Evaluation and Management of Osteoporosis

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No disclosures

Introduction to Osteoporosis

Osteoporosis: a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and increased risk of fracture

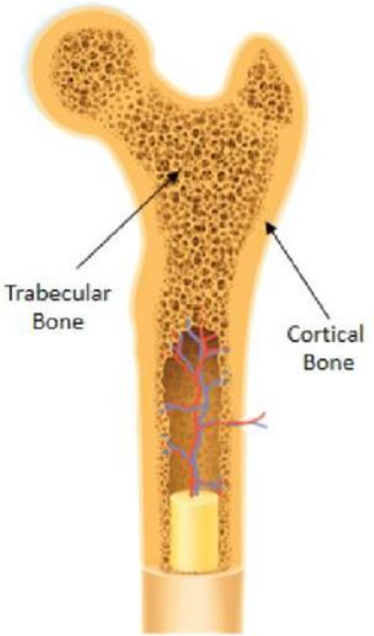
Diagnosis of osteoporosis can be made clinically in presence of fragility fracture, even in absence of low bone mineral density on imaging

Fragility fracture: a fracture sustained from force similar to a fall from a standing position or less that would not have occurred in healthy bone, except fractures of the skull, face, fingers, and toes

THE FUNCTION OF THE SKELETON DEPENDS ON THE PROPERTIES OF TRABECULAR AND CORTICAL BONE

Trabecular Bone

- A sponge-like network of delicate plates of bone known as trabeculae[1,2]
- 20% of skeletal mass[3]
- Essential functions
  - Mineral metabolism[4]
  - Strength and elasticity[4,5]
- Higher turnover rate compared to cortical bone[6,7]

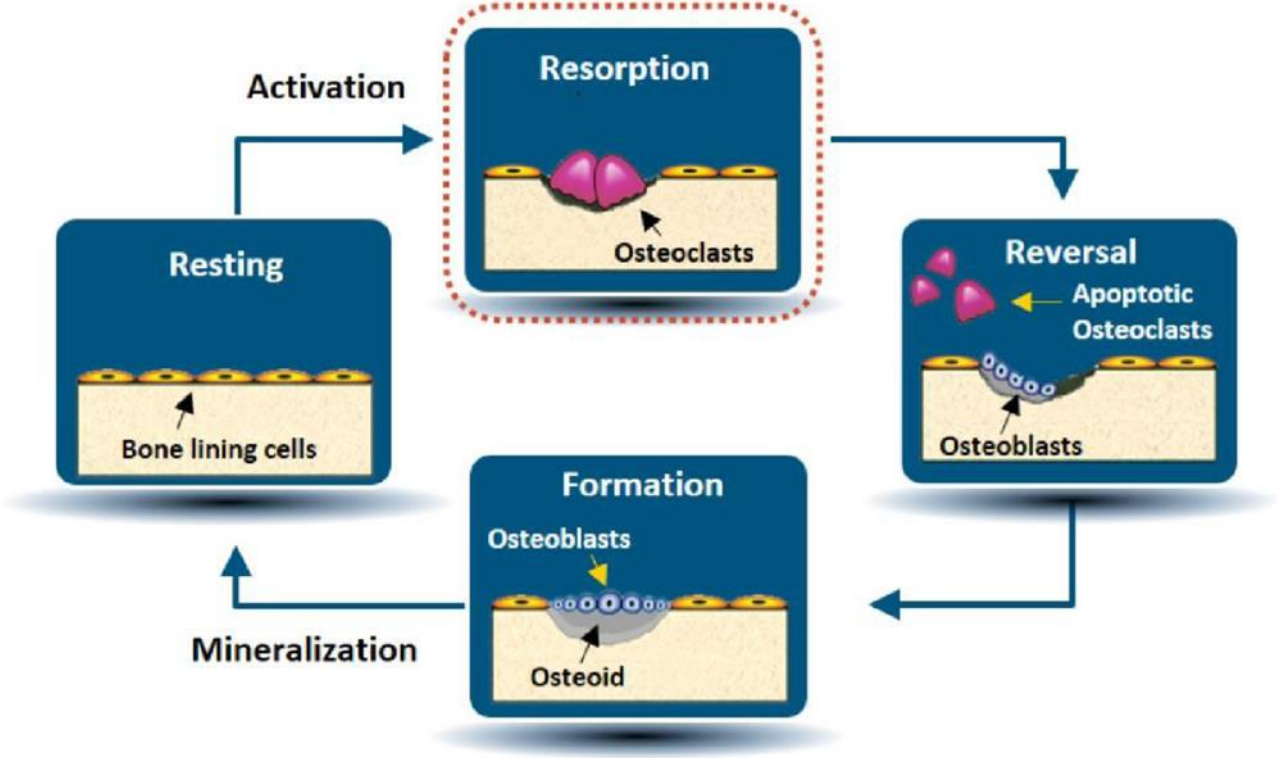


Cortical Bone

- Dense outer shell of compact bone; defines bone shape[1,5]
- 80% of skeletal mass[2]
- Essential functions
  - Provides biomechanical strength[8]
  - Attachment site for tendons and muscles[5]
  - Protects vital organs it surrounds[1]
- Turnover rate of 2%–3% per year[2,7,8]

1. Dempster DW. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism*. 6th ed. 2006:7-11. 2. Willems NMBK, et al. *Eur J Orthod*. 2014;36:479-485. 3. Ott SM. *Am J Nephrol*. 2018;47:373-375. 4. Feng X, McDonald JM. *Annu Rev Pathol Mech Dis*. 2011;6:121-145. 5. US Department of Health and Human Services. *Bone Health and Osteoporosis: A Report of the Surgeon General*. 2004. 6. Li N, et al. *Int J Endocrinol*. 2013:1-5. 7. Hruska KA, et al. *Semin Dial*. 2007;20:309-315. 8. Clarke B. *CJASN*. 2008;3(suppl 3):S131-S139.

THE BONE REMODELING CYCLE

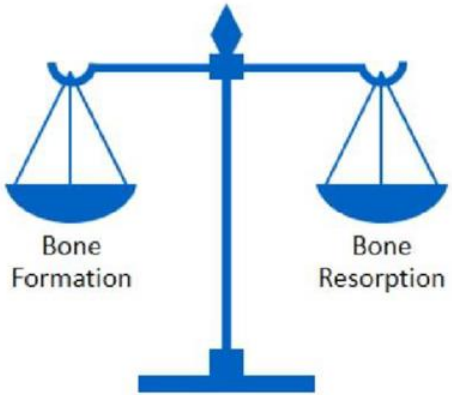


Adapted from: Baron R. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.* 5th ed. 2003:1-8

BONE REMODELING IS OUT OF BALANCE IN POSTMENOPAUSAL WOMEN[1]

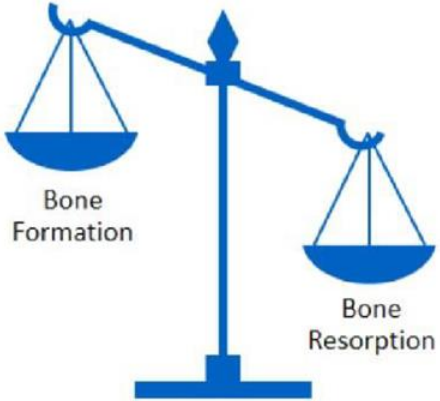
↓ Estrogen
↓ Testosterone
→ ↑ Osteoclast (Number and Activity)[2,3] → ↑ Bone Resorption → ↓ BMD → ↑ Risk of Fractures[4]

Normal Bone Remodeling



Osteoblast = Osteoclast
(Number and Activity)

