Nutrition & Cardiovascular Disease

Scientific Review of the Trials with Clinical Application and Case Presentations

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Objectives

1. To understand the role of **nutrition and dietary patterns in a lifestyle approach** for prevention and treatment of cardiovascular disease.
2. To understand how **specific macronutrients, micronutrients, and phytonutrients** impact prevention and treatment of cardiovascular disease.
3. To understand how **certain foods and actives** assist in cardiovascular disease prevention and treatment.
4. To understand the **scientific rationale and mechanisms** for clinical application of nutritional therapy in cardiovascular disease.

Overview

1. General dietary patterns and CVD
2. Macronutrients (protein/CHO/fat)
3. Micronutrients & phytonutrients
4. Clinical recommendations

6 Healing the Heart with Whole Foods and Food Bioactives

Deanna Minich and Benjamin Brown

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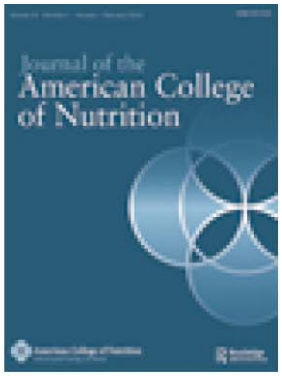

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Recent Science and Clinical Application of Nutrition to Coronary Heart Disease

Mark Houston, Deanna Minich, Stephen T. Sinatra, Joel K. Kahn & Mimi Guarneri

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Published online: 09 Jan 2018.

Dietary Patterns
&
Cardiovascular Disease

2015-2020 Dietary Guidelines for Americans

1. **Follow a healthy eating pattern across the lifespan.** All food and beverage choices matter. Choose a healthy eating pattern at an appropriate calorie level to help achieve and maintain a healthy body weight, support nutrient adequacy, and reduce the risk of chronic disease.
2. **Focus on variety, nutrient density, and amount.** To meet nutrient needs within calorie limits, choose a variety of nutrient-dense foods across and within all food groups in recommended amounts.
3. **Limit calories from added sugars and saturated fats and reduce sodium intake.** Consume an eating pattern low in added sugars, saturated fats, and sodium. Cut back on foods and beverages higher in these components to amounts that fit within healthy eating patterns.
4. **Shift to healthier food and beverage choices.** Choose nutrient-dense foods and beverages across and within all food groups in place of less healthy choices. Consider cultural and personal preferences to make these shifts easier to accomplish and maintain.
5. **Support healthy eating patterns for all.** Everyone has a role in helping to create and support healthy eating patterns in multiple settings nationwide, from home to school to work to communities.

Source: https://health.gov/dietaryguidelines/2015/guidelines/executive-summary/

2015-2020 Dietary Guidelines for Americans

A healthy eating pattern includes:[1]

- A variety of vegetables from all of the subgroups—dark green, red and orange, legumes (beans and peas), starchy, and other
- Fruits, especially whole fruits
- Grains, at least half of which are whole grains
- Fat-free or low-fat dairy, including milk, yogurt, cheese, and/or fortified soy beverages
- A variety of protein foods, including seafood, lean meats and poultry, eggs, legumes (beans and peas), and nuts, seeds, and soy products
- Oils

A healthy eating pattern limits:

- Saturated fats and *trans* fats, added sugars, and sodium
- Key Recommendations that are quantitative are provided for several components of the diet that should be limited. These components are of particular public health concern in the United States, and the specified limits can help individuals achieve healthy eating patterns within calorie limits:
- Consume less than 10 percent of calories per day from added sugars[2]
- Consume less than 10 percent of calories per day from saturated fats[3]
- Consume less than 2,300 milligrams (mg) per day of sodium[4]
- If alcohol is consumed, it should be consumed in moderation—up to one drink per day for women and up to two drinks per day for men—and only by adults of legal drinking age.[5]

Source: https://health.gov/dietaryguidelines/2015/guidelines/executive-summary/

To our benefit, the well-recognized global health concern that is cardiovascular disease (CVD) seems to have an accessible, effective solution – **food**.

- Food is medicine
- Food is information
- Food is connection

Minich and Brown, Nutritional and Integrative Strategies in Cardiovascular Medicine, 2015

Poly-pills vs. Poly-meals for the Poly-ills

Statin
Three different anti-hypertensives
Aspirin
Folic acid

"The "polypill" strategy could largely prevent 80% of heart attacks and strokes if taken by everyone aged 55 and older…It would be safe and have a greater impact on the prevention of disease in the Western world than any other single intervention". (statin, folate, ACE inhibitor, antiplatelet agent, diuretic)

Fruits & vegetables
Almonds
Chocolate
Wine
Fish
Garlic

Wald et al., British Medical J 2003; 525: 1-6.
Franco et al. Horm Metab Res. 2007 Sep;39(9):627-31.

But, food is different today.

“Food is different today than it was in the past; over 4,000 new agents have entered our food supply intentionally or inadvertently: almost none of those have been evaluated as potential causes of obesity or diabetes.”

Corkey BE. Banting lecture 2011: hyperinsulinemia: cause or consequence? Diabetes. 2012 Jan;61(1):4-13. doi: 10.2337/db11-1483.

Toxins and Risk of Cardiovascular Disease

- “These chemicals include persistent organic pollutants (POPs); the plastic exudates bisphenol A and phthalates; low molecular weight hydrocarbons (LMWHCs); and poly nuclear aromatic hydrocarbons (PAHs).” Zeliger HI. **Lipophilic chemical exposure as a cause of cardiovascular disease.** Interdiscip Toxicol. 2013 Jun;6(2):55-62. doi: 10.2478/intox-2013-0010.
- Gress S, Lemoine S, Séralini GE, Puddu PE. **Glyphosate-based herbicides potently affect cardiovascular system in mammals: review of the literature**. Cardiovasc Toxicol. 2015 Apr;15(2):117-26. doi: 10.1007/s12012-014-9282-y.
- He L, Chen Z, Dai B, Li G, Zhu G. **Low-level lead exposure and cardiovascular disease: the roles of telomere shortening and lipid disturbance.** J Toxicol Sci. 2018;43(11):623-630. doi: 10.2131/jts.43.623.

The power of “food”

A single fast food-style meal can increase serum IL-6 by 100%, peaking about 6 hours after a meal.

Sample meals included in the review:

- White bread, butter, cheese, milkshake
- Eggs, muffin, butter, sugary drink
- Sugar, heavy cream, chocolate syrup, powdered milk
- Bagel, cream cheese, potato, milk, apple juice

Adv Nutr. 2017 Mar 15;8(2):213-225. doi: 10.3945/an.116.014431. Print 2017 Mar. Magnitude and Timing of the Postprandial Inflammatory Response to a High-Fat Meal in Healthy Adults: A Systematic Review.
Emerson SR1,2, Kurti SP3,2, Harms CA3,2, Haub MD4,2, Melgarejo T4, Logan C5, Rosenkranz SK4,2.

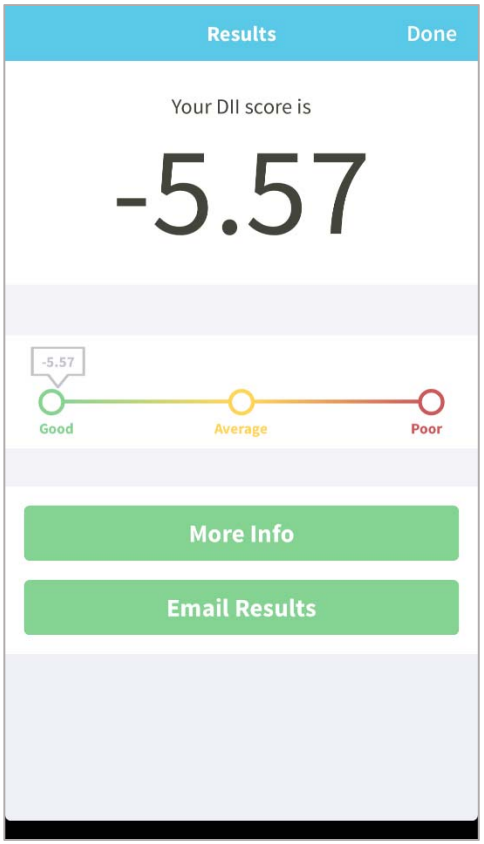
Adding vegetables to an inflammatory meal

Esposito et al. showed that adding 400 g of vegetables (100 g tomatoes, 200 g carrots, and 100 g peppers (184 mg vitamin C, 19.65 *mg* vitamin E, 15 mg -carotene, and 9.2 g fiber) to a high-fat meal (2 sausages, 6 bread slices, a small egg, butter, and olive oil) lessened the effects of fat on endothelial dysfunction.

Esposito K, Nappo F, Giugliano F, Giugliano G, Marfella R, Giugliano D. Effect of dietary antioxidants on postprandial endothelial dysfunction induced by a high-fat meal in healthy subjects. Am J Clin Nutr. 2003 Jan;77(1):139-43.

The Dietary Inflammatory Index (DII)

- Database with foods graded according to inflammatory parameters based on published studies (1)
- Look for the app called DII Screener to score your current diet
- Correlations in the literature between the DII and chronic diseases such as depression (2)



1) Shivappa, N., Steck, S.E., Hurley, T.G., Hussey, J.R., and Hébert, J.R. Designing and developing a literature-derived, population-based dietary inflammatory index. Publ Health Nutr. 2014; 17: 1689–1696; https://doi.org/10.1017/S1368980013002115. 2) Tolkien K, Bradburn S, Murgatroyd C. An anti-inflammatory diet as a potential intervention for depressive disorders: A systematic review and meta-analysis. Clin Nutr. 2018 Nov 20. pii: S0261-5614(18)32540-8. doi: 10.1016/j.clnu.2018.11.007. [Epub ahead of print]

Dietary inflammatory index and all-cause mortality in large cohorts

- “Inflammation is known to be related to the leading causes of death including cardiovascular disease, several types of cancer, obesity, type 2 diabetes, depression-suicide and other chronic diseases.”
- 18,566 participants in the "Seguimiento Universidad de Navarra" (SUN) cohort followed-up during 188,891 person-years and 6790 participants in the "PREvencion con DIeta MEDiterránea" (PREDIMED) randomized trial representing 30,233 person-years of follow-up
- **“In the meta-analysis of 12 cohorts, the DII was significantly associated with an increase of 23% in all-cause mortality (95% CI: 16%-32%, for the highest vs lowest category of DII).”**

Garcia-Arellano A, Martínez-González MA, Ramallal R, Salas-Salvadó J, Hébert JR, Corella D, Shivappa N, Forga L, Schröder H, Muñoz-Bravo C, Estruch R, Fiol M, Lapetra J, Serra-Majem L, Ros E, Rekondo J, Toledo E, Razquin C, Ruiz-Canela M; SUN and PREDIMED Study Investigators. Dietary inflammatory index and all-cause mortality in large cohorts: The SUN and PREDIMED studies. Clin Nutr. 2018 May 24. pii: S0261-5614(18)30175-4. doi: 10.1016/j.clnu.2018.05.003. [Epub ahead of print]

Select Features of an Inflammatory Diet

- High-heat cooking and frying
- High glycemic index/load
- Poor-quality trans fats
- Low in phytochemicals
- High-allergenic foods
- High sugar; high added sugar intake

It’s important to have the food conversation with all your patients.

The data say so.

Dietary advice for reducing cardiovascular risk

Compared to no advice, dietary advice increased fruit and vegetable intake by 1.25 servings/day.

Dietary fiber intake increased with advice by 5.99 g/day, while total dietary fat as a percentage of total energy intake fell by 4.49 % with dietary advice and saturated fat intake fell by 2.36 %.

Cochrane Database Syst Rev. 2007 Oct 17;(4):CD002128. **Dietary advice for reducing cardiovascular risk.** Brunner EJ, et al.

Is Behavioral Counseling Effective in Promoting a Healthy Lifestyle for Cardiovascular Disease Prevention in Persons With Cardiovascular Risk Factors?

Medium- and high-intensity diet and physical activity behavioral counseling in overweight or obese persons with CVD risk factors resulted in consistent improvements across a variety of important cardiovascular intermediate health outcomes up to 2 years.

Rockville (MD): Agency for Healthcare Research and Quality (US); 2014 Aug. Report No.: 13-05179-EF-1. U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews.

Do patients follow dietary guidance?

Patients' reasons for not complying with the prescribed diet included:

- 'already having satisfactory food habits' (34.7%);
- 'unwillingness to suffer nutritional deprivation' (33.3%);
- 'difficulties to conciliate a diet with family life' (27.8%) and
- 'taking cholesterol-lowering drugs' (22.2%).

Arch Cardiovasc Dis. 2012 Nov;105(11):557-65. doi: 10.1016/j.acvd.2012.06.005. Epub 2012 Nov 9.

Clinical Application: Dietary Patterns & CVD

- Diet record/food log
- 24-hour diet recall
- Food frequency
- Food photos
- Apps
- Food/lifestyle coaches
- Groups make a difference

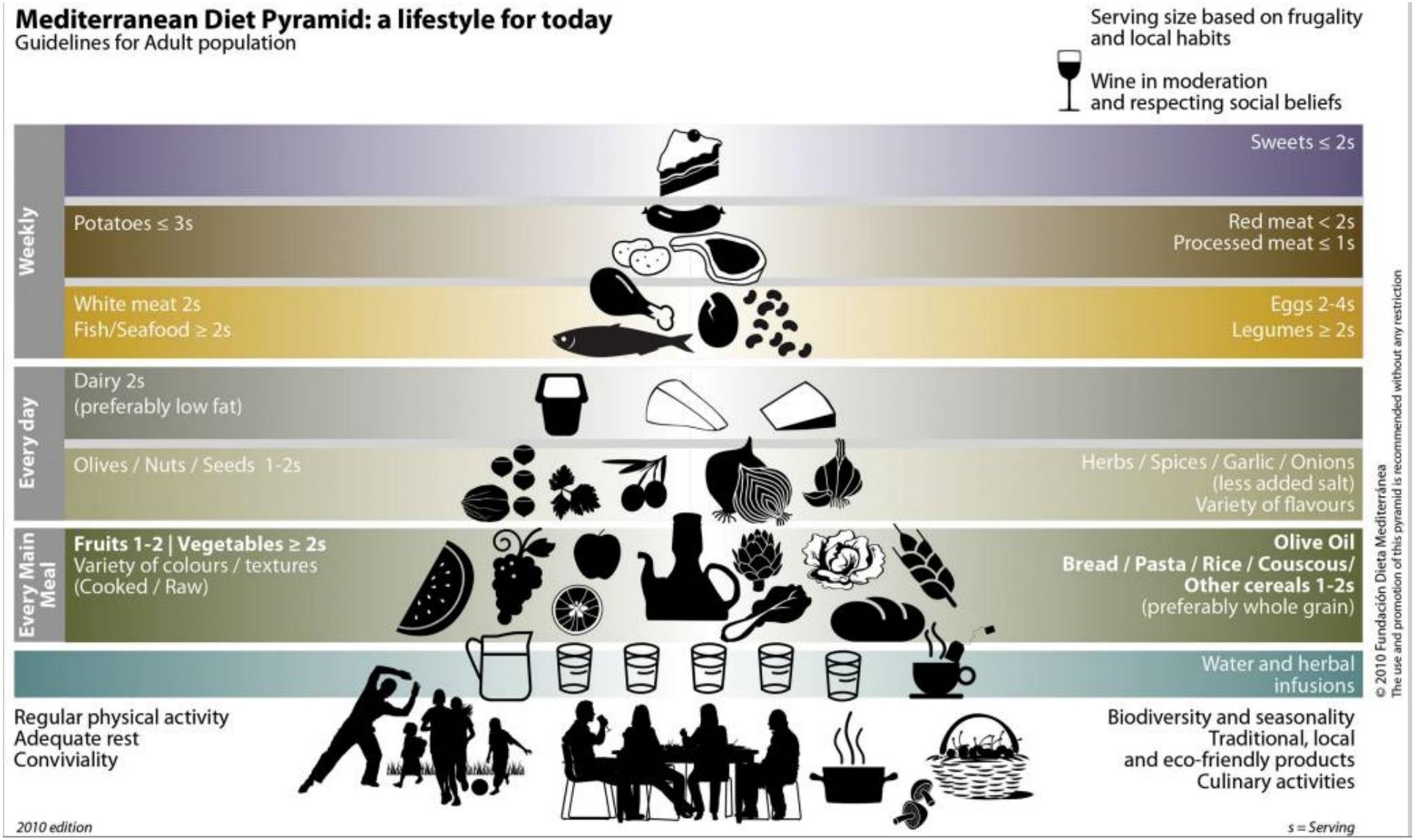
Research Publications on Dietary Patterns

Dietary Approach	Number of Pubmed citations as of 1/20/2019
Mediterranean Diet	4593
Vegan/vegetarian	3451
Ketogenic diet	2314
Elimination diet	721
Intermittent fasting	401
DASH diet	392
Paleolithic diet	128
MIND diet	12

Mediterranean Diet

- Emphasize fruit, vegetables, grains, nuts, legumes, dairy, olive oil; Small amounts poultry, fish, red meat, red wine
- Unknown which specific features responsible
- Lowers blood pressure
- Improves serum lipids: lowers TC, LDL, TG, increases HDL, lowers oxLDL and Lp(a). Improves LDL size and decreases LDL-P to a less atherogenic profile
- Improves T2DM and dysglycemia
- Improves oxidative defense and reduces oxidative stress: F-2 isoprostanes and 8-Oxo-2'-deoxyguanosine (8OHDG)
- Reduces inflammation: lowers (high sensitivity C reactive protein) hsCRP, interleukin – 6 (IL6), soluble vascular cell adhesion molecule (sI-VCAM) and soluble cell adhesion molecule (sI-CAM)
- Reduces thrombosis and factor VII after meals
- Decreases brain natriuretic peptide (BNP)
- Increases nitrates/nitrites
- Improves membrane fluidity
- Reduces MI, CHD and CVA
- Reduces homocysteine

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.



Dernini S, Berry EM. Mediterranean Diet: From a Healthy Diet to a Sustainable Dietary Pattern. Front Nutr. 2015 May 7;2:15. doi: 10.3389/fnut.2015.00015. eCollection 2015.

Mediterranean-Style Diet Improves Systolic Blood Pressure and Arterial Stiffness in Older Adults

- N=1142, one year intervention
- Significant reduction in SBP in males
- Significant reduction of arterial stiffness

Hypertension. 2019 Jan 14:HYPERTENSIONAHA11812259. doi: 10.1161/HYPERTENSIONAHA.118.12259. [Epub ahead of print]
Mediterranean-Style Diet Improves Systolic Blood Pressure and Arterial Stiffness in Older Adults. Jennings A1, Berendsen AM2, de Groot LCPGM2, Feskens EJM2, Brzozowska A3, Sicinska E3, Pietruszka B3, Meunier N4, Caumon E4, Malpuech-Brugère C1, Santoro A5,6, Ostan R6, Franceschi C5, Gillings R1, O' Neill CM1, Fairweather-Tait SJ1, Minihane AM1, Cassidy A1.

Mediterranean diet in large prospective cohort of women

- Prospective cohort design, baseline MED intake was assessed in 25 994 initially healthy US women in the Women's Health Study who were followed up to 12 years
- 40 biomarkers were evaluated
- "…higher MED intake was associated with approximately **one-fourth relative risk reduction** in CVD events."
- "The largest mediators of the CVD risk reduction of MED intake were **biomarkers of inflammation** (accounting for 29.2% of the MED-CVD association), glucose metabolism and insulin resistance (27.9%), and body mass index (27.3%)..."

Ahmad S, Moorthy MV, Demler OV, Hu FB, Ridker PM, Chasman DI, Mora S. Assessment of Risk Factors and Biomarkers Associated With Risk of Cardiovascular Disease Among Women Consuming a Mediterranean Diet. JAMA Netw Open. 2018 Dec 7;1(8):e185708. doi: 10.1001/jamanetworkopen.2018.5708.

PREDIMED:
Mediterranean Diet vs. Low-Fat Diet

- Three groups:
  - Med Diet + EVOO
  - Med Diet + nuts
  - Low-fat diet

"Among persons at high cardiovascular risk, a Mediterranean diet supplemented with extra-virgin olive oil or nuts reduced the incidence of major cardiovascular events."

N Engl J Med 2013;368:1279-90.
DOI:10.1056/NEJMoa1200303

The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals.

Results from clinical studies revealed the protective role of the Mediterranean diet on components of MS, like:

- Waist circumference
- High-density lipoprotein cholesterol
- Triglycerides
- Systolic and diastolic blood pressure
- Glucose

J Am Coll Cardiol. 2011 Mar 15;57(11):1299-313. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. Kastorini CM, et al.

The Mediterranean Diet Improves Heart Rate Variability

"After adjusting for energy intake, other nutritional factors, shared genes, and common environment, a 1-unit higher score was significantly associated with 3.9% to 13% higher time and frequency domain HRV parameters."

The Mediterranean dietary pattern is associated with higher HRV.

Dai J. et al. Circ Cardiovasc Qual Outcomes. 2010;3:00-00.

Transcriptomics and the Mediterranean Diet

- Monounsaturated fatty acid-rich diets prevented the expression of inflammatory genes in different tissues, an action also observed after the administration of olive oil phenolic compounds.
- Among these, tyrosol, hydroxytyrosol, and secoiridoids have been found to be particularly effective in cell cycle expression.
- Less explored terpenes, such as oleanolic acid, are important modulators of circadian clock genes.

Nutrients. 2017 May 9;9(5). pii: E472. doi: 10.3390/nu9050472.

DASH Diet

- Both DASH diets reduce BP and CHD.
- Both diets emphasize daily intake of fruits, vegetables, whole grains, beans, fiber, LF dairy products, poultry, fish, seeds and nuts, but limiting red meat, sweets and sugar containing beverages.
- The intake of potassium, magnesium and calcium are increased but with a variable restriction in dietary sodium.

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

DASH Diet

- Both DASH diets reduce BP and CHD.
- Both diets emphasize daily intake of fruits, vegetables, whole grains, beans, fiber, LF dairy products, poultry, fish, seeds and nuts, but limiting red meat, sweets and sugar containing beverages.
- DASH 2: DASH diet with additional salt restriction to 1500 mg per day.
- The intake of potassium, magnesium and calcium are increased but with a variable restriction in dietary sodium.

