Evidence-based Medicine
&
Nutrition Recommendations

Jim Mann

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Human Nutrition

Riddet Institute
FOOD | INNOVATION | HEALTH

UNIVERSITY of OTAGO
Te Whare Wānanga o Otāgo
NEW ZEALAND

EDGAR DIABETES & OBESITY RESEARCH
A UNIVERSITY OF OTAGO RESEARCH CENTRE

National SCIENCE Challenges
HEALTHIER LIVES
He Oranga Hauora

Statins for the Prevention of Cardiovascular Disease

	Relative risk	95% CI
All cause mortality	0.83	0.73, 0.95
Fatal & non fatal CVD	0.70	0.61, 0.79
Revascularisation rates	0.66	0.53, 0.83

Taylor et al, Cochrane Collaboration (2011)

CUT CARBS, QUIT SUGAR, FEEL FABULOUS

How to stay slim for life

PART FIVE
by Karen Thomson

SWITCHING to a sugar-free lifestyle may be the easiest and most effective way to lose weight. Happily, it is also an incredibly healthy way to live.

All this week in the Daily Mail we have been serialising a fascinating new book, Sugar Free, by Karen Thomson, the great-granddaughter of pioneering heart transplant surgeon Dr Christiaan Barnard, in which she lays out a simple and delicious plan that'll help you cut carbs, quit sugar and leave you feeling fabulous.

We have talked about losing weight, beating sugar addiction and getting the whole family involved, but today, in the final extract, we show you how to adapt the programme to ensure you can live happily and healthily sugar-free in the long-term.

More and more academics and medics around the world are leading the charge by quitting sugar and cutting back on carbohydrates, as research highlights the destructive impact on health of high blood sugar levels.

The sugar-free message forms an important part of the 'clean eating' and Paleo movements, which are gaining popularity among the rich and famous. However, unless you have a personal nutritionist on speed dial, it can be difficult to contemplate living your whole life without sugar, eating far fewer carbohydrates than is the norm.

IT'S NOT ABOUT SHORT TERM WEIGHT LOSS

THE very low-sugar diet plan we have been outlining all week can be easily adapted to provide a foolproof blueprint for a healthy diet whether you have excess weight to shift or not.

If you know you are addicted to sugar, and worry about the power it has over you, aim to reset your body. Keep sugar cravings at bay by sticking to the weight-loss version of the sugar-free eating plan for eight weeks, regardless of whether or not you have weight to lose.

This plan (explained in Monday's Mail) keeps total carbohydrates at 50g per day (or up to 120g if you're very active). If you relax your control too soon and let sugar and refined carbohydrates creep back before your system has truly settled, you run the risk of undoing the good work already done.

For the rest of us, it is just useful to think of the diet plan as a great starting point. Once your weight or cravings have settled, you can think about building on this plan to create a long-term blueprint that suits your life and your body.

After a few weeks without sugar, your body should start telling you what it needs to remain healthy — signals that will no longer be masked by sugar cravings and unexplainable hunger.

This means you can gradually increase your carbohydrate intake by enjoying a wider range of fruit and slightly more starchy vegetables and pulses until you find the ideal cut-off point that suits you. If you are naturally apple shaped, tend to have high or low blood sugar levels, or if you have diabetes, you might find it better to stick close to the 50g limit most days (but discuss this diet first with your GP or diabetes nurse).

Watch out for cravings, mood swings — often caused by intense highs and lows in your blood sugar — or weight gain. These are signs that your carbohydrate intake might have crept up and could do with a little adjusting.

To find your ideal level, gradually increase your carbohydrate intake by 5g per day while monitoring your weight, hunger and cravings (see chart on the final page for 5g carbohydrate comparisons).

The ideal sugar-free plan would keep you below 120g total carbs per day, and for your major source to be non-starchy fruit and veg.

CHOCOLATE REWARD

WHEN you reach your target weight and conquer your sugar addiction, celebrate by adding a daily 'dose' of dark chocolate (two squares of at least 70 per cent cocoa content) to your meal plan daily, if you would like.

WHAT IF YOU FALL OFF THE WAGON?

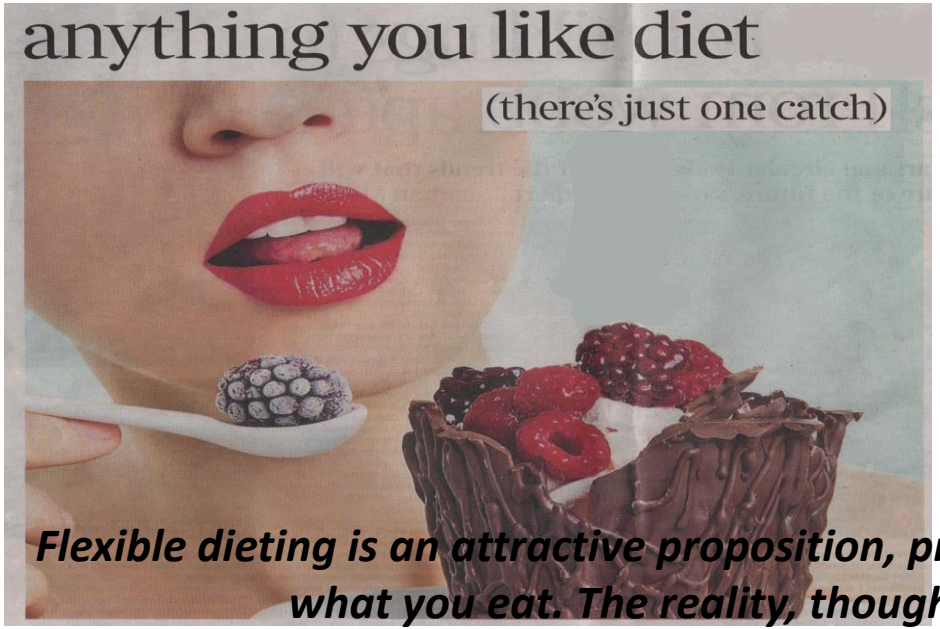
THERE will be times when even the most vigilant succumb to sugar's sweet temptation. It might be the tiny slice of birthday cake brought into work, or the tempting biscuits placed in front of you after you rushed out of the house without breakfast. If you've been battling sugar addiction for years and are hyper-sensitive to the white stuff, any brief taste can be enough to see you spiralling into a full binge. If this happens, don't worry — and don't give up.

Cut out all sugar or sweetness for the next day or two. Cook a wholesome, nourishing meal containing fat, protein and greens. But avoid dense vegetables for a few days to allow your blood sugar levels and insulin responses to settle.

Drink lots of water and herbal

TURN TO NEXT PAGE

Daily Mail, 8 July 2016



The Times, 5 July 2016

Flexible dieting is an attractive proposition, promising weight loss without restricting what you eat. The reality, though, is more mundane……’

Butter is good but olive oil is better

Katie Gibbons

Butter may be good for you but swapping dairy fat for olive oil will help you to live longer, according to a 30-year study of eating habits.

People who have frequent servings of unsaturated fat, found in fish and vegetable oils, are about 20 per cent more likely to live longer, research involving 120,000 people found.

The results, published in the journal *Jama Internal Medicine*, add to the growing body of evidence supporting a traditional Mediterranean diet — rich in fish, vegetables, nuts and olive oil — over a low-fat, high-carbohydrate approach.

Experts are increasingly calling for unsaturated fats to be introduced as an integral part of national dietary guidelines, with their importance promoted in a similar way to protein, vegetables and wholegrain. The recommendation follows news that butter, which has been demonised by doctors and dieticians for decades, is neutral for health and may even protect against diabetes.

A large-scale pilot study involving people with type 2 diabetes, the results of which were revealed in The Times, found that a diet low in carbohydrates and rich in protein and unsaturated fat could reduce blood glucose levels in weeks.

The latest study of 126,233 people, carried out at Harvard University, found that an increase of only 2 per cent in trans fats, which are present in margarines and other "low-fat" spreads, resulted in a 16 per cent higher chance of premature death.

Similar results were seen in people who often ate cheese, fatty red meat and other foods high in saturated fat. When compared with the same number of calories from carbohydrate, every 5 per cent increase in saturated fat intake was associated with an 8 per cent higher risk of overall mortality.

However, those who consumed large amounts of olive and sunflower oil, nuts and oily fish lived between 11 and 19 per cent longer. Replacing only 5 per cent of total calorie intake from saturated fat (about 15g) with the same quantity of polyunsaturated fat was associated with a 27 per cent lower risk of premature death from heart disease, cancer and other causes.

"We need to focus on food-based guidelines to help the public, as opposed to singling out single nutrients," said Aseem Malhotra, a cardiologist at Frimley Health NHS Foundation and an active member of the Action on Sugar campaign group. "A diet high in vegetables, olive oil, oily fish and nuts is most beneficial for heart health.

"Reducing consumption of refined carbohydrates and sugar is particularly beneficial for those with and at risk of type 2 diabetes.

"As far as butter is concerned its cardiovascular effects are neutral, with some suggestion that full-fat dairy may protect against type 2 diabetes."

