Osteoporosis

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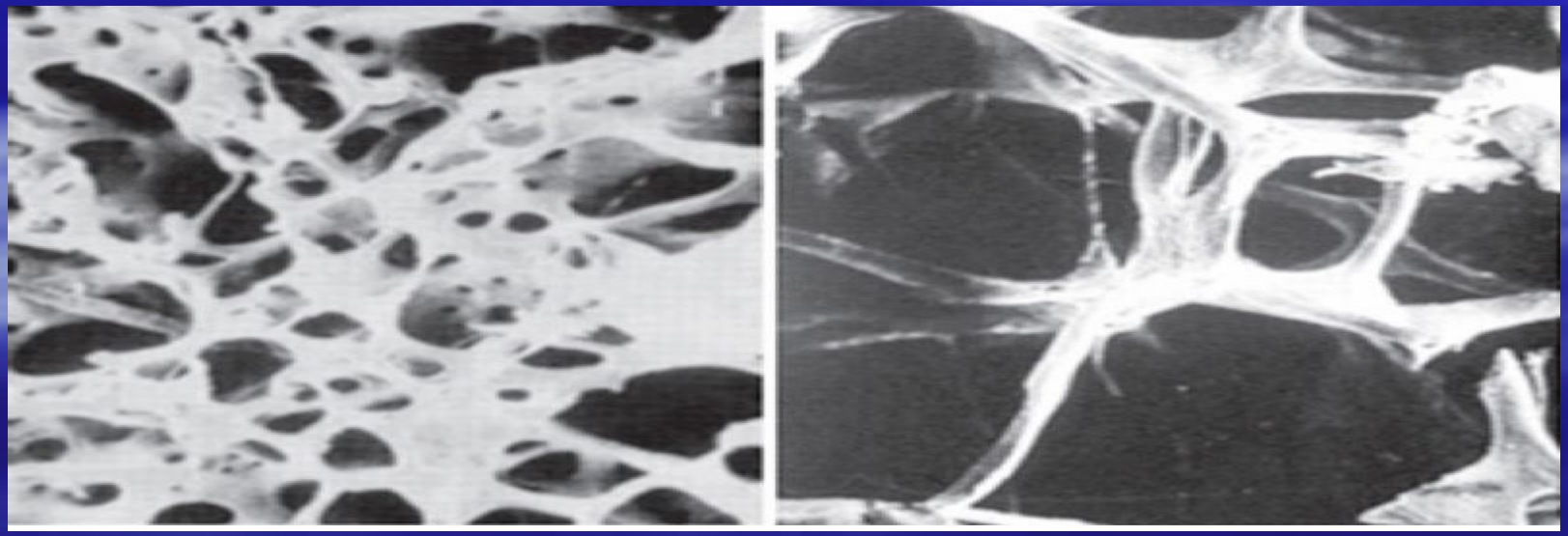
Definition of Osteoporosis