Osteoporosis



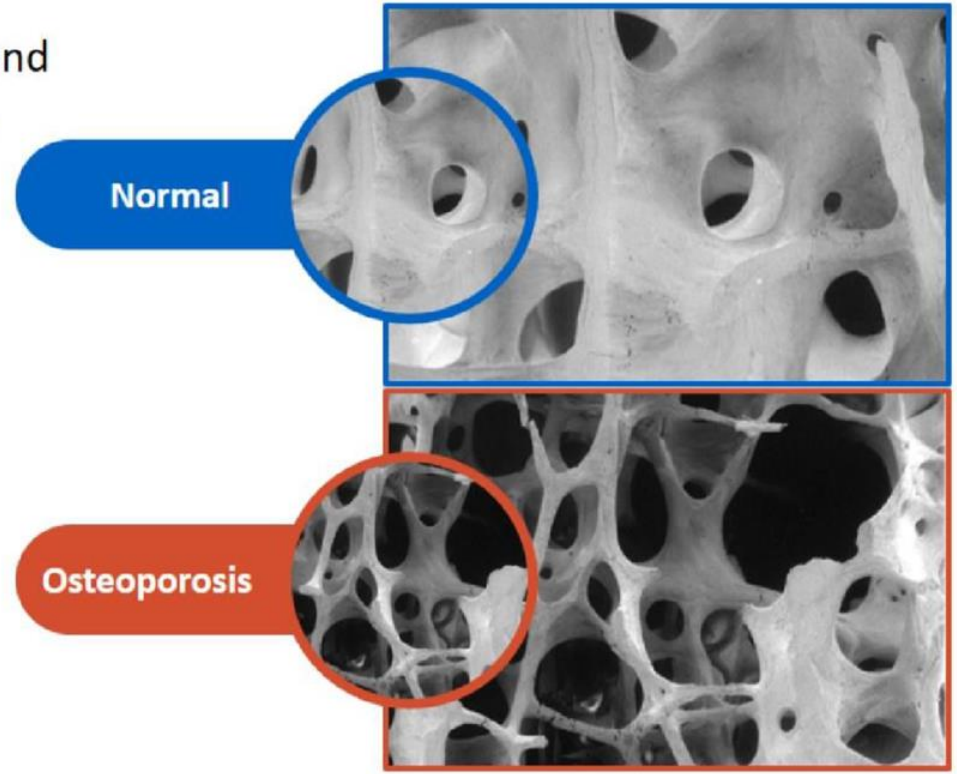
Osteoblast < Osteoclast
(Number and Activity)

BMD, bone mineral density.

1. US Department of Health and Human Services. Bone health and osteoporosis: a report of the surgeon general. 2004. Rockville, MD. 2. Raisz LG. *J Clin Invest.* 2005;115:3318-3325.
3. Michael H. *J Bone Miner Res.* 2005;20:2224-2232. 4. Boyle WJ, et al. *Nature.* 2003;423:337-342.

EFFECT OF INCREASED BONE LOSS OVER TIME

- The imbalance of bone resorption and formation, leading to osteoporosis, can cause:[1]
  - Impaired bone architecture
  - Compromised bone strength
  - Increased risk of fracture



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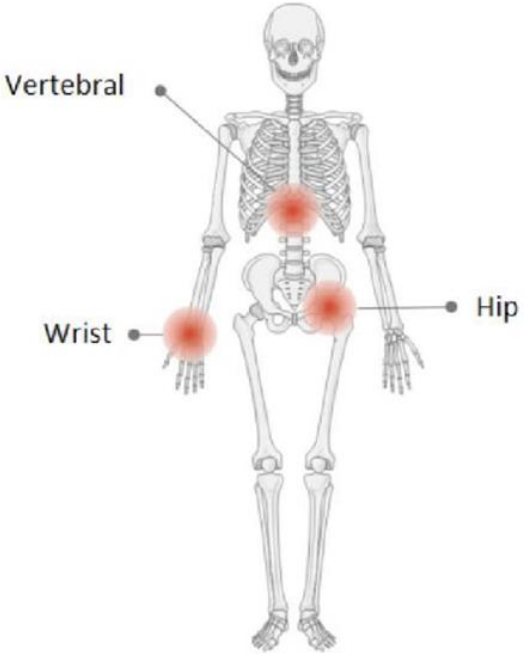
1. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. NIH Consensus Statement. *JAMA*. 2001;285:785-795.

FRACTURES AT MAJOR SKELETAL SITES IN ADULTS OLDER THAN 50 SHOULD BE FURTHER ASSESSED FOR OSTEOPOROSIS[1,2]

Major Sites of Osteoporosis-related Fractures[1,3]

Vertebral Fractures

Of all vertebral fractures in women, ~2/3 do not come to clinical attention[4]



Skeleton image used with permission from Servier Medical Art. www.servier.com. Creative Commons CC-BY-3.0.

1. Cosman F, et al. *Osteoporos Int.* 2014;25:2359-2381. 2. International Osteoporosis Foundation. Capture the Fracture. Available at: www.capturethefracture.org/about. Accessed April 7, 2020. 3. Burge R, et al. *J Bone Miner Res.* 2007;22:465-475. 4. Cooper C, et al. *J Bone Miner Res.* 1992;7:221-227.

OSTEOPOROSIS-RELATED FRACTURES CAN BE ASSOCIATED WITH DISABILITY AND LOSS OF INDEPENDENCE

Potential Impact of Osteoporosis-Related Fractures

Admission to nursing home or **long-term care** facilities[1]

Financial burden on patients and caregivers[2–5]

Decreased ability to perform **activities of daily living**[1,6,7]

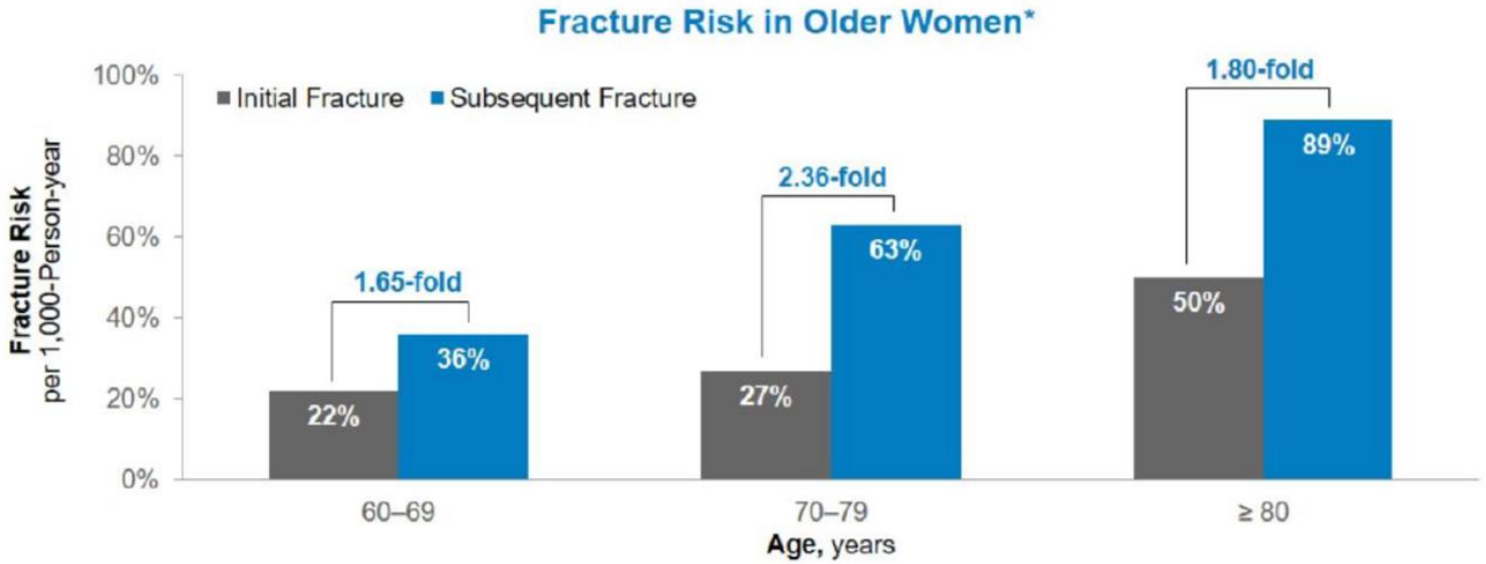
Worry about falls, future fracture, and potential for nursing home care[3,8]

Consequences such as **chronic pain** and **other complications**[6,9]

Skeleton image used with permission from Servier Medical Art. www.servier.com. Icons adapted and licensed (royalty-free) from the Noun Project, Inc. www.thenounproject.com.

1. Bentler SE, et al. *Am J Epidemiol*. 2009;170:1290-1299. 2. Tajeu GS, et al. *J Gerontol A Biol Sci Med Sci*. 2014;69:346-353. 3. National Osteoporosis Society. Life with Osteoporosis. October 2014. Available at: https://theros.org.uk/media/1859/life-with-osteoporosis.pdf. Accessed April 7, 2020. 4. Tarride J-E, et al. *Osteoporos Int*. 2012;23:2591-2600. 5. Kaffashian S, et al. *Age Ageing*. 2011;40:602-607. 6. Cosman F, et al. *Osteoporos Int*. 2014;25:2359-2381. 7. Fischer S, et al. *Osteoporos Int*. 2017;28:2843-2851. 8. Vass CD, et al. *Age Ageing*. 2014;43:i29. 9. Inacio MCS, et al. *Perm J*. 2015;19:29-36.

