

Modifying effects of dietary polyunsaturated fatty acid (PUFA) on levels of cholesterol and their implications for heart health

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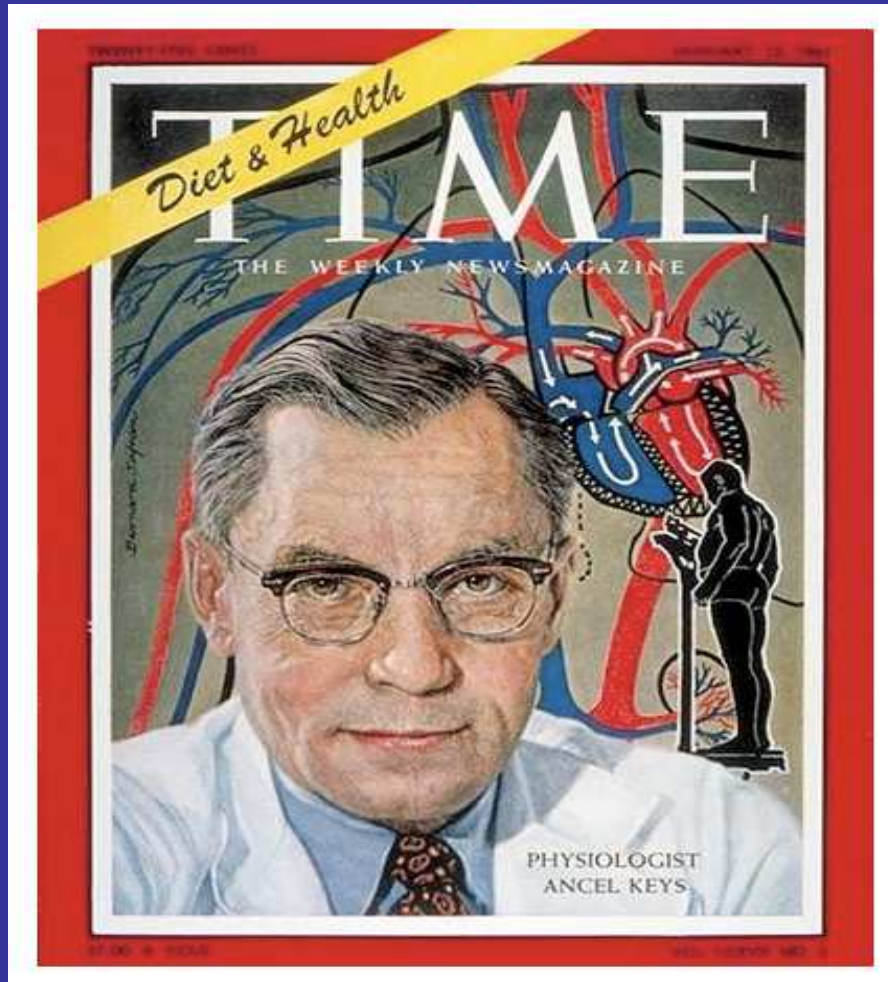
Outline of lecture

Classic “diet-heart” hypothesis

Limitations of cohort studies of diet and CHD

Limitations of trials of dietary advice to modify intake of dietary fat to reduce CHD risk

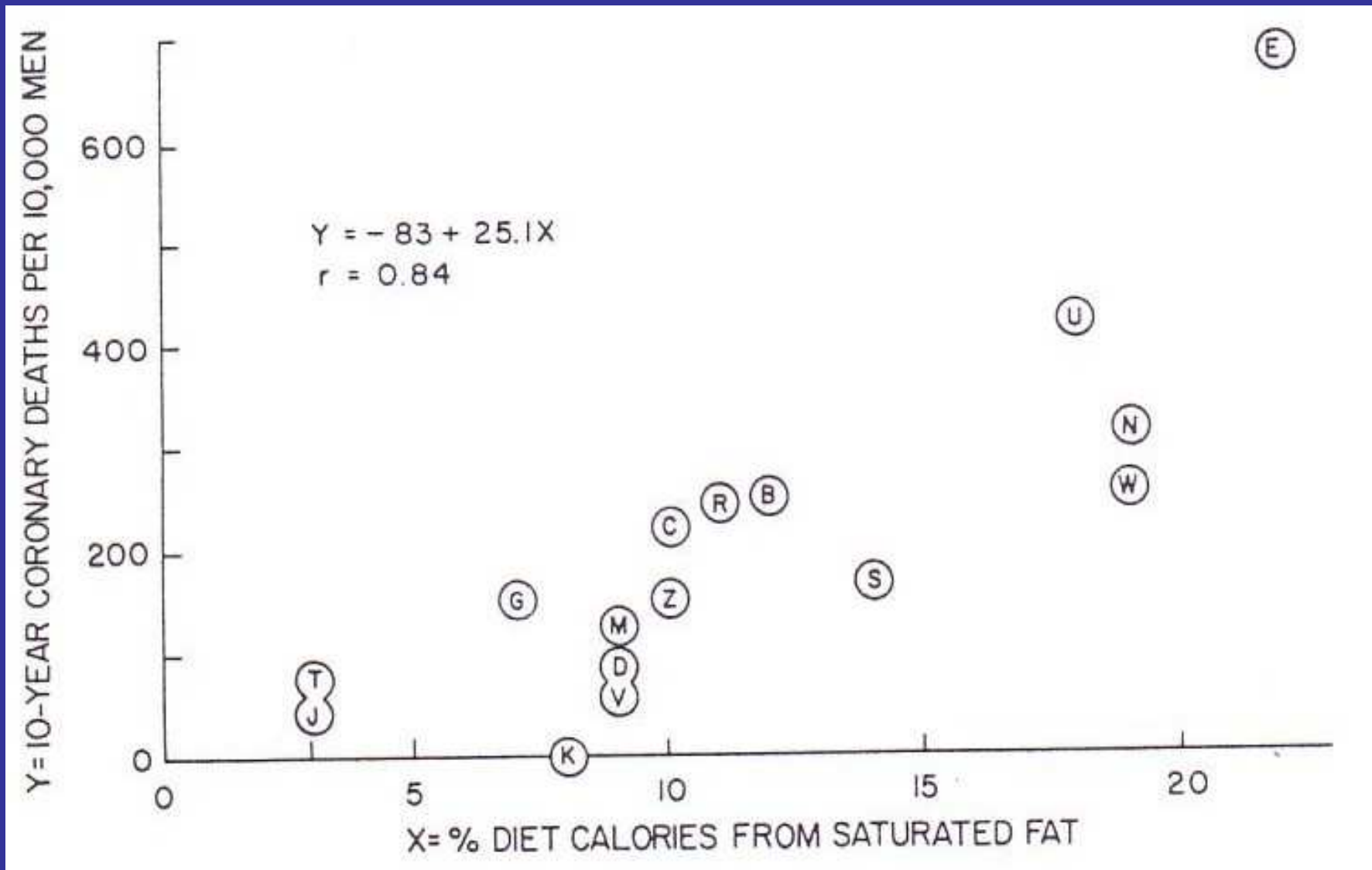
Importance of “metabolic ward” to assess the effects of dietary fat modification on blood lipids



