

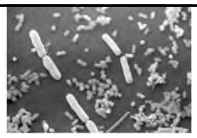


MONITORING VITAMINS & SUPPLEMENTS IN GERIATRIC PATIENTS

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Learning Objectives

1. Understand the regulations of vitamins and supplements in the United States
2. Identify the clinical symptoms and laboratory abnormalities that suggest the presence of vitamin deficiency in older adults
3. Determine the optimal vitamin supplementation regimens in treating vitamin deficiencies- with emphasis on vitamin D, thiamin, and iron; plus omega-3 fatty acid

History of Vitamin

- Terms come from "_____" and "Deficiency Diseases" as named by Casimir Funk, a Polish biochemist in 1912.
- Egyptians recorded symptoms of _____ as early as 1550 BC; in 1746 when James Lind, a British naval surgeon, discovered oranges and lemons were effective in improving these symptoms
- Industrial revolution was associated with an increase in _____ in children
- The "anti-beriberi factor" as described by Christiaan Eijkman, eventually named _____

Dietary Supplement Health and Education Acts (DSHEA) 1994

- Signed by President Clinton on October 25, 1994
- To meet the needs of consumers and manufacturers
- Congress stated that there may be a positive relationship between sound dietary practice and good health
- Goal of dietary supplement use is compatible with reduced health-care expenses, and disease prevention

http://vm.cfsan.fda.gov/~dms/dietsupp.html

DSHEA's Definition of DIETARY SUPPLEMENT

"….a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin, mineral, herbs or other botanicals, amino acids, a dietary substance used by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of any ingredient.…

http://vm.cfsan.fda.gov/~dms/dietsupp.html

DSHEA's Definition of DIETARY SUPPLEMENT

- is intended for ingestion in pill, capsule, tablet, or liquid form
- is not represented for use as a conventional food or as the sole item of a meal or diet.
- is labeled as a "dietary supplement"
- claims may not be made about the use of a dietary supplement to diagnose, prevent, mitigate, treat, or cure a specific disease

http://vm.cfsan.fda.gov/~dms/dietsupp.html

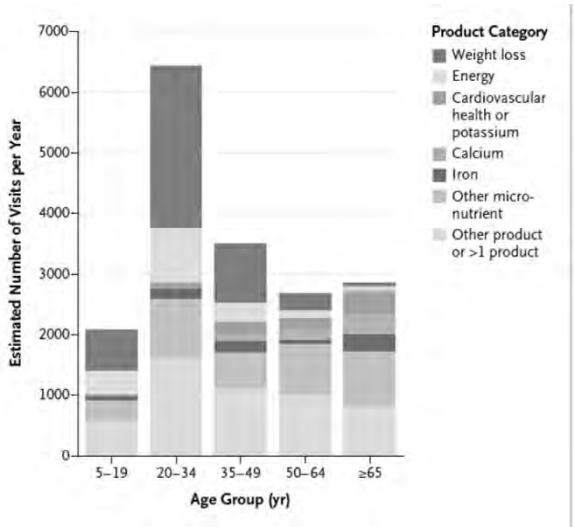
Prevalence of Micronutrient Use

- 75% of 75,000 study cohorts in WA state used at least one supplement in 10 year period
- 52 % of study population took vitamin or mineral supplements
- Between 64% to 81% of cancer survivors report using any vitamin or mineral supplements; 26% to 77% report using any multivitamins

Vitamins and Lifestyle Study (VITALS)
Dutch Health Care Consumer Panel Repor
Miller MF, et al. J Am Diet Assoc. 2008;108(3):483-494.
Grainger EM, et al. Urol Oncol 2008;26(2):125-132.
Ritchie MR. Proc Nutr Soc. 2007;66(4):479-482.
Velicer CM, et al. J Clin Oncol. 2008;26(4):665-673.
Bardia A, et al. J Support Oncol 2007;5(4):195-198.
Boon HS et al. BMC Womens Health 2007;7:4.

Supplements are not completely safe: National estimates of ED visits for ADE associated with supplement use (2004-13)

Geller AI, et al. New Engl J Med 2015;373:1531-40



Major Vitamins for Human's Health

Vitamin	Chemical Name	Complications associated with deficiency
Vitamin A	Retinol / Carotene	Night blindness
Vitamin B1	Thiamin	Polyneuropathy, psychosis
Vitamin B2	Riboflavin	Cheilosis, mouth sore
Vitamin B3	Niacin	Pellagra
Vitamin B5	Pantothenic acid	Non-specific presentations
Vitamin B6	Pyridoxine	Non-specific presentations
Vitamin B7	Biotin	Non-specific presentations
Vitamin B9	Folate	Anemia
Vitamin B12	Cobalamin	Anemia, neuropathy
Vitamin C	Ascorbate	Scurvy
Vitamin D	Ergocalciferol / cholecalciferol	Rickets, osteoporosis
Vitamin E	Tocopherol	Non-specific presentations
Vitamin K		Bleeding

Assessment approaches for vitamin status

- Diet history
- More diet history
- GI tract anatomy
- Lifestyle
- Physical exams
- Laboratory tests:
  - Plasma vitamin concentrations (e.g., vitamin D)
  - Functional tests (e.g., ETKA for thiamin)

A few things to keep in mind….

- Clinical data are under-reported due to knowledge deficiency and publication bias
- Oral micronutrients are dietary supplements regulated under DSHEA; hence quality cannot be guaranteed for many products
- Variance due to non-standardized analytical techniques
- Poor sensitivity and/or specificity of laboratory test for diagnosis (e,g., various assays exits for 25(OH)D)
- The timing of blood sampling and certain conditions may affect result interpretation (e.g., folate)

Photo courtesy of Shutterstock

Dietary Intake Recommendations for Key Micronutrients for Adults over 70 years old

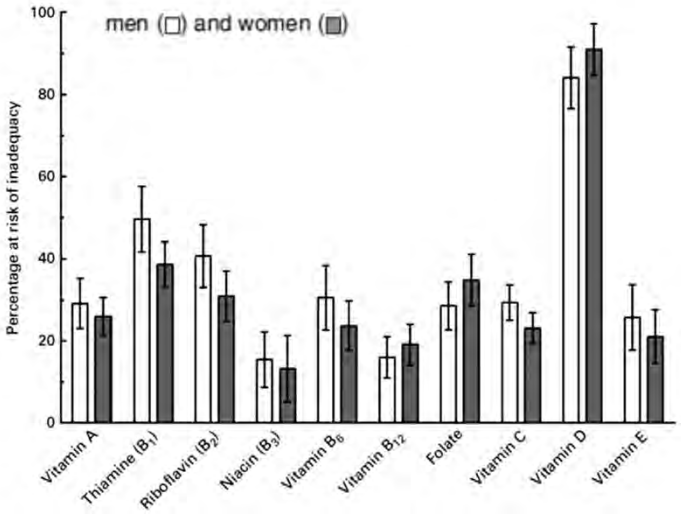
Micronutrient (RDA)	Men	Women
Vitamin A (μg/d)	900	700
Vitamin C (mg/d)	90	75
Vitamin D (IU/d)	800 *	800
Vitamin E (mg/d)	15	15
Folate (μg/d)	400	400
Vitamin B12 (μg/d)	2.4	2.4
Calcium (mg/d)	1200	1200
Zinc (mg/d)	11	8
Iron (mg/d)	8	8