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Paleolithic (Paleo) Diet

- 127 citations (1/15/2019)
  - **Plants:** Tubers, seeds, nuts, wild grown barley that was pounded as flour, legumes, and flowers.
  - **Animals**: Lean small game animals
  - **Seafood:** Shellfish and other smaller fish.
  - **Insects**: Insects and their products, including honey, honeycombs
- High satiety; possible iodine deficiency due to reduced table salt and dairy
- Improvements in cardiovascular and metabolic syndrome markers
  - "A Paleolithic diet improves fat mass and metabolic balance including insulin sensitivity, glycemic control, and leptin in subjects with type 2 diabetes." (1)

Lipids Health Dis. 2014 Oct 11;13:160. doi: 10.1186/1476-511X-13-160. Cardiovasc Diabetol. 2009 Jul 16;8:35. doi: 10.1186/1475-2840-8-35. Eur J Clin Nutr. 2009 Aug;63(8):947-55. doi: 10.1038/ejcn.2009.4. Epub 2009 Feb 11. Nutr J. 2013 Jul 29;12:105. doi: 10.1186/1475-2891-12-105. Nutr Res. 2015 Jun;35(6):474-9. doi: 10.1016/j.nutres.2015.05.002. Epub 2015 May 14. Challa HJ, Uppaluri KR. Paleolithic Diet. [Updated 2018 Oct 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482457/;
(1) Otten J#1, Stomby A#1, Waling M2, Isaksson A3, Tellström A1, Lundin-Olsson L4, Brage S5, Ryberg M1, Svensson M3, Olsson T1. Benefits of a Paleolithic diet with and without supervised exercise on fat mass, insulin sensitivity, and glycemic control: a randomized controlled trial in individuals with type 2 diabetes. Diabetes Metab Res Rev. 2017 Jan;33(1). doi: 10.1002/dmrr.2828. Epub 2016 Jun 30.

Ketogenic Diet

- 2310 citations (1/15/19)
- Rich in fat and low in carbohydrates (4:1 fat:nonfat ratio), designed to stimulate ketone formation
- Balanced net dietary acid load
- Important to assess duration when it comes to cardiovascular health
- Low toxin load (toxins are lipophilic)
- Moderate and not too low CHO (60-80 g)
- Adequate phytonutrients and green, alkaline-forming vegetables
- Healthy, quality proteins
- Healthy, quality fats
  - Coconut
  - Unsaturated fats

Hussain TA, Mathew TC, Dashti AA, Asfar S, Al-Zaid N, Dashti HM. Effect of low-calorie versus low-carbohydrate ketogenic diet in type 2 diabetes. Nutrition. 2012 Oct;28(10):1016-21. doi: 10.1016/j.nut.2012.01.016. Epub 2012 Jun 5; Kosinski C, Jornayvaz FR. Effects of Ketogenic Diets on Cardiovascular Risk Factors: Evidence from Animal and Human Studies. Nutrients. 2017 May 19;9(5). pii: E517. doi: 10.3390/nu9050517.

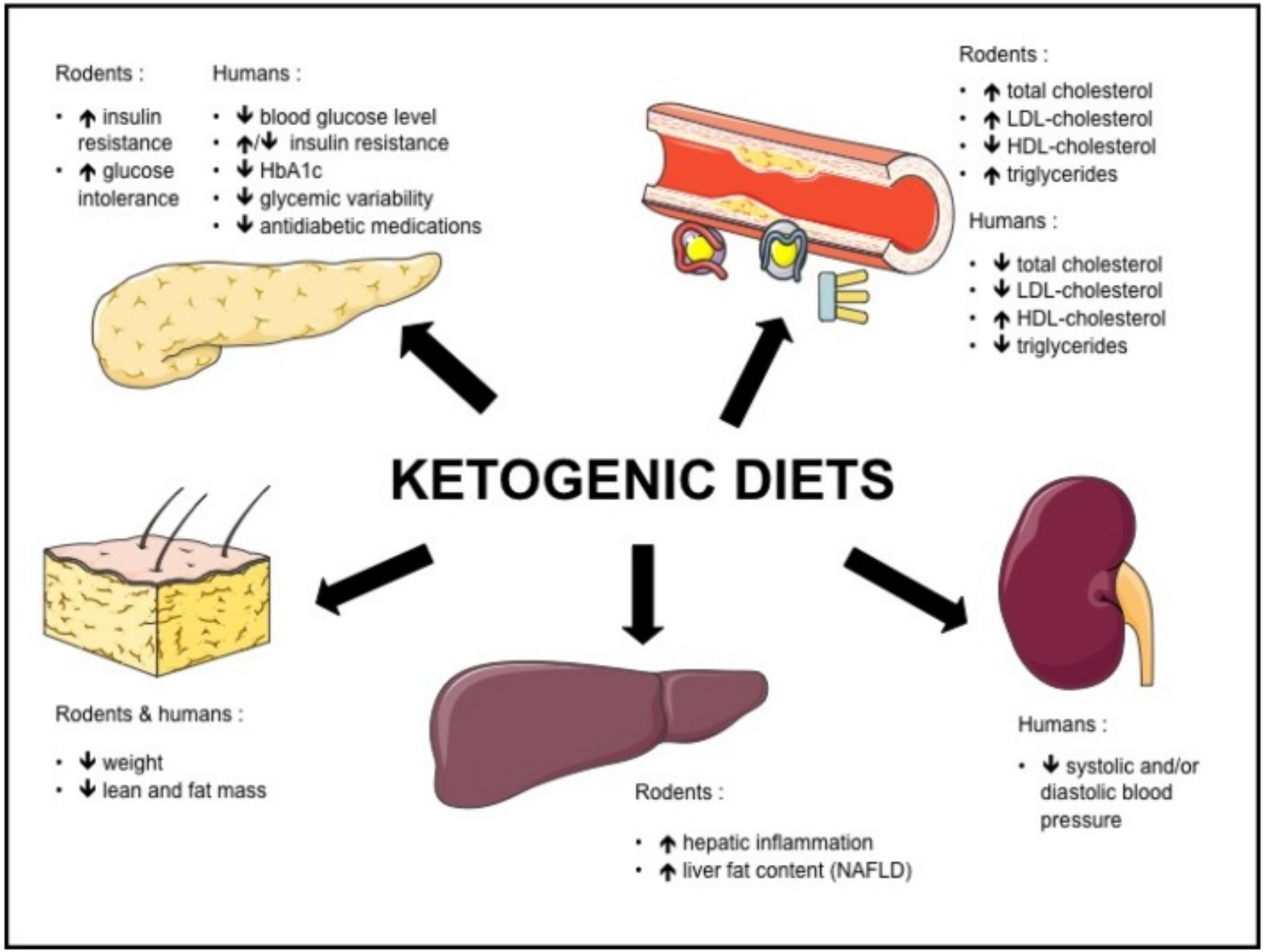


Image Credit: Kosinski C, Jornayvaz FR. Effects of Ketogenic Diets on Cardiovascular Risk Factors: Evidence from Animal and Human Studies. Nutrients. 2017 May 19;9(5). pii: E517. doi: 10.3390/nu9050517.

Elimination Diet

- Removes top allergens:
  - Corn, soy, wheat/gluten, shellfish, dairy, sugar
- Some additional modifications include removal of the following:
  - Nightshades, nuts, alcohol, caffeine, pork, citrus, histamines, oxalates, salicylates
- Goal is to remove these foods short-term and then reintroduce them sequentially to observe presence or absence of symptoms
- Reintroduction is to be personalized to the patient.

Elimination Diet

- Useful in food allergy, atopy, eczema
- Migraine, headaches, neurological and behavioral symptoms (e.g., ADHD)
- Gut disorders and dysfunction (e.g., IBS, leaky gut)
- Fibromyalgia

J Headache Pain. 2014 Oct 23;15:69. doi: 10.1186/1129-2377-15-69.
Gastroenterology. 2012 Jun;142(7):1451-9.e1; quiz e14-5. doi: 10.1053/j.gastro.2012.03.001. Epub 2012 Mar 3.
Altern Ther Health Med. 2011 Mar-Apr;17(2):36-44.

Vegan/Vegetarian Diets

- Significant evidence for reduced cardiovascular risk
  - "Vegetarian dietary patterns reduce CVD mortality and the risk of coronary heart disease (CHD) by 40%." (1)
- Reduced risk for various cancers
- Reduced inflammatory markers
- Potential nutrient deficiencies (vitamin B12, iron, protein, zinc, calcium, vitamin A, n-3 fatty acids and iodine) when imbalanced diets consumed

(1) Kahleova H, Levin S, Barnard ND. Vegetarian Dietary Patterns and Cardiovascular Disease. Prog Cardiovasc Dis. 2018 May - Jun;61(1):54-61. doi: 10.1016/j.pcad.2018.05.002. Epub 2018 May 22. J Am Heart Assoc. 2015 Oct 27;4(10):e002408. doi: 10.1161/JAHA.115.002408. Nutr Res. 2015 Feb;35(2):97-106. doi: 10.1016/j.nutres.2014.11.007. Epub 2014 Dec 3.
Forum Nutr. 2005;(57):147-56.

Fasting Regimens

- Intermittent fasting, food restriction, caloric restriction
- Results include weight loss and improvements in cardiometabolic health such as reductions in aortic vascular smooth muscle cell proliferation, C-reactive protein, adiponectin, leptin, total cholesterol, LDL cholesterol, triacylglycerol concentrations, systolic blood pressure and increases in LDL particle size in a relatively short time period
- Caloric restriction could be implemented by constructing a personalized diet based on nutrient-dense, low-energy foods such as vegetables, fruits, whole grains, nuts, fish, low-fat dairy products and lean meats**.**

"…calorie restriction (CR), intermittent fasting, and adjusted diurnal rhythm of feeding, with adequate intake of specific macronutrients and micronutrients, are powerful interventions not only for the prevention of cardiovascular disease but also for slowing the accumulation of molecular damage leading to cardiometabolic dysfunction."

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9. Quote from: Fontana L. Interventions to promote cardiometabolic health and slow cardiovascular ageing. Nat Rev Cardiol. 2018 Sep;15(9):566-577. doi: 10.1038/s41569-018-0026-8.

Advanced Glycation Endproducts (AGEs)

Advanced glycation endproducts and atherosclerosis

- Advanced glycation endproducts (AGEs) are a group of modified molecular species formed by nonenzymatic reactions between the aldehydic group of reducing sugars with proteins, lipids, or nucleic acids.
- Formation and accumulation of AGEs are related to the aging process and are accelerated in diabetes.
- AGEs are generated in hyperglycemia, but their production also occurs in settings characterized by oxidative stress and inflammation.

Biofactors. 2012 Apr 10. doi: 10.1002/biof.1018. [Epub ahead of print]
An update on advanced glycation endproducts and atherosclerosis. Del Turco S, Basta G.

Increased serum levels of advanced glycation endproducts predict total, cardiovascular and coronary mortality in women with type 2 diabetes:

A population-based 18 year follow-up study.

"Increased serum levels of AGEs predict total and CVD mortality in women with type 2 diabetes."

Diabetologia. 2007 Jul;50(7):1409-17. Epub 2007 May 4. **Increased serum levels of advanced glycation endproducts predict total, cardiovascular and coronary mortality in women with type 2 diabetes: a population-based 18 year follow-up study.**
Kilhovd BK, et al.

Examples of high-AGE foods

Food	AGE, kU/gram
Bacon	90.22
Cheese, white full fat	84.23
Pizza	68.24
Chicken breast, fried	61.22
Beef, fast food	54.17
Egg, fried in margarine	41.1
Vanilla cookie	32.2
Potatoes, small fried	28.8
Bread, toast	6.07

J Nutr. 2009 Jun;139(6):1219S-1227S. doi: 10.3945/jn.108.097998. Epub 2009 Apr 22. Misconceptions about high-fructose corn syrup: is it uniquely responsible for obesity, reactive dicarbonyl compounds, and advanced glycation endproducts?
White JS., Modified from Table 2

Inhibition of protein glycation by extracts of culinary herbs and spices

- In general, spice extracts inhibited glycation more than herb extracts, but inhibition was correlated with total phenolic content (R(2) = 0.89).
- The most potent inhibitors included extracts of cloves, ground Jamaican allspice, and cinnamon.
  Potent herbs tested included sage, marjoram, tarragon, and rosemary.

J Med Food. 2008 Jun;11(2):275-81. doi: 10.1089/jmf.2007.536. Inhibition of protein glycation by extracts of culinary herbs and spices. Dearlove RP1, Greenspan P, Hartle DK, Swanson RB, Hargrove JL.

AGEs matter

- A single meal consisting of a chicken breast, potatoes, carrots, tomatoes, and vegetable oil caused significant postprandial endothelial function and oxidative stress in type 2 diabetic patients when it underwent frying or broiling rather than when it was steamed or boiled (1).
- In a crossover design with healthy subjects fed for one month a meal containing either high-AGEs formed by cooking with high temperatures or low-AGE through mild steaming, it was reported that the high-AGE meals caused lower insulin sensitivity, omega-3 fatty acids, and vitamins C and E, and increased cholesterol and triglycerides (2).
- In contrast, diabetics following a low-AGE diet had lower inflammation and oxidative stress compared to eating a standard diet (3).

1. Effects of low- and high-advanced glycation endproduct meals on macro- and microvascular endothelial function and oxidative stress in patients with type 2 diabetes mellitus.
Negrean M, Stirban A, Stratmann B, Gawlowski T, Horstmann T, Götting C, Kleesiek K, Mueller-Roesel M, Koschinsky T, Uribarri J, Vlassara H, Tschoepe D. Am J Clin Nutr. **2007** May;85(5):1236-43. Erratum in: Am J Clin Nutr. **2007** Oct;86(4):1256.
2. A diet based on high-heat-treated foods promotes risk factors for diabetes mellitus and cardiovascular diseases. **Birlouez-Aragon** I, Saavedra G, Tessier FJ, Galinier A, Ait-Ameur L, Lacoste F, Niamba CN, Alt N, Somoza V, Lecerf JM. Am J Clin Nutr. **2010** May;91(5):1220-6. doi: 10.3945/ajcn.2009.28737. Epub **2010** Mar 24.
3. Dietary advanced glycation end products restriction diminishes inflammation markers and oxidative stress in patients with type 2 diabetes mellitus.
Luévano-Contreras C, Garay-Sevilla ME, Wrobel K, Malacara JM, Wrobel K. J Clin Biochem Nutr. **2013** Jan;52(1):22-6. doi: 10.3164/jcbn.12-40. Epub 2012 Dec 6.

Dietary Protein

Calorie Level of Pattern[a]	1,000	1,200	1,400	1,600	1,800	2,000	2,200
Food Group[b]	**Daily Amount[c]** of Food From Each Group (vegetable and protein foods subgroup amounts are per week)						
Vegetables	**1 c-eq**	**1½ c-eq**	**1½ c-eq**	**2 c-eq**	**2½ c-eq**	**2½ c-eq**	**3 c-eq**
Dark-green vegetables (c-eq/wk)	½	1	1	1½	1½	1½	2
Red and orange vegetables (c-eq/wk)	2½	3	3	4	5½	5½	6
Legumes (beans and peas) (c-eq/wk)	½	½	½	1	1½	1½	2
Starchy vegetables (c-eq/wk)	2	3½	3½	4	5	5	6
Other vegetables (c-eq/wk)	1½	2½	2½	3½	4	4	5
Fruits	**1 c-eq**	**1 c-eq**	**1½ c-eq**	**1½ c-eq**	**1½ c-eq**	**2 c-eq**	**2 c-eq**
Grains	**3 oz-eq**	**4 oz-eq**	**5 oz-eq**	**5 oz-eq**	**6 oz-eq**	**6 oz-eq**	**7 oz-eq**
Whole grains[d] (oz-eq/day)	1½	2	2½	3	3	3	3½
Refined grains (oz-eq/day)	1½	2	2½	2	3	3	3½
Dairy	**2 c-eq**	**2½ c-eq**	**2½ c-eq**	**3 c-eq**	**3 c-eq**	**3 c-eq**	**3 c-eq**
Protein Foods	**2 oz-eq**	**3 oz-eq**	**4 oz-eq**	**5 oz-eq**	**5 oz-eq**	**5½ oz-eq**	**6 oz-eq**
Seafood (oz-eq/wk)	3	4	6	8	8	8	9
Meats, poultry, eggs (oz-eq/wk)	10	14	19	23	23	26	28
Nuts seeds, soy products (oz-eq/wk)	2	2	3	4	4	5	5
Oils	**15 g**	**17 g**	**17 g**	**22 g**	**24 g**	**27 g**	**29 g**
Limit on Calories for Other Uses, calories (% of calories)[e,f]	150 (15%)	100 (8%)	110 (8%)	130 (8%)	170 (9%)	270 (14%)	280 (13%)

Source: https://health.gov/dietaryguidelines/2015/guidelines/executive-summary/

Dietary proteins

“There are no scientific arguments to increase the daily protein intake to more than 20% of total energy intake as recommended by the guidelines, in order to improve cardiovascular health.”

Int J Vitam Nutr Res. 2011 Mar;81(2-3):153-61. **Dietary proteins and atherosclerosis.** Darioli R.

Major dietary protein sources and risk of coronary heart disease in women

Prospective study with 84,136 women aged 30 to 55 years in the Nurses' Health Study

“These data suggest that high red meat intake increases risk of CHD and that CHD risk may be reduced importantly by shifting sources of protein in the US diet.”

Circulation. 2010 Aug 31;122(9):876-83. Epub 2010 Aug 16. **Major dietary protein sources and risk of coronary heart disease in women.** Bernstein AM, et al.

Major dietary protein sources and risk of coronary heart disease in women.

1 serving per day of nuts was associated with a 30% lower risk of CHD compared with 1 serving per day of red meat.

Similarly, compared with 1 serving per day of red meat, a lower risk was associated with 1 serving per day of low-fat dairy, poultry, and fish.

Circulation. 2010 Aug 31;122(9):876-83. Epub 2010 Aug 16. **Major dietary protein sources and risk of coronary heart disease in women.** Bernstein AM, et al.

Dietary protein sources and the risk of stroke in men and women.

- 84 010 women & 43 150 men
- Compared with 1 serving/day of red meat,
  - 1 serving/day of poultry was associated with a 27% lower risk of stroke,
  - nuts with a 17% lower risk,
  - fish with a 17% lower risk,
  - low-fat dairy with an 11% lower risk,
  - whole-fat dairy with a 10% lower risk.
- We did not see significant associations with exchanging legumes or eggs for red meat.

Stroke. 2012 Mar;43(3):637-44. Epub 2011 Dec 29. **Dietary protein sources and the risk of stroke in men and women.** Bernstein AM, et al.

Whey protein

- Long-term intake of several grams (typically 20 grams) of whey protein significantly reduces blood pressure, decreases TG and cholesterol levels, and lowers inflammation in patients with CVD.
- Type of whey protein needs to be considered: clinical trial data indicate that whey protein must be hydrolyzed to ACE inhibitor peptides for it to have anti-hypertensive properties
- Of note, certain whey protein preparations may result in a relatively higher insulin response relative to other protein sources

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Diets Higher in Protein Predict Lower High Blood Pressure Risk in Framingham Offspring Study Adults

- N=1361 men and women followed for a mean of 11.3 years
- Higher protein intakes were associated with lower mean SBP and DBP.
- Both animal and plant proteins lowered BP and led to statistically significant reductions in HBP risk

Am J Hypertens. 2014 Sep 6. pii: hpu157. [Epub ahead of print]

Total dietary protein and BP: Trial Data

- N=16 trials assessed
- In almost all the trials, high protein diet compared with high CHO diet.
- “Results suggest that increased intake of protein may be beneficial to BP, although no clear dose-response association could be distinguished.”
- Is it possible that a reduced intake of CHO is responsible?

Altorf-van der Kuil W, et al. **Dietary protein and blood pressure: a systematic review.** PLoS One. 2010 Aug 11;5(8):e12102.

Red meat consumption and mortality: Results from 2 prospective cohort studies

"Red meat consumption is associated with an increased risk of total, CVD, and cancer mortality. Substitution of other healthy protein sources for red meat is associated with a lower mortality risk."

Arch Intern Med. 2012 Apr 9;172(7):555-63. doi: 10.1001/archinternmed.2011.2287. Epub 2012 Mar 12. **Red meat consumption and mortality: results from 2 prospective cohort studies.** Pan A, et al.

Among highly educated persons, aged >45 years, a high consumption of red, total, and red + processed meat was related to increased all-cause mortality, compared with those with low consumption, whereas no significant associations were found for SFA intake. Dietary guidelines should specifically limit meat consumption and not relying only in limiting SFA intake.

Clin Nutr. 2017 Jun 19. pii: S0261-5614(17)30224-8. doi: 10.1016/j.clnu.2017.06.013. [Epub ahead of print]
Should we recommend reductions in saturated fat intake or in red/processed meat consumption? The SUN prospective cohort study.

TMAO

- Risk factor for CVD
- Production dependent on gut microbial metabolism
- Primary precursors of TMAO are from dietary sources of phosphatidylcholine, choline, and L-carnitine.
- “Once in the digestive tract, gut microbes aid in the catabolism of these compounds resulting in the production of trimethylamine (TMA) as a metabolic by-product. TMA is rapidly absorbed into the portal circulation and oxidized by hepatic enzymes, most notably flavin monooxygenase 3 (FMO3), which results in TMAO production.”
- In the systemic circulation, TMAO contributes to the activation of endogenous macrophage foam cells.

Erickson, M.L.; Malin, S.K.; Wang, Z.; Brown, J.M.; Hazen, S.L.; Kirwan, J.P. Effects of Lifestyle Intervention on Plasma Trimethylamine N-Oxide in Obese Adults. Nutrients 2019, 11, 179.

Short-term beef consumption promotes systemic oxidative stress, TMAO formation and inflammation in rats, and dietary fat content modulates these effects

Consumption of the beef diets resulted in higher urinary trimethylamine (4.5-fold) and TMAO (3.7-fold) concentrations ($P < 0.001$), compared to the chicken diets.

Van Hecke et al. Food Funct. 2016 Aug 17. [Epub ahead of print]

TMAO

- Wang et al. (1) showed that metabolism of phosphatidylcholine predicted CVD risk.
- A systematic review and meta-analysis of prospective studies (n=19,256) indicated that elevated concentrations of TMAO precursors (L-carnitine, choline, or betaine) was associated with 1.3 to 1.4 times higher risk for major adverse cardiovascular disease events and death compared with those who had low concentrations of these compounds (2).
- It remains to be explored how TMAO levels can be modulated through the gut through nutrients, antibiotics, probiotics, prebiotic fibers, and even fecal transplantation.

1. Wang Z, Klipfell E, Bennett BJ, Koeth R, Levison BS, Dugar B, Feldstein AE, Britt EB, Fu X, Chung YM, Wu Y, Schauer P, Smith JD, Allayee H, Tang WH, DiDonato JA, Lusis AJ, Hazen SL. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. Nature. 2011;472:57–63.