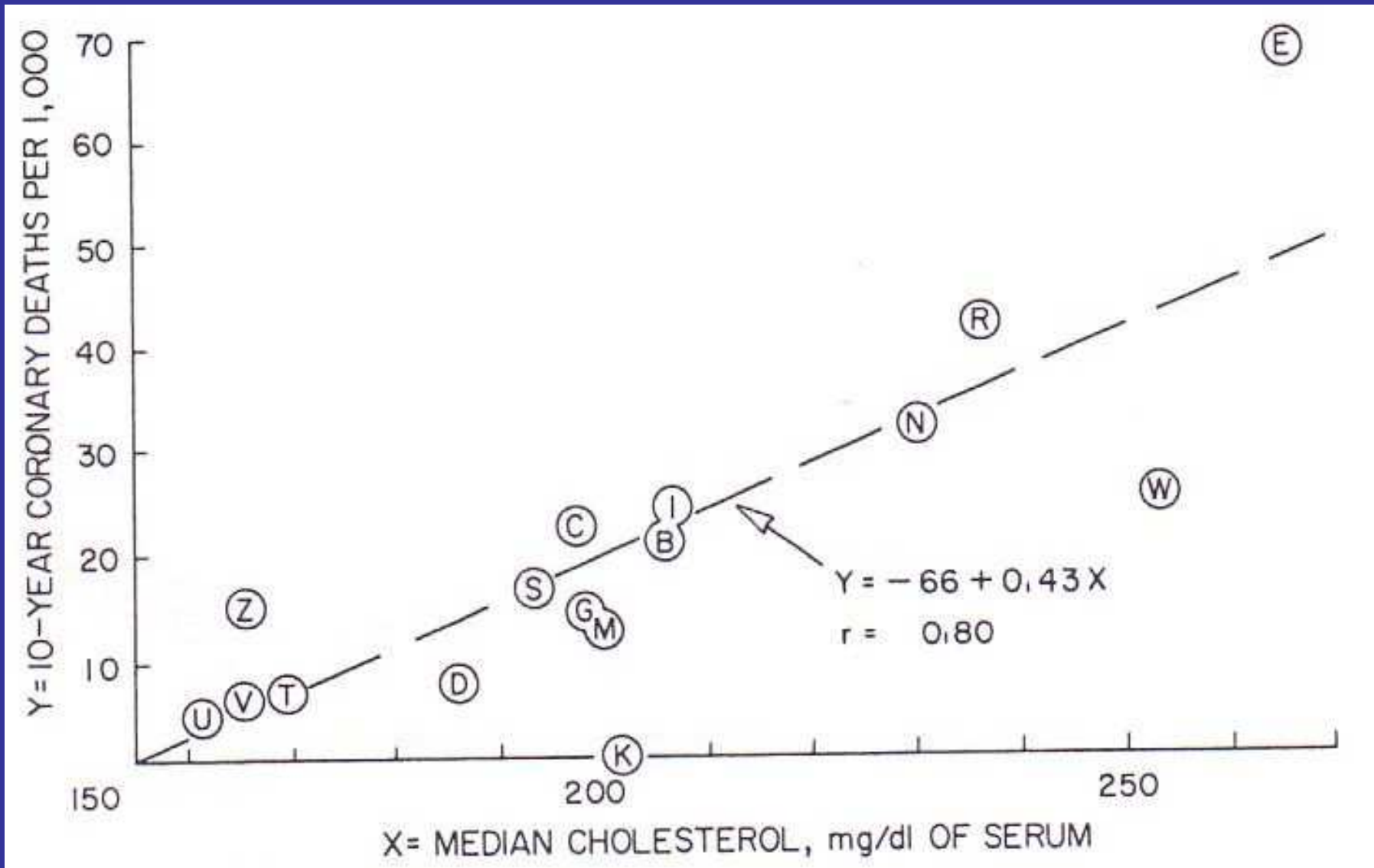
Ansel Keys (1904-2004)

“Keys advocated that replacing saturated by unsaturated fat would reduce blood cholesterol and the incidence of CHD. The resulting changes in the composition of food fats led to a doubling of the proportion of the unsaturated fatty acid, linoleic acid, in USA between 1960 and 1975. Rates of CHD in the US began to fall from 1968 onwards, and about half of the decline was ascribed to changes in lifestyle including diet”.

Saturated fat and risk of CHD mortality: Seven Countries Study



Total cholesterol and risk of CHD mortality: Seven Countries Study



Blood lipids and coronary disease (CHD)

Total cholesterol is composed of LDL-C and HDL-C, which are positive and negative risk factors for CHD, respectively

Decreasing intake of “bad fats” (saturated fats and trans fats), decreases total cholesterol and LDL-C

