THE GOOD, THE BAD, AND THE UGLY FATS

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Vegetable Oil Composition (approximations)

	Saturated %	Monosaturated %	Polyunsaturated %
Soybean Oil	18	24	58
Canola Oil	6	67	27
Grapeseed Oil	10	16	70
Olive Oil	17	74	9
Coconut Oil	53	37	10
Palm Oil	53	37	10
Beef	50	45	5
Chicken Breast	30	18	52
Fish	40	39	21
Milk (Whole)	62	30	4

AGEs= Glucose + Protein

- Glyceraldehyde + glucose + lipids + protein
- Glycolaldehyde + protein + lipid
- Methyl glyoxal + protein + lipid
- Acetaldehyde + protein + lipid

- Formation of AGES pathways
  - Maillard: amino group + glucose → Schiff Base → Amadori product → AGEs
  - Polyol:sorbitol → fructose → oxoaldehydes → AGEs
  - Lipid peroxidation → AGEs

What are AGEs?

- Advanced glycation end products (AGEs) are harmful molecules produced in the body during metabolic processes
  - AGEs promote
    - Oxidative stress
    - Inflammation
    - Apoptosis (cell injury and destruction)
    - Premature aging
    - Cardiovascular disease
    - Fatty liver disease
    - Neurodegenerative disease
    - Hypertension
    - Renal failure
    - Insulin resistance and pancreatic cell dysfunction

Damage by AGEs

- AGEs causes cellular damage, including:
  - Mitochondrial dysfunction
  - Promotion of ROS (reactive oxygen species)
  - Production of Nitrogen Reactive species
  - Nuclear factor kappa beta stimulation (NFk-beta), leading to inflammatory cellular response
  - Sirtuin-1, aging

- Extracellular damage affects:
  - Maturation of protein in walls
  - Collagen loss
  - Elastic tissue loss

Formation of AGEs Pathways

- Maillard reaction
- Polyol pathway (fructose production from glucose)
- Lipid peroxidation (of polyunsaturated fats)

Maillard Pathway

- Amino group of a protein molecule + glucose combined to make AGEs: Maillard reaction
- Polyol pathway: sorbitol → fructose → oxoaldehyde, results in AGEs
- Lipid peroxidation enhances AGEs

Methylglyoxal

- Drives Millard reaction 250x faster than glucose
- Derived from the breakdown of glycated proteins
- Produced in cooking and storage
- Produced with alcohol consumption and making
- Microbial fermentation

Endogenous AGEs

- Diabetes Mellitus e.g. Hemoglobin A1c
- CRF (lack of excretion of waste products)
- Liver disease
- Alcohol
- Cigarettes
- High Omega 6 fatty acid diet

Endogenous AGEs

- Endogenous AGEs: MOST IMPORTANT TO KEEP GLUCOSE LOW
- Continuous glucose monitoring can most effectively tell you which foods are causing a glucose spike thereby causes AGEs
- Another way to reduce endogenous AGEs is **FASTING**

- AGEs from Exogenous sources: Cooking and storing food and beverages
  - 90% end up in colon, affecting microbiome
  - 10% are absorbed into the body
  - 30% are excreted in the urine
  - 60% of what is absorbed, ends up in the tissues

Inhibitors of AGEs

Synthetic

Metformin

NSAIDs

Benfotiamine

Pyridoxamine

Naringenine

Hesperidin

Natural

Curcumin

Alpha lipoic acid

Flavanoids

Ginko

Celery

Red pepper

Parsely

Chamomile

Mint

Green Tea

Exogenous AGEs

- Frying
- Broiling
- Blackening
- Charring
- Baking
- Cereals

Damages by AGEs

- Cellular damage effects:
  - Mitochondrial dysfunction
  - Production of reactive oxygen species
  - Production of Nitrogen reactive species
  - Nuclear Factor kappa-Beta stimulation
  - Sirtuim-1 aging
- Extracellular damage:
  - Matrix proteins results in collagen loss
  - Elastic tissue loss

High vs. Low AGEs

High

- Animal foods
- Processed foods
- Dry/Direct heat cooking
  - Broiling
  - Air frying
  - Grilling
  - Roasting
  - BBQ
  - Baking

