# Protect Your Bones after Transplant or CAR T-cell Therapy

## Celebrating a Second Chance at Life
## Survivorship Symposium

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**Sarah Keller MD, MA**
Rheumatologist, Assistant Professor at the Cleveland Clinic Lerner School of Medicine

# Disclosures

- I have no financial disclosures.

# Agenda

- **Impact of BMT on bone health**
- Why osteoporosis and bone density loss matter
- How is osteoporosis diagnosed
- How to protect your bones
  - Regular bone density screening
  - Vitamin D and calcium supplementation
  - Weight-bearing and muscle-strengthening exercise
  - Optimization of lifestyle factors
  - Treatment in select patients

# Risk Factors for Bone Loss after Allogeneic BMT

- Induction and consolidation chemotherapeutic agents
- Glucocorticoids (e.g. dexamethasone, prednisone)
- Calcineurin inhibitors (e.g. tacrolimus, cyclosporine)
- Hypogonadism
- Total body irradiation
- Low body mass index (BMI)/rapid weight loss
- Prolonged immobilization
- Decrease in vitamin D/calcium
- Advanced age

*Transplant Int 2011 Sep;24(9):867-79;*
*Blood (2004) 103 (10): 3635–3643, J Bone Miner Res 1999 Mar; 14 (3): 342-50*

# Risk Factors for Bone Loss after Allogeneic/Autologous BMT

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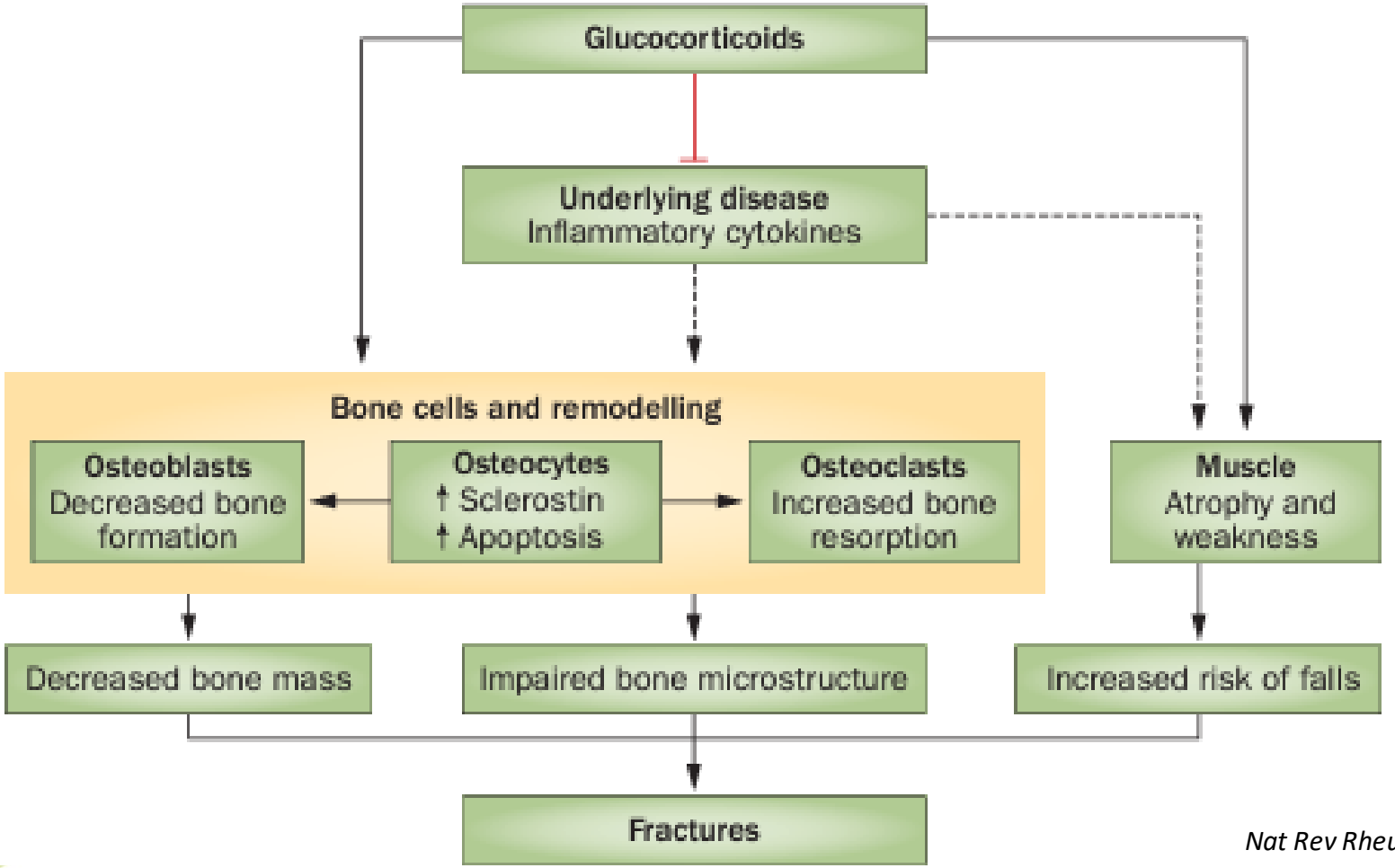
# Impact of BMT on Bone Health: Glucocorticoids