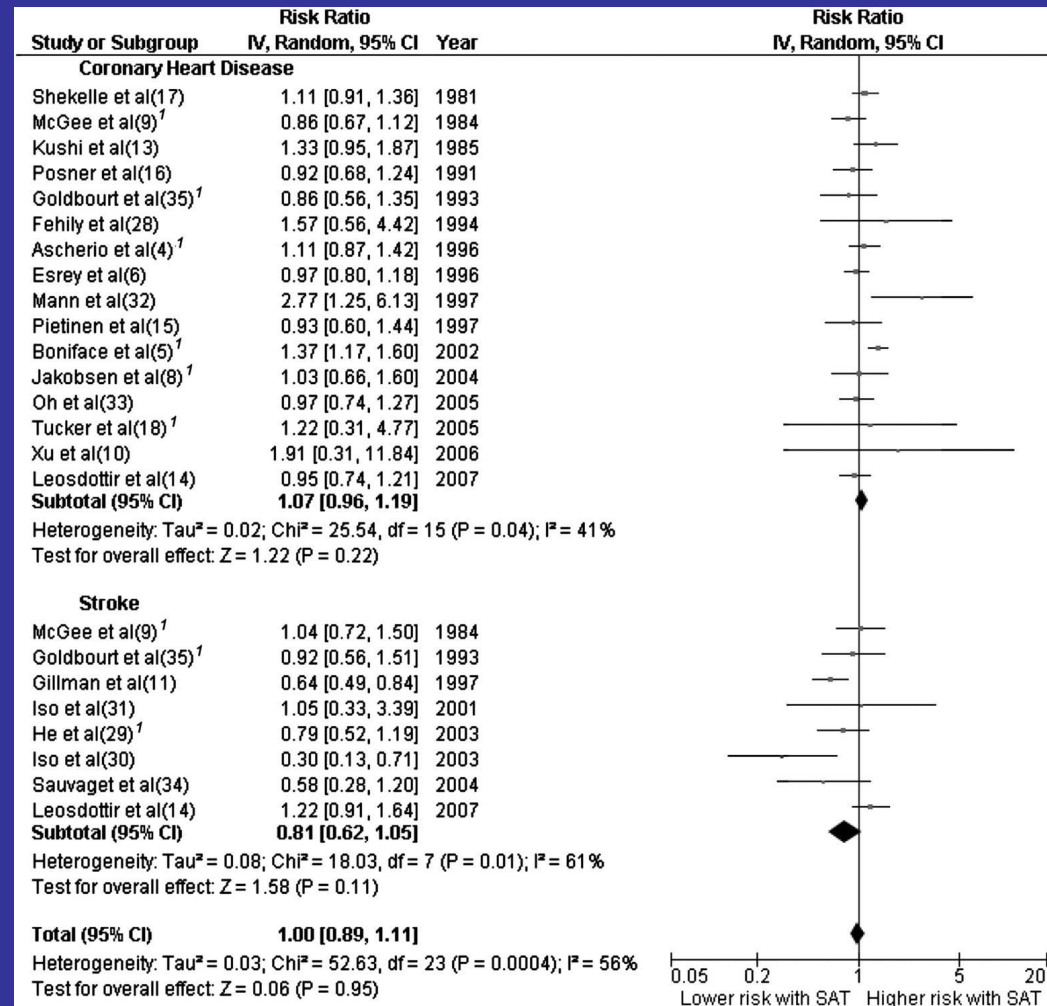
There remains uncertainty about the extent to which saturated fats should be replaced by unsaturates or by complex carbohydrates

Misinterpretation of the evidence: The Siri-Tarino et al. study

Meta-analysis of cohort studies of dietary intake of saturates and cardiovascular disease (11,000 CHD or stroke events among 347,747 individuals) examined the association of intake of saturated fat with CHD or stroke

Siri-Tarino et al. AJCN 2010;91; 535-46

Intake of saturated fat and risk of CHD and stroke

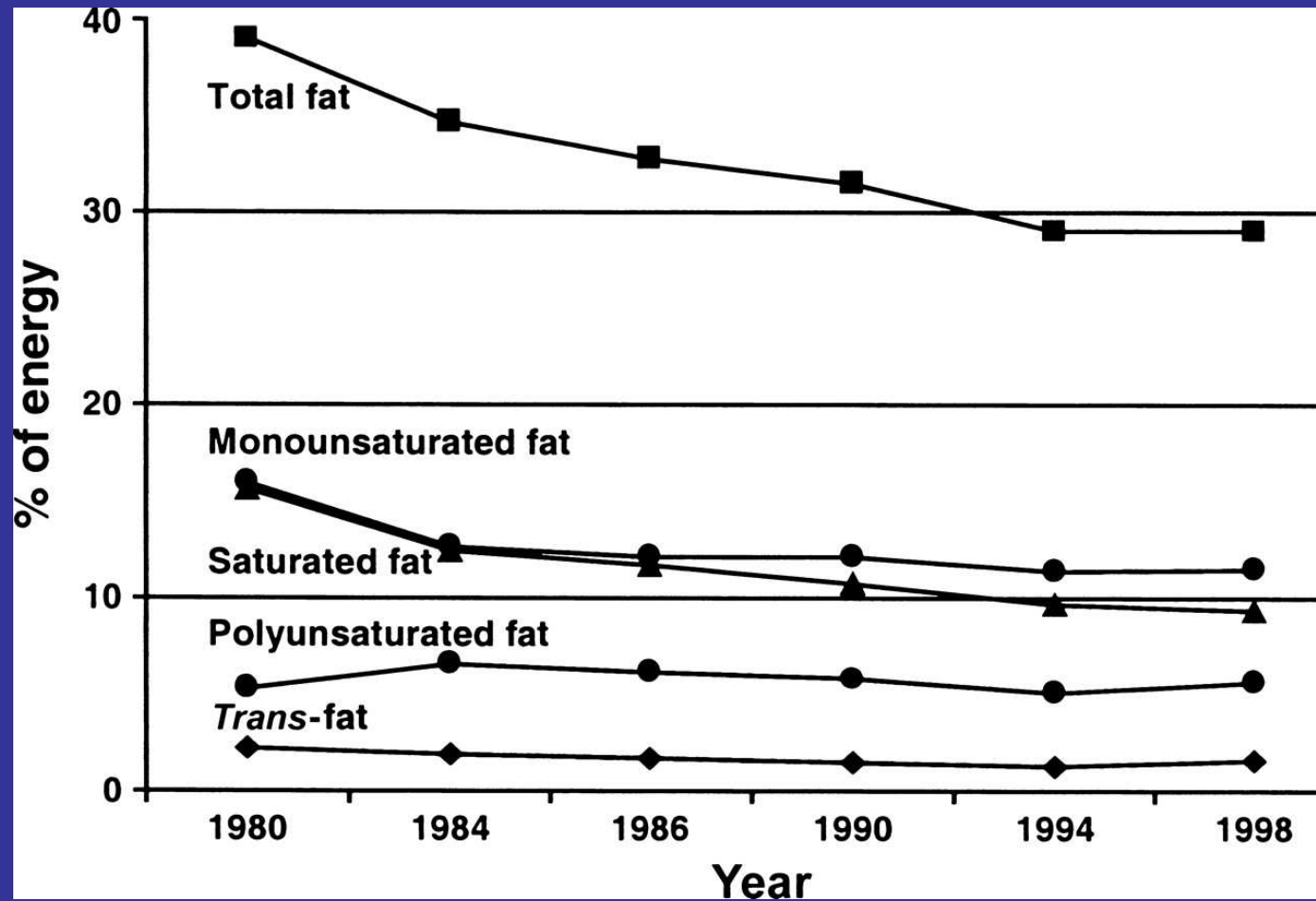


RR: 1.07 (0.96-1.19)

