Clinical Question 4

- How do we evaluate fracture risk in older men, and what are the therapeutic options?

1

Learning Objectives

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

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

2

Clinical Question 4

How do we evaluate fracture risk in older men, and what are the therapeutic options?

Osteoporotic fractures occur in men approximately one third as frequently as women but fractures in men have greater morbidity and mortality compared to women. BMD T-scores in men are calculated from a female reference databases, which can be used in FRAX to determine the 10-year fracture risk and to identify candidates for osteoporosis pharmacotherapy. Treatments include bisphosphonate, denosumab, and teriparatide.

3

Clinical Vignette

James
75 years old

James' History

- Follow-up visit post recent hip fracture
- History of COPD
- Previous smoker

Physical Exam & Tests

- Noted height loss (3 cm)
- Esophageal abnormalities due to GERD
- Femoral Neck T-score: -2.4

Medications

- Long-acting ß2-agonists (LABAs) and long-acting muscarinic antagonists (LAMAs)
- Statin, PPI

4

Men and Osteoporosis

- 1 in 5 men will suffer from an osteoporotic fracture during their lifetime
- 28% of all hip fractures occur in men[1]
- Lifetime risk of experiencing an osteoporotic fracture in men over the age of 50 is 13.1%[2,3]
- Men have the SAME risk factors for fracture as women
- By age 65, men catch up to women and lose bone mass at the same rate[4]
- It is estimated that by 2025, the total number of hip fractures in men will be similar to the current number reported in women[5]
- Compared to women, men who fracture a hip have an increased risk of mortality, and more comorbid diseases, despite their younger age at the time of fracture[6]
- **Fracture risk increases with:**[7]
  - → Parental history of fracture (especially hip)
  - → Systemic glucocorticoid use (≥3 months)†
  - → Rheumatoid arthritis, or other secondary causes of osteoporosis

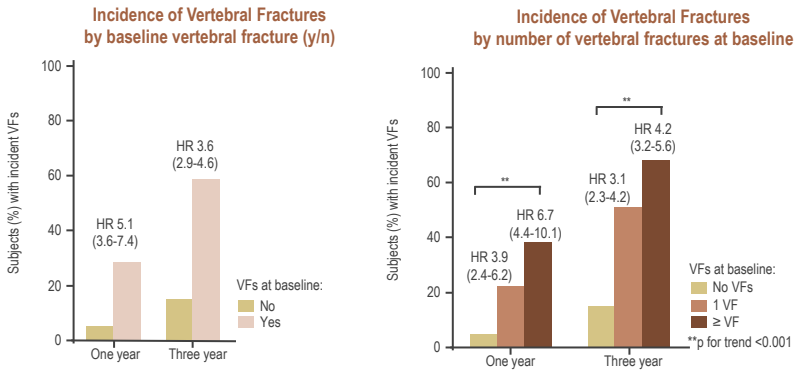
Men generally have higher rates of fracture related mortality – 37% of men who suffer a hip fracture will die within the year following that fractured hip.[1,8]

†≥3 months in the prior year of a prednisone equivalent dose ≥ 7.5mg daily.

1. Crilly RG et al Clin Med Insights Arthritis Musculoskelet Disord. 2016; 9:75-9; 2. Melton LJ, 3rd, et al. *J Bone Miner Res.* 1992; 7:1005; 3. https://www.cancer.ca/en/cancer-information/cancer-type/prostate/statistics/?region=on; 4.IOF 2017; 5. Seeman E. *Am J Med.* 1995; 98:76S–88S; 6. Gruber-Baldini et al. *J Am Geriatr Soc.* 2017;65(3):e64-e69; 7. Papaioannou, A, et al. *CMAJ.* 2010; 182:1864-1873. 8. https://osteoporosis.ca/about-the-disease/fast-facts/

5

High Imminent Vertebral Fracture Risk with COPD AND Previous Vertebral Fracture



Incidence of vertebral fractures (VFs) and adjusted hazard ratios within 1 and within 3 years.
ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints) study is a non-interventional, observational, multicenter study searching for underlying mechanisms of disease progression in conjunction with COPD.

van Dort, M.J., et al. J Bone Miner Res. 2018 Jul;33(7):1233-1241.

