

## Nutrition and Dietary Supplements What the Dental Team Should Know



### Tieraona Low Dog, M.D.

Chair: US Pharmacopeia Dietary  
Supplement Admissions, Evaluation and  
Labeling Expert Committee  
Clinical Associate Professor of Medicine  
University of Arizona (Retired)

National Geographic's:  
*Life Is Your Best Medicine*  
*Healthy At Home*  
*Fortify Your Life*  
*Guide to Medicinal Herbs*  
[www.DrLowDog.com](http://www.DrLowDog.com)

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## *Lifespan versus Health Span*

- Human **lifespan** has been steadily increasing, though slowing, which has led to a **rise in age-associated diseases**, including obesity, cardiovascular disease, type 2 diabetes, cancer, and neurodegenerative diseases.
- Our **health span** (time without significant age-related disease burden), however, is **not increasing at same rate**, resulting in **more life years suffering** from one or multiple diseases.
- We hope to **extend health span** and delay the onset of age-associated frailty and diseases; this is known as the **compression of morbidity**.

World Health Organization (2019) *World health statistics 2019: monitoring health for the SDGs: sustainable development goals*. Geneva, Switzerland: World Health Organization;

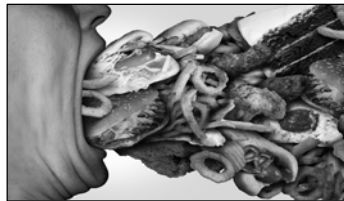
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## *Diet & Lifestyle*

Diseases linked to **unhealthful diet and lifestyle choices**, such as diabetes and cancer, are the **leading causes of death** in the United States, with high BMI and elevated blood glucose on the rise in all 50 states (tobacco use on the decline).

- Dietary factors**
- Tobacco consumption
- High blood pressure
- High BMI
- High plasma glucose
- Alcohol and drug use



The US Burden of Disease Collaborators. The State of US Health, 1990-2016 Burden of Diseases, Injuries, and Risk Factors Among US States. *JAMA* 2018;319(14):1444-1472.

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## *Diet and Health*

The relationship between diet and health is undisputed: **our bodies reflect what we eat and—just as importantly—what we do not or cannot eat.**

Dietary risks are complex: those associated with **'overnutrition'** and atherogenic diets and those related to **underconsumption of key micronutrients and macronutrients**. *Nutrition impacts almost all health conditions.*

Much of our food policy and public attention is oriented around the effects of **excess sugar, salt, and saturated fats**.

However, the **leading dietary risk factors for mortality are DIETS LOW in whole grains, fruit, nuts and seeds, vegetables, and omega-3 fatty acids.**

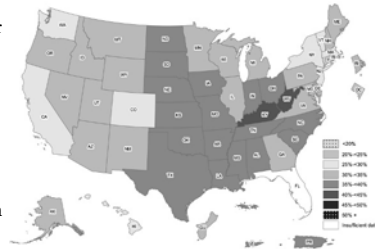
Ashish A, et al Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the global burden of disease study 2017. *Lancet* 2019;393(10184):1958-72. [https://doi.org/10.1016/S0140-6736\(19\)30453-6](https://doi.org/10.1016/S0140-6736(19)30453-6) <https://www.ncbi.nlm.nih.gov/patmed/3095488>

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## Obesity - A Growing Problem

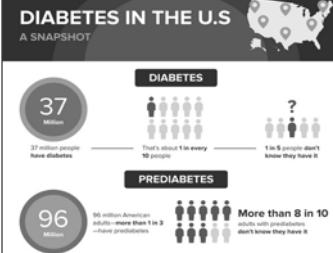
- **Globally:** 2.1 billion adults are overweight or obese<sup>1</sup>
  - **US:** highest # obese people (122 million)
  - **China:** second highest # obese people (88 million)
  - **<1%** of children/adolescents (5–19 years) obese in 1975, **124 million** in 2016
- **Unhealthy diets** account for up to **11 million avoidable premature deaths** per year.<sup>2</sup>



1. World Health Organization Obesity and Overweight <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight> Accessed December 12, 2022  
 2. Willet W, et al. Food in the Anthropocene: the EAT–Lancet Commission on healthy diets from sustainable food systems. *Lancet* 2019 February 2; 393, (10170): 447–492  
 Map Source: Behavioral Risk Factor Surveillance System <https://www.cdc.gov/dcsrt/data/prevalececcoccur.htm#mapall>. Accessed December 12, 2022

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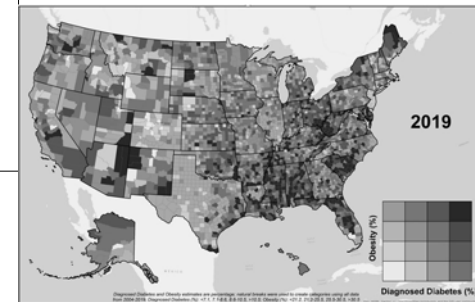


Source: <https://www.cdc.gov/diabetes/data/center/slides.html>  
 Accessed October 23, 2022

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Map of diagnosed diabetes vs obesity by county among US adults, 2019



## Heart Disease Death Rates, Total Population Ages 35+

### Heart Disease Death Rates, 2017 - 2019 Adults, Ages 35+, by County



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## Caloric Restriction?



Canto is 27-year-old monkey on CR diet, Owen is 29-year-old on unrestricted diet.

- 25-year study University of Wisconsin: **76 rhesus monkeys aged 7–14 years**, fed diet reduced in calories by **30%**.
- **Disease 3-fold greater in control group.** No evidence of diabetes in any caloric-restricted animal.<sup>1</sup>
- **2-year study** randomized 218 non-obese people to current diet or 25% caloric restriction (**11.7%** on average).<sup>2</sup>
  - **Statistically significant reduction in inflammatory markers, weight loss, improved mood, sleep duration, etc.**

1. [news.wisc.edu/monkey-caloric-restriction-study-shows-big-benefit-contradicts-earlier-study/](https://news.wisc.edu/monkey-caloric-restriction-study-shows-big-benefit-contradicts-earlier-study/)  
 2. Ravussin E, et al. *J Gerontol A Biol Sci Med Sci*. 2015;70(9):1097–104

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## *An Alternative? Intermittent Fasting*

- In our development as a species, food sources were abundant *and* scarce.
- Periods of **eating and fasting** probably the norm. **Thrifty gene theory** postulates fluctuations are necessary for **optimal metabolic function**.
- **Intermittent fasting** one way to replicate this evolutionary pattern.
- Evidence suggests our bodies respond to intermittent fasting in ways that may ultimately protect us from diseases of aging by **improving cardiovascular and cognitive function** and **reducing risk factors** for metabolic diseases.

Varady KA, et al. Alternate-day fasting and chronic disease prevention: a review of human and animal trials. *Am J Clin Nutr* 2007; 86(1): 7-13

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## *NEJM Review*

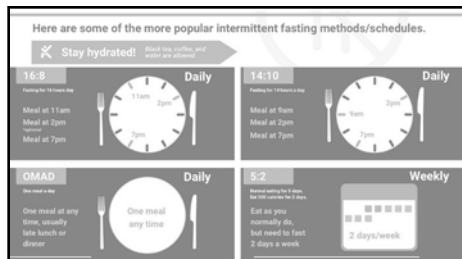
Dozens of animal and human studies reviewed to explain how fasting improves **metabolism, lowering blood sugar; lessens inflammation**, which improves range of issues from **pain and heart disease to asthma**; helps remove **toxins and damaged cells**, lowering risk for **cancer and improving brain function**.



deCabo R, et al. Effects of Intermittent Fasting on Health, Aging, and Disease. *N Engl J Med* 2019; 381:2541-2551

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## *Intermittent Fasting*

There are **many variations**. Three of the most popular are:

- **18/6 method:** restrict time you eat to 6 hrs./day and fast for 18 hours
- **16/8 method:** restrict time you eat to 8 hrs./day and fast for 16 hours
- **5:2 diet:** eat only 500–600 calories on two non-consecutive days, and eat normally the other five days
- **MAFD:** restrict to 500 calories every-other day.

