Osteoporosis

- Literally "porous bones," a skeletal disorder characterized by low bone mass and structural deterioration of bone tissue, with increase in susceptibility to fragility fracture.
- Multifactorial: genetic, hormonal, metabolic, mechanical and immunological factors.
- 75% percent of hip, spine and distal forearm fractures occur among those 65 years or older
- Roughly 30% of people over age 65 fall annually, with 10-15% of these falls resulting in fracture

Risk Factors

- Personal history of fracture after age 50
- Low bone density
- Female
- Thin and/or having a small frame
- Advanced age
- Family history of osteoporosis
- Estrogen deficiency, especially early or surgical menopause, amenorrhea
- Low lifetime calcium intake
- Use of certain medications
- Low testosterone levels in men
- Inactive lifestyle

Who Should Get a DXA?

Indications for BMD testing

Consider BMD testing in the following individuals:

- Women age 65 and older and men age 70 and older, regardless of clinical risk factors
- Younger postmenopausal women, women in the menopausal transition, and men age 50 to 69 with clinical risk factors for fracture
- Adults who have a fracture at or after age 50
- Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids in a daily dose ≥25 mg prednisone or equivalent for ≥3 months) associated with low bone mass or bone loss

DXA Scan

<table>
<thead>
<tr>
<th>T-score Description</th>
<th>BMD Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>BMD ≥ -1.0</td>
</tr>
<tr>
<td>Low bone mass (osteopenia)</td>
<td>BMD &gt; -2.5 and &lt; -1.0</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>BMD ≤ - 2.5</td>
</tr>
<tr>
<td>Severe (established) osteoporosis</td>
<td>BMD ≤ - 2.5 with history of fragility fracture</td>
</tr>
</tbody>
</table>

T-scores are based on the NHANES reference values for women aged 20-29 years. The same absolute values are used in men.

Guidance in the US

Consider FDA-approved medical therapies in postmenopausal women and men aged 50 years and older, based on the following:

- **A hip or vertebral** (clinical or morphometric) fracture
- **T-score ≤ -2.5** at the femoral neck or spine after appropriate evaluation to exclude secondary causes
- **Low bone mass** (T-score between -1.0 and -2.5 at the femoral neck or spine) and a **10-year probability of a hip fracture ≥ 3%** or a **10-year probability of a major osteoporosis-related fracture ≥ 20%** based on the US-adapted WHO FRAX algorithm
Height Loss

• Wisconsin study found prospective height loss is effective tool for identifying patients with vertebral fractures, low BMD, and vitamin D deficiency.

• Positive likelihood ratios for detecting vertebral fractures were:
  • 1.73 with 2 cm of height loss
  • 2.35 with 3 cm of height loss
  • 2.89 with 4 cm of height loss (1.57 inches)

• If significant height loss is present, the high positive likelihood ratios support a further workup.

Mikula AL, et al. Validity of height loss as a predictor for prevalent vertebral fractures, low bone mineral density, and vitamin D deficiency Osteoporosis Int 2017; 10.1007/s00198-017-3937
Bisphosphonates

• Most commonly prescribed medication for prevention and treatment of osteoporosis.
• Antiresorptive therapies reduce fracture risk by inhibiting osteoclasts, reducing bone turnover and increasing bone mass.
• Meta-analyses consistently show benefit over placebo, particularly for lowering risk of vertebral/hip fracture, in those at high risk.
• Bisphosphonates may cause dyspepsia, nausea, esophagitis and abdominal pain.

Bisphosphonates for Fracture Prevention in Post-Menopausal Women With Prior Fractures or With Very Low Bone Density (NNT = 100)

In Summary, for those who took the bisphosphonates:

<table>
<thead>
<tr>
<th>Benefits in NNT</th>
<th>Harms in NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 1 in 20 were helped (vertebral fracture prevented)</td>
<td>• A small number were harmed</td>
</tr>
<tr>
<td>• 1 in 100 were helped (hip fracture prevented)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Benefits in Percentage</th>
<th>Harms in Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 94% saw no benefit after 3 years of treatment</td>
<td>• A small percentage were harmed</td>
</tr>
<tr>
<td>• 5% avoided a vertebral fracture</td>
<td></td>
</tr>
<tr>
<td>• 3% avoided a hip fracture</td>
<td></td>
</tr>
</tbody>
</table>
Bisphosphonates for Fracture Prevention in Post-Menopausal Women Without Prior Fractures

