Vitamin D Controversy: 
Myth or Miracle?

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Disclosure

- Editor in Chief
  5 Minute Clinical Consult
- Author and Editor for *Up To Date*
- CCIPC/Pri Med Curriculum Committee
- Author/Editor: Rxpalm, Inc.
- Author/Editor: www.Epocrates.com
- Editor: www.Familydoctor.org
Objectives

1. Appreciate the epidemiology of Vitamin D Deficiency in the ambulatory setting
2. Revisit the metabolism of Vitamin D
3. Describe diagnosis & treat V. D Deficiency
4. Understand risks of V. D Deficiency
How Much Vitamin D do you take per Day?

- 1. 600 IU
- 2. 1000 IU
- 3. 2000 IU
- 4. 4000 IU
- 5. None
Theories:
Reduced Milk Consumption

Lower fat milks include: buttermilk (1.5 percent fat), plain and flavored reduced fat milk (2 percent fat), low-fat milk (1 percent fat), nonfat milk, and yogurt made from these milks (except frozen yogurt).
Why Is Everyone Vitamin D Deficient?

- Theories:
- ↓ Milk Consumption
- Fat Soluble → Need larger amount
Developed Nations

Rates of Obesity, 2007

US    74.1%
Argentina  69.4%
Greece  68.5%
New Zealand 68.4%
Mexico  68.1%
Australia   67.4%
Why is everyone Vitamin D Deficient?

- Theories:
  - ↓ Milk Consumption
  - Obesity

- Sun Exposure: Sunscreen, Windows, Walking
Vitamin D Winter: Very little if any vitamin D can be synthesized in the skin from November through February at latitudes north of 37 degrees.
Physiology of Vitamin D

- NOT a Vitamin; but rather a **hormone**
- Fat Soluble
- Vitamin D “job”: to maintain Serum Calcium
- Obtained from Diet or Sun Exposure
- UV B converts 7 dehydrocholesterol to D3
- Dietary Vitamin D3 & D2 thru. Intestine
- Both bound to Vit D3 binding protein.
Vitamin D — Calciferol; group of chemicals related to Vitamin D

Cholecalciferol (D3) In animal foods and supplements

Ergocalciferol (D2) from Plant sources

Calcidiol (25 Hydroxy D3) *** Serum Level

Calcitriol (1, 25 Hydroxy D3) Active Form
7-dehydrocholesterol → Cholecalciferol (Vitamin D3) → Calcidiol (25-hydroxy Vitamin D) → Calcitriol (1,25-dihydroxy Vitamin D)

Diet/supplements → Ergocalciferol (Vitamin D2) → Calcidiol (25-hydroxy Vitamin D) → 24,25-dihydroxyvitamin D

UV light skin → Liver

↓ Ca → ↑ PTH → Kidney

↑ Intestinal absorption of calcium, ↑ PTH-mediated bone resorption, ↓ Renal Ca++ and phosphate excretion
<table>
<thead>
<tr>
<th>Food</th>
<th>International Units (IU) per serving</th>
<th>Percent DV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cod liver oil, 1 Tablespoon</td>
<td>1,360</td>
<td>340</td>
</tr>
<tr>
<td>Salmon, cooked, 3½ ounces</td>
<td>360</td>
<td>90</td>
</tr>
<tr>
<td>Mackerel, cooked, 3½ ounces</td>
<td>345</td>
<td>90</td>
</tr>
<tr>
<td>Tuna fish, canned in oil, 3 ounces</td>
<td>200</td>
<td>50</td>
</tr>
<tr>
<td>Sardines, canned in oil, drained, 1¼ ounces</td>
<td>250</td>
<td>70</td>
</tr>
<tr>
<td>Milk, nonfat, reduced fat, and whole, vitamin D fortified, 1 cup</td>
<td>98</td>
<td>25</td>
</tr>
<tr>
<td>Margarine, fortified, 1 Tablespoon</td>
<td>60</td>
<td>15</td>
</tr>
<tr>
<td>Pudding, prepared from mix and made with vitamin D fortified milk, ½ cup</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td>Ready-to-eat cereals fortified with 10% of the DV for vitamin D, ¼ cup to 1 cup servings (servings vary according to the brand)</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>Egg, whole (vitamin D is found in egg yolk)</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>Liver, beef, cooked, 3½ ounces</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Cheese, Swiss, 1 ounce</td>
<td>12</td>
<td>4</td>
</tr>
</tbody>
</table>