*** 600 IU daily for 51-70 year-old**

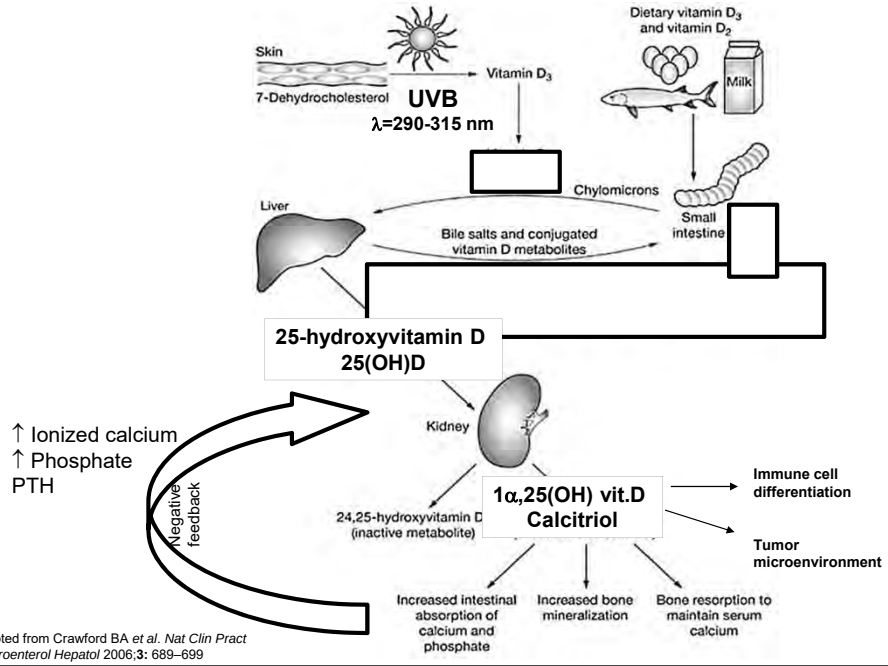
Institute of Medicine (IOM) 2010 Report (http://www.iom.edu/Reports/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D.aspx)

Risk of inadequate intake of vitamins among community-dwelling older adults

Ter Borg S et al. Br J Nutr 2015;113:1195-1206



Vitamin D- A Hormone and a Vitamin



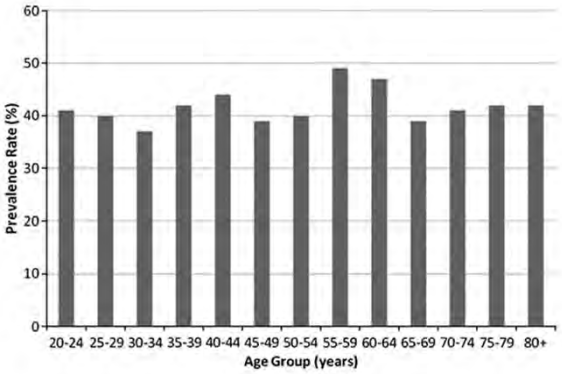
Adapted from Crawford BA *et al*. *Nat Clin Pract Gastroenterol Hepatol* 2006;**3:** 689–699

Prevalence of Vitamin D deficiency in U.S. Adults According NHANES (2005 to 2006)

Forrest KY et al. Nutrition Res 2011;31(1):48-54.

Definitions: Deficiency: 25(OH)D ≤ 20 ng/mL
Insufficiency: 25(OH)D 20.1 to 30 ng/mL

N = 4495



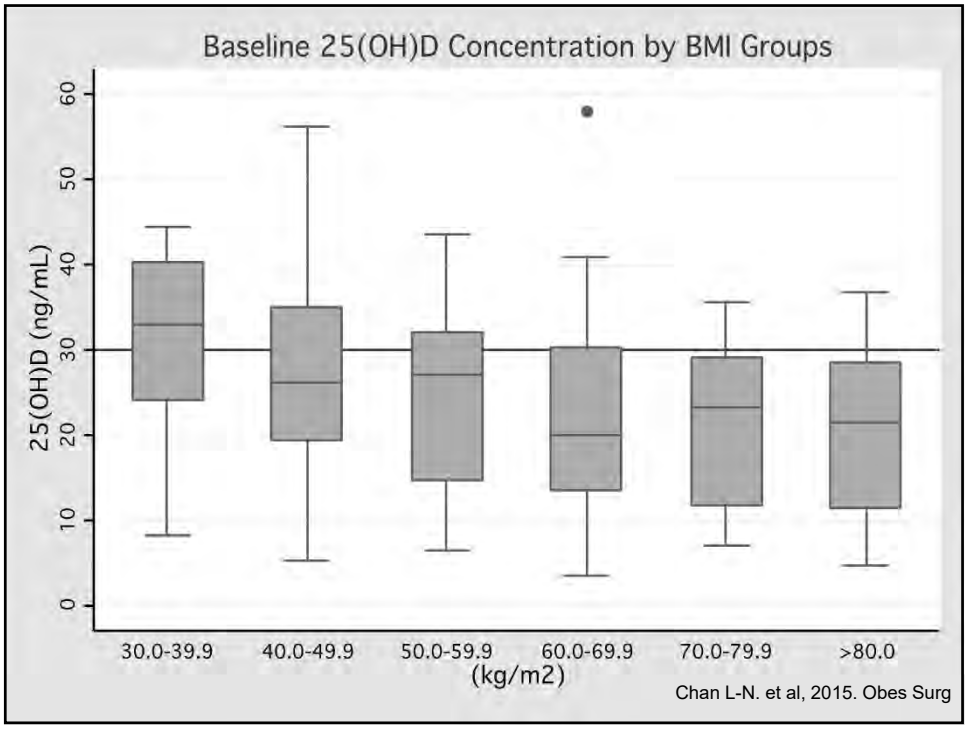
Mean vit. D =19.9 ± 8.5 ng/mL
20.1 ± 7.9 ng/mL in men
19.8 ± 9.0 ng/mL in women

Prevalence of vitamin D deficiency = 41.6%

Predictors of Vitamin D Deficiency in US Adults

Forrest KY et al. Nutrition Res 2011;31(1):48-54.

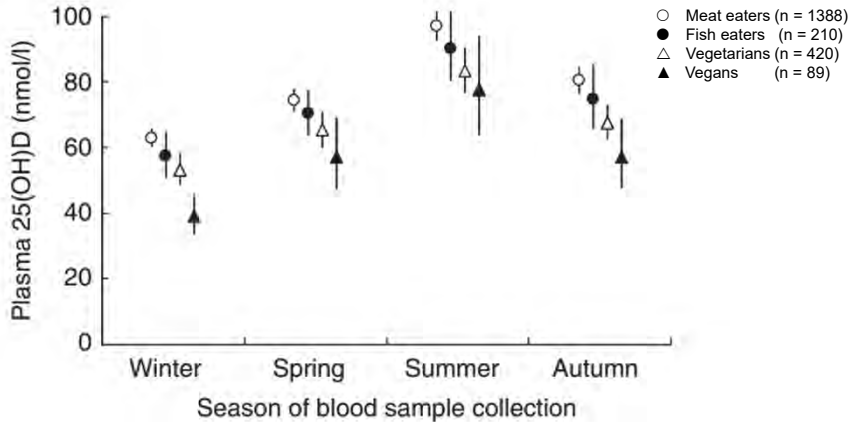
Predictors	**OR**	**95% CI**	***P***
African American (vs Caucasian)	9.6	6.3 – 14.5	<0.001
Hispanic (vs Caucasian)	3.2	2.1 – 4.9	<0.001
No college education	1.3	1.1 – 1.5	0.01
Poor/fair health status	1.8	1.4 – 2.3	<0.001
Obesity	1.9	1.6 – 2.3	<0.001
HDL < 40 mg/dL	1.4	1.1 – 1.8	0.03
Not consuming milk products daily	1.6	1.4 – 1.9	<0.001



Chan L-N. et al, 2015. Obes Surg

Comparison of 25(OH)D concentrations in British cohorts with different dietary habits

[Results from the EPIC-Oxford Study]



 # Conversion from nmol/L to ng/mL: divided by 2.5
European Prospective Investigation into Cancer and Nutrition (EPIC)

Crowe FL et al, Public Health Nutr. 2011;14(2):340-6.