Nita Forouhi, of the Medical Research Council's epidemiology unit at the University of Cambridge, said: "In the currently controversial dietary fat research landscape, this large study provides robust observational evidence for the health benefits of swapping saturated fat with polyunsaturated fat.

"It is now timely and appropriate to put effort into giving clear guidance on the health benefits and harms of the food sources of fat, moving beyond the issue of types of fat, the macronutrient."

High in unsaturated fat

- Olive oil
- Canola oil
- Soybean oil
- Raw nuts
- Avocados
- Olives
- Salmon
- Herring and mackerel
- Raw pumpkin
- Sunflower and chia seeds

Problems associated with RCTs involving nutrition interventions

*	NCDs have many causes
*	Large numbers required to study clinical outcomes
*	Nutritional causes of disease likely to have been present for many years
*	Difficult to achieve long term compliance
*	What is a true ‘CONTROL’ group?

Research approaches used to study nutrient-disease relationships

*	Comparisons between disease trends over time & food/nutrient consumption	+
*	Cross country comparisons	+
*	Case control studies	±
*	Cohort studies	++
*	RCTs	+++
*	Metaanalyses	++++
*	Experimental studies	++

Second Expert Report from WCRF/AICR (2007)

Evidence	Decreases risk	Increases risk
Convincing	Requires RCTs	
Probable	Cohort studies, dose response, mechanistic studies	

Convincing or **Probable** associations translate into recommendations

Limited: Suggestive	
Limited: No Conclusion	

GRADE

Author(s): Lisa A Te Morenga, Jim Mann
Date: 28 March 2012
Question: What is the effect of a reduction in free sugars intake in adults
Settings: General adult population.

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dietary sugar reduction	Control	Absolute (95% CI)		
Q1: What is the effect of a reduction in free sugars intake on body weight in adults											
5	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Potential publication bias[2]	397	414	MD 0.80 lower (0.39 to 1.21 lower)	⊕⊕⊕O MODERATE	IMPORTANT

[1] Three trials reported data for completers only, which could result in an overestimation of the effect thus the evidence was downgraded to moderate.

The initial quality of the evidence was downgraded from high to moderate because of potential risk of attrition bias as three studies reported data only for those who completed the treatment

Quality of evidence & importance determine strength of recommendations (*convincing* or *conditional)*

Nutrition Recommendations must consider **totality of evidence**

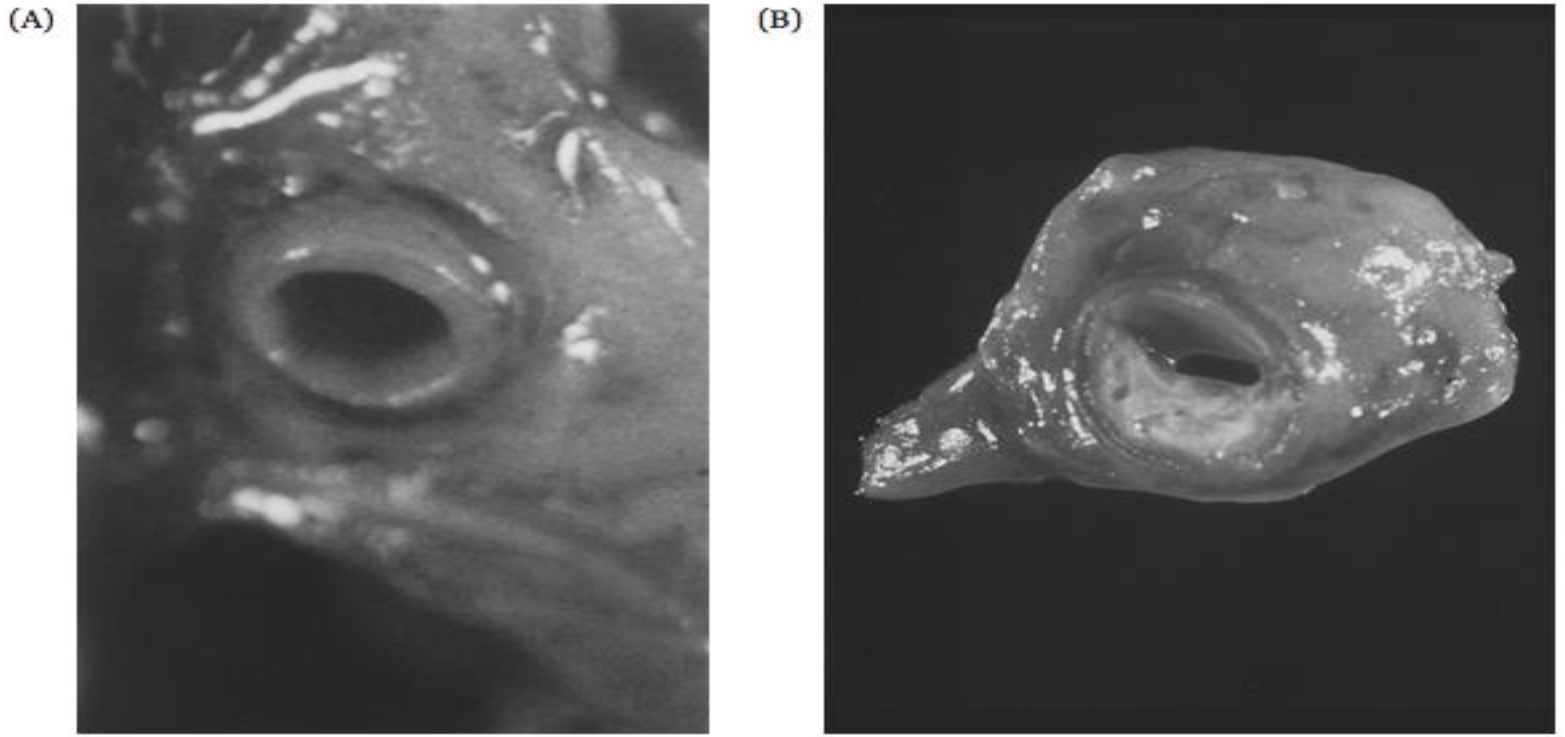


Fig. 21.1 A normal coronary artery (A) is contrasted with an artery showing atheromatous deposits (B).

Source: Mann JI, Chisholm A.Ch21
***Essentials of Human Nutrition* 4e (2012) Mann & Truswell (eds). OUP**

Source: Mann J. McLean R.

Ch 23.*Essentials of Human Nutrition* 5e (2017) Mann & Truswell eds. Oxford University Press

Table 23.1 Risk factors for coronary heart disease

Irreversible	• Male sex • Increasing age • Genetic traits, including monogenic and polygenic disorders of lipid metabolism
Potentially modifiable	• Cigarette smoking • Dyslipidaemia: increased levels of cholesterol, triglyceride, low-density and very-low-density lipoprotein, and apolipoprotein B; low levels of high-density lipoprotein; atypical lipoproteins • Oxidizability of low-density lipoprotein • Obesity, especially when centrally distributed (high waist circumference) • Elevated blood pressure and hypertension • Physical inactivity • Diabetes, hyperglycaemia, and insulin resistance • Increased thrombosis: increased haemostatic factors and enhanced platelet aggregation • High levels of inflammatory markers (e.g. CRP, IL-6, TNFα) • Impaired foetal nutrition • High levels of homocysteine
Psychosocial	• Stressful situations • Coronary-prone behaviour patterns: type A behaviour
Geographic	• Climate and season: cold weather

CRP, C-reactive protein; IL, interleukin; TNF, tumour necrosis factor.


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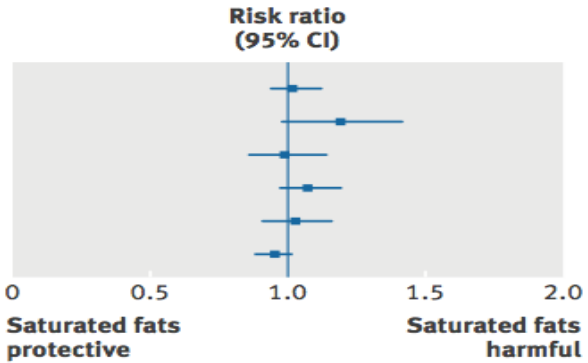
Fig 2: Summary most adjusted relative risks for saturated fat intake & all cause mortality, CHD mortality, CVD mortality, total CHD, ischemic stroke & type 2 diabetes

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



De Souza et al, BMJ 2015: 351:h3978

ORIGINAL CONTRIBUTION

Low-Fat Dietary Pattern and Risk of Cardiovascular Disease

The Women's Health Initiative Randomized Controlled Dietary Modification Trial

- 48835 women, postmenopausal, 50 to 79 y
- Randomised to intervention or comparison diet
- Follow-up 8.1 y

Intervention Intensive behavior modification in group and individual sessions designed to reduce total fat intake to 20% of calories and increase intakes of vegetables/fruits to 5 servings/d and grains to at least 6 servings/d. The comparison group received diet-related education materials.

Main Outcome Measures Fatal and nonfatal coronary heart disease (CHD), fatal and nonfatal stroke, and CVD (composite of CHD and stroke).