*DV = Daily Value. DVs are reference numbers developed by the Food and Drug Administration (FDA) to help consumers determine if a food contains a lot or a little of a specific nutrient. The DV for vitamin D is 400 IU (10 µg) for adults. Most food labels do not list vitamin D content unless a food has been fortified with this nutrient. The percent DV (%DV) listed on the table
Who is at RISK for VitD D

- Women at 50
- Dark Skinned Individuals
- Veiled
- Seniors/Nursing Home
- Chronics Aches
- Multiple Fractures
- Pregnant/PMS
- Malabsorption
How to Test

- **25 Hydroxy (OH) Vitamin D level**
  - Most sensitive measure of body stores
- **1,25 Vitamin D active form, but varies**
- **Interpretation:** IOM
  - WNL: 20-100 ng/ml (50-250 nmol/L)
  - Deficient: < 20 ng/ml (< 50 nmol/L)

- No need for PTH and Calcium *except*:
  - Serious Cardiac Arrhythmias
  - Renal Insufficiency
  - Malignancy
## Treatment

<table>
<thead>
<tr>
<th>25 Vitamin D* Status</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 – 100 ng/mL Sufficient (50-250 nmol/L)</td>
<td>800-4,000 IU D3/Day</td>
</tr>
<tr>
<td>&lt; 20 ng/mL Deficient (&lt;50 nmol/L)</td>
<td>50,000 IU D2/week (Ergocalciferol) x 12 Wk Then 2,000 D3/Day</td>
</tr>
<tr>
<td>? Calcium 600-1,000 mg/day; divided</td>
<td></td>
</tr>
</tbody>
</table>

**IOM/ES:** 19-70: 600 mg/d; >70: 800 IU/d  
**Tolerable Upper Intake Level (UL):** 4,000 IU/d
Newborns 400 IU/Day

  - “all children should be given 400 IU/day within a few days of birth.”
  - This is a doubling of their previous recommendation.

www.cdc.gov/breastfeeding/recommendations/vitamin_d.htm
D2 or D3?
Statistical, but no CLINICAL Differences

- RCT 64 adults: D2 vs D3 x 1 year
- 25 OH Vit D: D3 $\uparrow$ ~ 9ng/ml vs 6 in D2
  - J Clin Endocrin Met 2011; 96: 981

- RCT 33 adults: 50,000 D2 or D3 weekly; after 12 weeks,
  - D3 $\rightarrow$ 35% greater increase in 25 OH Vit D
  - J Clin Endocrin Met 2011; 96: E447
Relative Contraindications to Vitamin D Supplementation

- Sarcoid
- Tuberculosis
- Lymphoma
- Primary Hyperparathyroidism
- ? Renal Calculi
Why not just take extra Calcium?

Ca Does NOT ↓ Osteoporotic Fractures

- Cohort Study of 61,000 women x 19 years
- Influence of Ca intake and Fracture
- Ca Intake beyond 1st Quintile did NOT further reduce Fx Risk

BMJ 2011; 342: d1473
2010 Calcium Without Vitamin D Increases Risk of MI

- Meta Analysis of 15 trials, ~20,000 patients
- Age > 40 years; study > 1 year
- Median F/U > 3.5 years

- Ca alone ↑ MI (RR = 1.27; 95CI 1.02-1.67)
- NNH ~125

BMJ 2010; 341: c3691
What Outcomes are influenced by Vitamin D?
Vitamin D (>800 IU/Day) Reduces Hip and Non-Vertebral Fractures in Community Dwelling Adults aged ≥ 65 Years

