# OSTEOPOROSIS: Diagnosis and Treatment in 2019

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November 15, 2019

## Objectives

- Identify risk factors for bone loss
- Identify risk factors for fracture
- Define Dexa criteria for diagnosis
- Identify why, who, when & how to treat

### A Major Public Health Problem

- Osteoporosis is a major public health problem. More than 10 million Americans have osteoporosis, and an additional 43 million have low bone mass, according to data from the U.S. National Health and Nutrition Examination Survey.
- More than 2 million osteoporosis-related fractures occur each year in the United States, and more than 70% of these occur in women.
- More than 20% of postmenopausal women have prevalent vertebral fractures. As the most common osteoporotic fracture, vertebral fractures are a hallmark of the disease and indicate a high risk for future fractures. They are also associated with impaired pulmonary function and increased mortality risk, especially respiratory deaths. However, the majority of vertebral fractures (2/3) are asymptomatic.

Camacho PM, Petak SM, Binkley N et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2016 Update. Endocr Pract. 2016;22(Suppl 4):1-42.

Wright NC, Looker AC, Saag KG, Curtis JR, Delzell ES, Randall S, 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.

Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025. J Bone Miner Res. 2007;22:465-475. Puisto V et al. Vertebral fracture and cause-specific mortality: a prospective population study of 3,210 men and 3,730 women with 30 years of follow-up. Eur Spine J 2011; 20:2181–2186.

## Prevalence of Osteoporosis Increases With Age

- Age is an independent risk factor for osteoporotic fractures. The
  risk increases progressively with age, doubling every 5 to 10
  years. Nearly one-quarter (24.8%) of women 65 and older have
  osteoporosis. For women 80 and older, that figure rises to more
  than one-third (35.6%), according to a report from the CDC.
- In addition, more than half (52.3%) of women 65 and older have low bone mass (osteopenia). Although fracture risk is highest in women with osteoporosis, most women who experience a fracture have osteopenia, because there are many more women in this category.

The Centers for Disease Control and Prevention. "Percentage of Adults Aged 65 and Over With Osteoporosis or Low Bone Mass at the Femur Neck or Lumbar Spine: United States, 2005–2010." <a href="https://www.cdc.gov/nchs/data/hestat/osteoporosis/osteoporosis/2005/2010.htm">https://www.cdc.gov/nchs/data/hestat/osteoporosis/osteoporosis/2005/2010.htm</a>. Accessed August 2, 2018. Ross PD. "Risk Factors for Osteoporotic Fracture." New England Journal of Medicine 1998; 27: 289-301.

# Most Women with Osteoporosis Are Not Treated

- Postmenopausal osteoporosis is preventable and treatable, but only a small proportion of women at increased risk for fracture are evaluated and treated.
- Even among women with fractures, lack of treatment is common. Fewer than 1 in 4 women age 67 or older with an osteoporosis-related fracture undergoes bone density measurement or begins osteoporosis treatment.

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Kanis JA, Melton LJ 3rd, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. J Bone Miner Res. 1994;9:1137-1141.

#### Osteoporosis Affects Men Too

 Osteoporosis is an often asymptomatic disorder characterized by decreased bone strength and increased risk for bone fractures. Osteoporosis is less common in men than women, but it still affects a significant number of men. Of the 44 million Americans who have either osteoporosis or low bone mineral density (BMD), approximately 20% more than 8 million—are men.

NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA 2001; 285:785–795. Burge R et al. Incidence and economic burden of osteoporosis- related fractures in the United States. J Bone Miner Res 2007; 22:465–475. Nelson B et al. Osteoporosis in men: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2012; 97:1802-1822.

#### Men Are Often Overlooked

- Despite the substantial clinical burden of osteoporosis, the condition is commonly under-diagnosed and under-treated, especially in men.
- In one study of men and women 50 and older who were hospitalized for fragility hip fractures, only 4.5% of men were receiving any kind of osteoporosis treatment at discharge, compared with 27% of women. At 1 to 5 years of follow-up, only 11% of men had a BMD measurement, compared with 27% of women.
- In another, similar study of men and women with osteoporosis-related fractures, the vast majority of men (more than 95%) and more than half the women (51%) were not evaluated or treated according to current guideline or expert recommendations.