Low

- Naturally high carb foods
- Naturally high-water content foods
- High phytonutrients
- Raw, uncooked vegetables

AGEs

- Burgers and chicken nuggets: 7,800
- Processed cheese: 8,700
- Breakfast bar: 2,200
- Tofu: 5,900
- Butter: 26,000 in 3oz
- Margarine: 7,000
- Peanut butter: 7,000
- Fried chicken: 8,000 (poached is <1,100 and raw chicken is <800)
- Bacon: fried with no oil 90,000 in 3oz

Daily recommended AGEs limit: 15,000

Category/Food Item	Cooking Method	AGE (kU/100g)
Beef	Boiled	1538
	Roasted	6071
	Grilled	7416
	Broiled	11270
Poultry	Poached	1101
	Pan fried	4938
	Roasted and BBQ	18520
Salmon	Microwave	912
	Boiled	1082
	Broiled	3347
	Pan-fried	3083
Eggs	Poached	90
	Omelet, Pan	507
	Fried	2749
Cheese	American	8700

Food Group	Food Item	AGE (kU/serving)
Grains	Whole wheat bread	36
	Biscuit, oven baked	441
	Chips	865
Fruits/Vegies	Apple fresh	13
	Apple baked	45
	Eggplant, raw	116
	Eggplant, grilled	256
Milk	Milk, fat free	2
	Milk, whole	12
	Evaporated milk	86

Heating Oils- Not A Good Thing

- Worse for polyunsaturated fats
  - Because they breakdown into 24-decadienal (an aldehyde)
  - Easily oxidized in the body and hence alter out physiology leading to pro-inflammatory state
  - Best to worst:
    - Olive> Peanut> Canola> Corn> Soy> Sunflower> Safflower
- BEST temperature for frying 180-190°C (356-374 °F)
- AVOID smoke-point heating
  - It breaks down fats and triglycerols to free fatty acids + glycerol
  - Free fatty acids (FFA) are not good for you
  - Acrolein, a toxic substance, is produced at high temperatures

Heating Oils- Not A Good Thing

- Repeated heating of oil
  - Not good
  - Created FFA
  - Lowers smoke-point further
- Bad oils for frying
  - Soybean oil
  - Corn oil
  - Canola oil
  - Cottonseed oil
  - Safflower seed oil
- Transfats created by repeated heating of vegetable oils

	Smoke Point °C	Smoke Point °F
Butter	150	302
Coconut Oil	150	302
Peanut Oil	150	302
Lard	190	374
Olive Oil	200	392
Refined Coconut Oil	230	446
Ghee	250	482
Avocado Oil	270	518

Excess Linoleic Acid Syndrome

- Epidemic of this today because of our increased intake of vegetable oils- mostly due to processed food industry
- High Omega 6/Omega 3 ratio >1, nowadays >10!
- Causes high Arachidonic acid/ Omega 3 ratio
- Causes persistent inflammation
- Above is not supported by AHA/WHO
- Composition of cell membranes in ALL ORGANS, TISSUES, LDL and RBC's change, causing dysfunction
- LINOLEIC ACID found in SEED OILS
  - Normal levels were <20, now changed to <30!!

Transfats

- 1910- all partially hydrogenated vegetable seed oils are created to be SOLID at room temperature and MELTS in your mouth
  - Perfect for processed food preservation, shelf-life and sales.
- They are ANTI-PROSTACYCLINE
  - Cause vasoconstriction
  - Cause leukocyte adhesion
  - Cause platelet activation
  - Inhibit ARACHIDONIC ACID conversion to PROCYCLINES and Omega-3
  - Increase calcium intake into cells
- RESULTS: Endothelial cell wall dysfunction leading to CAD and cause FATTY LIVER

Vegetable Oils in Vitamin K2 Deficiency

- Soybean oil and Canola oil have HIGH vitamin K1, and some gets converted to K2 in tissues, although K1 causes CLOTS
  - Hydrogenation of soybean oil, canola oil causes increased Transfats but also DIHYDRO K1, which antagonizes vitamin K2 causing vitamin K2 deficiency (inhibits matrix gLA proteins + osteocalcin) causes non-osseous VASCULAR CALCIFICATION
  - DIHYDRO K1 inhibits testosterone production!!
  - Therefore, seed oils are linked to LOW TESTOSTERONE