Howard, JAMA 2006;295:655-66

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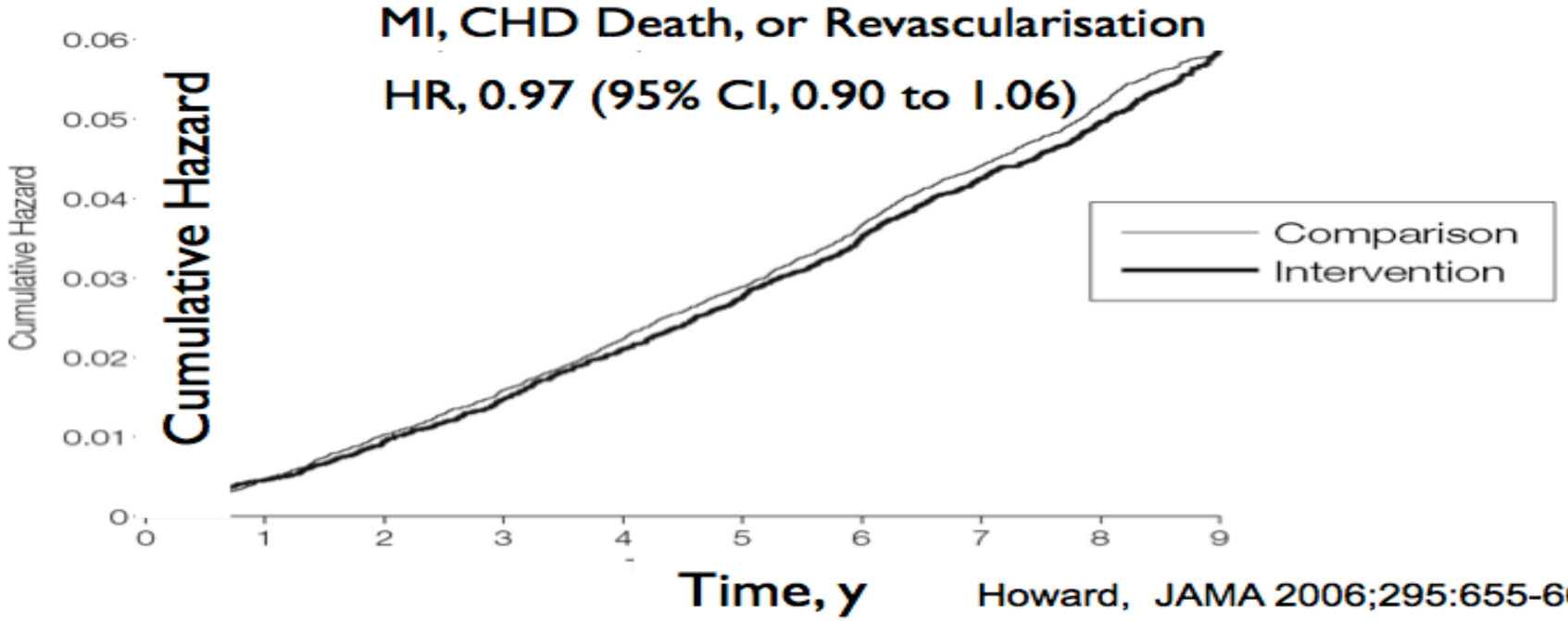
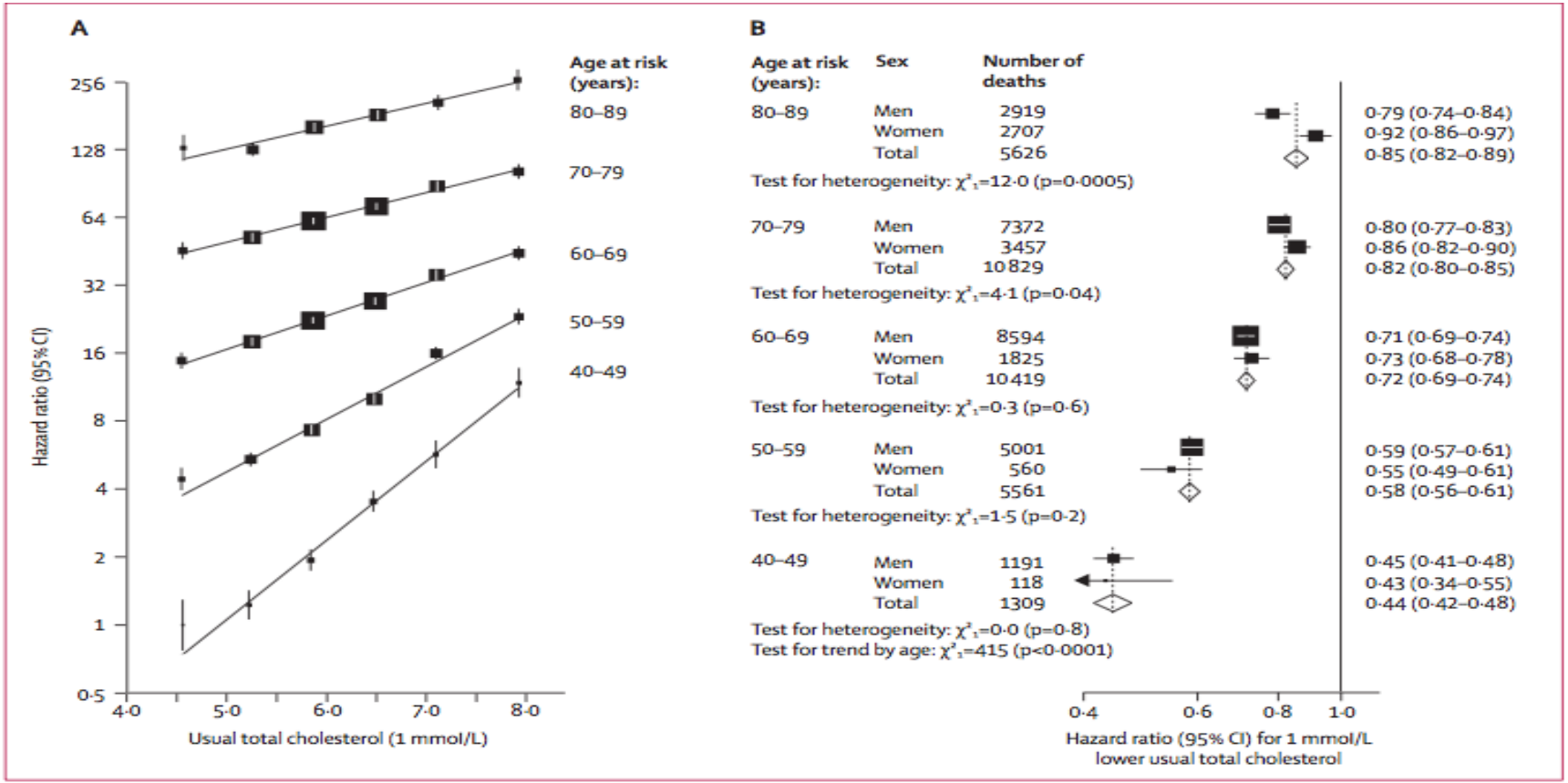
The Women's Health Initiative Randomized Controlled Dietary Modification Trial



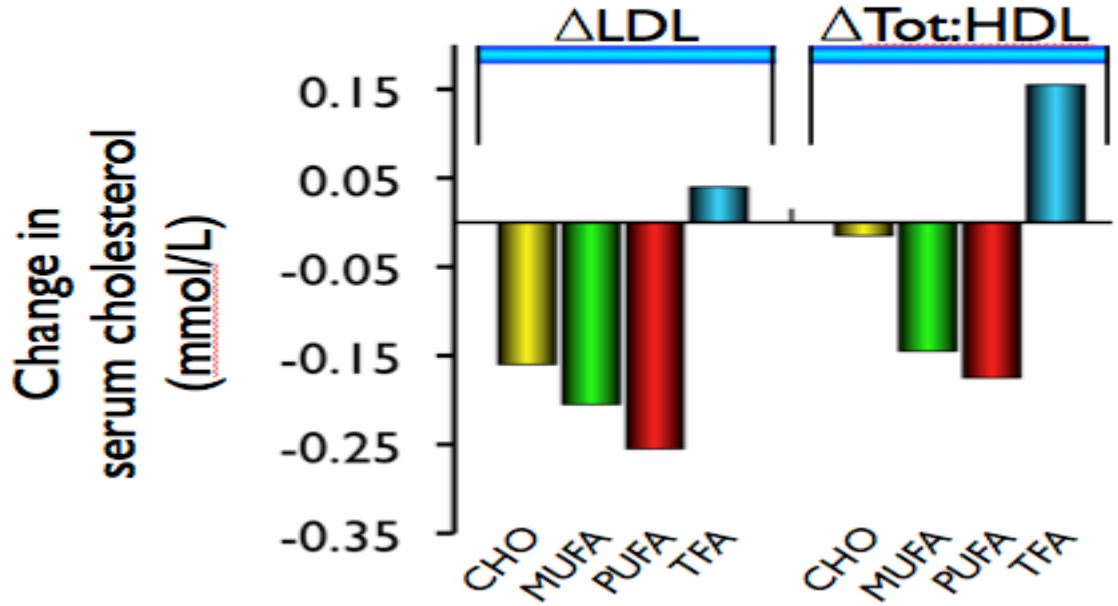
Howard, JAMA 2006;295:655-66



Prospective Studies Collaboration et al. Lancet. 2007; IHD Mortality

Replacing 5% total energy from SFA with:

