The use of and diet, habits and supplements to help prevent medical problems.

Part III: Diet Choices, Healthy Habits and Supplements

Every one desires to live long, but no one would be old.
- Jonathan Swift (1667-1745), Thoughts on Various Subjects, Moral and Diverting [1]

To lengthen thy life, lessen thy meals.
- Benjamin Franklin, Poor Richard's Almanack, June 1733 [2]

Calories are a primary cause of aging, and ***the*** limiting factor in lifespan.
Key insight: cutting calories slows the aging process and prolongs life.

Aging is due to a combination of years of age and total calories eaten in your lifetime[3];
The road to aging is paved with calories.
The simplest way to reduce calories is to reduce portion size: use a small plate!

By my calculations, **every calorie above the absolute minimum *ages your body and your mind* and hastens death by about 31 seconds** (+/- 10). This means that you age one day (and lose one day of life span) for every 2800 calories you eat - above a starvation diet with good nutrition (adequate protein, fats, vitamins and minerals). Carrying an extra pound of weight for one year costs 2 days of life span. In dollar terms, a candy bar might cost $20 in potential lost wages. (See "Effect of CR.XLS" for calculation details). A 40-year-old man can live 8 years longer by eating 25% less; a 15-year-old can live 16 years longer by eating 25% less. Slowing aging means MORE YOUTH, not more old age.

Turn this around: it is VERY expensive – in terms of money, aging, disability and early death – to keep your weight up!
Can **you** afford to stay plump?

Last updated 2007-01-17

NOTE: This document is very long. I have not revised it thoroughly. Much in the last half of the document is outdated. I think that no supplement, food, or habit - by itself or in combination with others - will be as effective as moderate caloric restriction (CR, to a BMI of about 18.5).

Table: Personal goals, many not yet achieved
These parameters are directly affected by lifestyle choices (diet, CR, exercise, supplements, etc.), and have substantial effects on lifespan, quality of life, and risk of serious disease.

Parameter	Goal	Current	Date
BMI (Weight)[4]	17 (115 lbs)	***20* (*138* lbs)**	2006-07-15
Blood pressure[5]	≤ 115/75	114/66	2006-05-11
LDL cholesterol[6]	< 80	*83*	2006-05-05
HDL cholesterol[7]	> 50	70	2006-05-05
HbA1c[8]	< 5.0	*5.5*	2001-10-01
Fasting glucose[9]	< 90 or < 81	*88*	2006-05-05
Fasting triglyceride[9]	< 150	58	2006-05-05

Table 1: Interventions

This table summarizes what I think are the most important interventions, in order of *importance to health*. Rating is my own assessment of the intervention, based on its importance *and* my confidence in the scientific backing to support it (1 = very important with strong suggestive evidence; 5 = possibly helpful, with some evidence to support it).

Rating	Intervention	What I do or think should be done
1	**Caloric restriction with optimal nutrition** (abbreviated CR or CRON) Note well: this is approximately twice as important as everything else put together!	Goal body mass index approximately 17, by reducing calories, not just by exercise. N.b., Exercise is very good, but exercising *without dieting* is not the best way to live longer or slow the aging process.
1	Modify fat intake, including increasing Omega-3 fat & monounsaturated fats (MUFAs)	Caloric restriction **Completely avoid** partially hydrogenated oils (trans fats) Avoid saturated fats, avoid most animal fat **Eat moderate amounts of**: tree nuts (unsalted & raw), wild salmon, freshly ground flaxseed, extra virgin olive oil, avocado Cook with olive oil, preferably extra virgin
1	Reduce cholesterol and triglyceride levels	**Caloric restriction** Avoid trans-saturated fats, animal fat Eat flax meal, fruits & vegetables, tree nuts, high-fiber foods, orange peel Avoid most carbs (rice, plain bread, sugar, potatoes, pasta, foods made largely of white flour, etc.) Consider statin drugs (*only* if cholesterol is too high and other things fail)
1	Keep blood pressure low (less than 115/75)	**Caloric restriction** **Low salt intake**, exercise daily, use potassium chloride (instead of salt, or 50/50 with salt if needed), limit alcohol intake, high folic acid (4 mg/day), take 6 mg of melatonin each night, eat a high protein diet (mostly vegetable-based), soluble fiber, magnesium
1	Take safety precautions	**Drive safely**, **use seat belts, drive in a safe car with air bags**, fire safety, follow government hazard preparation recommendations, hip protectors for the elderly
1	Take certain supplements	**Vitamins D**, B12, folate (about 4 mg / day vs. HTN), magnesium, benfotiamine, green tea extract, melatonin, glucosamine & chondroitin A little zinc & selenium; iron if really needed Avoid vitamin E supplements (*alpha* tocopherol) Possibly: R(+) ALA
1	Exercise daily	Run 1 mile each day, do calisthenics and stretching.
2	Reduction of homocysteine (a major risk factor for heart disease & Alzheimer's)	Caloric restriction Eat a low-methionine diet: this can be done by getting protein from vegetables instead of animals (milk, eggs or meat) Take supplemental vitamins: folate & B12
2	Reduce glycation (damages proteins & hardens arteries)	Caloric restriction Reduce or eliminate "useless" carbohydrates, cook meat at low temperatures, reduce mixing sugar and protein in cooked foods, benfotiamine Possibly: R(+) ALA
2	Avoid sun damage	Clothes, zinc oxide- or titanium dioxide- based sun block, hat, UV-protection sunglasses, eat orange peel *But*, be sure to take 800 units/day of supplemental vitamin D in the form of D3 Caloric restriction (*Perhaps - it reduces the area exposed to the sun*)

2	Reduce inflammation	Caloric restriction Floss & brush teeth, treat infections and skin problems If you have risk factors for heart attack (especially older men), take a baby aspirin each day or every other day
2	Vaccinations – keep up to date	Influenza shot yearly, Pneumovax, hepatitis B, chickenpox / shingles, tetanus, etc. In short, take all that are recommended
2	Eat a high-fiber diet	Fruit & vegetables; bran (insoluble fiber), whole grains, freshly ground flax seed Soluble fibers: glucomannan, psyllium, methylcellulose and guar (these are concentrated sources of soluble fiber, shown to lower cholesterol levels by 10%)
2	Medical tests periodically	Blood pressure, CBC, HbA1C, colonoscopy (starting at age 50), PSA, cholesterol (HDL & LDL) & lipids, CRP, eye exam for glaucoma, breast & pelvic exams for women
2	Greatly reduce in diet	Food! (i.e., caloric restriction) Salt, red meat (worst if grilled, charred or cooked at high temperatures), omega-6 fat (corn, soy & cottonseed oils etc.), cured meats, excess fluoride, saturated and trans-saturated fats Possibly: soy, peanuts
2	Increase the proportion of certain foods	Eat a variety of tree nuts, berries, spinach, kale, sprouts, broccoli & related veggies, tomato paste, coffee, green tea (only as extract capsules), pomegranate juice, fruit
3	Reduce iron load	Caloric restriction (less total iron intake) Give blood if you are a man, avoid iron supplements, reduce or eliminate red (mammal) meat *However, take care to avoid iron deficiency*
3	Avoid certain cooking techniques	Charred meat, over-cooking of fish or meat, high-temperature cooking of most foods, cooking with polyunsaturated oils such as canola, sunflower or flax oil, cooking sugars and meats together
4	Eat more than the RDA of protein	**From vegetable sources** such as broccoli, spinach, lentils, peas and tree nuts (n.b., vegetables like broccoli & spinach have far more protein per calorie than do beans and nuts)
5	Avoid aluminum (possible cause of Alzheimer's disease)	Use non-aluminum-based deodorants, minimize foods that use alum-based baking powder (read the label), drink reverse-osmosis filtered water, avoid certain foods with aluminum (some pickles), avoid aluminum foil on foods, etc. Possibly avoid antacids such as Mylanta (most are made with aluminum)

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Caloric restriction – eating less – is the main and by far most effective approach to improving health and prolonging life. Caloric restriction keeps you younger longer. In addition, there are certain choices of diet, habits and supplements to help prevent medical problems. All of them are documented in the tables and text below, with references. In brief:

1. Fats Modify your intake of fats.
   Increase certain fats:
   - Omega-3 fat: freshly ground flaxseed, salmon and canola
   - Monounsaturated fats: MUFAs, from tree nuts (not peanuts), avocados, & olives
   - Cook with olive oil

   Fats should comprise between 25-40% of your dietary calories.
   Avoid certain fats:
   - Trans-saturated fats (this is five times as bad for you as saturated fat!!): partially hydrogenated vegetable oils
   - Animal fats (especially mammalian): beef, pork, mutton, butter, whole milk etc.
   - Saturated fats: animal fat, palm oil & coconut oil, fully hydrogenated vegetable oil, brazil nuts
   - Excessive omega-6 fats: corn oil, corn-fed beef & pork, etc.
2. Exercise daily, in moderation.
3. Vitamins, minerals and supplements Take supplements or enough dietary vitamins to reduce

homocysteine (see Homocysteine, likely to be a major risk factor for heart disease, stroke & Alzheimer disease) take a few supplemental vitamins: folate, B12, D.

4. Take safety precautions: Drive safely, use seat belts, drive in cars with air bags, and practice fire safety.
5. Hypertension Keep blood pressure low (<115/75): very low salt intake, take supplemental potassium (substitute KCl (NuSalt) for some of the NaCl) & magnesium & folate, exercise, alcohol intake limited (women: ≤ 2/day; men ≤ 3/day), fruit and vegetables and low-fat dairy.
6. Vegetables & fruits Eat certain fruits & vegetables: a variety of nuts, legumes, tea (or tea extract capsules – this is what I do), pomegranate, berries, spinach, kale, sprouts, prunes, broccoli & the like, red pepper, tomato paste, vitamin C, selenium (in nuts), purple grape juice, pomegranate juice, turmeric (along with pepper), magnesium-rich foods (whole grains, nuts, leafy green vegetables). Eat foods with soluble fibers: flax, glucomannan, oat bran, psyllium and guar.
7. Avoid sun damage: Clothes, sun block, hat, and polycarbonate/UV-protection sunglasses.
8. Eat a "Mediterranean diet": olive oil, fish, vegetables, fruit, and red wine.
9. Nuts
10. Cholesterol and triglycerides
11. Meat
12. Methionine restriction seems to have a large positive effect on lifespan & prevention of diabetes. Animal protein sources (e.g., beef, pork, fish, milk, cheese, and eggs) have about twice as much methionine per gram of protein compared to vegetable protein sources (broccoli, lentils, peas, spinach, etc.). This may a reason that vegetarians are generally healthier than meat eaters.
13. Protein
14. Carbohydrates, glycemic index, and glycemic load
15. Advanced Glycation Endproducts and cooking methods
16. Bran and whole grains
17. Fiber (psyllium, guar, glucomannan etc.)
18. Tea and Coffee
19. Wine and alcohol
20. Toxins
21. Summaries of prevention measures for specific diseases
22. Brush your teeth
23. Safety measures
24. Genetics Obviously, this is not something you can do anything about in retrospect! However, identification of truly important factors might eventually lead to medical interventions that mimic the effects of the genes.

Caution #1: Many human studies show benefit from one or another intervention, such as eating vegetables, fish, or wine, etc. The inference that the intervention caused the benefit is not necessarily true, even when the study design is flawless (rare). Eating vegetables for example could simply be a marker for those with genes to protect against heart disease. The finding has to be supported by animal studies, a reasonable pathophysiological mechanism, etc. Other studies show benefit in animals, but have to be confirmed in humans. Thus, most of the recommendations in this document are based on suggestive – NOT CONCLUSIVE – data.

Caution #2: Be cautious about inferring cause from effect. For example, when people eat fruit and vegetables, there is a reduction in many diseases. This *may* be due directly to the fruit and vegetables, but it may be for other reasons, e.g. because these fruit and vegetables substituted for other foods that are bad for you. The suggestions in this document are particularly susceptible to this problem.

Warnings

Avoid Atkins' diet (in the early popular form). In one form, this diet promotes eating such things as animal fat, red meat, butter, trans-fats (margarine and many prepared foods) etc. This does help decrease

your appetite and you may lose a small amount of weight, but you run greatly increased risks of common, deadly and debilitating diseases such as heart disease, hypertension, stroke, cancer, Alzheimer disease and Parkinson disease. When you eat fatty foods (I do), you should do so carefully: eat mono-unsaturated fats (MUFA) found in nuts, olive oil, avocados etc. Also, specifically eat foods with omega-3 fats, such as wild salmon and possibly freshly ground flax seed. These fats are in fact GOOD for you and tend to prevent some of the problems that Atkins causes.

Folks, this web site interview [10] is worth reading in detail, by all. Why? Well, consider how much money and time you will spend on medical care for yourself, and then consider this quote from Walter Willett, MD (that I KNOW is backed up by outstanding data - I have reviewed this data myself): "The potential impact of healthy diet, when you combine it with not smoking and regular physical activity, is enormous. For example, our studies have shown that we could prevent about 82 percent of heart attacks, about 70 percent of strokes, over 90 percent of type 2 diabetes, and over 70 percent of colon cancer, with the right dietary choices as part of a health lifestyle. The best drugs can reduce heart attacks by about 20 or 30 percent, yet we put almost all of our resources into promoting drugs rather than healthy lifestyle and nutrition…Walter Willett is professor of epidemiology and nutrition at Harvard School of Public Health, a professor of medicine at the Harvard Medical School, and the author of *Eat, Drink, and Be Healthy: The Harvard Medical School Guide to Healthy Eating*."

Some of the supplements or diet modifications may interfere with each other. For example, two of the apparently most important factors are omega-3 fats (fish oil, etc.) and non-steroidal anti-inflammatory medications (NSAIDs: aspirin, Motrin, etc.) are thought to have beneficial effects due to their action on prostaglandins. However, omega-3 fats are precursors to the prostaglandins, while NSAIDs stop the conversion of precursors into prostaglandins. The effects of combining the two are unclear. In this case, fortunately, there is a prospective trial that partially answers the question, the Lyon Diet Heart Study.[11] To quote from this study in a discussion of the independent effects of aspirin use, cholesterol, and hypertension, "the data indicate that neither the Mediterranean dietary pattern nor any major bias has altered the usual and expected relationships between the major risk factors of CHD and recurrence." (CHD = coronary heart disease). Other evidence that combining the most important diet modifications have added positive effects can be found in the following studies:

1. A study of 7306 women followed for 31 years looked at "Risk groups were defined using national guidelines for values of systolic and diastolic blood pressure, serum cholesterol level, body mass index, presence of diabetes, and smoking status." It showed that "for women with favorable levels for all 5 major risk factors at younger ages, CHD and CVD are rare; **long-term and all-cause mortality are much lower** compared with others."[12]
2. One study in *short-lived, autoimmune disease-prone mice* showed that caloric restriction and fish oil had independent, positive effects on life span. Either one by itself increased life span of this mouse species by approximately 50%; combining the two nearly doubled the life span (to near normal).[13] n.b., this is NOT directly extensible to humans: both CR and fish oil improve autoimmune conditions; this experiment has not been repeated in normal mice.
3. Ross and Bras showed that combining caloric restriction with super-normal amounts of protein had an additive, positive effect on life span.[14]
4. A recent study from Oregon State University showed that *simultaneous* supplementation with acetyl-L-carnitine (ALCAR) and lipoic acid (LA) improves metabolic function while reducing oxidative stress.[15] In short, it improves mitochondrial function and decreases mitochondrial damage from oxidation: these functions *may* both improve function and extend life span (not proven yet to my knowledge). Another study confirmed this simultaneous beneficial effect on cognitive function in rats.[16] Carnitine is found in meat and fish; LA is found in spinach. I do not know if it best to supplement with ALCAR and LA (which I do not), or to eat spinach and fish or meat frequently, but I like the latter best. Juvenon is made up of

these supplements. Another study stated "After 25-month-old mice received basal diet together with 300 mg/l acetyl L-carnitine in the drinking water for 8 weeks, these levels were fully restored to those found in younger animals. Dietary supplementation with melatonin or acetyl L-carnitine partially reversed these changes. These findings suggest that dietary supplementation cannot merely arrest but indeed reverse some age-related increases in markers of oxidative and inflammatory events occurring with the cortex." [17]

5. "Data on the ingredients of the Polymeal were taken from the literature. The evidence based recipe included wine, fish, dark chocolate, fruits, vegetables, garlic, and almonds. Data from the Framingham heart study and the Framingham offspring study were used to build life tables to model the benefits of the Polymeal in the general population from age 50, assuming multiplicative correlations. **Results** Combining the ingredients of the Polymeal would reduce cardiovascular disease events by 76%. For men, taking the Polymeal daily represented an increase in total life expectancy of 6.6 years, an increase in life expectancy free from cardiovascular disease of 9.0 years, and a decrease in life expectancy with cardiovascular disease of 2.4 years. The corresponding differences for women were 4.8, 8.1, and 3.3 years."[18]

Some good web site sources for data used in this paper:

1. Harvard School of Public Health: Nutrition Source. http://www.hsph.harvard.edu/nutritionsource/ **Frankly, this web site is as good as or better than whole document that follows.**
2. Keeping Kids Healthy (http://www.keepkidshealthy.com/welcome/bmicalculator.html) – an outstanding, site including good objective information and a calculator to figure out if your child is "at risk for being overweight."
3. PubMED (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=journals) – Abstracts from all medical journals. Note: the quoted articles have references primarily to these PubMED abstracts.
4. American Journal of Clinical Nutrition (http://www.ajcn.org/)
5. Journal of Nutrition (http://www.nutrition.org/)
6. Circulation (http://circ.ahajournals.org/) – Heart disease journal
7. Hypertension (http://hyper.ahajournals.org/)
8. Stroke (http://stroke.ahajournals.org/)
9. USDA nutrient database (http://www.nal.usda.gov/fnic/cgi-bin/nut_search.pl)
10. Eicosanoid summary from the NIH (http://ods.od.nih.gov/eicosanoids)
11. American Institute for Cancer Research (http://www.aicr.org/)
12. Merck Manual (http://www.merck.com)
13. Botanical list of food families

The use of and diet, habits and supplements to help prevent medical problems.

(http://www.calgaryallergy.ca/Articles/botanical.htm)

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Meat

Category	Effect	Finding	Ref	Fig
Vegetarianism	Probably has a small beneficial effect on lifespan	From a well-thought out 2002 summary of many studies: "- vegetarians have low mortality compared with the general population - much of this benefit is attributable to non-dietary lifestyle factors such as the avoidance of smoking and a high socio-economic status - vegetarians have similar mortality to comparable non-vegetarians, although a vegetarian diet may confer an additional 1-2 years of life (at least among US Adventists)."	19	
	Less risk of one type of kidney stones	About 12% of kidney stones are from uric acid; gout is also caused by this. Uric acid comes mostly from meat. "The results indicate that the intake of a balanced vegetarian diet with a moderate animal protein and purine content, an adequate fluid intake and a high alkali-load with fruits and vegetables results in the lowest risk of uric acid crystallization compared to the omnivorous diets."	20	
Meat	Increased risk cardiovascular mortality from meat	A meta-analysis of 5 large prospective "Western diet" vegetarian studies showed that cardiovascular mortality is about 24% lower in vegetarians. (from other studies, part of this may be due to lower BMI)	21	
	Very low meat intake is associated with longer life expectancy	Review article: Very low meat intake is associated with longer life by 3.6 years. This effect may be at least partially due to factors other than meat: those with low meat intake also tend to be thinner and eat more healthy vegetables & nuts.	22	
	Increased risk of gout, especially from red meat and beer; skim milk decreases the risk.	"The multivariate relative risk of gout among men in the highest quintile of meat intake, as compared with those in the lowest quintile, was 1.41… and the corresponding relative risk associated with seafood intake was 1.51 … In contrast, the incidence of gout decreased with increasing intake of [low fat] dairy products; the multivariate relative risk among men in the highest quintile, as compared with those in the lowest quintile, was 0.56…The level of consumption of purine-rich vegetables and the total protein intake were not associated with an increased risk of gout." From the 2004-03-13 Science News summary of the article, **each daily serving of meat increased gout risk by 21%**, while each daily fish serving increased the risk by 7%. In addition, **each daily serving of beer increased risk by 49%. Skim milk decreases the risk by 21% per daily serving.**	23	
	Increased risk for diabetes (type 2, adult onset)	"We prospectively assessed the associations between major dietary patterns and risk of type 2 diabetes in women. Dietary information was collected in 1984, 1986, 1990, and 1994 from 69 554 women aged 38 to 63 years without a history of diabetes, cardiovascular disease, or cancer in 1984. We conducted factor analysis and identified 2 major dietary patterns: "prudent" and "Western." We then calculated pattern scores for each participant and examined prospectively the associations between dietary pattern scores and type 2 diabetes risks. RESULTS: The prudent pattern was characterized by higher intakes of fruits, vegetables, legumes, fish, poultry, and whole grains, while the Western pattern included higher intakes of red and processed meats, sweets and desserts, french fries, and refined grains. During 14 years of follow-up, we identified 2699 incident cases of type 2 diabetes. After adjusting for potential confounders, we observed a relative risk for diabetes of 1.49 (95% confidence interval [CI], 1.26-1.76, P for trend, <.001) when comparing the highest to lowest quintiles of the Western pattern. Positive associations were also observed between type 2 diabetes and red meat and other processed meats. **The relative risk for diabetes for every 1-serving increase in intake is 1.26 (95% CI, 1.21-1.42) for red meat, 1.38**	24	

		(95% CI, 1.23-1.56) for total processed meats, 1.73 (95% CI, 1.39-2.16) for bacon, 1.49 (95% CI, 1.04-2.11) for hot dogs, and 1.43 (95% CI, 1.22-1.69) for processed meats."		
	Hypertension	"Compared with quintile 1, the relative hazards of EBP for quintiles 2–5 of plant food intake were 0.83 (95% CI: 0.68, 1.01), 0.83 (0.67, 1.02), 0.82 (0.65, 1.03), and 0.64 (0.53, 0.90), respectively; *P* for trend = 0.01… positive dose-response relations for EBP were observed across increasing quintiles of meat intake (*P* for trend = 0.004)."	[25]	
Red meat	Colorectal cancer	"N-Nitroso compounds are suspected colorectal cancer (CRC) carcinogens to which individuals on a diet high in red meat (RM) may be particularly exposed… These data provide additional support for the hypothesis that nitrosamines are carcinogenic to the rectum in humans and that RM and, in particular, [processed meats] are significant sources of exposure for these compounds."	[26]	
	Increases risk of colorectal cancer	An NIH study found that the factors making the most difference are eating red meat (OR [odds ratio] = 2.0), pan-fried red meat (OR = 2.0) and well-done meat (OR = 1.7)	[27]	
	Increases risk of colorectal cancer	A meta-analysis of 13 studies found that "a daily increase of 100 g of all meat or red meat is associated with a significant 12–17% increased risk of colorectal cancer" and that the risk for processed meat was greater: "A significant 49% increased risk was found for a daily increase of 25 g of processed meat."	[28]	
	Increased risk of diabetes type 2	"Heme-iron intake from red meat sources is positively associated with the risk of type 2 diabetes. Total iron intake, heme-iron intake from non-red meat sources, and blood donations are not related to the risk of type 2 diabetes." (relative risk = 1.63, i.e. a 63% increased risk)	[29]	
	Increased risk of rheumatoid arthritis	"A study of 25 000 people living in Europe shows that those who ate the most red meat had double the risk of rheumatoid arthritis, compared to those who ate the least amount. And people who ate more protein overall, including other forms of meat and plant protein, also had a higher risk of the disease while eating fat did not seem to raise the risk, the researchers found."	[30]	
	US Government collusion in disinformation	"I first became aware of the food industry as an influence on government nutrition policies and on the opinions of nutrition experts when I moved to Washington, DC, in 1986 to work for the Public Health Service. My job was to manage the editorial production of the first-and as yet only-Surgeon General's Report on Nutrition and Health, which appeared as a 700-page book in the summer of 1988. This report was an ambitious government effort to summarize the entire body of research linking dietary factors such as fat, saturated fat, cholesterol, salt, sugar, and alcohol to leading chronic diseases. My first day on the job, I was given the rules: No matter what the research indicated, the report could not recommend "eat less meat" as a way to reduce intake of saturated fat, nor could it suggest restrictions on intake of any other category of food. In the industry-friendly climate of the Reagan administration, the producers of foods that might be affected by such advice would complain to their beneficiaries in Congress, and the report would never be published. This scenario was no paranoid fantasy; **federal health officials had endured a decade of almost constant congressional interference with their dietary recommendations.** As I discuss in Part I, agency officials had learned to avoid such interference by resorting to euphemisms, focusing recommendations on nutrients rather than on the foods that contain them, and giving a positive spin to any restrictive advice about food. Whereas "eat less beef" called the industry to arms, "eat less saturated fat" did not. "Eat less sugar" sent sugar producers right to Congress, but that industry could live with "choose a diet moderate in sugar." When released in 1988, the Surgeon General's Report recommended "choose lean meats" and suggested limitations on sugar intake only for people particularly	[31]	

		vulnerable to dental cavities."		
Bacon	Increased risk of bladder cancer	"In these 2 cohorts combined, frequent consumption of bacon was associated with an elevated risk of bladder cancer." (about double)	[32]	

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Inflammation

Category	Effect	Finding	Ref	Fig
Aspirin	Cardiovascular disease	There is no evidence that aspirin helps if you have low cardiovascular risk factors.	[33]	
	Cardiovascular disease	Aspirin only helps those with high risk factors for MI. "For 1000 patients with a 5% risk for coronary heart disease events over 5 years, aspirin would prevent 6 to 20 myocardial infarctions but would cause 0 to 2 hemorrhagic strokes and 2 to 4 major gastrointestinal bleeding events. For patients with a risk of 1% over 5 years, aspirin would prevent 1 to 4 myocardial infarctions but would cause 0 to 2 hemorrhagic strokes and 2 to 4 major gastrointestinal bleeding events."	[34]	
	Cancer (colon etc.)	Aspirin may help prevent digestive tract cancer. "The role of aspirin on the risk of cancers of the upper aerodigestive tract was investigated in the combined data of three Italian case-control studies, including 965 cases and 1779 hospital controls. The odds ratio was 0.33 for users of >/=5 years, and 0.51 for >/=5 years since first use."	[35]	
	Colon cancer	A randomized trial of patients who had previous colon adenomas showed that "Low-dose aspirin has a moderate chemopreventive effect on adenomas in the large bowel." However, as noted in an editorial in the same journal "The cumulative risk of major adverse effects most likely outweighs any benefit in the prevention of colorectal cancer, particularly when prevention due to screening is considered."	[36]	

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Glycation, Advanced Glycation Endproducts (AGEs), and cooking methods

Direct, non-enzymatic glycation damages your body tissue. This is what makes diabetics age so quickly. A recent English study suggests that even small elevations in blood sugar level (as measured via hemoglobin A_1C, or HbA_1C for short) have a large effect on the risk for heart attack. Glycation is simply the direct chemical reaction between glucose in your blood stream (from carbohydrates such as sugar, starches, fruits etc.) and your body's proteins. In college chemistry, you may have heard of this as the Maillard reaction. This reaction results in the proteins being degraded and losing their function: tissues become stiff, arteries hard, lenses opaque, spots form on your skin. This reaction is directly related to the glucose concentration in the blood, which is a complex interaction between what and when you eat, your body weight and body fat, your activity level, your body's insulin response, etc. This is too complex for me to sort out completely, but two things are clear (for non-diabetics): insulin responsiveness declines in obese people, and the glucose level rises fast after eating a lot of simple sugars (a soda, fruit juice, ice cream, etc.) Therefore, simply keep slender and avoid large quantities of sweets, just like your mother told you. Another approach is to eat many small meals each day instead of one or two large meals, to keep the peak glucose load down.

Glycation also occurs in the intestines and outside the body, and that the glycated proteins are readily absorbed. Thus, it is best to not marinate meat with fruit or in sugary liquids. I like plain soy sauce my self (or better, potassium chloride (KCl)). The most important and straightforward way to reduce glycation is caloric restriction. If you do nothing else, do this.

Advanced Glycation End-products (AGEs) are the ultimate end waste product of glycation damage. They form in the body, but also are present in cooked fats and proteins. The most important and straightforward ways to reduce AGE intake are 1) caloric restriction, 2) reduction of cooking time and temperature, especially for fats and proteins, and 3) avoidance of cooked fatty foods. See the "AGE" tab of the "Foods.xls" spreadsheet for the proportion of AGEs per 200 calories in some foods.

Glycation related to aging		"Glycation, a deleterious form of post-translational modification of macromolecules has been linked to diseases such as diabetes, cataract, Alzheimer's, dialysis related amyloidosis (DRA), atherosclerosis and Parkinson's as well as physiological aging… Macromolecular damage and biochemical changes that occur in aging and age-related disorders point to the process of glycation as the common event in all of them. This is supported by the fact that several age-related diseases show symptoms manifested by hyperglycemia."	[37]	
AGE formation	CR is the most effective way to reduce this	"…These results suggest that long-term feeding of specific dietary carbohydrates does not alter serum glucose concentrations or the rate of collagen glycation. Rather, **age-related accumulation of AGE is more closely related to caloric intake**."	[38]	
Advanced glycosylation end-products (AGEs) in the diet	AGEs can be absorbed when taken orally, and cause reduced insulin sensitivity in mice	"AGEs are abundant in exogenous sources such as foods, especially when prepared under elevated temperatures (11,12). After ingestion, 10% of preformed AGEs are absorbed into the human or rodent circulation (13,14), of which two-thirds are retained in tissues… reduced intake of dietary AGEs has been recently shown to decrease the incidence of type 1 diabetes in NOD mice (26) as well as the formation of atherosclerotic lesions in diabetic apolipoprotein E-deficient mice"	[39]	
	Dietary AGE has a large effect	Low AGE in the diet was achieved by using different cooking methods: "To vary the AGE content, foods, particularly meat, were exposed to different cooking methods. L-AGE subjects were instructed to boil, poach, stew or steam, avoid fried entrees, and reheat food indirectly using steam in a double boiler." This cut their circulating AGE levels by 55%. "…dietary glycotoxins contribute significantly to the elevated AGE levels in renal failure patients. Moreover, dietary restriction of AGE is an effective and feasible method to reduce excess toxic AGE and possibly cardiovascular associated mortality."	[40]	
		"**Foods of the fat group showed the highest amount of AGE content** with a mean of 100+/-19 kU/g. High values were also observed for the meat and meat-substitute group, 43+/-7 kU/g. The carbohydrate group contained the lowest values of AGEs, 3.4+/-1.8 kU/g. **The amount of AGEs present in all food categories was related to cooking temperature, length of cooking time, and presence of moisture.** Broiling (225 degrees C) and frying (177 degrees C) resulted in the highest levels of AGEs, followed by roasting (177 degrees C) and boiling (100 degrees C)."	[41]	
	Dietary AGE impairs wound healing	"Advanced glycoxidation end products (AGEs) are implicated in delayed diabetic wound healing. To test the role of diet-derived AGE on the rate of wound healing, we placed female db/db (+/+) (n = 55, 12 weeks old) and age-matched control db/db (+/-) mice (n = 45) on two diets that differed only in AGE content (high [H-AGE] versus low [L-AGE] ratio, 5:1) for 3 months. Full-thickness skin wounds (1 cm) were examined histologically and for wound closure... L-AGE-fed mice displayed more rapid wound closure at days 7 and 14 ($P < 0.005$) and were closed completely by day 21 compared with H-AGE nonhealed wounds. Serum AGE levels increased by 53% in H-AGE mice and decreased by 7.8% in L-AGE mice ($P < 0.04$) from baseline. L-AGE mice wounds exhibited lower skin AGE deposits, increased epithelialization, angiogenesis, inflammation, granulation tissue deposition, and enhanced collagen organization up to day 21, compared with H-AGE mice. Reepithelialization was the dominant mode of wound closure in H-AGE mice compared with wound contraction that prevailed in L-AGE mice. Thus, increased diet-derived AGE intake may be a significant retardant of wound closure in diabetic mice; dietary AGE restriction may improve impaired	[42]	

		diabetic wound healing."		
AGE absorption from foods	Cooking at high temperatures or with simple sugars produces absorbable AGEs	"To assess the kinetics of ingested AGEs, investigators at this center recently prepared, for five healthy persons and 38 diabetic patients with or without overt renal disease, a breakfast consisting of 56 gm of egg white cooked with or without 100 gm of fructose for one to three hours at 90°C. In the cooked fructose-containing mixture, the AGE content was more than 200 times that of the other food. Over the ensuing 48 hours, blood and urine were sampled. The high-AGE meal produced serum AGE elevations well correlated with severity of renal disease. In particular, renal clearance ranged from about 30% of absorbed AGEs in controls to less than 5% in diabetic patients with renal failure. The rest was retained in the body. Serum AGE analyses confirmed the ability of the absorbed AGEs to crosslink biologic macromolecules (in this case, radiolabeled fibronectin). It must immediately be said that the AGE content of one or another food has no simple relation to its sugar content. The more important relation is with the method of food preparation. Since the turn of the 20th century, food chemists have appreciated that the changes responsible for increasing the AGE content of a food--changes known to them as the Maillard reaction and to the rest of us, less formally, as the browning of raw foods by methods such as roasting or braising--depend directly on temperature and are greatly heightened by long exposure to high heat. Unfortunately, heat creates tastes that humans enjoy, or at least tastes for which humans in Western societies have developed an appetite. In recent decades, food manufacturers have been using their knowledge of Maillard chemistry to add appeal to natural foods and even to incorporate such appeal into synthetic foods (an example being the use of caramelized sugars in beverages such as Coca Cola). In consequence, the AGE content of the Western diet has increased vastly in the past 50 years. A few representative measurements may serve to illustrate the importance of cooking method. So far, our group has analyzed 300 to 400 foods, using an immunoassay that assesses a few of the many lipid- and protein-bound AGEs. By this test, roasted duck skin (220°C for 110 minutes) exhibited, weight for weight, almost 15 times the AGE content of a doughnut (160°C for five minutes). Cooking increased the doughnut's AGE content 24-fold and the duck skin's 101-fold."	[43]	
	Technical discussion of AGE	Free pdf paper at http://www.mssm.edu/msjournal/70/70_4_pages_232_241.pdf A popular discussion from the same author is at CBSnews: "The key to lowering AGEs, said Vlassara, is to cook for a short time in the presence of high humidity. This means either boiling or steaming meats for the minimum time required. Meat can be sautéed, she said, but it should be cut very thin and cooked quickly with a small amount of oil. She said one of the worst AGE offenders is turkey cooked in the traditional American way. "We cook for many hours," she said. "That would tend to make a tremendous number of AGEs."	[44]	
		High AGE diet led to kidney damage in diabetic and normal mice.	[45]	
High HbA1c is associated with vessel disease	Glycosylation results in carotid plaques, even in normal, non-diabetic people	"HbA1c measurements and ultrasonography of the carotid artery were performed in 5960 subjects (3026 women, 2934 men) 25 to 84 years of age...HbA1c was categorized into 5 groups: <5.0%, 5.0% to 5.4%, 5.5% to 5.9%, 6.0% to 6.4% and >6.4%. Carotid plaque prevalence increased with increasing HbA1c level (P for linear trend=0.002). **The OR for hard plaques versus no plaques was 5.8 in the highest HbA1c group (>6.4%) compared with subjects in the**	[46]	

		lowest group (<5.0%) after adjustment for several possible confounders. The risk of predominantly hard plaques was also significantly associated with HbA1c levels, although the ORs at each level were somewhat lower than for hard plaques… CONCLUSIONS: Metabolic changes reflected by HbA1c levels may contribute to the development of hard carotid artery plaques, even at modestly elevated levels."		
		"Glycosylated hemoglobin is an easily measured bio-chemical marker that strongly correlates with the level of ambient glycemia during a 2- to 3-month period… Khaw and colleagues (14) carefully analyzed the relationship of 1 hemoglobin A1c measurement to incident cardiovascular events in a 6-year cohort study of 10 232 diabetic and nondiabetic men and women age 45 to 79 years. After adjustment for systolic blood pressure, cholesterol level, body mass index, waist-to-hip ratio, smoking, and previous myocardial infarction or stroke, there was a 21% increase in cardiovascular events for every 1–percent-age point increase in hemoglobin A1c level above 5% (P 0.001). Similar relationships were observed for total mortality (22% for men [P 0.001] and 28% for women [P 0.01] per 1–percentage point increase in hemoglobin A1c level)."	[47] [48]	
High-normal glucose levels	Associated with higher risk of death	"Using the Framingham Heart Study data... After adjustment for systolic blood pressure, cholesterol, body mass index, cigarette smoking, and use of antihypertensive agents, they found that glucose was a strong, independent predictor of mortality… For men, **adjusted mortality risk increased very rapidly through the normal range (from 4.12% at 3.89 mmol/liter (70 mg/dl) to 12.26% at 5.55 mmol/liter (100 mg/dl))** and was flat at 12.26% thereafter. For women, risk was flat at 3.65% through the normal range and then increased rapidly, reaching 8.34% at 6.99 mmol/liter (126 mg/d), but increased much more slowly thereafter. Exactly analogous relations held for cardiovascular mortality. For men and women combined, noncardiovascular mortality increased from 1.82% at 3.89 mmol/liter to 2.06% at 5.55 mmol/liter to 2.29% at 6.99 mmol/liter (p for trend = 0.009). These findings suggest that although 5.55 mmol/liter (normal) may be a useful mortality risk division (albeit with different implications for the two sexes), 6.99 mmol/liter (diabetic) is not, especially for men."	[49]	
Pyridoxamine	Inhibits AGE formation	"[Pyridoxamine (PM)] has a strong lipid-lowering effect in streptozotocin (STZ)-induced diabetic and Zucker obese rats, and protects against the development of nephropathy in both animal models. PM also inhibits the development of retinopathy and neuropathy in the STZ-diabetic rat."	[50]	
Benfotiamine (a thiamine derivative)	AGE prevention	Benfotiamine blocks the formation of intracellular Advanced Glycation Endproducts (AGE), through boosting the activity of the enzyme transkelotase sufficiently to provide a metabolic "shunt" for excess intracellular (as opposed to blood) glucose, reducing the formation of highly reactive glycolytic intermediates called triosephosphates. "…benfotiamine treatment … prevented experimental diabetic retinopathy. The ability of benfotiamine to inhibit three major pathways simultaneously might be clinically useful in preventing the development and progression of diabetic complications."	[51]	
Glucose Alpha lipoic acid	Increases blood pressure & insulin resistance in rats alpha lipoic acid blocks this effect	Message: avoid glucose (sugars & starches); consider using alpha lipoic acid. "Chronic administration of glucose resulted in a 29% increase in blood pressure, 30% increase in glycemia, 286% increase in insulinemia, and 408% increase in insulin resistance index. Chronic glucose feeding also resulted in a 22% greater mitochondrial superoxide anion production in heart and in an increase of 63% in AGE content in aorta. Increases in blood pressure, aorta AGE content and heart mitochondrial superoxide production were prevented in the rats fed glucose supplemented with lipoic acid."	[52]	
Glycation	Strongly correlated with	"HbA1c was categorized into 5 groups: <5.0%, 5.0% to 5.4%, 5.5% to 5.9%, 6.0% to 6.4% and >6.4%. Carotid plaque prevalence	[53]	

	carotid plaques	increased with increasing HbA1c level (P for linear trend=0.002). The OR for hard plaques versus no plaques was 5.8 in the highest HbA1c group (>6.4%) compared with subjects in the lowest group (<5.0%) after adjustment for several possible confounders… Metabolic changes reflected by HbA_{1c} levels may contribute to the development of hard carotid artery plaques, even at modestly elevated levels."		

Go to TOC

Carbohydrates and insulin

One term used in discussing glycation is "glycemic index", or the much more useful measurement of "glycemic load". Some foods with high glycemic index and load include: all starches, potatoes, bread, rice, sugar, honey, and breakfast cereals (except all-bran cereals); sweet fruits also have a high glycemic load but have the benefit of nutrients. This web site has an extensive glycemic index list. So note: In fact, the glucose load from starch-based foods like bread, pizza, potatoes and noodles is equivalent to that from candy!!

Glycemic load refers to how much your blood glucose level rises after eating various foods. The glycemic load for sugar, rice, and bread would be very high; for asparagus and peanuts very low. If you want to minimize the glycation of your body's tissues, practice caloric restriction *and* eat foods with low glycemic loads (not too much starch).

Fructose ("fruit sugar") is equally important to glucose in the problem of glycation (J Nutr 2000 May;130(5):1247-55; PMID: 10801926). In lab rats it causes kidney damage and "…studies showed that long-term fructose intake adversely affected several age-related metabolic parameters." (Kizhner T, Werman MJ. Long-term fructose intake: Biochemical consequences and altered renal histology in the male rat. Metabolism. 2002 Dec;51(12):1538-47. PMID: 12489065). Much of it is (I think) converted to glucose quickly after ingestion. The major sources of fructose in our diet are table sugar (half fructose & half glucose), fruit, honey, and high-fructose corn syrup (corn syrup is a part of many prepared foods at the grocery store such as soft drinks, jams & yogurt). It is probably worth avoiding too much of the sweet fruits, although berries (blueberries, raspberries, strawberries, etc.) have much less sugar and seem to be fine.

Some foods with low glycemic load include: onions, mushrooms, yams and whole grain or 100% rye bread (pumpernickel are all good), but mostly lots more vegetable 'fruits', i.e. peppers, tomato, cucumber, squash, eggplant; cruciferous vegetables (cabbage, broccoli, cauliflower, kale, Brussels sprouts); and leafy green vegetables of all kinds.

One quick and easy way to effectively decrease the glycemic index of food is to decrease the rate of gastric emptying. This can be done by eating an acidic (e.g. a pickle, grapefruit juice, or a vinegar-based dressing) or fatty food (e.g. nuts, fish) with your meals. High-fiber food does not affect the glycemic index of a meal.

See the Scientific American 2002-12 issue for an updated food pyramid based on modern nutrition research.

