Geriatric Osteoporosis: an Overview

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Example for T-score = -2.0, 60 year old and Z-Score = -0.5
نمودار شیوع استوکیروز در ناحیه فمور به تفکیک سن

لاریجانی ب، حسین‌نژاد ا، موتاخدی ا، پاجویی م، بستن‌هاق MH، سلطانی A، میرفهیزی SZ، دشتی R.

داده‌های مرجع مادکیت تنها در جمعیت سالم از تهران، ایران: یک بررسی پایدار. 

BMC Musculoskelet Disord. 2005 Jul 2;6(1):38.
سیوگ اسپنوز در سون فرار
کمری به تفکیک سن

### Risk Assessment of menopausal and elderly people for evaluation

**With Relative Risk ≥ 2 (Major)**
- Age > 70
- Menopause < 45
- Hypogonadism
- Fragility Fracture
- Hip Fracture in Parents
- Glucocorticoids
- Malabsorption
- BMI < 18
- Immobilisation
- Chronic Renal Failure
- Transplantation

**With Relative Risk 1 - 2 (Moderate)**
- Estrogen Deficiency
- Calcium Intake < 500 mg/d
- Primary Hyperparathyroidism
- Rheumatoid Arthritis
- Anticonvulsivants
- Hyperthyroidism
- Diabetes Mellitus type 1
- Smoking
- Alcohol Excess
Age Is a Major Risk Factor for Fracture

## Falls and fractures

<table>
<thead>
<tr>
<th>Type of fracture</th>
<th>Percentage attributed to falls by older women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist</td>
<td>96</td>
</tr>
<tr>
<td>Proximal humerus</td>
<td>95</td>
</tr>
<tr>
<td>Hip</td>
<td>92</td>
</tr>
<tr>
<td>Ankle</td>
<td>88</td>
</tr>
<tr>
<td>Pelvis</td>
<td>80</td>
</tr>
<tr>
<td>Face</td>
<td>77</td>
</tr>
<tr>
<td>Tibia/fibula</td>
<td>65</td>
</tr>
<tr>
<td>Face</td>
<td>59</td>
</tr>
<tr>
<td>Vertebral</td>
<td>&lt;25</td>
</tr>
</tbody>
</table>

## Risk factors for falls

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Relative risk ratio/Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle weakness</td>
<td>4.4</td>
</tr>
<tr>
<td>History of falls</td>
<td>3.0</td>
</tr>
<tr>
<td>Gait deficit</td>
<td>2.9</td>
</tr>
<tr>
<td>Balance deficit</td>
<td>2.9</td>
</tr>
<tr>
<td>Walking aid use</td>
<td>2.6</td>
</tr>
<tr>
<td>Visual deficit</td>
<td>2.5</td>
</tr>
<tr>
<td>Arthritis</td>
<td>2.4</td>
</tr>
<tr>
<td>Impaired ADL</td>
<td>2.3</td>
</tr>
<tr>
<td>Depression</td>
<td>2.2</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>1.8</td>
</tr>
<tr>
<td>Psychoactive drugs</td>
<td>1.7</td>
</tr>
<tr>
<td>Age &gt;80</td>
<td>1.7</td>
</tr>
</tbody>
</table>

Common sites of fracture

\[
\begin{align*}
\frac{1}{2} & \quad \text{vertebral fracture} \\
\frac{1}{4} & \quad \text{Hip fracture} \\
\frac{1}{4} & \quad \text{colles’ fracture}
\end{align*}
\]

Am J Med 1998; 94-646
Clinical manifestations

- Chronic pain
- Height loss
- Kyphosis
- Decreased self-esteem
- Restrictive lung dx
- Constipation, abdominal pain
- Depression
2010 Guidelines for Bone Density Testing

• Screening
  – All women age 65 and older\textsuperscript{1,2}
  – All men age 70 and older\textsuperscript{1}

