

***Life Fortified:
The Case for Dietary Supplements***



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**Per 1994
Dietary Supplement Health Education Act**

- A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet.
- The "dietary ingredients" in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites.
- Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders.

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- Since passage of DSHEA, the marketplace has grown from roughly 4,000 products to more than 29,000.
- The sheer number and variation in products makes it difficult for clinicians to counsel patients about DS use.

Tsourounis, et al. Clin Pharmacol Ther 2010; 87(2):147-9

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Centers for Disease Control

- Recent findings have determined that *less than optimal biochemical levels* of vitamins and minerals are associated with risks of adverse health effects.
- “These health effects include cardiovascular disease, stroke, impaired cognitive function, cancer, eye diseases, poor bone health, and other conditions.”

CDC: 2nd National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population

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At Risk Populations

- Obesity (B1, B6, B12, D)
- Ethnic/racial minorities
 - Hispanics (B3, folate, D, magnesium, iron)
 - African Americans (iron, zinc, B6, D)
- Those with chronic disease
- Chronic medication use
- Families with food insecurity
- Those on restricted diets
 - Vegans - B6, B12, D, K, choline, iron, zinc, omega 3s

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Food Insecurity

- Food insecurity is a serious public health problem associated with poor cognitive and emotional development in children and with depression and poor health in adults.
- Prevalence rate 30.2% food insecurity in female-headed households ~ 3 times the national average, more than 12.4 million children.
- Even mildest form of food insecurity is associated with risk of poor cognitive, social, and emotional development of children younger than 3 years.

Chilton M, et al. Am J Public Health 2009; 99(7): 1203–1211

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Chronic Disease



- Many examples:
 - Cystic fibrosis
 - A, D, E, K, Ca, Fe, Zn
 - Diabetes
 - B1, B6, B12, C, D, Ca, Mg, Zn, choline
 - IBD
 - A, B6, B9, B12, D, E, K, Cr, Fe, Mg, Zn, omega 3
 - Sickle cell
 - Zinc, B9, D

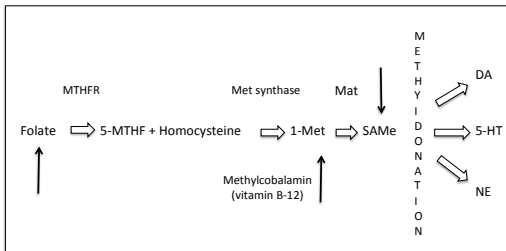
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B-Vitamins

- The B-vitamins are important for the metabolism of carbohydrates, fats and proteins and play a vital role in the production of fuel and energy for the body.
- There are eight B-vitamins that partner together, which is why you almost always want to take them together in balanced amounts.

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The "Stress" B- Vitamins



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Vitamin B6 (Pyroxidal-5-Phosphate)

- Critically involved in production of serotonin, dopamine, melatonin, hemoglobin, and converting tryptophan to niacin.
- Necessary for conversion of plant omega 3 (ALA) to docosahexaenoic acid (DHA).
- Deficiency increases risk for depression and impaired cognition, attention, memory and sleep.
- Serum PLP < 20 nmol/L indicates deficiency.

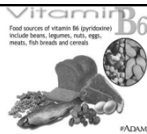
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Vitamin B6 and Health

- Meta-analysis of 13 prospective studies in the *Journal of the American Medical Association (2010)* found that PLP inversely correlated with colorectal cancer risk: for every 0.1 nmol/L increase in serum PLP concentration, colorectal cancer risk decreased by 49%.
- 2009 systematic review published in *Canadian Journal of Pharmacology* concluded that B6 improves depression, anxiety, and breast tenderness associated with PMS.
- American College of Obstetrics and Gynecology recommends 10-25 mg of vitamin B₆ every eight hours as first-line therapy for nausea and vomiting in pregnancy (morning sickness).