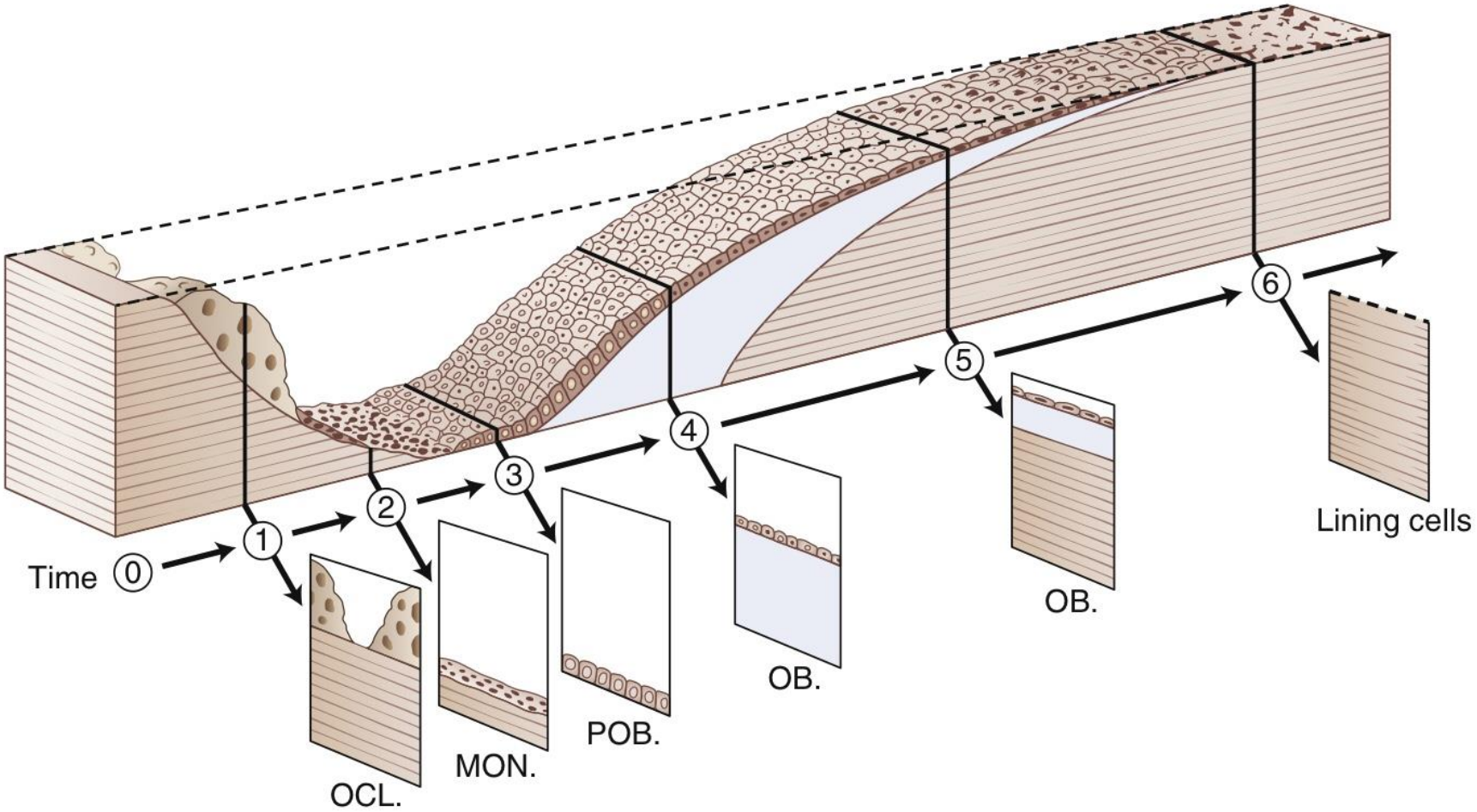
Osteoporosis is defined as a (silent) skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture.



World Health Organization Criteria for Classification of Osteopenia and Osteoporosis

(Z is to look for the zebras in Texas!)

Category	T Score
Normal	Above -1
Low bone density (osteopenia)	Between -1 and -2.4
Osteoporosis	-2.5 or below



Reconstruction of the remodeling sequence in human trabecular bone.

OCL: osteoclasts, MON: mononuclear cells, POB: pre-osteoblasts, OB: osteoblasts,

Each year, Americans experience over 2 million osteoporosis related fractures. (50 percent of women, and 25 percent of men above 50 years old will experience OP related fx.)

