
# Osteoporosis
# Assessment & Management

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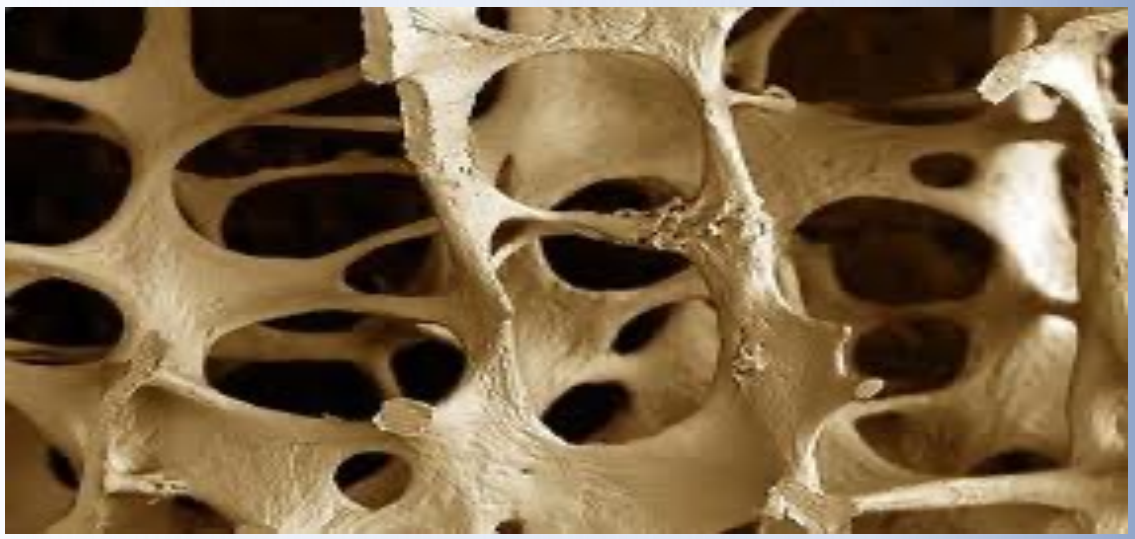
No disclosures to report



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# Epidemiology

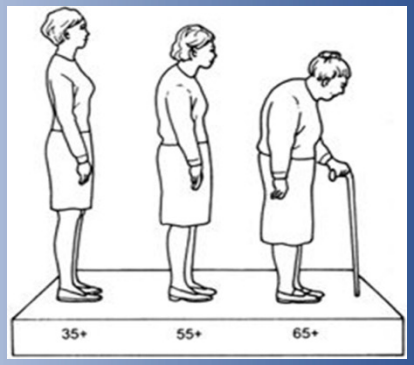
- 2 million osteoporotic fractures in the United States each year
- about 50 million people in the U.S. are at risk for fracture
  - Diabetes: 34 million
  - Hyperlipidemia: 94 million
  - Hypertension: 75 million*

# Epidemiology

- Lifetime probability of a hip fracture in women is 10-15%

- Lifetime probability of breast cancer is 12-13%

# Morbidity & Mortality




- **15-20% will die within 1 year of a hip fracture**
- 30% will have permanent disability
- 40% will be unable to walk independently
- 50% will no longer be able to live independently
- Mortality rates are higher for men than for women

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# Assessing Risk: Who to Screen?

- DEXA scan
  - All women 65 and older
  - All men 70 and older*
  - Patients 50 and older with any non-phalangeal fracture
  - Patients at higher risk….

