Optimizing Fracture Prevention in Primary Care

Optimizing Fracture Prevention in Primary Care
Faculty/Presenter Disclosure

- **Faculty:** Angela M. Cheung, MD, PhD, FRCPC, CCD
- **Relationships with commercial interests:**
  - **Grants/Research Support:** Amgen, Eli Lilly (all to UHN)
  - **Honoraria / Consulting:** Amgen, Eli Lilly
  - **Other: none**

Optimizing Fracture Prevention in Primary Care
Disclosure of Commercial Support

- **This program has received financial support from JCCP in the form of an educational grant.**
- **This program has received in-kind support from JCCP in the form of logistical support.**

- **<u>Potential for conflict(s) of interest</u>:**
  - Dr. Cheung has received funding from Amgen Canada whose product is being discussed in this program.
  - Amgen Canada benefits from the sale of a product that will be discussed in this program: Prolia (denosumab).

Optimizing Fracture Prevention in Primary Care
Disclosure of Commercial Support

Bias has been mitigated by the following:

- All program content was developed and peer-reviewed by an independent physicians steering group.
- All clinical recommendations are based on clinical guidelines and peer-reviewed evidence.
- No commercial or other non-commercial organization has had any input to the content of this program.

This slide deck has been reviewed and accredited by the College of Family Physicians of Canada and the Ontario Chapter.

Learning Objectives

Upon completion of this program, participants will be able to:

- Ensure validated diagnostic strategies are applied to postmenopausal patients.
- Implement effective risk assessment tools into regular patient visits to ensure assessment of all patients at risk for fracture.
- Evaluate current treatment strategies for patients at high risk for fracture.

Shift in Focus: Fracture Prevention vs. BMD

CMAJ REVIEW

2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary

"Focus now is on preventing fragility fractures and their negative consequences, rather than on treating low bone mineral density."

Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

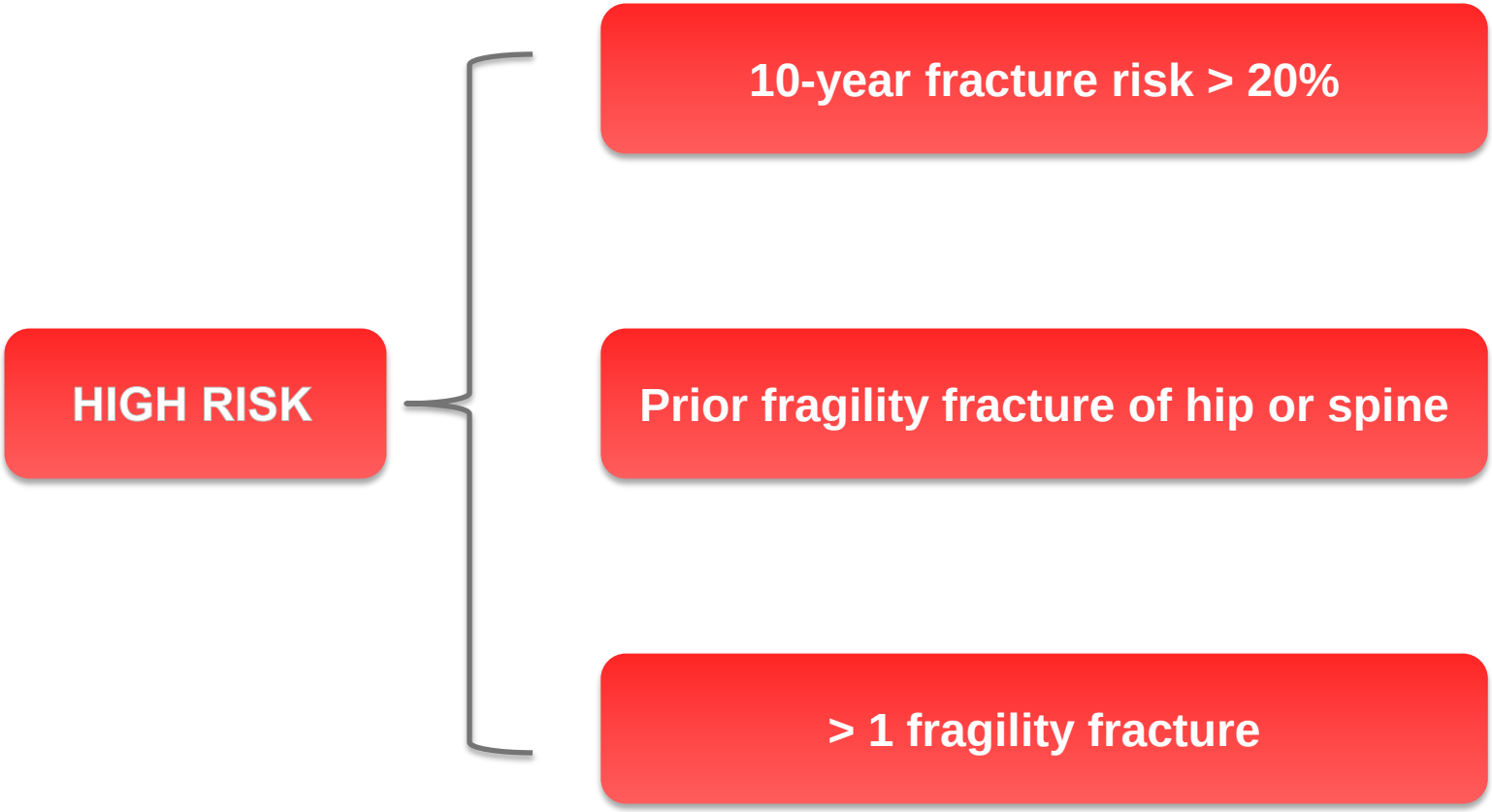
This Is Your Next Patient…

Alice is a 75-year-old female. She suffers from Type 2 Diabetes and has come into the office to refill her Metformin prescription.

On review of her history, you find out that she tripped and fell 3 months ago in her apartment and broke her hip.

Today, What Is Your Next Course of Action with Alice?

