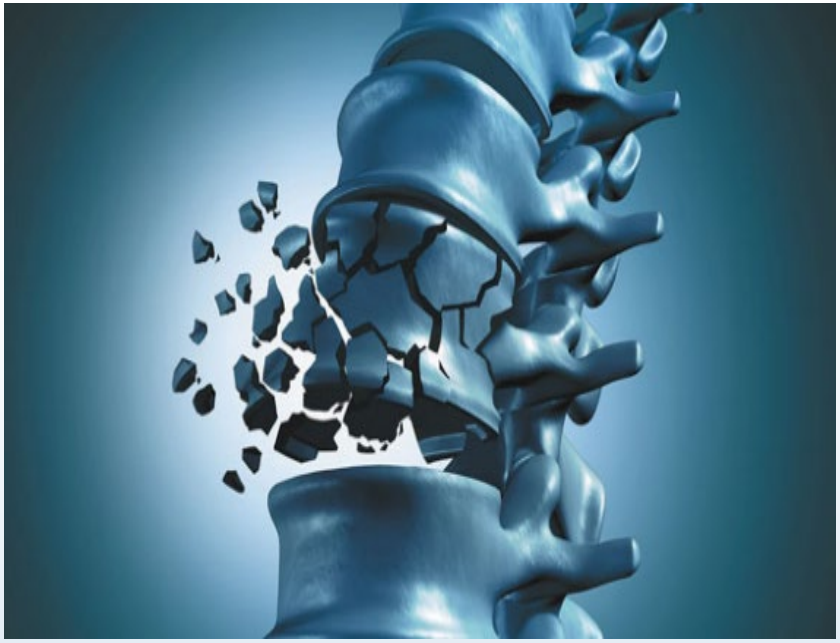
OSTEOPOROSIS



Grace Kim, MD
Assistant Professor
Division of Endocrinology
Albany Med Health System

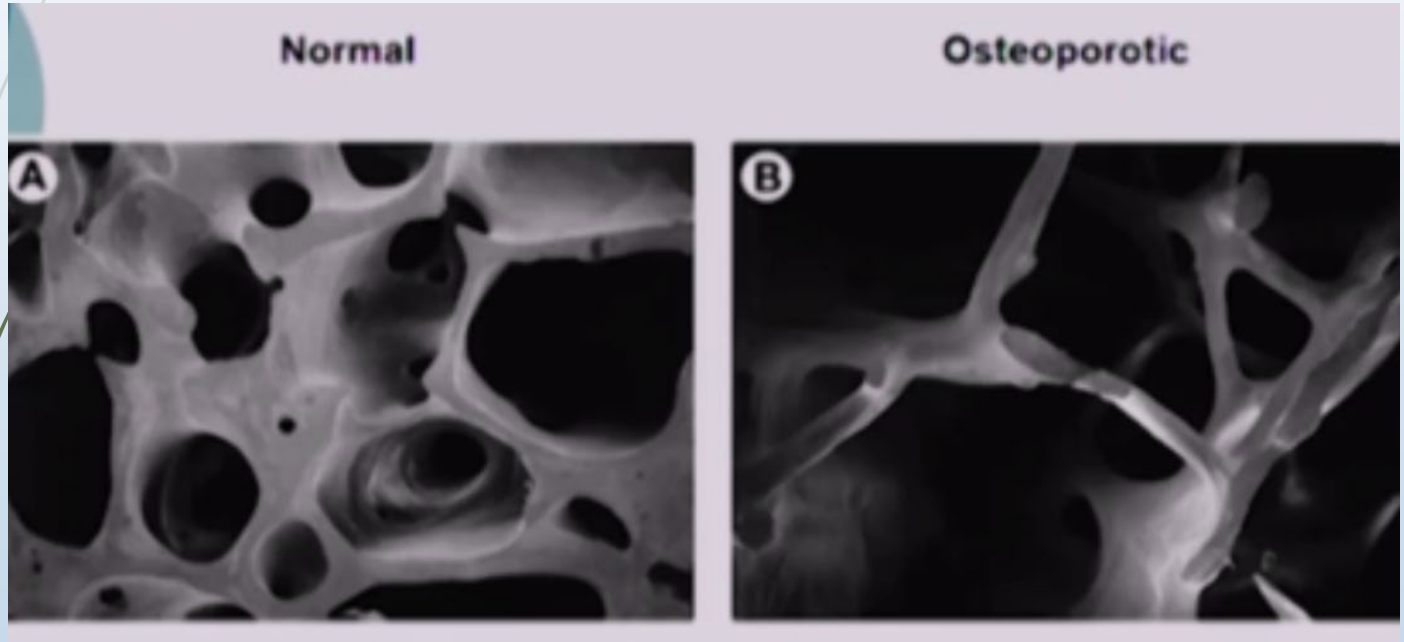
October 24, 2026

Outline

- Definition
- Epidemiology
- Diagnosis
  - Screening
  - Risk factors
  - Secondary causes of osteoporosis
  - FRAX
  - VFA
  - TBS
  - Bone turnover markers
- Fall prevention
- Pharmacotherapy

Definition of Osteoporosis

- "A systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture"



Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 1993; 94: 646–50.

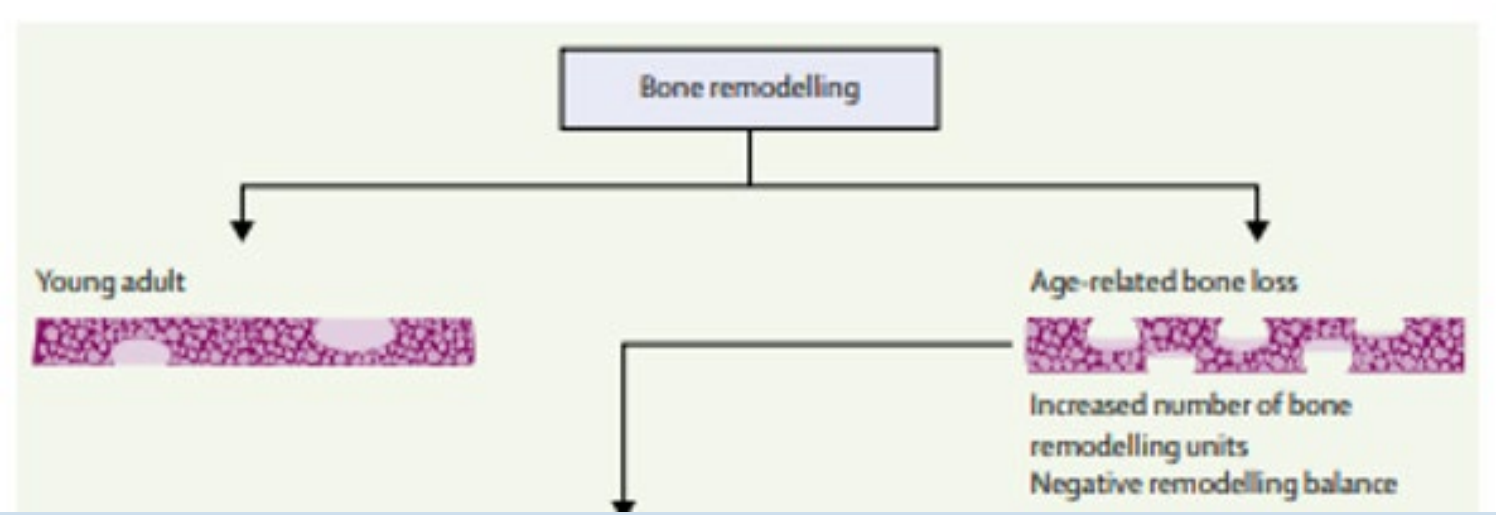
Definition of Osteoporosis

- Hip, spine and wrist are most likely to be affected.

- Amount of bone loss:
  - Age-related bone loss of 0.5 – 1% per year after age 18-25
  - Early menopausal bone loss of 1 – 2% per year.

Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 1993; 94: 646–50.

Pathophysiology of Age-related Bone Loss



Eriksen EF. Normal and pathological remodeling of human trabecular bone: three dimensional reconstruction of the remodeling sequence in normal s and in metabolic bone disease. Endocr Rev. 1986; 7: 379-408.