Seed Oil	Phytosterol content (mg/100g)
Olive Oil	288
Soy Oil	355
Rapeseed Oil	893
Corn Oil	990

- Foods. 2019. Aug 9: 344

Saturated Fats have Different Effect on LDL

- Olive oil: LDL↓
- Coconut oil: LDL↓
- Butter: LDL↑

- BMS 2018. Mar 6; 8(3)

Use of dietary linoleic acid for secondary prevention of coronary heart disease and death: evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis

Abstract

Objective To evaluate the effectiveness of replacing dietary saturated fat with omega 6 linoleic acid, for the secondary prevention of coronary heart disease and death.

Design Evaluation of recovered data from the Sydney Diet Heart Study, a single blinded, parallel group, randomized controlled trial conducted in 1966-73; and an updated meta-analysis including these previously missing data.

Setting Ambulatory, coronary care clinic in Sydney, Australia.

Participants 458 men aged 30-59 years with a recent coronary event.

Interventions Replacement of dietary saturated fats (from animal fats, common margarines, and shortenings) with omega 6 linoleic acid (from safflower oil and safflower oil polyunsaturated margarine). Controls received no specific dietary instruction or study foods. All non-dietary aspects were designed to be equivalent in both groups.

Outcome measures All cause mortality (primary outcome), cardiovascular mortality, and mortality from coronary heart disease (secondary outcomes). We used an intention to treat, survival analysis approach to compare mortality outcomes by group.

Results The intervention group (n=221) had higher rates of death than controls (n=237) (all cause 17.6% *v* 11.8%, hazard ratio 1.62 (95% confidence interval 1.00 to 2.64), P=0.05; cardiovascular disease 17.2% *v* 11.0%, 1.70 (1.03 to 2.80), P=0.04; coronary heart disease 16.3% *v* 10.1%, 1.74 (1.04 to 2.92), P=0.04). Inclusion of these recovered data in an updated meta-analysis of linoleic acid intervention trials showed non-significant trends toward increased risks of death from coronary heart disease (hazard ratio 1.33 (0.99 to 1.79); P=0.06) and cardiovascular disease (1.27 (0.98 to 1.65); P=0.07).

Conclusions Advice to substitute polyunsaturated fats for saturated fats is a key component of worldwide dietary guidelines for coronary heart disease risk reduction. However, clinical benefits of the most abundant polyunsaturated fatty acid, omega 6 linoleic acid, have not been established. In this cohort, substituting dietary linoleic acid in place of saturated fats increased the rates of death from all causes, coronary heart disease, and cardiovascular disease. An updated meta-analysis of linoleic acid intervention trials showed no evidence of cardiovascular benefit. These findings could have important implications for worldwide dietary advice to substitute omega 6 linoleic acid, or polyunsaturated fats in general, for saturated fats.

- *BMJ* 2013;346:e8707

Use of dietary linoleic acid for secondary prevention of coronary heart disease and death: evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis

Tables

Table 1| **Content of n-6 LA and n-3 α LNA in commercially available edible oils**

Cooking oil	LA (g per 100 g of cooking oil)	α LNA (g per 100 g of cooking oil)
Vegetable oil*	Depends on specific oil	Depends on specific oil
Safflower†	74.6	0.0
Sunflower†	65.7	0.0
Cottonseed	51.5	0.0
Corn	53.5	0.2
Soybean	50.3	7.0
Canola	18.6	9.1
Olive	9.8	0.8
Butter oil	2.3	1.4
Coconut	1.8	0.0

n-6 LA=omega 6 linoleic acid; n-3 α LNA=omega 3 α linolenic acid. Fatty acid contents of oils vary to some extent by season, latitude, and other conditions. USDA National Nutrient Database numbers: safflower 04510, sunflower 04510, cottonseed 04502, corn 04518, soybean 04669, canola 04582, olive 04053, butter 01003, coconut 04047.[9]

*Food items labeled "vegetable oil" may contain one or more of the above oils.

