Osteoporosis and Falls in LTC

Dr. John Puxty
Major source was:

2010 Clinical Practice Guidelines for the Diagnosis and Management of Osteoporosis in Canada
Definition of Osteoporosis

A skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture.
Fragility Fracture: Definition

A fracture occurring spontaneously or following minor trauma such as a fall from standing height or less\textsuperscript{1,2}

- Excluding craniofacial, hand, ankle and foot fractures

The Majority of Fractures in Canadian Women > Age 50 Are Fragility Fractures

Overall: 81%

<table>
<thead>
<tr>
<th>Age Group</th>
<th>% of All Fractures that are Fragility Fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>75.7%</td>
</tr>
<tr>
<td>60-69</td>
<td>80%</td>
</tr>
<tr>
<td>70-79</td>
<td>85%</td>
</tr>
<tr>
<td>80+</td>
<td>91.8%</td>
</tr>
</tbody>
</table>

Causes of Osteoporosis

- Age
- Life Style
- Estrogen deficiency
- Calcium deficiency & secondary hyperparathyroidism
- Androgen deficiency
- Changes in bone formation
- Secondary causes and medications
Secondary Causes of Osteoporosis

- Endocrine Disorders
- Marrow Disorders
- Organ Transplantation
- Gastrointestinal Disease
- Nutritional Disorders
- Genetic Disorders

- Drugs
  - Glucocorticoids
  - Excess thyroid supplement
  - Anticonvulsants
  - Methotrexate
  - Cyclosporine
  - Heparin
Epidemiology Osteoporosis (General)

- Prevalence in Canadian women aged 50 years and over was 12.1% at the lumbar spine and 7.9% at the femoral neck, with a combined prevalence of 15.8%. *(Canadian Multicentre Osteoporosis Study).*
- The prevalence of Osteoporosis increases with age from approximately 6% at 50 years of age to over 50% above 80 years of age.
- Expected to increase by about 40% by 2020.
- Estimated Direct costs in 2001 = $ 11.6 - 17.1 billion annually, or $6 - $40 million every single day in Canada.
- Lifetime prevalence of VCF in Caucasians:
  - 15% in **women**
  - 5 - 9% in **men**
- Mortality increased 2 - 3 fold in women and women after all types of osteoporotic fractures.
Prior Fracture Increase Risk for Subsequent Fracture

<table>
<thead>
<tr>
<th>Site of prior fracture</th>
<th>Risk of subsequent fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hip</td>
</tr>
<tr>
<td>Hip</td>
<td>2.3</td>
</tr>
<tr>
<td>Spine</td>
<td>2.3</td>
</tr>
<tr>
<td>Forearm</td>
<td>1.9</td>
</tr>
<tr>
<td>Minor Fracture</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Falls Facts - Hip Fractures (General)

- There are over 4.5 million seniors in Canada.
- This means for this year:
  - There will be 25,500 hip #s (hip fracture rate of 1.7%)
  - Only 8415 (1/3) will regain their previous level of function
  - 1785 (7%) will die within 30 days of hospitalization
  - 5100 (20%) will die within 1 year
  - $27,000 per person average cost to health care system
  - $6.9 billion total cost to healthcare system
Undertreatment of Osteoporosis Post Fracture in Women

A fracture is to osteoporosis what a heart attack is to cardiovascular disease. BUT... The treatment gap is far wider post fracture than post MI.\(^1\,^4\)

Currently, low BMD is the primary trigger for initiation of therapy. . .

**HOWEVER,** Most fragility fractures occur in those with a BMD in the non-osteoporotic range

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Post-fracture Care Gap: Comparison with Heart Attack

- Anti-osteoporosis medication post fracture: ~15%
- Beta-blockers post heart attack: ~80%

Therapeutic Care Gap: Most Men Do Not Receive Treatment for Osteoporosis after Fracture

Male Osteoporosis: Morbidity and Mortality

As compared to women, while lifetime fracture risk may be less:

- Men have higher rates of morbidity and mortality due to fractures.
- Men are twice as likely to die in hospital after a hip fracture.
- Men have a higher mortality rate than women one year after a hip fracture.