2. Heianza Y, Ma W, Manson JE, Rexrode KM, Qi L. Gut Microbiota Metabolites and Risk of Major Adverse Cardiovascular Disease Events and Death: A Systematic Review and Meta-Analysis of Prospective Studies. J Am Heart Assoc. 2017;6(7):e004947. Published 2017 Jun 29. doi:10.1161/JAHA.116.004947

Meat and CVD

Meats rich in visible fat and preservatives (red box on the left) have been demonstrated to increase cardiovascular risk while lean fresh red meat (green box on the right) has not

Int J Prev Med. 2017; 8: 40. Published online 2017 Jun 1. doi: 10.4103/ijpvm.IJPVM_206_16 **A Contemporary Review of the Relationship between Red Meat Consumption and Cardiovascular Risk** Sofia Bronzato and Alessandro Durante[1]

Lean Meat, Poultry, & Eggs

"Distinguishing processed from unprocessed meats is important to assess the association of meat with cardiovascular risk."

- Micha et al. 2010 found that processed meat intake was associated with a 42% greater risk of CVD, whereas unprocessed meat was not significantly associated with CVD risk.

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Lean Meat, Poultry, and Eggs

- AHA recommends that processed meat consumption be limited to 0 to ≤ 2 servings per week.
- Moderate egg consumption is advised (0.4 oz/d) due to cholesterol content.
- Consuming one egg/d does not increase CVD risk in healthy individuals, however, there is evidence that it may in individuals with or at high risk of CVD and T2DM.

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Eggs

- Negative reputation most likely began decades ago when the AHA recommended that dietary cholesterol consumption should be no more than 300 mg/day and that no more than 3 egg yolks should be consumed per week (1).
- An egg is a nutrient-dense food:
  - A medium-sized egg (50 g) contains 78 kcal, 6.3 g protein, 0.6 g carbohydrate, 5.3 g fat, of which 1.6 g is saturated, with 186 mg cholesterol (2).

1. American Heart Association. The National Diet-Heart Study.American Heart Association; 1968.
2. Kuang H, Yang F, Zhang Y, Wang T, Chen G. The Impact of Egg Nutrient Composition and Its Consumption on Cholesterol Homeostasis. Cholesterol. 2018;2018:6303810. Published 2018 Aug 23. doi:10.1155/2018/6303810

Eggs

- A systematic review (1) looked at egg intake and the risk for CVD in diabetics (6 randomized, controlled clinical trials) – egg intake did not impact major CVD risk factors.
  - As much as 6-12 eggs weekly had no effect on total cholesterol, LDL-cholesterol, triglycerides, fasting glucose, insulin, or C-reactive protein compared with control groups that had no eggs or less than two eggs weekly. HDL-cholesterol increases were seen in 4 of the 6 studies.
- A study (n= 37 men and women with metabolic syndrome) looked at consuming 3 whole eggs daily on a carbohydrate-restricted diet compared with an egg substitute; Favorable changes in lipids and, in the egg group only, a reduction in plasma tumor necrosis factor-α (2).
- No association of egg consumption in a prospective study (3) of a large cohort of Swedish men (n=39,610) followed for 10+ yrs for T2DM; however, in a meta-analysis (12 studies), **U.S.-based** studies had a positive association between frequent egg consumption and higher risk of T2DM.
- Relationship between meat and eggs?
  - A longitudinal study (4) (n=55,851 participants of the Adventist Health Study 2 who were followed for 5.3 years) showed that all stratifications of meat intake significantly increased the risk of type 2 diabetes compared with no meat intake. Egg intake on its own, as compared with no egg intake, was not associated with type 2 diabetes risk, but within the categories of egg intake, there was a rise in risk as meat intake increased. The converse was not true except for nonmeat-eaters consuming ≥5 eggs/week.

1. Can J Diabetes. 2017 Aug;41(4):453-463. doi: 10.1016/j.jcjd.2016.12.002. Epub 2017 Mar 27. Impact of Egg Consumption on Cardiovascular Risk Factors in Individuals with Type 2 Diabetes and at Risk for Developing Diabetes: A Systematic Review of Randomized Nutritional Intervention Studies. Richard C[1], Cristall L[1], Fleming E[1], Lewis ED[1], Ricupero M[2], Jacobs RL[1], Field CJ[3]. 2. Blesso CN, Andersen CJ, Barona J, Volk B, Volek JS, Fernandez ML. Effects of carbohydrate restriction and dietary cholesterol provided by eggs on clinical risk factors in metabolic syndrome. J Clin Lipidol. 2013 ;7(5):463-71. 3. Wallin A, Forouhi NG, Wolk A, Larsson SC. Egg consumption and risk of type 2 diabetes: a prospective study and dose-response meta-analysis. *Diabetologia*. 2016;59(6):1204-13. 4. Sabaté J, Burkholder-Cooley NM, Segovia-Siapco G, et al. Unscrambling the relations of egg and meat consumption with type 2 diabetes risk. *Am J Clin Nutr*. 2018;108(5):1121-1128.

Intake of up to 3 Eggs per Day Is Associated with Changes in HDL Function and Increased Plasma Antioxidants in Healthy, Young Adults

- Intake of 1 egg/d was sufficient to increase HDL function and large-LDL particle concentration;
- However, intake of 2-3 eggs/d supported greater improvements in HDL function as well as increased plasma carotenoids.
- Overall, intake of ≤3 eggs/d favored a less atherogenic LDL particle profile, improved HDL function, and increased plasma antioxidants in young, healthy adults.

J Nutr. 2017 Mar;147(3):323-329. doi: 10.3945/jn.116.241877.

Associations of egg consumption with cardiovascular disease in a cohort study of 0.5 million Chinese adults

- “Daily consumers also had an 18% lower risk of CVD death and a 28% lower risk of haemorrhagic stroke death compared to non-consumers.”
- “…a moderate level of egg consumption (up to <1 egg/day) was significantly associated with lower risk of CVD, largely independent of other risk factors.”

Qin C, et al. Associations of egg consumption with cardiovascular disease in a cohort study of 0.5 million Chinese adults. Heart. 2018 Nov;104(21):1756-1763. doi: 10.1136/heartjnl-2017-312651. Epub 2018 May 21.

Seafood

- Benefits related to EPA/DHA content
- Young children, nursing mothers, pregnant women, and women who may become pregnant should avoid 5 species of fish that are higher in mercury: Shark, Swordfish, King Mackerel, or Tilefish

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Seafood

- DGA recommends a **variety of seafood** to reduce amount of methyl mercury from any one seafood type.
- DGA recommends consuming **about 8 oz/wk** to reduce cardiac deaths among individuals with or without pre-existing CVD.
- Seafood contains nutrients such as **high-quality protein, vitamin D, various minerals** that may confer cardioprotective benefits beyond n-3 fatty acids.

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Fish

- High dietary intake of fish and fish oil supplements associated with low rate of CVD.
- Environmental contaminants of concern – methylmercury, polychlorinated biphenyls and dioxins, which can diminish the health benefits of omega-3 fats.

J Nutr Metab 2012;2012:569486. Epub 2012 Apr 10. **Functional foods and nutraceuticals in the primary prevention of cardiovascular diseases.** Alissa EM Ferns GA.

Dairy

The Takeaways: Low-Fat Dairy

- Milk and milk products improve insulin resistance, postprandial hyperglycemia, lower BP, increases nitric oxide, improves endothelial function, decreases inflammation and oxidative stress.
- Milk proteins, both caseins and whey proteins and buttermilk with MFGM (milk fat globule membrane) are a rich sources of angiotensin converting enzyme (ACE) inhibitory peptides that significantly reduce blood pressure.
- The pooled data from the meta-analysis indicates an average reduction in blood pressure of 4.8/2.2 mm Hg with milk peptides.

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Dairy consumption and risk of stroke in Swedish women and men

- 74 961 Swedish women and men
- Mean follow-up of 10.2 years
- Consumption of low-fat dairy foods was inversely associated with risk of total stroke and cerebral infarction.

Stroke. 2012 Jul;43(7):1775-80. Epub 2012 Apr 19. **Dairy consumption and risk of stroke in Swedish women and men.** Larsson SC, et al.

The effect of dairy consumption on the prevention of cardiovascular diseases: A meta-analysis of prospective studies

- This is the first meta-analysis of the relationship of total dairy intake with CVD.
- This study showed an inverse relationship between total dairy intake and CVD while no relationship was found for CHD.

J Cardiovasc Thorac Res. 2017;9(1):1-11. doi: 10.15171/jcvtr.2017.01. Epub 2017 Mar 18.

Dairy Products, Dairy Fatty Acids, and the Prevention of Cardiometabolic Disease: a Review of Recent Evidence

“Current evidence suggests null or weak inverse association between consumption of dairy products and risk of cardiovascular disease. However, replacing dairy fat with polyunsaturated fat, especially from plant-based foods, may confer health benefits.”

Curr Atheroscler Rep. 2018 Mar 21;20(5):24. doi: 10.1007/s11883-018-0724-z. Dairy Products, Dairy Fatty Acids, and the Prevention of Cardiometabolic Disease: a Review of Recent Evidence. Yu E1,2, Hu FB3,4,5.

Low-Fat Dairy

- Part of the DASH diet
- Clinical studies show consistent BP-lowering effects of dairy products (excluding butter)
- May be due to bioactive dairy peptides & specific micronutrients (e.g., Ca, Mg, K, vit D)
- Specific dairy peptides may inhibit ACE

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

A systematic review and meta-analysis of elevated blood pressure and consumption of dairy foods.

"This meta-analysis supports the inverse association between low-fat dairy foods and fluid dairy foods and risk of EBP."

J Hum Hypertens. 2012 Jan;26(1):3-13. doi: 10.1038/jhh.2011.3. Epub 2011 Feb 10. **A systematic review and meta-analysis of elevated blood pressure and consumption of dairy foods.** Ralston RA, et al.

Calcium

- BP lowering with Ca supplementation is modest, ranging from -2.6 to -1.27 mm Hg for SBP and -0.84 to -0.24 mm Hg for DBP.
- Question of whether increasing Ca intake leads to Ca deposits in atherosclerotic lesions (< UL of 1000-3000 mg/d depending on lifestage group), but data are inconsistent and inconclusive.
- Low vitamin D and/or vitamin K may be a consequence of CVD rather than a cause.

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Probiotics and Cholesterol Lowering

- “Supplementation of diet with fermented dairy products or lactic acid bacteria containing dairy products has shown the potential to reduce serum cholesterol levels.
- Various approaches have been used to alleviate this issue, including the use of probiotics, especially Bifidobacterium spp. and Lactobacillus spp.”

Role of probiotics' metabolites as epigenetic approach to control high cholesterol and colon cancer. Exp Diabetes Res. 2012;2012:902917. Epub 2012 May 3. **Cholesterol-lowering probiotics as potential biotherapeutics for metabolic diseases.** Kumar M, et al.

Probiotics and Cholesterol-Lowering

- "…there are numerous reports on cholesterol removal ability of probiotics and their hypocholesterolemic effects.
- Several possible mechanisms for cholesterol removal by probiotics are:
  - Assimilation of cholesterol by growing cells
  - Binding of cholesterol to cellular surface
  - Incorporation of cholesterol into the cellular membrane
  - Deconjugation of bile via bile salt hydrolase
  - Coprecipitation of cholesterol with deconjugated bile
  - Binding action of bile by fiber
  - Production of short-chain fatty acids by oligosaccharides."

Exp Diabetes Res. 2012;2012:902917. Epub 2012 May 3. Cholesterol-lowering probiotics as potential biotherapeutics for metabolic diseases. Kumar M, et al.

The effects of dietary and nutrient interventions on arterial stiffness: a systematic review.

"Consumption of Lactobacillus helveticus fermented milk that contained the bioactive tripeptides isoleucyl-prolyl-proline and valyl-prolyl-proline was shown to be effective in reducing arterial stiffness in hypertensive patients with small to moderate effects."

Am J Clin Nutr. 2011 Feb;93(2):446-54. Epub 2010 Dec 8. **The effects of dietary and nutrient interventions on arterial stiffness: a systematic review.** Pase MP, et al.

Summary:
Protein, Part 1

- Increased red meat intake is associated with heightened CVD risk.
- Inconclusive evidence that plant protein is superior to animal protein
- No scientific evidence to support energy intakes of protein that exceed 20%.
- Lean meat recommendations (DGA, 2010):
  - 1.8 oz. lean meat/2000 kcal diet/day
  - 1.5 oz. poultry/2000 kcal diet/day

Summary:
Protein, Part 2

- Processed meat associated with greater CVD risk compared with unprocessed meat; Limit servings to 0 to ≤ 2 servings/week
- Aim for moderate egg consumption for individuals with CVD risk and less if high meat
- Seafood
  - Avoid high mercury-containing fish
  - About 8 oz./week
  - High-quality, low contaminant fish oil supplements

Summary:
Protein, Part 3

- Soy foods
  - Generally good for cardiovascular health
  - Soy isoflavones may be more cardioprotective than protein
  - Other soy constituents to be identified
- Low-fat dairy most likely beneficial for CVD

Dietary Fat

Dietary Fats and Cardiovascular Disease: A Presidential Advisory From the American Heart Association

- “Taking into consideration the totality of the scientific evidence, satisfying rigorous criteria for causality, we conclude strongly that lowering intake of saturated fat and replacing it with unsaturated fats, especially polyunsaturated fats, will lower the incidence of CVD.
- This recommended shift from saturated to unsaturated fats should occur simultaneously in an overall healthful dietary pattern such as DASH (Dietary Approaches to Stop Hypertension) or the Mediterranean diet as emphasized by the 2013 American Heart Association/American College of Cardiology lifestyle guidelines and the 2015 to 2020 Dietary Guidelines for Americans.”

Circulation. 2017 Jun 15. pii: CIR.0000000000000510. doi: 10.1161/CIR.0000000000000510. [Epub ahead of print]
Dietary Fats and Cardiovascular Disease: A Presidential Advisory From the American Heart Association. Sacks FM, Lichtenstein AH, Wu JHY, Appel LJ, Creager MA, Kris-Etherton PM, Miller M, Rimm EB, Rudel LL, Robinson JG, Stone NJ, Van Horn LV; American Heart Association

Saturated Fatty Acids and Cardiovascular Disease: Replacements for Saturated Fat to Reduce Cardiovascular Risk

- While the 2015-2020 Dietary Guidelines for Americans advise substituting both monounsaturated and polyunsaturated fatty acids for SFA, evidence supports other nutrient substitutions that will also reduce CVD risk.
- For example, replacing SFA with whole grains, but not refined carbohydrates, reduces CVD risk. Replacing SFA with protein, especially plant protein, may also reduce CVD risk.
- While dairy fat (milk, cheese) is associated with a slightly lower CVD risk compared to meat, dairy fat results in a significantly greater CVD risk relative to unsaturated fatty acids.

Healthcare (Basel). 2017 Jun 21;5(2). pii: E29. doi: 10.3390/healthcare5020029.
Saturated Fatty Acids and Cardiovascular Disease: Replacements for Saturated Fat to Reduce Cardiovascular Risk.
Briggs MA1, Petersen KS2, Kris-Etherton PM3.

Fatty acids in cardiovascular health

High-density lipoprotein (HDL)-C increases with SFA intake.

Among individuals who are insulin resistant, a low-fat, high-carbohydrate diet typically has an adverse effect on lipid profiles (in addition to decreasing HDL-C, it also increases triglyceride and LDL particle concentrations).

Baum et al. Fatty acids in cardiovascular health and disease: A comprehensive update. J Clin Lipidology 2012; 6:216-234.

Refined carbohydrates vs. SFAs

"No clear benefit of substituting carbohydrates for SFAs has been shown, although there might be a benefit if the carbohydrate is unrefined and has a low glycemic index.

Furthermore, the effect of particular foods on CHD cannot be predicted solely by their content of total SFAs because individual SFAs may have different cardiovascular effects and major SFA food sources contain other constituents that could influence CHD risk."

Am J Clin Nutr. 2011 Apr;93(4):684-8. Epub 2011 Jan 26. The role of reducing intakes of saturated fat in the prevention of cardiovascular disease: where does the evidence stand in 2010? Astrup A, et al.

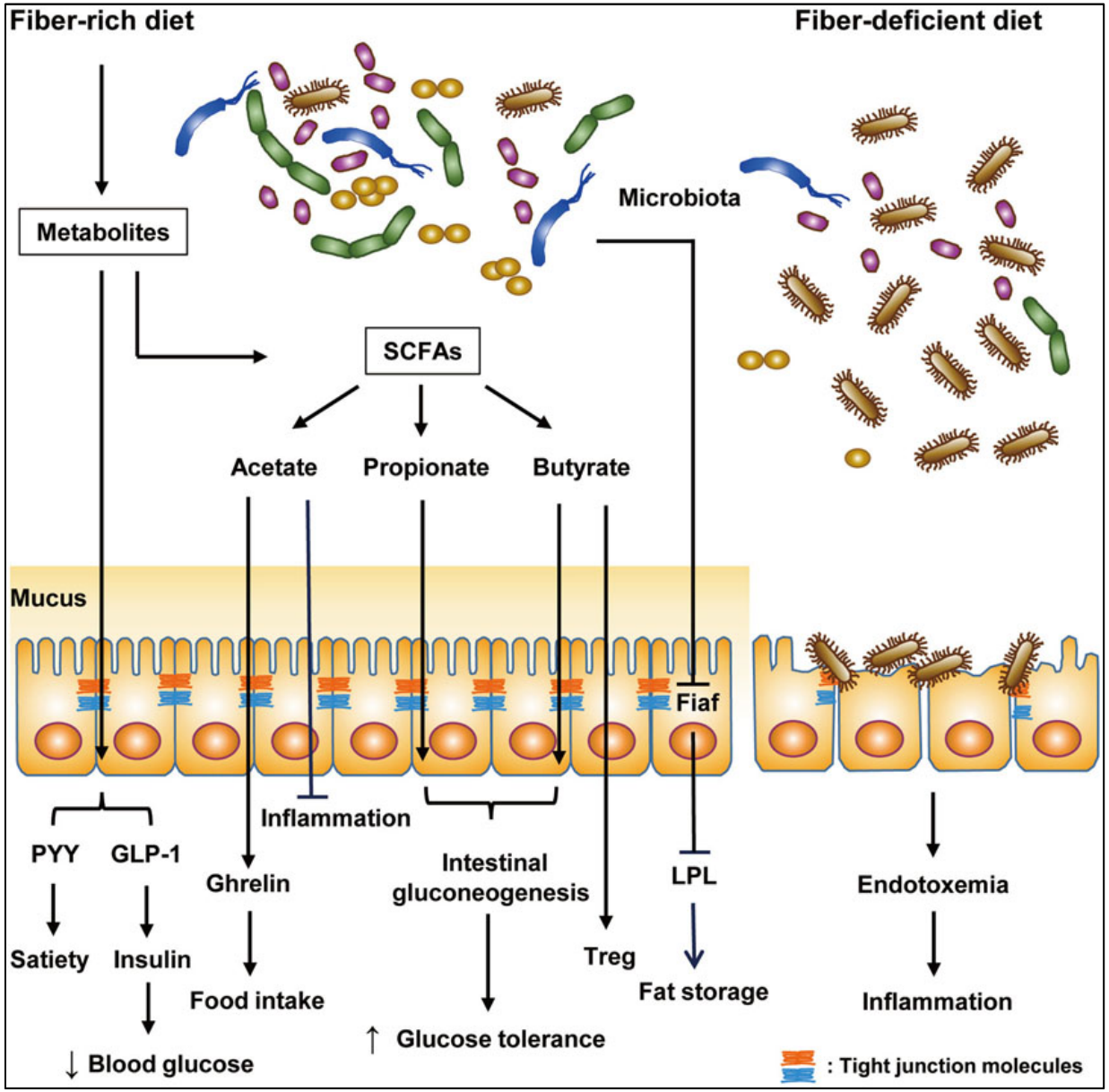
Metabolically-triggered inflammation

“There is evidence of a link between a form of low-grade systemic inflammation and several chronic diseases. This subclass of inflammation has been labelled ‘metaflammation’ (metabolically triggered inflammation), ‘paraflammation’, or ‘smouldering inflammation’.”

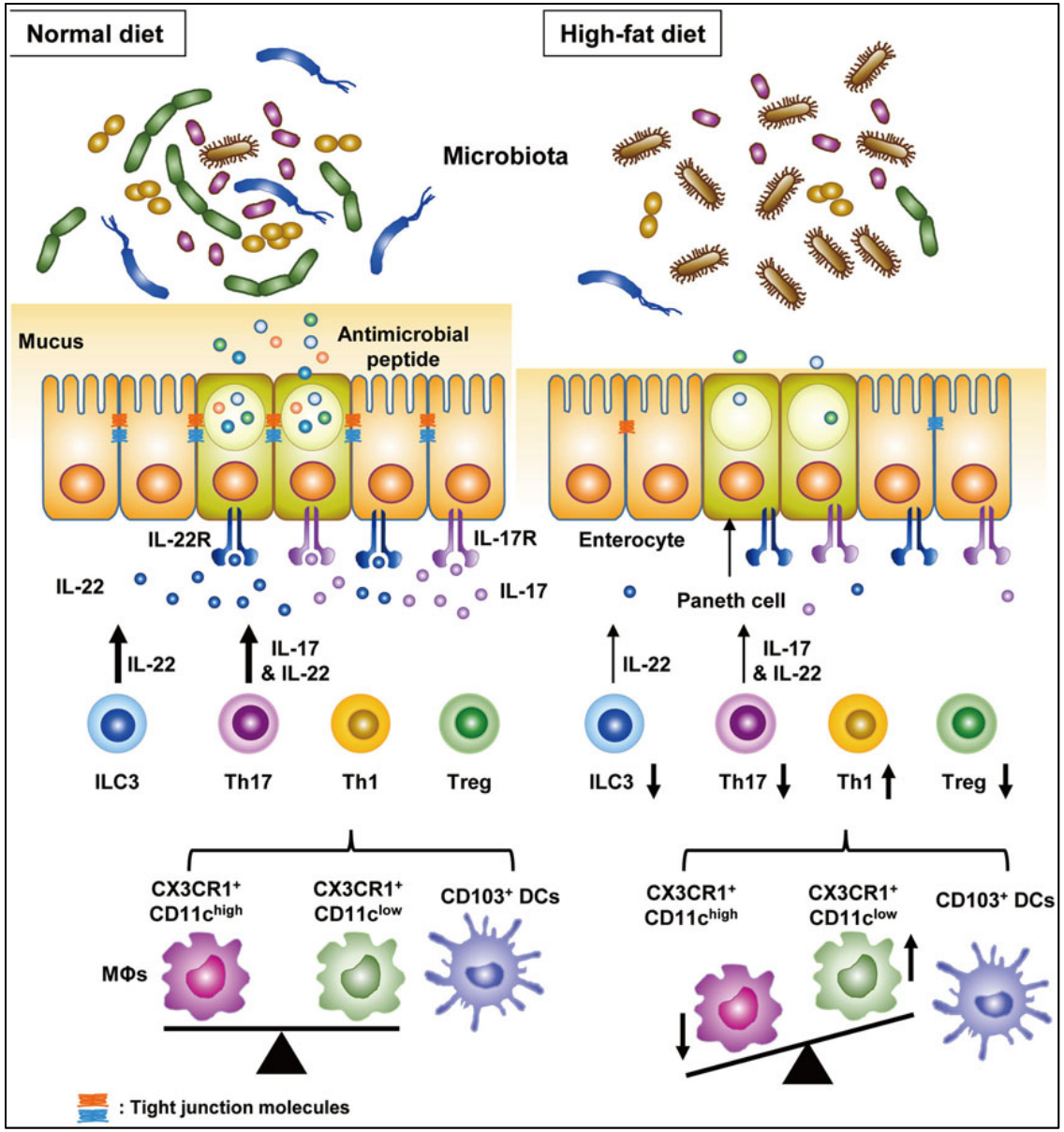
“It does not include the features of classical microbial-related inflammation (pain, redness, swelling and fever), and is characterized only by a mild increase in plasma levels of certain pro-inflammatory markers such TNF-a, IL-6 and C-reactive protein (CRP).”