Seasonal differences in Pre-vitamin D3 formation in Boston (42°N)

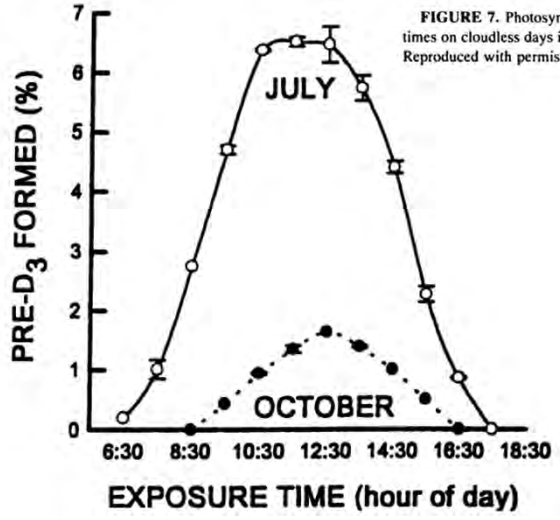
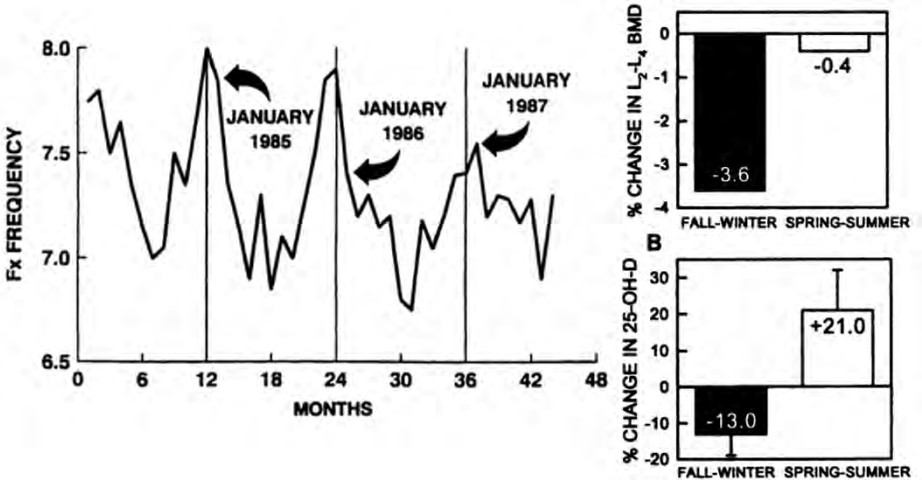


FIGURE 7. Photosynthesis of precholecalciferol (PRE-D_3) at various times on cloudless days in Boston in October (●) and July (○). $\bar{x} \pm$ SEM. Reproduced with permission (11).

Incidence of bone fracture as a function of season in women



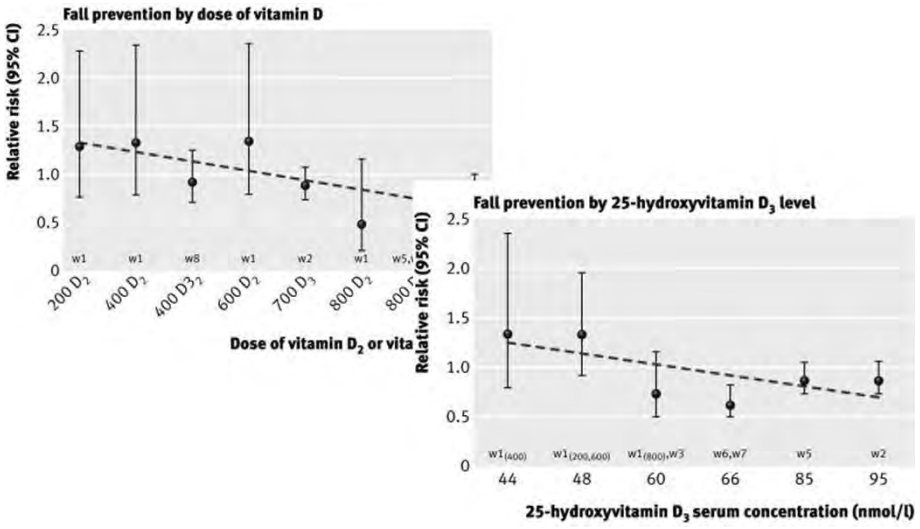
What is the prevalence of vitamin D deficiency in the Pacific Northwest ?

- Everyone thinks it is pretty high
- Large scale, surveillance data are lacking
- Seattle latitude: 47.6° N
  - Boston, MA: 42.4 ° N
  - International Falls, MN 48.6° N
  - Fargo, ND: 46.8° N
  - Green Bay, WI: 44.5° N
  - Quebec City, CAN: 46.8° N

- Unique diet and lifestyle in WA state compared with many metropolis/ major cities

Summation of fall prevention by dose and achieved 25(OH)D concentrations

Bischoff-Ferrari HA et al BMJ. 2009 Oct 1;339:b3692.



Vitamin D replacement
Method 1: "Simple Rule"

Cannell JJ et al. Expert Opin. Pharmacother. (2008) 9(1):107-118

- Every 1,000 IU/day of D2 or D3 given orally would raise serum 25(OH)D by 10 ng/mL over a period of 3 to 4 months.
- An "unofficial summary" of the dose-response curve based on many small trials.
- A simplified approach and co-variances such as sun exposure, dietary effect, GI symptoms, drug/nutrient interactions are not taken into consideration.

Vitamin D replacement
Method 2: "The Dutch Sliding Scale"

van Groningen et al. Eur J Endocrinol 2010;162:805-11.

- The Dutch have developed an weight-base equation based on the blood level:

  Total Vit. D dose (in IU) = 40 x (75 - current 25(OH)D level) x wt(kg).

- Note that the 25(OH)D level is measured in SI unit (nmol/L). So you need to convert our common unit from ng/mL to nmol/L by multiplying by 2.5.
- You can also rewrite the question to:

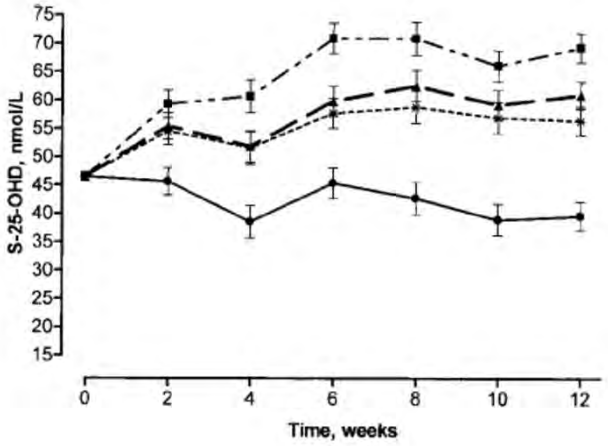
Total vitamin D Dose = 40 x (75 - (current 25(OH)D (ng/mL) x 2.5)) x wt (kg).

- Replace this amount with a weekly dose no more than 25,000 IU.
- The equation assumes that the dose-response relationship is linear, which is not true with increased fat mass. So, this method loses sensitivity in obese patients.