In Summary, for those who took the bisphosphonates:

<table>
<thead>
<tr>
<th>Benefits in NNT</th>
<th>Harms in NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• None were helped (fracture prevented after 3 years of medicine)</td>
<td>• A small number were harmed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Benefits in Percentage</th>
<th>Harms in Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 100% saw no benefit after 3 years of treatment</td>
<td>• A small percentage were harmed</td>
</tr>
</tbody>
</table>

Impact on Bone

- Bisphosphonates suppress bone resorption that occurs during normal healing process, delaying bone healing.
- Osteonecrosis of jaw is a serious adverse event associated with bisphosphonate use.
  - Exposed bone in the maxillofacial region that is present for 8 weeks or more
  - Current or previous bisphosphonate use
  - No history of radiation therapy to the jaw.
- Risk factors: older than 65 years, periodontitis, prolonged use of bisphosphonates (for more than 2 years), smoking, wearing dentures, and diabetes.

Osteonecrosis of Jaw after Tooth Extraction in Osteoporotic Patients on Oral Bisphosphonates

• Clinical records 320 osteoporotic patients who underwent tooth extraction while receiving oral bisphosphonates reviewed.
• All patients had healing period > 6 months following the extractions.
• 11 patients developed bisphosphonate related ONJ (3.44%) incidence
• Patients on ibandronate showed highest incidence rate (5.0%); however, no statistically significant difference found according to the drug type.
• The incidence of BRONJ increased with age, was greater in the mandible than the maxilla, and associated with a duration of administration of more than 3 years.


Atypical Femur Fractures

• Atypical femur fractures are rare but serious condition associated with use of bisphosphonates.
• Among women 68 years and older, treatment with bisphosphonate > 5 years associated with an increased risk of subtrochanteric or femoral shaft fractures.
• Bisphosphonates must be discontinued but ongoing metabolic management in the form of calcium and/or vitamin D supplements is advisable.
• Teriparatide (Forteo – parathyroid recombinent) therapy alternative treatment, very low bone density with fractures, or due to steroid use.
• Denosumab (Prolia, Xgeva) medication alternative, especially in reduced kidney function.

United States Preventive Services Task Force recommended against the use of estrogen/progestin for prevention of osteoporosis in women. Each woman must work with her practitioner individually on this question.

Table 1. Estimated Event Rate Differences Associated With the Use of Oral Estrogen and Progestin in Postmenopausal Women Compared With No Treatment

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Event Rate Difference per 10 000 Person-Years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events Prevented, n (95% CI)</td>
</tr>
<tr>
<td>Benefits</td>
<td></td>
</tr>
<tr>
<td>Total fractures</td>
<td>46 (29 to 63)</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>6 (1 to 10)</td>
</tr>
<tr>
<td>Harms</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>9 (2 to 15)</td>
</tr>
<tr>
<td>Deep venous thrombosis</td>
<td>12 (6 to 17)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>3 (4 to 14)</td>
</tr>
<tr>
<td>Invasive breast cancer incidence</td>
<td>8 (3 to 14)</td>
</tr>
<tr>
<td>Gallbladder disease</td>
<td>20 (11 to 29)</td>
</tr>
<tr>
<td>Dementia</td>
<td>22 (5 to 39)</td>
</tr>
<tr>
<td>Self-reported urinary incontinence</td>
<td>872 (591 to 1153)</td>
</tr>
</tbody>
</table>
Healthy Bones Start Early!

• Growth in bone size and strength happens during childhood and is not completed until roughly 25 years of age.
• The bone mass attained early in life is perhaps the most important determinant of lifelong skeletal health.

Exercise

• Physical activity and mechanical loading build peak bone mass, beginning in pre-pubertal years.
• Exercise consistently shown to prevent or reverse bone loss in the lumbar spine and femoral neck.
• Bone Estrogen Strength Training Study found postmenopausal women receiving 800 mg/d calcium citrate + structured exercise, increased muscle mass by 11-21% and BMD by ~2%.
• Review 37 studies found physical exercise has a positive impact on muscle mass and function in those aged 60 years and older.