†Varieties of safflower and sunflower oils with lower LA content are commercially available.

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Table 3| **Baseline and follow-up dietary data in the SDHS, for 426 participants with baseline and at least one follow-up diet record**

	Baseline*		Follow-up†				
Nutrient	Control (n=221)	Intervention (n=205)	Control (n=221)	Change from baseline	Intervention (n=205)	Change from baseline	P
PUFA‡	6.2 (3.2-9.2)	6.1 (3.0-9.2)	8.4 (6.7-10.9)	+2.2	15.4 (12.3-17.9)	+9.3§	<0.001
SFA‡	15.6 (13.0-18.7)	16.2 (13.4-19.3)	13.5 (11.4-15.6)	−2.1	9.3 (8.2-10.9)	−6.9	<0.001
PUFA:SFA ratio	0.41 (0.18-0.68)	0.38 (0.16-0.65)	0.63 (0.45-0.92)	+0.22	1.72 (1.31-2.08)	+1.34	<0.001
MUFA‡	14.7 (12.8-16.9)	14.6 (13.2-16.5)	14.0 (12.3-15.2)	−0.7	11.2 (10.1-12.7)	−3.4	<0.001
Total fat‡	39.2 (35.0-43.5)	40.2 (36.6-43.4)	38.1 (34.3-41.2)	−1.1	38.3 (36.1-46.3)	−1.9	0.87
Carbohydrate‡	40.5 (37.0-45.2)	39.9 (35.2-46.1)	40.6 (35.6-44.8)	+0.1	41.3 (36.1-46.3)	+1.4	0.31
Protein‡	14.1 (12.4-16.3)	14.4 (12.6-16.5)	15.3 (13.4-17.3)	+1.2	14.8 (13.4-16.8)	+0.4	0.25
Alcohol‡	2.3 (0.0-8.1)	2.4 (0.0-8.9)	4.0 (0.9-8.7)	+1.7	3.1 (0.7-8.9)	+0.7	0.42
Energy (kcal/day; 1 kcal=4.18 kJ)	2384 (2072-2770)	2423 (1972-2860)	2194 (1804-2524)	−190	2256 (1958-2574)	−167	0.07
Cholesterol (mg/day)	439 (344-593)	477 (355-621)	331 (269-408)	−108	238 (203-283)	−239	<0.001

*Data are median (interquartile range) from a single seven day food record administered before randomization.

†Data are median summaries (interquartile range), with each participant assigned one value based on the average of their seven day food records after randomization. Comparisons between diets were calculated with the Mann Whitney U test.

‡Data are percentage of food energy.

§From safflower oil.

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Table 4| **Risk factors for cardiovascular disease**

	Baseline		12 month follow-up		
	Control (n=237)	Intervention (n=221)	Control (n=192)	Intervention (n=179)	P*
Total cholesterol (mg/dL; 1 mg/dL=0.026 mmol/L)	282.0 (274.8 to 289.1)	281.3 (272.9 to 289.7)	266.5 (259.1 to 273.8)	243.9 (237.4 to 250.4)	<0.001
Triglycerides (mg/dL; 1 mg/dL=0.011 mmol/L)	185.9 (168.8 to 202.9)	189.0 (162.6 to 215.4)	151.8 (133.9 to 169.7)	135.5 (126.0 to 145.1)	0.06
Body mass index	25.4 (25.1 to 25.8)	25.1 (24.8 to 25.3)	24.5 (24.1 to 24.9)	24.3 (24.0 to 24.6)	0.26
Systolic blood pressure (mm Hg)	136.9 (134.2 to 139.6)	136.6 (133.9 to 139.3)	136.5 (133.4 to 139.5)	136.4 (133.8 to 139.0)	0.49
Diastolic blood pressure (mm Hg)	88.5 (86.9 to 90.0)	88.5 (86.9 to 90.2)	87.9 (86.0 to 89.9)	87.5 (85.7 to 89.3)	0.38

Data are mean (95% confidence interval) at baseline and 12 months after randomization.

*P values=between group differences, assessed by *t* test.