“Obesity is known to be associated with this form of inflammation.”

Arya et al. *British Journal of Nutrition* (2010), 104, 724–728.



Yang BG, Hur KY, Lee MS. Alterations in Gut Microbiota and Immunity by Dietary Fat. Yonsei Med J. 2017;58(6):1083-1091.



Yang BG, Hur KY, Lee MS. Alterations in Gut Microbiota and Immunity by Dietary Fat. Yonsei Med J. 2017;58(6):1083-1091.

Endotoxin Levels Increase After a Western-Style Diet

Supplementary Table 1. Diet Composition

	Energy (*kcal*)	Fat (% of total calories)	Saturated fat (% of total calories)	Carbohydrates (% of total calories)	Protein (% of total calories)	Fiber (*g*)	Calcium (*mg*)
Western-style diet	2209	40	20.8	40	20	12.5	450
Prudent-style diet	2214	20	5.8	60	20	31	1055

NOTE. The Western-style diet and the prudent-style diet were fed for approximately 4 weeks. The prudent-style diet contained less than 11% greater amounts of the "anti-inflammatory nutrients" 3-omega fatty acids, vitamin C, and vitamin E than the Western-style diet.

Pendyala S, Walker JM, Holt PR. A high-fat diet is associated with endotoxemia that originates from the gut. Gastroenterology. 2012 May;142(5):1100-1101.e2.

Single meals of stress

"…a single high-fat meal may be associated with heightened cardiovascular reactivity to stress and offer insight into the pathways through which a high-fat diet may affect cardiovascular function."

Jakulj et al., *J. Nutr*. 137: 935–939, 2007.

But it was only one meal…

"Baseline **endotoxin concentrations** were 8.2 pg/mL…but **increased significantly…by 50% after a high-fat meal**… plasma from whole blood treated with as little as 10 pg endotoxin/mL increased the endothelial cell expression of E-selectin, at least partly via tumor necrosis factor-–induced cellular activation."

Erridge et al. Am J Clin Nutr 2007;86:1286 –92.

Metainflammation after a meat meal

"We conclude that the metaflammatory reaction to ingestion of a 'new' form of hybridised beef (wagyu) is indicative of a low-grade, systemic, immune reaction when compared with lean game meat (kangaroo)."

Arya et al. *British Journal of Nutrition* (2010), 104, 724–728

Grass-fed vs. grain-fed beef

“Research spanning three decades supports the argument that grass-fed beef (on a g/g fat basis), has a more desirable SFA lipid profile (more C18:0 cholesterol neutral SFA and less C14:0 & C16:0 cholesterol elevating SFAs) as compared to grain-fed beef.

Grass-finished beef is also higher in total CLA (C18:2) isomers, TVA (C18:1 t11) and n-3 FAs on a g/g fat basis.

This results in a better n-6:n-3 ratio that is preferred by the nutritional community. Grass-fed beef is also higher in precursors for Vitamin A and E and cancer fighting antioxidants such as GT and SOD activity as compared to grain-fed contemporaries.”

Nutr J. 2010 Mar 10;9:10. **A review of fatty acid profiles and antioxidant content in grass-fed and grain-fed beef.** Daley CA, Abbott A, Doyle PS, Nader GA, Larson S.

Coconut oil

- No human clinical trial evidence
- Coconut oil is 92% SFA, mostly lauric acid C12:0 (MCFA) and myrisitic acid (C14:0) which acts mostly like a LCFA
- MCFA have rapid absorption, hepatic uptake and immediate oxidation for energy production.
- Both lauric and myristic acid increase LDL-C similar to other MCFA and LCFA, but increase HDL-C more
- MCT (medium chain triglycerides) which are C-10 or less have direct portal vein absorption and are more water soluble. Only 4% of coconut oil is MCT of C-10 or less fatty acids.
- Coconut oil should not be recommended at this time for prevention or treatment of CHD or CVD due to the lack of prospective studies on CV outcomes, the mixed effects on serum lipids, the content of LCFA and the fact that replacement of coconut oil with PUFA and MUFA reduces CHD risk.

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Conclusions on Saturated Fat

- Dietary SFA intake is associated with an increased CHD risk and reducing dietary SFA in isocaloric (ISC) replacement with PUFA, MUFA, omega-6 FA, whole grains and plant proteins decrease CHD risk.
- The source of the SFA is associated with the risk for CHD. Dietary intake of meat and animal fat have the greatest risk.
- LCFA are the most likely SFA associated with CHD risk. SCFA are not associated with CHD risk but additional studies are needed to confirm.
- The carbon chain number of the SFA, as odd or even, may be associated with CHD risk (e.g., C15 and C17 from dairy may be protective)
- Replacement of SFA with PUFA reduces CHD risk
- Replacement of SFA with MUFA reduces CHD risk
- Replacement of SFA with omega 6 FA decreases CHD risk
- Replacement of SFA with refined CHO increases CHD risk

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Industrialized-Produced TFAs

- Dyslipidemia
  - Increase TC, LDL-C, TG and VLDL
  - Lower HDL-C
  - Increase TC/HDL ratio
  - Increase apolipoprotein B
  - Increase lipoprotein (a) [Lp(a)]
- Increase in adipose tissue TFA levels
- Increase in TG and phospholipid TFA levels
- Increase insulin resistance, glucose and T2DM risk
- Increase thrombogenic risk and plaque vulnerability
- Increase risk of CHD and MI
- Increase risk of primary cardiac arrhythmias and sudden death
- Increase in all-cause mortality by 25% from lowest to highest quintile
- Increase of 2% in energy in total TFA intake results in 25% increase in CHD (CHD death and nonfatal MI)
- Hypertension, endothelial dysfunction, obesity, increased inflammation

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Essential Fatty Acid Families

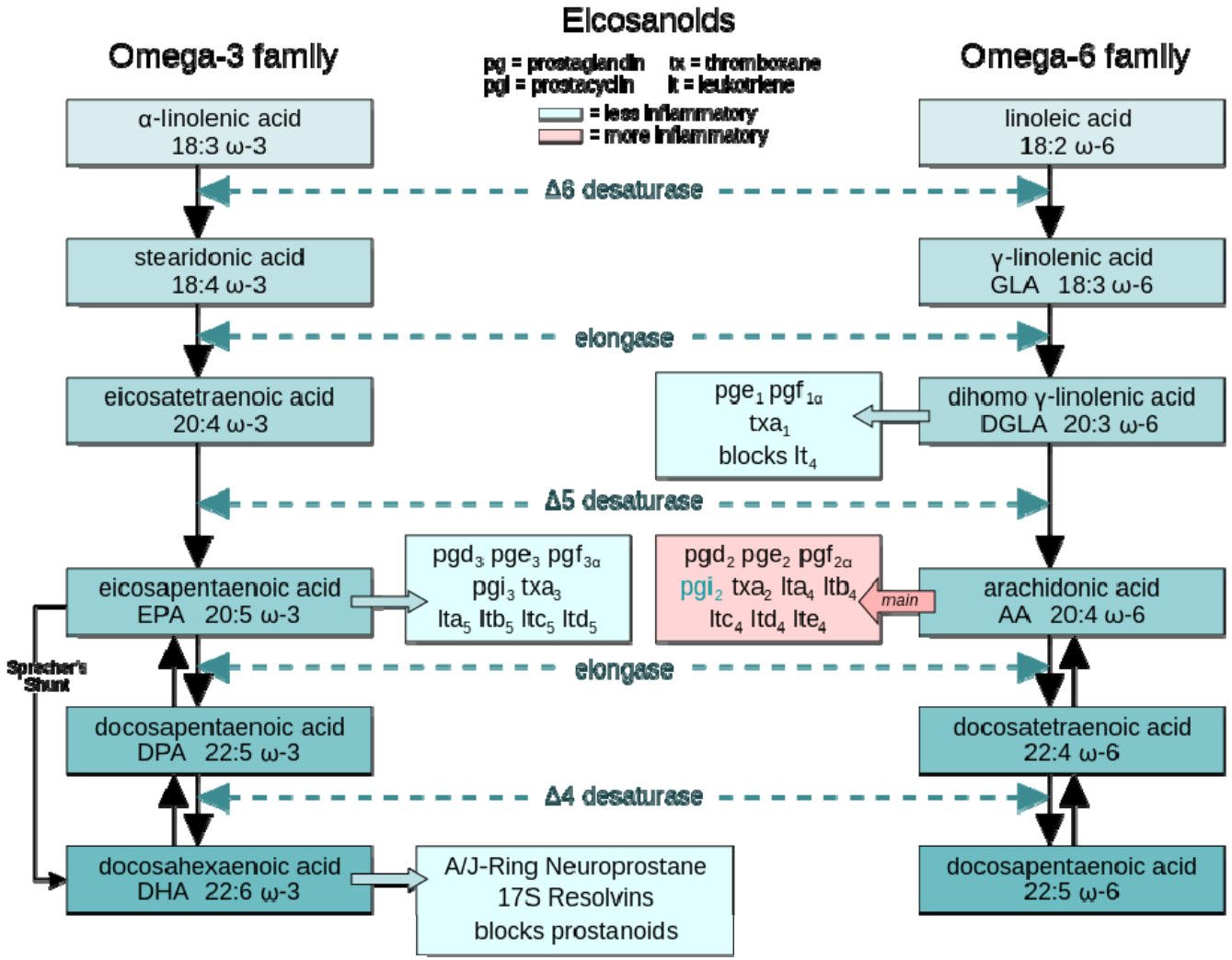


Image: Thoop, D. https://commons.wikimedia.org/w/index.php?curid=1630962

Too much omega-6 fat and too little omega-3 fat is inflammatory

- “Studies indicate that a high intake of omega-6 fatty acids shifts the physiologic state to one that is prothrombotic and proaggregatory, characterized by increases in blood viscosity, vasospasm, and vasoconstriction, and decreases in bleeding time.” (1)
- “Omega-3 fatty acids, however, have anti-inflammatory, antithrombotic, antiarrhythmic, hypolipidemic, and vasodilatory properties.” (1)

1. Curr Sports Med Rep. 2007 Jul;6(4):230-6.

The Omega-3 Index

- “In 2004, the 'ω-3 index' was described as the sum of eicosapentaenoic acid (EPA, 20:5 n-3) and docosahexaenoic acid (DHA, 22:6 n-3) in red blood cells (RBCs) as an index of coronary heart disease mortality.”
- Mean Omega-3 Index in the U.S. (4.3%)
- American women had a significantly higher Omega-3 Index than men
  (4.8% vs. 3.8%, $p < 0.001$)
- Ideal is 8% for cardiovascular health
- “…we estimate that risk for fatal CHD would have been reduced by about 30% moving from an Omega-3 Index of 4%-8%.”

Fielding BA. *Curr Opin Clin Nutr Metab Care*. 2017;20(5):360-365.

Thuppal SV, et al. *Nutrients.* 2017;9(9):930-41.

Harris WS, et al. *Atherosclerosis.* 2017;262:51-54.

Signs of fatty acid imbalance and inflammation

- Dry skin
- Dandruff
- Frequent urination
- Irritability
- Attention deficit
- Soft nails
- Alligator skin
- Allergies
- Lowered immunity
- Learning problems
- Poor wound healing
- Frequent infections
- Weakness
- Fatigue
- Dry, unmanageable hair
- Excessive thirst
- Brittle, easily frayed nails
- Hyperactivity
- “Chicken skin” on back of arms
- Dry eyes
- Patches of pale skin on cheeks
- Cracked skin on heels or fingertips

Omega-3 fatty acids

- "…the benefits of EPA + DHA supplementation for CVD prevention via supplements are supported if fish intake is low, particularly in individuals with elevated TG."
- "…pleiotropic effects and possible benefits for depression and inflammatory diseases…are supportive of the use of these n-3 fatty acids."

Baum et al. Fatty acids in cardiovascular health and disease: A comprehensive update. J Clin Lipidology 2012; 6:216-234.

Select Cardiovascular Benefits of Omega-3 Fatty Acids

- Decrease MI and CHD with concomitant use of statins
- Reduce stent restenosis
- Reduce post MI mortality
- Reduce plaque formation
- Reduce coronary artery calcification and atherosclerosis,
- Improve the lipid profile, lower glucose, improve insulin resistance and reduce blood pressure

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

More on omega-3 fats

- Beneficial effect of omega-3 fatty acids on cardiovascular morbidity and mortality
- Large secondary prevention trials of omega-3 fatty acids reported lower mortality due to reduced CV events. Reduction in sudden death has implicated an important role for an antiarrhythmic action of omega-3 fatty acids.
- Antithrombotic and antiinflammatory activity of omega-3 fatty acids may be key actions in reducing CV events and mortality.

Curr Opin Cardiol. 2012 Jul;27(4):412-9. Marine omega-3 fatty acids and coronary heart disease. Calder PC, Yaqoob P.

Omega-3 Index and Specialized Pro-Resolving Lipid Mediators

- "A doubling of the omega-3 index correlated with increases of 2.3-fold in 18-hydroxy-eicosapentaenoic acid (HEPE; $P < .0001$), 1.7-fold in 15-HEPE ($P = .03$), 1.9-fold in 5-HEPE ($P = .04$), and 3.6-fold in 4-hydroxy-docosahexaenoic acid ($P < .001$)."

- "Among subjects with symptomatic PAD who took oral fish oil supplements for 1 month, observed changes in the omega-3 index were strongly associated with increases in downstream mediators in the biochemical pathways of resolution."

Schaller MS, et al. *J Clin Lipidol*. 2017;11(5):1289-1295.

No Impact of Fish Oil Supplements on Bleeding Risk: a Systematic Review

- 52 publications were included; 32 publications on healthy subjects and 20 publications on patients undergoing surgery
- The majority of the included studies were randomized controlled trials or included a control group
- Overall, fish oil supplements reduced platelet aggregation in healthy subjects
- Fish oil exposure in surgical patients did not increase bleeding or blood transfusions either during or after surgery

Begtrup KM, et al. *Dan Med J*. 2017;64(5).

Vegetable oils

- Sources of MUFAs and PUFAs
- Extracted from plants such as olive, soybean, and sunflower
- Oils rich in unsaturated fatty acids also present in foods such as nuts, avocados, and olives

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Consider the total food source

"…relatively unrefined olive oil retains several lipophilic components, whereas highly refined olive oil has a low level of some of these potentially bioactive compounds."

Baum et al. Fatty acids in cardiovascular health and disease: A comprehensive update. Section by Kevin Maki, PhD, "Monounsaturated fatty acid intake and atherosclerotic cardiovascular disease risk." J Clin Lipidology 2012; 6:216-234.

Beneficial effects of polyphenol-rich olive oil in patients with early atherosclerosis

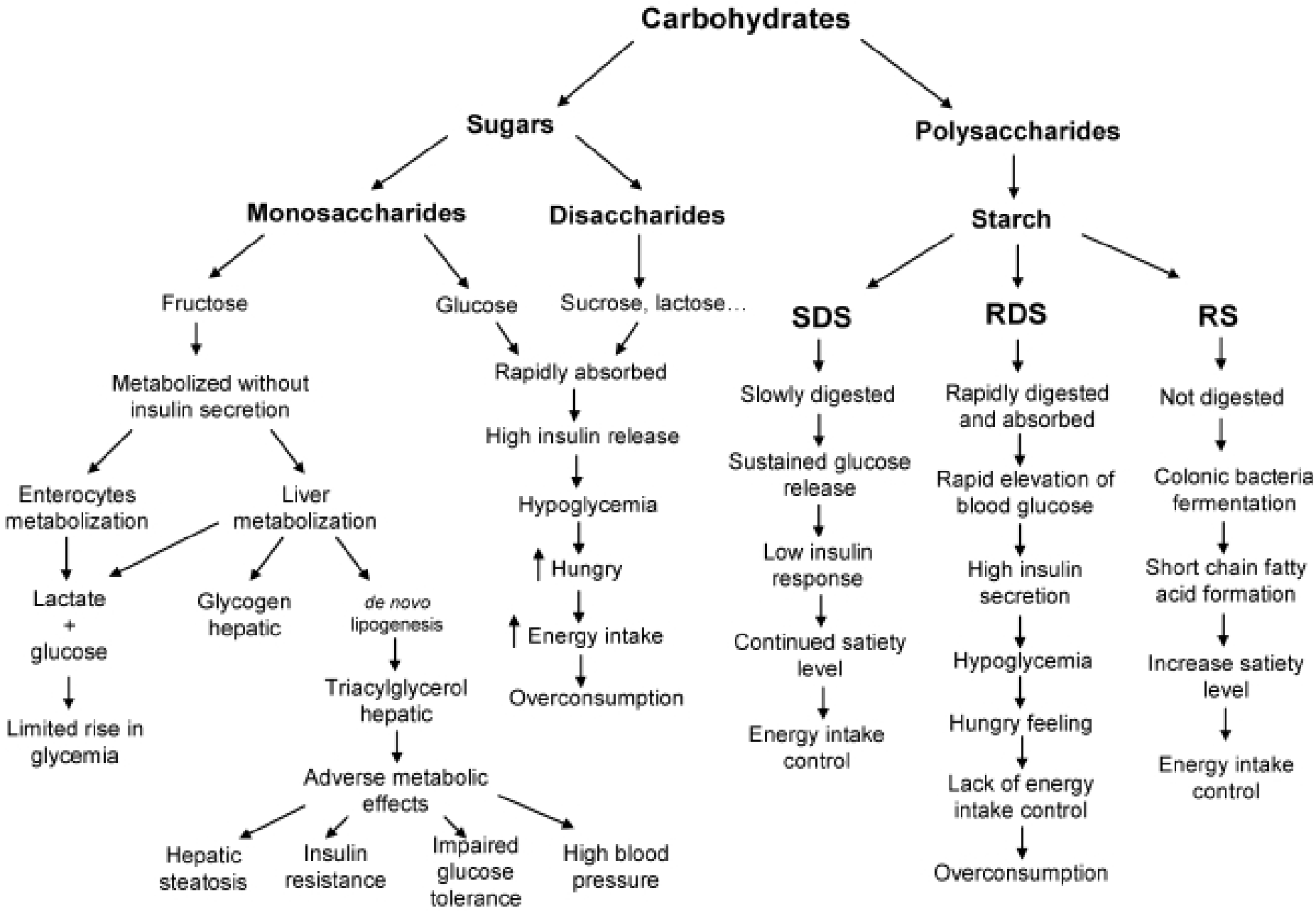
- OO significantly improved endothelial function
- Significant reduction in inflammatory parameters:
  - sICAM
  - White blood cells
  - Monocytes
  - Lymphocytes
  - Platelets

Eur J Nutr. 2012 Aug 8. [Epub ahead of print] **Beneficial effects of polyphenol-rich olive oil in patients with early atherosclerosis.** Widmer RJ, et al.

Summary:
Dietary Fat Intake

- High-fat may lead to metabolic endotoxemia and subsequent endothelial dysfunction & cardiovascular stress
- A moderate fat diet in which unsaturated fatty acids replace SFAs, and CHO are not increased, seems to be most preferred for cardiovascular health.
- Omega-3 PUFAs are important for reducing inflammation, thrombosis, and arterial stiffness.

Dietary Carbohydrate



Erik E. J. G. Aller, Itziar Abete, Arne Astrup, J. Alfredo Martinez, and Marleen A. van Baak. Starches, Sugars and Obesity. Nutrients. 2011 March; 3(3): 341–369. Published online 2011 Mar 14. doi: 10.3390/nu3030341

Glycemic Index

- The glycemic index of a food quantifies the area under the glycemic response curve (AUC) of a test food, compared to the same amount (usually 50 g of available carbohydrate) of a reference food, most often glucose or white bread.
- Generally, foods with a GI ≤ 55 are classified as low GI, whereas foods with a GI ≥ 70 are classified as high GI foods.

Nutrients. 2011 March; 3(3): 341–369.

Glycemic load, glycemic index and risk of cardiovascular diseases: Meta-analyses of prospective studies

- Dose-response meta-analysis found an increased RR of 1.18 per 50 unit increment of GL with cardiac event risk in Caucasians.
- High GL and GI were associated with significant increased risk of CVDs, specifically for women.

Atherosclerosis. 2012 Aug;223(2):491-6. Epub 2012 Jun 6. **Glycemic load, glycemic index and risk of cardiovascular diseases: Meta-analyses of prospective studies.** Ma XY, et al.

Do we need to question GI?

- A review of 73 scientific articles published between 2006 to 2018 (terms: glycemic index, glycemic load, diabetes, cardiovascular disease, body weight, satiety, and obesity) - the finding was an equivocal relationship between GI/GL and disease outcome (1).
- Several factors may determine an individual's glycemic response at each feeding, such as the microbiome (2).

1. Nutrients. 2018 Sep 22;10(10). pii: E1361. doi: 10.3390/nu10101361. Relevance of the Glycemic Index and Glycemic Load for Body Weight, Diabetes, and Cardiovascular Disease. Vega-López S1, Venn BJ2, Slavin JL3.

2. Cell. 2015 Nov 19;163(5):1079-1094. doi: 10.1016/j.cell.2015.11.001. **Personalized Nutrition by Prediction of Glycemic Responses.** Zeevi D[1], Korem T[1], Zmora N[2], Israeli D[3], Rothschild D[1], Weinberger A[1], Ben-Yacov O[1], Lador D[1], Avnit-Sagi T[1], Lotan-Pompan M[1], Suez J[4], Mahdi JA[4], Matot E[1], Malka G[1], Kosower N[1], Rein M[1], Zilberman-Schapira G[4], Dohnalová L[4], Pevsner-Fischer M[4], Bikovsky R[1], Halpern Z[5], Elinav E[6], Segal E[7].