Osteoporosis and Falls Facts in LTC

→ 40% of all nursing home admissions are related to falls.
→ 65-85% prevalence of osteoporosis estimated
→ Fractured hip incidence is twice that of age-matched controls and prognosis worse
→ Osteoporosis often undiagnosed or undertreated
Survey of LTC in Ontario and Manitoba 2005-06 (Giangregorio LM et al)

- Bisphosphonate use was reported in 38% residents
- Calcium and Vit D supplementation were reported in 27% (half not optimal)
- 10.3% residents were on a bisphosphonate but were not taking Vit D or Calcium
- Variables negatively associated with osteoporosis therapy: ≥6 comorbidities, wheelchair use, cognitive impairment, depression, swallowing difficulties
Key Changes from 2002\(^1\) to 2010\(^2\): Fracture Risk Assessment

- 10-year fracture risk prediction tools incorporate clinical risk factors beyond BMD for improved clinical decision making:
  - CAROC: Joint initiative of the Canadian Association of Radiologists and Osteoporosis Canada\(^3\) OR
  - FRAX: Fracture Risk Assessment Tool developed by the World Health Organization\(^4\)

- Increased focus on the clinical impact of fragility fractures

- Increased focus on the care gap that exists in the identification and treatment of high-risk individuals

Key Changes from 2002\textsuperscript{1} to 2010\textsuperscript{2}: Fracture Risk Assessment

- Higher daily vitamin D supplementation (D3)\textsuperscript{3}
  - 400 – 1000 IU for individuals < 50 years
  - 800 – 2000 IU for individuals > 50 years
- Lower daily calcium intake (from all sources): 1200 mg
- Updated evidence-based approach to therapies
# Recommendations for Clinical Assessment

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Recommended Elements of Clinical Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History</strong></td>
<td>Identify risk factors for low bone-mineral density (BMD), future fractures, and falls</td>
</tr>
<tr>
<td></td>
<td>- Prior fragility fractures</td>
</tr>
<tr>
<td></td>
<td>- Parental hip fracture</td>
</tr>
<tr>
<td></td>
<td>- Glucocorticoid use</td>
</tr>
<tr>
<td></td>
<td>- Current smoking</td>
</tr>
<tr>
<td></td>
<td>- High alcohol intake (&gt; 3 units per day)</td>
</tr>
<tr>
<td></td>
<td>- Rheumatoid arthritis</td>
</tr>
<tr>
<td></td>
<td>- Inquire about falls in the previous 12 months</td>
</tr>
<tr>
<td></td>
<td>- Inquire about gait and balance</td>
</tr>
</tbody>
</table>
## Recommendations for Clinical Assessment

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Recommended Elements of Clinical Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical examination</strong></td>
<td>Measure <strong>weight</strong> (weight loss of $\geq 10%$ since age 25 is significant)</td>
</tr>
<tr>
<td></td>
<td>Measure <strong>height</strong> annually (prospective loss $&gt; 2\text{cm}$)</td>
</tr>
<tr>
<td></td>
<td>(historical height loss $&gt; 6\text{ cm}$)</td>
</tr>
<tr>
<td></td>
<td>Measure <strong>rib to pelvis distance</strong> $\leq 2$ fingers' breadth</td>
</tr>
<tr>
<td></td>
<td>Measure <strong>occiput-to-wall distance</strong> (for kyphosis) $&gt; 5\text{cm}$</td>
</tr>
<tr>
<td></td>
<td>Assess fall risk by using Get-Up-and-Go Test (ability to get out of chair without using arms, walk several steps and return)</td>
</tr>
</tbody>
</table>
Importance of Height Loss

- Increased risk of vertebral fracture
  - Historical height loss (> 6 cm)\(^1,2\)
  - Measured height loss (< 2 cm)\(^3-5\)
- Significant height loss should be investigated by a lateral thoracic and lumbar spine X-ray

Appropriate Measurement of Height

- Use a wall-mounted stadiometer
- Instructions for subjects:
  - Shoes off
  - Heels, buttocks, and back against the upright board
  - Face directly forward, head stable
- Record height after exhalation

# Additional Tests for Clinical Identification of Vertebral Fracture

<table>
<thead>
<tr>
<th>Test</th>
<th>Rationale</th>
<th>Method</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rib-pelvis distance(^1)</td>
<td>To identify lumbar fractures</td>
<td>Measure the distance between the costal margin and the pelvic rim on the mid-axillary line</td>
<td>$&lt; 2$ fingerbreadths is associated with vertebral fractures</td>
</tr>
<tr>
<td>Occiput-to-wall distance(^2,3)</td>
<td>To help identify thoracic spine fractures</td>
<td>Stand straight with heels and back against the wall</td>
<td>$&gt; 5$ cm raises suspicion of vertebral fracture</td>
</tr>
</tbody>
</table>

