

Top Selling Dietary Supplements: What Dental Professionals Must Know



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Dietary Supplements Admissions Joint
Standard Setting Sub-Committee

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Your Life*", "*Healthy At Home*", and "*Life Is
Your Best Medicine*"

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Food is Foundational



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The State of American Nutrition

- Typical American diets exceed recommended intake levels in four categories: calories from solid fats and added sugars; refined grains; sodium; and saturated fats.
- CDC results indicate that <18% of adults in each state consumed the recommended amount of fruit and <14% consumed the recommended amount of vegetables.

www.cdc.gov/mmwr/preview/mmwrhtml/mm6426a1.htm Accessed December 20, 2016

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Women and Folate

- Women who are of reproductive age need 400 mcg/day of folate at least 2-3 months before pregnancy to reduce the risk of neural tube defects.
- Folic acid received through food fortification in the US is *less than 130 mcg/day*, making supplementation vitally important.
- Given that many women are avoiding gluten containing foods, the contribution from fortified foods is likely even lower.
- 10% of individuals have an abnormality in the MTHFR enzyme, which is involved in the metabolism of folate, leading to low levels of folate in spite of intake. This is why a number of supplement companies now use L-methylfolate (the active form) instead of folic acid.

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Food Fortification

- Many cereals are fortified with vitamins B1, B2, B3, B5, B9, B12, and C, as well as iron and calcium.
- This has both an upside and downside (providing key nutrients to women and children, especially low income individuals; potentially getting too much a nutrient; for instance iron in adult men).
- Further complicating the issue: **most non-GMO and/or organic cereals are not fortified.**

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Kashi® GoLean Crunch!® Honey Almond Flax	
Nutrition Facts	
Serving Size 2/3 Cup (53g/1.9 oz.)	
Amount Per Serving	
Calories 200 Calories from Fat 40	
	% Daily Value*
Total Fat 5g	10%
Saturated Fat 0.5g	1%
Trans Fat 0g	0%
Polyunsaturated Fat 2g	4%
Monounsaturated Fat 2.5g	5%
Cholesterol 0mg	0%
Sodium 140mg	6%
Potassium 330mg	9%
Total Carbohydrate 30g	12%
Dietary Fiber 4g	8%
Soluble Fiber 4g	8%
Insoluble Fiber 0g	0%
Sugars 12g	24%
Protein 5g	10%
Vitamin A 2%	Vitamin C 0%
Calcium 2%	Iron 6%

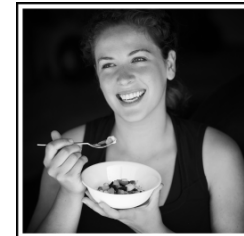
Cascadian Farm ORGANIC Granola	
Nutrition Facts	
Serving Size 1/2 Cup (30g)	
Amount Per Serving	
Calories 150 Calories from Fat 45	
	% Daily Value*
Total Fat 5g	10%
Saturated Fat 0.5g	1%
Trans Fat 0g	0%
Polyunsaturated Fat 2g	4%
Monounsaturated Fat 2.5g	5%
Cholesterol 0mg	0%
Sodium 140mg	6%
Potassium 330mg	9%
Total Carbohydrate 30g	12%
Dietary Fiber 4g	8%
Soluble Fiber 4g	8%
Insoluble Fiber 0g	0%
Sugars 12g	24%
Protein 5g	10%

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Vitamin B6 (Pyroxidal-5-Phosphate)

- Critically involved in production of serotonin, dopamine, melatonin, hemoglobin, protein metabolism, energy production, and more.
- Deficiency: depression; impaired cognition, attention, memory, and sleep. Increased risk for heart disease, stroke and colorectal cancer.
- Common OTC analgesics and oral contraceptives lower B6 levels. 30 MILLION Americans are deficient in B6.
- Need ~6 mg per day to maintain normal serum level.



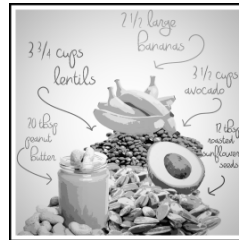
Larsson SC, et al. JAMA 2010; 303(11):1077-83
Morris MS, et al. Am J Clin Nutr 2008; 87(5):1446-54
Ulvik A, et al. Am J Clin Nutr 2014; 100(1):250-5

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To Get 1.5mg of B6 in Food

- 2.5 bananas
- 12 Tbsp. roasted sunflower seeds
- 8 ounces chicken breast
- 8 ounces sockeye salmon
- ~5 ounces cooked tuna
- ~5 ounces beef liver
- 3.5 cups raw diced avocado
- 3 cups sweet potatoes
- 15 cups of milk OR
- 20 Tbsp. peanut butter



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Case 41-year old Female

- Strict vegan for 2.5 years. Disturbance of taste (unable to sense flavor of variety of fruits and vegetables), fatigue after simple daily activities, paresthesia of the anatomic structures innervated by the mandibular division of the trigeminal nerve on her left side, disturbance of memory and slowing mental faculty. No meds. No significant medical or dental history.

Pontes HA, et al. *J Can Dent Assoc* 2009; 75(7):533-7.

