The Lipid Hypothesis of Atherosclerosis in 2016

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Topical/political Issues- Ravnskov/Malhotra

- LDL cholesterol not related to heart disease
- Saturated fat not related to heart disease
- People with high cholesterol die at a lower rate than those with low cholesterol
- High cholesterol protects against infection
- Infection is related to heart disease/heart failure
- Statins lower heart disease (by a trivial degree) by a different mechanism than lowering cholesterol
- Saturated fat helpful for heart disease (Malhotra)

Ranvskov et al 2016

- Believe if cholesterol is important then risk relationship should be same in 80 year olds as in 40 year olds
- Ignores 40 year exposure to high blood pressure and smoking that becomes more dominant in older individuals as well as age related vascular stiffening.
- 30 cohorts with a total of 68 094 elderly people, where all-cause mortality was recorded in 28 cohorts and CV mortality in 9 cohorts. Inverse association between all-cause mortality and LDL-C was seen in 16 cohorts (in 14 with statistical significance) representing 92% of the number of participants, where this association was recorded.
- In the rest, no association was found. In two cohorts, CV mortality was highest in the lowest LDL-C quartile and with statistical significance; in seven cohorts, no association was found.

Ranvskov et al 2016

- Concluded that cholesterol-lowering medication and diet be not used in those over 60.
- Nunan “1. Lack of a published protocol 2. Searching of only one database 3. Non-uniform application of inclusion/exclusion criteria 4. A lack of critical appraisal of the methods used in the included studies 5. No indication of the quality or uncertainty of the included data 6. *Issues with the accuracy of data extraction* 7. A lack of controlling for confounding due to the effect of lipid-lowering treatment *and HDL-C* levels presenting major bias and more likely underpinning the majority of the observed inverse associations.

Ranvskov et al 2016

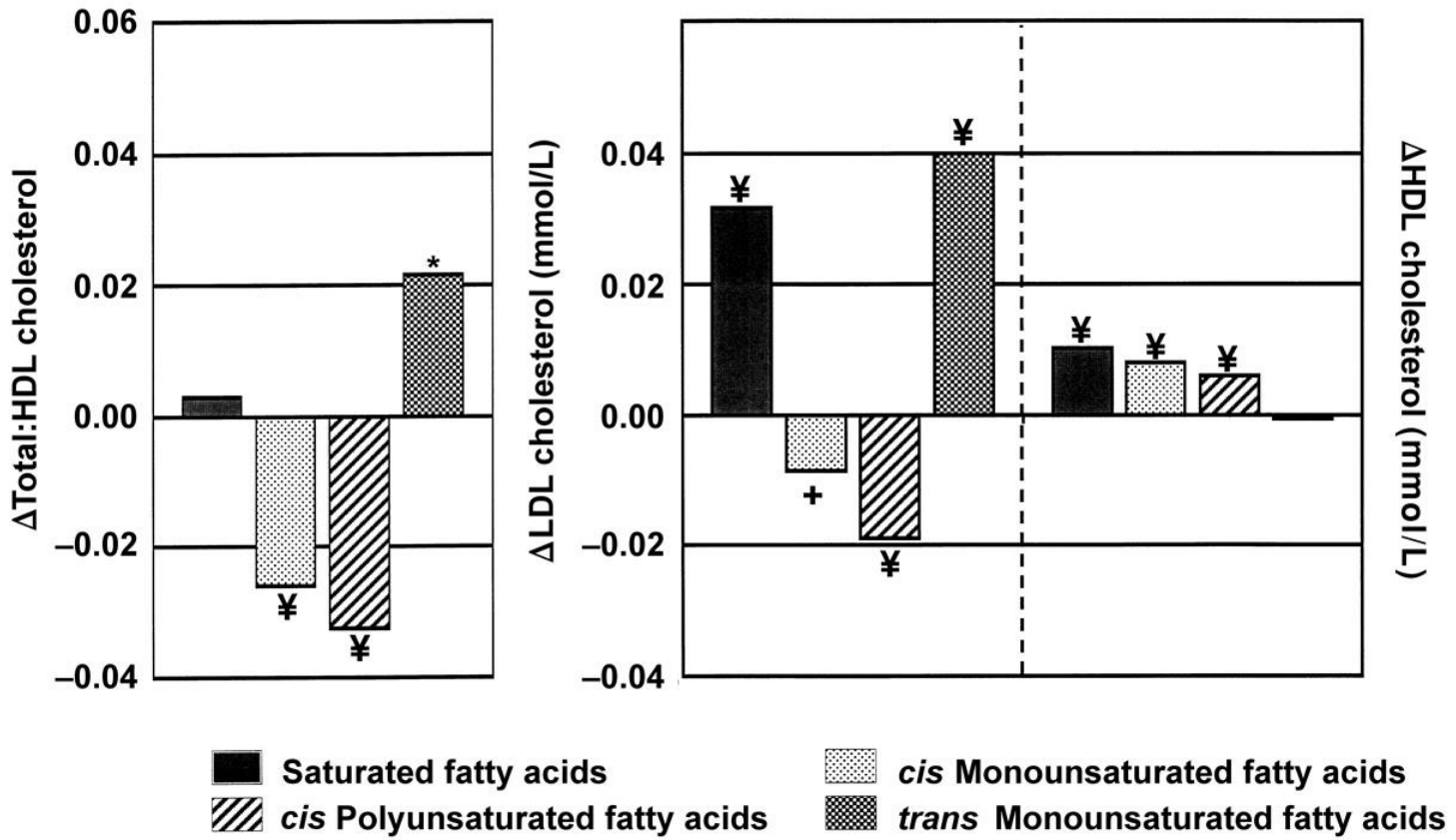
- Keller: “observational data only”
- Meta-analysis of eight controlled trials, including over 24,000 subjects with average age 73 years, (Savarese et al 2013), which proved that elderly patients with CV risk factors but without established cardiovascular (CV) disease actually do benefit from statin therapy. Statin therapy significantly reduced heart attacks by over 39%, and reduced strokes by over 23%, and non-significantly reduced all-cause mortality by 5.9%, and CV mortality by 9.3%

Mendelian randomization LDL cholesterol

- PCSK9 loss of function with R46L genotype in Copenhagen 103,000. LDL cholesterol 124mg/dl, 104 mg/dl and 97 mg/dl. 2 X $10^{-52.}$ 23% reduction in myocardial infarction (Langsted 2016)
- 9 polymorphisms that lower LDL in 312,000 people. 54% lower risk of IHD for each mmol/l lower LDL cholesterol. 3 fold greater than effect observed in statin studies (Ference 2012)
- NPC1L1 group had 2.4 mg/dl lower LDL-C and 4.8% lower risk of CHD, HMGCR group had 2.9 mg/dl lower LDL-C and 5.3% lower risk of CHD. The group with lower LDL-C mediated by both NPC1L1 and HMGCR polymorphisms had 5.8 mg/dl lower LDL-C and a 10.8% log-linearly additive lower risk of CHD (Ference 2015)

Predicted changes (Δ) in the ratio of serum total to HDL cholesterol and in LDL- and HDL-cholesterol concentrations when carbohydrates constituting 1% of energy are replaced isoenergetically with saturated, cis monounsaturated, cis polyunsaturated, or trans...

The American Journal of Clinical Nutrition



Ronald P Mensink et al. Am J Clin Nutr 2003;77:1146-1155

Benefit from replacement of saturated fat with CHO depends on effects of CHO on glucose/insulin and BP

Prospective Studies Collaboration 2007

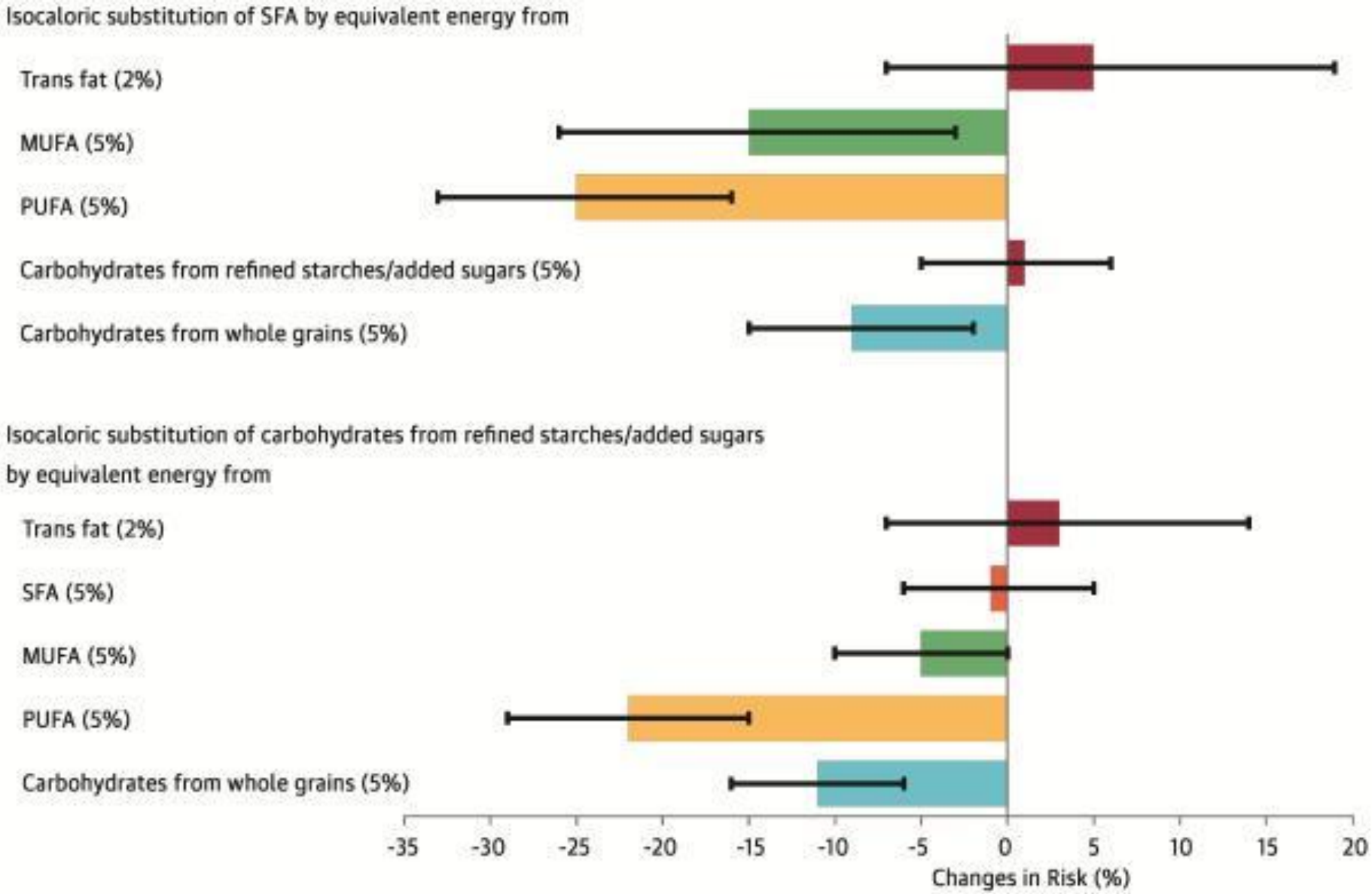
- 61 prospective observational studies, mostly in western Europe or North America, consisting of almost 900,000 adults without previous disease and with baseline measurements of total cholesterol and blood pressure.
- 12 million person years ages of 40 and 89 years, there were more than 55,000 vascular deaths (34,000 ischaemic heart disease [IHD], 12,000 stroke, 10,000 other).
- 1 mmol/L lower total cholesterol was associated with about a half (hazard ratio 0.44 [95% CI 0.42-0.48]), a third (0.66 [0.65-0.68]), and a sixth (0.83 [0.81-0.85]) lower IHD mortality in both sexes at ages 40-49, 50-69, and 70-89 years, respectively, with no apparent threshold

