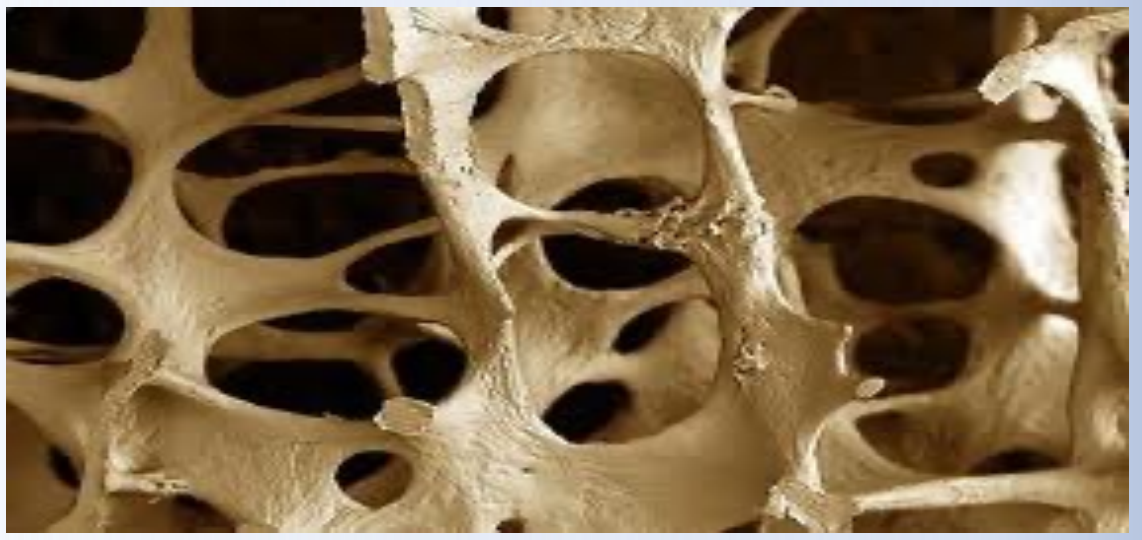
Osteoporosis

Assessment & Management

Dennis K-Borna, MD, FACSM

No disclosures to report



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Epidemiology

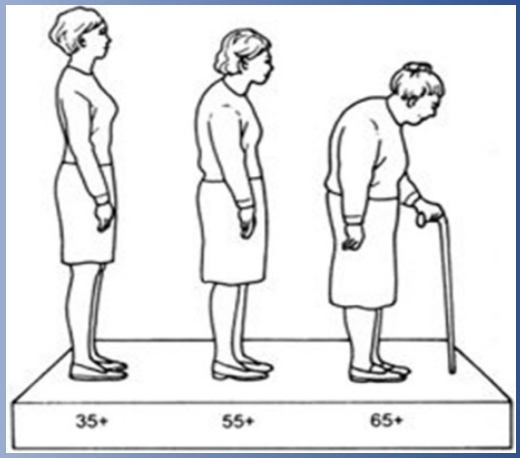
- 2 million osteoporotic fractures in the United States each year
- about 50 million people in the U.S. are at risk for fracture
  - Diabetes: 34 million
  - Hyperlipidemia: 94 million
  - Hypertension: 75 million*