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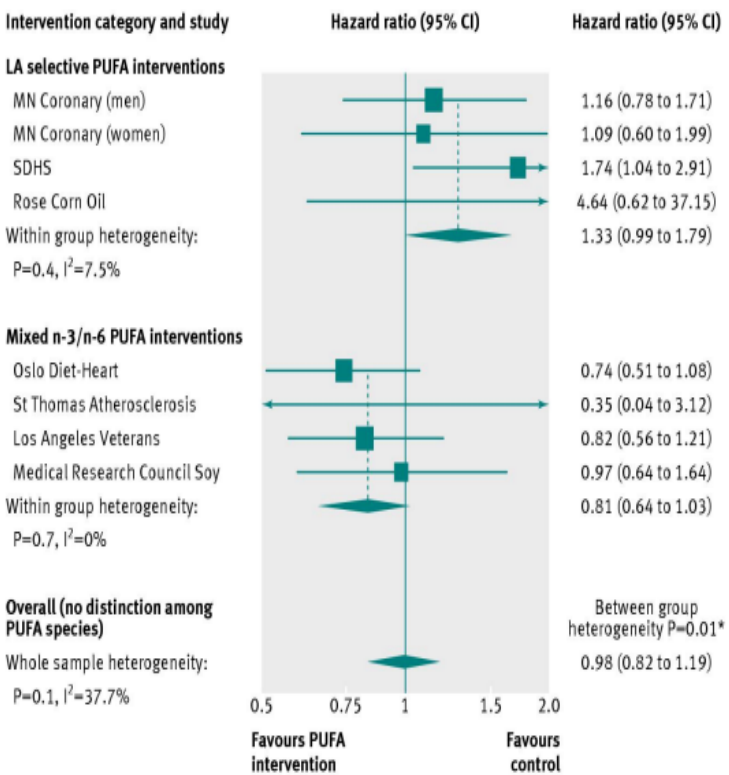

Fig 3 Updated meta-analysis of effects of LA selective interventions and mixed n-3/n-6 PUFA interventions on risk of death from coronary heart disease. LA selective interventions selectively increased n-6 LA without a concurrent increase in n-3 PUFAs. Mixed PUFA interventions increased n-3 PUFAs and n-6 LA. PUFA interventions replaced high SFA control diets in each trial. *Significant heterogeneity between groups. Full methods and results in part 8 of the web appendix