*Nat Rev Rheumatol. 2015 Feb;11(2):98-109.*

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# Why Osteoporosis and Bone Density Loss Matter

- Osteoporosis affects more than 10 million US adults (80% of whom are women)
- The direct cost is $17 billion; however, the indirect cost is far greater
- There are more than 2 million fractures annually
- By diagnosing osteoporosis and preventing fractures, we can increase patient survival, improve quality of life and decrease the large direct and indirect costs of this disease

*J Bone Miner Res. 2014 Nov;29(11):2520-2526*

# Osteoporosis and Bone Density Loss: Fractures

- A fracture occurs when a force (like a fall) is applied to osteoporotic bone
- The most dreaded osteoporotic fracture is the hip fracture
- Hip fractures are associated with increased morbidity and mortality, particularly in the first year following hip fracture

# Hip Fractures

- There is a 20% excess mortality during the first year following a hip fracture in women, and up to 50% excess risk of death in men
- Up to 40% of patients are no longer able to walk independently in the first year following hip fracture
- Up to 25% of patients are no longer able to live independently and require long-term care
- Up to 80% of patients are unable to carry out at least one independent activity of daily living following a hip fracture



*Am J Med. 1997;103(2A):12S-17S*

# Vertebral Compression Fractures

- The most common fractures in osteoporotic patients
- Like hip fractures, vertebral compression fractures are also associated with significant morbidity and mortality
- 20% of patients who have a vertebral fracture will have a recurrent vertebral fracture within 1 year, and up to 40% within 3 year
- Patients with a vertebral fracture are at double the risk for a subsequent hip fracture

*Bone. 2003;33(4):522-532, J Bone Miner Res. 1999;14(5):821-828, Osteoporosis International 2006: 17 (suppl 3); 365*