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Source	Population	Type of IF	Comparator	Duration of fasting	No. of included studies	Total participants	Outcomes	AMSTAR-2 rating
Coffi et al. <sup>22</sup> 2018	Adults with or without medical conditions	5:2 diets, MAFD	CER	3–6 mo	11	630	Body weight, fat-free mass, fat mass, HDL-C, LDL-C, TC, TG, FPG, HbA <sub>1c</sub> , fasting insulin, HOMA-IR, adverse events	Moderate
Harris et al. <sup>23</sup> 2018	Adults with overweight or obesity	5:2 diets, MAFD	RD or CER	3–6 mo	6	360	Body weight, fat-free mass, fat mass, waist circumference, HDL-C, LDL-C, TC, TG, FPG, insulin, SBP, DBP, adverse events	Moderate
Cho et al. <sup>6</sup> 2019	Adults without diabetes	MAFD, TRE, 0-calorie ADF	RD or CER	1–6 mo	12	545	BMI, body weight, fat-free mass, fat mass, FPG, HOMA-IR, adiponectin, leptin	Low
Roman et al. <sup>24</sup> 2019	Adults with overweight or obesity	5:2 diets, MAFD	CER	1–12 mo	9	782	Body weight, fat-free mass, fat mass, hip circumference, waist circumference	Low
Cui et al. <sup>25</sup> 2020	Adults	MAFD	RD	1–12 mo	7	269	BMI, body weight, fat-free mass, fat mass, HDL-C, LDL-C, TC, TG, FPG, HOMA-IR, SBP, DBP	Low
Meng et al. <sup>7</sup> 2020	Adults	5:2 diets, MAFD	RD or CER	1–12 mo	28	1528	HDL-C, LDL-C, TC, TG	Moderate
Moor et al. <sup>5</sup> 2020	Adults	TRE	RD or CER	4.6 to 3 mo	19	475	Body weight, fat-free mass, fat mass, HDL-C, LDL-C, TC, TG, FPG, SBP, DBP	Moderate
Park et al. <sup>26</sup> 2020	Adults	MAFD	RD, CER, or TRE	1–8 mo	8	728	BMI, body weight, fat-free mass, fat mass, waist circumference, HDL-C, LDL-C, TC, TG, FPG, insulin, SBP, DBP, CRP	Moderate
Pellegrini et al. <sup>9</sup> 2020	Adults who are healthy or with chronic disease not impacting outcomes	TRE	RD or CER	1–2 mo	11	452	BMI, body weight, fat-free mass, fat mass, HDL-C, LDL-C, TC, TG, FPG, fasting insulin, HOMA-IR, SBP, DBP	Low
Panera et al. <sup>8</sup> 2020	Adults with overweight or obesity	TRE	RD or TRE	1 to 3 mo	8	264	LDL-C, HDL-C, TC, TG, FPG, fasting insulin, HOMA-IR, ghrelin	Moderate
He et al. <sup>27</sup> 2021	Adults with overweight or obesity	5:2 diets, MAFD	CER	3–12 mo	11	850	Body weight, fat-free mass, fat mass, waist circumference, HDL-C, LDL-C, TC, TG, FPG, HbA <sub>1c</sub> , fasting insulin, HOMA-IR, SBP, DBP	Moderate

Abbreviations: AMSTAR-2, A Measurement Tool to Assess Systematic Reviews; BMI, body mass index; CER, continuous energy restriction; CRP, C-reactive protein; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL-C, low-density lipoprotein cholesterol; MAFD, modified alternate-day fasting; RD, regular diet; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; TRE, time-restricted eating; ADF, alternate-day fasting.

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## Intermittent Fasting and Weight Loss

- MADF and 5:2 diet only IF types associated with **statistically significant weight loss** in overweight/obese adults.
- MADF associated with **improvement** of several cardiovascular risk factors in first 2-12 months including **LDL-C, total cholesterol, triglycerides, and blood pressure.**
- **Earlier eating window** appears to offer wider health benefits.
- 3-month study **late time restricted eating** (eating window noon to 8 PM) found **no significant improvements** in weight loss, fasting insulin levels, fat mass, or blood lipid levels.

Patikorn C, et al. **Intermittent Fasting and Obesity-Related Health Outcomes: An Umbrella Review of Meta-analyses of Randomized Clinical Trials.** *JAMA Netw Open.* 2021;4(12):e2139538.  
 Lowe DA, et al. Effects of time-restricted eating on weight loss and other metabolic parameters in women and men with overweight and obesity: the treat randomized clinical trial. *JAMA Intern Med* 2020; 180: 1491–1499

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## One Thing in Common

Despite incredible variation in dietary patterns, **all have this in common:**

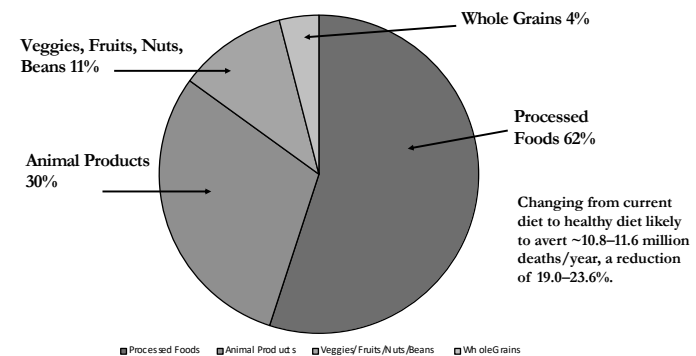
- **DRAMATIC** reduction/elimination of **ultra-processed foods**—industrial foods with little/no intact foods, often high in **added sugars, salts, artificial flavors, colors and other additives.**
- Individuals with **highest vs. lowest** intake of ultra-processed foods had a **31% increased likelihood of death** after adjusting for confounders.<sup>1</sup>
- In US: **57% of total calories for adults<sup>2</sup>** and **67% of total calories for children<sup>3</sup>** come from these foods.

1. Kim H, et al. *Public Health Nutr* 2019; 22(10):1777-1785. 2. Juul F, et al. *Am J Clin Nutr* 2022; 115(1):211-221  
 3. Wang L, et al. *JAMA* 2021; 326(6):519-530

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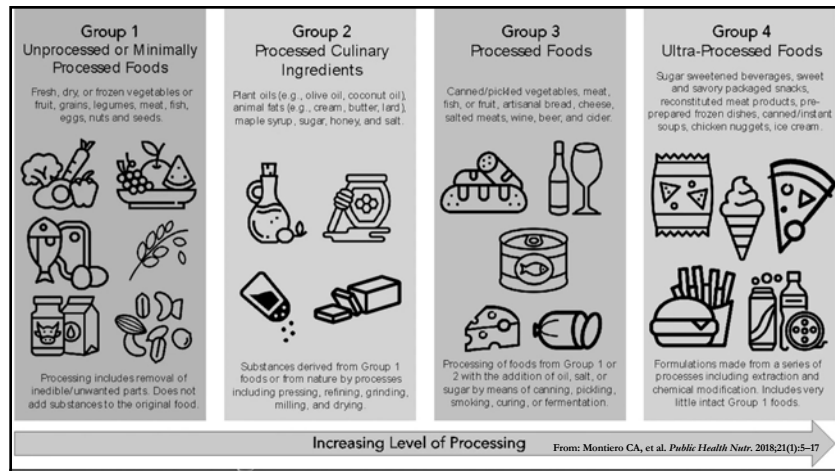
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## STANDARD AMERICAN DIET



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## The Rise of Ultra-Processed Foods

- UPF are "snacks, drinks, ready meals and many other products created **mostly or entirely** from substances extracted from foods or derived from food constituents with **little if any intact food**."<sup>1</sup>
- Quick, tasty, and often cheap.** Increasingly found in "health" foods.
- UPF from *animals or plants* has been shown to harm the microbiome and drive inflammation.<sup>2</sup>
- In US, **57% of total calories for adults<sup>3</sup> and 67% for children<sup>4</sup>** come from UPF.
- High consumption is associated with driving inflammation**
- Observational studies show an association between UPF and **cancer, heart disease, obesity, and other chronic health problems.**

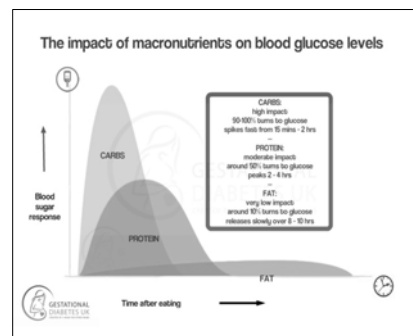
1. Willett W, et al. *Lancet* 2019 February 2; 393, (10170): 447-492.  
3. Judd P, et al. *Am J Clin Nutr* 2022; 115(1):211-221.