Category	Effect	Finding	Ref	Fig
Carbohydrates	Colon cancer	There may be an increased risk of colorectal cancer with high carbohydrate intake. "increased eCarb and total carbohydrate consumption are both associated with increased risk of CRC [colorectal cancer] in both sexes, and that among women, relative risk appears greatest for the right colon, whereas among men, relative risk appears greatest for the rectum" (**note: in another careful case-control study, carbohydrates dropped out as a risk factor in favor of calories**)	54	
	Low-carbohydrate, low iron, vegetable diet helps prevent progression of kidney damage	"In conclusion, [carbohydrate-restricted, low-iron-available, polyphenol-enriched] CR-LIPE was 40-50% more effective than standard protein restriction in improving renal and overall survival rates." (Polyphenols are found in tea, wine, etc.) Although this is a study of kidney failure patients, the implications may be much more widespread. *Perhaps* this type of diet is healthy for other organs as well.	55	

Blood glucose level	Post-prandial glucose level is more important than average	"**Most epidemiological data implicate postprandial hyperglycemia in the development of cardiovascular disease, whereas the link between fasting glycemia and diabetic complications is inconclusive**. Moreover, in many studies, postprandial glycemia is a better predictor of cardiovascular risk than HbA(1c) level. Postprandial glucose may have a direct toxic effect on the vascular endothelium, mediated by oxidative stress that is independent of other cardiovascular risk factors such as hyperlipidemia."	56	
	High levels damage mitochondria	"Four main molecular mechanisms have been implicated in glucose-mediated vascular damage. All seem to reflect a single hyperglycaemia-induced process of overproduction of superoxide by the mitochondrial electron-transport chain."	57	
	Fasting glucose >90, BMI >30, and triglyceride ≥150 => increased rate of subsequent diabetes	"We obtained blood measurements, data from physical examinations, and medical and lifestyle information from men in the Israel Defense Forces who were 26 to 45 years of age. RESULTS: A total of 208 incident cases of type 2 diabetes occurred during 74,309 person-years of follow-up (from 1992 through 2004) among 13,163 subjects who had baseline fasting plasma glucose levels of less than 100 mg per deciliter. A multivariate model, adjusted for age, family history of diabetes, body-mass index, physical-activity level, smoking status, and serum triglyceride levels, revealed a progressively increased risk of type 2 diabetes in men with fasting plasma glucose levels of 87 mg per deciliter (4.83 mmol per liter) or more, as compared with those whose levels were in the bottom quintile (less than 81 mg per deciliter [4.5 mmol per liter], P for trend <0.001). In multivariate models, men with **serum triglyceride levels of 150 mg per deciliter** … **combined with fasting plasma glucose levels of 91 to 99 mg per deciliter** …had a hazard ratio of 8.23 … for diabetes, as compared with men with a combined triglyceride level of less than 150 mg per deciliter and fasting glucose levels of less than 86 mg per deciliter … The joint effect of a body-mass index … of 30 or more and a fasting plasma glucose level of 91 to 99 mg per deciliter resulted in a hazard ratio of 8….as compared with a [BMI <] 25 and a fasting plasma glucose level of less than 86 mg per deciliter. CONCLUSIONS: Higher fasting plasma glucose levels within the normoglycemic range constitute an independent risk factor for type 2 diabetes among young men, and such levels may help, along with body-mass index and triglyceride levels, to identify apparently healthy men at increased risk for diabetes."	58	
Reduce glycemic load (eat less non-fiber carbohydrates)	Reduces heart attack risk	A prospective study of 75,521 American women showed that those with the lowest glycemic load had half the risk for heart attack of women with the highest glycemic load.	59	
	Reduced CRP level	Another study showed that high glycemic load caused raised C-reactive protein (CRP) levels. CRP is strongly correlated with heart attack risk.	60	
	High glycemic index and low cereal fiber diet are associated with Type 2 DM	From the nurses health study: "After adjustment for age, body mass index, family history of diabetes, and other potential confounders, glycemic index was significantly associated with an increased risk of diabetes (multivariate relative risks for quintiles 1-5, respectively: 1, 1.15, 1.07, 1.27, and 1.59; 95% CI: 1.21, 2.10; P for trend = 0.001). Conversely, cereal fiber intake was associated with a decreased risk of diabetes (multivariate relative risks for quintiles 1-5, respectively: 1, 0.85, 0.87, 0.82, and 0.64; 95% CI: 0.48, 0.86; P for trend = 0.004). Glycemic load was not significantly associated with risk … CONCLUSIONS**: A diet high in rapidly absorbed carbohydrates and low in cereal fiber is associated with an increased risk of type 2 diabetes.**"	61	
	High GI and GL are associated with increased risk of prostate	"ORs [odds ratios] of prostate cancer and the corresponding 95% CIs were derived using unconditional multiple logistic regression, including terms for age, study center, education, family history of prostate cancer, smoking, body mass index, physical activity, alcohol	62	

	cancer	consumption, intake of energy, fiber and lycopenes. Compared to the lowest quintile of GI, the ORs were 1.23, 1.24, 1.47 and 1.57 for subsequent levels of GI. The corresponding values for GL were 0.91, 1.00, 1.20 and 1.41…We found direct relations between dietary GI and GL and prostate cancer risk."		
	High GL lowers HDL even in young people	"The only significant correlations evident were negative correlations between HDL cholesterol and glycemic load (in relation to white bread), percentage carbohydrate, total dietary sugar, total carbohydrate, and fructose. On stepwise multiple regression analysis, glycemic load accounted for 21.1% of the variation in HDL cholesterol."	63	
	Reduces stroke risk	"Cereal fiber intake was inversely associated with total and hemorrhagic stroke risk; for total stroke, relative risk = 0.66 (95% confidence interval: 0.52, 0.83; p(trend) = 0.001) and for hemorrhagic stroke, relative risk = 0.51 (95% confidence interval: 0.33, 0.78; p(trend) = 0.01). Findings suggest that high intake of refined carbohydrate is associated with hemorrhagic stroke risk, particularly among overweight or obese women. In addition, high consumption of cereal fiber was associated with lower risk of total and hemorrhagic stroke." Note: The lifetime risk for stroke is about 20% for women and 10% for men.	64 65	
	High GI and GL (carbohydrate intake) ⇔ higher rate of cataracts … Maybe. I am not sure if they controlled for BMI etc.	"A modified Block food-frequency questionnaire was used to obtain dietary information from 3377 participants (aged 60-80 y; 56% were women) in the Age-Related Eye Disease Study (AREDS)... RESULTS: For participants in the highest quartile, dietary **GI was associated with a higher prevalence of all pure nuclear opacities [grade >2; odds ratio (OR): 1.29**; 95% CI: 1.04, 1.59; P for trend = 0.02] and moderate nuclear opacities (grade >/=4; OR: 1.43; 95% CI: 0.96, 2.14; P for trend = 0.052). The OR in a comparison of the highest with the lowest quartile of intake was 1.27 (95% CI: 0.99, 1.63; P for trend = 0.09) for cortical opacities of any severity (>0% of area opaque), and the OR increased somewhat for moderate cortical opacities (>5% of area opaque; OR: 1.71; 95% CI: 1.00, 2.95; P for trend = 0.056)." "Subjects were 417 Boston-area members of the Nurses' Health Study cohort aged 53-73 y... RESULTS: After multivariate adjustment, the **odds of cortical opacities** (LOCS III >/=1.0) among women in the highest tertile of carbohydrate intake (>/=200 g/d) **was 2.46 times** (95% CI: 1.30, 4.64; P for trend = 0.005) **that among women in the lowest tertile** (<185 g/d)."	66 67	
Glycemic load	Increases level of glucose in blood (bad)	"Stepwise increases in glycemic load produced significant and predictable increases in both glycemia (P < 0.001) and insulinemia (P < 0.001)." An interesting note: pasta has a relatively low glycemic index, while potatoes and rice are very high.	68	
Fructose	Causes diabetes in rats	"Sprague-Dawley rats fed a fructose-rich diet exhibit insulin resistance and hypertension, a pathologic status resembling human type II diabetes mellitus"	69	
Insulin score	Insulin Index	Reducing insulin response to foods may be as important as or more important than reducing glycemic index.	70	Figure
Cut down on sugars and fats	May delay or reduce the disease of aging	"Simultaneous consideration of the influence of the different types of carbohydrates and fats in human diets on mortality rates (especially the diseases of aging), and the probable retardation of such diseases by caloric restriction (CR) leads to the hypothesis that restriction of foods with a high glycemic index and saturated or hydrogenated fats would avoid or delay many diseases of aging and might result in life extension."	71	
	May reduce pancreas cancer risk	"The objective of the study was to examine prospectively the association of the consumption of added sugar (ie, sugar added to coffee, tea, cereals, etc) and of high-sugar foods with the risk of	72	

		pancreatic cancer in a population-based cohort study of Swedish women and men. DESIGN: A food-frequency questionnaire was completed in 1997 by 77 797 women and men aged 45-83 y who had no previous diagnosis of cancer or history of diabetes. The participants were followed through June 2005. RESULTS: During a mean follow-up of 7.2 y, we identified 131 incident cases of pancreatic cancer. The consumption of added sugar, soft drinks, and sweetened fruit soups or stewed fruit was positively associated with the risk of pancreatic cancer. The multivariate hazard ratios for the highest compared with the lowest consumption categories were 1.69 (95% CI: 0.99, 2.89; P for trend = 0.06) for sugar, 1.93 (1.18, 3.14; P for trend = 0.02) for soft drinks, and 1.51 (0.97, 2.36; P for trend = 0.05) for sweetened fruit soups or stewed fruit. CONCLUSION: **High consumption of sugar and high-sugar foods may be associated with a greater risk of pancreatic cancer.**"		

Go to TOC

Omega-3 fats

Category	Effect	Finding	Ref	Fig
Omega-3 fats	Cardiovascular disease	"Randomized trials have convincingly documented that omega-3 fatty acids can significantly reduce the occurrence of CVD events in patients with coronary artery disease. The strongest evidence to date is from studies in which marine-derived omega-3 fatty acids have been consumed as supplements or fish."	73	
		The AHA recommends that all adults eat fish (particularly fatty fish) at least two times a week (fatty fish have the omega-3 fats DHA and EPA). The AHA also recommends eating plant-derived omega-3 fatty acids (ALA, found in flax seed, canola oil, and walnuts).	74	
	Protect against sudden death, NOT vs. atherosclerosis	"Both clinical and animal-experimental evidence suggests that the effect of n-3 PUFAs on the risk of sudden cardiac death relates primarily to reduced vulnerability to ventricular fibrillation, rather than to a reduction in atherosclerosis or nonfatal myocardial infarction.."	75	
	Depression	"…percentages of n-3 PUFAs and ratios of n-6 to n-3 PUFAs were significantly lower and higher, respectively, in subjects with depressive disorders than in control subjects…"	76	
Fish intake	Protects against death in those with cardiovascular disease	"Compared with no consumption, consumption of fish tended to be associated with a lower risk of death [1–57 g/d, RR = 0.50 (0.20, 1.28); > 57 g/d, RR = 0.37 (0.14, 1.00); P for trend = 0.059]." I.e., if you have CAD, eat ~3 oz of fish each day.	77	
DHA and EPA (long-chain omega 3 fats)	Help infants develop neurologically	"A prospective, double-blind, randomized controlled study was conducted with 2 groups of healthy term infants [showed that] Supplementation of healthy term infants with [long-chain polyunsaturated fatty acids] during the first 2 mo of life reduces the occurrence of mildly abnormal [general movements]."	78	
	Intake of fish oil during pregnancy and lactation increases child's IQ	A randomized and double-blinded study of the effect of cod liver oil supplementation (with DHA and EPA) "Children who were born to mothers who had taken cod liver oil (n = 48) during pregnancy and lactation scored higher on the Mental Processing Composite of the K-ABC at 4 years of age as compared with children whose mothers had taken corn oil (n = 36; 106.4 [7.4] vs 102.3 [11.3])… The children's mental processing scores at 4 years of age correlated significantly with maternal intake of DHA and eicosapentaenoic acid during pregnancy… Maternal intake of very-long-chain n-3 PUFAs during pregnancy and lactation may be favorable for later mental development of children."	79	
	Help prevent breast cancer	High marine omega-3 (DHA and EPA) diet => 26% lesser risk of breast cancer; high n-6 fat diet (e.g., corn oil) => 87% greater risk of breast cancer.	80	
DHA	Depression	The omega-3 fat DHA found in fish may help prevent depression.	81	

		"Mildly depressed subjects had significantly reduced (-34.6%) adipose tissue docosahexaenoic acid (DHA) levels than non-depressed subjects. Multiple linear regression analysis indicated that depression related negatively to adipose tissue DHA levels."		

Go to TOC

Nuts (see also Fats for the benefits of MUFA)

Category	Effect	Finding	Ref	Fig
Nuts and monounsaturated fats	Cardiovascular disease	"Nuts such as pecans that are rich in monounsaturated fat may therefore be recommended as part of prescribed cholesterol-lowering diet of patients or habitual diet of healthy individuals."	82	
	All-cause mortality and ischemic heart disease (IHD)	"The protective effect of nut consumption on IHD is not offset by increased mortality from other causes. Moreover, frequency of nut consumption has been found to be inversely related to all-cause mortality in several population groups such as whites, blacks, and the elderly. Thus, **nut consumption may not only offer protection against IHD, but also increase longevity**." This protection is 18% for those eating 1 oz of nuts every day, even after all other factors are controlled for.	83	
Nuts	Interesting botany web site	Lots of information and pictures at http://waynesword.palomar.edu/ecoph8.htm	84	
	Reduce incidence of gallstones	From the Nurses' Health Study: eating more than 5 oz of nuts/week (either peanuts or other nuts) reduced the risk of cholecystectomy by 25%.	85	
		In a prospective long-term study, nuts and peanuts were both found to be associated with reduced incidence of gallstones. "After adjustment for age and other known or suspected risk factors, men consuming 5 or more units of nuts per week… had a significantly lower risk of gallstone disease (relative risk = 0.70…) than did men who never ate or who ate less than 1 unit per month … (1 unit = 1 ounce (0.028 kg) of nuts)."	86	
	Reduce bad lipids (LDL cholesterol)	A systematic review of human studies showed: "The results of 3 almond (50–100 g/d), 2 peanut (35–68 g/d), 1 pecan nut (72 g/d), and 4 walnut (40–84 g/d) studies showed decreases in total cholesterol between 2 and 16% and LDL cholesterol between 2 and 19% compared with subjects consuming control diets. Consumption of macadamia nuts (50–100 g/d) produced less convincing results. **In conclusion, consumption of ≈50–100 g (≈1.5–3.5 servings) of nuts ≥5 times/wk as part of a heart-healthy diet with total fat content (high in mono- and/or polyunsaturated fatty acids) of ≈35% of energy may significantly decrease total cholesterol and LDL cholesterol in normo- and hyperlipidemic individuals."**	87	
	Eating nuts does NOT tend to cause weight gain	"Review of the available data to date suggests that adding nuts to habitual diets of free-living individuals does not cause weight gain. In fact, nuts have a tendency to lower body weight and fat mass. In the context of calorie-restricted diets, **adding nuts produces a more lasting and greater magnitude of weight loss** among obese subjects while improving insulin sensitivity… there is sufficient evidence to promote the inclusion of nuts as part of healthy diets."	88	
Walnuts	Cardiovascular disease	Walnuts help prevent cardiovascular disease. "This study demonstrated that walnuts, when consumed as part of a low fat, low-cholesterol diet, have a beneficial effect on serum cardiovascular risk factors."	89	
	Protects the heart	"Substituting walnuts for monounsaturated fat in a Mediterranean diet improves endothelium-dependent vasodilation in hypercholesterolemic subjects. This finding might explain the cardioprotective effect of nut intake beyond cholesterol lowering."	90	
Almonds	Almond intake improves lipid profile	"Isoenergetic incorporation of ≈68 g of almonds (20% of energy) into an 8368-kJ (2000-kcal) Step I diet markedly improved the serum lipid profile of healthy and mildly hypercholesterolemic adults."	91	
	Help with dieting	"[Low calorie diet] supplementation with almonds, in contrast to complex carbohydrates, was associated with greater reductions in	92	

		weight/BMI (-18 vs -11%), waist circumference (WC) (-14 vs -9%), fat mass (FM) (-30 vs -20%) … and systolic blood pressure (-11 vs 0%)"		
Macadamia nuts	Favorably affect blood lipid levels, and cholesterol in particular	My take: nuts help against cholesterol, but you have to eat a lot. "… macadamia nuts (40-90 g/d), equivalent to 15% energy intake… Plasma total cholesterol and LDL cholesterol concentrations decreased by 3.0 and 5.3%, respectively, and HDL cholesterol levels increased by 7.9% in hypercholesterolemic men after macadamia nut consumption."	93	
Peanuts	Cause atherosclerosis in animals	"Peanut oil is unexpectedly atherogenic for rats, rabbits, and primates." This is probably from the lectin content. Additional note: relative to other nuts, peanuts have less good MUFA and more bad omega-6 fats.	94 95	

Go to TOC

Fats (MUFA, saturated, and trans fats etc.)

1. *Which* fats you eat and how much is very important. Also note that part of the body's response to diet modification is genetic (Am J Clin Nutr 2002 Feb;75(2):191-212; PMID: 11815309).

In summary:
BAD FATS: partially hydrogenated ("trans fats"), saturated fats, and omega-6 (in large quantities)
GOOD FATS: monounsaturated fats in moderate amounts, and omega-3 fats in small quantities
HOW MUCH FAT TO EAT: 35% of calories (+/- 10%), as part of a CR diet

BAD FATS

Definitely very important: try to **eliminate** partially hydrogenated vegetable oils. These have trans-fatty acids, shown to cause many health problems: see Margarine, Fatty Acids and Your Health. Hydrogenation makes oils solid, but trans-fats are a NON-FOOD: they are not easily metabolized in the body and accumulate over time, increasing your risk for heart attack (Eur J Clin Nutr 2000 Aug;54(8):618-25; PMID: 10951510). They may also increase the risk of adult-onset diabetes (Dietary fat intake and risk of type 2 diabetes in women. American Journal of Clinical Nutrition, Vol. 73, No. 6, 1019-1026, June 2001.) Eliminating these is very hard to do, as these make up margarine and are the major fat used in most prepared foods such as cookies, cake mixes, Raman noodles, bread, snacks, biscuits, etc. Read the labels!

Cut down on animal fat (except fish), saturated fats, and certain types of vegetable fats such as corn and safflower oil (Am J Clin Nutr 1999 Sep;70(3 Suppl):560S-569S; PMID: 10479232). This will help reduce the incidence of stroke, heart attack, and cancer.

The current Western diet is too rich in omega-6 fat from various vegetable sources, and this is thought to cause much disease. Current theory is that the ratio of omega-3 to omega-6 fat should be about 1 to 1; the average Western diet has a ratio of about 1 to 15! (See either of these National Institutes of Health sites discussing eicosanoids: 1 or 2) In order to get some balance, eat some source of omega-3 fat. I know of a few sources: small, fatty, cold-water fish (such as salmon, herring, cod and sardines), perilla oil (whatever that is!) and flax seed; there are probably several others. Corn, sunflower, safflower, soy, sesame and cottonseed oils have lots of omega-6 fat.

GOOD FATS

Modification of fat intake is far more important than how much cholesterol you eat. What is good fat? Mono-unsaturated fats (MUFA) and Omega-3 fats.

1. MUFA: Moderate quantities of mono-unsaturated fats are good, especially those found in olive oil, avocados, and nuts. [N.b., peanuts are not nuts but rather legume seeds; while they have MUFAs they have been shown to cause atherosclerosis (Lipids 1998 Aug;33(8):821-3; PMID: 9727614).]

A large study of 7th Day Adventists showed that the lifetime risk of IHD was reduced by approximately 31% in those who consumed nuts frequently (Am J Clin Nutr 1999 Sep;70(3 Suppl):532S-538S; PMID: 10479227). Another nut study showed a 47% reduction in sudden heart death in those who

ate nuts (Arch Intern Med 2002 Jun 24;162(12):1382-7; PMID: 12076237). A summary of data on nuts (Clin Cardiol 1999 Jul;22(7 Suppl):III11-5; PMID: 10410300) stated that "Four of the best and largest cohort studies in nutritional epidemiology have now reported that eating nuts frequently is associated with a decreased risk of coronary heart disease of the order of 30-50%. The findings are very consistent in subgroup analyses and unlikely to be due to confounding. Possible mechanisms include reduction in LDL cholesterol, the antioxidant actions of vitamin E, and the effects on the endothelium and platelet function of higher levels of nitric oxide." Another study showed that "Consumption of nuts was also significantly associated with a reduced risk of [Parkinson's Disease] (for >/=5/week vs <1/month, pooled RR, 0.57; 95% CI, 0.34 to 0.95)." (Zhang SM, Hernan MA, Chen H, Spiegelman D, Willett WC, Ascherio A. Intakes of vitamins E and C, carotenoids, vitamin supplements, and PD risk. Neurology. 2002 Oct 22;59(8):1161-9. PMID: 12391343.) A study based on the Nurses' Health Study showed that eating an ounce of nuts 5 times each week reduces the risk of type II diabetes by 27% (Jiang R, Manson JE, Stampfer MJ, Liu S, Willett WC, Hu FB. Nut and Peanut Butter Consumption and Risk of Type 2 Diabetes in Women. JAMA. 2002;288:2554-2560) Another study showed that substituting MUFA for saturated fats improved LDL levels and insulin sensitivity (Vessby B, Unsitupa M, Hermansen K, Riccardi G, Rivellese AA, Tapsell LC, Nalsen C, Berglund L, Louheranta A, Rasmussen BM, Calvert GD, Maffetone A, Pedersen E, Gustafsson IB, Storlien LH; KANWU Study. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU Study. Diabetologia. 2001 Mar;44(3):312-9. PMID: 11317662).

Caveat: a single study that was large, multi-center, and case-controlled found an association between high MUFA intake and macula degeneration (Arch Ophthalmol 2001 Aug;119(8):1191-9; PMID: 11483088).

2. Omega 3 fats (EPA and DHA) *in moderation* are particularly important, as summarized in a review article (Am J Clin Nutr 2000 Jan;71(1 Suppl):171S-5S; PMID: 10617967). Fatty fish (e.g., salmon) has a large amount of omega 3 fat and is probably good (Curr Opin Lipidol 2001 Feb;12(1):11-7; PMID: 11176197). EPA and DHA have beneficial anti-inflammatory effects; in people "Clinical studies have reported that oral fish oil supplementation has beneficial effects in rheumatoid arthritis and among some patients with asthma, supporting the idea that the n-3 PUFA in fish oil are anti-inflammatory." (Calder PC. Dietary modification of inflammation with lipids. Proc Nutr Soc. 2002 Aug;61(3):345-58. Review. PMID: 12296294). It even turns out that at least in mice fish fat does not induce nearly as much weight gain or hyperglycemia as does lard, soybean oil, or safflower oil (Metabolism 1996 Dec;45(12):1539-46; PMID: 8969289). On the other hand, an older study from 1995 (N Engl J Med 1995 Apr 13;332(15):977-82; PMID: 7885425) found that protection from heart attacks by fish intake was the same with 1 or 2 servings per week as with 5 or 6 servings per week (but see below: too much may be bad!), and another found that fish eaten 1-3 times reduced the incidence of stroke by 43% (He K, Rimm EB, Merchant A, Rosner BA, Stampfer MJ, Willett WC, Ascherio A. Fish consumption and risk of stroke in men. JAMA. 2002 Dec 25;288(24):3130-6. PMID: 12495393). Omega 3 fats probably protect against many, many diseases, including dry eyes, breast cancer, etc. EPA and DHA also increase the flexibility of the arteries, reducing pulse pressure and vascular resistance (Am J Clin Nutr 2002 Aug;76(2):326-30; PMID: 12145002). Studies show that omega-3 oil helps to prevent heart attacks and probably helps prevent depression or reduce bipolar psychosis. A large, multi-center, case-controlled study (Arch Ophthalmol 2001 Aug;119(8):1191-9; PMID: 11483088) showed that fish oil reduces the rate of macula degeneration while the omega-6 fat linoleic acid raises the risk, as does MUFA! The American Heart Association (AHA) currently recommends two servings per week of fatty fish (such as salmon). Note: because these oils are polyunsaturated they are subject to very rapid oxidation both outside and inside the body, and should always be used while still quite fresh (mainly for flavor). They (i.e. canola oil and flax oil) should not be used in cooking, as heat results in both still more rapid oxidation and conversion to the trans- form.

A meta-analysis of 11 randomized, controlled human trials with over 15,000 patients (Am J Med 2002 Mar;112(4):298-304; PMID: 11893369) found that "dietary and non-dietary intake of n-3 polyunsaturated fatty acids reduces overall mortality, mortality due to myocardial infarction, and sudden death in patients with coronary heart disease." (note, omega-3 is often abbreviated as n-3 or w-3.)

In addition, the type of omega-3 oil is important (EPA, DHA, and alpha-linolenic acid (ALA) – see this description of the essential fatty acids and deficiency symptoms). EPA and DHA are long-

chain omega-3 fats from fish, which in turn get it from eating cold-water marine food. Most fresh fish in the store is farm-raised fish, and some may have less EPA and DHA if they are fed on corn or the like. A table of EPA and DHA content of various fish can be found at: http://groups.yahoo.com/group/crsociety/message/2946.

For psychological health it may be that the more EPA the better, and the more DHA the worse. If you have problems with depression, the best way of getting this ratio of omega-3 oil may be to take a supplement such as OmegaBrite (EPA to DHA ratio of 7:1), Omega-3s "700" (The Solgar Vitamin Company), Pro-Omega from the company Nordic Naturals, GNC's Fish Body Oils 1000 (30 percent concentrated omega-3 fatty acids, with an EPA to DHA ratio of 1.5:1). For other health concerns, salmon is just fine!

DHA and EPA have also been associated with reduced ADHD (hyperactivity / attention deficit disorder) in children – a real breakthrough if this randomized prospective trial is confirmed!!

On the other hand, pregnant and nursing women probably need more DHA and should consider increasing intake of certain fatty fish, especially the wild salmon such as is found in canned salmon products. These fish have high DHA levels, critical to the development of the fetus and infant's brain. A recent study showed that breast-feeding is associated with enhanced stereopsis at age 3.5 y, as is a maternal DHA-rich antenatal diet, irrespective of later infant feeding practice (**Williams C, Birch EE, Emmett PM, Northstone K; Avon Longitudinal Study of Pregnancy and Childhood Study Team.** Stereoacuity at age 3.5 y in children born full-term is associated with prenatal and postnatal dietary factors: a report from a population-based cohort study. Am J Clin Nutr. 2001 Feb;73(2):316-22. PMID: 11157330 full text).

"Maternal intake of very-long-chain n-3 PUFAs during pregnancy and lactation may be favorable for later mental development of children." **Helland IB, Smith L, Saarem K, Saugstad OD, Drevon CA.** Intakes of essential n-6 and n-3 polyunsaturated fatty acids among pregnant Canadian women. Am J Clin Nutr. 2003 Feb;77(2):473-8. PMID: 12540410

"Pregnant and nursing women should be encouraged to consume seafood on a regular basis during pregnancy and lactation to furnish DHA for their infants" **Nettleton JA.** Are n-3 fatty acids essential nutrients for fetal and infant development? J Am Diet Assoc. 1993 Jan;93(1):58-64. Review. PMID: 8417094

On the DOWN SIDE: polyunsaturated fats (PUFAs) - and especially DHA from fish - can cause increased lipid peroxidation: they are chemically prone to oxidation. A diet rich in PUFAs "induces only after two days an increase in oxidized LDL/PUFAs for a factor up to two in young people and for a factor of more than two in old individuals" (Ann N Y Acad Sci 2002 Apr;959:30-44; PMID: 11976183). Indeed, oxidation of DHA *in the mitochondrial membranes* may be a prime cause of aging itself, and the level of DHA is lower in species with long life spans. I do not know however whether mitochondrial DHA or oxidized lipid levels are related to lipid intake. Perhaps of significance, one study found that CR reduced the mitochondrial DHA level (Biochem Biophys Res Commun 1987 Jun 30;145(3):1185-91; PMID: 3606601).

ALA is from flax seed (highest concentration) and certain other plant sources such as canola. (Note: canola is derived from the rape seed plant: canola was bred to have a lower – but not absent – level of a cardiac toxin.) ALA has been shown to reduce cardiac death (J Nutr Health Aging 2001;5(3):179-83; PMID: 11458289). Flax oil has the potential problem of associated increased rates of prostate cancer in four epidemiological studies. However, flax seed per se (as opposed to flax oil) has additional benefits of lignans and fiber that may make using *freshly* ground flax seed helpful overall in a healthy diet, particularly for women. In addition the studies showing problems were not controlled for proper use of the flax. Neither flax nor canola oil should be used for frying (use olive oil (best), or butter), nor should flax oil or anything other than freshly ground forms be used. Otherwise the risks may be increased due to oxidation of the oil. In addition, a study showed that the benefit of the Mediterranean Diet (rich in olive oil and fish) is at least in part from monounsaturated fatty acids (MUFA) or ALA. So getting the shorter chain omega-3 fats from vegetable sources probably does help, and the longer chain omega-3 fats from fish help even more.

The NIH has a table of omega-3 vs. omega-6 fatty acids, listed as short or long, 6 or 3 (slightly modified below).

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Omega6 Fatty Acids
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Linoleic Acid (LA)  ................ C18:2;9,12
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Gamma Linolenic Acid (GLA) ..... C18:3;6,9,12
Dihomogamma linolenic Acid (DGLA).... C20:3n6
Arachidonic Acid (AA) ............... C20:4n6

Omega 3 Fatty Acids
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Alpha Linolenic Acid (ALA), (LNA) ... C18:3;9,12,15
Eicosapentaenoic Acid(EPA) ..... C20:5n3
Docosahexaenoic Acid (DHA) ..... C22:6n3
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HOW MUCH FAT TO EAT

Epidemiological studies show that the countries that have the highest fat diet, such as the USA, UK and Canada, have the highest incidence of Alzheimer's disease, while the countries with the lowest intake of fat (i.e., Japan, Nigeria and China) have the lowest incidence. This correlation of Alzheimer's disease with high fat intake was recently confirmed in a controlled study of patients genetically predisposed to Alzheimer's, where low fat intake reduced the incidence by 50%! (Archives of Neurology, 2002-08). In addition there are numerous studies indicating lower risks of coronary artery disease with lower intake of certain fats - particularly animal fat, dairy fat, hydrogenated vegetable fats, tropical oils and egg yolks (Am J Clin Nutr 2002 Feb;75(2):191-212; PMID: 11815309); other studies show other positive effects of low fat intake (Clin Immunol Immunopathol 1990 Jan;54(1):103-16; PMID: 2293903). Still other studies find a higher rate of cancers (including prostate Cancer Epidemiol Biomarkers Prev 2002 Aug;11(8):719-25; PMID: 12163324) is associated with high-fat diets, even "good" MUFA fats. Of note is that this relationship is correlated with average body weight or calorie intake, and if that were taken into account, fat intake might drop out as a risk factor.

On the other hand, the amount of *good* fat in your diet should perhaps be about 20 to 40% of your total calories. In favor of the upper limit is that fat is more efficiently metabolized than carbohydrate, and metabolism of certain fats may produce fewer free radicals than that of carbohydrates. It is also much easier to maintain a moderate-fat diet: people on a low-fat diet tend to quit. In addition, low-fat diets are strongly correlated with an increased rate of ischemic strokes (Proc Nutr Soc 2002 May;61(2):287-98; PMID: 12133212,). My guess is that it is best to have a "normal" (about 35% of calories) intake of fat, but keep the total down by caloric restriction (again this comes up!)

A recent comprehensive review of diet and heart disease stated that "Compelling evidence from metabolic studies, prospective cohort studies, and clinical trials in the past several decades indicates that at least 3 dietary strategies are effective in preventing CHD: substitute nonhydrogenated unsaturated fats for saturated and trans-fats; increase consumption of omega-3 fatty acids from fish, fish oil supplements, or plant sources; and consume a diet high in fruits, vegetables, nuts, and whole grains and low in refined grain products. However, simply lowering the percentage of energy from total fat in the diet is unlikely to improve lipid profile or reduce CHD incidence. Many issues remain unsettled, including the optimal amounts of monounsaturated and polyunsaturated fats, the optimal balance between omega-3 and omega-6 polyunsaturated fats, the amount and sources of protein, and the effects of individual phytochemicals, antioxidant vitamins, and minerals." (Hu FB, Willett WC. Optimal Diets for Prevention of Coronary Heart Disease. JAMA 2002;288:2569-2578).

Of interest, the Mediterranean diet found that the following six foods led to reduction in risk of heart attacks, with the odds ratio given last (Eur J Nutr 41 (2002) 4, 153-160; PMID: 12242583). They also noted that "our results support the exclusion of refined cereals with a high glycaemic load as healthy elements of this pattern."

Food	gm/day	Odds ratio
Olive oil	10-18	0.34
Fiber	18-26	0.25
Fruit	365-570	0.32
Vegetables	482-583	0.36
Fish	77-106	0.28
Alcohol	0-7	0.49

Contraindications to fat modification: None that I know of.

Potential problems: Too much fish (of many types) is not good for children or potentially pregnant women because of tiny amounts of mercury in fish. See this FDA document (http://www.cfsan.fda.gov/~frf/sea-mehg.html) for a list of mercury levels, or possibly this EPA fish consumption advisory summary. Avoid bottom-dwelling fish, fresh-water fish, bluefin tuna (albacore too), mackerel, shark and tilefish (a.k.a. golden snapper): these large fish that live long enough to accumulate quantities of mercury and are thus potentially dangerous if you eat them frequently. Also avoid tuna steaks (canned tuna is better but not perfect). The Environmental Working Group says there are some fish considered safe for pregnant women, including farm-raised trout and catfish, shrimp, fish sticks, flounder (summer), wild pacific salmon, croaker, mid-Atlantic blue crab and haddock. Indeed, salmon and shrimp have almost no detectable mercury and are probably quite safe.

Reduce intake of highly processed and junk foods, such as boxed cookies, pudding mixes and fast food from places like McDonalds and Burger King, etc. These tend to have high quantities of partially hydrogenated oils, charred meat, and aluminum (an anti-caking agent that may be associated with neurological problems; however, aluminum is also found everywhere else including soil, cooking pots, antiperspirants, and municipal drinking water)

Category	Effect	Finding	Ref	Fig
Fats		This web site is an OUTSTANDING scientific summary of the various types of fats, their sources, what fats are found in various foods, why trans fats (partially hydrogenated oils) are bad, etc. http://www.scientificpsychic.com/fitness/fattyacids.html	96	
	Use MUFA fats and avoid saturated and trans-fats	A meta-analysis of 60 controlled trials showed that the ratio of HDL to total cholesterol was influenced by the type of fat eaten. "Lauric acid [coconut oil] greatly increased total cholesterol, but much of its effect was on HDL cholesterol. Consequently, oils rich in lauric acid decreased the ratio of total to HDL cholesterol. " "… risk is reduced most effectively when trans fatty acids and saturated fatty acids are replaced with cis unsaturated fatty acids."	97	
	Parkinson disease	"Estimating the association between PD [Parkinson disease] and risk of being in the highest versus the lowest intake quartile, there were **elevated odds ratios for total fat** (OR 1.94, 95% confidence interval [CI] : 1.05-3.58), **cholesterol** (OR 2.11, 95% CI: 1.14-3.90), **lutein** (OR 2.52, 95% CI: 1.32-4.84) and **iron** (OR 1.88, 95% CI: 1.05-3.38)." This study is from Detroit: most of the fat and cholesterol is from animal fat. The lutein (from broccoli and kale) correlation is somewhat worrisome.	98	
Saturated fat	Associated with reduced bone density	"These data indicate that [bone mineral density] is negatively associated with saturated fat intake, and that men may be particularly vulnerable to these effects."	99	
	Increases LDL cholesterol, worsens insulin resistance, increases cancer, may cause brain function problems	This site is a MSNBC nutrition article; basically a readable summary that emphasizes that saturated fat is bad for health.	100	
	Raises cholesterol	"**Regression analysis of the combined published data** on the effects of dietary fatty acids and cholesterol on serum cholesterol and lipoprotein cholesterol evaluated with groups of human subjects shows that 1) saturated fatty acids increase and are the primary determinants of serum cholesterol, 2) polyunsaturated fatty acids actively lower serum cholesterol, 3) monounsaturated fatty acids have no independent effect on serum cholesterol and, 4) dietary cholesterol increases serum cholesterol"	101	
Saturated and trans-fats	Alzheimer disease increased	Trans fats increase risk: "Risk … increased with consumption of trans-unsaturated fats" (relative risk = 2.4) Saturated fats increase risk (relative risk = 2.2)	102	
	Increase coronary heart disease	From the Nurses' Health Study. "We prospectively studied 80,082 women who were 34 to 59 years of age and had no known coronary disease, stroke, cancer, hypercholesterolemia, or diabetes in 1980.	103	

		Information on diet was obtained at base line and updated during follow-up by means of validated questionnaires. During 14 years of follow-up, we documented 939 cases of nonfatal myocardial infarction or death from coronary heart disease. Mutivariate analyses included age, smoking status, total energy intake, dietary cholesterol intake, percentages of energy obtained from protein and specific types of fat, and other risk factors. RESULTS: Each increase of 5 percent of energy intake from **saturated fat**, as compared with equivalent energy intake from carbohydrates, was associated with a 17 percent increase in the risk of coronary disease (**relative risk, 1.17**; 95 percent confidence interval, 0.97 to 1.41; P=0.10). As compared with equivalent energy from carbohydrates, **the relative risk for a 2 percent increment in energy intake from trans unsaturated fat was 1.93** (95 percent confidence interval, 1.43 to 2.61; P<0.001); that for a 5 percent increment in energy from monounsaturated fat was 0.81 (95 percent confidence interval, 0.65 to 1.00; P=0.05); and that for a 5 percent increment in energy from polyunsaturated fat was 0.62 (95 percent confidence interval, 0.46 to 0.85; P= 0.003). Total fat intake was not signficantly related to the risk of coronary disease (for a 5 percent increase in energy from fat, the relative risk was 1.02; 95 percent confidence interval, 0.97 to 1.07; P=0.55). **We estimated that the replacement of 5 percent of energy from saturated fat with energy from unsaturated fats would reduce risk by 42 percent** (95 percent confidence interval, 23 to 56; P<0.001) and that the replacement of 2 percent of energy from trans fat with energy from unhydrogenated, unsaturated fats would reduce risk by 53 percent (95 percent confidence interval, 34 to 67; P<.001). CONCLUSIONS: Our findings suggest that replacing saturated and trans unsaturated fats with unhydrogenated monounsaturated and polyunsaturated fats is more effective in preventing coronary heart disease in women than reducing overall fat intake."		
Animal fat	Parkinson disease greatly increased	"…**increasing intake of animal fats were strongly related to PD [Parkinson disease] (odds ratio, 5.3**; 95% confidence interval, 1.8-15.5; p for trend = 0.001)."	104	
	Saturated fats reduce insulin sensitivity	SFA (saturated fats) may thus be a cause of diabetes. "The plasma insulin response was significantly higher following the SFA meal than the other meals after both breakfast and lunch (P<0.006) although there was no effect of breakfast fatty acid composition on plasma glucose concentrations. Postprandial insulin sensitivity (SI(Oral)) was assessed for 180 min after each meal. SI(Oral) was significantly lower after lunch than after breakfast for all four test meals (P=0.019) following the same rank order (SFA < n-6 PUFA < n-3 PUFA < MUFA) for each meal. The present study demonstrates that a single meal rich in SFA reduces postprandial insulin sensitivity with 'carry-over' effects for the next meal."	105	
Trans fat	Are 2.5 to 10 times worse for you than saturated fat!	"**Compared to saturated fat, TFAs [trans fatty acids] are, gram to gram, associated with a considerably (2.5- to >10-fold) higher risk increment for IHD**." (IHD = Ischemic Heart Disease). "Danish government has decided that oils and fats containing more than 2% industrially produced TFAs will not be sold in Denmark after the January 1, 2004."	106	
	Trans fat sources	Margarine, frosting, crackers, biscuits, cookies, cakes and other baked goods all are bad sources. Approximately 21-36% of their fat is trans fat (from USDA analysis). Of course, margarine is the most concentrated form. If you use olive oil to bake something at home, this is not a problem. Note: about 5% of fat from cows (in beef, milk, and butter) are trans fats! This is based on USDA data. Thus, cow fat has about 1/5 of the trans fat that margarine does. Even so, this trans fat accounts for a large fraction of the heart risks from butterfat.		

	Increases asthma	A German survey found that "Frequent intake of margarine of any kind was positively associated with current asthma during the past 12 months in young adults aged 18 to 29 years (aOR, 2.33; 95% CI, 1.03-5.26). In subgroup analysis, the positive association was confined to frequent intake of low-fat margarine (4.51; 1.78-11.43) or the combination of low-fat margarine and low-fat butter (4.79; 1.84-12.44). Consumption of margarine of any kind was not related to hay fever, atopic dermatitis, and atopic sensitization to inhalant allergens." I do not know what "low-fat margarine" is in the German context.	107	
	Bad fats: Trans and saturated Fat should be 30-35% of energy intake	"there is a general consensus concerning the need to decrease the intake of trans and saturated fatty acids with regard to the risk of CHD" "A modest reduction in fat intake to 30-35% energy, with the bulk of carbohydrates being derived from complex carbohydrates from unrefined sources, would appear to be the best option for the prevention of obesity and cardiovascular disease."	108	
	Good fats: n-3, monounsaturated, CLA n-6 is bad fats	Review: "The cardioprotective effects of the long chain n-3 PUFAs found in oily fish and fish oil [3] have been confirmed by recent studies." "A recent study reported that the n-6 PUFA arachidonic acid can induce the production of damaging proinflammatory cytokines"	109	
Monounsaturated fats (MUFA)	High-MUFA diet helps lipid profiles in diabetics	"…17% to 20% [of calories from] monounsaturated fat… [resulted in] lower plasma total triglycerides by 18% (P=.027), lower very low-density lipoprotein triglycerides by 26% (P=.043), lower very low-density lipoprotein cholesterol by 48% (P=.043), higher apolipoprotein A1 by 7% (P=.018), smaller low-density lipoprotein particle size by 1% (P=.043), and longer low-density lipoprotein oxidation lag time by 25% (P=.043) were found after the high-monounsaturated-fat diet."	110	
	Reduces LDL cholesterol	"Plasma cholesterol concentrations decreased in a dose-dependent manner with increasing intakes of dietary MUFAs. This change was entirely accounted for by reduced LDL cholesterol"	111	
	Reduces clotting from two pathways	"In conclusion, a high-MUFA diet sustains potentially beneficial effects on platelet aggregation and postprandial activation of factor VII."	112	
	Reduces lipid oxidation	Rats given olive oil (MUFA) had less lipid oxidation than those given sunflower seed oil (n-6 polyunsaturated). "In conclusion, the type of dietary fat should be considered in studies on aging, since oxidative stress is directly modulated by this factor."	113	
	Reduced triglyceride (TG)	Calories from MUFA are better for you than calories from carbohydrate: "The MUFA-rich diet showed better effects on serum TG than the [carbohydrate]-rich diet, even with energy restriction and weight loss."	114	
	Reduced arteriosclerosis risk	A review states that "many observational epidemiological studies suggest that a high intake of monounsaturated fat is associated with reduced coronary risk"	115	
	Olive oil	"Olive oil supplementation alone improved the lipid profile but was more effective when coupled with dietary restriction. There was a synergistic beneficial action of dietary restriction and olive oil on serum lipids and myocardial antioxidant defences."	116	
	Reduced mortality rate	"After a median follow-up of 8.5 years, we investigated the possible role of MUFA, PUFA, and other selected food groups in protecting against all-causes mortality in a population-based, prospective study, conducted in one of the eight centers of the Italian Longitudinal Study on Aging (ILSA), Casamassima, Bari, Italy. Out of 704 elderly subjects (65-84 years), 278 nondemented persons agreed to participate at the first survey (1992-1993). During the follow-up, there were 91 deaths. A semi-quantitative food frequency questionnaire evaluating macronutrient daily intakes were performed at the first survey. Higher MUFA intake was associated with an increase of survival (hazard ratio 0.81, 95% CI 0.66-0.99),"	117	

	Reduced Parkinson Disease	"In the Rotterdam Study, a prospective population-based cohort study of people ages > or =55, the association between intake of unsaturated fatty acids and the risk of incident PD was evaluated among 5,289 subjects who were free of dementia and parkinsonism and underwent complete dietary assessment at baseline...After a mean follow-up of 6.0 years, 51 participants with incident PD were identified. Intakes of total fat, monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs) were significantly associated with a lower risk of PD, with an adjusted hazard ratio per SD increase of energy-adjusted intake of 0.69 (95% CI 0.52 to 0.91) for total fat, of 0.68 (95% CI 0.50 to 0.94) for MUFAs, and 0.66 (95% CI 0.46 to 0.96) for PUFAs. No associations were found for dietary saturated fat, cholesterol, or trans-fat. CONCLUSION: These findings suggest that high intake of unsaturated fatty acids might protect against Parkinson disease."	[118]	
	Reduced blood pressure	"Randomized, 3-period, crossover feeding study … Participants were 164 adults with prehypertension or stage 1 hypertension. Each feeding period lasted 6 weeks and body weight was kept constant. INTERVENTIONS: A diet rich in carbohydrates; a diet rich in protein, about half from plant sources; and a diet rich in unsaturated fat, predominantly monounsaturated fat. MAIN OUTCOME MEASURES: Systolic blood pressure and low-density lipoprotein cholesterol. RESULTS: Blood pressure, low-density lipoprotein cholesterol, and estimated coronary heart disease risk were lower on each diet compared with baseline. Compared with the carbohydrate diet, the **protein diet further decreased mean systolic blood pressure by 1.4 mm Hg** (P = .002) and by 3.5 mm Hg (P = .006) among those with hypertension **and decreased low-density lipoprotein cholesterol by 3.3 mg/dL** (0.09 mmol/L; P = .01), high-density lipoprotein cholesterol by 1.3 mg/dL (0.03 mmol/L; P = .02), and triglycerides by 15.7 mg/dL (0.18 mmol/L; P<.001). Compared with the carbohydrate diet, the **unsaturated fat diet decreased systolic blood pressure by 1.3 mm** Hg (P = .005) and by 2.9 mm Hg among those with hypertension (P = .02), had no significant effect on low-density lipoprotein cholesterol, **increased high-density lipoprotein cholesterol by 1.1 mg/dL** (0.03 mmol/L; P = .03), and lowered triglycerides by 9.6 mg/dL (0.11 mmol/L; P = .02). **Compared with the carbohydrate diet, estimated 10-year coronary heart disease risk was lower and similar on the protein and unsaturated fat diets.**"	[291][259]	
ɣ-linolenic acid (GLA) from borage oil	Reduces atopic dermatitis	"In a double-blind, randomized, placebo-controlled trial… Early supplementation with GLA in children at high familial risk does not prevent the expression of atopy as reflected by total serum IgE, but it tends to alleviate the severity of atopic dermatitis in later infancy in these children." Note: GLA is also found in pecans and walnuts.	[119]	
Lecithin	Mitochondria damage (aging)	Lecithin (in the form of phosphatidyl choline) may reduce mitochondrial DNA damage: if so, this one fact alone may be of great importance in reducing the rate of aging. HOWEVER, this is not easily obtained in the form and dosage used in the rodent experiments.	[120]	
	Low insulin => low mitochondria ROS	In a rat experiment, CR => lower mitochondrial reactive oxygen species (mtROS); insulin reversed this. It MAY be that by keeping insulin low (CR, low glycemic index, small meals etc.) we can mimic or enhance the effects of CR	[121]	
Omega 3		Omega 3 fats are associated with lower mortality in a very large meta-analysis "a systematic search of randomized controlled trials"; omega 3 fats out-performed statins! "Compared with control groups, risk ratios for overall mortality were 0.87 for statins (95% confidence interval [CI], 0.81-0.94), 1.00 for fibrates (95% CI, 0.91-1.11), 0.84 for resins (95% CI, 0.66-1.08), 0.96 for niacin (95% CI, 0.86-1.08), 0.77 for n-3 fatty acids (95% CI, 0.63-0.94),	[122]	

		and 0.97 for diet (95% CI, 0.91-1.04)…CONCLUSIONS: Statins and n-3 fatty acids are the most favorable lipid-lowering interventions with reduced risks of overall and cardiac mortality."		
Omega 3: ALA (short-chain) (?)		"Dietary polyunsaturated and more specifically linoleic fatty acid intake may have a substantial cardioprotective benefit that is also reflected in overall mortality. Dietary fat quality seems more important than fat quantity in the reduction of cardiovascular mortality in men."	123	
Omega 3: DHA and EPA (long-chain)	DHA / fish oil may be harmful to lifespan, in theory	This CR society e-mail summary by Michael Rae (AOR, Canada) explains how DHA / fish oil may theoretically be harmful for life span of very long life expectancy people, even if it is helpful for cardiac disease in obese people. "Michael Rae's Fish oil Accelerated Aging" (MiRFAA) hypothesis is based on the mitochondrial free-radical theory of aging (MiFRA). I think this might apply most to those who have a very long life expectancy because of CR since youth combined with good nutrition and habits. To quote Michael Rae from a CR Society post of 2004-05-11: "1. Across species, double bond content in the mitochondrial (mt) inner membrane (MIM) - and especially DHA content - is inversely correlated with max LS. 2. Within a species, double bond content in MIM increases with aging. 3. CR, the only anti-aging therapy per se (only therapy which extends max LS, maintains molecular fidelity, extends physiological functioning, etc) in mammals, retards this increase, apparently by lowering delta-5 desaturase activity & perhaps by modulatings phospholipids acyltransferase activity. 4. Feeding all animals yet tested longer-chain PUFA, such as DHA, increases DHA content in MIM. 5. This increase in MIM DHA increases the actual peroxidation of the MIM. Inductive conclusion, from the above & a few other tidbits: eating DHA will lead to more DHA in MIM; more DHA in MIM is in direct opposition to a known effect of CR, and correlates with aging within and across species." His advice to those who practice CR: "So: don't eat DHA. Avoid fatty fish, and don't take fish oil supplements."	124	
	Fish oil supplements do NOT have PCBs or mercury, two toxins present in fish meat	"In a previous study we showed that the amount of mercury in 5 over-the-counter brands of fish oil was negligible. …The levels of polychlorinated biphenyls and organochlorines were all below the detectable limit. CONCLUSIONS: Fish oil supplements are more healthful than the consumption of fish high in organochlorines. Fish oils provide the benefits of omega-3 fatty acids without the risk of toxicity. In addition, fish oil supplements have been helpful in a variety of diseases, including bipolar disorder and depression."	125	
	Fish consumption is associated with less hostility in young adulthood!	From an Oakland, California study: "…a sample of 3581 urban white and black young adults… Consumption of any fish rich in n-3 fatty acids, compared to no consumption, was also independently associated with lower odds of high hostility (OR=0.82; 95% CI=0.69-0.97; P=0.02). These results suggest that high dietary intake of DHA and consumption of fish rich in n-3 fatty acids may be related to lower likelihood of high hostility in young adulthood."	126	
	EPA may help treat depression and schizophrenia	"…we investigated whether membrane concentrations of these fatty acids might vary as a function of schizotypal traits in non-psychotic individuals… Our findings … are quite consistent with evidence that omega-3 fatty acids (notably EPA) can be useful in the treatment of schizophrenic illness." "Four out of five placebo-controlled double- blind trials of eicosapentaenoic acid (EPA) in the treatment of schizophrenia have given positive findings. In depression, two placebo-controlled trials have shown a strong therapeutic effect of ethyl-EPA added to	127	

		existing medication."		
	Improves cardiovascular risk factors and disease	The AHRQ (Agency for Healthcare Research and Quality, http://www.ahrq.gov/clinic/epcindex.htm#dietsup) review of very many of the largest randomized clinical trials found that: 1. Triglycerides: there is strong evidence that fish oils have a strong beneficial effect on (10-30%) that is dose-dependent 2. Blood pressure: a very small beneficial effect (2 mm Hg) 3. Cardiovascular mortality: there is evidence to support the hypothesis that fish, fish oil, or ALA supplement consumption reduces all-cause mortality and various CVD outcomes, although the evidence is strongest for fish or fish oil. It does NOT help with cholesterol, HDL cholesterol, LDL cholesterol, fasting blood sugar, or glycosylated hemoglobin or insulin.		
		"A meta-analysis of cohort studies was conducted to examine the association between fish intake and CHD mortality…A database was developed on the basis of 11 eligible studies and 13 cohorts, including 222 364 individuals with an average 11.8 years of follow-up… **Each 20-g/d increase in fish intake was related to a 7% lower risk of CHD mortality** (P for trend=0.03)."	128	
	Fish decreases the risk of stroke	A meta-analysis of 9 cohort studies found that "intake of fish is inversely related to risk of stroke, particularly ischemic stroke." "Compared with those who never consumed fish or ate fish less than once per month, the pooled [relative risks] for total stroke were 0.91 … for individuals with fish intake 1 to 3 times per month, 0.87 … for once per week, 0.82 … for 2 to 4 times per week, and 0.69 … for > or =5 times per week (P for trend=0.06)."	129	
		Do not eat fried fish or fish sandwiches. "In multivariate analyses, tuna/other fish consumption was inversely associated with total stroke (P = .04) and ischemic stroke (P = .02), with 27% lower risk of ischemic stroke with an intake of 1 to 4 times per week (hazard ratio [HR], 0.73; 95% confidence interval [CI], 0.55-0.98) and 30% lower risk with intake of 5 or more times per week (HR, 0.70; 95% CI, 0.50-0.99) compared with an intake of less than once per month. In contrast, fried fish/fish sandwich consumption was positively associated with total stroke (P = .006) and ischemic stroke (P = .003), with a 44% higher risk of ischemic stroke with consumption of more than once per week (HR, 1.44; 95% CI, 1.12-1.85) compared with consumption of less than once per month… Among elderly individuals, consumption of tuna or other broiled or baked fish is associated with lower risk of ischemic stroke, while intake of fried fish or fish sandwiches is associated with higher risk."	130	
	Fish consumption lowers heart disease (CHD) rate	Fish consumption lowers many risk factors for heart disease (HTN, cholesterol etc.) After controlling for BMI, smoking etc, a lower heart rate remains statistically significant.	131	
		The AHA Scientific Statement of 2003 is available as full free text and is well-worth reading. It gives a readable summary of very good evidence, with recommendations: "…0.3 to 0.5 g/d of EPA+DHA [from fish] and 0.8 to 1.1 g/d of α-linolenic acid [e.g., from flax]. Recently, the Food and Nutrition Board, Institute of Medicine, and The National Academies, in collaboration with Health Canada, released the Dietary Reference Intakes for Energy and Macronutrients.[107] The Acceptable Macronutrient Distribution Range (AMDR) for α-linolenic acid is estimated to be 0.6% to 1.2% of energy, or 1.3 to 2.7 g/d on the basis of a 2000-calorie diet. This is ≈10 times the current intake of EPA+DHA" "Patients with CHD should be encouraged to increase their	132	

		consumption of EPA and DHA to ≈1 g/d"		
	Fish decreases dementia	There is some evidence that eating fish can reduce the incidence of dementia (Alzheimer's disease and the like). One medium-term (approximately 5 yr. follow-up) study of >1000 French people found "a significant trend between increasing consumption of fish or seafood and decreasing incidence of dementia (P for trend = 0.0091)"	133	
	Reduces risk of prostate cancer	A prospective population study of 47,866 men for 14 yr. found that "The multivariate [relative risks] of total and advanced prostate cancer from comparisons of extreme quintiles of the combination of EPA and DHA were 0.89 (0.77, 1.04) and 0.74 (0.49, 1.08), respectively."	134	
		Eating fish per se (better than fish oil) may reduce prostate cancer incidence. "We followed 47882 men participating in the Health Professionals Follow-up Study… Eating fish more than three times per week was associated with a reduced risk of prostate cancer, and the strongest association was for metastatic cancer (multivariate relative risk, 0.56; 95% confidence interval, 0.37-0.86, compared with infrequent consumption, i.e., less than twice per month)."	135	
	Associated with better intelligence in old age	"This was an observational study of subjects born in 1936 whose mental ability was tested in 1947 and who were followed up in 2000–2001, at which time cognition, diet, food supplement use, and risk factors for vascular disease were assessed… Total erythrocyte n–3 fatty acids and the ratio of docosahexaenoic acid to arachidonic acid was associated with better cognitive function in late life before and after adjustment for childhood IQ."	136	
	Fish reduces risk of macula degeneration	"The US Twin Study of Age-Related Macular Degeneration comprises elderly male twins from the National Academy of Sciences-National Research Council World War II Veteran Twin Registry. To determine genetic and environmental risk factors for AMD, twins were surveyed for a prior diagnosis of AMD and underwent an eye examination, fundus photography, and food frequency and risk factor questionnaires. This environmental component of the study includes 681 twins: 222 twins with AMD (intermediate or late stages) and 459 twins with no maculopathy or early signs. Risk for AMD according to cigarette smoking and dietary fat intake was estimated using logistic regression analyses… **dietary omega-3 fatty intake was inversely associated with AMD (odds ratio, 0.55**; 95% confidence interval, 0.32-0.95) comparing the highest vs lowest quartile. **Reduction in risk of AMD with higher intake of omega-3 fatty acids was seen primarily among subjects with low levels (below median) of linoleic acid intake**, an omega-6 fatty acid (P trend<.001). **The attributable risk percentage was 32% for smoking and the preventive fraction was 22% for higher omega-3 intake**."	137	

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Mediterranean diet

In essence, a diet rich in olive oil, fish, vegetables, fiber, fruit, and red wine is healthy.