Strength and Balance Training Programs for Preventing Falls in the Elderly (NNT=11)

In summary, for at-risk elderly community dwellers who used balance and strength training:

<table>
<thead>
<tr>
<th>Benefits in NNT</th>
<th>Harms in NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 1 in 11 at-risk elderly were helped (avoid suffering a fall over a one year period)</td>
<td>• None were harmed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Benefits in Percentage</th>
<th>Harms in Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 91% saw no benefit</td>
<td>• 0% were harmed</td>
</tr>
</tbody>
</table>


Tai Chi

• Multiple studies show tai chi reduces the *risk of falls* in elders, post-stroke, and Parkinson’s.
• Systematic review found effective for relieving pain and improving physical function in those with osteoarthritis.
• Effect on bone mineral density in osteoporosis is difficult to assess given poor quality of studies.

Exercise and Protein

• Risk for sarcopenia increase as we age, increasing frailty and fall risk.

• **Protein intake and physical activity** are main anabolic stimuli for muscle protein synthesis.

• European guidelines recommend **20-25 grams high quality protein with each meal for women over age 50** with regular physical activity/exercise 3-5 times/week.


Protein and Fracture Risk

• Framingham Osteoporosis Study found **higher protein intakes** (60-83g/d versus 46g/d) in elders (mean 75 years) associated with a **37% decreased risk of hip fracture**.

• Women's Health Initiative found **20% increase in protein intake improved bone mineral density** and marginally lowered forearm fracture risk.

• **Protein intake and physical activity** are main stimuli for muscle protein synthesis and maintenance of bone strength.


Protein Intake and Fracture in Men

• **Osteoporotic Fractures in Men Research** (5,875 men; mean age 73.6 yrs), higher protein intake associated with **8% decreased risk of major osteoporotic fracture**.
• Increased dairy protein and non-dairy animal protein associated with **20% and 16% decreased risk of hip fracture**.
• **Plant protein not associated** with decreased risk of hip fracture.
• **Total protein** was associated with a **16% decreased risk of hip fracture but not clinical spine fracture.**
• Caution with high protein in those with **severe kidney disease.**

Langsetmo L, et al. The Association Between Protein Intake by Source and Osteoporotic Fracture in Older Men: A Prospective Cohort Study. *J Bone Miner Res* 2017; Mar;32(3):592-600

### Protein Rich Foods

<table>
<thead>
<tr>
<th>Food</th>
<th>Portion Size</th>
<th>Protein (g) (approximate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meat, fish, or poultry</td>
<td>75g (2 1/2 oz) / 125 mL (1/4 cup)</td>
<td>21</td>
</tr>
<tr>
<td>Firm tofu</td>
<td>150g / 175 mL (4% cup)</td>
<td>21</td>
</tr>
<tr>
<td>Eggs, chicken</td>
<td>2 large</td>
<td>13</td>
</tr>
<tr>
<td>Cheese</td>
<td>50 g (1 1/4 oz)</td>
<td>12</td>
</tr>
<tr>
<td>Fortified soy beverage</td>
<td>250 mL (1 cup)</td>
<td>6.85</td>
</tr>
<tr>
<td>Cooked dried beans, peas, or lentils</td>
<td>175 mL (4% cup)</td>
<td>12</td>
</tr>
<tr>
<td>Cow’s milk</td>
<td>250 mL (1 cup)</td>
<td>9</td>
</tr>
<tr>
<td>Yogurt</td>
<td>175 mL (4% cup)</td>
<td>8</td>
</tr>
<tr>
<td>Peanut butter or other nut spread</td>
<td>30 mL (1/2 tsp)</td>
<td>8</td>
</tr>
<tr>
<td>Nuts or seeds</td>
<td>60 mL (1/4 cup)</td>
<td>7</td>
</tr>
<tr>
<td>Bread</td>
<td>1 slice (35g)</td>
<td>3</td>
</tr>
<tr>
<td>Cereals, cold</td>
<td>30 g</td>
<td>3</td>
</tr>
<tr>
<td>Cereals, hot</td>
<td>175 mL (4% cup)</td>
<td>3</td>
</tr>
<tr>
<td>Pasta or rice</td>
<td>125 mL (4% cup)</td>
<td>3</td>
</tr>
<tr>
<td>Vegetables</td>
<td>125 mL (1/2 cup) or 250 mL (1 cup) lettuce</td>
<td>2</td>
</tr>
<tr>
<td>Fruit</td>
<td>1 fruit or 125 mL (1/4 cup)</td>
<td></td>
</tr>
</tbody>
</table>

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Inflammation

- Osteoporosis may be driven, in part, by chronic low grade inflammation.
- Pro-inflammatory cytokines (IL-1, IL-6, TNF-alpha), accelerate bone loss via activation of osteoclasts, inhibit collagen production in osteoblasts and enhance breakdown of the extracellular matrix.
- A large study of older women found almost a 50% increased risk of hip fracture in those with highest levels of inflammatory markers.