Prospective Studies Collaboration 2007

- Total/HDL cholesterol was the strongest predictor of IHD mortality (40% more informative than non-HDL cholesterol and more than twice as informative as total cholesterol).
- Total cholesterol was weakly positively related to ischaemic and total stroke mortality in early middle age (40-59 years), but this finding could be largely or wholly accounted for by the association of cholesterol with blood pressure.
- Moreover, a positive relation was seen only in middle age and only in those with below-average blood pressure; at older ages (70-89 years) and, particularly, for those with systolic blood pressure over about 145 mm Hg, total cholesterol was negatively related to haemorrhagic and total stroke mortality.
- The results for other vascular mortality were intermediate between those for IHD and stroke.

Lowering of cholesterol-drugs and diet

- Meta regression. 312 175 participants (mean age, 62 years; 24% women; mean baseline LDL-C level of 3.16 mmol/L from 49 trials with 39 645 major vascular events
- The RR for major vascular events per 1-mmol/L reduction in LDL-C level was 0.77 (95% CI, 0.71-0.84; P < .001) for statins and 0.75 (95% CI, 0.66-0.86; P = .002) for established non-statin interventions that work primarily via upregulation of LDL receptor expression (diet, bile acid sequestrants, ileal bypass, and ezetimibe) (between-group difference, P = .72).
- For these 5 therapies combined, the RR was 0.77 (95% CI, 0.75-0.79, P < .001) for major vascular events per 1-mmol/L reduction in LDL-C level (Silverman 2016)



NHS and HPFU 24-30 year follow up, FFQ every 4 years. 7667 incident cases of CHD. Li 2015

Epidemiology Diet and mortality-USA

- 3 439 954 person-years , 33 304 deaths NHS and HPFS
- Dietary total fat compared with total carbohydrates 0.84; *P* < .001 for trend)
- 1.08 (95% CI, 1.03-1.14) for saturated fat
- 0.81 (95% CI, 0.78-0.84) for PUFA
- 0.89 (95% CI, 0.84-0.94) for MUFA
- 1.13 (95% CI, 1.07-1.18) for *trans*-fat (*P* < .001 for trend for all)
- Replacing 5% of energy from saturated fats with equivalent energy from PUFA and MUFA was associated with estimated reductions in total mortality of 27% and 13% respectively
- ω-6 PUFA intake was 0.85 *P* < .001 for trend
- ω-3 PUFA intake 0.96 *P* = .002 for trend Wang 2016

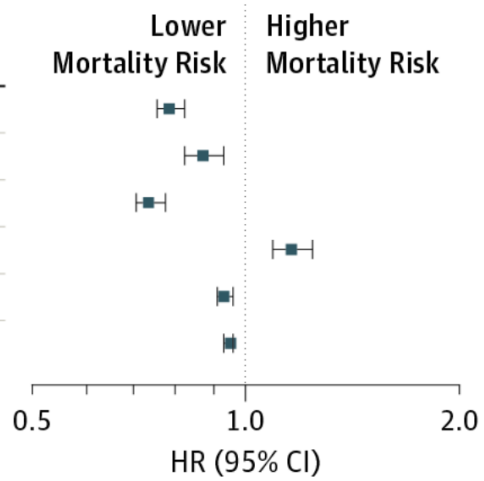
The JAMA Network

From: **Association of Specific Dietary Fats With Total and Cause-Specific Mortality**

JAMA Intern Med. 2016;176(8):1134-1145. doi:10.1001/jamainternmed.2016.2417

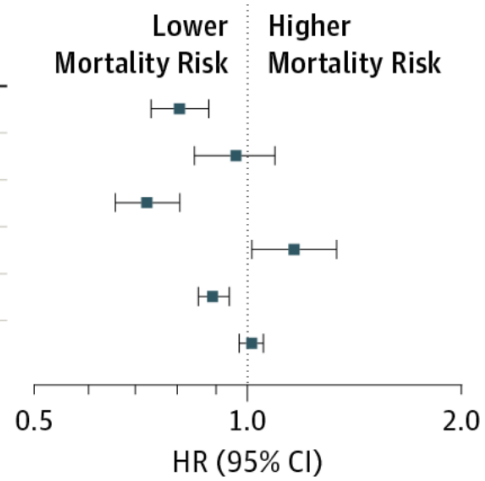
A Total mortality

	HR (95% CI)
UFAs, 5% of energy	0.78 (0.75-0.82)
MUFAs, 5% of energy	0.87 (0.82-0.93)
PUFAs, 5% of energy	0.73 (0.70-0.77)
Trans-fat, 2% of energy	1.16 (1.09-1.24)
ω-6 PUFAs, 2% of energy	0.93 (0.91-0.96)
ω-3 PUFAs, 0.3% of energy	0.95 (0.93-0.96)



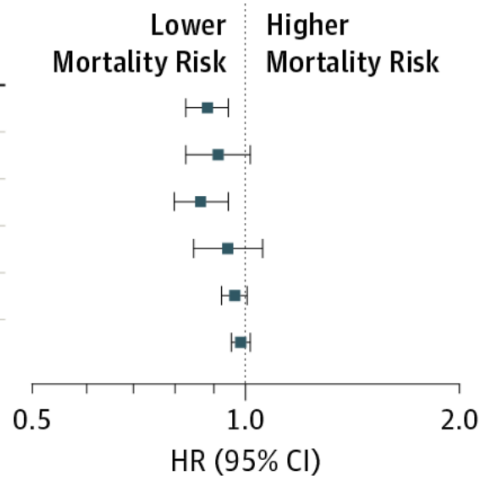
B Cardiovascular disease mortality

	HR (95% CI)
UFAs, 5% of energy	0.80 (0.73-0.88)
MUFAs, 5% of energy	0.96 (0.84-1.09)
PUFAs, 5% of energy	0.72 (0.65-0.80)
Trans-fat, 2% of energy	1.16 (1.01-1.33)
ω-6 PUFAs, 2% of energy	0.89 (0.85-0.94)
ω-3 PUFAs, 0.3% of energy	1.01 (0.97-1.05)



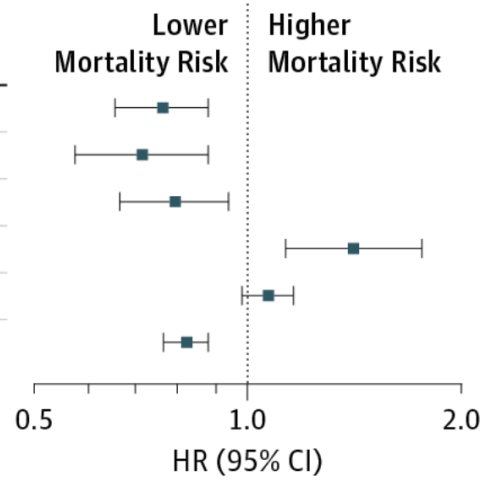
C Cancer mortality

	HR (95% CI)
UFAs, 5% of energy	0.88 (0.82-0.94)
MUFAs, 5% of energy	0.91 (0.82-1.01)
PUFAs, 5% of energy	0.86 (0.79-0.94)
Trans-fat, 2% of energy	0.94 (0.84-1.05)
ω-6 PUFAs, 2% of energy	0.96 (0.92-1.00)
ω-3 PUFAs, 0.3% of energy	0.98 (0.95-1.01)



D Neurodegenerative disease mortality

	HR (95% CI)
UFAs, 5% of energy	0.76 (0.65-0.88)
MUFAs, 5% of energy	0.71 (0.57-0.88)
PUFAs, 5% of energy	0.79 (0.66-0.94)
Trans-fat, 2% of energy	1.41 (1.13-1.76)
ω-6 PUFAs, 2% of energy	1.07 (0.98-1.16)
ω-3 PUFAs, 0.3% of energy	0.82 (0.76-0.88)