Risk of Subsequent Fracture Increases After Prior Fracture[1]



Once a patient has experienced a fracture, the chances of having another one are much higher[1]

*Not living in nursing homes.

1. Adapted from Center JR, et al. *JAMA*. 2007;297:387-394.

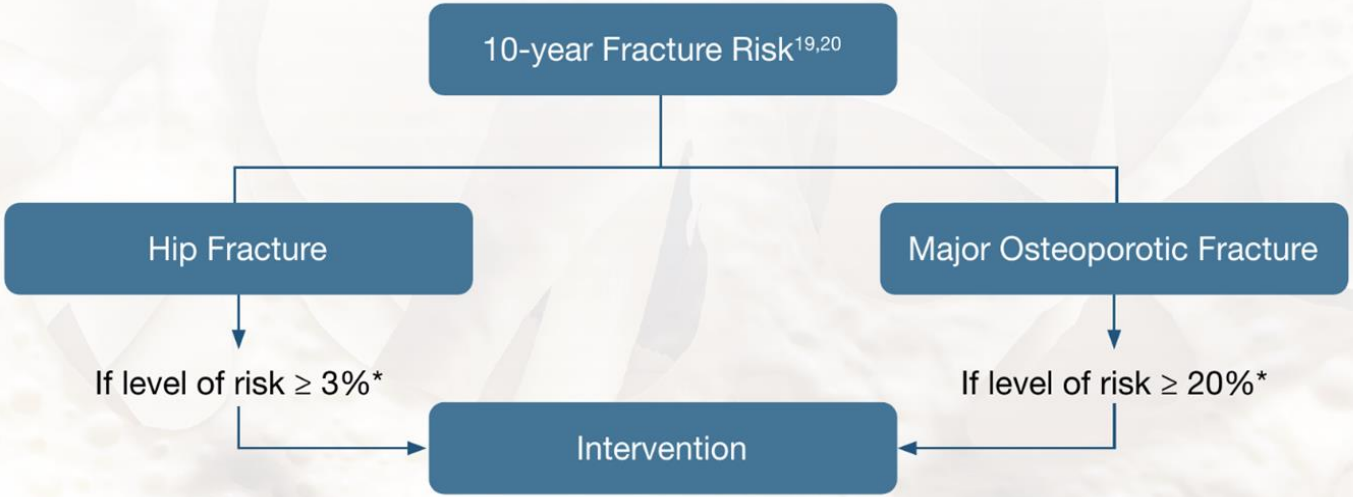
Updated PMO Guidelines: Recommendations for Fracture Risk Assessment

AACE Guidelines[1]	ENDO Guidelines[2]
• Evaluate all postmenopausal women aged ≥ 50 years for OP risk • A detailed history, physical exam, and clinical fracture risk assessment with FRAX™ or other fracture risk assessment tool should be included in the initial evaluation for OP • Consider BMD testing in women ≥ 65 years of age or based on clinical fracture risk profile • When BMD is measured, axial DXA measurement (lumbar spine and hip; 1/3 radius if indicated) should be used	• Evaluate all postmenopausal women for OP risk • Measure lumbar spine and hip BMD • Clinical fracture risk assessment using FRAX™ with femoral neck BMD

*Interpretation of FRAX™ scores may be influenced by exposure to glucocorticoids, information on lumbar spine BMD, trabecular bone score, hip axis length, falls history, immigration status and type 2 diabetes mellitus. †With a history of ≥ 4 cm height loss, kyphosis, recent or current long-term oral glucocorticoid therapy or a BMD T-score ≤ –2.5.
AACE = American Association of Clinical Endocrinologists; BMD = bone mineral density; DXA = dual-energy x-ray absorptiometry; ENDO = Endocrine Society; ESCEO = European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases; FRAX = Fracture Risk Assessment Tool; IOF = International Osteoporosis Foundation; OP = osteoporosis; PMO = postmenopausal osteoporosis.

1. Adapted from Camacho PM, et al. *Endocr Pract*. 2020;26 (Suppl 1):1-46. 2. Adapted from Shoback D, et al. *J Clin Endocrinol Metab*. 2020;105:587-594. 3. Adapted from Kanis JA, et al. *Osteoporos Int*. 2019;30:3-44.

FRAX® Calculator



*Represents National Osteoporosis Foundation recommended intervention thresholds.[21]
FRAX® is a trademark owned by the International Osteoporosis Foundation.

AACE, American Association of Clinical Endocrinologists; **BMD**, bone mineral density; **DXA**, dual energy X-ray absorptiometry; **FRAX**, fracture risk assessment tool; **MAPD**, Medicare Advantage Prescription Drug; **MOF**, major osteoporotic fracture; **TBS**, trabecular bone score

1. World Health Organization. *World Health Organ Tech Rep Ser*. 1994;843:1-129. **2.** U.S. Department of Health and Human Services. *Bone Health and Osteoporosis: A Report of the Surgeon General. 2004*. **3.** Bone Health and Osteoporosis Foundation. https://bonehealthandosteoporosis.org/wp-content/uploads/2015/12/Osteoporosis-Fast-Facts.pdf. Accessed September 29, 2022. **4.** International Osteoporosis Foundation. https://www.osteoporosis.foundation/facts-statistics/epidemiology-of-osteoporosis-and-fragility-fractures. Accessed September 29, 2022. **5.** NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. *JAMA*. 2001;285:785-795. **6.** Curtis JR, et al. *J Gen Intern Med*. 2009;24:956-962. **7.** Lewiecki EM, et al. *Osteoporos Int*. 2020;31:2069-2071. **8.** Lewiecki EM, et al. *Orthop Nurs*. 2022;41:125-134. **9.** Wright NC, et al. *J Bone Miner Res*. 2014;29:2520-2526. **10.** Lewiecki EM, et al. *JBMR Plus*. 2019;3:e10192. **11.** Boytsov NN, et al. *Am J Med Qual*. 2017;32:644-654. **12.** Black DM, et al. *J Bone Miner Res*.1999;14:821-828. **13.** Gehlbach S, et al. *J Bone Miner Res*. 2012;27:645-653. **14.** van Geel TACM, et al. *Ann Rheum Dis*. 2009;68:99-102. **15.** Singer A, et al. *Mayo Clin Proc*. 2015;90:53-62. **16.** Camacho PM, et al. *Endocr Pract*. 2020; 26(suppl 1):1-46. **17.** Lenchik L, et al. *Curr Rheumatol Rep*. 2018;20:74. **18.** Keaveny TM, et al. *Osteoporos Int*. 2020;31:1025-1048. **19.** Kanis JA, et al. *Osteoporos Int*. 2010;21:35-40. **20.** Cosman F, et al. *Osteoporos Int*. 2014;25:2359-2381. **21.** Kanis JA, et al. *Osteoporos Int*. 2020;31:1-12. **22.** Eisman JA, et al. *J Bone Miner Res*. 2012;27:2039-2046. **23.** Walters S, et al. *Clin Interv Aging*. 2017;12:117-127.

Risk Factors for Osteoporosis

- Low body weight
- Excessive alcohol intake
- Smoking
- Family history
- Glucocorticoid use
- Risk of falling due to other medical conditions
  - Including balance issues, hearing impairment, medications causing drowsiness, neuropathy, among others
- Risk of falling due to environmental factors
  - Including poor lighting, uneven walking surfaces, dogs
- Secondary causes of osteoporosis

Secondary Causes of Osteoporosis

Table 12
Causes of Secondary Osteoporosis in Adults[a]

Endocrine or metabolic causes	Nutritional/ GI conditions	Drugs	Disorders of collagen metabolism	Other
Acromegaly	Alcoholism	Anti-epileptic drugs[b]	Ehlers-Danlos syndrome	AIDS/HIV
Diabetes mellitus	Anorexia nervosa	Aromatase inhibitors	Homocystinuria due to cystathionine deficiency	Ankylosing spondylitis
Type 1	Calcium deficiency	Chemotherapy/ immunosuppressants	Marfan syndrome	Chronic obstructive pulmonary disease
Type 2	Chronic liver disease	Medroxyprogesterone acetate	Osteogenesis imperfecta	Gaucher disease
Growth hormone deficiency	Malabsorption syndromes/ malnutrition (including celiac disease, cystic fibrosis, Crohn disease, and gastric resection or bypass)	Glucocorticoids		Hemophilia
Hypercortisolism	Total parenteral nutrition	Gonadotropin-releasing hormone agents		Hypercalciuria
Hyperparathyroidism	Vitamin D deficiency	Heparin		Immobilization
Hyperthyroidism		Lithium		Major depression
Hypogonadism		Proton pump inhibitors		Myeloma and some cancers
Hypophosphatasia		Selective serotonin- reuptake inhibitors		Organ transplantation
Porphyria		SGLT2-inhibitors		Renal insufficiency/ failure
Pregnancy		Thiazolidinediones		Renal tubular acidosis
		Thyroid hormone (in supraphysiologic doses)		Rheumatoid arthritis
				Systemic mastocytosis
				Thalassemia

AIDS = acquired immunodeficiency syndrome; GI = gastrointestinal; HIV = human immunodeficiency virus; SGLT2 = sodium-glucose cotransporter 2.
[a]Not meant to be a complete list.
[b]Phenobarbital, phenytoin, primidone, valproate, and carbamazepine have been associated with low bone mass.