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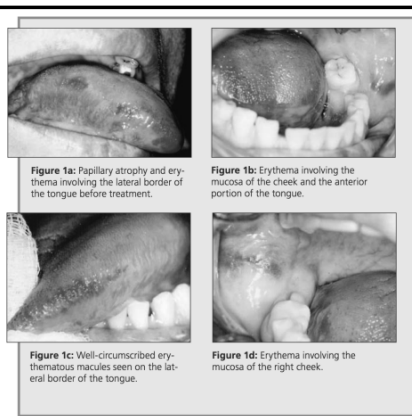


Figure 1a: Papillary atrophy and erythema involving the lateral border of the tongue before treatment.

Figure 1b: Erythema involving the mucosa of the cheek and the anterior portion of the tongue.

Figure 1c: Well-circumscribed erythematous macules seen on the lateral border of the tongue.

Figure 1d: Erythema involving the mucosa of the right cheek.

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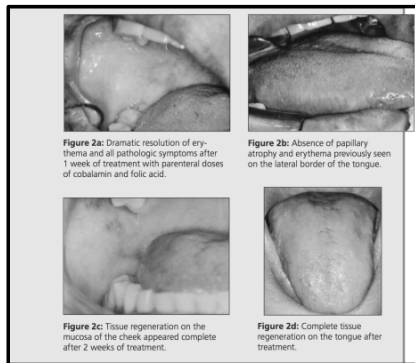
Lab Tests

Test	Normal range (female)	Patient's values
RBC count (cells/ μ L)	3.90–5.03	1.63
Hemoglobin (g/dL)	12.0–15.5	7.2
MCV (fL)	80–100	144
Hematocrit (%)	36–45	23.4
RDW (%)	13 \pm 1.5	25
Serum folate (ng/mL)	3–16	7.73
Serum cobalamin (pmol/L)	118–716	71.8

MCV = mean corpuscular volume; RBC = red blood cell; RDW = red cell distribution width.

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Patient treated with 1000 mcg B12 IM per week for 4 weeks .
Symptoms disappeared after 14 days of treatment.

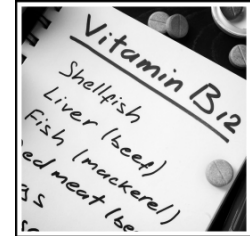
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Vitamin B12

- Found in animal and fortified foods. Key role in DNA synthesis, hematopoiesis and neurological function.
- Deficiency: megaloblastic anemia, neurological disorders (numbness/tingling feet, difficulty walking, memory loss, dementia) tongue soreness, constipation)
- American Academy of Neurology recommends elders and anyone with suspected dementia, be checked for B12 deficiency.
- Risk for deficiency: inadequate intake, impaired absorption, vegan, meds, obesity, elders, alcoholism
- **18 million Americans** deficient in vitamin B12
- Recommend > 20 mcg/d for those over age 50

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



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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.

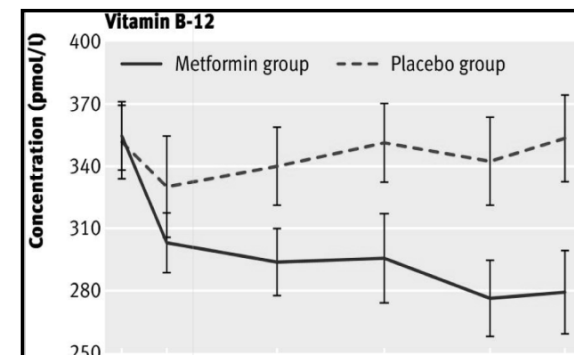


Meta analysis: 29 studies (8,089 patients) found **245% increased risk of B12 deficiency associated with metformin use.**

Niafar M, et al. Intern Emerg Med 2015; 10(1):93-1026

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De Jager, et al. BMJ 2010; 340:c2181

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Choline

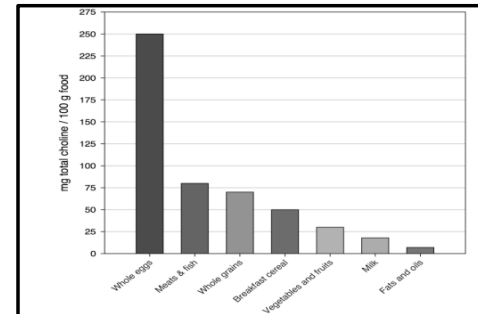
- Water soluble nutrient in the B-vitamin family that is particularly crucial during pregnancy and the first three years of a child's life.
- Deficiency may be associated with changes in brain function that negatively impact intelligence, memory, mood regulation, and stress response.
- Preclinical studies show choline partially ameliorates memory and learning deficits from prenatal alcohol exposure.
- Necessary for prevention of fatty liver disease.
- RDA for choline in pregnancy is 450 mg per day and 550 mg per day if breastfeeding.
- DV set in 2016: 550 mg per day



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Choline in Foods



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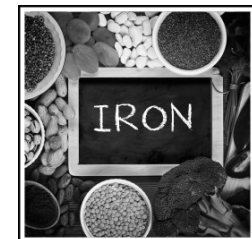
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Iron

WHO: Iron deficiency most common nutrient deficiency in world, affecting 2 billion people.