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

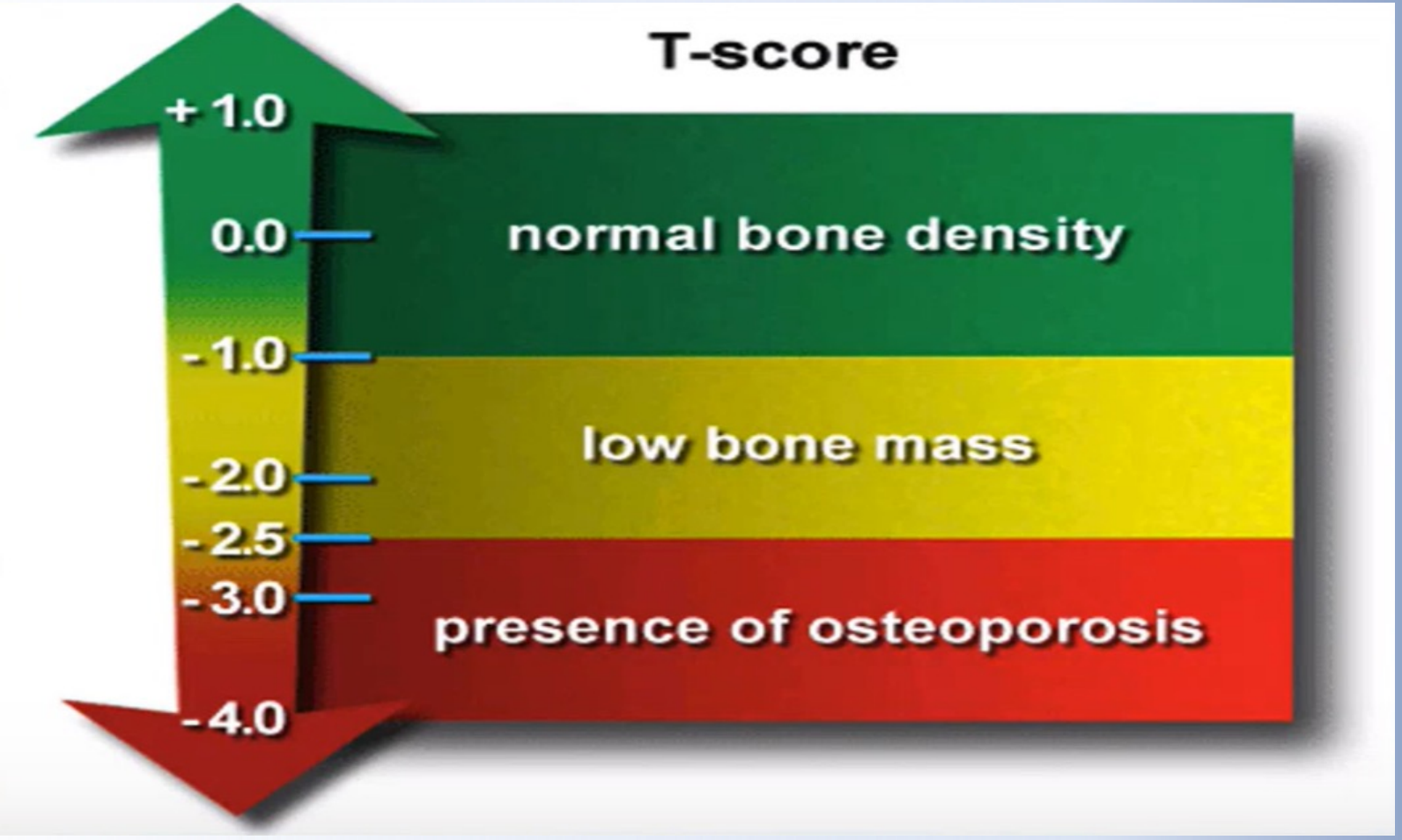
- Long-term glucocorticoid use
- Smokers
- Heavy alcohol use
- Inactivity
- Malabsorptive conditions
- Rheumatologic conditions
- Hematologic conditions
- Neuromuscular diseases

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
normal bone density
- 1.0
low bone mass
- 2.0
- 2.5
- 3.0
presence of osteoporosis
- 4.0

