

## Osteoporosis

**Compromised Bone Strength  
Predisposing to Increased Risk of  
FRAGILITY FRACTURES**

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## Disclosure

Michael McDermott has no conflict of interest or relationships to disclose in relation to this educational activity.

## Learning Objectives

- Discuss the diagnosis and evaluation of osteoporosis.
- Explain the individualized approach to managing osteoporosis according to degree of fracture risk.
- Review treatment of vitamin D deficiency in people with normal intestinal absorption and in those with malabsorption disorders.

## Osteoporosis

Fragility Fractures (Low Trauma)



**Vertebral Fractures**  
700,000/year  
2/3 Asymptomatic

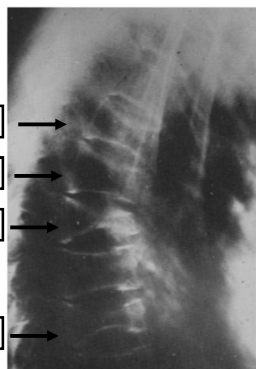


**Hip Fractures**  
300,000/year  
Disability/Mortality High



**Wrist Fractures**  
250,000/year

## Vertebral Fractures



Fragility Fracture →

Fragility Fracture →

Fragility Fracture →

Fragility Fracture →

Pain

Kyphosis

Scoliosis

Height Loss

Impaired Breathing

## Osteoporosis Diagnosis

Fragility Fracture Criteria

Presence Of:



Vertebral Fracture

Hip Fracture



**Fragility Fractures = Osteoporosis**  
Bone Density Testing Not Required for Diagnosis

### Osteoporosis Diagnosis

#### Bone Densitometry Criteria

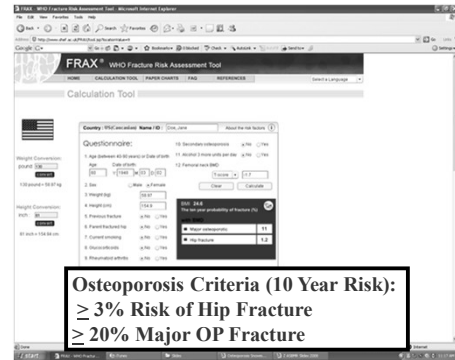
#### T-Score

- Normal > -1.0
- Osteopenia -1.0 to -2.5
- Osteoporosis < -2.5

**Overall Diagnosis: Made by T-Score at Lowest Site**

### Osteoporosis Diagnosis

#### FRAX Risk Criteria



### Low Bone Mass and Fractures are Not Always Osteoporosis

**Evaluate for Secondary or  
Contributing Causes**

### Differential Diagnosis

#### Causing / Contributing To Osteoporosis

- Osteomalacia
- Osteogenesis Imperfecta
- Hyperparathyroidism
- Hyperthyroidism
- Hyperprolactinemia
- Hypogonadism
- Cushing's Syndrome
- Celiac Disease
- Eating/Exercise Disorders
- Inflammatory Bowel Dz
- Primary Biliary Cirrhosis
- Multiple Myeloma
- Rheumatoid Arthritis
- Chronic Renal Failure
- Idiopathic Hypercalciuria
- Systemic Mastocytosis

#### High Risk Medications

Established: Glucocorticoids, Thyroid Hormone Excess,  
Anticonvulsants, Androgen Deprivation Rx.  
Probable: SSRIs, Proton Pump Inhibitors.

### Osteoporosis Evaluation

#### Secondary or Contributing Factors

#### Lab Tests

- Calcium
  - Creatinine
  - Alkaline Phosphatase
  - 25 OH Vitamin D
  - Thyroid (TSH)
  - Celiac Panel
  - Testosterone (Men)
  - 24 Hour Urine Calcium, Creatinine
- Calcium ↑ or ↓  
▪ PTH
- Anemia, Protein Gap ↑,  
or Calcium ↑ and PTH ↓  
▪ SPEP, UPEP

Camacho P. Endocrine Pract 2016; 22 (Suppl 4):1-42.

### Osteoporosis Treatment

#### Who Should be Offered Treatment?

**All Patients with Osteoporosis**

- Fragility Fracture
- T-Score < -2.5 (any site)
- FRAX 10 Year Risk Criteria


Camacho P. Endocrine Pract 2016; 22 (Suppl 4):1-42.  
Black DM, Rosen CJ. N Engl J Med 2016; 374:254-62.