Meta-analysis of 90 randomised controlled trials (RCT)

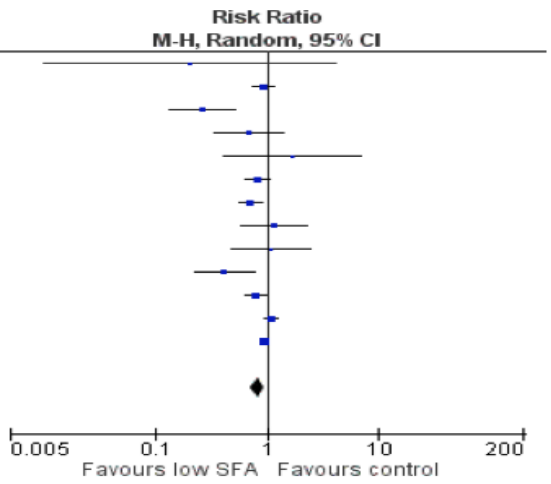


EJCN 2009;63:S22-33 AJCN 2003;77:1146-55

Forest plot of comparison between saturated fatty acid reduction *vs* usual diet for the primary outcome of combined cardiovascular disease.

Study or Subgroup	reduced SFA Events	Total	usual diet Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Black 1994	0	66	2	67	0.2%	0.20 [0.01, 4.15]
DART 1989	136	1018	147	1015	13.0%	0.92 [0.74, 1.15]
Houtsmuller 1979	8	51	30	51	3.7%	0.27 [0.14, 0.52]
Ley 2004	11	88	16	88	3.4%	0.69 [0.34, 1.40]
Moy 2001	5	117	3	118	1.0%	1.68 [0.41, 6.87]
MRC 1968	62	199	74	194	11.1%	0.82 [0.62, 1.07]
Oslo Diet-Heart 1966	64	206	90	206	11.7%	0.71 [0.55, 0.92]
Rose corn oil 1965	15	28	6	13	3.7%	1.16 [0.59, 2.29]
Rose olive 1965	11	26	5	13	2.7%	1.10 [0.48, 2.50]
STARS 1992	8	27	20	28	4.2%	0.41 [0.22, 0.78]
Veterans Admin 1969	97	424	122	422	12.5%	0.79 [0.63, 1.00]
WHI with CVD 2006	225	908	311	1369	15.3%	1.09 [0.94, 1.27]
WHI without CVD 2006	1132	18633	1777	27925	17.4%	0.95 [0.89, 1.03]
Total (95% CI)		**21791**		**31509**	**100.0%**	**0.83 [0.72, 0.96]**
Total events	1774		2603			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 34.25$, df = 12 (P = 0.0006); $I^2 = 65\%$
Test for overall effect: Z = 2.50 (P = 0.01)

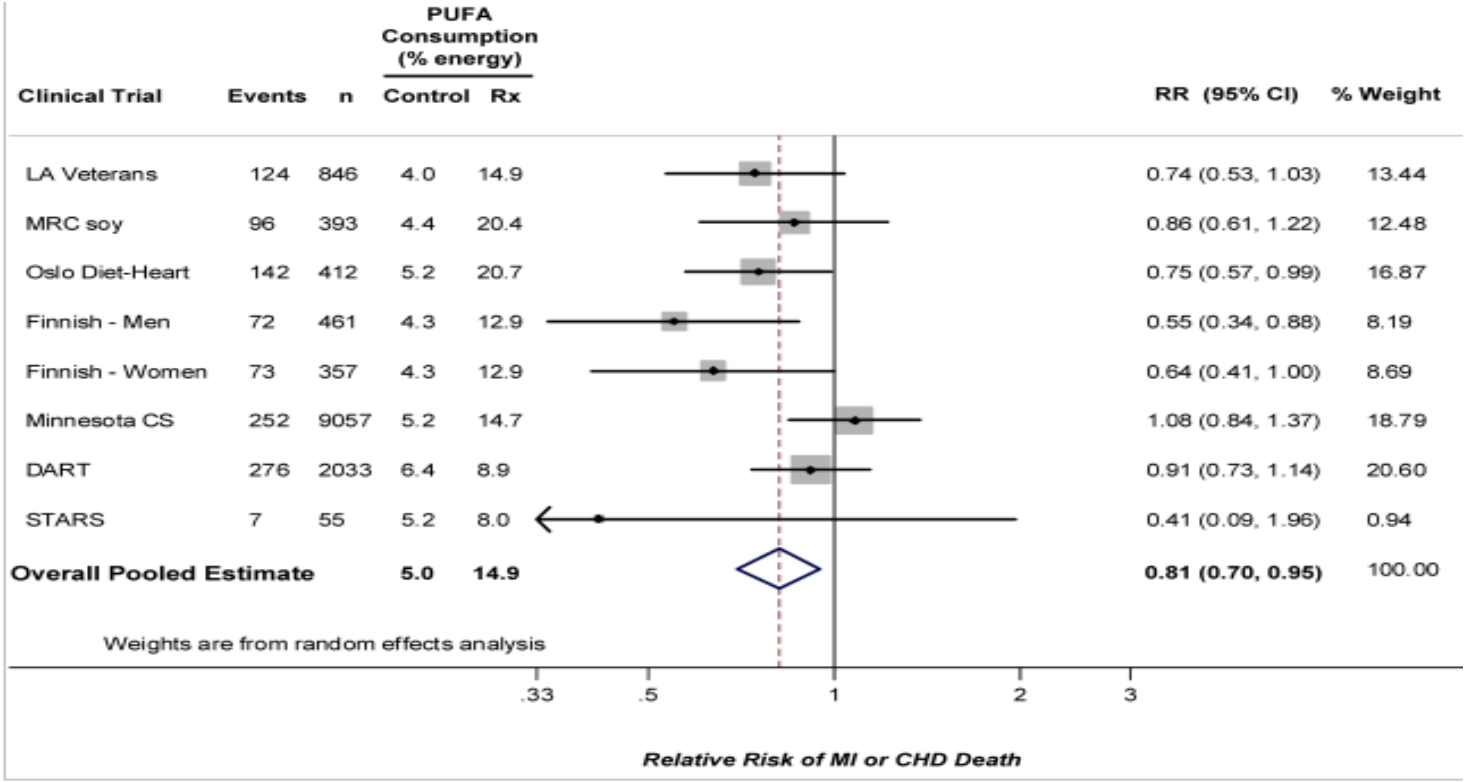


Source: Hooper et al, (2015) Cochrane Database of Systematic Reviews Issue 6

Hooper et al. CHD Events, subgroup analysis

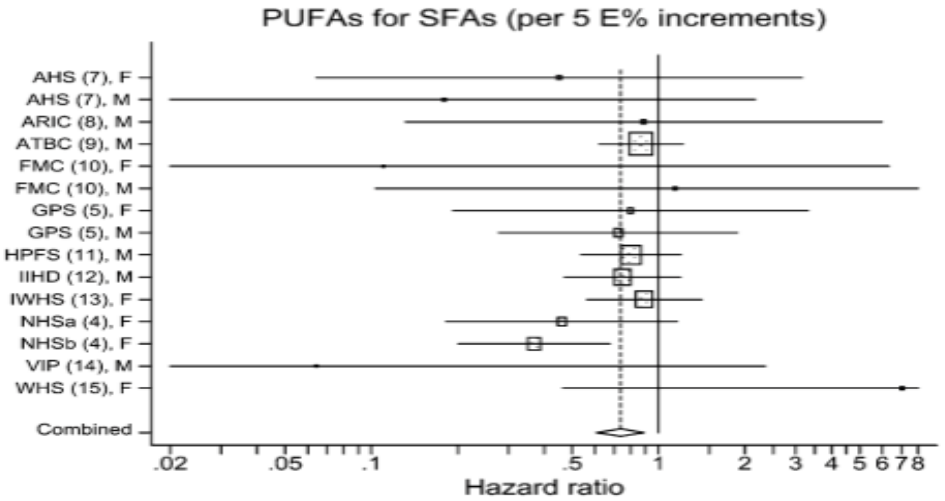
Subgroup by replacement	
	RR (95% CI)
PUFA replacement	0.76 (0.57, 1.00)
CHO replacement	0.98 (0.83, 1.14)
MUFA replacement	1.50 (0.62, 3.61)
Subgroup by TC reduction	
TC reduced by ≥0.2 mmol/l	0.75 (0.58, 0.99)
TC reduced by <0.2 mmol/l	1.03 (0.87, 1.21)

