Fracture risk assessment: From Basics to Baffling

William D Leslie MD FRCPC MSc CCD
By the end of this session attendees shall be able to:

• Understand how and why fracture risk assessment has changed over the past decade
• Understand how recent advances in fracture risk assessment enhance the quality of patient care
Incidence of Osteoporotic Fracture, Heart Attack, Stroke and Breast Cancer in Canadian Women


Fragility Fracture: Definition

- A fracture occurring spontaneously or following minor trauma such as a fall from standing height or less\(^1,2\)
  - Excluding face/head, hand, ankle, and foot fractures

Consequences of Fracture

- Increased risk of
  - Hospitalization\(^1\)
  - Institutionalization\(^2\)
  - Death\(^3-5\)
  - Subsequent fracture\(^6-8\)
  - Decreased quality of life\(^9-12\)
  - Economic burden on healthcare system\(^2\)

Death 1st Year Post Fracture
adjusted for age, comorbidity, home care/PCH status

Morin S. Osteoporo Int. 2010.
Post-fracture Care Gap: Comparison with Heart Attack

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

Percentage of individuals who received OP medication 1 year following major fracture in Canada, 2000–2001 to 2014–2015

“Up to” 26.1% in Women and 16.9% in Men
Increase up to 2008–2009 (p for trend <0.0001)
Followed by a Decline to 2014–2015 (p for trend <0.0001)

Morin SN et al. ASBMR 2018.
F.D.A. to Review Safety of Popular Bone Drugs

By DUFF WILSON
Published: September 5, 2011

Two advisory panels of the Food and Drug Administration will consider on Friday whether to recommend requiring women who use popular bone drugs like Fosamax to take “drug holidays” because of rising concerns about rare side effects with long-term use, according to people involved in the review.
Figure 1. Risks of major osteoporotic fracture and other rare events

- **Bis-ONJ**\(^*\): 1.03
- **Bis-AFF (8 y)**\(^†\): 78
- **Bis-AFF (2 y)**\(^†\): 2
- **Death by murder**\(^‡\): 1.62
- **Fatal MVA**\(^§\): 8.4
- **Major osteoporotic fracture in low-risk women**\(^∥\): 650
- **Major osteoporotic fracture in moderate-risk women**\(^∥\): 1600
- **Major osteoporotic fracture in high-risk women**\(^∥\): 3100

INCENTDENCE PER 100 000 PERSON-YEARS

• “...all Canadians, wherever they live, have the right to effective bone care and fracture prevention programs”
2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary

Key Changes from 2002\textsuperscript{1} to 2010\textsuperscript{2}

• Increased focus on the importance of fragility fractures

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

Most Fragility Fractures in Older Women Occur with Low Bone Mass ("Osteopenia")

Treatment initiation:
High risk fracture = vertebral, hip, multiple

Initial BMD Testing

Assessment of fracture risk

Low risk

Moderate risk

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
10-year MOF Risk Assessment

FRAX Canada

CAROC 2010

Calculation Tool

WOMEN

LOW RISK (<10%)
MODERATE RISK
HIGH RISK (>20%)

Weight Conversion
Pounds → Kgs
Height Conversion
Inches → Cms
10-year Risk Assessment: CAROC

- Semiquantitative method for estimating 10-year absolute risk of a major osteoporotic fracture* in postmenopausal women and men over age 50
  - Three zones (low: < 10%, moderate, high: > 20%)
- Considers two additional risk factors
  - Fragility fracture after age 40
  - Recent prolonged systemic glucocorticoid use (at least 3 m last year prednisone > 7.5 mg daily)

* Fractures of the thigh bone, vertebra, forearm, and shoulder

Example: 65 year old woman

- Femoral neck T-score = -2.8
- Based on age and T-score alone = **moderate risk**

Example: 65 year old woman

- Femoral neck T-score = -2.8
- Based on age and T-score alone = moderate risk

- History of fragility fracture or prolonged systemic glucocorticoid use would shift her to high risk

CAROC: Women ≠ Men

A. Papaioannou et al. CMAJ 2010;182:1864-73
B. Lentle et al. CARJ 62:243-250, 2011
10-year Risk Assessment: FRAX

Canadian FRAX uses:

- 2005 national hip fracture data
- 2004 national mortality data
- Estimates non-hip fractures from hip fractures
- Predictions validated in >45,000 Canadians

Fraser L. Osteoporos Int 2010.
The site and reference technology is DXA at the femoral neck. T-scores are based on the NHANES reference values for women aged 20-29 years. The same absolute values are used in men.
- Without CAROC risk factors: 13% - moderate risk
- History of fragility fracture: 21% - high risk
- Systemic glucocorticoids: 21% - high risk
**FRAX vs Updated 2010 CAROC**

Same risk category 90% of cases

## First Line Therapies with Grade A Evidence for Fracture Prevention

<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>
Importance of Prior Major Fracture: Re-fracture in 40,062 women and 17,721 men

Morin SN et al. ASBMR 2018.
Importance of Vertebral Fractures

Fracture Risk Assessment

Other Factors that Warrant Consideration for Pharmacological Therapy?
E.G. LATERAL THORACOLUMBAR IMAGING TO IDENTIFY VERTEBRAL FRACTURES

High Risk
10-year fracture risk > 20%
or
Prior fragility fracture of hip or SPINE
or
More than one fragility fracture

Good evidence of benefit from pharmacotherapy

Case Finding with VFA
Proportions Dispensed Medication By VFA Results & Risk Category

Schousboe JT et al. ASBMR 2018.
To Treat or Not to Treat?

- 70 year old woman:
  - Breast cancer starting AI therapy
  - Low Bone Mass / Osteopenic
  - FRAX MOF 31%
Follow Up

- 72 year old woman:
  - Breast cancer on AI therapy for 2 years
  - No anti-osteoporosis tx
  - Low Bone Mass / Osteopenic
  - FRAX MOF 7.3%
Prior fracture: fell on the ice, injured wrists, x-ray no fracture
Parental hip fracture: adopted
Glucocorticoids: in conjunction with adjuvant breast chemotx
Rheumatoid arthritis: now indicates fibromyalgia
79 year old woman

- Left “wrst” fracture age 55
  - fell while curling
- Right radius/ulna fracture age
  - stepped off curb
- Type 2 diabetes
  - since age 50
- Father hip fracture
  - age 102

**FRAX Canada without BMD:**
- no risk factors: 17%
  + prior fracture: 28%
  + prior fracture + parent hip fracture: 44%
  + prior fracture + RA (diabetes proxy): 38%
79 year old woman

- Left "wrist" fracture age 55
  - X fell while curling
- Right radius/ulna fracture age
  - stepped off curb
- Type 2 diabetes
  - since age 50
- Father hip fracture
  - X age 102

FRAX Canada with BMD (femur neck T-score -2.2):
- no risk factors: 16%
- + prior fracture: 23%
- + prior fracture + parent hip fracture: 39%
- + prior fracture + RA (diabetes proxy): 29%
79 year old woman

• Left “wrist” fracture age 55
  • fell while curling
• Right radius/ulna fracture age
  • stepped off curb
• Type 2 diabetes
  • since age 50
• Father hip fracture
  • age 102

CAROC with BMD (femur neck T-score -2.2):
• no risk factors: moderate risk
+ prior fracture: high risk
When in doubt....
<table>
<thead>
<tr>
<th>FRAX:</th>
<th>CAROC:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Quantitative</td>
<td>• Semi-quantitative</td>
</tr>
<tr>
<td>• More risk factors</td>
<td>• Simpler</td>
</tr>
<tr>
<td>• Computer based</td>
<td>• Table / graphic based</td>
</tr>
<tr>
<td>• Widely used in 2018</td>
<td>• Widely used in 2010</td>
</tr>
<tr>
<td>• Does not include falls and other risk factors</td>
<td>• Does not include falls and other risk factors</td>
</tr>
<tr>
<td>• Requires clinical judgment</td>
<td>• Requires clinical judgment</td>
</tr>
</tbody>
</table>
Concluding Thoughts

• Osteoporosis is much more than DXA
• We have good tools to improve post fracture care