Gluten free diet and nutrient deficiencies: A review

- Increased glycemic index and glycemic load
- Increased saturated and hydrogenated fatty acids
- Low in fiber due to high starch and/or refined flours
- Low in micronutrients, especially vitamin D, B12, folate
- Low in minerals, such as Fe, Zn, Mg, Ca

Vici G, Belli L, Biondi M, Polzonetti V. Gluten free diet and nutrient deficiencies: A review. Clin Nutr. 2016 Dec;35(6):1236-1241. doi: 10.1016/j.clnu.2016.05.002. Epub 2016 May 7.

Minerals

“One of the most common deficiencies from a GFD are an insufficient amount of Ca, Fe, Mg, and Zn. This is mainly because the most of popular gluten-free (GF) raw materials are poor in minerals.”

Rybicka I. **The Handbook of Minerals on a Gluten-Free Diet.** Nutrients. 2018 Nov 5;10(11). pii: E1683. doi: 10.3390/nu10111683.

Toxic metals in GF foods

- “Foods containing rice were significantly higher in As, Hg and Pb and lower in Se, Fe, Cu and Zn.
- Wheat-based foods were higher in Cd. Mercury concentrations were low (<3.5 ng/g); speciation was predominantly methylmercury.
- Arsenic and mercury in rice were correlated.
- GF foods contained significantly more As and Hg.
- Eating a wide variety of GF grains may reduce contaminant exposure and increase micronutrient status compared to a rice-based GF diet.”

Punshon T, Jackson BP. Essential micronutrient and toxic trace element concentrations in gluten containing and gluten-free foods. Food Chem. 2018 Jun 30;252:258-264. doi: 10.1016/j.foodchem.2018.01.120.

Accumulation of Heavy Metals in People on a GF Diet

- We collected NHANES survey data on blood levels of lead, mercury, and cadmium from subjects who were on a GFD (n = 115) and participants who were not on a GFD (n = 11,239).
- In an analysis of data collected from NHANES, persons on a GFD had significantly higher urine levels of **total arsenic and blood levels of mercury, lead, and cadmium than persons not avoiding gluten**.

Raehsler SL, Choung RS, Marietta EV, Murray JA. Accumulation of Heavy Metals in People on a Gluten-Free Diet. Clin Gastroenterol Hepatol. 2018 Feb;16(2):244-251. doi: 10.1016/j.cgh.2017.01.034. Epub 2017 Feb 20.

Impact of gluten-free diet on cardiovascular risk factors. A retrospective analysis in a large cohort of coeliac patients

"A gluten-free diet significantly affects cardiovascular risk factors in coeliac patients, but changes do not consistently point towards worse or better risk profiles, thus suggesting that the diet is unlikely to be atherogenic."

Dig Liver Dis. 2013 May 17. pii: S1590-8658(13)00147-3. doi: 10.1016/j.dld.2013.04.001. [Epub ahead of print]

Cardiovascular risk factors

- “A total of 5372 articles were identified, from which 27 were included.
- Overall study quality was low and restricted to patients with celiac disease.
- Consistent findings across studies included an increase in total cholesterol, high density lipoprotein, fasting glycaemia, and body mass index (while remaining within the healthy weight range).”

Potter MDE, Brienesse SC, Walker MM, Boyle A, Talley NJ. Effect of the gluten-free diet on cardiovascular risk factors in patients with coeliac disease: A systematic review. J Gastroenterol Hepatol. 2018 Apr;33(4):781-791. doi: 10.1111/jgh.14039. Epub 2018 Feb 14.

Metabolic Alterations in Celiac Disease Occurring after Following a Gluten-Free Diet

- “CD patients showed an increased risk of developing both MS and HS after following a GFD.
- MS was reported in 3.24% of the cases at the time of CD diagnosis and in 14.59% after GFD ($p < 0.0001$).
- HS was reported in 1.7% at the time of diagnosis and in 11.1% after GFD ($p < 0.0001$).
- With regard to metabolic sub-categories, the prevalence of the increase in WC, hypertension, reduction of HDL cholesterol, hyperglycemia, hypercholesterolemia, and BMI > 25 was significantly higher after GFD compared to baseline at CD diagnosis.”

Digestion. 2018 Dec 14:1-7. doi: 10.1159/000495749. [Epub ahead of print]

Riceabetes

- “A high intake of rice is associated with a high incidence and prevalence of diabetes.
- While this may be partially due to the high glycemic index carbohydrate content, it may also be due to a high arsenic level found in rice.
- Arsenic increases insulin resistance and decreases beta-cell function through oxidative stress, high cytokine levels, activation of NF-kappa B and increased amyloid formation in the pancreatic beta cells.”

Bell DS[1]. Riceabetes: is the association of type 2 diabetes with rice intake due to a high carbohydrate intake or due to exposure to excess inorganic arsenic? Postgrad Med. 2015;127(8):781-2. doi: 10.1080/00325481.2015.1098518. Epub 2015 Oct 9.

Differential Effects of Carbohydrates on Inflammation

"In the **oat and wheat bread and potato group**, circulating concentrations of **IL-1 and IL-6 tended to increase**, whereas in the **rye-pasta group they tended to decrease**."

Kallio et al. Am J Clin Nutr 2008;87:1497–503.

Are all sweeteners the same?

Agave nectar, sucrose, fructose, glucose, brown rice syrup, xylitol, corn syrup, corn syrup solids, polyols, xylitol, sorbitol, fructose, glucose, dextrose, sucrose, brown rice syrup, evaporated cane juice, erythritol, NutraSweet, Splenda, aspartame, brown sugar, Demerara sugar, Stevia, invert sugar, lactose, maltodextrin, maltose, maple syrup, confectioner's sugar, turbinado sugar, fruit juice concentrate, honey, barley malt, cane sugar, date sugar, caramel…

Added sugars and refined grains

- Contribute a significant portion of calories to the American diet (e.g., sugar-sweetened beverages, SSB)
- High-glycemic foods
- Consumption of CHOs, particularly sugars and refined grains, are positively associated with several CVD risk factors, including elevated TG, low HDL-C, and decreased insulin sensitivity.

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Sugar-sweetened beverages and hypertension

"Over the duration of the study, a reduction of **one 12-oz serving of sugar-sweetened beverages per day** was associated with an **average of 1.8 mmHg reduction in systolic blood pressure** and **an average of 1.1 mmHg reduction in diastolic blood pressure**."

Feig DI Future Cardiol. 2010 Nov;6(6):773-6. **Sugar-sweetened beverages and hypertension.**

High Fructose Corn Syrup and Vascular Health

- Consumption of HFCS (20%) increased serum triglyceride, VLDL and insulin levels as well as blood pressure.
- Resveratrol supplementation efficiently restored HFCS-induced deteriorations.
- Thus, intake of HFCS leads to vascular dysfunction by decreasing vasoprotective factors and provoking oxidative stress in association with metabolic disturbances.

Food Chem Toxicol. 2012 Jun;50(6):2135-41. Epub 2012 Mar 23. **High-fructose corn syrup causes vascular dysfunction associated with metabolic disturbance in rats: Protective effect of resveratrol.** Akar F, et al.

Honey as a medicinal food

- Rich in polyphenols shown to exhibit several biological activities: antimicrobial, anti-inflammatory, antioxidant, cardioprotective properties, and anticancer
- Polyphenol-enriched fraction from honey can suppress cancer in an in vivo model
- To date, approximately 300 varieties of honey have been identified, which are characterized by a different mixture of approximately 30 different polyphenols.

Alleva R, Manzella N, Gaetani S, Ciarapica V, Bracci M, Caboni MF, Pasini F, Monaco F, Amati M, Borghi B, Tomasetti M. (2016) Organic honey supplementation reverses pesticide-induced genotoxicity by modulating dna damage response. Mol Nutr Food Res. 2016 Apr 30. doi: 10.1002/mnfr.201600005. [Epub ahead of print]

Summary:
Carbohydrate & Sugar Intake

- Glycemic load & glycemic index are associated with CVD risk.
- Added sugars like HFCS may have adverse effects on cardiovascular health.

Plant-Based Foods

Eat plant foods, reduce chronic disease

- CVD
- Cancer
- Diabetes
- Alzheimer's disease
- Cataracts
- Age-related functional decline

Liu et al. Journal of Food Science Vol. 78, S1, 2013

Why plant foods for cardiovascular health?

"High intakes of potassium and magnesium are recommended in conjunction with sodium restriction."

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

The phytonutrient gap

- 69% fall short in green
- 78% fall short in red
- 86% fall short in white
- 88% fall short in purple/blue
- 79% fall short in yellow/orange

America's Phytonutrient Report, Nutrilite Health Institute, 2009;

Phytochemicals

"Understanding the complex role of diet in such chronic diseases is challenging since a typical diet provides **more than 25,000 bioactive food constituents**, many of which may modify a multitude of processes that are related to these diseases."

Carlsen MH, Halvorsen BL, Holte K, Bøhn SK, Dragland S, Sampson L, Willey C, Senoo H, Umezono Y, Sanada C, Barikmo I, Berhe N, Willett WC, Phillips KM, Jacobs DR Jr, Blomhoff R. The total antioxidant content of more than 3100 foods, beverages, spices, herbs and supplements used worldwide. Nutr J. 2010 Jan 22;9:3. doi: 10.1186/1475-2891-9-3.

The Family of Phytochemicals

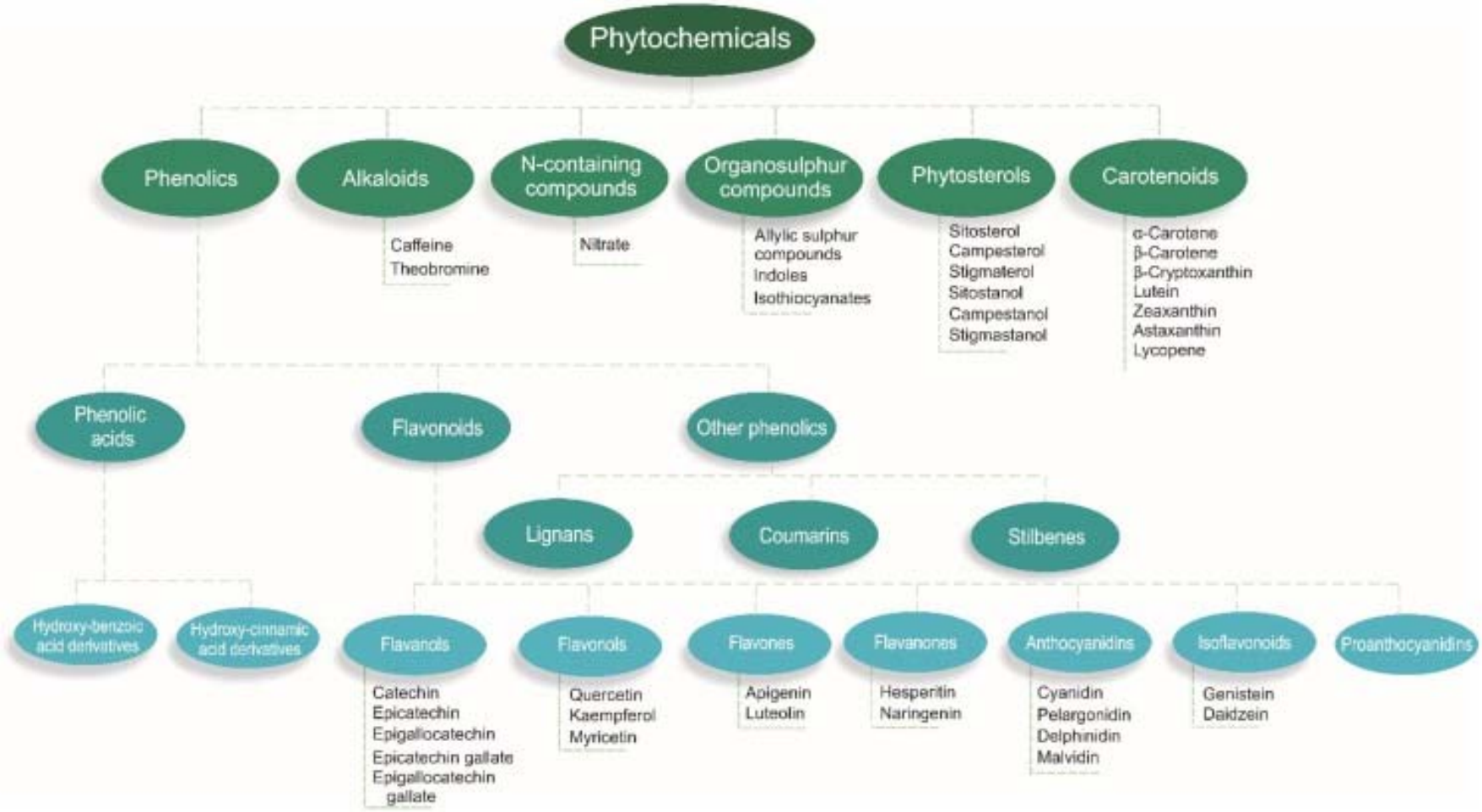


Image Credit: Blekkenhorst LC, Sim M, Bondonno CP, Bondonno NP, Ward NC, Prince RL, Devine A, Lewis JR, Hodgson JM. Cardiovascular Health Benefits of Specific Vegetable Types: A Narrative Review. Nutrients. 2018 May 11;10(5). pii: E595. doi: 10.3390/nu10050595.

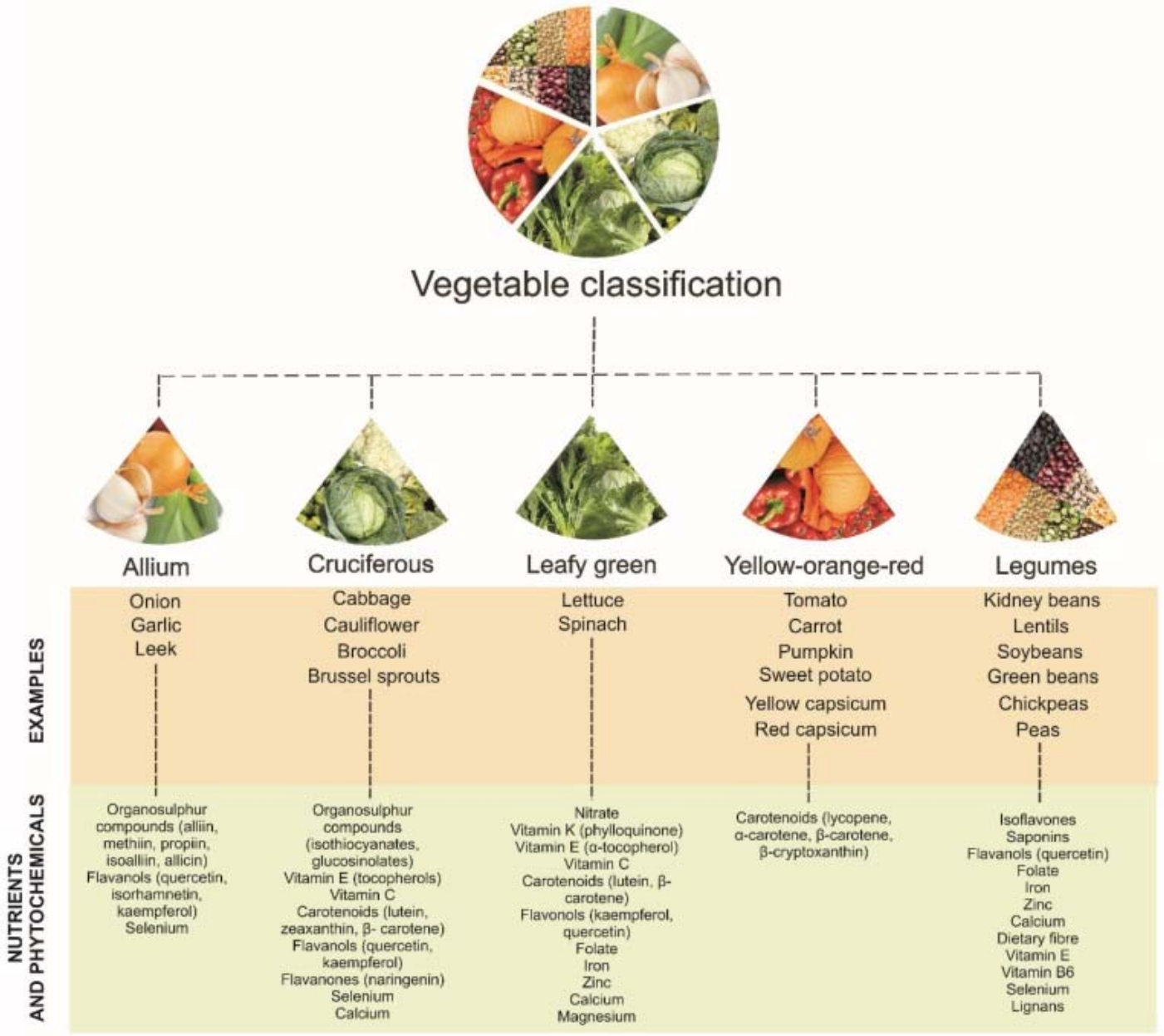


Image Credit: Blekkenhorst LC, Sim M, Bondonno CP, Bondonno NP, Ward NC, Prince RL, Devine A, Lewis JR, Hodgson JM. Cardiovascular Health Benefits of Specific Vegetable Types: A Narrative Review. Nutrients. 2018 May 11;10(5). pii: E595. doi: 10.3390/nu10050595.

THE PLEIOTROPIC EFFECTS OF PHYTOCHEMICALS

- Anti-inflammatory
- Insulin-sensitizing
- Stress response

Choose fewer and more phytochemicals:

Phytochemical Diversity

"These findings indicate that botanical diversity plays a role in determining the bioactivity of high-VF diets and that smaller amounts of many phytochemicals may have greater beneficial effects than larger amounts of fewer phytochemicals."

J Nutr.2006 Aug;136(8):2207-12. Dietary botanical diversity affects the reduction of oxidative biomarkers in women due to high vegetable and fruit intake. Thompson HJ, Heimendinger J, Diker A, O'Neill C, Haegele A, Meineck B, Wolfe P, Sedlacek S, Zhu Z, Jiang W.

PLANT DIVERSITY AND FOOD VARIETY ARE KEY TO GOOD HEALTH.

Med Hypotheses. 2018 Nov;120:28-42. doi: 10.1016/j.mehy.2018.08.002. Epub 2018 Aug 9.

Ancestral Diet

Over 3000 species

Modern Diet

100-400 species

Dietary variety is a protective factor for elevated systolic blood pressure.

"There was a positive correlation between diastolic blood pressure and sugar and cholesterol intake, and a negative one with intake of fiber, portions of oil and fats and diet quality.

Dietary variety with ≥ 8 food items showed a protective effect for alterations in systolic blood pressure…"

Arq Bras Cardiol. 2012 Apr;98(4):338-343. Epub 2012 Mar 15. **Dietary variety is a protective factor for elevated systolic blood pressure.** [Article in English, Portuguese]. Oliveira EP, et al.

Increase your variety!

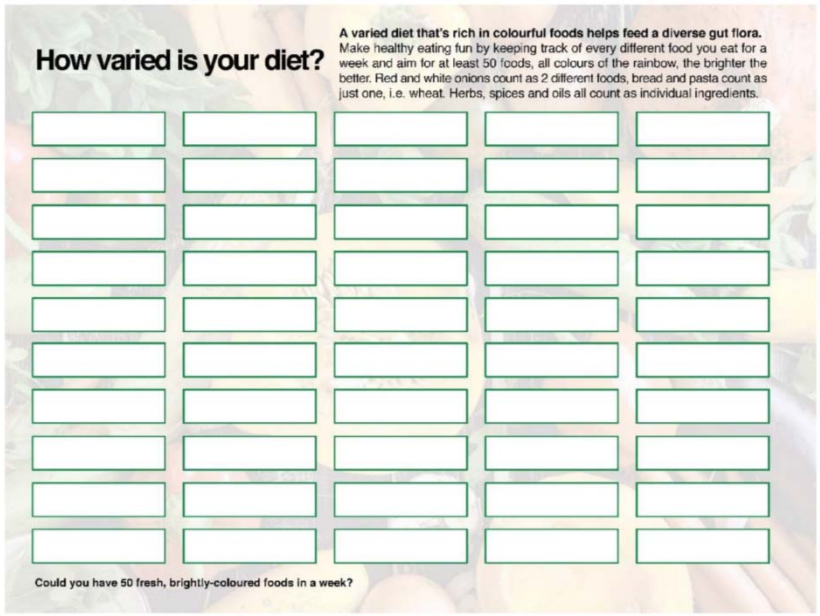
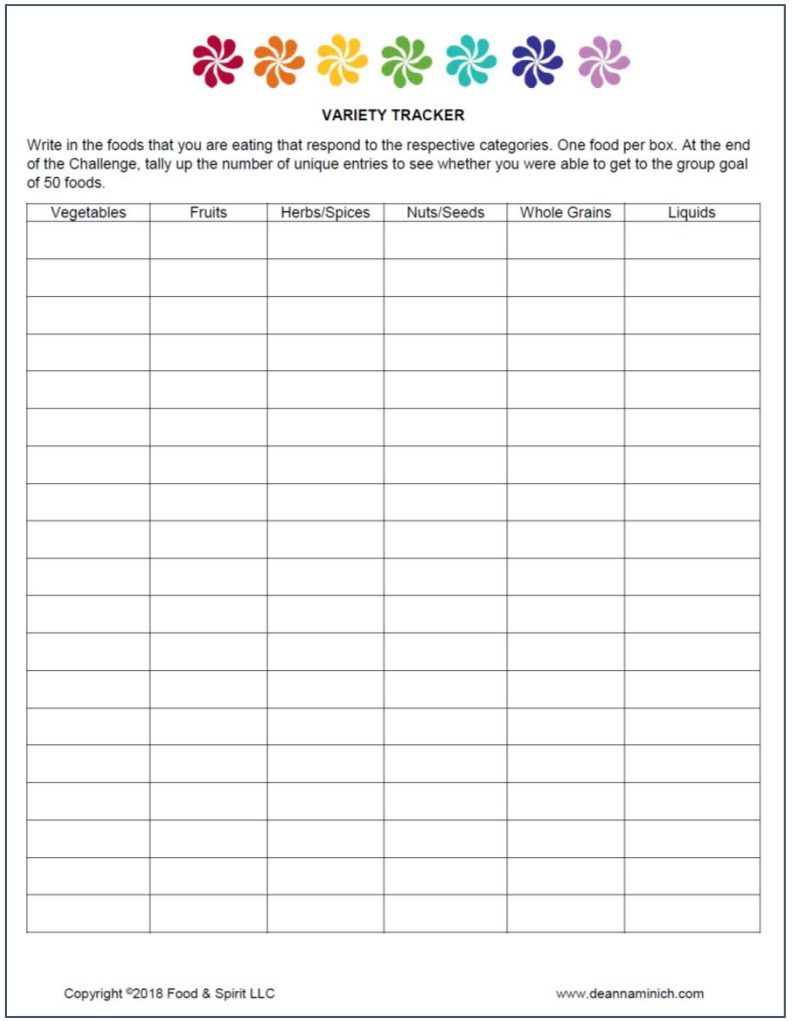


Figure 3. The author's "50-food challenge" chart is an example of a simple, but powerful data collection tool used in clinical practice to engage with patients in a light-hearted way so that they report back to their practitioner on their dietary diversity. The rationale is to motivate patients to vary the foods they have every day, so that they're increasing their micronutrient diversity, thereby feeding different classes of gut microbes.