Laboratory Testing – Ruling Out Secondary Causes

- CBC, CMP
- TSH, FT3, FT4
- PTH intact
- 25 hydroxy vitamin D
- Serum/ urine electrophoresis
- 24-hour urinary calcium excretion in select patients
- Celiac disease panel

Table 6
2020 AACE Diagnosis of Osteoporosis in Postmenopausal Women

1. T-score –2.5 or below in the lumbar spine, femoral neck, total proximal femur, or 1/3 radius
2. Low-trauma spine or hip fracture (*regardless of bone mineral density*)
3. T-score between –1.0 and –2.5 **and** a fragility fracture of proximal humerus, pelvis, or distal forearm
4. T-score between –1.0 and –2.5 **and** high FRAX® (or if available, TBS-adjusted FRAX®) fracture probability based on country-specific thresholds

Abbreviations: AACE = American Association of Clinical Endocrinologists; FRAX® = fracture risk assessment tool; TBS = trabecular bone score.

Updated PMO Guidelines Provide Similar Characterization of Fracture Risk[1-3]

	HIGH RISK	VERY HIGH RISK
AACE[1]	❑ Fragility fractures in the absence of other metabolic bone disorders even with normal BMD, *or* ❑ T-score ≤ −2.5 in the lumbar spine, femoral neck, total hip, or 1/3 radius even in the absence of a prevalent fracture, *or* ❑ FRAX™ ≥ 20% MOF *or* ≥ 3% hip	❑ Recent fracture (< 12 months), *or* ❑ Fractures while on approved osteoporosis therapy, *or* ❑ Multiple fractures, *or* ❑ Fractures while on drugs causing skeletal harm, *or* ❑ Very low T-score (e.g., < −3.0), *or* ❑ High fall risk or history of injurious falls, *or* ❑ Very high fracture probability by FRAX™ (e.g., major osteoporosis fracture > 30%*, hip fracture > 4.5%*) or other validated fracture risk algorithm to be at very high fracture risk
ENDO[2]	❑ Prior spine or hip fracture, *or* ❑ T-score ≤ −2.5, *or* ❑ FRAX™ ≥ 20% MOF *or* ≥ 3% hip	❑ Multiple spine fractures AND ❑ T-score at the hip or spine of −2.5 or below

*Per AACE, these FRAX estimates are not based on published evidence and are only examples of levels of risk warranting special consideration.[4]
AACE = American Association of Clinical Endocrinologists; BMD = bone mineral density; ENDO = Endocrine Society; FRAX = Fracture Risk Assessment Tool; MOF = major osteoporotic fracture.

1. Adapted from Camacho PM, et al. *Endocr Pract*. 2020;26 (Suppl 1):1-46. 2. Adapted from Shoback D, et al. *J Clin Endocrinol Metab*. 2020;105:587-594. 3. Adapted from Kanis JA, et al. *Osteoporos Int*. 2020;31:1-12. 4. Watts NB et al. *Endocr Pract*. 2021. doi: https://doi.org/10.1016/j.eprac.2021.02.001.

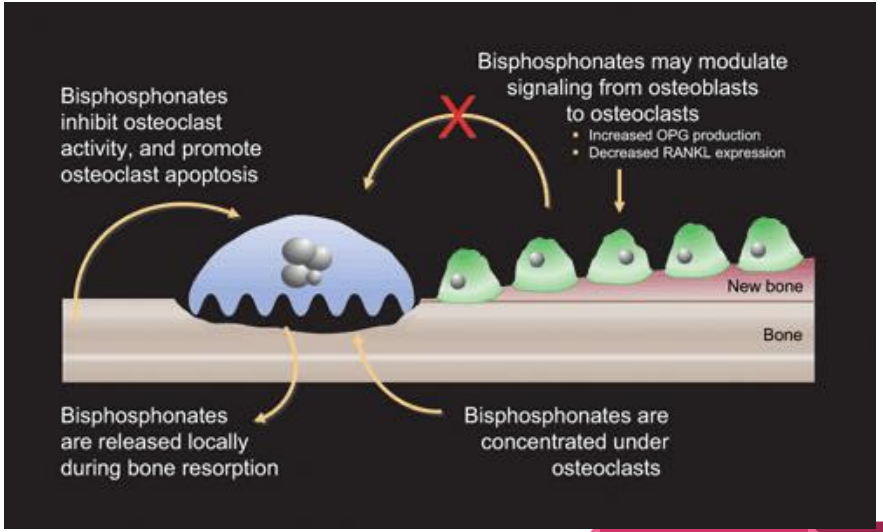
Lifestyle Recommendations for Osteoporotic Patients

- 1200 mg of elemental calcium through **diet** or supplement
  - 8 ounces of milk = 6 ounces of yogurt = 1.5 ounces of cheese = 300 mg calcium
- Vitamin D levels above 40 mg/dl
- At least 800-1000 IU per day, preferably administered with food
  - Doses may vary depending on secondary absorption issues
- Weight bearing exercises
- Reduce alcohol consumption
- Smoking cessation
- Environmental accommodations
- Risk reduction of fall
  - Glasses for visually impaired, walker or cane

Pharmacotherapy for Osteoporotic Patients

Bisphosphonates:

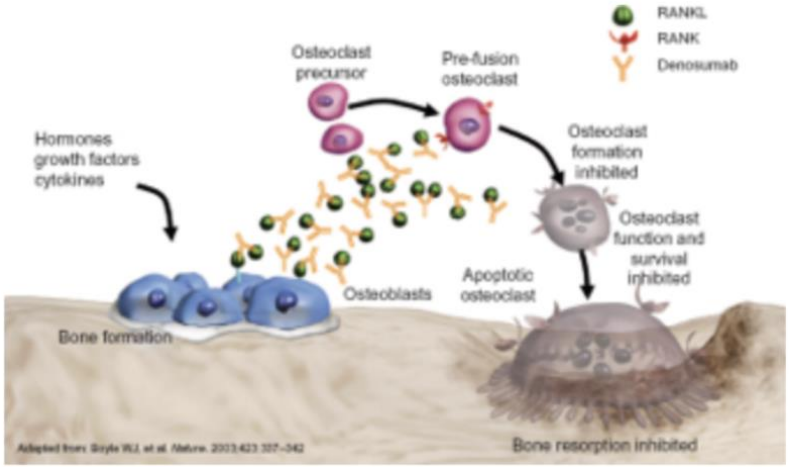
- Alendronate, Risedronate, Ibandronate, Zoledronic acid
  - Ibandronate does not improve BMD at spine
  - Alendronate and Risedronate comparison trial showed relatively greater BMD in hip and spine with Alendronate, however, benefits didn't translate into fracture risk reduction
- Act by decreasing osteoclast activity
- Contraindications: GFR < 35, history of esophageal disorders or malabsorption