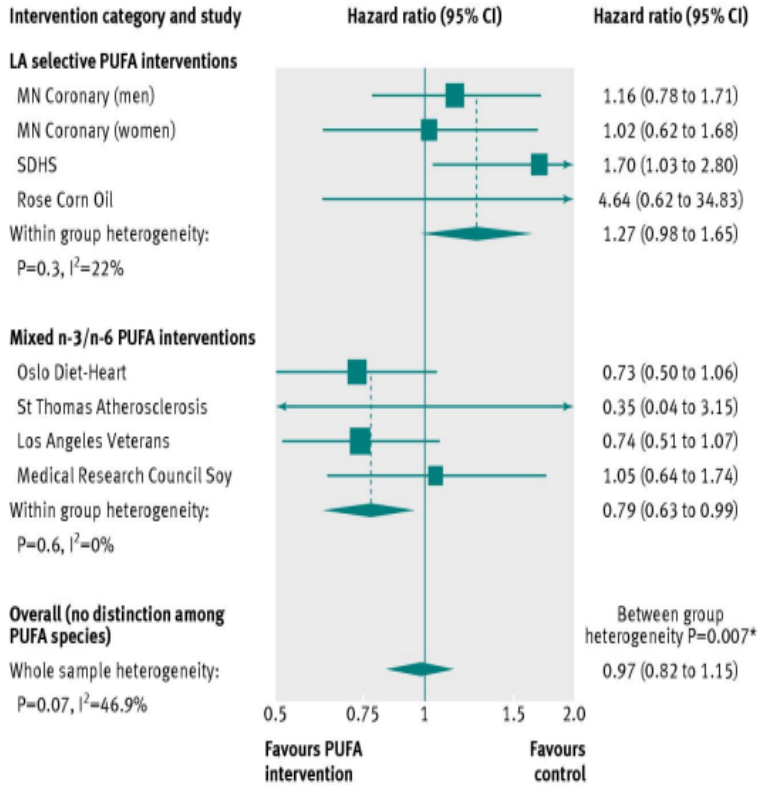

Fig 4 Updated meta-analysis of effects of LA selective interventions and mixed n-3/n-6 PUFA interventions on risk of cardiovascular death. LA selective interventions selectively increased n-6 LA without a concurrent increase in n-3 PUFAs. Mixed PUFA interventions increased n-3 PUFAs and n-6 LA. PUFA interventions replaced high SFA control diets in each trial. *Significant heterogeneity between groups. Full methods and results in part 8 of the web appendix

- *BMJ* 2013;346:e8707

Test of Effect of Lipid Lowering by Diet on Cardiovascular Risk

The Minnesota Coronary Survey

Ivan D. Frantz Jr., Emily A. Dawson, Patricia L. Ashman, Laël C. Gatewood, Glenn E. Bartsch, Kanta Kuba, and Elizabeth R. Brewer

The Minnesota Coronary Survey was a 4.5-year, open enrollment, single end-time, double-blind, randomized clinical trial that was conducted in six Minnesota state mental hospitals and one nursing home. It involved 4393 institutionalized men and 4664 institutionalized women. The trial compared the effects of a 39% fat control diet (18% saturated fat, 5% polyunsaturated fat, 16% monounsaturated fat, 446 mg dietary cholesterol per day) with a 38% fat treatment diet (9% saturated fat, 15% polyunsaturated fat, 14% monounsaturated fat, 166 mg dietary cholesterol per day) on serum cholesterol levels and the incidence of myocardial infarctions, sudden deaths, and all-cause mortality. The mean duration of time on the diets was 384 days, with 1568 subjects consuming the diet for over 2 years. The mean serum cholesterol level in the pre-admission period was 207 mg/dl, falling to 175 mg/dl in the treatment group and 203 mg/dl in the control group. For the entire study population, no differences between the treatment and control groups were observed for cardiovascular events, cardiovascular deaths, or total mortality. A favorable trend for all these end-points occurred in some younger age groups.
(Arteriosclerosis 9:129–135, January/February 1989)

Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968-73)

Christopher E Ramsden,[1,2] Daisy Zamora,[3] Sharon Majchrzak-Hong,[1] Keturah R Faurot,[2] Steven K Broste,[4] Robert P Frantz,[5] John M Davis,[3,6] Amit Ringel,[1] Chirayath M Suchindran,[7] Joseph R Hibbeln[1]

Objective: To examine the traditional diet-heart hypothesis through recovery and analysis of previously unpublished data from the Minnesota Coronary Experiment (MCE) and to put findings in the context of existing diet-heart randomized controlled trials through a systematic review and meta-analysis.

Conclusions: Available evidence from randomized controlled trials shows that replacement of saturated fat in the diet with linoleic acid effectively lowers serum cholesterol but does not support the hypothesis that this translates to a lower risk of death from coronary heart disease or all causes. Findings from the Minnesota Coronary Experiment add to growing evidence that incomplete publication has contributed to overestimation of the benefits of replacing saturated fat with vegetable oils rich in linoleic acid.

Associations of fat and carbohydrate intake with cardiovascular disease and mortality: prospective cohort study of UK Biobank participants

Frederick K Ho,[1] Stuart R Gray,[2] Paul Welsh,[2] Fanny Petermann-Rocha,[1,2] Hamish Foster,[1] Heather Waddell,[2] Jana Anderson,[1] Donald Lyall,[1] Naveed Sattar,[2] Jason M R Gill,[2] John C Mathers,[3] Jill P Pell,[1] Carlos Celis-Morales[1,2,4,5]

Objective: To investigate the association of macronutrient intake with all cause mortality and cardiovascular disease (CVD), and the implications for dietary advice.