According to the Canada Osteoporosis Guidelines, a Patient Who Has Experienced a Hip Fracture Is Considered High Risk and Should Be on Pharmacological Therapy



Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

The Osteoporosis Canada Guidelines Recommend Treating Patients at High Risk with the Following[1]

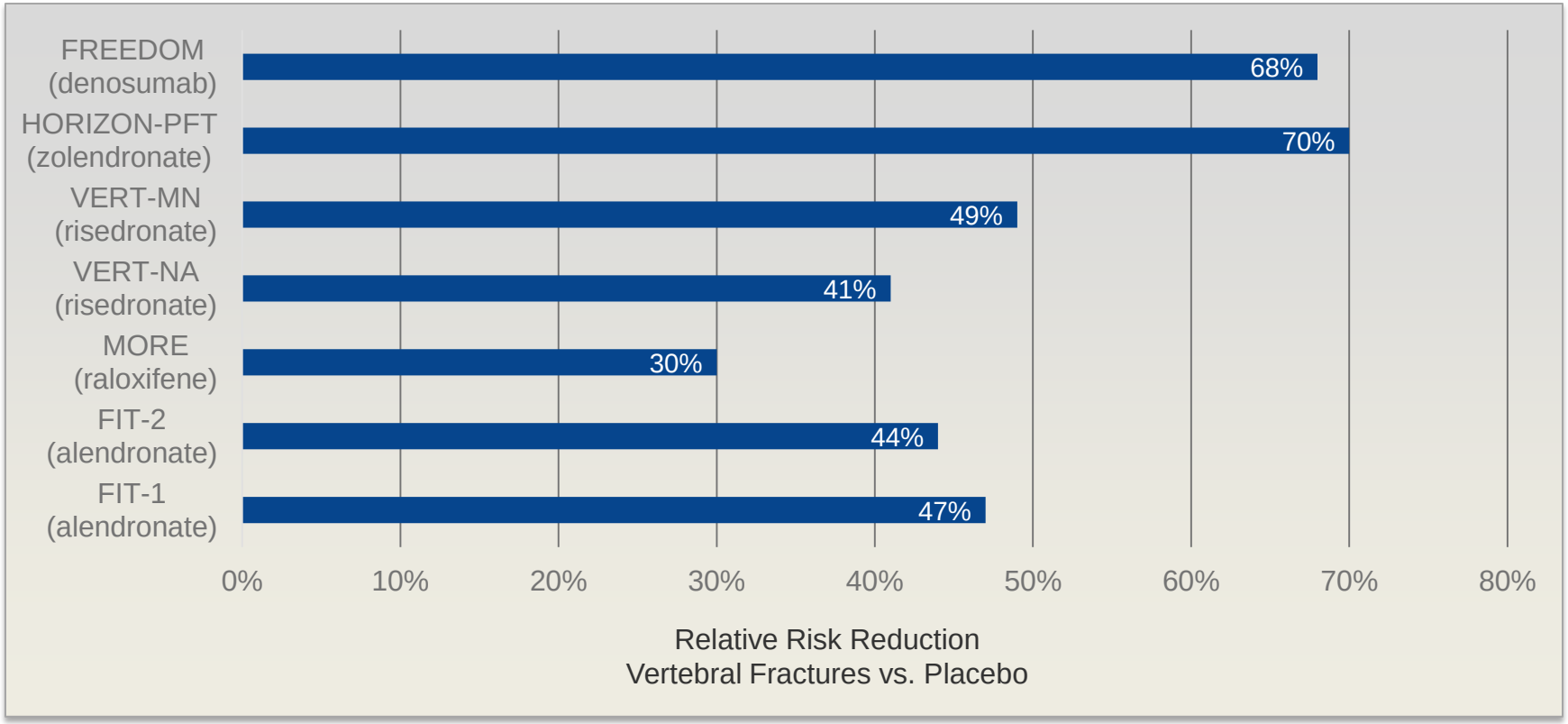
Therapeutic Options for Fracture Prevention in PMO Women[1*†]