### Fall Prevention



**Prevents Fractures**  
May be Most Effective Measure in the Elderly

### Exercise




Aerobic

Resistance

**Builds: Bone and Muscle**  
**Improves: Balance**

### Calcium Nutrition

**Milk**  
300 mg / 8 oz



**Yogurt**  
300 mg / Cup

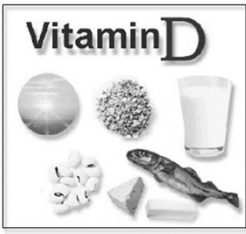
**Cheese**  
300 mg / Oz


**Dairy Products**  
Calcium Phosphate

If Dairy Intake Inadequate: Add Calcium Supplements  
Total Calcium Intake Goal: 1000-1500 mg/day

### Vitamin D Nutrition

**Vitamin D**





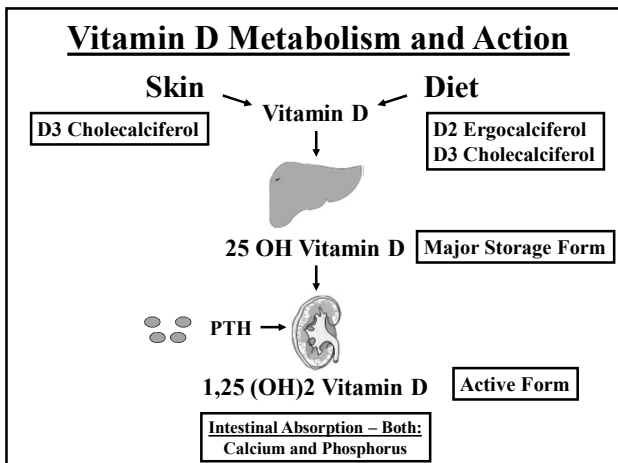
Sunlight

Fatty Fish

Dairy

Supplements

Vitamin D Supplements: Usually Needed  
Total Vitamin D Intake Goal: 1000 Units/day



### Vitamin D Deficiency

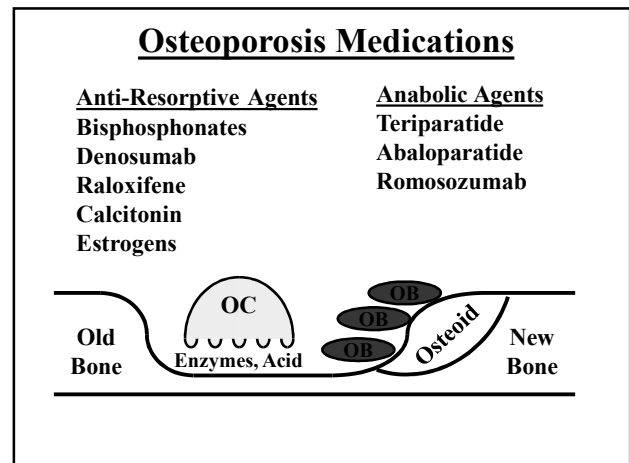
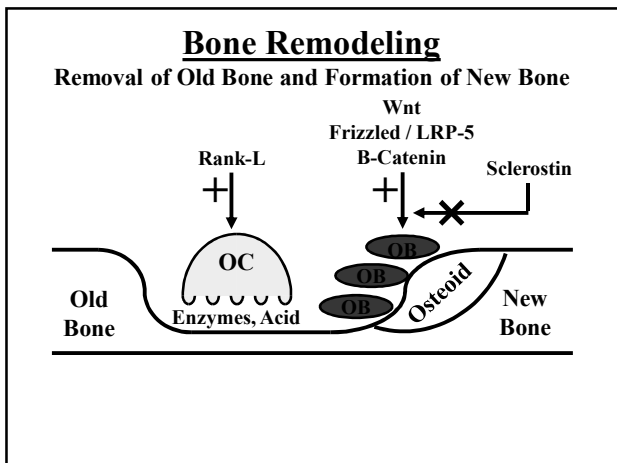
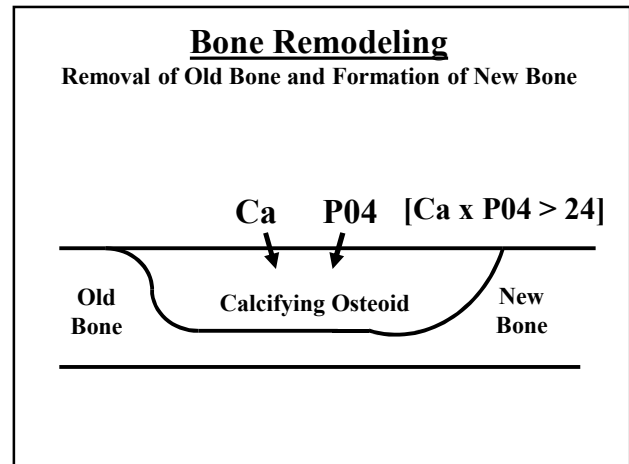
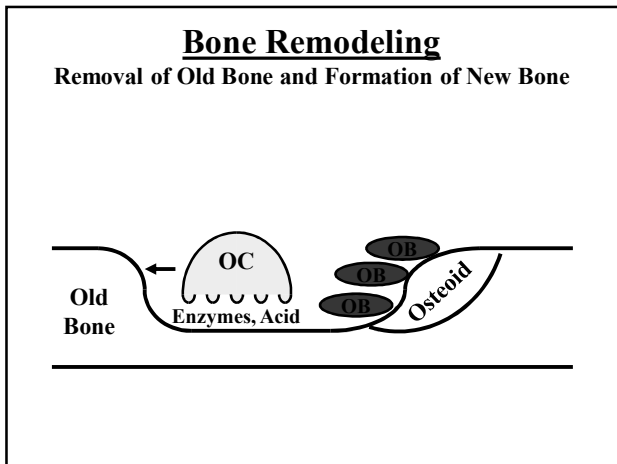
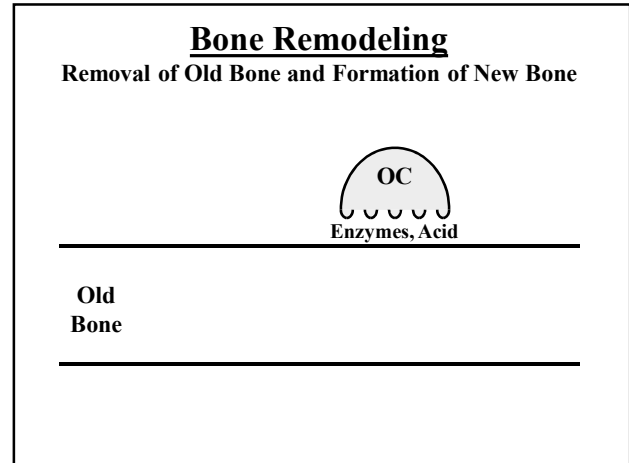
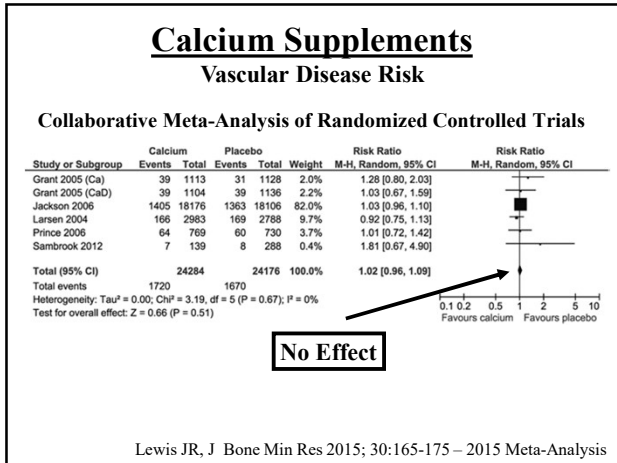
Replacement