6

Clinical Vignette

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- LABA/LAMA
- Statin
- PPI

What factors would guide your decision to initiate OP therapy for James?

Would you initiate therapy for James?

7

When to do a BMD[1]

In Women and Men

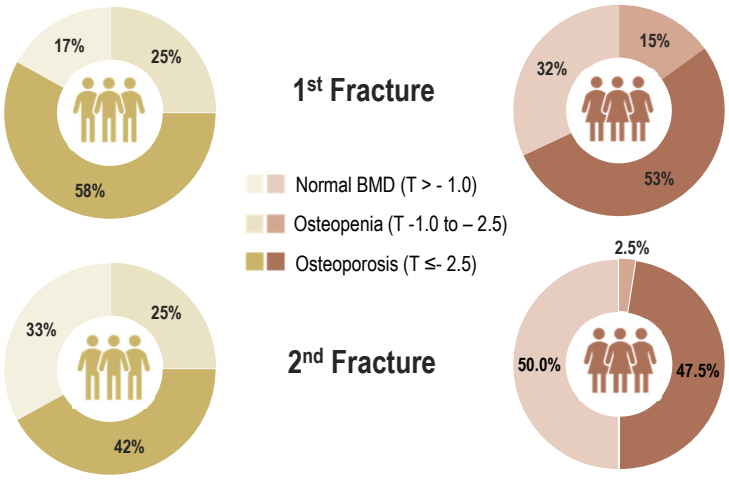
Aged ≥ 65 years	Aged 50-64 years	Aged <50 years
Everyone	**One or more risk factors for fracture:** ▪ Fragility fracture after age 40 ▪ Parental hip fracture ▪ Vertebral fracture or osteopenia identified on radiography ▪ Medication with high risk of bone loss (i.e. steroids) ▪ Smoking, alcohol (≥3/d) ▪ Disorders associated with osteoporosis (i.e. RA) ▪ Low weight or major weight loss	▪ 2°causes of osteoporosis (i.e. malabsorption) ▪ Prior fragility fracture ▪ Medication with high risk of bone loss

Clinical Note:
If you are ordering unrelated imaging (e.g. chest x-ray) for your patient, consider adding "rule out vertebral fracture" on the order[2]

1. Papaioannou A, et al. *CMAJ.* 2010;182:1864-1873; 2. Steering Group Communications Feb 9th 2012.

8

Men Usually have Fractures at a Higher Bone Density than Women



* Lowest BMD at lumbar spine or hip

Langsetmo L et al. CaMos Res Gr J Bone Miner Res 2009 Sep;24(9):1515-22.

9

Checklist for Fracture and OP Risk Factors

HISTORY

- Age >65 yrs
- History of fragility fracture
- Parental history of hip fracture
- Systemic glucocorticoid use [cumulative exposure >5 g] (≥3 months)
- Comorbidity (e.g. rheumatoid arthritis, celiac disease, COPD, chronic liver disease)
- Medications that may cause OP
- Smoke or excess alcohol
- Menopausal status
- Fall Risk

PHYSICAL EXAM

- Kyphosis?
- Loss of height (2 cm or 3/4") as measured by HCP
- Rib to Pelvis < 2 finger breadths
- Occiput to wall > 3 finger breadths

IMAGING / LABS

- Bone mineral density
- Osteopenia noted on routine X ray
- Standard lab test for osteoporosis assessment
- Labs:
  - Calcium, corrected for albumin
  - Thyroid stimulating hormone (TSH)
  - Complete blood count
  - Serum protein electrophoresis for patients with vertebral fractures
  - Creatinine o 25-hydroxy vitamin D (25-OH-D)*
  - Alkaline phosphatase

FALLS RISK

- Has the patient experienced frequent falls (i.e. fallen ≥2 times in the past year)?
- Unsteady walk and poor balance?
- Is assistance needed to get up from a chair?
- Assistive device needed (cane, walker, wheelchair)?
- Can the patient complete a "Get-up and Go Test"?