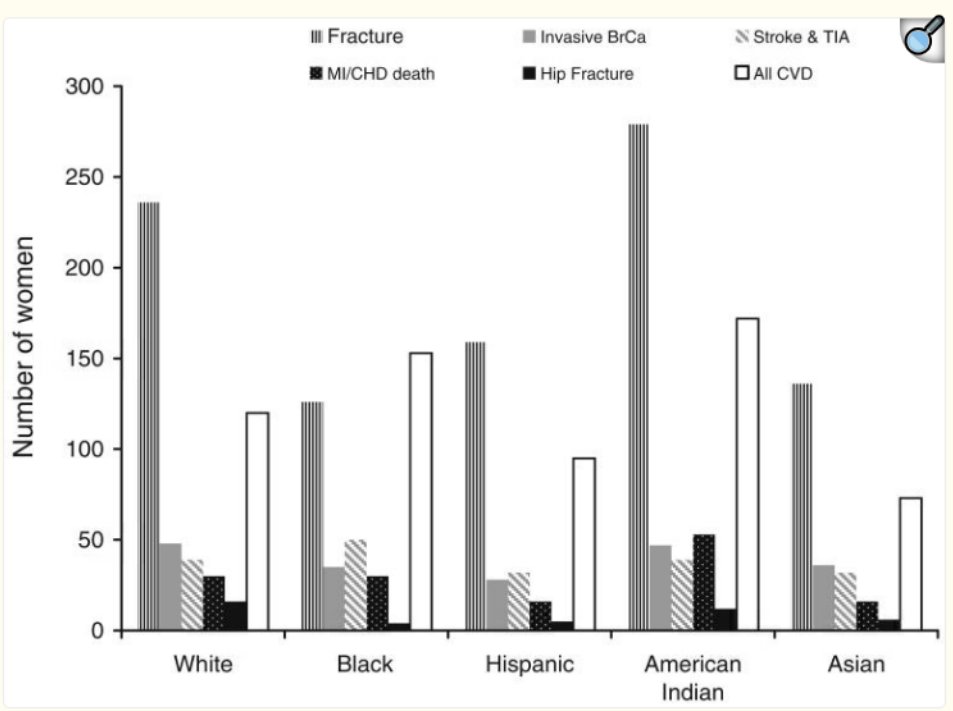
A Public Health Problem

- National Osteoporosis Foundation (NOF) estimates 10.2 million Americans have osteoporosis and additional 43.4 million have low bone mass.
- More than 2 million osteoporosis-related fractures occur annually in the US; more than 70% in women.
- According to International Osteoporosis Foundation, economic impact in US alone is estimated to be $52 billion per year (including hospitalizations, medication, rehabilitation, and long-term care.

Wright NC, Looker AC, Saag KG, et al. The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. J Bone Miner Res. 2014;29:2520-2526.

AACE/American College of Endocrinology Clinical Practive Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

Comparative Risks



Open in a new tab

The estimated number of cases that will occur in 10,000 women in one year: total fractures, hip fractures, invasive breast cancer, stroke and TIA, MI, CHD death and all CVD (including MI, CHD death, angina, CHF, DVT, coronary revascularization, TIA and stroke)

Cauley JA et al. Incidence of fractures compared to cardiovascular disease and breast cancer: the Women's Health Initiative Observational Study. Osteoporosis Int. PMC: 2009.

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*) **Definition**: "**Fragility fractures** are **fractures that result from mechanical forces that would not ordinarily result in fracture**, known as low-level (or 'low energy') trauma. The World Health Organization (WHO) has quantified this as forces equivalent to a fall from a standing height or less."
- 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.

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

Vertebral Fractures

- 30% are symptomatic
- Only sign is loss of height
- Highest incidence and prevalence: North America and Asia
- Increase risk for other fractures including HIP fracture
- Most common fracture associated with skeletal fragility
  - Source of substantial morbidity and mortality

High prevalence of asymptomatic vertebral fractures in post-menopausal women receiving chronic glucocorticoid therapy: a cross-sectional outpatient study. Angeli et al. Bone. August 2006. 39(2):253259.

Hip Fractures

- Most occur after age 80, usually in women
  - 25% hip fractures occur in men
  - pain and inability to weight bear
- Most require surgical fixation
- Result in a reduction in functional status and Quality of Life
- 30% mortality
- 51% (of 2.7 million hip fractures worldwide in 2010) were calculated to be potentially preventable

Oden A, McCloskey EV, Johansson H, Kanis JA. Assessing the impact of osteoporosis on the burden of hip fractures. Calcified Tissue International. November 2012; Volume 92: 42–49 (2013).

Indications for BMD Testing

- All women 65 years of age or older
- All postmenopausal women
- With a history of fracture(s) without major trauma
- With osteopenia identified radiographically
- Starting or taking long-term systemic glucocorticoid therapy (≥ 3 months)
- Other perimenopausal or postmenopausal women with risk factors for osteoporosis if willing to consider pharmacologic interventions
- Low body weight (< 127 lb or body mass index < 20 kg/m2)
- Long-term systemic glucocorticoid therapy (≥ 3 months)
- Family history of osteoporotic fracture
- Early menopause
- Current smoking
- Excessive consumption of alcohol
- Secondary osteoporosis

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

Causes of Secondary Osteoporosis in Adults

- **Endocrine or metabolic causes**
  - Acromegaly
  - Diabetes mellitus Type 1 & Type 2
  - Growth hormone deficiency
  - Hypercortisolism
  - Hyperparathyroidism
  - Hyperthyroidism
  - Hypogonadism
  - Porphyria
  - Pregnancy

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

Causes of Secondary Osteoporosis in Adults

- **Nutritional/GI conditions**
  - Alcoholism
  - Anorexia nervosa
  - Calcium deficiency
  - Chronic liver disease
  - Malabsorption syndromes/malnutrition (including celiac disease, cystic fibrosis, Crohn disease, and gastric resection or bypass)
  - Vitamin D deficiency

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

Causes of Secondary Osteoporosis in Adults

- **Drugs**
  - Anti-epileptic drugs
  - Aromatase inhibitors
  - Chemotherapy/immunosuppressants
  - Medroxyprogesterone acetate
  - Glucocorticoids
  - Gonadotropin-releasing hormone agents
  - Heparin
  - Lithium
  - Proton pump inhibitors
  - SGLT-2 inhibitors
  - Thiazolidinediones
  - Thyroid hormone (in supraphysiologic doses)

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

SGLT-2 inhibitors

- The effect of SGLT-2i on bone fracture is controversial.
- Large meta-analyses and RCTs indicate that the use of SGLT-2i did not show an association with increased risk of bone fracture
- Assessment of BMD and fracture risk should be considered, especially for patient with a high risk of fracture.
- Based on its significant benefit on cardiovascular and chronic kidney disease outcomes, SGLT-2i are still an outstanding choice