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

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%

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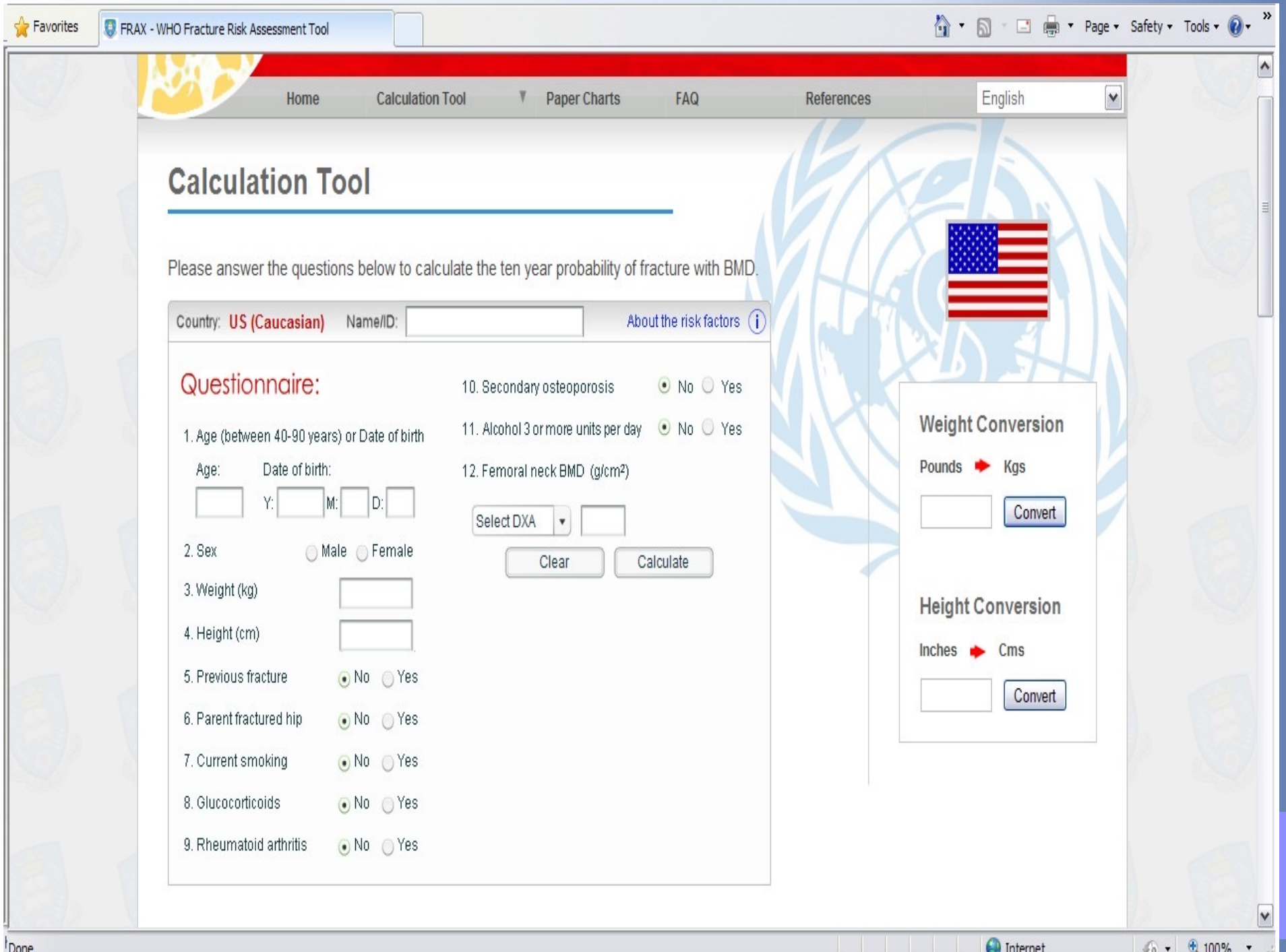
Favorites
FRAX - WHO Fracture Risk Assessment Tool
Page
Safety
Tools
Home
Calculation Tool
Paper Charts
FAQ
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English
Calculation Tool
Please answer the questions below to calculate the ten year probability of fracture with BMD.
Country: US (Caucasian)
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
Done
Internet
100%

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

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

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Calculation Tool
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Name/ID:
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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 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

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

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

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
- Severe hypocalcemia if advanced CKD
- **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 ≥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