Omega 3 Fatty Acids

- In animals, marine omega 3 attenuates bone loss associated with estrogen decline; EPA enhances calcium absorption, reduces calcium excretion and increases calcium deposition in bone.
- Findings from observational and randomized controlled trials suggest higher fatty fish intake strongly linked with reduced risk of fragility fracture and improving muscle health.
Tea
(Camellia sinensis)

- Tea drinkers (black and green) have been consistently shown to have higher bone density, improved hip structure and less bone density loss in both men and women.


Coffee and Bone Health

- Meta-analysis 10 prospective cohort studies with 205,930 participants showed no significant association between coffee intake and risk of hip fracture.
- Swedish study 61,433 women born in 1914-1948, followed up from 1987-2008. High coffee intake (≥4 cups daily) versus low intake (<1 cup daily) was associated with a 2%-4% lower bone density, depending on site that did not translate into an increased risk of fracture.

Alcohol

• Moderate alcohol intake has no known negative effect on bone and may be associated with slightly higher bone density and lower risk of fracture in postmenopausal women.
• However, more than two drinks per day for women or three drinks a day for men may be detrimental to bone health and increases the risk of falling.


What About Drug Induced Nutrient Deficiencies?

• Drug-induced nutrient deficiencies are an important yet poorly appreciated category of adverse drug reactions.
• Some drugs may cause marginal nutrient deficiencies with serious consequences.
• The major risk factors for developing a drug induced nutrient deficiency is the lack of awareness by the prescribing clinician and long duration of drug therapy.
Drug Induced Osteoporosis

- 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


Glucocorticoids

- Used to treat wide range of diseases (respiratory, autoimmune, inflammatory, malignancies, dermatological, etc.)
- Reduces intestinal calcium absorption and increases urinary excretion; decreases testosterone in men and estrogen in women causing increased bone resorption. **Causes muscle weakness and atrophy.**
- Glucocorticoid-induced osteoporosis most common cause of secondary osteoporosis and confers a substantial risk for future fractures.
  - Daily dose: 2.5-7.5 mg/d RR hip fracture 1.77; vertebral fracture 2.59;
  - Daily dose > 7.5 mg/d RR hip fracture 2.27; vertebral fracture 5.18.

Proton Pump Inhibitors and Fracture

- FDA concluded patients taking high doses of PPIs and/or taking one year or more are at highest risk. Warning label mandated.
- Recent study of adverse event reporting at FDA showed that PPI also increases fracture of ribs and other sites.
- American Geriatrics Society recommends against use of PPIs for longer than eight weeks in older adults, except in high-risk patients, due to the potential risk of bone loss, fractures and C. difficile infection


Serotonin and Serotonin/Norepinephrine Reuptake Inhibitors

- SSRIs and SNRIs prescribed for depression, anxiety, peripheral neuropathy, fibromyalgia, PMS, and chronic musculoskeletal pain.
- Serotonin transporter found in all main types of bone cells, including osteoclasts, osteoblasts, and osteocytes. Dose and duration of SSRIs contribute to fracture risk (>3–5 years). May increase risk of falls.
- Canadian 10-year longitudinal study found SSRI and SNRI use increased fragility fractures in patients over 50.
- Meta-analysis 34 studies (>1 million patients) found 38% increased risk for vertebral fracture, 42% increased risk for nonvertebral fracture, and 47% increased risk for hip fracture.
- Ensure appropriate calcium and vitamin D supplementation and weight bearing activities. Currently no guidelines that deal with fracture prevention.

