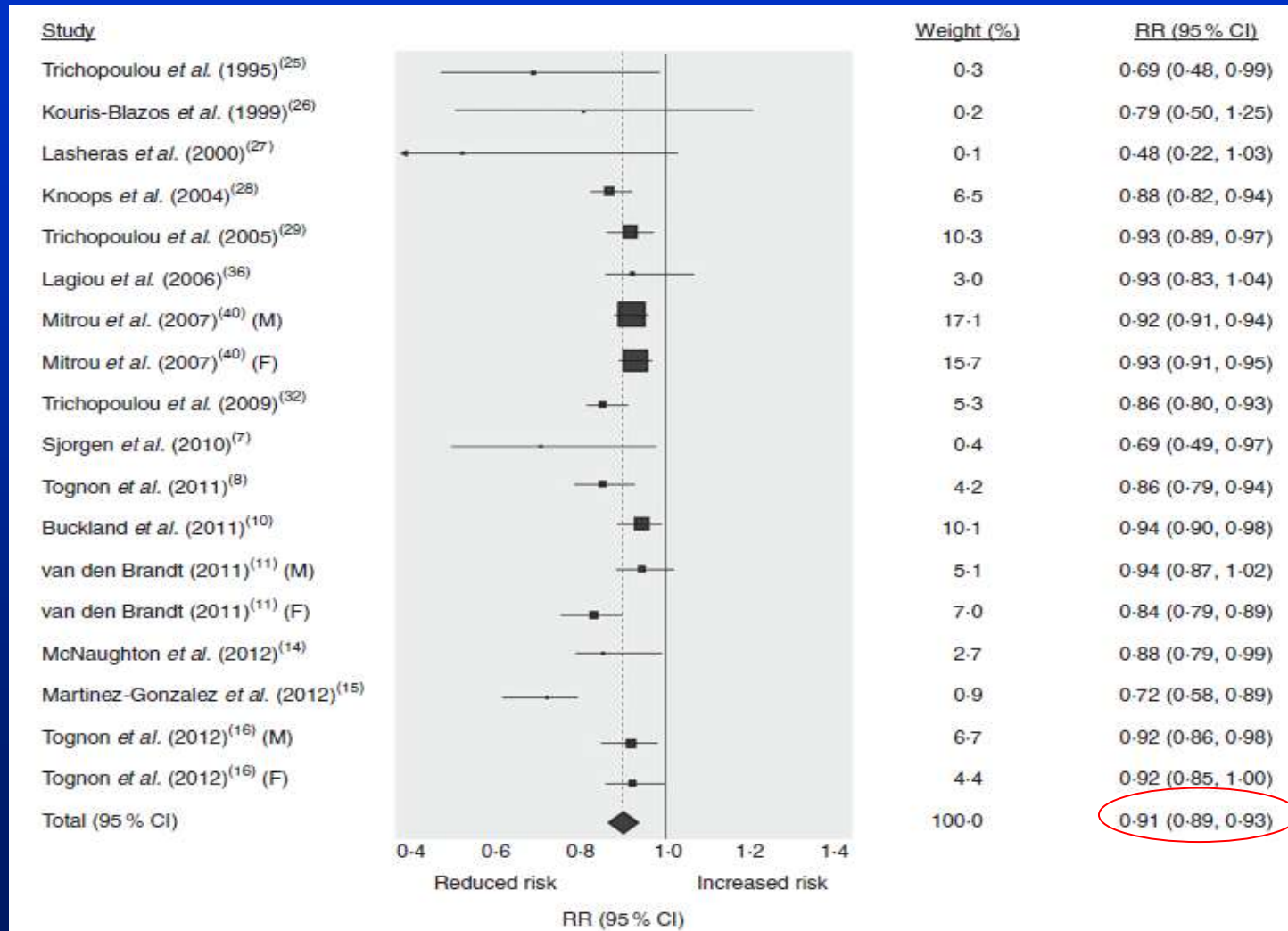
Protective factor	Hazard ratio all-cause mortality
Alcohol included in MDS	0.86
MDS without alcohol	0.77
Alcohol	0.78
MDS and alcohol independently	0.60

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# Meta-analysis of Mediterranean Diet Score and cardiovascular disease