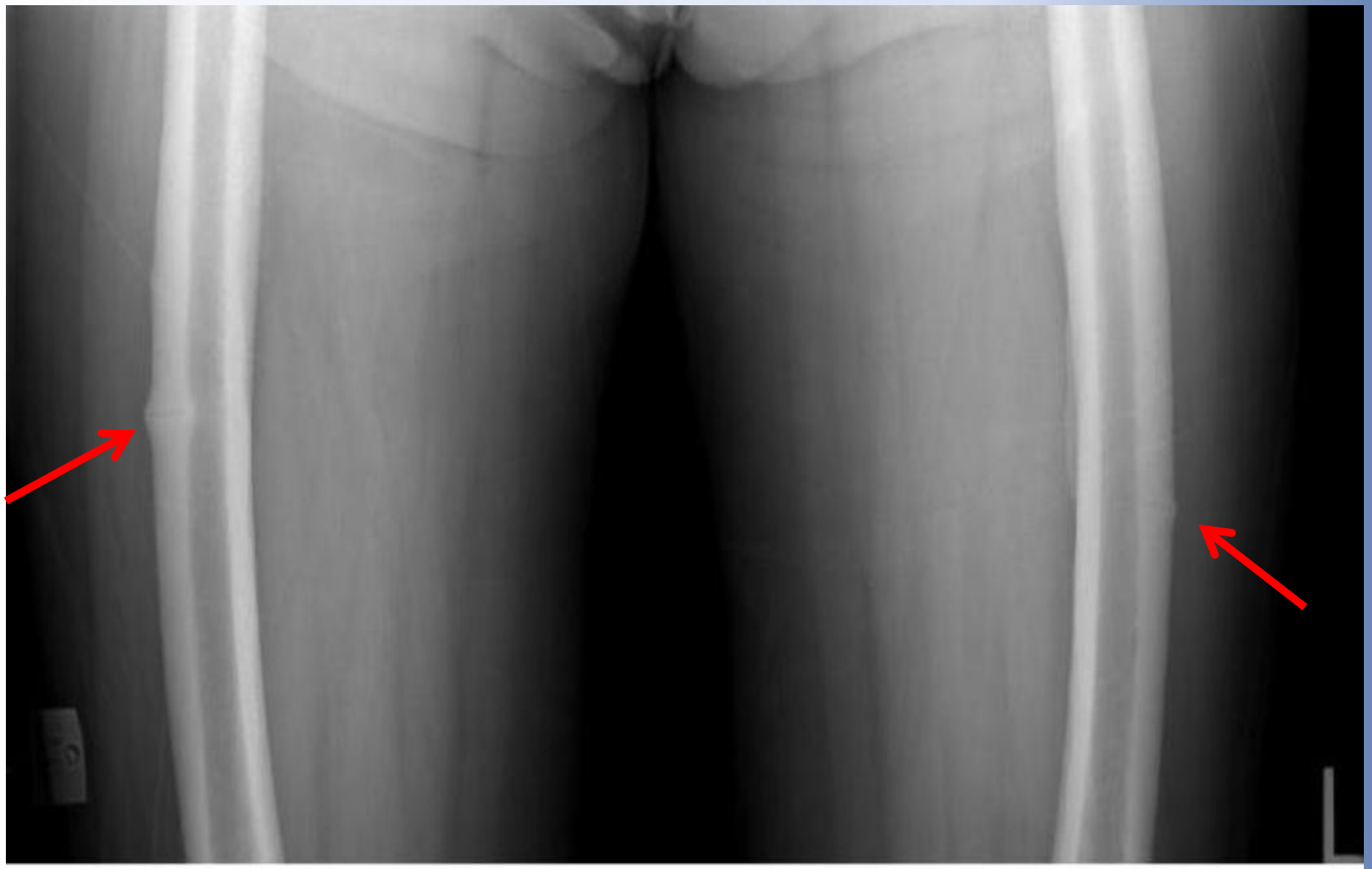
Contraindications to Alendronate

- 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

Bisphosphonates – Adverse Effects

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

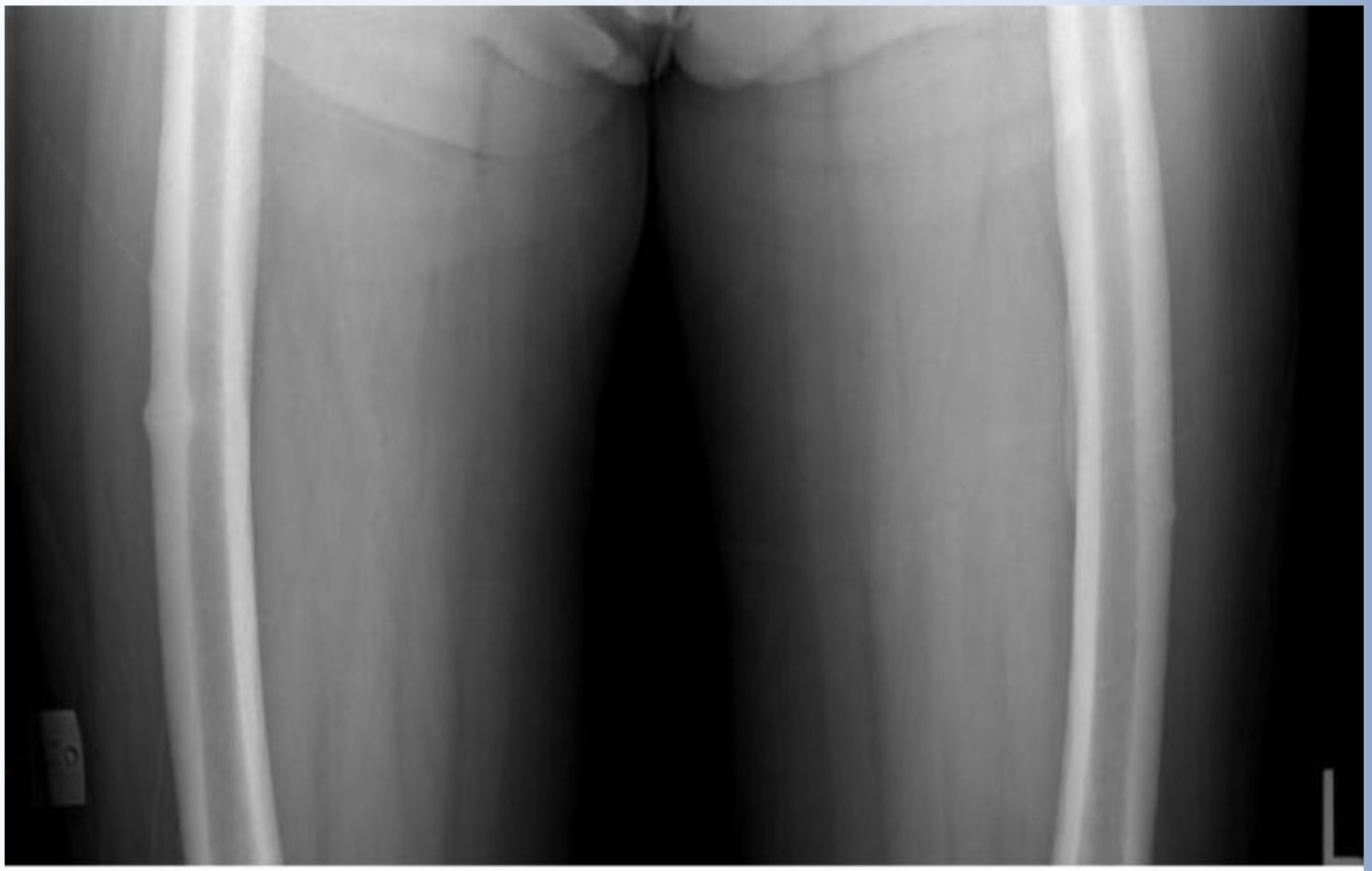
Atypical Femur Fractures



Atypical Femur Fractures