## Diagnosing Osteoporosis

 Postmenopausal osteoporosis can be diagnosed based on the World Health Organization (WHO) definition: a bone mineral density (BMD) T-score of -2.5 or below in the lumbar spine, femoral neck, total hip, and/or 33% (one-third) radius.

World Health Organization Criteria for Classification of Osteopenia and Osteoporosis			
Category	T-score		
Normal	-1.0 or above		
Low bone mass (osteopenia) <sup>n</sup>	Between -1.0 and -2.5		
Osteoporosis	-2.5 or below		

<sup>&</sup>lt;sup>a</sup> Fracture rates within this category vary widely. The category of "osteopenia" is useful for epidemiology studies and clinical research but is problematic when applied to individual patients and must be combined with clinical information to make treatment decisions.

Note: this is table 4 from the AACE Guidelines.

Camacho PM, Petak SM, Binkley N et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2016 Update. Endocr Pract. 2016;22(Suppl 4):1-42.

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## Additional Diagnostic Criteria

- In addition to the WHO bone mineral density criteria, these may also be used to diagnose osteoporosis:
  - Low-trauma spine or hip fracture, regardless of BMD
  - Osteopenia or low bone mass (T-score between -1 and -2.5) with a fragility fracture of proximal humerus, pelvis, or possibly distal forearm
  - Low bone mass or osteopenia and high FRAX® (<u>Fracture Risk Assessment Tool</u>) fracture probability based on country-specific thresholds

# Screening for Postmenopausal Osteoporosis

- All postmenopausal women age 50 or older should undergo clinical assessment for osteoporosis and fracture risk, including a detailed history and physical examination. Tools such as FRAX should be used when available.
- BMD testing is the gold standard in diagnosing osteoporosis. However, this test is not always available. The decision to measure BMD should be based on an individual's clinical fracture risk profile and skeletal health assessment.

### Screening Recommendations

- Both the AACE and the U.S. Preventive Services Task Force recommend BMD testing for all women aged 65 and older as well as younger postmenopausal women at increased risk for bone loss and fracture based on fracture risk analysis.
- BMD measurement is not recommended in children, adolescents, healthy young men, or premenopausal women, unless there is a significant fracture history or there are specific risk factors for bone loss.

Nelson HD, Haney EM, Dana T, Bougatsos C, Chou R. Screening for osteoporosis: an update for the U.S. Preventive Services Task Force. Ann Intern Med. 2010;153: 99-111.

## Who Should Be Tested?

- The Endocrine Society recommends BMD testing in all men 70 or older.
- Men age 50-69 should be tested if they have a history of fracture or other risk factors including the following:
  - Delayed puberty
  - Hypogonadism
  - Hyperparathyroidism
  - Hyperthyroidism
  - Chronic obstructive pulmonary disease
  - Use of glucocorticoids or GnRH agonists
  - Alcohol abuse or smoking

#### Clinical Presentation

- Fracture is the single most important manifestation of postmenopausal osteoporosis. Osteoporotic fractures are usually caused by low-energy injuries such as a fall from standing height.
- Vertebral fractures, however, may occur during routine daily activities, without a specific fall or injury. In clinical practice, it may be difficult or impossible to reconstruct the mechanical force applied to bone in a particular fall.

#### Clinical Presentation

- Osteoporosis-related fractures can lead to pain, disability, and deformity. They reduce quality and quantity of life.
- Hip fractures are the most serious consequence of postmenopausal osteoporosis. Women with hip fracture have an increased mortality of 12% to 20% during the subsequent two years. More than 50% of hip fracture survivors are unable to return to independent living. Many survivors require long-term nursing home care
- Other low-trauma, osteoporosis-related fractures include those of the proximal humerus, pelvis, and in some cases the distal forearm.