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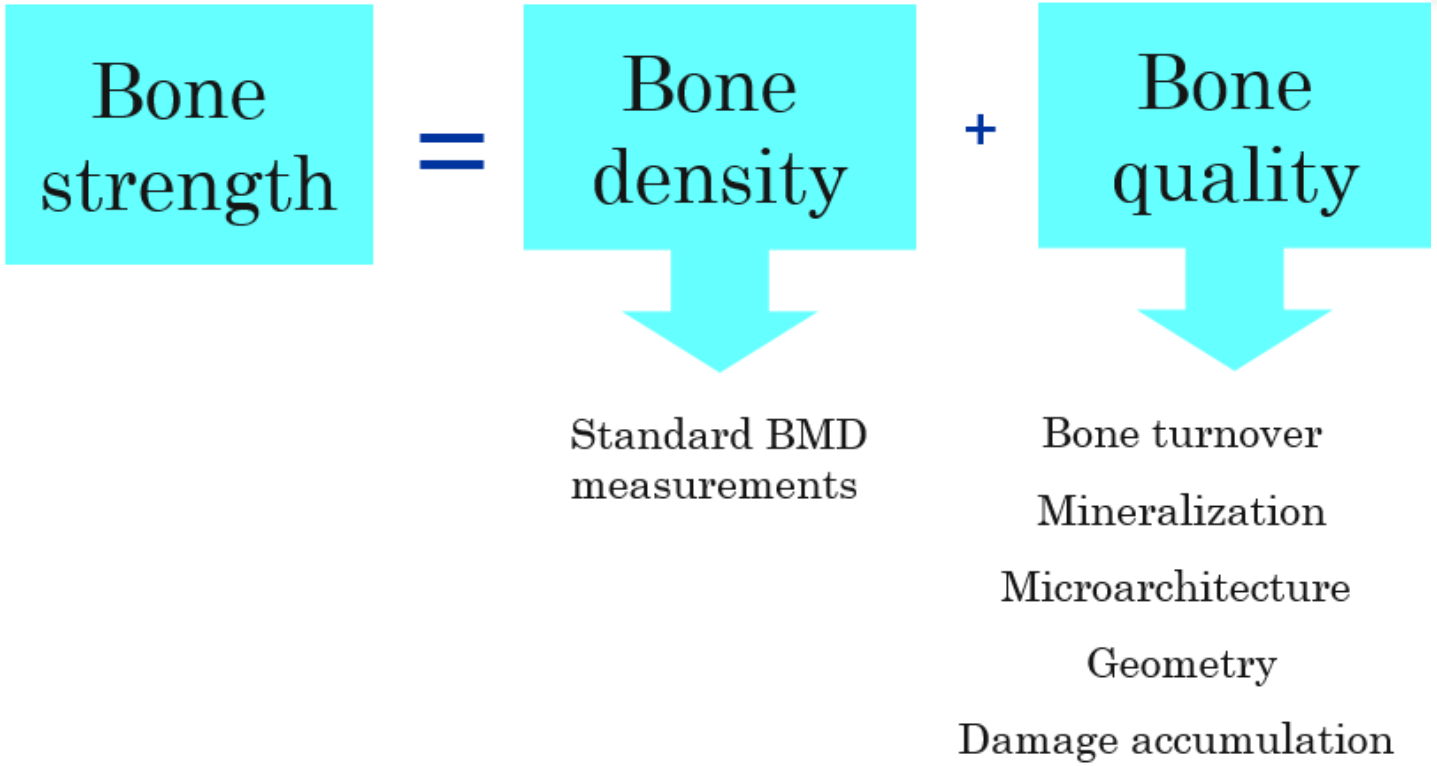
# Bone Density: Key Component of Bone Strength




*ARP, Advanced Rheumatology Course, Activity 16*

# Methods of Diagnosing Osteoporosis

- Bone mineral density (BMD) measurement: T-score ≤ -2.5
- Fragility fracture
  - Hip fracture (with or without BMD measurement)
  - Clinical vertebral, proximal humerus or pelvis fracture with osteopenia
- Incidental radiographic vertebral fracture
- FRAX score
  - Hip fracture risk ≥ 3% or major osteoporosis fracture ≥ 20%

