Clinical Question 3

- How do we evaluate fracture risk in postmenopausal women with a view to identifying women who would benefit from osteoporosis pharmacotherapy?

1

Learning Objectives

Upon completion of this module, participants will be better able to:

- Identify clinical and diagnostic risk factors which further increase the risk of fractures in post menopausal women
- Apply evidence-based management protocols to prevent future fractures in post menopausal women
- Assess patients on treatment for occurrence of side effects and select appropriate therapies based on the patient characteristics

2

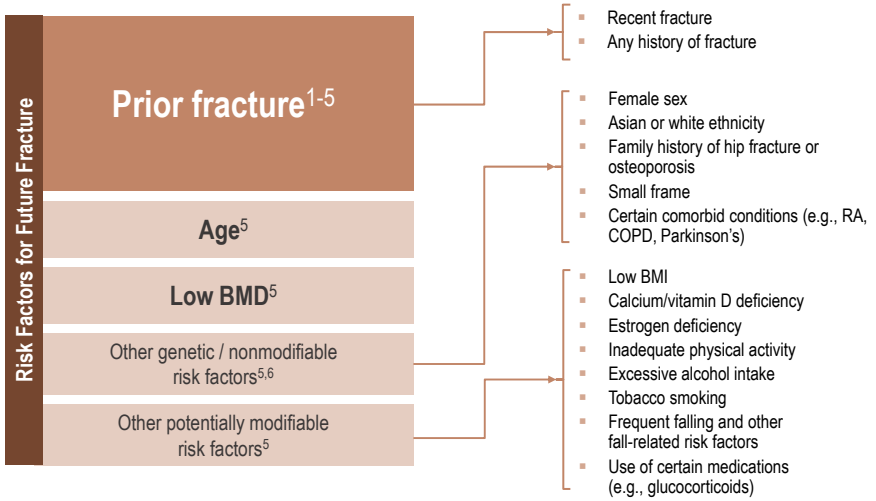
Clinical Question 3

How do we evaluate fracture risk in postmenopausal women with a view to identifying women who would benefit from osteoporosis pharmacotherapy?

It is important to consider the routine evaluation of fracture risk in postmenopausal women in order to determine those requiring osteoporosis therapy in addition to calcium, vitamin D, exercise, and lifestyle advice. At age 65, a bone health assessment in a woman without other risks will identify features of peak bone mineral density in addition to declines in the 1.5 decades of postmenopausal life. In a woman with risk factors, evaluation at an earlier stage of her postmenopausal life may be warranted. FRAX incorporates clinical risk factors with femoral neck bone mineral density to identify patients at high 10-year fracture risk who would be candidates for osteoporosis treatment. Cut points of >20% for major osteoporotic fracture risk or >3% for hip fracture risk are aligned with a cost economic approach to osteoporosis therapy.

3

Several Factors Contribute to Long-Term Fracture Risk

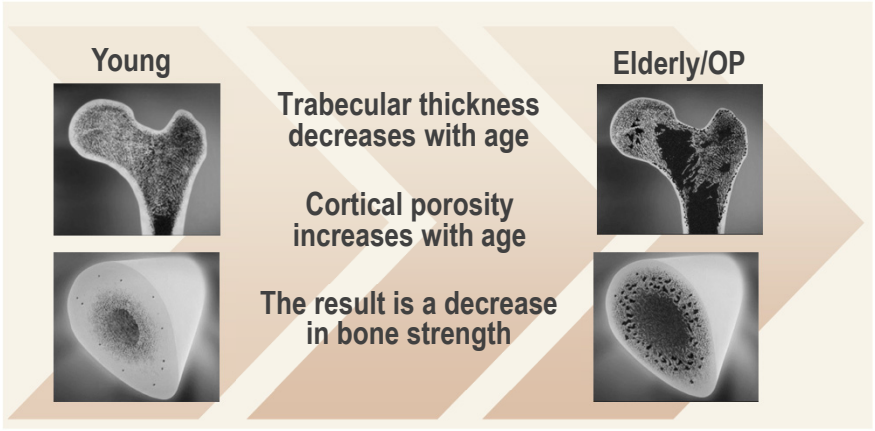


BMD = bone mineral density; BMI = body mass index; COPD = chronic obstructive pulmonary disease; RA = rheumatoid arthritis

1. Kanis JA, et al. *Bone*. 2004;35:375-382. 2. Kanis JA, et al. *Lancet*. 2002;359:1929-1936. 3. Black DM, et al. *J Bone Miner Res*. 1999;14:821-828. 4. Eisman JA, et al. *J Bone Miner Res*. 2012;27:2039-2046. 5. Cosman F, et al. *Osteoporos Int*. 2014;25:2359-2381. 6. US Department of Health and Human Services. Bone health and osteoporosis: a report of the surgeon general. 2004. Rockville, MD.

4

The Impact of Aging and Osteoporosis on Bone



Davison SK, et al. *Semin Arthritis Rheum* 2006;36:22-31; Mosekilde L. *Technol Health Care* 1998;6:287-297; Seeman E, et al. *J Bone Miner Res* 2010;25:1886-1894. Image courtesy of David Dempster.