Calcium

- **Calcium** found in the bones and teeth of humans and animals in the form of calcium salts. Found in seashells and limestone—the word “calcium” is from Latin root for “lime.”
- Most abundant mineral in our body, roughly 99% stored in our bones, balance used to maintain healthy BP, nerve and muscle function.
- According to NHANES data, more than 50% of these populations do not get adequate calcium in their diet:
  - Children age 9-13
  - Girls 14-18
  - Women 51-70
  - People > 70 years old

<table>
<thead>
<tr>
<th>Life Stage</th>
<th>Age</th>
<th>Males (mg/day)</th>
<th>Females (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>0-6 months</td>
<td>200 (AI)</td>
<td>200 (AI)</td>
</tr>
<tr>
<td>Infants</td>
<td>6-12 months</td>
<td>260 (AI)</td>
<td>260 (AI)</td>
</tr>
<tr>
<td>Children</td>
<td>1-3 years</td>
<td>700</td>
<td>700</td>
</tr>
<tr>
<td>Children</td>
<td>4-8 years</td>
<td>1,000</td>
<td>1,000</td>
</tr>
<tr>
<td>Children</td>
<td>9-13 years</td>
<td>1,300</td>
<td>1,300</td>
</tr>
<tr>
<td>Adolescents</td>
<td>14-18 years</td>
<td>1,300</td>
<td>1,300</td>
</tr>
<tr>
<td>Adults</td>
<td>19-50 years</td>
<td>1,000</td>
<td>1,000</td>
</tr>
<tr>
<td>Adults</td>
<td>51-70 years</td>
<td>1,000</td>
<td>1,200</td>
</tr>
<tr>
<td>Adults</td>
<td>71 years &amp; older</td>
<td>1,200</td>
<td>1,200</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>14-18 years</td>
<td>-</td>
<td>1,300</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>19-50 years</td>
<td>-</td>
<td>1,000</td>
</tr>
<tr>
<td>Breast-feeding</td>
<td>14-18 years</td>
<td>-</td>
<td>1,300</td>
</tr>
<tr>
<td>Breast-feeding</td>
<td>19-50 years</td>
<td>-</td>
<td>1,000</td>
</tr>
</tbody>
</table>
Calcium and Vitamin D: Fracture

- Meta-analysis by National Osteoporosis Foundation: eight studies (n= 30,970 participants) found that all studies showed calcium plus vitamin D supplementation produced a statistically significant 15% reduced risk of total fractures and 30% reduced risk of hip fractures.


Contributors to Lower Calcium

- One of first signs of calcium deficiency is **muscle cramping**. Long term deficiency leads to poor bone development/loss of bone mineral density, numbness and tingling in the fingers, convulsions, lethargy, poor appetite, and abnormal heart rhythms.

- **Sodium**: high sodium intake increases urinary calcium excretion. 1,000 mg/d of calcium needed per 2,000 mg/d sodium intake.

- **High protein** intake increases calcium excretion BUT it also increases absorption, overall, a **neutral** effect.

- **Caffeine** very modestly increases urinary excretion (~3 mg loss)
Calcium Supplements

- **Calcium citrate or chelate** best for > 50 years or taking drugs to suppress stomach acid. No need to take with food

- Do not take calcium at the same time as other medications (thyroid, bisphosphonates, phenytoin, tetracycline)

- **ONLY supplement the difference between the calcium in your diet and what you need.**

---

**Calcium Calculator: A Quick Estimate**

<table>
<thead>
<tr>
<th>Food</th>
<th># Servings/Day</th>
<th>Estimated Calcium per serving, in mg</th>
<th>Calcium in mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk (8 ounces)</td>
<td>X 300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yogurt (6 ounces)</td>
<td>X 300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hard Cheese (1 ounce)</td>
<td>X 200</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soy milk, fortified (8 ounce)</td>
<td>X 300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orange juice, fortified (8 ounce)</td>
<td>X 300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tofu, firm calcium set (4 ounces)</td>
<td>X 300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All foods not included above</td>
<td>X 250</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Calcium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al for your gender and age group</td>
<td>Subtract total calcium from Al</td>
<td>Supplement this amount</td>
<td></td>
</tr>
</tbody>
</table>
Reach for the Prebiotics

- Prebiotics alter gut microbiome and increase in calcium absorption in adolescents and postmenopausal women and increase in BMD and strength in animal models.
- Prebiotic rich foods: garlic, onions, bananas, artichokes, asparagus, whole wheat, soybeans


Vitamin D

- Fat soluble vitamin (technically not a vitamin as it can be made from cholesterol in the skin upon exposure to UV light)
- Primary forms:
  - Vitamin D$_2$ (ergocalciferol) presents in plants
  - Vitamin D$_3$ (cholecalciferol) present in the liver, skin of animals
  - Vitamin D$_3$ $\rightarrow$ 25(OH)D (calcidiol) in the liver $\rightarrow$ 1,25(OH)$_2$D (calcitriol) in the kidneys
• **Deficiency** often more **severe in elders** due to environmental and biological factors.