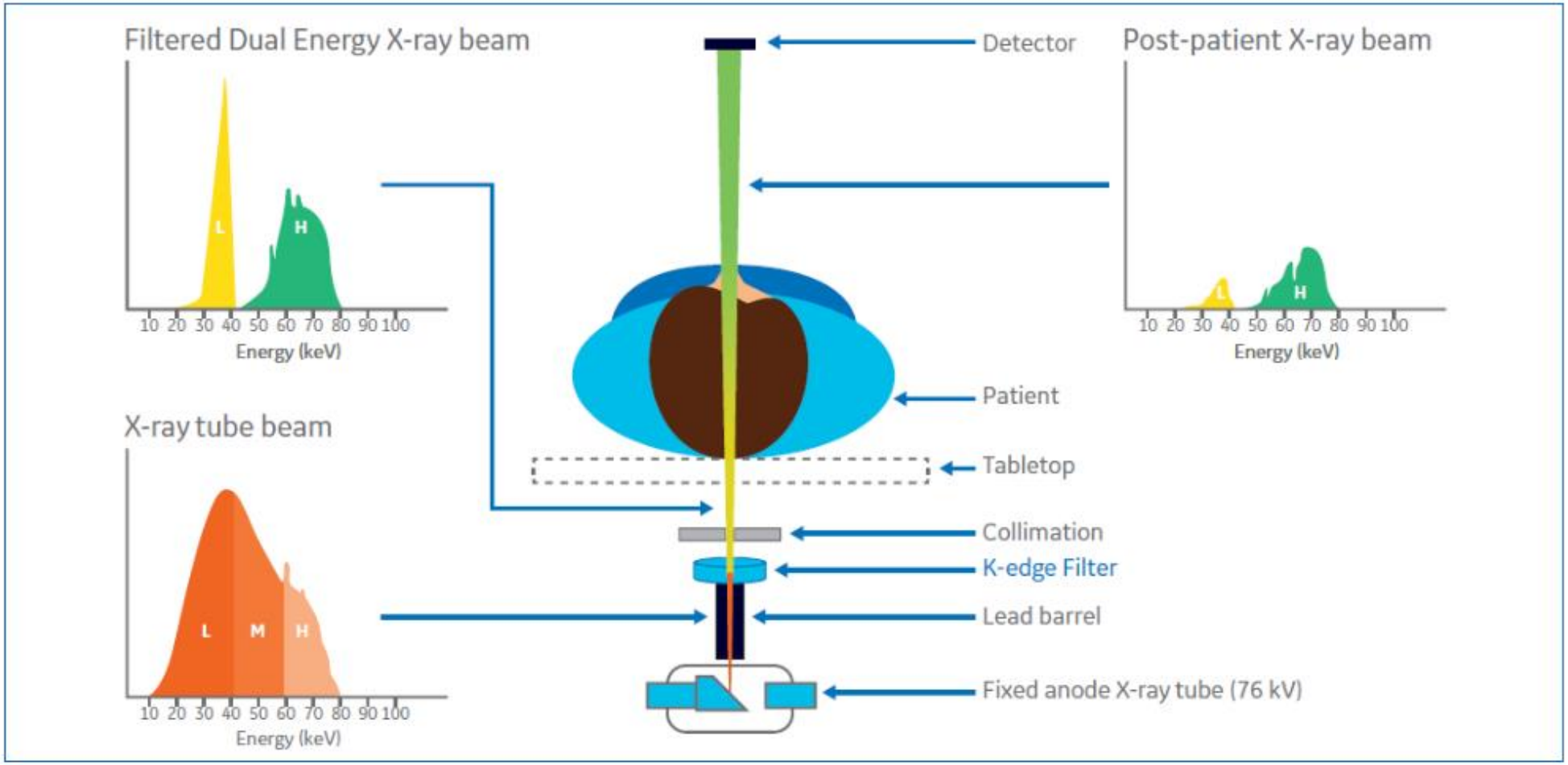
*Osteoporos Int (2014) 25:1439–1443*

# Dual Energy X-ray Absorptiometry (DXA) Scan

- DXA scan measures bone density
- DXA scanner is a radiographic machine that produces high energy and low energy x-ray beams
- These beams are passed through the patient
- X-rays that are absorbed by bone are measured for each beam
- Bone density is determined based on energy differences between the two beams
- Radiation energy is detected and converted into an areal density ($g/cm^2$)

*BMJ 2002 Aug 31; 325(7362): 484*

# How DXA is Obtained




*BMJ. 2002 Aug 31; 325(7362): 484*

# When to Screen: General Population

- Screening guidelines vary
- Most groups recommend screening in women > 65
- National Osteoporosis Foundation:
  - Women > 65 and men > 70
  - Post-menopausal women and men 50-69, depending on risk factor profile
  - Post-menopausal women and men 50-69 with a fragility fracture as an adult

*Cosman et al. Clinician's Guide to Prevention and Treatment of osteoporosis. 2014. volume 25 pp 2359-2381. Developed by an expert committee of the Natonal Osteoporosi Foundation (NOF)*

# When to Screen: Daily Glucocorticoid Use

- Lower threshold to screen patients on glucocorticoids (GC)
- Recommendations vary by group
- American College of Rheumatology 2017 guidelines:
  - Perform fracture risk assessment of all patients on GC at the start of treatment
  - Screen adults ≥ 40 years by obtaining DXA within 6 months of starting GC
  - Screen adults < 40 years with by obtaining DXA if history of previous osteoporosis or other significant risk factors