# Patients at Increased Risk

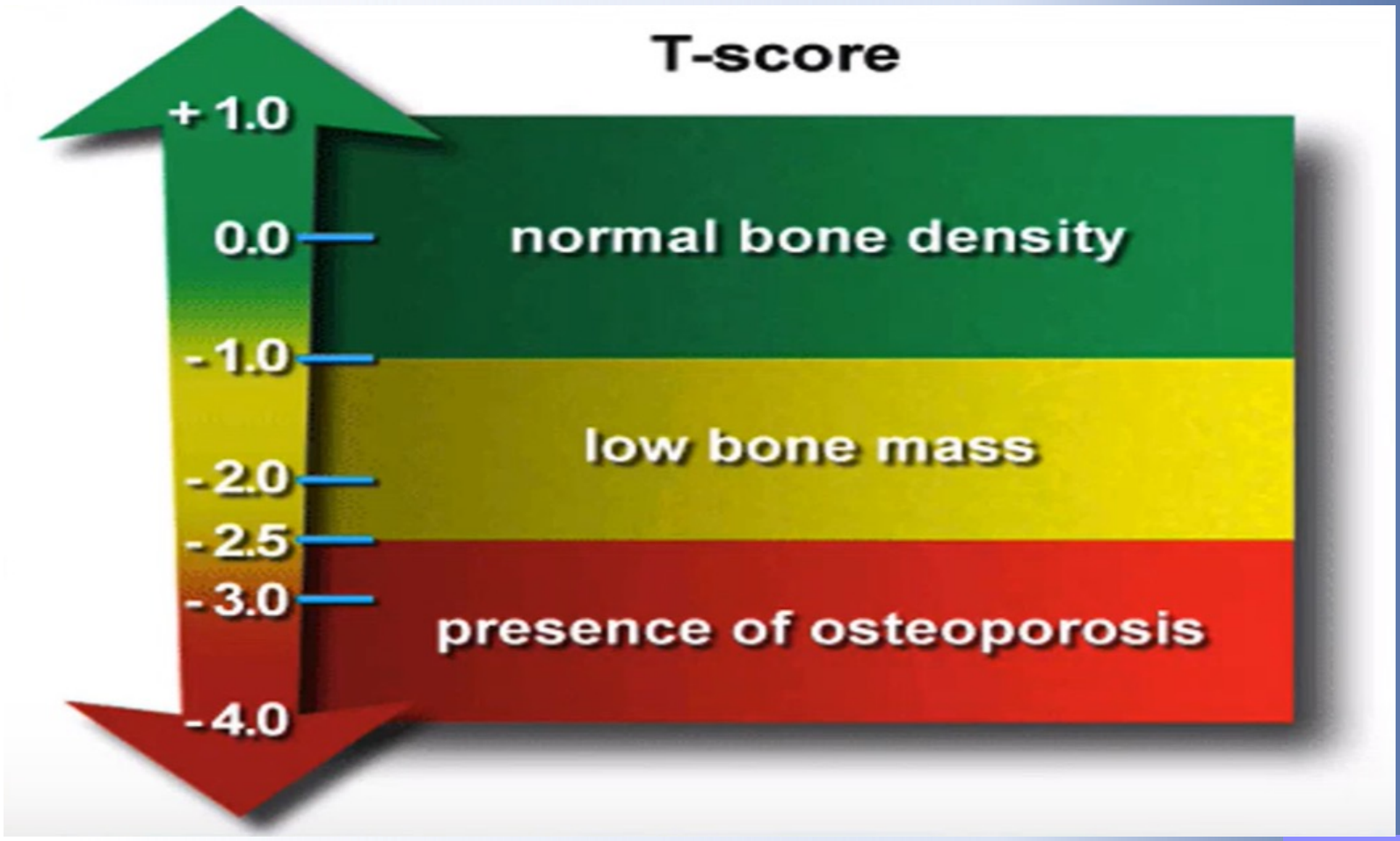
- Long-term glucocorticoid use
- Smokers
- Heavy alcohol use
- Inactivity
- Malabsorptive conditions
- Rheumatologic conditions
- Hematologic conditions
- Neuromuscular diseases

# Patients at Increased Risk

- Postmenopausal women <65
  - FRAX score for major osteoporotic fracture >8.4% should get DEXA scan
  - OST (osteoporosis self-assessment tool)
    - Score < 2 should get DEXA scan
    - OST = $\frac{\text{(weight in kg) – (age)}}{5}$

# Patients at Increased Risk

# DEXA Scan


T-score
+1.0
0.0
-1.0
-2.0
-2.5
-3.0
-4.0
normal bone density
low bone mass
presence of osteoporosis

# DEXA Scan Rescreening

- For women 65 and older who are not taking prescription antifracture medication, suggested rescreening intervals are based on initial T-score:

| Initial T-score | Suggested Minimum Interval |
|---|---|
| ≥ -1.4 | 10 years |
| -1.5 to -1.9 | 5 years |
| -2.0 to -2.4 | 2 years |

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# Who to Treat?