Dose-response relationship of Vitamin D Supplementation

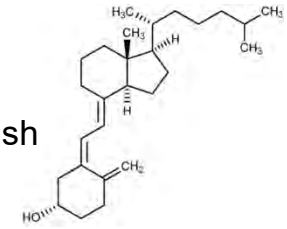
(Adopted from Viljakainen HT et al, J Am Coll Nutr 2006;25(5):429–435)

Intervention: Vitamin D_3 0, 200, 400 or 800 IU of daily for 12 weeks

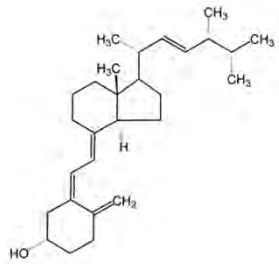


The Numbers Game: D2 vs D3

- Vitamin D3: Cholecalciferol
  - Endogenous vitamin D
  - Meat-based sources, including fish

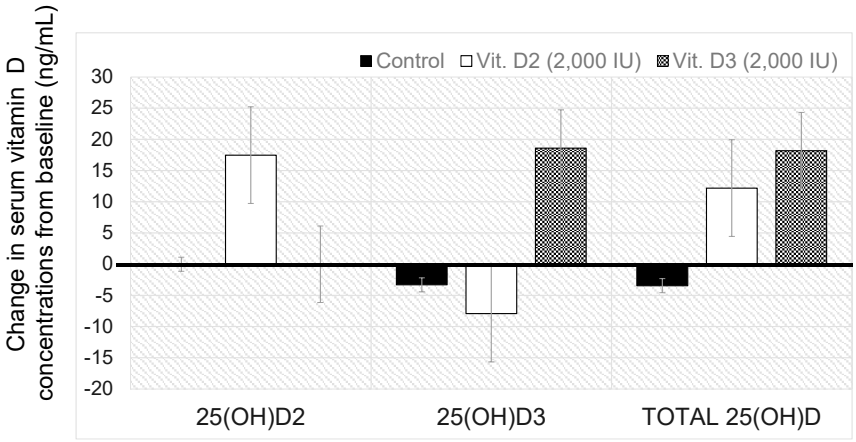


- Vitamin D2: Ergocalciferol
  - Plant-based sources



Changes in vitamin D profile after supplementation with placebo, vit D2, or vit D3. for 8 weeks

Lehmann U, et al. J Clin Endocrinol Metab 2013;98: 4339–45



Dietary, Supplemental & Pharmaceutical Sources

Source	Vitamin D Content
Natural sources	
Salmon	
Fresh, wild (3.5 oz)	About 600–1000 IU of vitamin D_3
Fresh, farmed (3.5 oz)	About 100–250 IU of vitamin D_3 or D_2
Canned (3.5 oz)	About 300–600 IU of vitamin D_3
Sardines, canned (3.5 oz)	About 300 IU of vitamin D_3
Mackerel, canned (3.5 oz)	About 250 IU of vitamin D_3
Tuna, canned (3.6 oz)	About 230 IU of vitamin D_3
Cod liver oil (1 tsp)	About 400–1000 IU of vitamin D_3
Shiitake mushrooms	
Fresh (3.5 oz)	About 100 IU of vitamin D_2
Sun-dried (3.5 oz)	About 1600 IU of vitamin D_2
Egg yolk	About 20 IU of vitamin D_3 or D_2
Exposure to sunlight, ultraviolet B radiation (0.5 minimal erythemal dose)†	About 3000 IU of vitamin D_3
Fortified foods	
Fortified milk	About 100 IU/8 oz, usually vitamin D_3
Fortified orange juice	About 100 IU/8 oz vitamin D_3
Infant formulas	About 100 IU/8 oz vitamin D_3
Fortified yogurts	About 100 IU/8 oz, usually vitamin D_3
Fortified butter	About 50 IU/3.5 oz, usually vitamin D_3
Fortified margarine	About 430 IU/3.5 oz, usually vitamin D_3
Fortified cheeses	About 100 IU/3 oz, usually vitamin D_3
Fortified breakfast cereals	About 100 IU/serving, usually vitamin D_3
Supplements	
Prescription	
Vitamin D_2 (ergocalciferol)	50,000 IU/capsule
Drisdol (vitamin D_2) liquid supplements	8000 IU/ml
Over the counter	
Multivitamin	400 IU vitamin D, D_2, or D_3‡
Vitamin D_3	400, 800, 1000, and 2000 IU

Holick 2007

Effect of cooking on vit. D content in fish

	IU/3.5 oz (N)
Farmed salmon, raw	274 ± 16 (6)
Farmed salmon, microwaved	272 ± 1 (2)
Farmed salmon, baked	248 ± 3 (2)
Farmed salmon, fried	142 ± 21 (2)

Risk of Falls and Fracture Changed Over Time with high-Dose Vitamin D Supplementation

Sanders et al. JAMA 2010;303(18):1815-22

Table 4. Temporal Pattern of Risk in Falls and Fracture 0 to 3 Months and 4 to 12 Months After Treatment

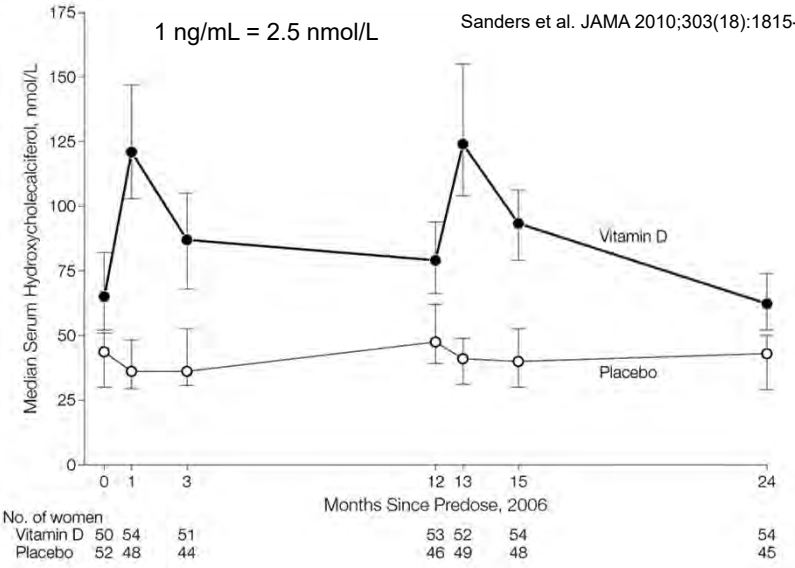
	Incidence Rate Ratio for Vitamin D Group, Estimate (95% Confidence Interval)[a]	*P* Value
Time after treatment, mo		
Falls		
Within 3	1.31 (1.12-1.54)	.001
After 3	1.13 (0.99-1.29)	.08
Fracture		
Within 3	1.53 (0.95-2.46)	.08
After 3	1.18 (0.91-1.54)	.21

[a] The incidence rate ratio refers to the risk ratio of the vitamin D group compared with the placebo group. The rate ratio within 3 months after treatment is significantly different from the rate ratio of the remaining 9 months after treatment for falls ($P = .02$) but not for fracture ($P = .36$).

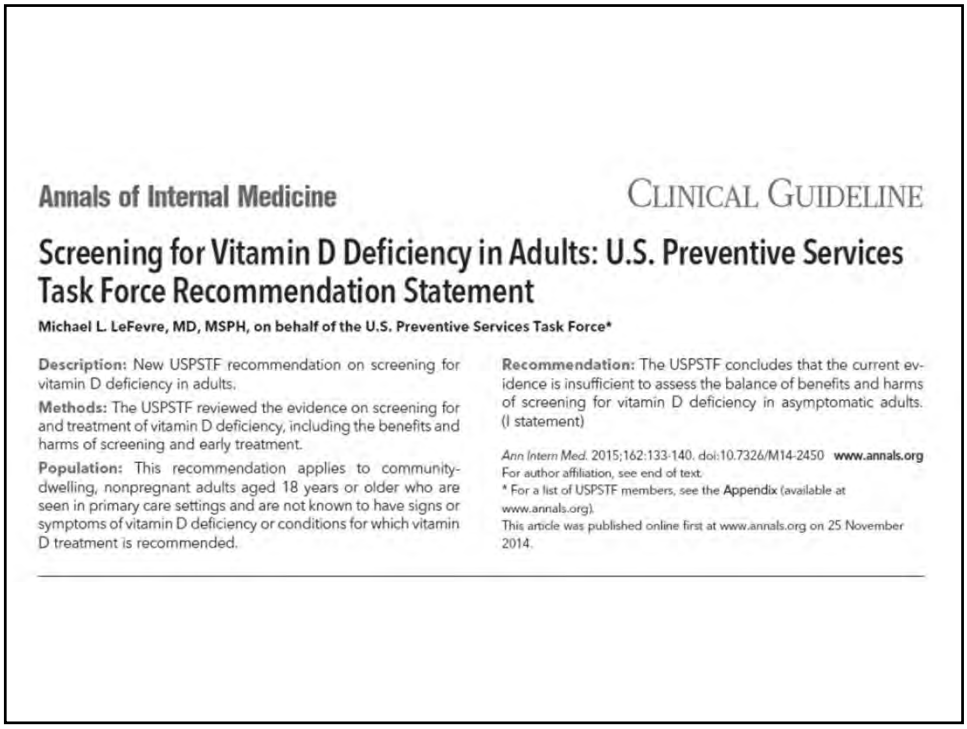
Figure 4. Serum 25-Hydroxycholecalciferol Levels Before Dose, and at 1, 3, and 12 Months After Dose

