Osteoporosis Management in Older Adults

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Professor of Medicine, University of Toronto
Disclosures

Relationship with Commercial Entities:
Honoraria from: Amgen, Eli Lilly, Merck
Grants to institution: Amgen, Eli Lilly

Relationship with Non-commercial Entities:
Chair, Osteoporosis Canada Scientific Advisory Council
Chair, Canadian Bone Strength Working Group
Director, CESHA at University of Toronto
Director, Osteoporosis Program at University Health Network / Mount Sinai Hospital
Learning Objectives

1) Understand the epidemiology and risks associated with osteoporosis

2) Appreciate the latest developments in the pharmacological management of osteoporosis

3) Be aware of some of the current controversies around the treatment of osteoporosis
EPIDEMIOLOGY AND RISKS OF OSTEOPOROSIS
Prevalence of Fractures in Canadian Women

Annual incidence of common diseases

- **Osteoporotic fractures**
  - Pelvis: 10,300
  - Hip: 30,000
  - Wrist: 32,700
  - Vertebral: 38,900
  - Other: 41,500
  - Total: 153,400

- **Heart Attack**: 49,220

- **Stroke**: 22,700

- **Breast Cancer**:

Osteoporosis and Fractures
Missing the Bridge?

Angela M. Cheung, MD, PhD
Allan S. Detsky, MD, PhD

On August 1, 2007, a bridge on Interstate 35W collapsed during rush-hour traffic near Minneapolis, Minnesota, with tragic consequences. Engineers commissioned by the National Transportation Safety Board are still investigating the cause of this structural failure, and the final report is expected by fall 2008. The bridge buckled because its load exceeded the strength of its structure.
Patients’ first response...

- The floor was slippery
- I was clumsy
- The store owner should have cleaned up the spill
- It was an accident
75.7% of all fractures that are fragility fractures

Overall: 81%

Post-fracture Care Gap: Comparison with Heart Attack

How do we shift this paradigm?

% of patients being treated

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

In women with hip fractures:

- Fracture begets future fracture
- 40% had prior fracture

- Deteriorated quality of life
- 40% need assistance walking

- Long-term care admission
- 18% enter LTC

- Mortality
- 23% die within 1 year

**Lifetime risk of hip fracture in women >50 is 12.1%**

NEJM Case
PHARMACOLOGICAL MANAGEMENT
Age & Risk of Fracture with Low BMD

Risk increases with age

Kanis et al, Osteopor Int 2001
Two Tools for Fracture Risk Assessment

These tools incorporate other risk factors for fracture in addition to BMD

2. FRAX® tool available at: [http://www.shef.ac.uk/FRAX/tool.jsp](http://www.shef.ac.uk/FRAX/tool.jsp)
Calculating 10-Year Absolute Fracture Risk for Postmenopausal Women: CAROC

Lumbar spine or total hip T-score ≤ -2.5: consider the individual to be at least at moderate risk

Calibrated using Canadian fracture data and have been directly validated in Canadians²

*At least three months cumulative use during the preceding year at a prednisone-equivalent dose ≥ 7.5 mg daily

High 10-Year Fracture Risk

Those with:

- Hip Fractures
- Vertebral Fractures
- >2 fragility fractures
- >1 fragility fracture + steroid use
Most patients >age 75 are at Moderate to High risk of Fracture based on age alone.
2010 Treatment Guidelines

- Low risk (<10%): Lifestyle Modification
- Moderate risk: ?
- High risk (>20%): Treat

Moderate Risk

Treat if:

- Over 65 with wrist fracture
- Lumbar spine $<$ Femoral neck T-score
- Medications (e.g. AI, ADT)
- Conditions (e.g. RA)
- Falls
- Patient preference
Consequences of Falls in Osteoporotic Patients

- Falls are a major contributor to fractures:
  - Over 90% of hip fractures are the result of a fall
  - Up to 14% of falls result in hip fractures

# Pharmocological therapy

## First Line Therapies with Evidence for Fracture Prevention in Postmenopausal Women*

<table>
<thead>
<tr>
<th>Type of Fracture</th>
<th>Antiresorptive Therapy</th>
<th>Bone Formation Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bisphosphonates</td>
<td>Denosumab</td>
</tr>
<tr>
<td></td>
<td>Alendronate</td>
<td>Risedronate</td>
</tr>
<tr>
<td>Vertebral</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hip</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Non-Vertebral+</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