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Black DM and Rosen CJ. Postmenopausal Osteoporosis. The New England Journal of Medicine 2016; 374:254-262.

To identify coexisting medical conditions that cause or contribute to bone loss, an appropriate
medical evaluation is indicated for all women with postmenopausal osteoporosis. Some causes
of secondary osteoporosis include the following.

Endocrine or metabolic causes	Nutritional/GI conditions	Drugs	Disorders of collagen metabolism	Other
Acromegaly	Alcoholism	Antiepileptic drugsa	Ehlers-Danlos syndrome	AIDS/HIVa
Diabetes mellitusType 1Type 2 Growth hormone deficiency Hypercortisolism Hyperparathyroidism Hyperthyroidism Hypogonadism Hypogonadism Porphyria Pregnancy	Anorexia nervosa  Calcium deficiency  Chronic liver disease  Malabsorption syndromes/ malnutrition (including celiac disease, cystic fibrosis, Crohn's disease, and gastric resection or bypass)  Total parenteral nutrition  Vitamin D deficiency	Aromatase inhibitors  Chemotherapy/ immunosuppressants  Depo-Provera  Glucocorticoids  Gonadotropin-releasing hormone agents  Heparin  Lithium  Proton pump inhibitors	Homocystinuria due to cystathionine deficiency Marfan syndrome Osteogenesis imperfecta	Ankylosing spondylitis Chronic obstructive pulmonary disease Gaucher disease Hemophilia Hypercalciuria Immobilization Major depression Myeloma and some cancers
Note: This is table 11 from the AACE gu	sidelines.	Selective serotonin reuptake inhibitors Thiazolidinediones Thyroid hormone (in supraphysiologic doses)		Organ transplantation  Renal insufficiency/ failure  Renal tubular acidosis  Rheumatoid arthritis  Systemic mastocytosis  Thalassemia

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- Because causes of secondary osteoporosis are common even in apparently healthy, postmenopausal women, laboratory testing should be considered for all women with osteoporosis. Laboratory evaluation could include:
  - Complete blood cell count (CBC)
  - Comprehensive metabolic panel (includes calcium, albumin, and creatinine tests)
  - Serum 25-hydroxyvitamin D
  - Phosphate
  - 24-hour urine collection for calcium, sodium, and creatinine.

- If medical history, physical findings, or laboratory test results suggest causes of secondary osteoporosis, additional laboratory evaluation is warranted and may include, but is not limited to, the following.
  - Serum intact parathyroid hormone (PTH) concentration for possible primary or secondary hyperparathyroidism
  - · Serum thyrotropin
  - Tissue transglutaminase antibodies for suspected celiac disease
  - Serum protein electrophoresis and free kappa and lambda light chains for suspected myeloma
  - Urinary free cortisol or other tests for suspected adrenal hypersecretion

Note: This is taken from table 12 in the AACE guidelines.

- Serum tryptase, urine N-methylhistidine, or other tests for mastocytosis
   Bone marrow aspiration and biopsy to look for marrow-based diseases
- Undecalcified iliac crest bone biopsy with double tetracycline labeling (recommended for patients with bone disease and renal failure to establish the correct diagnosis and direct management)
- Genetic testing for unusual features that suggest rare metabolic bone diseases

- Lifestyle modifications may improve musculoskeletal integrity and balance, preserve bone strength, and prevent future fractures. These include:
- An adequate intake of calcium and vitamin D
  - Daily supplementation with vitamin D<sub>3</sub> at a dose of 1,000 to 2,000 IU is typically needed to maintain an optimal serum 25(OH)D level.
  - For adults age 50 and older, the recommended calcium intake (dietary plus supplements if necessary) is 1,200 mg/day.
- Lifelong participation in regular, weight-bearing, resistance exercise
- Balance-improving exercises to minimize falls
- Avoiding tobacco and excessive use of alcohol
- Eliminating potential risk factors for falling.