	Sticking with the diet significantly reduces risk of heart disease, death and cancer.	"…a population-based, prospective investigation involving 22,043 adults in Greece who completed an extensive, validated, food-frequency questionnaire at base line. Adherence to the traditional Mediterranean diet was assessed by a 10-point Mediterranean-diet scale that incorporated the salient characteristics of this diet… A higher degree of adherence to the Mediterranean diet was associated with a reduction in total mortality (adjusted hazard ratio for death associated with a two-point increment in the Mediterranean-diet score, 0.75 …). An inverse association with greater adherence to this diet was evident for both death due to coronary heart disease (adjusted hazard ratio, 0.67 …) and death due to cancer (adjusted hazard ratio, 0.76 …)…Greater adherence to the traditional	138	

		Mediterranean diet is associated with a significant reduction in total mortality."		
	Lessens rates of all-cause mortality, coronary heart disease, cardiovascular diseases, and cancer	"Healthy Ageing: a Longitudinal study in Europe (HALE) population, comprising individuals enrolled in the Survey in Europe on Nutrition and the Elderly: a Concerned Action (SENECA) and the Finland, Italy, the Netherlands, Elderly (FINE) studies, includes 1507 apparently healthy men and 832 women, aged 70 to 90 years in 11 European countries. This cohort study was conducted between 1988 and 2000. MAIN OUTCOME MEASURES: Ten-year mortality from all causes, coronary heart disease, cardiovascular diseases, and cancer. RESULTS: During follow-up, 935 participants died: 371 from cardiovascular diseases, 233 from cancer, and 145 from other causes; for 186, the cause of death was unknown. Adhering to a Mediterranean diet (hazard ratio [HR], 0.77; 95% confidence interval [CI], 0.68-0.88), moderate alcohol use (HR, 0.78; 95% CI, 0.67-0.91), physical activity (HR, 0.63; 95% CI, 0.55-0.72), and nonsmoking (HR, 0.65; 95% CI, 0.57-0.75) were associated with a lower risk of all-cause mortality (HRs controlled for age, sex, years of education, body mass index, study, and other factors). Similar results were observed for mortality from coronary heart disease, cardiovascular diseases, and cancer. The combination of 4 low risk factors lowered the all-cause mortality rate to 0.35 (95% CI, 0.28-0.44)."	139	
	Lessens risk of Alzheimer Disease	"There is converging evidence that composite dietary patterns such as the Mediterranean diet (MeDi) is related to lower risk for cardiovascular disease, several forms of cancer, and overall mortality…METHODS: A total of 2,258 community-based nondemented individuals in New York were prospectively evaluated every 1.5 years. Adherence to the MeDi (zero- to nine-point scale with higher scores indicating higher adherence) was the main predictor in models that were adjusted for cohort, age, sex, ethnicity, education, apolipoprotein E genotype, caloric intake, smoking, medical comorbidity index, and body mass index. RESULTS: There were 262 incident AD cases during the course of 4 (+/-3.0; range, 0.2-13.9) years of follow-up…**Compared with subjects in the lowest MeDi tertile, subjects in the middle MeDi tertile had a hazard ratio of 0.85 (95% confidence interval, 0.63-1.16) and those at the highest tertile had a hazard ratio of 0.60** (95% confidence interval, 0.42-0.87) for AD (p for trend = 0.007). INTERPRETATION: We conclude that higher adherence to the MeDi is associated with a reduction in risk for AD."	140	

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Homocysteine

2. Reduce the homocysteine level in your blood by taking about 1 mg (1000 mcg) of folate (folic acid) each day. No, your nor al diet does NOT have enough folate, even if you eat vegetables and fruit. The Recommended Daily Allowance (RDA) is 400 mcg and is too little. Common multivitamins have 400 mcg of folate. Folate works in coordination with vitamins B6 and B12 to reduce the homocysteine level in your blood. In fact, folate should be taken with B12 to prevent nerve damage if you happen to have B12 deficiency (rare in youth). Folate definitely does the following:
    a. Reduces the risk for heart attack and other blood vessel disease.
    b. Greatly reduces the risk for spina bifida if taken during early pregnancy.

In addition, folate probably also reduces your risk for strokes, certain cancers (colon and breast), (along with B6 and B12: JAMA 2002-08-29) recurrence of clogged arteries after an angioplasty, and depression.

Perhaps the best way to reduce homocysteine is caloric restriction. In one epidemiologic study "Plasma [homocysteine] level correlated positively with age, body mass index, and waist-to-hip ratio ($P < 0.0001$)." (Chan SJ, Chang CN, Hsu JC, Lee YS, Shen CH. Homocysteine, vitamin B(6), and lipid in cardiovascular disease. Nutrition. 2002 Jul-Aug;18(7-

8):595-8. PMID: 12093437).

Coffee, especially when prepared in the European fashion (very thick and muddy), may increase homocysteine levels (Urgert R, van Vliet T, Zock PL, Katan MB. Heavy coffee consumption and plasma homocysteine: a randomized controlled trial in healthy volunteers. Am J Clin Nutr. 2000 Nov;72(5):1107-10. PMID: 11063436). Although regular coffee increases homocysteine levels ("The increase in homocysteine concentrations 4 h after consumption of 0.45 L coffee relative to consumption of 3 placebo capsules was 19% ($P = 0.0001$)." **Verhoef P, Pasman WJ, van Vliet T, Urgert R, Katan MB. Contribution of caffeine to the homocysteine-raising effect of coffee: a randomized controlled trial in humans. American Journal of Clinical Nutrition, Vol. 76, No. 6, 1244-1248, December 2002**), only decaffeinated coffee has been shown to be associated with a higher rate of heart attack (increased by 25% when compared to non-drinkers; Sesso HD, Gaziano JM, Buring JE, Hennekens CH. Coffee and tea intake and the risk of myocardial infarction. Am J Epidemiol. 1999 Jan 15;149(2):162-7. PMID: 9921961).

Of interest, the best form of vitamin B6 (pyridoxine) may be pyridoxamine. Pyridoxamine directly helps to prevent oxidation of lipids that should also reduce the rate of cardiovascular disease.

Category	Effect	Finding	Ref	Fig
Homocysteine	Associated with lower mental function in the elderly	"Elevated plasma tHcy has an independent, graded association with concurrent cognitive impairment as measured with the MMSE [Mini-Mental State Examination] in healthy elderly community dwellers."	141	
		"Participants were from the Veterans Affairs Normative Aging Study. Cognitive function was assessed with the Mini-Mental State Examination and on the basis of measures of memory, verbal fluency, and constructional praxis, which were adapted from the revised Wechsler Adult Intelligence Scale and the Consortium to Establish a Registry for Alzheimer's Disease batteries at 2 time points. At baseline, dietary intakes were assessed with a food-frequency questionnaire, and blood was drawn for the measurement of B vitamins and homocysteine. Results: **Over a mean 3-y follow-up, declines in constructional praxis, measured by spatial copying, were significantly associated with plasma homocysteine, folate, and vitamins B-6 and B-12 and with the dietary intake of each vitamin**. Folate (plasma and dietary) remained independently protective against a decline in spatial copying score after adjustment for other vitamins and for plasma homocysteine. **Dietary folate was also protective against a decline in verbal fluency**. A high homocysteine concentration was associated with a decline in recall memory. Conclusions: **Low B vitamin and high homocysteine concentrations predict cognitive decline.** Spatial copying measures appear to be most sensitive to these effects in a general population of aging men."	142	
	Associated findings	More evidence that folate and B-12 may help: "The unadjusted mean tHcy was 21.5% (approximately 1.9 micro mol/L) higher in men than in women, 11.8% (approximately 1.1 micro mol/L) higher in non-Hispanic whites than in Mexican Americans, 42% (approximately 3.7 micro mol/L) higher in persons aged >/= 70 y than in persons aged < 30 y, and 10.9% (approximately 1.0 micro mol/L) higher in supplement nonusers than in supplement users. The tHcy concentration was negatively associated with serum folate ($P < 0.0001$ for trend), RBC folate ($P < 0.0001$ for trend), and serum vitamin B-12 ($P < 0.0036$ for trend).."	143	
	Associated quite high rates of death from heart disease	A 24-year study of 1368 middle-age women showed that elevated homocysteine levels (tHcy) were associated with much higher rates of heart attack (AMI) and death from heart attack. "For the fifth tHcy quintile, relative risk was 1.86 (95% CI 1.06 to 3.26) for AMI and 5.14 (95% CI 2.22 to 11.92) for death due to AMI."	144	
	Associated with depression	"Those in the upper tertile for serum tHcy had a more than twofold (odds ratio: 2.30; 95% CI: 1.35, 3.90; $P = 0.002$) higher risk of being depressed than did those in the lowest tertile for serum tHcy. The results remained significant after adjustment for the month of study, history of ischemic heart disease, smoking habits, alcohol consumption, marital status, education, and socioeconomic status in adulthood (**odds ratio: 2.23**; 95% CI: 1.30, 3.83; $P = 0.004$)."	145	

	Reduced by folate supplements	"From the dose-response curve, the adequate daily dose of folic acid was estimated to be 392 micro g [mcg], which decreased plasma homocysteine concentrations 22%." (note: standard folate pills and vitamins are at 400 mcg)	146	

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Cholesterol and triglycerides

Category	Effect	Finding	Ref	Fig
HDL cholesterol level	Brain function Longevity	"Plasma HDL levels correlated significantly with MMSE (r =.32; p <.0001). Each decrease in plasma HDL tertile (74.9 +/- 2.1, 50.6 +/- 0.5, and 36.8 +/- 1.0 mg/dl) was associated with a significant decrease in MMSE (23.4 +/- 1.5, 17.7 +/- 1.8, and 12.4 +/- 1.8; p <.04 for each plasma HDL tertile)… This underscores the protective effects of increased plasma HDL and its role in maintaining superior cognition in longevity." "Families of centenarians have high levels of plasma high-density lipoprotein (HDL) cholesterol"	147	
	High non-HDL cholesterol is bad for the heart	"SUMMARY Non-HDL cholesterol is a potent predictor of cardiovascular risk among a broad range of individuals with and without cardiovascular disease and is prognostic over a wide range of follow-up periods."	148	
LDL level	Should be below 100, perhaps below 80	Intensive statin therapy => LDL average = 79 => no progression of atheroma burden, while those with LDL = 110 => progression. In other words, this is good evidence that LDL cholesterol should be very low indeed.	149	
Cholesterol-lowering diet	Diet is as good as statin drugs	A cholesterol-lowering diet ("a diet high in plant sterols …, soy protein…, viscous fibers… and almonds…") works as well as statins in a controlled, prospective study. Both interventions reduced cholesterol and CRP by about 30%. But note: phytoestrogens per se from soy & other plant foods do not seem to lower heart disease risk	150 151 152	
Statins	C E & β-carotene do NOT help; statins do	Long PDF file summarizing the results of a study: vitamins C, E & β-carotene do not reduce risk of cancer, cardiovascular disease or any other major outcome. On the other hand, the statins substantially reduce the risk for vascular events (stroke or heart attack)	153	
	Lower risk of POAG glaucoma	"…Longer duration of statin use was associated with a lower risk of open-angle glaucoma (P for trend =.04) primarily among subjects with 24 months or more of use (OR, 0.60) …a protective association was also observed among those who used nonstatin cholesterol-lowering agents (OR, 0.59)"	154	

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Whole grains and bran

Whole grains (e.g. whole wheat, oat bran) have advantages including decreased risk of heart disease and improving insulin sensitivity (vs. diabetes.) One study (Am J Clin Nutr 2002 Sep;76(3):535-40; PMID: 12197996) found a 30% reduction in the rate of diabetes in men who ate whole grain foods, and recommended replacing refined grain foods with whole grain ones.

Category	Effect	Finding	Ref	Fig
Whole grains	Whole grains are associated with lower mortality and heart disease	"Whole-grain breakfast cereal intake was inversely associated with total and CVD-specific mortality, independent of age; body mass index; smoking; alcohol intake; physical activity; history of diabetes, hypertension, or high cholesterol; and use of multivitamins. Compared with men who rarely or never consumed whole-grain cereal, men in the highest category of whole-grain cereal intake (>/= 1 serving/d) had multivariate-estimated relative risks of total and CVD-specific mortality of 0.83…"	155	

	Associated with lower risk for adult-onset diabetes	"An inverse association between whole-grain intake and the risk of type 2 diabetes was found. The similar result for cereal fiber intake suggests that the whole-grain association is due to cereal fiber or another factor related to cereal fiber intake."	156	
	Good for bowel health and lower blood glucose	"High-fiber rye and wheat food consumption improved several markers of bowel and metabolic health relative to that of low-fiber food. Fiber from rye appears more effective than that from wheat in overall improvement of biomarkers of bowel health."	157	
	Diabetes type 2	Whole grains and grain fiber may help prevent diabetes. "An inverse association between whole-grain intake and the risk of type 2 diabetes was found. The similar result for cereal fiber intake suggests that the whole-grain association is due to cereal fiber or another factor related to cereal fiber intake."	158	
		"cross-sectional association between whole- and refined-grain intake, cardiovascular disease risk factors, prevalence of the metabolic syndrome, and the incidence of cardiovascular disease mortality in the same cohort of older adults. DESIGN: The nutritional status of 535 healthy persons aged 60-98 y…The results showed a significant inverse trend between whole-grain intake and the metabolic syndrome (P for trend = 0.005) and mortality from cardiovascular disease (P for trend = 0.04), independent of demographic, lifestyle, and dietary factors. Fasting glucose concentrations and body mass index decreased across increasing quartile categories of whole-grain intake (P for trend = 0.01 and 0.03, respectively), independent of confounders, whereas intake of refined grain was positively associated with higher fasting glucose concentrations (P for trend = 0.04) and a higher prevalence of the metabolic syndrome (P for trend = 0.01). CONCLUSION: Whole-grain intake is a modifiable dietary risk factor, and older and young adults should be encouraged to increase their daily intake to >/=3 servings/d."	159	
	Helps to prevent obesity	"Women who consumed more whole grains consistently weighed less than did women who consumed less whole grains (P for trend < 0.0001). Over 12 y, those with the greatest increase in intake of dietary fiber gained an average of 1.52 kg less than did those with the smallest increase in intake of dietary fiber (P for trend < 0.0001) independent of body weight at baseline, age, and changes in covariate status. Women in the highest quintile of dietary fiber intake had a 49% lower risk of major weight gain than did women in the highest quintile (OR = 0.51; 95% CI: 0.39, 0.67; P < 0.0001 for trend)."	160	
		A prospective study of whole grain intake and development of diabetes type II found a 30% reduced risk after adjusting for BMI.	161	
	Reduces periodontitis risk	"We prospectively followed 34 160 male US health professionals aged 40-75 y at the outset. We updated medical and lifestyle information biennially with questionnaires and diet every 4 y by using a validated food-frequency questionnaire…**Men in the highest quintile of whole-grain intake were 23% less likely to get periodontitis than were those in the lowest quintile**"	162	
	Associated with lower rate of heart disease Bran may be the active part	"This was a prospective cohort study of 42 850 male health professionals aged 40–75 y at baseline in 1986 who were free from cardiovascular disease, cancer, and diabetes. Daily whole-grain, bran, and germ intakes were derived in grams per day from a detailed semiquantitative dietary questionnaire… The hazard ratio of CHD in men with the highest intake of added bran was 0.70 (95% CI: 0.60, 0.82) compared with men with no intake of added bran (P for trend ≤ 0.001). Added germ was not associated with CHD risk…This study … suggests that the bran component of whole grains could be a key factor in this relation."	163	
Oat bran	Reduces cholesterol	"The most significant decreases in total cholesterol (-67.7 +/- 37.2 mg/dl; p < 0.01), low-density lipoprotein cholesterol (-56.3 +/- 35.1 mg/dl; p < 0.01), and apolipoprotein B (-42.4 +/- 34.1 mg/dl; p < 0.01) were found with the combination of the fat-modified and oat bran enriched food."	164	

		"The oat bran was incorporated into the daily cooking process (bread and bread rolls 20-30 g, sauces and desserts 15-20 g), not detectable for the patients at all."		
		"34 premenopausal women (age: 22-53 years) were randomly assigned either to the control group (no supplement) or to the treatment group, which received 2 oat bran-enriched muffins per day (28 g/day of oat bran) during 4 weeks. RESULTS: Supplementation with oat bran had a beneficial effect on plasma HDL-C levels. Indeed, compared to the control group (n = 16), a mean increase in plasma HDL-C levels of 11.2% was observed in women eating the oat bran supplement (n = 18) (p = 0.01), whereas the total cholesterol/HDL-C ratio decreased by 7.0% (p = 0.002)."	165	

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Flax

Category	Effect	Finding	Ref	Fig
Flax	Enterolactones lower the rate of cardiovascular disease and death Flax seed intake increases enterolactones	"Owing to its phenolic structure, enterolactone and its plant lignan precursors, which are converted by intestinal bacteria to enterolactone, are potential antioxidants… Our data suggest that a high serum enterolactone level is associated with reduced CHD- and CVD-related mortality in middle-aged Finnish men. These results add to the evidence supporting the importance of whole grain foods, fruits, and vegetables in the prevention of premature death from CVD." And "…death decreased linearly across quartiles of serum enterolactone concentration." "The percentage of flaxseed supplemented test food out of total dietary intake was 20% of energy… Serum enterolactone concentration was doubled during flaxseed supplementation."	166 167	
	Flax lowers cholesterol and triglycerides dramatically, and better than soy	From a USDA study, where 20% of calories were from ground flax seed: "In obese rats flaxseed meal had significant cholesterol lowering effect compared to control rats (41%)." "The marked hypotriglyceridemic and hypocholesterolemic effects of flaxseed meal may have important therapeutic implications in patients with hypertriglyceridemia and hypercholesterolemia…"	168	

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Exercise

Category	Effect	Finding	Ref	Fig
Exercise	Cardiovascular disease	"There is an inverse association between relative intensity of physical activity (an individual's perceived level of exertion) and risk of CHD"	169	
	Helps prevent strokes	"Low cardiorespiratory fitness was comparable with systolic blood pressure, obesity, alcohol consumption, smoking, and serum low-density lipoprotein cholesterol level as a risk factor for stroke."	170	
	Reduces visceral fat (a risk factor for diabetes)	"participants who exercised at a level equivalent to 17 miles of jogging each week saw significant declines in visceral fat, subcutaneous abdominal fat and total abdominal fat"…" participants who did not exercise had an 8.6 percent increase in visceral fat after eight months, while those participants who exercised at the highest amount saw a 8.1 percent decrease in visceral fat."	171	
	Greatly reduced risk of hypertension	"We prospectively followed 8302 Finnish men and 9139 women aged 25 to 64 years without a history of antihypertensive drug use, coronary heart disease, stroke, and heart failure at baseline… **Multivariate-adjusted hazards ratios of hypertension associated with light, moderate, and high physical activity were 1.00, 0.63, and 0.59 in men (Ptrend<0.001), and 1.00, 0.82, and 0.71 in women (Ptrend=0.005), respectively**. This association persisted both in subjects who were overweight and in those who were not. Multivariate-adjusted hazards ratios of hypertension based at different levels of body mass index (<25, 25 to 29.9, and >/=30) were 1.00, 1.18, and 1.66 for men (Ptrend<0.001), and 1.00, 1.24, and 1.32 for	172	

		women (Ptrend=0.007), respectively."		
	Helps keep bones tough and prevent fractures	The primary factor determining bone density and mass is body weight. However, bone mass does not necessarily prevent fractures: thin runners have thin but tough bones. http://www.usc.edu/projects/nexus/faculty/dept-ldsg/wiswell/article.htm		
	Reduces the risk of stroke (CVA) by 27%	"a meta-analysis… [of] 23 studies… For cohort studies, **highly active individuals" (equivalent to running 15-20 min/day, or exercising 30 min/day) "had a 27% lower risk of stroke incidence or mortality** … than did low-active individuals. We observed similar results in moderately active individuals compared with inactive persons (RRs =0.80 …)… We conclude that moderate and high levels of physical activity are associated with reduced risk of total, ischemic, and hemorrhagic strokes."	[173]	
	Increases longevity by 9% in rats, but not maximum life span	"As in previous studies, wheel running modestly increased average longevity (approximately 9%), but had no effect on maximal life span." [174] HOWEVER, from the same author in an earlier paper "the beneficial effects of food restriction and exercise on survival are not additive or synergistic." [175] Steven Spindler's studies of mice show a "squaring of the longevity curve" with exercise; CR however has a far greater effect.		Fig
	Reduces mortality	"A cohort study of vegetarians and health-conscious persons in Germany was followed-up prospectively for 21 years, including 1,225 vegetarians and 679 health-conscious nonvegetarians. Standardized mortality ratios compared with the German general population were calculated for all causes and specific causes… RESULTS: Standardized mortality ratios for all-cause mortality was significantly below 100: 59 [95% confidence interval (95% CI), 54-64], predominantly due to a deficit of deaths from circulatory diseases. Within the cohort, vegetarian compared with nonvegetarian diet had no effect on overall mortality [rate ratio (RR), 1.10; 95% CI, 0.89-1.36], whereas **moderate and high physical activity significantly reduced risk of death (RR, 0.62,** 0.64), adjusted for age, sex, smoking, alcohol intake, body mass index, and educational level."	[176]	
	Too much exercise may have a long-term detrimental effect	"We conclude that the rate of decline in maximal aerobic capacity during middle and older age is greater in endurance-trained men than in their sedentary peers"	[177]	
	Improves insulin sensitivity	A randomized controlled trial of diet and exercise in 45 obese women found that "Body weight decreased by approximately 6.5% within both weight loss groups and was unchanged in the exercise without weight loss and control groups. In comparison with controls, cardiorespiratory fitness improved within the exercise groups only ($p < 0.01$). Reduction in total, abdominal, and abdominal subcutaneous fat within the exercise weight loss group was greater ($p < 0.001$) than within all other groups… In comparison with the control group, insulin sensitivity improved within the exercise weight loss group alone ($p < 0.001$). DISCUSSION: Daily exercise without caloric restriction was associated with substantial reductions in total fat, abdominal fat, visceral fat, and insulin resistance in women. Exercise without weight loss was also associated with a substantial reduction in total and abdominal obesity."	[178]	
	Reduces risk for Alzheimer Disease and dementia	"Participants were randomly selected from the survivors of a population-based cohort previously surveyed in 1972, 1977, 1982, or 1987. 1449 persons (72.5%) age 65-79 years participated in the re-examination in 1998 (mean follow-up, 21 years). 117 persons had dementia and 76 had AD. Multiple logistic regression methods were used to analyse the association between leisure-time physical activity and dementia or AD. FINDINGS: **Leisure-time physical activity at midlife at least twice a week was associated with a reduced risk of dementia and AD (odds ratio [OR] 0.48** [95% CI 0.25-0.91] and	[179]	

		0.38 [0.17-0.85], respectively), even after adjustments for age, sex, education, follow-up time, locomotor disorders, APOE genotype, vascular disorders, smoking, and alcohol drinking. The associations were more pronounced among the APOE varepsilon4 carriers. INTERPRETATION: Leisure-time physical activity at midlife is associated with a decreased risk of dementia and AD later in life. Regular physical activity may reduce the risk or delay the onset of dementia and AD, especially among genetically susceptible individuals."		
		"1740 persons older than age 65 years without cognitive impairment …were followed biennially to identify incident dementia… During a mean follow-up of 6.2 years (SD, 2.0), 158 participants developed dementia (107 developed Alzheimer disease). **The incidence rate of dementia was 13.0 per 1000 person-years for participants who exercised 3 or more times per week compared with 19.7 per 1000 person-years for those who exercised fewer than 3 times per week. The age- and sex-adjusted hazard ratio of dementia was 0.62** (95% CI, 0.44 to 0.86; P = 0.004). The interaction between exercise and performance-based physical function was statistically significant (P = 0.013). The risk reduction associated with exercise was greater in those with lower performance levels. Similar results were observed in analyses restricted to participants with incident Alzheimer disease."	[180]	
	Reduces risk of macula degeneration (AMD)	"The 15-year cumulative incidence of AMD was determined through four examination phases at five-year intervals of a population-based study conducted in Beaver Dam, Wisconsin, initiated in 1988-1990 (n=3,874 men and women between ages of 43-86 years)… After controlling for age, gender, arthritis history, systolic blood pressure, body mass index, smoking history, and education, **persons with an active lifestyle (defined as regular activity >/= 3 times/week) at baseline were less likely to develop exudative AMD (odds ratio [OR]= 0.3**, 95% confidence interval [CI]=0.1-0.7) compared to persons without an active lifestyle. After multivariate adjustment, **increased categories of number of blocks walked per day decreased the risk of exudative AMD (OR=0.7**, 95% CI=0.6-0.97). Physical activity was not related to the incidence of early AMD or pure geographic atrophy. CONCLUSIONS: These data show a protective effect of physical activity for incident exudative AMD, independent of body mass index and other confounders."	[181]	
	Reduced risk of colon cancer	"We investigated several aspects of the role of physical activity in colon and rectal cancer etiology that remain unclear in the European Prospective Investigation into Nutrition and Cancer. This cohort of 413,044 men and women had 1,094 cases of colon and 599 cases of rectal cancer diagnosed during an average of 6.4 years of follow-up. We analyzed baseline data on occupational, household, and recreational activity to examine associations by type of activity, tumor subsite, body mass index (BMI), and energy intake. **The multivariate hazard ratio for colon cancer was 0.78 [95% confidence interval (95% CI), 0.59-1.03] among the most active participants when compared with the inactive, with evidence of a dose-response effect (P(trend) = 0.04)**. For right-sided colon tumors, the risk was 0.65 (95% CI, 0.43-1.00) in the highest quartile of activity with evidence of a linear trend (P(trend) = 0.004). Active participants with a BMI under 25 had a risk of 0.63 (95% CI, 0.39-1.01) for colon cancer compared with the inactive."	[182]	

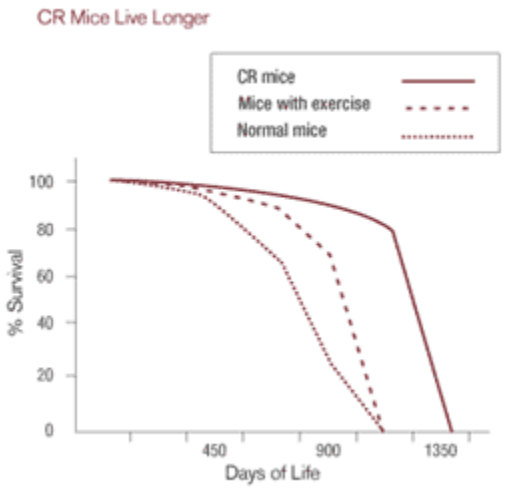

Figure. Survival curve for mice: normal, on CR diet or given exercise. Exercise "squares the curve"; CR shifts the curve to the right. Both help average lifespan, but the effects of CR are much greater.

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Tea and coffee

Potential problems: Caffeine and liquids also give a very small, temporary rise in blood pressure. If you want less caffeine, "rinse" the tea bag first for a few seconds with hot water: caffeine dissolves more easily than the antioxidants, so most of it is washed away. In addition, to my mind green tea tastes bad. When I drink it (not often), I add sweetener and spiced tea to make it palatable. Another problem with tea is oxalic acid that is present in tea just as it is in spinach. Calcium from milk either in the tea or just before or after should prevent its absorption.

Category	Effect	Finding	Ref	Fig
Caffeine	Raises intraocular pressure (IOP)	"In patients with normotensive glaucoma who drank regular coffee, the mean +/- SD changes in IOP at 30, 60, and 90 minutes were 0.9 +/- 0.5, 3.6 +/- 1.1, and 2.3 +/- 0.66 mm Hg, respectively; in those who drank decaffeinated coffee, they were 0.75 +/- 0.36, 0.70 +/- 0.4, and 0.4 +/- 0.6 mm Hg, respectively."	183	
	May help prevent Alzheimer disease	A retrospective, case control study of 54 AD pts and 54 controls found that "Using a logistic regression model, caffeine exposure during this period was found to be significantly inversely associated with AD (odds ratio=0.40, 95% confidence interval=0.25-0.67), whereas hypertension, diabetes, stroke, head trauma, smoking habits, alcohol consumption, non-steroid anti-inflammatory drugs, vitamin E, gastric disorders, heart disease, education and family history of dementia were not statistically significantly associated with AD."	184	
Tea	Lowers BP in rats	In rats "systolic and diastolic BP were significantly lower in the BTP and GTP groups than in the controls… because the amounts of polyphenols used in this experiment correspond to those in approximately 1 L of tea, the regular consumption of black and green tea may also provide some protection against hypertension in humans."	185	
	Lowers BP in people	"Compared with nonhabitual tea drinkers, the risk of developing hypertension decreased by 46% for those who drank 120 to 599 mL/d and was further reduced by 65% for those who drank 600 mL/d or more after carefully adjusting for age, sex, socioeconomic status, family history of hypertension, body mass index, waist-hip ratio, lifestyle factors (total physical activity, high sodium intake, cigarette smoking, alcohol consumption, and coffee drinking), and dietary factors (vegetable, fruit, unrefined grain, fish, milk, visible-fat food, and deep fried food intake)… CONCLUSION: Habitual	186	

		moderate strength green or oolong tea consumption, 120 mL/d or more for 1 year, significantly reduces the risk of developing hypertension in the Chinese population."		
	Benefits may be eliminated if you drink milk at the same time	"Experimental and clinical studies indicate that tea exerts protection against cardiovascular diseases…METHODS AND RESULTS: A total of 16 healthy female volunteers consumed either 500 mL of freshly brewed black tea, black tea with 10% skimmed milk, or boiled water as control. Flow-mediated dilation (FMD) was measured by high-resolution vascular ultrasound before and 2 h after consumption. **Black tea significantly improved FMD in humans compared with water, whereas addition of milk completely blunted the effects of tea.** To support these findings, similar experiments were performed in isolated rat aortic rings and endothelial cells. Tea induced vasorelaxation in rat aortic rings and increased the activity of endothelial nitric oxide synthase by phosphorylation of the enzyme in endothelial cells. **All effects were completely inhibited by the addition of milk to tea.** Of the various kinds of milk proteins, the **caseins accounted for these inhibiting effects of milk**, probably by formation of complexes with tea catechins. CONCLUSION: Milk counteracts the favourable health effects of tea on vascular function. This finding indicates the need for particular awareness in the interpretation and design of studies comprising nutritional flavonoids."	[187]	
Green tea	Cancer	Green tea helps prevent cancer BUT YOU NEED 10+ CUPS PER DAY!! You can get this much EGCG with supplement capsules, such as two of AOR's EGCG MAX capsules per day.	[188] [189]	
	Breast cancer	"Compared to women who did not drink green tea regularly (i.e., less than once a month), there was a significant trend of decreasing risk with increasing amount of green tea intake, adjusted odds ratios being 1.00, 0.71 (95% confidence interval [CI] 0.51-0.99) and 0.53 (95% CI 0.35-0.78), respectively, in association with no, 0-85.7 and >85.7 ml of green tea per day."	[190]	
Green tea extract	Flavenols are absorbed as well as from green tea itself	"Our observations suggest that green tea extract supplements retain the beneficial effects of green and black tea and may be used in future chemoprevention studies to provide a large dose of tea polyphenols without the side effects of caffeine associated with green and black tea beverages."	[191]	
	Helps you lose weight	"After a 2-wk diet run-in period, healthy Japanese men were divided into 2 groups with similar BMI and waist circumference distributions. A 12-wk double-blind study was performed in which the subjects ingested 1 bottle oolong tea/d containing 690 mg catechins (green tea extract group; n = 17) or 1 bottle oolong tea/d containing 22 mg catechins (control group; n = 18). Results: Body weight, BMI, waist circumference, body fat mass, and subcutaneous fat area were significantly lower in the green tea extract group than in the control group."	[192]	
Coffee	High intake appears associated with heart attack	A case control study showed "…the odds ratios for moderate (<300 mL/d), heavy (300-600 mL/d), and very heavy (>600 mL/d), consumption, relative to no consumption, were 0.69 (95% CI, 0.50-0.86), 1.56 (95% CI, 1.10-2.34) and 3.10 (95% CI, 1.82-5.26), respectively, after controlling for the presence of hypertension, hypercholesterolemia, diabetes mellitus, family history of premature coronary heart disease, physical activity status, smoking habits, BMI, alcohol consumption, triglycerides, consumption of several food items, depression scale score and education status."	[193]	
		"A total of 41 836 postmenopausal women aged 55-69 y at baseline were followed for 15 y. After exclusions for cardiovascular disease, cancer, diabetes, colitis, and liver cirrhosis at baseline, 27 312 participants remained, resulting in 410 235	[194]	

		person-years of follow-up and 4265 deaths. The major outcome measure was disease-specific mortality. RESULTS: … the hazard ratio of death attributed to cardiovascular disease was 0.76 (95% CI: 0.64, 0.91) for consumption of 1-3 cups/d, 0.81 (95% CI: 0.66, 0.99) for 4-5 cups/d, and 0.87 (95% CI: 0.69, 1.09) for >/=6 cups/d. The hazard ratio for death from other inflammatory diseases was 0.72 (95% CI: 0.55, 0.93) for consumption of 1-3 cups/d, 0.67 (95% CI: 0.50, 0.90) for 4-5 cups/d, and 0.68 (95% CI: 0.49, 0.94) for >/=6 cups/d."		
	Not associated with hypertension	A 2002 analysis of recent studies of coffee and hypertension found no association.	[195]	
		"Prospective cohort study conducted in the Nurses' Health Studies (NHSs) I and II of 155,594 US women free from physician-diagnosed hypertension followed up over 12 years …no linear association between caffeine consumption and risk of incident hypertension was observed after multivariate adjustment"	[196]	
	Homocysteine	"The increase in homocysteine concentrations 4 h after consumption of [two cups of] coffee relative to consumption of 3 placebo capsules was 19% (P = 0.0001). Caffeine treatment had a much weaker acute effect on homocysteine (4%; P = 0.09). Effects of caffeine were stronger in women than in men, but the effects of coffee did not differ significantly between men and women. CONCLUSIONS: Caffeine is partly responsible for the homocysteine-raising effect of coffee. Coffee, but not caffeine, affects homocysteine metabolism within hours after intake, although the effect is still substantial after an overnight fast."	[197]	
	May protect against stroke and all-cause mortality	A Japanese study of "2,855 men and women aged 40-79 years in 1989, and during the subsequent 9.9 years of follow-up. Using the Cox regression model to adjust for potential confounding factors, we calculated the multivariate hazard ratios of death from all causes separately for men and women. The multivariate hazard ratio of mortality for men who consumed two or more cups of coffee per day, compared with those who consumed less than half a cup per day, was 0.43 (95% confidence interval, 0.30-0.63), and the ratio for those who consumed half to one cup of coffee per day was 0.70 (95% confidence interval, 0.52-0.94)."	[198]	
	Appears to protect against diabetes type 2 Drinking 6 cups/day reduces risk by about 30%	A large, prospective 18-year Swedish follow-up study showed that "Associated hazard ratios, after adjustment for age, smoking, low physical activity, education and body mass index were 0.55 (0.32-0.95), 0.39 (0.20-0.77) and 0.48 (0.22-1.06) for daily consumption of three to four, five to six and seven cups or more, respectively, with a consumption of less than two per day as reference." A large, prospective Dutch study showed that "After adjustment for potential confounders, individuals who drank at least seven cups of coffee a day were 0.50 (95% CI 0.35-0.72, p=0.0002) times as likely as those who drank two cups or fewer a day to develop type 2 diabetes." This was also found in the Nurses' Health Study: "The authors found an inverse association between coffee intake and type 2 diabetes after adjustment for age, body mass index, and other risk factors. The multivariate relative risks for diabetes according to regular coffee consumption categories (0, <1, 1 to 3, 4 to 5, or > or =6 cups per day) in men were 1.00, 0.98, 0.93, 0.71, and 0.46 (95% CI, 0.26 to 0.82; P = 0.007 for trend), respectively. The corresponding multivariate relative risks in women were 1.00, 1.16, 0.99, 0.70, and 0.71 (CI, 0.56 to 0.89; P < 0.001 for trend), respectively. For decaffeinated coffee, the multivariate relative risks comparing persons who drank 4 cups or more per day with nondrinkers were 0.74 (CI, 0.48 to 1.12) for men and 0.85 (CI, 0.61	[199] [200] [201]	

		to 1.17) for women. Total caffeine intake from coffee and other sources was associated with a statistically significantly lower risk for diabetes in both men and women. CONCLUSIONS: These data suggest that long-term coffee consumption is associated with a statistically significantly lower risk for type 2 diabetes." And again in a study from Finland in JAMA: "After adjustment for confounding factors (age, study year, body mass index, systolic blood pressure, education, occupational, commuting and leisure-time physical activity, alcohol and tea consumption, and smoking), the HRs [Hazard Ratios] of DM associated with the amount of coffee consumed daily (0-2, 3-4, 5-6, 7-9, > or =10 cups) were 1.00, 0.71 … 0.39 … 0.39 … and 0.21 …(P for trend<.001) in women, and 1.00, 0.73 …0.70 … 0.67 … and 0.45 … (P for trend =.12) in men, respectively. In both sexes combined, the multivariate-adjusted inverse association was significant (P for trend <.001) and persisted when stratified by younger and older than 50 years; smokers and never smokers; healthy weight, overweight, and obese participants; alcohol drinker and nondrinker; and participants drinking filtered and nonfiltered coffee. CONCLUSION: **Coffee drinking has a graded inverse association with the risk of type 2 DM**" A large review in JAMA (2005) of 9 cohort studies found that "The [Relative Risk] of type 2 diabetes was 0.65 (95% confidence interval [CI], 0.54-0.78) for the highest (>or=6 or >or=7 cups per day) and 0.72 (95% CI, 0.62-0.83) for the second highest (4-6 cups per day) category of coffee consumption compared with the lowest consumption category (0 or <or=2 cups per day)."	202 203	
	Associated with lower risk of breast cancer	"A hospital-based, case-control study … 1932 cases with primary, incident breast cancer and 1895 hospital controls with nonneoplastic conditions… Among premenopausal women, consumption of regular coffee was associated with linear declines in breast cancer risk (P for trend = 0.03); consumers of >/=4 cups/d experienced a 40% risk reduction (odds ratio = 0.62, 95% CI 0.39-0.98)."	204	
Carbonated soft drinks	Associated with lower risk of esophageal cancer	"we examined CSD [Carbonated soft drinks] as a risk factor for esophageal and gastric cancers in a U.S. multicenter, population-based case-control study. Associations between CSD intake and risk were estimated by adjusted odds ratios (ORs), comparing the highest versus lowest quartiles of intake. All statistical tests were two-sided. Contrary to the proposed hypothesis, CSD consumption was inversely associated with esophageal adenocarcinoma risk (highest versus lowest quartiles, OR = 0.47, 95% confidence interval = 0.29 to 0.76; Ptrend = .005)"	205	

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Antioxidants

Free radicals. These are intermediate chemical reactants, a by-product of living and processing the food we eat! They are very reactive and cause slow, continuous damage to cells and tissues all over the body, and may account for part of the aging process in the brain. As we age, free radicals are produced in greater amounts. The body has several systems to neutralize these reactive chemicals, especially bilirubin "bilirubin is a major physiologic antioxidant cytoprotectant" (Baranano DE, Rao M, Ferris CD, Snyder SH. Biliverdin reductase: a major physiologic cytoprotectant. Proc Natl Acad Sci U S A. 2002 Dec 10;99(25):16093-8. PMID: 12456881)), glutathione and uric acid. Mutant lab animals with defects in these systems age and die rapidly. Fortunately there are a few things you can do to reduce the effect of free radicals.

First, you can reduce the production of free radicals by eating less (see the section on caloric restriction). This is by far the cheapest and most effective (in theory) approach, with the fewest side effects! In fact fasting for a day temporarily reduces the level of free radical damage by a very large amount, about 1/3.

Second, you can reduce the risk of damage from free radicals by getting a portion of your calories monounsaturated fat (MUFA) from nuts, and reducing polyunsaturated fats such as corn oil and other sources rich in omega-6 fats.

Third, you can get a *variety* (Int J Epidemiol 2002 Aug;31(4):847-54) of antioxidants from vegetables (especially spinach, broccoli and related vegetables), nuts and fruits (especially blueberries, strawberries, raspberries [shown to reduce risk of cancer in the lab], prunes and purple grape juice), green or black tea, and other things. Antioxidant-rich blueberries, spinach and strawberries have been shown to improve brain function in rats. Blueberries have also been shown to be equal to CR in protecting brain function in rats (Mech Ageing Dev 1999 Nov;111(2-3):141-54; PMID: 10656533). On the other hand, antioxidants in general have NOT been shown to reduce the risk of coronary heart disease (Am J Clin Nutr 2002 Feb;75(2):191-212; PMID: 11815309). Tea and flavenoids, however, HAVE recently been shown to be associated with a very large drop in heart disease – up to 70%! (Am J Clin Nutr 2002 May;75(5):880-6; PMID: 11976162) I think it is best not to place too much emphasis on antioxidants. They probably help up to a point, but are secondary and perhaps not worth fretting about too much if you eat lots of fruit and vegetables and drink tea. N.b., simultaneous intake of milk may eliminate the antioxidant qualities of tea (Int J Food Sci Nutr 2000 Sep;51(5):309-15; PMID: 11103296).

Note: studies on the effect of antioxidants in lifespan of lab mammals show NO EFFECT, or even a detriment (for coenzyme Q-10, a popular supplement).

Caveat: tea from tea bags has a substantial amount of fluoride, in part from the fluoridated pesticides used on tea leaves (the same applies to other fruit and vegetables, such as grapes). Fluoride gets permanently deposited in bone. It is a highly toxic poison (read the label on your toothpaste!) It increases the density of bone but actually weakens it (perhaps making it more brittle), making it prone to fractures. One study showed a small but significant increase in hip fractures in areas where there was a moderate or high level of fluoride in the water (J Bone Miner Res 2001 May;16(5):932-9; PMID: 11341339). You need fluoride in toothpaste to harden your teeth to tooth decay, but I think it is best to avoid excess fluoride ingestion if you plan to live long! Fortunately, the tea extract in commonly available capsules is said to have little or no fluoride.