2. Smeat R, et al. *Lancet Gastroenterol Hepatol* 2022 Dec;7(12):1128-1140  
4. Wang L, et al. *J Am A 2021; 526(6):519-530*

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## Refined Carbohydrates

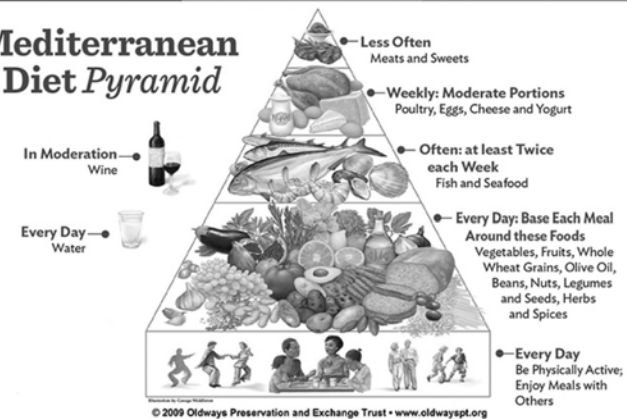
- Overdo processed/refined carbs, **blood sugar rises, insulin released, store extra glucose as fat, drive inflammation.**
- Blood sugar goes up and then can plummet, **leaving one tired and disrupting sleep/wake cycle.**
- Eating lots of carbs makes one crave lots of carbs (dopamine rush).**
- High sugar diets cause **dysbiosis and degrade intestinal barrier, leading to systemic inflammation.**



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## Mediterranean Diet Pyramid



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### Mediterranean Diet for 5 Years for Heart Disease Prevention (Without Known Heart Disease)

61 for prevented stroke, heart attack, or death

Benefits in NNT	Harms in NNT
<ul style="list-style-type: none"> <li>1 in 61 were helped (avoiding a stroke, heart attack, or death)</li> </ul>	<ul style="list-style-type: none"> <li>None were harmed (diet effects)</li> </ul>

7447 subjects followed for an average of roughly five years, demonstrated a clear reduction in their combined endpoint of strokes, heart attacks, and death.

Estruch R, Ros E, Salas-Salvadó J, et al; PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med*. 2013 Apr 4;368(14):1279-90. doi: 10.1056/NEJMoa1200303.

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### Mediterranean Diet for Secondary Prevention After Heart Attack

30 for mortality

Benefits in NNT	Harms in NNT
<ul style="list-style-type: none"> <li>1 in 18 were helped (preventing repeat heart attack)</li> <li>1 in 30 were helped (preventing death)</li> <li>1 in 30 were helped (preventing cancer)</li> </ul>	<ul style="list-style-type: none"> <li>None were harmed</li> </ul>

Benefits in Percentage	Harms in Percentage
<ul style="list-style-type: none"> <li>94% saw no benefit</li> <li>6% were helped by preventing a repeat heart attack</li> <li>3% were helped by preventing death</li> <li>3% were helped by preventing cancer</li> </ul>	<ul style="list-style-type: none"> <li>0% were harmed</li> </ul>

To compare saving a life post-heart attack with this diet (NNT= 30) and with statins (NNT=83) suggests that diet is nearly three times more powerful as a life-saving tool. Cancers were also reduced,

<https://www.thennt.com/nnt/mediterranean-diet-for-post-heart-attack-care/>

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### Statin Drugs Given for 5 Years for Heart Disease Prevention (Without Known Heart Disease)

104 for non-fatal heart attack

Benefits in NNT	Harms in NNT
<ul style="list-style-type: none"> <li>None were helped (life saved)</li> <li>1 in 104 were helped (preventing heart attack)</li> <li>1 in 154 were helped (preventing stroke)</li> </ul>	<ul style="list-style-type: none"> <li>1 in 50 were harmed (develop diabetes*)</li> <li>1 in 10 were harmed (muscle damage)</li> </ul>


Effect of statins for people who have never had a heart attack or stroke (most of the people who currently take statins). They do lower cholesterol in most people who took them. But it takes 5 years of daily statin therapy to achieve a 1.6% chance of avoiding a heart attack, and a 0.37% chance of avoiding a stroke. There continues to be a debate over the true benefit/risk of statins. Almost all studies have been industry sponsored.

<https://www.thennt.com/nnt/statins-for-heart-disease-prevention-without-prior-heart-disease-2/>

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### Mediterranean Diet Inflammation & Memory



- Dietary Inflammatory Index** based on measuring inflammation in the body in response to specific foods (1,900 studies).
- Mediterranean diet associated with lower dementia risk.** Researchers evaluated inflammatory potential of diet in relation to mild cognitive impairment/dementia risk using the **DII** during an average follow up of **9.7 years during Women's Health Initiative Memory Study**.
- Higher inflammatory scores** were significantly associated with **greater cognitive decline and earlier onset of cognitive impairment**.

Hayden KM, et al. The association between an inflammatory diet and global cognitive function and incident dementia in older women: The Women's Health Initiative Memory Study. *Alzheimer's & Dementia* 2017; May 19, pii: S1552-5260(17)30185-1.

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### Inflammatory Food Ratings

FOOD	SERVING SIZE	SERVING SIZE (GRAMS)	IF RATING
AGAVE NECTAR	1 TBSP	21	-74
ALMOND BUTTER	¼ CUP	64	100
CHEESE, CHEDDAR	1 OUNCE	28.35	-20
CHICKEN BREAST, RSTD	3 OUNCES	85	-19
MILK, WHOLE	1 CUP	246	-46
OLIVE OIL	1 TBSP	14	74
ONIONS, COOKED	½ CUP	105	240
RICE, WHITE	1 CUP	158	-153
SPINACH	1 CUP	30	75
SALMON, SOHO BAKED	3 OUNCES	85	450
TURMERIC	½ TSP	1.5	338

200 or higher	Strongly anti-inflammatory
101 to 200	Moderately anti-inflammatory
0 to 100	Mildly anti-inflammatory
-1 to -100	Mildly inflammatory
-101 to -200	Moderately inflammatory
-201 or lower	Strongly inflammatory

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### C-Reactive Protein and Cardiovascular Risk

- Coronary artery disease once considered primarily **lipid accumulation mediated disease**, now shown to involve ongoing **inflammatory response**.
- C-reactive protein (CRP)** is a sign of inflammation in the body. There should be no detectable (hs)CRP in healthy individual.
- hs-CRP improves risk prediction at all levels of LDL cholesterol.

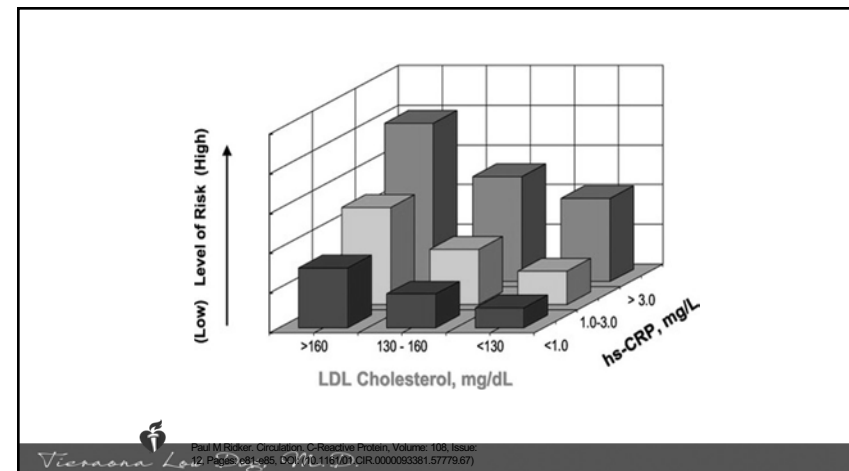
hs-CRP Value	Cardiovascular Disease Risk Level*
< 1 mg/L	low risk
1-3 mg/L	average risk
> 3 mg/L	high risk

\* Risk levels published in 2003. American Heart Association / Centers for Disease Control and Prevention Scientific Statement

Christodoulidis G, et al. Cardiol Rev 2014 Jan 15

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## Sugar & Cardiovascular Risk

- **Diets high in sugar increase total-, LDL-cholesterol, and triglycerides.** To match cholesterol increases seen with *typical* sugar consumption, you'd need to **consume saturated fat at a level ~40% of daily calories** (typical intake is ~10 %).
- Human/animal data show high sugar diets **impair glucose tolerance, cause insulin resistance, elevate uric acid, and alter platelet function.**
- **Added sucrose and fructose** increases **leptin resistance** (satiety hormone), increasing weight gain; causes **NAFLD**, most common cause of liver disease in US, and is a **strong risk factor for coronary heart disease.**
- American Heart Association recommends **women limit added sugar intake to 6 tsp/d** (25 g); **men limit to 9 tsp/d** (37.5 g). Americans consume roughly triple this amount.