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Black DM and Rosen CJ. Postmenopausal Osteoporosis. The New England Journal of Medicine 2016; 374:254-262.

- The AACE strongly recommends pharmacologic therapy for the following patients:
  - Those with osteopenia or low bone mass 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 33% radius.
  - Those with a T-score between -1.0 and -2.5 in the spine, femoral neck, total hip, or 33% radius, if the FRAX® 10-year probability for major osteoporotic fracture is ≥20% or the 10year probability of hip fracture is ≥3% (in the U.S.) or above the country-specific threshold in other countries or regions.

Camacho PM, Petak SM, Binkley N et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2016 Update. Endocr Pract. 2016;22(Suppl 4):1-42.

Black DM and Rosen CJ. Postmenopausal Osteoporosis. The New England Journal of Medicine 2016; 374:254-262.

 A number of agents are approved by the U.S. Food and Drug Administration for prevention and/or treatment of postmenopausal osteoporosis. Full prescribing information should be reviewed before recommending any specific agent.

Drug	Prevention	Treatment
Alendronate (Fosamax)	5 mg PO daily 35 mg PO weekly	10 mg PO daily 70 mg PO weeklyb 70 mg + Dc
Calcitonin (Miacalcin, Fortical)	_	200 IU intranasally once daily, or 100 IU SQ qod
Denosumab (Prolia)	_	60 mg SQ every 6 mo
Estrogen (multiple formulations)	Multiple regimens	_
Ibandronate (Boniva, generic form)	2.5 mg PO daily 150 mg PO monthly	2.5 mg PO daily 150 mg PO monthly 3 mg IV every 3 mo
Raloxifene (Evista)	60 mg PO daily	60 mg PO daily
Risedronate (Actonel, Atelvia, generic form)a	5 mg PO daily 35 mg PO weekly 150 mg PO monthly	5 mg PO daily 35 mg PO weekly 150 mg PO monthly
Abaloparatide (Tymlos)	_	80 mcg subcutaneously daily
Teriparatide (Forteo)	_	20 μg SQ daily
Zoledronic acid (Reclast, generic infusion form)	5 mg IV every 2nd y	5 mg IV once yearly

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 There are no-head-to-head trials comparing the efficacy of approved drugs. However, four agents (alendronate, risedronate, zoledronic acid, and denosumab) have evidence for broad anti-fracture efficacy (spine, hip, and non-vertebral fracture risk reduction). These should be considered as initial options for most patients who are candidates for pharmacologic therapy.

- Patients who have lower or moderate fracture risk can be started on oral agents.
- Injectable agents such as teriparatide, abaloparatide, denosumab, or zoledronic acid can be considered as initial therapy for those who have the highest fracture risk.

- For patients at high risk of spine fracture but not at risk for hip or non-vertebral fractures, ibandronate and raloxifene may be appropriate. Raloxifene has the additional benefit of reducing breast cancer risk.
- Denosumab is the agent of choice for patients with renal insufficiency. The AACE cautions against using in dialysis patients and those with stage 5 kidney disease due to risk of hypocalcemia.

## Sequential Therapy: Follow Anabolic Therapy with Antiresorptive Agents

 Treatment with anabolic agents (teriparatide, abaloparatide) should always be followed by antiresorptive therapy to prevent bone density decline and loss of fracture efficacy. The rationale for using an antiresorptive agent after anabolic therapy is based on both the limited period that anabolic therapy is used and on data showing that bone mineral density declines if antiresorptive therapy is not initiated.

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Leder BZ. Optimizing sequential and combined anabolic and antirespriptive osteoporosis therapy. Journal of Bone and Mineral Research 2018; 2:62-68.

