# FRAGILITY FRACTURES

Stephanie Stradley, MS, ATC, PA-C
The Ohio State University Wexner Medical Center

# DISCLOSURES

*I have no relevant relationships with ineligible companies to disclose*

# FRAGILITY FRACTURES

*Objectives*

- Define fragility fracture
- Identify risk factors
- Discuss the pathophysiology of osteoporosis and the basic science of bone metabolism
- Review the epidemiology, diagnosis and management of fragility fractures
- Summarize the daily recommendations and dosing for vitamin D and calcium
- Overview of osteoporosis medicines

# FRAGILITY FRACTURE - DEFINITION

- Fracture that results from a low energy trauma that would not ordinarily result in a fracture. Example: Hip fracture after a fall from standing height.
- Osteoporosis causes loss of bone mass and deterioration of bone microarchitecture with a consequent reduction in bone stiffness and strength, thus resulting in an increased risk of fragility fractures.
- Osteoporosis is diagnosed based on presence of fragility fractures in the absence of other metabolic bone disorders and even with a normal bone mineral density
- Exclude fractures of the face, skull, fingers, toes
- Common sites for fragility fractures (areas with large proportion of trabecular bone)
  - Spine, Hip (Proximal Femur), Wrist (Distal Radius), Shoulder (Proximal Humerus)

Pietri, M., & Lucarini, S. (2007). The orthopaedic treatment of fragility fractures. Clinical cases in mineral and bone metabolism : the official journal of the Italian Society of Osteoporosis, Mineral Metabolism, and Skeletal Diseases, 4(2), 108–116.
American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis—2020 Update,Endocrine Practice,Volume 26, Supplement 1,2020,Pages 1-46,ISSN 1530-891X,

# Fragility Fracture Sites (cont.)

Ribs

Clavicle

Humerus (shaft, distal)

Olecranon

Radial head

Pelvis (ring and acetabular)

Distal femur

Tibia (plateau, shaft, pilon)

# Other Fracture Types to Consider:

- Insufficiency fracture – Fracture resulting from normal stress on abnormal bone (**no trauma**). Often associated with osteopenic bone and fragility. Often managed the same as a Fragility Fractures.
- Stress fracture – Fracture resulting from abnormal stress on normal bone
- Atypical femur fracture – Uncommon complication of long-term use of bisphosphonates (Slow bone resorption by reducing osteoclast function to treat osteoporosis. ) Low energy or atraumatic femoral diaphyseal fracture resulting from slow bone turnover and a lack of remodeling of “old” bone into new bone. Difficult to heal and often require specialist intervention (orthopedic and endocrinology)
- Pathologic fracture – result of diseased, weakened bone due to focal pathology such as tumors

# Fragility Fractures

*Morbidity & Mortality*

- These injuries cause significant pain and disability and lead to reduced quality of life
- Hip and vertebral fractures are associated with decreased life expectancy
- **Overall, 24-35% of hip fracture patients 50 and older will die within one year of their fracture (NOF, 2017)**

# Risk Factors

# Risk Factors for Osteoporosis & Fracture

*Non-Modifiable Risk Factors*

- Increased age
- Gender (female)
- Race (white ethnic background)
- Family History (genetics)
- Prior fracture
- Early menopause

Pouresmaeili, F., Kamalidehghan, B., Kamarehei, M., & Goh, Y. M. (2018). A comprehensive overview on osteoporosis and its risk factors. Therapeutics and clinical risk management, 14, 2029–2049. https://doi.org/10.2147/TCRM.S138000

# Risk Factors for Osteoporosis & Fracture

*Modifiable Risk Factors*

- Nutrition
- Low body weight
- Physical inactivity/immobility
- Frequent falls
- Nicotine use
- Vitamin D insufficiency
- Use of glucocorticoids
- Alcohol consumption
- Medical history: Endocrine disorders, Thyroid disorders, Type I Diabetes, RA

# Risk Factors for Falls

- Age
- Environmental risk
- Previous falls
- Dehydration
- Depression
- Poor vision
- Sarcopenia
- Urgent urinary incontinence
- Malnutrition
- Neurological risk factors

Adapted from Cosman et al[13] with modification.

1CRFs for fracture risk assessment from tool FRAX®. BMD: Bone mineral density; CRFs: Clinical risk factors; IBD: Inflammatory bowel diseases; BMI: Body mass index.