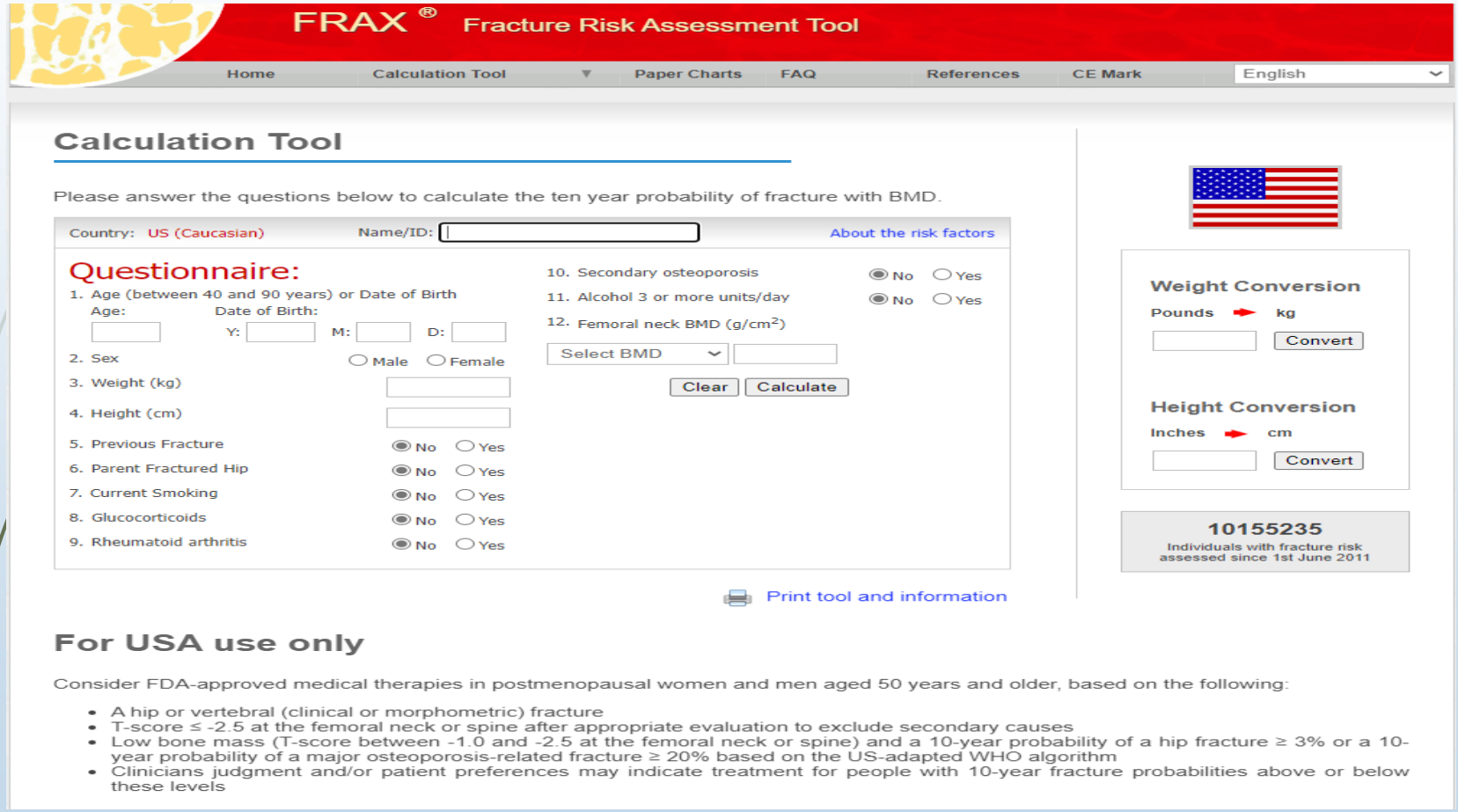
Dong B et al. The Extraglycemic Effect of SGLT-2i on Mineral and Bone Metabolism and Bone Fracture. Endocrinol. 2022 Jul 7;13:918350.

FRAX (Fracture Risk Assessment Tool)

- Low BMD as measured by DXA is **NOT** a perfect predictor of fracture risk.
- To predict fracture risk among people with low bone density to guide treatment decisions.
- Indicated for those with BMD in osteopenia range and not on pharmacological treatment yet.
- Recommend treatment if:
  - 10-yr probability of hip fracture ≥ 3% or 10-yr probability of major osteoporosis-related fracture ≥ 20%.

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

FRAX (Fracture Risk Assessment Tool)



LATERAL VERTEBRAL ASSESSMENT





Source: International Osteoporosis Foundation.

Indications for VFA

- Women age ≥ 70 or men age ≥ 80 years if BMD T-score at the spine, total hip, or femoral neck is ≤ -1.0.
- Women age 65-69 and men age 70-79 if BMD T-score at the spine, total hip, or femoral neck is ≤ -1.5.
- Postmenopausal women and men age ≥ 50 yr with specific risk factors:
  - Low trauma fracture during adulthood
  - Historical height loss of ≥4 cm (1.5 inches)
  - Prospective height loss of ≥ 2 cm (0.8 inches)
  - Recent or ongoing glucocorticoid treatment

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

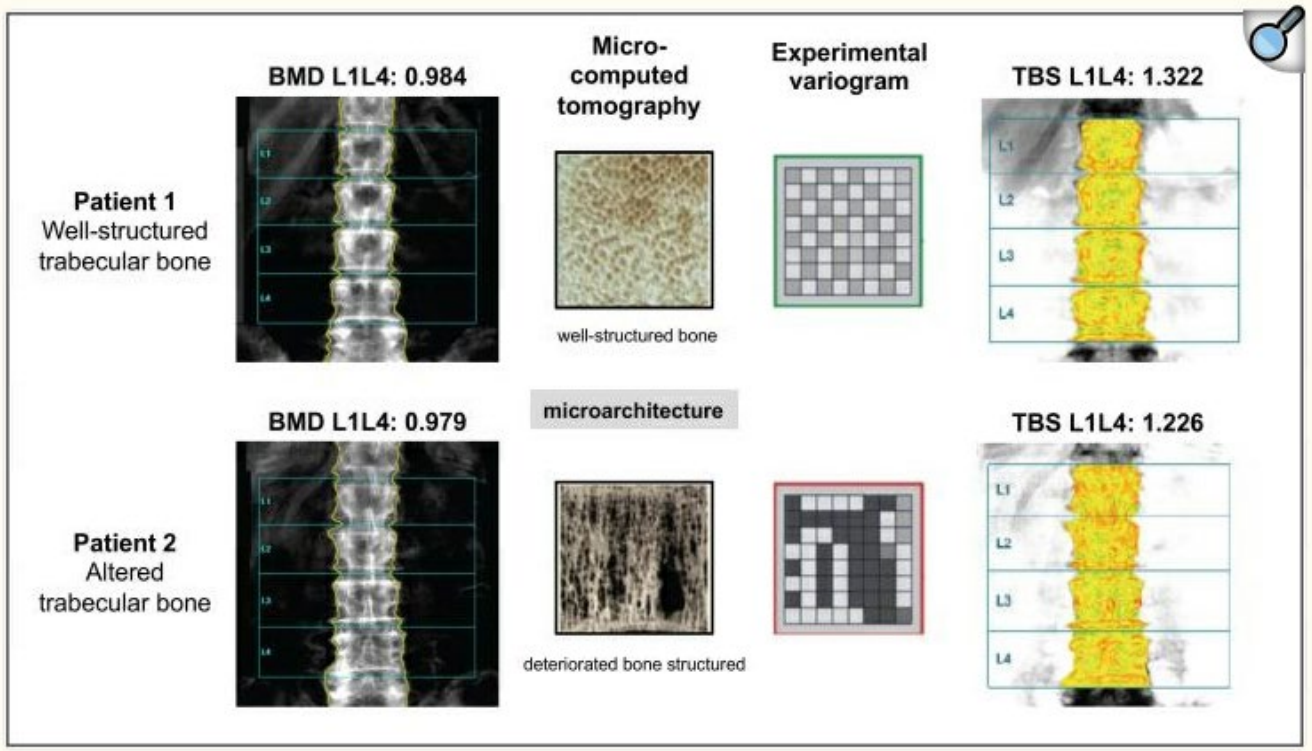
Trabecular Bone Score (TBS)

- Textural index that evaluates pixel gray-level variations in LS DXA image providing an indirect parameter of trabecular architecture and bone quality.
- Substantial evidence supporting the use of TBS to assess vertebral, hip, and major osteoporotic fracture risk in postmenopausal women
- Particularly useful as an adjunct to BMD for fracture risk assessment in conditions associated with increased fracture risk, such as T2DM, chronic corticosteroid excess, and other conditions where in BMD readings are often misleading.

Palomo T et al. Update on trabecular bone score. Arch Endocrinol Meta. 2022 Nov 10;66(5): 694-706.

Trabecular Bone Score (TBS)

Figure 1. Concept of TBS – the figure presents an example of two different patients with equivalent BMD but different TBS.



Palomo T et al. Update on trabecular bone score. Arch Endocrinol Meta. 2022 Nov 10;66(5): 694-706.

Trabecular Bone Score (TBS)

- There is no consensus about TBS cutoff points (TBS ≥ 1.350 is considered normal, TBS = 1.200-1.350 is "partially degraded" bone, and TBS ≤ 1.200 indicates "degraded" bone in postmenopausal women
- While a low TBS is associated with a greater risk of fracture, a threshold value to initiate treatment has not been determined yet
- International Society of Clinical Densitometry recommended against the use of TBS as a single parameter to guide treatment decisions, but suggest to adjust FRAX probabilities using TBS values to assist in treatment decisions

Palomo T et al. Update on trabecular bone score. Arch Endocrinol Meta. 2022 Nov 10;66(5): 694-706.