- **Meta-analyses** on Vitamin D supplementation and fracture
- 11 double-blind, randomized, controlled trials of oral vitamin D supplementation in those 65 years of age or older.
- 31,022 persons (mean age, 76 years; 91% women) with 1111 incident hip fractures and 3770 nonvertebral fractures.
- Reduction shown with intake: 800 IU daily; (792-2000 IU)
- **30% reduction in the risk of hip fracture** (hazard ratio, 0.70; 95% CI, 0.58 to 0.86) and a **14% reduction in the risk of any nonvertebral fracture** (hazard ratio, 0.86; 95% CI, 0.76 to 0.96).
- Benefits consistent across subgroups defined by age groups

Figure 1. Threshold Assessment for the Risk of Fracture, According to Quartile of Baseline 25-Hydroxyvitamin D Level.
2012: USPSTF Recommends Exercise or PT + Vitamin D (800 IU/D) for Adults ≥ 65 years

Annals of Internal Medicine

Prevention of Falls in Community-Dwelling Older Adults: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 1996 U.S. Preventive Services Task Force (USPSTF) recommendation statement on counseling to prevent household and recreational injuries, including falls.

Methods: The USPSTF reviewed new evidence on the effectiveness and harms of primary care-relevant interventions to prevent falls in community-dwelling older adults. The interventions were grouped into 5 main categories: multifactorial clinical assessment (with or without direct intervention), clinical management (with or without screening), clinical education or behavioral counseling, home hazard modification, and exercise or physical therapy.

Recommendations: The USPSTF recommends exercise or physical therapy and vitamin D supplementation to prevent falls in community-dwelling adults aged 65 years or older who are at increased risk for falls. (Grade B recommendation)

The USPSTF does not recommend automatically performing an in-depth multifactorial risk assessment in conjunction with comprehensive management of identified risks to prevent falls in community-dwelling adults aged 65 years or older because the likelihood of benefit is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of the circumstances of prior falls, comorbid medical conditions, and patient values. (Grade C recommendation)


For author affiliation, see end of text.
* For a list of the members of the USPSTF, see the Appendix (available at www.annals.org).
This article was published at www.annals.org on 29 May 2012.
Vit D and Fall Prevention

**Strength & Balance**

- Meta analysis (13 studies):
  - 800 - 1,000 IU/d
  - Vit D Supplementation →
  - Improved strength and balance

*J Am Geriatr Soc. 2011 Dec;59(12): 2291*
& the obvious: Osteoporosis

- Osteoporosis:
  Most studies of Rx (Bisphosphonates, etc.) ALSO include Vitamin D, Calcium and Weight Bearing Exercise

- "Based on relationship between 25(OH)D, bone mineral density, bone turnover, lower extremity function, & falls, supplementation should aim to increase 25(OH)D levels” > 30 ng/ml range

Clin Endocrinol (Oxf). 2009 Sep 10
Obesity

- 2 Year Vit D Weight Loss Trial, 300+ Patients
- Baseline; Higher BMI $\rightarrow$ Lower 25 OH Vit D
- After 2 Years & Adjusting for age, sex, baseline BMI, total fat intake, and diet group assignment
- **Highest D intake lost additional 5.6 Kg x 2 yrs**
- ? Fecal Fat Excretion
- Higher Intake Ca & Vit D $\rightarrow$ Greater Wt Loss

Obesity & Depression

- Cross Sectional, then **RCT** of Vit D on Depression in Obese Patients
- 440+, BMI: 28-47, \( \sqrt{25} \) VD & Beck Dep Inventory
- Subjects with Low Vit D -> Higher Beck scores
- RCT: D3--40K, 20K/week vs Placebo x 1 Yr
- 1Yr: ↓ Beck in 40K & 20K D3, ↓ PTH; No Δ Placebo
- **Treat patients with Depression with Vitamin D**

Multiple Sclerosis & VDD

- Strong Epidemiologic data that **Poor Vitamin D status increases risk for MS**
- Some observational data shows VDD may predict poor clinical course in those with MS
- MS patients higher risk of falls & Osteoporosis
- Initial **Clinical trial data of MS patients treated with high dose Vitamin D pending till 2015**
- Suggested serum goal of 30-60 ng/mL