# Fall Prevention

- Stay physically active
- Have your eyes and hearing tested
- Find out about the side effects of medicine
- Get enough sleep. Limit the amount of alcohol you drink.
- Stand up slowly
- Use assistive devices to feel steady when walking and be very careful when walking on wet or icy surfaces
- Wear non-skid, rubber-soled, low-heeled shoes, or lace-up shoes with non-skid soles that fully support the feet

# Fall Prevention

*Continued*

- Always tell your doctor if you have fallen since your last checkup, even if you aren't hurt when you fall
- Minimize clutter
- Adequate lighting in the home
- Avoid loose clothing
- Install grab bars/handrails
- Remove trip hazards such as rugs, cords, or uneven floorboards

# Pathophysiology of osteoporosis and basic science of bone metabolism

# OSTEOPOROSIS

*Osteoporosis literally means "porous bone."*

- When bone resorption is occurring at a higher rate than mineral deposition, bones become weaker and more fragile…**leading to fracture**
- Occurs with aging due to daily remodeling; bone formation phase typically takes longer than the resorption phase, therefore an increase in remodeling activity usually results in a net loss of bone
- Osteoclast and osteoblast activity is influenced by multiple factors (hormones, diet, exercise, etc). Any factor that tips the balance in favor of osteoclasts can lead to osteoporosis.

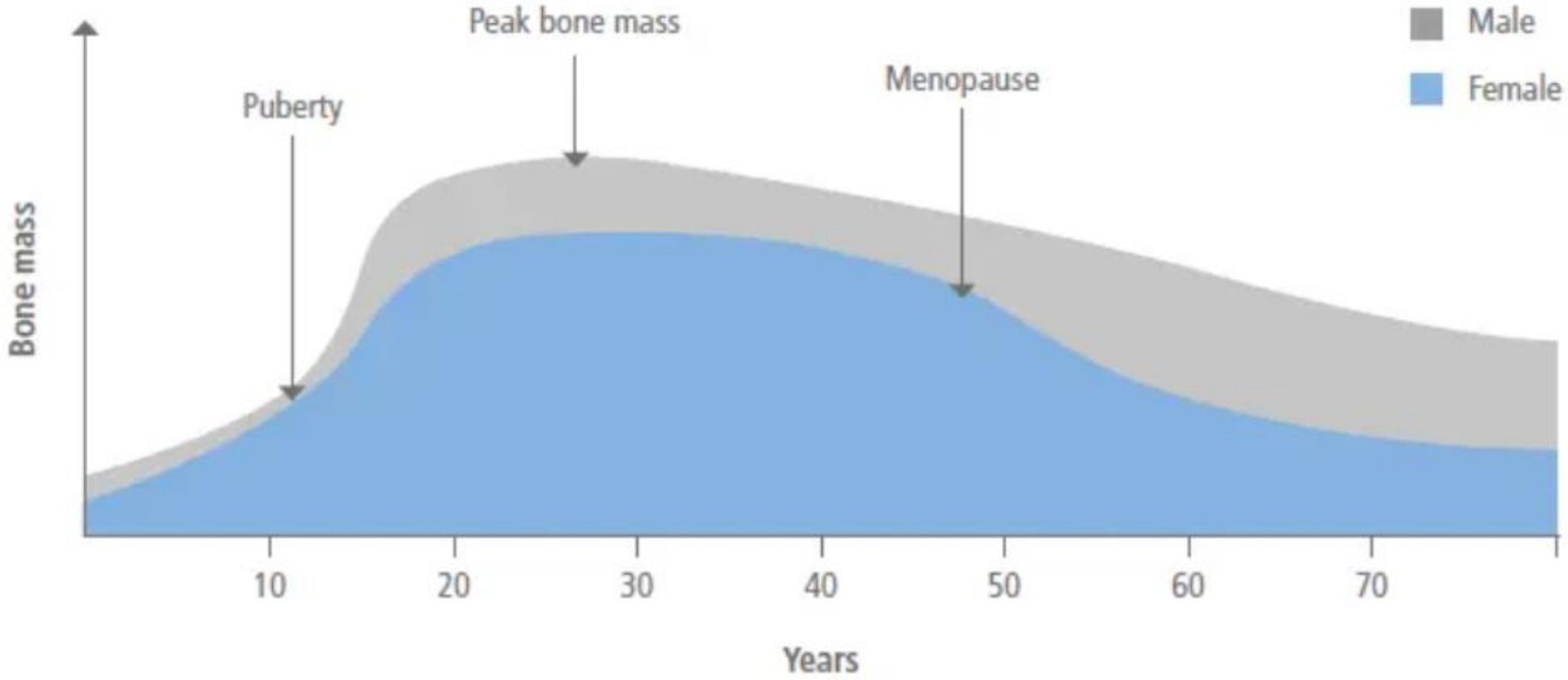
# Osteoclast & Osteoblast

Osteoclasts: cells that degrade bone to initiate normal bone remodeling and mediate bone loss in pathologic conditions by increasing their resorptive activity.