EVENITY™ is the first and only bone builder that works differently with a dual effect<sup>1-3</sup> EVENITY™ works with the body's natural ability to increase bone formation and, to a lesser extent, decrease bone resorption¹

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#### **Original Article**

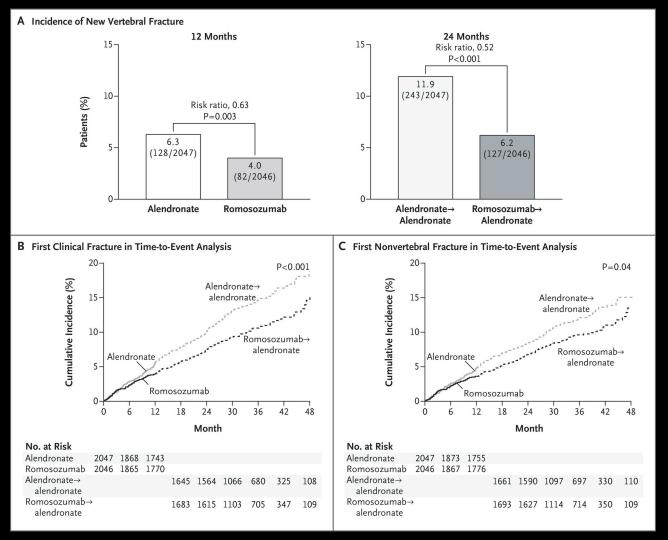
## Romosozumab or Alendronate for Fracture Prevention in Women with Osteoporosis

Kenneth G. Saag, M.D., Jeffrey Petersen, M.D., Maria Luisa Brandi, M.D., Andrew C. Karaplis, M.D., Ph.D., Mattias Lorentzon, M.D., Ph.D., Thierry Thomas, M.D., Ph.D., Judy Maddox, D.O., Michelle Fan, Ph.D., Paul D. Meisner, Pharm.D., and Andreas Grauer, M.D.

N Engl J Med Volume 377(15):1417-1427 October 12, 2017

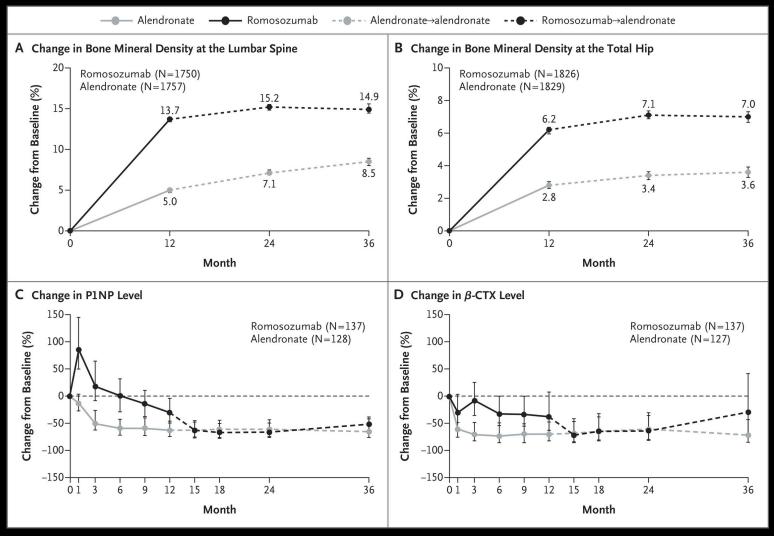


#### Incidence of New Vertebral, Clinical, and Nonvertebral Fracture.



Saag KG et al. N Engl J Med 2017;377:1417-1427

### Percentage Change from Baseline in Bone Mineral Density and Levels of Bone-Turnover Markers.







#### AACE/ACE 2016 POSTMENOPAUSAL OSTEOPOROSIS TREATMENT ALGORITHM

Lumbar spine or femoral neck or total hip T-score of ≤ -2.5, a history of fragility fracture, or high FRAX® fracture probability\*

Evaluate for causes of secondary osteoporosis

Correct calcium/vitamin D deficiency and address causes of secondary osteoporosis

- Recommend pharmacologic therapy
- · Education on lifestyle measures, fall prevention, benefits and risks of medications

No prior fragility fractures or moderate fracture risk\*\*

- Alendronate, denosumab, risedronate, zoledronic acid\*\*\*
- Alternate therapy: Ibandronate, raloxifene

