How long will your bones remain standing?

Using the FRAX Tool

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Osteoporosis Definition

A skeletal disease characterized by low bone mass, deterioration of bone tissue with disruption of bone architecture, resulting in compromised bone strength and an increase in the risk of fracture.

Clinician’s Guide to Prevention and Treatment of Osteoporosis;
National Osteoporosis Foundation, 2008

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Osteoporosis

Osteoporosis Can Lead to Irreversible Deterioration of Bone Structure

WHO Diagnostic Classifications

T-score ≥ -1 = Normal

T-score between -1 and -2.5 = low bone mass (osteopenia)

T-score ≤ -2.5 = Osteoporosis

T-score ≤ -2.5 and fragility fracture = Severe Osteoporosis

Osteoporosis

• 1 of 2 Caucasian females = osteoporotic Fx
• 1 of 5 Caucasian males = osteoporotic Fx

• Fractures cause chronic pain, disability, and increased mortality
• Hip Fxs cause 10-20% excess mortality in 1 yr
• 20% of hip Fx pts require long term nursing home care
• Only 40% regain their pre fracture level of independence
Economic Toll

Cause 432,000 hospital admissions
2.5 million office visits
180,000 nursing home admissions per year
2 million fractures/yr cost $20 billion/yr

Incidence of Osteoporosis

Osteoporosis (and low BMD) is a risk factor for fractures

Just as HTN is a risk factor for stroke
and
Hyperlipidemia is a risk factor for cardiac events.
Osteoporosis

• < 30% of elderly women are screened for osteoporosis
• Only 22% of patients with osteoporotic fractures are treated to prevent recurrence
• Compared to 94% of post MI patients.

Osteoporosis

• 10 million Americans have osteoporosis
• 33.6 million Americans have low bone mass (at the hip)
• = 3 X more patients with low bone mass than those with osteoporosis

Based on Data from NHANES III

Osteoporotic Fractures

• Most Fractures Occur in People without Osteoporosis
  only
• 44 % of women
• 21 % of men
who sustained a non vertebral fracture had Osteoporosis by BMD

Schult et al. Bone, 2004;34:195-202
BMD and fractures

Who to treat

• NOF has always recommended treating pts with Osteoporosis (T-score < -2.5)

• Which patients should be treated with low bone mass?

• Would like to treat those at high risk, but avoid those at low risk

Low bone mass dilemma

• Who is at higher risk of fracture?

• 54 yr old smoker with T-score of -2.0

  or

• 81 yr old no risk factors and T-score of -1.6
Risk Factors for Fracture: Age

10 Year risk: Age & Risk of Fracture with Low BMD

Risk increases with age

Vertebral fracture risk related to BMD and Previous Fractures

Combined Effect of Bone Density and Prevalent Fractures

Risk of Hip fractures influenced by BMD and number of risk factors

Annual Risk of Hip Fractures

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Fracture Risk Reporting

- T-score alone does not provide a complete assessment of fracture risk
- Combination of clinical risk factors with BMD may provide a better way of identifying patients for treatment
- Use 10 yr probability of risk of fracture
- Focus on hip fracture

FRAX

Tool developed by the WHO for world wide use to predict fracture risk
Combines BMD and clinical risk factors to better predict fracture risk

Predicts 10 year probability of:
1) major osteoporotic fracture (hip, spine, wrist, humerus)
2) Hip fracture

FRAX TOOL

- Data from 59,232 patients from 12 large observational studies from Europe, North America, Australia, and Asia
- Used to identify risk factors that increased fracture risk
- This data used to develop the FRAX tool to calculate the 10 year probability of developing an osteoporotic fracture
- Validated in other observational studies
**FRAX Intervention Thresholds**

- Intervention threshold not calculated by FRAX tool or by the WHO
- Intervention threshold determined by each individual country
- (In USA this was determined by the NOF)

- Based on costs of treatment, resources in each country, and priority of osteoporosis in each country