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Vitamin B6 Deficiency



- **30 million people are deficient (PLP < 20nmol/L)**
- In 2012, Tuft’s University researchers confirmed as inflammation in body rises, B6 levels falls.
- Even marginally low PLP levels (20–30 nmol/L) are associated with increased risk of CAD and stroke.
- Women are almost twice as likely to be deficient in B6 as men and deficiency rates for blacks (15.7%) are higher than for whites (10.7%).

CDC 2nd National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population

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To Get 1.5 mg B6 in Food

- 2.5 bananas
- 12 Tbsp. roasted sunflower seeds
- 8 ounces chicken breast
- 8 ounces sockeye salmon
- 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.

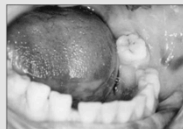


Figure 1b: Erythema involving the mucosa of the cheek and the anterior portion of the tongue.



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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Vitamin B12

- Found in animal and fortified foods. Key role in DNA synthesis, hematopoiesis and neurological function.
- Deficiency damages myelin sheath covering cranial, spinal, and peripheral nerves, resulting in neurological damage.
- Myelination primarily occurs during fetal development and early infancy but continues through early adulthood.
- Risk: inadequate intake, veganism, malabsorption, medications, obese, insulin resistant adolescents.
- MMA level > 271 nmol/L is most reliable measure of deficiency (aim for serum B12 500-800 pg/ml)

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

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Vitamin B12

- Scientific review > 40 studies found that low levels of vitamin B12 are associated with dementia, Alzheimer's, and Parkinson's disease.
- American Academy of Neurology recommends elders and anyone with suspected dementia, be checked for B12 deficiency.

Moore E, et al. International Psychogeriatrics (2012), 24:4, 541-556

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Metabolism of B12

- Enters stomach, HCL and pepsin separate B12 from protein in animal food
- Free B12 joined to protein called intrinsic factor (IF) made by parietal cells in stomach.
- B12-IF travels to ileum where, if calcium is adequate, it is absorbed.

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Obese Adolescents with Insulin Resistance



- 103 adolescents with pre-diabetes enrolled in 12 month RESIST trial. Baseline data used for analysis, no participant was taking metformin.
- *One-third of the obese adolescents were classified with low or borderline vitamin B12 status.*
- Concerning as many will likely take metformin.
- RDA is 1.2 mcg/d kids 4-8 years, and 1.8 mcg/d for ages 9-13 years of age.

Ho M, et al. *Nutrients* 2014; 6(12): 5611-5618.

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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.

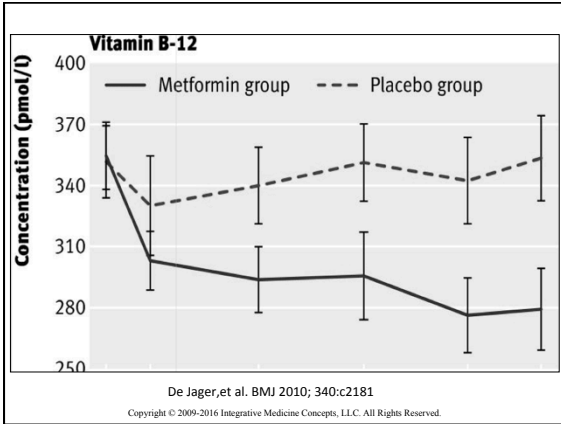


Diabetic Medications

Drug Classification	Nutrient Depletion
Sulfonylureas	Coenzyme Q10
Biguanides	Folic acid, vitamin B12

- Study of 390 patients with type 2 diabetes randomized to metformin (850 mg) or placebo TID for 4.3 years.
- Compared with placebo, metformin treatment was associated with a mean decrease in vitamin B-12 concentration of -19%.

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Riboflavin (B2)

- Crucial for absorption and use of iron. Primary source in western diet is dairy & fortified foods.
- Laboratory data in UK found 95% of 15-18 year old girls had low riboflavin levels.
- Five year study in China found strong correlation between low riboflavin and iron deficiency anemia.
- Consider B-vitamins in girls with iron deficiency who may be at risk for low dietary intake.

Powers HJ. Am J Clin Nutr 2003; 77(6):1352-60

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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 permanent 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.