In a study of death rates related to diet and other factors (Epidemiology 1997 Mar;8(2):168-74; PMID: 9229209): the mortality hazard ratios with ... increasing [amounts of]... nuts (1.00, 0.60, 0.56), fruits (1.00, 0.38, 0.57), and green salads (1.00, 0.54, 0.65). Thus the often heard exhortation to eat more fruits, vegetables & nuts. All of these foods have antioxidants of various kinds.

Another study from rural Japan found that people with the highest levels of serum antioxidants (carotenes, lycopene, beta-cryptoxanthin, canthaxanthin, zeaxanthin, lutein; NOT tocopherols (vit E) or retinol (vit A)) had the lowest levels of cancer and all-cause mortality (Int J Vitam Nutr Res 2002 Jul;72(4):237-50; PMID: 12214561).

A Finnish study found that high lycopene levels were associated with intima-media thickening of the common carotid artery, that has been shown to predict coronary events (Rissanen TH, Voutilainen S, Nyyssönen K, Salonen R, Kaplan GA and Salonen JT. Serum lycopene concentrations and carotid atherosclerosis: the Kuopio Ischaemic Heart Disease Risk Factor Study. American Journal of Clinical Nutrition, Vol. 77, No. 1, 133-138, January 2003), thus lycopene may help prevent heart disease and stroke.

Lutein & zeaxanthin have also been shown to be at low levels in the maculae (the central part of the retina) of patients with macula degeneration (AMD). In AMD patients who took high-dose lutein supplements, these levels returned to normal (Bernstein PS, Zhao DY, Wintch SW, Ermakov IV, McClane RW, Gellermann W. Resonance Raman measurement of macular carotenoids in normal subjects and in age-related macular degeneration patients. Ophthalmology. 2002 Oct;109(10):1780-7. PMID: 12359594). There is also evidence that people with the highest food intake of lutein and zeaxanthin (e.g. spinach & kale) have the lowest rate of AMD (Seddon JM, Ajani UA, Sperduto RD, Hiller R, Blair N, Burton TC, Farber MD, Gragoudas ES, Haller J, Miller DT, et al. Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. Eye Disease Case-Control Study Group. JAMA. 1994 Nov 9;272(18):1413-20. PMID: 7933422). What is not yet proven is whether these supplements can prevent, slow or reverse AMD. This is being studied: a pilot study states that "results suggest that increasing the level of retinal antioxidants might influence macular function early in the disease process, as well as in normal aging." (Falsini B, Piccardi M, Iarossi G, Fadda A, Merendino E, Valentini P. Influence of short-term antioxidant supplementation on macular function in age-related maculopathy: a pilot study including electrophysiologic assessment. Ophthalmology. 2003 Jan;110(1):51-60; discussion 61. PMID: 12511345)

Food	Lutein & zeaxanthin per serving (mg)
Kale	26
Collard greens	15
Spinach, fresh cooked	13
Turnip greens	12
Broccoli	4
Spinach, frozen cooked	4
Squash	3
Peas	2
Sweet corn	1.5
Lettuce	1.5
Brussels sprouts	1

The best research seems to show that antioxidants of most (if not all) kinds can prolong the mean lifespan of lab animals but NOT the maximum lifespan (Barja G. Rate of generation of oxidative stress-related damage and animal longevity. Free Radic Biol Med. 2002 Nov 1;33(9):1167-1172. PMID: 12398924). This implies that antioxidants help reduce the risk of certain diseases, but do not slow the aging process itself. To do both, practice caloric restriction.

Here is a useful summary using the antioxidant analysis called ORAC. The antioxidant foods on top of the list have the most effect ON THIS ARTIFICIAL TEST OF UNCERTAIN VALUE per calorie. In vivo, spinach comes out on top of several tested (see the USDA article Cans Foods Forestall Aging?), but there are many different types of anti-oxidants, and it may be best to eat a variety (Int J Epidemiol 2002 Aug;31(4):847-54) of them every day. The list below is of many but not by any means all anti-oxidant food sources. ORAC/Cal – the most "bang for the buck":

Food sorted by ORAC per calorie	ORAC/cal	ORAC/100 gm
Clove oil (Syzigium aromaticum)	**11,985**	10,786,875
Wolfberries	**633**	25,300
Thyme oil (Thymus vulgaris)	**177**	159,590
Oregano oil (Origanum compactum)	**170**	153,007
Mountain Savory oil (Satureja montana)	**126**	113,071
Spinach	**57**	1,260
Strawberries	**51**	1,540
Blueberries	**43**	2,400
Blackberries	**39**	2,036
Kale	**35**	1,770
Broccoli Flowers	**32**	890
Red bell pepper	**26**	710
Raspberries	**25**	1,220
Prunes	**24**	5,770
Brussels sprouts	**23**	980
Beets	**20**	840
Plums	**17**	949
Oranges	**16**	750
Eggplant	**15**	390
Grapefruit, pink	**15**	483
Cherries	**13**	670
Onion	**12**	450
Red grapes	**10**	739
Kiwi fruit	**10**	602
Raisins	**9**	2,830

Corn 5 400

Food	ORAC/ Cal	ORAC/ g
Cauliflower	15.6	3.9
Cabbage	14	3.5
Garlic	13.1	19.5
Onion	11.8	4.5
Cantaloupe	8.6	3
White grape	6.7	4.5
Apricot	4.2	2
Sweet potato (yams)	3	3.5

Interestingly, red & violet onions have about three times as much of the antioxidant quercetin as common onions. This finding matches the correlation between color and antioxidants found in colored vegetables.

Recent data also show that the ORAC and FRAP (ferric reducing antioxidant capacity) values of vegetable are not only dependent on species, but also highly dependent on geographical origin and harvest time (J Agric Food Chem 2002 May 22;50(11):3122-8; PMID: 12009973).

Remarkably, some essential oils (spice oils) have far more antioxidant power on ORAC assays than fruits and vegetables. Cloves come out on top, with two drops of oil equivalent to 2.5 cups of blueberries. Clove oil (eugenol) is used as a local anesthetic by dentists; ground cloves contain 15% eugenol and are tasty in some foods. I like to put them on thawed frozen blackberries & blueberries!

Category	Effect	Finding	Ref	Fig
Antioxidants	Link to a table	USDA web site with list of flavenoid content of many foods, such as berries, tea, etc. Of interest is that green tea has much more of many flavenoids than prepared tea powders etc.	206	
	ORAC is NOT the best measure of effect	Well thought out quote from Michael Rae: "I've often ranted about people citing ORAC and other test-tube measures of alleged antioxidant capacity to draw conclusions about the health value of various foods. In brief, the 2 biggest issues are that (1) because different kinds of antioxidants quench different kinds of radicals, any existing measure of 'antioxidant capacity' can only represent a narrow range of a given substance's antioxidant effects; [ORAC only measures phenolic antioxidant donor capacity. So for example, gamma tocopherol has a much lower ORAC than alpha, which against SOME ROS (say, hydroxyl radical) is an accurate assay of their relative potency -- but gamma is much more powerful against peroxynitrite and other nitrogen-based "free radicals," and ORAC totally misses this. It also can't account for the compartmentalization & distribution of specific antioxidant molecules: whether they work in the fluids of the body or in the membranes, whether they can be transported actively into various key compartments or are only able to dissolve & diffuse, etc]; and (2) because of different absorption & metabolism of various antioxidant compounds (esp phenolics [which are the antioxidants whose value is always put in the most impressive light by ORAC and in which fruit is rich]), something can have gangbuster antioxidant activity in a test tube & be irrelevant in vivo because the compound in the food just doesn't get into your system. (There is also the whole question of whether something's simply being an antioxidant actually constitutes a health benefit)."	207	
	Which flavenoids matter for heart disease?	A case-control study from Greece found that only "Flavan-3-ols, which are largely found in wine and tea, are inversely associated with, and may be protective against, coronary heart disease." Also, "an increase of about 21 mg per day corresponding to a 24% decrease in CHD risk. The inverse association between flavan-3-ols and CHD risk was largely accounted for by the intake of wine and to a lesser extent tea." Flavan-3-ols, specifically the catechins, are abundant in	208	

		ripe fruits, leaves, tea and red wine.		
	Numerous antioxidant data	FDA (PDF-format) document lists a large number of antioxidant compounds and activity in foods. Note: this does NOT necessarily correspond with benefit to humans.	209	
	Do NOT affect lifespan	Two of the most touted antioxidants do not improve lifespan of mice. "…alpha-lipoic acid or coenzyme Q(10)… had no impact on longevity or tumor patterns compared with control mice fed the same number of calories, whereas [caloric restriction] increased maximum life span by 13% ($p < .0001$) and reduced tumor incidence." n.b., this has been confirmed elsewhere with these and other supplements.	210	
Dietary beta carotene, vitamin C & E, and zinc	Linked to slightly lower macula degeneration rates	"Recently, high-dose supplementation with beta carotene, vitamins C and E, and zinc was shown to slow the progression of AMD. OBJECTIVE: To investigate whether regular **dietary** intake of antioxidants is associated with a lower risk of incident AMD. DESIGN: Dietary intake was assessed at baseline in the Rotterdam Study (1990-1993) using a semiquantitative food frequency questionnaire. Incident AMD until final follow-up in 2004 was determined by grading fundus color transparencies in a masked way according to the International Classification and Grading System. SETTING: Population-based cohort of all inhabitants aged 55 years or older in a middle-class suburb of Rotterdam, the Netherlands. PARTICIPANTS: Of 5836 persons at risk of AMD at baseline, 4765 had reliable dietary data and 4170 participated in the follow-up. MAIN OUTCOME MEASURE: Incident AMD, defined as soft distinct drusen with pigment alterations, indistinct or reticular drusen, geographic atrophy, or choroidal neovascularization. RESULTS: Incident AMD occurred in 560 participants after a mean follow-up of 8.0 years (range, 0.3-13.9 years). Dietary intake of both vitamin E and zinc was inversely associated with incident AMD. The hazard ratio (HR) per standard deviation increase of intake for vitamin E was 0.92 (95% confidence interval [CI], 0.84-1.00) and for zinc was 0.91 (95% CI, 0.83-0.98). An above-median intake of all 4 nutrients, beta carotene, vitamin C, vitamin E, and zinc, was associated with a 35% reduced risk (HR, 0.65; 95% CI, 0.46-0.92) of AMD. Exclusion of supplement users did not affect the results. CONCLUSION: In this study, a high dietary intake of beta carotene, vitamins C and E, and zinc was associated with a substantially reduced risk of AMD in elderly persons."	211	
		A popularized summary website of AMD macula degeneration risk factors.	212	

Go to TOC

Vegetables and fruits

DO NOT do the Atkins diet! It is bad for you.

I have heard that the "South Beach Diet" advocates avoiding unhealthy types of fats etc., thus it may be a variant that is quite good for you. I do not know!

Category	Effect	Finding	Ref	Fig
How to eat	Eat with oil for absorption of carotenoids	No oil => no absorption!	213	
Vegetables	High intake is associated with longer lifespan	A 30-year follow-up study of 1536 Italian males showed a 1-year gain in lifespan of non-smokers (2 years in smokers).	214	
	Associated with a reduced rate of cognitive decline	"a prospective cohort study of 3,718 participants, aged 65 years and older of the Chicago Health and Aging Project. Participants completed a food frequency questionnaire and were administered at least two of three cognitive assessments at baseline, 3-year, and 6-year follow-ups. … The mean cognitive score at baseline for the analyzed cohort was 0.18 (range: -3.5 to 1.6), and the overall mean change in score per year was a decline of 0.04 standardized units. In mixed effects models adjusted for age, sex, race, and education,	215	

		compared with the rate of cognitive decline among persons in the lowest quintile of vegetable intake (median of 0.9 servings/day), the rate for persons in the fourth quintile (median, 2.8 servings/day) was slower by 0.019 standardized units per year (p = 0.01), a **40% decrease**, and by 0.018 standardized units per year (p = 0.02) for the fifth quintile (median, 4.1 servings/day), or a 38% decrease in rates. The association remained significant (p for linear trend = 0.02) with further control of cardiovascular-related conditions and risk factors. Fruit consumption was not associated with cognitive change. CONCLUSION: **High vegetable but not fruit consumption may be associated with slower rate of cognitive decline with older age**."		
	Reduces kidney stones from uric acid	Uric acid (think gout, kidney stones) comes from purine metabolism; purine comes from DNA in cells, most concentrated in meat. Thus meat => these problems. "The ingestion of the vegetarian diet … led to a further significant reduction in the risk of uric acid crystallization by 93% compared to [the Western type diet]."	216	
		Some people are sensitive to the bitter taste of some vegetables. It turns out that the gene (TAS2R38) that is associated with being a "PTC taster" (phenylthiocarbamide) correlates well with avoiding vegetables in children! PTC strips is the common test often used in high school genetics.	217	
Fruit and vegetables	May help prevent dementia	Fruit (blueberries and strawberries) and vegetables (spinach) may help prevent neuronal aging (dementia), perhaps via anti-oxidant properties.	218	
		From Reuters: [Researchers] "divided the dogs into four groups that got either standard care; a diet supplemented with tomatoes, carrot granules, citrus pulp, spinach flakes and supplements; standard care plus extra exercise and play; or the special diet and the special play and exercise regime. A second set of 17 dogs aged 1 to 3 got either a standard or fortified diet. Tests included having to find a hidden treat. The older dogs clearly benefited from the special diet and the special exercise program, the researchers said. All 12 of the older beagles that got a supplemented diet and exercise could solve a difficult problem, compared to eight of 10 dogs that got the enriched diet alone and two of eight dogs that got no special treatment."	219	
	Lower LDL levels	"Fruit and vegetable consumption was inversely related to LDL: in the categories 0–1.9, 2.0–2.9, 3.0–3.9, and ≥4 servings/d, multivariate-adjusted mean (95% CI) LDL concentrations were 3.36 (3.28, 3.44), 3.35 (3.27, 3.43), 3.26 (3.17, 3.35), and 3.17 (3.09, 3.25) mmol/L, respectively, for men (*P* for trend < 0.0001) and 3.35 (3.26, 3.44), 3.22 (3.14, 3.30), 3.21 (3.13, 3.29), and 3.11 (3.04, 3.18), respectively, for women (*P* for trend < 0.0001)."	220	
	Improve bone health in girls	"High fruit and vegetable intakes have beneficial effects on the bone area of the radius and whole body in early pubertal girls."	221	
	There is only a modest effect on chronic disease	"Of the food groups analyzed, green leafy vegetable intake showed the strongest inverse association with major chronic disease and cardiovascular disease. For an increment of one serving per day of green leafy vegetables, relative risks were 0.95 (95% CI = 0.92 to 0.99) for major chronic disease and 0.89 (95% CI = 0.83 to 0.96) for cardiovascular disease. CONCLUSIONS: Increased fruit and vegetable consumption was associated with a modest although not statistically significant reduction in the development of major chronic disease. The benefits appeared to be primarily for cardiovascular disease and not for cancer." My thoughts: there still may be some fruit and vegetables that are good at preventing certain types of cancer.	222	
		"Current evidence supports the inclusion of whole grains, fruits and vegetables, and lean sources of animal proteins including low-fat dairy products in dietary therapies for insulin resistance. Those who wish to follow a low-carbohydrate diet should be encouraged to follow a new menu low in fat, and with most of the protein derived	223	

		from plant sources."		
	Lower C-Reactive Protein (CRP)	"…high intake (8 servings/d) of vegetables and fruit significantly increased total carotenoid concentrations in plasma … C-reactive protein was significantly reduced at week 8 in the subjects who consumed 8 servings/d of vegetables and fruit compared with those who consumed 2 servings/d."	[224]	
	Reduced risk of stroke	A meta-analysis of prospective studies "including 90,513 men, 141,536 women, and 2,955 strokes" showed "**The risk of stroke was decreased by 11%... for each additional portion per day of fruit, by 5% ... for fruit and vegetables, and by 3% ... for vegetables**."	[225]	
		A meta-analysis in Lancet "Eight studies, consisting of nine independent cohorts, met the inclusion criteria. These groups included 257,551 individuals (4917 stroke events) with an average follow-up of 13 years. Compared with individuals who had less than three servings of fruit and vegetables per day, **the pooled relative risk of stroke was 0.89 (95% CI 0.83-0.97) for those with three to five servings per day, and 0.74 (0.69-0.79) for those with more than five servings per day.** Subgroup analyses showed that fruit and vegetables had a significant protective effect on both ischaemic and haemorrhagic stroke…Our results provide strong support for the recommendations to consume more than five servings of fruit and vegetables per day, which is likely to cause a major reduction in strokes."	[226]	
	Associated with reduced risk of oral cancer	Meta-analysis: "A comprehensive, systematic bibliographic search of medical literature published up to September 2005 was conducted to identify relevant studies. Separate meta-analyses were conducted for fruit and vegetable consumption. The effect of portion or daily intake of fruit or vegetables on the risk of oral cancer was calculated. A multivariate meta-regression analysis was performed to explore heterogeneity. This multivariate meta-regression analysis examined the effect of quality score, the type of cancers included, citrus fruit and green vegetable consumption, and the time interval for dietary recall of the studies on the role of fruit or vegetable consumption in the risk of oral cancer. The presence of publication bias was assessed with a funnel plot for asymmetry. RESULTS: Sixteen studies (15 case-control studies and 1 cohort study) met the inclusion criteria and were included in the meta-analysis. **The combined adjusted odds ratio (OR) estimates showed that each portion of fruit consumed per day significantly reduced the risk of oral cancer by 49%** (OR: 0.51; 95% CI: 0.40, 0.65). **For vegetable consumption, the meta-analysis showed a significant reduction in the overall risk of oral cancer of 50%** (OR: 0.50; 95% CI: 0.38, 0.65)…The consumption of fruit and vegetables is associated with a reduced risk of oral cancer."	[227]	
	Reduces risk of coronary heart disease (CHD)	A meta-analysis of studies found "The pooled RRs were calculated for each additional portion of fruit and/or vegetables consumed per day, and the linearity of the associations were examined. Nine studies were eligible for inclusion in the meta-analysis that consisted of 91,379 men, 129,701 women, and 5,007 CHD events. **The risk of CHD was decreased by 4% …for each additional portion per day of fruit and vegetable intake and by 7% … for fruit intake**…This meta-analysis of cohort studies shows that fruit and vegetable consumption is inversely associated with the risk of CHD. The causal mechanism of this association, however, remains to be demonstrated."	[228]	
Broccoli & other crucifers (Brussels sprouts, cauliflower, etc.)	Helps prevent certain cancer	Broccoli and related vegetables have been shown to reduce the rate of certain cancers. This is NOT because of antioxidant activity; instead they contain certain molecules (glucosinolate, isothiocyanates (ITC) and indoles) that induce an increase in the body's production of what is called "Phase 2 enzymes". These enzymes detoxify certain carcinogens by causing an increase in glutathione-S-transferase (GST) activity. The response to these vegetables appears to be dependent on your genes. The most potent vegetable inducer of this is	[229]	

		broccoli sprouts, easily grown at home (I do).		
	Helps prevent stomach ulcers and cancers	In addition, the nutrient sulphorophane is found in broccoli and broccoli sprouts: it has been shown to kill Heliobacter pylori, a common pathogenic bacterium that causes stomach cancer and stomach ulcers.	230	
	Acidic salad dressing increases; long cooking eliminates sulforaphane	"Broccoli contains sulforaphane, an anticarcinogen with multiple chemoprotective effects. Upon disruption of broccoli tissue, bioactive sulforaphane … are … formed by myrosinase-dependent hydrolysis of glucoraphanin, a glucosinolate precursor. Since production of these compounds occurs only after the plant tissue is disrupted" "A pH of 3.5, typical of many salad dressings, significantly increased sulforaphane from 17% to 41% of detected glucoraphanin hydrolysis products, at the expense of sulforaphane nitrile. …Steam blanching longer than 1 minute significantly decreased production of [sulforaphane + sulforaphane nitrile] to <3% of pre-steamed, indicating inactivation of myrosinase."	231	
		"We conclude that a diet containing phase 2 protein inducers" [*e.g. broccoli sprouts*] "also reduces the risk of developing cardiovascular problems of hypertension and atherosclerosis."	232	
	Slow mental aging	"We prospectively examined fruit and vegetable intake in relation to cognitive function and decline among aging women. Participants were followed from in 1976 with biennial questionnaires, and food frequency questionnaires were administered in 1984, 1986, and every 4 years thereafter. From 1995 to 2001, we administered, by telephone, six cognitive tests measuring general cognition, verbal memory, category fluency, and working memory. We repeated assessments two years later for 13,388 women (>90% follow-up)… Fruits were not associated with cognition or cognitive decline. However, total vegetable intake was significantly associated with less decline. Specifically, on a global score combining all tests, women in the highest quintile of **cruciferous vegetables** declined slower (by 0.04 unit; 95% confidence interval, 0.003, 0.07; p trend = 0.1) compared with the lowest quintile. Women consuming the most **green leafy vegetables** also experienced slower decline than women consuming the least amount (by 0.05 unit; 95% confidence interval, 0.02, 0.09; p trend < 0.001). **These mean differences were equivalent to those observed for women about 1 to 2 years apart in age**."	233	
Garlic & Onions	May help prevent prostate cancer	"Men in the highest of three intake categories of total allium vegetables [garlic, onions etc.] (>10.0 g/day) had a statistically significantly lower risk (odds ratio [OR] = 0.51, 95% confidence interval [CI] = 0.34 to 0.76; P(trend)<.001) of prostate cancer than those in the lowest category (<2.2 g/day)."	234	
	May reduce the risk of getting a cold	"One hundred forty-six volunteers were randomized to receive a placebo or an allicin-containing garlic supplement, one capsule daily, over a 12-week period between November and February… The active-treatment group had significantly fewer colds than the placebo group (24 vs 65, P < .001). The placebo group, in contrast, recorded significantly more days challenged virally (366 vs 111, P < .05) and a significantly longer duration of symptoms (5.01 vs 1.52 days, P < .001)."	235	
Hot peppers (capsaicin)	Associated with higher rates of stomach cancer – in Mexicans who eat a LOT	"The risk of [gastric cancer] was increased (OR = 1.71; 95% CI = 0.76-3.88) among high-level consumers of CAP (90-250 mg of capsaicin per day, approximately 9-25 jalapeno peppers per day) as compared to low-level consumers (0-29.9 mg of capsaicin per day, approximately 0 to less than 3 jalapeno peppers per day; p for trend p = 0.026)"	236	
Lutein and zeaxanthin	Associated with lower risk of macula degeneration	A review states that "Until scientifically sound knowledge is available we recommend for patients judged to be at risk for AMD to: alter their diet to more dark green leafy vegetables, wear UV protective lenses and a hat when outdoors."	237	
	Study data	"The FDA recently reviewed intervention and observational studies	238	

	showing a benefit is weak	that evaluated the role of lutein and zeaxanthin in reducing the risk of age-related macular degeneration and cataracts. On the basis of this evidence-based review, the FDA concluded that **no credible evidence exists for a health claim about the intake of lutein or zeaxanthin (or both) and the risk of age-related macular degeneration or cataracts**."		
	Associated with MUCH lower risk of prostate cancer (*98%* less in one comparison)	These are INCREDIBLE results. The odds ratios are truly extraordinary (maybe unbelievably so), so I am including the entire abstract: "To determine whether dietary intake of lycopene and other carotenoids has an etiological association with prostate cancer, a case-control study was conducted in Hangzhou, southeast China during 2001-2002. The cases were 130 incident patients with histologically confirmed adenocarcinoma of the prostate. The controls were 274 hospital inpatients without prostate cancer or any other malignant diseases. Information on usual food consumption, including vegetables and fruits, was collected by face-to-face interviews using a structured food frequency questionnaire. The risks of prostate cancer for the intake of carotenoids and selected vegetables and fruits rich in carotenoids were assessed using multivariate logistic regression, adjusting for age, locality, education, income, body mass index, marital status, number of children, family history of prostate cancer, tea drinking, total fat and caloric intake. The prostate cancer risk declined with increasing consumption of lycopene, alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein and zeaxanthin. Intake of **tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk.** The adjusted odds ratios for the highest versus the lowest quartiles of intake were **0.18** (95% CI: 0.08-0.41) for **lycopene**, 0.43 (95% CI: 0.21-0.85) for **alpha-carotene** [from carrots, squash, tomatoes etc.], **0.34** (95% CI: 0.17-0.69) for **beta-carotene**, **0.15** (95% CI: 0.06-0.34) for **beta-cryptoxanthin** [from red bell peppers, papaya, cilantro, oranges etc.] and **0.02** (95% CI: 0.01-0.10) for **lutein and zeaxanthin**. The corresponding dose-response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer."	[239]	
	Oil is needed for good absorption	Lipids from avocado (in salad) increased carotenoid absorption from salsa by 2.6 to 4.4 times.	[240]	
Fiber	Fruit fiber and cereal fiber reduce heart risk	"We analyzed the original data from 10 prospective cohort studies from the United States and Europe to estimate the association between dietary fiber intake and the risk of coronary heart disease…. After adjustment for demographics, body mass index, and lifestyle factors, **each 10-g/d increment of energy-adjusted and measurement error–corrected total dietary fiber was associated with a 14% … decrease in risk of all coronary events and a 27% … decrease in risk of coronary death.** For cereal, fruit, and vegetable fiber intake [Relative Risks] corresponding to 10-g/d increments were 0.90…, 0.84…, and 1.00 …, respectively, for all coronary events and 0.75 …, 0.70 …, and 1.00…, respectively, for deaths… Consumption of dietary fiber from cereals and fruits is inversely associated with risk of coronary heart disease." Note: Vegetable fiber was NOT protective!	[241]	
Citrus rinds	Reduce cholesterol	"Using hamster models with diet-induced high cholesterol, the researchers showed that feeding them food containing 1 percent [citrus peel-derived] PMFs [(polymethoxylated flavones)] lowered levels of LDL cholesterol by 32 to 40 percent."	[242] [243]	
	Reduce the risk of cancer, both in people and rodents	"…case-control study was designed to determine the usual citrus consumption patterns of an older Southwestern population and to then evaluate how this citrus consumption varied with history of squamous cell carcinoma (SCC) of the skin… the most striking feature was the protection purported by citrus peel consumption (OR = 0.66, 95% CI = 0.45-0.95). Moreover, there was a dose-response relationship between higher citrus peel in the diet and degree of risk	[244]	

		lowering." "Monoterpenes are nonnutritive dietary components found in the essential oils of citrus fruits and other plants. A number of these dietary monoterpenes have antitumor activity. For example, d-limonene, which comprises >90% of orange peel oil, has chemopreventive activity against rodent mammary, skin, liver, lung and forestomach cancers." How in the world do you eat it? Remember marmalade, kumquats, and fruitcake! Cooked citrus peel with added sweetener (I like sucralose, but anything will do) adds spice to a berry mix. My favorite combination is a mix of (mostly frozen berries) blueberries, blackberries, raspberries, strawberries, cooked orange peel and fiber mix (guar & psyllium [Wal-Mart's sugar-free Metamucil substitute]) spiced with sucralose & ground cloves, moistened with red wine.	[245]	
Vegan diet	Not more healthy than a lean meat + veggies diet Better for heart disease than the standard ("unhealthy") diet.	"Just cutting animal products out of your diet will not make you healthier. … vegans tend to have worse mortality rates than other groups. The largest meta-study to look at the relative merits of various diets (in terms of rates of mortality) found: "There were no significant differences between vegetarians and nonvegetarians in mortality from cerebrovascular disease, stomach cancer, colorectal cancer, lung cancer, breast cancer, prostate cancer, or all other causes combined." However, "**Mortality from ischemic heart disease was 24% lower in vegetarians than in nonvegetarians.**"	[246] [247]	
Overview	A summary of ways to prevent cancer, from JAMA	"Obesity and overweight have been linked to development of several cancers, including breast, colon, and uterine. Eating healthful foods in smaller portions can help to reduce or maintain weight in a healthful range. • Eat at least 5 servings of fruit and vegetables every day. • Limit your intake of saturated fats from meats, full-fat dairy products, and processed foods. • Include high--fiber choices (whole-grain breads and cereals, raw fruits and vegetables). • Avoid foods that have been charred or blackened because they may have higher levels of carcinogens....."	[248]	
Vegetarian diet needs supplements	B12 Taurine			
Vegetarian diet	Reduces risk of heart disease	"A cohort study of vegetarians and health-conscious persons in Germany was followed-up prospectively for 21 years, including 1,225 vegetarians and 679 health-conscious nonvegetarians. Standardized mortality ratios compared with the German general population were calculated for all causes and specific causes… RESULTS: Standardized mortality ratios for all-cause mortality was significantly below 100: 59 [95% confidence interval (95% CI), 54-64], predominantly due to a deficit of deaths from circulatory diseases. Within the cohort, vegetarian compared with nonvegetarian diet had no effect on overall mortality [rate ratio (RR), 1.10; 95% CI, 0.89-1.36], whereas moderate and high physical activity significantly reduced risk of death (RR, 0.62, 0.64), adjusted for age, sex, smoking, alcohol intake, body mass index, and educational level. **Vegetarian diet was however associated with a reduced RR of 0.70 (95% CI, 0.41-1.18) for ischemic heart disease, which could partly be related to avoidance of meat**."	[249]	
Fruit	Macula degeneration	"We conducted a prospective follow-up study of women in the Nurses' Health Study and men in the Health Professionals Follow-up Study. We followed 77 562 women and 40 866 men who were at least 50 years of age and had no diagnosis of ARM or cancer at baseline for up to 18 years for women and up to 12 years for men. Fruit and vegetable intakes were assessed with a validated	[250]	

		semiquantitative food-frequency questionnaire up to 5 times for women and up to 3 times for men during follow-up. RESULTS: A total of 464 (329 women and 135 men) incident cases of early ARM and 316 (217 women and 99men) cases of neovascular ARM, all with visual loss of 20/30 or worse due primarily to ARM, were diagnosed during follow-up. Fruit intake was inversely associated with the risk of neovascular ARM. Participants who consumed 3 or more servings per day of fruits had a pooled multivariate relative risk of 0.64 (95% confidence interval, 0.44-0.93; P value for trend =.004) compared with those who consumed less than 1.5 servings per day. The results were similar in women and men. However, intakes of vegetables, antioxidant vitamins, or carotenoids were not strongly related to either early or neovascular ARM. CONCLUSION: These data suggest a protective role for fruit intake on the risk of neovascular ARM."		
	Alzheimer disease	"After adjustment for potential confounders, the **hazard ratio for probable Alzheimer's disease was 0.24 (95% confidence interval [CI], 0.09-0.61) comparing subjects who drank juices at least 3 times per week with those who drank less often than once per week** with a hazard ratio of 0.84 (95% CI, 0.31-2.29) for those drinking juices 1 to 2 times per week (P for trend < .01). This inverse association tended to be more pronounced among those with an apolipoprotein Eepsilon-4 allele and those who were not physically active."	[251]	
Blueberries	Brain function	"…rats given dietary supplements of fruit and vegetable extracts with high antioxidant activity for 8 months beginning at 6 months of age retarded age-related declines in neuronal and cognitive function. The present study showed that such supplements (strawberry, spinach, or blueberry …) fed for 8 weeks to 19-month-old Fischer 344 rats were also effective in reversing age-related deficits in several neuronal and behavioral parameters"	[252]	
	Mental function in people	A prospective, randomized study of 100 Americans age >60 showed that "Among those receiving wild blueberries, significant improvement occurred in decision speed (t-test $p = 0.025$) and self-reported aches and pains ($p = 0.017$), energy level ($p = 0.002$), sharpness ($p = 0.001$), sleep quality ($p = 0.017$), mood ($p = 0.010$), peacefulness ($p = 0.005$) and overall health ($p = 0.001$). Blueberry group response times improved by 4.2%, decreasing from 39.96 to 38.27 centiseconds, more than twice the improvement in the control group. Actual decision speeds were not displayed during the study so speed improvement could not influence self-reported health. Adjustments to balance decision speed predictions, error rates and within-measurement decision-speed improvement (our measures of expectation and motivation) in blueberry and control groups did not significantly change these results. Two blueberry recipients reported hearing improvement that was confirmed by an independent observer"	[253]	
Tomato	Lycopene alone does not prevent prostate cancer; tomato does	"Consumption of tomato powder but not lycopene inhibited prostate carcinogenesis, suggesting that tomato products contain compounds in addition to lycopene that modify prostate carcinogenesis."	[254]	
Pomegranate		From a small study, pomegranate juice may help reduce carotid artery stenosis.	[255]	
		A moderate size prospective, randomized, double-blind study showed decreased cardiac ischemia in heart disease patients who drank six oz./day of pomegranate juice.	[256]	
Red grapefruit	Lowers triglyceride levels	"Fifty-seven hyperlipidemic patients, ages 39-72 years…During 30 consecutive days of the investigation the diets of the patients of the red and blond dietary groups were daily supplemented with one equal in weight fresh red or blond grapefruit, respectively…Diet supplemented with fresh red grapefruit positively influences serum	[257]	

		lipid levels of all fractions, especially serum triglycerides and also serum antioxidant activity."		
Legumes	Associated with long life in people	"The 'Food Habits in Later Life' (FHILL) is a cross-cultural study conducted under the auspices of the International Union of Nutritional Sciences (IUNS) and the World Health Organization (WHO). Baseline data on food habits, health status and social variables were collected from five cohorts aged 70 and over (Japanese in Japan, Swedes in Sweden, Anglo-Celtic in Australia, Greeks in Australia and Greece). Objective: To identify protective dietary predictors amongst long-lived elderly people (n=785) … Food items were grouped into nine food groups based on key features of the Traditional Mediterranean Diet (vegetables, legumes, fruits and nuts, cereals (including starchy roots), dairy products, meat, fish, monounsaturated: saturated ratio, and ethanol). All-cause mortality data were obtained from up to seven years follow-up. Alternative Cox Proportional Hazard model adjusted to age at enrolment (in 5-year interval), gender, and smoking was developed to analyse the survival data...Results: Only for legumes intake was the result plausible, consistent and statistically significant across collective FHILL cohort's data. **There is a 7% - 8% reduction in mortality hazard ratio for every 20g increase in daily legume intake** with adjustment for location/ethnicity …The significance of legumes persisted even after controlling for age at enrolment (in 5-year interval), gender, and smoking. Legumes have been associated with long-lived food cultures such as the Japanese (soy, tofu, natto, miso), the Swedes (brown beans, peas), and the Mediterranean people (lentils, chickpeas, white beans)."	258	
	Associated with reduced risk of prostate cancer	"multicenter case-control study …Intake of legumes (whether total legumes, soyfoods specifically, or other legumes) was inversely related to prostate cancer (OR for highest relative to lowest quintile for total legumes = 0.62; P for trend = 0.0002); …Intakes of yellow-orange and cruciferous vegetables were also inversely related to prostate cancer, especially for advanced cases, among whom the highest quintile OR for yellow-orange vegetables = 0.67 (P for trend = 0.01) and the highest quintile OR for cruciferous vegetables = 0.61 (P for trend = 0.006). Intake of tomatoes and of fruits was not related to risk. Findings were generally consistent across ethnic groups. **These results suggest that legumes (not limited to soy products) and certain categories of vegetables may protect against prostate cancer**."	259	

Go to TOC

Alcohol and wine

Wine or purple grape juice – the jury is still out. Purple grape juice in moderate amounts is probably good for you; if you are a man over 40 or a woman over 50 you could substitute a *small* glass of red wine (Circulation 2001 Jan 23;103(3):472-5; PMID: 11157703) each day. There is some evidence that alcohol itself has an independent beneficial effect in small quantities by increasing HDL levels, or possibly by the anti-AGE effect of its metabolite acetaldehyde (Proc Natl Acad Sci U S A 1999 Mar 2;96(5):2385-90; PMID: 10051651). . In addition, for men who drink moderately at least 5 days per week there is also a 36% reduction in the incidence of diabetes (Diabetes 2001 Oct;50(10):2390-5; PMID: 11574424). A drink of any kind of alcohol beverage 3 to 5 times per week seems to reduce the risk of heart attack in men by about 35% in a large recent study (**Mukamal KJ, Conigrave KM, Mittleman MA, Camargo CA Jr, Stampfer MJ, Willett WC, Rimm EB. Roles of drinking pattern and type of alcohol consumed in coronary heart disease in men. N Engl J Med. 2003 Jan 9;348(2):109-18. PMID: 12519921**.) Polyphenols may be the active component, and these may be more potent in red wine than in grape juice. Red wine has the same antioxidants found in purple grape juice. Apparently white wine or other drinks with alcohol may not be helpful. Burgundy and cabernet sauvignon (perhaps these are the same thing?) have the highest antioxidant level of those tested in vitro.

Light alcohol intake also seems to be associated with a smaller risk of strokes (Stroke 2001 Sep;32(9):1939-46; PMID: 11546878); however the same study showed that there is dose-dependant shrinkage of the brain with alcohol use, and long-term, moderate or high intake of alcohol is one of the causes of cancer (but on the other hand, the catechins in red wine help to prevent cancer in animals American Journal of Clinical Nutrition, Vol. 76, No. 4, 865-872, October 2002) In other words, you might have a smaller risk of strokes per se but gradually lose your brain in the process from the toxic effects of alcohol. Another recent study of 6500 patients in Britain showed a lower rate of cardiovascular disease among those who drank moderately, but the overall death rate from all causes was actually larger. Wine may be associated with lower risk of dementia (Truelsen T, Thudium D, Gronbaek M; Copenhagen City Heart Study. Amount and type of alcohol and risk of dementia: the Copenhagen City Heart Study. Neurology. 2002 Nov 12;59(9):1313-9. PMID: 12427876), but it is possible that associated factors other than wine may be at work (e.g. perhaps those who drink wine have a better lifestyle), or factors in the wine other than alcohol. To my gestalt, it is better if you can control your risk for stroke and heart attack by other means than alcohol (diet, aspirin, blood pressure control).

Problems: Alcohol has several risks: alcoholism, especially if you are young or genetically prone to it, breast cancer ("results suggest that about 4% of the breast cancers in developed countries are attributable to alcohol." Alcohol, tobacco and breast cancer - collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the disease. Br J Cancer. 2002 Nov 18;87(11):1234-1245. PMID: 12439712), other cancers, hypertension, and stroke. The metabolite of ethanol (acetaldehyde) is itself toxic, with hundreds of articles about its toxicity. And worst of all, about 10% of all people may be susceptible to alcoholism: this is most likely in those who start drinking at a young age. These are the reasons for the age recommendations. For many people (and indeed in general!) it may not be worth drinking any wine at all.

Category	Effect	Finding	Ref	Fig
Alcohol	Reduces dementia and cognitive loss	Moderate drinking among the elderly is associated with half the risk of dementia. "Compared with abstention, consumption of 1 to 6 drinks weekly is associated with a lower risk of incident dementia among older adults." Michael Rae (CR society list, 2004-10-14) did a careful review of eleven studies on the effects of alcohol on dementia, and concluded that "The evidence on alcohol & dementia shows a clear trend toward a protective effect, most clearly for wine"	260 261	
		From the Nurses Health Study "Our data suggest that in women, up to one drink per day does not impair cognitive function and may actually decrease the risk of cognitive decline."	262	
	Reduced risk of ischemic stroke	"After adjusting for other risk factors compared with those who did not drink in the past year, moderate drinkers had a reduced risk of IS (0.67; 95% CI, 0.46 to 0.99) and IS, myocardial infarction, or vascular death (0.74; 95% CI, 0.59 to 0.94)."	263	
	Reduces risk of CVD (heart disease)	"From the Physicians' Health Study enrollment cohort of 88 882 men who provided self-reported information on alcohol intake, we identified a group of 14 125 men with a history of current or past treatment for hypertension who were free of myocardial infarction, stroke, cancer, or liver disease at baseline…These results, which require confirmation in other large-scale studies, suggest that light to moderate alcohol consumption is associated with a reduction in risk of total and CVD mortality in hypertensive men."	264	
		"This cross-sectional study was performed using data from the population-based Rotterdam Coronary Calcification Study. Data on alcohol consumption were available for 1795 individuals without coronary heart disease. Mean +/- SD age of the participants was 71 +/- 5.7 years. Coronary calcification was detected on electron beam computed tomographic scans and quantified as a calcium score by the Agatston method… A U-shaped association was found between alcohol consumption and coronary calcification…**The risk of extensive coronary calcification was 50% lower in individuals who**	265	

		consumed 1 to 2 alcoholic drinks per day than in nondrinkers."		
	Reduces all-cause mortality	This epidemiologic study for 10 years found that moderate alcohol reduces all-cause mortality in men *after* age 35. However, before age 35, it increases the risk of death. Makes sense to me: young men may die of accidents and violence due to alcohol.	266	
		"We undertook a 23-year prospective study of 12 000 male British doctors aged 48-78 years in 1978…ischaemic heart disease (RR 0.72, CI 0.58-0.88, P = 0.002), respiratory disease (RR 0.69, CI 0.52-0.92, P = 0.01), and **all-cause (RR 0.88, CI 0.79-0.98, P = 0.02) mortality were significantly lower than in the non-drinkers**."	267	
		"We performed a **meta-analysis of prospective studies** on alcohol dosing and total mortality. METHODS: We searched PubMed for articles available until December 2005, supplemented by references from the selected articles. Thirty-four studies on men and women, for a **total of 1 015 835 subjects** and 94 533 deaths, were selected. Data were pooled with a weighed regression analysis of fractional polynomials. RESULTS: A J-shaped relationship between alcohol and total mortality was confirmed in adjusted studies, in both men and women. **Consumption of alcohol, up to 4 drinks per day in men and 2 drinks per day in women, was inversely associated with total mortality, maximum protection being 18% in women (99% confidence interval, 13%-22%) and 17% in men** (99% confidence interval, 15%-19%). Higher doses of alcohol were associated with increased mortality... CONCLUSIONS: **Low levels of alcohol intake (1-2 drinks per day for women and 2-4 drinks per day for men) are inversely associated with total mortality in both men and women**."	268	
	Increases breast cancer risk (by a small amount)	"Compared with women who reported drinking no alcohol, the relative risk of breast cancer was 1.32 (1.19-1.45, P<0.00001) for an intake of 35-44 g per day alcohol, and 1.46 (1.33-1.61, P<0.00001) for >/=45 g per day alcohol. The relative risk of breast cancer increased by 7.1% (95% CI 5.5-8.7%; P<0.00001) for each additional 10 g per day intake of alcohol, i.e. for each extra unit or drink of alcohol consumed on a daily basis… If the observed relationship for alcohol is causal, these results suggest that about 4% of the breast cancers in developed countries are attributable to alcohol."	269	
	Increases the risk of hypertension	"drinking outside meals appears to have a significant effect on hypertension risk independent of the amount of alcohol consumed."	270	
		For 40 gm alcohol per day, "compared with control-abstinence, both **red wine and beer increased awake systolic BP (2.9 and 1.9 mm Hg, respectively; P<0.05) and asleep [heart rate] (5.0 and 4.4 bpm; P<0.05**)."	271	
	… but moderate amounts are safe	"Heavy alcohol consumption increases risk for hypertension, which is in itself a strong risk factor for cardiovascular disease (CVD)... OBJECTIVE: To assess whether alcohol consumption is inversely associated with CVD among men with hypertension. DESIGN: **Prospective** cohort study. SETTING: United States. PARTICIPANTS: **11,711 men with hypertension** from the Health Professionals Follow-Up Study. MEASUREMENTS: Alcohol consumption was assessed every 4 years by using a food-frequency questionnaire. Incident cases of nonfatal myocardial infarction (MI), fatal coronary heart disease, and stroke were documented from 1986 to 2002. RESULTS: During follow-up, 653 patients with MI were documented. **Compared with patients abstaining from alcohol, the hazard ratio for participants with MI consuming 0.1 to 4.9 grams of alcohol per day was 1.09 (95% CI, 0.86 to 1.37); consuming 5 to 9.9 grams of alcohol per day was 0.81 (CI, 0.60 to 1.08 g/d);**	272	

		consuming 10 to 14.9 grams of alcohol per day was 0.68 (CI, 0.51 to 0.91 g/d); consuming 15 to 29.9 grams of alcohol per day was 0.72 (CI, 0.54 to 0.97 g/d); consuming 30 to 49.9 grams of alcohol per day was 0.67 (CI, 0.48 to 0.94 g/d); and consuming 50 or more grams of alcohol per day was 0.41 (CI, 0.22 to 0.77 g/d) (P < 0.001 for trend). Associations were similar for fatal and nonfatal MI. Alcohol consumption was not associated with total death or death due to CVD. **Risks for total and ischemic stroke for patients consuming 10 to 29.9 g of alcohol per day were 1.40 (CI, 0.93 to 2.12) and 1.55 (CI, 0.90 to 2.68) compared with that of abstainers.**.. CONCLUSIONS: In this population of men with hypertension, moderate alcohol consumption was associated with a decreased risk for MI but not with risks for total death or death due to CVD."		
Red wine	May decrease risk of prostate cancer	"Each additional glass of red wine consumed per week showed a statistically significant 6% decrease in relative risk"	[273]	
	Resveratrol (found in red wine) improves lifespan in mice	"resveratrol shifts the physiology of middle-aged mice on a high-calorie diet towards that of mice on a standard diet and significantly increases their survival."	[274]	

Go to TOC

Fiber

Personal note: I find glucomannan the most palatable and easy to use fiber. I like to mix it with my food, often with spices (garlic, onion powder & NuSalt). All soluble fibers absorb more fluid over time, so go easy at first. You may find your stomach swelling up as the day goes on. It is most effective at slowing absorption of glucose when mixed with food.