~600 K Vertebral

~300 K Hip

~400 K Wrist

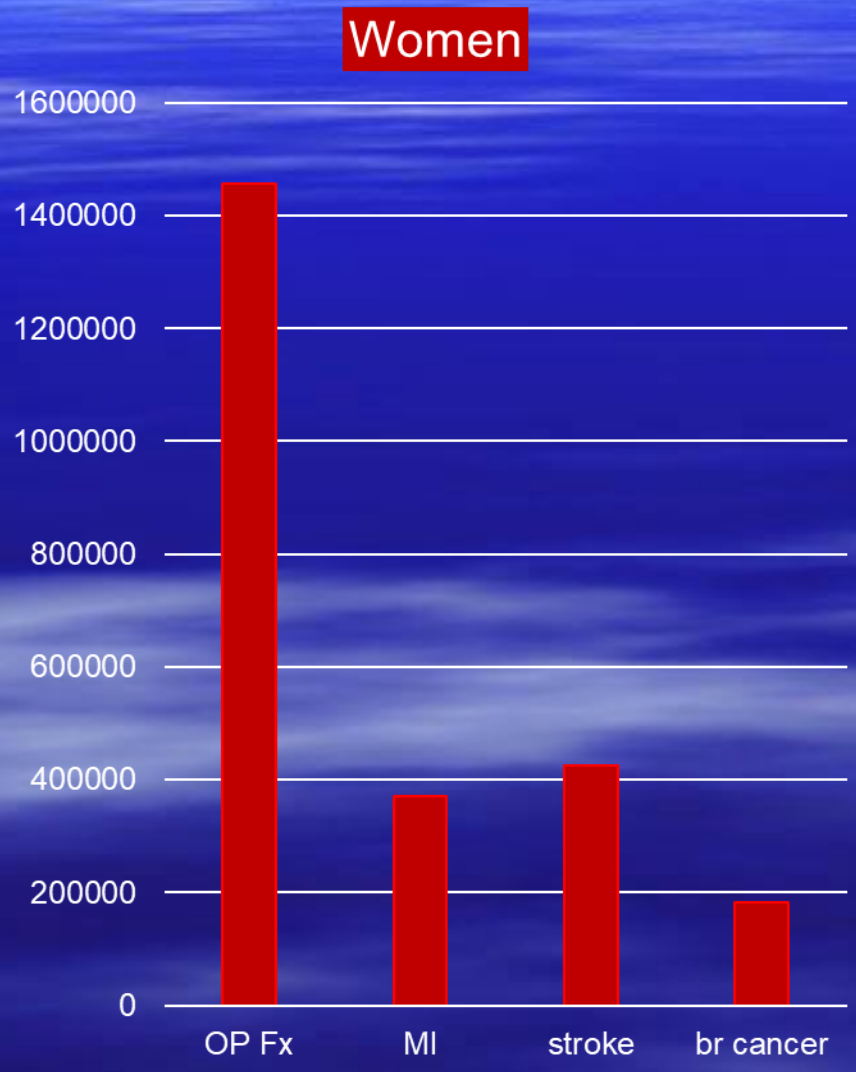
~135 K pelvic

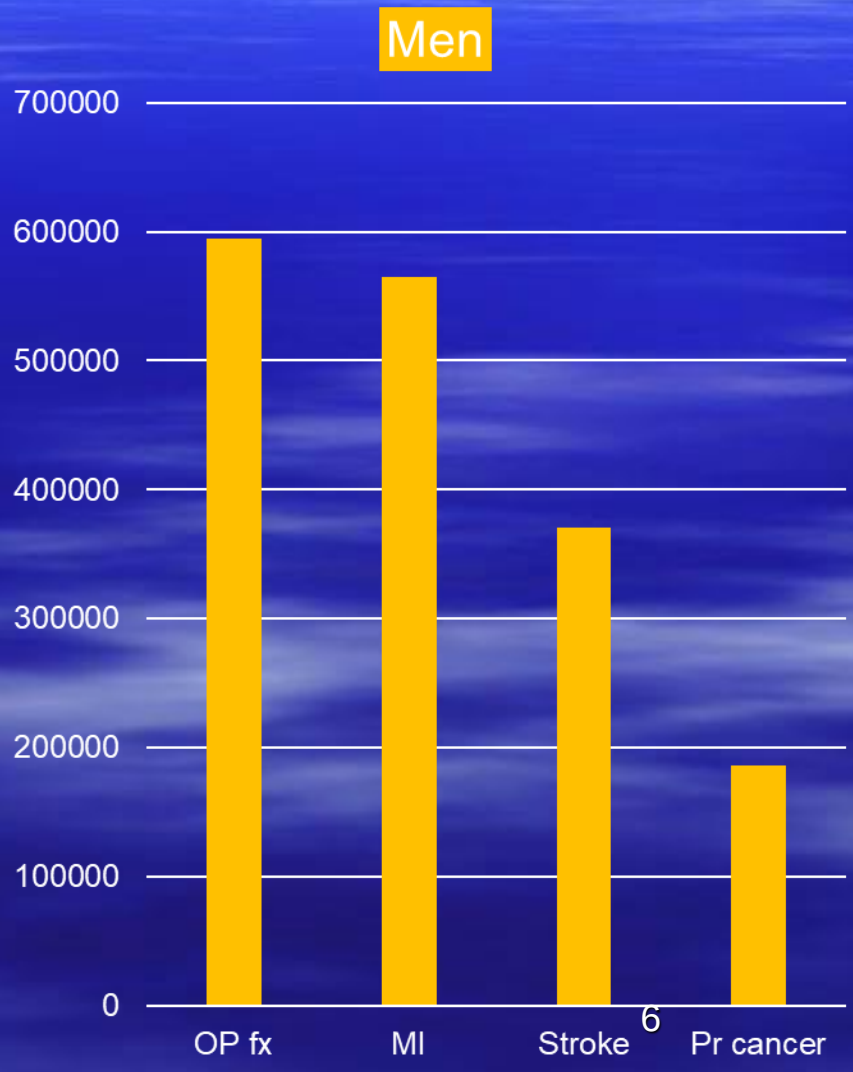
~600 K other

In the year following **vertebral fracture, 26 percent** of patients will fracture another bone

Women with hip fractures are at *4 fold greater* risk of a *second hip fracture*.

44m Americans have low bone mass, of these 10m with osteoporosis. ~80 percent are women





Who Needs to Be Screened for Osteoporosis?

- Women 65 years old or older.
- ?Men ≥70 years. (At least men with evidence of radiologic osteopenia, ***hypogonadism, ETOH heavy use***, or loss of 1.5 inches of height or more)
- Younger postmenopausal women or men 50-70 years with risk factors (family history, steroid use, smoking, heavy ETOH use, PHPT, Hyperthyroidism, intestinal disorders, RA, *Parental history of a hip fracture*).
- Women or men who have experienced a fracture, especially a low trauma fx.
- Starting or taking long-term systemic glucocorticoid therapy ***(3 months or longer at a prednisone dose of 5 mg or above)***

Best screening test: DEXA

- Use a central dual-energy x-ray absorptiometry (DXA) measurement