Chhabra R, et al. *Mayo Clin Proc.* 2013;88:1259-65; Vasselli JR, et al. *Advances in Nutrition (Bethesda, Md)* 2013;4:164-75.

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## Magnesium and CRP

- Patients with low Mg intake **have increased likelihood of serum hs-CRP  $\geq 3.0$  mg/L.**
- **Elevated serum hs-CRP is decreased by Mg supplementation** in patients with chronic disease.<sup>1</sup>
- **Meta-analysis** 8 RCTs: Mg supplementation (320-500 mg/d) significantly decreased level of **serum hs-CRP by an average of -1.33 mg/L.**<sup>2</sup>
- Supplements: magnesium oxide likely to cause diarrhea; **citrate, malate, and glycinate** gentler on GI. **L-threonate** may have superior brain penetration.
- **Caution** using supplements in those with severe kidney dysfunction.

1. Nielsen FH. Dietary magnesium and chronic disease. *Adv Chronic Kidney Dis* 2018 May;25(5):230-235.

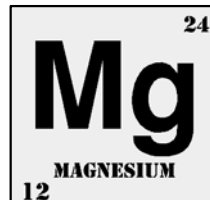
2. Masidi M, et al. Effect of magnesium supplements on serum C-reactive protein: a systematic review and meta-analysis. *Arch Med Sci* 2018 June; 14(4): 707-716.

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## Magnesium and Diabetes

- **Insulin resistance** repeatedly shown to **decrease magnesium** levels and **diabetics** with low magnesium show a **more rapid disease progression** and an increased risk for **diabetes-related complications.**
- A vicious forward feeding cycle is created.
- **Magnesium supplementation** shown to **improve glucose metabolism and insulin sensitivity** in those with type-2 diabetes.



Gommers LM, et al Hypomagnesemia in Type 2 Diabetes: A Vicious Circle? *Diabetes* 2016;65(1):3-1

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## Magnesium and Heart Disease



- 2013 **meta-analysis** of 16 studies with more than **313,000 participants** found:
  - Higher blood levels associated with a **30% lower risk of cardiovascular disease.**
  - Dietary magnesium (per 200-mg/d increment) associated with a **22% lower risk of fatal ischemic heart disease.**
- Magnesium important in maintaining blood pressure and **supplementation (365 to 450 mg/d)** shown to **significantly lower blood pressure** in those with **insulin resistance, prediabetes, and other chronic diseases.**
- Mg involved in heart's electrical conduction and hypomagnesemia, hypokalemia and other electrolyte disturbances may trigger **cardiac arrhythmias.**

Del Gobbo LC, et al. *Am J Clin Nutr* 2013; 98(1):160-73. Dibaba DT, et al. *Am J Clin Nutr* 2017; 106(3):921-929.

Barbagallo M et al. *Nutrients* 2021 Feb; 13(2): 463.

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## Magnesium Deficiency

- People with magnesium deficiency can present with **insulin resistance, menstrual cramps, leg cramps, migraines, fatigue, anxiety and mild elevations in blood pressure.**
- In **more severe cases** of deficiency, **seizures, tingling and numbness in the arms and legs, bizarre muscle movements (especially of the eyes and face), personality changes, and coronary spasms** can occur.
- Many medications can deplete magnesium (e.g., **diuretics, PPIs, OCPs, gout medication, B2-agonists, steroids**, etc.).
- Mg is necessary for **vitamin D synthesis, transport, and activation**; hence, **Mg deficits** impair production of **active form of vitamin D**.

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Magnesium Content in Foods

### Nuts and Seeds

■ Almonds, dry	1/4 cup	105
■ Brazil nuts, dry	1/4 cup	80
■ Cashews, dry roasted	1/4 cup	89
■ Peanuts, dry or oil roasted	1/4 cup	67
■ Peanut Butter	2 Tbsp	50
■ Pecans, dry	1/4 cup	38
■ Sesame Seeds, roasted whole	1 oz.	101
■ Soybeans, roasted	1/4 cup	63
■ Sunflower Seeds, dry	1/4 cup	128
■ Walnuts, chopped	1/4 cup	63

Magnesium Content in Foods

### Fruits

■ Apricots, canned	3 halves	8.0
■ Banana	1 medium	33.0
■ Cherries, canned, pitted	1/2 cup	16.0
■ Grapefruit, fresh	1/2 cup	9.5
■ Orange, fresh	1 medium	13.0
■ Peach, fresh, pared	1 medium	6.0
■ Peach, canned in syrup	1/2 cup	6.0
■ Pear, fresh	1 medium	9.0
■ Pear, canned in syrup	1/2 cup	5.5
■ Pineapple, canned	1/2 cup	17.5
■ Strawberries, raw	1/2 cup	8.0

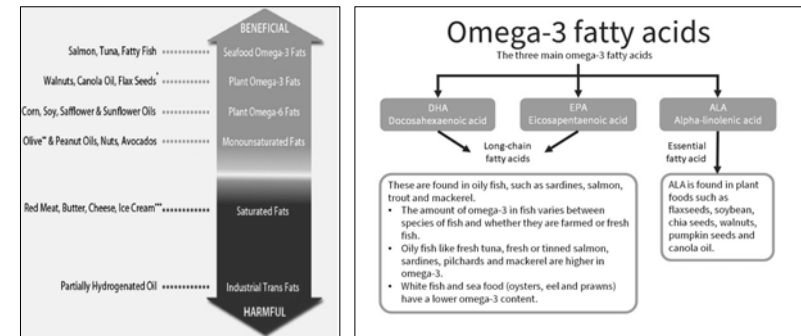
*Viannna Low Dog, M.D.*

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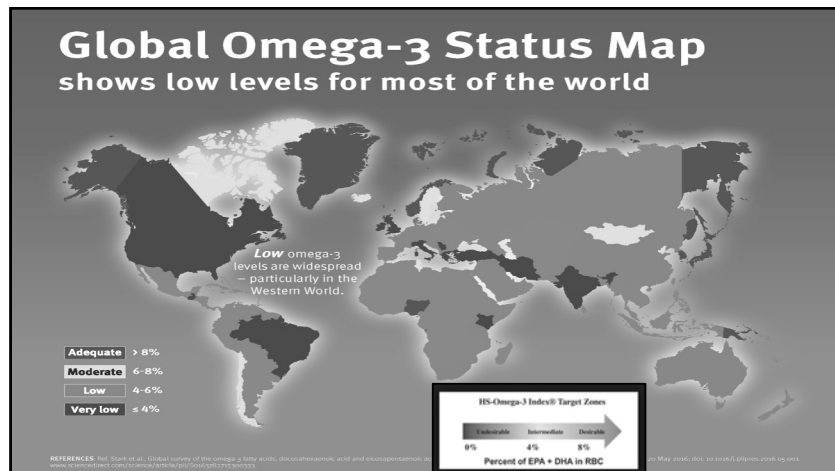
35



Fish concentrate EPA and DHA from algae, their primordial source.

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### American Heart Association

- “Omega-3 fish oil supplements prescribed by a healthcare provider may help **prevent death** from heart disease in patients **who recently had a heart attack** and may **prevent death and hospitalizations** in patients with **heart failure**.”



Siscovick DS, et al. *Circulation* 2017; Mar 13.

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### EPA & DHA Health Benefits

- Crucial for **brain/eye** development of baby first **1,000 days of life**
- **Lower triglycerides**
- Mildly **lowers blood pressure**
- **Reduces inflammation**
- Reduces risk of **heart disease**
- May **improve eye health**
- May **reduce the risk of asthma**
- May **reduce fat in the liver**
- May **alleviate menstrual cramping**
- May improve **cognitive function, depression, anxiety, and ADHD**

Mehran D, et al. *JAMA Intern Med* 2021 May 1;181(5):631-649.