- Iron deficiency anemia accounts for 20% of all global maternal deaths.
- Necessary for growth and development and essential component of hemoglobin.
- Iron promotes resistance to disease; improves health of the teeth, skin, and bones; maintains energy
- Meta-analysis found that iron supplementation *improved attention, concentration, and IQ*.
- Iron promotes resistance to disease; improves health of the teeth, skin, and bones; maintains energy.
- Two forms of iron: heme and non-heme. Meat contains both forms, while plants and fortified foods contain only non-heme iron. We absorb roughly 18% of iron present in meat, compared to about 10% in plants



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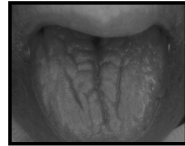
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• Review of Systems May Yield

- Shortness of breath
- Fatigue
- Sensitivity to cold
- Muscular weakness
- Low blood pressure
- Restless legs
- Pica (chew ice or non-food items)

• Physical Exam Findings

- Nonspecific pallor of the mucous membranes
- *Cheilosis*
 - fissures at the corners of the mouth
- *Koilonychia*
 - spooning of the fingernails



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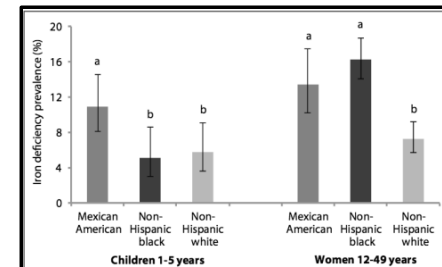


Figure H.3.a. Age-adjusted prevalence estimates of low body iron stores (< 0 mg/kg) in U.S. children and women by race/ethnicity, National Health and Nutrition Examination Survey, 2003–2006.

Error bars represent 95% confidence intervals. Bars not sharing a common letter differ within children and women ($p < 0.05$). Age adjustment was done using direct standardization.

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Recommended dietary allowances for iron for infants, children, and adult women

Age	Infants and children	Women	Pregnant	Breastfeeding
7 to 12 months	11 mg	n/a	n/a	n/a
1 to 3 years	7 mg	n/a	n/a	n/a
4 to 8 years	10 mg	n/a	n/a	n/a
9 to 13 years	8 mg	n/a	n/a	n/a
14 to 18 years	n/a	15 mg	27 mg	10mg
19 to 50 years	n/a	18 mg	27 mg	9 mg
51+ years	n/a	8 mg	n/a	n/a

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To Get 18mg of Iron in Food

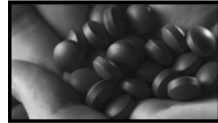
- 4 cups of raisins
- 3-5 cups instant oatmeal
- 3 cups Special K cereal**
- 3 cups cooked lentils
- 2.2 cups canned white beans
- 10 ounce beef liver
- 45 ounce chicken breasts
- 15 cups broccoli
- 3 cups cooked spinach



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Warning: Iron



- People who are not at risk of iron deficiency (teenage boys, adult men, women with infrequent menstrual cycles, and postmenopausal women) should *NOT* take multivitamins that contain iron or iron supplements unless instructed to do so by their health care provider.

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Vitamin C

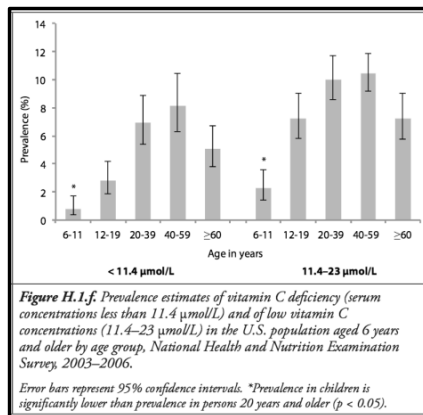
- Potent antioxidant, activates folate, needed to convert tryptophan to serotonin, cofactor in synthesis of carnitine, thyroxine, norepinephrine, dopamine and immune cells
- Vitamin C levels decline rapidly during periods of emotional and physical strain, and illness.
- As levels fall, collagen synthesis impaired: bruise more easily, skin becomes thick and dry, wounds take longer to heal, joints hurt, fatigue.
- At-risk populations include those with iron overload, neurologic conditions and history of chemotherapy.
- Recommend 200 mg 1-2 times daily.



Golriz F, et al. *Pediatr Radiol* 2016; Oct 24

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Zinc

- Zinc plays a vital role in our immune response.
- Marginal zinc deficiency can also diminish the activity of other important immune cells such as macrophages, neutrophils, and natural killer cells.
- WHO estimates marginal zinc status results in the deaths of > 780,000 children under the age five every year from diarrheal diseases, pneumonia, and malaria.
- Not effectively stored, must be continuously replaced in the diet.



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Zinc: Benefits



- Zinc lozenges have been shown to lead to a significant reduction in the duration of cold at a dose of ≥ 75 mg/day
- Study found half of women undergoing chemotherapy for gynecological cancer experienced altered taste. Serum zinc level consistently below lower limit of normal.
- RDBPCT of adult patients with head and neck cancers received zinc sulfate (50 mg, three times a day) or placebo at start of radiation through one month post. Zinc prevented radiation induced taste alterations.