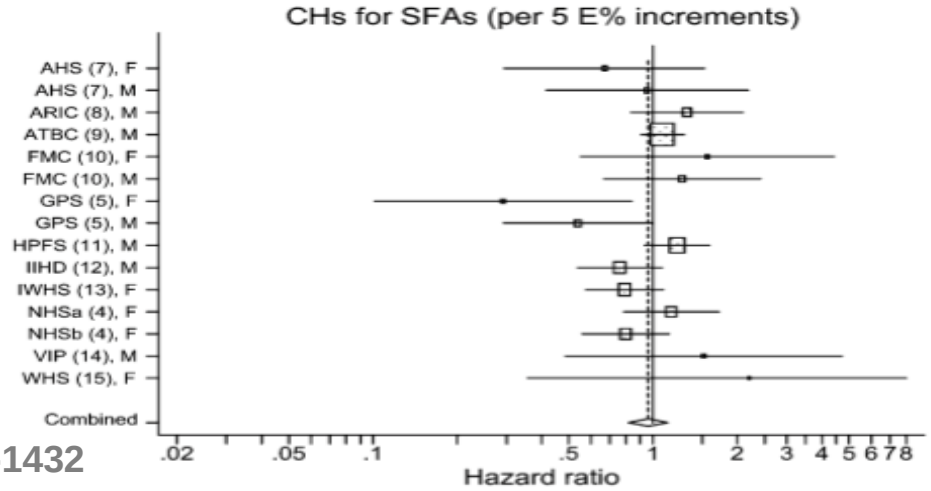
Fig 2. Meta-analysis of RCTs evaluating effects of increasing PUFA consumption in place of SFA & occurrence of CHD events



Mozaffarian et al, PLoS Med 2010 7(3): e1000252

Coronary deaths

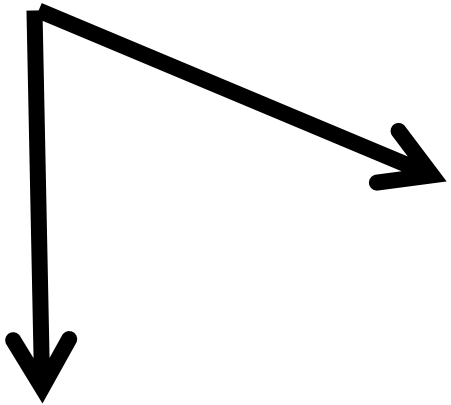




Jakobsen et al, Am J Clin Nutr 2009; 89:1425-1432

“Additional analyses” in WHI

Women who reached low levels of saturated fat intake
compared with those who did not

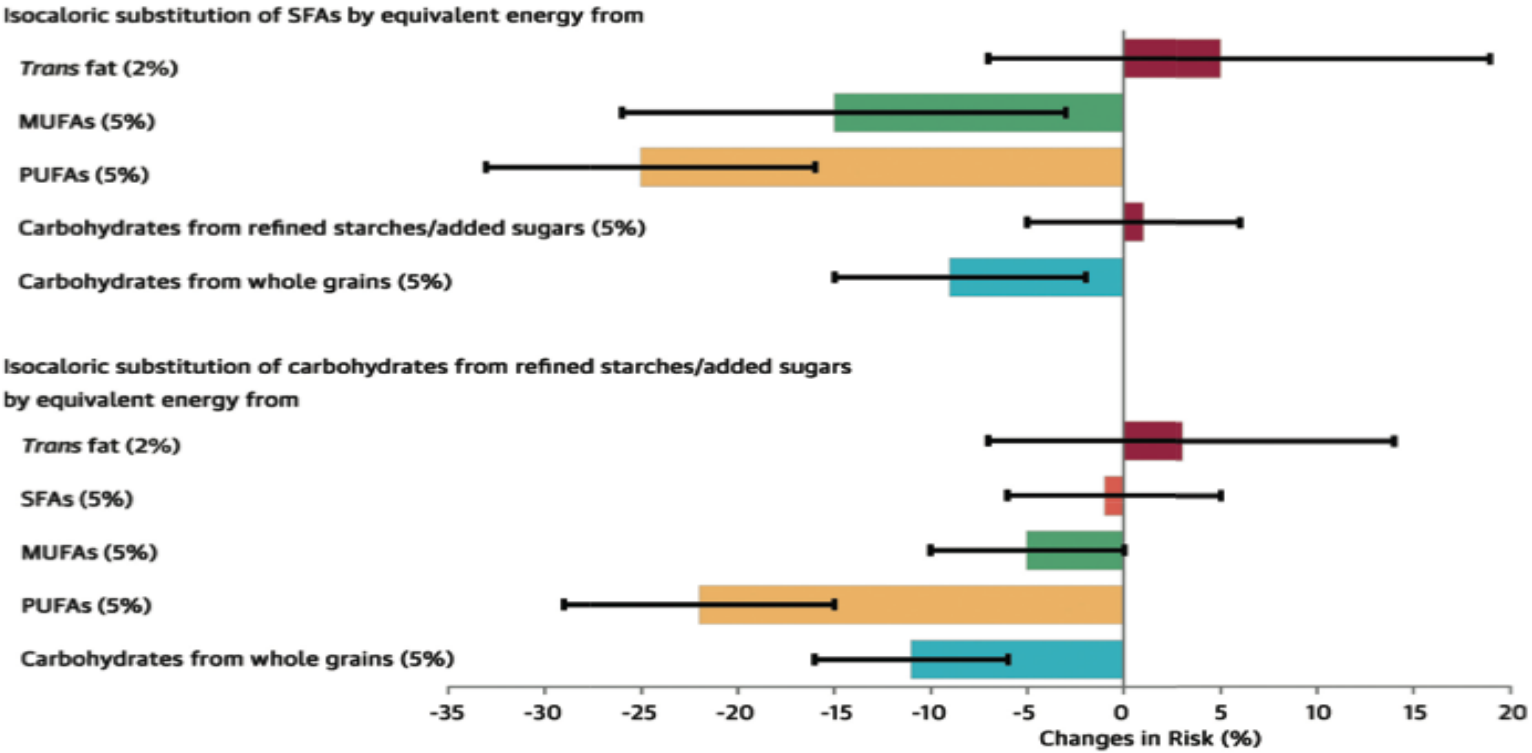


LDL-chol decreased
0.26 mmol/L (95%CI, 0.17-0.36)

CHD risk: HR 0.81 (95%CI, 0.69-0.96; *P*<0.001)

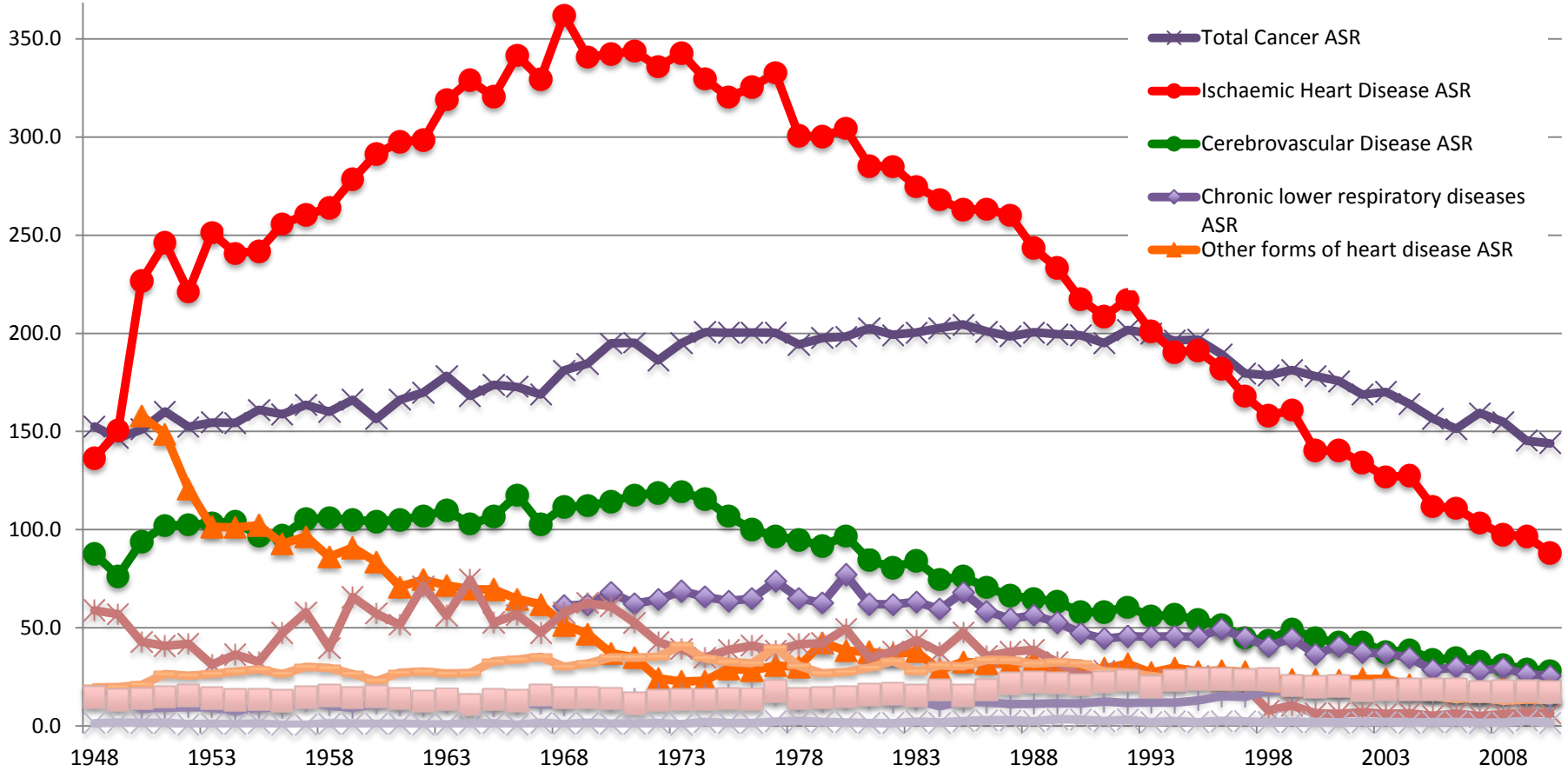
Howard, JAMA 2006;295:655-66

Fat, carbohydrates and heart disease: Estimated percentage of changes in the risk of coronary heart disease associated with isocaloric substitution of 1 dietary component for another