Pharmacotherapy for Osteoporotic Patients

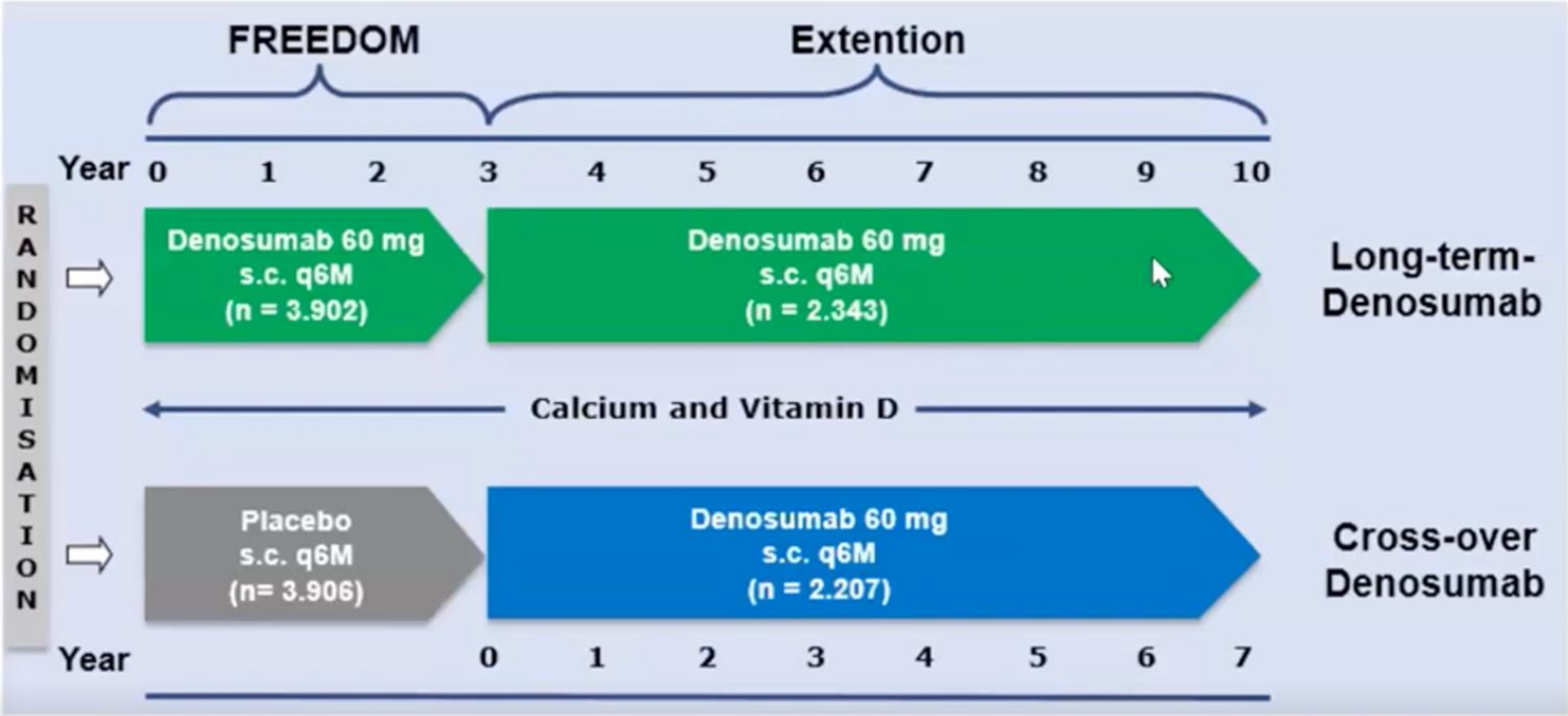
Denosumab:

- Human monoclonal antibody against RANK ligand
  - Surface of osteoclast and osteoclast precursors
  - RANK - RANKL interaction is the key mediator of osteoclastic activation
- Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months (FREEDOM) Trial of 7,808 women with postmenopausal osteoporosis
  - Showed “broad-spectrum” antifracture efficacy as early as 12 months after starting therapy
- Studies have reported and safe and effective use for up to 10 years
- Contraindications: hypocalcemia, vitamin D deficiency
- Renal insufficiency is not a contraindication
- Drug holidays are not recommended while using Denosumab



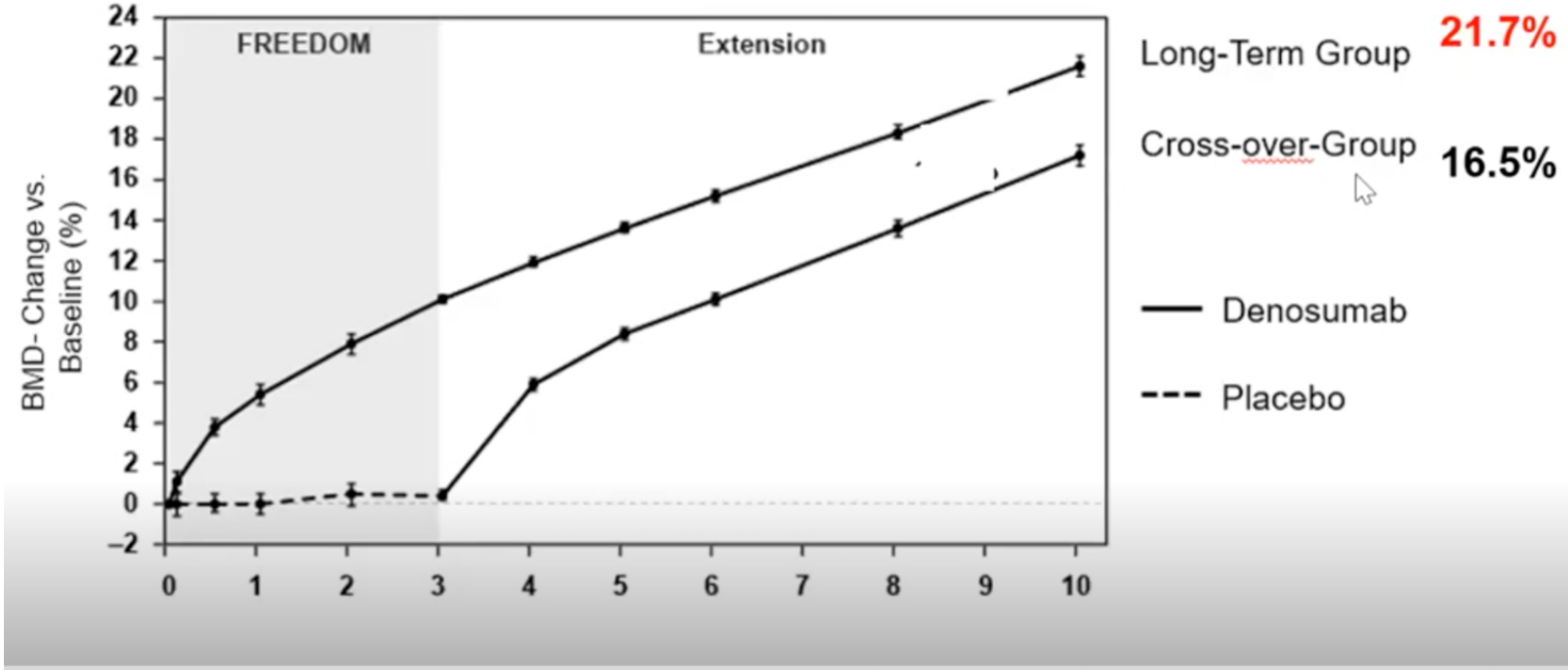
10-Year Analysis of FREEDOM-Extention Trial

Denosumab in the Treatment of postmenopausal osteoporosis



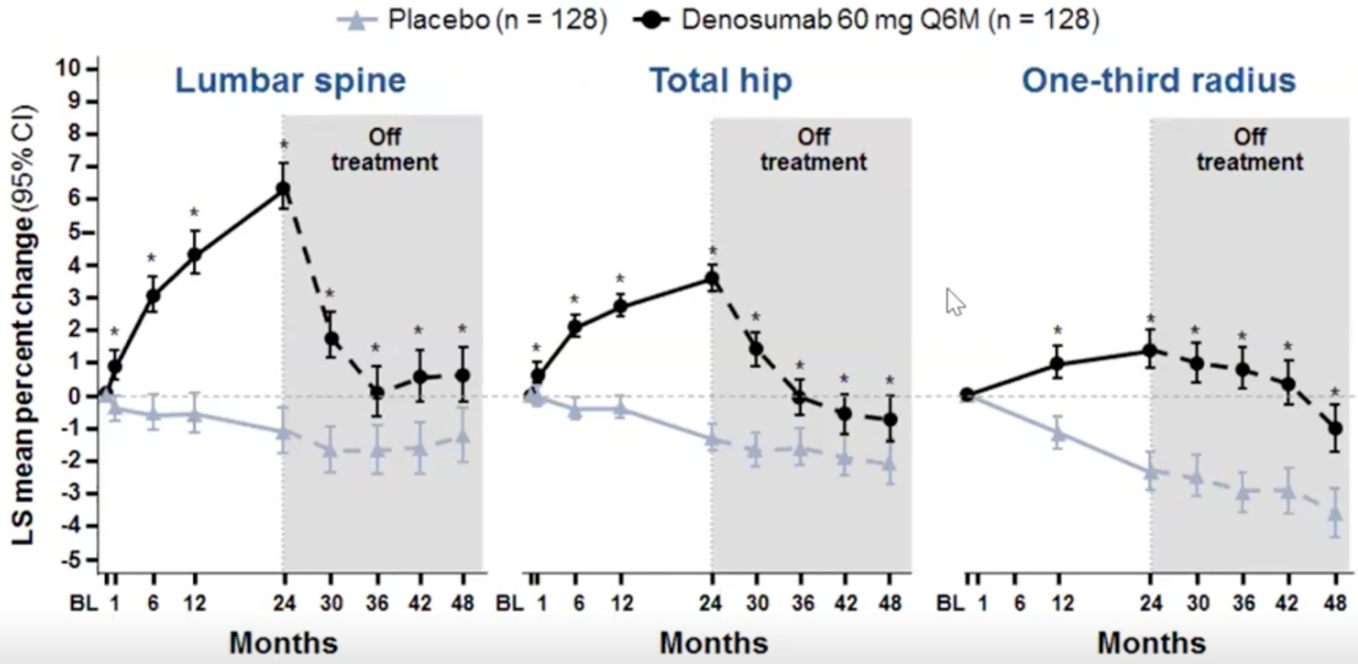
Adapted from Bone HG, et al. *Lancet Diabetes Endocrinol.* 2017;5: 513-523