Osteoblasts:  large cells responsible for the synthesis and mineralization of bone during both initial bone formation and later bone remodeling.

# BONE MASS

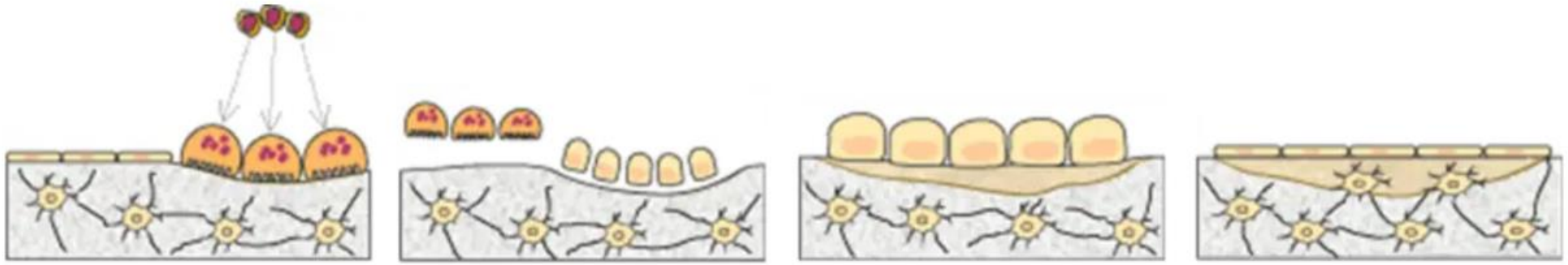
*Peak bone mass is achieved for both males and females by the mid-twenties. Thereafter, a gradual decline into old age occurs in men, while a plateau followed by an accelerated period of bone loss for several years after the menopause occurs in women.*




Bone mass throughout the life cycle

# Remodeling of Normal Adult Bone:

*The five phases of bone remodeling: Activation,  Resorption, Reversal, Formation, Quiescence*



Activation and resorption
Preosteoclasts are stimulated and differentiate under the influence of cytokines and growth factors into mature active osteoclasts, which can digest mineral matrix (old bone).

Reversal
End of resorption.

Formation
Osteoblasts synthesize new bone matrix.

Quiescence
Osteoblasts become resting bone lining cells on the newly formed bone surface

The five phases of bone remodelling

# Secondary Causes of Osteoporosis & Increased Fracture Risk

*Diseases/Disorders*

- Hypogonadism
- Hyperparathyoridism
- Chronic liver disease
- Inflammatory diseases (RA, celiac, IBD)
- Renal disease
- Diabetes
- Multiple Myeloma
- Vitamin D deficiency
- s/p gastric bypass
- s/p organ transplant
- s/p total hysterectomy

# Secondary Causes of Osteoporosis & Increased Fracture Risk

*Medications*

- Aluminum (antacids)
- Anticonvulsants
- Aromatase inhibitor
- Cancer chemotherapeutic agents
- Depo-medroxyprogesterone (Depo Provera Shot)
- Glucocorticoids (>5mg/d prednisone > 3 months)
- Lithium
- Methotrexate
- PPI
- SSRI

# Epidemiology, Diagnosis & Management

# Fragility Fractures

*A Costly Problem*

- 1056 fragility fractures per 100,000 people
- 2.5 million medical office visits
- 430,000 hospital admissions
- 180,000 nursing home admissions
- Direct medical care costs between $12.2 and $17.9 billion per year

*J Am Acad Orthop Surg.* 2010; 18:278-285. *Geriatric Orthopaedic Surgery and Rehabilitation.* 2015; 6(2): 58-120. U.S. Department of Health and Human Services. Bone Health and Osteoporosis: A Report of the Surgeon General. Rockville, MD: US Department of Health and Human Services; 2004.