Category	Effect	Finding	Ref	Fig
Soluble fiber	Glucomannan	A randomized clinical trial showed that daily glucomannan "supplement improved blood lipid levels by enhancing fecal excretion of neutral sterol and bile acid and alleviated the elevated glucose levels in diabetic subjects." It reduced cholesterol by 11% and LDL by 20%.	[275]	
		"Decreases in serum cholesterol (total, 12.4+/-3.1%, P<0.004; LDL, 22+/-3.9%, P<0.002; total/HDL ratio, 15.2+/-3.4%, P<0.003; and LDL/HDL ratio, 22.2+/-4.1%, P< 0.002), apolipoprotein (apo) B (15.1+/-4.3%, P<0.0004), apo B/A-1 ratio (13.1+/-3.4%, P< 0.0003), and serum fructosamine (5.2+/-1.4%, P<0.002) were observed during [glucomannan] treatment compared with [wheat bran]-control. Fasting blood glucose, insulin, triglycerides, HDL cholesterol, and body weight remained unchanged. CONCLUSIONS: A diet rich in high-viscosity KJM improves glycemic control and lipid profile, suggesting a therapeutic potential in the treatment of the insulin resistance syndrome."	[276]	
	Notes on soluble fiber, such as which soluble fiber type best?	Glucomannan is white, is very easy to mix, has no taste and absorbs a huge amount of water. It is very useful in preparing foods – use it like corn starch. Downside: expense. Guar is hard to mix (unless mixed in with something else like psyllium), and has a distinct taste. Needs to be very finely ground up. Psyllium: Good against constipation. Needs to be ground finely (don't get the rough stuff).		
	Psyllium reduces hunger and postprandial glucose levels	In a randomized, controlled clinical trial: "After the meal, hunger feelings and energy intake were significantly lower during the psyllium session than during the placebo session (13% and 17% lower respectively; P < 0.05). Postprandial increase in serum glucose, triglycerides and insulin levels was less with psyllium than with placebo (P < 0.05)."	[277]	

	Protects against carotid blood vessel narrowing Raises HDL	"A significant inverse association was observed between IMT progression and the intakes of viscous fiber ($P = 0.05$) and pectin ($P = 0.01$). Correction for measurement error increased the magnitude of these estimated effects. The ratio of total to HDL cholesterol was inversely related to the intakes of total fiber ($P = 0.01$), viscous fiber ($P = 0.05$), and pectin ($P = 0.01$)."	278	
	Reduces the rise in blood glucose with a meal	"guar gum supplementation attenuated the blood glucose response after the meals"	279	
		"Varying the amount of psyllium incorporated into the cereal from 0 to 20% resulted in a **linear dose-dependent reduction of the glycemic index** (GI) (GI = 101 -2.2 x % psyllium; r = 0.950; p less than 0.002)…the mechanism of action relates to a **reduced rate of digestion** rather than carbohydrate malabsorption."	280	
		"A high intake of dietary fiber, particularly of the soluble type, above the level recommended by the ADA, improves glycemic control, decreases hyperinsulinemia, and lowers plasma lipid concentrations in patients with type 2 diabetes."	281	
	Reduces blood pressure	"Results suggest that a diet containing soluble fiber-rich whole oats can significantly reduce the need for antihypertensive medication and improve BP control. Considering the lipid and glucose improvements as well, increased consumption of whole oats may significantly reduce cardiovascular disease risk."	282	
Fiber	Reduces LDL Reduces colon cancer risk factors	"The diets were: high-vegetable, fruit, and nut (very-high-fiber, 55 g/1,000 kcal)… Compared with the starch-based and low-fat diets, the high-fiber vegetable diet resulted in the largest reduction in low-density lipoprotein (LDL) cholesterol (33% +/- 4%, P <.001) and the greatest fecal bile acid output (1.13 +/- 0.30 g/d, P =.002), fecal bulk (906 +/- 130 g/d, P <.001), and fecal short-chain fatty acid outputs (78 +/- 13 mmol/d, P <.001). Nevertheless, due to the increase in fecal bulk, the actual concentrations of fecal bile acids were lowest on the vegetable diet (1.2 mg/g wet weight, P =.002). Maximum lipid reductions occurred within 1 week… We conclude that very high-vegetable fiber intakes reduce risk factors for cardiovascular disease and possibly colon cancer."	283	
	Reduces CRP levels (likely to => reduced risk of heart disease)	"We examined the association between dietary fiber and serum concentration of C-reactive protein (CRP), a possible predictor of cardiovascular events, using data from the National Health and Nutrition Examination Survey 1999–2000. Among 3920 participants □20 y old, dietary fiber intake was inversely associated with serum CRP concentration. The [adjusted] odds ratio (OR) for increased CRP concentration (>3.0 mg/L) was … 0.59…Our findings indicate that fiber intake is independently associated with serum CRP concentration and support the recommendation of a diet with a high fiber content."	284	

Go to TOC

Hypertension and salt (see also CR, Exercise**)**

Keep your blood pressure *lower* than 129/85 (both numbers are important, and optimal BP is < 115/75), no matter your age. The longest study (25 years follow-up on 10,874 patients) showed that Life expectancy was shortened by 2.2 years for men with high-normal blood pressure and by 4.1 years for those with stage 1 hypertension, where high-normal is a reading of 130-139 (systolic pressure) over 85-89 (diastolic pressure) and stage 1 hypertension is 140-159 over 90-99.

A huge review of blood pressure studies on 1 million patients showed that there is a two-fold increase in risk

of death from stroke or ischemic heart disease, no matter the baseline blood pressure (down to at least 115/75) and no matter the age (within the age range of 40-89 yr). "Throughout middle and old age, usual blood pressure is strongly and directly related to vascular (and overall) mortality, without any evidence of a threshold down to at least 115/75 mm Hg." (Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002; 360: 1903-13.)

A DASH diet (low salt, low fat, high vegetables and fruit diet) can lower your blood pressure by 7 to 11 mm Hg, and again Miller ER 3rd, Erlinger TP, Young DR, Jehn M, Charleston J, Rhodes D, Wasan SK, Appel LJ. Results of the Diet, Exercise, and Weight Loss Intervention Trial (DEW-IT). Hypertension. 2002 Nov;40(5):612-8. PMID: 12411452. Note that caloric restriction does this by its nature: by reducing the *amount* of calories there is usually a natural reduction in the amount of saturated fat and salt intake – another good reason to practice caloric restriction, if you need one. In practice, those who practice caloric restriction typically seem to drop their blood pressure by 10-20 mm Hg! Two other methods that seem to have merit in reducing BP are moderate exercise and reducing alcohol intake.

Category	Effect	Finding	Ref	Fig
Blood pressure	Lower is MUCH better	"At ages 40-69 years, each difference of 20 mm Hg usual SBP (or, approximately equivalently, 10 mm Hg usual DBP) is associated with more than a twofold difference in the stroke death rate, and with twofold differences in the death rates from IHD and from other vascular causes. …Throughout middle and old age, usual blood pressure is strongly and directly related to vascular (and overall) mortality, without any evidence of a threshold down to at least 115/75 mm Hg." Note: SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure.	285	
		A population based "prospective study of a random sample of 1700 Danish men and women, aged 41 to 72 years" found both cardiovascular death and all-cause mortality over a period averaging 9.5 years. The cardiovascular death relative risk for "10 mm Hg increments in systolic and 5 mm Hg increments in diastolic ambulatory blood pressure were 1.51 (1.28 to 1.77) and 1.43 (1.26 to 1.61). The corresponding figures for all cause mortality were 1.18 (1.06 to 1.31) and 1.18 (1.09 to 1.28)"	286	
		Richard Martin, a senior lecturer in epidemiology and public health at the University of Bristol in Britain stated "**A one percent reduction in population systolic blood pressure levels is associated with about a 1.5 percent reduction in all-cause mortality**"	287	
	Higher BP reduces brain function at all ages	"In this 20-year longitudinal study, we examined the relationship between baseline blood pressure and cognitive decline for 529 participants using 2 age groups (18 to 46 years and 47 to 83 years)… Results indicated that higher levels of baseline systolic blood pressure, diastolic blood pressure, mean arterial pressure, and blood pressure categories … were significantly associated with decline in Visualization/Fluid abilities in both younger and older age groups. Young adults are as susceptible to blood pressure-related longitudinal decline in cognitive performance as are older adults." "Cerebral white matter lesions are frequently observed on magnetic resonance imaging (MRI) scans in elderly people and are associated with stroke and dementia… 1805 nondemented subjects aged 65 to 75 years were sampled from ongoing community-based studies that were initiated 5 to 20 years before the MRI. …We performed logistic regression analyses adjusted for potential confounders in 1625 people with complete data. Concurrently and formerly assessed diastolic and systolic blood pressure levels were positively associated with severe white matter lesions… Higher blood pressure was associated with an increased risk of severe white matter lesions." "Controlling for potential confounders, **each 10 mmHg increase in**	288 289 290	

		supine SBP was associated with a 2.31-fold increase … in risk for impairment in psychomotor speed and set shifting" "For each additional year of [hypertension] treatment there was a reduction in the risk of incident dementia (**hazard ratio [HR]=0.94**, 95% CI, 0.89 to 0.99)... Results suggest that in hypertensive men, the duration of the antihypertensive treatment is associated with a reduced risk for dementia and cognitive decline."	[291]	
Salt reduction, exercise, weight loss, reducing alcohol	Lower hypertension	A US Government NIH summary of "Prevention of Primary Hypertension" is available as a PDF file. A summary of the most-proven approaches to prevention of hypertension is on page 17, and recommends: 1. **Exercise 30 minutes/day** 2. Maintain a **low BMI** (18.5-24.9) 3. **Limit alcohol** to essentially no more than one drink/day 4. **Reduce salt** intake to < 6 gm/day 5. Get enough dietary **potassium** 6. Good diet: **fruits, vegetables, low-fat dairy, low in saturated and total fat** (the DASH diet)	[292]	
Exercise		"Vigorous exercise reduces day time ambulatory BP and, in combination with calorie restriction, had a synergist effect to reduce night-time and 24 h BP. 4. Exercise is a positive and effective adjunct to other lifestyle measures in the prevention of hypertension. Adherence to either supervised or unsupervised moderate-intensity exercise is sufficient to reduce BP in the short and long term."	[293]	
Salt	There is a linear effect of salt intake on BP => stroke and heart attack	"A reduction of 3 g/d predicts a fall in blood pressure of 3.6 to 5.6/1.9 to 3.2 mm Hg (systolic/diastolic) in hypertensives and 1.8 to 3.5/0.8 to 1.8 mm Hg in normotensives. The effect would be doubled with a 6 g/d reduction and tripled with a 9 g/d reduction. A conservative estimate indicates that a reduction of 3 g/d would reduce strokes by 13% and ischemic heart disease (IHD) by 10%."	[294]	
	The Institute of Medicine recommends 1.5 gm sodium/day and ≥ 4.7 gm potassium/day	"The Institute of Medicine serves as adviser to the nation to improve health. As an independent, scientific adviser, the Institute of Medicine strives to provide advice that is unbiased, based on evidence, and grounded in science." On 2004-02-11 they recommended 1.5 gm sodium/day (down from 2.4 gm), and to get far more dietary potassium than is now common.	[295]	
	High salt intake is associated with high risk for gastric cancer	"… the frequency categories of highly salted foods such as salted fish roe and salted fish preserves were strongly associated with the risk in both sexes. Restriction of salt and salted food intake is a practical strategy to prevent gastric cancer in areas with high risk."	[296]	
	Salt reduction reduces blood pressure in children too	"To assess the effect of reducing salt intake on blood pressure in children, we carried out a **meta-analysis** of controlled trials…Ten trials of children and adolescents with 966 participants …Salt intake was reduced by 42% (interquartile range [IQR]: 7% to 58%). There were significant reductions in blood pressure: systolic: -1.17 mm Hg (95% CI: -1.78 to -0.56 mm Hg; P<0.001); diastolic: -1.29 mm Hg (95% CI: -1.94 to -0.65 mm Hg; P<0.0001)… a modest reduction in salt intake causes immediate falls in blood pressure and, if continued, may well lessen the subsequent rise in blood pressure with age. This would result in major reductions in cardiovascular disease. These results in conjunction with other evidence provide strong support for a reduction in salt intake in children."	[297]	
Potassium	Lowers BP	A review of randomized trials found: "A total of 40 sodium trials and 27 potassium trials in adults with a minimum duration of 2 weeks were selected for analysis… Sodium reduction (median: -77 mmol/24	[298]	

		h) was associated with a change of -2.54 mmHg (95% CI: -3.16, -1.92) in systolic blood pressure and -1.96 mmHg (-2.41, -1.51) in diastolic blood pressure. Corresponding values for increased potassium intake (median: 44 mmol/24 h) were -2.42 mmHg (-3.75, -1.08) and -1.57 mmHg (-2.65, -0.50). Blood pressure response was larger in hypertensives than normotensives, both for sodium (systolic: -5.24 vs -1.26 mmHg, P < 0.001; diastolic: -3.69 vs -1.14 mmHg, P < 0.001) and potassium (systolic: -3.51 vs -0.97 mmHg, P=0.089; diastolic: -2.51 vs -0.34 mmHg, P=0.074)." Bottom line: get more potassium and less sodium!		
		A recent summary measures to prevent hypertension states that "… modifiable factors might decrease blood pressure and even prevent the development of hypertension. Thus, present national recommendations and guidelines include lifestyle modifications ranging from **weight loss** in case of obesity, engagement in regular isotonic **physical activity**, **reduced sodium** diet (<100 mmol/d), **supplementation of potassium**, and **alcohol moderation** (<1 ounce of ethanol or its equivalent per day)."	[299]	
		Adding KCl or K citrate to the diet reduces blood pressure. This study of hypertensives found a ~12 point systolic and 5 point diastolic BP reduction.	[300]	
	Lowers rate of cardiovascular disease deaths in the elderly	"Five kitchens of a veteran retirement home were randomized into 2 groups (experimental or control) and veterans assigned to those kitchens were given either potassium-enriched salt (experimental group) or regular salt (control group) for approximately 31 mo. Information on death, health insurance claims, and dates that veterans moved in or out of the home was gathered. RESULTS: Altogether, 1981 veterans, 768 in the experimental [x (+/-SD) age: 74.8 +/- 7.1 y] and 1213 in the control (age: 74.9 +/- 6.7 y) groups, were included in the analysis. The experimental group had better CVD survivorship than did the control group. The incidence of CVD-related deaths was 13.1 per 1000 persons (27 deaths in 2057 person-years) and 20.5 per 1000 (66 deaths in 3218 person-years) for the experimental and control groups, respectively. **A significant reduction in CVD mortality (age-adjusted hazard ratio: 0.59; 95% CI: 0.37, 0.95) was observed in the experimental group.** Persons in the experimental group lived 0.3-0.90 y longer and spent significantly less (approximately US $426/y) in inpatient care for CVD than did the control group, after control for age and previous hospitalization expenditures…The effect was likely due to a major increase in potassium and a moderate reduction in sodium intakes."	[301]	
Vegetables and fruit	Lower BP	A 7-year study found that a "prospective cohort study of 1,710 employed men in Chicago, Illinois, initially aged 41-57 years… diets higher in fruits and vegetables and lower in meats (except fish) may reduce the risk of developing high BP."	[302]	
		"In a Mediterranean population with an elevated [vegetable] fat consumption, a high fruit and vegetable intake is inversely associated with BP levels."	[303]	
Vegetarian diet	Lowers BP	"Evidence that vegetarian dietary patterns lower blood pressure (BP) comes from both population studies and randomized controlled trials in normotensive and hypertensive subjects. 2. The effect has been shown most clearly in those who keep to a strict lacto-ovo vegetarian diet characterized by a relatively low intake of saturated fat, a high polyunsaturated/saturated fat ratio, and a high intake of fruit, vegetables and other fibre containing products. Randomized controlled dietary trials suggest the effects are independent of dietary sodium, additive to that of calorie restriction, and not due to the	[304]	

		absence of meat protein per se."		
Melatonin		"We conducted a randomized, double-blind, placebo-controlled, crossover trial in 16 men with untreated essential hypertension to investigate the influence of acute (single) and repeated (daily for 3 weeks) oral melatonin (2.5 mg) intake 1 hour before sleep on 24-hour ambulatory blood pressure … Repeated melatonin intake reduced systolic and diastolic blood pressure during sleep by 6 and 4 mm Hg, respectively. … Repeated (but not acute) melatonin also improved sleep… In patients with essential hypertension, repeated bedtime melatonin intake significantly reduced nocturnal blood pressure."	305	
Protein	High protein intake diet is correlated with a small decrease in BP	Note: this type of study is fraught with potential problems. In an Okinawan cohort, "…both [systolic] BP and [diastolic] BP tended to be lower in those with higher daily protein intake, particularly in men."	306	
		A randomized control trial showed that both high protein and soluble vegetable fiber (from psyllium in this case) significantly lower blood pressure. "Relative to control subjects, the net reduction in 24-hour systolic blood pressure was 5.9 mm Hg with fiber and with protein. Findings were independent of age, gender, and change in weight, alcohol intake, or urinary sodium and potassium. Relative to reduced fiber and protein intake, **dietary protein and soluble fiber supplements lower blood pressure additively in hypertensives**."	307	
Protein and MUFAs	Reduce BP and improve lipids	"Randomized, 3-period, crossover feeding study … Participants were 164 adults with prehypertension or stage 1 hypertension. Each feeding period lasted 6 weeks and body weight was kept constant. INTERVENTIONS: A diet rich in carbohydrates; a diet rich in protein, about half from plant sources; and a diet rich in unsaturated fat, predominantly monounsaturated fat. MAIN OUTCOME MEASURES: Systolic blood pressure and low-density lipoprotein cholesterol. RESULTS: Blood pressure, low-density lipoprotein cholesterol, and estimated coronary heart disease risk were lower on each diet compared with baseline. Compared with the carbohydrate diet, the **protein diet further decreased mean systolic blood pressure by 1.4 mm Hg** (P = .002) and by 3.5 mm Hg (P = .006) among those with hypertension **and decreased low-density lipoprotein cholesterol by 3.3 mg/dL** (0.09 mmol/L; P = .01), high-density lipoprotein cholesterol by 1.3 mg/dL (0.03 mmol/L; P = .02), and triglycerides by 15.7 mg/dL (0.18 mmol/L; P<.001). Compared with the carbohydrate diet, the **unsaturated fat diet decreased systolic blood pressure by 1.3 mm** Hg (P = .005) and by 2.9 mm Hg among those with hypertension (P = .02), had no significant effect on low-density lipoprotein cholesterol, **increased high-density lipoprotein cholesterol by 1.1 mg/dL** (0.03 mmol/L; P = .03), and lowered triglycerides by 9.6 mg/dL (0.11 mmol/L; P = .02). **Compared with the carbohydrate diet, estimated 10-year coronary heart disease risk was lower and similar on the protein and unsaturated fat diets.**"	308	
Olive oil	Associated with lower BP	"Olive oil intake…is inversely associated with both systolic and diastolic blood pressure."	309	
		"We evaluated the effects of a moderate consumption of olive oil on lipid profile, BMI, and blood pressure (BP) in a group of 160 healthy men …The study was a randomized, cross-over trial …General linear models showed that the administration of the sequence of the 3 olive oils was responsible for a 3% decrease in systolic BP (SBP) (P < 0.05), but not in diastolic BP, in the non-Mediterranean subjects… this study suggest that a **moderate consumption of olive oil may be used as an effective tool to reduce SBP of healthy men** who do not	310	

		typically consume a Mediterranean diet."		
Folate at high doses (5 mg/day – 8 times more than the RDA)	Lowers BP	"Forty-one asymptomatic men with normal or high-normal ambulatory blood pressure (systolic: >130 to <145 mm Hg; diastolic: >80 to <90 mm Hg) participated. The study had a randomized, placebo-controlled, double-blind, crossover design that incorporated 3-wk treatments with 5 mg folic acid/d or matching placebo; each treatment was separated by a 4-wk washout phase. RESULTS: Folic acid reduced brachial pulse pressure by 4.7 +/- 1.6 mm Hg (P < 0.05) without changing mean arterial pressure…Folic acid is a safe and effective supplement that targets large artery stiffness and may prevent isolated systolic hypertension."	311	
Low fat dairy	Associated with lower rate of HTN (only **low-fat** dairy)	"a prospective study conducted in 5880 university graduates in Spain, aged >20 y in 2000 (x age: 37 y), free of hypertension and cardiovascular disease at baseline, and followed-up with mailed questionnaires for a median of 27 mo…One hundred eighty new cases of hypertension were identified. The hazard ratio of hypertension between extreme quintiles of low-fat dairy product consumption was 0.46 (95% CI: 0.26, 0.84; P for trend = 0.02) after adjustment for the main known risk factors for hypertension and several dietary factors… low-fat dairy consumption, but not whole-fat dairy consumption, was associated with a lower risk of incident hypertension."	312	
		"5880 university graduates in Spain … mean age: 37 y … followed-up with mailed questionnaires for a median of 27 mo… One hundred eighty new cases of hypertension were identified. The hazard ratio of hypertension between extreme quintiles of low-fat dairy product consumption was 0.46 (95% CI: 0.26, 0.84; P for trend = 0.02) after adjustment for the main known risk factors for hypertension and several dietary factors. No significant association between whole-fat dairy products or total calcium intake and incident hypertension was seen."	313	
Sleep	≤ 5 hr/night raises BP (obesity risk too)	"Sleep durations of </=5 hours per night were associated with a significantly increased risk of hypertension (hazard ratio, 2.10; 95% CI, 1.58 to 2.79) in subjects between the ages of 32 and 59 years, and controlling for the potential confounding variables only partially attenuated this relationship. The increased risk continued to be significant after controlling for obesity and diabetes, which was consistent with the hypothesis that these variables would act as partial mediators. Short sleep duration could, therefore, be a significant risk factor for hypertension."	314	

Go to TOC

Vitamins, minerals, supplements and spices

Other possible supplements

I simply do not have enough reliable information on these things to comment much, but they look promising based on various claims. I await better studies.

Metformin (antidiabetic drug) has been shown to substantially increase lifespan in rodent models, an average of 21%!

Hormone replacement therapy for those older than age 50 (natural production of hormones such as melatonin, growth hormone, sex hormones, etc. decline dramatically at about this age, possibly with detrimental effects). Unfortunately hormone replacement may also increase the rates of aging and cancer (such as prostate cancer). I think this is likely to be a BAD idea in all cases I know of.

A combination of R(+) alpha lipoic acid and acetyl-L-carnitine that appears to simultaneously increase energy ("youthfulness") in rats, and act as a potent antioxidant where it counts – the mitochondria.

The former helps you feel better as you age, the latter may help slow the aging process. Sounds "too good to be true", but has the positive signs of support by the NIH, and research done at UC Berkeley. These positive effects have been confirmed anecdotally in people; a high-quality clinical trial is currently under way. Racemic alpha lipoic acid is currently available as a dietary supplement "Juvenon" – at a cost: $39.95 + S&H. I have started taking this myself… Note: the racemic alpha lipoic acid is a mixture of R and S enantiomers (mirror-images); the R form is active, the S form is at best inactive, and at worst harmful. Articles supporting R(+) alpha lipoic acid are: (FASEB J 1998 Sep;12(12):1183-9; PMID 9737721, FASEB J 1999 Feb;13(2):411-8 ; PMID 9973329, Antioxid Redox Signal 2000 Fall;2(3):473-83 ; PMID 11229361, FASEB J 2001 Mar;15(3):700-6 ; PMID 11259388, Proc Natl Acad Sci U S A 2002 Feb 19;99(4):1870-5; PMID 11854487, Proc Natl Acad Sci U S A 2002 Feb 19;99(4):1876-81; PMID 11854488, Proc Natl Acad Sci U S A 2002 Feb 19;99(4):2356-61; PMID 11854529, Hagen TM, Moreau R, Suh JH, Visioli F. Mitochondrial decay in the aging rat heart: evidence for improvement by dietary supplementation with acetyl-L-carnitine and/or lipoic acid. Ann N Y Acad Sci. 2002 Apr;959:491-507. Review. PMID: 11976222; Hagen TM, Liu J, Lykkesfeldt J, Wehr CM, Ingersoll RT, Vinarsky V, Bartholomew JC, Ames BN. Feeding acetyl-L-carnitine and lipoic acid to old rats significantly improves metabolic function while decreasing oxidative stress. Proc Natl Acad Sci U S A. 2002 Feb 19;99(4):1870-5. PMID: 11854487).

Creatine seems to improve brain function as well as sports performance. "we tested the hypothesis that oral creatine supplementation (5 g d(-1) for six weeks) would enhance intelligence test scores and working memory performance in 45 young adult, vegetarian subjects in a double-blind, placebo-controlled, cross-over design. Creatine supplementation had a significant positive effect ($p < 0.0001$) on both working memory (backward digit span) and intelligence (Raven's Advanced Progressive Matrices), both tasks that require speed of processing. These findings underline a dynamic and significant role of brain energy capacity in influencing brain performance." (**Rae C, Digney AL, McEwan SR, Bates TC.** Oral creatine monohydrate supplementation improves brain performance: a double-blind, placebo-controlled, cross-over trial. Proc R Soc Lond B Biol Sci. 2003 Oct 22;270(1529):2147-50. PMID: 14561278)

See also homocysteine.

Category	Effect	Finding	Ref	Fig
Recommended vitamin doses		This web site has a list. "The Dietary Reference Intakes (DRI) are the most recent set of dietary recommendations established by the Food and Nutrition Board of the Institute of Medicine, 1997-2001. They replace previous RDAs"	315	
Folate	Reduces colon cancer risk by 40%	"Epidemiologic and clinical studies indicate that dietary folate intake and blood folate levels are inversely associated with colorectal cancer risk. Collectively, these studies suggest an □40% reduction in the risk of colorectal cancer in individuals with the highest dietary folate intake compared with those with the lowest intake."	316	
	Strongly associated with reduced dementia	A study of 228 subjects found that low folate levels or high homocysteine levels were strongly associated with mild cognitive development, vascular dementia, and Alzheimer disease. (approximately 3-fold increased risk)	317	
	Associated with decreased risk of HTN	"younger women who consumed at least 1000 microg/d of total folate (dietary plus supplemental) had a decreased risk of hypertension"	318	
	Dose-response reduction in homocysteine. Maximum effect is at about 0.8 mg	"daily doses of 0.2, 0.4, 0.8, 2.0, and 5.0 mg folic acid were associated with reductions in homocysteine of 13% (95% CI: 10%, 16%), 20% (17%, 22%), 23% (21%, 26%), 23% (20%, 26%), and 25% (22%, 28%), respectively. Vitamin B-12 (x: 0.4 mg/d) produced 7% (95% CI: 4%, 9%) further reduction in homocysteine concentrations, but vitamin B-6 had no significant effect."	319	
Folate and B12	Older people need them	"…significant vitamin B12 deficiency increased with age in all three studies, from about 1 in 20 among people aged 65-74 years to 1 in 10 or even greater among people aged 75 years or greater. The prevalence of folate deficiency also increased with age, and was similar to that for vitamin B12 deficiencies…"	320	
Vitamin D	Supplements help	"Relative risk of falling in the groups supplemented with vitamin D	321	

	vs osteoporosis	was 0.48 (95% CI 0.26-0.90) compared with controls. CONCLUSION: Vitamin D supplementation, either orally or with injected vitamin D, suppresses parathyroid hormone, increases bone mineral density and reduces falls." [Note from other sources: exercise also helps; calcium supplements and milk may not.]		
	Take cholecalciferol (D3), NOT ergocalciferol (D2)	"vitamin D(3) [chlecalciferol] has proven to be the more potent form of vitamin D in all primate species, including humans…the form of vitamin D used in major preparations of prescriptions in North America is vitamin D(2)…Vitamin D(2), or ergocalciferol, should not be regarded as a nutrient suitable for supplementation or fortification."	322	
	May help prevent multiple sclerosis (MS)	This could explain the long-observed fact that those who grow up in northern areas tend to have a higher incidence of MS. "Intake of vitamin D from supplements was also inversely associated with risk of MS; the RR comparing women with intake of >or=400 IU/day with women with no supplemental vitamin D intake was 0.59 (95% CI = 0.38 to 0.91; p for trend = 0.006). No association was found between vitamin D from food and MS incidence."	323	
		"Prospective, nested case-control study among more than 7 million US military personnel who have serum samples stored in the Department of Defense Serum Repository. Multiple sclerosis cases were identified through Army and Navy physical disability databases for 1992 through 2004, and diagnoses were confirmed by medical record review. Each case (n = 257) was matched to 2 controls by age, sex, race/ethnicity, and dates of blood collection. Vitamin D status was estimated by averaging 25-hydroxyvitamin D levels of 2 or more serum samples collected before the date of initial multiple sclerosis symptoms. MAIN OUTCOME MEASURES: Odds ratios of multiple sclerosis associated with continuous or categorical levels (quantiles or a priori-defined categories) of serum 25-hydroxyvitamin D within each racial/ethnic group. RESULTS: **Among whites (148 cases, 296 controls), the risk of multiple sclerosis significantly decreased with increasing levels of 25-hydroxyvitamin D (odds ratio [OR] for a 50-nmol/L increase in 25-hydroxyvitamin D, 0.59**; 95% confidence interval, 0.36-0.97). In categorical analyses using the lowest quintile (<63.3 nmol/L) as the reference, the ORs for each subsequent quintile were 0.57, 0.57, 0.74, and 0.38 (P = .02 for trend across quintiles). Only the OR for the highest quintile, corresponding to 25-hydroxyvitamin D levels higher than 99.1 nmol/L, was significantly different from 1.00 (OR, 0.38; 95% confidence interval, 0.19-0.75; P = .006). **The inverse relation with multiple sclerosis risk was particularly strong for 25-hydroxyvitamin D levels measured before age 20 years**…**The results of our study suggest that high circulating levels of vitamin D are associated with a lower risk of multiple sclerosis**."	324	
	You should take MORE than the RDA	"The recommended adequate intakes for vitamin D are inadequate, and, in the absence of exposure to sunlight, a minimum of 1000 IU vitamin D/d is required to maintain a healthy concentration of 25(OH)D in the blood."	325	
	The upper limit of vitamin D intake should be no less than **10,000 IU** per day	"Except in those with conditions causing hypersensitivity, there is no evidence of adverse effects with serum 25(OH)D concentrations <140 nmol/L, which require a total vitamin D supply of 250 microg (10000 IU)/d to attain. Published cases of vitamin D toxicity with hypercalcemia, for which the 25(OH)D concentration and vitamin D dose are known, all involve intake of > or = 1000 microg (40000 IU)/d. Because vitamin D is potentially toxic, intake of >25 microg (1000 IU)/d has been avoided even though the weight of evidence shows that the currently accepted, no observed adverse effect limit	326	

		of 50 microg (2000 IU)/d is too low by at least 5-fold."		
	May help prevent some cancers	"Inverse correlations are found for UV-B radiation for a number of cancers, with those for bladder, breast, endometrial, ovarian, prostate, and renal cancer, and multiple myeloma and NHL having the strongest correlations in this and ongoing multicountry ecologic studies. These studies add further support for the role of UV-B radiation and vitamin D in reducing the risk of a large number of cancers."	327	
		"**daily intake of 1,000 international units (IU) or 25 micrograms(*μg*) of vitamin D3 may lower the risk of developing colon, breast, prostate and ovarian cancers by up to 50 percent**…Vitamin D supplements may be needed to supplement dietary sources of vitamin D, which are likely not enough to provide 1,000 IU daily recommended by the researchers of the current study. One glass of milk may offer only 100 IU of vitamin D." "Vitamin D status differs by latitude and race, with residents of the northeastern United States and individuals with more skin pigmentation being at increased risk of deficiency. A PubMed database search yielded 63 observational studies of vitamin D status in relation to cancer risk, including 30 of **colon**, 13 of **breast**, 26 of **prostate**, and 7 of **ovarian** cancer, and several that assessed the association of vitamin D receptor genotype with cancer risk. The majority of studies found a protective relationship between sufficient vitamin D status and lower risk of cancer. The evidence suggests that efforts to improve vitamin D status, for example by **vitamin D supplementation, could reduce cancer incidence and mortality at low cost, with few or no adverse effects.**"	328 329	
	May help prevent periodontal disease	A study of 11,202 subjects found that for those >50 yr of age, "Compared with men in the highest $25(OH)D_3$ [vitamin D] quintile, those in the lowest quintile had a mean [periodontal attachment loss] that was 0.39 mm (95% CI: 0.17, 0.60 mm) higher; in women, the difference in [periodontal attachment loss] between the lowest and highest quintiles was 0.26 mm (0.09, 0.43 mm)."	330	
	May help prevent infection	Detailed in a summary article in Science News	331	
	Good summary article	From Science News. The messages: Vitamin D helps prevent muscle problems, immune problems, etc. and you need to take much more vitamin D than the RDA.	332	
	Made on sun exposure	From Wikipedia, "**At higher latitudes, total vitamin D input from sunlight is usually insufficient, especially in the winter**." "Vitamin D_3... is derived from animal sources and is made in the skin when 7-dehydrocholesterol reacts with UVB ultraviolet light with wavelengths 290 to 315 nm. **These wavelengths are present in sunlight at sea level when the sun is more than 45°** above the horizon, or when the UV index is greater than 3." Note: the best way to get enough vitamin D3 is from (cheap) supplements, because UV exposure (sunlight) results in skin cancers.		
Vitamins C & E	Associated with reduced Alzheimer Disease risk	A cross-sectional, prospective study from Utah of 4740 people > 64 yr. old found that "Use of vitamin E and C (ascorbic acid) supplements in combination was associated with reduced AD prevalence (adjusted odds ratio, 0.22; 95% confidence interval, 0.05-0.60) and incidence (adjusted hazard ratio, 0.36; 95% confidence interval, 0.09-0.99). A trend toward lower AD risk was also evident in users of vitamin E and multivitamins containing vitamin C, but	333	

		we saw no evidence of a protective effect with use of vitamin E or vitamin C supplements alone, with multivitamins alone, or with vitamin B-complex supplements."		
Vitamin E (alpha-tocopherol)	Does NOT help prevent heart disease	"…strong support for a lack of statistically significant or clinically important effects of vitamin E on cardiovascular disease."	334	
	Associated with HIGHER all-cause mortality	"PURPOSE: To perform a meta-analysis of the dose-response relationship between vitamin E supplementation and total mortality by using data from randomized, controlled trials. PATIENTS: 135,967 participants in 19 clinical trials… A dose-response analysis showed a statistically significant relationship between vitamin E dosage and all-cause mortality, with increased risk of dosages greater than 150 IU/d… CONCLUSION: High-dosage (> or =400 IU/d) vitamin E supplements may increase all-cause mortality and should be avoided."	335	
Iron	Too low an iron level is bad	Very low iron levels (iron deficiency) causes increased mitochondrial oxidation => accelerated aging and neural decay.	336	
	Iron supplements may possibly cause intestinal damage	An 80 mg iron dose study found "These data show that a single dosage of ferrous sulfate induces oxidative damage … in the small intestine in vivo in healthy volunteers." Review of iron's effects on the bowel	337 338	
Acetyl-L-carnitine	May reduce age-related changes in brain lipids	"…changes in membrane lipid metabolism and/or composition represent one of the alterations occurring in rat brain with aging, and that long-term feeding with acetyl-L-carnitine can be useful in normalizing these age-dependent disturbances."	339	
Curcumin	Should be eaten with pepper	The possibly beneficial compound curcumin is found in the spice turmeric. However, it is almost completely metabolized by the intestine and liver by glucuronidation. Piperine found in peppers inhibits this metabolism. "Concomitant administration of piperine 20 mg produced much higher concentrations from 0.25 to 1 h post drug ($P < 0.01$ at 0.25 and 0.5 h; $P < 0.001$ at 1 h), the increase in bioavailability was 2000%." Peppers have about 6% piperine, which accounts for its pungent flavor (see http://www-ang.kfunigraz.ac.at/~katzer/engl/generic_frame.html?Curc_lon.html) . Turmeric has about 4% curcumin (http://www-ang.kfunigraz.ac.at/~katzer/engl/generic_frame.html?Curc_lon.html) .	340	
	Associated with lesser cognitive decline	"The authors investigated the association between usual curry consumption level and cognitive function in elderly Asians. In a population-based cohort (n = 1,010) of nondemented elderly Asian subjects aged 60-93 years in 2003, the authors compared Mini-Mental State Examination (MMSE) scores for three categories of regular curry consumption…Those who consumed curry "occasionally" and "often or very often" had significantly better MMSE scores than did subjects who "never or rarely" consumed curry."	341	
Calcium	Associated with lower rate of colon cancer	"After adjustment for known risk factors, adenoma risk was lower by 12% for participants in the highest quintile of total calcium intake (>1767 mg/d) than for participants in the lowest quintile (<731 mg/d) (odds ratio: 0.88; 95% CI: 0.76, 1.02; *P* for trend = 0.04). The protective association between total calcium and colorectal adenoma was largely due to calcium supplement use, with a 27% decrease in adenoma risk for participants taking >1200 mg/d than for nonusers of supplements (odds ratio: 0.73; 95% CI: 0.56, 0.91; *P* for trend = 0.005)."	342	

	Lower rate of stroke and death	"The multivariate relative risk for men with highest versus lowest quintiles of dairy calcium intake was 0.53 (95% CI, 0.34 to 0.81) for total stroke, 0.46 (0.23 to 0.91) for hemorrhagic stroke, and 0.53 (0.29 to 0.99) for ischemic stroke; corresponding relative risks for women were 0.57 (0.38 to 0.86), 0.51 (0.28 to 0.94), and 0.50 (0.27 to 0.95). CONCLUSIONS: Dietary calcium intake from dairy products was associated with reduced mortality from stroke for Japanese men and women."	[343]	
Magnesium	High intake associated with 33% lower rate of diabetes type 2	"We followed 85,060 women and 42,872 men who had no history of diabetes… After 18 years of follow-up in women and 12 years in men… After adjusting for age, BMI, physical activity, family history of diabetes, smoking, alcohol consumption, and history of hypertension and hypercholesterolemia at baseline, the relative risk (RR) of type 2 diabetes was 0.66 (95% CI 0.60-0.73; P for trend <0.001) in women and 0.67 (0.56-0.80; P for trend <0.001) in men, comparing the highest with the lowest quintile of total magnesium intake… **This study supports the dietary recommendation to increase consumption of major food sources of magnesium, such as whole grains, nuts, and green leafy vegetables**."	[344]	
	Sources of magnesium[345]	**Source** / **Serving** / **Magnesium (mg)** 100% Bran Cereal (e.g. All Bran) / 1/2 cup / 128.7 Spinach, chopped / 1/2 cup cooked / 78.3 Almonds / 1 ounce / 81.1 Oat bran / 1/2 cup dry / 96.4		
	Associated with a lower rate of colon cancer (in dietary sources)	"a population-based prospective cohort of 61,433 women aged 40 to 75 years without previous diagnosis of cancer at baseline from 1987 to 1990… During a mean of 14.8 years (911 042 person-years) of follow-up, 805 incident colorectal cancer cases were diagnosed. After adjustment for potential confounders, we observed an **inverse association of magnesium intake with the risk of colorectal cancer** (P for trend = .006). Compared with women in the lowest quintile of	[346]	

		magnesium intake, the multivariate rate ratio (RR) was 0.59 (95% confidence interval [CI], 0.40-0.87) for those in the highest quintile. The inverse association was observed for both colon (**RR, 0.66**; 95% CI, 0.41-1.07) and rectal cancer (**RR, 0.45**; 95% CI, 0.22-0.89)."		
		"a cohort of 35,196 Iowa women initially free of cancer and aged 55-69 years in 1986. Intakes of magnesium and other nutrients were assessed by food frequency questionnaire at baseline. Over 17 years of follow-up through 2002, 1,112 women developed colorectal cancer. After adjustment for age, energy, other nutrients, and risk factors for colorectal cancer, the hazard ratios of colorectal cancer across quintiles of magnesium intake were 1.00, 0.96, 0.83, 0.87, and 0.80 (95% confidence interval: 0.62, 1.03; ptrend = 0.06). The association was largely absent for rectal cancer but, for colon cancer, the hazard ratios were 1.00, 1.00, 0.88, 0.85, and 0.77 (95% confidence interval: 0.58, 1.03; ptrend = 0.04). These findings offer further evidence that a diet high in magnesium may reduce the occurrence of colon cancer among women."	[347]	
	Associated with better muscle function in the elderly	"From among 1453 randomly selected community residents completing a home interview, 1138 men (46%) and women (aged 66.7 ± 15.2 y; x̄ ± SD) with complete data on muscle performance and serum magnesium who were not severely cognitively compromised … were included in the analysis. Muscle performance was evaluated by grip strength, lower-leg muscle power, knee extension torque, and ankle extension isometric strength and was normalized for age and body mass index (BMI) within each sex. Results: After adjustment for age, sex, BMI, laboratory variables, presence of chronic diseases, muscle area, muscle density, and physical activity level, **serum magnesium concentrations were significantly associated with indexes of muscle performance**, including grip strength …, lower-leg muscle …, knee extension torque …, and ankle extension strength"	[348]	
	Associated with lesser severity of asthma	"37 patients (aged 7-19 years, 19 males) were randomized in two groups: magnesium (n=18, 300 mg/day) and placebo (n=19), during 2 months. …The primary outcome was bronchial reactivity…The magnesium group presented fewer asthma exacerbations and used less salbutamol compared to the placebo group. Conclusions: **Oral magnesium supplementation helped to reduce bronchial reactivity** to methacholine, to diminish their allergen-induced skin responses and to provide better symptom control in pediatric patients with moderate persistent asthma treated with inhaled fluticasone."	[349]	
Selenium	May help reduce the risk of prostate cancer	"A large body of epidemiological evidence, including observational, case-control, cohort and randomized controlled clinical trials, support the proposition that selenium may prevent prostate cancer in humans."	[350]	
Benfotiamine (a niacin derivative, available as a supplement)	Helps prevent glucose damage to the retina	"Three of the major biochemical pathways implicated in the pathogenesis of hyperglycemia induced vascular damage (the hexosamine pathway, the advanced glycation end product (AGE) formation pathway and the diacylglycerol (DAG)-protein kinase C (PKC) pathway) are activated by increased availability of the glycolytic metabolites glyceraldehyde-3-phosphate and fructose-6-phosphate. We have discovered that the lipid-soluble thiamine derivative benfotiamine can inhibit these three pathways, as well as hyperglycemia-associated NF-kappaB activation, by activating the pentose phosphate pathway enzyme transketolase, which converts glyceraldehyde-3-phosphate and fructose-6-phosphate into pentose-5-phosphates and other sugars. In retinas of diabetic animals, benfotiamine treatment inhibited these three pathways and NF-kappaB activation by activating transketolase, and also prevented	[351]	

		experimental diabetic retinopathy. The ability of benfotiamine to inhibit three major pathways simultaneously might be clinically useful in preventing the development and progression of diabetic complications."		
	Helps prevent damage from glucose (AGEs, diabetes)	Benfotiamine helps prevent diabetic nephropathy (kidney disease)	352	
Make sure your nutrition is adequate	CR mice live longer with optimal diet	Six groups of mice were studied with variations in diet quality (standard diet vs. enriched for protein, vitamins and minerals) and % CR. The CR mice survived longer than the ad lib mice; the CR + optimal diet survived longest of all and were healthiest.	353	
B12	Helps prevent osteoporosis	From the Framingham Offspring Osteoporosis Study (1996-2001): "Both men and women with vitamin B12 concentrations <148 pM had lower average BMD than those with vitamin B12 above this cut-off. These differences were significant ($p < 0.05$) for men at most hip sites and for women at the spine."	354	
	Deficiency is common in the elderly	"This was a cross-sectional survey of 84 nondemented elderly participants (aged >69 y) from the Welsh cohort…Nearly one-half (43%) of the persons selected had likely metabolically significant vitamin B-12 deficiency." And this was associated with decreased mental function.	355	
Calcium	May NOT prevent osteoporosis		356	
Beta carotene, vitamins C and E, and zinc		"Dietary intake was assessed at baseline in the Rotterdam Study (1990-1993) using a semiquantitative food frequency questionnaire. Incident AMD until final follow-up in 2004 was determined by grading fundus color transparencies in a masked way according to the International Classification and Grading System. SETTING: Population-based cohort of all inhabitants aged 55 years or older in a middle-class suburb of Rotterdam, the Netherlands. PARTICIPANTS: Of 5836 persons at risk of AMD at baseline, 4765 had reliable dietary data and 4170 participated in the follow-up. MAIN OUTCOME MEASURE: Incident AMD, defined as soft distinct drusen with pigment alterations, indistinct or reticular drusen, geographic atrophy, or choroidal neovascularization. RESULTS: Incident AMD occurred in 560 participants after a mean follow-up of 8.0 years (range, 0.3-13.9 years). Dietary intake of both vitamin E and zinc was inversely associated with incident AMD. The hazard ratio (HR) per standard deviation increase of intake for vitamin E was 0.92 (95% confidence interval [CI], 0.84-1.00) and for zinc was 0.91 (95% CI, 0.83-0.98). An above-median intake of all 4 nutrients, beta carotene, vitamin C, vitamin E, and zinc, was associated with a 35% reduced risk (HR, 0.65; 95% CI, 0.46-0.92) of AMD. Exclusion of supplement users did not affect the results. CONCLUSION: In this study, a high dietary intake of beta carotene, vitamins C and E, and zinc was associated with a substantially reduced risk of AMD in elderly persons."	357	

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General and Broad recommendations

Category	Effect	Finding	Ref	Fig
Overall diet recommendations vs. coronary heart disease	Cut some fats Increase intake of whole grains, omega-3 fats,	"**Compelling evidence from metabolic studies, prospective cohort studies, and clinical trials in the past several decades indicates that at least 3 dietary strategies are effective in preventing CHD: substitute nonhydrogenated unsaturated fats for**	358	

(CHD)	fruit and vegetables	**saturated and trans-fats; increase consumption of omega-3 fatty acids from fish, fish oil supplements, or plant sources; and consume a diet high in fruits, vegetables, nuts, and whole grains and low in refined grain products**. … Substantial evidence indicates that diets using nonhydrogenated unsaturated fats as the predominant form of dietary fat, whole grains as the main form of carbohydrates, an abundance of fruits and vegetables, and adequate omega-3 fatty acids can offer significant protection against CHD. Such diets, together with regular physical activity, avoidance of smoking, and maintenance of a healthy body weight, may prevent the majority of cardiovascular disease in Western populations."		
Fats and carbohydrates	Altering fat and carbohydrate intake works better than medicine to reduce cardiovascular disease risk factors	A thorough review of the literature to date. Among other things: 1. **Diet works better than medicine**: "The reductions in cardiovascular disease (CVD) caused by these dietary therapies compare favorably with drug treatments for hyperlipidemia and hypertension." 2. "The n-3 polyunsaturated fats in fish oils suppress cardiac arrhythmias and reduce triglycerides, but they have little effect on LDL or HDL cholesterol levels." 3. "…triglycerides increase … when carbohydrate increases, except when low glycemic index foods are used."	[359]	
		"Diets higher in MUFA, higher in fiber with a low glycemic index continue to show advantages in reducing risk and risk factors for chronic disease, especially those associated with insulin resistance. The simple classification of diets into high-fat versus high-carbohydrate appears less helpful in predicting the metabolic outcome."	[360]	
Food pyramid	Revised based on modern nutritional understanding	Base of pyramid is whole grains, specific vegetable oils, vegetables, fruit and nuts! This is worth looking at on line (see the reference).	[361]	
Breakfast		One study looked at the breakfast habits of "...262 volunteers aged between 21 and 85 years, mean age: 60.9 years... The results showed that those who consumed breakfast cereal every day reported better mental and physical health than those who consumed it less frequently. This association was still present when demographic factors [including] other aspects of diet were covaried."	[362]	
		Another study evaluated the effects of breakfast and coffee on 142 volunteers. "…The results showed that those who consumed breakfast cereal had a more positive mood at the start of the test sessions, performed better on a spatial memory task, and felt calmer at the end of the test session than those in the no breakfast condition. Ingestion of caffeine had no effect on initial mood or working memory, but it did improve encoding of new information and counteracted the fatigue that developed over the test session. Caffeine increased blood pressure and pulse rate, whereas breakfast cereal consumption only had an effect on pulse."	[363]	
		A meta-analysis of three studies (not including the above two studies) concluded that breakfast improves memory-task performance.	[364]	
		"[Omitting breakfast] impairs fasting lipids and postprandial insulin sensitivity and could lead to weight gain if the observed higher energy intake was sustained."	[365]	
Protein	Vegetable protein in large amounts may help vs. HTN and heart disease	"Recent evidence suggests that an increased intake of protein, particularly plant protein, may lower blood pressure and reduce the risk of cardiovascular disease. However, the data are not sufficiently compelling to advocate an increased consumption of protein."	[366]	