• Test postmenopausal women and men >50 if\textsuperscript{1}:
  – Fracture after age 50
  – Clinical risk factors for osteoporosis
  – Conditions/medications associated with bone loss
    o COPD, RA, hyperparathyroidism, celiac disease, IBD
    o Oral glucocorticoids, anticonvulsants, proton pump inhibitors, SSRIs, aromatase inhibitors

Dual Energy Xray Absorptiometry (DXA)

- Currently most widely used
- Bone mineral analysis
- Gold standard is DEXA of hip or spine
- Takes ~ 10 minutes
**IN THE NAME OF GOD**
**BONE MINERAL DENSITOMETRY UNIT**
Endocrine and Metabolism Research Center
Shariati Hospital – North Kargar Ave. Tehran, Iran Tel: 84902133

**Date: 82/03/06**

**Risk factor assessment for osteoporosis and osteoporotic fractures in your patient**

**Menopause**

<table>
<thead>
<tr>
<th>Femur (Total)</th>
<th>Lumbar spine (L3-L4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMD:</strong> 0.554</td>
<td><strong>BMD:</strong> 0.705</td>
</tr>
<tr>
<td>T-score: 1 <strong>-3.7</strong> (55% of normal young adult)</td>
<td>T-score: 1 <strong>-4.1</strong> (59% of normal young adult)</td>
</tr>
<tr>
<td>Z-score: 2 <strong>-1.8</strong> (72% of age matched)</td>
<td>Z-score: 2 <strong>-1.7</strong> (78% of age matched)</td>
</tr>
</tbody>
</table>

**Diagnosis:** Osteoporotic (according to WHO criteria)

Relative risk of fracture: 13

(There is decreased height of L1 & L2, so relative risk of fracture can't be estimated, but it is at least 17.1.)

**C: General Preventive and Therapeutic Recommendations (After secondary causes were ruled out):**

- According to decreased height of L1 & L2 more investigation is suggested for local disorders.
- Optimal calcium intake (diet* and drug = 1500 mg/day) + exercise + vitamin D (800 IU/day) and etidronate (400 mg/day for 14 days and repeat every 3 months) or alendronate (10 mg/day with plain water, at least 1/2 hours before the first food).
- 2- and/or calcitonin 200 IU/day (as nasal spray).
- 3- An evaluation of the risk of falling and a preventive program should be undertaken.
- 4- Repeat of BMD after 2 years is suggested.

*each glass of milk or yogurt contains 300 and 400mg calcium respectively.

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**Notice:** The interpretation of reported findings and final decision making (including the above mentioned recommendations) must be done by original patient's physician.

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1- The number of standard deviations (SD) the adult patient’s BMD is above or below the mean, for the young normal reference population.
2- The number of standard deviations (SD) the patient’s BMD is above or below the mean, for the age match reference population.
3- WHO criteria for osteoporosis:
   - Normal: a value for BMD greater than 1 SD of the young adult mean
   - Osteopenia: a value for BMD more than 1 SD but less than 2.5 SD below the young adults mean
   - Osteoporosis: a BMD value 2.5 SD or greater below the young adult mean
4- Secondary causes: hypogonadism, hypercortisolism, hyperparathyroidism, hyperthyroidism, hyperprolactinemia, diabetes, thalassemia, acromegaly, malabsorption, anorexia nervosa, vitamin D deficiency, chronic liver disease, myocardia, rheumatoid arthritis, renal disease; use of levotyroxine, anticonvulsant, corticosteroid or heparin.
5- Changes in BMD values at femoral region equal to or more than 0.05 g/cm2 or 5.6%, are considered significant.
6- Changes in BMD values at lumbar region equal to or more than 0.03 g/cm2 or 2.8%, are considered significant.
Physician:
75 years 01/01/1928
145 cm 59 kg White Female
SSN:

Left FEMUR BONE DENSITY

Acquired: 05/21/2003 (4.6d)
Analyzed: 05/21/2003 (4.6d)
Printed: 05/21/2003 (4.6d)

atasha00.f64

TOTAL Comparison to Reference

T Score

AGE (years)