Source: Li Y, et al. *J Am Coll Cardiol*. 2015; 66(14): 1538-48

Deaths from heart disease & other causes: NZ



Quality assessment							No of participants (study event rate %)		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Reduced saturated fat intake	Usual saturated fat intake	Relative effect (95% CI)	Absolute effects (per 10,		
7	RCTs	no serious risk of bias[2]	serious inconsistency[8]	no serious indirectness[4]	no serious imprecision[9]	none[6]	390/1953 (20%)	494/1942 (25.4%)	**RR 0.73** (0.58 to 0.92)	**687 fewer** (from 204 fewer to 1068 fewer)	⊕⊕⊕O MODERATE	CRITICAL

Table 25:
GRADE profile: What is the effect of replacing some saturated fat with PUFA on risk of CVD in adults? Hooper et al, Reduction in saturated fat intake for cardiovascular disease (Review) Cochrane Database Syst Rev 2015

Comparison of WHO (2003), FAO (2008), Nordic (2012/13)

	WHO (2003)	FAO ** (2008)	NORDIC (2012/13)
Total fat (%)	15-30%	(15) 20-35%	25-40%
Saturated fatty acids	<10%	<10%	<10%
Unsat fatty acids			
Cis PUFA	6-10%	6-11%	5-10% *
n-6	5-8%	2.5-9%	Not specified
n-3	1-2%	0.5 – 2%	Not specified
Cis MUFA	By difference	By difference	10-20%
trans	<1%	<1%	As low as possible
Cholesterol	<300mg		

* at least 1% n-3 PUFA: ** WHO withdrew support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BMJ 2017;357:j2241 doi: 10.1136/bmj.j2241 (Published 2017 May 10)

RESEARCH NEWS

Red meat consumption is linked to higher risk of death from most major causes

Zosia Kmietowicz

The BMJ

RESEARCH

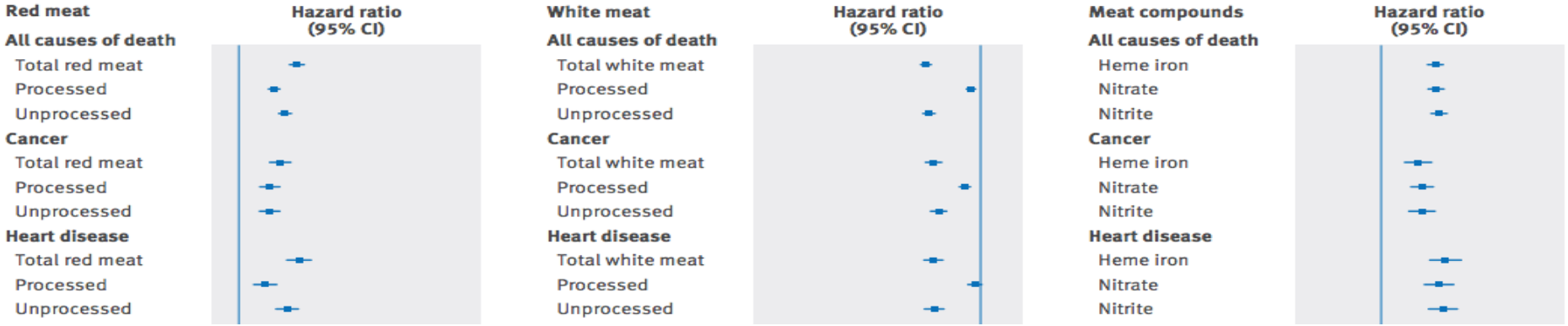
OPEN ACCESS

Mortality from different causes associated with meat, heme iron, nitrates, and nitrites in the NIH-AARP Diet and Health Study: population based cohort study

Arash Etemadi, Rashmi Sinha, Mary H Ward, Barry I Graubard, Maki Inoue-Choi, Sanford M Dawsey, Christian C Abnet

BMJ 2017;357:j1957http://dx.doi.org/10.1136/bmj.j1957

Fig 1. Association between intake of different types of red meat, different types of white meat, & meat associated compounds & mortality in NIH-AARP Diet & Health Study



BMJ 2017;357:j1957http://dx.doi.org/10.1136/bmj.j1957

BMJ 2017;357:j2190 doi: 10.1136/bmj.j2190 (Published 9 May 2017)

EDITORIALS

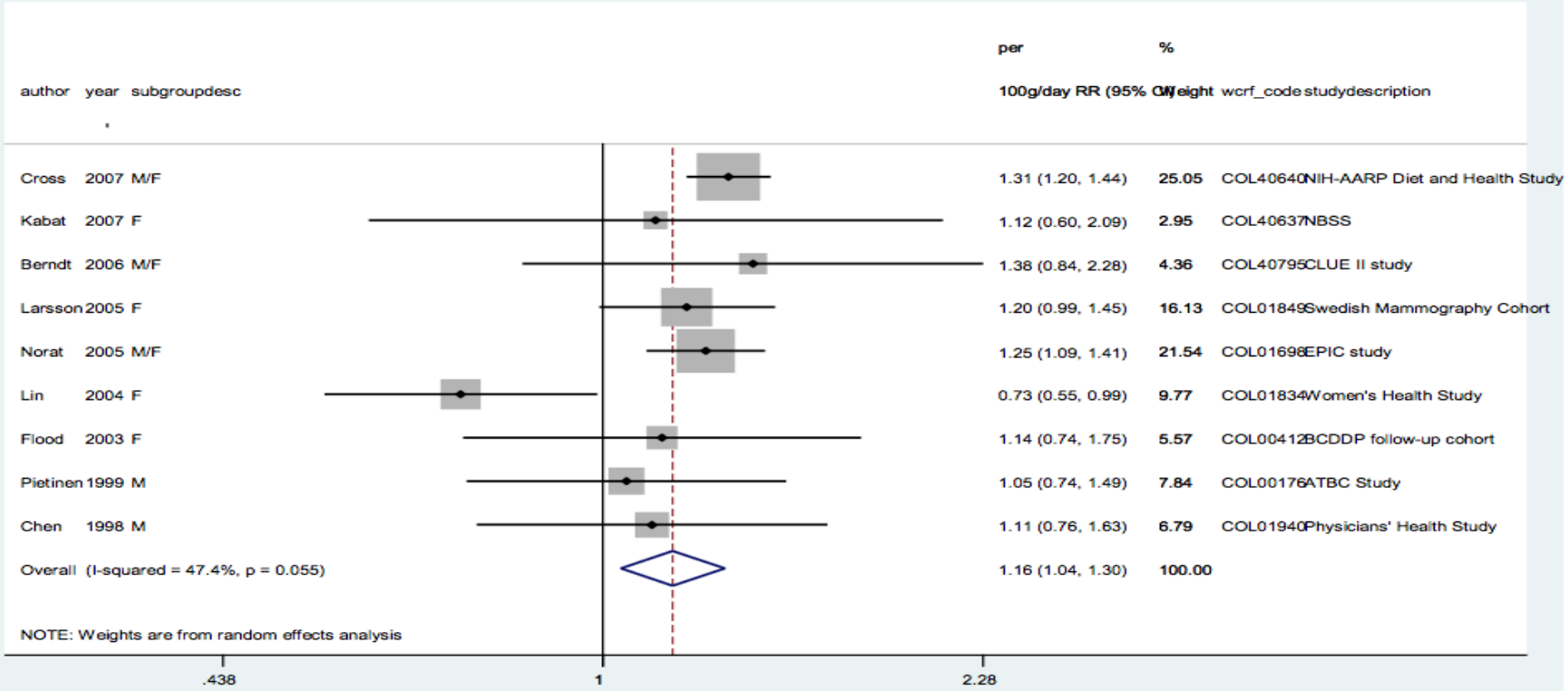
Red and processed meat, and human and planetary health

Contemporary meat consumption harms human health and is equally bad for the planet