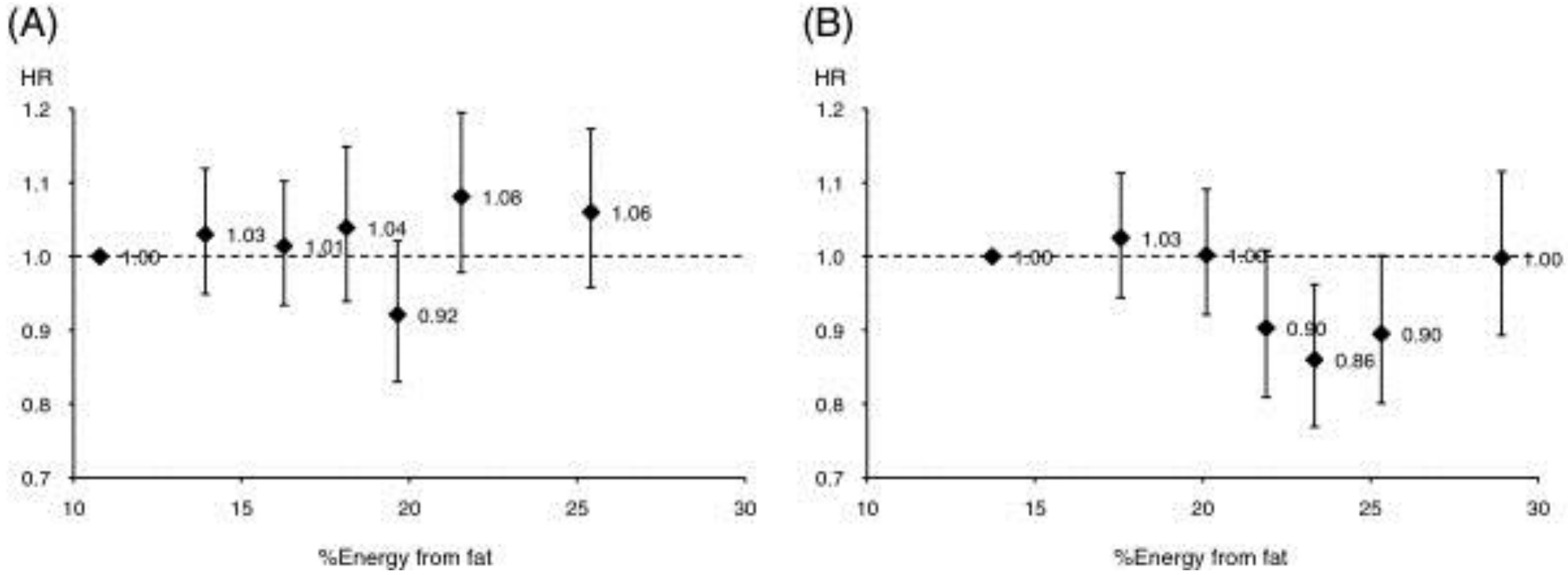
Predimed

- 336 CVD cases, 414 deaths
- CVD: total fat, mono, poly 0.58 (0.39, 0.86), 0.50 (0.31, 0.81), and 0.68 (0.48, 0.96) for extreme quintiles
- CVD: higher saturated fatty acid (SFA) and trans-fat intakes were associated with 81% (HR: 1.81; 95% CI: 1.05, 3.13) and 67% (HR: 1.67; 95% CI: 1.09, 2.57) higher risk
- SFAs from pastries and processed foods were associated with a higher risk of CVD (Guasch-Ferre 2015)

High Glycemic Load/high sugar diets

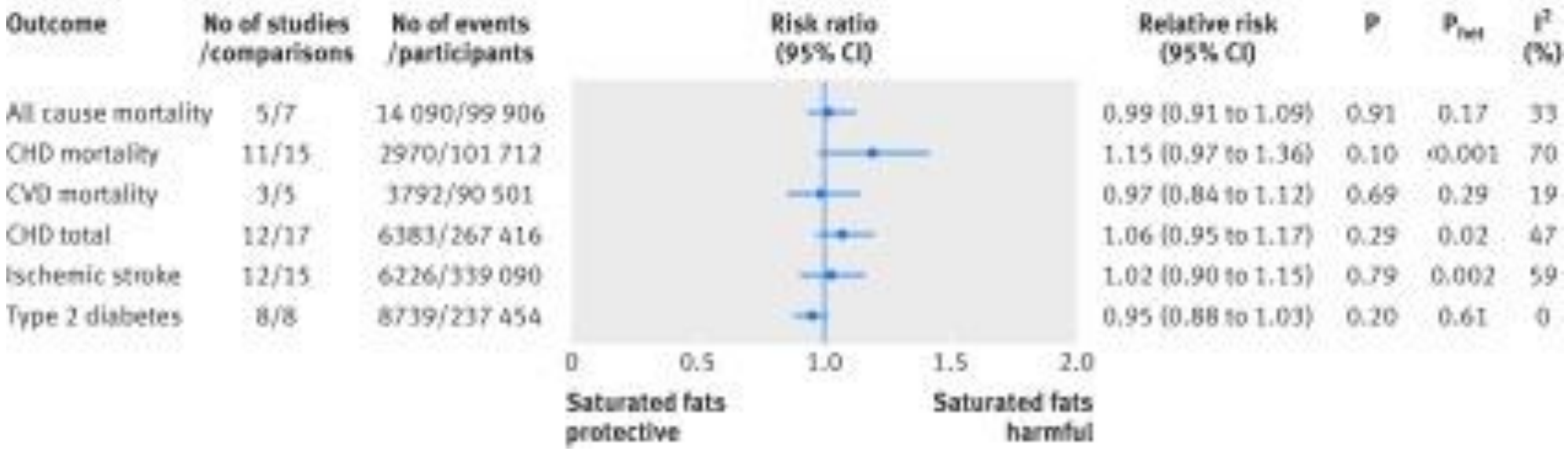
- Associated with more CVD
- Compatible with lipid hypothesis-increased endothelial dysfunction-increases endothelial adhesion molecule expression
- Increased inflammation enhances lipid accumulation
- Glycation of LDL enhances uptake
- Saturated fat and low quality CHO should both be avoided

Japan-an outlier with low fat intake



Women top quintile of intake for SFA, MUFA, and PUFA: 0.91 (95% CI, 0.83–1.00), 0.91 (0.83–0.99) and 0.88 (0.80 - 0.97), respectively (trend *P* across quintiles, 0.020, 0.012, and 0.029, respectively). Causes of death other than cancer and cardiovascular disease contributed most to decreases in HRs for total and types of fat. 28% fat optimal (Wakai 2014)

Saturated fat vs total carbohydrate (BMJ 2015)

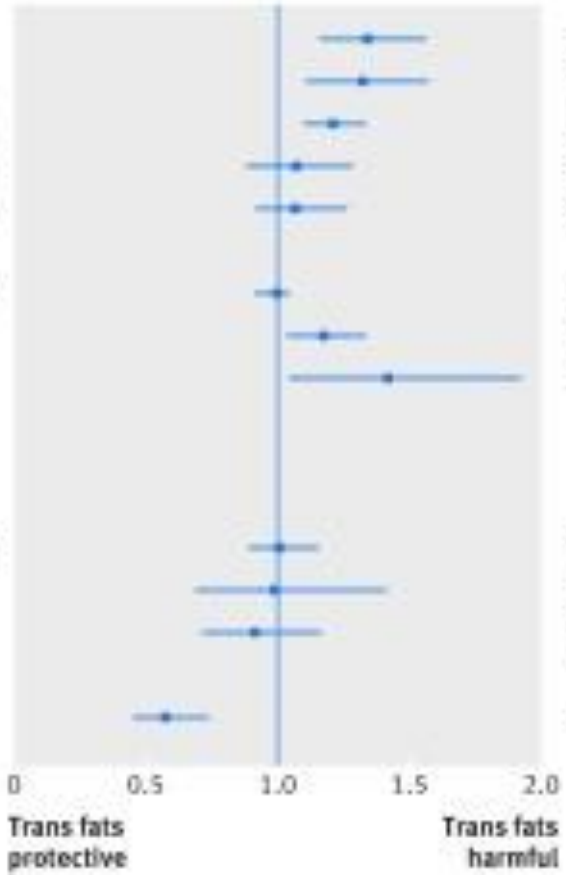


Outcome	No of studies /comparisons	No of events /participants	Relative risk (95% CI)	P	P_{het}	I^2 (%)
All cause mortality	5/7	14 090/99 906	0.99 (0.91 to 1.09)	0.91	0.17	33
CHD mortality	11/15	2970/101 712	1.15 (0.97 to 1.36)	0.10	<0.001	70
CVD mortality	3/5	3792/90 501	0.97 (0.84 to 1.12)	0.69	0.29	19
CHD total	12/17	6383/267 416	1.06 (0.95 to 1.17)	0.29	0.02	47
Ischemic stroke	12/15	6226/339 090	1.02 (0.90 to 1.15)	0.79	0.002	59
Type 2 diabetes	8/8	8739/237 454	0.95 (0.88 to 1.03)	0.20	0.61	0

Very similar to Nurses and HPFU combined and Siri-Tarino 2010. de Souza 2015

Trans fats

Outcome	No of studies /comparisons	No of events /participants	Relative risk (95% CI)	P	P_{het}	I^2 (%)
Total trans fats						
All cause mortality	2/2	2141/20 346	1.34 (1.16 to 1.56)	<0.001	0.07	70
CHD mortality	5/6	1234/70 864	1.28 (1.09 to 1.50)	0.003	0.66	0
CHD total	6/7	4579/145 922	1.21 (1.10 to 1.33)	<0.001	0.43	0
Ischemic stroke	3/4	1905/190 284	1.07 (0.88 to 1.28)	0.50	0.03	67
Type 2 diabetes	6/6	8690/230 135	1.10 (0.95 to 1.27)	0.21	0.01	66
Industrial trans fats						
All cause mortality	1/2	11 890/71 464	0.98 (0.92 to 1.04)	0.52	0.52	0
CHD mortality	2/2	3018/93 394	1.18 (1.04 to 1.33)	0.009	0.68	0
CHD total	2/2	454/69 848	1.42 (1.05 to 1.92)	0.02	0.22	34
Ischemic stroke	0	0/0	-	-	-	-
Type 2 diabetes	0	0/0	-	-	-	-
Ruminant trans fats						
All cause mortality	1/2	11 890/71 464	1.04 (0.92 to 1.18)	0.51	0.31	4
CHD mortality	2/3	3018/93 394	1.01 (0.71 to 1.43)	0.95	0.01	79
CHD total	3/4	828/73 546	0.93 (0.73 to 1.18)	0.55	0.13	46
Ischemic stroke	0	0/0	-	-	-	-
Type 2 diabetes	5/5	1153/12 942	0.58 (0.46 to 0.74)	<0.001	0.22	30



Interventions-Cochrane

- 15 randomised controlled trials 59,000 participants,
- Reducing dietary saturated fat reduced the risk of cardiovascular events by 17% (0.72 to 0.96, 13 comparisons, 53,300 participants of whom 8% had a cardiovascular event, I^2 65%, GRADE moderate quality of evidence),
- All-cause mortality and cardiovascular mortality –not significant
- Some evidence that reducing saturated fats reduced the risk of myocardial infarction (fatal and non-fatal, RR 0.90; 95% CI 0.80 to 1.01; 11 trials, 53,167 participants
- No effect on stroke (Hooper 2015)