Lumbar Spine: Cumulative BMD increase **21.7%** in the Long-Term Group and **16.5% in** the Cross-Over-Group



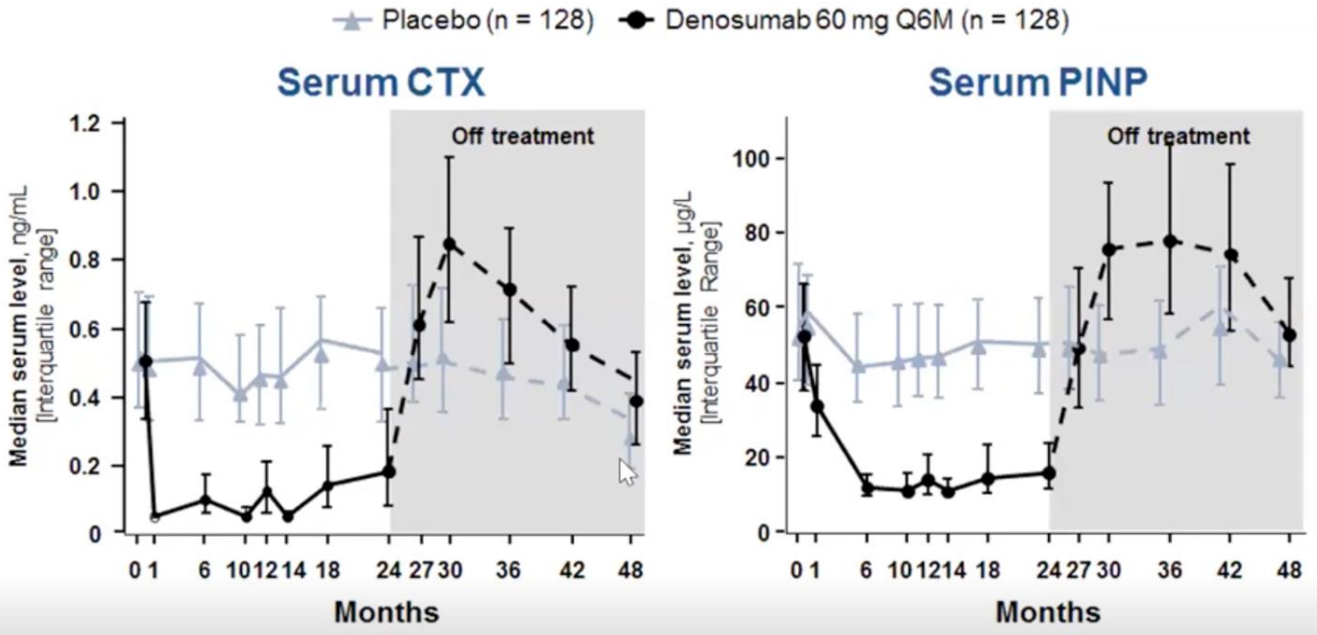
Adapted from Bone HG, et al. *Lancet Diabetes Endocrinol.* 2017;5: 513-523

Effects of Denosumab Discontinuation on BMD



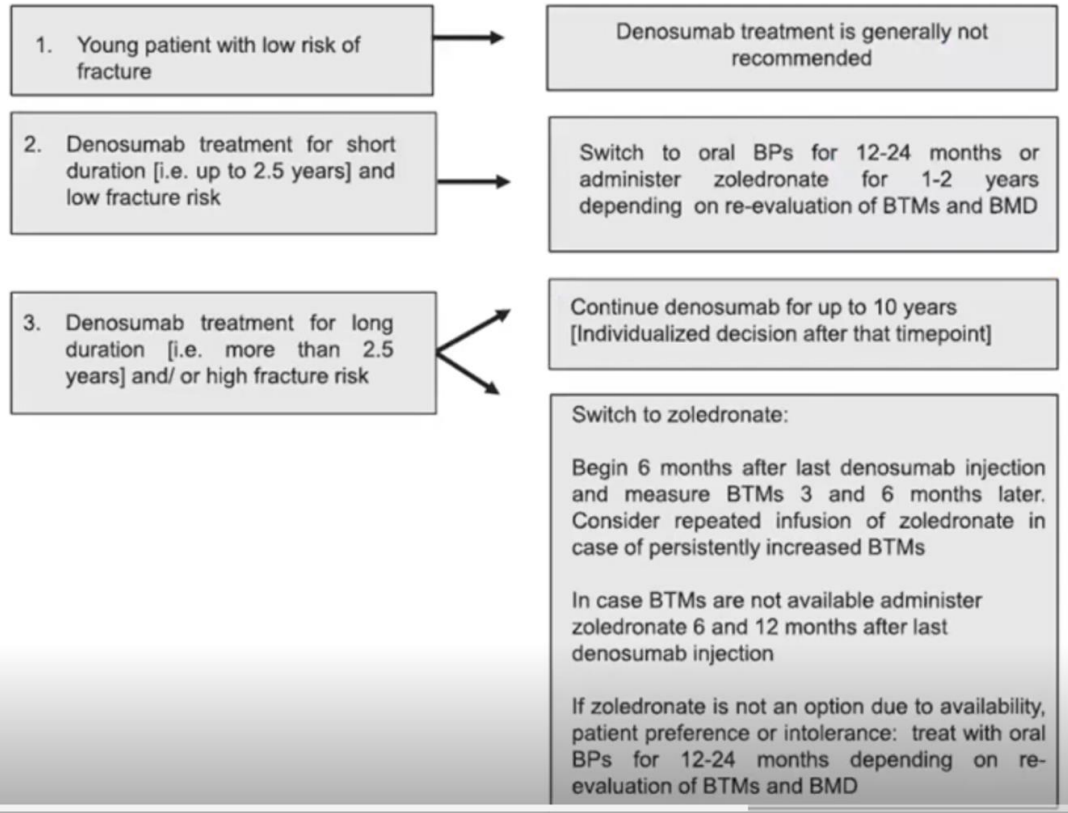
Adapted from Bone HG, et al. *J Clin Endocrinol Metab.* 2011;96: 972-980