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### Greater Longevity with a Higher Omega-3 Index



Postmenopausal women with an Omega-3 Index over 8% were 30% less likely to die than those with an Index under 4% over 15 years.

### Recovering from a Heart Attack with Omega-3s: The OMEGA-REMODEL Study



Patients who had recently had a heart attack and were then treated with omega-3 fatty acids for 6 months had healthier hearts if their Omega-3 Index reached 11% compared to those with lower levels.

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**The Omega-3 Index and Risk for Fatal CHD**



Data from 10 prospective cohort studies including >24,000 subjects showed that an Omega-3 Index of 8% or greater was associated with the lowest risk for fatal CHD.

**Total Mortality and the Omega-3 Index: Heart and Soul**




People with the highest Omega-3 Index levels lived longer than those with the lowest levels.

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## Omega 3 Fatty Acids – Healthy Muscles

- Chronic low-grade inflammation also contributes to the **loss of muscle mass, strength and functionality**, referred to as sarcopenia, as it affects both muscle protein breakdown and synthesis through several signaling pathways.
- Omega-3 fatty acids stimulate muscle protein synthesis in older adults and may be useful for the **prevention and treatment of sarcopenia**.



Dalle S, et al. Front Physiol 2017; Dec 12;8:1045  
Ticinesi A, et al. Nutrients 2016; Mar 29;8(4):186

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## Omega 3 and Prostate Cancer?

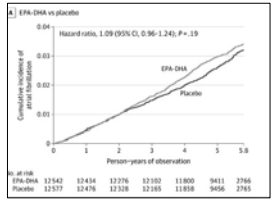
- SELECT trial raised concerns** about potential link between omega-3s and increased prostate cancer/aggressive cancer.
- European Food Safety (EFSA) concluded, “there is **no evidence** for a role of EPA and/or DHA intake in the development of prostate cancer.”
- Also, “**supplemental intake of EPA and DHA combined at doses up to 5 g/d does not give rise to safety concerns for adults.**”
- FDA: safe supplemental level **2 g/d and total EPA/DHA at 3 g/d**

*EFSA Journal 10(7): doi:10.2903/j.efsa.2012.2815*

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## Heart Arrhythmias?



	n	Events	Person-years
EPA-DHA	12542	12434	12276
Placebo	12537	12476	12328
<b>Total</b>	<b>25079</b>	<b>24910</b>	<b>24604</b>

Albert CM, et al. Effect of Marine Omega-3 Fatty Acid and Vitamin D Supplementation on Incident Atrial Fibrillation: A Randomized Clinical Trial. *JAMA* 2021 Mar 16;325(11):1061-107

- Omega-3s have been said to **reduce and increase** the risk of heart arrhythmias.
- Randomized clinical trial **25,119 women/men aged 50 years or older** without cardiovascular disease, cancer, or AF **failed to show any effect (positive or negative)** with **1 gram/d marine omega-3, 2,000 IU vitamin D, or combo**.

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- Vitamin D deficiency can cause **osteomalacia** leading to **musculoskeletal pain** in the pelvis, shoulders, low back, and proximal muscles.
- Deficiency common worldwide but **more severe in elders** due to environmental/biological factors.
- Impaired mobility can limit time spent outdoors and **decreased synthesis of vitamin D in skin**
- As aging advances, intestinal resistance to 1,25(OH)<sub>2</sub>D **impairs uptake of calcium** and **decline in renal function reduces activation of vitamin D**.

### Vitamin D



Wintermeyer E, et al. Crucial Role of Vitamin D in the Musculoskeletal System. *Nutrients* 2016; Jun 1;8(6). pii: E319.

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### Vitamin D: Bones, Balance, and Infection

- Low vitamin D increases risk of **falls** and **gait instability**. Exercise, calcium and vitamin D supplementation all been shown to decrease falling in elders.
- Meta-analysis by National Osteoporosis Foundation: eight studies (n= 30,970 participants): **calcium plus vitamin D supplementation** produced significant **15 % reduced risk total fractures and 30% reduced risk hip fracture**.
- Vitamin D supplementation also protects against **acute respiratory tract infection**, especially in those who were most deficient.

Tricco AC, et al. Comparisons of Interventions for Preventing Falls in Older Adults: A Systematic Review and Meta-analysis. *JAMA* 2017; Nov 7;318(17):1687-1699.

Weaver CM. Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation. *Osteoporosis Int* 2016 Jan;27(1):367-76

Martineau AR, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ* 2017; Feb 15;356:g6583.

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### Statins, Vitamin D, and Myopathy

- Meta-analysis: nine cohort studies (n=2906 patients) revealed that the 25OHD level of patients with statin-related myopathy was significantly lower than that of patients without myopathy and subset of studies found that statin tolerance improved to 89% (p < 0.001) after vitamin D supplementation.
- Patients should have levels corrected to sufficient levels (>30 ng/mL).

Hou G, et al. *Am J Cardiovasc Drugs* 2022 Mar;22(2):183-193.

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### Vitamin D Deficiency

- **Serum 25(OH)D level** is used to determine vitamin D status. According to the American Endocrine Society:
  - **Sufficiency is 30 ng/mL** (75 nmol/L) and above (range 30-100 ng/mL)
  - **Insufficiency defined as 20–29 ng/mL**
  - **Deficiency defined as <20 ng/mL** (<50 nmol/L)
  - **Severe deficiency <12 ng/mL** (<30 nmol/L)
- **66.8 million Americans** 1 year and older: levels between **12-20 ng/ml**
- **23 million Americans** 1 year and older: levels **less than 12 ng/ml**
  - Most at risk were *women and non-Hispanic black*.
- **2000 IU per day appears necessary to maintain sufficient levels.**
- Vitamin D best taken alongside **vitamin K and magnesium**.

CDC 2nd National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population Copyright Medicine Lodge Ranch, LLC. Holick MF, et al. *J Clin Endocrinol Metab* 2011; 96(7):1911-30. All rights reserved.

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## A Note on Protein



- Framingham Osteoporosis Study found **higher protein** intakes (60-83g/d versus 46g/d) in elder men and women (mean 75 years) associated with a **37% decreased risk of hip fracture**.
- Women's Health Initiative: **20% increase in protein intake** (15-18% of energy intake) improved BMD maintenance and marginally lowered forearm fracture risk.
- European guidelines recommend **20-25 grams high quality protein with each meal for women over age 50** with regular physical activity/exercise 3-5 times/week.

Mitra D, et al. *Osteoporosis Int* 2011; 22(1):345-349.  
 Beasley JM, et al. *Am J Clin Nutr* 2014; 99(4):934-940.  
 Rizzoli R, et al. *Maturitas* 2014 Sep;79(1):122-32.

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## How Much Protein?



- ~0.8 g/kg body weight for adults
  - (Multiply weight in lb. x 0.36)
  - 150 pounds = 55 g/d
  - 180 pounds = 65 g/d
- 1.0-1.2 g/kg for those over age 60\*
  - 150 pounds = 69-81 grams
  - 180 pounds = 81-98 grams
- 1.2-1.5 g/kg competitive athletes

*\*Not for those with kidney disease.*

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## Prescription Meds and Nutrients: Just a Glimpse

- Widespread use of **prescription drugs** for management of chronic health conditions can make it difficult to **maintain adequate levels of specific nutrients**.
- **PPI drugs** are commonly prescribed and are also available over-the-counter. Long-term use can **increase the risk of fracture, cause magnesium levels to plummet, and interfere with B12 absorption**, as well as increasing the risk of *C. difficile* infection.
- With increasing prevalence of type-2 diabetes, we will continue to see increase in **metformin use, a drug known to deplete vitamin B12**.

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## Metformin With Proton Pump Inhibitors: A Polypharmacy Recipe for Neuropathy via Vitamin B12 Depletion

Zdilla MJ. *Clin Diabetes* 2015; 33(2):90-5.