Observational cohorts- diet effects

- 61,239 men and 73,216 women (aged 40-74 y) from 2 population-based prospective studies in Shanghai, China.
- 2954 deaths in men and 4348 deaths in women during mean follow-ups of 6.5 and 12.0 y, respectively.
- A higher CHFP score was associated with lower total mortality with multivariable-adjusted HRs of 0.67 (95% CI: 0.60, 0.75) in men and 0.87 (95% CI: 0.80, 0.95) in women when extreme quartiles were compared (both P-trend < 0.005).
- Decreased risks associated with a higher CHFP score were observed for cardiovascular disease, cancer, and diabetes mortality, particularly in men.
- A significantly lower total mortality was shown for adherence to specific recommendations on vegetables, fruit, legumes, fish, and eggs but not *grains, dairy, meat, fat, and salt*. A higher DASH score and AHEI also predicted lower mortality from all causes, cardiovascular disease, and diabetes but not cancer (Yu 2014)

Diet-observational cohorts

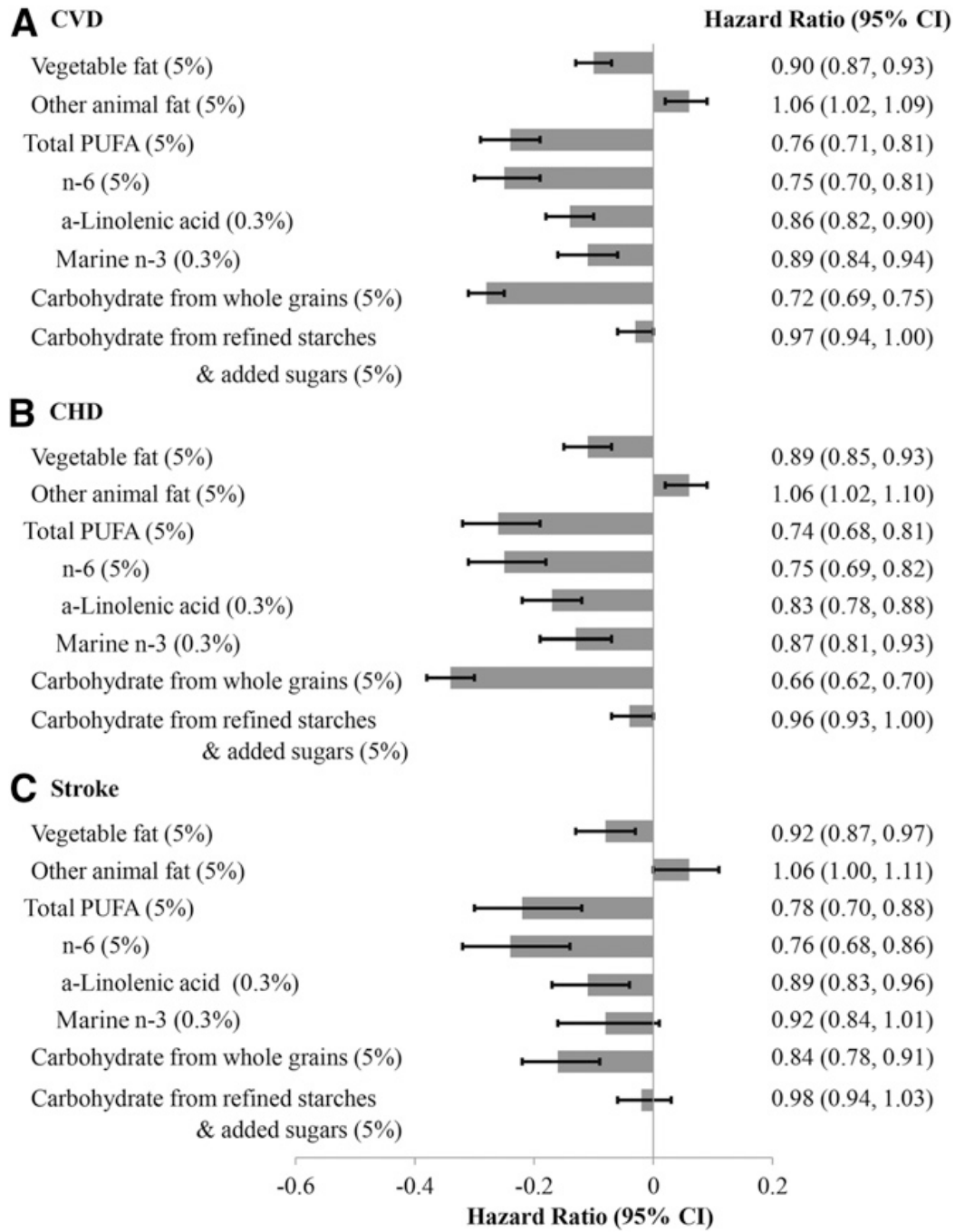
- 10 prospective cohort studies from Europe and the United States comprising a total sample of 281,874 men and women >60 years free from chronic diseases at baseline.
- Components of the Healthy Diet Indicator (HDI) included saturated fatty acids, polyunsaturated fatty acids, mono- and disaccharides, protein, cholesterol, dietary fiber, and fruit and vegetables
- During 3,322,768 person-years of follow-up, 12,492 people died of CVD. An increase of 10 HDI points (complete adherence to an additional WHO guideline) was, on average, not associated with CVD mortality (HR: 0.94; 95% CI: 0.86, 1.03), CAD mortality (HR: 0.99; 95% CI: 0.85, 1.14), or stroke mortality (HR: 0.95; 95% CI: 0.88, 1.03).
- Adherence to the HDI was associated with reduced CVD mortality in the southern European cohorts (HR: 0.87; 95% CI: 0.79, 0.96; I(2) = 0%) and in the US cohort (HR: 0.85; 95% CI: 0.83, 0.87;) Jankovic 2015

Epidemiology-N3 fats

- 16 countries, 45 637 unique individuals, and 7973 total CHD, 2781 fatal CHD, and 7157 nonfatal MI events, with ω-3 measures in total plasma, phospholipids, cholesterol esters, and adipose tissue.
- ALA, DPA, and DHA were associated with a lower risk of fatal CHD - 0.90-0.91
- DPA associated with total CHD 0.94 , others not
- Non Fatal MI-no relationship
- Phospholipids and total plasma stronger (Del Gobbo 2016)

Dairy-a major source of saturated fat (Nurses +HPFU)

- Dairy fat not associated with total CVD, CHD or stroke. For 5% energy 1.01, 1.03 and 0.99
- Not protective
- Substitution of 5% energy from PUFA or vegetable fat -24% and 10% reduction in CVD
- Substitution of 5% energy from other animal fat was associated with a 6% increase in CVD. Could be meat protein not fat per se (Chen 2016)
- Note milk intake and risk of overall CVD [2283 events 4 studies; relative risk (RR): 0.94 per 200 mL/d; 95% CI: 0.89, 0.99]. No association with CHD, stroke, total mortality. Total dairy low of high fat-not associated with CHD (Soedamah-Muthu 2011)


A CVD
Hazard Ratio (95% CI)
Vegetable fat (5%)
0.90 (0.87, 0.93)
Other animal fat (5%)
1.06 (1.02, 1.09)
Total PUFA (5%)
0.76 (0.71, 0.81)
n-6 (5%)
0.75 (0.70, 0.81)
a-Linolenic acid (0.3%)
0.86 (0.82, 0.90)
Marine n-3 (0.3%)
0.89 (0.84, 0.94)
Carbohydrate from whole grains (5%)
0.72 (0.69, 0.75)
Carbohydrate from refined starches & added sugars (5%)
0.97 (0.94, 1.00)
B CHD
Vegetable fat (5%)
0.89 (0.85, 0.93)
Other animal fat (5%)
1.06 (1.02, 1.10)
Total PUFA (5%)
0.74 (0.68, 0.81)
n-6 (5%)
0.75 (0.69, 0.82)
a-Linolenic acid (0.3%)
0.83 (0.78, 0.88)
Marine n-3 (0.3%)
0.87 (0.81, 0.93)
Carbohydrate from whole grains (5%)
0.66 (0.62, 0.70)
Carbohydrate from refined starches & added sugars (5%)
0.96 (0.93, 1.00)
C Stroke
Vegetable fat (5%)
0.92 (0.87, 0.97)
Other animal fat (5%)
1.06 (1.00, 1.11)
Total PUFA (5%)
0.78 (0.70, 0.88)
n-6 (5%)
0.76 (0.68, 0.86)
a-Linolenic acid (0.3%)
0.89 (0.83, 0.96)
Marine n-3 (0.3%)
0.92 (0.84, 1.01)
Carbohydrate from whole grains (5%)
0.84 (0.78, 0.91)
Carbohydrate from refined starches & added sugars (5%)
0.98 (0.94, 1.03)
-0.6
-0.4
-0.2
0
0.2
Hazard Ratio (95% CI)

Cheese

	REG (*n* = 50)		RED (*n* = 51)		CHO (*n* = 49)		*P*	
	Week 12	Change from baseline	Week 12	Change from baseline	Week 12	Change from baseline	REG vs. RED	REG vs. CHO
LDL-C, mmol/L	3.51 ± 0.11	0.17 ± 0.07	3.45 ± 0.13	0.09 ± 0.08	3.43 ± 0.11	0.03 ± 0.06	0.42	0.1