Bone turnover markers

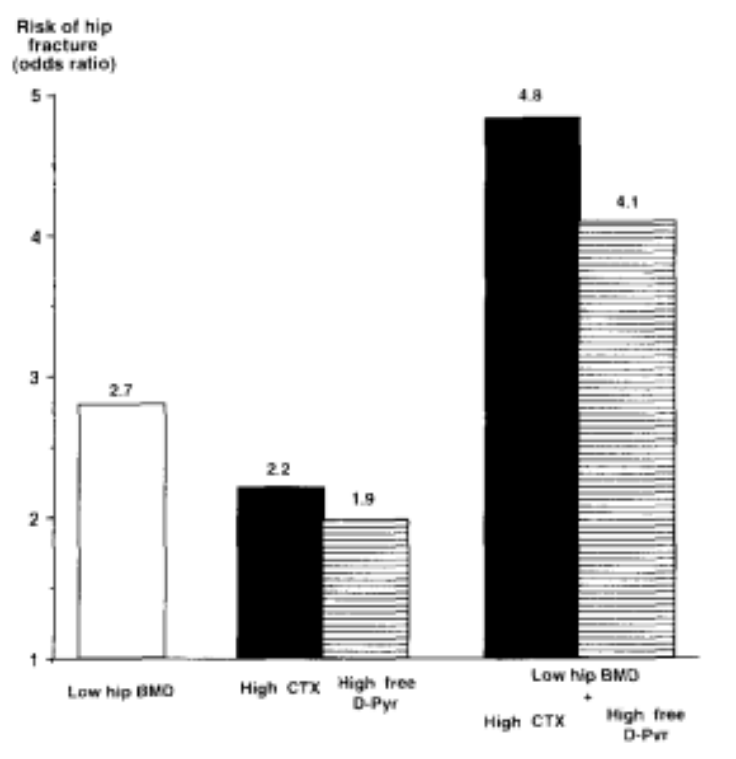
- Resorption
  - C-telopeptide (CTX)
    - Serum
  - N-telopeptide (NTX)
    - Urine
- Formation
  - Bone specific Alkaline Phosphatase
  - Osteocalcin
  - Carboxy-terminal propeptide of type 1 collagen (P1NP)

Bone Turnover Markers

- Predict risk of fracture independently of BMD in untreated patients and help determine the need for treatment
- Predict rapidity of bone loss in untreated patient
- Predict extent of fracture risk reduction when repeated after 3-6 months treatment with FDA-approved therapies
- Predict magnitude of BMD increases with FDA-approved therapies
- Help determine adequacy of patient compliance or malabsorption of medication if given oral bisphosphonate therapy
- Help determine duration of "drug holiday" and when if medication should be restarted (Data are limited without peer-reviewed trials supporting this approach)

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

Prediction of Hip Fracture by Bone Markers



Gamero P, et al. Markers of Bone Resorption Predict Hip Fracture in Elderly Women: The EPIDOS Prospective Study J Bone Miner Res. 1996;11:1531-1538.

Fall Prevention

- Every 13 seconds, an older adult is seen in an emergency department for a fall.
- Falls are the leading cause of hospitalizations among people age 65 and older.
- Falls are the leading cause of hip fractures, which can cause disability and even death.
- Muscle strengthening, balance training, correction of visual impairment may improve mobility and reduce risk of falls.

https://americanbonehealth.org/stepping-out-strong

Measures for Prevention of Falls

- Anchor rugs
- Minimize clutter
- Remove loose wires
- Use nonskid mats
- Install handrails in bathrooms, halls, and long stairways
- Light hallways, stairwells, and entrances
- Encourage patient to wear sturdy, low-heeled shoes

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

Who Needs Pharmacologic Therapy?

- Those with a T-score between − 1.0 and − 2.5 in the spine, femoral neck, total hip, or 1/3 radius and a history of fragility fracture of the hip or spine.
- Those with a T-score of − 2.5 or lower in the spine, femoral neck, total hip, or 1/3 radius.
- Those with a T-score between − 1.0 and − 2.5 in the spine, femoral neck, total hip, or 1/3 radius, if the FRAX (or if available, TBS-adjusted FRAX) 10-year probability for major osteoporotic fracture is ≥ 20% or the 10-year probability of hip fracture is ≥ 3%.

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

PHARMACOTHERAPY

BISPHOSPHONATES

- First introduced in the 1990s
- Reduce the activity of bone-resorbing osteoclasts

Drug	Treatment
Alendronate (Fosamax)	10 mg PO daily 70 mg PO weekly
Risedronate (Actonel, Atelvia)	5 mg PO daily 35 mg PO weekly 150 mg PO monthly
Zoledronate (Reclast)	5 mg IV once yearly
Ibandronate (Boniva)	2.5 mg PO daily 150 mg PO monthly

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

BISPHOSPHONATES

- Considered as initial options for most patients without contraindications
- Contraindication: eGFR <30 for risedronate and ibandronate or eGFR <35 for alendronate and zoledronate
- Oral bisphosphonates are contraindicated if:
  - Inability to follow the dosing regimen
  - The presence of anatomic or functional esophageal abnormalities
  - Presence of GI malabsorption

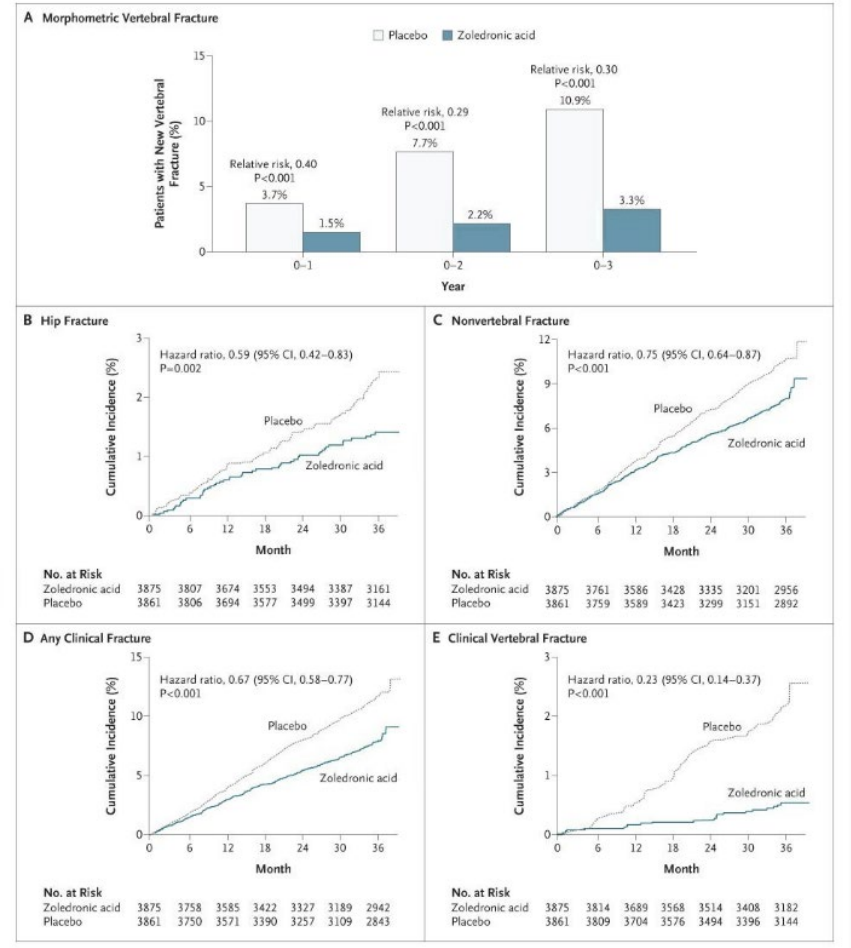
AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

BISPHOSPHONATES

- Most common cause of poor outcomes, particularly with oral BPs, is treatment nonadherence
- An estimated 50% of patient who start oral BPs stop taking within 3 to 6 months.
- Bone turnover markers can help assess adherence to oral BP therapy