+ In clinical trials, non-vertebral fractures are a composite endpoint including hip, femur, pelvis, tibia, humerus, radius, and clavicle.
* For postmenopausal women, ✓ indicates first line therapies and Grade A recommendation. For men requiring treatment, alendronate, risedronate, and zoledronic acid can be used as first line therapies for prevention of fractures [Grade D].
** Estrogen or hormone therapy can be used as first line therapy in women with menopausal symptoms.
Special Considerations for the Geriatrics Population

- Falls risk
- Sarcopenia
- Poor Nutrition
- Poor Renal Function
- Multiple Comorbidities and Medications

How many times has she fallen in the past 12 months?
Fall Prevention Strategies

- Assessment of fall risk: on admission/after a fall
- Patient education on risk of falls
- Environmental modification: reduction of fall hazards
- Reduce use of restraints for patients in care
- Adequate vitamin D
- Medication review
- Exercise: Tai chi, balance and strength training
- Hip protectors
- Compliant flooring

Registered Nurse Association of Ontario (RNAO) Prevention of Falls and Falls injuries in Older Adults – Recommendations.
Exercise

To order:
416-340-4800 ext 5926
osteoporosis@uhn.ca
Assistive Devices
Different Types of Hip Protectors
Conditions
SmartCells: commercially available compliant floor for injury prevention

Installation of compliant flooring (SmartCells) in a demonstration bedroom of Delta View Rehabilitation Centre in Delta, BC
CURRENT CONTROVERSIES
Calcium and Vitamin D Supplementation in Postmenopausal Women

John F. Aloia, Ruban Dhaliwal, Albert Shieh, Mageda Mikhail, Shahidul Islam, and James K. Yeh

CBC News closed with: “People should consult their physicians before taking more than 800IU of vitamin D”
Effects of vitamin D supplements on bone mineral density: a systematic review and meta-analysis

CBS News: Vitamin D supplements won’t help bones in healthy adults
Vitamin D

- Oversimplification of action of vitamin D

- Adequacy – aiming for serum 25-hydroxyvitamin D levels: ≥75nmol/L (2010 OC guidelines)
  ≥50nmol/L (IOM guidelines for healthy adults)

- Reid meta-analysis: baseline mean serum 25-hydroxyvitamin D level > 50nmol/L in 15 studies

- Canadian Guidelines: 400IU – 2000IU a day is safe
Calcium Supplements and Fracture Prevention

Douglas C. Bauer, M.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author’s clinical recommendations.

A 62-year-old healthy woman presents for routine care. She has no history of fracture, but she is worried about osteoporosis because her mother had a hip fracture at 72 years of age. She exercises regularly and has taken over-the-counter calcium carbonate at a dose of 1000 mg three times a day since her menopause at 54 years of age.
Calcium – potential benefits

• US Preventive Services Task Force meta-analysis 2011:
  – 16 RCTs → 12% reduction in all fractures
  – institutionalized elderly RR= 0.71 (95%CI: 0.57-89)
  – community-dwelling RR=0.89 (95%CI: 0.76-1.04) p=0.07

• Tang et al meta-analysis 2007:
  9 RCTs → 10% reduction in all fractures

• Reid et al meta-analysis 2008:
  3 RCTs → 50% increase in hip fractures
Calcium – potential harm

• Cardiovascular:

  Bolland 1\textsuperscript{st} meta-analysis 2010:
  15 RCTs of Ca alone OR= 1.31 (95\%CI: 1.02 - 1.67)

  Bolland 2\textsuperscript{nd} meta-analysis 2011:
  15 RCTs of Ca+/-D OR= 1.21 (95\%CI: 1.01 - 1.44)

• Wang et al meta-analysis 2010 (Included all WHI)
  Ca + D: RR = 1.04 (95\%CI: 0.92 - 1.18)
  Ca alone: RR = 1.14 (95\%CI: 0.92 -1.42)
Calcium

• Other side effects: constipation and bloating, constipation and bloating -- mild
kidney stones: RR = 1.17 (dose-dependent)

• Current guidelines for total calcium intake per day:
  2010 Osteoporosis Canada = 1200mg/day (diet + supplements)
  2011 IOM = 1200mg/day (F>age50)
  = 1000-1200mg/day (M>age 50)
Osteonecrosis of the Jaw