*Expert Rev Neurother.* 2012 Sep;12(9):1101-12
Late Breaking News

- **Hepatitis C**: RCT Peg α IF + Ribavirin +/- D3
  - Sustained Virologic Response (Undetectable HCV)
  - Week 4: 44 vs 17%
  - Week 12: 94% vs 48%
  - Week 24: 86 vs 42%
  - World J Gastro 2011: 17(47): 5184

- **Type 1 DM**
  - Observational Study Military Personal
  - 25 OH VD < 17 ng/mL Tripled Ris of Type 1 DM

- **Alzheimer Disease**:
  - Observational Study
  - > 1800 IU/D → ↓ AD Risk in Women
  - J Gerentol 2012
Pre Menstrual Syndrome

- PMS is related to cyclic decrease in Calcium and increase in PTH
- Nurses’ Health Study II Case/Control 1000+
- Highest Vit D (~700 IU/D) RR of PMS of 0.59
- Similar trend with Calcium Intake

Vit D and Calcium **MAY** reduce PMS

Vitamin D & Cancer

1. Sys. Review of 63 *Observation* Studies

**Adequate Vit D Levels -> ↓ Risk**

- 30 Colon Cancer (20/30)
- 13 Breast Cancer (9/13)
- 26 Prostate Cancer (13/26)
- Low VD Level → ↑ Ovarian Cancer (7)


2. Women with Non Melanoma SC on Vit D had lower rates of Melanoma

*J Clin Oncol.* 2011 Aug 1;29(22):3078-84
Colon Cancer

- Meta-analysis of 5 studies
- highest quintile (> 33 ng/ml)
- 50% reduction in colo-rectal cancer risk.

HTN & Vitamin D:  
≈ NaCl Restriction

1. Hypertension NHANES III data (IOM Ob)
2. **BP lower in highest Quintile of 25 VD v lowest.**
   - Elevations of Blood Pressure were highest in Non-Hispanic Blacks compared to Whites.
     Am J Hypertension 2007; 20:713

2. **HTN: Vit D. Suppl. (8-12 weeks) → ↓ BP**
   - Average ↓: Systolic > 5 mmHg (NNT=3), Diastolic > 5 mmHg (NNT=7)
     J Clin Endo Met 2001; 86(4): 1633
Vit D Def. -> Increased Risk of MI

- **Case Control Study of 18,000+ Men**
- **If Deficient (\(\leq 15\) ng/mL) RR=2.09**
  
  *after adjusting for:*
  
  FHx CAD, BMI, EtOH, Activity level, Diabetes mellitus, HTN, Ethnicity, LDL

**Vitamin D Def increases risk of MI**

- **If \(\leq30\) ng/mL \(\Rightarrow\) RR=1.60

VDD & CHD: Kansas

- **Cohort** Study of ~ 11,000 found VDD:
- Associated w/ HTN, CAD, and DM (p <0.05).
- **VDD Strong predictor of all-cause death** (odds ratios 2.64, 95% CI 1.901 to 3.662, p <0.0001) adjusting for multiple clinical variables.
- **Vitamin D supplementation conferred** ‘substantial survival benefit” (OR death 0.39).

*Am J Cardiol.* 2011 Nov 7
Vitamin D Deficiency & ↑ Risk of All Cause Mortality

- Melamed: Cohort 13,000 NHANES

- Lowest quartile of 25 OH Vitamin D → ↑ Risk of All Cause Mortality

- Mortality RR=1.26 (95% CI 1.08 - 1.46)

What *Decreases* Risk of All Cause Mortality?