- Start treatment in patients with hip or vertebral fractures**
- Start treatment in patients with a T-score **≤-2.5** SD at femoral neck, total hip, or spine on DEXA
- Treat postmenopausal women and men aged 50+ with osteopenia (T-score **-1 to -2.4**) with increased fracture risks
  - a 10-year **hip fracture** probability of **3%** or more or
  - a 10-year **major osteoporosis-related fracture** probability of **20%** or more
- Osteoporosis based on clinical judgment

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# FRAX

- **www.shef.ac.uk/FRAX**
- The gold standard tool for assessing fracture risk
- In some cases, can be calculated without a DEXA score
- Can be quite useful for some of us if we aren't sure

Welcome to FRAX - Windows Internet Explorer

http://www.shef.ac.uk/FRAX/

File Edit View Favorites Tools Help

Favorites | Welcome to FRAX

Page Safety Tools

# FRAX® WHO Fracture Risk Assessment Tool

Home | Calculation Tool | Paper Charts | FAQ | References | English

- Asia
- Europe
- North America
- Latin America
- Oceania

- Canada
- US (Caucasian)
- US (Black)
- US (Hispanic)
- US (Asian)

## Welcome to FRA

The FRAX® tool has been deve
individual patient models that i
bone mineral density (BMD) at the femoral neck.

Dr. John A Kanis
Professor Emeritus,
University of Sheffield

The FRAX® models have bee
based cohorts from Europe, North America, Asia and Australia. In their most sophisticated form, the FRAX® tool is computer-driven and is available on this site. Several simplified paper versions, based on the number of risk factors are also available, and can be downloaded for office use.

The FRAX® algorithms give the 10-year probability of fracture. The output is a 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture).

**Web Version 3.1**

View Release Notes

**Links**

www.iofbonehealth.org

www.nof.org

www.jpof.or.jp

www.esceo.org

**FRAX available as iPhone App**

View in iTunes

http://www.shef.ac.uk/FRAX/tool.jsp?country=9

Internet 100%

# Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: US (Caucasian) Name/ID: About the risk factors

## Questionnaire:

1. Age (between 40-90 years) or Date of birth
   Age: Date of birth: Y: M: D:
2. Sex ○ Male ○ Female
3. Weight (kg)
4. Height (cm)
5. Previous fracture ◉ No ○ Yes
6. Parent fractured hip ◉ No ○ Yes
7. Current smoking ◉ No ○ Yes
8. Glucocorticoids ◉ No ○ Yes
9. Rheumatoid arthritis ◉ No ○ Yes
10. Secondary osteoporosis ◉ No ○ Yes
11. Alcohol 3 or more units per day ◉ No ○ Yes
12. Femoral neck BMD (g/cm²)

Select DXA

Clear Calculate

### Weight Conversion

Pounds → Kgs

Convert

### Height Conversion

Inches → Cms

Convert

# Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: US (Caucasian) Name/ID: About the risk factors

## Questionnaire:

1. Age (between 40-90 years) or Date of birth
   Age: 65 Date of birth: Y: M: D:
2. Sex ○ Male ◉ Female
3. Weight (kg) 68.04
4. Height (cm) 167.64
5. Previous fracture ◉ No ○ Yes
6. Parent fractured hip ◉ No ○ Yes
7. Current smoking ◉ No ○ Yes
8. Glucocorticoids ◉ No ○ Yes
9. Rheumatoid arthritis ◉ No ○ Yes
10. Secondary osteoporosis ◉ No ○ Yes
11. Alcohol 3 or more units per day ◉ No ○ Yes
12. Femoral neck BMD (g/cm²)
    T-Score -2.1

Clear Calculate

BMI 24.2

The ten year probability of fracture (%)

with BMD

| | |
|---|---|
| Major osteoporotic | 11 |
| Hip fracture | 1.8 |

### Weight Conversion

Pounds → kg

150 Convert

### Height Conversion

Inches → cm

66 Convert

**01130944**

Individuals with fracture risk assessed since 1st June 2011

Home | Calculation Tool | Paper Charts | FAQ | References | English

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11. Alcohol 3 or more units per day: No / Yes
12. Femoral neck BMD (g/cm²)
    T-Score: -2.1

Clear | Calculate

BMI 24.2

The ten year probability of fracture (%)

with BMD

| | |
|---|---|
| Major osteoporotic | 12 |
| Hip fracture | 3.1 |

### Weight Conversion

Pounds → kg

150 Convert

### Height Conversion

Inches → cm

66 Convert

**01141754**

Individuals with fracture risk assessed since 1st June 2011

# Treatment – Primary Prevention

- According to the Bone Health and Osteoporosis Foundation (BHOF), all people aged 50 and above should:
  - be encouraged to engage in regular weightbearing and muscle strengthening exercises to reduce the risk of falls
  - safety-proof their home
  - avoid smoking and excessive alcohol
  - take 1000-1200mg of calcium daily*
  - take 800-1000 IU of vitamin D