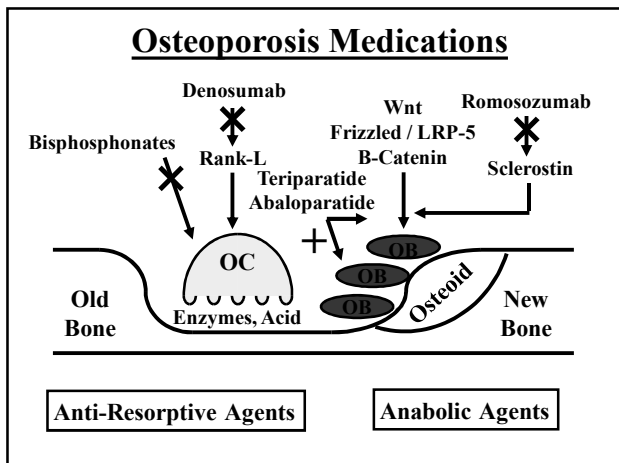
<u>25 OH Vit D</u>	<u>Treatment</u>
▪ < 10 ng/ml	50,000 U D2 BIW x 3 months
▪ 10-20 ng/ml	50,000 U D2 QW x 3 months
▪ 20-30 ng/ml	2,000 U D3 QD x 3 months

Maintenance

- Optimal Intake: 1,000 U QD
- Safe Intake: 2,000-4,000 U QD

Dawson Hughes B, Am J Clin Nutr 2004; 80:1763-6S





### Osteoporosis Medications

#### Fracture Reduction

Vertebral Fractures	RR	Hip Fractures	RR
Alendronate	0.57	Alendronate	0.61
Risedronate	0.61	Risedronate	0.73
Ibandronate	0.67	Zoledronic Acid	0.60
Zoledronic Acid	0.38	Denosumab	0.56
Denosumab	0.32	Romosozumab	0.44
Teriparatide	0.27		
Abaloparatide	0.14		
Romosozumab	0.33		
Calcitonin	0.65		
Raloxifene	0.59		
Estrogens	0.65		

RR: compared with placebo  
 Barrionuevo P. J Clin Endocrinol Metab 2019; 104:1623-30.  
 Eastell R. J Clin Endocrinol Metab 2019; 104:1595-1622.  
 Shoback D. J Clin Endocrinol Metab 2020; 105:587-594.