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## Vitamin B12

- **Atrophic gastritis affects 10%-30% of people over 60 years of age** causing malabsorption of food bound vitamin B12.
- Low vitamin B<sub>12</sub> concentrations can cause serious problem; **peripheral neuropathy, balance disturbances, cognitive disturbances, physical disability, and greater loss of bone density.**
- Risk: inadequate intake, veganism, malabsorption, medications (PPI, metformin), obesity, aging
- **18 million Americans are** deficient in vitamin B12.
- Supplement with 20-100 mcg per day.

Niafar M, et al. Intern Emerg Med 2015; 10(1):93-102.

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	Nonpregnant/ nonlactating females	Pregnant (age 14 to 18 years)	Pregnant (age 19 to 30 years)	Pregnant (age 31 to 50 years)	Upper limit
<b>Minerals</b>					
Calcium	1000 mg	1300 mg	1000 mg	1300 mg	2500 mg
Iron	18 mg	27 mg	27 mg	27 mg	45 mg
Magnesium	310 to 360 mg	400 mg	350 mg	360 mg	350* mg
Phosphorus	700 mg	1250 mg	700 mg	700 mg	4000 mg
Zinc	8 mg	12 mg	11 mg	11 mg	40 mg
Iodine	150 mcg	220 mcg	220 mcg	220 mcg	1110 mcg
Selenium	55 mcg	60 mcg	60 mcg	60 mcg	400 mcg
<b>Vitamins</b>					
Vitamin A	700 mcg RAE	750 mcg RAE	770 mcg RAE	770 mcg RAE	3000 mcg RAE
Vitamin D	600 international units	600 international units	600 international units	600 international units	4000 international units
Vitamin E	15 mg	15 mg	15 mg	15 mg	1000 mg
Vitamin K	90 mcg	75 mcg	90 mcg	90 mcg	ND
Vitamin C	75 mg	80 mg	85 mg	85 mg	2000 mg
Thiamin	1.1 mg	1.4 mg	1.4 mg	1.4 mg	ND
Riboflavin	1.1 mg	1.4 mg	1.4 mg	1.4 mg	ND
Niacin	14 mg	18 mg	18 mg	18 mg	35 mg
Vitamin B6	1.3 mg	1.9 mg	1.9 mg	1.9 mg	100 mg
Vitamin B12	2.4 mcg	2.6 mcg	2.6 mcg	2.6 mcg	ND
Choline	425 mg	450 mg	450 mg	450 mg	3500 mg
Folate	400 mcg DFE	600 mcg DFE	600 mcg DFE	600 mcg DFE	1000 mcg DFE

RAE: retinol activity equivalents; DFE: dietary folate equivalents; ND: not determinable, due to lack of data of adverse effects and concern with regard to lack of ability to handle excess amounts.  
\* Applies only to supplemental magnesium.

From: Garner CD. Nutrition in Pregnancy. Dietary Requirements and Supplements. Up to Date October 22, 2022

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## Choline



- Component of acetylcholine, sphingomyelin, and phosphatidylcholine, necessary for the development of fetal central nervous system and cognition.
- In 2017, the American Medical Association House of Delegates voted to recommend “evidence based” amounts of choline in all prenatal vitamins,<sup>1</sup> highlighting the importance of **maternal choline intake during pregnancy/lactation**; insufficient choline and other key nutrients during first 1,000 days post-conception may result in lifelong **deficits in brain function** despite subsequent nutrient repletion.<sup>2</sup>
- AI for choline is 450 mg/d pregnancy and 550 mg/d lactation.<sup>3</sup>
- Dietary choline: **eggs, meats, poultry, seafood, dairy are good sources**. Plant sources: navy beans, Brussels sprouts, broccoli, spinach contain lower amounts.

1. <https://www.ama-assn.org/delivering-care/public-health/ama-backs-global-health-reports-calling-for-fortified-diets>

2. Schwarzenberg SJ. *Pediatrics*. 2018;141. doi: 10.1542/peds.2017-3716. 3. Wallace TC, Fulgoni VL. *Nutrients*. 2017 Aug 5;9(8):839.

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Figure 3. Total choline in selected foods

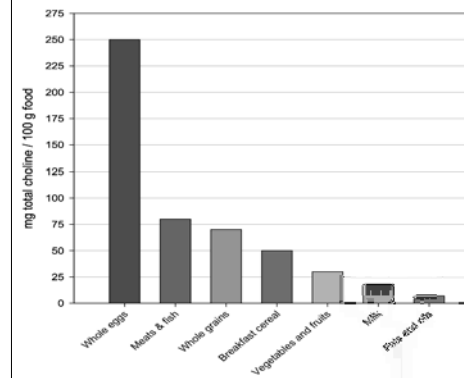


Image: USDA Database for the Choline Content of Common Foods

<https://www.ars.usda.gov/ARSUserFiles/80400535/Data/Choline/Choln02.pdf>  
Accessed November 8, 2022

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## Iodine

- Iodine requirements **increase by ≥ 50% in pregnancy** due to increase in maternal thyroid hormone production; fetus does not have fully functional thyroid gland until **20 weeks gestation**. Essential for **normal brain/nervous system** development.<sup>1</sup>
- American Thyroid Association recommends **150 mcg/d potassium iodide** for pregnant/lactating women in US/Canada (not necessary if taking meds for hypothyroidism).<sup>2</sup>
- Women in US ages 20–39 had median urine iodine concentrations **bordering on insufficiency**.<sup>3</sup>
- NHANES: 72.2% of pregnant women used any dietary supplement; only 17.8% used a dietary supplement with iodine. 75.0% of lactating women used a dietary supplement; however, only 19.0% used a dietary supplement with iodine. Far below current recommendations.<sup>4</sup> *Low iron further impairs thyroid metabolism, which is also prevalent in this population.*
- Prolonged exposure to **iodine levels >1100 mcg per day** may trigger autoimmune thyroiditis and result in hypothyroidism.<sup>5</sup>

1. Belsho-Turhan K, et al. *Nutrients*. 2019 Dec; 11(12): 2891. 2. Alexander EK, et al. *Thyroid*. 2017; 27:315. 3. Pfeiffer CM, et al. *J Nutr*. 2013; 143(6): DOI:10.3945/jn.112.172658. 4. Gupta PM, et al. *Nutrients*. 2018 Mar 29;10(4):422. 5. Rayman MP, et al. *Proc Nutr Soc*. 2019 Feb;78(1):34-44.

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## Docosahexaenoic Acid (DHA)

- Cochrane analysis: high quality evidence **preterm birth < 37 weeks** and **early preterm birth < 34 weeks** reduced in women receiving omega-3 LCPUFA compared with no omega-3. Moderate evidence of **reduced perinatal death**.<sup>1</sup>
- Analysis of 2003–2012 NHANES data for 788 pregnant women in the US found daily consumption approximately **66 mg DHA and 34 mg EPA**.<sup>2</sup>
- Recommendation pregnant/breastfeeding women: consume **8-12 ounces** low-mercury **seafood** per week. Many global scientific/expert committees recommend **200 mg/d DHA**.<sup>3</sup> **Algal derived** supplements are available for vegetarians/vegans.

1. Middleton P, et al. *Cochrane Database Syst Rev*. 2018 Nov 15;11(11):CD003402. 2. Nordgren TM, et al. *Nutrients*. 2017;9(3):197. doi: 10.3390/nu9030197. 3. GOED Global Recommendations for EPA and DHA Intake. [https://www.wisefat.org/assets/globalrecommendationsummary12nov2014landscape\\_3.pdf](https://www.wisefat.org/assets/globalrecommendationsummary12nov2014landscape_3.pdf). Accessed November 11, 2022.

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## Supplementation for Breastfed Infants

- **Insufficient iron intake** in infants <12 months of age typically due to:<sup>1</sup>
  - **Breastfeeding without initiation of adequate iron supplementation** by 6 months age
  - **Formula with insufficient iron fortification**
  - **Early transition to cow's milk** (before 12 months).
- Breastfed infants **1 mg/kg/d iron at 4 months**, continued until eating iron rich foods.<sup>1</sup>
- Studies show only **2-19% breastfed** infants receive the **recommended 400 IU/d of direct vitamin D** supplementation, leaving majority at **high risk** for vitamin D deficiency.<sup>2</sup>
- Breastmilk of strict **vegans** can be **low in vitamin B12** if supplementation is not adequate. Important to evaluate diet/supplement use to ensure adequate B12 levels in the infant.<sup>3</sup>

1. Meek, J. Y., Noble, L., & Section on Breastfeeding. Policy Statement: Breastfeeding and the Use of Human Milk. *Pediatrics* 2022; 150(1): e2022057988.
2. Umaretnya, P. J., et al. *The Annals of Family Medicine* 2017; 15(1): 68-70.
3. Dror DK, et al. *Adv Nutr* 2018;9:358e-66e.