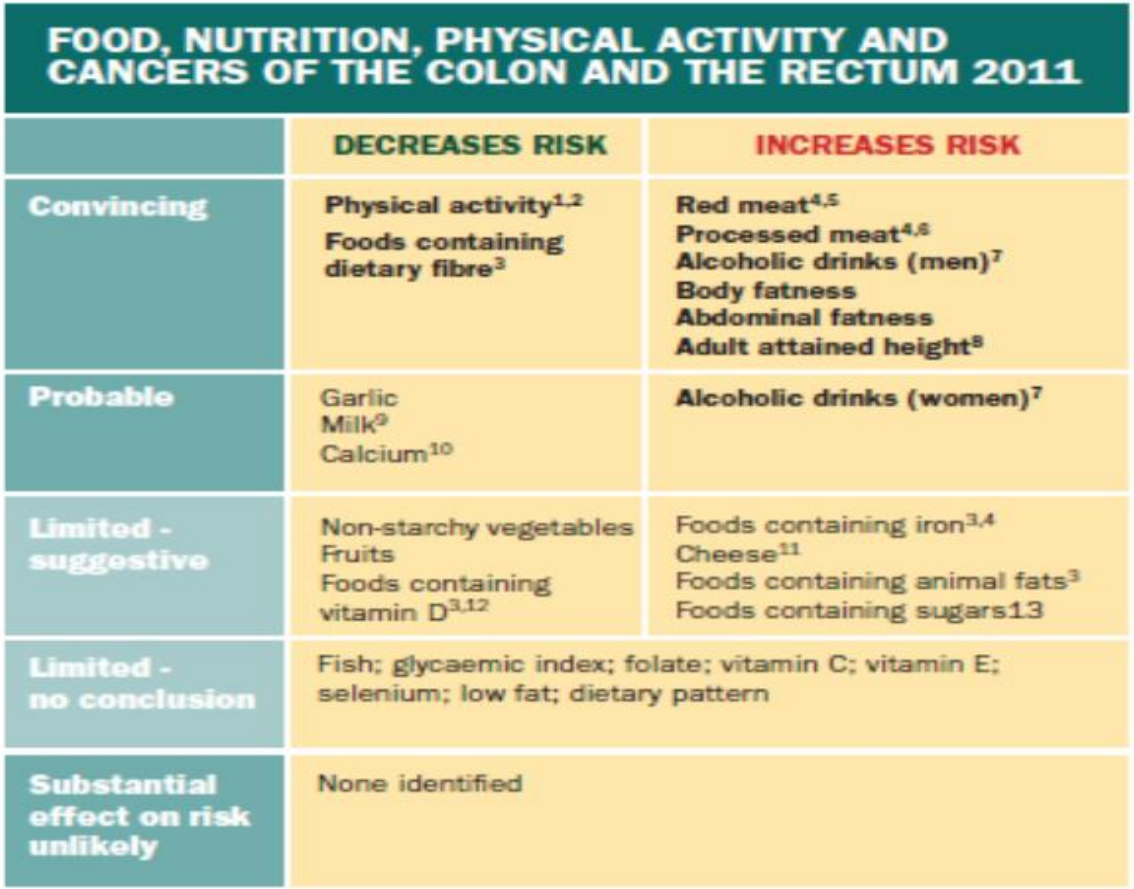
John D Potter *professor of epidemiology*

Centre for Public Health Research, Massey University, Wellington, New Zealand

Figure 47 Dose-response meta-analysis of red and processed meat and colorectal cancer – per 100g/d



World Cancer Research Fund (WCRF). Continuous Update Project Report, 2011



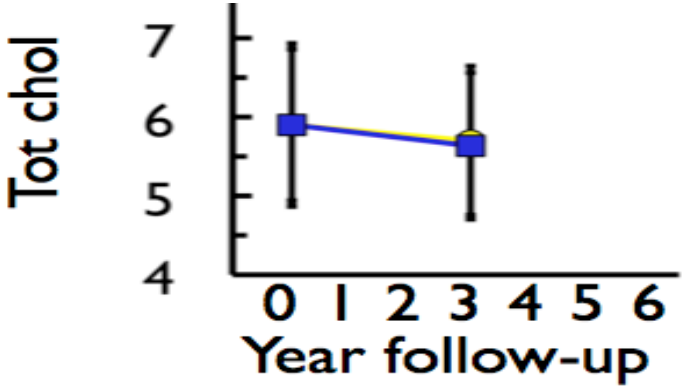
FOOD, NUTRITION, PHYSICAL ACTIVITY AND CANCERS OF THE COLON AND THE RECTUM 2011		
	DECREASES RISK	**INCREASES RISK**
Convincing	**Physical activity[1,2]** **Foods containing dietary fibre[3]**	**Red meat[4,5]** **Processed meat[4,6]** **Alcoholic drinks (men)[7]** **Body fatness** **Abdominal fatness** **Adult attained height[8]**
Probable	Garlic Milk[9] Calcium[10]	**Alcoholic drinks (women)[7]**
Limited - suggestive	Non-starchy vegetables Fruits Foods containing vitamin D[3,12]	Foods containing iron[3,4] Cheese[11] Foods containing animal fats[3] Foods containing sugars13
Limited - no conclusion	Fish; glycaemic index; folate; vitamin C; vitamin E; selenium; low fat; dietary pattern	
Substantial effect on risk unlikely	None identified	

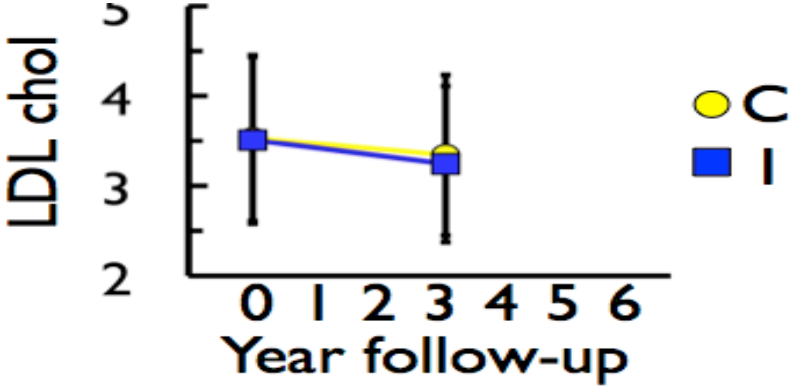
World Cancer Research Fund (WCRF). Continuous Update Project Report, 2011

Nutrition recommendations must consider totality of evidence and utilise standard procedures for assessing quality and importance

Anecdotal evidence and social media have the potential to generate advice which may be detrimental to human health

WHI plasma cholesterol (mmol/L)