*Arthritis Rheumatol. 2017 Aug;69(8):1521-153*

# When to Screen: Transplant Population

- Ideally, a DXA should be obtained prior to transplant
- Rate of bone density loss is highest in the first 3-6 months after BMT
- Should get a repeat scan at least every two years if your bone density is in the
  - osteoporosis range (T-score ≤ -2.5)
  - osteopenia range (T-score between -1.0 and -2.5)

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# Get Bone Density Scans Every 2 Years

- Make sure your doctor or provider orders a bone density scan, if not before your transplant, then as soon as possible after transplant
- Follow up with regular bone density (DXA) scans every 2 years if your bone density is in the osteoporotic or osteopenic range
- If you are on steroids, you can get a DXA every year
- Many transplant centers work closely with a metabolic bone clinic, but if not, request to see an expert in metabolic bone health

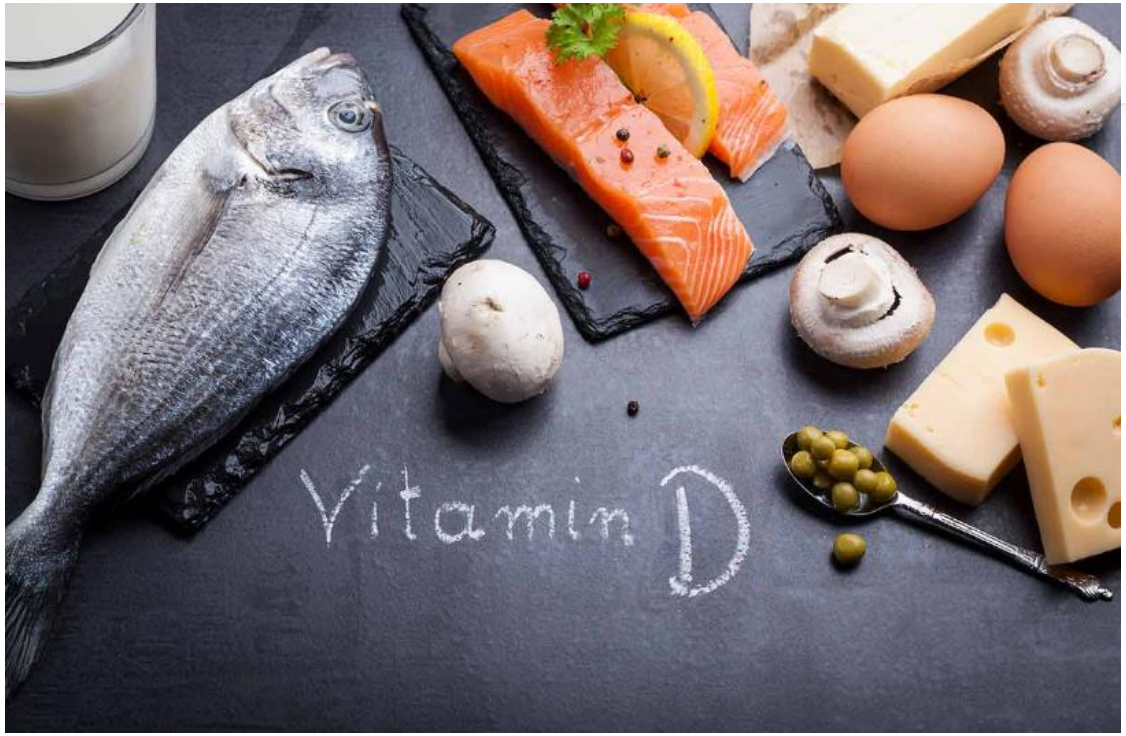
# Optimize Calcium Intake

- 1200-1500 mg of daily calcium (including dietary intake + supplement)
- Total daily intake may include both dietary sources (from dairy and leafy green vegetables) and supplements if necessary
- Calcium intake from supplements should be split at least twice a day to maximize absorption