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**Intervention Thresholds**

- In USA NOF recommends treatment for patients with T-score between -1.0 and -2.5 (low bone mass or osteopenia)
  
  AND

- 10 year probability of major fracture of ≥ 20 %

- 10 year probability of hip fracture of ≥ 3 %

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## Risk Factors used in FRAX

- Prior fracture
- Parental hip Fx
- Current smoking
- Systemic corticosteroids
- Alcohol intake > 2 units/day
- Rheumatoid arthritis
- Current age
- Femoral neck BMD
- BMI (without BMD)
- Secondary osteoporosis (without BMD)
Risk Factors Included in FRAX®
Independent contribution after age and T-score

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>RR</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior fracture</td>
<td>1.62</td>
<td>(1.30-2.01)</td>
</tr>
<tr>
<td>Parental history of hip fracture</td>
<td>2.28</td>
<td>(1.48-3.51)</td>
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<tr>
<td>Current smoking</td>
<td>1.60</td>
<td>(1.27-2.02)</td>
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<tr>
<td>Systemic corticosteroids</td>
<td>2.25</td>
<td>(1.60-3.15)</td>
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<tr>
<td>Alcohol intake &gt; 2 units daily</td>
<td>1.70</td>
<td>(1.10-2.42)</td>
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<tr>
<td>Rheumatoid arthritis</td>
<td>1.74</td>
<td>(0.94-3.20)</td>
</tr>
</tbody>
</table>

Risk Factors

AGE

The model accepts ages between 40 and 90 years. If ages below or above are entered, the program will compute probabilities at 40 and 90 respectively.

Risk Factors

Sex

Male or female. Enter as appropriate.
Risk Factors

Weight

This should be entered in kilograms. The FRAX Tool will convert pounds into kg.

Risk Factors

Height

This should be entered in centimeters. The FRAX Tool will convert inches to cm.

Risk Factors

Previous Fracture

A previous fracture is a fracture in adult life occurring spontaneously, or secondary to trauma which in a healthy person would not have resulted in a fracture. The number of fractures is not taken into account. Therefore, with multiple fractures, the probability of fracture will be underestimated.
Risk Factors

Parental Hip Fracture

Is there a history of a hip fracture in a patient’s mother or father?

Risk Factors

Current Smoking

Does the patient currently smoke tobacco?

The higher the exposure, the greater the risk. However, this is not taken into account and, therefore, the tool assumes average exposure.

Risk Factors

Glucocorticoids

This assumes a dose of 5 mg or more for more than 3 months.

The effect is dose dependent; the higher the dose, the greater the risk. However, this is not taken into account. Therefore, actual risk may be underestimated.
Risk Factors

Rheumatoid Arthritis
The patient must have a confirmed diagnosis of rheumatoid arthritis.

Risk Factors

Secondary Osteoporosis
Does the patient have a disorder strongly associated with osteoporosis?
These include type I diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (< 45 yrs), chronic malnutrition or malabsorption, or chronic liver disease.

Risk Factors

Alcohol 3 or more units per day
A unit of beer is equal to a standard glass of beer (285 ml).
A unit of spirits is equal to 30 ml.
A unit of wine is a medium sized glass (120 ml).
A unit of aperitif is equal to 60 ml.
The risk is dose dependent. Therefore, risk may be underestimated.
Risk Factors

Bone Mineral Density (BMD)

Select the DXA manufacturer and then enter the femoral neck BMD (in gm/cm²). Total femur BMD may also be used. In patients without a DXA, the field should be left blank.
Where to Find FRAX™

- Now
  - http://www.shef.ac.uk/FRAX
- Future
  - DXA
  - CD
  - PDA

Where to find FRAX

- Is now on new versions of DXA software
- Is currently available as iPhone App

When to Use FRAX

Postmenopausal women and men ≥ 50 years of age with osteopenia (low bone mass) who do NOT qualify for treatment based on other treatment indications.
When Not to Use FRAX

- Patients who meet other treatment indications
- Treated patients
- Normal T-score (> -1.0)
- Osteoporotic patients (T-score < -2.5)
- Premenopausal women
- Men < 50 years of age
- Children

Incorrect use of FRAX

- Consumer Reports “5 minute consult”

- 65 year old teacher
- No risk factors
- BMD T-score -2.6 (hip?)