Jiang X, et al. Trends Endocrinol Metab 2014; 25(5):263-73.
Jiang X, et al. FASEB J. 2012;26(8):3563-3574.
Wozniak JR, et al. Nutr Res 2013; 33(11):897-904

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Choline in Pregnancy

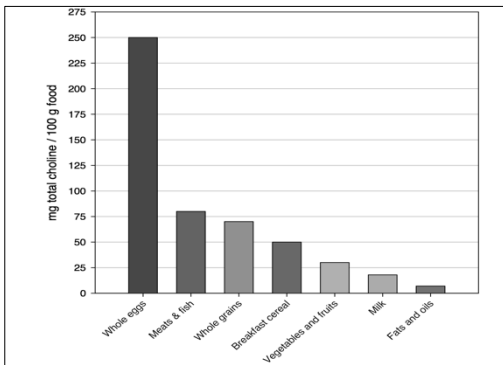


- Suboptimal intake of choline was found in 95% of pregnant women in Boston.
- Low choline intake increases the risk of neural tube defects by up to 4 times.
- RDA for choline in pregnancy is 450 mg per day and 550 mg per day if breastfeeding.

Shaw GM, et al. *Am. J. Epidemiol.* 2004; 160, 102–109
Brunst KJ, et al. *Public Health Nutr* 2014; 17(9):1960-70
Jiang X, et al. *FASEB J.* 2012;26(8):3563–3574.

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Choline in Foods: <http://naldc.nal.usda.gov/download/47335/PDF>



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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.
- Meta-analysis found that iron supplementation improved attention, concentration, and IQ.
- Iron deficiency increases the risk of lead toxicity

Falkingham M, et al. *Nutr J* 2010; 25;9:4.
 Calarge C, et al. *J Child Adolesc Psychopharmacol.* 2010;20(6):495–502

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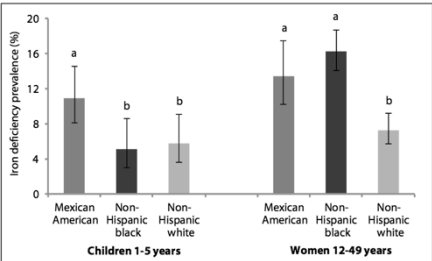


Figure H.3.a. Age-adjusted prevalence estimates of low body iron stores (< 0 mg/kg) in U.S. children and women by race/ethnicity, National Health and Nutrition Examination Survey, 2003–2006.

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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Iron in Food

- 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.
- You can increase absorption of non-heme iron if meal contains vitamin C.

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To Get 18 mg of Iron in Food

- 4 cups raisins
- 3–5 cups instant oatmeal
- 3 cups Special K cereal
- 3 cups cooked lentils
- 2.2 cups canned white beans
- 10 ounces beef liver
- 45 ounces chicken breast
- 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.
- When taking supplements: Look for iron bisglycinate, ferrous bisglycinate, or iron glycinate on the label. Take with vitamin C and *NOT* with calcium.

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Vitamin C



- Plays a role in activating folic acid, assists in conversion of tryptophan to serotonin, and is a cofactor in synthesis of carnitine, thyroxin, norepinephrine, and dopamine.
- Vitamin C levels decline rapidly during periods of emotional and physical strain, and illness.
- As levels fall, collagen synthesis is impaired: bruise more easily, skin becomes thick and dry, wounds take longer to heal, joints hurt, fatigue.
- 15.7 million Americans have vitamin C deficiency.

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Vitamin C and Common Cold



- “Given the consistent effect of vitamin C on the duration and severity of colds in the regular supplementation studies, and the low cost and safety, it may be worthwhile for common cold patients to test on an individual basis whether therapeutic vitamin C is beneficial for them.”
- Dose of 200-500 mg per day is probably a good target.

Hemila H, et al. Cochrane Database Syst Rev 2013; Jan 31:1.CD 000980.