Recommendations for Clinical Assessment

- Recognition and reporting of vertebral fractures is of paramount importance.
- Several different types of radiologic investigations can be ordered, depending on the clinical needs.
- Vertebral fractures are under reported in emergency department radiology reports.
# Recommendations for Clinical Assessment

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>A fragility fracture is a major risk factor for predicting another fracture</td>
<td>Level 1</td>
</tr>
<tr>
<td>Fractures of the hip and of the vertebra are associated with significant morbidity and mortality</td>
<td>Level 1</td>
</tr>
<tr>
<td>There is an important osteoporosis care gap in Canada</td>
<td>Level 1</td>
</tr>
<tr>
<td>A history of a fall in the past year is predictive of future falls</td>
<td>Level 1</td>
</tr>
</tbody>
</table>
**Recommendations for Clinical Assessment**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with osteoporosis need only limited laboratory investigations performed: complete blood count, calcium corrected for albumin, creatinine, alkaline phosphatase, and thyroid stimulating hormone</td>
<td>D</td>
</tr>
<tr>
<td>Measurement of serum 25-OH-D is recommended among individuals with the following conditions: treatment with pharmacologic therapy for osteoporosis, recurrent fractures, bone loss despite osteoporosis treatment, or those with co-morbid conditions that affect vitamin D absorption or action</td>
<td>D</td>
</tr>
<tr>
<td>Serum protein electrophoresis should be performed in individuals with vertebral fractures</td>
<td>D</td>
</tr>
<tr>
<td>In selected patients, based on clinical assessment, additional biochemical testing should be considered to rule out secondary causes of osteoporosis</td>
<td>D</td>
</tr>
</tbody>
</table>
Indications for BMD Testing in Older Adults (Age > 50 Years)

- All women and men age ≥ 65
- Postmenopausal women, and men aged 50 – 64 with clinical risk factors for fracture:
  - Fragility fracture after age 40
  - Prolonged glucocorticoid use†
  - Other high-risk medication use*
  - Parental hip fracture
  - Vertebral fracture or osteopenia identified on X-ray
  - Current smoking
  - High alcohol intake
  - Low body weight or major weight loss
  - Rheumatoid arthritis
  - Other disorders strongly associated with osteoporosis

† At least three months cumulative therapy in the previous year at a prednisone-equivalent dose ≥ 7.5 mg daily;
* e.g. aromatase inhibitors, androgen deprivation therapy.
## BMD Reporting Categories

<table>
<thead>
<tr>
<th>Age</th>
<th>Category</th>
<th>Criteria*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50 years</td>
<td>Below expected range for age</td>
<td>Z-score ≤ -2.0</td>
</tr>
<tr>
<td></td>
<td>Within expected range for age</td>
<td>Z-score &gt; -2.0</td>
</tr>
<tr>
<td>≥ 50 years</td>
<td>Severe (established) osteoporosis</td>
<td>T-score ≤ -2.5 with fragility fracture</td>
</tr>
<tr>
<td></td>
<td>Osteoporosis</td>
<td>T-score ≤ -2.5</td>
</tr>
<tr>
<td></td>
<td>Low bone mass</td>
<td>T-score -1.0 to -2.5</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>T-score ≥ -1.0</td>
</tr>
</tbody>
</table>
Absolute 10-year Fracture-Risk Tools

Tools validated in Canada (choice based on personal preference and convenience)

- CAROC: Joint initiative of the Canadian Association of Radiologists and Osteoporosis Canada¹
- FRAX: Fracture Risk Assessment Tool developed by the World Health Organization²

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10-year Risk Assessment for Women (CAROC Basal Risk)
10-year Risk Assessment for Men (CAROC Basal Risk)

![Graph showing risk assessment for men with the Y-axis representing femoral neck T-score and the X-axis representing age. The graph categorizes risk into Low Risk (<10%), Moderate Risk, and High Risk (>20%).]