Singh M, et al. Cochrane Database Syst Rev 2013; 6:CD001364
 Nishijima S, et al. Gynecol Oncol 2013; 131(3):674-8.
 Najafzade N, et al. J Res Med Sci 2013; 18(2):123-6

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Zinc and Oral Health

- One sign of zinc deficiency is red, swollen, and tender gums that may bleed after brushing.
- A review of clinical trials found “moderate quality evidence that zinc supplements improve overall taste improvement in patients with zinc deficiency/idiopathic taste disorders.”
- Zinc deficiency detected in 28% of recurrent aphthous stomatitis patients compared to controls.

Nagraj SK, et al. Cochrane Database Syst Rev 2014; 2014 Nov 26;11:CD010470.
 Ozler GS. J Laryngol Otol 2014; 128(6):531-3

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Zinc

- Zinc concentrations high in prostate gland, testes, and sperm. Deficiency might contribute to lower testosterone and infertility in men.
- Vegetarians need 50% more zinc due to lower absorption of zinc from plant foods. DV= 15 mg
- ACE inhibitors and thiazides deplete zinc
- Take 2 hours apart from medication, especially quinolones and tetracycline antibiotics.
- Do not take > 40 mg/d for more than a couple of months without supplementing copper.



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Calcium Calculator: A Quick Estimate

Food	# Servings/Day	Estimated Calcium per serving, in mg	Calcium in mg
Milk (8 ounces)		X 300	=
Yogurt (6 ounces)		X 300	=
Hard Cheese (1 ounce)		X 200	=
Soy milk, fortified (8 ounce)		X 300	=
Orange juice, fortified (8 ounce)		X 300	=
Tofu, firm calcium set (4 ounces)		X 300	=
All foods not included above		X 250	=
		Total Calcium	=
AI for your gender and age group		Subtract your total calcium from AI	=
		Supplement this amount	

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Deficiency

- One of the first signs of calcium deficiency is muscle cramping.
- Muscle aches of thighs and arms, with minimal exertion, could indicate a deficiency of calcium, vitamin D, and/or magnesium.
- Long term deficiency leads to poor bone development/loss of bone mineral density
- Necessary for dentin, bony tissue synthesis and mineralization.

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Calcium and PMS



- Two systematic reviews of PMS treatments concluded there was sufficient evidence to recommend calcium for PMS.
- Given that many women, especially adolescents, do not meet the adequate intake recommendations for dietary calcium, a 3-month trial of 500 mg BID calcium is reasonable.

Freeman EW. Expert Opin Pharmacother 2010; 11(17):2879-89
Whelan AM, et al. Can J Clin Pharmacol 2009; 16(3):e407-29

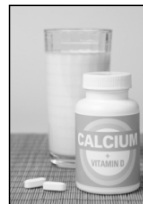
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Calcium Supplements

- You need roughly 1000 mg per day of calcium **from all sources**, depending upon age.
- Chelated calcium (citrate, malate)
 - Best for those over 50 years old or those taking drugs to suppress stomach acid
- Do not take at the same time as other medications (thyroid, bisphosphonates, phenytoin, tetracycline)

Spence LA, et al. Nutr Rev 2013; 71(1):15-22



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Drug Induced Osteoporosis

- These drugs include:
 - Glucocorticoids (steroids) – 1:5 cases of osteoporosis
 - Aromatase inhibitors (breast cancer)
 - Anti-androgen therapy (prostate cancer)
 - Proton pump inhibitors (heartburn)
 - Antiretroviral drugs (HIV, hepatitis)
 - SSRIs (antidepressants) and antipsychotics
 - Anticonvulsants (epilepsy)
 - Loop diuretics (e.g. lasix)
 - Heparin and oral anticoagulants

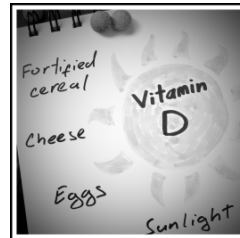
Mazziotti G, et al. Am J Med 2010; 123:877-84

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Vitamin D

- Vitamin D interacts with more than 1000 genes
- Necessary for calcium, magnesium, and phosphorus homeostasis; dentin, bony tissue synthesis; mineralization; and bone sufficiency
- Modulates chronic inflammation of the gums associated with gingivitis or periodontal disease
- Low vitamin D in adults causes muscle weakness and lower back and hip pain.
- Obesity increases the risk of deficiency.



Kim Y, et al. Br J Cancer 2014; 110(11):2772-84.
Ma Y, et al. J Clin Oncol 2011; 29(28):3775-82

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Endocrine Society Clinical Practice Guidelines

- Serum 25(OH)D level used to evaluate high-risk folks
 - Insufficiency defined as 21-29 ng/mL
 - **Deficiency defined as <20 ng/mL**
- Maximum tolerable limits (without supervision):
 - 1,000 IU/day for infants to age 6 months
 - 1,500 IU/day for ages 6 months to 1 year
 - 2,500 IU/day ages 1 to 3 years
 - 3,000 IU/day for ages 4 to 8 years
 - 4,000 IU/day anyone older than 8 years

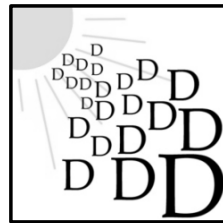
Holick MF, et al. J Clin Endocrinol Metab 2011; 96(7):1911-30

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Endocrine Society Guidelines

- Obese children and adults should be given at **least twice or three times** the vitamin D requirements previously specified, as should all individuals taking anticonvulsant medications, glucocorticoids, antifungals such as ketoconazole and medications for HIV/AIDS.