- In the absence of fracture, osteoporosis is defined as a T-score of -2.5 or below in the spine (anteroposterior), **femoral neck**, or total hip. *In PHPT always include the forearm* (or include it regardless!)
- **Osteoporosis is defined as the presence of a fracture of the hip or spine** (low trauma fx) **[in the absence of other bone conditions]**

Laboratory Tests to Consider in Screening for Secondary Osteoporosis

- Complete blood cell count
- COMP. iPTH with ica if serum calcium is high.
- Serum 25-hydroxyvitamin D
- Thyroid function test
- 24 hour urine collection for calcium
- Other labs are directed by the clinical history, and the Z score!

Non-pharmacologic Measures for Treatment of Osteoporosis

- Maintain adequate vitamin D intake; supplement vitamin D, if needed, to maintain serum levels of 25-hydroxyvitamin D between 30 and 60 ng/mL
- Daily calcium intake (up to 1200 mg a day from diet/supplements)
- Exercise, including weight bearing.
- Limit alcohol intake (to no more than 2 servings per day for men and no more than 1 serving per day for women)

Non-pharmacologic Measures for Treatment of Osteoporosis

- Maintain adequate protein intake.
- Consider the use of hip protectors in individuals with a high risk of falling.
- Take measures to reduce the risk of falling.
- Consider referral for physical therapy and occupational therapy.