# Treatment – Primary Prevention

- According to the United States Preventive Services Task Force (USPSTF):
  - exercise to prevent falls
  - insufficient evidence to assess balance risks/benefits for vitamin D and calcium for primary prevention

  - recommends against ≤ 400 IU/day of vitamin D or ≤ 1000 mg/day of calcium in postmenopausal women

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# Calcium

- **Dietary supplementation is considered safest**
- **No more than 2000mg/day of supplements**
- **Calcium carbonate**
  - cheapest
  - max absorption with 500mg doses
  - better absorption after meals
  - helps with heartburn
- **Calcium citrate**
  - best absorption
  - preferred if on acid-blocking medication
  - preferred if history of renal stones

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# Treatment

- First-line treatment of osteoporosis is with **bisphosphonates**
  - alendronate (Fosamax)
    - 70mg, once weekly
  - ibandronate (Boniva)
    - 150mg, once monthly
    - lack of evidence for non-vertebral fx risk
  - zolendronic acid (Reclast)
    - IV, once yearly
  - risedronate (Actonel)
    - best tolerated
    - most expensive


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# Bisphosphonates

- Bisphosphonates reduce the incidence of vertebral fractures by almost 50% over 3 years
- Alendronate has a little better data than the other bisphosphonates
- The number needed to treat to prevent **one** hip fracture per year is about **100**

# Other Medications

**Estrogen receptor modulator**

**Raloxifene (Evista)**

- May reduce vertebral fractures by 30-55%
- Not clinically proven to reduce hip fractures
- Incidentally lowers breast cancer risk
- Increased risk of hot flashes, leg cramps, and blood clots/DVTs

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# Other Medications

## Calcitonin

- Intranasal
- Can help the pain associated with vertebral fractures
- Questionably decreases risk for new vertebral fractures in established osteoporosis, but no evidence of significant effect on hip fractures
- Not frequently used for fracture prevention

# Other Medications

## Parathyroid hormone analogs

- Teriparatide (Forteo)
- Abaloparatide (Tymlos)
- Daily subcutaneous injections
- May reduce hip fractures by 65%, and other nonvertebral fractures by 53%
- May increase risk of osteosarcoma
- Used for a maximum of two years

# Other Medications

**Receptor activator of nuclear factor kappa-B (RANK) ligand inhibitor**

- Denosumab (Prolia, Xgeva)
- Monoclonal antibody bone-modifying agent, used for bony metastases
- Subcutaneous injection every 6 months
- Cardiovascular, neurologic, and gastrointestinal side effects are not uncommon
- **Possibly worse bone density and increased fracture risk after discontinuation**
- Possible alternative for women at high risk for fracture who cannot take bisphosphonates

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# Other Medications

## Sclerostin Inhibitors

- Romosoxumab (Evenity)
- Monoclonal antibody bone-modifying agent
- Subcutaneous injection monthly for 12 months
- **Increased risk of MI, stroke, and cardiovascular death**
- Possible alternative for women at high risk for fracture who cannot take bisphosphonates
- Unlike the PTH analogs, can be used again after stopping

# Treatment

- First check: creatinine, calcium, albumin, and vitamin D level
  - GFR should be $\geq$30
  - Hypocalcemia can be worsened by bisphosphonates
  - Albumin to get the corrected calcium
  - Vitamin D level should be above 20 ng/ml before initiating treatment with bisphosphonates
    - If vitamin D level is below 20 ng/ml, treat with vitamin D2 -- 50,000 units once weekly for 6-12 weeks
    - Re-check a level before starting bisphosphonates

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# Contraindications to Alendronate

- True Allergy
- Renal
  - GFR <30
- Gastrointestinal
  - esophageal stricture
  - achalasia
  - inability to remain upright for 30 minutes
  - history of bariatric surgery
  - IV bisphosphonate may be a good choice
- Endocrine
  - hypocalcemia