### Osteoporosis Medications

#### Combination Therapy

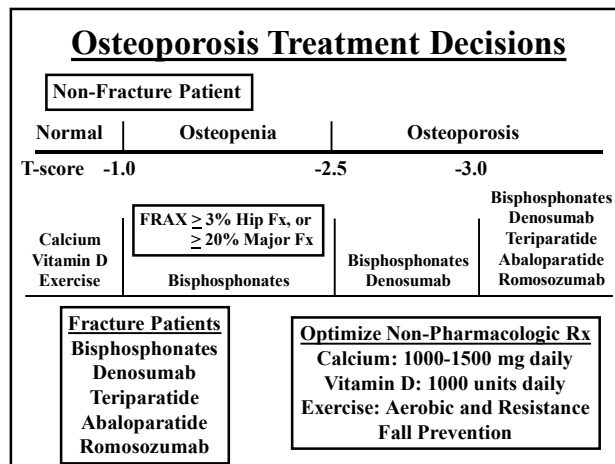
Anabolic	Anti-Resorptive	Outcome
Teriparatide	+ Alendronate	No Synergy
Teriparatide	+ Zoledronic Acid	BMD Synergy
Teriparatide	+ Denosumab	BMD Synergy

Combination Therapy Not Recommended Yet

Sequential Therapy Is Recommended

Cosman F. J Bone Min Res 2012; 26:503-11  
 Leder B. J Clin Endocrinol Metab 2014; 99:1694-1700  
 Camacho P. Endocrine Pract 2016; 22 (Suppl 4):1-42.



### Case

A 67 y.o. woman recently sustained painful vertebral fractures at T10 and T11.

PMH: None      Family Hx: Hip Fracture - Mother

Calcium/Vitamin D: 1500 mg / 1000 U daily

Meds: None

Lab: Calcium 9.6 mg/dl, 25 Vitamin D 32 ng/ml,  
TSH 1.4 mU/L, Cr 1.1 mg/dl, SPEP normal

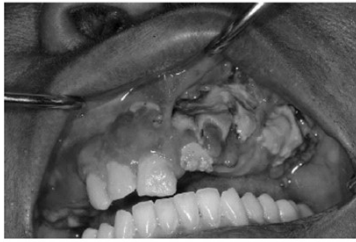
DEXA: Spine T-score -3.7, Fem Neck T-score -3.4

What treatment do you recommend for Osteoporosis?

- ### Osteoporosis Medications
- #### Risk Stratification
- Low / Moderate Risk**
- Oral Bisphosphonate (Alendronate, Risedronate)
  - Zoledronic Acid (Reclast)
  - Denosumab (Prolia)
- High Risk\***
- Zoledronic Acid (Reclast)
  - Denosumab (Prolia)
  - Teriparatide (Forteo, Bonsity)
  - Abaloparatide (Tymlos)
  - Romosozumab (Evenity)
- High Risk\*:** Old Age, Prior Fractures, Very Low BMD, High Fall Risk, Glucocorticoid Use

**Osteonecrosis of the Jaw (ONJ)**

Non-Healing Exposed Bone for  $\geq$  8 Weeks



**FIGURE 1.** Exposed necrotic maxillary bone in a patient receiving zoledronic acid for 6 months. The patient had posterior maxillary extractions performed 4 months earlier. (Courtesy of Dr Jay Neugarten, New Hyde Park, NY.)

Ruggiero S, J Oral Maxillofac Surg 2004; 62:524-34

**Osteonecrosis of the Jaw (ONJ)**

**Highest Risk**

**High Dose Anti-Resorptive Rx for Cancer**

**Periodontal Disease / Poor Oral Hygiene**

**Stop Anti-Resorptive Rx for 3 Months (Dental Work)**

**Reasonable - No Data for Efficacy**

**Anabolic Agents Are Not Associated with ONJ**

Ruggiero S, J Oral Maxillofac Surg 2014; 72:1938  
Khan AA, J Bone Min Res 2015; 30:3-23

**Atypical Femur Fractures**



THE NEW ENGLAND  
JOURNAL OF MEDICINE

Lenart B, N Engl J Med 2008;358:1304-6

**Atypical Femur Fractures**

- **Femoral Shaft Fractures**
- **Non-Healing Stress Fractures**
- **Thigh Pain → Often No Prior Trauma**
- **Prolonged Anti-Resorptive Rx (> 5 years)**

**Anabolic Agents Are Not Associated with AFF**

Shane E, J Bone Min Res 2014; 29:1-23

**Case**

A 62 y.o. woman diagnosed with osteoporosis by BMD 7 years ago. No history of fragility fractures.