1 ng/mL = 2.5 nmol/L

Sanders et al. JAMA 2010;303(18):1815-22



Study	Population characteristics	Treatment groups	Number of participants	Mean age (years)	Pre/post 25 (OH)D (nmol/l;mean)	Follow up (moths)	Outcomes
Latham 2003 [21]	Recruited from geriatric rehabilitation center, institutionalized	Oral vit D_2 300000 IU once	108	80	37 to 60 at 3 months	6	Mortality
		Placebo	114	79	48 to 48 at 3 months		
Trivedi 2003 [14]	Elderly man and woman, community dwelling	Oral vit D_3 100000 IU every 4 months	1027	75	74 at 48 months	60	Mortality, fracture
		Placebo	1011	75	53 at 48 months		
Harwood 2004 [22]	Elderly women after hip fracture, community dwelling	Vit D_2 300,000 IU/im/ once	30	80	28 to 41 at 12 months	12	Mortality
		Vit D_2 300,000 IU/im/ once + 1,000 mg calcium	25	81	30 to 48 at 12 months		
		No treatment	35	81	30 to 27 at 12 months		
Dhesi 2004 [23]	Ambulatory elderly with a history of fall institutionalized	Vit $D_2$600000IU/im/once	62	77	27 to 44 at 6 months	6	Fall
		Placebo	61	77	25 to 31 at 6 months		
Law 2006 [24]	Recruited from residential care home institutionalized	Oral vit D_2 100000 IU every 3 months	1762	85	59 to 77 at 3 months	10	Mortality Fracture
		No treatment	1955	85	NA		
Lyons 2007 [25]	Nursing home residents institutionalized	Oral vit D_2 100000 IU every 4 months	1725	84	80/NA	36	Mortality fracture
		Placebo	1715	84	54/NA		
Smith 2007 [16]	Elderly man and woman, community dwelling	Vit D_2 300,000 IU/im/ year	4727	79	56.5 to 68 at 4 months	36	Mortality fracture
		Placebo	4713	79	NA		
Sanders 2010 [15]	Ambulatory elderly women at risk for fractures, community dwelling	Oral vit D_3 500000 IU annually for 3–5 yerrs	1131	77	53/NA	36–60	Mortality fracture
		Placebo	1125	77	45/NA		fall
Glendenning 2012 [26]	Older women, community dwelling	Oral vit $D_3$150000 IU every 3 months + calcium 1300 daily	353	77	65 to 75 at 9 months	9	Fall
		Calcium 1300 daily	333	77	66 to 60 at 9 months		



Annals of Internal Medicine

CLINICAL GUIDELINE

Screening for Vitamin D Deficiency in Adults: U.S. Preventive Services Task Force Recommendation Statement

Michael L. LeFevre, MD, MSPH, on behalf of the U.S. Preventive Services Task Force*

Description: New USPSTF recommendation on screening for vitamin D deficiency in adults.

Methods: The USPSTF reviewed the evidence on screening for and treatment of vitamin D deficiency, including the benefits and harms of screening and early treatment.

Population: This recommendation applies to community-dwelling, nonpregnant adults aged 18 years or older who are seen in primary care settings and are not known to have signs or symptoms of vitamin D deficiency or conditions for which vitamin D treatment is recommended.

Recommendation: The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for vitamin D deficiency in asymptomatic adults. (I statement)

Ann Intern Med. 2015;162:133-140. doi:10.7326/M14-2450 **www.annals.org**
For author affiliation, see end of text.
* For a list of USPSTF members, see the **Appendix** (available at www.annals.org).
This article was published online first at www.annals.org on 25 November 2014.

SUMMARY: Optimal vitamin D management for elderly patients in the Pacific Northwest

- Prevalence of vitamin D deficiency is 63% in obese patients undergoing bariatric surgery in our region
- No fewer than 600 IU per day
- Higher intake is likely needed although published interventional trials are lacking [optimal range 600 to 2,000]
- In spite of USPSTF recommendation, monitor 25(OH) D annually may be beneficial due to the regional risk factors:
  - Routine practice in at-risk patients
  - At least once in healthy individuals as surveillance
- Deficiency can be treated by weekly dose of 50,000 IU x8 weeks or an increase in daily maintenance therapy
- Avoid doses over 100,000 IU unless in established history of malabsorption

Case Discussion

Craig is a 72-year-old man who has just visited his PCP for his annual check-up. He was told by his PCP that his vitamin D level is low and that he should take additional vitamin D supplements.

PMH: Hypertension, hyperlipidemia, T2DM

Allergies: NKDA; allergic to shellfish; lactose intolerance

His most recent cholesterol is 173 mg/dL, with LDL of 112 mg/mL and triglyceride 132 mg/dL. He has been taking atorvastatin 20 mg QD since 12 years ago. He also metformin, benazepril and HCTZ.

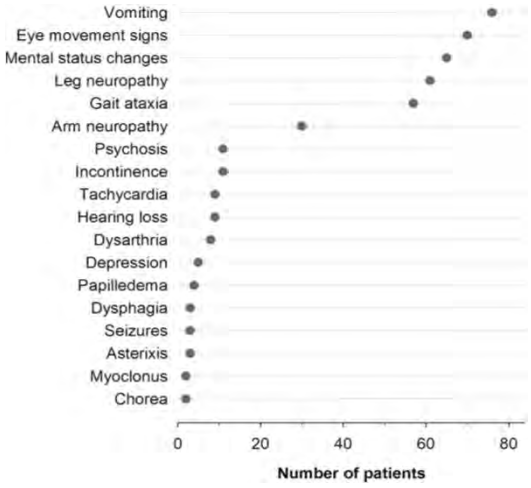
His vitamin D level is 14.4 ng/mL (from a week ago).

Thiamin Absorption Profile

- Total thiamin pool in humans ~ 25 – 30 mg with little reserve → clinical deficiency can occur within 2 weeks of poor intake
- Humans obtain thiamin through TWO sources:
  - Diet: mostly as thiamin pyrophosphate (TPP), which is hydrolyzed in the small intestine to form free thiamin
  - bacterial source: through synthesis by the microbes of the large intestine
- Food rich in thiamin:
  - Lentils, green peas, brown rice, wheat cereal, milk, orange, cantaloupe

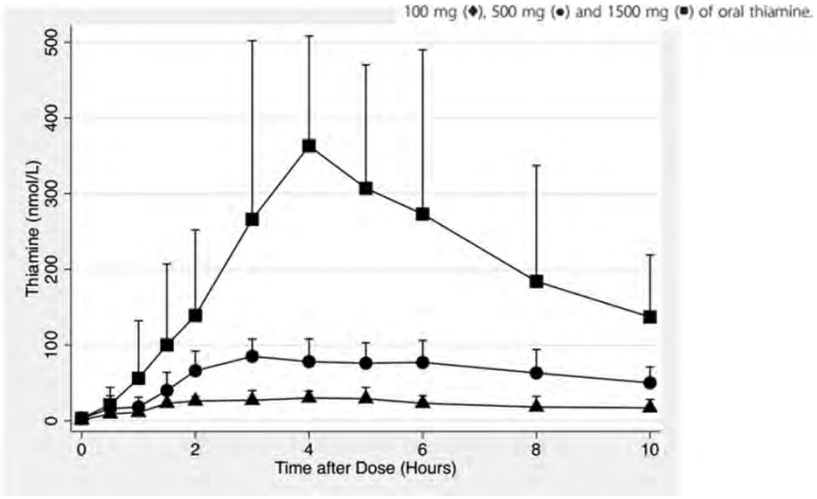
Reported Symptoms in Patients with Confirmed Wernicke Encephalopathy

Aasheim ET. Ann Surg 2008;248:714-20.