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Toxins and carcinogens

Category	Effect	Finding	Ref	Fig
Iron and manganese	Associated with increased risk of Parkinson Disease	"Subjects with an iron intake in the highest quartile compared with those in the lowest quartile had an increased risk of PD (odds ratio = 1.7, 95% CI: 1.0, 2.7, trend p = 0.016). There was an apparent joint effect of iron and manganese; dietary intake above median levels of both together conferred a nearly doubled risk compared with lower intakes of each nutrient (odds ratio = 1.9…"	367	
Iron	Supplements damage the GI tract	A review discusses the toxic effects of iron supplements, particularly when taken with vitamin C. "Co-supplementation of ferrous salts with vitamin C exacerbates oxidative stress in the gastrointestinal tract, predisposing individuals to ulceration, inflammatory disorders, and exacerbation of existing chronic disorders and may cause cancer."	368	
Mercury	Even LOW LEVEL exposure in ADULTS affects neurologic performance	"The strongest effects of mercury on persons in this study were detected on tests of fine motor speed and dexterity (Bead Threading) and response inhibition (errors of commission or "false alarms" on the timed visual search and attention tasks). The size of the effects increased with hair mercury concentration, consistent with a dose-dependent effect…the public health impacts of MeHg exposure at levels often encountered by adults in North America [2] may be inducing adverse effects on neurobehavioral performance."	369	
Polycyclic aromatic hydrocarbons (PAH)	Smoke flavor has small amounts of PAH and is safer than grilling	"…the flavoring obtained from poplar wood presents the highest number and concentrations of both total and carcinogenic PAHs, even though the levels of these latter are very low."	370	
	How to reduce PAHs from grilling	From AICR: Best, do not grill! Also: pre-heat the meat, use sauces and marinades for flavor, use low-fat meat, grill far from hot coals or flames.	371 372	
Risk factors for Parkinson Disease	Lead & copper, insecticide, family history, smoking	A "health system population-based case-control study of epidemiological risk factors" found that ">20 years joint occupational exposure to lead and copper (p=0.009; population attributable risk [PAR]=3.9%), occupational exposure to insecticides (p=0.002; PAR=8.1%), a positive family history of PD in first- and second-degree relatives (p=0.001; PAR=12.4%), and smoking </=30 pack-years or not smoking (p=0.005; PAR=41.4%)." Altogether these could account for 54% of Parkinson Disease.	373	
Aluminum	May cause Alzheimer Disease (n.b., there is very limited epidemiologic evidence)	"Aluminum (Al) has been etiologically and epidemiologically related to several neurologic conditions, including Alzheimer's disease (AD)." In rats, chronic high dose aluminum exposure, "The experimental animals had impaired spatial memory, with lower and more fluctuant performance at Morris water maze…The brains of experimental animals, studied by optical microscopy, displayed a massive cellular depletion in the hippocampal formation, …The hippocampus contained extracellular accumulations of Al and amyloid … These behavioral and neuropathological modifications associated with long-term exposure to Al are reminiscent of those observed in AD."	374	
Aluminum and Fluoride	High concentration in tea, may cause toxic accumulations	"Tea plant takes up a large quantity of aluminium (Al) and fluoride (F) from acidic soils. It has been known that fluorosis can be developed for people who consume a large quantity of tea made from brick tea, a low quality tea consisting mainly of old tea leaves in China."	375	
Pesticides	Some fruit and vegetables have more than others *I personally think this does not matter much*	See the table at http://www.foodnews.org/reportcard.php 12 Most Contaminated . Apples . Bell Peppers . Celery . Cherries . Imported Grapes		

	compared to other factors	. Nectarines . Peaches . Pears . Potatoes . Red Raspberries . Spinach . Strawberries 12 Least Contaminated . Asparagus . Avocados . Bananas . Broccoli . Cauliflower . Corn (sweet) . Kiwi . Mangos . Onions . Papaya . Pineapples . Peas (sweet)		
Soy	May (very limited evidence) be associated with cognitive decline	"Poor cognitive test performance, enlargement of ventricles and low brain weight were each significantly and independently associated with higher midlife tofu consumption…Odds ratios comparing endpoints among "high-high" with "low-low" consumers were mostly in the range of 1.6 to 2.0."	[376]	
	Worsens heart disease in a mouse model that may or may not be relevant to humans	"We report that dietary modification from a soy-based diet to a casein-based diet radically improves disease indicators and cardiac function in a transgenic mouse model of hypertrophic cardiomyopathy. On a soy diet, males with a mutation in the alpha-myosin heavy chain gene progress to dilation and heart failure. However, males fed a casein diet no longer deteriorate to severe, dilated cardiomyopathy."	[377]	
Vitamin E (alpha-tocopherol)	Associated with HIGHER all-cause mortality	"PURPOSE: To perform a meta-analysis of the dose-response relationship between vitamin E supplementation and total mortality by using data from randomized, controlled trials. PATIENTS: 135,967 participants in 19 clinical trials… A dose-response analysis showed a statistically significant relationship between vitamin E dosage and all-cause mortality, with increased risk of dosages greater than 150 IU/d… CONCLUSION: High-dosage (> or =400 IU/d) vitamin E supplements may increase all-cause mortality and should be avoided."	[378]	
Lead	Is at a high level in chocolate	"lead concentrations of manufactured cocoa and chocolate products were as high as 230 and 70 ng/g, respectively, which are consistent with market-basket surveys that have **repeatedly listed lead concentrations in chocolate products among the highest reported for all foods.** One source of contamination of the finished products is tentatively attributed to atmospheric emissions of leaded gasoline, which is still being used in Nigeria. Because of the high capacity of cocoa bean shells to adsorb lead, contamination from leaded gasoline emissions may occur during the fermentation and sun-drying of unshelled beans at cocoa farms." Equal Exchange sources their cocoa from cooperatives in the Dominican Republic, where leaded gasoline has been totally banned since 1999, so the lead issue SHOULD be largely obviated.	[379] [380]	
Air pollution	Correlated with high risk of heart attack	Perhaps fine particulates. "The findings of the study support the hypothesis that particles can induce cardiovascular disease through inflammatory pathways, suggestive of a greater toxicity of traffic-related particles."	[381]	
Copper	Associated with late-life mental decline, when in	Multi-vitamins often have 2 mg of copper; this may be one of the causes of mental decline or Alzheimer Disease. Those with the highest copper and bad fat intake added the equivalent of 19 years to	[382]	

	association with trans or saturated fats	their ages in terms of mental decline. "Evidence from prospective epidemiologic studies and animal models suggests that intakes of dietary fats and copper may be associated with neurodegenerative diseases… **Among persons whose diets were high in saturated and trans fats, higher copper intake was associated with a faster rate of cognitive decline.** In multiple-adjusted mixed models, the difference in rates for persons in the highest (median, 2.75 mg/d) vs lowest (median, 0.88 mg/d) quintiles of total copper intake was -6.14 standardized units per year (P<.001) or the equivalent of 19 more years of age. There was also a marginally statistically significant association (P = .07) with the highest quintile of food intake of copper (median, 1.51 mg/d) and a **strong dose-response association with higher copper dose in vitamin supplements.** Copper intake was not associated with cognitive change among persons whose diets were not high in these fats."		
	Associated with higher death rate	"Data from the Paris Prospective Study 2, a cohort of 4035 men age 30-60 years at baseline, were used to assess the association between serum zinc, copper, and magnesium and all-cause, cancer, and cardiovascular disease mortality…During 18-year follow up, 339 deaths occurred, 176 as a result of cancer and 56 of cardiovascular origin. Relative risks (RRs) for each element were inferred using Cox's proportional hazard model after controlling for various potential confounders. RESULTS: **High copper values (4th quartile) were associated with a 50% increase in RRs for all-cause deaths** … **High magnesium values were negatively related to mortality with a 40% decrease in RR for all-cause**"	[383]	
Cinnamon	Contains coumarin	Coumarin (also used in rat poison) can cause cancer and liver damage. The levels of coumarin in cinnamon can be very high. A little on applesauce is OK, but large quantities are not. "Ceylon cinnamon" has substantially lower levels of coumarin than cassia or Chinese cinnamon (1/10th).	[384]	
Stevia		"In one of the rat studies (14), a 13-week dose-finding study, cell necrosis in the liver of all treated males was reported (lowest dose equivalent to 155 mg/kg bw) "	[385]	

Cholesterol

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Ultraviolet light

Get out of the sun, and use maximum sun block (SPF 45 to 50) if you have to be out in the sun. The sun block should be broad spectrum, protecting well against both UVA and UVB; microfine / micronized zinc oxide is perhaps the best. UVB is far more damaging than UVA, but there is far more UVA from the sun. UVA exposure has been shown to damage mitochondria, in effect hastening aging (Koch H, Wittern KP, Bergemann J. In human keratinocytes the Common Deletion reflects donor variabilities rather than chronologic aging and can be induced by ultraviolet A irradiation. J Invest Dermatol. 2001 Oct;117(4):892-7. PMID: 11676829). Sun block should be re-applied frequently depending on what you are doing. A sign in the Dermatology Clinic at my hospital says "Wear sun block all day, every day." A suntan is not enough to protect you. Besides causing the very common skin cancer, sunlight (along with smoking) is responsible for much of the premature skin aging changes, including wrinkles. If you wonder if it really makes a difference, just look at the top and bottom of your forearm. The top was exposed to the sun a lot: if you are like me it is covered with spots, wrinkles, and blemishes. The bottom is relatively protected and is child-like. The best protection is to avoid exposure by wearing clothes and a hat; UV-protecting sunglasses or polycarbonate glasses will protect your eyes and eyelids.

Potential problems: Sunlight helps your body make the active form of vitamin D: just make sure you get enough vitamin D in your diet.

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Protein

When I was growing up – indeed, until recently – I thought that the primary sources of protein were meat, cheese, beans and nuts. Well… there are two primary issues in choosing quality protein.

1. "Completeness" of the protein: does the protein in your whole diet contain enough of each of the essential amino acids? Protein from limited vegetables alone may not be complete, while protein from meat is.
2. What proportion of the food calories is from protein? For example, it is easy to think that salmon is a better source of protein than spinach. However, only 43% of the calories in salmon are protein, while 50% of spinach's calories are protein. Vegetables like spinach and broccoli (43%) have more protein per calorie than nuts (4-20%), peanut butter (19%), most meats, cheese (24%) or skim milk (40%).

Category	Effect	Finding	Ref	Fig
Vegetable protein	Lessens risk of cholecystectomy (from gallstones)	From the Nurses' Health Study, "the relative risk for animal protein intake was 1.07 (95% CI: 0.98, 1.15; p for trend = 0.08), whereas the relative risk for vegetable protein intake was 0.79 (95% CI: 0.71, 0.88; p for trend < 0.0001), with a significant dose-response relation… These results suggest that increased consumption of vegetable protein in the context of an energy-balanced diet can reduce the risk of cholecystectomy in women."	386	
	Good for bone health (and animal protein is bad)	"Our analysis includes 8,178 female study participants of the European Prospective Investigation into Cancer and Nutrition (EPIC) Potsdam Study. Ultrasound bone measurements were performed on the right os calcis, and BUA was determined. Dietary intake was assessed by a standardized food frequency questionnaire. We applied linear regression models to estimate the association between dietary protein and BUA. RESULTS: After multivariate adjustment, high intake of animal protein was associated with decreased BUA values (beta = -0.03; p = 0.010) whereas high vegetable protein intake was related to an increased BUA (beta = 0.11; p = 0.007). The effect of dietary animal protein on BUA was modified by calcium intake. CONCLUSION: **High consumption of protein from animal origin may be unfavourable, whereas a higher vegetable protein intake may be beneficial for bone health.** Our results strengthen the hypothesis that high calcium intake combined with adequate protein intake based on a high ratio of vegetable to animal protein may be protective against osteoporosis."	387	
Total protein	Lessens the risk of heart attack	"The study was a prospective cohort study. RESULTS: We examined the association between dietary protein intake and incidence of ischemic heart disease in a cohort of 80082 women aged 34-59 y and without a previous diagnosis of ischemic heart disease, stroke, cancer, hypercholesterolemia, or diabetes in 1980. Intakes of protein and other nutrients were assessed with validated dietary questionnaires. We documented 939 major instances of ischemic heart disease during 14 y of follow-up. After age, smoking, total energy intake, percentages of energy from specific types of fat, and other ischemic heart disease risk factors were controlled for, **high protein intakes were associated with a low risk of ischemic heart disease**; when extreme quintiles of total protein intake were compared, **the relative risk was 0.74** (95% CI: 0.59, 0.94). Both animal and vegetable proteins contributed to the lower risk. This inverse association was similar in women with low- or high-fat diets."	388	
	Lowers BP and improves lipids	"Randomized, 3-period, crossover feeding study … Participants were 164 adults with prehypertension or stage 1 hypertension. Each	291	

		feeding period lasted 6 weeks and body weight was kept constant. INTERVENTIONS: A diet rich in carbohydrates; a diet rich in protein, about half from plant sources; and a diet rich in unsaturated fat, predominantly monounsaturated fat. MAIN OUTCOME MEASURES: Systolic blood pressure and low-density lipoprotein cholesterol. RESULTS: Blood pressure, low-density lipoprotein cholesterol, and estimated coronary heart disease risk were lower on each diet compared with baseline. Compared with the carbohydrate diet, the **protein diet further decreased mean systolic blood pressure by 1.4 mm Hg** (P = .002) and by 3.5 mm Hg (P = .006) among those with hypertension **and decreased low-density lipoprotein cholesterol by 3.3 mg/dL** (0.09 mmol/L; P = .01), high-density lipoprotein cholesterol by 1.3 mg/dL (0.03 mmol/L; P = .02), and triglycerides by 15.7 mg/dL (0.18 mmol/L; P<.001). Compared with the carbohydrate diet, the **unsaturated fat diet decreased systolic blood pressure by 1.3 mm** Hg (P = .005) and by 2.9 mm Hg among those with hypertension (P = .02), had no significant effect on low-density lipoprotein cholesterol, **increased high-density lipoprotein cholesterol by 1.1 mg/dL** (0.03 mmol/L; P = .03), and lowered triglycerides by 9.6 mg/dL (0.11 mmol/L; P = .02). **Compared with the carbohydrate diet, estimated 10-year coronary heart disease risk was lower and similar on the protein and unsaturated fat diets.**"		

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Methionine restriction

75% reduction appears to slow the aging process and prolong lifespan in rats. People can do something like this by eating vegetables instead of meat: this results in a reduction of ~50% in methionine.

Category	Effect	Finding	Ref	Fig
Methionine restriction	RESTRICTION of this amino acid may slow aging and prolong life …At least in RATS	"A diet deficient in the amino acid methionine has previously been shown to extend lifespan in several stocks of inbred rats. We report here that a methionine-deficient (Meth-R) diet also increases maximal lifespan in … mice. Compared with controls, Meth-R mice have significantly lower levels of serum IGF-I, insulin, glucose and thyroid hormone. Meth-R mice also have higher levels of liver mRNA for MIF (macrophage migration inhibition factor), known to be higher in several other mouse models of extended longevity. Meth-R mice are significantly slower to develop lens turbidity and to show age-related changes in T-cell subsets. They are also dramatically more resistant to oxidative liver cell injury induced by injection of toxic doses of acetaminophen. The spectrum of terminal illnesses in the Meth-R group is similar to that seen in control mice. Studies of the cellular and molecular biology of methionine-deprived mice may, in parallel to studies of calorie-restricted mice, provide insights into the way in which nutritional factors modulate longevity and late-life illnesses." Note: methionine is present in all natural proteins. Meats are highest in methionine: typically 2.5 to 3.0% of meat and dairy protein is methionine; typically 0.9 to 1.5% of vegetable protein is methionine. Yet another reason to keep meat intake low, and eat your veggies!	[389]	
		"… methionine restriction-related life span extension is not a consequence of reduced energy intake. By feeding the methionine restricted diet to a variety of rat strains we determined that lowered methionine in the diet prolonged life in strains that have differing pathological profiles in aging, indicating that this intervention acts by altering the rate of aging, not by correcting some single defect in a single strain."	[390]	

		"…lifelong reduction in the concentration of a single dietary component, the essential amino acid L-methionine, from 0.86 to 0.17% of the diet results in a **30% longer life span** of male Fischer 344 rats."	391	
	Effects are additive to CR … in rats	"Reduced dietary methionine intake (0.17% methionine, MR) and calorie restriction (CR) prolong lifespan in male Fischer 344 rats… MR rats show significantly reduced visceral fat compared to CF and PF with concomitant decreases in basal insulin, glucose, and leptin, and increased adiponectin and triiodothyronine…In a separate cohort, insulin responses of older MR animals as measured by oral glucose challenge are similar to young animals. Longitudinal assessments of MR and CF through 112 weeks of age reveal that MR prevents age-associated increases in serum lipids… Collectively, the results indicate that MR reduces visceral fat and preserves insulin activity in aging rats independent of energy restriction."	392	
	May reduce risk of colon cancer	"[formation of preneoplastic aberrant crypt foci (ACF)] formation was markedly reduced in rats fed the MR diet with ACF containing >/= 4 crypts/focus being reduced by over 80% compared to controls... These results show that MR inhibits colonic tumor development in the rat, an effect that occurs primarily during post-initiation phases of carcinogenesis and may be due, in part, to an inhibition of colonic cell proliferation."	393	
	May NOT be additive to CR	"Recently, methionine restriction has received wide acclaim including speculation that it may play a role in FR-induced life extension. In my opinion, work on rats done in our laboratory makes it unlikely that this speculation is correct, at least for that species (4). We found that a long term 40% reduction in food intake without a reduction in methionine intake extends the life of rats to the same extent as a 40% reduction of both food and methionine intake does (Table 1). Thus, it is clear that methionine intake need not be decreased for FR to markedly extend the life of rats."	394	

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Summaries of preventative measures for specific diseases

Category	Effect	Finding	Ref	Fig
Alzheimer Disease		Thorough summary with lots of references, in a free PDF document. "Epidemiology studies, including both regional incidence and the analysis of specific risk factors for Alzheimer's disease indicate that substantial prevention of the disease, in the 50-70 percent range, is a practical possibility for the United States."	395	
Heart disease		The American Heart Association "Diet and Lifestyle Recommendations Revision 2006" states: "Specific goals are to consume an overall healthy diet; aim for a healthy body weight; aim for recommended levels of low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides; aim for normal blood pressure; aim for a normal blood glucose level; be physically active; and avoid use of and exposure to tobacco products. The recommendations are to balance caloric intake and physical activity to achieve and maintain a healthy body weight; consume a diet rich in vegetables and fruits; choose whole-grain, high-fiber foods; consume fish, especially oily fish, at least twice a week; limit intake of saturated fat to <7% of energy, trans fat to <1% of energy, and cholesterol to <300 mg/day by choosing lean meats and vegetable alternatives, fat-free (skim) or low-fat (1% fat) dairy products and minimize intake of partially hydrogenated fats; minimize intake of beverages and foods with added sugars; choose and prepare foods with little or no salt; if you consume alcohol, do so in moderation; and when you eat food prepared outside of the home, follow these Diet and Lifestyle Recommendations. By adhering to these diet and	396	

		lifestyle recommendations, Americans can substantially reduce their risk of developing cardiovascular disease, which remains the leading cause of morbidity and mortality in the United States."		
Osteoporosis	Avoid colas	"Soft drink consumption may have adverse effects on bone mineral density (BMD), but studies have shown mixed results. In addition to displacing healthier beverages, colas contain caffeine and phosphoric acid (H(3)PO(4)), which may adversely affect bone. OBJECTIVE: We hypothesized that consumption of cola is associated with lower BMD. DESIGN: BMD was measured at the spine and 3 hip sites in 1413 women and 1125 men in the Framingham Osteoporosis Study by using dual-energy X-ray absorptiometry. Dietary intake was assessed by food-frequency questionnaire. We regressed each BMD measure on the frequency of soft drink consumption for men and women after adjustment for body mass index, height, age, energy intake, physical activity score, smoking, alcohol use, total calcium intake, total vitamin D intake, caffeine from noncola sources, season of measurement, and, for women, menopausal status and estrogen use. RESULTS: Cola intake was associated with significantly lower ($P < 0.001$-0.05) BMD at each hip site, but not the spine, in women but not in men. The mean BMD of those with daily cola intake was 3.7% lower at the femoral neck and 5.4% lower at Ward's area than of those who consumed <1 serving cola/mo. Similar results were seen for diet cola and, although weaker, for decaffeinated cola. No significant relations between noncola carbonated beverage consumption and BMD were observed. Total phosphorus intake was not significantly higher in daily cola consumers than in nonconsumers; however, the calcium-to-phosphorus ratios were lower. CONCLUSIONS: Intake of cola, but not of other carbonated soft drinks, is associated with low BMD in women. Additional research is needed to confirm these findings."	397	

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Brush your teeth

Category	Effect	Finding	Ref	Fig
Brush teeth	Periodontal disease may => vascular disease	"multiple logistic regression analysis identified periodontal disease as a principal independent predictor of the common carotid [disease]… The present results indicate that periodontal disease is associated with the development of early atherosclerotic carotid lesions." So brush your teeth!!	398	
		"Dental status, oral hygiene, and particularly tooth loss are associated with the degree of carotid stenosis and predict future progression of the disease."	399	
	Periodontal disease may => prostate cancer			

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Safety measures

Category	Effect	Finding	Ref	Fig
Hip fracture prevention	Hip protectors Reduce hip fractures by half	Hip protectors reduce hip fractures by half in the elderly. "We randomly assigned 1801 ambulatory but frail elderly adults (1409 women and 392 men; mean age, 82 years), … either to a group that wore a hip protector or to a control group…The respective rates of hip fracture were 21.3 and 46.0 per 1000 person-years."	400	

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Genetics

Category	Effect	Finding	Ref	Fig
Lipoprotein size	Lesser **small** LDL and HDL particles was very strongly correlated with human lifespan and overall health	"NMR-measured lipoprotein profiles were analyzed in 165 families from the Leiden Longevity Study, consisting of 340 long-lived siblings (females >91 y, males >89 y), 511 of their offspring, and 243 partners of the offspring. Offspring had larger (21.3 versus 21.1 nm; p = 0.020) and fewer (1,470 versus 1,561 nmol/l; p = 0.011) LDL particles than their same-aged partners. This effect was even more prominent in the long-lived siblings (p < 10(-3)) and could be pinpointed to a reduction specifically in the concentration of small LDL particles. No differences were observed for HDL particle phenotypes. The mean LDL particle sizes in 259 90-y-old singletons from a population-based study were similar to those in the long-lived siblings and thus significantly larger than in partners of the offspring, suggesting that the relevance of this phenotype extends beyond familial longevity. A low concentration of small LDL particles was associated with better overall health among both long-lived siblings (p = 0.003) and 90-y-old singletons (p = 0.007). CONCLUSIONS: Our study indicates that LDL particle profiles mark both familial and sporadic human longevity already in middle age."	401	

3. Avoid charring or browning meat: this induces the formation of "heterocyclic amines" (heterocyclic amines are carcinogens, e.g. they cause cancer) and advanced glycosylation end-products (AGEs). Instead boil or *low-power* microwave it and reduce how much you eat. This is probably most important for red meat (mammals including beef and pork); the risk may be lower for white meat (fowl & fish). A study from the University of South Carolina (reported in Journal of the National Cancer Institute 1998-11-18) found a five-fold increase in breast cancer rates in women who consistently ate well-done red meat. Another study found a similarly increased incidence of pancreatic cancer from food that was fried, smoked, salty, high in refined sugar or dehydrated; and a *low* incidence with raw food intake and the use of microwave ovens to cook food (Cancer Epidemiol Biomarkers Prev 1995 Dec;4(8):895-9; PMID: 8634663). In addition, roasted nuts, cereal, milk products, etc. have AGEs; probably it is best to eat these with as little cooking and at as low temperatures as reasonable.

   One study found that "…dietary AGEs promote inflammatory mediators, leading to tissue injury. Restriction of dietary AGEs suppresses these effects." (Vlassara H, Cai W, Crandall J, Goldberg T, Oberstein R, Dardaine V, Peppa M, Rayfield EJ. Inflammatory mediators are induced by dietary glycotoxins, a major risk factor for diabetic angiopathy. Proc Natl Acad Sci U S A. 2002 Nov 12. PMID: 12429856)

   Processed meats (such as hot dogs) also have been associated with an increased risk of Type II diabetes (Diabetes Care 2002 Mar;25(3):417-24; PMID: 11874924), as well as an increased risk of colon cancer.
   Contraindications: None.
   Potential problems: Meat does not taste quite as good.
4. Cooking protein or fat in combination with simple sugars (glucose or fructose, such as corn syrup, Bar-B-Q sauce, fruit, milk, etc. – but NOT table sugar (sucrose)) will also cause formation of substantial amounts of advanced glycosylation end-products (AGEs). 10% of these dietary AGEs are absorbed from the gut, and only 30% of the absorbed AGEs are excreted by the kidneys. The rest may be deposited around the body and cause an eventual toxic buildup, as occurs in diabetics (Diabetes Metab (Paris) 2001, 27, 535-542). The known or hypothesized toxic effects of these AGEs are primarily vascular. AGE ingestion also is seems to raise the risk for diabetes in lab rats.

   Note that AGEs are in nearly all food we eat – another reason to be on caloric restriction! This is especially clearly seen in diabetics ("dietary restriction of AGE food intake may greatly reduce the burden of AGEs in diabetic patients and possibly improve prognosis." Proc Natl Acad Sci U S A 1997 Jun 10;94(12):6474-9;

PMID: 9177242) but in my opinion probably applies to all.

AGEs are tasty! They are responsible for the good flavor of coffee (see Scientific American, June 2002) and perhaps other foods such as grilled meat and chocolate. While AGEs are in these foods it is not at all clear that they are harmful. For example, coffee has been *extensively* studied and has been found to be virtually harmless.

Whether ingested AGEs are clinically significant for normal people is an open question. Certainly AGEs formed in the body – especially those associated with diabetes, smoking, and sunlight exposure – are highly correlated with aging effects and are inversely correlated with lifespan.
Contraindications: None.
Potential problems: Meat does not taste quite as good.

5. Colon cancer may be caused in part by red meat (doubles risk) and cured meats (including bacon, cured ham, salami, corned beef and pastrami). These meats cause the formation of carcinogenic N-nitroso compounds by bacteria in the feces, and may thus be a risk factor in colon cancer. Dairy products and soy do not (soy may cause problems on estrogen-sensitive tissues and the thyroid, but may also help prevent prostate cancer: whether it is beneficial overall is unclear). It is probably best to avoid eating large quantities of these meats. In addition, colon cancer risk may be reduced by 40% by eating a high-fiber diet. Perhaps the major factor associated with colon cancer is high body mass index. Factors that may decrease the risk: legumes (beans), broccoli and the like, NSAIDs, and folate. (Lipkin M, Reddy B, Newmark H, Lamprecht SA. Dietary factors in human colorectal cancer. Annu Rev Nutr. 1999;19:545-86. Review. PMID: 10448536)
6. Avoid processed, cured and smoked meats such as hot dogs, bacon, smoked foods and lunchmeats: nitrites and the smoke processing seem to be the cause of much of stomach cancer. (Int J Cancer 1999 Mar 15;80(6):852-6; PMID: 10074917: Of various sources of N-nitroso compounds, intake of smoked and salted fish was significantly (RR = 2.58, 95% CI 1.21-5.51) and intake of cured meat was non-significantly (RR = 1.84, 95% CI 0.98-3.47) associated with risk of colorectal cancer. No similar association was observed for intake of other fish or other meat). Smoked meats may be the cause of the very high stomach cancer rates in Japan and Italy. *Simultaneous* vitamin C & E intake may provide some protective effect against the carcinogenic properties of nitrites, by helping prevent formation in the gut.
Contraindications: None.
Potential problems: None.
7. Many of the foods that are best for your health are also full of oxalic acid, a substance that causes kidney stones. No fun if you get them! Fortunately, you can prevent the absorption of the oxalic acid in your intestines by drinking milk (or taking some other source of calcium: I prefer milk in fat-free cheese on my spinach: "Dietary calcium lowers the risk of nephrolithiasis due to a decreased absorption of dietary oxalate that is bound by intestinal calcium." Braz J Med Biol Res 2002 Jun;35(6):669-75; PMID: 12045831, and "Daily urine oxalate excretion/creatinine decreased curvilinearly as estimated dietary Ca intake increased … as the ratio of estimated dietary calcium to dietary oxalate increased" Kidney Int 1996 Jan;49(1):200-8; PMID: 8770968) at the same meal you eat foods high in oxalate (spinach, rhubarb, chard, beets, cocoa, peanuts, bran, berries, etc.) In addition, the biggest risk factor for excretion of oxalate is body weight (Kidney Int 1996 Jan;49(1):200-8; PMID: 8770968), so if you are on CR this may not matter so much. For a listing of oxalic acid levels in a variety of vegetables, check this USDA web site or this kidney stone prevention site. I hypothesize that it is good to eat a milk-derived food when eating the following: spinach, rhubarb, chard, okra, sweet potato, radish, lettuce, carrots, green beans and Brussels sprouts (each of these – especially the first three – has moderate concentrations of oxalic acid *and* is often eaten in significant amounts).
Contraindications: None.
Potential problems: None.
8. Eat lots of vegetables and some fruit, especially tomatoes, broccoli (broccoli sprouts are best, and also other vegetables in the cabbage family have the same protective effects), purple grape juice, and berries (at least 1 cup and preferably 2 cups each day of blueberries, raspberries, and/or strawberries). These seem to help prevent cancer and stroke. The American Institute for Cancer Research recommends five to 10 servings of fruits and vegetables a day for cancer protection.

Tomatoes (especially cooked) are the source of lycopene. Lycopene is available in highest concentrations in tomato paste, and may be better absorbed if eaten with oil. "Among 72 studies identified, 57 reported inverse associations between tomato intake or blood lycopene level and the risk of cancer at a defined anatomic site; 35 of these inverse associations were statistically significant… The evidence for a benefit was strongest for cancers of the prostate, lung, and stomach." Giovannucci E. Tomatoes, tomato-based products, lycopene, and cancer: review of the epidemiologic literature. J Natl Cancer Inst. 1999 Feb 17;91(4):317-31. Review. PMID: 10050865.

Broccoli sprouts in particular have been found to have especially high concentrations of glucoraphanins (10-50 times more than mature flowerets), and have been shown to prevent and slow the growth of breast cancer in rats (Proc Natl Acad Sci U S A 1997 Sep 16;94(19):10367-72; PMID: 9294217). To get sufficient protective quantities of glucoraphanins from mature broccoli flowerets would require approximately 20% of your food to be from broccoli alone. The benefits of eating broccoli-family vegetables are probably due to induction by glucoraphanins of "Phase 2 enzymes" that detoxify carcinogens, rather than from any antioxidant effects.

Part of the protection from eating lots of fruits and vegetables may simply be avoidance of relatively bad food.

Contraindications: None.

Potential problems: Gas. Try cooking the vegetables more or eating different types and amounts.

9. Exercise regularly and moderately (30 minutes each day). This has repeatedly been shown to have several beneficial long-term health effects, including substantially reduced rates of diabetes & (at least) colon cancer, preservation of mental function & bone strength, and reduced risk of cardiovascular disease ("Women in increasing quintiles of energy expenditure measured in metabolic equivalents (the MET score) had age-adjusted relative risks of coronary events of 1.00, 0.73, 0.69, 0.68, and 0.47, respectively (P for trend, <0.001). In multivariate analyses, the inverse gradient between the total MET score and the risk of cardiovascular events remained strong (adjusted relative risks for increasing quintiles, 1.00, 0.89, 0.81, 0.78, and 0.72, respectively; P for trend <0.001). Walking and vigorous exercise were associated with similar risk reductions, and the results did not vary substantially according to race, age, or body-mass index. A brisker walking pace and fewer hours spent sitting daily also predicted lower risk." Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women: is "no pain, no gain" passe? JAMA. 2001 Mar 21;285(11):1447-54. PMID: 11255420; Manson JE, Greenland P, LaCroix AZ, Stefanick ML, Mouton CP, Oberman A, Perri MG, Sheps DS, Pettinger MB, Siscovick DS. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. N Engl J Med. 2002 Sep 5;347(10):716-25. PMID: 12213942; and from a 12-year study of 44,452 men: "Total physical activity, running, weight training, and walking were each associated with reduced CHD risk. Average exercise intensity was associated with reduced risk…" Tanasescu M, Leitzmann MF, Rimm EB, Willett WC, Stampfer MJ, Hu FB. Exercise type and intensity in relation to coronary heart disease in men. JAMA. 2002 Oct 23;288(16):1994-2000. PMID: 12387651). There is also a suggestion that moderate exercise may be associated with longer life, but the effect is hard to differentiate from other lifestyle changes (Schnohr P, Parner J, Lange P. [Joggers live longer. The Osterbro study] Ugeskr Laeger. 2001 May 7;163(19):2633-5. Danish. PMID: 11360357; Fraser GE, Shavlik DJ. Ten years of life: Is it a matter of choice? Arch Intern Med. 2001 Jul 9;161(13):1645-52. PMID: 11434797.)

   Note that over-exertion may be harmful, both directly on the joints, and if you have to eat a lot to make up for calories used in exercise this partially defeats caloric restriction principles. Exercise helps keep your bones strong, helping to prevent osteoporosis-related fractures.

   Contraindications: Ask your doctor first before starting an exercise program!

   Potential problems: The increased metabolism of exercise causes some free radical induced damage and DNA damage. Exercise does NOT seem to affect life span (Epidemiology 1997 Mar;8(2):168-74; PMID: 9229209)! Instead, I think of it as a way to improve the life I have.
10. Floss your teeth every day, in addition to brushing after every meal. This reduces your risk for heart attack and stroke, probably by reducing the chronic, low-grade gum infections.

    Contraindications: None.

    Potential problems: None.
11. Get your vaccinations! Influenza and pneumonia kill lots of people, especially after age 65 yr.
12. Most supplements (except vitamins A, E, & B12) should be taken in small doses several times each day instead of once a day. Just like medications they are not stored in the body, lasting about 4 hours, and thus may be best if taken three or four times per day. In my opinion, this includes folate, red grapes (grape juice or grape seed extract), tea, broccoli, and (for those with heart attack risk factors)

aspirin. An easy way to do this is to eat good food at every meal and take supplements with each meal and at bedtime. You should probably not take any supplemental vitamin A if you can avoid it: too much is quite toxic, and most people get plenty in the vegetables they eat.

13. Treat any infections. Chronic sinusitis and gingivitis (bad oral health) have been shown to predispose to heart disease!
    Recently the bacterium that causes stomach ulcers, *Heliobacter pylori*, has been strongly associated with stomach cancer (N Engl J Med 2001 Sep 13;345(11):784-9; PMID: 11556297). They estimated that if this infection can be identified and treated with antibiotics we could eliminate the #10 cause of cancer death in America. Approximately 35% of Americans have *H. pylori* infection and do not know it: this appears to be associated with a 2.9% risk of this cancer. Fortunately, broccoli and broccoli sprouts contain a beneficial nutrient (sulphorophane) that kills *H. pylori*, and they contain it in sufficient concentrations to prevent this infection.
14. ***If*** you have risk factors for heart disease (obesity, high blood pressure, diabetes, smoking, family history, etc.), consider taking low-dose, non-buffered (the buffer has aluminum) aspirin, perhaps ¼ tablet every other day. This does two things:
    c. Reduces your risk for heart attacks (the #1 killer!) by 40%.
    d. May reduce your risk for colon cancer (the #2 cancer killer after lung cancer - and you can avoid this by not smoking) by 20%.
    e. May reduce the overall risk for strokes (although it increases the risk of a hemorrhagic stroke).

    Do not take both ibuprofen and aspirin together.
    Contraindications: stomach upset or gastritis with aspirin, bleeding problems. The cardiac benefit may also not be worth the risks for those with few risk factors for heard disease.
    Potential problems: hemorrhagic stroke, bleeding problems, stomach upset, gastrointestinal bleed (can be very serious or deadly!), and if you have kidney problems it may cause an increased rate of kidney failure. The risk/benefit ratio has been worked out for cardiac problems: for this purpose it is best to take aspirin only if you have cardiac risk factors. On the other hand, I think that this analysis did not take the reduced colon cancer risk into account.

Things I think may be worth trying because they probably work or may work

15. The risk of Alzheimer's disease is lower in populations with higher education, nonsteroidal anti-inflammatory drugs, wine consumption, coffee consumption, and regular physical activity (Am J Epidemiol 2002 Sep 1;156(5):445-53; PMID: 12196314).
16. Consider taking some sort of non-steroidal anti-inflammatory drug (NSAID) such as Motrin (SEE WARNING BELOW). This probably reduces the risk for Alzheimer's disease and cataracts. Low-dose aspirin appears not to do this. A recent study from Holland of 7000 people (N Engl J Med 2001 Nov 22;345(21):1515-21; PMID: 11794217) showed an 80% drop in the incidence of Alzheimer's for those taking NSAIDs for more than 2 years. Low dose worked as well as high dose. Another study showed that Motrin has a direct effect preventing the production of the protein associated with Alzheimer's. The National Institute on Aging (NIA) launched a new clinical trial at the end of January 2001, called the Alzheimer's Disease Anti-Inflammatory Prevention Trial (ADAPT), to test naproxen and celecoxib (Celebrex) with regards to Alzheimer's prevention. So in 20 years we will know the answer – but that may be too late for some of us! See Ophthalmology 2001;108:1400-1408. Also, the combination of an NSAID and vitamin E reduces atherosclerosis in mice with high cholesterol levels by 80% (Circulation 2001 Oct 16;104(16):1940-5; PMID: 11602498). If you take ibuprofen (vs. Alzheimer's disease, etc.) and aspirin (vs. heart disease), be sure to take the aspirin first and wait for about 2 hours: ibuprofen blocks the usefulness of aspirin.
    Potential problems: **This is a potentially fatal drug.** It can cause bleeding problems, stomach upset, gastrointestinal bleed (can be very serious!), liver and kidney problems. Be careful of long-term use!! – I really am unsure on the long-term risk/benefit ratio of this one, but since I have no stomach or renal problems, the several studies indicating such a dramatic benefit had convinced me personally to take low-dose Motrin two times each day. Unfortunately this also caused me to become hyponatremic (low level of sodium found in a blood test: no symptoms, but it could indicate potential for causing kidney or other problems, so I stopped the Motrin.)
17. Glucosamine and chondroitin may reduce the chance of getting osteoarthritis, the most common kind of arthritis. Certainly they have been shown to reduce the symptoms. Both of these are the body's natural joint lubricants (JAMA 2000 Mar 15;283(11):1469-75; PMID: 10732937). To get these you need to take tablets. "Dr. Theo" has a comprehensive web site discussion, with studies, analysis and recommendations. From this site it appears that it is necessary for full effect to take both glucosamine and chondroitin, and to take the chondroitin in doses of at least 1200 mg/day. Because the chondroitin is expensive and quite variable in the available formulations, the Dr. Theo site recommends several brands shown to have high quality by HPLC testing.
    (Lancet 2001 Jan 27;357(9252):251-6; PMID: 11214126):

    Two hundred twelve patients with mild to moderate arthritis were randomly assigned a 1500 mg daily glucosamine sulfate supplement or a placebo for a period of three years in a double-blind trial. X-ray films of the knee were taken at the beginning and the conclusion of the study to measure joint space width, in order to assess cartilage loss. The study participants completed questionnaires in which symptoms such as pain, joint function and stiffness were scored.

    At the conclusion of the study, participants who received the placebo had significant mean and minimum joint-space narrowing, showing cartilage loss. The majority of the group of 106 patients receiving glucosamine sulfate had no significant joint-space narrowing. Evaluation of the questionnaires showed an improvement of symptoms in the glucosamine group and a worsening of symptoms in the placebo group. Even in the small group of patients who received glucosamine and experienced joint-space narrowing, symptomatic relief was noted.

    Note: Caloric Restriction has also been shown to significantly delay the onset of osteoarthritis in dogs.
    Potential problems: Get good-quality supplements.
18. A high-fiber diet probably helps prevent heart disease (J Nutr 1999 Jul;129(7 Suppl):1457S-66S; PMID: 10395621). This has been found to be strongly true from epidemiology (in comparative studies of populations of people such as vegetarians and 7th-Day Adventists) and animal studies. This is true for fiber from cereals (e.g., wheat & oat), fruits and vegetables. "In general … soluble fibers, such as psyllium, oat bran, guar and pectin, decrease serum cholesterol and LDL cholesterol concentrations without affecting serum triglycerides." (Beans have soluble fiber too.) "(Insoluble fibers such as) wheat bran intake decreased serum

triglyceride concentrations in humans (but) does not have a significant effect on serum cholesterol concentrations." Part of this positive effect is probably from associated nutrients. The reduction in cholesterol and triglyceride is approximately 10%. For most people the most important thing to reduce is cholesterol. In addition, high-fiber diets tend to reduce overall food intake. Nonetheless, caloric restriction itself has by far the greatest effect in reduction of these risk factors. My take is to practice caloric restriction, and include a balanced variety high-fiber, low-calorie foods as part of this diet.

Both psyllium (Am J Clin Nutr 2000 Feb;71(2):472-9; PMID: 10648260) and guar have been shown to decrease cholesterol levels significantly. If you get these, start slowly!! Both increase the stool volume substantially, resulting in several bowel movements each day. If you eat too much you can get in real trouble from this, with abdominal pain: follow the directions on the bottles. I like the finely-ground psyllium-based Metamucil equivalent from Wal-Mart, mixed with a little guar powder and ground cloves, then mixed with cold diet orange soda. (weird, I know…)

19. If you are a man, donate blood regularly (about three times per year) and avoid iron supplements. Iron is a pro-oxidant (as opposed to an anti-oxidant); it enhances the production of the highly reactive and toxic hydroxyl radical, thus stimulating oxidative damage. It is associated with chronic damage to the brain, skin, liver, and muscle. Excess and even "normal" iron levels can cause an increased risk for heart attacks. A recent article (Ann N Y Acad Sci 2002 Jun;967:342-51) showed that patients with iron deficiency had much better heart disease risk factors (lower BP, higher HDL, lower LDL, etc.); these probably beneficial things were reversed by supplementing with iron! A major review article in Diabetes stated that high iron levels seem to cause diabetes type 2, and "Iron depletion has been demonstrated to be beneficial in coronary artery responses, endothelial dysfunction, insulin secretion, insulin action, and metabolic control in type 2 diabetes" (Diabetes 2002 Aug;51(8):2348-54; PMID: 12145144; the full text is at http://www.medscape.com/viewarticle/439591_1); another stated that iron may be "a major factor of (accelerated) ageing." (Polla AS, Polla LL, Polla BS. Iron as the malignant spirit in successful ageing. Ageing Res Rev. 2003 Jan;2(1):25-37. PMID: 12437994)
Potential problems: 1) Ouch! 2) You may develop iron-deficiency anemia if you give too much blood. Not likely for most men: I had been donating blood about four to six times per year and avoiding iron supplements for about 25 yr., and only recently had low iron levels – low enough to actually cause iron deficiency anemia requiring supplements! Of note, it appears that both iron deficiency and high-dose iron supplementation may cause mitochondrial damage (Proc Natl Acad Sci U S A 2002 Feb 19;99(4):2264-9; PMID: 11854522), possibly the cause of most aging changes.
20. There is one study that implies we should eat lots of protein: the higher the protein, the longer the life span for both ad lib (eat-what-you-want) and caloric restricted rodents. From this post, about 75% down the message (slightly edited):

Days survived	Ad lib			CR		
protein % =>	**10**	**22**	**51**	**10**	**22**	**51**
900	8	2	6	93	116	149
1000	0	0	1	48	85	122
1200	0	0	0	5	61	91
1300	0	0	0	0	31	59
1400	0	0	0	0	11	24
1500	0	0	0	0	1	10
1600	0	0	0	0	0	3

Further, the highest-protein groups had the lowest ratios of malignant to benign tumors, and the lowest AGE-SPECIFIC tumor rates of all isocaloric groups: that is, the low-protein group had fewer cancers only because they died sooner -- their rate of tumor formation was higher. (Ross MH, Bras G. Influence of protein under-and overnutrition on spontaneous tumor prevalence in the rat. J Nutr 1973;103: 944-963.)

This is only one study, and an old one at that, but they used a lot of animals (1600) and I know of no contradictory evidence. However, there are design and interpretation problems that limit the usefulness of the study, such as their source of protein (casein), carbohydrate (sugar) and fat (corn oil). It appears to me from reading the paper that 1) older rats seemed to be the ones to most benefit from a high protein diet, and 2) the CR rats needed the same quantity of protein, but because their total diet was restricted they did better

on diets with a higher protein fraction.

Note: older people may need proportionally more protein in their diet than young people. A study of old rats showed that a 27% (by calories) protein diet worked best for elderly rats, and noted in regard to people that "Protein-energy malnutrition is common in the elderly" (Walrand S, Chambon-Savanovitch C, Felgines C, Chassagne J, Raul F, Normand B, Farges MC, Beaufrere B, Vasson MP, Cynober L. Aging: a barrier to renutrition? Nutritional and immunologic evidence in rats. Am J Clin Nutr. 2000 Sep;72(3):816-24. PMID: 10966905).

Potential problems: high-protein diets may cause 1) Problems for the kidneys, that may not be a big problem for those on CR (Masoro EJ, Iwasaki K, Gleiser CA, McMahan CA, Seo EJ, Yu BP. Dietary modulation of the progression of nephropathy in aging rats: an evaluation of the importance of protein. Am J Clin Nutr. 1989 Jun;49(6):1217-27. PMID: 2729159). 2) Calcium loss and potential kidney stones (Reddy ST, Wang CY, Sakhaee K, Brinkley L, Pak CY. Effect of low-carbohydrate high-protein diets on acid-base balance, stone-forming propensity, and calcium metabolism. Am J Kidney Dis. 2002 Aug;40(2):265-74. PMID: 12148098).