Type of Fracture	Anti-resorptive Therapy						Bone Formation Therapy
	Bisphosphonates			Denosumab	Raloxifene	Estrogen (Hormone Therapy)‡	Teriparatide
	Alendronate	Risedronate	Zoledronic Acid				
Vertebral	✓	✓	✓	✓	✓	✓	✓
Hip	✓	✓	✓	✓	–	✓	–
Nonvertebral[Δ]	✓	✓	✓	✓	–	✓	✓
Route of Administration	Oral	Oral	IV infusion	Subcutaneous injection	Oral	Oral	Subcutaneous injection

* Based on GRADE A evidence as assessed in the Osteoporosis Canada 2010 Clinical Practice Guidelines for the Diagnosis and Management of Osteoporosis in Canada
† For postmenopausal women, ✓ indicates first-line therapies and Grade A recommendations
‡ Hormone therapy (estrogen) can be used as first-line therapy in women with menopausal symptoms
Δ In clinical trials, nonvertebral fractures are a composite endpoint including hip, femur, pelvis, tibia, humerus, radius, and clavicle

1. Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

Fracture Risk Reduction in Clinical Trials

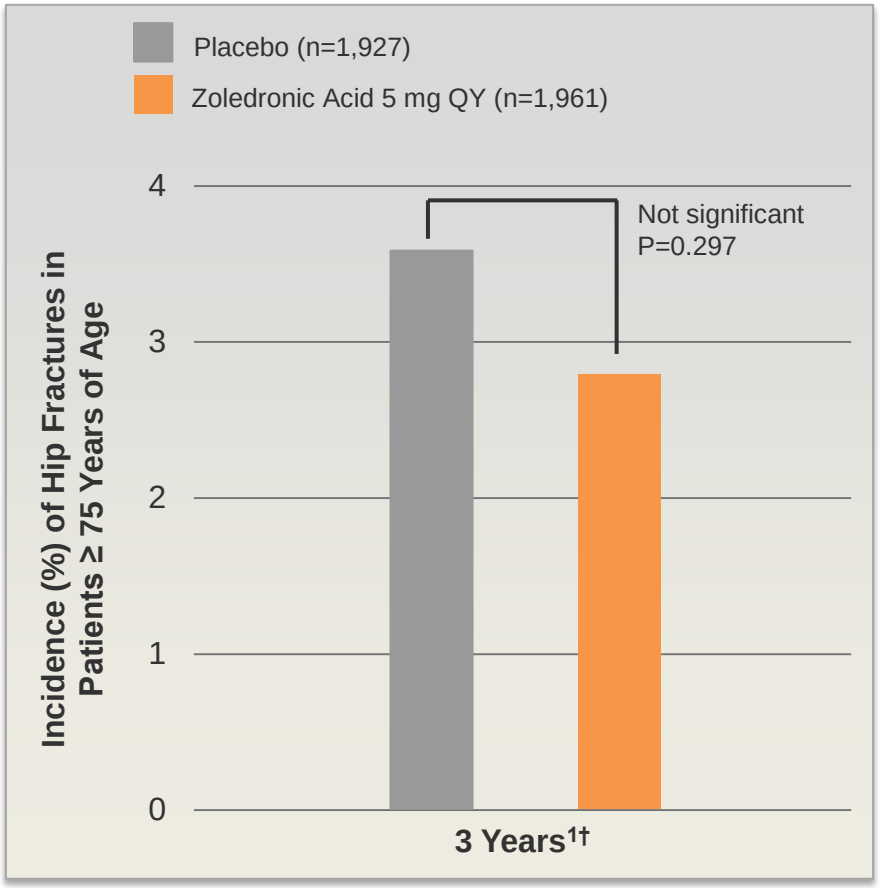


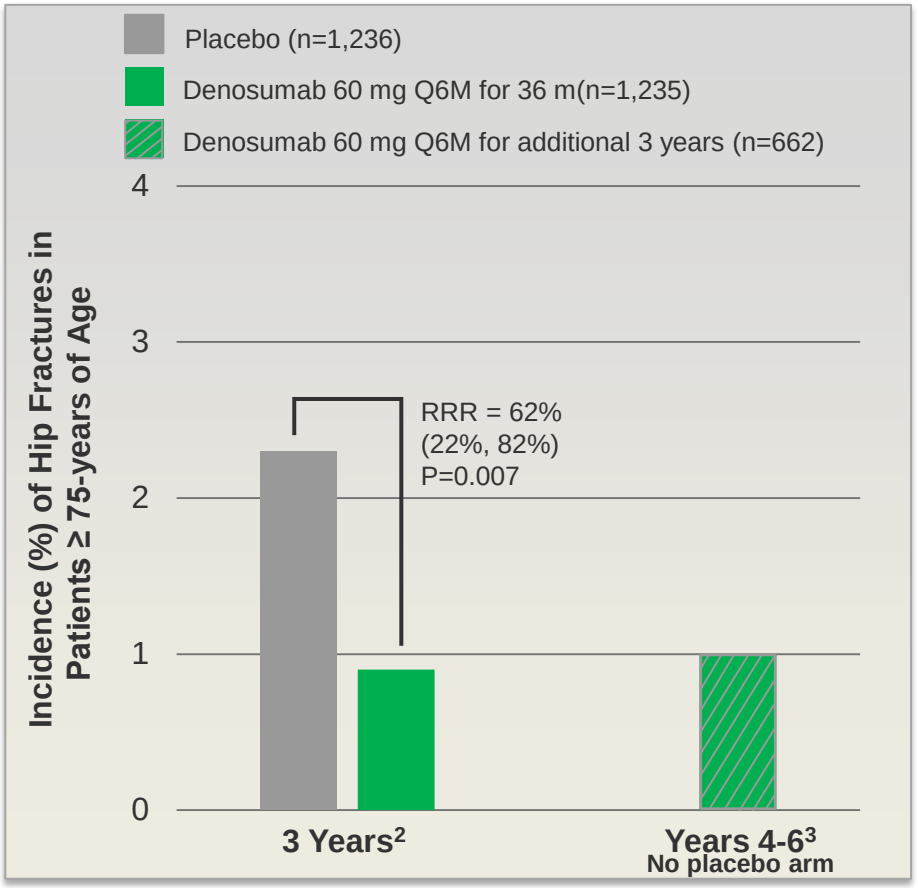
These data are not meant to predict fracture efficacy difference between the antiresorptive therapies.
Head-to-head fractures studies have not been conducted.

Data reported for 3 years of treatment with the exception of FIT-2 at 4 years

1. Black DM, et al. Lancet. 1996;348:1535–41 (FIT-1); 2. Cummings SR, et al. JAMA.1998;280(24):2077-82 (FIT-2); 3. Ettinger B, et al. JAMA. 1999;282:637-45 (MORE); 4. Harris ST, et al. JAMA.1999;282:1344-52 (VERT-NA); 5. Reginster J, et al. Osteoporos Int. 2000;11:83–91 (VERT-MN); 6. Black DM, et al. N Engl J Med. 2007;356:1809-22 (HORIZON-PFT); 7. Cummings SR, et al. N Engl J Med. 2009;361:756-765 (FREEDOM).