- Seatbelts
- Clean Water
- Vaccines
- Exercise
2007 Vit. D Supplementation Decreases of All Cause Mortality

- Meta Analysis: 18 studies of 57,000+ Adults
- Examined Risk of Death Any Cause in RCT Vitamin D Supplementation
- Average dose
- > 500 IU/D

- Vit D Supplementation Decrease in All Cause Mortality (RR = 0.93)
- Autier: Arch Int Med 2007;167(16): 1730
2011 Systematic Review on VD Supplementation

- **Cochrane Systematic Review**: 50 trials, 90,000+
- **Vitamin D Supp**:
  - **DECREASE ALL CAUSE MORTALITY**
  - Vitamin D decreased mortality → RR 0.97
  - Subgroup Analysis: **Older women best outcomes**

Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD007470
What Didn’t Improve in RCT of Vitamin D Supplementation

- Chronic Myalgias/Fibromyalgia
- Upper Respiratory Tract Infections
- “Cure” Psoriasis (? Maybe oral for Tx....)
- Seasonal Affective Disorder
- Treat Osteoarthritis pain
- COPD exacerbations
- Academic Achievement in Adolescents
- Diabetes Prevention
Vitamin D testing: Coding

- Pre Menstrual Synd 625.4
- Arthralgias 719.49
- Fatigue 780.79
- Diabetes (T2) 250.00
- Malabsorption 579.8
- Irritable Bowel Synd 564.1
- Menopausal Disorder 627.8
Is this Real?

- MOST data is *observational* research, rather than RCT’s
- Reference Range of 25 OH Vitamin D based loosely on suppressing PTH
- OTC Drug-- little initiative to study
- Analogous to Treating ↑ Homocysteine or Vitamin E and CHD
Data Summary

Good SR Data:
- **Lower Risk of Falls/Fx**
- **Lower Risk of Some Cancers**
- **↓ All Cause Mortality**

Intermediate Data:
- PMS, HTN
- CHD Risk

**Benefit:**
- Osteoporosis, Depression, Obesity

2,000-4,000 IU/Day
Screen those at risk: Seniors, Women at 50, Dark Skinned, Veiled, Home Bound & NH, DM, Multiple Fx, Pregnant, Malabsorption, CHD, Depression

Test: 25 OH Vitamin D

Treat according to status

Prevention for all: 2-4,000 IU/Day + ?Ca
(No known benefit to higher doses)

Weight Bearing Exercise
Endocrine Society 12/2011-12

Endocrine Society Task force: Consensus Statement

General screening for vitamin D deficiency is not recommended.
Screening for high risk: osteoporosis, obesity, or history of falls.
Vitamin D deficiency is serum (25[OH]D) level <20 ng/mL.
Recommended intake adults is 600 IU (800 IU for those aged >70).
Blacks and other dark-skinned higher risk for deficiency.

Both D2 (ergocalciferol) & D3 (cholecalciferol) are acceptable.

Treatment of vitamin D deficiency is indicated mainly for skeletal reasons; evidence also suggests that treatment lowers the incidence of falls in older adults.

Vitamin D, Obesity and Diabetes

- Calcium + D during weight-loss enhances weight loss & lipoprotein profile in T2DM

- Treating Vit. D in T2DM improves insulin secretion

- VDD associated w/ ↑ SubQ & Visceral adiposity
  - Diabetes. 2010 Jan;59(1):242-8
Children: NHANES
Prevalence of VDD in Children

- 1-21 years 2001–2004 ($n = 6275$)
- 25 OH Vit D & Cardiovascular risk factors
- 70% were Insufficient; >10% deficient

Risk Factors for Vit D Def:
- Older children, Dark Skinned Children, Obese
- Girls
- Kids who drank milk less than once a week
- Kids who spent > 4 hours/day Screen Time
- “turn off TV (and computer) & send them outside”

Kumar; Pediatrics 2009; doi:10.1542/peds.2009-0051
VitD D Prevalence

- **Seasonal Variation:**
  - Boston: 30% Winter vs. 11% Summer

- **Adolescent Females:**
  - 54% Insufficient 17% Deficient
    - J. Adolescent Health; 2005; 75e1-e5

- **African American Females:**
  - 12% Severely Deficient

- **Seniors with Deficiency:**
  - NH Residents: 38%; Housebound dwellers 54%
    - JAMA 1995; 274( 21): 1683-6