5

Frequent Falling is Associated with Serious Injury and a Greater Risk of Fracture

- **Women with osteoporosis and without a fall***
  → Fracture risk: 2.8 (95% CI, 0.6-12.8; P<.10)
- **Women with osteoporosis and a fall***
  → Fracture risk: 24.8 (95% CI, 6.9-88.6; P<.0001)

*Compared with women without osteoporosis and without a fall, fracture risk age- and BMI-adjusted.
Nevitt MC, et al. *J Gerontol Med Sci*. 1991;46(5):M164-70; Geusens P, et al. *Arch Phys Med Rehabil*. 2002; 83(7):903-6.

6

High Alcohol Consumption Decreases Bone Remodeling and Increases Fracture Risk

- **Consuming > 4 units of alcohol/day can double the risk of hip fracture**
- **Heavy alcohol consumption is associated with:**
  - → Decreased BMD
  - → Impaired bone quality
  - → Increased fracture risk
  - → Increased risk of falls

Likely due to a decrease in bone remodelling

Kanis JA, et al. *Osteoporos Int.* 2005;16:737-42; Gaddini GW, et al. *Alcohol Clin Exp Res.* 2016;40(4):657-71.

7

Comorbidities Significantly Contribute to Fracture Risk

Global Longitudinal Study of Osteoporosis in Women (GLOW)

- **Co-morbidities that contributed most to fracture prediction*:**
  - → Parkinson's disease
  - → Multiple sclerosis
  - → COPD
  - → Osteoarthritis
  - → Heart disease
- **Increasing co-morbidity index† associated with increasing fracture risk**

*in a Cox regression model with FRAX risk factors as additional predictors.
†weighted value for each co-morbidity based on parameter estimates from the Cox regression model.
COPD: chronic obstructive pulmonary disease.
Dennison EM, et al. *Bone.* 2012;50(6):1288-93.

8

Potential Medications Contributing to Falls or Adverse Events leading to Falls in the Elderly

Adverse Drug Effect	Medication(s)
Agitation	Antidepressants, caffeine, neuroleptics, stimulants
Cognitive impairment, confusion	Benzodiazepines, narcotics (opioids), neuroleptics, any anticholinergic
Dizziness, orthostatic hypotension	Anticonvulsants, antidepressants, antihypertensives, benzodiazepines, narcotics, neuroleptics
Gait abnormalities, extrapyramidal reactions	Antidepressants, metoclopramide, neuroleptics
Increased urination	Diuretics
Postural disturbances (balance issues)	Anticonvulsants, benzodiazepines, neuroleptics
Sedation, drowsiness	Anticonvulsants, antidepressants, benzodiazepines, narcotics, neuroleptics
Syncope	Beta-blockers, nitrates, vasodilators (ie alpha1-adrenergic blockers like doxazosin)
Visual disturbances (blurring)	Neuroleptics, anticholinergics

Ruddock B. *DIRC*. 2004;137(6):17-18.

9

Checklist for Fracture and OP Risk Factors

- Anticonvulsants
- Antipsychotic drugs
- Antiretroviral drugs
- Aromatase inhibitors
- Chemotherapeutic/transplant drugs
- Furosemide
- Glucocorticoids
- Heparin (long-term)
- Hormonal/endocrine therapies
- Methotrexate
- Proton Pump Inhibitors (PPI)
- Selective Serotonin Reuptake Inhibitors (SSRI)
- Thyroxine (excessive)

Hodgson SF, Watts NB, et al. *Endocr Pract* 2003;9:544-564; Jacobs-Kosmin D. (2011). Medscape CME. Accessed May 25th 2011. http://emedicine.medscape.com/article/330598-overview

10

OC Guideline Recommendations

	Antiresorptive Therapy				Bone Formation Therapy
	Bisphosphonates			Denosumab	Teriparatide
	Oral Branded	Oral Generic	IV		
OC Guideline Recommendations					
Vertebral	✓	✓	✓	✓	✓
Hip	✓	✓	✓	✓	-
Non-vertebral	✓	✓	✓	✓	✓
OC Guideline Recommendations for Long-Term Care Patients					
High Risk	✓	✓	✓	✓	Suggested treatment
High Risk with dysphagia			✓	✓	Suggested treatment
High Risk with CrCl <30 mL/min				✓†	

†Clinical monitoring of serum calcium levels is recommended because of higher risk of hypocalcemia; consider referral to specialist.
Adapted from: Papaioannou A, et al. *CMAJ*. 2015;187(15):1135-1144.

11

BMD Responses to Antiresorptive Therapy at 3 years in Pivotal Clinical Trials

	Antiresorptive Therapy				
	Bisphosphonates				
vs. Placebo from Baseline	Alendronate (FIT 1)[1]	Risedronate 5 mg Daily (VERT-MN)[2]	Risedronate Weekly[3]	Zoledronic Acid (HORIZON)[4]	Denosumab (FREEDOM)[5]
Change in Lumbar Spine BMD	6.2%	5.9%	5.2% at 24 months	6.7%	8.8%
Change in femoral neck BMD	4.1%	3.1%	N/A	5.1%	5.2%

1. Black DM, et al. *Lancet*. 1996;348:1535-1541 (FIT 1); 2. Reginster J, et al. *Osteoporos Int*. 2000;11(1):83-91 (VERT-MN); 3. Actonel/Actonel DR (risedronate sodium) Product Monograph. Sanofi-Aventis Canada Inc. Laval, QC. July 15, 2011; 4. Black DM, et al. *N Engl J Med*. 2007;356:1809-1822. (HORIZON); 5. Cummings SR, et al. *N Eng J Med*. 2009;361:756-765 (FREEDOM).

12