Region

BMD \(^1,7\) g/cm\(^2\)

Young-Adult \(^2\) %

Age-Matched \(^3\) %

TOTAL 0.694 69 -2.6 88 -0.8

Image not for diagnosis
0.75ma:Medium DPXMD 1.2x1.2mm 1.68mm
717888:413593 275.88-207.34:145.17
%Fat = 18.9(1.354) Neck Angle = 56

1 - See appendix on precision and accuracy.
   Statistically 68% of repeat scans will fall within 1 SD. (±0.02 g/cm\(^2\))
2 - USA Femur Reference Population. Young Adult Ages 20-45. See Appendices.
3 - Matched for Age, Weight(25-100kg), Ethnic.
7 - Standardized BMD for TOTAL is 648 mg/cm\(^2\). See J Bone Miner Res 1994; 9:1503-1514

Comments:
1 - See appendix on precision and accuracy. Statistically 68% of repeat scans will fall within 1 SD. (±0.02 g/cm²)
2 - USA AP Spine Reference Population, Young Adult Ages 20-45. See Appendices.
3 - Matched for Age, Weight (25-100kg), Ethnic.
4 - WHO T-score categories are: >1.0 SD = normal; -1.0 to -2.5 SD = osteopenia; <-2.5 SD = osteoporosis.

Comments:
Assessment of unexplained osteoporosis

- Weight loss
- Diarrhea
- Bone pain
- Muscle weakness
- Obesity
- Skin rash
- Hyperandrogenism
- Nephrolithiasis
- Thyrotoxicosis
- Malabsorption
- Osteomalacia, FX’s malignancy
- Cushing’s syndrome
- Hypercalciuria

EVALUATIONS

• CBC
• Ca, P, Alk P, Cr
• URIN Ca
• Testosterone in male

Management
PROFET (prevention of falls in the elderly trial): Preventing falls in patients presenting to A&E

Patients aged > 65 attending A & E with a fall
  – 184 randomised to medical and Occupational Therapy assessment
  – 213 controls

- Medical assessment and treatment of cause of fall
  – 72% balance impairment
  – 59% visual impairment
  – 34% cognitive impairment
  – 28% reduced muscle power
  – 20% peripheral neuropathy
  – 17% cardiovascular disorders

- Home visit: safety education and environmental adaptations

Close et al, Lancet 1999
PROFET: results

• 12 months later:
  – **183** falls in intervention group
  – **510** falls in controls \( (p=0.0002) \)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odds ratio (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in any fall</td>
<td>0.39 (0.23-0.66)</td>
</tr>
<tr>
<td>Reduction in recurrent falls</td>
<td>0.33 (0.16-0.68)</td>
</tr>
<tr>
<td>Reduction in hospital admission</td>
<td>0.61 (0.35-1.05)</td>
</tr>
</tbody>
</table>

Effective interventions

2. Muscle strengthening and balance retraining
   – Individually prescribed
   – Delivered in patient’s home by a health professional
   \[ RR \, 0.80 \, (95\% \, C.I. \, 0.66-0.98) \]

3. Home hazard assessment and modification
   – Professionally prescribed
   – In those who have fallen (only)
   \[ RR \, 0.66 \, (95\% \, C.I. \, 0.54-0.81) \]
Effective interventions

4. Withdrawal of psychotropic medication
   RR 0.34 (95% CI 0.16-0.74)

5. Cardiac pacing for fallers with Carotid Sinus Syndrome
   WMD -5.20 (95% CI -9.4- -1.0)

6. Tai Chi group exercise intervention
   RR 0.51 (95% CI 0.36-0.73)
Hip protectors

Cochrane review 2006

- Meta-analysis of 11 trials in care home settings: Reduction in incidence of hip fracture (RR 0.77 (95% C.I. 0.62-0.97) (but weak cluster randomisation methodology in 7 trials)

- Meta-analysis of 3 individually randomised trials in community settings: No reduction (RR 1.16 (95% C.I. 0.85-1.59)

- Poor acceptance (median 68%) and compliance rates (median 56%)

- Conclusion: hip protectors are ineffective for those living at home and their effectiveness in an institutional setting is uncertain.