PMH: None      Family Hx: Osteoporosis - MGM

Calcium/Vitamin D: 1200 mg / 600 U daily

Meds: Alendronate 70 mg weekly for 7 years

Lab: Calcium 9.4 mg/dl, 25 Vitamin D 48 ng/ml

BMD: Spine T-score -2.2, Fem Neck T-score -1.9

Significant  $\uparrow$  over 7 years, stable past 2 years

**Do you recommend a bisphosphonate drug holiday?**

**Osteoporosis Medications**

**When Should Drug Holidays be Considered?**

**Bisphosphonates – Oral (daily, weekly, monthly)**

- After 5 Years (Low / Moderate Risk Patients)
- After 6-10 Years (High Risk Patients)

**Zoledronic Acid – IV (annually)**

- After 3 Doses (Low / Moderate Risk Patients)
- After 6 Doses (High Risk Patients)

**Denosumab – SQ (every 6 months)**

**Holiday Not Recommended. If stopped, must replace.**

**Teriparatide (2 yr) / Abaloparatide (2 yr) / Romosozumab (1 yr)**

**Holiday Not Recommended. If stopped, must replace.**

Camacho P, Endocrine Pract 2016; 22 (Suppl 4):1-42.  
Qaseem A, Ann Intern Med 2017; 166:818-39

**Case**

A 66 y.o. woman diagnosed with osteoporosis by BMD 11 years ago. No history of fragility fractures.

PMH: None      Family Hx: Osteoporosis - MGM

Calcium/Vitamin D: 1200 mg / 600 U daily

Meds: Bisphosphonate drug holiday x 4 years.

Lab: Calcium 9.7 mg/dl, 25 Vitamin D 54 ng/ml

DEXA: Spine T-score -2.6, Fem Neck T-score -2.4  
Significant ↓ during past 2 years (> LSC)

**Do you recommend ending the bisphosphonate drug holiday?**

**Osteoporosis Medications**

**When Should Bisphosphonate Holidays End?**

- **Fragility Fracture Occurs**
- **BMD ↓ (> Least Significant Change)**
- **Bone Turnover Markers ↑ by 30% or into upper half of reference range)**
  - Serum C-Telopeptide (CTX)
  - Urine N-Telopeptide (NTX)
  - Bone Specific Alkaline Phosphatase (BSAP)

Adapted from: Camacho P. Endocrine Pract 2016; 22 (Suppl 4):1-42.

**Case**

A 63 y.o. woman is being treated for osteoporosis. Recently fell and sustained a right wrist fracture.

PMH: Osteoporosis, Type 2 DM      Family Hx: Negative

Calcium Intake: 1200 mg/d (diet plus supplements)

Meds: Alendronate (4 years), Metformin

PE: Ht 5'5" Wt 162 lb.      Otherwise normal

Lab: Calcium 9.2 mg/dl, 25 Vitamin D 36 ng/ml

<b>BMD:</b>	<u>T-score</u>	<u>Change (2 Year)</u>
Spine (L2-L4)	-2.6	-0.2 g/cm <sup>2</sup> (< LSC)
Femoral Neck	-2.2	-0.1 g/cm <sup>2</sup> (< LSC)

**Is this considered a treatment failure?**

**Failure to Respond to Therapy**

**Definition**

- **Development of 2 or more fragility fractures**
- **BMD decrease > Least Significant Change**

Lewiecki M, J Clin Densitom 2003; 6:307-14

**Failure to Respond to Therapy**

**Causes and Management**

- **Poor compliance → Education**
- **Calcium / Vitamin D deficiency → Correct**
- **Co-morbid conditions → Correct**
- **Harmful medications → Adjust**
- **Wrong dose or dose interval → Correct**
- **Lack of efficacy → Change Medication**

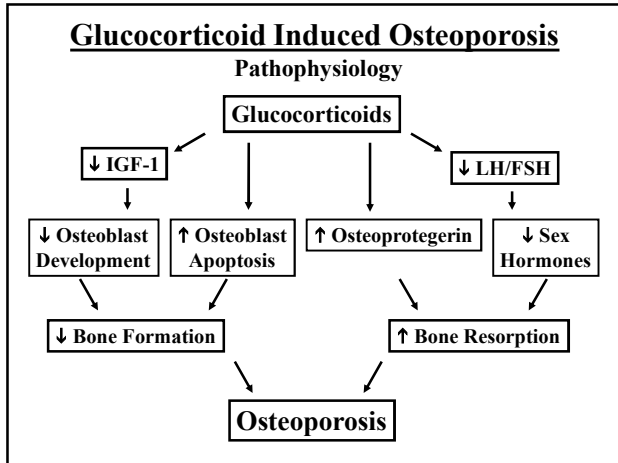
Lewiecki M, J Clin Densitom 2003; 6:307-14