Effects of Denosumab Discontinuation on BTMs



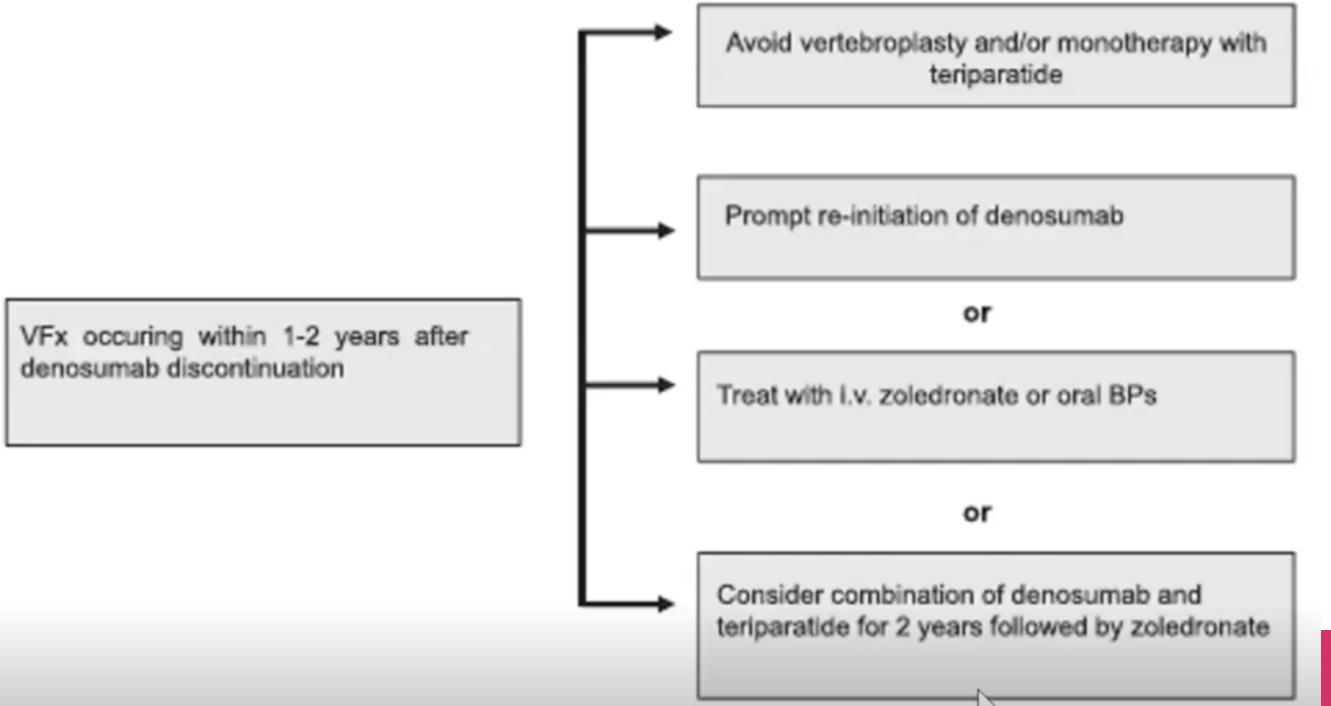
Adapted from Bone HG, et al. *J Clin Endocrinol Metab.* 2011;96: 972-980

Recommendations for Clinicians



Tsourdi E et al., *J Clin Endocrinol Metab.* 2020; dgaa756.

Recommendations for Clinicians



Tsourdi E et al., *J Clin Endocrinol Metab*. 2020; dgaa756.

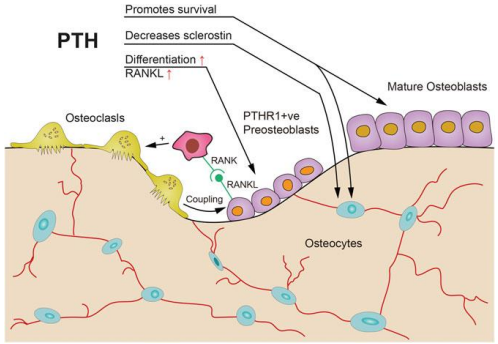
Risk Factors for Antiresorptive Therapy

- The incidence of osteonecrosis of the jaw (ONJ) and atypical femur fracture (AFF) is much lower with oral or IV bisphosphonate therapy for osteoporosis, than when used for treatment of cancer
- Bisphosphonate data shows order of 1/10,000 to 1/100,000 patients per year
- Denosumab therapy of osteoporosis, with 5.2 cases per 10,000 patient-years

Pharmacotherapy for Osteoporotic Patients

Teriparatide and Abaloparatide - PTH and PTHrP Analogs:

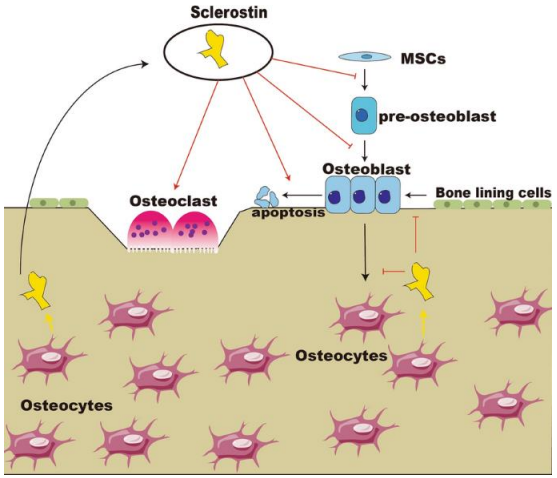
- Recommended for postmenopausal women (PMW) with osteoporosis who are at high risk of fracture
- Recommended dose 20 mcg sc daily injection for a duration of 2 years for reduction of vertebral and nonvertebral fractures
- After completion of course, follow with treatment with anti-resorptive osteoporosis therapies to maintain bone density gains and reduce fracture risk



Pharmacotherapy for Osteoporotic Patients

Romosozumab:

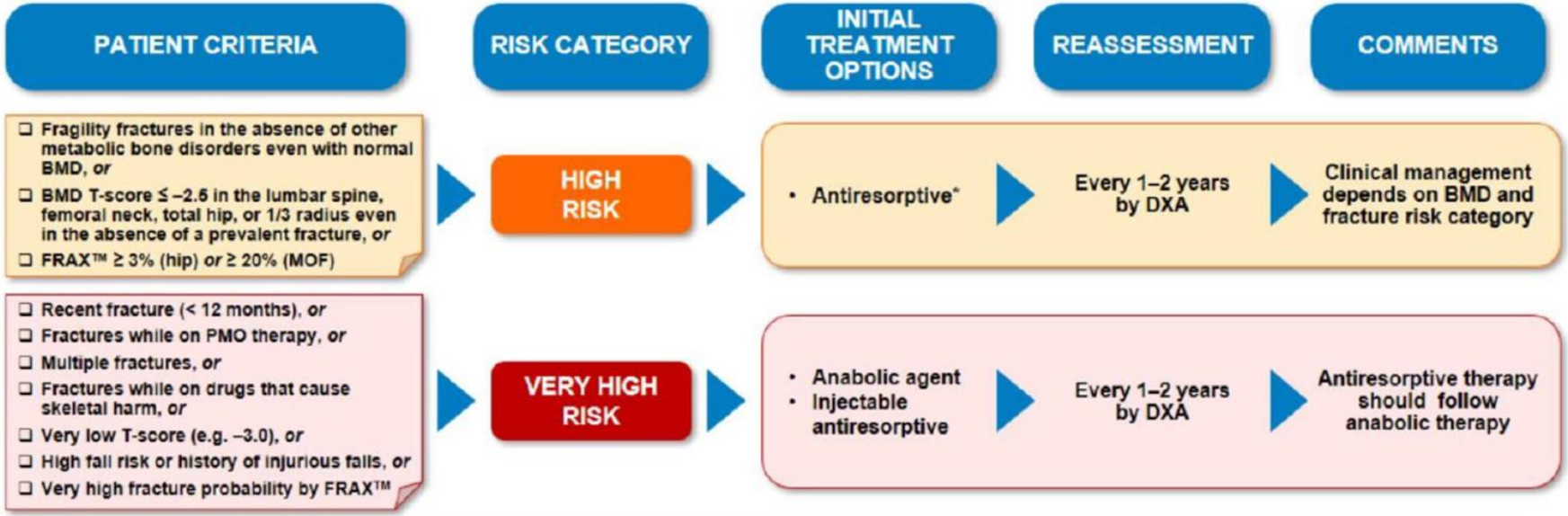
- Recommended for PMW with severe osteoporosis and high risk of fracture or history of multiple vertebral fractures
- Recommended for a duration of 1 year
- Recommended dosage is 210 mg monthly by subcutaneous injection
- Women at high risk of cardiovascular disease or stroke should not be treated with Romosozumab
- After completion of course, follow with treatment with anti-resorptive osteoporosis therapies to maintain bone density gains and reduce fracture risk



Pharmacotherapy for Osteoporotic Patients

- **Selective Estrogen Receptor Modulators:**
  - Recommended for PMW with osteoporosis at high risk of fracture and any of the following characteristics:
    - Patient has low risk of deep vein thrombosis (DVT)
    - Patient is not recommended to use bisphosphonates or denosumab
    - Patient has high risk of breast cancer
- **Menopausal Hormone Therapy:**
  - Recommended for PMW at high risk of fracture and any of the following characteristics:
    - Patient is under 60 years of age or <10 years past menopause
    - Patient has low risk of DVT
    - Patient is not recommended to use bisphosphonates or denosumab
    - Patient has bothersome vasomotor symptoms
    - Patient has not had MI or stroke
    - Patient does not have breast cancer
  - Recommended that estrogen is used only in women with hysterectomy