Parker et al. BMJ 2006
Vitamin D and Calcium in the Prevention of Fracture in Elderly Institutionalized Women

## Calcium Intake Recommendations From the IOM

<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>Estimated Requirement (mg/day)</th>
<th>Recommended Dietary Allowance (mg/day)</th>
<th>Upper Level Intake (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants 0 to 6 months</td>
<td>*</td>
<td>*</td>
<td>1,000</td>
</tr>
<tr>
<td>Infants 6 to 12 months</td>
<td>*</td>
<td>*</td>
<td>1,500</td>
</tr>
<tr>
<td>1–3 years old</td>
<td>500</td>
<td>700</td>
<td>2,500</td>
</tr>
<tr>
<td>4–8 years old</td>
<td>800</td>
<td>1,000</td>
<td>2,500</td>
</tr>
<tr>
<td>9–13 years old</td>
<td>1,100</td>
<td>1,300</td>
<td>3,000</td>
</tr>
<tr>
<td>14–18 years old</td>
<td>1,100</td>
<td>1,300</td>
<td>3,000</td>
</tr>
<tr>
<td>19–30 years old</td>
<td>800</td>
<td>1,000</td>
<td>2,500</td>
</tr>
<tr>
<td>31–50 years old</td>
<td>800</td>
<td>1,000</td>
<td>2,500</td>
</tr>
<tr>
<td>51–70 year-old male</td>
<td>800</td>
<td>1,000</td>
<td>2,000</td>
</tr>
<tr>
<td>51–70 year-old female</td>
<td>1,000</td>
<td>1,200</td>
<td>2,000</td>
</tr>
<tr>
<td>&gt;70 years old</td>
<td>1,000</td>
<td>1,200</td>
<td>2,000</td>
</tr>
</tbody>
</table>

* For infants, adequate intake is 200 mg/day for 0 to 6 months of age and 260 mg/day for 6 to 12 months of age.

Available Forms and Recommended Dosing

• Adequate calcium intake is fundamental to all prevention and treatment programs for postmenopausal osteoporosis.

• To minimize gastrointestinal side effects and enhance absorption, patients should take calcium in conjunction with food.
Calcium Replacement

• Don’t exceed to more than 500mg elemental ca per Doses

• At least 6 hours between doses

• Change the diet if patients compliance is acceptable

• Bedtime is better for single doses?
## Generations of Bisphosphononates

<table>
<thead>
<tr>
<th>Generation</th>
<th>Chemical modification</th>
<th>Examples</th>
<th>Antiresorptive potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>Short alkyl or halide side chain</td>
<td>Etidronate, Clodronate</td>
<td>1, 10</td>
</tr>
<tr>
<td>Second</td>
<td>Cyclic side chain Amino-terminal group</td>
<td>Tiludronate, Pamidronate, Alendronate</td>
<td>10, 100, 100-1000</td>
</tr>
<tr>
<td>Third</td>
<td>Cyclic side chain</td>
<td>Risedronate, Ibandronate, Zoledronate</td>
<td>1000-10,000, 1000-10,000, 10,000+</td>
</tr>
</tbody>
</table>

Effects of alendronate on the risk of fragility fractures-FIT1

Adapted from Black DM et al  *Lancet* 348:1535-41, 1996
Pharmacology

- Stable analogues of pyrophosphate
- The oral bioavailability is low, between 1% and 3%, and is impaired by food, calcium, iron, coffee, tea, and orange juice.
- These drugs are quickly cleared from plasma, with about 50% deposited in bone and 50% excreted in urine.