Holick MF, et al. J Clin Endocrinol Metab 2011; 96(7):1911-30

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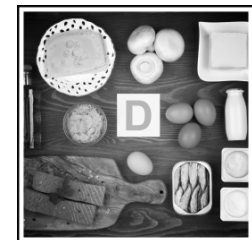
Vitamin D

CDC found:

- ~90 million Americans are vitamin D deficient
- Most individuals should take 1,000-2,000 IU vitamin D3 per day with dinner

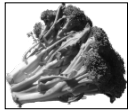
To get 600 IU/d Vitamin D3:

- 3-4 ounces sockeye salmon, cooked
- 11.4 ounces water-packed tuna
- 26 oil-packed sardines
- 15 large eggs
- 5 cups fortified milk
- 30-45 ounces yogurt

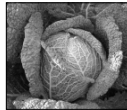


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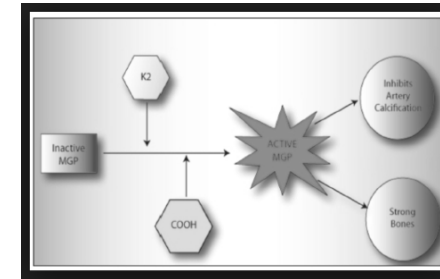
Vitamin K



- There are two main forms of vitamin K.
 - Phylloquinone, or vitamin K1, is synthesized by plants and makes up 90% of the vitamin K obtained in the diet. Best sources are green leafy vegetables. Fat-soluble so should be eaten with some healthy fat.
 - Menaquinone, vitamin K2, is result of bacterial action in GI tract converting K1 to K2 or obtained directly from food sources such as meat, egg yolks, fermented dairy and soy (e.g, miso, natto).

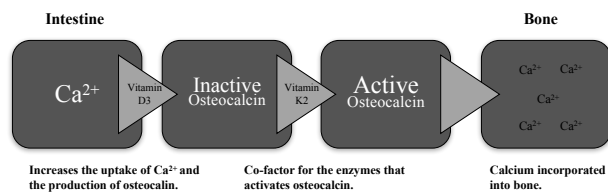
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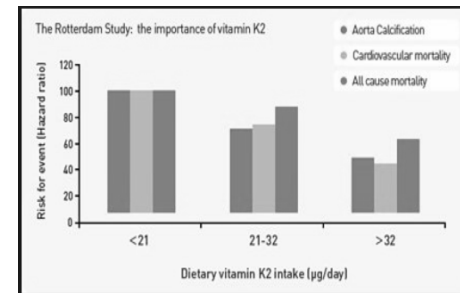
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Geleijnse JM, et al. J Nutr. 2004;134(11):3100-5.

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Magnesium

- Low magnesium intakes and serum levels associated with type 2 diabetes, metabolic syndrome, inflammation, high blood pressure, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer.
- 50% of U.S. population consumes less than the required amount of daily magnesium.
- FDA requires warning that proton pump inhibitors can cause dangerously low magnesium levels.



Rosanoff A, et al. Nutr Rev 2010;70(3):153-64

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To Get 400 mg Magnesium

- 115 almonds, whole
- 2.5 cups boiled spinach
- 6.5 cups soymilk, plain or vanilla
- 17 slices whole wheat bread
- 3.5 cups cooked black beans
- 4.7 cups cooked brown rice
- 9 cups raw, cubed avocado
- 3 cups pumpkin seeds

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Magnesium and the Heart

- Low serum magnesium levels associated with higher all-cause and cardiovascular mortality.
- Review of 44 studies shows Mg supplements enhance blood-pressure lowering effect of BP medications in stage 1 hypertension when given 230-460 mg/d.
- Nurses Health Study (88,375 women) found that for every 0.25-mg/dL increment in plasma magnesium –41% lower risk of sudden cardiac death. Women with lowest levels of magnesium also had significantly increased risk of stroke.

Reffelmann, et al. Atherosclerosis 2011 Nov;219(1):280-4.
Rosanoff, et al. Magnes Res 2010 Mar;23(1):27-40.
Chiuve, et al. Am J Clin Nutr. 2011;93(2):253-60.
Akarolo-Anthony SN, et al. Stroke 2014; 45(10):2881-6

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Proton Pump Inhibitors

Drug Classification	Nutrient Depletion
Proton pump inhibitors	Magnesium, iron, calcium, vitamin B12, folic acid, zinc, vitamin C, vitamin D (?)
H2 antagonists	folic acid

- FDA issued a MedWatch warning and label change for PPIs due to low magnesium levels associated with long-term use.
- “Those taking medications, generally more than one year, may end up with low magnesium, which can put them at risk for seizures, irregular heartbeats, and muscle spasms.”
- Review of nine studies (n=115,455) found that the odds of *developing hypomagnesemia increased by 75% if taking PPIs*.
- FDA advises magnesium levels be checked before and periodically during treatment.