# Epidemiology

*Incidence*

- 10 million Americans and 200 million people worldwide have osteoporosis
- 34 million Americans have osteopenia
- 1.5 million osteoporotic fractures occur each year
  - 700,000 are vertebral fractures
  - 300,000 are hip fractures
  - 200,000 are wrist fractures

# Epidemiology

*Demographics*

- Male: Female ratio is 1:4
- Age:
  - Osteoporosis
    - postmenopausal osteoporosis is highest in women aged 50-70 years
    - senile osteoporosis begins after 70 years
    - secondary osteoporosis begins at any age
  - Fractures
    - Wrist fractures occur most commonly at age 50-60 years
    - Vertebral fractures occur most commonly at age 60-70 years
    - Hip fractures occur most commonly at age 70-80 years

# Once you identify the Fragility Fracture

**Communicate three simple messages** to people aged 65 years or older with a hip or vertebral fracture (as well as to their family/caregivers) consistently throughout the fracture care and healing process:

- Their broken bone likely means they have osteoporosis and are at high risk for breaking more bones, especially over the next 1 to 2 years;
- Breaking bones means they may suffer declines in mobility or independence—for example, have to use a walker, cane, or wheelchair, or move from their home to a residential facility, or stop participating in favorite activities—and they will be at higher risk of dying prematurely;
- Most importantly, there are actions they can take to reduce their risk, including regular follow-up with their usual health care provider as for any other chronic medical condition.

Conley RB, Adib G, Adler RA, et al. Secondary Fracture Prevention: Consensus Clinical Recommendations from a Multistakeholder Coalition. J Orthop Trauma. 2020;34(4):e125-e141. doi:10.1097/BOT.0000000000001743

# Fragility Fracture Evaluation

- History & Physical
  - Family history, secondary causes, height loss, prior fracture history, etc.
- DXA
  - Not essential prior to starting therapy if a patient > 65 years has sustained a hip or vertebral fragility fracture
- FRAX (Fracture Risk Assessment Tool)
- Labs
- Fall Risk

# Fragility Fracture Evaluation

*History & Physical*

- Mechanism
- Timing
- LOC? Syncope? Chest pain?
- Ambulatory status
- Assistive devices
- Home? Assisted living? SNF?
- Comorbid illnesses? Life expectancy?
- Cognition

# Fragility Fracture Evaluation

*WHO – Bone mineral density diagnosis via DXA*

**TABLE 1**

**World Health Organization criteria for diagnosing osteoporosis using bone density measurements**

| CATEGORY | T SCORE |
|---|---|
| Normal | Not more than 1.0 standard deviations (SD) below the young adult mean |
| Osteopenia | Between 1.0 and 2.5 SD below the young adult mean |
| Osteoporosis | More than 2.5 SD below the young adult mean |
| Severe or established osteoporosis | More than 2.5 SD below the young adult mean with a fracture |

http://www.clevelandclinicmeded.com/medicalpubs/ccjm/Jan06/watts.ht m

# Fragility Fracture Evaluation

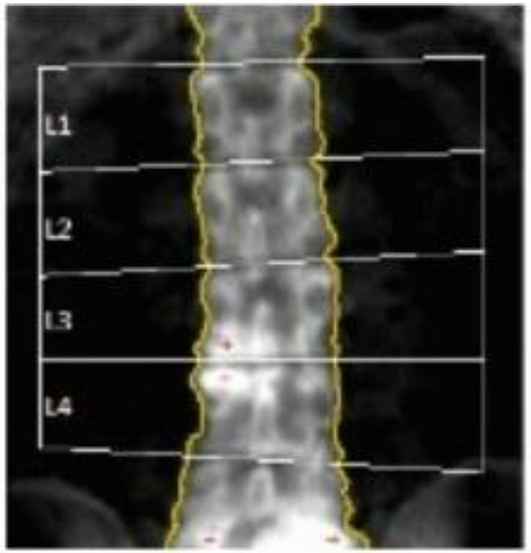
*DXA*

## Dual Energy X-ray Absorptiometry (DEXA or DXA)

- Used to aid in the diagnosis of osteoporosis and the monitoring of treatment efficacy
- Most commonly include hip and lumbar spine.  Forearm is an option if both hips or spine contains hardware.
- T-score: comparison by standard deviation to a young adult population. Use for postmenopausal women and men > 50 years.
  - Greater than or equal to 1.0 normal
  - <-1.0 to >-2.5 osteopenia
  - <-2.5 osteoporosis
- Z score: Age matched controls - used for premenopausal women, men < 50 years, and children
  - <-2.0 below expected range warrants additional workup