RR: 0.81 (0.62-1.05)

Siri-Tarino: “No significant evidence for concluding that dietary saturated fat is associated with CHD risk”

Trends in intakes of total fat and specific types of fat over time in the Nurses' Health Study, United States, 1980-2000

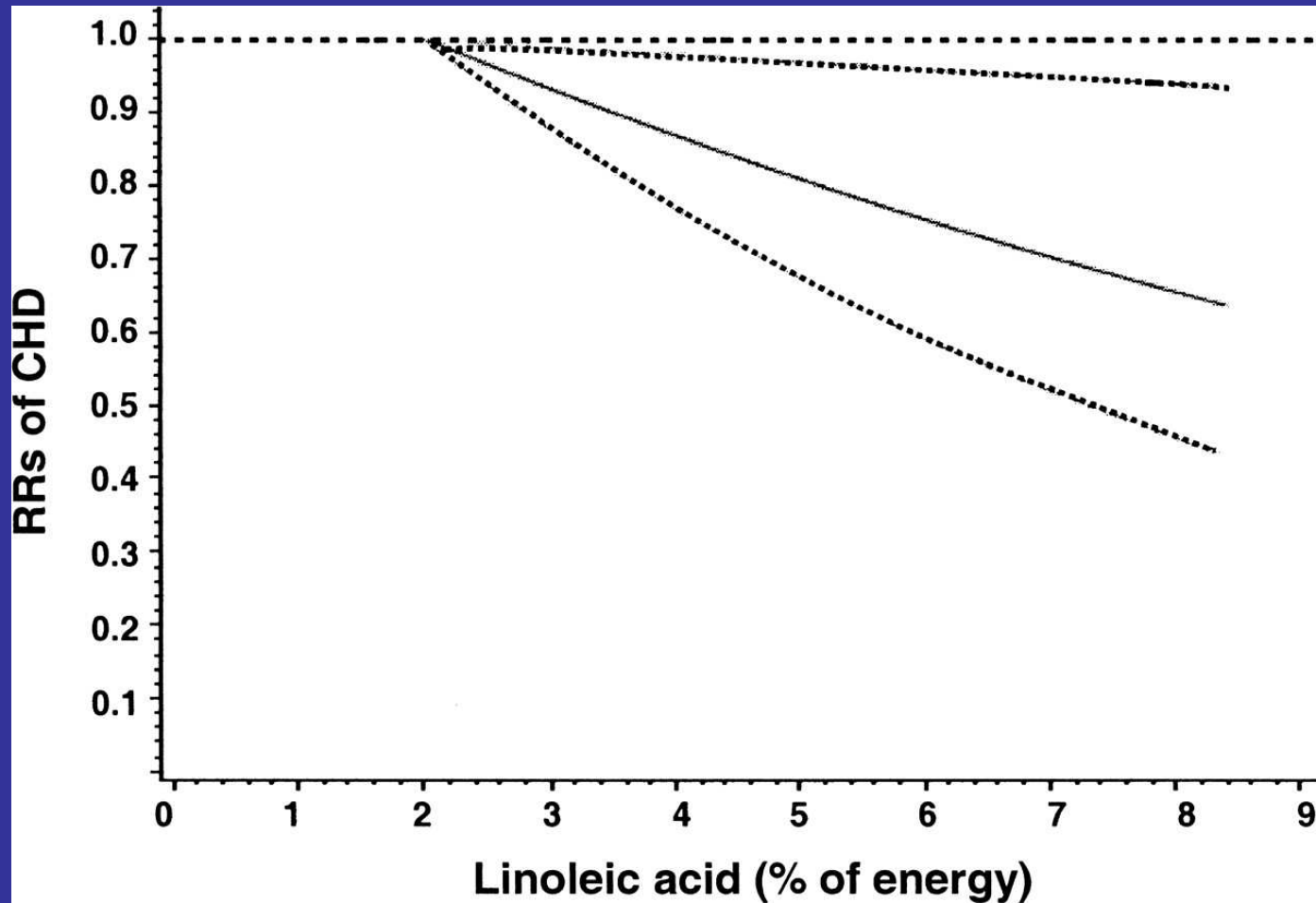


Intake of dietary fat and CHD risk: Nurses' Health Study

TABLE 2. Relative risks of coronary heart disease according to intake of specific types of dietary fat, Nurses' Health Study, United States, 1980–2000

	Quintile					<i>P</i> _{trend}
	1 (lowest)	2	3	4	5 (highest)	
Total fat						
Median (% of energy)	28.3	32.6	35.6	38.7	44.0	
Age-adjusted RR*	1	0.97	1.02	1.17	1.26	0.001
95% CI*		0.84, 1.12	0.88, 1.18	1.01, 1.35	1.07, 1.47	
Multivariate† RR	1	0.94	0.91	0.98	0.92	0.49
95% CI		0.81, 1.08	0.79, 1.06	0.84, 1.15	0.77, 1.09	
Saturated fat						
Median (% of energy)	10.1	11.9	13.3	14.8	17.6	
Age-adjusted RR	1	1.05	1.16	1.35	1.52	<0.0001
95% CI		0.91, 1.21	1.00, 1.34	1.16, 1.56	1.30, 1.79	
Multivariate‡ RR	1	0.94	0.96	1.01	0.97	0.93
95% CI		0.80, 1.11	0.79, 1.16	0.81, 1.26	0.73, 1.27	
Monounsaturated fat						
Median (% of energy)	10.6	12.5	13.8	15.3	18.0	
Age-adjusted RR	1	1.01	1.11	1.18	1.30	0.0003
95% CI		0.87, 1.16	0.96, 1.28	1.02, 1.37	1.11, 1.53	
Multivariate‡ RR	1	0.94	0.95	0.91	0.82	0.19
95% CI		0.79, 1.11	0.78, 1.17	0.72, 1.16	0.62, 1.10	
Polyunsaturated fat						
Median (% of energy)	4.1	5.0	5.6	6.3	7.4	
Age-adjusted RR	1	0.93	0.81	0.83	0.80	0.002
95% CI		0.81, 1.07	0.70, 0.94	0.72, 0.97	0.69, 0.94	
Multivariate‡ RR	1	0.98	0.83	0.84	0.75	0.004
95% CI		0.84, 1.14	0.70, 0.99	0.70, 1.02	0.60, 0.92	
Trans-fat						
Median (% of energy)	1.3	1.6	1.9	2.2	2.8	
Age-adjusted RR	1	1.11	1.31	1.24	1.39	<0.0001
95% CI		0.96, 1.28	1.14, 1.52	1.07, 1.44	1.19, 1.63	
Multivariate‡ RR	1	1.08	1.29	1.19	1.33	0.01
95% CI		0.92, 1.26	1.09, 1.53	0.99, 1.44	1.07, 1.66	