# Meta-analysis of Mediterranean Diet Score and all-cause mortality



# Mediterranean diets and changes in risk factors

## The PREDIMED Study

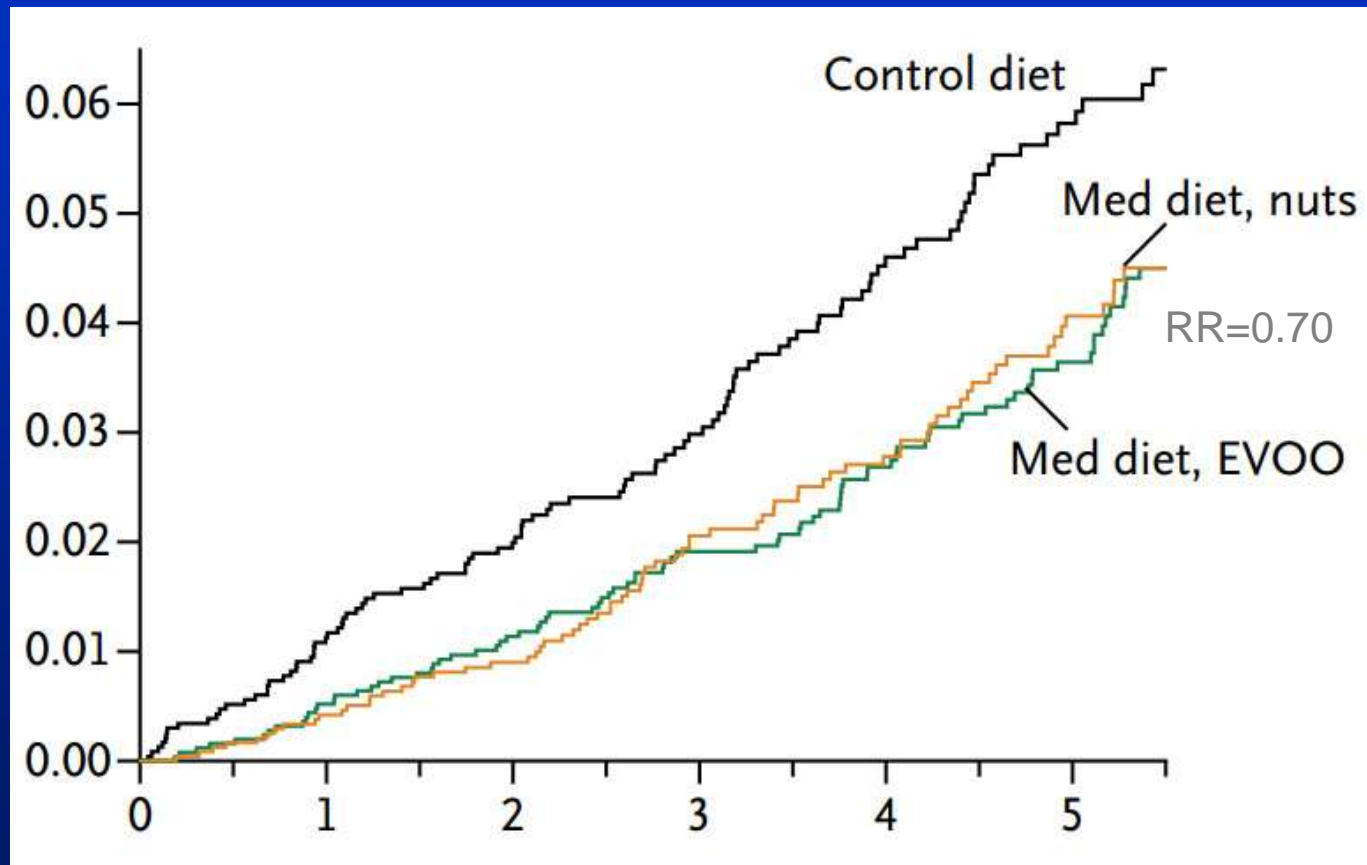
Variable	Mediterranean diet with olive oil vs low-fat diet	Mediterranean diet with nuts vs low-fat diet
LDL cholesterol (mmol/L)	-0.10	-0.09
HDL cholesterol (mmol/L)	+0.08***	+0.04**
Systolic BP (mm Hg)	-5.9***	-7.1***
Fasting glucose (mmol/L)	-0.39*	-0.30*
Fasting insulin (mmol/L)	-16.7***	-20.4***
C-Reactive protein (mg/L)	-0.54**	+0.33