FRAX Clinical Risk Factors

- Parental hip fracture
- Prior fracture
- Glucocorticoid use
- Current smoking
- High alcohol intake
- Rheumatoid arthritis
FRAX Tool: On-line Calculator

Calculation Tool

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

Country: Canada

Questionnaire:
1. Age (between 40-90 years) or Date of birth
   Age: 59
   Date of birth: Y: _ _ _ M: _ _ D: _ _
2. Sex
   Male
3. Weight (kg) 55.5
4. Height (cm) 154
5. Previous fracture
   No
6. Parent fractured hip
   No
7. Current smoking
   No
8. Glucocorticoids
   No
9. Rheumatoid arthritis
   No
10. Secondary osteoporosis
    No
11. Alcohol 3 or more units per day
    No
12. Femoral neck BMD (g/cm²)
    T-Score: -2.0

BMI 23.4
The ten year probability of fracture (%)
with BMD
- Major osteoporotic 7.5
- Hip fracture 1.0

www.shef.ac.uk/FRAX.
Modalities Used to Prevent Fracture

➡ Lifestyle modifications
- Vitamin D
- Calcium
- Exercise
- Falls prevention

➡ Pharmacologic therapy
- Bisphosphonates
- Other anti-resorptives
  - Calcitonin
  - Denosumab
  - Hormone therapy
  - Raloxifene
- Parathyroid hormone
- Combination therapy
## Recommended Vitamin D Supplementation

<table>
<thead>
<tr>
<th>Group</th>
<th>Recommended Vitamin D Intake (D3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults &lt;50 without osteoporosis or conditions affecting vitamin D absorption</td>
<td>400 – 1000 IU daily (10 mcg to 25 mcg daily)</td>
</tr>
<tr>
<td>Adults &gt; 50 or high risk for adverse outcomes from vitamin D insufficiency (e.g., recurrent fractures or osteoporosis and comorbid conditions that affect vitamin D absorption)</td>
<td>800 – 2000 IU daily (20 mcg to 50 mcg daily)</td>
</tr>
</tbody>
</table>

Recommended Calcium Intake

- From diet and supplements combined: **1200 mg daily**
- Evidence shows a benefit of calcium on reduction of fracture risk\(^1\)
- Concerns about serious adverse effects with high-dose supplementation\(^2-4\)
  - Renal calculi in older women
  - Cardiovascular events in older women
  - Prostate cancer in older men

## Summary Statements for Calcium & Vitamin D

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D3 with calcium supplementation increases bone density in postmenopausal women and men over age 50 and reduces the risk of fractures</td>
<td>Level 1</td>
</tr>
<tr>
<td>Vitamin D3 at daily doses of 800 IU (20 mcg) with calcium (1000 mg) reduces the risk of hip and non-vertebral fractures in elderly populations in institutions</td>
<td>Level 1</td>
</tr>
<tr>
<td>The evidence in community-dwelling individuals is less strong</td>
<td>Level 2</td>
</tr>
<tr>
<td>There is evidence that daily 800 IU (20 mcg) vitamin D3 reduces fall risk, particularly in trials that adequately ascertained falls</td>
<td>Level 2</td>
</tr>
<tr>
<td>A daily intake of 1000 IU vitamin D3 (25 mcg)—a commonly available safe dose—will raise serum 25-OH-D level on average by 15 – 25 nmol/L</td>
<td>Level 2</td>
</tr>
</tbody>
</table>
Nonpharmacologic Interventions Associated with Reduction in Falls

- Exercise-focused interventions for community-dwelling older people
- Tai chi, gait, and balance training
- Home safety assessment (only effective in those at high risk for falls)
- Cataract removal

Benefits of Exercise: Fractures and Bone Health

- Programs > 1 year including aerobic exercises and strength training have demonstrated positive effects on BMD and thoracic kyphosis but have limited evidence for fracture reduction\(^1\)

- Moderate to vigorous exercise has demonstrated an ability to reduce hip fracture risk\(^2\)

Bone Health Protection Strategies

Promoting Exercises:

- Resistance exercises improve mobility, balance and strength.
- Gait training, stairs, muscle strengthening, coordination and postural training, parallel bar exercise, walking, Tai Chi
- Wheelchair dependent older adults can use free weights.
Promoting the use of Hip Protectors

Hip protectors are padded undergarments designed to decrease the impact of a fall on the hip by either absorbing or shunting energy away from the hip, thus decreasing the risk of hip fracture.

Who should wear Hip Protectors?

Most promising studies indicate that for high risk LTC resident with a history of hip fracture, using hard-shelled hip protectors seems to reduce the number of fractures.