Park CH, et al. PLoS One 2014; Nov 13;9(11):e112558.

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Magnesium for Migraines



Sun-Edelstein C, Mauskop A. Clin J Pain. 2009 Jun;25(5):446-52.
Pringsheim T, et al. Can J Neurol Sci 2012; 39(Suppl) S1-S9
Mauskop A, et al. J Neural Transm 2012; 119(5):575-9.

- Studies show that migraineurs have low brain Mg during migraine attacks and may have systemic Mg deficiency.
- Mg reduces recurrent pediatric migraine and tension headaches.
- Canadian Headache Society gave magnesium citrate a strong recommendation for prophylaxis of migraine.
- Dose generally 300-400 mg/d. Diarrhea most common side effect (glycinate and citrate forms less GI complaints than oxide).

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Iodine in Pregnancy

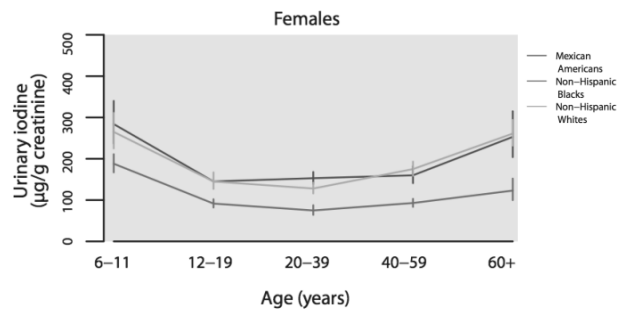


- Many reproductive aged women in US have marginal iodine status; salt in processed foods is not iodized.
- Deficiency associated with pregnancy loss and prematurity, and neurocognitive defects in the baby.
- Mild to moderate iodine deficiency associated with higher incidence of ADHD and lower IQ in the baby.
- American Thyroid Association recommends pregnant/lactating women supplement: 150 mcg/d potassium iodide.

Council on Environmental Health, et al. *Pediatrics* 2014; 133(6):1163-6.

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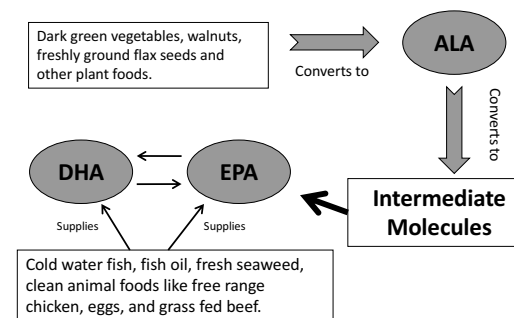


CDC 2nd National Report on Biochemical Indicators of Diet and Nutrition. The WHO recommends that the median UI in pregnancy be 150-249 mcg/L.

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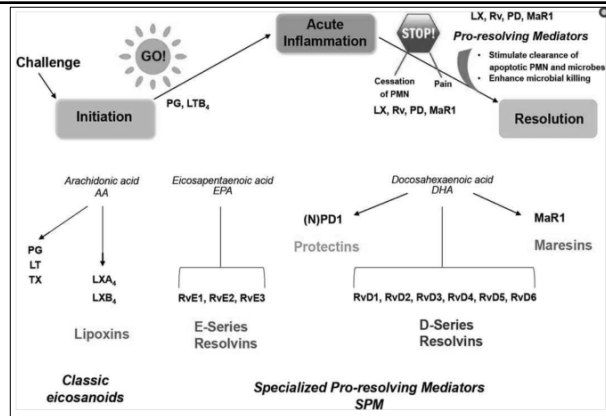
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Omega 3 Fatty Acids from Plants and Animals



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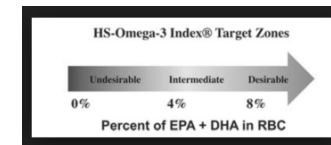
Serhan CN, Chiang N. *Curr Opin Pharmacol* 2013; 13(4):632-40.

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No Fish Story: The Omega 3 Index

- Omega-3 Index test is now the gold standard for omega-3 biostatus testing. It is used as a compliance marker for randomized controlled trials with fish oil supplements, and in epidemiological research.
- In 2008 Dr. Bernadine Healy, cardiologist and past President of the AHA and first woman Director of the NIH said, "Before long, your personal Omega-3 Index just could be the new cholesterol—the number you want to brag about."



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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."
- There was insufficient evidence to evaluate the role of fish oil supplements in primary prevention of CVD.

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

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Omega 3 and Pregnancy

- Critical for neurological and early visual development, particularly in 3rd trimester.
- Reduces risk of allergies
- Reduces risk of preterm labor and birth
- Increases birth weight
- FDA recommends 2-3 servings of low mercury fatty fish per week during pregnancy.



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Omega 3 and Asthma

- Reduced intake of omega-3 fatty acids may be a contributing factor to the increasing prevalence of wheezing disorders.
- Reviewers found that supplementation with omega-3 fatty acids in the third trimester of pregnancy reduced the absolute risk of persistent wheeze or asthma and infections of the lower respiratory tract in offspring by approximately 33%.