Exposed non-healing bone for 6 to 8 weeks
### Incidence of BP associated ONJ (# cases/# pts -Rx filled)

<table>
<thead>
<tr>
<th></th>
<th>Overall number of patients ODB +PP</th>
<th>Number of cancer patients (IV bisphosphonate) Brogan Rx data</th>
<th>Number of patients with osteoporosis or metabolic bone disease Brogan Rx data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number in Ontario with bisphosphonate use at any time between 2004 - 2006</td>
<td>583,513</td>
<td>2,825</td>
<td>580,688</td>
</tr>
<tr>
<td>Number of patients* with ONJ between 2004 – 2006</td>
<td>32</td>
<td>19</td>
<td>13</td>
</tr>
<tr>
<td>Three – year cumulative incidence</td>
<td>~5 per 100,000</td>
<td>~7 per 1,000</td>
<td>~2 per 100,000</td>
</tr>
<tr>
<td>Average annual incidence</td>
<td>~2 per 100,000</td>
<td>~2 per 1,000</td>
<td>~1 per 100,000</td>
</tr>
</tbody>
</table>
Other risk factors

- Cancer (lymphoma, breast, prostate, multiple myeloma)
- Chemo and radiation
- High dose bisphosphonates for high calcium levels or for bone mets
- Steroids
- Diabetes
- Poor dental hygiene
- Invasive dental procedure
Atypical femur fractures (AFFs)

- low-trauma stress fractures
- in subtrochanteric or shaft region of the femur
- can be associated with bisphosphonate or denosumab therapy
Hip Fractures

- **Subcapital**
- **Femoral neck**
- **Inter trochanteric**
- **Subtrochanteric**

**Fractures:**
- Subcapital neck fracture
- Transcervical neck fracture
- Intertrochanteric fracture
- Subtrochanteric fracture
- Fracture of the greater trochanter
- Fracture of the lesser trochanter
Radiographic Images of AFFs

Transverse fracture line
Subtrochanteric

Transverse fracture line
Mid-diaphyseal

Focal Periosteal Reaction on Lateral cortex
Oblique extension
Medial spike
Imaging using other modalities

Plain X-rays

Bone Scan

MRI

DXA

Incidence of Complete AFFs

Ontario CANADA Data

Bisphosphonate Use and the Risk of Subtrochanteric or Femoral Shaft Fractures in Older Women

Laura Y. Park-Wyllie, PharmD, MS, Ph
Muhammad M. Mandani, PharmD, MA, MPH

Context: Osteoporosis is associated with significant morbidity and mortality. Oral bisphosphonates have become a mainstay of treatment, but concerns have emerged that long-term use of these drugs may suppress bone remodeling, leading to unusual fractures.

~1-2/1000 py after 6 - 7 years

Kaiser Permanente California Data

ORIGINAL ARTICLE

Incidence of Atypical Nontraumatic Diaphyseal Fractures of the Femur


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2. Department of Research and Evaluation, Kaiser Permanente Southern California, Gardena, CA, USA
3. Bone Center of Excellence at Cedars-Sinai Medical Center, West Hollywood, CA, USA
4. Department of Orthopedic Surgery, Maimonides Medical Center, Brooklyn, NY, USA
5. Department of Medicine, University of Washington, Seattle, WA, USA

ABSTRACT

Bisphosphonates reduce the rate of osteoporotic fractures in clinical trials and community practice. “Atypical” nontraumatic fractures of the femur have been observed with increased frequency in women treated with bisphosphonates. The authors conducted a nested case-control study to identify the risk of atypical femur fractures associated with bisphosphonate use.

Main Outcome Measures: The primary analysis examined the association between atypical femur fractures and a history of bisphosphonate use, adjusting for potential confounders.