# Optimize Vitamin D Intake

Sunlight Diet Supplements


- The NOF (National Osteoporosis Foundation) recommends 800 to 1000 international units (IU) of vitamin D per day for adults aged 50 years and older
- Aim for vitamin D 25-OH D level of ≥30


Vitamin D


Vitamin d Foods
JustChartIt.com
Salmon
450 to 500 IU
Vitamin d
Tuna
200 to 250 IU
Vitamin d
Fortified Milk
100 to 120 IU
Vitamin d
Egg
20 to 44 IU
Vitamin d
Button Mushrooms
7 IU
Vitamin d
Shiitake Mushrooms
18 IU
Vitamin d
Portobello Mushrooms
10 IU
Vitamin d
Maitake Mushroom
1123 IU
Vitamin d
Fortified Tofu
100 IU
Vitamin d
Fortified Bread
20 to 40 IU
Vitamin d
Fortified Yogurt
80 to 116 IU
Vitamin d
Beef Liver
36 IU
Vitamin d
Sardines
42 - 70 IU
Vitamin d
Mackerel
998 IU
Vitamin d
Chicken
2 IU
Vitamin d
Beef
6 IU
Vitamin d
JustChartIt.com

# Weight-Bearing and Muscle-Strengthening Exercise

- Weight-bearing Exercise:
  - Running/jogging
  - Walking
  - Hiking
  - Jumping rope/jumping jacks
  - High-impact aerobics (step, Zumba)
  - Dancing
  - Stair climbing
- Muscle-strengthening Exercise
  - Lifting free weights
  - Using weight machines
  - Using elastic exercise bands
  - Lifting your own body weight (squats, lunges)
  - Functional moving (standing from sitting position)
  - Balance exercises

# How Much Exercise?

- Aim for at least 3 times per week
- Start at a low level and progress slowly
- Exercising too vigorously may increase risk of injury, including fractures

# Activities to Avoid

- Activities that:
  - put excessive force on forward flexion of the spine
    - Certain yoga or Pilates positions where you bend forward
  - increase the risk of falling
  - require sudden, forceful movement
  - require forceful twisting motion (unless the person is accustomed to such movement)
  - put undue force/pressure on the spine
    - Horse-back riding, extreme skiing, bungee jumping
- Be careful not to lift too much

# Modify Risk Factors

- Advanced age
- Female sex
- Menopause
- Prior fracture
- Family history of osteoporosis and/or fracture
- Low body weight, weight loss
- Smoking, excessive alcohol and caffeine consumption
- Low sunlight exposure and/or low vitamin D intake
- Low calcium intake
- Medications (glucocorticoids, androgen deprivation agents, aromatase inhibitors, proton pump inhibitors etc.)

*Bone. 2004; 34:195-202*
*J. Bone Miner Res. 2005; 20: 1813-1819*
*Slide modified from ISCD "Use of Bone Densitometry for the Diagnosis of Osteoporosis*