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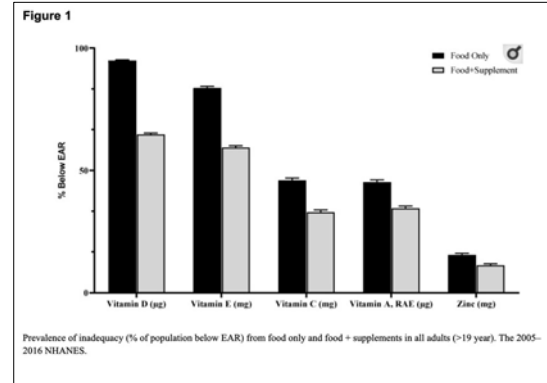
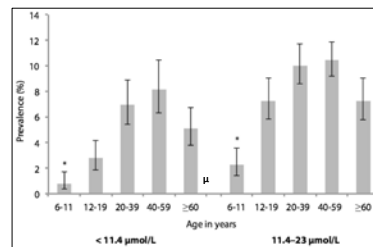


Image from: Reider CA, et al. Inadequacy of Immune Health Nutrients: Intakes in US Adults, the 2005–2016 NHANES. *Nutrients* 2020 Jun; 12(6): 1735.

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## Prevalence of Vitamin C Deficiency and Low Vitamin C Concentration in US Population



**Figure H.1.f.** Prevalence estimates of vitamin C deficiency (serum concentrations less than 11.4 µmol/L) and low vitamin C concentrations (11.4-23 µmol/L) in the U.S. population aged 6 years and older by age group. National Health & Nutrition Examination Survey, 2003-2006.

Error bars represent 95% of confidence intervals. \*Prevalence in children is significantly lower than prevalence in persons 20 years and older ( $p < 0.05$ ).

NOTE: *scurvy induced* when dietary vitamin C intake < 10 mg/d and/or plasma vitamin C levels *below 11 µmol/L*.

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## “Picky” Eater?

- **Healthy 4-year-old boy** seen by ortho/rheumatology with **right-leg pain and progressively worse limping**, became **unable to weight bear**.
- Intermittent **non-blanching rash arms and legs** past 2 years, topical emollients not effective. **Bleeding when brushing teeth, gingivitis**.
- Diet primarily waffles, yogurt, pasta with butter, goldfish crackers, peanut butter, chicken nuggets, and water.
- Workup negative except for **iron, vitamins C and D deficiencies**.
- **100 mg ascorbic acid q 8 hours x 7 days**, then 1 x daily with iron and vitamin D.
- **Limp and rash completely disappeared within weeks**.

Nastro A, et al. Scurvy Due to Selective Diet in a Seemingly Healthy 4-Year-Old Boy. *Pediatrics* September 2019; 144 (3) e20182824.

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MAIN FUNCTIONS	GOOD SOURCES	
<ul style="list-style-type: none"> <li>Antioxidant defense</li> <li>Enhances immune function</li> <li>Needed to make collagen, carnitine, and the neurotransmitters serotonin and norepinephrine</li> </ul>	<b>Fruit</b> <ul style="list-style-type: none"> <li>Kiwifruit, 1 medium-sized, 90 mg</li> <li>Strawberries (whole), 1 cup, 85 mg</li> </ul>	<b>Vegetables</b> <ul style="list-style-type: none"> <li>broccoli • kale • tomatoes</li> <li>Sweet Red Pepper, ½ cup chopped, 95 mg</li> </ul>
<b>DAILY RECOMMENDATION</b> <div style="text-align: center;"> <div style="background-color: black; color: white; border-radius: 50%; width: 60px; height: 60px; display: flex; align-items: center; justify-content: center; margin: 0 auto;"> <div style="text-align: center;"> <b>400</b> mg </div> </div> <p>All Adults</p> </div>	<b>SPECIAL NOTES</b> <ul style="list-style-type: none"> <li>Heat destroys vitamin C. Try to eat fresh foods and cook by steaming, microwaving, or stir-frying.</li> <li>Vitamin C in food is identical to vitamin C in supplements.</li> <li>The Daily Recommendation listed is specific to the LPI based on extensive review of the scientific evidence. The Institute of Medicine's Recommended Dietary Allowance (RDA) is 90 mg/day for men and 75 mg/day for women.</li> </ul>	


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## Zinc

- Improves **mucociliary clearance**, strengthens **epithelial integrity**, regulating **tight junction** proteins important for **mucosal membranes**, direct antibacterial against *S. pneumoniae*<sup>1</sup> preserves antiviral immunity.
- Deficiency/inadequacy affects **30%** of global population; responsible **~800,000 deaths** (e.g., diarrhea, pneumonia).<sup>2</sup>
- ~ **4% children** (<10 y), **8.6% males** (≥10 y), **8.2% females** (≥10 y) **below** serum zinc cutoff.<sup>3</sup>
- 35–45% US adults over 60 years** have daily intake below estimated average requirement.




1. Eijkelkamp B.A. et al. *PLoS Pathogens*, 2019; 15 (8): e1007  
 2. Wu, D, et al. *Front Immunol* 2019; doi: 10.3389/fimmu.2018.03160  
 3. Henninger SR, et al. *The Journal of Nutrition* 2018; 148(8): 1341-51

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## Zinc & Immune Health

- Suboptimal zinc levels **increase risk for infectious diseases**. Mild zinc deficiency is largely sub-clinical, unnoticed in most people.
- Study 420 nursing home patients: **29%** zinc deficient even after one-year taking MVI with 7 mg zinc.
- Those with serum levels > 70 µg/dL had lower incidence of pneumonia, shorter duration of illness, less total antibiotic use.



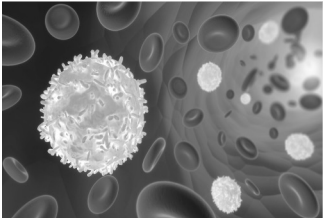
Meydani SN, et al. Serum zinc and pneumonia in nursing home elderly. *Am J Clin Nutr* 2007; 86, 1167–1173

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## Vitamins B6

- Folate and vitamins B6 and B12** all necessary for **production of white blood cells**, crucial for immune health.
- Low vitamin B6** significantly associated with **impaired humoral and cell-mediated immunity**; and increased inflammation.
- Supplementing critically ill patients with B6** increases immune response.
- 30 million Americans deficient in B6** (deficiency increases with age, higher in non-Hispanics, women on oral contraceptives, and those with inflammatory disorders)



Cheng CH, et al. Vitamin B6 supplementation increases immune responses in critically ill patients. *Eur J Clin Nutr* 2006;60:1207–1213.

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## Oral Health & Systemic Disease

- **1891:** first oral microbiologist Willoughby D. Miller put forward theory of **oral focal infections**, suggesting that **oral microbial infection** can affect other parts of the body, related to a **variety of systemic diseases**.
- **1912:** Frank Billings **speculated that infection of the teeth** may be the cause of **rheumatoid arthritis, nephritis, endocarditis, and other diseases**.
- **Periodontal inflammation** leads to loss of connective tissues/bones. **Extensive inflammatory cell infiltration** appears in connective tissue near periodontal pocket epithelium. This **low-grade inflammation** may disturb the health of body or worsen other systemic diseases.

Miller WD. The human mouth as a focus of infection. *Lancet* 1891; 138: 340-342

Billings F. Chronic focal infections and their etiologic relations to arthritis and nephritis. *Arch. Intern. Med* 1912; IX, 484-498 (1912).