Linoleic acid intake and risk of CHD: Nurses' Health Study, United States, 1980-2000



Oh, K. et al. Am. J. Epidemiol. 2005 161:672-679

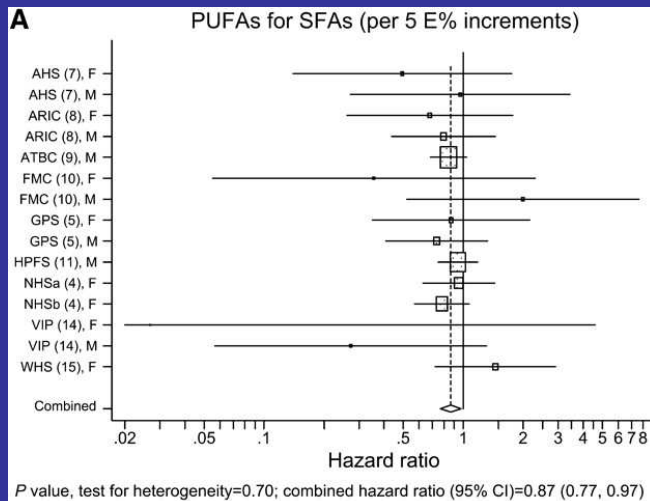
Meta-analysis of cohort studies: Effect of replacing SFA by PUFA, carbohydrate or by MONO on CHD

A meta-analysis involving individual data from 11 cohort studies (5249 CHD events, 455 CHD deaths in 344,696 people)

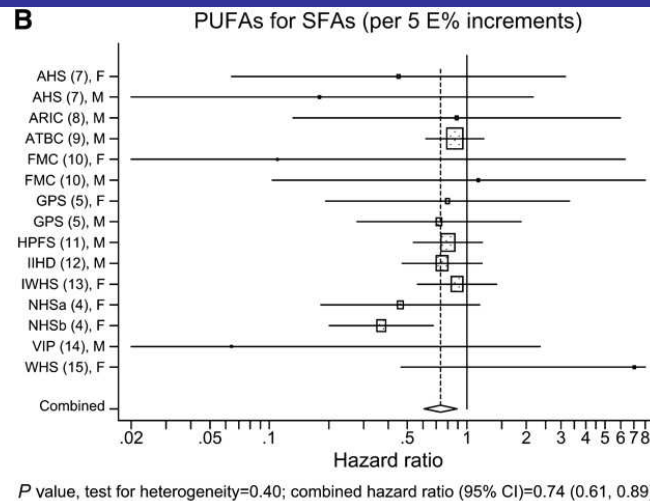
The effects on CHD risk of replacement of SFA by PUFA, carbohydrate or by MONO were assessed

Effect of replacing SFA by PUFA or by carbohydrate on CHD: (A) Coronary events & (B) coronary deaths

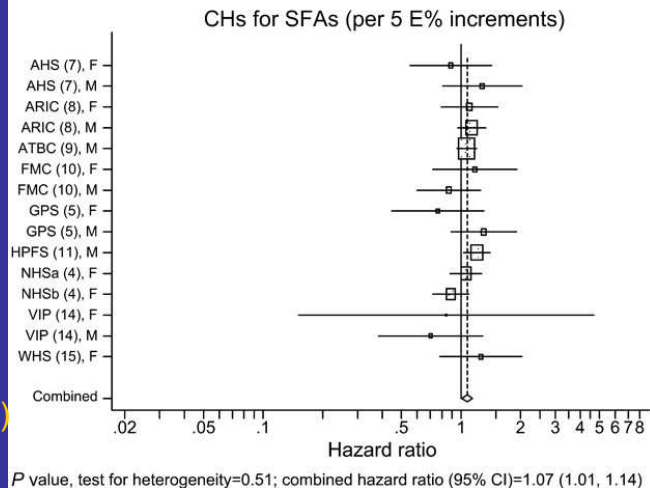
HR: 0.87 (0.77-0.97)



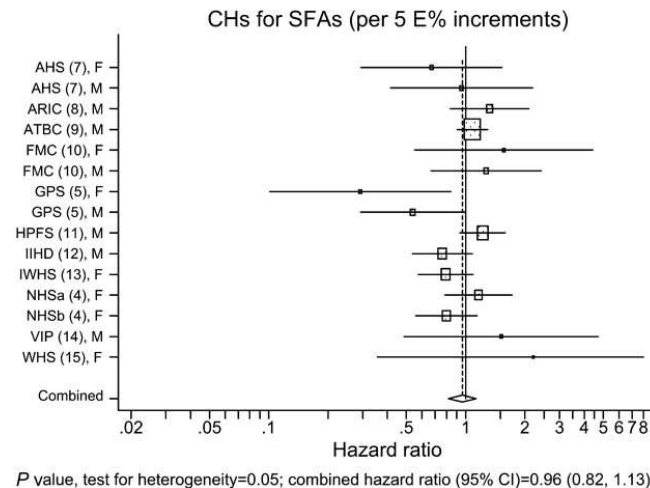
HR: 0.74(0.61-0.89)



HR: 1.07 (1.01-1.14)



HR: 0.96(0.82-1.13)