**Failure to Respond to Therapy**

**Change Medication**

- **Zoledronic Acid**
- **Denosumab**
- **Teriparatide**
- **Abaloparatide**
- **Romozosumab**

Lewiecki M, J Clin Densitom 2003; 6:307-14

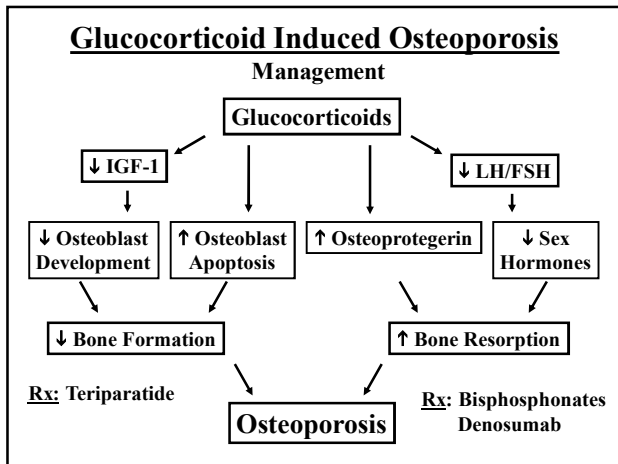


**Glucocorticoid Induced Osteoporosis**  
Management

**Non-Pharmacological Measures:** All people

**Medication:** Prednisone  $\geq 7$  mg/day for  $\geq 3$  months

- Fragility fractures
- Postmenopausal women
- Premenopausal women and men with T score  $< -1.0$



**Chronic Kidney Disease**  
Stage 4, Stage 5

- Optimize Lifestyle (Calcium, Vitamin D, Exercise)
- Control Serum Phosphorus (reduce  $\uparrow$  PTH)
- Order Bone Specific Alkaline Phosphatase and PTH
  - Adynamic bone disease unlikely if  $\uparrow$  BSAP and PTH  $> 100$
- Stage 4 CKD (eGFR 15-30)
  - Denosumab or low dose bisphosphonate
- Stage 5 CKD (eGFR  $< 15$ )
  - Low dose bisphosphonate

**Case**

A 68 year old woman complains of back pain. Spine films show 2 new vertebral fractures.

PMH: Hypertension    Meds: Lisinopril  
PE: BP 136/84    P 80    Ht 5'9"    Wt 145 lb.

Normal otherwise

Lab: Ca 11.6    Phos 3.0    PTH 123 (nl: 10-65)  
BMD: Spine T-score -2.8    Hip T-score -3.2

What is the cause of her vertebral fractures?  
What is the most appropriate management?

**Case**

A 42 year old woman complains of weakness and thigh pain. Bowel habits normal. Wears a veil.

Meds: none    Cigarettes: none    Etoh: none  
PE: Ht 5'8"    Wt 135 lb.    normal exam  
Lab: Ca 7.4    Phos 2.4    Alk Phos 215  
BMD: Spine T-score -2.5    Hip T-score -3.1  
Serum PTH: 112 pg/ml (nl, 10-65)  
Serum 25 Vitamin D: 5 ng/ml (nl, 30-100)

What is the cause of her pain, weakness and low BMD?  
Why is her PTH elevated?  
What is the most appropriate management?



**Nutritional Vitamin D Deficiency**  
**Laboratory**

- ↓ Serum Calcium
- ↓ Serum Phosphate
- ↓ Serum 25 OH Vitamin D
- ↑ Serum PTH (2<sup>o</sup> HPTH)
- ↑ Serum Alkaline Phosphatase  
(suggests Osteomalacia)

**Vitamin D Deficiency**

**25 OH Vit D Treatment**

- < 10 ng/ml 50,000 U D2 BIW x 3 months
- 10-20 ng/ml 50,000 U D2 QW x 3 months
- 20-30 ng/ml 2,000 U D3 QD x 3 months

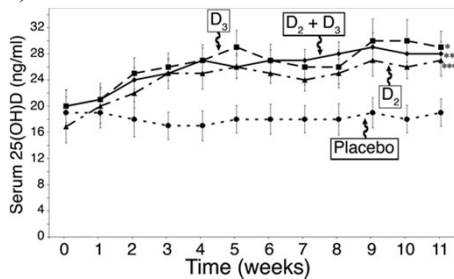
**Maintenance**

- Optimal Intake: 1,000 U QD
- Safe Intake: 2,000-4,000 U QD

Williams SE. Cleve Clin J Med 2022; 89:154-60.  
Holick M, N Engl J Med 2007; 357:266-81  
Dawson Hughes B, Am J Clin Nutr 2004; 80:1763-6S