Studies looking at the community are not as successful, mainly due to compliance with wearing them.

(Brown et al, 2008; Sawka et al. 2007; Sawka et al., 2005)
## Summary Statement for Other Nonpharmacologic Therapies

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight bearing, balance and strengthening exercises can improve outcomes in individuals with osteoporosis</td>
<td>Level 2</td>
</tr>
<tr>
<td>Exercise-focused interventions improve balance and reduce falls in community-dwelling older people</td>
<td>Level 2</td>
</tr>
<tr>
<td>Hip protectors may reduce the risk of hip fractures in long-term care residents; however adherence with their use may pose a challenge for the older adult</td>
<td>Level 2</td>
</tr>
</tbody>
</table>
Medications Indicated for Osteoporosis in Canada

- Bisphosphonates—oral and IV
- Calcitonin
- Denosumab (RANK ligand inhibitor)
- Hormone therapy
- Raloxifene (SERM)
- Teriparatide (PTH analogue)
<table>
<thead>
<tr>
<th>Statement</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate prevents vertebral, non-vertebral, hip, and wrist fractures in post-menopausal women</td>
<td>Level 1</td>
</tr>
<tr>
<td>Cyclical etidronate prevents vertebral fractures, but has not demonstrated risk reductions for other non-vertebral fracture types</td>
<td>Level 1</td>
</tr>
<tr>
<td>Risedronate prevents vertebral, non-vertebral, and hip fractures in post-menopausal women</td>
<td>Level 1</td>
</tr>
</tbody>
</table>
### Summary Statements for Pharmacotherapy (Cont'd)

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoledronic acid prevents vertebral, non-vertebral, hip fractures in men and women</td>
<td>Level 1</td>
</tr>
<tr>
<td>Hormone therapy prevents vertebral, non-vertebral, and hip fractures, but is recommended for women with moderate to severe vasomotor symptoms</td>
<td>Level 1</td>
</tr>
<tr>
<td>Raloxifene and calcitonin reduce vertebral fractures, but have not demonstrated risk reductions for non-vertebral fractures</td>
<td>Level 1</td>
</tr>
</tbody>
</table>
### Summary Statements for Pharmacotherapy (Cont'd)

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teriparatide reduces vertebral and non-vertebral fractures</td>
<td>Level 1</td>
</tr>
<tr>
<td>Denosumab reduces vertebral, non-vertebral, and hip fractures</td>
<td>Level 1</td>
</tr>
</tbody>
</table>
# Oral Bisphosphonates: Summary

<table>
<thead>
<tr>
<th>Drug (Brand name)</th>
<th>Dosing Schedules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate (Fosamax®, Fosavance®)</td>
<td>10 mg daily 70 mg weekly</td>
</tr>
<tr>
<td>Risedronate (Actonel®)</td>
<td>5 mg daily 35 mg weekly 150 mg monthly</td>
</tr>
<tr>
<td>Etidronate (Didrocal®)</td>
<td>Cyclical therapy of daily 200 mg for 14 days followed by calcium supplements for 10 weeks</td>
</tr>
<tr>
<td>Zoledronic Acid (Aclasta®)</td>
<td>5 mg intravenously once yearly</td>
</tr>
</tbody>
</table>
## Other Medications: Summary

<table>
<thead>
<tr>
<th>Drug (Brand name)</th>
<th>Dosing Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcitonin (Miacalcin®)</td>
<td>200 IU intranasally daily</td>
</tr>
<tr>
<td>Denosumab (Prolia®)</td>
<td>60 mg subcutaneous injection every six months</td>
</tr>
<tr>
<td>Raloxifene (Evista®)</td>
<td>60 mg daily</td>
</tr>
<tr>
<td>Teriparatide (Forteo®)</td>
<td>20 μg subcutaneously daily</td>
</tr>
</tbody>
</table>
## Recommendations for High-risk Individuals

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>For menopausal women requiring osteoporosis treatment, alendronate, denosumab, risedronate, and zoledronic acid can be used as first-line therapies for prevention of hip, non-vertebral, and vertebral fractures</td>
<td>A</td>
</tr>
<tr>
<td>For menopausal women requiring osteoporosis treatment, teriparatide can be used as a first-line therapy for prevention of non-vertebral and vertebral fractures</td>
<td>A</td>
</tr>
<tr>
<td>For menopausal women requiring osteoporosis treatment, raloxifene can be used as a first-line therapy for prevention of vertebral fractures</td>
<td>A</td>
</tr>
</tbody>
</table>
## Recommendations for High-risk Individuals (Cont'd)