Effect of Anti-resorptive Therapy on Hip Fractures in Patients ≥ 75 Years Of Age*





* Post-hoc analysis of pivotal trials. †Data not available for this age group beyond 3 years. RRR=relative risk reduction

Adapted from: 1. Boonen S, et al. J Am Geriatr Soc. 2010;58(2):292-9. 2. Boonen S, et al. J Clin Endocrinol Met. 2011;96:1727-1736.
3. Papapoulos S, et al. Poster Presentation at ASBMR 2012.FR0391;SA0391.

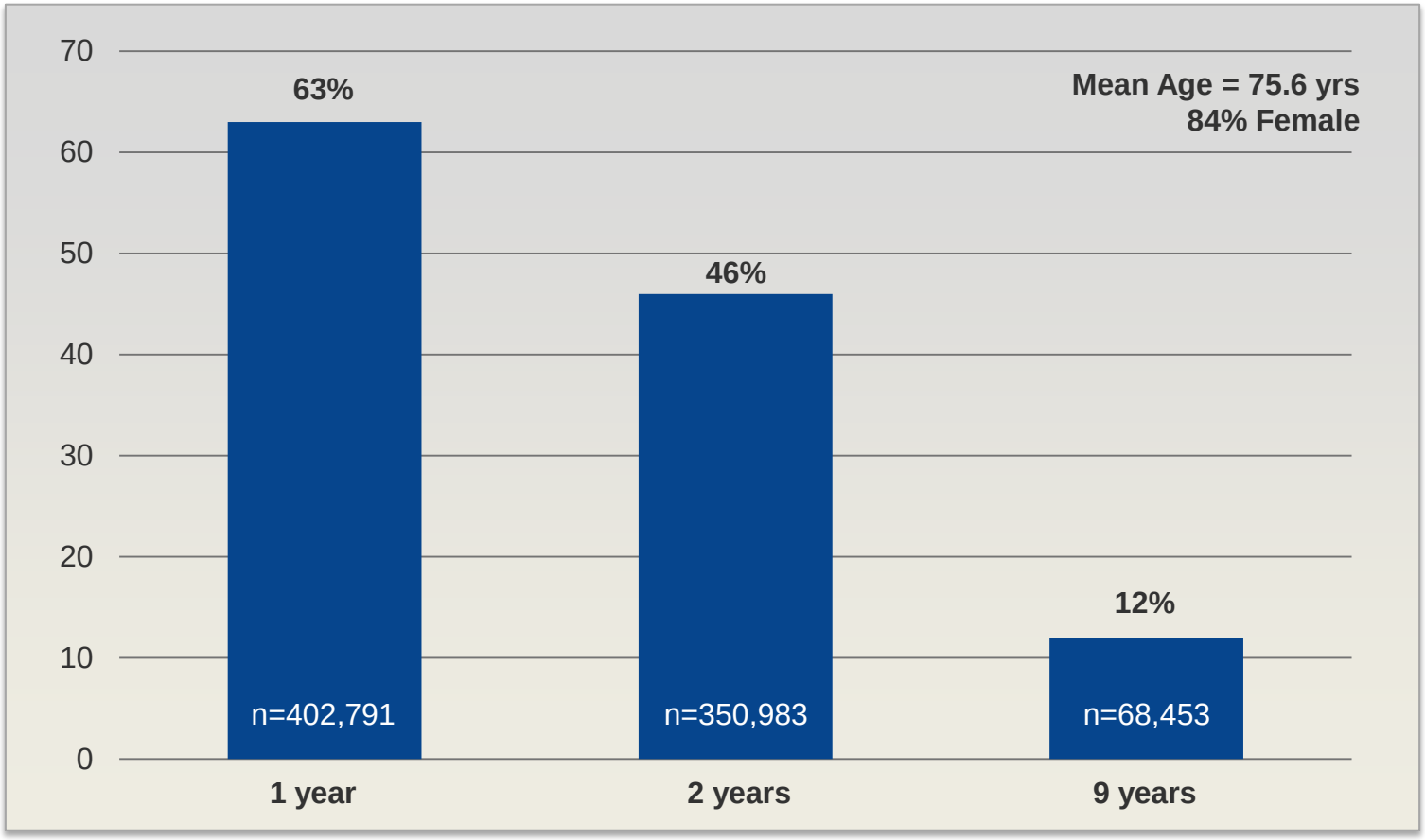
What if Alice was currently on therapy but…

- **was not adherent to her osteoporosis therapy?**
- **was intolerant of her oral bisphosphonates?**

What if Alice was not adherent to her OP therapy?