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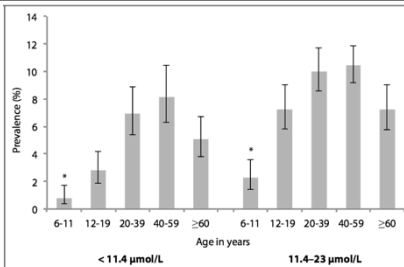
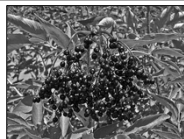


Figure H.1.f. Prevalence estimates of vitamin C deficiency (serum concentrations less than 11.4 µmol/L) and of low vitamin C concentrations (11.4–23 µmol/L) in the U.S. population aged 6 years and older by age group, National Health and Nutrition Examination Survey, 2003–2006.

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

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Elderberry *Sambucus nigra*



- Anthocyanidins have potent antiviral and immune priming effects.
- Antimicrobial activity against Gram-positive bacteria *Streptococcus pyogenes* and group C and G *Streptococci*, and Gram-negative *Moraxella catarrhalis*.
- Elderberry flavonoids inhibit H1N1 to roughly same degree as tamiflu and amantadine. Elderberry extract reduces symptoms when administered to patients with influenza A or B.
- Take elderberry extracts as instructed on label (crude equivalent 5000-6000 mg) 1-4 times per day

Krawitz C, et al. BMC Complement Altern Med 2011; 11:16.
Roschek, et al. Phytochemistry 2009; 70(10):1255-61.
Zakay-Rones Z, et al. J Int Med Res 2004; 32(2):132-40.

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Supplement Facts		
Serving Size: 2 teaspoons (10 ml)		
Servings Per Container: 24		
	Amount Per Serving	% DV
Calories	20	
Total Carbohydrate	6 g	2%†
Standardized Elderberry BioActives Extract (berry) from 6.4 g (6,400 mg) of premium cultivar berries	100 mg	**
Supplement Facts		
Serving Size: 2 Capsules		
Servings Per Container: 30		
	mg	%DV
Calories	30	
Alcohol Free Concentrated Extract Of: Black Elderberry berries (Sambucus nigra)*	800 mg	†
†Daily Value not established. * = Organic ingredient Each 2 capsules contain 5,000 mg crude herb equivalent.		

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Zinc

- Zinc plays a vital role in our immune response.
- Need zinc to activate T-lymphocytes, immune cells responsible for destroying cells infected with viruses or bacteria, or cancerous.
- 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 in Children

- Meta-analysis concluded zinc supplementation reduces frequency, severity, and duration of diarrheal episodes in children under five years of age.
- Zinc supplementation in children (2-59 months) reduced incidence and prevalence of pneumonia.
- When supplemented for at least five months, zinc reduces cold incidence, school absenteeism and prescription of antibiotics in children.

Aggarwal R, et al. Pediatrics. 2007;119(6):1120-1130
 Lassi ZS, et al. Cochrane Database Syst Rev 2010; 8:12:CD005978
 Singh M, et al. Cochrane Database Syst Rev 2011; 16:2:CD001364

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Zinc: Treatment of Common Cold



- Zinc administered within 24 hours of onset of symptoms reduces the duration of common cold symptoms in healthy people
- Zinc lozenges formulation have been shown to lead to a significant reduction in the duration of cold at a dose of ≥ 75 mg/day

Singh M, et al. Cochrane Database Syst Rev 2013; 6:CD001364

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Zinc and Growth in Children



- Prevalence of zinc deficiency high in low-income minority children in the US, especially among African Americans and Hispanic adolescents, 28.4% (females) and 24.5% (males) had zinc deficiency.

Brown KH, et al. Food Nutr Bull 2009; 30(15):S12-40
Cole CR, et al. Am J Clin Nutr 2010; 91(4):1027-34.
De la Cruz-Gongora V, et al. Salud Publica Mex 2012; 54(2):135-45.

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Zinc and the Senses

- Zinc is necessary for sense of smell, which accounts for about 80% of your sense of taste!
- Also important for oral health; one sign of zinc deficiency is red, swollen, and tender gums that may bleed after brushing.
- Zinc helps protect cells that line the mouth in those undergoing chemotherapy or radiation.