"Increasing the diversity of brightly-coloured plant foods, even in small amounts, can have a dramatic effect on SCFA production."



VARIETY TRACKER

Write in the foods that you are eating that respond to the respective categories. One food per box. At the end of the Challenge, tally up the number of unique entries to see whether you were able to get to the group goal of 50 foods.

Vegetables	Fruits	Herbs/Spices	Nuts/Seeds	Whole Grains	Liquids

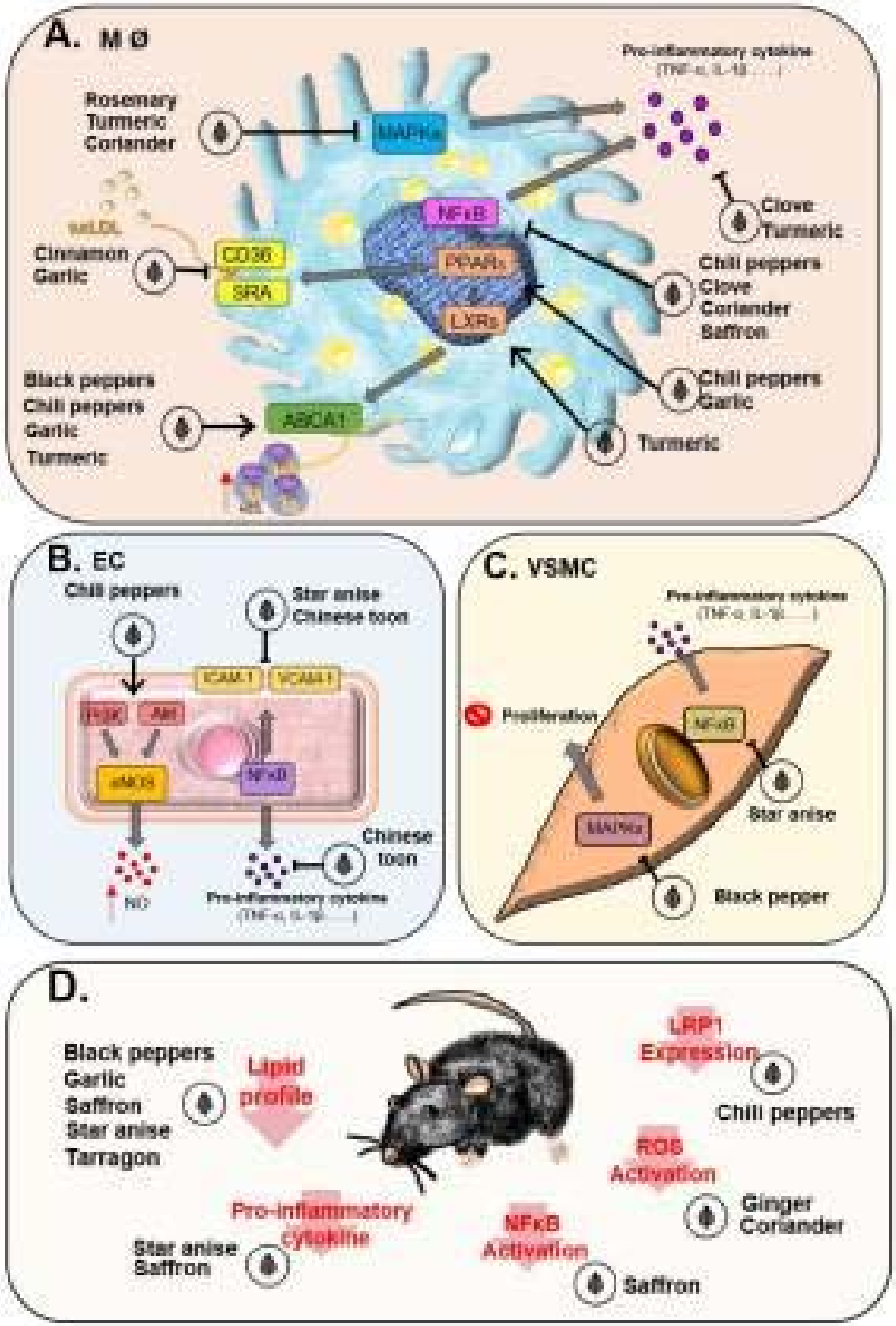
www.deannaminich.com

Microorganisms. 2018 Apr 25;6(2). pii: E35. doi: 10.3390/microorganisms6020035.
Harnessing the Power of Microbiome Assessment Tools as Part of Neuroprotective Nutrition and Lifestyle Medicine Interventions.Toribio-Mateas M

Atheroprotective effects of spices in vitro and in vivo

Tsui, P.-F.; Lin, C.-S.; Ho, L.-J.; Lai, J.-H. Spices and Atherosclerosis. Nutrients 2018, 10, 1724

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6266658/



Anti-inflammatory spices to block inflammatory vascular receptors

- Curcurmin (turmeric) blocks TLR 4, NOD 1, and NOD 2
- Cinnamaldehyde (cinnamon) blocks TLR 4
- Sulforaphane (broccoli) blocks TLR 4
- Resveratrol (nutritional supplement, red wine, grapes) blocks TLR 1
- Epigallocatechin gallate (EGCG) (green tea) blocks TLR 1
- Luteolin (celery, green pepper, rosemary, carrots, oregano, oranges, olives) block TLR 1
- Quercetin (tea, apples, onion, tomatoes, capers) block TLR 1

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Combine foods for synergy

- ***Green Tea + Citrus:*** Vitamin C may help in the intestinal transport of catechins in green tea (1)
- ***Turmeric + Black pepper:*** Piperine enhances the serum concentration, extent of absorption and bioavailability of curcumin in both rats and humans with no adverse effects (2).
- ***Chopped Garlic + Time:*** Let garlic sit after crushing it to allow beneficial enzymes to increase (3).

1. J Food Sci. 2013 May;78(5):C685-90. 2. Planta Med. 1998 May;64(4):353-6. 3. http://www.whfoods.com/genpage.php?tname=foodspice&dbid=60

Find a colorful community:

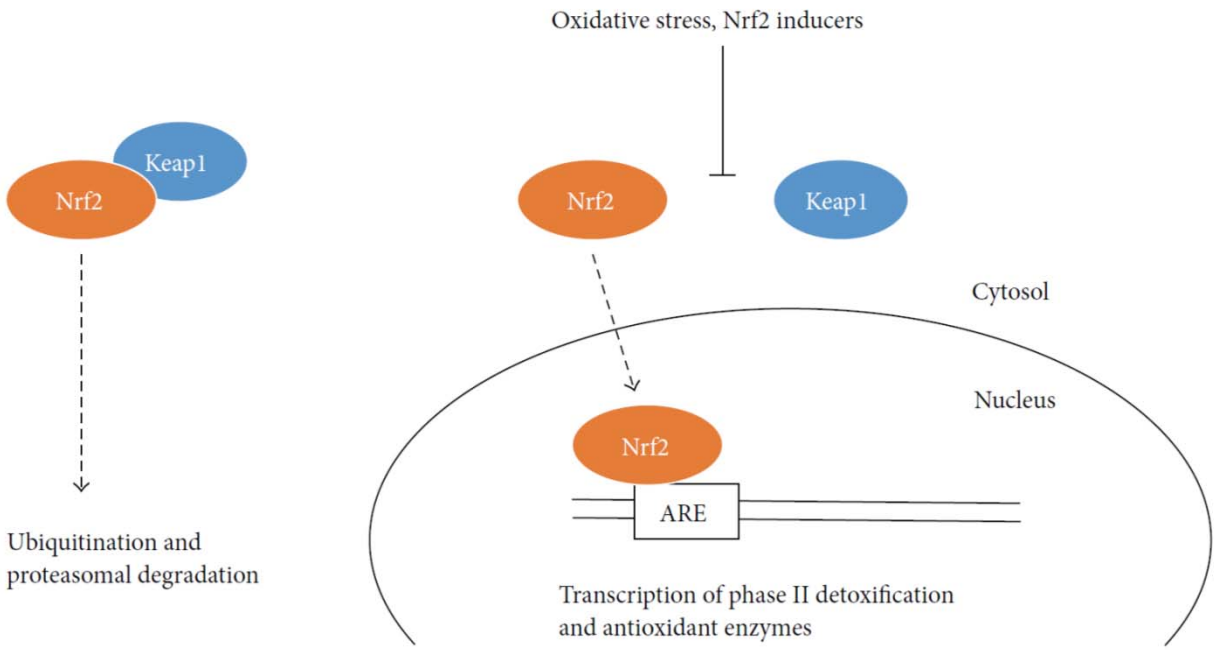
Your tribe determines your fruit and vegetable intake

Lower levels of friend contact were associated with reduced variety of fruits and vegetables in a graded trend for both genders; the trend was more pronounced among men.

Soc Sci Med. 2013 Aug 28. pii: S0277-9536(13)00470-X. doi: 10.1016/j.socscimed.2013.08.018. [Epub ahead of print]

Nrf2 Nutritional Inducers:

Endogenous Detoxification Enzyme Upregulation



- Fish oil
- Lycopene
- Curcumin
- Cruciferous vegetables
- Garlic
- Catechins
- Resveratrol
- Ginger
- Purple sweet potato
- Isoflavones
- Coffee
- Rosemary
- Blueberry
- Pomegranate
- Naringenin
- Ellagic acid
- Astaxanthin
- Gamma-tocopherol

Hodges RE, Minich DM. Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. J Nutr Metab. 2015;2015:760689..

The evidence for fruits, vegetables & whole grains

- Convincing body of evidence to suggest that a plant-based dietary pattern beneficially impacts cardiovascular health
- F&V are low in energy, sodium and SFA and high in nutrient density, providing significant amounts of fiber and micronutrients

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

FV and Blood Pressure

- FV intake is associated with lower BP
- Greater BP effect is due to higher potassium content
- Limited evidence for an inverse trend between FV consumption and LDL levels
- Greater LDL lowering effect is due to soluble fiber and sterols

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Effects of chronic consumption of fruit and vegetable puree-based drinks on vasodilation, plasma oxidative stability and antioxidant status

"Overall, the findings obtained in the present study showed that FVPD [fruits and vegetables as puree-based drinks] were a useful vehicle to increase fruit and vegetable intake, significantly increasing dietary and plasma phytochemical concentrations with a trend towards increased endothelium-dependent vasodilation."

J Hum Nutr Diet. 2012 Jul 26. doi: 10.1111/j.1365-277X.2012.01279.x. [Epub ahead of print] **Effects of chronic consumption of fruit and vegetable puree-based drinks on vasodilation, plasma oxidative stability and antioxidant status.** George TW, et al.

The evidence for fruits, vegetables & whole grains

- Fruit & vegetable intake > 5 servings/d is associated with the lowest risk of CVD
- Highest risk with an intake <3 servings/d.

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Colorful food categories connected to chronic disease markers

- Associations of colors of fruits and vegetable subgroups and cardiometabolic risk factors
- 3-year changes of cardiometabolic risk factors in adults
- Higher intake of red/purple FV may be related to lower weight and abdominal fat gain
- Yellow, green and white FV may be related to lipid parameters.

Mirmiran P, Bahadoran Z, Moslehi N, Bastan S, Azizi F. Colors of fruits and vegetables and 3-year changes of cardiometabolic risk factors in adults: Tehran lipid and glucose study. Eur J Clin Nutr. 2015 Apr 8. doi: 10.1038/ejcn.2015.49. [Epub ahead of print]

Lycopene

- Greater intakes of lycopene associated with increased CV health
- 5-yr results of the prospective observational Women's Health Study of 39,876 initially disease-free women indicated that the risk for developing any form of CVD was inversely proportional to long-term plasma lycopene concentration.

Nutrition. 2012 Jun;28(6):605-10. Epub 2012 Apr 4. **Novel phytonutrient contributors to antioxidant protection against cardiovascular disease.** Riccioni G, et al.

Red and Blue Phytonutrients Reduce MI Risk

- 93,600 women included in the Nurses' Health Study II
- Greater intake of anthocyanin, a bioactive compound in red and blue fruits and vegetables, was associated with a lower heart attack risk in young and middle-aged women.
- The relative risk of heart attack decreased by 17% for every 15-mg increase in anthocyanin intake.

High anthocyanin intake is associated with a reduced risk of myocardial infarction in young and middle-aged women. Cassidy A, Mukamal KJ, Liu L, Franz M, Eliassen AH, Rimm EB. Circulation. 2013 Jan 15;127(2):188-96. doi: 10.1161/CIRCULATIONAHA.112.122408.

Beet root juice

- Raw beet juice (250 mL) or cooked beet (250 g) for blood pressure?
- Randomized, crossover, 24 subjects with HTN
- Took each food for 2 weeks and then washed out for 2 weeks, then switched.
- More improvement in lipids with RBJ.
- Equal improvement on BP and inflammation.

J Hum Hypertens. 2016 Jun 9. doi: 10.1038/jhh.2016.34. [Epub ahead of print]

Orange Fruits & Vegetables:
Coronary Heart Disease (CHD)

- Prospective study with 20,069 men and women aged 20-65 yrs
- Each 25 g/d increase in the intake of deep orange fruit and vegetables was inversely associated with CHD.
  - Carrots, their largest contributor (60%), were associated with a 32% lower risk of CHD.

Br J Nutr. 2011 Nov;106(10):1562-9. doi: 10.1017/S0007114511001942. Epub 2011 Jun 8. **Colours of fruit and vegetables and 10-year incidence of CHD.** Oude Griep LM[1], Verschuren WM, Kromhout D, Ocké MC, Geleijnse JM.

Nuts and seeds

- Contain MUFAs and PUFAs
- When replacing SFA food sources, they reduce CVD risk via their effects on blood lipids
- Plant sterols and dietary fiber content also important.
- Clinical studies demonstrate that 1 to 2 oz/d of nuts lowers LDL-C by 2% to 19%.
- Obese subjects experience a smaller decrease in LDL-C from nuts compared with lean subjects
- May have other actives (antioxidants, polyphenols) that help to reduce CVD risk.
- Reduces susceptibility of LDL to oxidation, improves endothelial function, and reduces inflammation

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Nut consumption: A systematic review and meta-analysis of prospective studies

- N=23 prospective studies
- 1 serving of nuts associated with 19% reduction in CAD and 34% reduction in hypertension
- A higher consumption of nuts was associated with reduced risk of CAD and hypertension but not stroke or T2D.

Am J Clin Nutr. 2014 May 7;100(1):270-277. [Epub ahead of print]

Whole Grains

- Epidemiological evidence suggests an inverse relationship between whole grain intake and CVD risk.
- 20 to 40% reduction in atherosclerotic CVD risk when comparing habitual consumers of whole grains versus seldom consumers (Jacobs and Gallaher, 2004).
- Mechanisms: Antioxidants and phytonutrients, including polyphenols

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM.

Whole Grains

- Short-term whole grain intake, specifically oats, was associated with lower total cholesterol and LDL-C compared with refined grains.
- Lipid-lowering effects occur with intakes as low as 12 to 33 g/d of fiber from foods.
- In the NCEP ATPIII, an increase in viscous fiber of 5 to 10 g/d achieved an LDL-lowering of approximately 3 to 5%.
- Not all studies show a lipid lowering effect, likely due to differences in fiber viscosity.

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM

The Mighty Avocado

"There are eight preliminary clinical studies showing that avocado consumption helps support cardiovascular health."

Half avocado (68 grams):

Fiber 4.6 g
Potassium 345 mg
Folate 60 mg
MUFAs 6.7 g
114 kcal

Critical Reviews in Food Science and Nutrition, 53:738–750 (2013)

Avocado + Burger

- Increased vasoconstriction 2 h after hamburger ingestion, but no difference when avocado was added;
- IL-6 increased significantly at 4 hours in postprandial serum after consumption of the hamburger, but no change was observed when avocado was added.
- Postprandial serum triglyceride concentration increased, but did not further increase when avocado was ingested with the burger compared to burger alone despite the added fat and calories from the avocado.

N=11 healthy subjects, two acute eating occasions

Li Z, Wong A, Henning SM, Zhang Y, Jones A, Zerlin A, Thames G, Bowerman S, Tseng CH, Heber D. Hass avocado modulates postprandial vascular reactivity and postprandial inflammatory responses to a hamburger meal in healthy volunteers. Food Funct. 2013 Feb 26;4(3):384-91. doi: 10.1039/c2fo30226h.

Half Avocado (68 grams):

Fiber 4.6 g
Potassium 345 mg
Folate 60 mg
MUFAs 6.7 g
114 kcal

Dietary Sources of Nitrates

Nitrate Content, mg/100 g of fresh weight	Vegetable varieties
Very low (<20)	Artichoke, asparagus, broad bean, eggplant, garlic, onion, green bean, mushroom, pea, pepper, potato, summer squash, sweet potato, tomato, watermelon
Low (20-50)	Broccoli, carrot, cauliflower, cucumber, pumpkin, chicory
Middle (50-100)	Cabbage, dill, turnip, Savoy cabbage
High (100-250)	Celeriac, Chinese cabbage, endive, fennel, kohlrabi, leek, parsley
Very high (>2,500)	Celery, cress, chervil, lettuce, red beetroot, spinach, rocket (rucola)

Curr Atheroscler Rep. 2011 Dec;13(6):484-92. **Dietary nitrates, nitrites, and cardiovascular disease.** Hord NG.

Dietary nitrates and nitrites

"It has been estimated that 1 serving of a high-nitrate vegetable, like spinach, results in more nitric oxide production from the reduction of nitrate to nitrite, and nitrite to NO, than what is endogenously formed by all the three NOS isoforms combined during a day."

Hord NG. **Dietary nitrates, nitrites, and cardiovascular disease.** Curr Atheroscler Rep. 2011 Dec;13(6):484-92.

Seaweed & Sea Vegetables

- Wakame (*Undaria pinnatifida*) is most popular edible seaweed in Japan.
- 3.3 g of dried wakame consumed for 4 weeks significantly reduced both the SBP (14 ± 3 mmHg) and DBP (5 ±2 mmHg).
- Contain most of seawater's 771 minerals and rare earth elements, fiber and alginate in colloidal form.
- ACE-inhibition activity from various peptides contained in the matrix

Expert Rev Cardiovasc Ther. 2010 Jun;8(6):821-33. **Nutrition and nutraceutical supplements in the treatment of hypertension.**
Houston MC.

Cocoa, blood pressure, and vascular function

"…intervention studies strongly suggest that cocoa has several beneficial effects on cardiovascular health, including the lowering of blood pressure, the improvement of vascular function and glucose metabolism, and the reduction of platelet aggregation and adhesion.

Curr Hypertens Rep.2012 Aug;14(4):279-84. **Cocoa, blood pressure, and vascular function.** Sudano I, et al.

Summary:

Fruits, Vegetables, Whole Grains, Legumes, & Nuts

- Good evidence that intake of fruits, vegetables, and whole grains help to mitigate CVD risk.
- Fiber is an important constituent that helps to decrease plasma cholesterol, CVD risk and blood pressure.
- Legumes & nuts have cardiovascular health benefit.
- Olive oil and olive phytochemicals appear to provide cardiovascular benefits.
- Phytosterols in food (vegetable origin) help to lower LDL-C due to their ability to block cholesterol absorption in the intestine.

Beverages

Don’t drink out of cans.

- N= 60
- 3 study site visits:
  - 2 glass bottles
  - 2 cans
  - 1 glass bottle, 1 can
- Urinary BPA concentration, blood pressure, and HRV was measured 2 hours after the consumption of each beverage.
- The urinary BPA concentration increased after consuming canned beverages by >1600% compared with that after consuming glass bottled beverages.
- SBP increased by ≈4.5 mm Hg after consuming 2 canned beverages compared with that after consuming 2 glass bottled beverages, and the difference was statistically significant.

Hypertension. 2015 Feb;65(2):313-9.

Coffee and Tea and Cardiovascular Health

- Tea and coffee have been associated with risk of cardiovascular disease (CVD), both positively and negatively.
- Epidemiological data suggest that black and green tea may reduce the risk of both coronary heart disease and stroke by between 10 and 20%.
- Experimental and clinical trial data generally indicate either neutral or beneficial effects on risk factors and pathways linked to the development of CVD.
- Inconclusive evidence on coffee; any detrimental effects of coffee may be associated with the acute pressor effects, most likely due to caffeine at high daily intakes, and lipids from boiled coffee can contribute to raised serum cholesterol.

Food Funct. 2012 Mar 29. [Epub ahead of print] **Effects of tea and coffee on cardiovascular disease risk.** Bøhn SK, et al.

Coffee and Tea and Cardiovascular Health

- Note SNPs for metabolism and excretion of tea and coffee compounds are also associated with differential biological effects.
- Potential mechanisms by which tea and coffee phytochemicals can exert effects for CVD protection include the regulation of vascular tone through effects on endothelial function, improved glucose metabolism, increased reverse cholesterol transport and inhibition of foam cell formation, inhibition of oxidative stress, immunomodulation and effects on platelet function (adhesion and activation, aggregation and clotting).
- Although many biologically active compounds have been identified with known biological effects, tea and coffee contain many unidentified compounds with potential bioactivity.

Food Funct. 2012 Mar 29. [Epub ahead of print] **Effects of tea and coffee on cardiovascular disease risk.** Bøhn SK, et al.

Coffee Consumption and Mortality From All Causes, Cardiovascular Disease, and Cancer: A Dose-Response Meta-Analysis

- The largest risk reductions were observed for 4 cups/day for all-cause mortality (16%, 95% confidence interval: 13, 18) and 3 cups/day for CVD mortality (21%, 95% confidence interval: 16, 26).
- Coffee consumption was not associated with cancer mortality. Findings from this meta-analysis indicate that coffee consumption is inversely associated with all-cause and CVD mortality.

Am J Epidemiol. 2014 Aug 24. pii: kwu194. [Epub ahead of print]

Coffee and its consumption: benefits and risks

Average cup of instant coffee contains about 100 mg caffeine per 240 mL

Table 1 Safe limits for caffeine

Age group	Caffeine (mg/day)
Healthy adults	400—450
Pregnant Women	300
Children (4–6 years)	45

Source: Nawrot et al., 2003

Crit Rev Food Sci Nutr. 2011 Apr;51(4):363-73. **Coffee and its consumption: benefits and risks.** Butt MS, Sultan MT.