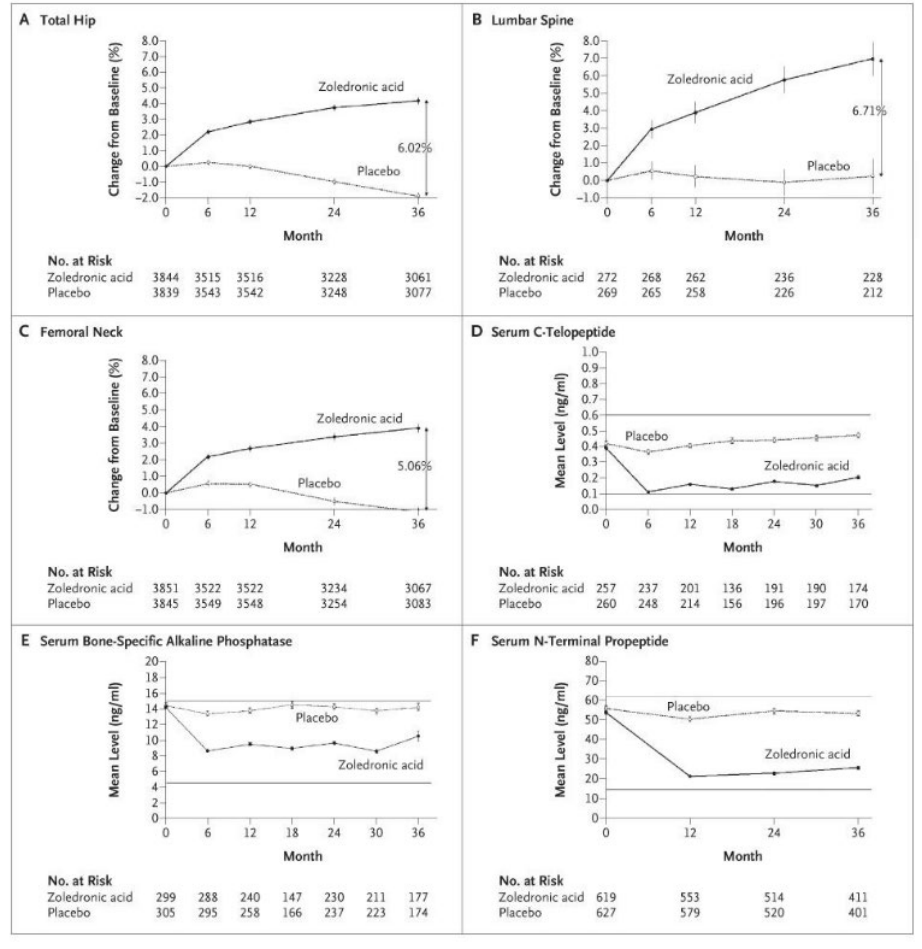
Adler RA et al. Managing Osteoporosis Patients after Long-Term Bisphosphonate Treatment. J Bone Miner Res. 2016 Jan;31(1):16–35.

HORIZON Pivotal Fracture Trial



Black DM et al. Once-Yearly Zoledronic Acid for Treatment of Postmenopausal Osteoporosis. NEJM 2007.

HORIZON Pivotal Fracture Trial



Black DM et al. Once-Yearly Zoledronic Acid for Treatment of Postmenopausal Osteoporosis. NEJM 2007.

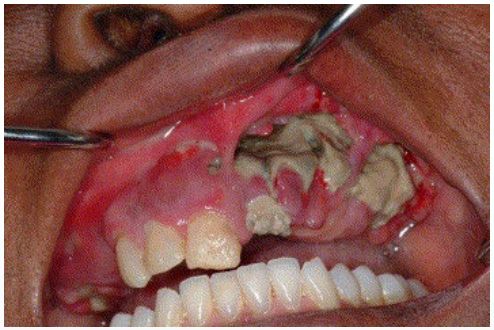
Atypical Femoral Fracture (AFF)



- Subtrochanteric region with long-term BP therapy
- Occur after little or no trauma
- Prodromal groin or thigh pain in ~70% of patient with AFF

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

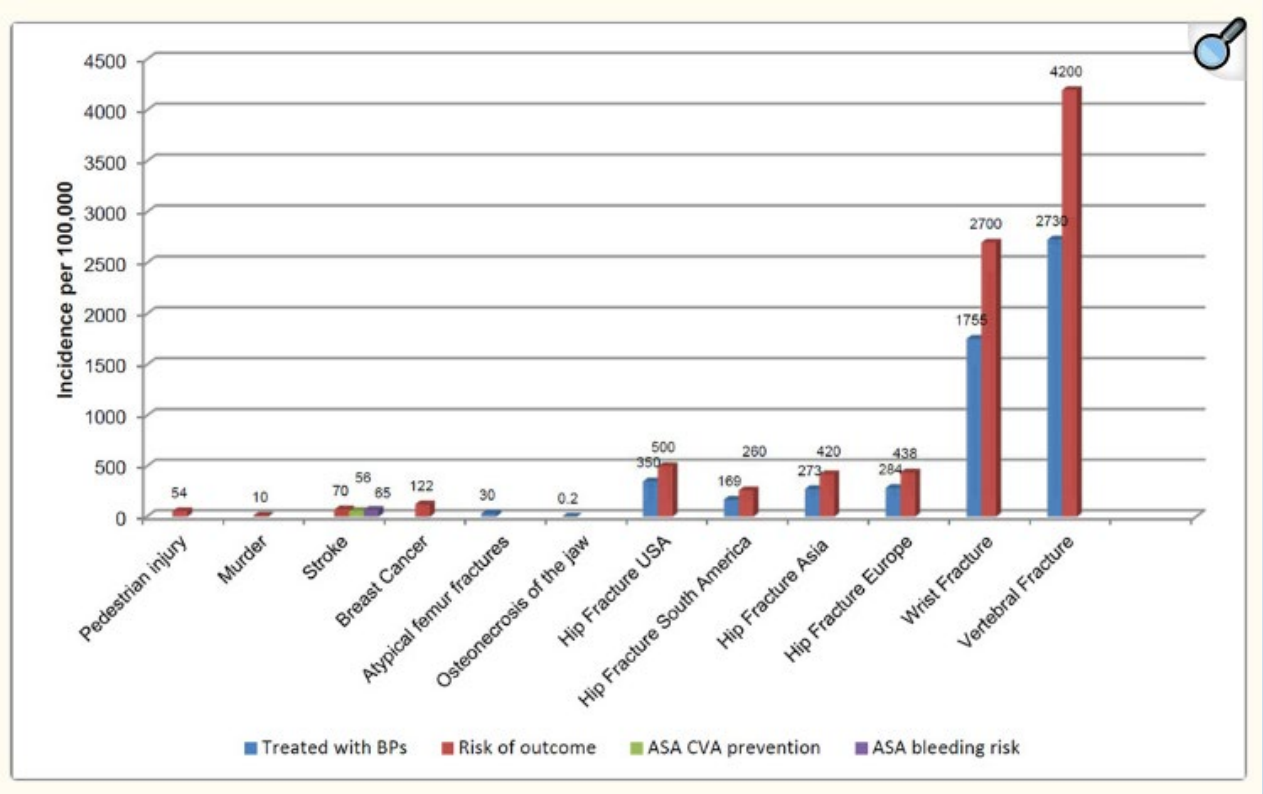
Osteonecrosis of Jaw



- The presence of exposed bone in the maxillofacial region that did not heal within 8 weeks after identification
- Incidence range from 1/10,000 to 1/100,000 patient per year.
- Risk Factors: dental pathologic conditions, invasive dental procedures, smoking, and poor dental hygiene, concomitant GC and/or chemotherapy
- May delay the initiation of therapy until the dental issues have been corrected

Adler RA et al. Managing Osteoporosis Patients after Long-Term Bisphosphonate Treatment. J Bone Miner Res. 2016 Jan;31(1):16–35.