Pharmacology

• Alendronate should be taken
  – with approximately 8 ounces of water on an empty stomach,
  – at least 1/2 hour before the first food, beverage, or orally administered medication of the day
  – patient should remain upright (seated or standing)

• Ingesting it within 2 hours after a meal, may substantially reduce or abolish the absorption of alendronate.

Contraindications: PO forms

- Hypersensitivity
- Hypocalcemia
- Inability to remain upright for at least 1/2 hour
- Esophageal abnormalities (achalasia or stricture).
- Active upper gastrointestinal disease.
- Alendronate should be used with caution in patients who have more severe renal insufficiency. (creatinine clearance less than 30 mL/min).
Calcitonin: mechanisms

- Diminution in the number of osteoclasts.
- Change in their appearance (shrinkage of cells, loss of ruffled border).
- Shortening of life span
Nasal Calcitonin: Efficacy at the Spine and Hip

(PROOF: 5-Year study of 1255 women, average age 68, with 1-5 prevalent vertebral fractures)

N = 1255 osteoporotic postmenopausal women.

NS = Not significant.

Calcitonin

- 50 to 100 units daily (sc. im)
- 200 units (one puff/day intranasally delivers 30 doses)
- Intranasal in alternating nostrils
- Keep medication at room temperature

• 15% of nasal salmon calcitonin users will experience nasal irritation (rhinitis) over a 5-year period.

Clinical Practice Guidelines For The Diagnosis And Management Of Osteoporosis In Canada
CMAJ 2002;167(10 Suppl):s1-s34 Revised On Aug. 26, 2004
Clinical Outcomes of the WHI trial (Estr.+Progestin)

16700 women with 5.2 yrs follow-up

% difference vs. placebo

- CHD: +29%
- Stroke: +41%
- VTD: +112%
- Breast Cancer: +26%
- Colorectal Cancer: -37%

NNH

1429 1250 555 1250 1666

WHI, JAMA 2002
Raloxifene as a SERM

Dimensional Model of Raloxifene -3

**Basic Side Chain**
- Estrogen antagonist
  - Uterus
  - Breast

**Benzothiophene moiety**
- Estrogen agonist
  - Bone
  - Serum lipids
  - Vascular endothelium
  - Central nervous system

Structural features adapted from Brzozowski AM et al., Nature 1997;389:753-58
Effect of Raloxifene on Incident Vertebral Fractures in Postmenopausal Women With Osteoporosis

3-year clinical trial of 7705 women with PMO age 31-80
Multiple Outcomes of Raloxifene Evaluation (MORE)


* RR=0.5, 95% CI=0.3-0.7. ‡RR, 0.7, 95% CI=0.6-0.9.
†RR=0.6, 95% CI=0.4-0.9. §RR, 0.5, 95% CI=0.4-0.6.
**Raloxifene Use for The Heart Trial Design**

- **Participant**: Randomly assigned 10,101 postmenopausal women (mean age, 67.5 years) with CHD or multiple risk factors for CHD.

- **Intervention**: 60 mg of raloxifene daily or placebo and Fo: 5.6 years.

- **Primary outcomes**: coronary events (i.e., death from coronary causes, myocardial infarction, or hospitalization for an acute coronary syndrome) and invasive breast cancer.

Cumulative Incidence of the Primary Outcomes of Coronary Events
(Death from Coronary Causes, Nonfatal Myocardial Infarction, or Hospitalization for an Acute Coronary Syndrome Other Than Myocardial Infarction)

raloxifene and breast cancer

Cumulative Incidence of Invasive Breast Cancer

Pharmacology

• **Excretion:** Primarily feces; urine (0.2%)

• **Take this medicine at a similar time of day.**

• **Take this medicine with or without food.**
Adverse Reactions

- **>10%:**
  - Cardiovascular: Hot flashes
  - Neuromuscular & skeletal: Arthralgia

- **1-10%:**
  - Peripheral edema, and leg cramps, DVT (similar to HRT)
Contraindications