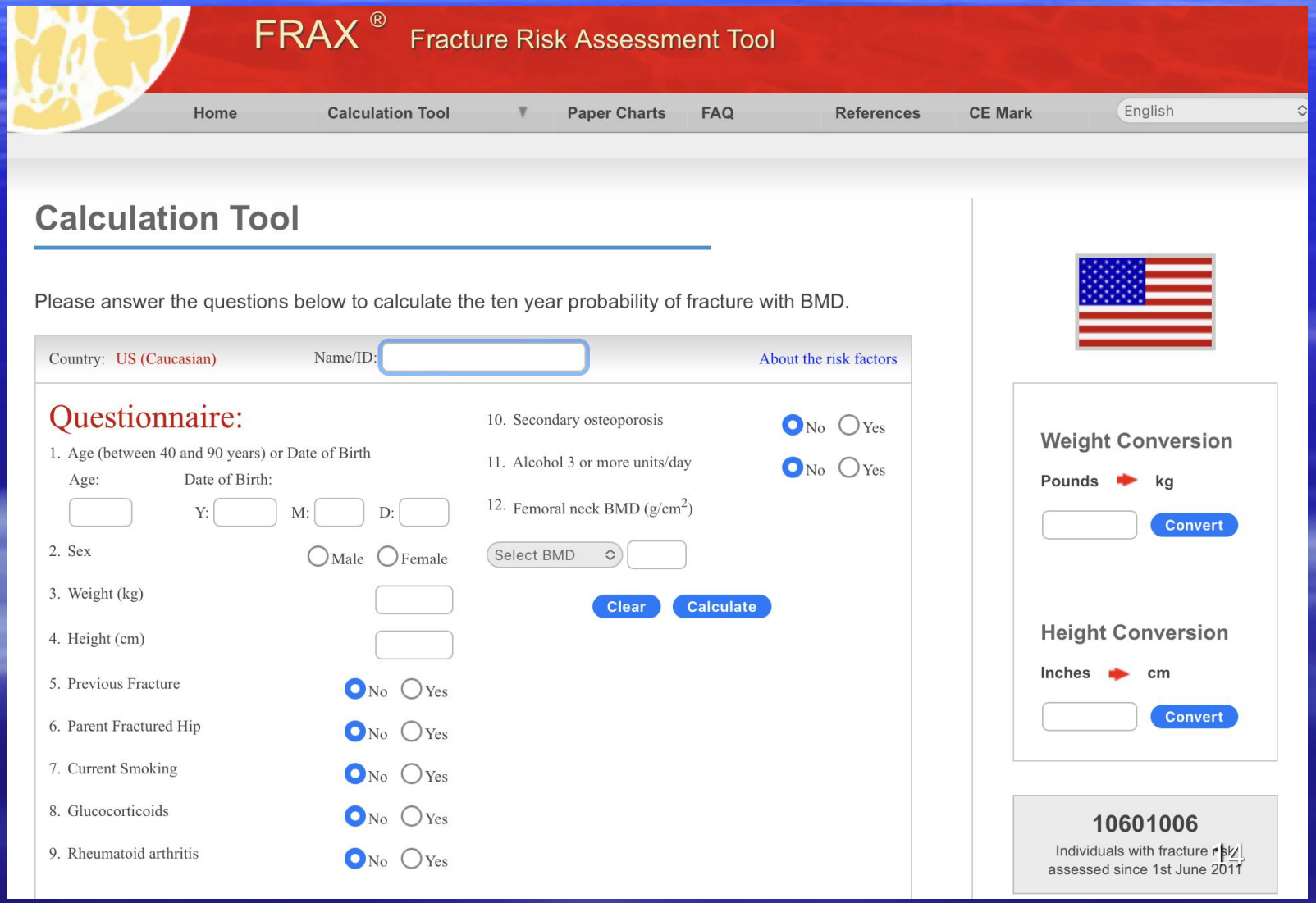
Some Measures for Prevention of Falls

- Anchor rugs
- Remove loose wires
- Use nonskid mats
- Install handrails
- Light hallways, stairways, and entrances
- Low heel shoes
- Hip protectors for patients who are predisposed to falling

Who requires Pharmacologic Therapy?

- Those patients with a history of a low trauma fracture of **the hip or spine** (regardless of the T score!)
- Patients without a history of fractures but with a T-score of -2.5 or lower. (osteoporosis dx)
- Patients with a T-score between -1.0 and -2.4 **if FRAX major osteoporotic fracture probability is ≥20% or hip fracture probability is ≥3%** (osteopenia dx)
- FRAX **≥10% or hip ≥1% if on long term glucocorticoid tx. Zoledronic acid, alendronate, denosumab and teriparatide are approved for the treatment of glucocorticoid-induced osteoporosis**

FRAX is a very helpful tool, but clinical judgement remains the critical element!



What Drugs Can Be Used to Treat Osteoporosis?