DEFINITION OF A FRAGILITY FRACTURE:* A fracture that occurs ***spontaneously*** or following a ***minor trauma*** such as:

- Fall from a standing height (i.e. on the ice)
- Fall from a sitting position
- Fall from a supine position (bed or reclining deck chair < 1 metre high)
- Fall after having missed 1 to 3 steps in a staircase
- After a movement outside of the typical plane of motion or coughing

*Fragility fracture includes all bones, except skull and face, patella, hands and feet, cervical spine.
Osteoporosis Canada 2016. Checklist for Risk of Broken Bones and Osteoporosis. Accessed July 8th 2016. http://www.osteoporosis.ca/osteoporosis-and-you/diagnosis/risk-factors/.
Bessette L et al. Contemp Clin Trials. 2008;29:194-210. Brown JP, et al. J Bone Miner Res. 2007;23(Suppl 1):M350.

10

Long-Term Fracture Risk Can Be Quantified Using FRAX® or Other Risk-Assessment Tools

- FRAX® provides conservative estimate of 10-year fracture risk but does not necessarily identify patients with shorter-term risk who require urgent intervention (pharmacological) to prevent subsequent fractures[1-3]

Input[1] → **Calculator[1]** → **Output[1]**

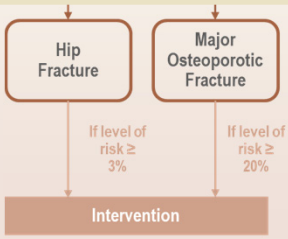
In men, absolute BMD value for femoral neck (rather than T-score) should be entered into FRAX because FRAX converts the BMD into a female T-score.

BMD

Fracture History

Other Characteristics

- Smoking
- Alcohol use
- Rheumatoid arthritis
- Glucocorticoids use
- Etc



FRAX® is a registered trademark of Professor J.A. Kanis. University of Sheffield.
BMD = bone mineral density; FRAX = fracture risk assessment tool.
1. FRAX. https://www.shef.ac.uk/FRAX/. Accessed March 15, 2018. 2. Kanis JA, et al. *Osteoporos Int*. 2011;22:2395-2411. 3. Silverman SL, et al. *Curr Osteoporos Rep*. 2010;8:192-197

11

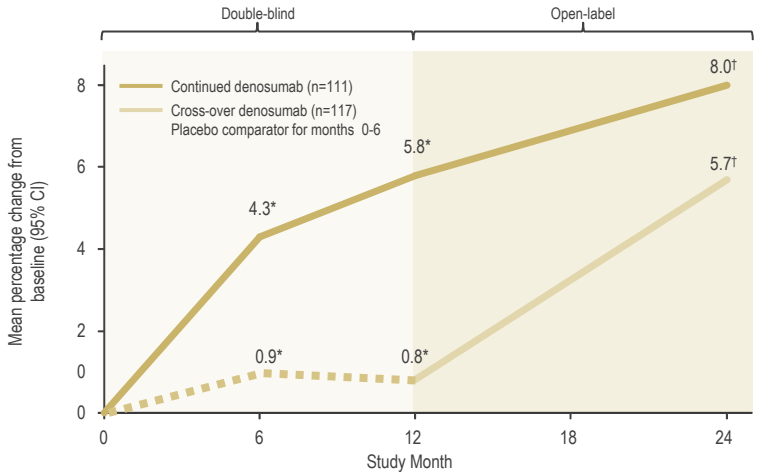
Male: BMD Responses to Bisphosphonate Therapy with 24-Month Treatment