Change in whole blood thiamin concentration over time with 3 different oral doses

Smithline HA et al.BMC Clin Pharmacol 2012 Feb 4;12:4



Suggested Regimens in the Treatment of Thiamin Deficiency

Frank LL. JPEN 2015;39(5):503-20.

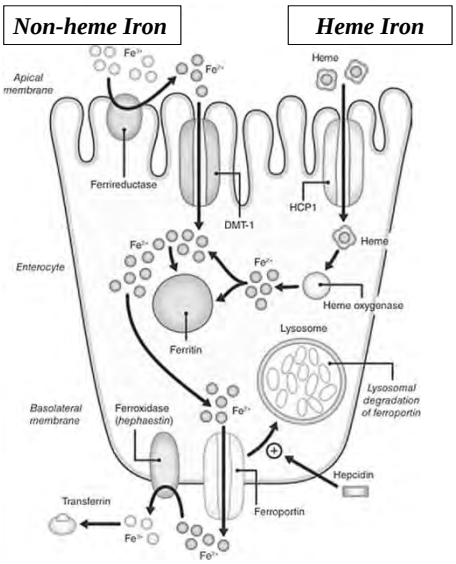
Condition	Suggested Treatment Regimen(s)
Alcoholism	Typical treatment from CIWA protocol: 100 mg IV thiamin, once daily, for 3–5 days[18,82]
	Royal College of Physicians: >500 mg IV thiamin, once or twice daily, for 3–5 days.[21,75,77]
	European Federation of Neurological Societies: 200 mg thiamin, 3 times daily, preferably IV, before any carbohydrates are given[78]
Refeeding syndrome	200–300 mg oral or IV thiamin, once daily, before feeding begins[118]
Critical illness	100 mg IV thiamin, once daily[55]; up to 400 mg, twice daily[20]
Heart failure	For cardiac insufficiency: 50 mg/kg[109] to 100 mg thiamin, once or twice daily[105]
	For heart failure: 200 mg IV thiamin daily[107] or 300 mg oral thiamin daily[108]
	If high lactate levels: 100 mg IV thiamin, once daily[55]; up to 400 mg, twice daily[20]
Renal failure	200 mg IV thiamin, once daily, until clinical symptoms resolve, then 100 mg/d oral thiamin as maintenance dose[137]
Bariatric surgery	Mild deficiency: 100 mg oral thiamin, two[54] to three[21] times daily until symptoms resolve or 100 mg IV thiamin for 7–14 days[99]
	Severe deficiency: A minimum of 250 mg thiamin, once daily, given parenterally or intramuscularly, for at least 3–5 days[54,100]
	500 mg/day IV thiamin for 3–5 days followed by 250 mg/d for 3–5 days or until resolutions of symptoms, then consider treatment with 100 mg/d orally, usually indefinitely or until risk factors have been resolved[99]
	European Federation of Neurological Societies: 200 mg IV thiamin, 3 times daily[78]

CIWA, Clinical Institute Withdrawal for Alcohol; IV, intravenously.

Summary- Thiamin in elderly patients

- At risk for deficiency:
  - Chronic alcohol use
  - Decreased oral intake for more than 1 week
  - Vomiting for more than 3-5 days
- Empirical thiamin supplementation:
  - Presented clinic, ED, or hospital with persistently low appetite
  - ED or hospital admission with acute altered mental status or other neurological deficits
  - History of major GI tract surgery
- IV vs PO thiamin
  - All symptomatic patients should receive IV therapy initially
  - Empirical prophylaxis/ asymptomatic patients may receive oral therapy

Intestinal Absorption of Iron



- HCP1, aka PCFT or SLC46A1, is a minor mechanism in transporting heme iron
- It is the primary transport protein for folate absorption, expressed primarily in the duodenum and proximal jejunum
- SLC46A1 is enhanced by vitamin D but inhibited by alcohol

Figure adapted from: Rizvi S et al. Am J Gastroenterol 2011; 106:1872–1879
Chan L-N, Mike LA. J Parenter Enteral Nutr 2014;38:656-72

Iron supplementation

Chan L-N, Mike LA. *J Parenter Enteral Nutr* 2014;38:656-72

- Duodenum is the primary site where iron, especially non-heme iron, is absorbed
- Iron transport is a saturable process; thus, increasing the oral dose of iron does not translate to a proportional increase in the amount absorbed
- Iron uptake also takes place in the colon, although the relative absorption efficiency is only about 1/10 of that from the duodenum
- Heme iron has higher fractional absorption (15%–35%) than does non-heme iron (2%–20%)
- The bioavailability of iron sulfate from iron supplements can approach 60% in severe cases of iron-deficiency anemia

Oral Iron Supplements

Salt Form	Elemental Iron % (w/w)	Formulations
Fumarate	33 %	Tablets, Chewable tablets
Sulfate, dried	30 %	Capsules, Tablets, ER tablets
Sulfate	20 %	Oral solution, Oral tablets EC tablets, Film-coated tablets
Bisglycinate	20 %	Capsules, Oral tablets
Ammonium citrate (Ferric)	18 %	Capsules
Gluconate	12 %	Oral tablets
Carbonyl iron	100 %	Tablets, Chewable tablets Oral suspension
Polysaccharide complex	100 %	Capsules, Oral solutions Film-coated tablets
Heme polypeptide	100%	Capsules

Clinical Pearl:
Iron Supplementation Therapy

- The goal of treatment should be directed at restoring hemoglobin concentrations and replenishing iron stores (i.e., normalize ferritin)
- Hemoglobin ↑ by 1–2 g/dL in the first 2 weeks and then 0.7–1 g/dL per week thereafter
- Repletion of iron stores will take longer (≥ 3 months)
- Ferrous sulfate 200 mg twice daily is usually better tolerated by most patients than 325 mg thrice daily

⇨ Ferrous sulfate 325 mg TID is <u>NOT</u> more effective than regimens with lower iron content but is associated with more GI side effects and low adherence

Case Discussion

Craig is a 72-year-old man who has just visited his PCP for his annual check-up. He was told by his PCP that his vitamin D level is low and that he should take additional vitamin D supplements.

PMH: Hypertension, hyperlipidemia, T2DM,

Allergies: NKDA; allergic to shellfish; lactose intolerance

His most recent cholesterol is 173 mg/dL, with LDL of 112 mg/mL and triglyceride 132 mg/dL. He has been taking atorvastatin 20 mg QD since 12 years ago. His vitamin D level is 14.4 ng/mL (from a week ago). He takes metformin for his diabetes and benazepril 20 mg QD and HCTZ 25 mg QD for hypertension

Hgb 11.8 g/dL MCV 73 fL RDW 15.5%

Fish and Omega-3 Fatty Acid Intake and Risk of Coronary Heart Disease in Women – Sub-study from Nurse Health Study