Biggaard H, et al. N Engl J Med 2016; Dec 29;375(26):2530-9

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Fish Oil

- Supplementation is an alternative to eating fish; however, all supplements are not equal.
- Randomized, crossover study of 35 healthy individuals compared four popular brands/types of omega 3 fatty acids:
 - Concentrated triglyceride (rTG)
 - Ethyl ester (EE)
 - Phospholipid krill oil (PL)
 - Triglyceride salmon oil (TG)

Laidlaw M, et al. Lipids Health Dis 2014; 13:99

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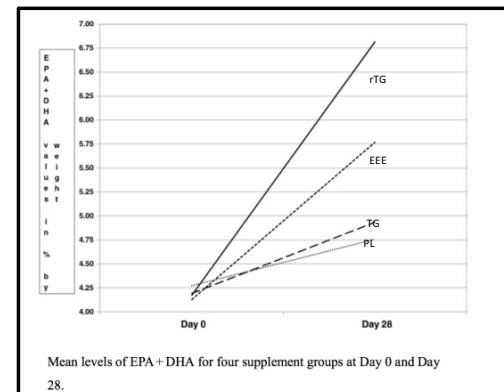
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Dosing According to Manufacturer's Recommendations

TRT	Product	EPA & DHA per capsule*	Tested values	Label use: caps/day	Daily dosage of EPA + DHA
rTG	Nordic Naturals ProOmega®	325 mg EPA	329.6 mg EPA	2	EPA: 650 mg
	Triglyceride	225 mg DHA	226.0 mg DHA		DHA: 450 mg
EE	Minami MorEPA®	756 mg EPA	774.2 mg EPA	1	EPA: 756 mg
	Platinum Ethyl Ester	228 mg DHA	233.7 mg DHA		DHA: 228 mg
PL	Source Naturals ArcticPure®	75 mg EPA	78.0 mg EPA	2	EPA: 150 mg
	Krill Oil Phospholipid	45 mg DHA	46.7 mg DHA		DHA: 90 mg
TG	New Chapter			2	
	Wholemega® Salmon	90 mg EPA	96.4 mg EPA		EPA: 180 mg
	Oil Triglyceride	110 mg DHA	109.5 mg DHA		DHA: 220 mg

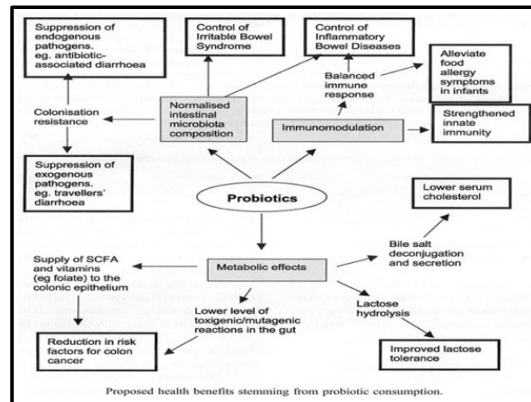
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Probiotics and Oral Health

- A systematic review of probiotic strains for caries prevention showed promising results but only a few studies have demonstrated clear clinical outcomes.
- More than 14 strains have been researched.
- A continuous regular almost daily intake is probably required.

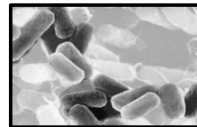


Cagetti MG, et al. Nutrients 2013; 5(7):2530-50

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Antibiotic Associated Diarrhea (AAD)



1. Results from an imbalance in the colonic microbiota
2. Probiotic treatment can reduce the incidence and severity of AAD
3. Efficacy of probiotic AAD prevention is dependent on the probiotic strain(s) used and on the dosage.

- *Saccharomyces boulardii* 500 mg BID
- *Lactobacillus* GG 1 billion colony forming units BID
- *Lactobacillus reuteri* 1 billion colony forming units BID

Go to usprobioticguide.com for up to date product recommendations.

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Melatonin

- Maintains 24-hour circadian rhythm.
- Melatonin, when taken several *hours* before sleep, can shorten the time it takes to fall asleep, as well as help you stay asleep.
- 2010 review (*Annals of Pharmacotherapy*) concluded that melatonin is a well-tolerated and efficacious treatment for children with ADHD that have chronic difficulty falling asleep. Studies included children 6-14 years old and melatonin doses ranged from 3 to 6 mg.
- Our natural production of melatonin may decline with age. In Europe, sustained-release melatonin is approved for adults 55 years and older who have primary insomnia.

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Depression?

- 2014 Danish study published in *Breast Cancer Research and Treatment* randomized 54 women diagnosed with breast cancer and without depression to receive 6 mg of melatonin or placebo starting one week before their cancer surgery for a total of three months.⁵
- Only 11% of women in melatonin group experienced depression versus 45% in the placebo group.
- A double-blinded placebo-controlled study found that taking 3 mg of melatonin at night for six months significantly improved symptoms of depression in perimenopausal and post-menopausal women.

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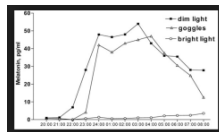
Melatonin and Heartburn?