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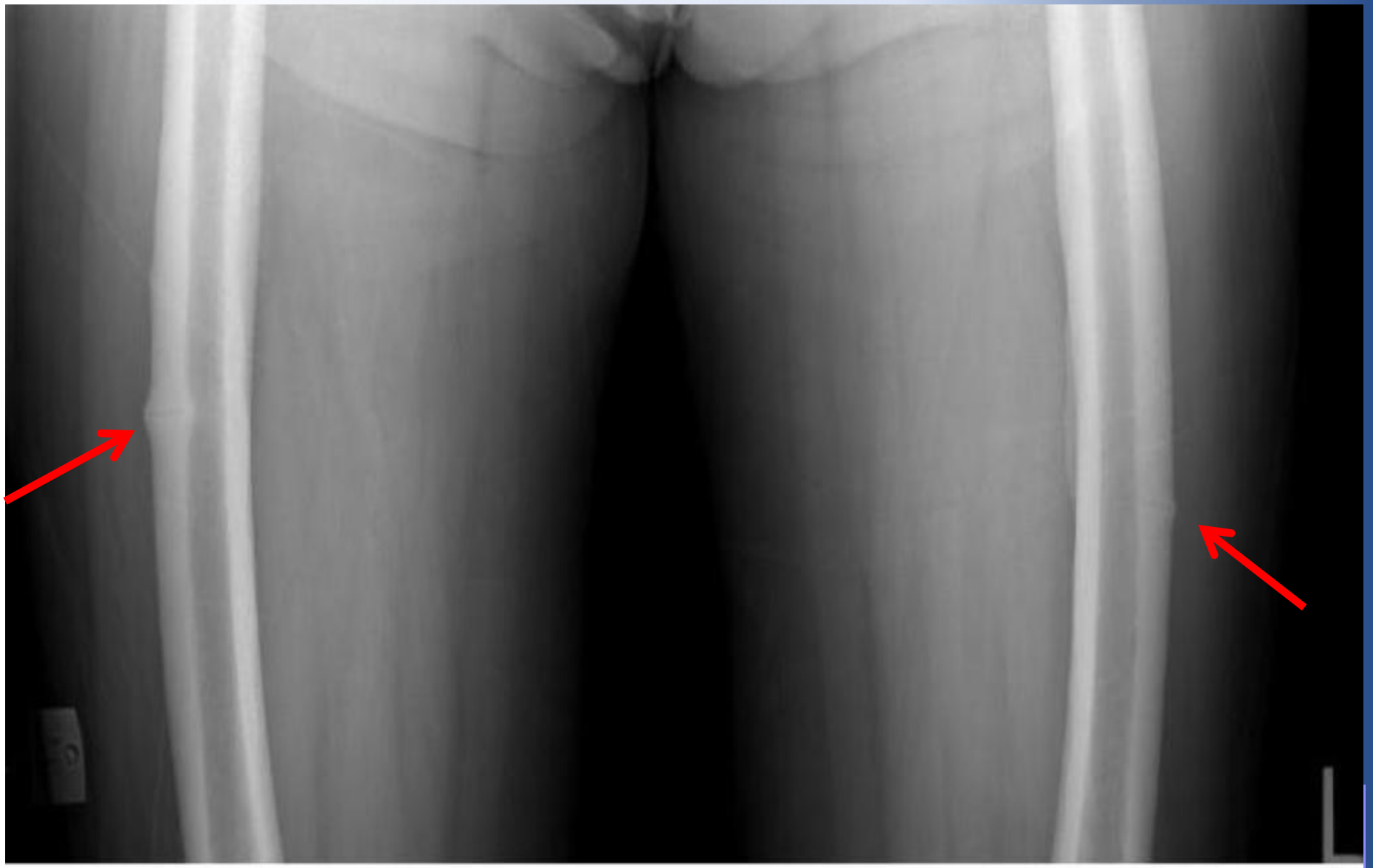