CHD events

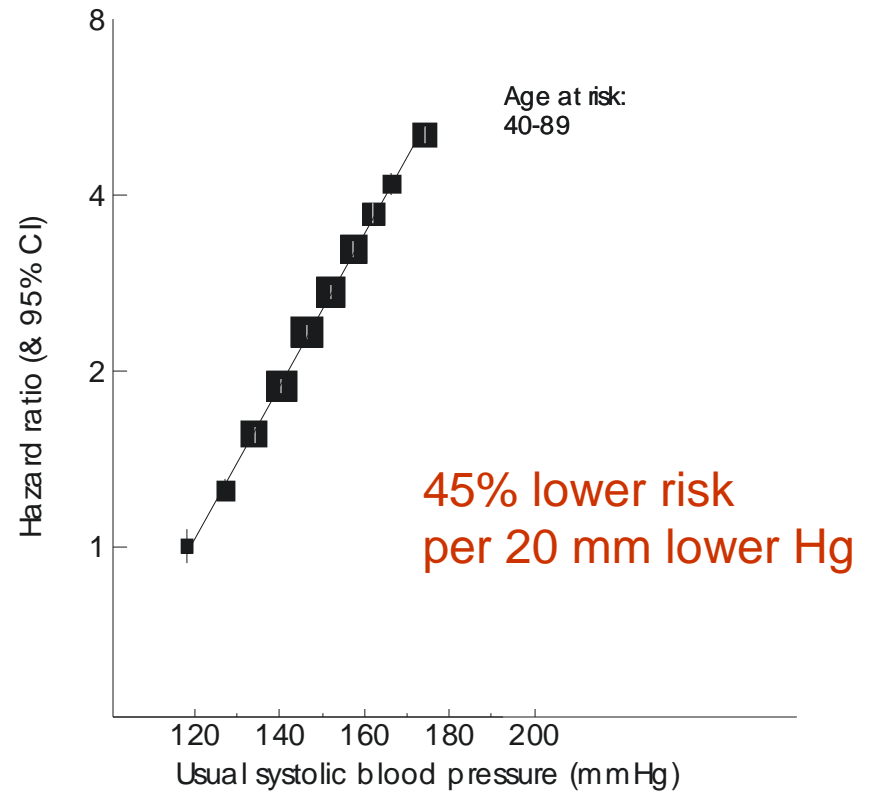
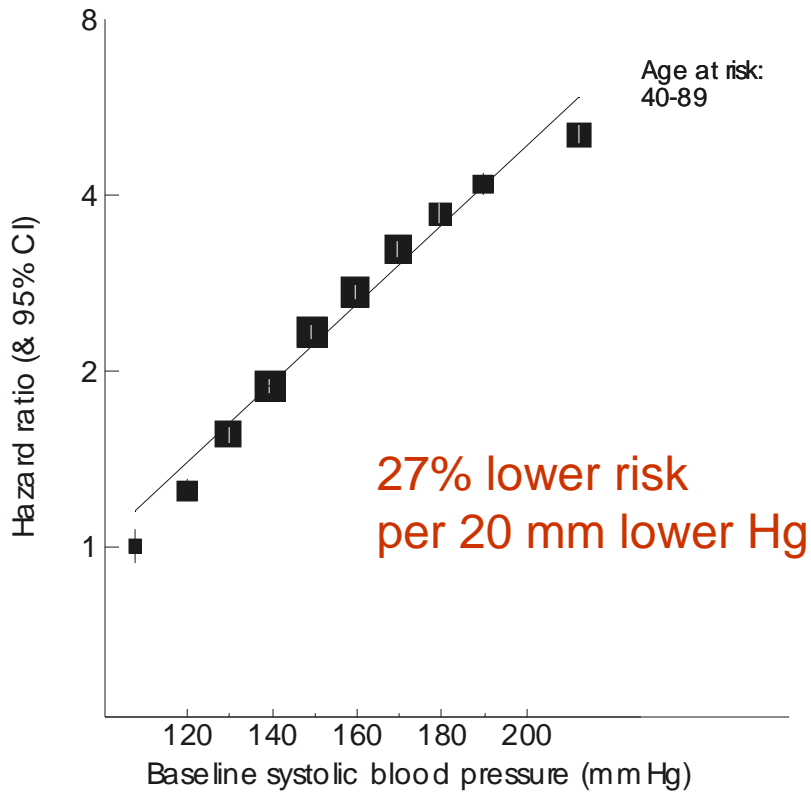
CHD deaths

Limitations of cohort studies

Imprecision in assessment of dietary intake results in an inability to rank individuals reliably by long-term usual intake

Such imprecision results in systematic underestimation of risk referred to as regression dilution bias (Liu et al. 1978)

Blood pressure and risk of CHD mortality: Underestimation of risk due to regression dilution bias



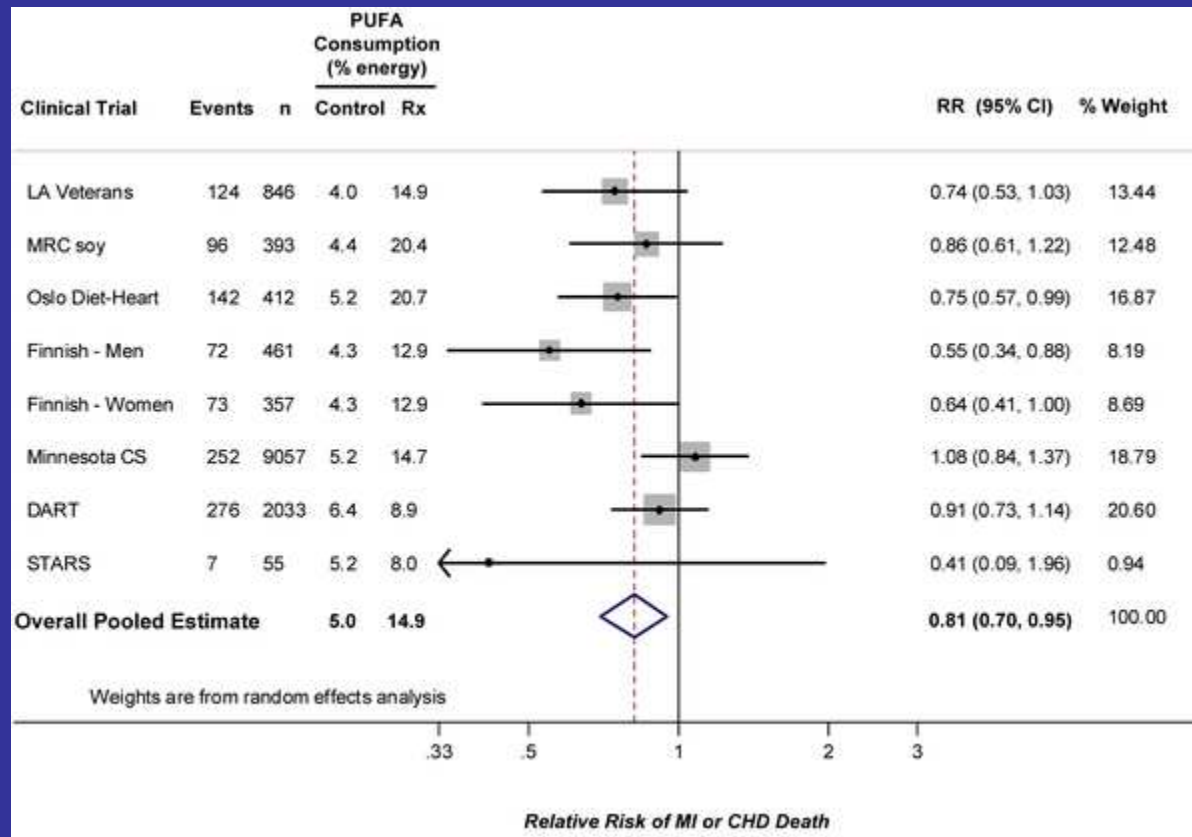
Trials of dietary advice to reduce intake of SAFA and increase intake of PUFA