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## Oral Microbiota Among Most Diverse

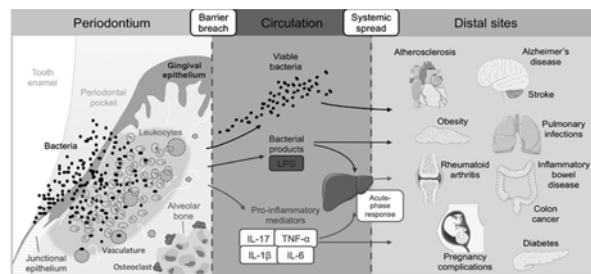
- **700 microbial species:** bacteria, fungi, viruses, archaea, and protozoa form complex ecological community. Oral microbiota generally exist as **biofilm**.
- Despite different etiologies, **periodontitis and caries** driven by feedforward loop between **microbiota and host** (inflammation and dietary sugars, respectively) that favors **emergence and persistence of dysbiosis**.<sup>1</sup>
- Increasing evidence suggests an association with dysbiosis of **oral ecosystem**, and development of **diabetes, CVD, and certain cancers**.<sup>2</sup>

1. Lamont RJ, et al. The oral microbiota: dynamic communities and host interactions. *Nature Reviews Microbiology* 2018; 16: 745-59

2. Zhang Y, et al. Human oral microbiota and its modulation for oral health, *Biomedicine & Pharmacotherapy* 2018; 99:883-93

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- Severe periodontitis affects 743 million people worldwide.
- Bacteria can enter bloodstream and translocate to extra-oral tissue: **lung, heart, gut, placenta, brain inflamed joints, etc.** Study found **100%** of patients with CVD had *P. gingivalis* arterial colonization, found in brains of those with AD.

From: Konkel JE, et al. Distal Consequences of Oral Inflammation *Front. Immunol* 2019; <https://doi.org/10.3389/fimmu.2019.01403>

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## Oral Microbiota & Gut Inflammation

- Adults produce >1000 mL/d of **saliva**, carrying **oral microbes to the GI tract**. Bacteria can also enter GI tract via **bloodstream**.
- Inflammation caused by *P. gingivalis* in oral cavity can **alter intestinal microbial communities, disrupt intestinal barrier, induce endotoxemia, and trigger a systemic inflammatory response**.
- *F. nucleatum* can migrate to intestine, **inhibiting the immune response mediated by T cells**, and promoting progression of IBD.

Peng X, et al. *International Journal of Oral Science* 2022; 14, 14.

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## Probiotics



- **Live microorganisms** administered in adequate amounts confer *health benefit to the host*.
- Regulate/modulate immune functions, **reduce risk intestinal infection**.
- Improve **intestinal barrier functions**, **reduce endotoxemia**.
- Induce hypo-responsiveness to **food antigens**.
- Improve **glucose control** and **reduce inflammatory cytokines**.
- Inhibit tumorigenesis and **may inhibit cancer progression**.

Gianotti L. et al. *World J Gastroenterol*. 2010;16:167–175  
Szulinska M, et al. *Nutrients* 2018, 10(6), 773; <https://doi.org/10.3390/nu10060773>

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Outcome	Reference	No of studies/ participants	Evidence of benefit?	Prevention and treatment of Crohn's disease and ulcerative colitis	Seo Lora et al (2015) <sup>111</sup>	14/821 ulcerative colitis 8/374 Crohn's disease	Yes
Clostridium difficile associated diarrhoea in adults and children	Goldenberg et al (2017) <sup>111</sup>	39/9955	Yes	Prevention of Clostridium difficile associated diarrhoea in children with cystic fibrosis	Arvanthani et al (2016) <sup>112</sup>	9/275	Yes
Necrotizing enterocolitis	Al Falah et al (2014) <sup>113</sup> Rees et al (2017) <sup>114</sup>	17/5338	Yes	Type 2 diabetes fasting glucose, glycated haemoglobin (HbA1c)	Abbari et al (2016) <sup>115</sup>	13/805	Yes
Antibiotic associated diarrhoea in children	Goldenberg et al (2015) <sup>116</sup>	26/3898	Yes	Type 2 diabetes fasting glucose, insulin level	Zhang et al (2016) <sup>117</sup>	7/425	Yes
Probiotics for preventing acute upper respiratory tract infections	Hao et al (2015) <sup>118</sup>	12/3720	Yes	Necrotizing enterocolitis in pre-term neonates with focus on Lactobacillus reuteri	Athalye-Jape et al (2016) <sup>119</sup>	6/1778	Yes
Urinary tract infections	Schwenger et al (2015) <sup>120</sup>	9/735	No	Reduction of serum concentration of C reactive protein	Masidi et al (2017) <sup>121</sup>	19/935	Yes
Prevention of asthma and wheeze in infants	Azad et al (2013) <sup>122</sup>	6/1364	No	Cardiovascular risk factors in patients with type 2 diabetes	Hendjani et al (2017) <sup>123</sup>	11/641	Yes
Prevention of eczema in infants and children	Mansfield et al (2014)	16/2797	Yes	Reduction of total cholesterol and low density lipoprotein cholesterol	Wu et al (2017) <sup>124</sup>	15/976	Yes
Prevention of invasive fungal infections in preterm neonates	Agrawal et al (2015) <sup>125</sup>	19/4912	Unclear	Depressive symptoms	Wallace and Milne (2017) <sup>126</sup>	6/1080	Yes
Prevention of nosocomial infections	Manzanares et al (2015) <sup>128</sup>	30/2972	Yes	Vulvovaginal candidiasis in non- pregnant women	Xie et al (2018) <sup>125</sup>	10/1656	Yes
Treatment of rotavirus diarrhoea in infants and children	Ahmadi et al (2015) <sup>121</sup>	14/1149	Yes				

From: Valdes AM, et al. Role of gut microbiota in nutrition and health. *BMJ* 2018;361:e2179

*Viernona Low Dog, M.D.*

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**AEProBio Clinical Guide to Probiotic Products Available in Canada**  
Applications, Dosage Forms and Clinical Evidence to Date - 2023 Edition

Introduction Adult Health Vaginal Health Pediatric Health Functional Foods References About

**Find the appropriate probiotic:**

Adult Health Vaginal Health Pediatric Health Functional Foods

**WHAT is this:**  
A Practice Tool to Assist with Clinical Decision Making for Appropriate Probiotic Therapy for Your Patients

**WHO is the intended user:**  
This Clinical Guide is designed to translate scientific evidence available for probiotic products to practical, clinically relevant information. It is intended to be used as a clinical decision-making tool, enabling clinicians to easily select the appropriate product, dose, and formulation for a specific indication.

**WHY is this needed:**  
Currently, the body of evidence for probiotic interventions is growing along with popular demand for these products. There is evidence to support the use of probiotic products for a variety of indications beyond gut health, however, applications and results are strain-specific.

**HOW is this tool reviewed:**  
A systematic literature review using pre-defined inclusion criteria was undertaken to identify studies of defined clinical outcomes for specific probiotic strains. Commercially available products containing said strains were

[www.probioticchart.ca](http://www.probioticchart.ca)

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Brand	pH
Simple Truth	5.0
Le Bleu	5.0
Dasani	5.0
Aquafina	5.0
Tap Water	6.5
Chlorine in Valley	6.5
Spring Water	6.5
Pellegrino	6.5
Just Water	6.5
Icelandic Glacial	6.5
Voss	7.0
Smart Water	7.0
LifeWater	7.0
Kroger	7.0
Hydrogen Water	7.0
Fiji	7.0
Aqua Panna	7.0

Independent testing of various bottled waters.

<https://watertestingkits.com/7-facts-about-ph-of-bottled-water/>

*Viernona Low Dog, M.D.*

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## *Resources*

- Identifying Drug-Nutrient Interactions:
  - <https://lpi.oregonstate.edu/mic/drug-nutrient-interactions>
  - [https://www.drugs.com/drug-interactions/multivitamin\\_vitamins.html](https://www.drugs.com/drug-interactions/multivitamin_vitamins.html)
  - <https://familydoctor.org/drug-nutrient-interactions-and-drug-supplement-interactions/>
  - <https://medlineplus.gov/druginformation.html>
  - <https://naturalmedicines.therapeuticresearch.com> (paid subscription)
- Micronutrient Information
  - <https://lpi.oregonstate.edu/mic>
  - <https://ods.od.nih.gov>
  - [https://www.who.int/health-topics/micronutrients#tab=tab\\_1](https://www.who.int/health-topics/micronutrients#tab=tab_1)
- Micronutrient Calculator
  - <https://www.nal.usda.gov/human-nutrition-and-food-safety/dri-calculator>
  - <https://www.osteoporosis.foundation/educational-hub/topic/calcium-calculator>

*Veronica Low Dog, M.D.*