- Use drugs with **proven antifracture efficacy**:
- Use alendronate (**Fosomax**), risedronate (**Actonel**), zoledronic acid (**Reclast**), and ? denosumab (**Prolia**) as the ***first line*** of therapy.
- Use ibandronate (***Boniva***) as a ***second-line*** agent
- Use raloxifene (Evista) as a second- or third-line agent
- Use teriparatide (Forteo), abaloparatide (Tymlos) and romosozumab (Evenity) for patients with very high fracture risk or patients in whom bisphosphonate therapy has failed.
- Use calcitonin as the last line of therapy (Or in case of Painful spine Fracture)
- ?Advise against the use of combination therapy

Bisphosphanates

- Fosamax, Actonel, Boniva, or Reclast
- Oral intake or IV

- The most widely used drugs for treatment of osteoporosis

- Contraindicated in advanced renal disease

- Fosamax has been studied in trials up to 10 years

Prolia: is a fully human monoclonal antibody to the receptor activator of nuclear factor kappaB ligand (RANKL). By blocking the binding of RANKL to RANK, it reduces osteoclast formation, function, and survival, which results in decreased bone resorption and increased bone density.

Evenity is a monoclonal antibody to **sclerostin**, an endogenous inhibitor of bone formation. It was approved by the US FDA for the treatment of postmenopausal osteoporosis in 2019.

Raloxifene is a selective estrogen receptor modulator approved for the treatment of postmenopausal osteoporosis; however, it is considered a second-line agent because it only decreases the risk of vertebral fractures and has no effect on hip or other nonvertebral fracture risk.

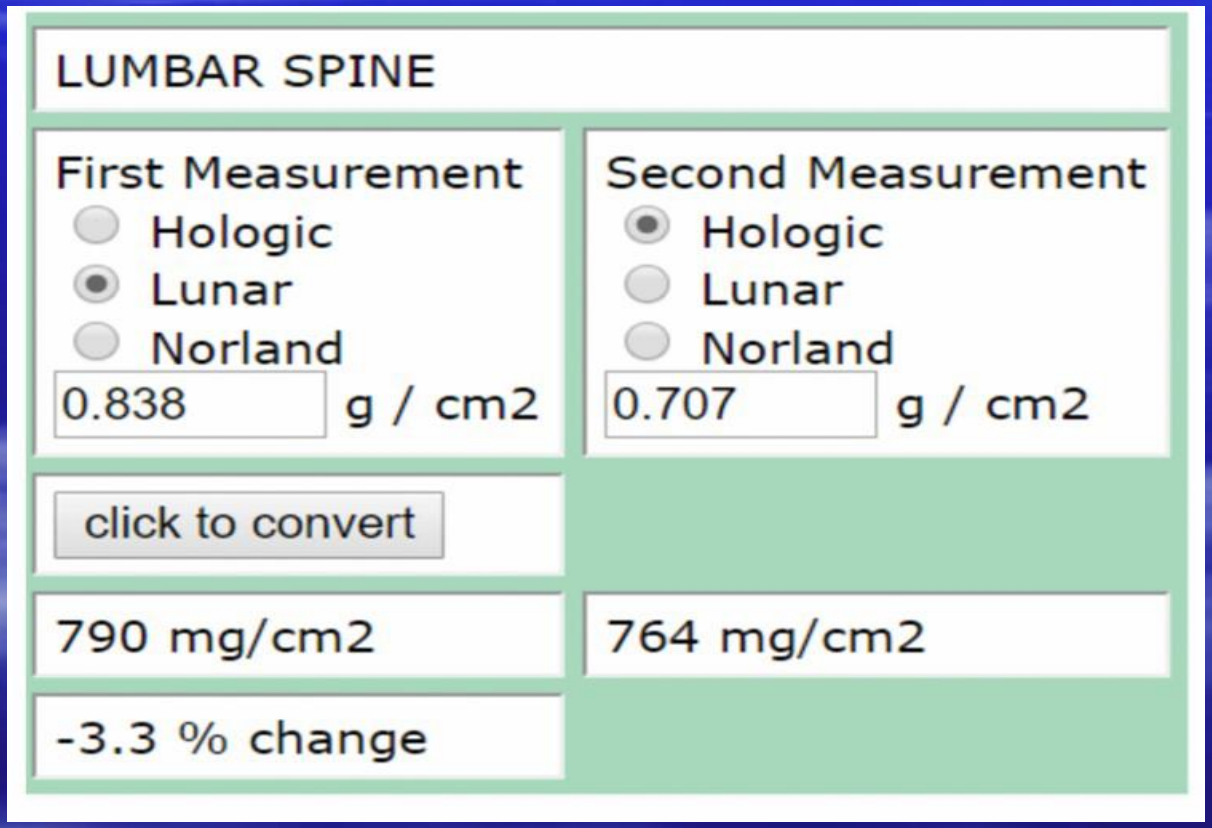
How Is Treatment Monitored?