• Limited time spent outdoors and **decreased synthesis of vitamin D in skin** makes it difficult to maintain adequate levels even with sun exposure.

• As aging advances, **intestinal resistance to 1,25(OH)2D impairs the uptake of calcium** and a decline in renal function reduces activation of vitamin D.

### Osteomalacia

• In adults, **vitamin D deficiency can cause osteomalacia (lower bone mineralization)**, which can lead to musculoskeletal pain, usually in the pelvis, shoulders or proximal muscles.

• **Pain increased by mild pressure on the sternum or anterior tibial bone are typical or suspected symptoms.**

• Vitamin D has been shown to **positively affect muscle strength, muscle size and neuromuscular performance.**

Endocrine Society Clinical Practice Guidelines for Vitamin D

- 90 million Americans have vitamin D levels less than 20 ng/mL
- 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 for vitamin D (without supervision):
  - 1,000 IU/day for infants to age 6 months
  - 1,500 IU/day for ages 6 months to 1 year
  - 2,500 IU/day ages 1 to 3 years
  - 3,000 IU/day for ages 4 to 8 years
  - 4,000 IU/day anyone older than 8 years


Fragility Fractures

- Fragility fractures associated with decreased quality of life, increased disability, more frequent hospital admission and an increased risk of mortality.
- While a multimodal approach is important for fall protection, vitamin D supplementation alone, or in combination with calcium, has been shown to significantly reduce the risk of falling in elders.

**Vitamin D**

- Most individuals should take 1,000-2,000 IU vitamin D3 per day with dinner
- Study found that **taking with fat increased serum levels by 32%** compared to when vitamin D was taken without fat.

To get 600 IU/d Vitamin D3:
- 3-4 ounces sockeye salmon, cooked
- 11.4 ounced water-packed tuna
- 26 oil-packed sardines
- 15 large eggs
- 5 cups fortified milk OR
- 30-45 ounces yogurt


---

**Vitamin K**

- Two main forms of vitamin K.
  - **Phyloquinone, or vitamin K1**, 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). Subtypes: MK4, MK7, etc.
Intestine

Ca\(^{2+}\)

Increases the uptake of Ca\(^{2+}\) and the production of osteocalcin.

Inactive Osteocalcin

Vitamin D3

Bone

Active Osteocalcin

Vitamin K2

Ca\(^{2+}\) Ca\(^{2+}\) Ca\(^{2+}\) Ca\(^{2+}\)

Co-factor for the enzymes that activates osteocalcin.

Calcium incorporated into bone.

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Vitamin K Review

- Calcium, vitamins D and K supplementation contribute independently and collectively to bone health.
- Beneficial role of vitamin K, particularly vitamin K2 as MK-7, in bone and cardiovascular health is reasonably well supported scientifically, with several preclinical, epidemiological, and clinical studies published over the last decade.


Magnesium

- Low magnesium associated with type 2 diabetes, metabolic syndrome, inflammation, high blood pressure, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer.
- 50% of U.S. population consumes less than the required amount of daily magnesium.
- Magnesium plays a structural role in bones, cell membranes and chromosomes.
- Magnesium required for the conversion of vitamin D to active form.
- Magnesium deficiency reduces number and function of osteoblasts and increases activity and number of osteoclasts.

Multivitamin

• A multivitamin can provide other nutrients important for bones:
  • Boron
  • Zinc
  • Copper
  • Manganese
  • Vitamin C

Summary

• The maintenance of healthy bones and muscles requires a lifetime of being physically active, consuming adequate amounts of protein, calcium, vitamins D and K, and a host of other minerals and trace minerals.
• Minimizing the risk of falls, particularly as we age is a key strategy (e.g., lights in bathroom at night, removal of throw rugs, cane, etc.)
• Medications should strongly be considered for those with a FRAX that indicates high risk for fracture.