Hu FB et al. JAMA. 2002;287(14):1815-1821

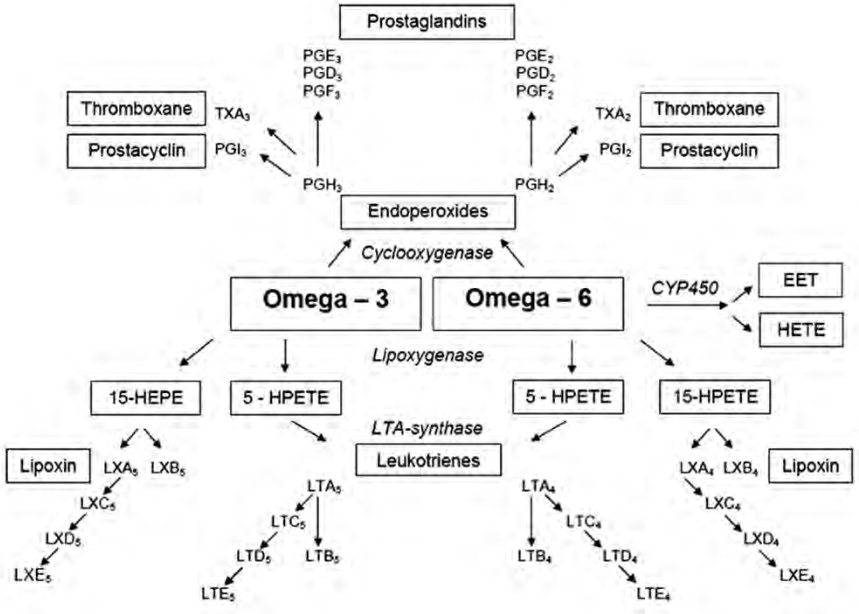
- The multivariable relative risks (RRs) of CHD were 0.79 (95% confidence interval [CI], 0.64-0.97) for fish consumption 1 to 3 times per month, 0.71 (95% CI, 0.58-0.87) for once per week, 0.69 (95% CI, 0.55-0.88) for 2 to 4 times per week, and 0.66 (95% CI, 0.50-0.89) for 5 or more times per week (P for trend = .001).

- Similarly, women with a higher intake of omega-3 fatty acids had a lower risk of CHD, with multivariable RRs of 1.0, 0.93, 0.78, 0.68, and 0.67 (P<.001 for trend) across quintiles of intake.

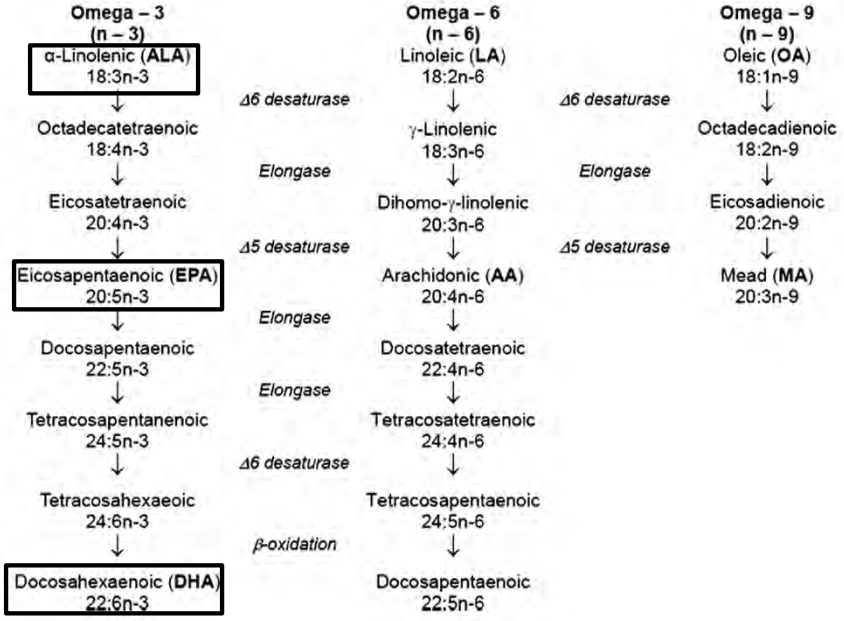
w3-PUFA and Outcomes of Interest in geriatrics

- Hypertriglyceridemia
- Atrial fibrillation
- Alzheimer's disease
- Macular degeneration
- Depression

W-3/w-6 FA and Their Downstream Products



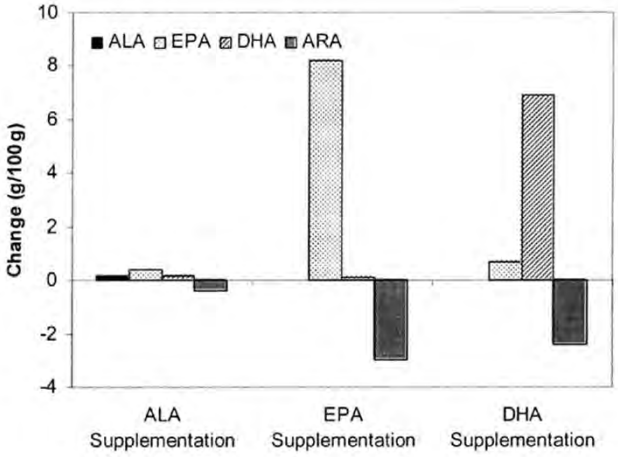
Metabolic Pathways of w3/w6/w9 FAs



Cross-study effects of:

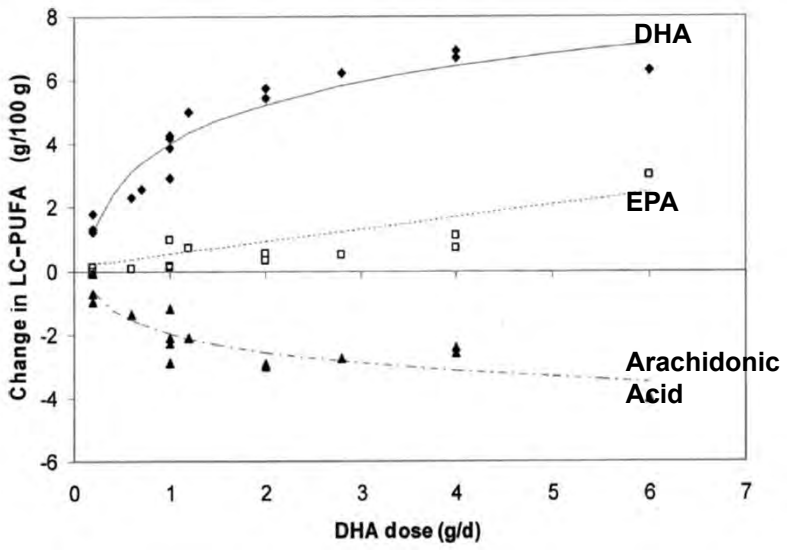
- ***3.7 g α-linolenic acid (ALA)/d (canola oil),***
- ***4 g pure eicosapentaenoic acid (EPA) ethyl ester, or***
- ***4 g pure docosahexaenoic acid (DHA) ethyl ester***

on the change in plasma phospholipid fatty acid concentrations.



Arterburn LM et al. Am J Clin Nutr 2006;83(suppl):1467S–76S

Regression Analysis of Dose-Response Curve of DHA on Plasma Profile of DHA, EPA and AA



	EPA	DPA[2]	DHA	Combined EPA+DHA
			mg/100 g	
Anchovy	763	41	1292	2055
Herring, Atlantic	909	71	1105	2014
Salmon, farmed	862	393	1104	1966
Salmon, wild	411	368	1429	1840
Mackerel, Atlantic	504	106	699	1203
Bluefish	323	79	665	988
Sardines, Atlantic	473	0	509	982
Trout	259	235	677	936
Golden bass (tilefish)	172	143	733	905
Swordfish	127	168	772	899
Tuna, white (albacore)	233	18	629	862
Mussels	276	44	506	782
Striped bass	169	0	585	754
Shark	258	89	431	689
Pollock, Atlantic	91	28	451	542
Oysters, wild	274	16	210	484
King mackerel	174	22	227	401
Tuna, light (skipjack)	91	17	237	328
Snapper	48	22	273	321
Flounder and sole	168	34	132	300
Clams	138	104	146	284
Grouper	35	17	213	248
Halibut	80	20	155	235
Lobster	117	6	78	195
Scallops	72	5	104	176
Blue crab	101	9	67	168
Cod, Pacific	42	5	118	160
Shrimp	50	5	52	102
Catfish, farmed	20	18	69	89
Eggs	0	7	58	58
Chicken breast	10	10	20	30
Beef	2	4	1	3
Pork	0	10	2	2