~1/1000 py after 8 - 9.9 years

Identified by diagnostic or procedure codes and adjudicated by examination of radiographs. Bisphosphonate exposure was derived from internal pharmacy records. The results showed that 142 patients had atypical fractures of the hip, 128 had bisphosphonate exposure. There was no significant correlation between duration of use and age, and bone density (T-score). The age-adjusted incidence rates for atypical fractures were 1.78/100,000/year (95% confidence interval [CI], 1.5-2.0) with exposure from 0.1 to 1.9 years, and increased to 1.03 (95% CI, 0.9-1.16) with exposure from 10 to 9.9 years. We conclude that the incidence of atypical fractures of the femur increases with longer duration of bisphosphonate use. The site is much lower than the expected rate of dislocating hip fractures in elderly osteoporotic patients. Patients at risk for osteoporotic fractures should not be discouraged from initiating bisphosphonates, because clinical trials have documented that these medicines can substantially reduce the incidence of typical hip fractures. The increased risk of atypical fractures should be taken into consideration when continuing bisphosphonates beyond 5 years. © 2012 American Society for Bone and Mineral Research.
## Is long-term therapy still effective?*

In long-term trials, BMD continued to increase or remained stable.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Pivotal Study Extension</th>
<th>Treatment Duration (yrs)</th>
<th># of Participants</th>
<th>% Change Lumbar Spine BMD †</th>
<th>% Change Total Hip BMD †</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risedronate¹</td>
<td>VERT-MN</td>
<td>7</td>
<td>68</td>
<td>11.5</td>
<td>3.9</td>
</tr>
<tr>
<td>Alendronate²</td>
<td>FLEX</td>
<td>10</td>
<td>86</td>
<td>13.7</td>
<td>6.7</td>
</tr>
<tr>
<td>Zoledronic Acid³</td>
<td>HORIZON (interim analysis of 9 year study)</td>
<td>6</td>
<td>616</td>
<td>12.1</td>
<td>4.3</td>
</tr>
<tr>
<td>Denosumab⁴</td>
<td>FREEDOM (interim analysis of 10 year study)</td>
<td>6</td>
<td>2343</td>
<td>15.2</td>
<td>7.5</td>
</tr>
</tbody>
</table>

* Not head to head analyses: Results cannot be compared due to differing study populations and methodologies.
† Represents % change from BL of Pivotal Trial.
² Represents 10 mg dose only.

“Drug Holiday” for low and moderate risk

2010 CAROC tool: Assessment of Basal 10-year Fracture Risk

<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
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- **Low risk (<10%)**
- **Moderate risk**
- **High risk (> 20%)**
Summary

1) the epidemiology and risks associated with osteoporosis

2) the latest developments in the pharmacological management of osteoporosis

3) the current controversies around the treatment of osteoporosis
Which of the conditions below is most common in women age 50 and over?

a. Heart disease
b. Breast cancer
c. Stroke
d. Osteoporotic fractures
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d. Osteoporotic fractures
Which of the patients below are at high risk of another major osteoporotic fracture in the next 10 years?

a. Those with BMD T-score less than or equal to -2.5 and on prednisone 10mg a day for the past year
b. Those with hip fractures irrespective of BMD
c. Those with vertebral fractures irrespective of BMD
d. Those with more than 1 fragility fracture irrespective of BMD
e. All of the above
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Which of the following drug therapies is/are first line therapy/ies for osteoporosis in the elderly?

a. Oral bisphosphonates (daily, weekly, monthly)
b. Intravenous bisphosphonate once a year
c. Subcutaneous denosumab every 6 months
d. Subcutaneous teriparatide every day for 2 years
e. All of the above
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e. All of the above
WHI Calcium/Vit D

- 36,282 women age 50 to 79 yrs -- 1000 mg calcium with 400 IU Vit D$_3$ (CaD) versus placebo

- After 7 yrs:
  - non-significant reductions hip, clinical vertebral and total fracture.
  - CHD and cancer similar in the 2 groups

- Mean Ca intake in placebo group = 1154mg/ day
WHI Calcium/Vit D: 5 yrs after Trial

- 86% of participants
- CaD n=15025 and PBO n=14837
- Fractures were self-reported

- Vertebral fractures: HR 0.87 (0.76, 0.98)
- Clinical vertebral fractures: HR 0.83 (0.71, 0.98)
- Hip fractures: HR 0.95 (0.78, 1.15)
- Total fractures: HR 1.00 (0.94, 1.06)

- No difference: total cancers, CVD, mortality
• **Height loss** can be a warning sign of a spine fracture (a broken bone in your back).

• A spine fracture may be caused by **osteoporosis**, a condition that causes bones to break easily.

• You may not be aware of a broken bone in your back because 66% are painless.

• If you have a spine fracture, **effective treatment** is available to reduce your risk of another broken bone.
Questions?

THANK YOU!