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>For menopausal women requiring osteoporosis treatment and who require treatment for vasomotor symptoms, hormone therapy can be used as a first-line therapy for prevention of hip, non-vertebral, and vertebral fractures</td>
<td>A</td>
</tr>
<tr>
<td>Clinicians should avoid prescribing more than one anti-resorptive agent concurrently for fracture reduction</td>
<td>A</td>
</tr>
<tr>
<td>For menopausal women intolerant of first-line therapies, calcitonin or etidronate can be considered for prevention of vertebral fractures</td>
<td>B</td>
</tr>
<tr>
<td>For men requiring osteoporosis treatment, alendronate, risedronate, and zoledronic acid can be used as first-line therapies for prevention of fractures</td>
<td>D</td>
</tr>
</tbody>
</table>
**Recommendation for Duration of Therapy**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals at high risk for fracture should continue osteoporosis therapy without a drug holiday</td>
<td>A</td>
</tr>
</tbody>
</table>

- Evidence supporting recommendations for duration of treatment is limited
- Data for the above recommendation come from the FLEX study (long-term alendronate treatment)\(^1\) and the risedronate discontinuation study\(^2\)

### Summary Statements for Special Groups

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporosis therapies including alendronate, risedronate, and teriparatide reduce the risk of vertebral fractures and maintain BMD in those prescribed glucocorticoids for 3 months or longer</td>
<td>Level 1</td>
</tr>
<tr>
<td>Etidronate, zoledronic acid, and calcitonin maintain BMD in those prescribed glucocorticoids for 3 months or longer</td>
<td>Level 2</td>
</tr>
<tr>
<td>Bisphosphonates and denosumab maintain BMD in women prescribed aromatase inhibitors and men prescribed androgen-deprivation therapy</td>
<td>Level 1</td>
</tr>
</tbody>
</table>
## Summary Statements on Treatment Initiation

<table>
<thead>
<tr>
<th>Statement</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Multiple fractures confer greater risk than a single fracture</td>
<td>Level 1</td>
</tr>
<tr>
<td>Prior fractures of the hip and vertebra carry greater risk than other fracture sites</td>
<td>Level 1</td>
</tr>
<tr>
<td>Pharmacologic intervention, when based on prior fragility fractures affecting the vertebra or hip, has shown fracture benefit in clinical trials</td>
<td>Level 1</td>
</tr>
</tbody>
</table>
### Summary Statements on Treatment Initiation (Cont'd)

<table>
<thead>
<tr>
<th>Statement</th>
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<tbody>
<tr>
<td>In patients who initiated glucocorticoids, fractures can occur quickly (within three to six months) with prednisone doses as low as 2.5 – 7.5 mg daily with a rapid decline in fracture risk toward baseline after cessation</td>
<td>Level 1</td>
</tr>
<tr>
<td>Rapid BMD loss in untreated individuals may be an independent risk for fracture</td>
<td>Level 2</td>
</tr>
</tbody>
</table>
# Recommendations on Treatment Initiation

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>In individuals over age 50, fragility fracture of the hip or vertebra, or more than one fragility fracture event, constitutes a high risk for future fracture and such individuals should be offered pharmacologic therapy</td>
<td>A</td>
</tr>
<tr>
<td>For those at moderate risk (10% – 20% probability for major osteoporotic fracture over 10 years), lateral radiographs or Vertebral Fracture Assessment (VFA) of the thoracolumbar spine is recommended for further risk stratification and in clinical decision-making regarding pharmacologic interventions</td>
<td>A</td>
</tr>
</tbody>
</table>
## Recommendations on Treatment Initiation (Cont'd)

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacologic therapy should be offered to patients at high absolute risk (&gt; 20% probability for major osteoporotic fracture over 10 years)</td>
<td>D</td>
</tr>
<tr>
<td>For those at moderate fracture risk, patient preference and additional clinical risk factors that are not already incorporated in the risk assessment system should be used to guide pharmacologic management decisions</td>
<td>D</td>
</tr>
</tbody>
</table>
**Recommendation for Adverse Events**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential benefits and risks of the prescribed agent should be discussed with each patient prior to initiating therapy to support informed decision-making</td>
<td>D</td>
</tr>
</tbody>
</table>
Considerations for Monitoring