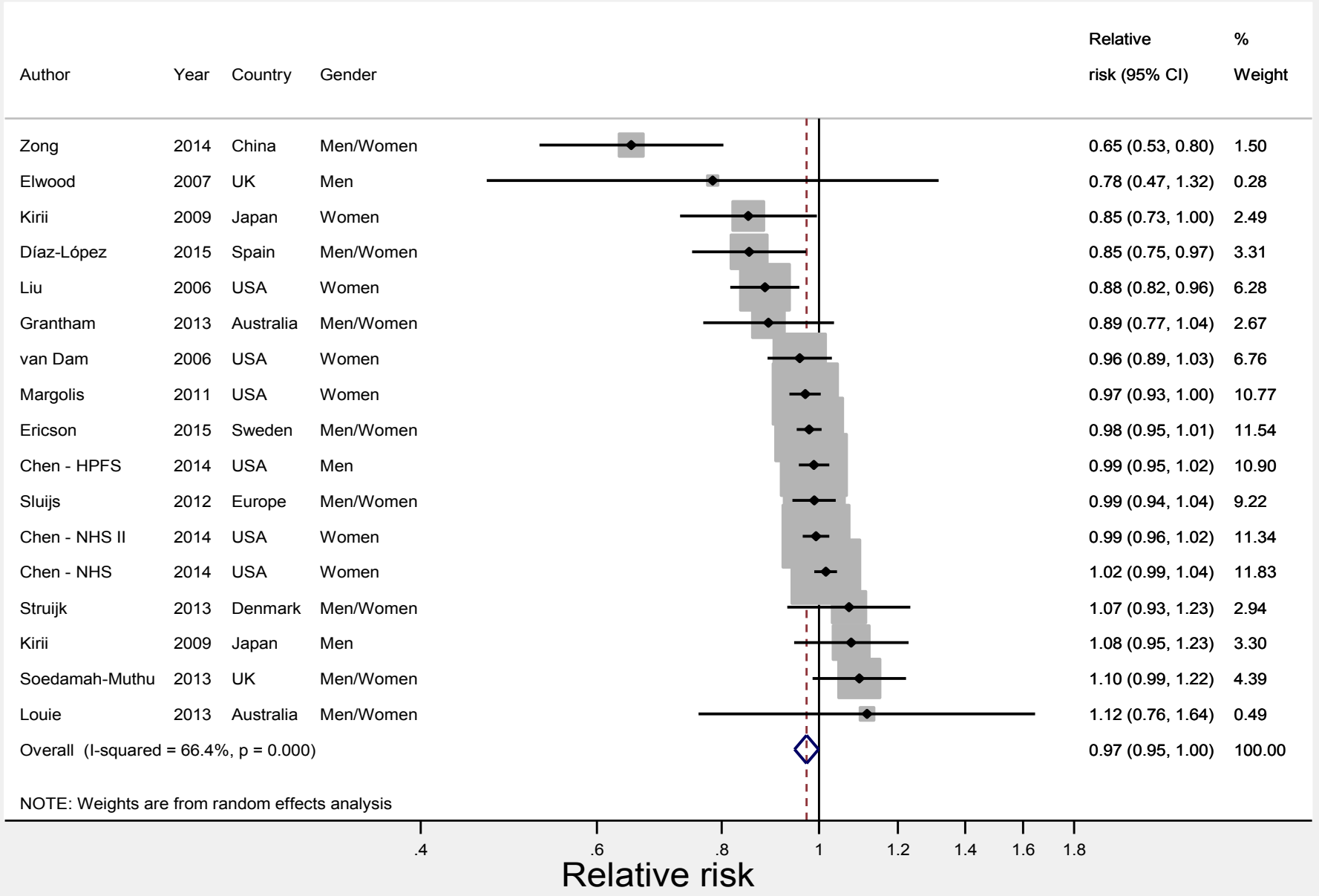
80g/d per 10MJ cheese (25-32% and 13-16% fat)
90 and 25g/d per 10MJ bread and jam. Raziani 2016
N=139 completed.

Red Meat as a source of saturated fat

- Red Meat: total mortality for a 1-serving-per-day increase was 1.13 for unprocessed red meat and 1.20 for processed red meat. 1.18 and 1.21 for CVD mortality and 1.10 and 1.16 for cancer mortality.
- 1 serving per day of other foods (including fish, poultry, nuts, legumes, low-fat dairy, and whole grains) for 1 serving per day of red meat were associated with a 7% to 19% lower mortality risk.
- 9.3% of deaths in men and 7.6% in women could be prevented at the end of follow-up if all individuals consumed <0.5 servings per day (approximately 42 g/d) of red meat (Pan 2012)
- Meta analysis total mortality 1.1 (n = 6 studies) for processed meat, and 1.29 (n = 5 studies) for total red meat (Larsson 2014)

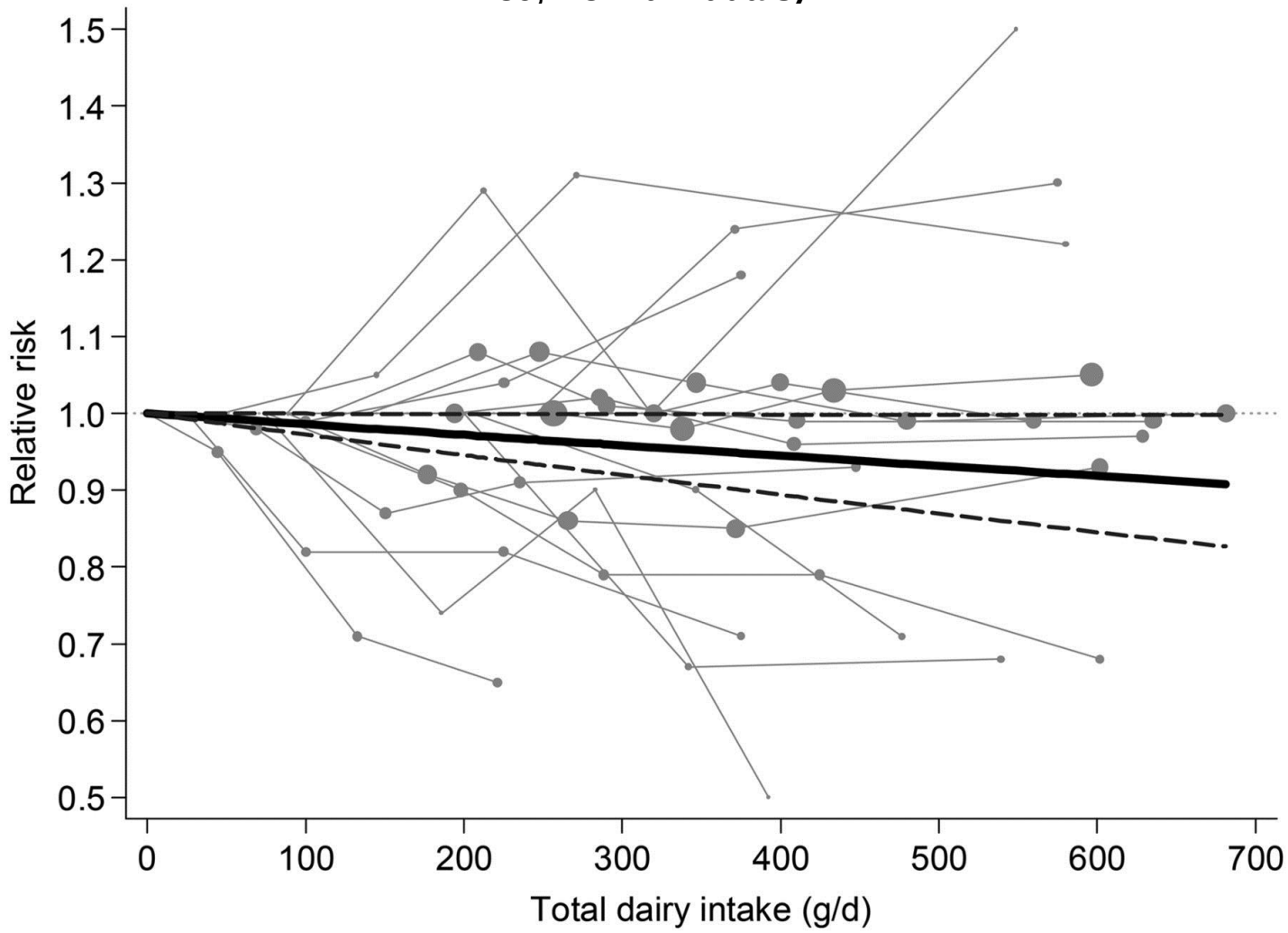
Dairy epidemiology of incident type 2 DM

- Gijsberg et al 2016 examined 22 cohort studies comprised of 579,832 individuals and 43,118 T2D cases. Meta analysis number 6
- 3% reduction per 200g/day ($p=0.04$) with high heterogeneity (ie not reliable). Low fat dairy had a similar but non-significant relationship.
- 80g/day of yogurt reduced the incidence of diabetes by 18% ($p<0.001$) while 10g/day of ice-cream reduced the risk by 19% ($p<.001$) but both had high heterogeneity.
- The dose response for these two foods was non-linear and no benefit was obtained from consuming larger amounts ?behaviour