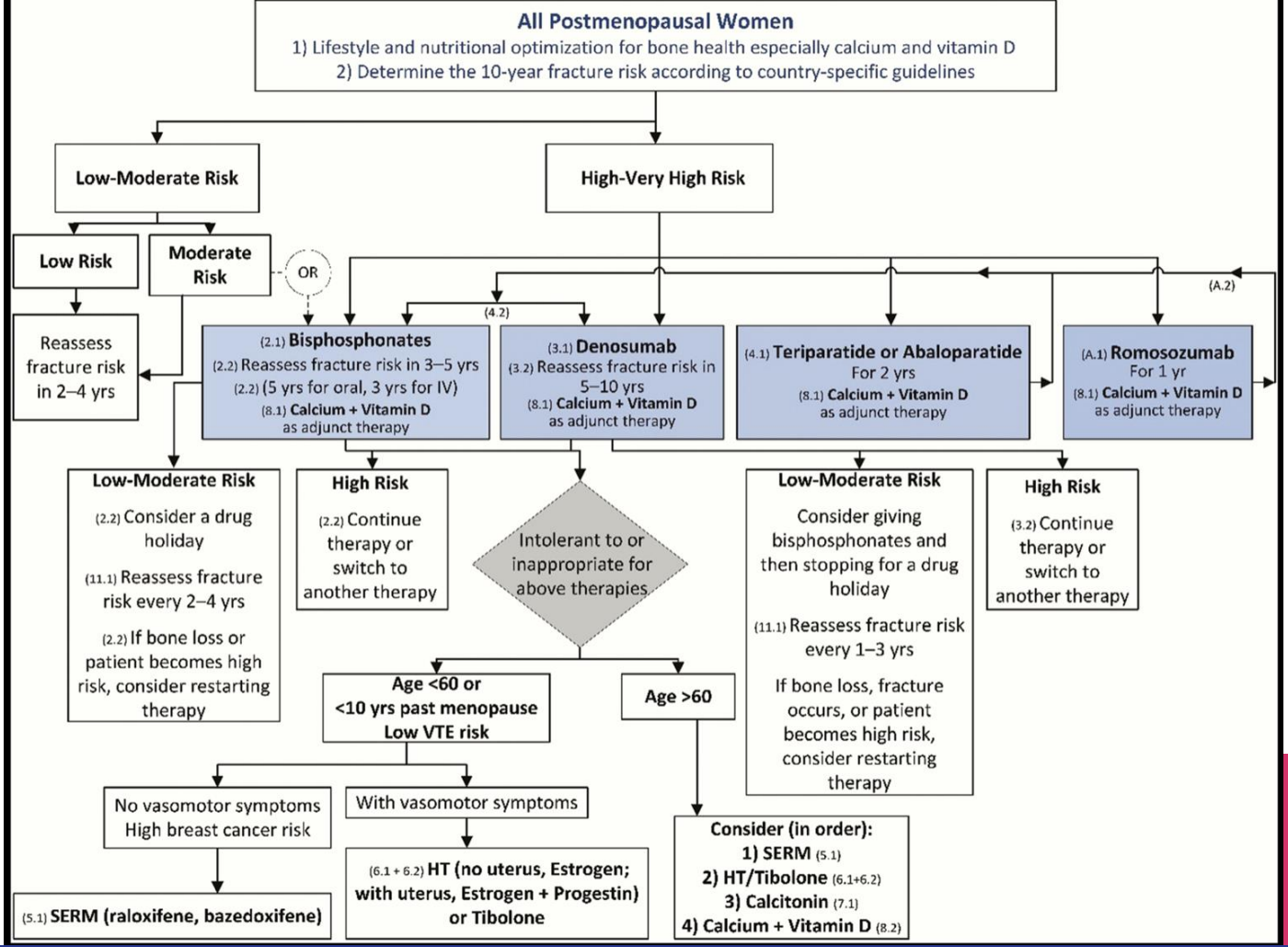
Updated AACE Guidelines for the Management of PMO[1]



Injectable agents† are recommended as initial therapy for patients who are at very highest fracture risk, who might not tolerate or absorb oral medications, and those with decreased adherence[1]

*SERMs are included as alternative initial treatment options. †Agents include anabolic therapies and injectable antiresorptives.
AACE = American Association of Clinical Endocrinologists; BMD = bone mineral density; DXA = dual-energy X-ray absorptiometry; FRAX = Fracture Risk Assessment Tool; MOF = major osteoporotic fracture; PMO = postmenopausal osteoporosis; SERM = selective estrogen receptor modulator.

1. Adapted from Camacho PM, et al. *Endocr Pract*. 2020;26(Suppl 1):1-46.


All Postmenopausal Women
1) Lifestyle and nutritional optimization for bone health especially calcium and vitamin D
2) Determine the 10-year fracture risk according to country-specific guidelines
Low-Moderate Risk
High-Very High Risk
Low Risk
Moderate Risk
OR
Reassess fracture risk in 2–4 yrs
(4.2)
(A.2)
(2.1) Bisphosphonates
(2.2) Reassess fracture risk in 3–5 yrs
(2.2) (5 yrs for oral, 3 yrs for IV)
(8.1) Calcium + Vitamin D as adjunct therapy
(3.1) Denosumab
(3.2) Reassess fracture risk in 5–10 yrs
(8.1) Calcium + Vitamin D as adjunct therapy
(4.1) Teriparatide or Abaloparatide
For 2 yrs
(8.1) Calcium + Vitamin D as adjunct therapy
(A.1) Romosozumab
For 1 yr
(8.1) Calcium + Vitamin D as adjunct therapy
Low-Moderate Risk
(2.2) Consider a drug holiday
(11.1) Reassess fracture risk every 2–4 yrs
(2.2) If bone loss or patient becomes high risk, consider restarting therapy
High Risk
(2.2) Continue therapy or switch to another therapy
Intolerant to or inappropriate for above therapies
Low-Moderate Risk
Consider giving bisphosphonates and then stopping for a drug holiday
(11.1) Reassess fracture risk every 1–3 yrs
If bone loss, fracture occurs, or patient becomes high risk, consider restarting therapy
High Risk
(3.2) Continue therapy or switch to another therapy
Age <60 or <10 yrs past menopause Low VTE risk
Age >60
No vasomotor symptoms High breast cancer risk
With vasomotor symptoms
(5.1) SERM (raloxifene, bazedoxifene)
(6.1 + 6.2) HT (no uterus, Estrogen; with uterus, Estrogen + Progestin) or Tibolone
Consider (in order):
1) SERM (5.1)
2) HT/Tibolone (6.1+6.2)
3) Calcitonin (7.1)
4) Calcium + Vitamin D (8.2)

Sequential therapy

Table 2
Effects of the Second Medication on Bone Mineral Density With Specific Sequences

Transition	Effect of the second agent on BMD
Antiresorptive to antiresorptive	
Bisphosphonates to denosumab[35-38]	Modest increase in spine and hip BMDs
Denosumab to bisphosphonates [43,46-52]	Moderate decrease in spine and hip BMD after long-term denosumab Maintenance in spine and hip BMD after short-term denosumab
Osteoanabolic to antiresorptive	
Teriparatide to bisphosphonates[64]	Increase in spine and hip BMD
Teriparatide to denosumab[65,66]	Increase in spine and hip BMD, larger than with bisphosphonates
Abaloparatide to bisphosphonates[59]	Increase in spine and hip BMD[a]
Romosozumab to bisphosphonates[61]	Increase in spine and hip BMD[a]
Romosozumab to denosumab[58,60]	Increase in spine and hip BMDs, larger than with bisphosphonates[a]
Antiresorptive to osteoanabolic	
Bisphosphonates to teriparatide[70,71,73]	Increase in spine BMD, blunted compared with that in de novo teriparatide In hip BMD, a decrease for at least 1 year and a modest increase at 18-24 mo
Bisphosphonates to romosozumab[71,72]	Increase in spine and hip BMD, blunted compared with those in de novo romosozumab
Denosumab to teriparatide[66]	Transient (6-mo) decrease in spine BMD followed by a modest increase More sustained and larger decrease in hip BMD[b]
Denosumab to romosozumab[15,72,76]	Increase in spine BMD, blunted compared with that in de novo romosozumab Maintenance in hip BMD

Abbreviation: BMD = bone mineral density.
[a] These transitions were also associated with continued antifracture efficacy in pivotal randomized controlled trials.

Secondary osteoporosis

- Glucocorticoid Induced
- Secondary to gonadal antagonist /aromatase inhibitors /therapy (prostate/breast cancer patients)
- Post transplant patients

Thank you