Meta-analysis of clinical trials of PUFA and CHD conducted in the 1960's and 1970's

7 trials involving 13,614 participants assessed the effect on CHD risk of average of dietary intake of PUFA of 15% vs 5%

(Mozaffarian et al. 2010)

Meta-analysis of trials of dietary advice to increase intake of PUFA



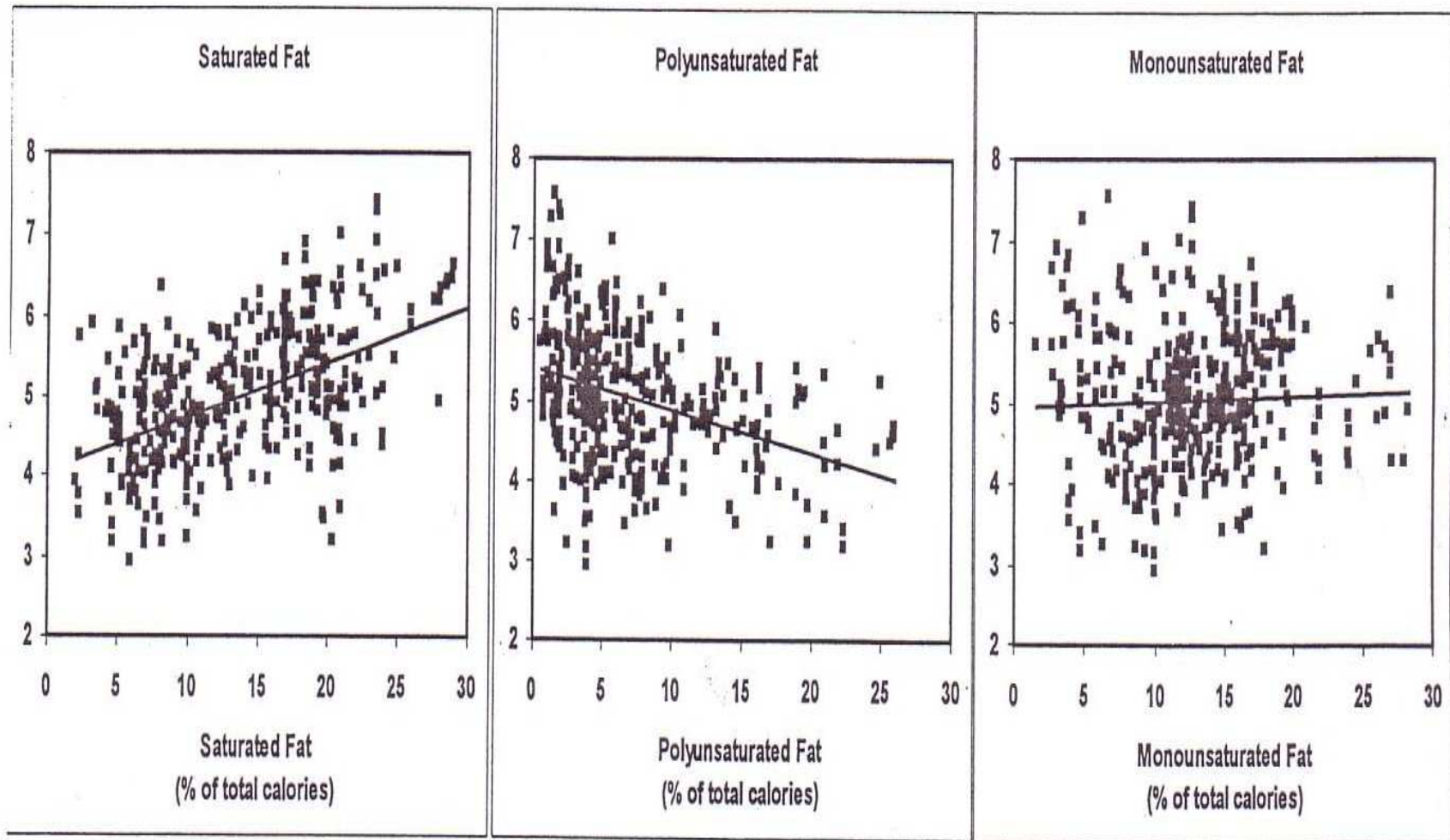
Metabolic ward studies

Metabolic ward studies are dietary trials conducted over several weeks in which all food consumed is provided