**Vitamin D Sources (D2 or D3)**

68 Subjects: Age 18-84, End of Winter  
RCT: 1,000 U D2 or D3 or 500 D2/ 500 D3 or Placebo QD



THE JOURNAL OF  
CLINICAL  
ENDOCRINOLOGY  
& METABOLISM

Holick MF, J Clin Endocrinol Metab 2008; 93:677-81

**Case**

A 54 y.o. woman is being treated for osteoporosis. She has recently sustained 2 vertebral fractures on therapy. Calcium Intake: 1200 mg/d (diet plus supplements) Meds: Risedronate (5 years), Levothyroxine 125 mcg PE: Ht 5'5" Wt 162 lb. Tenderness over T-spine. Lab: Ca 8.8 mg/dl, 25 D 8 ng/ml, PTH 101 pg/ml

**Would you order additional tests?**

**Case**

A 54 y.o. woman is being treated for osteoporosis. She has recently sustained 2 vertebral fractures on therapy. Calcium Intake: 1200 mg/d (diet plus supplements) Meds: Risedronate (5 years), Levothyroxine 125 mcg PE: Ht 5'5" Wt 162 lb. Tenderness over T-spine. Lab: Ca 8.8 mg/dl, 25 D 8 ng/ml, PTH 101 pg/ml

Celiac Panel: strongly positive

**What do you recommend now?**

**Case**

A 54 y.o. woman is being treated for osteoporosis. She has recently sustained 2 vertebral fractures on therapy. Calcium Intake: 1200 mg/d (diet plus supplements) Meds: Risedronate (5 years), Levothyroxine 125 mcg PE: Ht 5'5" Wt 162 lb. Tenderness over T-spine. Lab: Ca 8.8 mg/dl, 25 D 19 ng/ml, PTH 101 pg/ml Celiac Panel: strongly positive

Gluten free diet recommended and explained.

She requests vitamin D intake through "natural" sources.

**What do you advise?**

### Vitamin D Sources

Natural Sources	Vitamin D Content
<b>Salmon</b>	
Fresh, Wild (3.5 oz)	600-1000 U D3
Fresh, Farmed (3.5 oz)	100-250 U D3 or D2
Canned (3.5 oz)	100-600 U D3
Sardines, Canned (3.5 oz)	300 U D3
Mackerel, Canned (3.5 oz)	250 U D3
Tuna, Canned (3.5 oz)	230 U D3
Cod Liver Oil (1 tsp)	400-1000 U D3
Egg Yolk	20 U D3 or D2
<b>Shiitake Mushrooms</b>	
Fresh (3.5 oz)	100 U D2
Sun-dried (3.5 oz)	1600 U D2
Sunlight/UVB (0.5 MED*)	3000 U D3

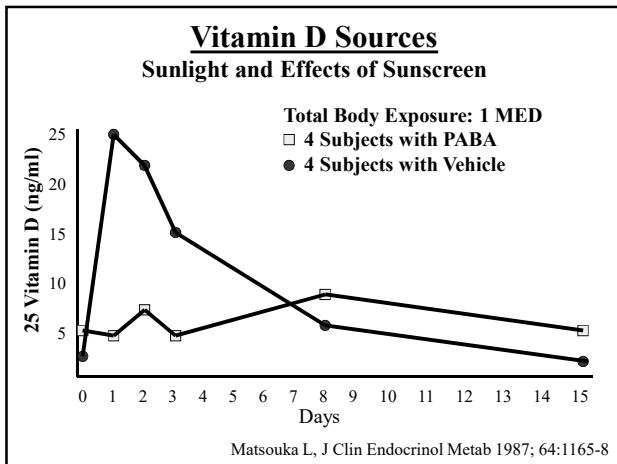
\* MED = Minimal Erythematous Dose  
Arm + Leg exposure to sunlight for 5-10 minutes

Holick M, N Engl J Med 2007; 357:266-81

### Vitamin D Sources

Fortified Foods	Vitamin D Content
Milk (fortified) (8 oz)	100 U D3
OJ (fortified) (8 oz)	100 U D3
Yogurt (fortified) (8 oz)	100 U D3
Infant Formulas (8 oz)	100 U D3
Cereals (fortified) (Serving)	100 U D3
Cheese (fortified) (3 oz)	100 U D3
Margarine (fortified) (3.5 oz)	430 U D3
Butter (fortified) (3.5 oz)	50 U D3

Holick M, N Engl J Med 2007; 357:266-81



### Vitamin D Sources Sunlight and Various Effects

Cause	Vitamin D Synthesis
<b>Sunscreen</b>	
SP8	↓ 92.5%
SP15	↓ 99%
<b>Pigmentation</b>	
	↓ 99%
<b>Ageing (age 70)</b>	
	↓ 75%
<b>Season + Latitude</b>	
	> 35 Latitude (Atlanta), minimal Vitamin D from Nov – Feb of each year