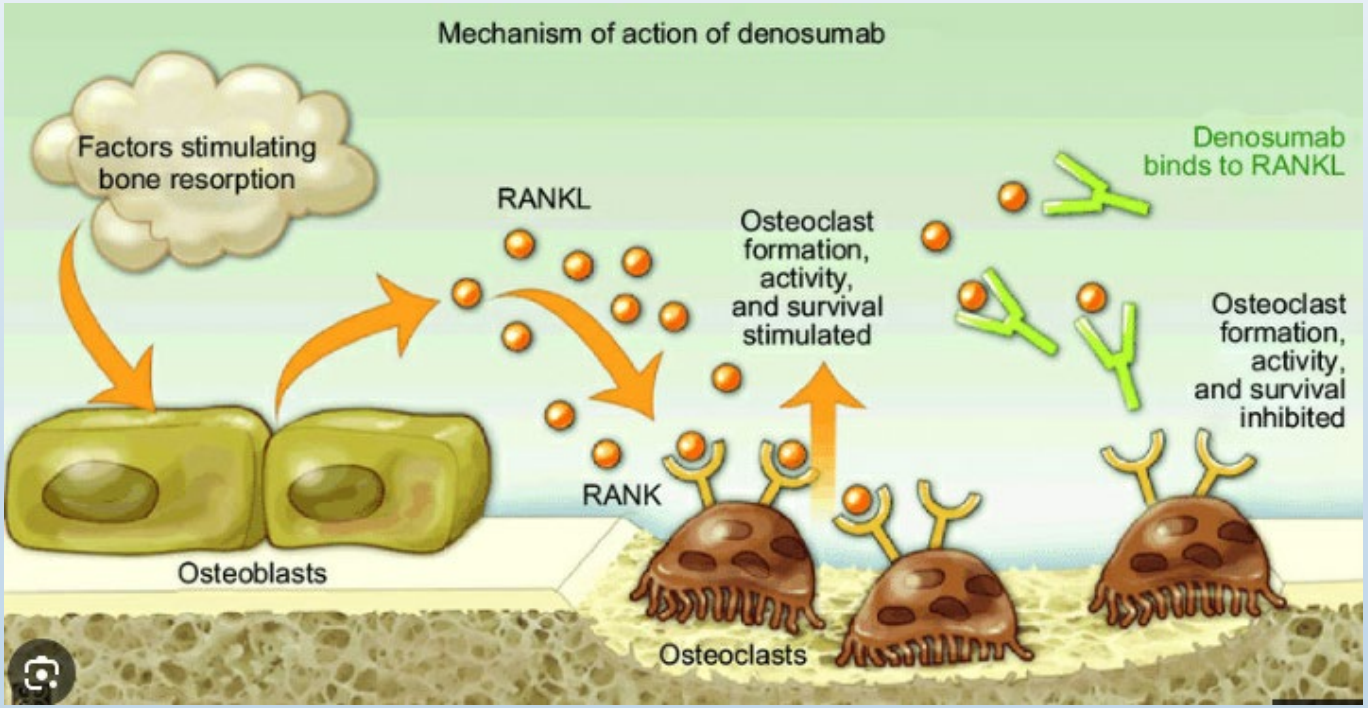
Comparative Risks with Bisphosphonate Use and Other Health Outcomes



Adler RA et al. Managing Osteoporosis Patients after Long-Term Bisphosphonate Treatment. J Bone Miner Res. 2016 Jan;31(1):16–35.

Denosumab (Prolia)

- Monoclonal antibody that binds to RANKL and blocks osteoclast proliferation, function and survival, subsequently reducing bone resorption.



Denosumab (Prolia)

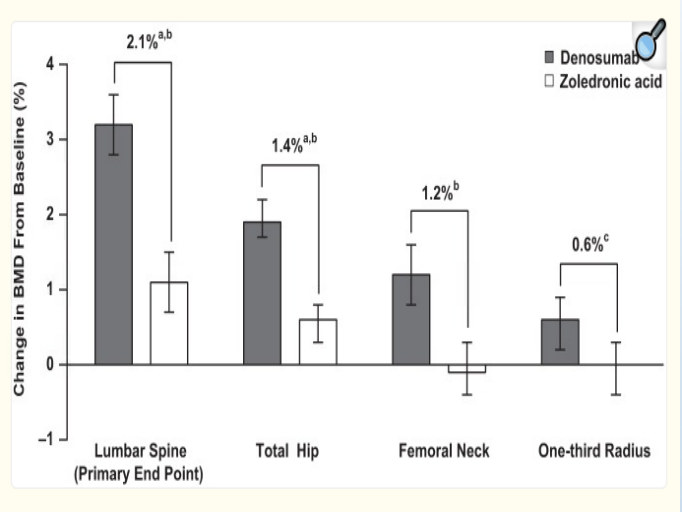
- 60 mg SQ every 6 months of denosumab showed "broad-spectrum" antifracture efficacy as early as 12 months after starting therapy [FREEDOM Trial]
- Switching from BPs to denosumab results in additional gains in BMD
- Denosumab is NOT contraindicated in patients with renal insufficiency, and no dose adjustment is required in these patients.

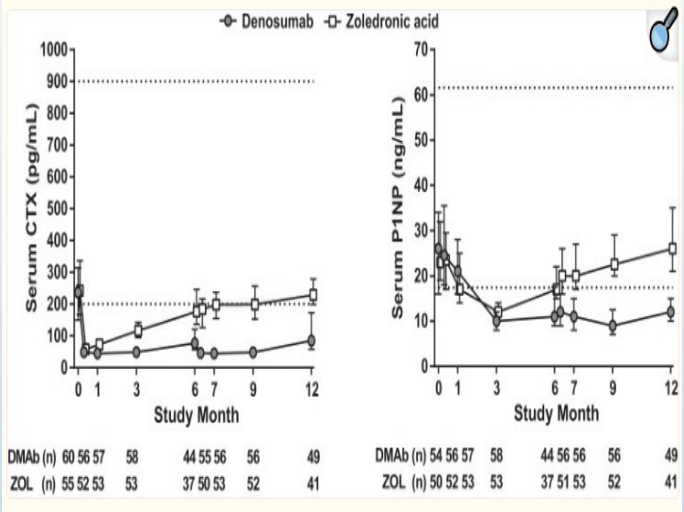
Miller PD, Pannacciulli N, Brown JP, et al. Denosumab or zoledronic acid in postmenopausal women with osteoporosis previously treated with oral bisphosphonates. JCEM. 2016;101:3163-3170.

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

Denosumab or Zoledronic Acid in Postmenopausal Women With Osteoporosis Previously Treated With Oral Bisphosphonates

Miller PD, Pannacciulli N, Brown JP, et al. JCEM. 2016;101:3163-3170.





Denosumab—Cessation warning

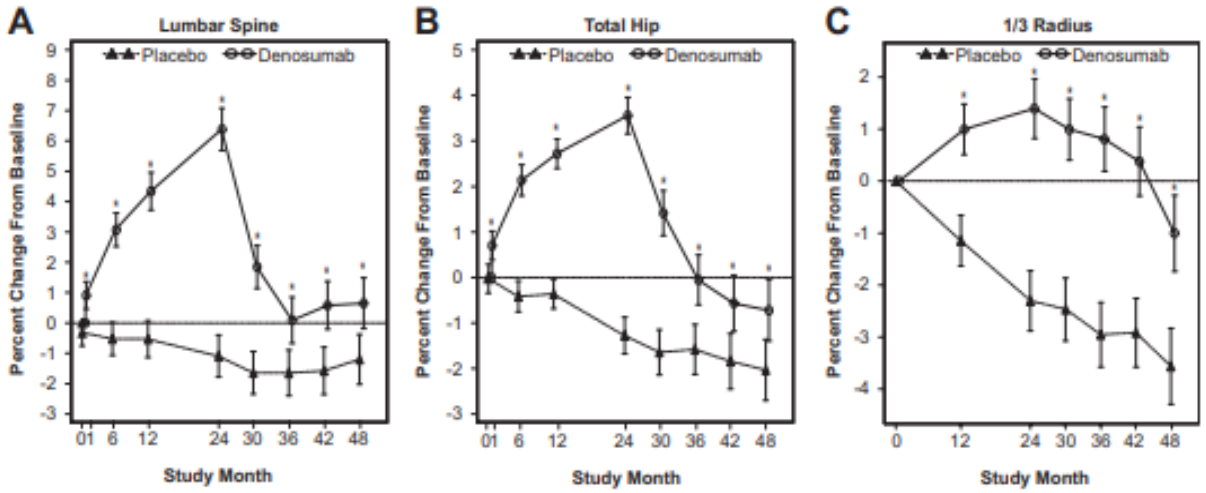


FIG. 3. Percentage change from month 0 in Lumbar Spine (A), Total Hip (B), and 1/3 Radius (C) BMD over 48 months. Percentage change from month 0 in BMD is presented as least squares means and 95% confidence intervals based on a repeated measures model that adjusts for treatment, strata, visit, month 0 value, densitometer type, treatment-by-visit interaction, and month 0 value-by-densitometer type interaction. Includes participants enrolled in the off-treatment phase with observed values at month 0 and the time point of interest [n = 110–128 (placebo) and n = 109–128 (denosumab)]. *, $P \leq 0.0071$.