- Melatonin inhibits gastric acid secretion, increases gastrin, which stimulates contraction of lower esophageal sphincter.
- Study of 60 patients with GERD by endoscopy compared to controls. Received:
 - 3 mg melatonin
 - 20 mg omeprazole
 - 3 mg melatonin + 20 mg omeprazole
- Heartburn/epigastric pain decreased after 4 weeks and completely resolved in 8 weeks in all three groups.
- Only groups with melatonin has improved sphincter function.

Kandil TS, et al. *BMC Gastroenterol* 2010;10:7.

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Safety

- Short term use of melatonin at even very high doses is not associated with any significant side effects.
- Long-term treatment is not associated with any significant side effects, comparable to placebo.
- Safety data in pregnancy, lactation is still being evaluated.

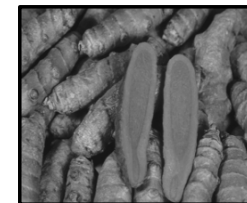
Andersen LP, et al. *Clin Drug Investig* 2015; Dec 21

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Turmeric Rhizome (*Curcuma longa* and others)

- Rhizomes provide bright yellow-orange culinary spice and dye.
- Yellow pigments = curcuminoids, one example is curcumin.
- Long history of medicinal use for respiratory, skin, digestive and inflammatory conditions in India.
- More than 65 clinical trials have shed light on its *potential* role in CVD, diabetes, cancer, fatty liver, arthritis, neuro/psych disorders.



Kunnumakkara AB, et al. *Br J Pharmacol* 2016; Sep 17. doi: 10.1111/bph.13621.

Prasad S, et al. *Biotechnol Adv* 2014; 32(6):1053-1064

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Turmeric for Depression?

- A mini meta-analysis of 6 studies found curcumin reduced depression symptoms, particularly in middle-aged patients when given at higher doses for longer periods of time.
- Authors concluded, “there is supporting evidence that curcumin administration reduces depressive symptoms in patients with major depression.”
- Is this an impact on microbiome? Is it due to systemic reduction in inflammation? *Intriguing.*



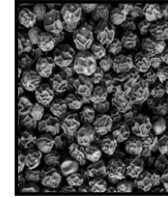
Al-Kawari D, et al. *Phytother. Res* 2016; 30(2):175-83

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Absorption and Safety Issues

- Low aqueous solubility of curcumin and its rapid metabolism and elimination from the body have constituted *major obstacles* to clinical use.
- Nanoencapsulation, curcumin complexed with phosphatidylcholine, and inclusion of the black pepper alkaloid, piperine, enhance tissue distribution and bioavailability.
- Note: Piperine causes inhibition of CYP3A4 and at doses of **20 mg or more** can cause *clinically relevant drug interactions* especially for drugs with narrow therapeutic indices.
- If taking prescription meds, choose phytosome bound turmeric/curcumin product.
- Dose generally 1200-1800 mg per day of turmeric extract standardized to 95% curcumin, taken in divided doses.



Bedada SK, et al. *Drug Res* 2016; Oct 24

Gurley BJ, et al. *Planta Med* 2012; 78(13):1490-514

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Read the Label Carefully

Supplement Facts		
Serving Size: 1oz.		
Servings Per Container: 16		
	Amt. Per Serving	% Daily Value
Organic Turmeric Root Extract (Supercritical CO2 Extraction)	500mg	*
Organic Black Pepper Fruit Extract (Standardized to 95% Piperine)	10mg	*

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Alpha Lipoic Acid (LA)

- A water and fat-soluble antioxidant that readily crosses the blood/brain barrier, where it acts as a neuroprotectant.
- One small double-blinded, placebo controlled 12-month study published in 2014 in the *Journal of Alzheimer's Disease* found that the combination of fish oil (975 mg EPA and 675 mg DHA) and LA (600 mg) slowed both cognitive and functional decline in people with dementia.
- Randomized, double-blinded, placebo-controlled clinical trials have shown LA to be both safe and effective for the treatment of diabetic neuropathy, helping to improve the numbness, tingling, and loss of muscle strength that accompanies the disorder.
- Drug pregabalin (Lyrica) acts more quickly than LA to relieve pain, studies show that they are otherwise therapeutically equivalent.
- 600 mg 1-2 times per day. Good safety data – *may* impact thyroid hormones and blood sugar.

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Diabetic Neuropathy

- Randomized, double-blinded, placebo-controlled clinical trials have shown LA to be both safe and effective for the treatment of diabetic neuropathy, helping to improve the numbness, tingling, and loss of muscle strength that accompanies the disorder.
- Drug pregabalin (Lyrica) acts more quickly than LA to relieve pain, studies show that they are otherwise therapeutically equivalent.
- 600 mg 1-2 times per day. Good safety data – *may* impact thyroid hormones and blood sugar.

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Resources

- *Fortify Your Life*, Tieraona Low Dog, MD with National Geographic
- Dietary Supplement Label Database: dslid.nlm.nih.gov
- NIH National Center for Complementary and Integrative Health (NCCIH): nccih.nih.gov
- Office of Dietary Supplements: ods.od.nih.gov
- Linus Pauling Institute: lpi.oregonstate.edu
- Consumer Labs: www.consumerlabs.com
- Natural Medicines Comprehensive Database: naturaldatabase.com

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