A Practical Approach to Interpretation of Dual-Energy X-ray Absorptiometry (DXA) for Assessment of Bone Density. Curr Radiol Rep 2, 48 (2014). https://doi.org/10.1007/s40134-014-0048-x



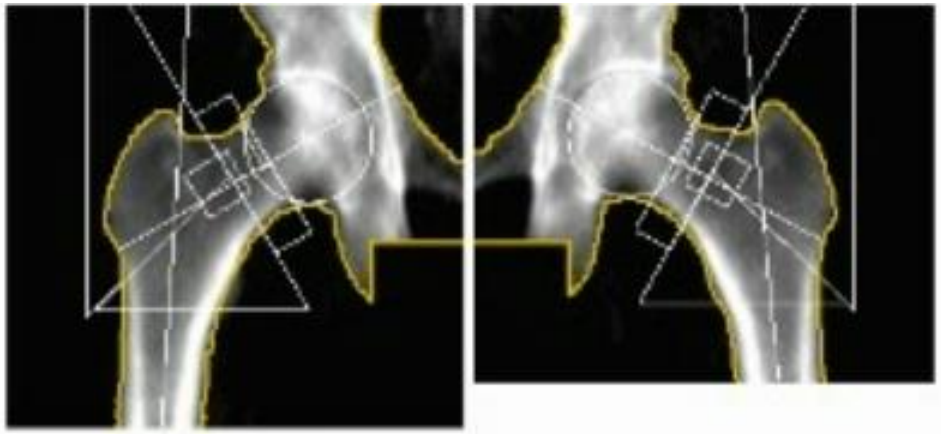
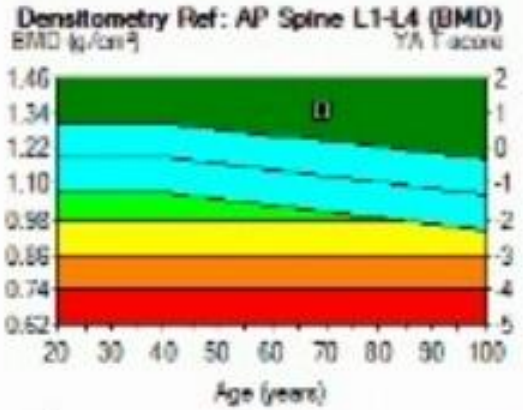



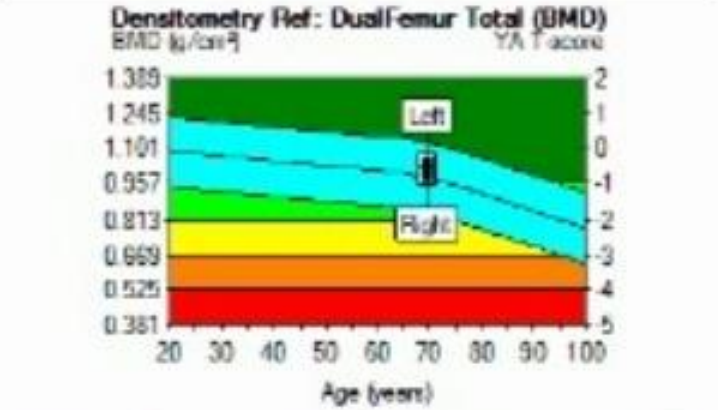
Image not for diagnosis

HAL chart results unavailable

Image not for diagnosis

(Right = 121.8 mm) (Left = 121.3 mm)




| Region | 1 BMD (g/cm²) | 27 Young Adult T-score | 3 Age Matched Z-score | 11 WHO Classification |
|---|---|---|---|---|
| AP Spine L1-L4 | 1.345 | 1.0 | 1.8 | - |
| DualFemur Total | | | | |
| Left | 1.034 | -0.5 | 0.4 | - |
| Right | 0.983 | -0.8 | 0.0 | - |
| Mean | 1.008 | -0.6 | 0.2 | - |
| Difference | 0.051 | 0.4 | 0.4 | - |