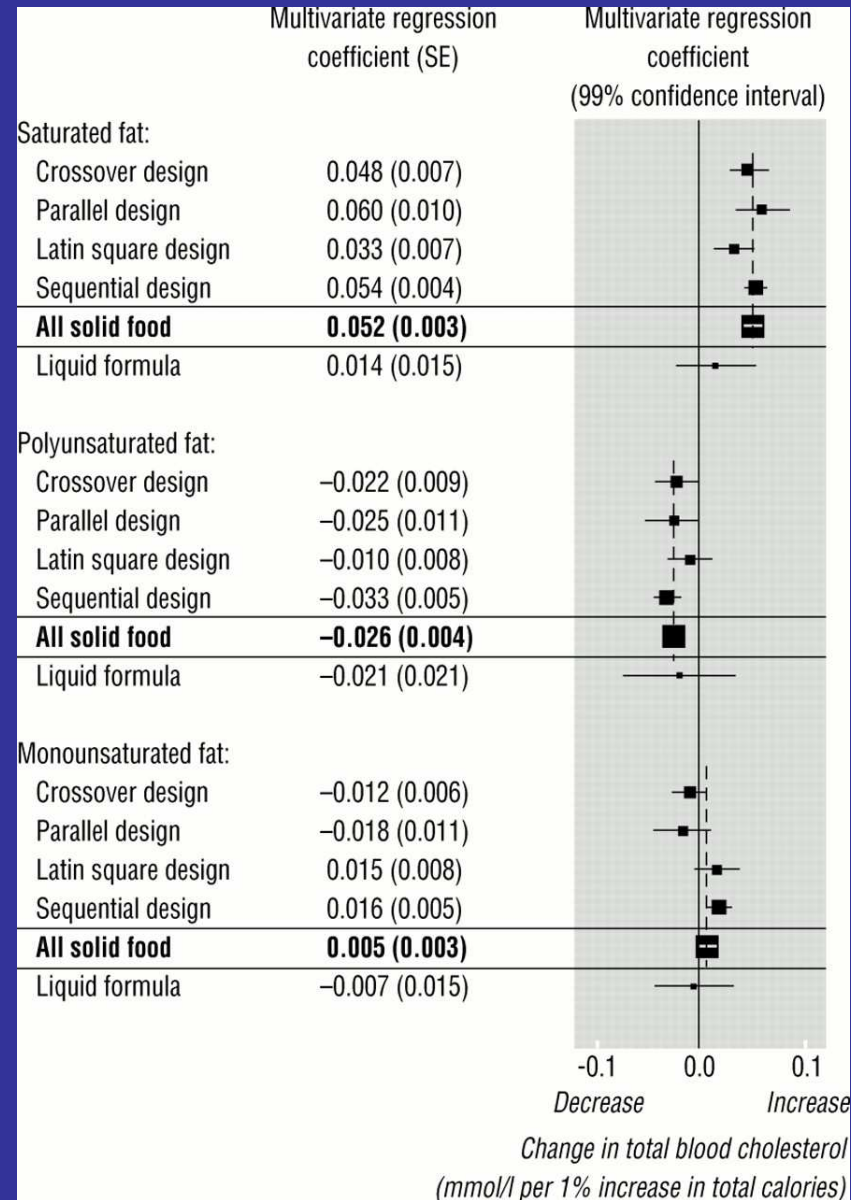
Participants have a fixed caloric intake and the amount and type of fat consumed is recorded

Blood lipids are measured at the end of the intervention period

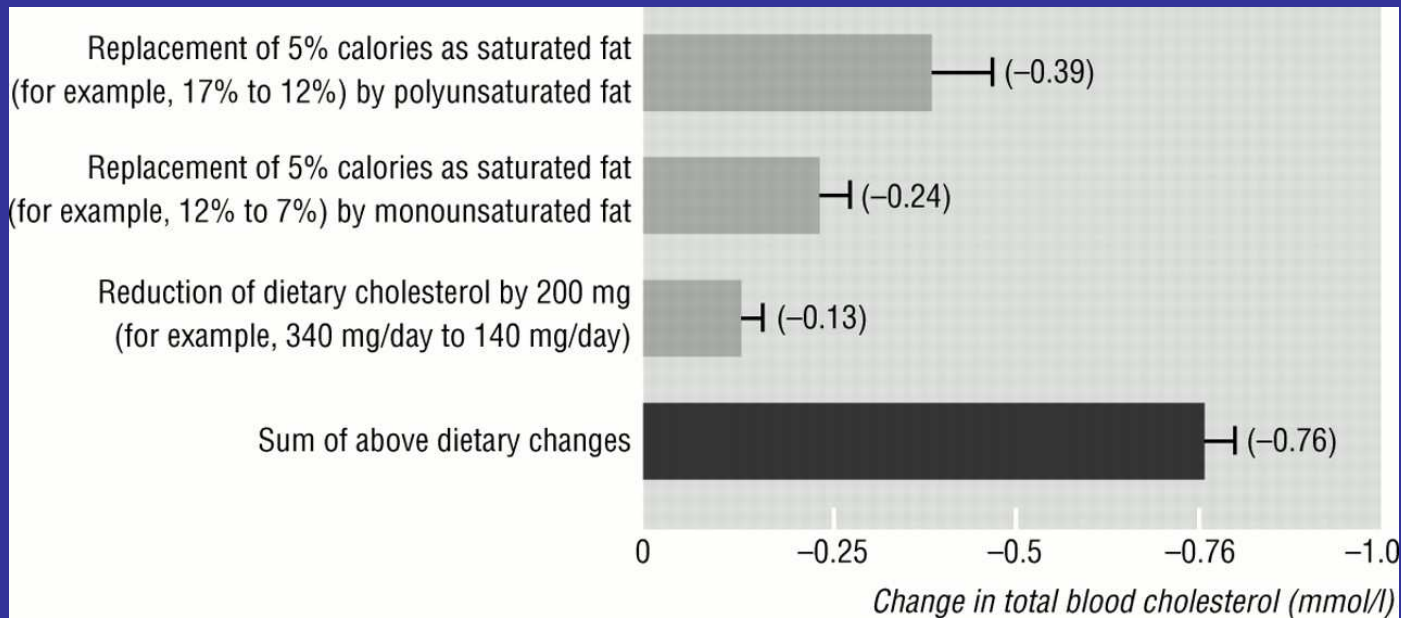
Meta-analysis of metabolic ward studies (n=395 dietary experiments)



Multivariate regression coefficients of effects of dietary saturated, polyunsaturated, and monounsaturated fats on blood total cholesterol concentration in metabolic ward studies.



Mean (SE) changes in blood total cholesterol associated with replacing dietary saturated fat by polyunsaturated and monounsaturated fats and with reducing dietary cholesterol



Clarke, R. et al. *BMJ* 1997;314:112

An updated meta-analysis of the metabolic ward studies

The present meta-analysis (103 studies involving 500 dietary experiments) assesses the effects on a wider range of lipid markers

The analysis assessed the effects on LDL-C, ApoB, HDL-C, ApoA₁, total cholesterol and total/HDL ratio of replacement of SAFA or TFA by PUFA, MONO or by carbohydrate

Replacement of SAFA by PUFA

Large trials of PUFA demonstrate benefits for CHD risk of advice to replace SAFA by polyunsaturates rather than by carbohydrate

Metabolic ward studies confirm importance for lipids of replacement of SAFA (and of TFA) by PUFA rather than by carbohydrate

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