21. Reducing salt intake may decrease your risk of high blood pressure, which in turn affects heart disease and stroke. A study of actual salt intake (measured by urinary sodium excretion) as a risk factor, high sodium intake predicted mortality and risk of coronary heart disease, independent of other cardiovascular risk factors, including blood pressure. The hazards ratios for coronary heart disease, cardiovascular disease, and all-cause mortality, associated with a 100 mmol increase in 24 h urinary sodium excretion, were 1.51 (95% CI 1.14-2.00), 1.45 (1.14-1.84), and 1.26 (1.06-1.50), respectively, in both men and women. (Tuomilehto J, Jousilahti P, Rastenyte D, Moltchanov V, Tanskanen A, Pietinen P, Nissinen A. Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study. Lancet. 2001 Mar 17;357(9259):848-51. PMID: 11265954.)
    However, there was a significant interaction between sodium excretion and body mass index for cardiovascular and total mortality; sodium predicted mortality in men who were overweight. Thus much or most of the correlation may be due to weight alone. Certainly short-term salt intake modulates blood pressure; the long-term effects in thin people are not clear to me. I still like my foods to taste good!
    Another study states that the long-term effects of a low-salt diet seem to be uncertain. "Without knowledge of the sum of the multiple effects of a reduced sodium diet, no single universal prescription for sodium intake can be scientifically justified." (Grassi G, Dell'Oro R, Seravalle G, Foglia G, Trevano FQ, Mancia G. Short- and long-term neuroadrenergic effects of moderate dietary sodium restriction in essential hypertension. Circulation. 2002 Oct 8;106(15):1957-61. PMID: 12370219)
22. Aluminum may cause Alzheimer's disease. The evidence on this is unclear: there is some epidemiologic data to support it, and aluminum is found in Alzheimer's brain plaques. Studies are hard to do, of course! Aluminum-based antiperspirants may be the worst cause, perhaps because of absorption rates. On the other hand, aluminum-based antacids (Mylanta etc.) may be safe. Aluminum is also found in baking powder (sodium aluminum sulfate), buffered aspirin and some pickles (alum).
23. Vitamin E may reduce the risk of prostate cancer, perhaps by 1/3, and may reduce the incidence of carotid vascular disease (Am J Clin Nutr 2002 Sep;76(3):582-7; PMID: 12198003). There are two main forms available: alpha tocophererol (from almonds, hazelnuts, olive oil and avocado; this is the standard vitamin E supplement) and gamma tocophererol (best source is peas; also in pecans & walnuts, and to a lesser extent from cashews) Peanuts do not have any vitamin E. Generally if supplements are taken (as opposed to natural sources such as nuts), the alpha form should be taken only with the gamma as well: both are needed, and too much alpha actually leads to depletion of gamma (Am J Clin Nutr 2001 Dec;74(6):714-22; PMID: 11722951). Indeed, supplementation with vitamin E has been shown to be harmful to the elderly in fighting off respiratory infections (JAMA 2002 Aug 14;288(6):715-21; PMID: 12169075); Other studies show it is NOT beneficial to the heart, and may cause other harm. I think it is better to eat a variety of nuts, which in addition have monounsaturated fats and have been shown in epidemiologic studies to be good for you.
    Besides the tocophererols, tocotrienols are a variant of vitamin E and are found in palm oil and some grains. It may be best to get all of these forms of vitamin E. Again, I think that good foods are the best source, not high-dose supplements.
24. Selenium may possibly reduce overall cancer rates by up to 50% (based indirectly on just one study that needs confirmation). Selenium is a necessary part of the body's anti-oxidant system. Glutathione peroxidase is a selenium-dependant enzyme found primarily in the cytoplasm (70%) but also in the

mitochondria (30%). Requiring four selenium atoms per active molecule, this enzyme scavenges lipid peroxides throughout the membrane surfaces and quenches H_2O_2, converting it to water.

Evidence exists that supplementation with selenium is able to increase the levels of glutathione peroxidase in patients. Selenium is found in nuts (especially Brazil nuts, though in quite variable concentrations; (Brazil nuts may be prone to toxic fungus growth[402] (aspergillus); they also have a lot of omega 6 and saturated fats: I avoid them)) and supplements.

Caveat: too much can be toxic, causing hair loss and skin problems.

25. Grazing vs. two or three square meals. How you eat your meals may make a difference. Here is one instance where common wisdom is probably wrong: it is probably best to have very small meals with snacks in between – as long as the total calorie intake is the same – and restricted – of course! One study showed the grazing habit was associated with lower cholesterol & vascular disease (J Cardiovasc Risk 1999 Feb;6(1):19-22; PMID: 10197288). This is just one study, but it seems to have been well-done, with very significant results ($P < 0.001$ for both measurements), and makes sense in light of other data. The reasons might be as follows: small meals lead to lesser increases in levels of post-prandial glucose, fats, insulin, etc., with resulting lesser damage from these things.

    Problem: needs confirmation.

    Incidentally, studies also show that it is easier for people to eat fewer calories if the food is relatively bulky (i.e., not rich). This is a behavioral aide, but also corresponds with eating more nutritional foods such as vegetables.

References

1 http://www.giga-usa.com/gigaweb1/quotes2/quautswiftjonathanx004.htm
2 http://sln.fi.edu/qa98/musing9/almanack1733.html
3 *Modified from* **Gruber RP, Kalamas AD.** Measuring human age by estimating lifetime caloric consumption. Gerontology 2000 Jan-Feb;46(1):44-6; PMID: 11111228
4 **Field AE, Coakley EH, Must A, Spadano JL, Laird N, Dietz WH, Rimm E, Colditz GA.** Impact of overweight on the risk of developing common chronic diseases during a 10-year period. Arch Intern Med. 2001 Jul 9;161(13):1581-6. PMID: 11434789
5 **Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration.** Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002 Dec 14;360(9349):1903-13. PMID: 12493255
6 **Nissen SE, Tuzcu EM, Schoenhagen P, Brown BG, Ganz P, Vogel RA, Crowe T, Howard G, Cooper CJ, Brodie B, Grines CL, DeMaria AN; REVERSAL Investigators.** Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial. JAMA. 2004 Mar 3;291(9):1071-80. PMID: 14996776
7 **Atzmon G, Gabriely I, Greiner W, Davidson D, Schechter C, Barzilai N.** Plasma HDL levels highly correlate with cognitive function in exceptional longevity. J Gerontol A Biol Sci Med Sci. 2002 Nov;57(11):M712-5. PMID: 12403798
8 **Jorgensen L, Jenssen T, Joakimsen O, Heuch I, Ingebretsen OC, Jacobsen BK.** Glycated Hemoglobin Level Is Strongly Related to the Prevalence of Carotid Artery Plaques With High Echogenicity in Nondiabetic Individuals. The Tromso Study. Circulation. 2004 Jul 12 [Epub ahead of print] PMID: 15249512
9 Normal fasting plasma glucose levels and type 2 diabetes in young men. N Engl J Med. 2005 Oct 6;353(14):1454-62. PMID: 16207847
10 http://www.pbs.org/wgbh/pages/frontline/shows/diet/interviews/willett.html
11 **de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N.** Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation. 1999 Feb 16;99(6):779-85. PMID: 9989963
Free full text at http://circ.ahajournals.org/cgi/content/full/99/6/779
12 **Daviglus ML, Stamler J, Pirzada A, Yan LL, Garside DB, Liu K, Wang R, Dyer AR, Lloyd-Jones DM, Greenland P.** Favorable cardiovascular risk profile in young women and long-term risk of cardiovascular and all-cause mortality. JAMA. 2004 Oct 6;292(13):1588-92. PMID: 15467061
13 **Jolly CA, Muthukumar A, Avula CP, Troyer D, Fernandes G.** Life span is prolonged in food-restricted autoimmune-prone (NZB x NZW)F(1) mice fed a diet enriched with (n-3) fatty acids. J Nutr. 2001 Oct;131(10):2753-60. PMID: 11584100; Full text
14 **Ross MH, Bras G.** Influence of protein under- and overnutrition on spontaneous tumor prevalence in the rat. J Nutr. 1973 Jul;103(7):944-63. No abstract available. PMID: 4351915
15 **Hagen TM, Liu J, Lykkesfeldt J, Wehr CM, Ingersoll RT, Vinarsky V, Bartholomew JC, Ames BN.** Feeding acetyl-L-carnitine and lipoic acid to old rats significantly improves metabolic function while decreasing oxidative stress. Proc Natl Acad Sci U S A. 2002 Feb 19;99(4):1870-5. Erratum in: Proc Natl Acad Sci U S A 2002 May 14;99(10):7184. PMID: 11854487
Free full text article at http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=11854487
16 **Liu J, Atamna H, Kuratsune H, Ames BN.** Delaying brain mitochondrial decay and aging with mitochondrial antioxidants and metabolites. Ann N Y Acad Sci. 2002 Apr;959:133-66. Review. PMID: 11976193
17 **Sharman EH, Vaziri ND, Ni Z, Sharman KG, Bondy SC.** Reversal of biochemical and behavioral parameters of brain aging by melatonin and acetyl L-carnitine. Brain Res. 2002 Dec 13;957(2):223-30. PMID: 12445964
18 http://bmj.bmjjournals.com/cgi/content/full/329/7480/1447?ehom
19 http://www.ivu.org/oxveg/Talks/veglongevity.html
20 **Siener R, Hesse A.** The effect of a vegetarian and different omnivorous diets on urinary risk factors for uric acid stone formation. Eur J Nutr. 2003 Dec; 42(6): 332-7. PMID: 14673606
21 **Key TJ, Fraser GE, Thorogood M, Appleby PN, Beral V, Reeves G, Burr ML, Chang-Claude J, Frentzel-Beyme R, Kuzma JW, Mann J, McPherson K.** Mortality in vegetarians and nonvegetarians: detailed findings from a collaborative analysis of 5 prospective studies. Am J Clin Nutr. 1999 Sep;70(3 Suppl):516S-524S. PMID: 10479225 free full text
22 **Singh PN, Sabate J, Fraser GE.** Does low meat consumption increase life expectancy in humans? Am J Clin Nutr. 2003 Sep;78(3 Suppl):526S-532S. Review. PMID: 12936945
23 **Choi HK, Atkinson K, Karlson EW, Willett W, Curhan G.** Purine-rich foods, dairy and protein intake, and the risk of gout in men. N Engl J Med. 2004 Mar 11;350(11):1093-103. PMID: 15014182
24 **Fung TT, Schulze M, Manson JE, Willett WC, Hu FB.** Dietary Patterns, Meat Intake, and the Risk of Type 2 Diabetes in Women. Arch Intern Med. 2004 Nov 8;164(20):2235-2240. PMID: 15534160
25 http://www.ajcn.org/cgi/content/abstract/82/6/1169
26 **Le Marchand L, Donlon T, Seifried A, Wilkens LR.** Red meat intake, CYP2E1 genetic polymorphisms, and colorectal cancer risk. Cancer Epidemiol Biomarkers Prev. 2002 Oct;11(10 Pt 1):1019-24. PMID: 12376502
27 **Butler LM, Sinha R, Millikan RC, Martin CF, Newman B, Gammon MD, Ammerman AS, Sandler RS.** Heterocyclic amines, meat intake, and association with colon cancer in a population-based study. Am J Epidemiol. 2003 Mar

1;157(5):434-45. PMID: 12615608
28 **Sandhu MS, White IR, McPherson K.** Systematic review of the prospective cohort studies on meat consumption and colorectal cancer risk: a meta-analytical approach. Cancer Epidemiol Biomarkers Prev. 2001 May;10(5):439-46. PMID: 11352852 free full text
29 **Jiang R, Ma J, Ascherio A, Stampfer MJ, Willett WC, Hu FB.** Dietary iron intake and blood donations in relation to risk of type 2 diabetes in men: a prospective cohort study. Am J Clin Nutr. 2004 Jan;79(1):70-5. PMID: 14684399
30 http://www.iol.co.za/index.php?set_id=1&click_id=31&art_id=qw110201472111B243
31 Marrion Nestle, "Food Politics" http://tinyurl.com/5ftkp
32 Meat intake and bladder cancer risk in 2 prospective cohort studies. Am J Clin Nutr. 2006 Nov;84(5):1177-83. PMID: 17093172
33 **Boltri JM, Akerson MR, Vogel RL.** Aspirin prophylaxis in patients at low risk for cardiovascular disease: a systematic review of all-cause mortality. J Fam Pract. 2002 Aug;51(8):700-4. Review. PMID: 12184966
34 **Hayden M, Pignone M, Phillips C, Mulrow C.** Aspirin for the primary prevention of cardiovascular events: a summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med. 2002 Jan 15;136(2):161-72. PMID: 11790072
35 **Bosetti C, Talamini R, Franceschi S, Negri E, Garavello W, Vecchia CL.** Aspirin use and cancers of the upper aerodigestive tract. Br J Cancer. 2003 Mar 10;88(5):672-4. PMID: 12618872
36 **Baron JA, Cole BF, Sandler RS, Haile RW, Ahnen D, Bresalier R, McKeown-Eyssen G, Summers RW, Rothstein R, Burke CA, Snover DC, Church TR, Allen JI, Beach M, Beck GJ, Bond JH, Byers T, Greenberg ER, Mandel JS, Marcon N, Mott LA, Pearson L, Saibil F, van Stolk RU.** A randomized trial of aspirin to prevent colorectal adenomas. N Engl J Med. 2003 Mar 6;348(10):891-9. PMID: 12621133
37 **Suji G, Sivakami S.** Glucose, glycation and aging. Biogerontology. 2004;5(6):365-73. PMID: 15609100
38 **Lingelbach LB, Mitchell AE, Rucker RB, McDonald RB.** Accumulation of advanced glycation endproducts in aging male Fischer 344 rats during long-term feeding of various dietary carbohydrates. J Nutr. 2000 May;130(5):1247-55. PMID: 10801926 free full text at
39 **Hofmann SM, Dong HJ, Li Z, Cai W, Altomonte J, Thung SN, Zeng F, Fisher EA, Vlassara H.** Improved insulin sensitivity is associated with restricted intake of dietary glycoxidation products in the db/db mouse. Diabetes. 2002 Jul;51(7):2082-9. PMID: 12086936
40 **Uribarri J, Peppa M, Cai W, Goldberg T, Lu M, He C, Vlassara H.** Restriction of dietary glycotoxins reduces excessive advanced glycation end products in renal failure patients. J Am Soc Nephrol. 2003 Mar;14(3):728-31. PMID: 12595509
Full text at http://www.jasn.org/cgi/reprint/14/3/728.pdf
41**Goldberg T, Cai W, Peppa M, Dardaine V, Baliga BS, Uribarri J, Vlassara H.** Advanced glycoxidation end products in commonly consumed foods. J Am Diet Assoc. 2004 Aug;104(8):1287-91. PMID: 15281050
42 Adverse effects of dietary glycotoxins on wound healing in genetically diabetic mice. Diabetes. 2003 Nov;52(11):2805-13. PMID: 14578300
43 http://www.hosppract.com/issues/2000/11/eldvlas.htm
44 http://www.cbsnews.com/stories/2002/11/12/health/main529028.shtml
45 Prevention of diabetic nephropathy in mice by a diet low in glycoxidation products. Diabetes Metab Res Rev. 2002 May-Jun;18(3):224-37. Erratum in: Diabetes Metab Res Rev. 2002 Jul-Aug;18(4):332. PMID: 12112941
46 **Jorgensen L, Jenssen T, Joakimsen O, Heuch I, Ingebretsen OC, Jacobsen BK.** Glycated Hemoglobin Level Is Strongly Related to the Prevalence of Carotid Artery Plaques With High Echogenicity in Nondiabetic Individuals. The Tromso Study. Circulation. 2004 Jul 12 [Epub ahead of print] PMID: 15249512
47 **Gerstein HC.** Glycosylated hemoglobin: finally ready for prime time as a cardiovascular risk factor. Ann Intern Med. 2004 Sep 21;141(6):475-6. No abstract available. PMID: 15381522
48 **Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N.** Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. Ann Intern Med. 2004 Sep 21;141(6):413-20. PMID: 15381514
49 The predictive role of blood glucose for mortality in subjects with cardiovascular disease. Am J Epidemiol. 2006 Feb 15;163(4):342-51. Epub 2005 Dec 22. PMID: 16373527
50 **Metz TO, Alderson NL, Thorpe SR, Baynes JW.** Pyridoxamine, an inhibitor of advanced glycation and lipoxidation reactions: a novel therapy for treatment of diabetic complications. Arch Biochem Biophys. 2003 Nov 1;419(1):41-9. Review. PMID: 14568007
51 **Hammes HP, Du X, Edelstein D, Taguchi T, Matsumura T, Ju Q, Lin J, Bierhaus A, Nawroth P, Hannak D, Neumaier M, Bergfeld R, Giardino I, Brownlee M.** Benfotiamine blocks three major pathways of hyperglycemic damage and prevents experimental diabetic retinopathy. Nat Med. 2003 Mar;9(3):294-9. PMID: 12592403
52 **Midaoui AE, Elimadi A, Wu L, Haddad PS, de Champlain J.** Lipoic acid prevents hypertension, hyperglycemia, and the increase in heart mitochondrial superoxide production. Am J Hypertens. 2003 Mar;16(3):173-9. PMID: 12620694
53 **Jorgensen L, Jenssen T, Joakimsen O, Heuch I, Ingebretsen OC, Jacobsen BK.** Glycated hemoglobin level is strongly related to the prevalence of carotid artery plaques with high echogenicity in nondiabetic individuals: the Tromso study. Circulation. 2004 Jul 27;110(4):466-70. Epub 2004 Jul 12. PMID: 15249512

54 **Borugian MJ, Sheps SB, Whittemore AS, Wu AH, Potter JD, Gallagher RP.** Carbohydrates and colorectal cancer risk among Chinese in North America. Cancer Epidemiol Biomarkers Prev. 2002 Feb;11(2):187-93. PMID: 11867506
55 **Facchini FS, Saylor KL.** A Low-Iron-Available, Polyphenol-Enriched, Carbohydrate-Restricted Diet to Slow Progression of Diabetic Nephropathy. Diabetes. 2003 May;52(5):1204-1209. PMID: 12716753
56 **Ceriello A, Hanefeld M, Leiter L, Monnier L, Moses A, Owens D, Tajima N, Tuomilehto J.** Postprandial glucose regulation and diabetic complications. Arch Intern Med. 2004 Oct 25;164(19):2090-5. PMID: 15505121
57 **Brownlee M.** Biochemistry and molecular cell biology of diabetic complications. Nature. 2001 Dec 13;414(6865):813-20. PMID: 11742414
58 Normal fasting plasma glucose levels and type 2 diabetes in young men. N Engl J Med. 2005 Oct 6;353(14):1454-62. PMID: 16207847
59 Am J Clin Nutr 2000 Jun;71(6):1455-61; PMID: 10837285
60 Am J Clin Nutr 2002 Mar;75(3):492-8; PMID: 11864854
61 **Schulze MB, Liu S, Rimm EB, Manson JE, Willett WC, Hu FB.** Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women. Am J Clin Nutr. 2004 Aug;80(2):348-56. PMID: 15277155
62 **Augustin LS, Galeone C, Dal Maso L, Pelucchi C, Ramazzotti V, Jenkins DJ, Montella M, Talamini R, Negri E, Franceschi S, La Vecchia C.** Glycemic index, glycemic load and risk of prostate cancer. Int J Cancer. 2004 Nov 10;112(3):446. PMID: 15382070
63 **Slyper A, Jurva J, Pleuss J, Hoffmann R, Gutterman D.** Influence of glycemic load on HDL cholesterol in youth. Am J Clin Nutr. 2005 Feb;81(2):376-9. PMID: 15699224
64 **Oh K, Hu FB, Cho E, Rexrode KM, Stampfer MJ, Manson JE, Liu S, Willett WC.** Carbohydrate intake, glycemic index, glycemic load, and dietary fiber in relation to risk of stroke in women. Am J Epidemiol. 2005 Jan 15;161(2):161-9. PMID: 15632266
65 The lifetime risk of stroke: estimates from the framingham study. Stroke. 2006 Feb;37(2):345-50. Epub 2006 Jan 5. PMID: 16397184
66 Dietary carbohydrate intake and glycemic index in relation to cortical and nuclear lens opacities in the Age-Related Eye Disease Study. Am J Clin Nutr. 2006 May;83(5):1177-84. PMID: 16685063
67 Carbohydrate intake and glycemic index in relation to the odds of early cortical and nuclear lens opacities. Am J Clin Nutr. 2005 Jun;81(6):1411-6. PMID: 15941895
68 **Brand-Miller JC, Thomas M, Swan V, Ahmad ZI, Petocz P, Colagiuri S.** Physiological validation of the concept of glycemic load in lean young adults. J Nutr. 2003 Sep;133(9):2728-32. PMID: 12949357
69 **Wu LY, Juan CC, Hwang LS, Hsu YP, Ho PH, Ho LT.** Green tea supplementation ameliorates insulin resistance and increases glucose transporter IV content in a fructose-fed rat model. Eur J Nutr. 2004 Apr;43(2):116-24. Epub 2004 Jan 06. PMID: 15083319
70 http://venus.nildram.co.uk/veganmc/insulin.htm
71 **Archer VE.** Does dietary sugar and fat influence longevity? Med Hypotheses. 2003 Jun;60(6):924-9. PMID: 12699727
72 Consumption of sugar and sugar-sweetened foods and the risk of pancreatic cancer in a prospective study. Am J Clin Nutr. 2006 Nov;84(5):1171-6. PMID: 17093171
73 **Kris-Etherton PM, Harris WS, Appel LJ.** Omega-3 fatty acids and cardiovascular disease: new recommendations from the American Heart Association. Arterioscler Thromb Vasc Biol. 2003 Feb 1;23(2):151-2. Review. PMID: 12588750
74 **Kris-Etherton P, Daniels SR, Eckel RH, Engler M, Howard BV, Krauss RM, Lichtenstein AH, Sacks F, St Jeor S, Stampfer M, Grundy SM, Appel LJ, Byers T, Campos H, Cooney G, Denke MA, Kennedy E, Marckmann P, Pearson TA, Riccardi G, Rudel LL, Rudrum M, Stein DT, Tracy RP, Ursin V, Vogel RA, Zock PL, Bazzarre TL, Clark J.** AHA scientific statement: summary of the Scientific Conference on Dietary Fatty Acids and Cardiovascular Health. Conference summary from the Nutrition Committee of the American Heart Association. J Nutr. 2001 Apr;131(4):1322-6. No abstract available. PMID: 11285345 Free full text
75 **Siscovick DS, Lemaitre RN, Mozaffarian D.** The fish story: a diet-heart hypothesis with clinical implications: n-3 polyunsaturated fatty acids, myocardial vulnerability, and sudden death. Circulation. 2003 Jun 3;107(21):2632-4. PMID: 12782612
76 **Tiemeier H, Van Tuijl HR, Hofman A, Kiliaan AJ, Breteler MM.** Plasma fatty acid composition and depression are associated in the elderly: the Rotterdam Study. Am J Clin Nutr. 2003 Jul;78(1):40-46. PMID: 12816769
77 **Erkkila AT, Lehto S, Pyorala K, Uusitupa MI.** n-3 Fatty acids and 5-y risks of death and cardiovascular disease events in patients with coronary artery disease. Am J Clin Nutr. 2003 Jul;78(1):65-71. PMID: 12816772
78 **Bouwstra H, Dijck-Brouwer DJ, Wildeman JA, Tjoonk HM, Van Der Heide JC, Boersma ER, Muskiet FA, Hadders-Algra M.** Long-chain polyunsaturated fatty acids have a positive effect on the quality of general movements of healthy term infants. Am J Clin Nutr. 2003 Aug;78(2):313-318. PMID: 12885715
79 **Helland IB, Smith L, Saarem K, Saugstad OD, Drevon CA.** Maternal supplementation with very-long-chain n-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. Pediatrics. 2003 Jan;111(1):e39-44. PMID: 12509593
80 **Gago-Dominguez M, Yuan JM, Sun CL, Lee HP, Yu MC.** Opposing effects of dietary n-3 and n-6 fatty acids on mammary carcinogenesis: The Singapore Chinese Health Study. Br J Cancer. 2003 Nov 3;89(9):1686-92. PMID: 14583770

81 **Mamalakis G, Tornaritis M, Kafatos A.** Depression and adipose essential polyunsaturated fatty acids. Prostaglandins Leukot Essent Fatty Acids. 2002 Nov;67(5):311-8. PMID: 12445491
82 **Rajaram S, Burke K, Connell B, Myint T, Sabate J.** A monounsaturated fatty acid-rich pecan-enriched diet favorably alters the serum lipid profile of healthy men and women. J Nutr. 2001 Sep;131(9):2275-9. PMID: 11533266
83 **Sabate J.** Nut consumption, vegetarian diets, ischemic heart disease risk, and all-cause mortality: evidence from epidemiologic studies. Am J Clin Nutr. 1999 Sep;70(3 Suppl):500S-503S. Review. PMID: 10479222 free full text
84 http://waynesword.palomar.edu/ecoph8.htm
85 http://www.ajcn.org/cgi/content/abstract/80/1/76
86 **Tsai CJ, Leitzmann MF, Hu FB, Willett WC, Giovannucci EL.** A Prospective Cohort Study of Nut Consumption and the Risk of Gallstone Disease in Men. Am J Epidemiol. 2004 Nov 15;160(10):961-968. PMID: 15522852
87 **Mukuddem-Petersen J, Oosthuizen W, Jerling JC.** A Systematic Review of the Effects of Nuts on Blood Lipid Profiles in Humans. J. Nutr. 135:2082-2089, September 2005. REF
88 Nuts, body weight and insulin resistance. Br J Nutr. 2006 Nov;96 Suppl 2:S79-86. PMID: 17125537
89 **Morgan JM, Horton K, Reese D, Carey C, Walker K, Capuzzi DM.** Effects of walnut consumption as part of a low-fat, low-cholesterol diet on serum cardiovascular risk factors. Int J Vitam Nutr Res. 2002 Oct;72(5):341-7. PMID: 12463111
90 **Ros E, Nunez I, Perez-Heras A, Serra M, Gilabert R, Casals E, Deulofeu R.** A Walnut Diet Improves Endothelial Function in Hypercholesterolemic Subjects. A Randomized Crossover Trial. Circulation. 2004 Mar 22 [Epub ahead of print] PMID: 15037535
91 **Joan Sabaté, Ella Haddad, Jay S Tanzman, Pera Jambazian and Sujatha Rajaram.** Serum lipid response to the graduated enrichment of a Step I diet with almonds: a randomized feeding trial. Am J Clin Nutr. 2003 Jun;77(6):1379-84. PMID: 12791613
92 **Wien MA, Sabate JM, Ikle DN, Cole SE, Kandeel FR.** Almonds vs complex carbohydrates in a weight reduction program. Int J Obes Relat Metab Disord. 2003 Nov;27(11):1365-72. PMID: 14574348
93 **Garg ML, Blake RJ, Wills RB.** Macadamia Nut Consumption Lowers Plasma Total and LDL Cholesterol Levels in Hypercholesterolemic Men. J Nutr. 2003 Apr;133(4):1060-3. PMID: 12672919
94 **Kritchevsky D, Tepper SA, Klurfeld DM.** Lectin may contribute to the atherogenicity of peanut oil. Lipids. 1998 Aug;33(8):821-3. PMID: 9727614
95 **Satchithanandam S, Flynn TJ, Calvert RJ, Kritchevsky D.** Effect of peanut oil and randomized peanut oil on cholesterol and oleic acid absorption, transport, and distribution in the lymph of the rat. Lipids. 1999 Dec;34(12):1305-11. PMID: 10652990
96 http://www.scientificpsychic.com/fitness/fattyacids.html
97 **Mensink RP, Zock PL, Kester AD, Katan MB.** Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. Am J Clin Nutr. 2003 May;77(5):1146-55. PMID: 12716665
98 **Johnson CC, Gorell JM, Rybicki BA, Sanders K, Peterson EL.** Adult nutrient intake as a risk factor for Parkinson's disease. Int J Epidemiol. 1999 Dec;28(6):1102-9. PMID: 10661654 free full text at http://ije.oupjournals.org/cgi/reprint/28/6/1102.pdf
99 Dietary Saturated Fat Intake Is Inversely Associated with Bone Density in Humans: Analysis of NHANES III. J Nutr. 2006 Jan;136(1):159-65. PMID: 16365076
100 http://msnbc.msn.com/id/12867692/
101 Dietary fat and serum lipids: an evaluation of the experimental data. Am J Clin Nutr. 1993 Jun;57(6):875-83. Review. Erratum in: Am J Clin Nutr 1993 Aug;58(2):245. PMID: 8503356
102 **Morris MC, Evans DA, Bienias JL, Tangney CC, Bennett DA, Aggarwal N, Schneider J, Wilson RS.** Dietary fats and the risk of incident Alzheimer disease. Arch Neurol. 2003 Feb;60(2):194-200. PMID: 12580703
103 Dietary fat intake and the risk of coronary heart disease in women. N Engl J Med. 1997 Nov 20;337(21):1491-9. PMID: 9366580
104 **Logroscino G, Marder K, Cote L, Tang MX, Shea S, Mayeux R** Dietary lipids and antioxidants in Parkinson's disease: a population-based, case-control study. Ann Neurol. 1996 Jan;39(1):89-94. PMID: 8572672
105 **Robertson MD, Jackson KG, Fielding BA, Williams CM, Frayn KN.** Acute effects of meal fatty acid composition on insulin sensitivity in healthy post-menopausal women. Br J Nutr. 2002 Dec;88(6):635-40. PMID: 12493085
106 **Stender S, Dyerberg J.** Influence of Trans Fatty Acids on Health. Ann Nutr Metab. 2004 [Epub ahead of print] PMID: 14679314
107 **Bolte G, Winkler G, Holscher B, Thefeld W, Weiland SK, Heinrich J.** Margarine Consumption, Asthma, and Allergy in Young Adults: Results of the German National Health Survey 1998. Ann Epidemiol. 2005 Mar;15(3):207-213. PMID: 15723766
108 **Sanders TA.** High- versus low-fat diets in human diseases. Curr Opin Clin Nutr Metab Care. 2003 Mar;6(2):151-5. PMID: 12589184
109 **Calder PC, Deckelbaum RJ.** Fat as a physiological regulator: the news gets better. Curr Opin Clin Nutr Metab Care. 2003 Mar;6(2):127-31. PMID: 12589182
110 **Strychar I, Ishac A, Rivard M, Lussier-Cacan S, Beauregard H, Aris-Jilwan N, Radwan F, Yale JF.** Impact of a

high-monounsaturated-fat diet on lipid profile in subjects with type 1 diabetes. J Am Diet Assoc. 2003 Apr;103(4):467-474. PMID: 12669010
111 **Gill JM, Brown JC, Caslake MJ, Wright DM, Cooney J, Bedford D, Hughes DA, Stanley JC, Packard CJ.** Effects of dietary monounsaturated fatty acids on lipoprotein concentrations, compositions, and subfraction distributions and on VLDL apolipoprotein B kinetics: dose-dependent effects on LDL. Am J Clin Nutr. 2003 Jul;78(1):47-56. PMID: 12816770
112 **Williams CM, Smith RD, Kelly CN, Fielding BA, Hauton D, Silva KD, Nydahl MC, Miller GJ, Williams CM.** Long-term monounsaturated fatty acid diets reduce platelet aggregation in healthy young subjects. Br J Nutr. 2003 Sep;90(3):597-607. PMID: 13129466
113 **Ochoa JJ, Quiles JL, Ibanez S, Martinez E, Lopez-Frias M, Huertas JR, Mataix J.** Aging-related oxidative stress depends on dietary lipid source in rat postmitotic tissues. J Bioenerg Biomembr. 2003 Jun;35(3):267-75. PMID: 13678277
114 **Colette C, Percheron C, Pares-Herbute N, Michel F, Pham TC, Brillant L, Descomps B, Monnier L.** Exchanging carbohydrates for monounsaturated fats in energy-restricted diets: effects on metabolic profile and other cardiovascular risk factors. Int J Obes Relat Metab Disord. 2003 Jun;27(6):648-56. PMID: 12833107
115 **Perez-Jimenez F, Lopez-Miranda J, Mata P.** Protective effect of dietary monounsaturated fat on arteriosclerosis: beyond cholesterol. Atherosclerosis. 2002 Aug;163(2):385-98. Review. PMID: 12052487
116 **Faine LA, Diniz YS, Galhardi CM, Rodrigues HG, Burneiko RC, Santana LS, Cicogna AC, Novelli EL.** Synergistic action of olive oil supplementation and dietary restriction on serum lipids and cardiac antioxidant defences. Can J Physiol Pharmacol. 2004 Nov;82(11):969-975. PMID: 15644936
117 **Solfrizzi V, D'Introno A, Colacicco AM, Capurso C, Palasciano R, Capurso S, Torres F, Capurso A, Panza F.** Unsaturated fatty acids intake and all-causes mortality: a 8.5-year follow-up of the Italian Longitudinal Study on Aging. Exp Gerontol. 2005 Apr;40(4):335-43. PMID: 15820615
118 Dietary fatty acids and the risk of Parkinson disease: the Rotterdam study. Neurology. 2005 Jun 28;64(12):2040-5. PMID: 15985568
119 **van Gool CJ, Thijs C, Henquet CJ, van Houwelingen AC, Dagnelie PC, Schrander J, Menheere PP, van den brandt PA.** Gamma-linolenic acid supplementation for prophylaxis of atopic dermatitis--a randomized controlled trial in infants at high familial risk. Am J Clin Nutr. 2003 Apr;77(4):943-51. PMID: 12663296
120 **Seidman MD, Khan MJ, Tang WX, Quirk WS.** Influence of lecithin on mitochondrial DNA and age-related hearing loss. Otolaryngol Head Neck Surg. 2002 Sep; 127(3): 138-44. PMID: 12297801
121 **Lambert AJ, Merry BJ.** Effect of Caloric Restriction on Mitochondrial Reactive Oxygen Species Production and Bioenergetics - REVERSAL BY INSULIN. Am J Physiol Regul Integr Comp Physiol. 2003 Sep 11 [Epub ahead of print] PMID: 12969875
122 **Studer M, Briel M, Leimenstoll B, Glass TR, Bucher HC.** Effect of different antilipidemic agents and diets on mortality: a systematic review. Arch Intern Med. 2005 Apr 11;165(7):725-30. PMID: 15824290
123 **Laaksonen DE, Nyyssonen K, Niskanen L, Rissanen TH, Salonen JT.** Prediction of Cardiovascular Mortality in Middle-aged Men by Dietary and Serum Linoleic and Polyunsaturated Fatty Acids. Arch Intern Med. 2005 Jan 24;165(2):193-9. PMID: 15668366
124 http://calorierestriction.org/post/?a=ind0108&p=172706
125 **Melanson SF, Lewandrowski EL, Flood JG, Lewandrowski KB.** Measurement of organochlorines in commercial over-the-counter fish oil preparations: implications for dietary and therapeutic recommendations for omega-3 fatty acids and a review of the literature. Arch Pathol Lab Med. 2005 Jan;129(1):74-7. PMID: 15628911
126 **Iribarren C, Markovitz JH, Jacobs DR, Schreiner PJ, Daviglus M, Hibbeln JR.** Dietary intake of n-3, n-6 fatty acids and fish: Relationship with hostility in young adults-the CARDIA study. Eur J Clin Nutr. 2004 Jan; 58(1): 24-31. PMID: 14679363
127 **Richardson AJ, Cyhlarova E, Ross MA.** Omega-3 and omega-6 fatty acid concentrations in red blood cell membranes relate to schizotypal traits in healthy adults. Prostaglandins Leukot Essent Fatty Acids. 2003 Dec;69(6):461-6. PMID: 14623500
128 **He K, Song Y, Daviglus ML, Liu K, Van Horn L, Dyer AR, Greenland P.** Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies. Circulation. 2004 Jun 8;109(22):2705-11. PMID: 15184295
129 **He K, Song Y, Daviglus ML, Liu K, Van Horn L, Dyer AR, Goldbourt U, Greenland P.** Fish consumption and incidence of stroke: a meta-analysis of cohort studies. Stroke. 2004 Jul;35(7):1538-42. Epub 2004 May 20. PMID: 15155968
130 **Mozaffarian D, Longstreth WT Jr, Lemaitre RN, Manolio TA, Kuller LH, Burke GL, Siscovick DS.** Fish Consumption and Stroke Risk in Elderly Individuals: The Cardiovascular Health Study. Arch Intern Med. 2005 Jan 24;165(2):200-206. PMID: 15668367
131 **Dallongeville J, Yarnell J, Ducimetiere P, Arveiler D, Ferrieres J, Montaye M, Luc G, Evans A, Bingham A, Hass B, Ruidavets JB, Amouyel P.** Fish consumption is associated with lower heart rates. Circulation. 2003 Aug 19;108(7):820-5. Epub 2003 Aug 11. PMID: 12912821
132 free full text at http://atvb.ahajournals.org/cgi/content/full/23/2/e20#TBL2
133 **Barberger-Gateau P, Letenneur L, Deschamps V, Peres K, Dartigues JF, Renaud S.** Fish, meat, and risk of dementia: cohort study. BMJ. 2002 Oct 26;325(7370):932-3. PMID: 12399342

134 http://www.ajcn.org/cgi/content/abstract/80/1/204
135 **Augustsson K, Michaud DS, Rimm EB, Leitzmann MF, Stampfer MJ, Willett WC, Giovannucci E.** A prospective study of intake of fish and marine fatty acids and prostate cancer. Cancer Epidemiol Biomarkers Prev. 2003 Jan;12(1):64-7. PMID: 12540506
136 http://www.ajcn.org/cgi/content/abstract/80/6/1650
137 Cigarette Smoking, Fish Consumption, Omega-3 Fatty Acid Intake, and Associations With Age-Related Macular Degeneration: The US Twin Study of Age-Related Macular Degeneration. Arch Ophthalmol. 2006 Jul;124(7):995-1001. PMID: 16832023
138 **Trichopoulou A, Costacou T, Bamia C, Trichopoulos D.** Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003 Jun 26;348(26):2599-608. PMID: 12826634
139 Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. JAMA. 2004 Sep 22;292(12):1433-9. PMID: 15383513
140 Mediterranean diet and risk for Alzheimer's disease. Ann Neurol. 2006 Apr 18; PMID: 16622828
141 **Ravaglia G, Forti P, Maioli F, Muscari A, Sacchetti L, Arnone G, Nativio V, Talerico T, Mariani E.** Homocysteine and cognitive function in healthy elderly community dwellers in Italy. Am J Clin Nutr. 2003 Mar;77(3):668-73. PMID: 12600859
142 http://www.ajcn.org/cgi/content/abstract/82/3/627
143 **Ganji V, Kafai MR.** Demographic, health, lifestyle, and blood vitamin determinants of serum total homocysteine concentrations in the third National Health and Nutrition Examination Survey, 1988-1994. Am J Clin Nutr. 2003 Apr;77(4):826-33. PMID: 12663279
144 http://circ.ahajournals.org/cgi/content/abstract/109/5/601
145 http://www.ajcn.org/cgi/content/abstract/80/6/1574
146 **van Oort FV, Melse-Boonstra A, Brouwer IA, Clarke R, West CE, Katan MB, Verhoef P.** Folic acid and reduction of plasma homocysteine concentrations in older adults: a dose-response study. Am J Clin Nutr. 2003 May;77(5):1318-23. PMID: 12716688
147 **Atzmon G, Gabriely I, Greiner W, Davidson D, Schechter C, Barzilai N.** Plasma HDL levels highly correlate with cognitive function in exceptional longevity. J Gerontol A Biol Sci Med Sci. 2002 Nov;57(11):M712-5. PMID: 12403798
148 **Bittner V.** Non-high-density lipoprotein cholesterol and cardiovascular disease. Curr Opin Lipidol. 2003 Aug;14(4):367-71. PMID: 12865734
149 **Nissen SE, Tuzcu EM, Schoenhagen P, Brown BG, Ganz P, Vogel RA, Crowe T, Howard G, Cooper CJ, Brodie B, Grines CL, DeMaria AN; REVERSAL Investigators.** Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial. JAMA. 2004 Mar 3;291(9):1071-80. PMID: 14996776
150 **Jenkins DJ, Kendall CW, Marchie A, Faulkner DA, Wong JM, de Souza R, Emam A, Parker TL, Vidgen E, Lapsley KG, Trautwein EA, Josse RG, Leiter LA, Connelly PW.** Effects of a dietary portfolio of cholesterol-lowering foods vs lovastatin on serum lipids and C-reactive protein. JAMA. 2003 Jul 23;290(4):502-10. PMID: 12876093
151 **Jenkins DJ, Kendall CW, Marchie A, Faulkner DA, Wong JM, de Souza R, Emam A, Parker TL, Vidgen E, Trautwein EA, Lapsley KG, Josse RG, Leiter LA, Singer W, Connelly PW.** Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants. Am J Clin Nutr. 2005 Feb;81(2):380-7. PMID: 15699225
152 **Sacks FM.** Dietary phytoestrogens to prevent cardiovascular disease: early promise unfulfilled. Circulation. 2005 Feb 1;111(4):385-7. No abstract available. PMID: 15687122
153 http://www.lipidsonline.org/slides/cme_pdf/talk027.pdf
154 **McGwin G Jr, McNeal S, Owsley C, Girkin C, Epstein D, Lee PP.** Statins and other cholesterol-lowering medications and the presence of glaucoma. Arch Ophthalmol. 2004 Jun;122(6):822-6. PMID: 15197056
155 **Liu S, Sesso HD, Manson JE, Willett WC, Buring JE.** Is intake of breakfast cereals related to total and cause-specific mortality in men? Am J Clin Nutr. 2003 Mar;77(3):594-9. PMID: 12600848
156 **Montonen J, Knekt P, Jarvinen R, Aromaa A, Reunanen A.** Whole-grain and fiber intake and the incidence of type 2 diabetes. Am J Clin Nutr. 2003 Mar;77(3):622-9. PMID: 12600852
157 **McIntosh GH, Noakes M, Royle PJ, Foster PR.** Whole-grain rye and wheat foods and markers of bowel health in overweight middle-aged men. Am J Clin Nutr. 2003 Apr;77(4):967-74. PMID: 12663299
158 **Montonen J, Knekt P, Jarvinen R, Aromaa A, Reunanen A.** Whole-grain and fiber intake and the incidence of type 2 diabetes. Am J Clin Nutr. 2003 Mar;77(3):622-9. PMID: 12600852
159 Whole-grain intake is inversely associated with the metabolic syndrome and mortality in older adults. Am J Clin Nutr. 2006 Jan;83(1):124-31. PMID: 16400060
160 http://www.ajcn.org/cgi/content/abstract/78/5/920
161 **Fung TT, Hu FB, Pereira MA, Liu S, Stampfer MJ, Colditz GA, Willett WC.** Whole-grain intake and the risk of type 2 diabetes: a prospective study in men. Am J Clin Nutr. 2002 Sep;76(3):535-40. PMID: 12197996
162 Whole-grain and fiber intakes and periodontitis risk in men. Am J Clin Nutr. 2006 Jun;83(6):1395-400. PMID: 16762952
163 http://www.ajcn.org/cgi/content/abstract/80/6/1492

164 Effect of an oat bran enriched diet on the atherogenic lipid profile in patients with an increased coronary heart disease risk. A controlled randomized lifestyle intervention study. Ann Nutr Metab. 2003;47(6):306-11. PMID: 14520027
165 Effect of an oat bran-rich supplement on the metabolic profile of overweight premenopausal women. Ann Nutr Metab. 2005 May-Jun;49(3):141-8. Epub 2005 May 24. PMID: 15942159
166 **Vanharanta M, Voutilainen S, Rissanen TH, Adlercreutz H, Salonen JT.** Risk of cardiovascular disease-related and all-cause death according to serum concentrations of enterolactone: Kuopio Ischaemic Heart Disease Risk Factor Study. Arch Intern Med. 2003 May 12;163(9):1099-104. PMID: 12742810
167 **Tarpila S, Aro A, Salminen I, Tarpila A, Kleemola P, Akkila J, Adlercreutz H.** The effect of flaxseed supplementation in processed foods on serum fatty acids and enterolactone. Eur J Clin Nutr. 2002 Feb;56(2):157-65. PMID: 11857049
168 **Bhathena SJ, Ali AA, Haudenschild C, Latham P, Ranich T, Mohamed AI, Hansen CT, Velasquez MT.** Dietary Flaxseed Meal is More Protective Than Soy Protein Concentrate Against Hypertriglyceridemia and Steatosis of the Liver in an Animal Model of Obesity. J Am Coll Nutr. 2003 Apr;22(2):157-64. PMID: 12672712 (USDA study)
169 **Lee IM, Sesso HD, Oguma Y, Paffenbarger RS Jr.** Relative intensity of physical activity and risk of coronary heart disease. Circulation. 2003 Mar 4;107(8):1110-6. PMID: 12615787
170 **Kurl S, Laukkanen JA, Rauramaa R, Lakka TA, Sivenius J, Salonen JT.** Cardiorespiratory fitness and the risk for stroke in men. Arch Intern Med. 2003 Jul 28;163(14):1682-8. PMID: 12885683
171 http://www.sciencedaily.com/releases/2003/05/030529081315.htm
172 **Hu G, Barengo NC, Tuomilehto J, Lakka TA, Nissinen A, Jousilahti P.** Relationship of Physical Activity and Body Mass Index to the Risk of Hypertension: A Prospective Study in Finland. Hypertension. 2004 Jan;43(1):25-30. Epub 2003 Dec 01. PMID: 14656958
173 **Lee CD, Folsom AR, Blair SN.** Physical activity and stroke risk: a meta-analysis. Stroke. 2003 Oct;34(10):2475-81. Epub 2003 Sep 18. PMID: 14500932
174 **Holloszy JO.** Longevity of exercising male rats: effect of an antioxidant supplemented diet. Mech Ageing Dev. 1998 Feb 16;100(3):211-9. PMID: 9578110
175 **Holloszy JO.** Mortality rate and longevity of food-restricted exercising male rats: a reevaluation. J Appl Physiol. 1997 Feb;82(2):399-403. PMID: 9049716
176 **Chang-Claude J, Hermann S, Eilber U, Steindorf K.** Lifestyle determinants and mortality in German vegetarians and health-conscious persons: results of a 21-year follow-up. Cancer Epidemiol Biomarkers Prev. 2005 Apr;14(4):963-8. PMID: 15824171
177 **Pimentel AE, Gentile CL, Tanaka H, Seals DR, Gates PE.** Greater rate of decline in maximal aerobic capacity with age in endurance-trained than in sedentary men. J Appl Physiol. 2003 Jun;94(6):2406-13. Epub 2003 Jan 17. PMID: 12533496
178 **Ross R, Janssen I, Dawson J, Kungl AM, Kuk JL, Wong SL, Nguyen-Duy TB, Lee S, Kilpatrick K, Hudson R.** Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. Obes Res. 2004 May;12(5):789-98. PMID: 15166299
179 Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. Lancet Neurol. 2005 Nov;4(11):705-11. PMID: 16239176
180 Exercise is associated with reduced risk for incident dementia among persons 65 years of age and older. Ann Intern Med. 2006 Jan 17;144(2):73-81. PMID: 16418406
181 Physical Activity and the 15-year Cumulative Incidence of Age-related Macular Degeneration: The Beaver Dam Eye Study. Br J Ophthalmol. 2006 Oct 31; PMID: 17077116
182 Physical activity and risk of colon and rectal cancers: the European prospective investigation into cancer and nutrition. Cancer Epidemiol Biomarkers Prev. 2006 Dec;15(12):2398-407. PMID: 17164362
183 **Avisar R, Avisar E, Weinberger D.** Effect of coffee consumption on intraocular pressure. Ann Pharmacother. 2002 Jun;36(6):992-5. PMID: 12022898
184 **Maia L, de Mendonca A.** Does caffeine intake protect from Alzheimer's disease? Eur J Neurol. 2002 Jul;9(4):377-82. PMID: 12099922
185 **Negishi H, Xu JW, Ikeda K, Njelekela M, Nara Y, Yamori Y.** Black and Green Tea Polyphenols Attenuate Blood Pressure Increases in Stroke-Prone Spontaneously Hypertensive Rats. J Nutr. 2004 Jan;134(1):38-42. PMID: 14704290
186 **Yang YC, Lu FH, Wu JS, Wu CH, Chang CJ.** The protective effect of habitual tea consumption on hypertension. Arch Intern Med. 2004 Jul 26;164(14):1534-40. PMID: 15277285
187 Addition of milk prevents vascular protective effects of tea. Eur Heart J. 2007 Jan 9; PMID: 17213230
188 **Jankun J, Selman SH, Swiercz R, Skrzypczak-Jankun E.** Why drinking green tea could prevent cancer. Nature. 1997 Jun 5;387(6633):561. No abstract available. PMID: 9177339
189 http://www.aor.ca/MedicalAbsDetail.asp?abs_id=84
190 **Wu AH, Yu MC, Tseng CC, Hankin J, Pike MC.** Green tea and risk of breast cancer in Asian Americans. Int J Cancer. 2003 Sep 10;106(4):574-9. PMID: 12845655
191 http://www.ajcn.org/cgi/content/abstract/80/6/1558
192 http://www.ajcn.org/cgi/content/abstract/81/1/122
193 **Panagiotakos DB, Pitsavos C, Chrysohoou C, Kokkinos P, Toutouzas P, Stefanadis C.** The J-shaped effect of coffee

consumption on the risk of developing acute coronary syndromes: the CARDIO2000 case-control study. J Nutr. 2003 Oct;133(10):3228-32. PMID: 14519815
194 Consumption of coffee is associated with reduced risk of death attributed to inflammatory and cardiovascular diseases in the Iowa Women's Health Study. Am J Clin Nutr. 2006 May;83(5):1039-46. PMID: 16685044
195 **Rust J.** Coffee intake over 33 years is not associated with developing hypertension. J Clin Hypertens (Greenwich). 2002 Nov-Dec;4(6):434. No abstract available. PMID: 12461309
196 Habitual caffeine intake and the risk of hypertension in women. JAMA. 2005 Nov 9;294(18):2330-5. PMID: 16278361
197 **Verhoef P, Pasman WJ, Van Vliet T, Urgert R, Katan MB.** Contribution of caffeine to the homocysteine-raising effect of coffee: a randomized controlled trial in humans. Am J Clin Nutr. 2002 Dec;76(6):1244-8. PMID: 12450889
198 **Iwai N, Ohshiro H, Kurozawa Y, Hosoda T, Morita H, Funakawa K, Okamoto M, Nose T.** Relationship between coffee and green tea consumption and all-cause mortality in a cohort of a rural Japanese population. J Epidemiol. 2002 May;12(3):191-8. PMID: 12164320
199 **Rosengren A, Dotevall A, Wilhelmsen L, Thelle D, Johansson S.** Coffee and incidence of diabetes in Swedish women: a prospective 18-year follow-up study. J Intern Med. 2004 Jan;255(1):89-95. PMID: 14687243
200 **van Dam RM, Feskens EJ.** Coffee consumption and risk of type 2 diabetes mellitus. Lancet. 2002 Nov 9;360(9344):1477-8. PMID: 12433517
201 **Salazar-Martinez E, Willett WC, Ascherio A, Manson JE, Leitzmann MF, Stampfer MJ, Hu FB.** Coffee consumption and risk for type 2 diabetes mellitus. Ann Intern Med. 2004 Jan 6;140(1):1-8. PMID: 14706966
202 **Tuomilehto J, Hu G, Bidel S, Lindstrom J, Jousilahti P.** Coffee consumption and risk of type 2 diabetes mellitus among middle-aged Finnish men and women. JAMA. 2004 Mar 10;291(10):1213-9. PMID: 15010442
203 Coffee consumption and risk of type 2 diabetes: a systematic review. JAMA. 2005 Jul 6;294(1):97-104. PMID: 15998896
204 Consumption of coffee, but not black tea, is associated with decreased risk of premenopausal breast cancer. J Nutr. 2006 Jan;136(1):166-71. PMID: 16365077
205 Carbonated soft drink consumption and risk of esophageal adenocarcinoma. J Natl Cancer Inst. 2006 Jan 4;98(1):72-5. PMID: 16391374
206 http://www.nal.usda.gov/fnic/foodcomp/Data/Flav/flav.html
207 CR society post, 2006-04-09
208 **Lagiou P, Samoli E, Lagiou A, Tzonou A, Kalandidi A, Peterson J, Dwyer J, Trichopoulos D.** Intake of specific flavonoid classes and coronary heart disease-a case-control study in Greece. Eur J Clin Nutr. 2004 Dec;58(12):1643-1648. PMID: 15226759
209 http://www.nal.usda.gov/fnic/foodcomp/Data/Flav/flav.pdf
210 **Lee CK, Pugh TD, Klopp RG, Edwards J, Allison DB, Weindruch R, Prolla TA.** The impact of alpha-lipoic acid, coenzyme Q10 and caloric restriction on life span and gene expression patterns in mice. Free Radic Biol Med. 2004 Apr 15;36(8):1043-57. PMID: 15059645
211 Dietary intake of antioxidants and risk of age-related macular degeneration. JAMA. 2005 Dec 28;294(24):3101-7. PMID: 16380590
212 http://www.agingeye.net/maculardegen/maculardegeninformation.php
213 **Brown MJ, Ferruzzi MG, Nguyen ML, Cooper DA, Eldridge AL, Schwartz SJ, White WS.** Carotenoid bioavailability is higher from salads ingested with full-fat than with fat-reduced salad dressings as measured with electrochemical detection. Am J Clin Nutr. 2004 Aug;80(2):396-403. PMID: 15277161
214 Vegetable Intake and Long-term Survival among Middle-aged Men in Italy. Ann Epidemiol 2003;13:424–430.s
215 Associations of vegetable and fruit consumption with age-related cognitive change. Neurology. 2006 Oct 24;67(8):1370-6. PMID: 17060562
216 **Siener R, Hesse A.** The effect of a vegetarian and different omnivorous diets on urinary risk factors for uric acid stone formation. Eur J Nutr. 2003 Dec;42(6):332-7. PMID: 14673606
217 http://msnbc.msn.com/id/14059947/
218 **Joseph JA, Denisova NA, Bielinski D, Fisher DR, Shukitt-Hale B.** Oxidative stress protection and vulnerability in aging: putative nutritional implications for intervention. Mech Ageing Dev. 2000 Jul 31;116(2-3):141-53. Review. PMID: 10996014
219 **Milgram NW, Head E, Zicker SC, Ikeda-Douglas CJ, Murphey H, Muggenburg B, Siwak C, Tapp D, Cotman CW.** Learning ability in aged beagle dogs is preserved by behavioral enrichment and dietary fortification: a two-year longitudinal study. Neurobiol Aging. 2005 Jan;26(1):77-90. PMID: 15585348
220 **Djousse L, Arnett DK, Coon H, Province MA, Moore LL, Ellison RC.** Fruit and vegetable consumption and LDL cholesterol: the National Heart, Lung, and Blood Institute Family Heart Study. Am J Clin Nutr. 2004 Feb;79(2):213-7. PMID: 14749225
221 **Tylavsky FA, Holliday K, Danish R, Womack C, Norwood J, Carbone L.** Fruit and vegetable intakes are an independent predictor of bone size in early pubertal children. Am J Clin Nutr. 2004 Feb;79(2):311-7. PMID: 14749239
222 **Hung HC, Joshipura KJ, Jiang R, Hu FB, Hunter D, Smith-Warner SA, Colditz GA, Rosner B, Spiegelman D, Willett WC.** Fruit and vegetable intake and risk of major chronic disease. J Natl Cancer Inst. 2004 Nov 3;96(21):1577-84.