Results: 4780 (2.4%) participants died over a mean 10.6 (range 9.4-13.9) years of follow-up, and 948 (0.5%) and 9776 (5.0%) experienced fatal and non-fatal CVD events, respectively, over a mean 9.7 (range 8.5-13.0) years of follow-up. Non-linear associations were found for many macronutrients. Carbohydrate intake showed a non-linear association with mortality; no association at 20-50% of tota energy intake but a positive association at 50-70% of energy intake (3.14 *v* 2.75 per 1000 person years, average hazard ratio 1.14, 95% confidence interval 1.03 to 1.28 (60-70% *v* 50% of energy)). A similar pattern was observed for sugar but not for starch or fibre. A higher intake of monounsaturatec fat (2.94 *v* 3.50 per 1000 person years, average hazard ratio 0.58, 0.51 to 0.66 (20-25% *v* 5% of energy)) and lower intake of polyunsaturated fat (2.66 *v* 3.04 per 1000 person years, 0.78, 0.75 to 0.81 (5-7% *v* 12% of energy)) and saturated fat (2.66 *v* 3.59 per 1000 person years, 0.67, 0.62 to 0.73 (5-10% *v* 20% of energy)) were associated with a lower risk of mortality. A dietary risk matrix was developed to illustrate how dietary advice can be given based on current intake.

Conclusion: Many associations between macronutrient intake and health outcomes are non-linear. Thus dietary advice could be tailored to current intake. Dietary guidelines on macronutrients (eg, carbohydrate) should also take account of differential associations of its components (eg, sugar and starch).

Hiding unhealthy heart outcomes in a low-fat diet trial: the Women's Health Initiative Randomized Controlled Dietary Modification Trial finds that postmenopausal women with established coronary heart disease were at increased risk of an adverse outcome if they consumed a low-fat 'heart-healthy' diet

Timothy David Noakes

Abstract

The Women's Health Initiative Randomized Controlled Dietary Modification Trial (WHIRCDMT) was designed to test whether the US Department of Agriculture's 1977 Dietary Guidelines for Americans protects against coronary heart disease (CHD) and other chronic diseases. The only significant finding in the original 2006 WHIRCDMT publication was that postmenopausal women with CHD randomised to a low-fat 'heart-healthy' diet in 1993 were at 26% greater risk of developing additional CHD events compared with women with CHD eating the control diet. A 2017 WHIRCDMT publication includes data for an additional 5 years of follow-up. It finds that CHD risk in this subgroup of postmenopausal women had increased further to 47%–61%. The authors present three post-hoc rationalisations to explain why this finding is 'inadmissible': (1) only women in this subgroup were less likely to adhere to the prescribed dietary intervention; (2) their failure to follow the intervention diet increased their CHD risk; and (3) only these women were more likely to not have received cholesterol-lowering drugs. These rationalisations appear spurious. Rather these findings are better explained as a direct consequence of postmenopausal women with features of insulin resistance (IR) eating a low-fat high-carbohydrate diet for 13 years. All the worst clinical features of IR, including type 2 diabetes mellitus (T2DM) in some, can be 'reversed' by the prescription of a high-fat low-carbohydrate diet. The Women's Health Study has recently reported that T2DM (10.71-fold increased risk) and other markers of IR including metabolic syndrome (6.09-fold increased risk) were the most powerful predictors of future CHD development in women; blood low-density lipoprotein-cholesterol concentration was a poor predictor (1.38-fold increased risk). These studies challenge the prescription of the low-fat high-carbohydrate heart-healthy diet, at least in postmenopausal women with IR, especially T2DM. According to the medical principle of 'first do no harm', this practice is now shown to be *not* evidence-based, making it scientifically unjustifiable, perhaps unethical.

Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial

Objective: To test the hypothesis that a dietary intervention, intended to be low in fat and high in vegetables, fruits, and grains to reduce cancer, would reduce CVD risk.

Conclusions: Over a mean of 8.1 years, a dietary intervention that reduced total fat intake and increased intakes of vegetables, fruits, and grains did not significantly reduce the risk of CHD, stroke, or CVD in postmenopausal women and achieved only modest effects on CVD risk factors, suggesting that more focused diet and lifestyle interventions may be needed to improve risk factors and reduce CVD risk.

- JAMA. 2006 Feb 8;295(6):655-66