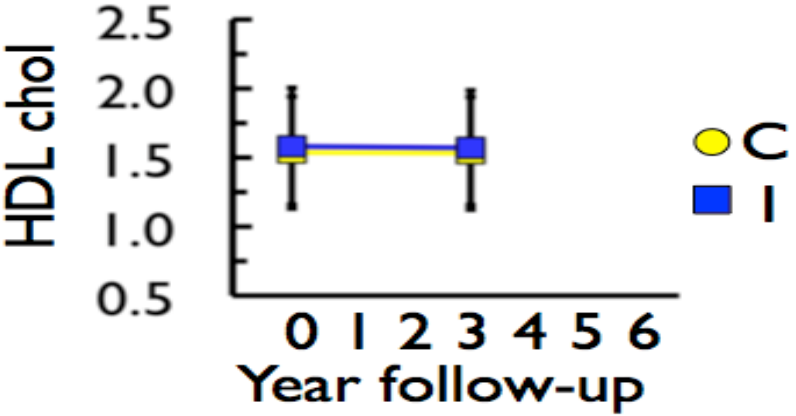


Fig.3 Effects on CDH risk of consuming PUFA, CHO, or MUFA in place of SFA

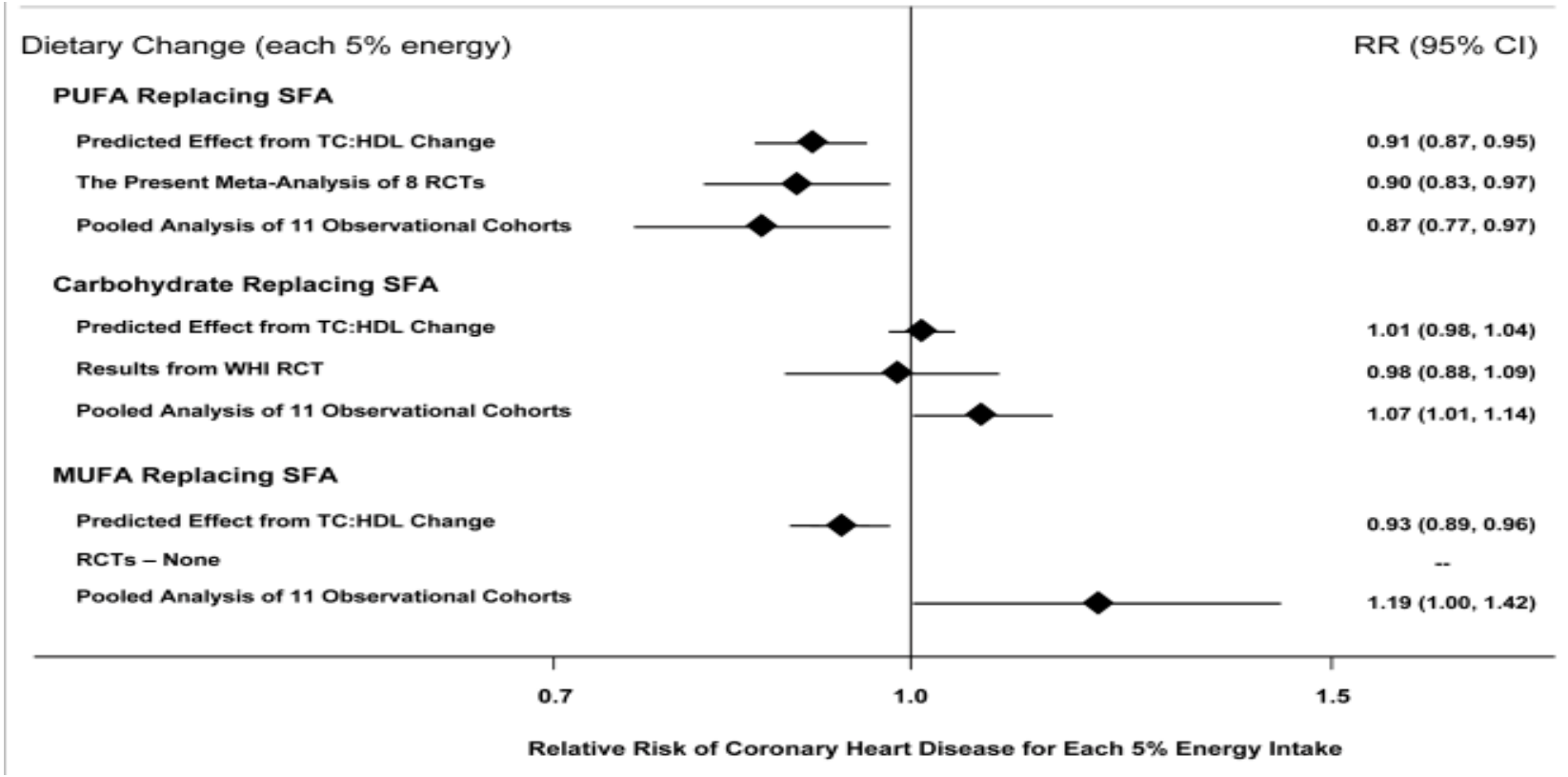


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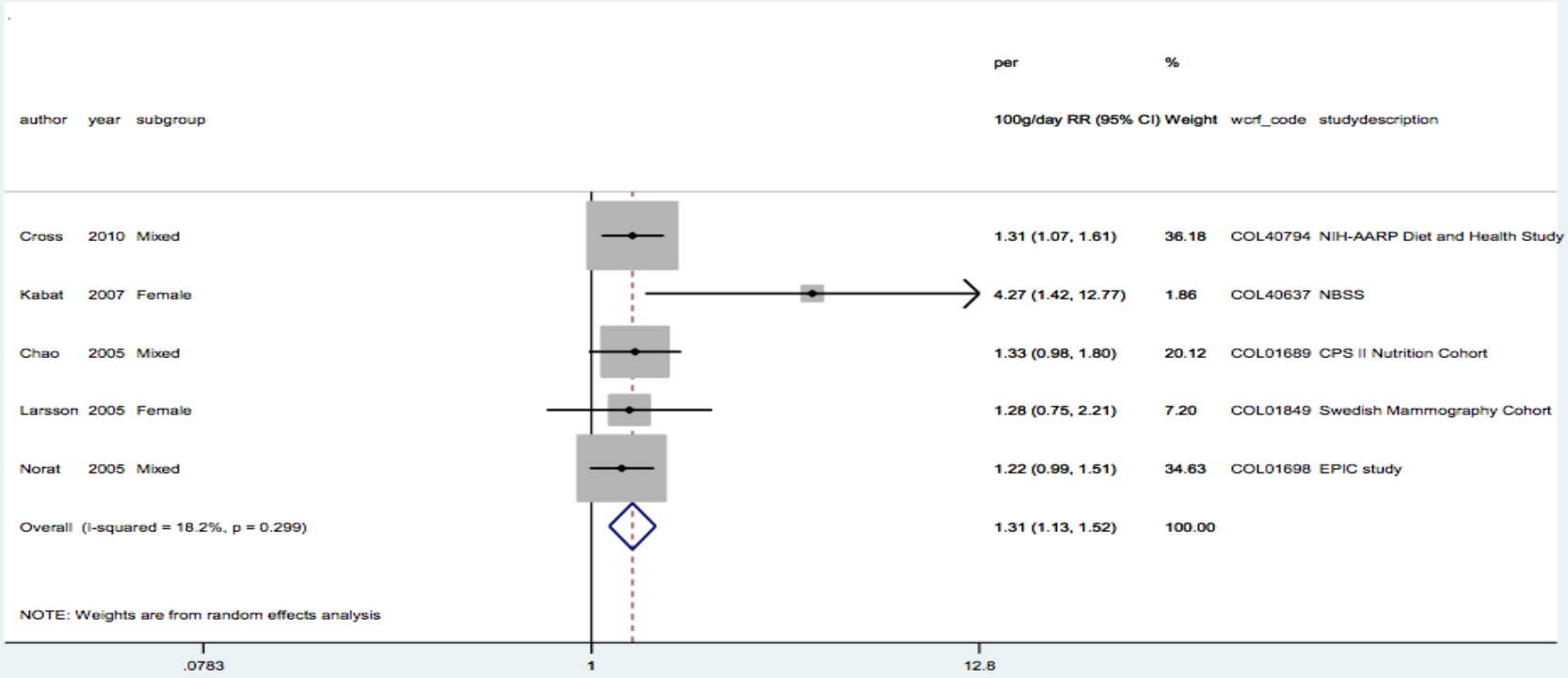
Figure 55 Dose-response meta-analysis of red and processed meat and rectal cancer



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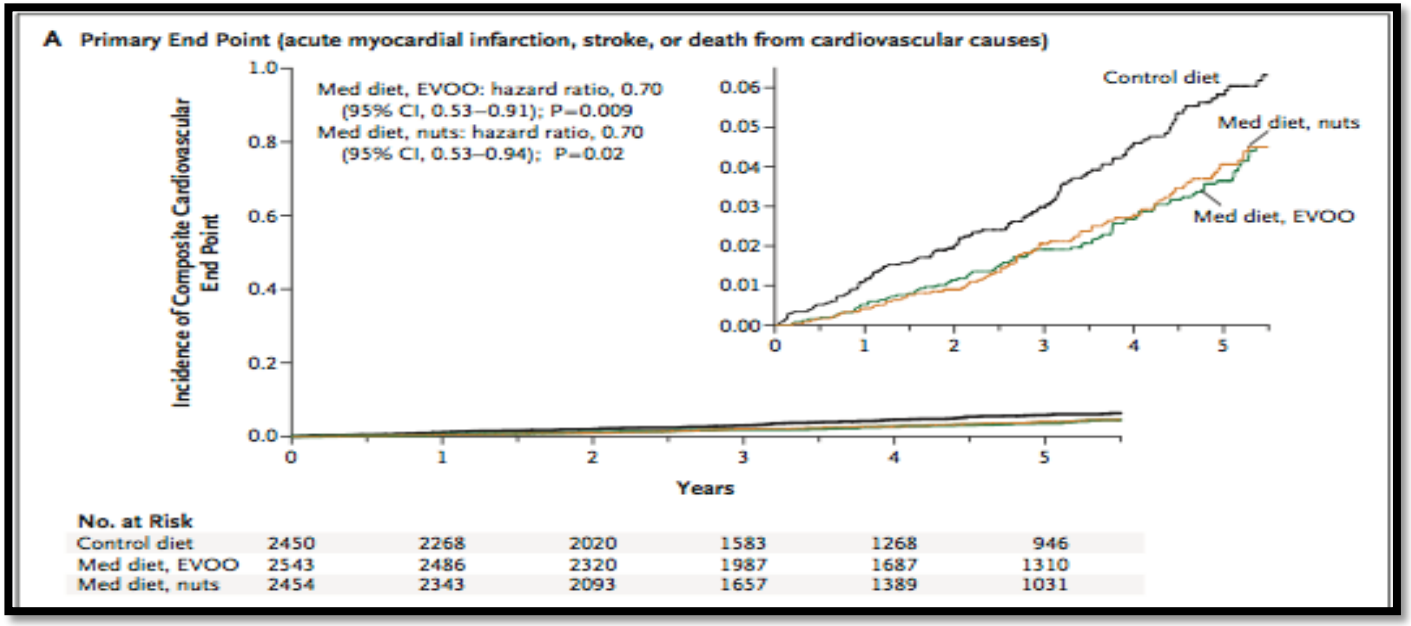

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