PMID: 15523086
223 **Schwenke DC.** Insulin resistance, low-fat diets, and low-carbohydrate diets: time to test new menus. Curr Opin Lipidol. 2005 Feb;16(1):55-60. PMID: 15650564
224 A 4-wk intervention with high intake of carotenoid-rich vegetables and fruit reduces plasma C-reactive protein in healthy, nonsmoking men. Am J Clin Nutr. 2005 Nov;82(5):1052-8. PMID: 16280438
225 Fruit and vegetable consumption and risk of stroke: a meta-analysis of cohort studies. Neurology. 2005 Oct 25;65(8):1193-7. PMID: 16247045
226 Fruit and vegetable consumption and stroke: meta-analysis of cohort studies. Lancet. 2006 Jan 28;367(9507):320-6. PMID: 16443039
227 Association between fruit and vegetable consumption and oral cancer: a meta-analysis of observational studies. Am J Clin Nutr. 2006 May;83(5):1126-1134. PMID: 16685056
228 Fruit and Vegetable Consumption and Risk of Coronary Heart Disease: A Meta-Analysis of Cohort Studies. J Nutr. 2006 Oct;136(10):2588-2593. PMID: 16988131
229 Lancet 2000 Aug 26;356(9231):724-9; PMID: 11085692
230 Proc Natl Acad Sci U S A 2002 May 28;99(11):7610-5; PMID: 12032331
231 N. V. Matusheski and E. H. JEFFERY. Processing conditions improve the yield of the anticarcinogen sulforaphane from broccoli. Department of Food Science and Human Nutrition, University of Illinois Institute of Food Technology 2002 Annual Meeting. Abstract
232 **Wu L, Ashraf MH, Facci M, Wang R, Paterson PG, Ferrie A, Juurlink BH.** Dietary approach to attenuate oxidative stress, hypertension, and inflammation in the cardiovascular system. Proc Natl Acad Sci U S A. 2004 May 4;101(18):7094-9. Epub 2004 Apr 21. PMID: 15103025
233 **Kang JH, Ascherio A, Grodstein F.** Fruit and vegetable consumption and cognitive decline in aging women. Ann Neurol. 2005 Apr 25;57(5):713-720 [Epub ahead of print] PMID: 15852398
234 **Hsing AW, Chokkalingam AP, Gao YT, Madigan MP, Deng J, Gridley G, Fraumeni JF Jr.** Allium vegetables and risk of prostate cancer: a population-based study. J Natl Cancer Inst. 2002 Nov 6;94(21):1648-51. PMID: 12419792
235 **Josling P.** Preventing the common cold with a garlic supplement: a double-blind, placebo-controlled survey. Adv Ther. 2001 Jul-Aug;18(4):189-93. PMID: 11697022
236 **Lopez-Carrillo L, Lopez-Cervantes M, Robles-Diaz G, Ramirez-Espitia A, Mohar-Betancourt A, Meneses-Garcia A, Lopez-Vidal Y, Blair A.** Capsaicin consumption, Helicobacter pylori positivity and gastric cancer in Mexico. Int J Cancer. 2003 Aug 20;106(2):277-82. PMID: 12800206
237 **Mozaffarieh M, Sacu S, Wedrich A.** The role of the carotenoids, lutein and zeaxanthin, in protecting against age-related macular degeneration: A review based on controversial evidence. Nutr J. 2003 Dec 11;2(1):20. PMID: 14670087 http://www.nutritionj.com/content/2/1/20 (free full text)
238 Lutein and zeaxanthin intakes and risk of age-related macular degeneration and cataracts: an evaluation using the Food and Drug Administration's evidence-based review system for health claims. Am J Clin Nutr. 2006 Nov;84(5):971-4. PMID: 17093145
239 **Jian L, Du CJ, Lee AH, Binns CW.** Do dietary lycopene and other carotenoids protect against prostate cancer? Int J Cancer. 2004 Oct 28;113(6):1010-1014 PMID: 15514967
240 http://www.nutrition.org/cgi/content/abstract/135/3/431
241 **Pereira MA, O'Reilly E, Augustsson K, Fraser GE, Goldbourt U, Heitmann BL, Hallmans G, Knekt P, Liu S, Pietinen P, Spiegelman D, Stevens J, Virtamo J, Willett WC, Ascherio A.** Dietary fiber and risk of coronary heart disease: a pooled analysis of cohort studies. Arch Intern Med. 2004 Feb 23;164(4):370-6. PMID: 14980987, http://archinte.ama-assn.org/cgi/content/abstract/164/4/370
242 **Kurowska EM, Manthey JA.** Hypolipidemic effects and absorption of citrus polymethoxylated flavones in hamsters with diet-induced hypercholesterolemia. J Agric Food Chem. 2004 May 19;52(10):2879-86. PMID: 15137829
243 http://www.sciencedaily.com/releases/2004/05/040512041238.htm
244 **Hakim IA, Harris RB, Ritenbaugh C.** Citrus peel use is associated with reduced risk of squamous cell carcinoma of the skin. Nutr Cancer. 2000;37(2):161-8. PMID: 11142088
245 **Crowell PL.** Prevention and therapy of cancer by dietary monoterpenes. J Nutr. 1999 Mar;129(3):775S-778S. Review. PMID: 10082788
246 http://www.veganoutreach.org/healthargument.html
247 **Key TJ, Fraser GE, Thorogood M, Appleby PN, Beral V, Reeves G, Burr ML, Chang-Claude J, Frentzel-Beyme R, Kuzma JW, Mann J, McPherson K.** Mortality in vegetarians and nonvegetarians: detailed findings from a collaborative analysis of 5 prospective studies. Am J Clin Nutr. 1999 Sep;70(3 Suppl):516S-524S. PMID: 10479225
248 JAMA, May 26, 2004; 291 (20) 2510 http://jama.ama-assn.org/cgi/content/extract/291/20/2510
249 **Chang-Claude J, Hermann S, Eilber U, Steindorf K.** Lifestyle determinants and mortality in German vegetarians and health-conscious persons: results of a 21-year follow-up. Cancer Epidemiol Biomarkers Prev. 2005 Apr;14(4):963-8. PMID: 15824171
250 **Cho E, Seddon JM, Rosner B, Willett WC, Hankinson SE.** Prospective study of intake of fruits, vegetables, vitamins, and carotenoids and risk of age-related maculopathy. Arch Ophthalmol. 2004 Jun;122(6):883-92. PMID: 15197064

251 Fruit and vegetable juices and Alzheimer's disease: the Kame Project. Am J Med. 2006 Sep;119(9):751-9. PMID: 16945610
252 **Joseph JA, Shukitt-Hale B, Denisova NA, Bielinski D, Martin A, McEwen JJ, Bickford PC.** Reversals of age-related declines in neuronal signal transduction, cognitive, and motor behavioral deficits with blueberry, spinach, or strawberry dietary supplementation. J Neurosci. 1999 Sep 15;19(18):8114-21.PMID: 10479711
253 R. Martin, R.J. Coppings, K.E. Gerstmann, J.A. Joseph, A.C. Kokesh, B. Kristal, D. Mathew, B. Sachs, A. Pruchnicki, R. Schnoll, A. Wetherell. THE 2002 BLUEBERRY HEALTH STUDY: DAILY BLUEBERRIES IMPROVE DECISION-SPEED AND AGE-RELATED HEALTH INDICATORS.
http://www.americanaging.org/past_meetings/AGE03/abs/Martin.htm.
254 **Boileau TW, Liao Z, Kim S, Lemeshow S, Erdman JW Jr, Clinton SK.** Prostate carcinogenesis in N-methyl-N-nitrosourea (NMU)-testosterone-treated rats fed tomato powder, lycopene, or energy-restricted diets. J Natl Cancer Inst. 2003 Nov 5;95(21):1578-86. PMID: 14600090
255 Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation. Clin Nutr. 2004 Jun;23(3):423-33. PMID: 15158307
256 Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. Am J Cardiol. 2005 Sep 15;96(6):810-4. PMID: 16169367
257 http://pubs.acs.org/cgi-bin/abstract.cgi/jafcau/asap/abs/jf058171g.html
258 Legumes: the most important dietary predictor of survival in older people of different ethnicities. Asia Pac J Clin Nutr. 2004;13(Suppl):S126. PMID: 15294666
259 Vegetables, fruits, legumes and prostate cancer: a multiethnic case-control study. Cancer Epidemiol Biomarkers Prev. 2000 Aug;9(8):795-804. PMID: 10952096
260 **Mukamal KJ, Kuller LH, Fitzpatrick AL, Longstreth WT Jr, Mittleman MA, Siscovick DS.** Prospective study of alcohol consumption and risk of dementia in older adults. JAMA. 2003 Mar 19;289(11):1405-13. PMID: 12636463
261 **Anttila T, Helkala EL, Viitanen M, Kareholt I, Fratiglioni L, Winblad B, Soininen H, Tuomilehto J, Nissinen A, Kivipelto M.** Alcohol drinking in middle age and subsequent risk of mild cognitive impairment and dementia in old age: a prospective population based study. BMJ. 2004 Sep 4;329(7465):539. Epub 2004 Aug 10. PMID: 15304383
Larrieu S, Letenneur L, Helmer C, Dartigues JF, Barberger-Gateau P. Nutritional factors and risk of incident dementia in the PAQUID longitudinal cohort. J Nutr Health Aging. 2004;8(3):150-4. PMID: 15129300
Luchsinger JA, Tang MX, Siddiqui M, Shea S, Mayeux R Alcohol intake and risk of dementia. J Am Geriatr Soc. 2004 Apr;52(4):540-6. PMID: 15066068
Letenneur L, Larrieu S, Barberger-Gateau P. Alcohol and tobacco consumption as risk factors of dementia: a review of epidemiological studies. Biomed Pharmacother. 2004 Mar;58(2):95-9. Review. PMID: 14992790
Truelsen T, Thudium D, Gronbaek M; Copenhagen City Heart Study. Amount and type of alcohol and risk of dementia: the Copenhagen City Heart Study. Neurology. 2002 Nov 12;59(9):1313-9. PMID: 12427876
Schlienger JL. [Beneficial and deleterious effects of alcoholic beverages] Rev Prat. 1999 Feb 15;49(4):367-72. Review. French. PMID: 10319684
Leibovici D, Ritchie K, Ledesert B, Touchon J. The effects of wine and tobacco consumption on cognitive performance in the elderly: a longitudinal study of relative risk. Int J Epidemiol. 1999 Feb;28(1):77-81. PMID: 10195668
Orgogozo JM, Dartigues JF, Lafont S, Letenneur L, Commenges D, Salamon R, Renaud S, Breteler MB. Wine consumption and dementia in the elderly: a prospective community study in the Bordeaux area. Rev Neurol (Paris). 1997 Apr;153(3):185-92. PMID: 9296132
Galanis DJ, Joseph C, Masaki KH, Petrovitch H, Ross GW, White L. A longitudinal study of drinking and cognitive performance in elderly Japanese American men: the Honolulu-Asia Aging Study. Am J Public Health. 2000 Aug;90(8):1254-9. PMID: 10937006
Leroi I, Sheppard JM, Lyketsos CG. Cognitive function after 11.5 years of alcohol use: relation to alcohol use. Am J Epidemiol. 2002 Oct 15;156(8):747-52. PMID: 12370163
Ruitenberg A, van Swieten JC, Witteman JC, Mehta KM, van Duijn CM, Hofman A, Breteler MM. Alcohol consumption and risk of dementia: the Rotterdam Study. Lancet. 2002 Jan 26;359(9303):281-6. PMID: 11830193
Huang W, Qiu C, Winblad B, Fratiglioni L. Alcohol consumption and incidence of dementia in a community sample aged 75 years and older. J Clin Epidemiol. 2002 Oct;55(10):959-64. PMID: 12464371
262 **Stampfer MJ, Kang JH, Chen J, Cherry R, Grodstein F.** Effects of Moderate Alcohol Consumption on Cognitive Function in Women. N Engl J Med. 2005 Jan 20;352(3):245-253. PMID: 15659724
263 Moderate Alcohol Consumption Reduces Risk of Ischemic Stroke. The Northern Manhattan Study. Stroke. 2005 Nov 23; [Epub ahead of print] PMID: 16306464
264 **Malinski MK, Sesso HD, Lopez-Jimenez F, Buring JE, Gaziano JM.** Alcohol consumption and cardiovascular disease mortality in hypertensive men. Arch Intern Med. 2004 Mar 22;164(6):623-8. PMID: 15037490
265 **Vliegenthart R, Oei HH, van den Elzen AP, van Rooij FJ, Hofman A, Oudkerk M, Witteman JC.** Alcohol consumption and coronary calcification in a general population. Arch Intern Med. 2004 Nov 22;164(21):2355-60. PMID: 15557415
266 **Arndt V, Rothenbacher D, Krauledat R, Daniel U, Brenner H.** Age, alcohol consumption, and all-cause mortality. Ann Epidemiol. 2004 Nov;14(10):750-3. PMID: 15519897

267 **Doll R, Peto R, Boreham J, Sutherland I.** Mortality in relation to alcohol consumption: a prospective study among male British doctors. Int J Epidemiol. 2005 Jan 12; [Epub ahead of print] PMID: 15647313
268 Alcohol dosing and total mortality in men and women: An updated meta-analysis of 34 prospective studies. Arch Intern Med. 2006 Dec 11-25;166(22):2437-45. PMID: 17159008
269 **Hamajima N, Hirose K, Tajima K, et al.** Alcohol, tobacco and breast cancer--collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. Br J Cancer. 2002 Nov 18;87(11):1234-45. PMID: 12439712
270 **Stranges S, Wu T, Dorn JM, Freudenheim JL, Muti P, Farinaro E, Russell M, Nochajski TH, Trevisan M.** Relationship of Alcohol Drinking Pattern to Risk of Hypertension. A Population-Based Study. Hypertension. 2004 Oct 11; [Epub ahead of print] PMID: 15477381
271 **Zilkens RR, Burke V, Hodgson JM, Barden A, Beilin LJ, Puddey IB.** Red wine and beer elevate blood pressure in normotensive men. Hypertension. 2005 May;45(5):874-9. Epub 2005 Apr 18. PMID: 15837829
272 Alcohol consumption and risk for coronary heart disease among men with hypertension. Ann Intern Med. 2007 Jan 2;146(1):10-9. PMID: 17200217
273 **Schoonen WM, Salinas CA, Kiemeney LA, Stanford JL.** Alcohol consumption and risk of prostate cancer in middle-aged men. Int J Cancer. 2005 Jan 1;113(1):133-40. PMID: 15386436
274 Resveratrol improves health and survival of mice on a high-calorie diet. Nature. 2006 Nov 1; PMID: 17086191
275 **Chen HL, Sheu WH, Tai TS, Liaw YP, Chen YC.** Konjac supplement alleviated hypercholesterolemia and hyperglycemia in type 2 diabetic subjects--a randomized double-blind trial. J Am Coll Nutr. 2003 Feb;22(1):36-42. PMID: 12569112
276 **Vuksan V, Sievenpiper JL, Owen R, Swilley JA, Spadafora P, Jenkins DJ, Vidgen E, Brighenti F, Josse RG, Leiter LA, Xu Z, Novokmet R.** Beneficial effects of viscous dietary fiber from Konjac-mannan in subjects with the insulin resistance syndrome: results of a controlled metabolic trial. Diabetes Care. 2000 Jan;23(1):9-14. PMID: 10857960
277 **Rigaud D, Paycha F, Meulemans A, Merrouche M, Mignon M.** Effect of psyllium on gastric emptying, hunger feeling and food intake in normal volunteers: a double blind study. Eur J Clin Nutr. 1998 Apr;52(4):239-45. PMID: 9578335
278 **Wu H, Dwyer KM, Fan Z, Shircore A, Fan J, Dwyer JH.** Dietary fiber and progression of atherosclerosis: the Los Angeles Atherosclerosis Study. Am J Clin Nutr. 2003 Dec;78(6):1085-91. PMID: 14668268
279 **Uusitupa M, Aro A, Korhonen T, Tuunainen A, Sarlund H, Penttila I.** Blood glucose and serum insulin responses to breakfast including guar gum and cooked or uncooked milk in type 2 (non-insulin-dependent) diabetic patients. Diabetologia. 1984 Jun;26(6):453-5. PMID: 6088333
280 **Wolever TM, Vuksan V, Eshuis H, Spadafora P, Peterson RD, Chao ES, Storey ML, Jenkins DJ.** Effect of method of administration of psyllium on glycemic response and carbohydrate digestibility. J Am Coll Nutr. 1991 Aug;10(4):364-71. PMID: 1654354
281 **Chandalia M, Garg A, Lutjohann D, von Bergmann K, Grundy SM, Brinkley LJ.** Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. N Engl J Med. 2000 May 11;342(19):1392-8. PMID: 10805824
282 **Pins JJ, Geleva D, Keenan JM, Frazel C, O'Connor PJ, Cherney LM.** Do whole-grain oat cereals reduce the need for antihypertensive medications and improve blood pressure control? J Fam Pract. 2002 Apr;51(4):353-9. PMID: 11978259
283 **Jenkins DJ, Kendall CW, Popovich DG, Vidgen E, Mehling CC, Vuksan V, Ransom TP, Rao AV, Rosenberg-Zand R, Tariq N, Corey P, Jones PJ, Raeini M, Story JA, Furumoto EJ, Illingworth DR, Pappu AS, Connelly PW.** Effect of a very-high-fiber vegetable, fruit, and nut diet on serum lipids and colonic function. Metabolism. 2001 Apr;50(4):494-503. PMID: 11288049
284 **Ajani UA, Ford ES, Mokdad AH.** Dietary fiber and C-reactive protein: findings from national health and nutrition examination survey data. J Nutr. 2004 May;134(5):1181-5. PMID: 15113967
285 **Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration.** Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002 Dec 14;360(9349):1903-13. PMID: 12493255
286 **Hansen TW, Jeppesen J, Rasmussen S, Ibsen H, Torp-Pedersen C.** Ambulatory blood pressure and mortality: a population-based study. Hypertension. 2005 Apr;45(4):499-504. Epub 2005 Mar 7. PMID: 15753229
287 http://msnbc.msn.com/id/4422326/
288 **Elias PK, Elias MF, Robbins MA, Budge MM.** Blood pressure-related cognitive decline: does age make a difference? Hypertension. 2004 Nov;44(5):631-6. Epub 2004 Oct 04. PMID: 15466661
289 **van Dijk EJ, Breteler MM, Schmidt R, Berger K, Nilsson LG, Oudkerk M, Pajak A, Sans S, de Ridder M, Dufouil C, Fuhrer R, Giampaoli S, Launer LJ, Hofman A.** The association between blood pressure, hypertension, and cerebral white matter lesions: cardiovascular determinants of dementia study. Hypertension. 2004 Nov;44(5):625-30. Epub 2004 Oct 04. PMID: 15466662
290 **Kuo HK, Sorond F, Iloputaife I, Gagnon M, Milberg W, Lipsitz LA.** Effect of blood pressure on cognitive functions in elderly persons. J Gerontol A Biol Sci Med Sci. 2004 Nov;59(11):1191-4. PMID: 15602074
291 Reducing the Risk of Dementia. Efficacy of Long-Term Treatment of Hypertension. Stroke. 2006 Apr 6; PMID: 16601212
292 http://www.nhlbi.nih.gov/health/prof/heart/hbp/pphbp.pdf

293 Exercise and blood pressure: applying findings from the laboratory to the community setting. Clin Exp Pharmacol Physiol. 2006 Sep;33(9):868-71. PMID: 16922823
294 **He FJ, MacGregor GA.** How Far Should Salt Intake Be Reduced? Hypertension. 2003 Nov 10 [Epub ahead of print] PMID: 14610100
295 http://www.iom.edu/
http://www4.nas.edu/news.nsf/6a3520dc2dbfc2ad85256ca8005c1381/25778ef9e449bc8385256e37005168c4?OpenDocument
296 **Tsugane S, Sasazuki S, Kobayashi M, Sasaki S.** Salt and salted food intake and subsequent risk of gastric cancer among middle-aged Japanese men and women. Br J Cancer. 2004 Jan 12;90(1):128-34. PMID: 14710219
297 Importance of Salt in Determining Blood Pressure in Children: Meta-Analysis of Controlled Trials. Hypertension. 2006 Nov;48(5):861-869. Epub 2006 Sep 25. PMID: 17000923
298 **Geleijnse JM, Kok FJ, Grobbee DE.** Blood pressure response to changes in sodium and potassium intake: a metaregression analysis of randomised trials. J Hum Hypertens. 2003 Jul;17(7):471-80. PMID: 12821954
299 **Slama M, Susic D, Frohlich ED.** Prevention of hypertension. Curr Opin Cardiol. 2002 Sep;17(5):531-6. Review. PMID: 12357131
300 **He FJ, Markandu ND, Coltart R, Barron J, Macgregor GA.** Effect of Short-Term Supplementation of Potassium Chloride and Potassium Citrate on Blood Pressure in Hypertensives. Hypertension. 2005 Apr;45(4):571-574. Epub 2005 Feb 21. PMID: 15723964
301 Effect of potassium-enriched salt on cardiovascular mortality and medical expenses of elderly men. Am J Clin Nutr. 2006 Jun;83(6):1289-96. PMID: 16762939
302 **Miura K, Greenland P, Stamler J, Liu K, Daviglus ML, Nakagawa H.** Relation of Vegetable, Fruit, and Meat Intake to 7-Year Blood Pressure Change in Middle-aged Men: The Chicago Western Electric Study. Am J Epidemiol. 2004 Mar 15;159(6):572-80. PMID: 15003961
303 **Alonso A, de la Fuente C, Martin-Arnau AM, de Irala J, Martinez JA, Martinez-Gonzalez MA.** Fruit and vegetable consumption is inversely associated with blood pressure in a Mediterranean population with a high vegetable-fat intake: the Seguimiento Universidad de Navarra (SUN) Study. Br J Nutr. 2004 Aug;92(2):311-9. PMID: 15333163
304 **Beilin LJ, Burke V.** Vegetarian diet components, protein and blood pressure: which nutrients are important? Clin Exp Pharmacol Physiol. 1995 Mar;22(3):195-8. Review. PMID: 7554413
305 **Scheer FA, Van Montfrans GA, Van Someren EJ, Mairuhu G, Buijs RM.** Daily Nighttime Melatonin Reduces Blood Pressure in Male Patients With Essential Hypertension. Hypertension. 2004 Jan 19 [Epub ahead of print] PMID: 14732734
306 **Iseki K, Iseki C, Itoh K, Sanefuji M, Uezono K, Ikemiya Y, Fukiyama K, Kawasaki T.** Estimated protein intake and blood pressure in a screened cohort in Okinawa, Japan. Hypertens Res. 2003 Apr;26(4):289-94. PMID: 12733696
307 **Burke V, Hodgson JM, Beilin LJ, Giangiulioi N, Rogers P, Puddey IB.** Dietary protein and soluble fiber reduce ambulatory blood pressure in treated hypertensives. Hypertension. 2001 Oct;38(4):821-6. PMID: 11641293
308 Effects of Protein, Monounsaturated Fat, and Carbohydrate Intake on Blood Pressure and Serum Lipids: Results of the OmniHeart Randomized Trial. JAMA. 2005 Nov 16;294(19):2455-2464. PMID: 16287956
309 http://www.ajcn.org/cgi/content/abstract/80/4/1012
310 Moderate Consumption of Olive Oil by Healthy European Men Reduces Systolic Blood Pressure in Non-Mediterranean Participants. J Nutr. 2007 Jan;137(1):84-87. PMID: 17182805
311 Folic acid supplementation for 3 wk reduces pulse pressure and large artery stiffness independent of MTHFR genotype. Am J Clin Nutr. 2005 Jul;82(1):26-31. PMID: 16002796
312 Low-fat dairy consumption and reduced risk of hypertension: the Seguimiento Universidad de Navarra (SUN) cohort. Am J Clin Nutr. 2005 Nov;82(5):972-9. PMID: 16280427
313 Low-fat dairy consumption and reduced risk of hypertension: the Seguimiento Universidad de Navarra (SUN) cohort. Am J Clin Nutr. 2005 Nov;82(5):972-9. PMID: 16280427
314 Short Sleep Duration as a Risk Factor for Hypertension. Analyses of the First National Health and Nutrition Examination Survey. Hypertension. 2006 Apr 3; PMID: 16585410
315 http://www.crnusa.org/about_recs.html
316 **Kim YI,** Role of Folate in Colon Cancer Development and Progression. J. Nutr. 133:3731S-3739S, November 2003
317 http://www.ajcn.org/cgi/content/abstract/80/1/114
318 **Forman JP, Rimm EB, Stampfer MJ, Curhan GC.** Folate intake and the risk of incident hypertension among US women. JAMA. 2005 Jan 19;293(3):320-9. PMID: 15657325
319 Dose-dependent effects of folic acid on blood concentrations of homocysteine: a meta-analysis of the randomized trials. Am J Clin Nutr. 2005 Oct;82(4):806-812. PMID: 16210710
320 **Clarke R, Grimley Evans J, Schneede J, Nexo E, Bates C, Fletcher A, Prentice A, Johnston C, Ueland PM, Refsum H, Sherliker P, Birks J, Whitlock G, Breeze E, Scott JM.** Vitamin B12 and folate deficiency in later life. Age Ageing. 2004 Jan;33(1):34-41. PMID: 14695861
321 **Harwood RH, Sahota O, Gaynor K, Masud T, Hosking DJ.** A randomised, controlled comparison of different calcium and vitamin D supplementation regimens in elderly women after hip fracture: The Nottingham Neck of Femur (NONOF) Study. Age Ageing. 2004 Jan;33(1):45-51. PMID: 14695863

322 The case against ergocalciferol (vitamin D2) as a vitamin supplement. Am J Clin Nutr. 2006 Oct;84(4):694-7. PMID: 17023693
323 **Munger KL, Zhang SM, O'Reilly E, Hernan MA, Olek MJ, Willett WC, Ascherio A.** Vitamin D intake and incidence of multiple sclerosis. Neurology. 2004 Jan 13; 62(1): 60-5. PMID: 14718698
324 Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. JAMA. 2006 Dec 20;296(23):2832-8. PMID: 17179460
325 **Holick MF.** Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. Am J Clin Nutr. 2004 Mar;79(3):362-71. PMID: 14985208
326 http://www.ajcn.org/cgi/content/full/69/5/842
327 **Grant WB.** Ecologic studies of solar UV-B radiation and cancer mortality rates. Recent Results Cancer Res. 2003;164:371-7. Review. PMID: 12899536
328 http://www.foodconsumer.org/777/8/Review_Vitamin_D_may_lower_cancer_risk.shtml
329 The Role of Vitamin D in Cancer Prevention. Am J Public Health. 2005 Dec 27; [Epub ahead of print] PMID: 16380576
330 http://www.ajcn.org/cgi/content/abstract/80/1/108
331 Science News, 2006-11-11, p312
332 Part I: http://www.sciencenews.org/articles/20041009/bob8.asp
Part II: http://www.sciencenews.org/articles/20041016/bob9.asp
333 **Zandi PP, Anthony JC, Khachaturian AS, Stone SV, Gustafson D, Tschanz JT, Norton MC, Welsh-Bohmer KA, Breitner JC.** Reduced risk of Alzheimer disease in users of antioxidant vitamin supplements: the cache county study. Arch Neurol. 2004 Jan; 61(1): 82-8. PMID: 14732624
334 **Eidelman RS, Hollar D, Hebert PR, Lamas GA, Hennekens CH.** Randomized trials of vitamin E in the treatment and prevention of cardiovascular disease. Arch Intern Med. 2004 Jul 26;164(14):1552-6. PMID: 15277288
335 **Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E.** Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. Ann Intern Med. 2005 Jan 4;142(1):37-46. Epub 2004 Nov 10. PMID: 15537682
336 Ames BN. Review Article: Delaying the Mitochondrial Decay of Aging-a Metabolic Tune-up. Alzheimer Dis Assoc Disord. 2003 Apr-Jun;17(2 Suppl):S54-7. No abstract available. PMID: 12813210
337 **Troost FJ, Saris WH, Haenen GR, Bast A, Brummer RJ.** New method to study oxidative damage and antioxidants in the human small bowel: effects of iron application. Am J Physiol Gastrointest Liver Physiol. 2003 Aug;285(2):G354-9. Epub 2003 Apr 30. PMID: 12724133
338 http://www.nutritionj.com/content/pdf/1475-2891-3-2.pdf
339 **Aureli T, Di Cocco ME, Capuani G, Ricciolini R, Manetti C, Miccheli A, Conti F.** Effect of long-term feeding with acetyl-L-carnitine on the age-related changes in rat brain lipid composition: a study by 31P NMR spectroscopy. Neurochem Res. 2000 Mar;25(3):395-9. PMID: 10761985
340 **Shoba G, Joy D, Joseph T, Majeed M, Rajendran R, Srinivas PS.** Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. Planta Med. 1998 May;64(4):353-6. PMID: 9619120
341 **Curry Consumption and Cognitive Function in the Elderly** American Journal of Epidemiology Advance Access published on July 26, 2006 Am. J. Epidemiol. 2006 164: 898-906 PMID: 16870699
342 AJCN http://www.ajcn.org/cgi/content/abstract/80/5/1358
343 Dietary Intake of Calcium in Relation to Mortality From Cardiovascular Disease. The JACC Study. Stroke. 2005 Dec 8; [Epub ahead of print] PMID: 16339476
344 **Lopez-Ridaura R, Willett WC, Rimm EB, Liu S, Stampfer MJ, Manson JE, Hu FB.** Magnesium Intake and Risk of Type 2 Diabetes in Men and Women. Diabetes Care. 2004 Jan;27(1):134-140. PMID: 14693979
345 http://my.webmd.com/content/Article/78/95930.htm?pagenumber=2
346 **Larsson SC, Bergkvist L, Wolk A.** Magnesium intake in relation to risk of colorectal cancer in women. JAMA. 2005 Jan 5;293(1):86-9. PMID: 15632340
347 Magnesium Intake and Reduced Risk of Colon Cancer in a Prospective Study of Women. Am J Epidemiol. 2005 Nov 30; [Epub ahead of print] PMID: 16319289
348 http://www.ajcn.org/cgi/content/abstract/84/2/419
349 Oral magnesium supplementation in asthmatic children: a double-blind randomized placebo-controlled trial. Eur J Clin Nutr. 2007 Jan;61(1):54-60. Epub 2006 Jun 21. PMID: 16788707
350 **Klein EA.** Selenium: Epidemiology and Basic Science. J Urol. 2004 Feb;171(2):S50-S53. PMID: 14713754
351 **Hammes HP, Du X, Edelstein D, Taguchi T, Matsumura T, Ju Q, Lin J, Bierhaus A, Nawroth P, Hannak D, Neumaier M, Bergfeld R, Giardino I, Brownlee M.** Benfotiamine blocks three major pathways of hyperglycemic damage and prevents experimental diabetic retinopathy. Nat Med. 2003 Mar;9(3):294-9. Epub 2003 Feb 18. PMID: 12592403
352 **Babaei-Jadidi R, Karachalias N, Ahmed N, Battah S, Thornalley PJ.** Prevention of incipient diabetic nephropathy by high-dose thiamine and benfotiamine. Diabetes. 2003 Aug;52(8):2110-20. PMID: 12882930
353 **Weindruch R, Walford RL, Fligiel S, Guthrie D.** The retardation of aging in mice by dietary restriction: longevity, cancer, immunity and lifetime energy intake. J Nutr. 1986 Apr;116(4):641-54. PMID: 3958810
354 **Tucker KL, Hannan MT, Qiao N, Jacques PF, Selhub J, Cupples LA, Kiel DP.** Low plasma vitamin B12 is

associated with lower BMD: the Framingham Osteoporosis Study. J Bone Miner Res. 2005 Jan;20(1):152-8. Epub 2004 Oct 25. PMID: 15619681
355 Methylmalonic acid and cognitive function in the Medical Research Council Cognitive Function and Ageing Study. Am J Clin Nutr. 2006 PMID: 17158424
356 **Feskanich D, Willett WC, Stampfer MJ, Colditz GA.** Milk, dietary calcium, and bone fractures in women: a 12-year prospective study. Am J Public Health. 1997 Jun;87(6):992-7. PMID: 9224182
357 Dietary intake of antioxidants and risk of age-related macular degeneration. JAMA. 2005 Dec 28;294(24):3101-7. PMID: 16380590
358 **Hu FB, Willett WC.** Optimal diets for prevention of coronary heart disease. JAMA. 2002 Nov 27;288(20):2569-78. Review. PMID: 12444864
359 **Sacks FM, Katan M.** Randomized clinical trials on the effects of dietary fat and carbohydrate on plasma lipoproteins and cardiovascular disease. Am J Med. 2002 Dec 30;113 Suppl 9B:13S-24S. Review. PMID: 12566134
360 **Hung T, Sievenpiper JL, Marchie A, Kendall CW, Jenkins DJ.** Fat versus carbohydrate in insulin resistance, obesity, diabetes and cardiovascular disease. Curr Opin Clin Nutr Metab Care. 2003 Mar;6(2):165-76. PMID: 12589186
361 http://www.sciam.com/article.cfm?articleID=0007C5B6-7152-1DF6-9733809EC588EEDF&catID=2
362 **Smith AP.** Breakfast cereal consumption and subjective reports of health. Int J Food Sci Nutr. 1999 Nov;50(6):445-9. PMID: 10719585
363 **Smith AP, Clark R, Gallagher J.** Breakfast cereal and caffeinated coffee: effects on working memory, attention, mood, and cardiovascular function. Physiol Behav. 1999 Aug 1;67(1):9-17. PMID: 10463623
364 **Benton D, Parker PY.** Breakfast, blood glucose, and cognition. Am J Clin Nutr. 1998 Apr;67(4):772S-778S. PMID: 9537627 free full text at http://www.ajcn.org/cgi/reprint/67/4/772S.pdf
365 **Farshchi HR, Taylor MA, Macdonald IA.** Deleterious effects of omitting breakfast on insulin sensitivity and fasting lipid profiles in healthy lean women. Am J Clin Nutr. 2005 Feb;81(2):388-96. PMID: 15699226
366 **Appel LJ.** The effects of protein intake on blood pressure and cardiovascular disease. Curr Opin Lipidol. 2003 Feb;14(1):55-9. PMID: 12544662
367 **Powers KM, Smith-Weller T, Franklin GM, Longstreth WT Jr, Swanson PD, Checkoway H.** Parkinson's disease risks associated with dietary iron, manganese, and other nutrient intakes. Neurology. 2003 Jun 10;60(11):1761-1766. PMID: 12796527
368 **Fisher AE, Naughton DP.** Iron supplements: the quick fix with long-term consequences. Nutr J. 2004 Jan 16;3(1):2. PMID: 14728718
Free full text at http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=14728718
369 **Yokoo EM, Valente JG, Grattan L, Schmidt SL, Platt I, Silbergeld EK.**Low level methylmercury exposure affects neuropsychological function in adults. Environ Health. 2003 Jun 4;2(1):8. Epub 2003 Jun 04. PMID: 12844364 free full text
370 **Guillen MD, Sopelana P, Partearroyo MA.** Polycyclic aromatic hydrocarbons in liquid smoke flavorings obtained from different types of wood. Effect of storage in polyethylene flasks on their concentrations. J Agric Food Chem. 2000 Oct;48(10):5083-7. PMID: 11052782
371 http://www.cheshire-med.com/services/dietary/nutrinew/grill.html
372 http://www.inchem.org/documents/ehc/ehc/ehc202.htm#SubSectionNumber:1.5.5
373 **Gorell JM, Peterson EL, Rybicki BA, Johnson CC.** Multiple risk factors for Parkinson's disease. J Neurol Sci. 2004 Feb 15;217(2):169-74. PMID: 14706220
374 **Miu AC, Andreescu CE, Vasiu R, Olteanu AI.** A behavioral and histological study of the effects of long-term exposure of adult rats to aluminum. Int J Neurosci. 2003 Sep;113(9):1197-211. PMID: 12959739
375 **Wong MH, Fung KF, Carr HP.** Aluminium and fluoride contents of tea, with emphasis on brick tea and their health implications. Toxicol Lett. 2003 Jan 31;137(1-2):111-20. Review. PMID: 12505437
376 **White LR, Petrovitch H, Ross GW, Masaki K, Hardman J, Nelson J, Davis D, Markesbery W.** Brain aging and midlife tofu consumption. J Am Coll Nutr. 2000 Apr;19(2):242-55. PMID: 10763906
Free full text at http://www.jacn.org/cgi/content/full/19/2/242
377 Soy diet worsens heart disease in mice. J Clin Invest. 2006 Jan;116(1):209-16. PMID: 16395406
378 **Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E.** Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. Ann Intern Med. 2005 Jan 4;142(1):37-46. Epub 2004 Nov 10. PMID: 15537682
379 Lead contamination in cocoa and cocoa products: isotopic evidence of global contamination. Environ Health Perspect. 2005 Oct;113(10):1344-8. PMID: 16203244 free full text at http://ehp.niehs.nih.gov/members/2005/8009/8009.html
380 http://www.globalexchange.org/campaigns/fairtrade/cocoa/
381 Inflammatory markers and particulate air pollution: characterizing the pathway to disease. Int J Epidemiol. 2006 Jul 14; PMID: 16844771
382 Dietary Copper and High Saturated and trans Fat Intakes Associated With Cognitive Decline. Arch Neurol. 2006 Aug;63(8):1085-1088. PMID: 16908733
383 Zinc, copper, and magnesium and risks for all-cause, cancer, and cardiovascular mortality. Epidemiology. 2006 May;17(3):308-14. PMID: 16570028
384 http://www.bfr.bund.de/cd/8487

385 http://europa.eu.int/comm/food/fs/sc/scf/out34_en.pdf
386 **Tsai CJ, Leitzmann MF, Willett WC, Giovannucci EL.** Dietary Protein and the Risk of Cholecystectomy in a Cohort of US Women: The Nurses' Health Study. Am J Epidemiol. 2004 Jul 1;160(1):11-8. PMID: 15229112
387 The relation between dietary protein, calcium and bone health in women: results from the EPIC-Potsdam cohort. Ann Nutr Metab. 2005 Sep-Oct;49(5):312-8. Epub 2005 Aug 4. PMID: 16088096
388 Dietary protein and risk of ischemic heart disease in women. Am J Clin Nutr. 1999 Aug;70(2):221-7. PMID: 10426698
389 Methionine-deficient diet extends mouse lifespan, slows immune and lens aging, alters glucose, T4, IGF-I and insulin levels, and increases hepatocyte MIF levels and stress resistance. Aging Cell. 2005 Jun;4(3):119-25. PMID: 15924568
390 Nutritional control of aging. Exp Gerontol. 2003 Jan-Feb;38(1-2):47-52. PMID: 12543260
391 Low methionine ingestion by rats extends life span. J Nutr. 1993 Feb;123(2):269-74. PMID: 8429371
392 Methionine restriction decreases visceral fat mass and preserves insulin action in aging male Fischer 344 rats independent of energy restriction. Aging Cell. 2006 Jun 26; [Epub ahead of print] PMID: 16800846
393 Methionine restriction inhibits colon carcinogenesis. Nutr Cancer. 2006;54(2):202-8. PMID: 16898864
394 Caloric restriction and aging: controversial issues. J Gerontol A Biol Sci Med Sci. 2006 Jan;61(1):14-9. Review. PMID: 16456190
395 **Jansson ET.** Alzheimer disease is substantially preventable in the United States - review of risk factors, therapy, and the prospects for an expert software system. Med Hypotheses. 2005;64(5):960-7. PMID: 15780492
Free full text at http://www.deptplanetearth.com/pdfdocs/ADprevention.pdf
396 http://circ.ahajournals.org/cgi/content/abstract/114/1/82
397 Colas, but not other carbonated beverages, are associated with low bone mineral density in older women: The Framingham Osteoporosis Study. Am J Clin Nutr. 2006 Oct;84(4):936-42. PMID: 17023723
398 **Soder PO, Soder B, Nowak J, Jogestrand T.** Early carotid atherosclerosis in subjects with periodontal diseases. Stroke. 2005 Jun;36(6):1195-200. Epub 2005 May 5. PMID: 15879347
399 Dental and Periodontal Status and Risk for Progression of Carotid Atherosclerosis. The Inflammation and Carotid Artery Risk for Atherosclerosis Study Dental Substudy. Stroke. 2006 Aug 3; PMID: 16888276
400 http://content.nejm.org/cgi/content/short/343/21/1506
http://www.hipprotector.com/
401 Lipoprotein particle profiles mark familial and sporadic human longevity. PLoS Med. 2006 Dec;3(12):e495. PMID: 17194192
402 **Bayman P, Baker JL, Mahoney NE.** Aspergillus on tree nuts: incidence and associations. Mycopathologia. 2002;155(3):161-9. PMID: 12617503