• Contraindications
• Capability of pregnant
• who have had venous thromboembolic disease
• Warnings / Precautions
• Like HRT
Osteoblast apoptosis ↓ → Lining cell differentiation ↑ → Osteoblast number ↑ → Bone formation ↑ → Bone mass ↑ → Bone strength ↑

Osteoclast ↑ → Bone resorption ↑ → Serum calcium ↑

Once daily

Continuous

RankL ↑ → OPG ↓ → Osteoclast ↑ → Bone resorption ↑ → Serum calcium ↑
Effect of PTH on Fracture Risk in Postmenopausal Women

clinical trial of 1637 women with PMO and >= 1 vertebral fractures treated an average 18 months

RR=0.35, 95% CI=0.22-0.55. †RR=0.47, 95% CI=0.25-0.88.
†RR=0.31, 95% CI=0.19-0.50. §RR=0.46, 95% CI=0.25-0.86.

Clinical Pharmacology

- **Injection, solution:** 250 mcg/mL (3 mL) [prefilled syringe, delivers teriparatide 20 mcg/dose]
- Administer by SC injection into the thigh or abdominal wall.
- No dosage adjustment required.
- Bioavailability and half-life increase with Clcr <30 mL/minute.
After exclusion of secondary causes, treat postmenopausal women and men age 50 and older who have:

- **Osteoporosis**
  - **Clinical diagnosis:** Hip or spine fracture
  - **DXA diagnosis:**
    - T-score -2.5 or below in the spine or hip

- **T-scores between -1.0 and -2.5 and**

- **10-year risk of fractures:**
  - ≥3% for hip fracture
  - or
  - ≥20% for a major osteoporotic fracture
Calculation Tool

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

**Questionnaire:**

1. Age (between 40-90 years) or Date of birth
   - Age: 70
   - Date of birth: Y: [ ] M: [ ] D: [ ]

2. Sex
   - Male [ ] Female [ ]

3. Weight (kg)
   - 49.9

4. Height (cm)
   - 165.1

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)
    - Hologic [ ] 0.605
    - T-score: -2.1

**BMI 18.3**

The ten year probability of fracture (%)

- Major osteoporotic [ ] 17
- Hip fracture [ ] 4.9
Table 4: Average 10-year probability (%) of an osteoporotic fracture* by sex, age and BMD expressed as T-score (adapted from Kanis et al.*

<table>
<thead>
<tr>
<th>Age; years</th>
<th>Overall average probability</th>
<th>1</th>
<th>0</th>
<th>-1</th>
<th>-2</th>
<th>Below -2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>3.3</td>
<td>1.8</td>
<td>2.7</td>
<td>4.2</td>
<td>6.3</td>
<td>9.2</td>
</tr>
<tr>
<td>55</td>
<td>3.9</td>
<td>1.9</td>
<td>3.0</td>
<td>4.6</td>
<td>7.0</td>
<td>10.4</td>
</tr>
<tr>
<td>60</td>
<td>4.9</td>
<td>2.5</td>
<td>3.6</td>
<td>5.4</td>
<td>7.9</td>
<td>11.6</td>
</tr>
<tr>
<td>65</td>
<td>5.9</td>
<td>3.0</td>
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<td>13.0</td>
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<tr>
<td>70</td>
<td>7.6</td>
<td>3.4</td>
<td>5.1</td>
<td>7.4</td>
<td>10.9</td>
<td>16.2</td>
</tr>
<tr>
<td>75</td>
<td>10.4</td>
<td>4.1</td>
<td>6.3</td>
<td>9.6</td>
<td>14.4</td>
<td>21.5</td>
</tr>
<tr>
<td>80</td>
<td>13.1</td>
<td>5.3</td>
<td>7.7</td>
<td>11.1</td>
<td>15.8</td>
<td>23.2</td>
</tr>
<tr>
<td>85</td>
<td>13.1</td>
<td>5.3</td>
<td>7.5</td>
<td>10.4</td>
<td>14.3</td>
<td>21.4</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>6.0</td>
<td>2.4</td>
<td>3.8</td>
<td>5.9</td>
<td>9.2</td>
<td>13.9</td>
</tr>
<tr>
<td>55</td>
<td>7.8</td>
<td>2.6</td>
<td>4.1</td>
<td>6.7</td>
<td>10.7</td>
<td>16.8</td>
</tr>
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<td>12.0</td>
<td>19.1</td>
<td>33.1</td>
</tr>
</tbody>
</table>