Bone HG, et al. Effects of Denosumab Treatment and Discontinuation on Bone Mineral Density and Bone Turnover Markers in Postmenopausal Women with Low Bone Mass JCEM 2011.

Denosumab—Cessation warning

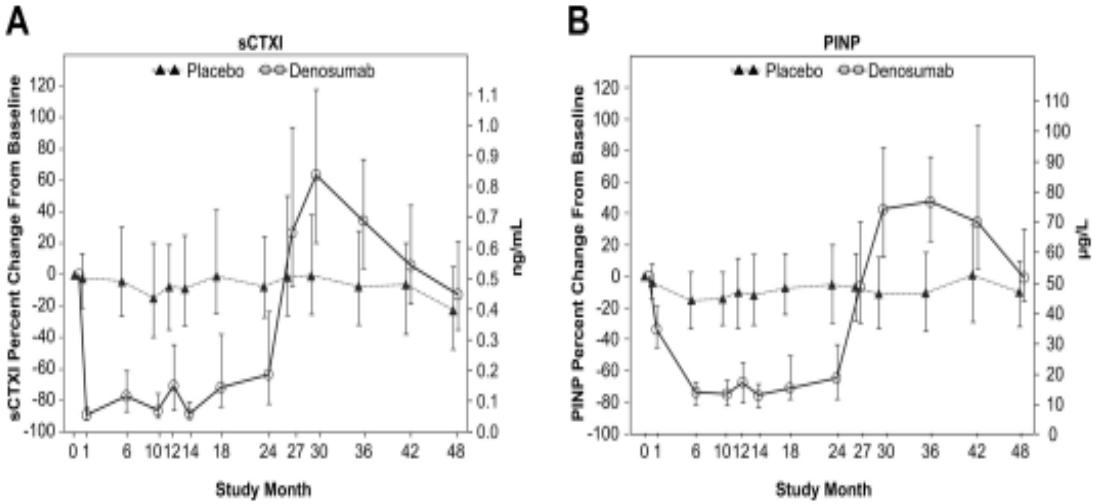
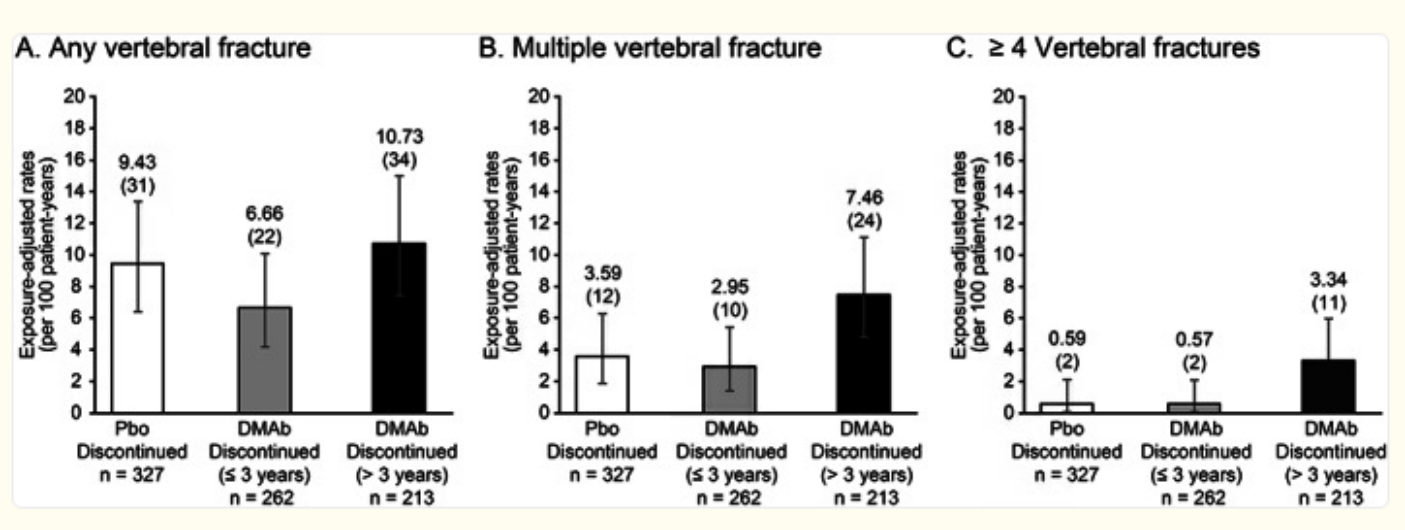


FIG. 4. Percentage change from month 0 in sCTXI (A) and PINP (B) over 48 months. Percentage change from month 0 in BTM are presented as medians and interquartile ranges (*left vertical axes*). Approximate corresponding concentrations are presented for reference (*right vertical axes*). The interquartile ranges shown on the graphs only apply to the percentage change axes. Includes participants enrolled in the off-treatment phase with observed values at the time point of interest [n = 113–128 (placebo) and n = 110–128 (denosumab)].

Bone HG, et al. Effects of Denosumab Treatment and Discontinuation on Bone Mineral Density and Bone Turnover Markers in Postmenopausal Women with Low Bone Mass JCEM 2011.

Multiple Vertebral Fractures After Denosumab Discontinuation: FREEDOM and FREEDOM Extension Trials Additional Post Hoc Analyses

Cosman F et al. J Bone Miner Res. 2022 Oct 12; 37(11):2112-2120.



Effectiveness of Sequential Treatment with Zoledronic Acid Following Discontinuation of Denosumab in Osteoporosis: A Narrative Review

Quyang H et al. Drug Des Devel Ther. 2025 Nov 9;19:10013-10031.

- Sequential administration of Zoledronic acid following Denosumab discontinuation is recommended.

- This approach can partially preserve the BMD gains achieved with Denosumab, dampen the rebound increase in bone turnover markders and offer some protection against vertebral fracture.

Anabolic Agents

- Preferable for patients at very high risk of fracture as initial therapy

Drug
Teriparatide (Forteo)
Abaloparatide (Tymlos)
Romosozumab (Evenity)

AACE/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of Postmenopausal Osteoporosis-2020 Update.

Teriparatide

- PTH 1-34 analog
- 20 µg, daily self-administered SQ injection
- 24 months, can be longer (Nov 2020: removal of black box warning for potential risk of osteosarcoma)
- BMD increase over median follow-up of 21 months (compared to placebo)
  - LS: 9%; TH: 2.6%; FN 3%
- 65% lower risk of new vertebral fracture; 53% lower risk of nonvertebral fracture (compared to placebo)
- Precautions: Paget's disease, bone cancer, prior skeletal radiation, renal stones or disease a/w urinary calcium increase, unexplained high alkaline phosphatase

Neer RM et al. NEJM 2001; 344(19): pp. 1434-1441.

Abaloparatide

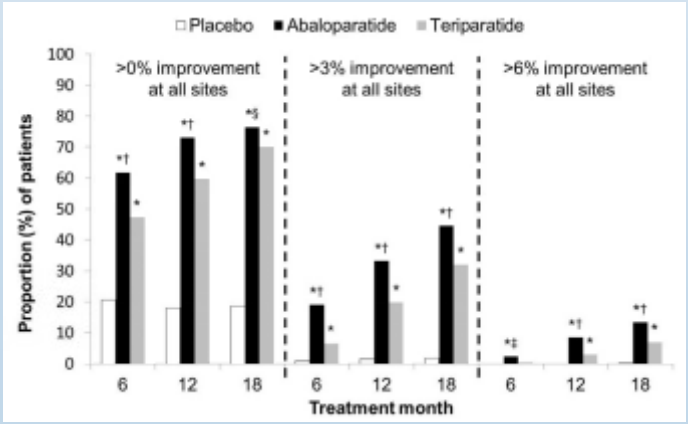
- PTHrP analog
- 80 µg, daily self-administer SQ injection
- 24 months, can be longer (Dec 2021: removal of black box warning for potential risk of osteosarcoma)
- BMD increase at 18 months (compared to placebo)
  - LS: 11.2%; TH 4.2%; FN 3.6%
- 86% lower risk of vertebral fracture; 43% lower risk of nonvertebral fracture (compared to placebo)
- Precautions: Paget's disease, bone cancer, prior skeletal radiation, renal stones or disease a/w urinary calcium increases, unexplained high alkaline phosphatase

Miller et al. JAMA. 2016: Vol.316, No.7.