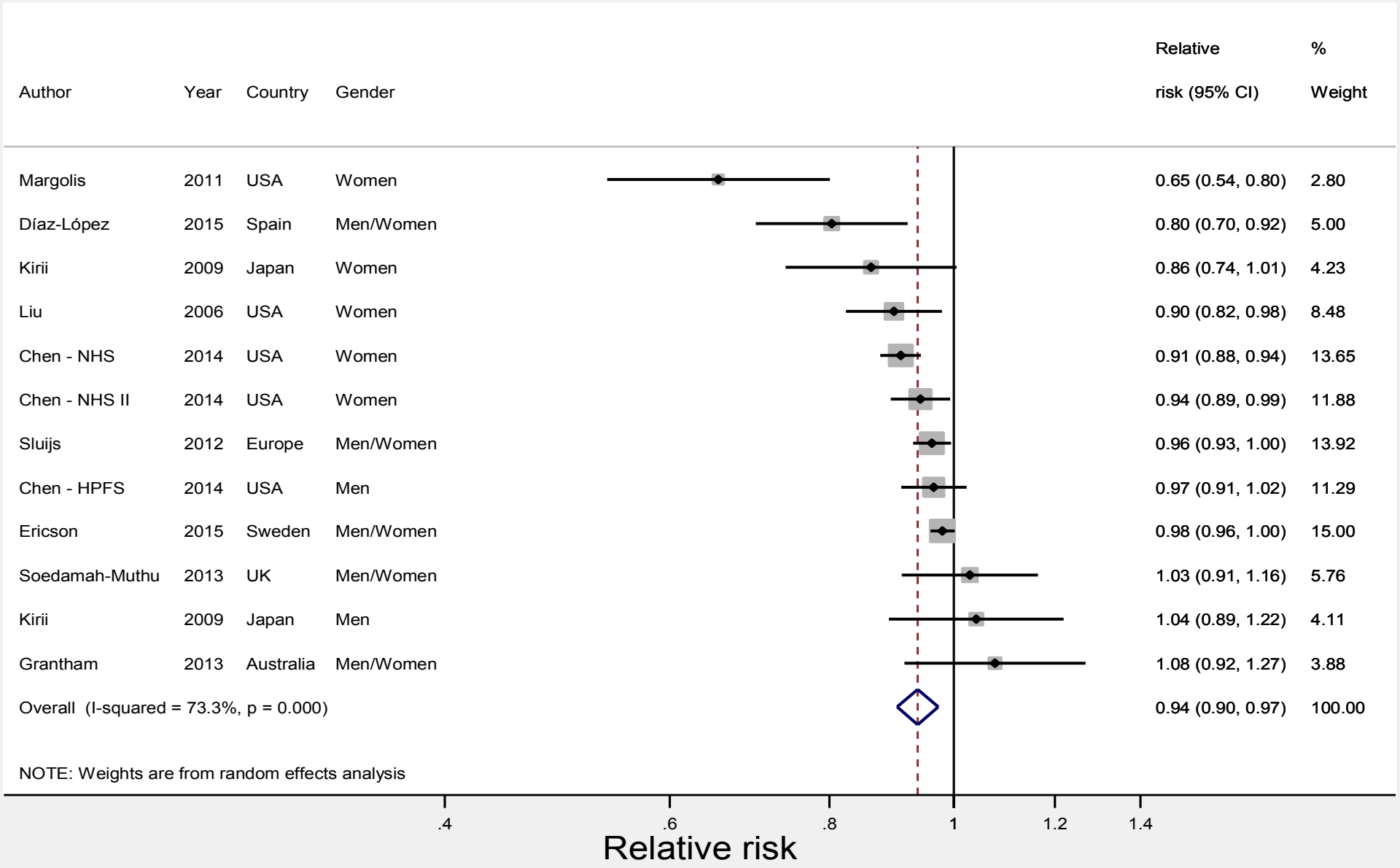

Author
Year
Country
Gender
Relative risk (95% CI)
% Weight
Zong 2014 China Men/Women 0.65 (0.53, 0.80) 1.50
Elwood 2007 UK Men 0.78 (0.47, 1.32) 0.28
Kirii 2009 Japan Women 0.85 (0.73, 1.00) 2.49
Díaz-López 2015 Spain Men/Women 0.85 (0.75, 0.97) 3.31
Liu 2006 USA Women 0.88 (0.82, 0.96) 6.28
Grantham 2013 Australia Men/Women 0.89 (0.77, 1.04) 2.67
van Dam 2006 USA Women 0.96 (0.89, 1.03) 6.76
Margolis 2011 USA Women 0.97 (0.93, 1.00) 10.77
Ericson 2015 Sweden Men/Women 0.98 (0.95, 1.01) 11.54
Chen - HPFS 2014 USA Men 0.99 (0.95, 1.02) 10.90
Sluijs 2012 Europe Men/Women 0.99 (0.94, 1.04) 9.22
Chen - NHS II 2014 USA Women 0.99 (0.96, 1.02) 11.34
Chen - NHS 2014 USA Women 1.02 (0.99, 1.04) 11.83
Struijk 2013 Denmark Men/Women 1.07 (0.93, 1.23) 2.94
Kirii 2009 Japan Men 1.08 (0.95, 1.23) 3.30
Soedamah-Muthu 2013 UK Men/Women 1.10 (0.99, 1.22) 4.39
Louie 2013 Australia Men/Women 1.12 (0.76, 1.64) 0.49
Overall (I-squared = 66.4%, p = 0.000) 0.97 (0.95, 1.00) 100.00
NOTE: Weights are from random effects analysis
.4
.6
.8
1
1.2
1.4
1.6
1.8
Relative risk

Spaghetti plot for the linear association between total dairy intake and diabetes risk (RR: 0.97 per 200 g/d; 95% CI: 0.95, 1.00; P = 0.044), including 16 studies (17 study populations; n = 489,113 individuals).

The American Journal of Clinical Nutrition

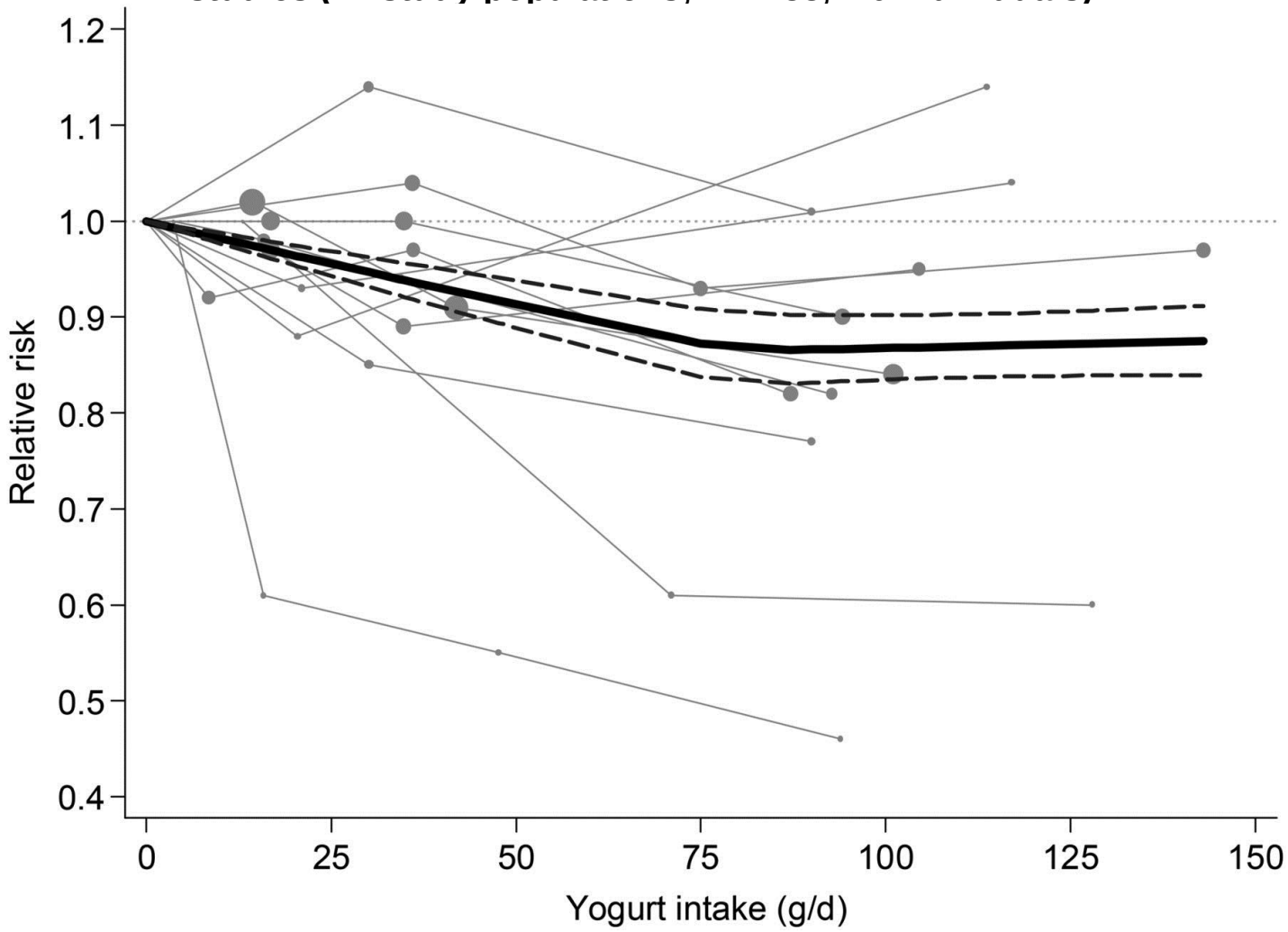


Lieke Gijsbers et al. Am J Clin Nutr 2016;103:1111-1124

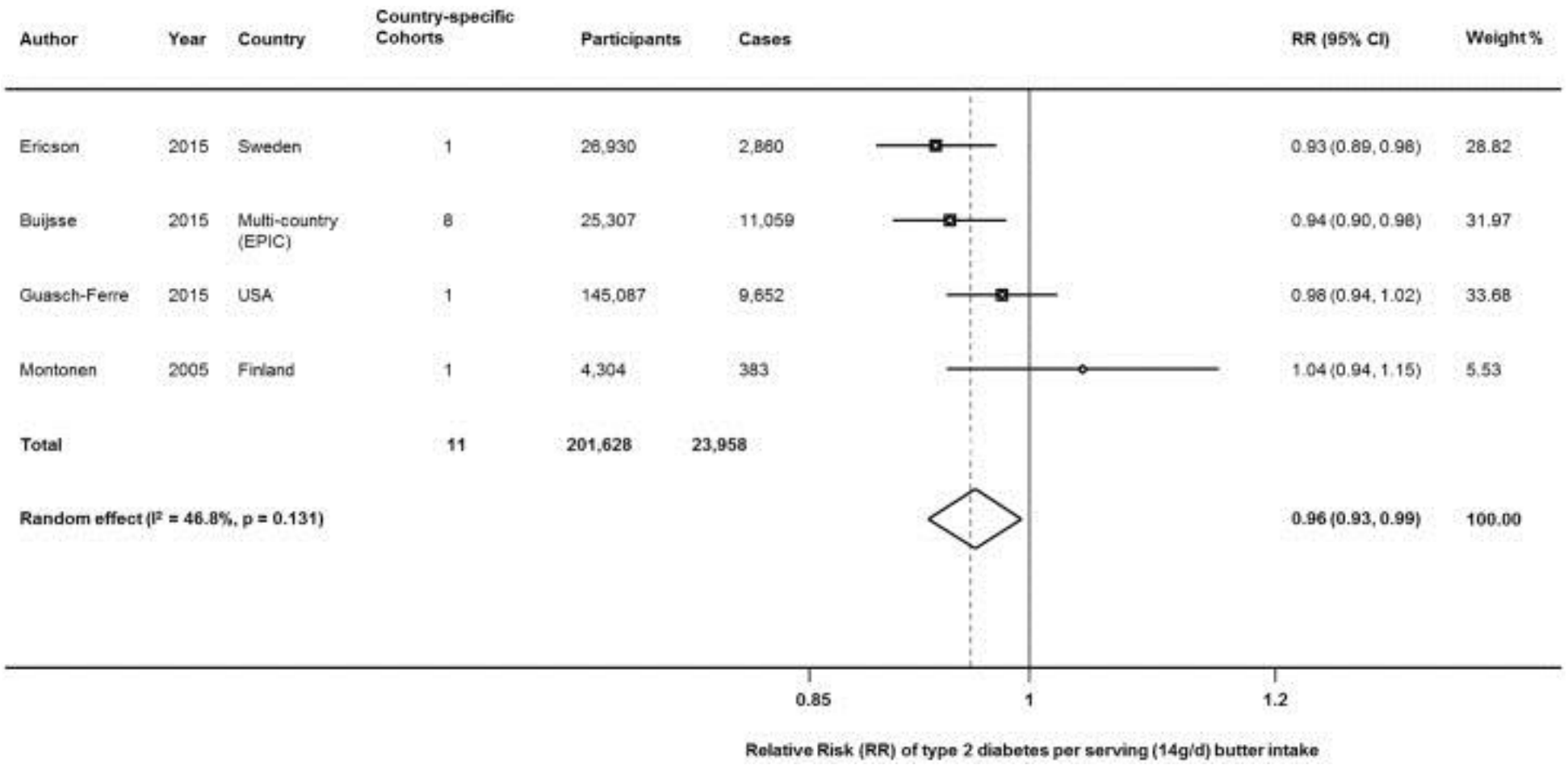

Author
Year
Country
Gender
Relative risk (95% CI)
% Weight
Margolis 2011 USA Women 0.65 (0.54, 0.80) 2.80
Díaz-López 2015 Spain Men/Women 0.80 (0.70, 0.92) 5.00
Kirii 2009 Japan Women 0.86 (0.74, 1.01) 4.23
Liu 2006 USA Women 0.90 (0.82, 0.98) 8.48
Chen - NHS 2014 USA Women 0.91 (0.88, 0.94) 13.65
Chen - NHS II 2014 USA Women 0.94 (0.89, 0.99) 11.88
Sluijs 2012 Europe Men/Women 0.96 (0.93, 1.00) 13.92
Chen - HPFS 2014 USA Men 0.97 (0.91, 1.02) 11.29
Ericson 2015 Sweden Men/Women 0.98 (0.96, 1.00) 15.00
Soedamah-Muthu 2013 UK Men/Women 1.03 (0.91, 1.16) 5.76
Kirii 2009 Japan Men 1.04 (0.89, 1.22) 4.11
Grantham 2013 Australia Men/Women 1.08 (0.92, 1.27) 3.88
Overall (I-squared = 73.3%, p = 0.000) 0.94 (0.90, 0.97) 100.00
NOTE: Weights are from random effects analysis
.4
.6
.8
1
1.2
1.4
Relative risk