Holick M, N Engl J Med 2007; 357:266-81

### Case

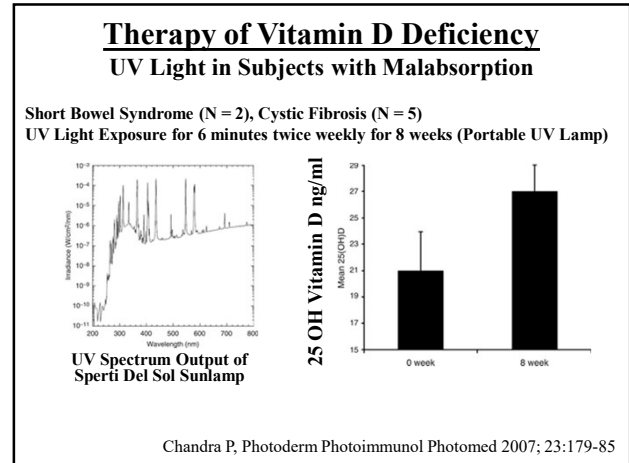
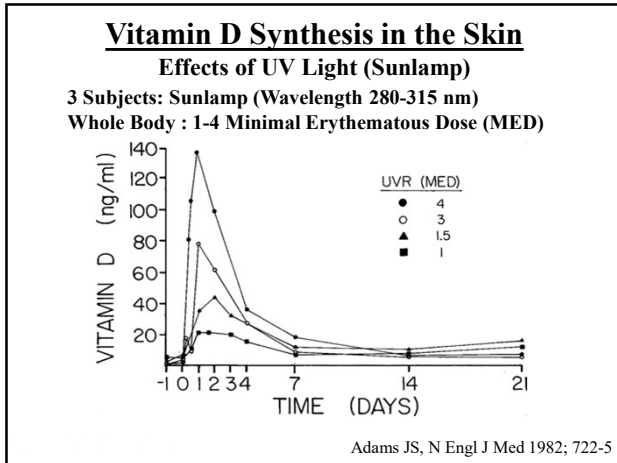
A 33 y.o. woman with malabsorption disorder.  
**PMH:** Crohn's disease since age 12  
 Multiple bowel resections, Colectomy  
**Meds:** Calcium 2400 mg/day, 4 Multivitamins,  
 Prednisone 10 mg/day, Pentasa  
**PE:** Ht 5'2" Wt 102 lb. Otherwise normal  
**Lab:** Calcium 8.6 mg/dl 25 Vitamin D < 5 ng/ml  
**BMD:**

	T-score	Z-score
Spine (L2-L4)	-2.99	-2.25
Femoral Neck	-2.53	-1.87

How would you manage her vitamin D deficiency?

### 33 year old woman with malabsorption

Vitamin D Dose	25 Vitamin D	Calcium	PTH
Multivitamins 4/day	< 5 ng/ml	8.6 mg/dl	
50,000 U BIW	22 ng/ml	9.4 mg/dl	30 pg/ml
50,000 U TIW	19 ng/ml	9.3 mg/dl	
50,000 U 5/Wk	20 ng/ml	8.6 mg/dl	
50,000 U QD	30 ng/ml	9.7 mg/dl	
50,000 U QD	5 ng/ml	8.1 mg/dl	132 pg/ml
50,000 U QD x 4 + 100,000 U QD x 3	12 ng/ml	9.1 mg/dl	49 pg/ml
100,000 U QD	11 ng/ml	9.2 mg/dl	45 pg/ml
100,000 U QD x 4 + 150,000 U QD x 3	26 ng/ml	9.1 mg/dl	
100,000 U QD x 4 + 150,000 U QD x 3	42 ng/ml	9.8 mg/dl	
100,000 U QD x 4 + 150,000 U QD x 3	30 ng/ml	9.3 mg/dl	



### Therapy of Vitamin D Deficiency

Malabsorption

Malabsorption	Prevention and Maintenance
Oral Vitamin D	D2 (Ergocalciferol Rx) 50,000 U QW, QOD, QD or Higher as Needed
Sunlight / UVB Device	280-315 nm Wavelength

Holick M, N Engl J Med 2007; 357:266-81

### Therapy of Vitamin D Deficiency

IM Vitamin D Injection

**Injectable Vitamin D given under the supervision of health care professional.**

**Single-day dosing may be 15,000 micrograms (600,000 IU) of vitamin D.**

Mayo Clinic Website

<http://www.zalmo.com/vitamins.html>

- ### Summary of Osteoporosis Management
- **Diagnosis:** Fragility Fracture, T-score  $\leq$  -2.5, or FRAX Risk Criteria
  - **Evaluation:** Search for cause of secondary bone loss
  - **Treatment:** All patients with diagnosis of osteoporosis
  - **Lifestyle Measures:** Calcium + Vitamin D Nutrition, Exercise and Fall Prevention
  - **Medications:** Anti-Resorptive or Anabolic Drugs to Reduce Fractures