Teriparatide and Abaloparatide

- Both showed to increase BMD and reduce the risk of vertebral and nonvertebral fractures in women with postmenopausal osteoporosis

- Head-to-head trial, gains in BMD were greater with abaloparatide compared with teriparatide at all 3 anatomical sites (total hip, femoral neck, & lumbar spine). Fracture reduction was also greater with abaloparatide



Miller PD et al. Bone 2019.

Romosozumab

- Monoclonal antibody against sclerostin
- 210 mg, monthly physician-administered SQ injection
- 12 months
- At 12 months (compared to placebo)
  - LS: 13.3%; TH 6.9%; FN 5.9%
- 73% lower risk of new vertebral fracture; 36% lower risk of clinical fracture (compared to placebo)
- Precautions: FDA black box warning: do not initiate in patients who have had a MI or stroke within the past year. Careful evaluation of risk-benefit in patients with CV risk factors.

Cosman F et al. Romosozumab treatment in postmenopausal women with osteoporosis. NEJM 2016; 375(16): pp.1532-1543.

Romosozumab vs teriparatide transitioning from oral BP therapy

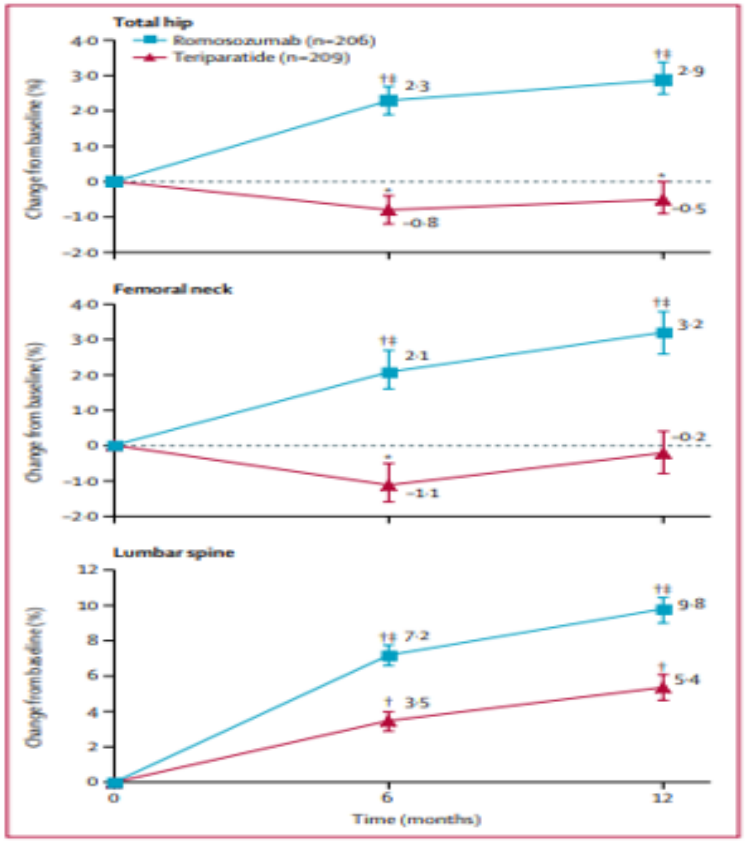
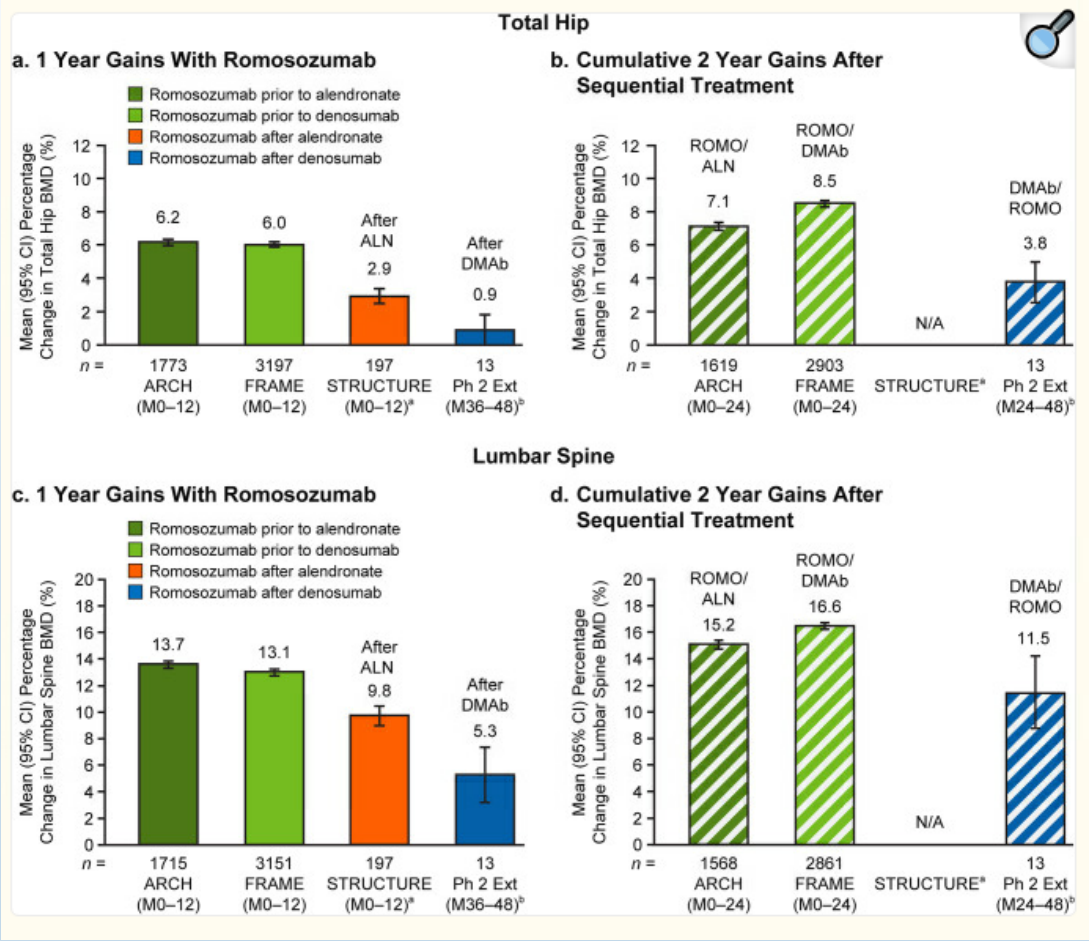


Figure 2: **Percentage change from baseline in areal bone mineral density at the total hip, femoral neck, and lumbar spine by dual energy x-ray absorptiometry**
Data are least-squares means and 95% CI. *p<0·05 versus baseline. †p<0·0001 versus baseline. ‡p<0·0001 versus teriparatide.

Langdahl BL, et al., Lancet 2017.

Romosozumab and antiresorptive treatment: the importance of treatment sequence

Cosman F et al. Osteoporos Int. 2022 Feb 15;33(6):1243-1256.



Sequential Therapy for Long-Term Treatment

- For patient who discontinue denosumab, follow-on antiresorptive therapy is required to prevent the overshoot in bone remodeling and minimize subsequent bone loss
- Transitioning from denosumab to teriparatide (and most likely abaloparatide) should be avoided as this leads to accelerated bone remodeling and rapid bone loss
- In postmenopausal women who have not received any prior bone-target therapy, the greatest gains in bone mass are achieved with the initial use of a bone-forming drug followed by an antiresorptive
- Initial therapy with a BP may modestly diminish the bone effects of subsequent bone-forming drugs but prior antiresorptive use is not a contraindication to anabolic therapy.

Ramchand SK, et al., JCEM 2024.

Take Home Message

- Chronic condition requiring long-term management in most patients
- Most patient will require more than one drug during the treatment course
- Know which drugs to start and in what sequence


Thank You