Spaghetti plot for the nonlinear association (P-nonlinearity: <0.001) between yogurt intake and diabetes risk (RR: 0.86 at 80 g/d compared with 0 g/d; 95% CI: 0.83, 0.90; P < 0.001), including 11 studies (12 study populations; n = 438,140 individuals).

The American Journal of Clinical Nutrition



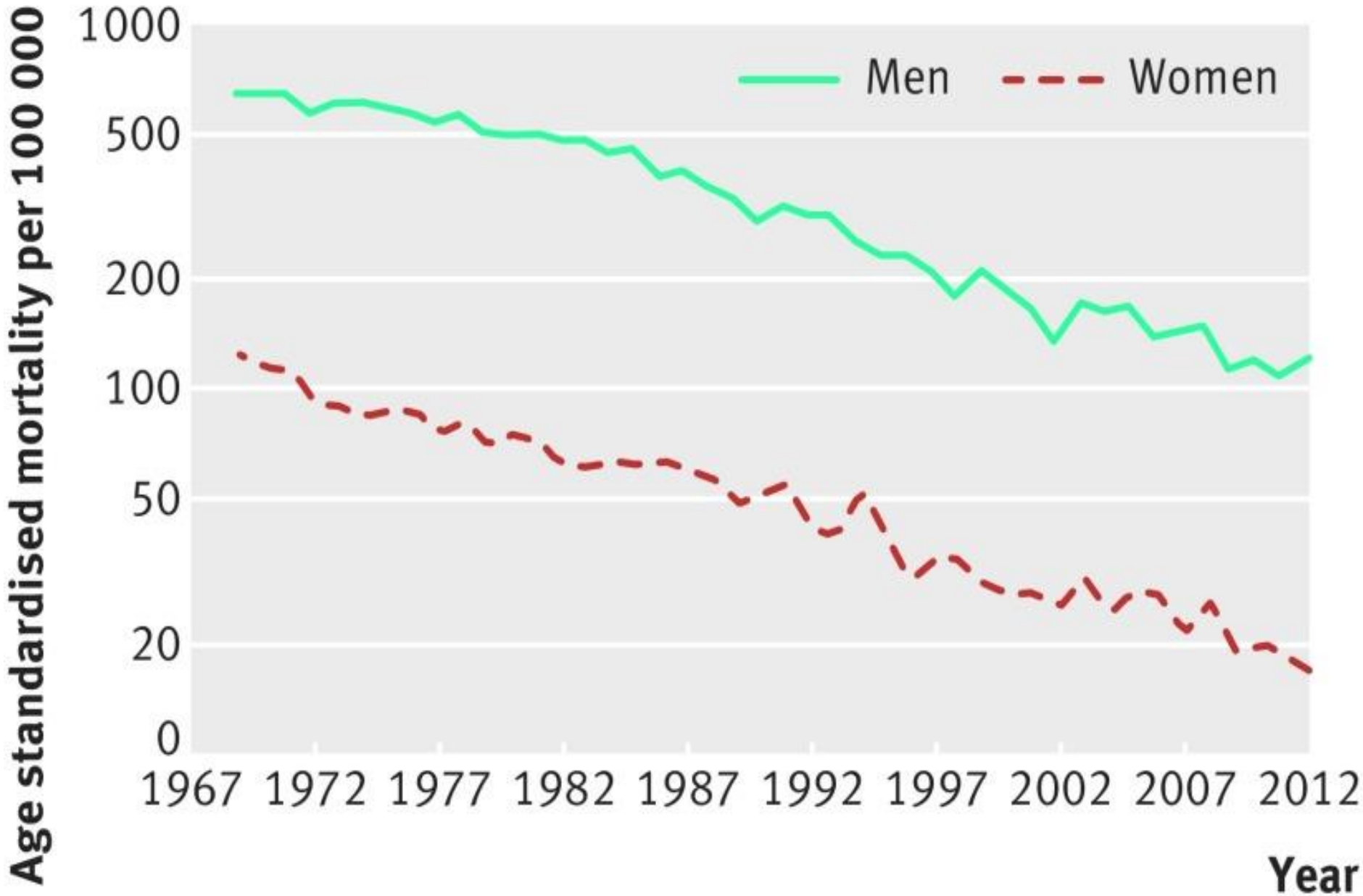
Lieke Gijsbers et al. Am J Clin Nutr 2016;103:1111-1124