Adherence to Oral Bisphosphonates Is Poor

Percentage of New BP Users Persistent with Therapy over Time[1]



Estimations based on Ontario Drug Benefit pharmacy claims.
Persistence with therapy was defined as continuous treatment with no interruption exceeding 60 days.
BP=bisphosphonate

Burden AM, et al. Osteoporos Int. 2012;23(3):1075-82.

Factors Associated with Non-adherence to Therapy

In decreasing order of importance:[1]

- Side effects
- Concerns about BP therapy
- Dissatisfaction with medication
- Practical difficulties with BP therapy (dosing, fasting requirement and avoidance of co-administration with calcium)

1. Carr AJ, et al. Osteoporos Int. 2006;17:1638-1644.

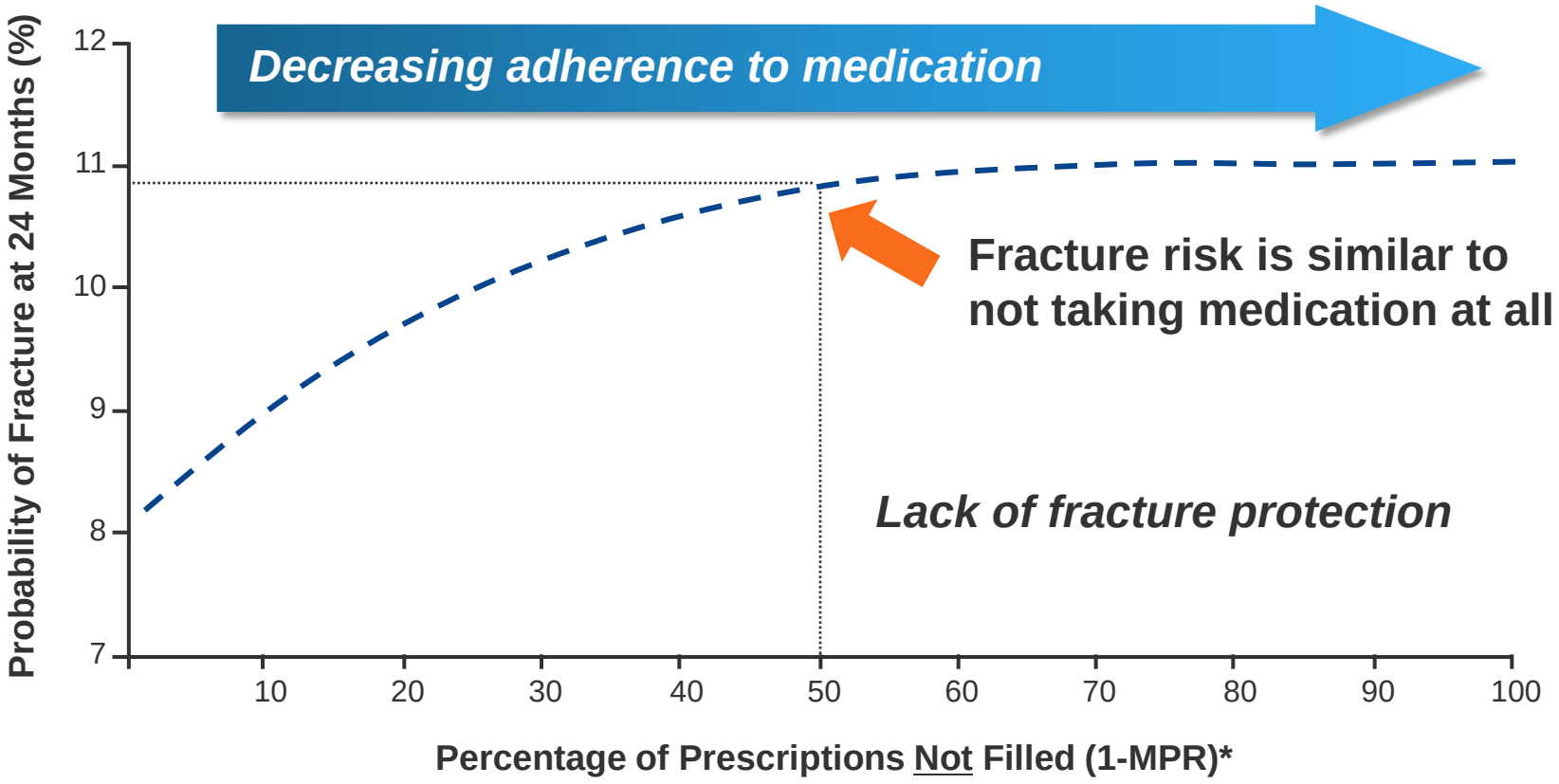
Oral Bisphosphonates Are Complex to Take

Instructions for oral BP‡

- Take in the morning, at least 1/2 hour before breakfast
- Remain sitting upright for at least 1 hour (in practice, 30 minutes is sufficient)
- Take only with water
- Take alone, with no other medications
- Calcium supplements should be taken at a different time

‡ Risedronate and Actonel delayed-release (DR) tablets need to be taken with food, best with breakfast.