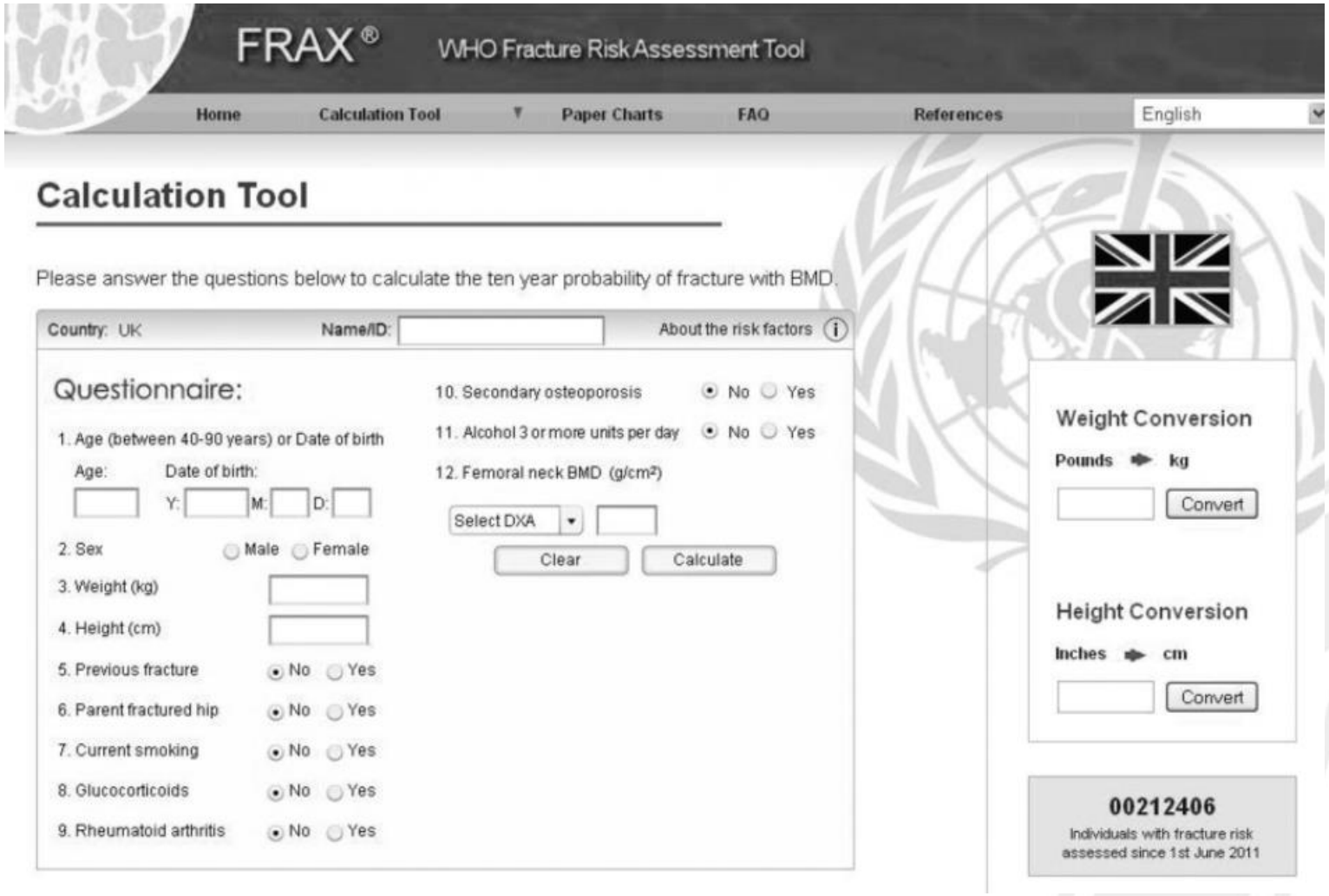
# Fragility Fracture Evaluation

*FRAX*

- Fracture risk assessment tool
- Uses select risk factors to estimate the 10-year fracture risk of sustaining a fragility fracture
- National Institute for Health and Clinical Excellence algorithm for the use of fragility fracture risk calculators
- https://www.sheffield.ac.uk/FRAX/tool.aspx?country=9

# Fragility Fracture Evaluation

*FRAX*



# 2020 AACE Diagnosis of Osteoporosis in Postmenopausal Women (American Association of Clinical Endocrinology)

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

# Fragility Fracture Evaluation

*Labs to consider to detect secondary osteoporosis:*

- CBC (Complete Blood Count)
- CMP (Comprehensive Metabolic Panel)
- Serum 25-hydroxyvitamin D
- PTH (hyperparathyroidism)
- TSH
- Phosphate
- Magnesium
- Prealbumin
- 24-hour urine for calcium, sodium, creatinine (malabsorption or hypercalciuria? Want patient's vit D level and calcium intake normal prior to test)