\*p<0.05; \*\*p<0.01; \*\*\*p<0.001

Estruch et al. Ann Intern Med 2006;145:1-11

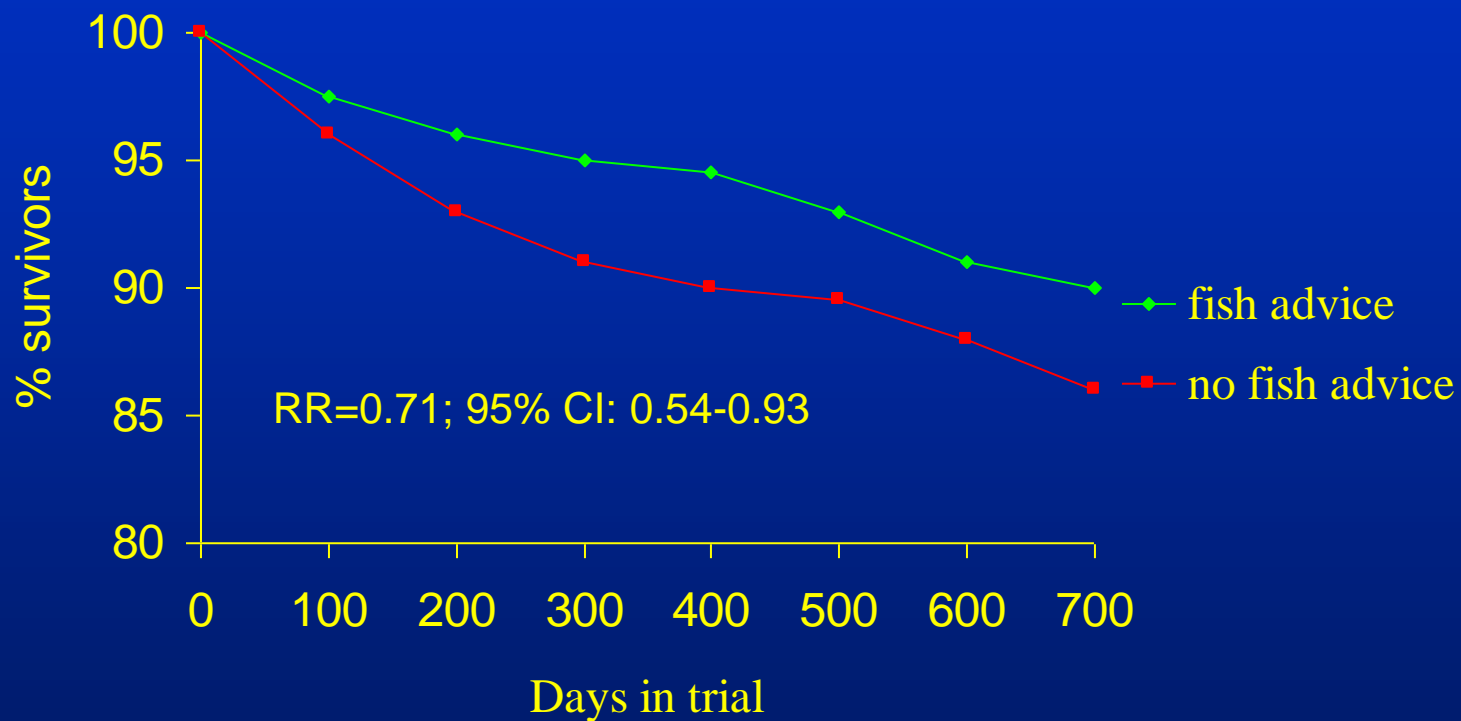


# CVD incidence to additional nuts and olive oil. The PREDIMED Study



Estruch et al. N Engl J Med 2013;368:1279-90

# Survival to fish advice. DART-I trial



Burr et al. Lancet 1989;ii:757-61

# Effects of dietary interventions on CVD events and mortality in Randomized Controlled Trials

Effect parameter	MA	DART	PREDIMED	
SAFA replaced by PUFA (%E)	10			
Extra portions oily fish/week		2		
Extra virgin olive oil (ml/d)			50	
Extra nuts (g/d)				30
Total cholesterol (mmol/L)	-0.8*	N.S.	N.S.	N.S.
CVD events			-30*	-28*
CHD death (%)	-20*	-33*	-20	-26
Total death (%)	-2	-29*	-18	-3

MA = Meta-Analysis

N.S. = Not Significant

\* = P<0.05

# Conclusions

- RCTs showed that replacement of SAFA by PUFA reduces CHD but not all-cause mortality
- RCTs showed that foods e.g. oily fish, extra virgin olive oil and nuts reduce CHD mortality at least as much as replacement of SAFA by PUFA
- Prospective cohort studies showed that the Mediterranean diet score is an example of an a priori defined dietary pattern that is strongly inversely related to survival



## What is the Seven Countries Study?

The Seven Countries Study (SCS for short) is the first major study to investigate diet and lifestyle along with other risk factors for cardiovascular disease, across contrasting countries and cultures and over an extended period of time. [Read more](#) about this study.



## About the study

Learn more about the history, study design and main study questions of the SCS. [Read more.](#)

## The 7 Countries



[Read more](#) about the countries.

## Study findings

Discover what the SCS brought to light by reading about the main results. [Read more.](#)

## Investigators

Get to know the people behind the SCS, and their relationships and careers. [Read more.](#)