- **Arizona Adults**
  - 25% Significantly deficient
Vitamin D Metabolism

D3 Cholecalciferol
D2 Ergocalciferol
Children:

NHANES & Heart Disease

- 3,500+ 12- to 19-year-olds in NHANES database.
- After controlling for CHD risk factors -- *low vitamin D increased risk of Adult CHD*.
- Compared highest quartile 25 OH Vit D levels vs. lowest:
  - a 2.36-fold higher risk of high blood pressure
  - a 2.54-fold higher risk of high cholesterol levels
  - a 50% higher risk of low HDL cholesterol
  - Almost fourfold risk of Metabolic Syndrome & CHD.
- Both obese and non-obese VDD had ↑ risk for CHD.

- Reis; Sept. 2009; Pediatrics 2009; 124(3): e371-e379
FIG. 1. Relationship between serum 25(OH)D and outcome parameters

Cohort of 1,300 +, 65-85 (IOM Ob)

Threshold for Optimal Performance =
50-60 nmol/l
Or
20-25 mg/dL
Ca and Low Dose Vitamin D May Not be a good idea either

- Reanalysis of Ca Supp in WHI

- 1 Gm Ca + Vit D 400 IU/d; 36,000 women x 7 Yr for CHD Events & MI/Fatal MI, CVA, etc.

- Ca + low dose Vit D $\rightarrow$ ↑ MI & CVA (RR= 1.15)

- **Conclusion**: “Ca supplementation w or w/o Vitamin D modestly increases risk of CV events, esp. MI. The reassessment of Ca supplementation in Osteoporosis management is warranted.”

BMJ 2011; 342: d2040
Is it Vitamin D or PTH?

- Cohort of Osteoporotic Fx in Men x 7+ Yrs
- No Association between 25 OH Vit D and all cause mortality
- HIGH PTH was associated with an increased risk of All Cause Mortality and CV Mortality

J. Clin Endo Met 2010; 95: 4625
Metabolic Effects of Vitamin D

- Decreased Serum Calcium ->
- Induces ↑ PTH ->
- Increase Renal Conversion to 1,25 Vit D:
  1. Increase intestine Ca & PO4 absorption,
  2. Decreased renal excretion of Ca & PO4, and
  3. Increase *Osteoclast* activity in the bone->

Osteomalacia and Osteoporosis
VitD D in Pregnancy

- Pittsburg: Vit D status @ 4-21 wk gestation & delivery in 200 white & 200 AA women and in cord blood neonates
- > 90% used prenatal vitamins (400 IU).
- @ Term: AA Women: 29% Def; 54% Insuf.
- @ Term: AA Neonates: 46% Def; 47% Insuf.
- @ Term: W Women: 5% Def 42% Insuf.
- @ Term: W Neonates: 9.7% Def; 56%

Journal of Nutrition 2007 Feb; 137(2) 447-452
Why not give more to mom?

- "amount of vitamin D to achieve the lower level of normal in the mother of 32 mg/ml or 80 nmol/L (400 IU in PNV) does not translate into adequate levels in her milk, and for baby.

- “mother is replete but on the lower end so her infant is obligated to receive 400 IU/day vitamin D to ensure adequacy in that infant.“

- Nice Dosing Chart

*Clinical Lactation, 2011, Vol. 2(1), 27-31*
Table 1. Suggested Vitamin D Supplementation Regimen for Pregnant and Lactating Women, Infants, and Children