# Vitamin D & Calcium Supplementation

# Osteoporosis Treatment

## Optimize Vitamin D

- AACE and the Endocrine Society recommend serum 25(OH)D ≥ 30 ng/mL to define vitamin D sufficiency
- Vitamin D3 is the preferred supplement
- 1,000 IU-4,000 IU Vitamin D3 daily is considered a safe dose for adults. There are guidelines for higher dose to treat vitamin D deficiency
- Use caution replacing vitamin D in patients at risk for hypercalciuria/hypercalcemia and in patients with renal disease

# Osteoporosis Treatment

## Optimize Calcium

- Calcium goal for adults > 50 years is 1,200 mg/day (recommended not to have a total more than 1,500 mg/day)
- Dietary sources are preferred with supplement as needed to reach daily goal
- No more than 600 mg calcium per dose
- 24-hour urine calcium collection is the best method for evaluating calcium intake and absorption

**Calcium Carbonate**

- Pros: affordable, less tablets to achieve desired dose
- Cons: constipation, bloating, requires gastric acid for absorption –take with meals

**Calcium Citrate**

- Pros: absorption is not dependent on gastric acid, less GI complaints
- Cons: more expensive, more tablets to achieve desired dose

# OSU Guidelines

| | | |
|---|---|---|
| **Calcium Intake**<br>• Assess dietary intake. Supplementation may be required if dietary intake is inadequate | | |
| | Age | Dose |
| Men | 50-70<br>>70 | 1000 mg/day<br>1200 mg/day |
| Women | >50 | 1200 mg/day |
| **Vitamin D intake** | | |
| | Medication/Dose | Comments |
| All patients Age >50 | 800-1000 IU/day | Higher doses may be required to maintain recommended 25OH vitamin D level ≥ 30 ng/ml |
| 25-OH Vitamin D Level <30 ng/ml | • Start ergocalciferol 50,000 units weekly x 12 weeks, then<br>• 1000 units daily | May adjust as needed to maintain target level |
| 25-OH Vitamin D Level <20 ng/ml | • Start ergocalciferol 50,000 units weekly x 12 weeks, then<br>• 2000 units daily | May adjust as needed to maintain target level |
| **Exercise** | Recommend regular weight-bearing, muscle strengthening exercise and balance training in collaboration with Physical Therapy | |

# Osteoporosis Treatment

- Fall Prevention
- Consider medications that increase fall risks, Environmental changes (handrails, lighting, throw rugs, etc), Therapy/exercise
- Address Other Modifiable Risk Factors
- Nicotine cessation, Alcohol intake reduction, Limit Caffeine intake ,Adequate protein, Exercise
- Pharmacological therapy

# Goals of Treatment

- Fracture Prevention
  - A fracture on treatment does not mean treatment failure, but does warrant further investigation
- Stable or increased BMD
  - Same machine, same technician
  - Medicare covers a repeat DXA every 2 years
  - Expect to see changes earlier in the spine (trabecular bone)
- Bone Turnover Markers
  - BTMs decrease with antiresorptive therapy
  - BTMs increase with anabolic therapy

# When to Consider Referral?

- Refer anytime you identify a fragility fracture, and your office/system is not set up to evaluate and manage osteoporosis.  Addressing secondary fracture prevention is the responsibility of the orthopedic provider.
- Recurrent fractures or continued bone loss despite treatment
- Atypical femur fractures
- Abnormally low bone density
- Abnormal or unexplained lab results
- Comorbidities that complicate treatment (CKD, hyperparathyroidism, malabsorption, etc)

# Medication Overview

# Pharmacological therapies approved for the treatment of osteoporosis in post menopausal women

*Antiresorptive: inhibit bone resorption*

Bisphosphonates
- Alendronate (Fosamax)
- Ibandronate (Boniva)
- Risedronate (Actonel)
- Zolendronate (Reclast)

Denosumab (Prolia)

Calcitonin

Selective Estrogen-Receptor Modulators/Estrogens (Raloxifene/Evista)

Teriparatide (Forteo)

Abaloparatide (Tymlos)

Romosumab (Evenity)