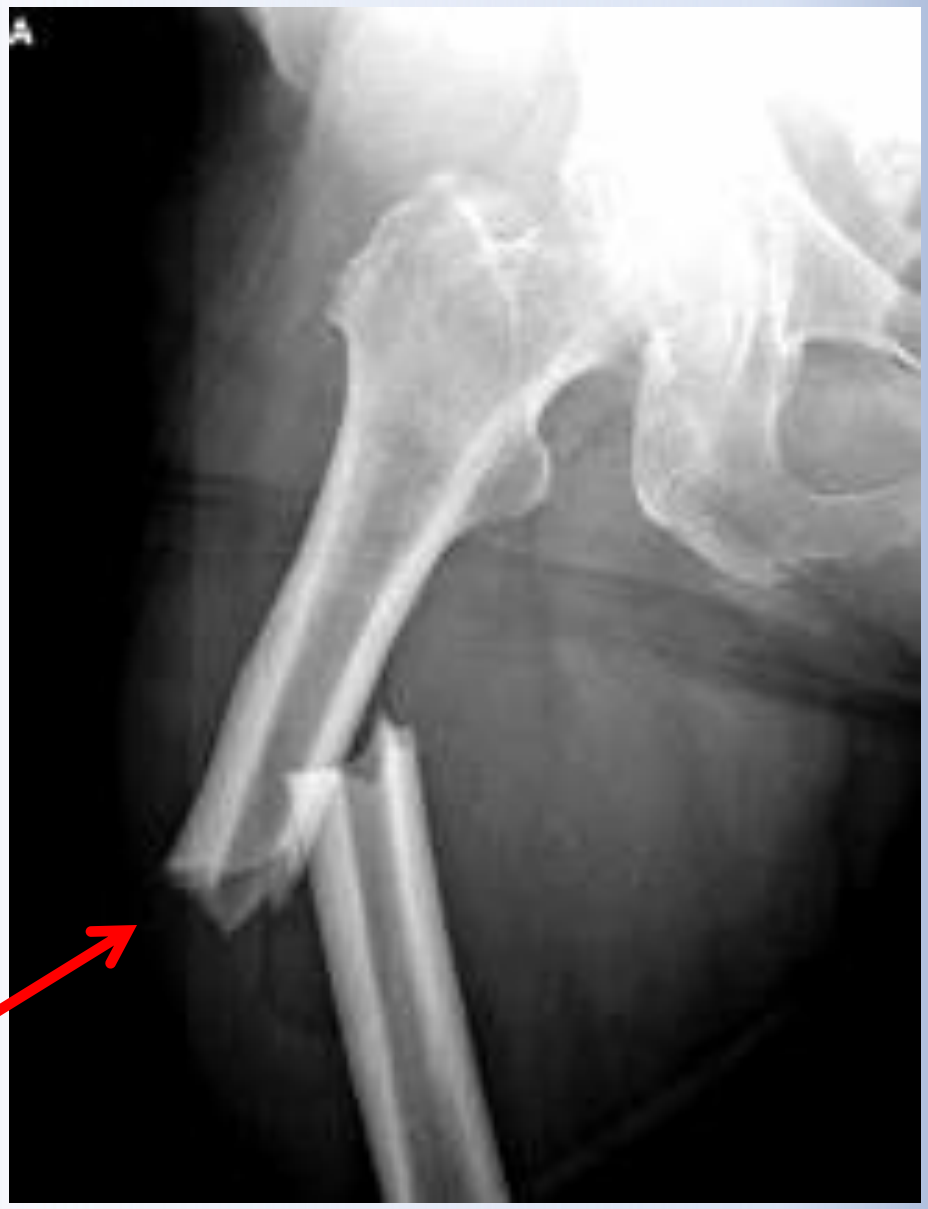
# Bisphosphonates – Adverse Effects