	Antiresorptive Therapy		
	Bisphosphonates		
from Baseline	Alendronate[1]	Risedronate Weekly[3]	Zoledronic Acid[4]
Change in Lumbar Spine BMD	5.3%	4.5%	6.1%
Change in femoral neck BMD	2.6%		

* vs. placebo; † vs. weekly alendronate
1. Orwoll E, et al. *N Engl J Med* 2000;343:604-10; 2. Boonen S, et al. *J Bone Miner Res* 2009;24(4):719-25; 3. Orwoll ES, et al. *J Bone Miner Res* 2010;25:2239–2250.

12

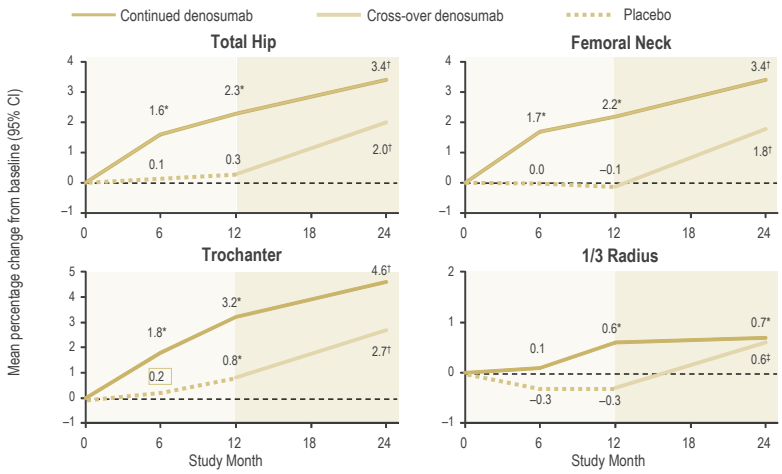
Male: ADAMO Continued BMD Increases With 24-Months of Denosumab Treatment at Lumbar Spine



*p < 0.05 vs double-blind baseline. †p < 0.0001 vs double-blind and open-label baseline. CI = confidence interval.
Adapted from: Langdahl BL, et al. *J Clin Endocrin Metab* 2015;100(4):1335-134. doi:10.1210/jc.2014-4079

13

Male: Continued BMD Increases with Denosumab at 24 Months: Total Hip, Femoral Neck, Trochanter, 1/3 Radius



Data are least square means.*p < 0.05 vs double-blind baseline; †p < 0.0001 vs double-blind and open-label baseline; ‡p < 0.05 vs double-blind and open-label baseline.
Adapted from Langdahl BL, et al. *J Clin Endocrin Metab* 2015;100(4):1335-134. DOI:10.1210/jc.2014-4079

14

Teriparatide: BMD Increases in Male OP

Mean Percent Change in BMD from Baseline to Endpoint in Men with Primary Hypogonadal OP Treated for a Median of 10 months

	Teriparatide (N=151)	Placebo (N=147)
Lumbar spine BMD	5.9†	0.5
Femoral Neck BMD	1.5‡	0.3
Total Hip BMD	1.2	0.5
Trochanter BMD	1.3	1.1
Distal 1/3 radius BMD	-0.5	-0.2

†p<0.001 compared with placebo; ‡p<0.05 compared with placebo.
Forteo-Drug Label Information. DailyMed. February 10, 2015. Accessed on June 1, 2016 at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aae667c5-381f-4f92-93df-2ed6158d07b0.

15

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What factors would guide your choice for OP therapy for James?

How would you address adherence with BPs?

What therapy would you start James on?

16

Discussion: Clinical Takeaways

1. Men are at high fracture risk, similar to women with the same risk factors
2. Men have a higher mortality risk than women after hip fracture
3. Treatment for men is the same as for women
4. For men we have to think of it!...It is not spontaneous

17