# Osteoporosis Treatment Considerations

- Stratify risk to help determine treatment choice and duration: high risk, very high risk for fracture
- Alendronate, Risedronate, Zoledronate, and Denosumab have evidence for antifracture efficacy (spine, hip, and nonvertebral fracture risk reduction) in the absence of contraindications, consider as initial options for most patients who are candidates for treatment (high risk)
- Consider starting anabolic therapy for very high risk
- Recent fracture (within the past 12 months)
- Fractures while on approved osteoporosis therapy

# Osteoporosis Treatment Considerations

- Multiple fractures
- Fractures while on drugs causing skeletal harm (long-term glucocorticoids)
- Very low T-score (less than − 3.0)
- High risk of falls or history of injurious falls
- Very high fracture probability by FRAX® (major osteoporosis fracture > 30%, hip fracture > 4.5%)

# Osteoporosis Treatment Considerations

*Bisphosphonates*

- Alendronate, Ibandronate, Risedronate, and Zoledronate
- MOA: reduce the activity of osteoclasts
- Prior to starting: check kidney function, calcium level, dental health/hygiene, discuss adverse effects (atypical femur fracture, osteonecrosis of the jaw)
- Alendronate (weekly) and risedronate (weekly or monthly) most common oral agents
- Must be taken after a prolonged fast (usually fasting overnight and taken in the morning soon after arising) ,swallowed with a full glass of water (with at least a 30-minute wait after ingestion before other medications, food, or beverages other than water)

# Osteoporosis Treatment Considerations

*Bisphosphonates*

- Caution with patients with esophageal diseases/disorders and GI malabsorption
- In the absence of contraindications, consider starting inpatient after a hip fracture
- Zoledronate (IV, once/year)
- Contraindicated in hypocalcemia
- Flu like symptoms after administration - pre medicate with acetaminophen to reduce symptoms
- Treatment duration
- When to consider a drug holiday ?

# Osteoporosis Treatment Considerations

*Denosumab (Prolia)*

- Subcutaneous injection every 6 months
- MOA: monoclonal antibody, reduces the differentiation of precursor cells into mature osteoclasts and decreases the function and survival of activated osteoclasts
- Contraindicated in patients with hypocalcemia, hypoparathyroidism, osteomalacia
- Can be used in patients with renal disease (unlike bisphosphonates)
- Adverse effects include AFF and ONJ (like bisphosphonates)
- Rapid bone loss after discontinuation. Common to follow with IV bisphosphonate, may not be fully effective.

# Osteoporosis Treatment Considerations

*Raloxifiene (Evista)*

- Selective Estrogen Receptor Modulator
- Approved for prevention of postmenopausal osteoporosis and reduction of breast cancer risk in women with postmenopausal osteoporosis and high risk of breast cancer
- Risk of VTE
- Efficacy limited to reduction of vertebral fractures

# Osteoporosis Treatment Considerations

*Teriparatide (Forteo) & Abaloparatide (Tymlos)*

- Daily subcutaneous injection
- MOA: Parathyroid hormone analogs
- Indicated for postmenopausal women who are at high or very high fracture risk, or who have failed previous osteoporosis treatment.
- Teriparatide is approved for glucocorticoid induced osteoporosis and osteoporosis in men
- Prior to starting: serum calcium, 25 (OH) D, PTH, alkaline phosphatase (r/o Paget disease)
- **Black Box Warning:** occurrence of osteosarcomas in rats treated with very high doses.  Do not use in patients at risk of osteosarcoma.
- Treatment duration limited to 2 years total
- Follow treatment with bisphosphonate or denosumab to help prevent bone loss after discontinuation

# Osteoporosis Treatment Considerations

*Romosumab (Evenity)*

- Monthly subcutaneous injection
- MOA: monoclonal antibody, sclerostin inhibitor (sclerostin is produced in osteocytes, prevents bone formation)
  - Sclerostin binds with the Wnt receptor and inhibits the differentiation of precursor cells into osteoblasts.  Blocking sclerostin →increased osteoblast activity
- Can be used in patients with prior radiation treatment (unlike the PTH analogs)
- Not currently approved for male osteoporosis
- **Black Box Warning :** should not be used in patients at high risk for cardiovascular events or who have had recent MI or stroke
- Treatment duration is currently limited to one year total

# Thank you!

# Resources

American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis—2020 Update https://pro.aace.com/disease-state-resources/bone-and-parathyroid/clinical-practice-guidelines/clinical-practice

International Osteoporosis Foundation https://www.osteoporosis.foundation/

Bone Health & Osteoporosis Foundation https://www.bonehealthandosteoporosis.org/

Own the Bone https://www.ownthebone.org/