Reassess at least yearly for response to therapy and fracture risk

Increasing or stable BMD and no fractures

Consider a drug holiday after 5 years of oral and 3 years of IV bisphosphonate therapy

Resume therapy when a fracture occurs, BMD declines beyond LSC, BTM's rise to pretreatment values or patient meets initial treatment criteria

Progression of bone loss or recurrent fractures

- Assess compliance
- Re-evaluate for causes of secondary osteoporosis and factors leading to suboptimal response to therapy
- Switch to injectable antiresorptive if on oral agent
- Switch to teriparatide if on injectable antiresorptive or at very high risk of fracture

Prior fragility fractures or indicators of higher fracture risk\*\*

- Denosumab, teriparatide, zoledronic acid\*\*\*
- Alternate therapy: Alendronate, risedronate

Reassess at least yearly for response to therapy and fracture risk

Denosumab

Continue therapy or consider adding teriparatide if progression of bone loss or recurrent fractures Teriparatide for up to 2 years

Sequential therapy with oral or injectable antiresorptive agent Zoledronic acid

- If stable, continue therapy for 6 years\*\*\*\*
- If progression of bone loss or recurrent fractures, consider switching to teriparatide
- 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%. Non-US countries/regions may have different thresholds.
- \*\* Indicators of higher fracture risk in patients with low bone density would include advanced age, frailty, glucocorticoids, very low T scores, or increased fall risk.
- \*\*\* Medications are listed alphabetically.
- \*\* Consider a drug holiday after 6 years of IV zoledronic acid. During the holiday, another agent such as teriparatide or raloxifene could be used.





- 50 yoWF in good health, menopause w/o HRT age 45, +FH oporosis in M age 75
- Requests Dexa showing T-score L total hip
   -1.2 & L1-4 spine -1.1
- Diagnosis?
- Treatment?

Dx: Osteopenia

Rx: Calcium & vitamin D supplementation
Repeat Dexa in 2 years
If fracture + and/or T-scores < -2.0, then
rx treatment warranted. Repeat Dexa 1 year
after 1 year of rx treatment change in rx

- 80 yoWF s/p fall, L hip fx. Menopause age 50, no HRT. PMH HBP, hypercalcemia (10.5),
   25(OH) vit D 22, +kidney stones
- 3 mos postop ORIF L hip, Dexa shows T-scores:
- R total hip -2.8, femoral neck -3.0, L1-4 spine
  -2.2 & proximal 1/3 L radius -3.4
- Diagnosis?
- Treatment?

- Diagnosis: Osteoporosis hip, spine & wrist,
- Fracture L hip
- Hypercalcemia, low vit D & kidney stone hx raise concern for underlying primary hyperparathyroidism. PTH level 110 (n, 15-65)
- Treatment: Forteo, Tymlos or Evenity?
- Prolia?
- Calcium, vitamin D?

- Diagnosis: Osteoporosis hip, spine & wrist,
- Fracture L hip
- Hypercalcemia, low vit D & kidney stone hx raise concern for underlying primary hyperparathyroidism. PTH level 110 (n, 15-65)
- Treatment: Forteo, Tymlos or Evenity?
- Prolia
- Calcium, vitamin D?

- 73 yoWM . PMH HBP, compression fx L3. Ca
   9.4, 25 vit D 30, testosterone 420
- L total hip -2.2, femoral neck -2.5, L1,2,4 spine
   -2.4 (calcification artifact) & proximal 1/3
   L radius -2.4
- Diagnosis?
- Treatment?

Diagnosis: Osteoporosis, fx L3

Treatment: Forteo, Tymlos or Evenity?

Prolia?

Calcim 600-1200 mg/d?

Vitamin D3 2000 u/d?

Diagnosis: Osteoporosis, fx L3

Treatment: Forteo, Tymlos or Evenity

Calcim 600-1200 mg/d

Vitamin D3 2000 u/d

Prolia after 1-2 yr anabolic rx

## QUESTIONS?

## THANK YOU