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Zinc and Taste

- 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.

Nishijima S, et al. *Gynecol Oncol* 2013; 131(3):674-8.
 Najafizade N, et al. *J Res Med Sci* 2013; 18(2):123-6

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Zinc and Oral Health

- 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 and Men

- Men have a higher daily requirement for zinc because it is used for the production of testosterone, making it an important nutrient for male sexual maturation and reproduction.
- Zinc concentrations very high in the prostate gland, testes, and in sperm. Deficiency of this important trace mineral might contribute to lower testosterone and infertility in men.

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Zinc



- Zinc deficiency: loss of appetite; lack of taste or smell; poor wound healing; acne; hair loss; lack of menstrual period; night blindness; and depression
- Vegetarians need as much as 50% more zinc due to lower absorption of zinc from plant foods. DV= 15 mg
- ACE inhibitors and thiazide diuretics deplete zinc
- Best absorbed on empty stomach. Do not take more than 40 mg per day for more than a few days without medical supervision. Take 2 hours apart from medication, especially quinolones and tetracycline antibiotics.

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Life Stage Group	Calcium			Vitamin D		
	Estimated Average Requirement (mg/day)	Recommended Dietary Allowance (mg/day)	Upper Level Intake (mg/day)	Estimated Average Requirement (IU/day)	Recommended Dietary Allowance (IU/day)	Upper Level Intake (IU/day)
Infants 0 to 6 months	*	*	1,000	**	**	1,000
Infants 6 to 12 months	*	*	1,500	**	**	1,500
1-3 years old	500	700	2,500	400	600	2,500
4-8 years old	800	1,000	2,500	400	600	3,000
9-13 years old	1,100	1,300	3,000	400	600	4,000
14-18 years old	1,100	1,300	3,000	400	600	4,000
19-30 years old	800	1,000	2,500	400	600	4,000
31-50 years old	800	1,000	2,500	400	600	4,000
51-70 year old males	800	1,000	2,000	400	600	4,000
51-70 year old females	1,000	1,200	2,000	400	600	4,000
>70 years old	1,000	1,200	2,000	400	800	4,000
14-18 years old, pregnant/lactating	1,100	1,300	3,000	400	600	4,000
19-50 years old, pregnant/lactating	800	1,000	2,500	400	600	4,000

*For infants, Adequate Intake is 200 mg/day for 0 to 6 months of age and 260 mg/day for 6 to 12 months of age.
**For infants, Adequate Intake is 400 IU/day for 0 to 6 months of age and 400 IU/day for 6 to 12 months of age.

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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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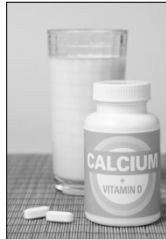
Deficiency

- 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.

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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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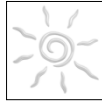
Drug Induced Osteoporosis

- 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



- Controls calcium and phosphorous levels, necessary for strong bones, muscle contraction, nerve conduction, and general function of all our cells.
- There is a growing body of data that show vitamin D is also critically important for respiratory, cardiovascular and immune health.

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Vitamin D and Breast Cancer



- Some research suggests serum 25(OH)D level of 47 ng/ml is associated with a 50% lower risk of breast cancer.
- Review of 30 studies show that high vitamin D status is *strongly associated with better breast cancer survival.*

Mohr SB, et al. *Anticancer Res* 2011;31(9):2939-48
Kim Y, et al. *Br J Cancer* 2014; 110(11):2772-84.

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Vitamin D and Colorectal Cancer



- Review ~ 1,000,000 participants found 10 ng/mL increment in blood 25(OH)D level conferred a *26% reduction in risk.*
- Higher serum 25(OH)D is associated with lower mortality of patients with colorectal cancer.
- Colorectal cancer patients with deficient levels of serum 25(OH)D should have levels restored to range (30-50ng/ml).

Ma Y, et al. *J Clin Oncol* 2011; 29(28):3775-82
Weinstein SJ, et al. *Int J Cancer* 2014; doi: 10.1002/ijc.29157.
Mohra SB, et al. *J Steroid Biochem Mol Biol* 2014; S0960-0760(14)00316-1.