In Order for Medication to Be Effective, Adherence Is Essential

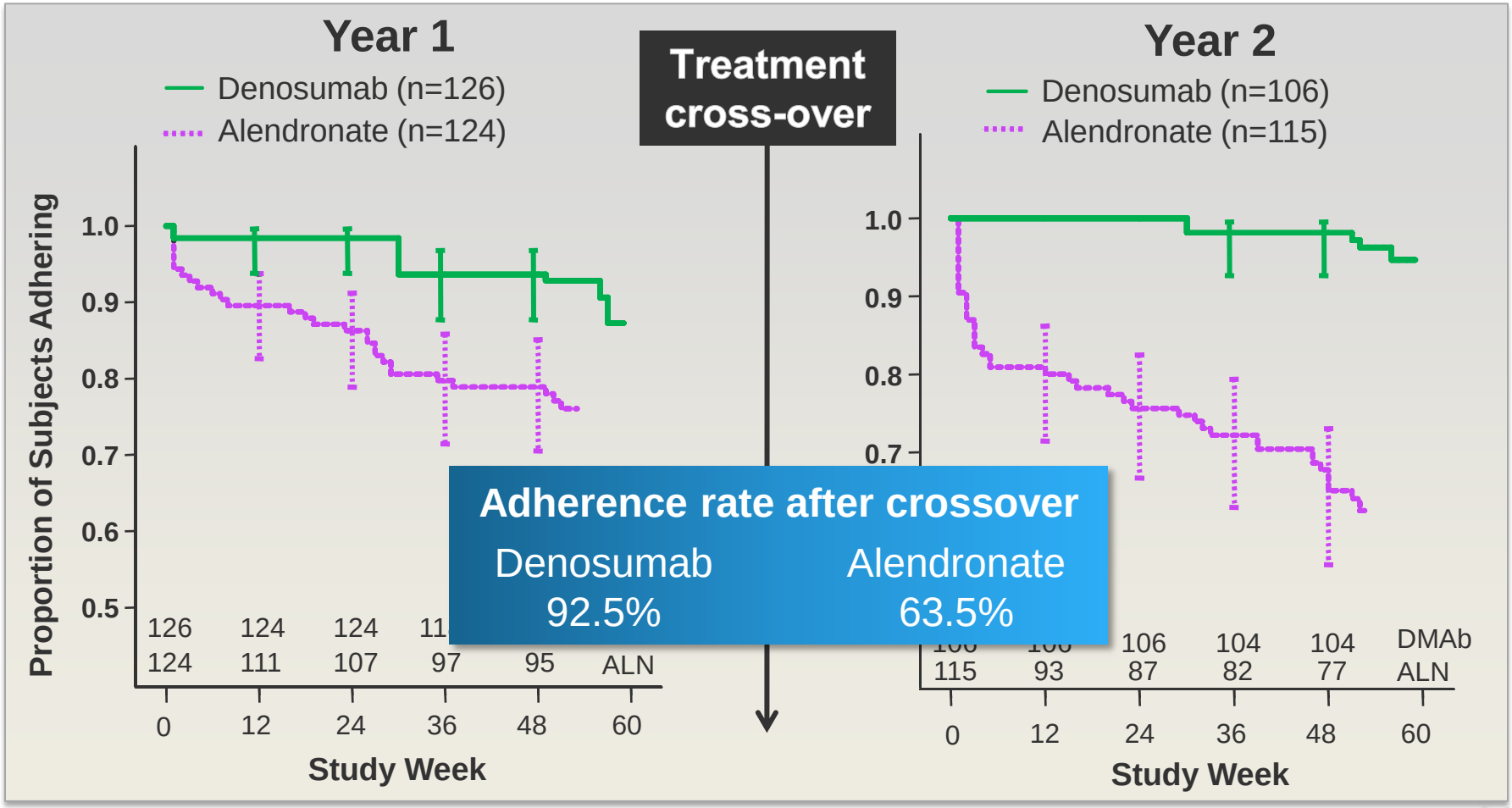


*MPR measures refill compliance: the percentage of time a medication was available.
MPR=medication possession ratio
Based on a study of 35,537 patients from two claims databases