➤ *Rationale for monitoring:* To identify individuals with continued BMD loss, despite appropriate osteoporosis treatment

➤ *Aspects of monitoring*
  - Serial BMD measurements
  - Assessment of adherence
  - Bone turnover markers (BTMs)?
When to Refer to Specialist Care: General

- Fracture on first-line therapy with optimal adherence
- Significant loss on follow-up BMD on first-line therapy with optimal adherence
- Intolerance of first- and second-line agents
When to Refer to Specialist Care: Special Populations

- Referrals to physicians with an interest or expertise in osteoporosis
  - Secondary causes of osteoporosis outside the comfort zone of the individual primary care physician
  - Patients with extremely low BMD
- Referrals to other specialists
  - Complex individuals with multiple comorbidities, such as those with frequent falling, Alzheimer’s disease, stroke, and Parkinson’s disease
Encourage basic bone health for all individuals over age 50, including regular active weight-bearing exercise, calcium (diet and supplementation) 1200 mg daily, vitamin D 800-2000 IU (20-50µg) daily and fall-prevention strategies.

**Age < 50 yr**
- Fragility fractures
- Use of high-risk medications
- Hypogonadism
- Malabsorption syndromes
- Chronic inflammatory conditions
- Primary hyperparathyroidism
- Other disorders strongly associated with rapid bone loss or fractures

**Age 50-64 yr**
- Fragility fracture after age 40
- Prolonged use of glucocorticoids or other high-risk medications
- Parental hip fracture
- Vertebral fracture or osteopenia identified on radiography
- High alcohol intake or current smoking
- Low body weight (< 60 kg) or major weight loss (> 10% of body weight at age 25)
- Other disorders strongly associated with osteoporosis

**Age ≥ 65 yr**
- All men and women

Initial BMD Testing
Integrated Approach, Continued

Evaluation of fracture risk

Low risk
(10-year fracture risk < 10%)

Moderate risk
(10-year fracture risk 10%-20%)

Lateral thoracolumbar radiography (T4-L4) or vertebral fracture assessment may aid in decision-making by identifying vertebral fractures

Factors warranting consideration of pharmacologic therapy...

High risk
(10-year fracture risk > 20% or prior fragility fracture of hip or spine or > 1 fragility fracture)

Good evidence of benefit from pharmacotherapy

Always consider patient preference

Unlikely to benefit from pharmacotherapy
Reassess in 5 yr
Integrated Approach, Continued

Initial BMD Testing

Assessment of fracture risk

Low risk
(10-year fracture risk < 10%)

Unlikely to benefit from pharmacotherapy
Reassess in 5 yr

Moderate risk
(10-year fracture risk 10%-20%)

Lateral thoracolumbar radiography (T4-L4) or vertebral fracture assessment may aid in decision-making by identifying vertebral fractures

Factors warranting consideration of pharmacologic therapy...

High risk
(10-year fracture risk > 20% or prior fragility fracture of hip or spine or > 1 fragility fracture)

Always consider patient preference

Good evidence of benefit from pharmacotherapy
**Moderate risk**
(10-year fracture risk 10%-20%)

Lateral thoracolumbar radiography (T4-L4) or vertebral fracture assessment may aid in decision-making by identifying vertebral fractures

*Factors warranting consideration of pharmacologic therapy:*
- Additional vertebral fracture(s) (by vertebral fracture assessment or lateral spine radiograph)
- Previous wrist fracture in individuals aged > 65 or those with T-score ≤ -2.5
- Lumbar spine T-score much lower than femoral neck T-score
- Rapid bone loss
- Men undergoing androgen-deprivation therapy for prostate cancer
- Women undergoing aromatase inhibitor therapy for breast cancer
- Long-term or repeated use of systemic glucocorticoids (oral or parenteral) not meeting conventional criteria for recent prolonged use
- Recurrent falls (≥ 2 in the past 12 mo)
- Other disorders strongly associated with osteoporosis, rapid bone loss or fractures

*Good evidence of benefit from pharmacotherapy*

Repeat BMD in 1-3 yr and reassess risk
Treatment Calcium

- Calcium can decrease bone turnover and diminish bone loss in certain conditions; it was found to diminish hip fractures when given with vitamin D in elderly institutionalized patients.