Overall Benefit of Bisphosphonates

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

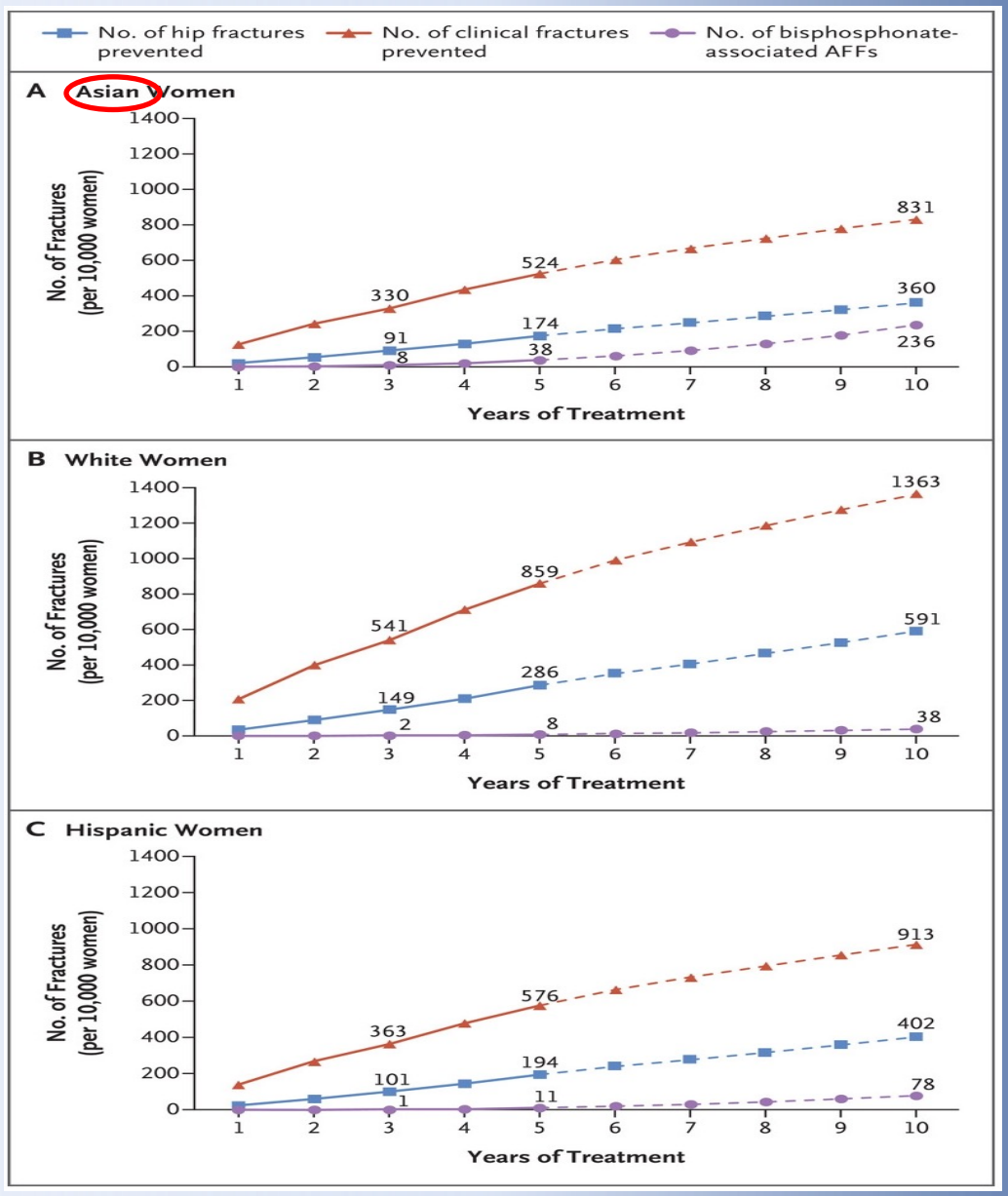


Years of Rx with a oral Bisphosphonate	Risk/Year per 100,000 for an Atypical Femur Fracture
<1 year	2 in 100,000
1 - 1.9 years	2 in 100,000
2 - 2.9 years	3 in 100,000
3 - 3.9 years	12 in 100,000
4 - 4.9 years	16 in 100,000
5 - 5.9 years	24 in 100,000
6 - 6.9 years	43 in 100,000
7 - 7.9 years	78 in 100,000

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)

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

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

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

Questions/Comments