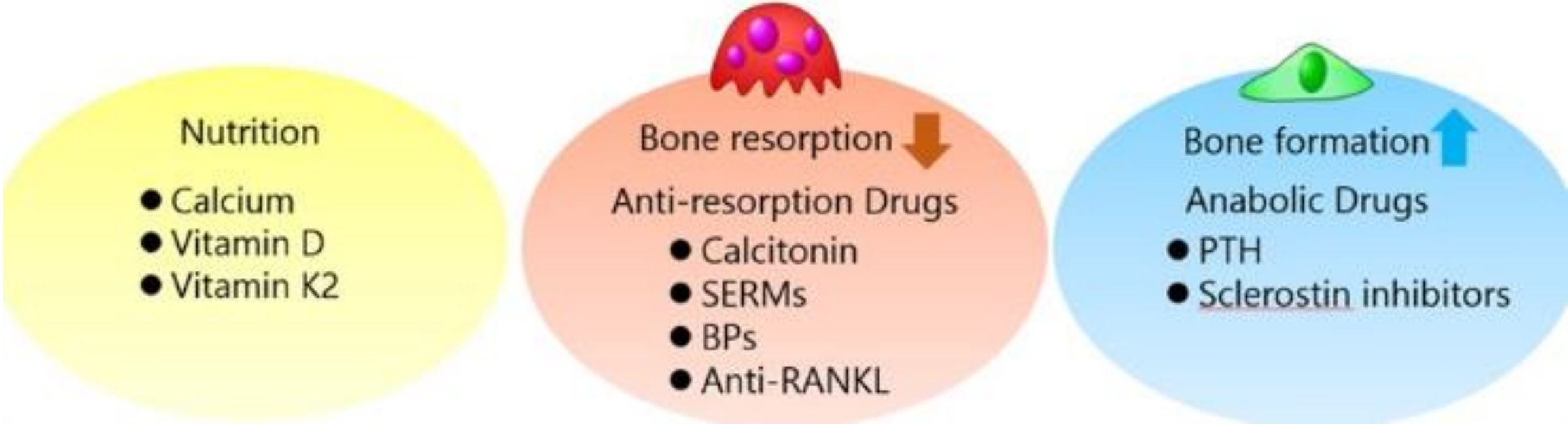
# Some People Require Treatment

- Bone mineral density (BMD) measurement: T-score ≤ -2.5
- Fragility fracture
  - Hip fracture
  - Clinical vertebral, proximal humerus or pelvis fracture with osteopenia
- Incidental radiographic vertebral fracture
- Increased FRAX
- Long term prednisone use

# Some People Require Treatment: Chronic Prednisone

- If you are on chronic prednisone (for more than 3-6 months) you may need to be treated with anti-osteoporosis medications
- Lack of consensus about which patients should receive therapy to prevent bone loss and fractures
- There are some guidelines for clinicians
- Prednisone > 7.5 mg daily for 3-6 months
- Duration of therapy may be as short as one year

# Osteoporosis Medication



# Effect of Osteoporosis Medications

| Medication | Does/Frequency | Fracture Risk Reduction (in post-menopausal osteoporosis) | Comments |
|---|---|---|---|
| Bisphosphonates | | | |
| Alendronate | 70 mg by mouth weekly | 35-65% Vertebral<br>23% Non-vertebral<br>45-55% Hip | Can cause hypocalcemia and esophagitis. |
| Risedronate | 35 mg by mouth weekly | 41% Vertebral<br>39% Non-vertebral<br>30% Hip | Can cause hypocalcemia and esophagitis. |
| Ibandronate | 150 mg by mouth monthly | 62% Vertebral | Can cause hypocalcemia and esophagitis. No evidence of hip fracture protection |
| Zoledronate | 5 mg IV annually | 70% Vertebral<br>25% Non-vertebral<br>41% Hip | Can cause hypocalcemia. 32% have an acute phase reaction with their first infusion consisting of fever, myalgias and flu-like symptoms lasting 24-72 hours [55] |

# Effect of Osteoporosis Medications

| Medication | Does/Frequency | Fracture Risk Reduction (in post-menopausal osteoporosis) | Comments |
|---|---|---|---|
| Raloxifene<br>Evista | 60 mg by mouth daily | 30% Vertebral | No data for hip fracture prevention |
| Denosumab<br>Prolia and Xgeva | 60 mg subcutaneously every 6 months | 68% Vertebral<br>20% Non-vertebral<br>40% Hip | Can cause hypocalcemia and musculoskeletal pain. Cannot be stopped/delayed due to increased risk of multiple rebound vertebrail compression factors [58] |
| Teriparatide | 20 mcg subcutaneously daily x 2 years | 65% Vertebral<br>40% Non-vertebral | Contraindicated if history of radiation. Must be followed by anti-resorptive therapy to avoid loss of bone marrow density gains |
| Abaloparatide | 80 mcg subcutaneously daily x 2 years | 86% Vertebral<br>43% Non-vertebral | Contraindicated if history of radiation. Must be followed by anti-resorptive therapy to avoid loss of bone mineral density gains |
| Romosozumab<br>Evenity | 210 mg subcutaneously Monthly x 1 year | 73% Vertebral | Contraindicated if history of heart attack or stroke in the past yaer<br>Must be followed by anti-resorptive therapy to avoid loss of bone mineral density gains |

# Summary

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# Questions?

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# Let Us Know How We Can Help You


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