Alcohol

- Depends on amount consumed as well as individual's characteristics.
- Epidemiologic studies have shown that moderate alcohol consumption (1-2 drinks/day) is associated with lower risk of CVD and all-cause mortality among middle-aged and older adults.
- Heavy drinking increases CVD risk.

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM. Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Alcohol and inflammation

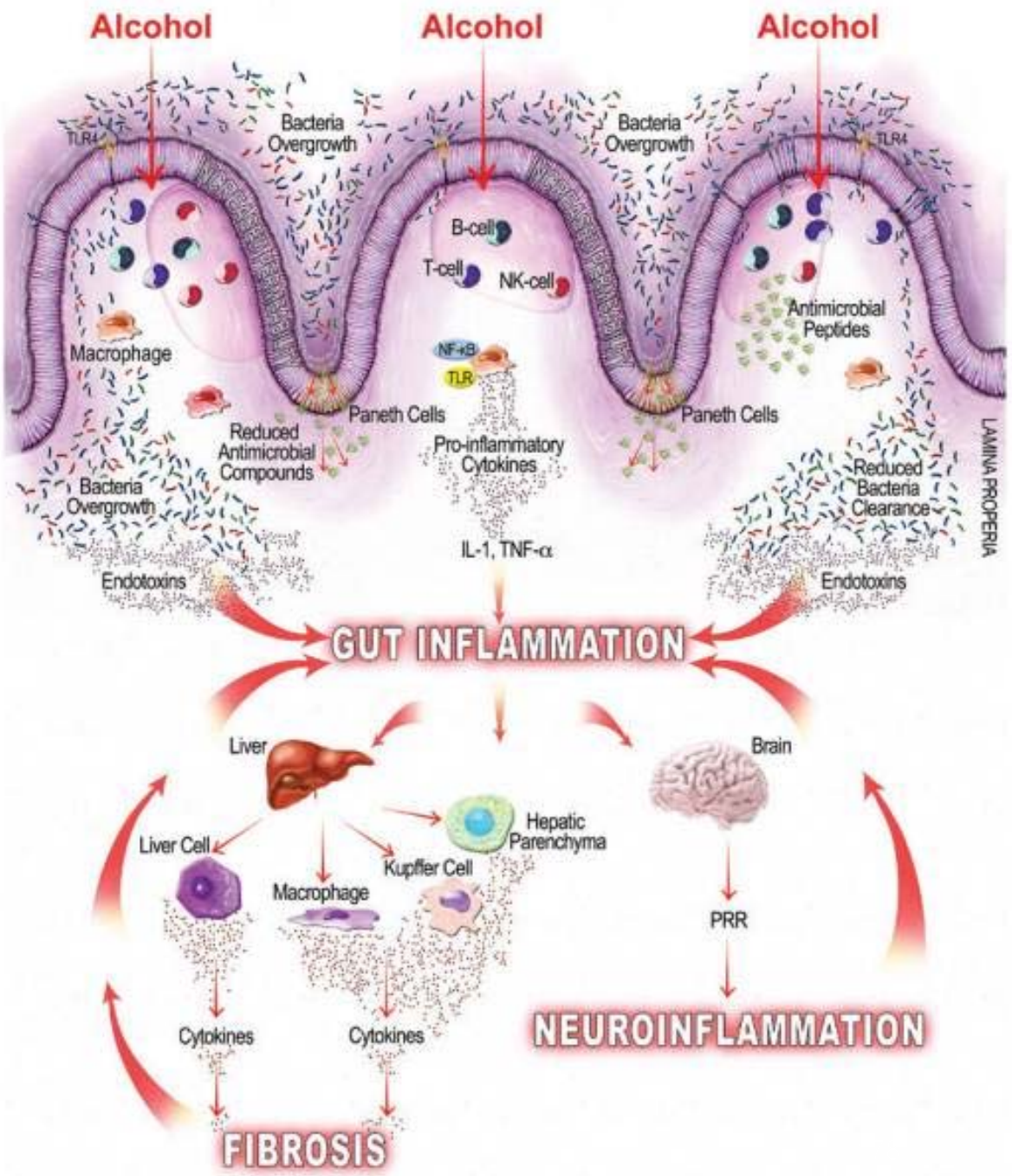


Image Credit: Bishehsari F, Magno E, Swanson G, et al. Alcohol and Gut-Derived Inflammation. Alcohol Res. 2017;38(2):163-171.

Alcohol

- May lower fibrinogen levels and decrease platelet aggregation, thus delaying formation of blood clots
- HDL-C and TG are generally increased by alcohol consumption (variable effects)
- Children, adolescents, women who are pregnant or may become pregnant should avoid alcohol completely.
- Not recommended for non-drinkers to start drinking.
- Healthy adults to limit consumption to 1 drink/d (0.6 fl oz. of alcohol) for women and up to 2 drinks/d for men.
- For example, 5 fl oz of wine containing 12% alcohol provides 0.6 fl oz. of alcohol, and therefore serves as one drink.

Curr Atheroscler Rep. 2011 Dec;13(6):499-507. **Dietary Guidelines for Americans 2010: implications for cardiovascular disease.** Flock MR, Kris-Etherton PM. Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Summary:
Coffee, Tea, Alcohol

- The data on coffee and tea for cardiovascular health remain inconclusive.
- Acute effects of caffeine appear to be detrimental to vessel health; however, chronic consumption of modest amounts of coffee/caffeine do not seem to negatively impact cardiovascular health.
- Coffee, tea, alcohol contain potentially beneficial compounds for cardiovascular function.
- Recommendations for coffee/tea/alcohol should be tailored to the patient, accounting for genetic polymorphisms, lifestyle, and co-existing conditions.

Summary:
Here is my process

- Look at labs
- Evaluate what they CAN do
- Encourage good dietary principles first so that the foundation is set
  - Macros/micros/phytos
  - Variety/Diversity
  - Diurnal rhythm
  - Spices, smoothie, teas
- Complete protein, quality fats/oils and plants throughout the day
- Supportive tribe
- Tailor foods to SNPs and ancestry
- Use dietary supplements for any vitamin/mineral gap as per labs or NPE/symptoms

Reference: Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent Science and Clinical Application of Nutrition to Coronary Heart Disease. J Am Coll Nutr. 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.

Table 1. Summary of Nutrition, Nutrients, and Daily Intake.

Nutrient	Daily intake
Diets that benefit cardiovascular health:	
Mediterranean diet and MD + ALA	
DASH 1 and 2	
Vegetarian diet	
• Potential for nutrient deficiencies, including vitamin B12, vitamin D, omega-3 fatty acids, iron, calcium, carnitine, zinc, and protein	
Paleolithic diet	
Caloric restriction and intermittent fasting	
Low AGEs	
Alkaline diet	
• No definitive results but appears in line with DASH and TMD	
Fats:	Less than 35% total caloric intake
SFA	< 7%–9% of total diet
• LCFA and MCFA have variable effects, with LCFA having a higher risk; SCFA are neutral	Replace with PUFA or MUFA
Coconut oil	
• No recommendation for prevention or treatment of CHD or CVD, but it is a possible substitute for high glycemic carbohydrates in low amounts	
Trans fat	Avoid trans fat
PUFA:	Omega-3 to omega-6 ratio at 4:1
Omega-3 fatty acids	>1 gram of EPA + DHA per day
• Opt for balanced formulation with DHA, EPA, GLA, and gamma-delta tocopherols	1.1 gram/day for women 1.6 gram/day for men ~2% total daily calories
MUFA (178):	50 grams/day
Extra virgin olive oil	
Diet elements:	
Animal protein	
• Avoid processed red meat	
• Aim for lean cuts	
Fish	1–2 servings/week
• Choose fish with high omega-3 content and low mercury levels	20 grams/day
Nuts	>5 servings/week; 28 grams/day
Vegetables and fruits	200–800 grams/day
• Dark leafy greens have the strongest effect on CHD risk	
Milk and milk products	
• Intake has an inverse association with CVD	
Eggs	*6–12 eggs per week as part of a healthy cardiovascular diet*
• No association with increased risk, except possibly for diabetics	
Special recommendation for diabetics	
Refined carbohydrates, sugar, and sugar substitutes	Reduce or eliminate from diet
Alcohol	1–2 drinks/day for women 2–4 drinks/day for men
Isolated nutrients and neutraceutical supplements	
Curcumin	
Cinnamaldehyde (cinnamon)	
Sulforaphane (broccoli)	
Resveratrol	
Luteolin	
Quercetin	
Caffeine:	Caffeinated coffee for slow metabolizers:
• Different effect on fast metabolizers compared to slow metabolizers	59 and younger <2–3 cups Older than 59 <1 cup
Soy protein	15 to 30 grams/day
Whey protein	20 grams/day
Gluten	
• No link even in those with celiac disease	
• Choose 100% whole grains	
Sodium	Low sodium to potassium ratio
Potassium	4.7 grams/day, preferably from food
Magnesium	

Thank You!

Dietary Protocols for Cardiovascular Disease

Putting the Science into Application

Angina Pectoris:

Dietary Factors to Consider

1. Meal size

– Patients with postprandial angina may benefit from consuming small, frequent meals compared with larger, less frequent meals.

Am J Clin Nutr.1984 Mar;39(3):421-6. **Effect of meal size on myocardial oxygen requirements: implications for postmyocardial infarction diet.** Bagatell CJJ Heymsfield SB.

Gaby A. Nutritional Medicine, 2011

Angina Pectoris:

Dietary Factors to Consider

2. Reactive hypoglycemia

– Possibility that patients who experience postprandial angina could benefit from consuming small, frequent meals as opposed to larger, less frequent meals.

- Angina can be triggered by reactive hyperglycemia.
- In these patients experience, relief experienced with dietary modifications to stabilize blood glucose.
- Result from lack of availability of glucose for heart for energy production and from release of epinephrine in response to low glucose.
- Suspect for patients with angina in late A.M., late afternoon, or middle of night.

Diabetes Care. 2011 May;34(5):1164-70. Epub 2011 Mar 18. **Evidence linking hypoglycemic events to an increased risk of acute cardiovascular events in patients with type 2 diabetes.** Johnston SS.
Eur Heart J.2010 Jul;31(13):1557-64. Epub 2010 Jun 2.; **Glycaemic control in acute coronary syndromes: prognostic value and therapeutic options.** De Caterina R, et al.
Gaby A. Nutritional Medicine, 2011

Angina Pectoris:

Treatment of Reactive Hypoglycemia

- Avoiding refined sugar, other refined carbohydrates (white flour, white rice), caffeine, and alcohol
- Consume 6 small meals per day (or have snacks in between main meals)
- Avoidance of honey, molasses, fruit juices, and some vegetable juices.
- Follow a high-protein, and high-complex carbohydrate diet
- Caffeine worsens hypoglycemia-induced symptoms.
- Look for food allergies with an elimination diet, as they are often associated with reactive hypoglycemia.

Gaby A. Nutritional Medicine, 2011

Angina Pectoris:

Dietary Factors to Consider

3. Allergy

- Determine food allergy and intolerance
- Elimination diet
- Histamine-containing foods
- Sulfates, salicylates

- Histamine can provoke coronary artery spasm.
- Transient chest pain and ECG changes indicative of ischemia may be associated with or part of an acute allergic reaction.

Heart Vessels. 2010 May;25(3):263-6. Epub 2010 May 29. **Coronary vasospasm secondary to allergic reaction following food ingestion: a case of type I variant Kounis syndrome.** Wada T, et al. [Nutrition **allergy** causes missdiagnosis of **angina pectoris**]. Reinstein H. Hippokrates. 1968 May 31;39(10):376-9.

Gaby A. Nutritional Medicine, 2011

Arrhythmias:

Dietary Factors to Consider

1. Allergy
2. Caffeine
3. Alcohol
4. Food additives (MSG)
5. Ensure sufficient dietary Mg, K, omega-3s

Gaby A. Nutritional Medicine, 2011

Atherosclerosis:

Dietary Factors to Consider

1. Meal frequency

– Eating small, frequent meals compared with large, less, frequent meals to improve serum lipid levels and glucose intolerance

Reduced prevalence of ischemic heart disease in men consuming 5 or more meals daily compared with those who consumed 3 or fewer per day.

Lancet.1968 Jul 27;2(7561):190-1. **Meal frequency and ischaemic heart-disease.** Fábry P, et al.

Gaby A. Nutritional Medicine, 2011

Atherosclerosis:

Dietary Factors to Consider

2. Optimize cooking and storage methods to reduce atherogenic compounds formed in food: oxidized cholesterol, lipid peroxides, AGEs.

- Keep foods high in cholesterol (butter, dairy products, and meats) or PUFAs (vegetable oils and nuts) in refrigerator and in airtight containers.
- Use olive oil, coconut oil, grapeseed oil for cooking rather than sunflower, safflower, or corn oil
- Choose boiling, poaching, stewing over frying, broiling, and roasting to help decrease AGEs.

Gaby A. Nutritional Medicine, 2011

Atherosclerosis:

Dietary Factors to Consider

3. Reduce or avoid certain foods and food compounds.

- Sucrose
- Dietary cholesterol and saturated fat
- Boiled or poached eggs (rather than fried) in non-diabetics up to 1 per day; however, less than 1 per week in patients with diabetes.
- Trans fatty acids
- Sodium chloride

Gaby A. Nutritional Medicine, 2011

Atherosclerosis:

Dietary Factors to Consider

4. Emphasize certain foods and food compounds.

- Monounsaturated fat sources over PUFAs
- Virgin, unfiltered olive oil high in phenolics
- 2-4 servings of nuts per week
- Whole grains
- Soy isoflavones
- Dietary fiber
- Fruits and vegetables
- Purple grape juice (4-16 ml/kg BW for 2-8 weeks)
- Pomegranate juice (250 ml/day)
- Garlic
- For alcohol drinkers, up to 2 drinks per day for men and 1 drink per day for women; non-drinkers should not be encouraged to drink for CVD risk reduction.

Gaby A. Nutritional Medicine, 2011

Hypercholesterolemia:

Dietary Factors to Consider

1. Meal frequency
   - Eating small, frequent meals compared with large, less, frequent meals may help lower total- and LDL-C levels
   - Having a regular eating pattern

"Skipping breakfast, eating infrequently (1 meal per day), and having irregular meal frequency may increase total and LDL-C levels."

Am J Clin Nutr. 2005 Feb;81(2):388-96. **Deleterious effects of omitting breakfast on insulin sensitivity and fasting lipid profiles in healthy lean women.** Farshchi HR, et al. Am J Clin Nutr. 2005 Jan;81(1):16-24. **Beneficial metabolic effects of regular meal frequency on dietary thermogenesis, insulin sensitivity, and fasting lipid profiles in healthy obese women,** Farshchi HR, et al.

Gaby A. Nutritional Medicine, 2011

Hypercholesterolemia:

Dietary Factors to Consider

2. Reducing dietary cholesterol intake
   - Oxidized cholesterol created during processing high-temp heating is highly atherogenic.

"Although relatively small effect: reducing cholesterol intake of 100 mg/day most likely results in a 4 mg/dl decrease in serum cholesterol"

Avoid cholesterol oxidation products: dried egg products (found in pancake mixes, baby foods, cake mixes, noodles, military rations), powdered milk, grated cheeses, french fries, processed meats, butter, heated butter and lard.

Gaby A. Nutritional Medicine, 2011

Hypercholesterolemia:

Dietary Factors to Consider

3. Note dietary fat intake
   - Consider quality
   - Consider quantity

- 10-20 en% help to lower serum total and LDL-C levels
- Consider the effect of metabolic endotoxemia with high-fat meals
- Minimize animal-based long-chain saturated fat and avoid trans fat
- MUFAs and PUFAs preferable but do not heat on high temps.
- Balance the omega-6/omega-3 ratio.

Gaby A. Nutritional Medicine, 2011

Hypercholesterolemia:

Dietary Factors to Consider

4. Foods to include

- Rice bran oil
- Nuts
- Sesame seeds
- Fiber
- Oat bran
- Barley & rye
- Whole soybeans
- Legumes
- Grapefruit
- Yogurt

Gaby A. Nutritional Medicine, 2011

- Rice bran oil contains heart healthy phytochemicals (gamma-oryzanol, tocotrienols)
- Nuts: Walnuts, almonds, pistachios, pecans, hazelnuts, and macadamia nuts
- Sesamin in sesame seeds to help with lowering LDL-C through reduced cholesterol absorption & reduced HMG-CoA activity.
- High fiber assists with increasing fecal excretion of bile acids, resulting in increased conversion of cholesterol to bile in the liver.
- Consumption of 1 red grapefruit per day for 30 days reduced mean serum total and LDL-C more than yellow grapefruit

J Agric Food Chem. 2006 Mar 8;54(5):1887-92. **Red grapefruit positively influences serum triglyceride level in patients suffering from coronary atherosclerosis: studies in vitro and in humans.** Gorinstein S, et al.

Platelet Aggregation:

Dietary Factors to Consider

1. Foods to consider

- Low-fat, whole foods
- Mediterranean diet
- Tomato juice
- Garlic
- Onion
- Cocoa & chocolate
- Alcohol & red wine
- Grape juice
- Black tea

Gaby A. Nutritional Medicine, 2011

- Tomato juice at 250 mL/day in type 2 diabetics resulted in reduced platelet aggregation compared with placebo.
- Garlic cloves, garlic oil, garlic powder shown to be efficacious.
- Onion due to quercetin content
- Cocoa flavanols and procyanidins
- Alcohol and red wine partly due to trans resveratrol and ethanol content (don't advise for patients if they don't drink alcohol)
- Grape juice due to flavonoids & resveratrol content.

JAMA. 2004 Aug 18;292(7):805-6.
Tomato juice and platelet aggregation in type 2 diabetes.
Lazarus SA, et al.

Platelet Aggregation:

Dietary Factors to Consider

2. Foods to exclude or reduce

- Sucrose

"…high glucose levels enhanced platelet reactivity to agonist stimulation through elevated osmolality. This occurred via superoxide anion production, which enhanced platelet P-selectin expression (secretion), and PKC signaling, which enhanced TRAP-induced fibrinogen binding (aggregablity)."

r J Haematol. 2006 May;133(3):315-22. **High glucose levels enhance platelet activation: involvement of multiple mechanisms.** Sudic D.

Gaby A. Nutritional Medicine, 2011

Platelet Aggregation:

Dietary Factors to Consider

3. Investigate food allergy
   - Elimination diet

"In patients with food allergies, ingestion of an allergenic food resulted in a significant decrease in platelet count within 90 minutes."

Storck H. et al. Int Arch Allergy 1955; 6:372-384.

Gaby A. Nutritional Medicine, 2011

Hypertension:

Dietary Factors to Consider

1. Consider metabolic detoxification if environmental toxin burden is high

- Relationship of HTN to blood lead and cadmium
- Patients with occupational exposure to lead include plumbers, glass manufacturers, printers, plastics or battery manufacturers, and construction workers.
- Sources of cadmium include cigarette smoke, water pipes, fertilizers.

Gaby A. Nutritional Medicine, 2011

Hypertension:

Dietary Factors to Consider

2. Studied dietary approaches:

- DASH diet
- Mediterranean diet
- Vegetarian diet
- Raw foods
- Examine food allergy

Gaby A. Nutritional Medicine, 2011

Hypertension:

Dietary Factors to Consider

3. Foods to emphasize:

- Onions
- Garlic
- Whole oats
- Soy
- Pomegranate juice
- Sesame oil
- Chocolate

Gaby A. Nutritional Medicine, 2011

Hypertension:

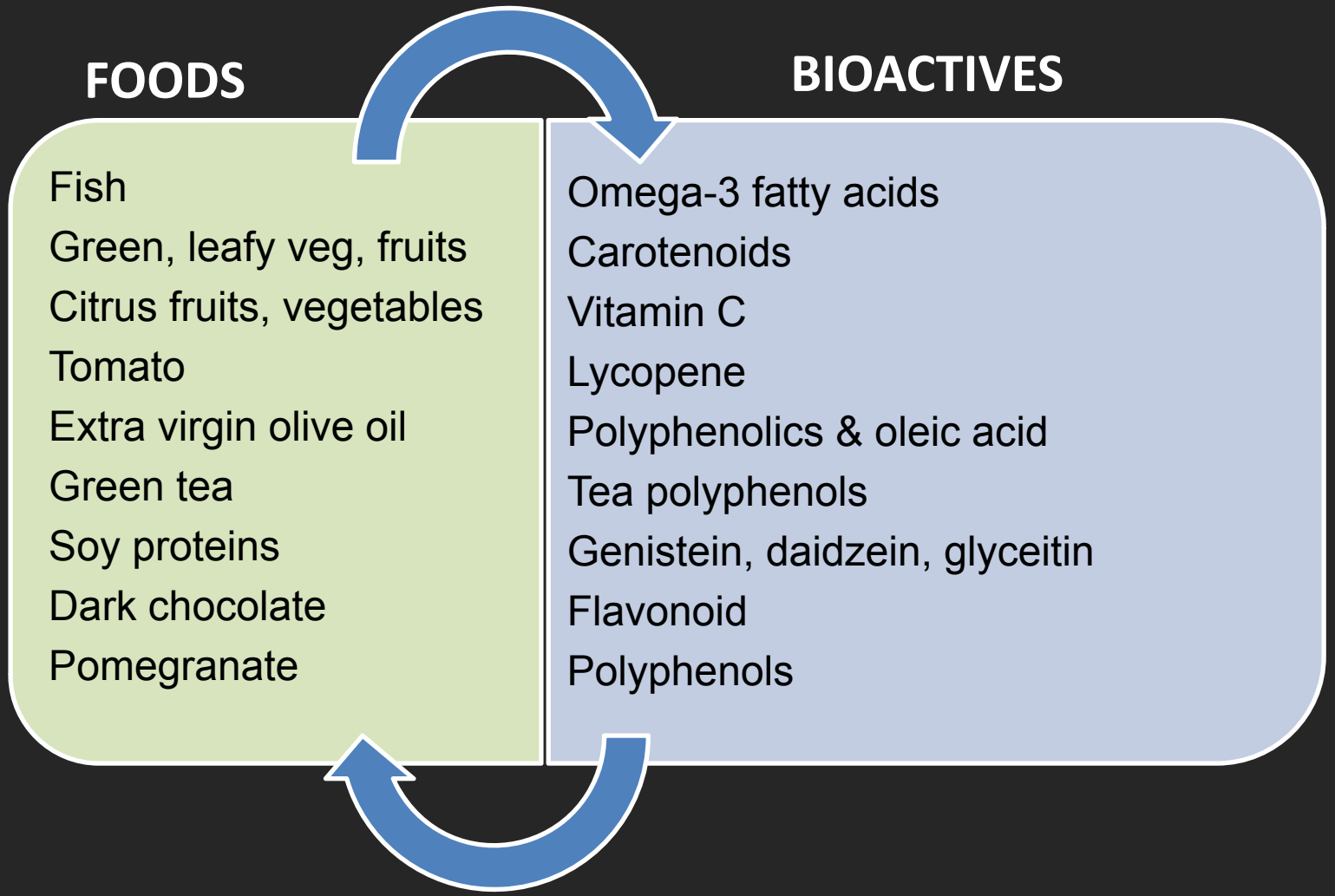
Dietary Factors to Consider

4. Foods to decrease:

- Sodium chloride
- Sucrose
- Caffeine
- Oils exposed to high heat

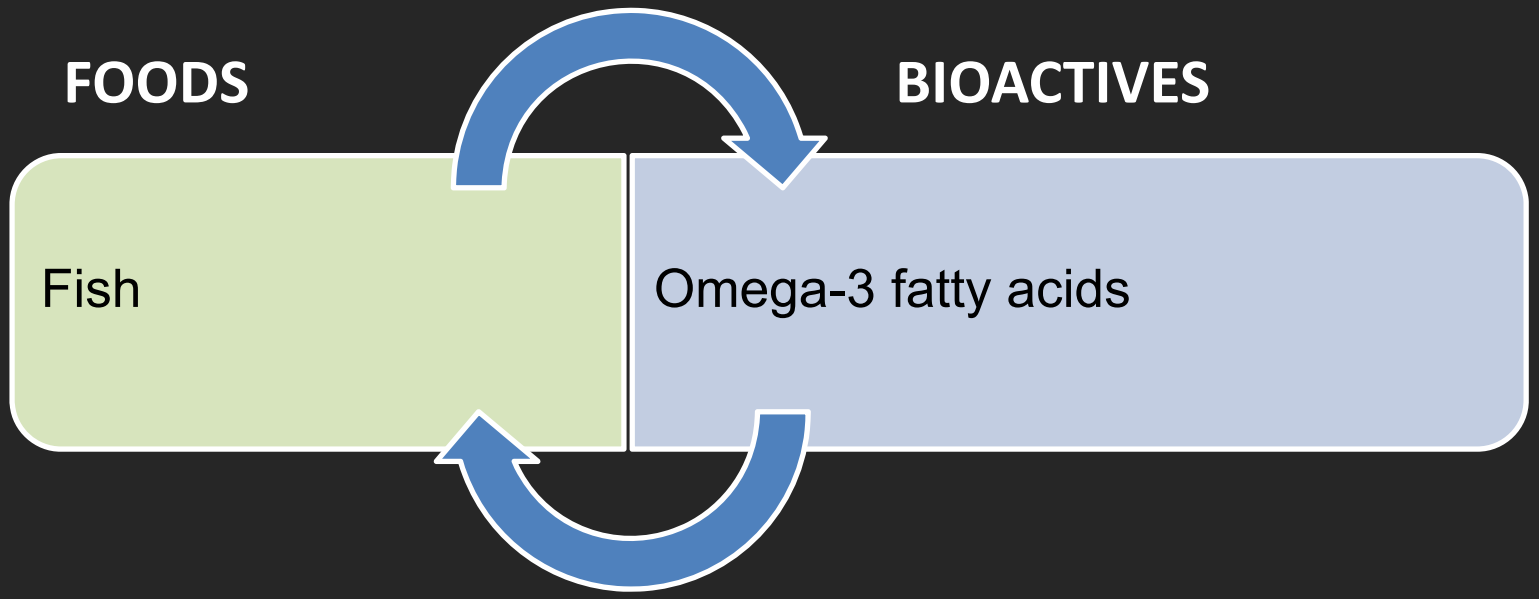
Gaby A. Nutritional Medicine, 2011

Foods & reduction of LDL-C oxidation



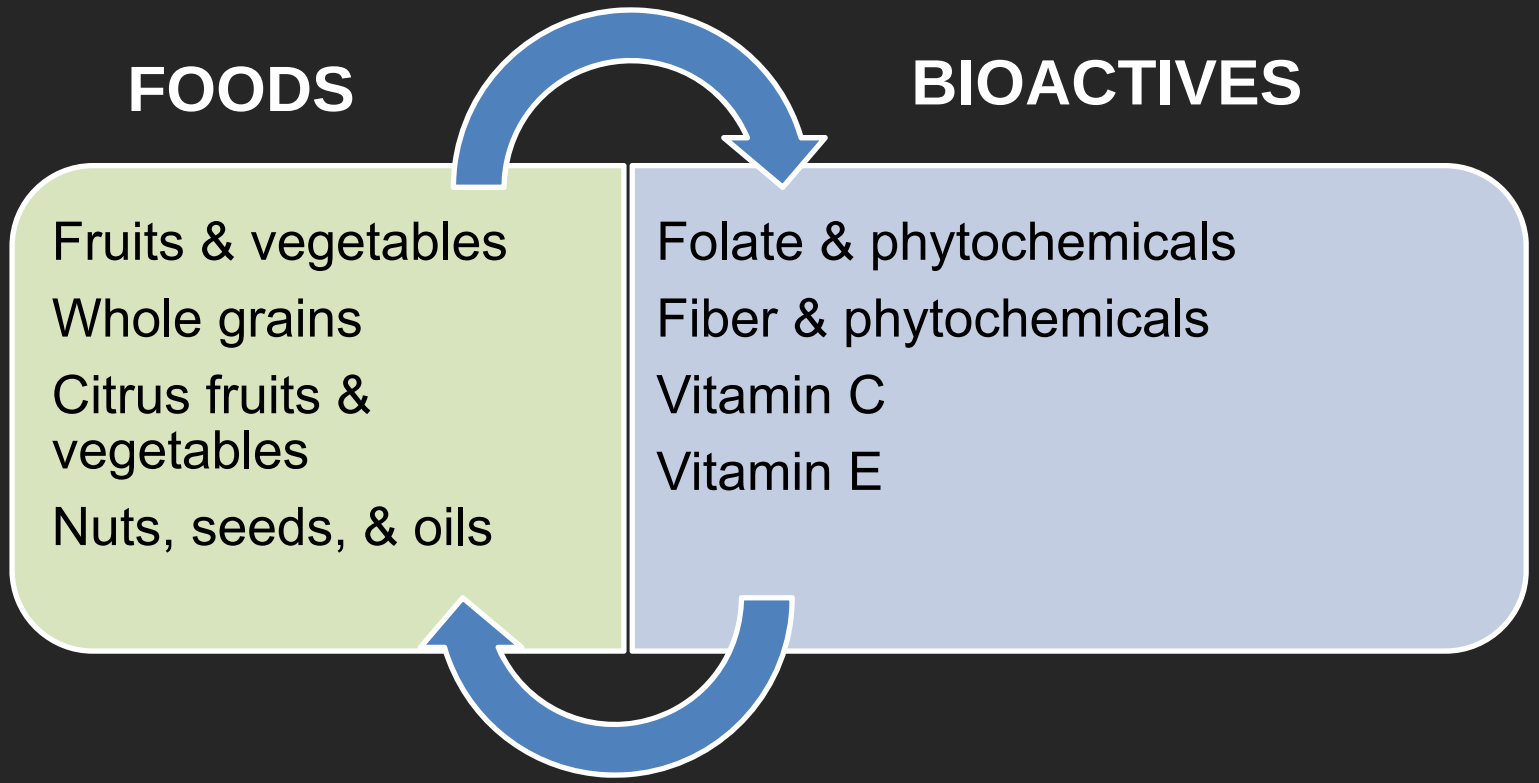
J Nutr Metab. 2012;2012:569486. Epub 2012 Apr 10. **Functional foods and nutraceuticals in the primary prevention of cardiovascular diseases.** Alissa EM, Ferns GA.

Foods that lower blood triglycerides



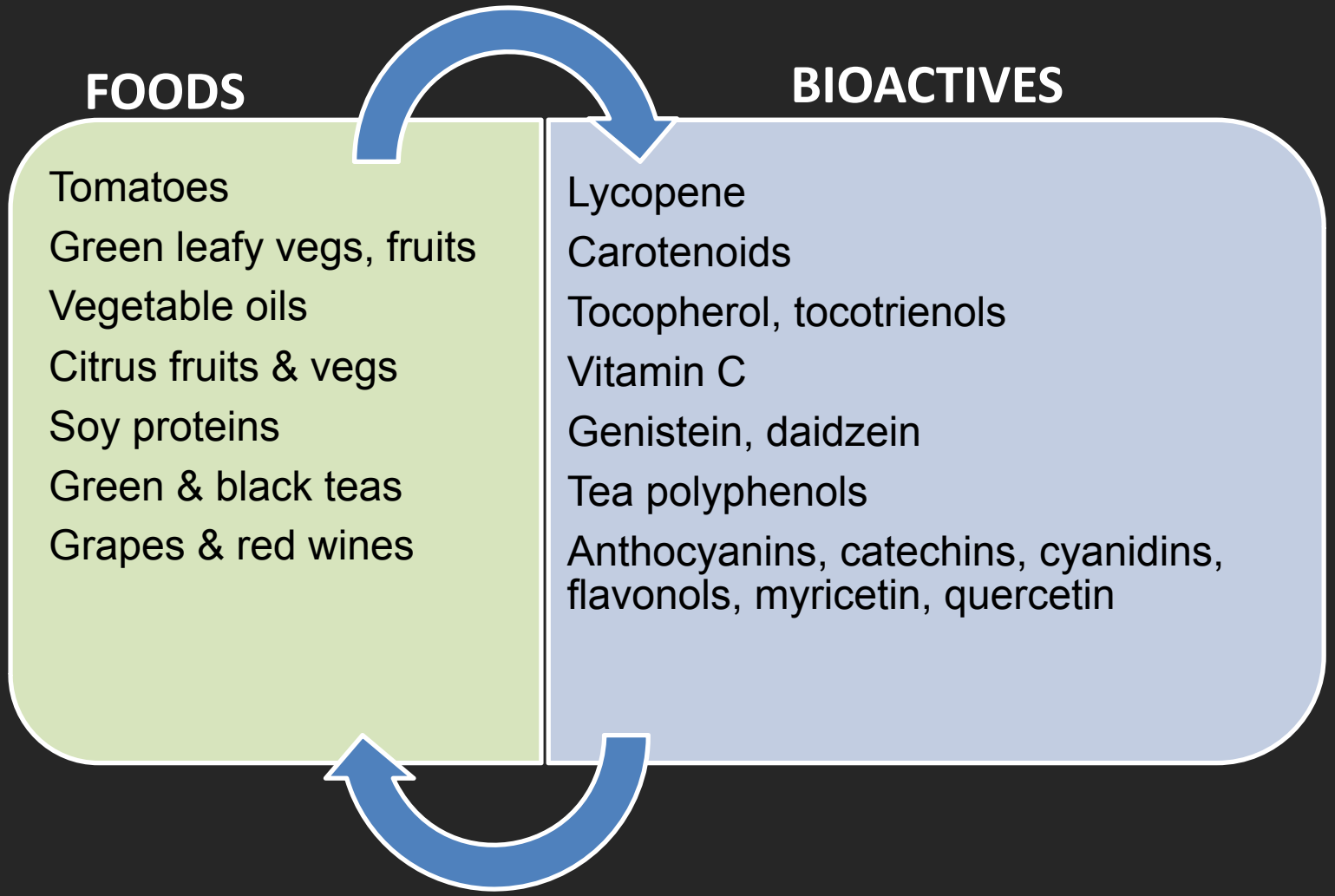
J Nutr Metab.2012;2012:569486. Epub 2012 Apr 10. **Functional foods and nutraceuticals in the primary prevention of cardiovascular diseases.** Alissa EM, Ferns GA

Foods & homocysteine reduction



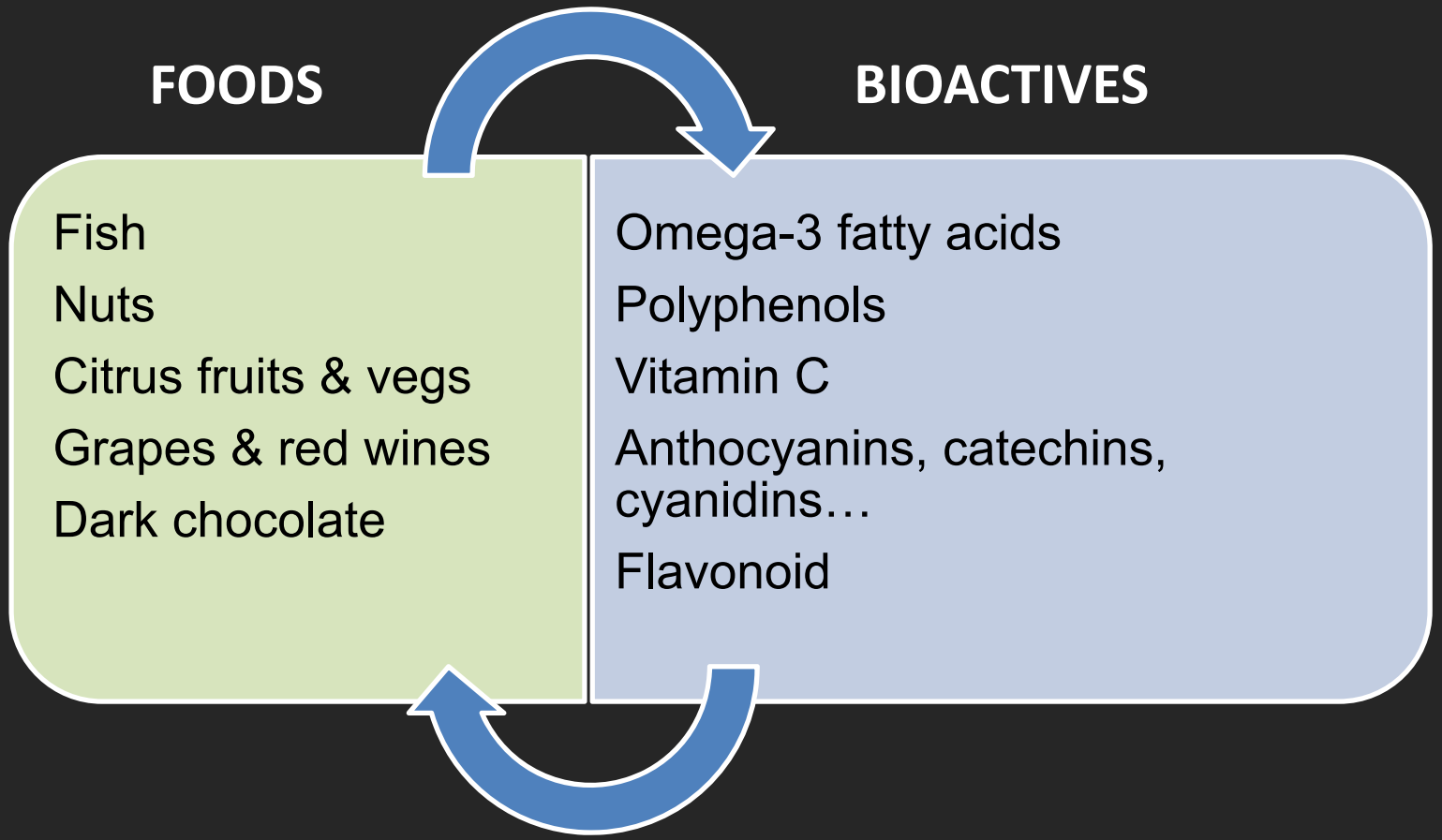
J Nutr Metab.2012;2012:569486. Epub 2012 Apr 10. **Functional foods and nutraceuticals in the primary prevention of cardiovascular diseases.** Alissa EM Ferns GA

Foods & antioxidant action improvement



J Nutr Metab.2012;2012:569486. Epub 2012 Apr 10. **Functional foods and nutraceuticals in the primary prevention of cardiovascular diseases.** Alissa EM Ferns GA

Foods & endothelial function improvement



J Nutr Metab.2012;2012:569486. Epub 2012 Apr 10. **Functional foods and nutraceuticals in the primary prevention of cardiovascular diseases.** Alissa EM Ferns GA

Don’t forget drug-induced nutrient depletion!

- Magnesium
- Coenzyme Q10
- Zinc
- B12/folic acid
- Vitamin D

Case Study

- 67 year old female who presented with a long-standing, severe obesity problem.
- She had severe osteoarthritis and degenerative damage in both knees, causing severe pain and marked restriction of activities.
- On her initial appointment, she could barely walk into the office from the handicapped parking spot. However, at this time, surgery could not be done because of her excessive weight, making successful surgery very unlikely.

Case Study

- Her orthopedist insisted that she reduce from her present weight of 258 pounds to less than 200 pounds before he would even begin to initiate any procedures.
- Also, M was having a number of other medical problems related to her obesity including poor sleep, averaging only two to four hours a night, varicose veins, hypertension, depression, low energy and GERD.
- She also had hypothyroidism, depression, and fatigue.
- To cope with chronic heartburn, M. had to take at least eight Tums daily; in addition, she had tried numerous other acid-blocking medications to no avail. Other medications included Lexapro 5-10 mg daily, Levoxyl 25 mcg daily, Lisinopril 40 mg daily, Triamterene-HCTZ 37.5/25 mg daily, Tylenol arthritis formula 2 daily, and Motrin as needed (often 4-6 daily).
- She had a cholecystectomy in the 1980's.
- M's family history was positive for Diabetes Mellitus and she had great concern she also would develop this problem.

Case Study

Measurements and Lab:

- Height: 64 inches
- Weight: 258 pounds
- Blood Pressure: 140/72
- % Body Fat: 40.6
- Waist Circumference: 51 inches
- Electrocardiogram (EKG): Abnormal, Atrial Fibrillation
- TSH: 2.43 (normal)
- Fasting Glucose: 82 (normal)
- Total Cholesterol 224: goal under 200
- Triglycerides 120: normal
- HDL Cholesterol 61: normal
- LDL 143: goal under 100

Case Study

Assessment:

(1) Obesity, markedly impairing the patient's lifestyle
(2) Osteoarthritis of the knees, severe
(3) Hyperlipidemia, (elevated cholesterol and LDL cholesterol)
(4) Varicose Veins
(5) Hypothyroid
(6) Hypertension
(7) Depression
(8) Fatigue
(9) GERD, causing chronic heartburn with acid reflux, aggravated by obesity
(10) Sleep Disorder, previously diagnosed by a specialist to have Obstructive Sleep Apnea secondary to the patient's weight.

Case Study

PLAN:

- Modified Mediterranean Food Plan and started her on Cardiometabolic Medical Food, 2 scoops twice daily. For micronutrient support of her metabolism, we also started **blood sugar support** tablets, one twice daily.
- For exercise, it was suggested that she start a "4 minute mini-walk program," in which she was advised to walk slowly around her house for 4 minutes and then rest.
- Hopefully, she could work up to five such efforts daily for a total of 20 minutes of controlled walking.
- the hope was that as she lost weight and felt better, we could gradually increase her walking.

Case Study

ONE MONTH LATER

- She weighed 244.2 pounds and felt much better. Her blood pressure was 118/76 and she was walking five to ten minutes at a time on her treadmill.

TWO MONTHS LATER

- M continued to feel better and her blood pressure continued to improve. She cut her blood pressure medication down and noted her heartburn was improving. Her weight was 234.6 pounds, blood pressure 108/62, and her lab showed a remarkable improvement in cholesterol, dropping to 152, and LDL cholesterol, now at 89.

Case Study

SIX MONTHS LATER

- Our patient is positive and happier with her life. She is decreasing all of her medications and walking 30 minutes daily on her treadmill! Her weight is 194.8 pounds and blood pressure 122/68.

SEVEN MONTHS LATER

- M is now wearing a pedometer. She is thrilled to share that she felt well enough to go on a family vacation to Disneyland with six grandchildren. This would have been impossible seven months ago. M averaged walking 7000-10000 steps daily for nine days in a row at Disneyland! Her heart is no longer in atrial fibrillation; it now is in regular sinus rhythm. Her weight is 188.8 pounds and blood pressure 108/68.

Case Study

ONE YEAR LATER
M continues to follow her diet and now takes medical food two scoops daily. Her EKG is completely normal. She has excellent energy, is walking 4-5 miles daily, and is off all of her medications except for her thyroid and an occasional Ibuprofen or Acetaminophen. M weighs 164 pounds with a 38 inch waist and body fat of 25.9 %.

TWENTY-ONE MONTHS LATER
M weighs 142 pounds, follows the food plan and lifestyle protocol and continues to take her medical food, two scoops daily. She is walking several miles daily with little discomfort. She has not gone back to her orthopedist and has no plans at this time for any surgery.

M said she has not felt this vigorous and healthy since she was a teenager!!


Other Forms of
Nourishment for the
Heart

Laughter

- “Heart rate and blood pressure increased significantly while watching the comedy, whereas no such changes were seen while watching the documentary.
- Carotid arterial compliance (by simultaneous application of ultrasound imaging and applanation tonometry) increased (10%) significantly immediately after watching the comedy and returned to baseline 24 hours after the watching, whereas it did not change significantly throughout the documentary condition.”

Am J Cardiol. 2010 Sep 15;106(6):856-9. **Effect of mirthful laughter on vascular function.** Sugawara J, et al.

Optimism

"Findings suggest that positive psychological well-being protects consistently against CVD, independently of traditional risk factors and ill-being.

Specifically, optimism is most robustly associated with restorative health behaviors and biological function…"

Psychol Bull. 2012 Jul;138(4):655-91. Epub 2012 Apr 16. **The heart's content: The association between positive psychological well-being and cardiovascular health.** Boehm JK, Kubzansky LD.

Happiness

“Depressive feelings were associated with increased risk, while happiness/optimism was associated with reduced risk of VTE.”

Thromb Haemost. 2012 Mar;107(3):485-93. Epub 2012 Feb 8. **Emotional states and future risk of venous thromboembolism: the Tromsø Study.** Enga KF, et al.

Forgiveness

- “Higher levels of forgiveness were associated with lower levels of anxiety, depression, and perceived stress as well as lower total cholesterol to HDL and LDL to HDL ratios after controlling for age and gender.”
- “…among cardiac patients, forgiveness may be associated with reduced risk for future cardiovascular events.”

Int J Behav Med. 2009;16(3):205-11. Epub 2009 Feb 20. **Relationship between forgiveness and psychological and physiological indices in cardiac patients.** Friedberg JP, et al.

Summary

- Foods significantly impact cardiovascular health.
- A whole foods dietary pattern complete with a variety of vegetables, fruits, whole grains, and low-fat dairy appears to present the best evidence for reducing cardiovascular disease risk.
- Certain bioactives within food address specific mechanisms related to cardiovascular function.