*Wrist, hip, proximal humerus, vertebra.
When Clinical Judgment Is Needed

FRAX® may underestimate fracture risk:

- Some risk factors (glucocorticoids, smoking, alcohol, fractures) are dose dependent, but FRAX® can’t consider dose
- Some risk factors that increase the risk of fractures independently of their effect on BMD are not included in FRAX®:
  - Falls
  - Frailty
  - Some diseases and medications (immobilization, diabetes, anticonvulsants, SSRIs, PPIs, TZDs)

Therapeutic Algorithm

History & PH.EX & Evaluations

Estimation of Ca intake

- 1000-1500 mg total Ca
- Low doses bedtime
- <=500 mg/dose
- With meal

800 IU daily or
50,000 IU/W FOR 8 w PO then
50,000/1-2 mo PO
or 100,000 IU of vitamin D3 once every 3 months
...

Ca
VD
Bone Mineral Density and Fracture Risk after Withdrawal of Teriparatide

Lindsay R. et al, Arch Int Med. 2004; 164:2024
Persistence of Treatment Effect with Continued Use

- Strong and consistent evidence
  - Antiresorptive effect assessed by BMD or histomorphometry persists for at least 7 years for RIS and 10 years for ALN
- No evidence that patients become refractory to treatment
- Fracture risk reduction, direct evidence:
  - ALN 4 years
  - IBN 3 years
  - RIS 5 years
  - ZLN 3 years
Bisphosphonate Holidays

- In patients at high risk for fractures, continued treatment seems reasonable. Consider a drug holiday of 1 to 2 years after 10 years of treatment.

- For lower risk patients, consider a “drug holiday” after 4 to 5 years of stability.

- Follow BMD and bone turnover markers during a drug holiday period, and reinitiate therapy if bone density declines or markers increase.

Follow-up

- Assessment of adherence to recommended program
- Assessment of stature and skeletal integrity (radiographic assessment if height loss $>2$ cm in a year or historical height loss $>4$ cm)
- Periodic assessment of BMD

(AACE recommends annual reassessment)
## Precision Error

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<thead>
<tr>
<th>Location</th>
<th>Short Term (PE)</th>
<th>Long Term (LSC)</th>
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<td>&gt; 2.8%</td>
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<tr>
<td>FEMURE</td>
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<tr>
<td>RADIUS</td>
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Precision is center specific.
How Should Clinicians Respond to Follow-up BMD Results?

BMD CHANGES

- Same (Within LSC)
  - NO CHANGE
  - EVALUATE
Referral to a specialist center

- Male patients
- Patients on long-term steroids
- Patients with disproportionately low scores $Z <-2, T <-3$
- Patients with endocrine disease e.g. hyperparathyroidism, hypogonadism, hypercortisolism, hyperthyroidism
- Is a candidate for combination therapy
- Is a candidate for teriparatide therapy (parathyroid hormone)
- Patients with pathological fracture and borderline BMD
- No responses (loss of BMD or fracture)
- Drug intolerance or complications

AACE, Endocrine Practice 2003
Conclusion

Multifactorial assessment

- Falls history
- Gait, balance and mobility
- Medication review
- Functional ability/ fear of falling
- Neurological examination
- Urinary continence
- Osteoporosis risk
- Visual impairment
- Cognitive impairment
- Cardiovascular examination
- Medication review