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Recommended Daily Vitamin D Intake (IU/day)</th>
<th>Caveats to Ponder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates</td>
<td>400 IU/day</td>
<td>This includes premature neonates and infants. More data are needed to determine what the IU/kg requirements are of preterm infants and neonates born to mothers with frank vitamin D deficiency.</td>
</tr>
<tr>
<td>Infants &lt; 1 year</td>
<td>400 IU/day up to 10 kg; then 25-50 IU/kg</td>
<td></td>
</tr>
<tr>
<td>Children 1-2 yrs</td>
<td>25-50 IU/kg</td>
<td>For example, a child weighing 20 kg would be given 500-1,000 IU/day. Another child weighing 25 kg would be given 625-1,250 IU/day. One could give the lower dose during summer months and the higher dose during winter months.</td>
</tr>
<tr>
<td>Children 2-5 yrs</td>
<td>25-50 IU/kg up to 30 kg</td>
<td></td>
</tr>
<tr>
<td>Children 5-12 yrs</td>
<td>25 IU/kg up to 50 kg</td>
<td></td>
</tr>
<tr>
<td>Children 12-17 yrs</td>
<td>&gt;50 kg</td>
<td>2,000-4,000 IU/day depending on BMI</td>
</tr>
<tr>
<td>Pregnant Women</td>
<td>&gt;45 kg</td>
<td>4,000 IU vitamin D/day</td>
</tr>
<tr>
<td>Lactating Women</td>
<td></td>
<td>Likely 6,400 IU/day with refinement of recommendation once Lactation RCT vitamin D studies have been completed and analyzed.</td>
</tr>
</tbody>
</table>

*This is a conservative guide. If an individual has an increased BMI or a history of malabsorption, then that individual may require higher daily vitamin D supplementation. It would be prudent to check levels if increasing intakes beyond these recommendations. The ultimate goal is to attain circulating 25(OH)D levels to that individual that would mimic living in a sun-rich environment with daily sun exposure.*
Other Papers on Cancer


Weight and Gender may play a role….

- Prospective association of vitamin D concentrations with mortality in postmenopausal women: from the Women's Health Initiative (WHI).

- Multivariate-adjusted HRs compared quartiles 1 (lowest) to 4 (highest) of 25(OH)D found no difference in all-cause mortality, CVD mortality, and cancer mortality.

- Increased mortality risk of women in lowest quartile with a normal waist circumference but no increased risk in women with obesity

*Am J Clin Nutr.* 2011 Dec;94(6):1471-8
Observational study of 1300 women on development of ARMD & 25 OH Vit D

Overall: no significant relationship was observed between early AMD and 25(OH)D

A significant age interaction suggested selective mortality bias in women aged 75 years and older

↑ 25(OH)D Vit D was associated with decreased odds ratio (0.52) of early AMD

Calcitriol (1,25 OH Vit D) inhibits growth of some types of malignant cells in vitro (including Breast Cancer cells)

Calcitriol also inhibits the growth of estrogen receptor positive (ER+) BCa cells and

Decreases expression of aromatase, the enzyme that catalyzes estrogen synthesis in BCa cells

*Steroids*. 2012 Sep;77(11):1107-12
Outcomes: Falls

- **Falls Meta Analysis** of 5 RCTs
  - Healthy, mobile adults, Age > 60
  - 700-1000 IU/day
  - **Decreased Risk of Fall by Almost 20%**
  - NNT to prevent one fall = 15
    

- **Meta Analysis** of 10 studies over 36 months
  - 41% of patients vitamin D fell compared to 48% of control patients
  - Vitamin D supplementation (>= 800 IU per day) reduces falls in adults older than 60 years. **NNT = 15**

Fracture SR data w/ VD Supplementation

800 IU ->

↓ Hip Fracture RR = 0.74

↓ Vertebral Fracture RR = 0.77

Bischoff-Ferrari,: JAMA 293(18): 2257
2011 Hold the Calcium: Ca + Vit D in Women ↑ CHD RISK

- Reanalysis of WHI data
- Meta Analysis of subset of data (28,000)
- RR MI/CVA 1.15(1.03-1.27)
- RR without Ca Unknown
- HOLD the Ca+

BMJ 2011; 342: d2040
Why Is Everyone Vitamin D Deficient?

- **Theories:**
  - ↓ Milk Consumption
  - Obesity
  - Sun Exposure

- **PPI Use:**
  - PPI $\rightarrow$ ↑ pH $\rightarrow$ ↓ Ca Absorption $\rightarrow$ ↑ PTH