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Vitamin D?



- Large consortium of eight cohort studies from Europe and US (26,018 men and women aged 50-79 years) the bottom 25(OH)D quintile was associated with increased all-cause and cardiovascular mortality and with cancer mortality in subjects with a history of cancer but not in subjects without.
- These relationships were compellingly consistent across countries, sexes, age groups.

Schottker B, et al. BMJ 2014; 348: g3656.

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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:
 - 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

“For clinical care, it appears that all current (testing) methodologies are adequate if one targets a 25(OH)D value higher than current cut points; for example, a value of 40 ng/ml (100 nmol/L) is without toxicity and virtually ensures that the individuals ‘true’ value is greater than 30 ng/ml (75nmol/L).”

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

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Deficiency/Insufficiency



- **66.8 million Americans** 1 year and older had vitamin D levels between 12-20 ng/ml
- **23 million Americans** 1 year and older had serum levels less than 12 ng/ml
- Most at risk were women and non-Hispanic blacks.

CDC 2nd National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population

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To Get 600 IU Vitamin D in Food

- 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

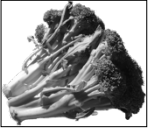
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American Endocrine Society




- All adults who are vitamin D deficient should be treated with 50,000 IU of vitamin D2/D3 once a week for 8 weeks or its equivalent of 6000 IU of vitamin D2/D3 daily to achieve a blood level of 25(OH)D *above 30 ng/ml*, followed by maintenance therapy of 1500–2000 IU/d.

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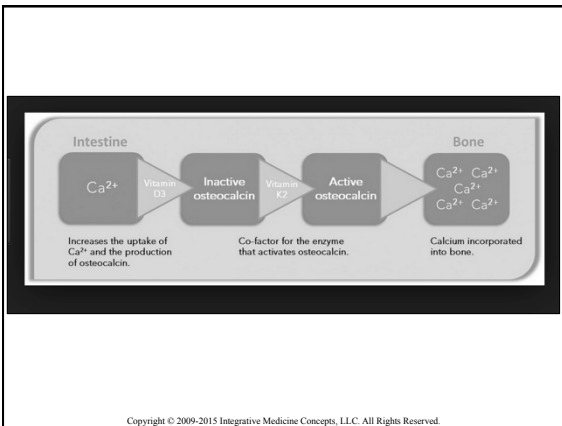


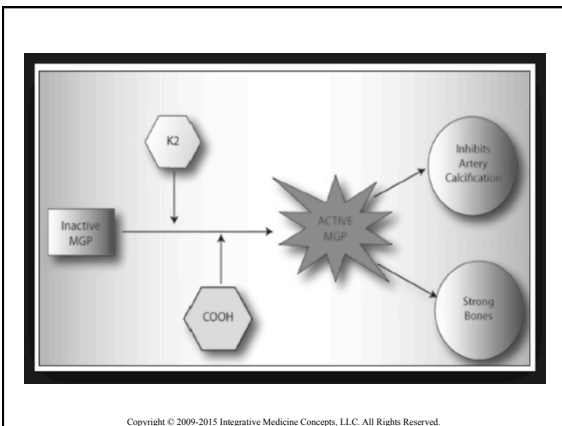
Vitamin K

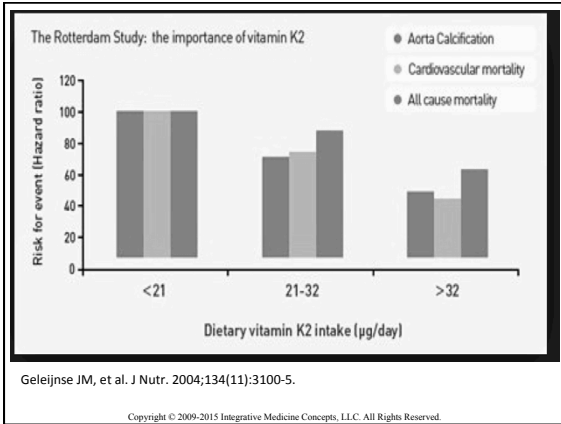


- There are two main forms of vitamin K.
 - Phylloquinone, or vitamin K1, is synthesized by plants and makes up 90% of the vitamin K obtained in the diet. Best sources are green leafy vegetables. Fat-soluble so should be eaten with some healthy fat.
 - Menaquinone, vitamin K2, is result of bacterial 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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"Dietary Supplements"