- Obtain a baseline DXA, and repeat DXA ever 1 to 2 years until findings are stable. Continue with follow-up DXA every 2 years or at a less frequent interval
- Follow-up of patients should be in the same facility, with the same machine, and, if possible, with the same technologist
- Bone turnover markers may be used at baseline to identify patients with high bone turnover and can be used to follow the response to therapy

http://courses.washington.edu/bonephys/opBMDs.html

BMD values are higher with GE-Lunar vs Hologic, and Norland values are between the other two

A change of 8-10 percent between the two tests is considered significant.



What Is Successful Treatment of Osteoporosis?

- BMD is **stable or increasing**, and no fractures are present
- For patients taking antiresorptive agents, bone turnover markers at or below the median value for premenopausal women are achieved.
- ***One fracture is not necessarily evidence of failure***
- Consider alternative therapy or reassessment for secondary causes of bone loss for patients who have **recurrent fractures** while receiving therapy.

How Long Should Patients Be Treated?

- For treatment with **bisphosphonates**, if osteoporosis is mild, consider a “drug holiday” after **4 to 5 years of stability**.
- If fracture risk is high, consider a drug holiday of 1 to 2 years after 10 years of treatment.
- Follow BMD and bone turnover markers during a drug holiday period, and ***reinitiate therapy if bone density declines substantially, bone turnover markers increase, or a fracture occurs***

Some Causes of Secondary Osteoporosis

- **Endocrine disorders**: acromegaly, diabetes, PHPT, *Hypogonadism.*
- **Nutritional**: *alcoholism,* anorexia nervosa, chronic liver disease, Vitamin D deficiency, Malabsorption
- **Medicines**: glucocorticoids, antiepileptics, chemotherapy
- **Rare Disorders** (of the collagen metabolism): osteogenesis imperfecta, Marfan, Ehlers-Danlos
- HIV

Surgical Treatment of Osteoporotic Fractures

- Vertebroplasty and Kyphoplasty for vertebral fx for pain relief
- They involve percutaneous injection of bone cement under into a collapsed vertebra.
- Kyphoplasty also involves the introduction of inflatable bone tamps into the fractured vertebral body prior to fixation of the fracture with bone cement
- Kyphoplasty my help reversal of the vertebral deformity
- Both may increase the risk of vertebral fx in the adjacent vertebrae.

Precautions: ONJ, subtrochanteric fx

- **ONJ is defined as exposed necrotic bone in the maxillofacial region, not healing after 8 weeks in patients with no history of craniofacial radiation. It appears as areas of exposed yellow or white hard bone with smooth or ragged borders.Risk factors** for developing ONJ include dosage and duration of exposure to bisphosphonate therapy, intravenous administration of bisphosphonate therapy, glucocorticoids, cancer and anticancer therapy, cigarette, smoking, poorly fitting dentures, and preexisting dental disease.
- ONJ can occur with any treatment except Forteo, or Tymlos (so it has been reported with the other bone builder, EVENITY)
- Use the car seat analogy. **0.6-0.7 % risk, but 50 percent prevention of serious injury**.

Forteo which is an osteoanabolic agent, would be the most appropriate drug to treat severe osteoporosis, with active ONJ. Teriparatide may also promote ONJ healing (off-label use), but limited data support its efficacy in this regard.

Case 1

78 year old man. Referred to endocrinology for adrenal tumor. Work up confirmed pheochromocytoma. Cured after surgical resection. No history of a fx. His wife is a patient of the practice for osteoporosis. He requested a DEXA for himself!

T L1-L4 -0.5

T femoral neck -0.3

T total hip 0

Read as normal. I requested T score of the forearm, and it was -3!!