Omega-3 fatty acid on preventing or slowing the progression of age-related macular degenration

Lawrenson JG, et al. Cochrane Database Syst Rev. 2015 Apr 9;4:CD010015

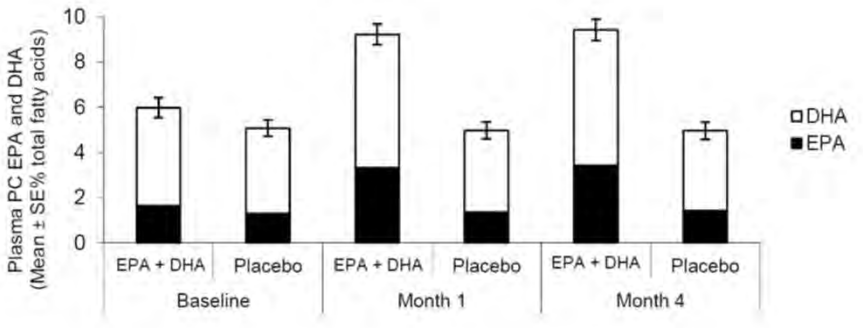
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)
	Assumed risk	Corresponding risk		
	No omega 3 fatty acids (placebo)	Omega 3 fatty acids		
Loss of 3 or more lines of VA at 24 months	100 per 1000	114 per 1000 (53 to 245)	RR 1.14, 95% CI 0.53 to 2.45	236 (1 study)
Loss of 3 or more lines of VA at 36 months	150 per 1000	187 per 1000 (104 to 339)	RR 1.25, 95% CI 0.69 to 2.26)	230 (1 study)
Incidence of CNV at 24 months	100 per 1000	106 per 1000 (47 to 240)	RR 1.06, 95% CI 0.47 to 2.40	224 (1 study)
Incidence of CNV at 36 months	150 per 1000	168 per 1000 (80 to 357)	RR 1.12, 95% CI 0.53 to 2.38	195 (1 study)
Progression of AMD over 5 years	300 per 1000	290 per 1000 (259 to 325)	HR 0.96 (0.84 to 1.1)	2343 (2 studies)
Adverse effects	500 per 1000	505 per 1000 (470 to 545)	RR 1.01, 95% CI 0.94 to 1.09	2343 (2 studies)

CNV: Choroidal neovascularization

Does w-3FA supplementation improve cognition in older adults?

Phillips MA et al. Int. J. Mol. Sci. 2015, 16, 24600-24613

Treatment arm: 600 mg EPA + 625 mg DHA per day
Placebo arm: Olive oil



Plasma phosphatidylcholine EPA and DHA in the omega-3 and placebo groups

Primary outcome measure performance scores over the study duration

Phillips MA et al. Int. J. Mol. Sci. 2015, 16, 24600-24613

Outcome Measure		Omega-3 PUFA Group	Placebo Group	*p for Main Effect of Treatment*
MMSES7	Baseline	24.3 (3.2)	23.4 (4.1)	$F(1,73) < 1, p = 0.711$
	Month 1	24.4 (3.9)	23.4 (4.6)	
	Month 4	24.4 (4.1)	23.3 (4.7)	
MMSEWB	Baseline	25.0 (2.8)	24.2 (3.7)	$F(1,73) < 1, p = 0.576$
	Month 1	25.3 (3.4)	24.2 (3.8)	
	Month 4	25.3 (3.4)	23.3 (4.1)	
Immediate verbal memory	Baseline	16.2 (4.3)	16.0 (5.9)	$F(1,73) = 0.461, p = 0.499$
	Month 1	17.4 (5.1)	17.4 (6.7)	
	Month 4	16.1 (5.2)	16.7 (6.3)	
Delayed verbal memory	Baseline	3.5 (2.7)	3.1 (3.0)	$F(1,73) < 1, p = 0.463$
	Month 1	3.9 (3.1)	3.9 (3.3)	
	Month 4	3.4 (2.9)	3.5 (3.2)	
Recognition verbal memory	Baseline	6.4 (3.3)	6.4 (3.6)	$F(1,73) < 1, p = 0.463$
	Month 1	7.4 (3.8)	7.3 (3.8)	
	Month 4	7.1 (3.4)	6.3 (4.1)	
Mood	Baseline	2.7 (2.4)	2.3 (2.0)	$F(1,73) < 1, p = 0.548$
	Month 1	2.3 (3.2)	2.3 (3.1)	
	Month 4	2.3 (2.9)	2.1 (2.5)	

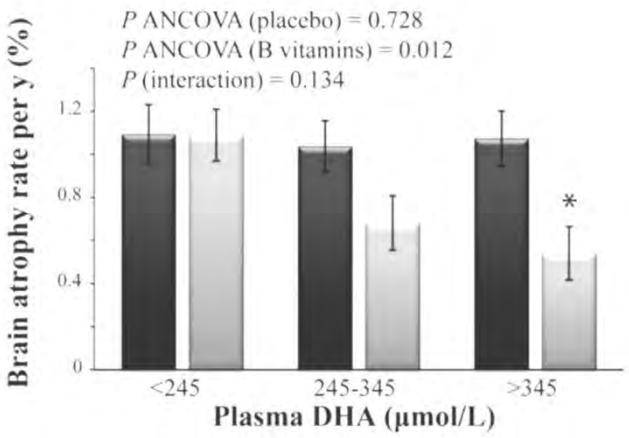
MMSES7, mini–mental state examination Serial Sevens;
MMSEWB, mini–mental state examination World Backwards;

W3FA- Alzheimer disease/ Dementia

Higher plasma w3FA concentration is associated with a slightly lower brain atrophy rates among older adults ONLY if they are receiving high-dose vitamin B

Jernerén F. et al. Am J Clin Nutr 2015; 102:215–21

Vitamin B regimen(TrioBe Plus; Meda AB/Recip AB) once daily for 24 mo
[content = 0.8 mg folic acid, 0.5 mg, vitamin B-12, and 20 mg vitamin B-6]



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Clinical Pearl: Micronutrient Supplementation

Micronutrient	Key risk factor for deficiency	Duration of treatment for deficiency	Special remarks
Thiamin	• ↓ oral intake or vomiting ≥ 1 week • Chronic alcoholism	At least 3-5 days; supplementation for 1-2 weeks	IV or IM should be used in the presence of neurological symptoms
Iron	• Blood loss • Malabsorption	3 months or until ferritin is normal	Start at 325 mg iron sulfate QD (NOT TID) or equivalent to minimize GI toxicity
Vitamin D	• ↓ oral intake • Obesity	At least 8 weeks	D2 vs D3 does not matter clinically based on current knowledge; Seasonal variation

APPENDIX 1:
Herbal supplements most commonly used by elderly patients based on published studies between 2001-2011

de Souza Silva JE et al. Arch Gerontol and Geriatr 2014;59:227–233

Supplement	Claimed benefits	Potential major risks
Gingko biloba	Enhance memory Improve circulation	Drug interactions (HIV meds) Increased bleeding risks
Garlic	Control cholesterol Antihypertensive Enhance immune function Anti-thrombotic effect	Increased bleeding risks Decreased absorption of INH
Ginseng	Boost energy Improve mental performance Enhance immune function	Drug interactions (inducer of CYP3A4)
Aloe vera	Improve constipation Treat skin disorders Improve osteoarthritis Lower blood sugar	Abdominal cramps Diarrhea Hypoglycemia ?

APPENDIX 2:
Other herbal supplements commonly used by American adults

Supplement	Common Uses
Chondroitin	Treat osteoarthritis
Coenzyme Q10	Various uses, including treatment of hypertension
Cranberry extracts	Prevent heart disease and cancer, treat UTI
Echinacea	Prevent/fight common cold
Flax seeds	Prevent heart disease
Glucosamine	Treat osteoarthritis
Saw palmetto	Treat benign prostatic hypertrophy
St. John's wort	Depression

Additional information: National Center for Complementary and Integrative Health (https://nccih.nih.gov/)