- Gastrointestinal issues
  - Difficulty swallowing
  - Gastric ulcer
  - Esophageal inflammation
- Atrial fibrillation?
- Osteonecrosis of the jaw
- Atypical femur fractures*

# Atypical Femur Fractures

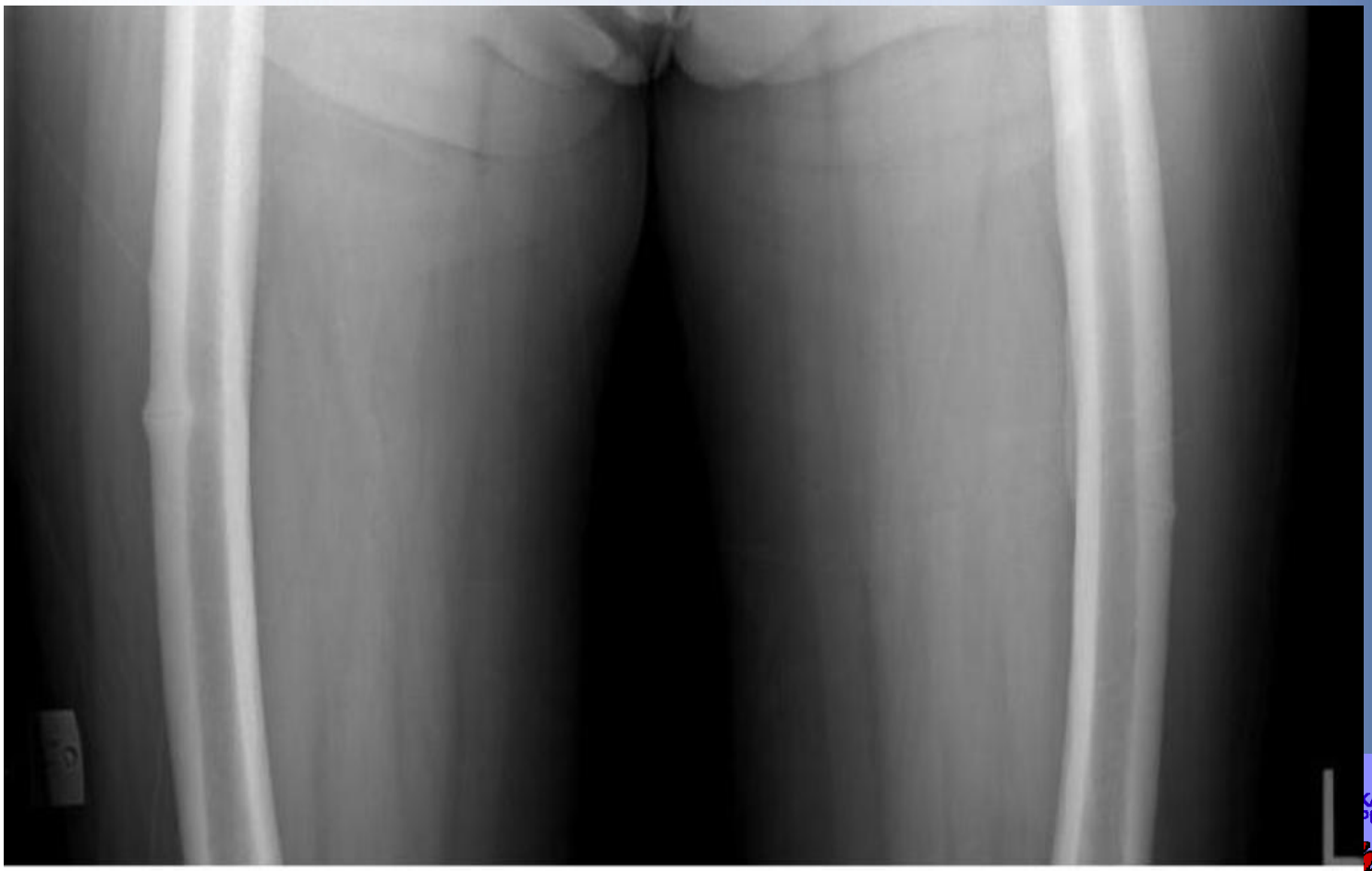


# Atypical Femur Fractures



# Overall Benefit of Bisphosphonates

- **NNT for alendronate is about 100 patients**
- **NNH for alendronate is about 5000 patients***