(Screen for PHPT, Initiate treatment with a bisphosphonate or Prolia)

Case 2

63 year old woman. Dx with osteoporosis at age 61. No history of HRT. No Fx. PCP treated with oral alendronate for 2 years. Pt reports regular and compliant intake of the medicine along with supplements and regular exercise. No smoking or ETOH consumption.

Prior to tx: T spine -2.7, T neck -2, TT hip -1.8

2 years after tx: T spine -2.9, T neck -2.2, TT hip -2.2

What is the best tx option?

Reclast or Prolia are reasonable options. However, Reclast is not life time tx like prolia

Case 3

70 year old woman. Dx with osteopenia. FRAX did not qualify her for tx yet. PCP did 2 years later a F/U DEXA which showed slight decrease in T score at the spine and the hip.

The decrease is reported at 3 percent at the spine and 2.2 percent at the hip

Her new FRAX score is 14 and 2 percent.

Do you treat? OK for this patient to continue supplement, and weight bearing exercise

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A significant change is ***a 5 percent*** or more change in either direction.

Case 4

68 year old woman. Dx with osteopenia at age 56. Her F/U DEXA showed stability over the years. She leads a healthy life style.

Her FRAX has been steady at 8 and 1 percent.

Her mother suffered from a hip fx at age 89.

What should you do now?

Recalculate the FRAX for this pt, even with her stable DEXA

A parental hip fx is a major risk for this pt. her recalculated FRAX for her went up to 22 and 3.3 percent!

Tx is started!

Case 5

73 year old woman. Moved from Florida. Her PCP treated her with Fosamax for osteoporosis for the last 2 years. Her new PCP in Connecticut did DEXA for F/U.

Her Florida DEXA was GE lunar, and her CT DEXA was Hologic.

The CT readings came lower.

PCP asked: what is the most appropriate action?

(slide 20)

We calculated the change in the measurements and turned out to be only 3.3 percent. *This is below the cutoff of 8-10 percent*. Conclusion: Stable DEXA so OK to cont Fosamax!

Case 6

75 year old man. + Hypogonadism. On T tx. His worst baseline T score is at the femoral neck and it was -4.

2 years after Tx with T, this improved to -3.1.

He also has GERD treated with omeprazole and Pepcid.

Do you add osteoporosis tx?

Yes!

Best is a ***bisphosphonate.***

With his GERD, best option is Reclast.

Cont T tx.

Case 7

58 year old woman. Referred for an incidental finding of a vertebral compression fx (L11) of infeterminate age.

DEXA showed normal T at spine, femoral neck, and Hip. T score at forearm was done and it was osteopenia **-2.2.**

Do you treat? Do you use Foreto?

Tx is indicated due to a vertebral fx in a postmenopausal tx.

While initiating Forteo is reasonable in a young woman with a vertebral fx, I noticed the significantly lower T score at the forearm, compared to the rest of her readings. While her calcium was normal, I suspected a normocalcemic PHPT. My work up was consistent with this dx. Cured with surgery. Treated with Reclast. Forteo was a contraindicated medicine in her!

Case 8

68 year old woman. On Prolia tx for osteoporosis. Will have a tooth implant. Surgeon will not do it unless Prolia is stopped. Tx duration will be up to a year.

What is a practical way of approaching this pt?

Invasive dental work increases risk of ONJ.

***Stopping Prolia may increase risk of fragility fx as early as 8-9 months after stopping the Prolia*.**

No consensus how to proceed, My answer is,

One option is to treat with Forteo if not contraindicated and once pt is done with dental work, stop it and resume Prolia,

Or give an infusion of Reclast, 6 months after last Prolia injection, and ask the surgeon to start working on the toot 3-4 months after the infusion

Case 9

64 year old woman. RA. On dexamethasone tx (8 mg a day) since age 40. Current height is 60 inches. Prior to glucocorticoid tx her height was 68 inches. Referred to me in 2003 for tx. Was on Actonel and HRT by then. Active fx, and multiple.

I started her on **Forteo. After finishing 2 years**, I started her on zoledronic acid, for few years. She became Fx free till 2019, and she was by then on active tx with Prolia.

What is the best tx option in your opinion?

Stopped Prolia. Treated her with Evenity **for a year, then restarted her back on Prolia.** 2 years post tx and is still FX free

(My first pt to go on Forte, and my first pt to go on Evenity!!)

THANK YOU!