- FRAX tool results:
  - 10 year risk of hip fx: 2.9%

- Pt told she did not need Rx
Problems with FRAX

- Original fracture risk was over estimated
- Now adjusted using new data base of US fracture rates
- Changes now incorporated into FRAX version 3.0 (September 2009)
- Requires Internet access

FRAX NOF Guideline Limitations*

- Identifies patients for treatment where limited evidence exists as to treatment efficacy (osteopenia NOT osteoporosis)
- Only uses BMD at the femoral neck
- Some risk factors are categorical vs variable ie;
  - prior Fx History (how many fractures)
    - 1 vert Fx increases risk 4X
    - Multiple vert Fxs increase risk 10 X
  - Glucocorticoid use (dose, duration)
    - ACR recommends a bisphosphonate for chronic steroid use > 5 mg and T-score < -1.0

*Personal opinions of M McClung MD at 11th Annual Santa Fe Bone Symposium 2010
McCloskey EV et al, Osteoporosis Int 2009;20:811-7

Summary of Recommendations

- Recommend BMD testing for women ≥ 65, men ≥ 70
- Calcium (1200-1500 mg/day)
- Vitamin D (800 – 1000 IU /day)
- Regular weight – bearing and muscle strengthening exercise
- Fall Prevention (consider hip protectors if increased fall risk)
- Avoid smoking and excessive alcohol
- Use of FDA approved medicine for those with T-scores < -2.5, or with fragility fractures of hip or spine, or osteopenia and a FRAX 10 year risk : at hip or ≥3% or of any major osteoporotic fx ≥20%
FDA-Approved Medications

<table>
<thead>
<tr>
<th>Drug</th>
<th>PMO Treatment</th>
<th>GIO (Women, Men)</th>
<th>Men Treatment</th>
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<tbody>
<tr>
<td>Estrone</td>
<td>✔️</td>
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<tr>
<td>Alendronate (PO)</td>
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<td>Estrogen</td>
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<tr>
<td>Calcitonin</td>
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<tr>
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<tr>
<td>Denosumab</td>
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Fracture Risk Reduction in Randomized Clinical Trials

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<th>Nonvertebral</th>
<th>Hip</th>
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Summary

- FRAX™ provides better estimation of fracture risk than qualitative estimation of relative risk.
- New NOF guide better identifies patients most likely to benefit from therapy than over-reliance on BMD with former guide.
- Optimal use of these tools requires full understanding of their limitations and good clinical judgment.
Case 1 - Osteopenia

- Which one of these patients is at higher risk for fractures?

- 53 year old smoker with T-score of –2.0

- 81 year old with no previous fractures and T-score of –1.6

Case 1 - Osteopenia

- 53 year old smoker T-score –2.0
- 10 year risk of hip fx = 1.5%
- 10 year risk of major osteoporotic fx = 7%

- 81 year old without fx T-score -1.6
- 10 year risk of hip fx = 3.6%
- 10 year risk major osteoporotic fx =13%

Old Guide vs. New Guide

<table>
<thead>
<tr>
<th>Case</th>
<th>Old Guide</th>
<th>New Guide</th>
</tr>
</thead>
<tbody>
<tr>
<td>55 year-old Caucasian woman (120 lbs, 5-2’) with T-score = -2.1</td>
<td>Treat (T-score &lt; -2.0)</td>
<td>Don’t Treat (10 year risk of major fracture 10%, hip 1.5%)</td>
</tr>
<tr>
<td>80 year-old Caucasian woman (120 lbs, 5-2’) with T-score = -1.1</td>
<td>Don’t Treat (T-score &gt; -1.5)</td>
<td>Treat (10 year risk of major fracture 24%, hip 2.4%)</td>
</tr>
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</table>
The Beginning of a new Era