- Not sufficient by itself to have major impact on fracture risk, but necessary with other treatments.

- Recommend total intake of approximately 1500 mg elemental calcium daily in patients with Osteopenia or Osteoporosis.
Treatment Vitamin D

- 25-Hydroxy-Vitamin D levels are a good reflection of Vitamin D stores and should probably be measured in all patients with Osteopenia or Osteoporosis; optimal levels are probably > 80 nmol/L.

- Vitamin D3 1000 IU daily or Vitamin D2 50,000 IU once weekly safe for most patients.
One suggested approach to use of biphosphonates

- Treat all compression fracture patients with drug (alendronate or risedronate) known to reduce both vertebral and hip fractures

- If treat 25 people with VCF with biphosphonates ($ 500 per year) for 3 years then cost is $37,500 per hip fracture prevented
Treatment Bisphosphonates

- Compounds with marked affinity for solid-phase calcium phosphate, on the surface of which they bind strongly.
- Main effect is to inhibit resorption and reduce bone turnover, but at large doses can also inhibit mineralization.
- Newer agents much more potent at inhibiting resorption than etidronate.
- Alendronate & risedronate reduce vertebral & non-vertebral fractures by about 50% in osteoporotic patients.
- Poor oral bioavailability.
- Side effects: Esophageal irritation, diarrhea.
Bisphosphonates

Approved for Osteoporosis Therapy:

- Alendronate 10 mg PO OD or 70 mg once weekly
- Risedronate 5 mg PO OD or 35 mg once weekly
- Etidronate 400 mg PO OD x 2 weeks every three (3) months
- Zoledronic Acid 4 mg IV once p.a.
Treatment Hormone Replacement Therapy

- HRT reduces vertebral and non-vertebral fracture rates through inhibition of bone resorption.

- For years, use was justified on the basis of epidemiologic data showing CV benefit outweighing smaller risk of increased breast cancer and VTE.

- HERS II and WHI studies showed no CV benefit of combined CEE/MPA and possible harm.

- Women’s Health Initiative showed ↓ hip fracture risk w/ E+P and E alone; however, use only if benefits outweigh risks (CHD, stroke, breast cancer).
Treatment SERMs

- “Designer Estrogens”
- Bind to Estrogen receptors and produce variable tissue-specific Estrogen agonist vs. antagonist response.
- Potential to provide benefits of Estrogen replacement therapy without increased risks.
- Approved for Osteoporosis therapy:
  - Raloxifene 60 mg PO OD
SELECTIVE ESTROGEN RECEPTOR MODULATORS (SERMs) - Raloxifene

- Estrogen agonist activity on bones (antiresorptive) and lipids.
- Estrogen antagonist activity on breasts and uterus.
- MORE study: 30% to 50% reduction in *vertebral fractures* in osteoporotic women treated with Raloxifene for three years.
- Pooled data from Raloxifene trials indicate 54% reduction in new primary breast cancer.
- Probable benefits to brain and heart.
- Side effects: VTE, hot flashes.
Treatment Calcitonin

- Natural polypeptide that inhibits bone resorption.
- PROOF study showed 200 IU/d nasal salmon calcitonin reduced vertebral fractures by 33 - 36%.
- Useful in relieving pain of acute vertebral fractures.
- Approved for Osteoporosis therapy:
  - Nasal Salmon Calcitonin 200 IU=1 spray/d
  - IM/SC Salmon Calcitonin 100 IU/d
- Side effects: Flushing, nausea, allergic.
Treatment Parathyroid Hormone

- Intermittent parathyroid infusion (as opposed to continuous exposure) stimulates bone formation.
- Newly approved for severe Osteoporosis therapy:
  - Teriparatide 20 mcg SC OD x two (2) years
PTH - Teriparatide

- Biosynthetic human parathyroid hormone (1 - 34).
- NEJM study of PMP women with prior vertebral fracture showed 65% reduction in new vertebral fractures, and 35% reduction in new non-vertebral fractures.
- Combination therapy with HRT improves BMD compared to HRT alone, whereas concomitant alendronate delays or attenuates anabolic effect of teriparatide.
- Side effects: Dizziness, headaches, leg cramps, nausea, hyperCa; Osteosarcoma in rats given much higher life-long doses.
- Reserved for severe Osteoporosis because of high cost and undetermined long-term side effects.