Magnesium

Mg²⁴
MAGNESIUM
12

- Low magnesium intakes and low blood levels have been associated with type 2 diabetes, metabolic syndrome, elevated CRP, hypertension, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer.
- 48% of US population consumes less than the required amount of daily magnesium.

Rosanoff A, et al. Nutr Rev 70(3):153-64.
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Magnesium and Blood Pressure

- 3954 apparently healthy Mexican children were enrolled in a cross-sectional study.
- Hypomagnesemia (<1.8 mg/dL) identified in:
 - 27.3% with prehypertension 6-10 years old
 - 36.0% with prehypertension 11-15 years old
 - 45.6% with hypertension 6-10 years old
 - 49.6% with hypertension 11-15 years old

Guerrero-Romero F, et al. J Pediatr 2015; 50022-3476(15)01120-8.
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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 I 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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Ulcer/GERD Medications

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

- There were 118.5 million prescriptions for PPIs in 2010 with roughly \$11.4 billion in sales. These numbers do not include over-the-counter sales for PPIs.
- esomeprazole magnesium (Nexium) - omeprazole (Prilosec)
- pantoprazole sodium (Protonix) - rabeprazole sodium (Aciphex)
- lansoprazole (Prevacid) - dexlansoprazole (Dexilant)
- omeprazole and sodium bicarbonate (Zegerid)

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FDA Safety Advisory

- 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 hypomagnesia increased by 75% if taking PPIs.*
- FDA advises magnesium levels be checked before and periodically during treatment.
- HOWEVER, serum magnesium levels poorly correlate with body stores – check RBC mag for more accurate level.

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

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Magnesium for Migraines

- 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).

Sun-Edelstein C, Mausekopp A. Clin J Pain. 2009 Jun;25(5):446-52.
 Pringsheim T, et al. Can J Neurol Sci 2012; 39(2Suppl) S1-S9
 Mausekopp A, et al. J Neural Transm 2012; 119(5):575-9.

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Butterbur Extract (*Petasites hybridus*)

- Butterbur has a Level A (highest) recommendation for migraine prevention in adults from the American Academy of Neurology and American Headache Society and is “strongly recommended”
- Extracts should be PA free and contain ~7.5% petasin.
 - Children 6-9 years take 25 milligrams BID
 - Children 9-13 take 50 milligrams BID.
 - Children > 13 yrs. and adults take 75 mg BID

Holland S, et al. Neurology 2012; 78(17): 1346-53

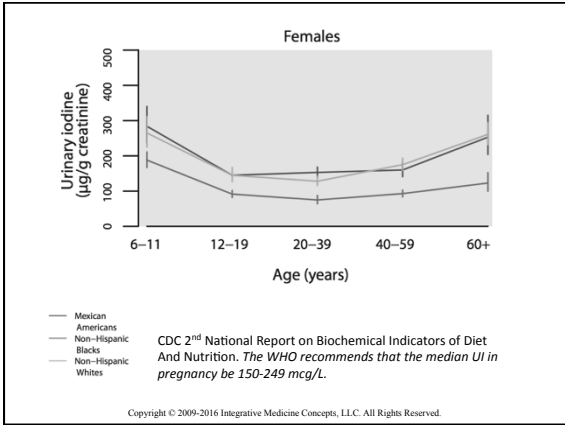
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Iodine in Pregnancy

- Many reproductive aged women in US have marginal iodine status; salt in processed foods is not iodized.
- Deficiency associated with pregnancy loss and prematurity, cretinism, and neurocognitive defects in the fetus.
- 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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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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