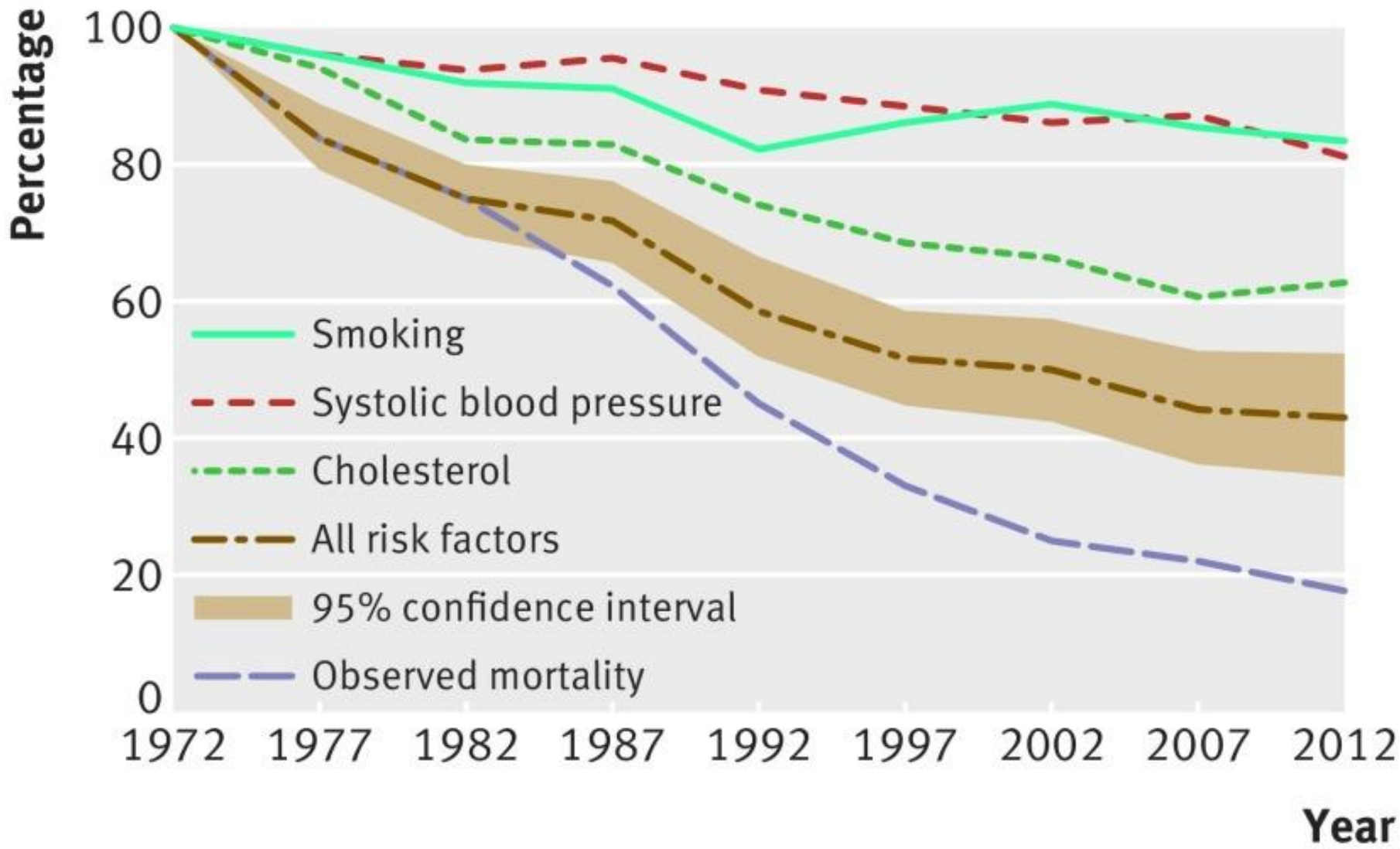


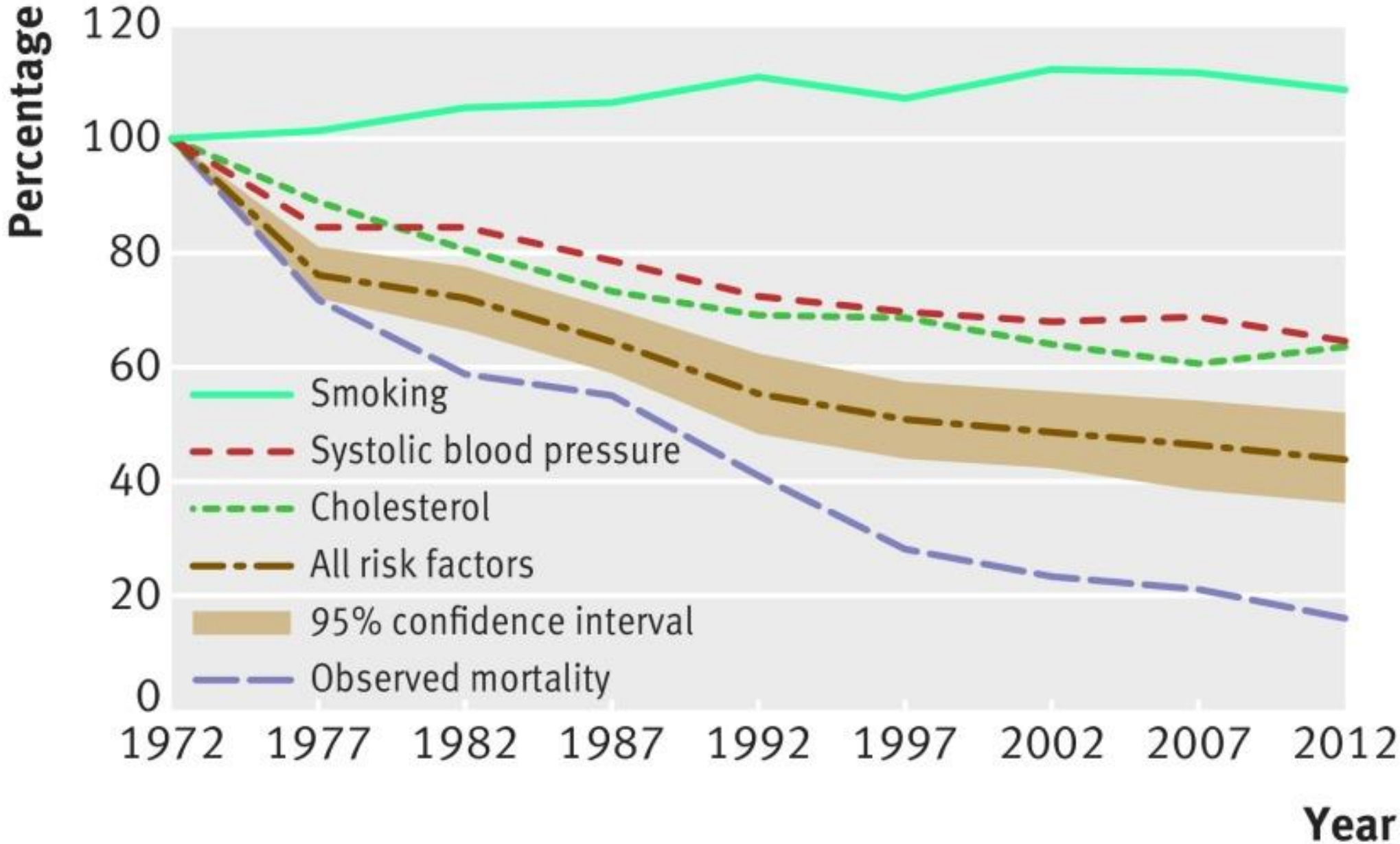
Butter consumption was weakly associated with all-cause mortality (N = 9 country-specific cohorts; per 14g(1 tablespoon)/day: RR = 1.01, 95%CI = 1.00, 1.03, P = 0.045) Pimpin 2016. Note this is compared with CHO not margarine or olive oil

Finnrisk

- 34,525 men and women aged 30-59 years FINRISK studies 1972 and 2012.
- During the 40 year study period, levels of the three major cardiovascular risk factors decreased except for a small increase in serum cholesterol levels between 2007 and 2012.
- From years 1969-1972 to 2012, coronary heart disease mortality decreased by 82% (from 643 to 118 deaths per 100,000 people) and 84% (114 to 17) among men and women aged 35-64 years, respectively.
- During the first 10 years of the study, changes in these three target risk factors contributed to nearly all of the observed mortality reduction.
- Since the mid-1980s, the observed reduction in mortality has been larger than predicted. In the last 10 years of the study, about two thirds (69% in men and 66% in women) of the reduction could be explained by changes in the three main risk factors, and the remaining third by other factors.

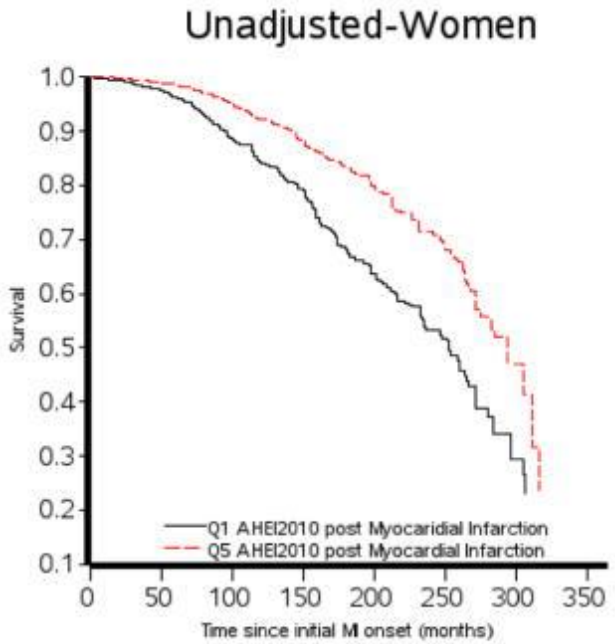

Age standardised mortality per 100 000
1000
500
200
100
50
20
0
Men
Women
1967
1972
1977
1982
1987
1992
1997
2002
2007
2012
Year

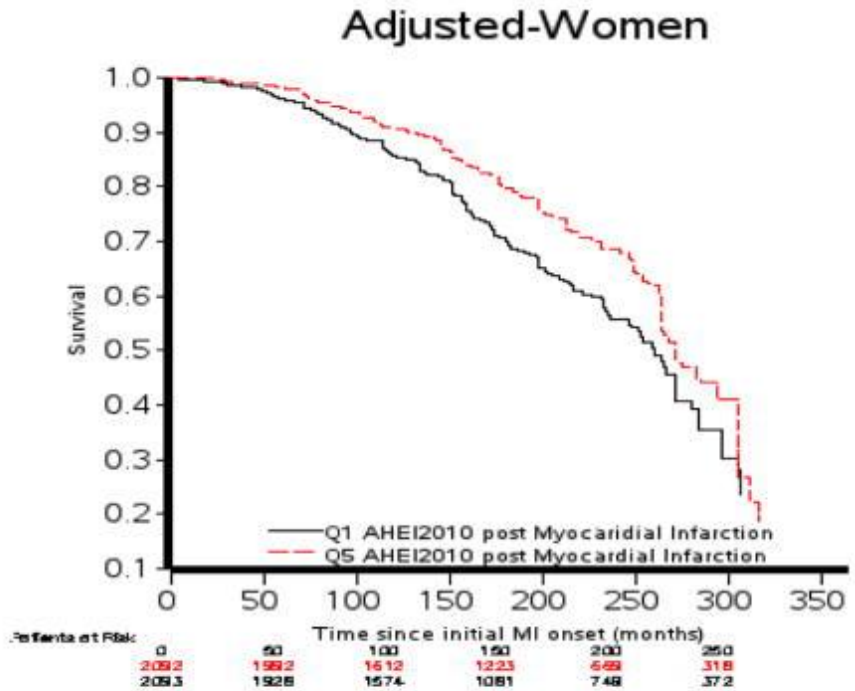

Percentage
100
80
60
40
20
0
Smoking
Systolic blood pressure
Cholesterol
All risk factors
95% confidence interval
Observed mortality
1972
1977
1982
1987
1992
1997
2002
2007
2012
Year

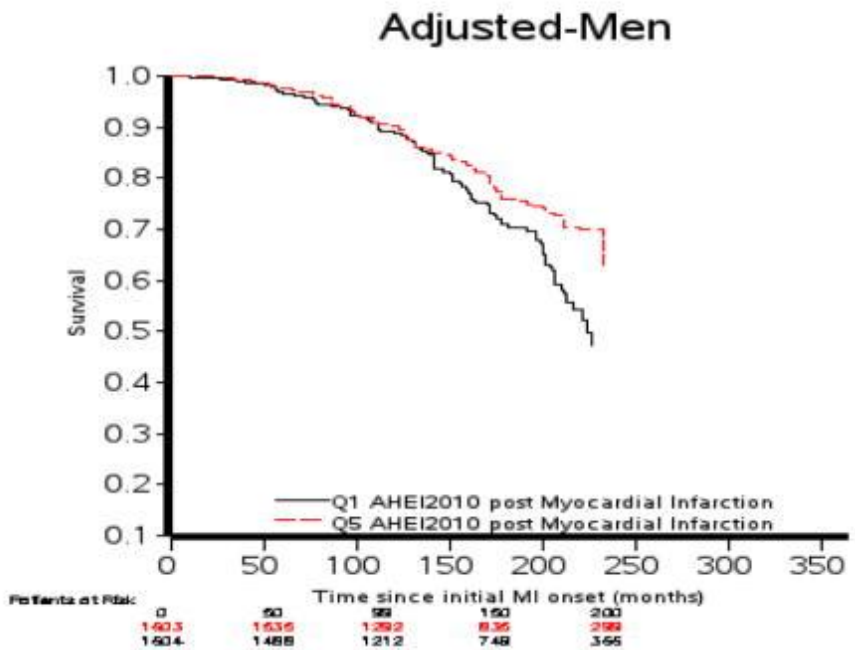

Percentage
120
100
80
60
40
20
0
Smoking
Systolic blood pressure
Cholesterol
All risk factors
95% confidence interval
Observed mortality
1972
1977
1982
1987
1992
1997
2002
2007
2012
Year

Diet Quality-Nurses and HPFU

- 1 394 702 person-years of follow-up, 11 793 CVD cases.
- Those with the greatest improvement in diet quality scores had a 7% to 8% lower CVD risk in the subsequent 4-year period - 0.92 for the Alternative Healthy Eating Index; 0.93 for the Alternative Mediterranean Diet score; and 0.93 for the Dietary Approach to Stop Hypertension; all P for trend <0.05).
- In the long term, increasing the diet scores from baseline to the first 4-year follow-up was associated with lower CVD risk during the next 20 years by 7-9%
- A decrease in diet quality scores was associated with significantly elevated risk of CVD in subsequent time periods (Sotos-Prieto 2015)







24% decrease in all cause mortality. Secondary prevention Li 2013

Conclusions

- Replacement of saturated fat with high GI, low fibre carbohydrate of no value
- Replacement with PUF, Mono or high quality CHO can reduced CVD by 10-25% and total mortality by up to 27%
- No advantage to increasing saturated fat from either dairy or meat- may increase inflammation and postprandial lipemia
- Improving diet quality good for both primary and secondary prevention