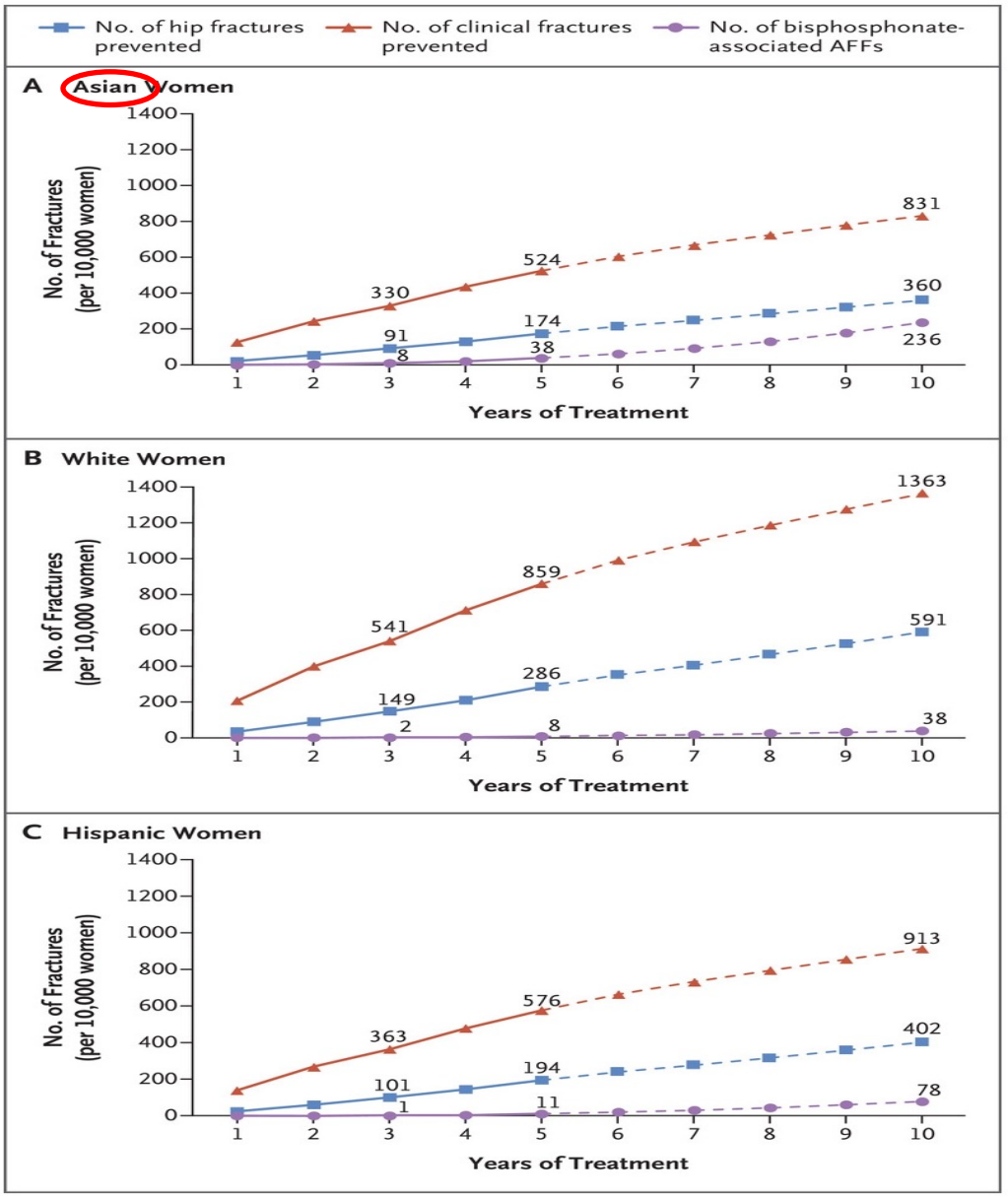


| Years of Rx with a oral Bisphosphonate | Risk/Year per 100,000 for an Atypical Femur Fracture |
|---|---|
| <1 year | 2 in 100,000 |
| 1 - 1.9 years | 2 in 100,000 |
| 2 - 2.9 years | 3 in 100,000 |
| 3 - 3.9 years | 12 in 100,000 |
| 4 - 4.9 years | 16 in 100,000 |
| 5 - 5.9 years | 24 in 100,000 |
| 6 - 6.9 years | 43 in 100,000 |
| 7 - 7.9 years | 78 in 100,000 |

Dell R, Greene D, Ott S, et al. A retrospective analysis of all atypical femur fractures seen in a large California HMO from the years 2007 to 2009. ASBMR 2010 Annual Meeting, Toronto, Canada. 2010

# Atypical Femur Fractures

- Highest incidence in **Asian** women
- Glucocorticoid use > 1 year also a risk factor
- Benefit still outweighs risk




D.M. Black, E.J. Geiger, R. Eastell, *et al.* **Atypical femur fracture risk versus fragility fracture prevention with bisphosphonates**
N. Engl. J. Med., 383 (8) (2020), pp. 743-753

# Drug Holiday

- After 5 years of oral bisphosphonate therapy (or 3 years of IV bisphosphonate), there should be a drug holiday if:
  - DEXA T-score is better than -2.5, **and**
  - No history of fragility fracture, **and**
  - Not on bone-losing medication
- Reassess with DEXA scan every 2 years
  - Resume treatment for any of the above changing or for bone loss >5% between tests

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# Summary

- Osteoporotic hip fractures affect as many as 1 in 8 women, resulting in 10-20% excess mortality
- Screening with DEXA is recommended in:
  - all women 65 and older
  - all men 70 and older*
  - fracture patients 50 and older
  - higher risk patients (50 and older)

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# Summary

- Primary prevention in people 50+ (BHOF):
  - 1000-1200mg of calcium daily
  - 800-1000 IU of vitamin D
  - regular weightbearing and muscle strengthening exercises to reduce the risk of falls
  - safety-proofing the home
  - avoid smoking and excessive alcohol

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# Summary

- Start treatment in patients with:
  - a hip or a vertebral fracture
  - a Dexa T-score of -2.5 or lower
  - a FRAX 10-year probability of:
    - 3% or more for hip fracture

      or
    - 20% or more for major osteoporotic fracture

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# Summary

- Bisphosphonates are the medication of choice to treat osteoporosis
  - Most side effects are gastrointestinal in nature
  - Serious side effects are rare but notable
  - Benefits outweigh serious risks by 50 to 1
  - A 5-year timespan of treatment is currently recommended, with reassessment and a possible 2-year drug holiday
  - A repeat DXA scan can be checked at 2 years

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# Questions/Comments