1. Siris ES, et al. Mayo Clin Proc. 2006;81:1013-1022.

In Order for Medication to Be Effective, Adherence Is Essential

Open-label, Randomized, Cross-over Study of Denosumab Subcutaneous 60 mg Q6M and Oral Alendronate 70 mg QW

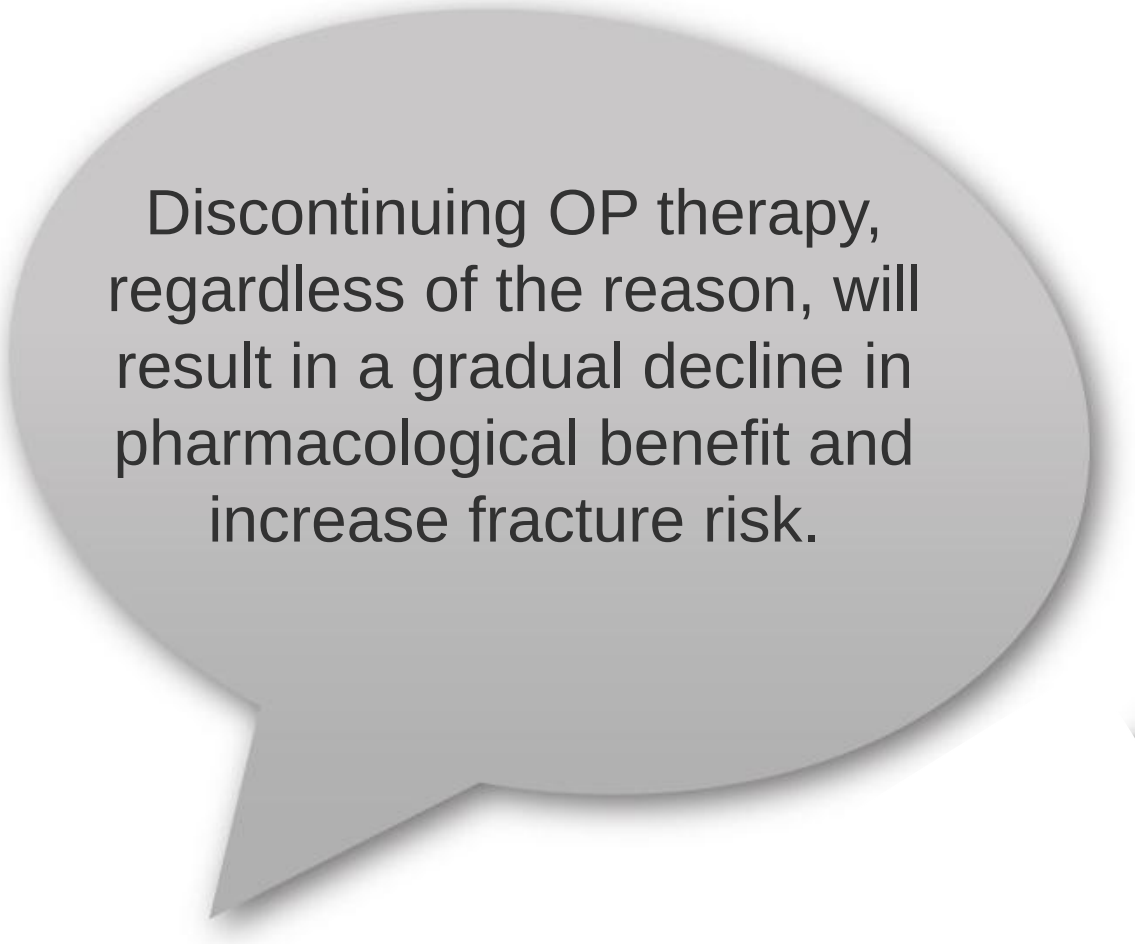


For each treatment group, time points with > 95% cumulated subjects were excluded

Freemantle N, et al. Osteoporos Int. 2012;23(1):317-26.

What if Alice was intolerant of her oral BP?

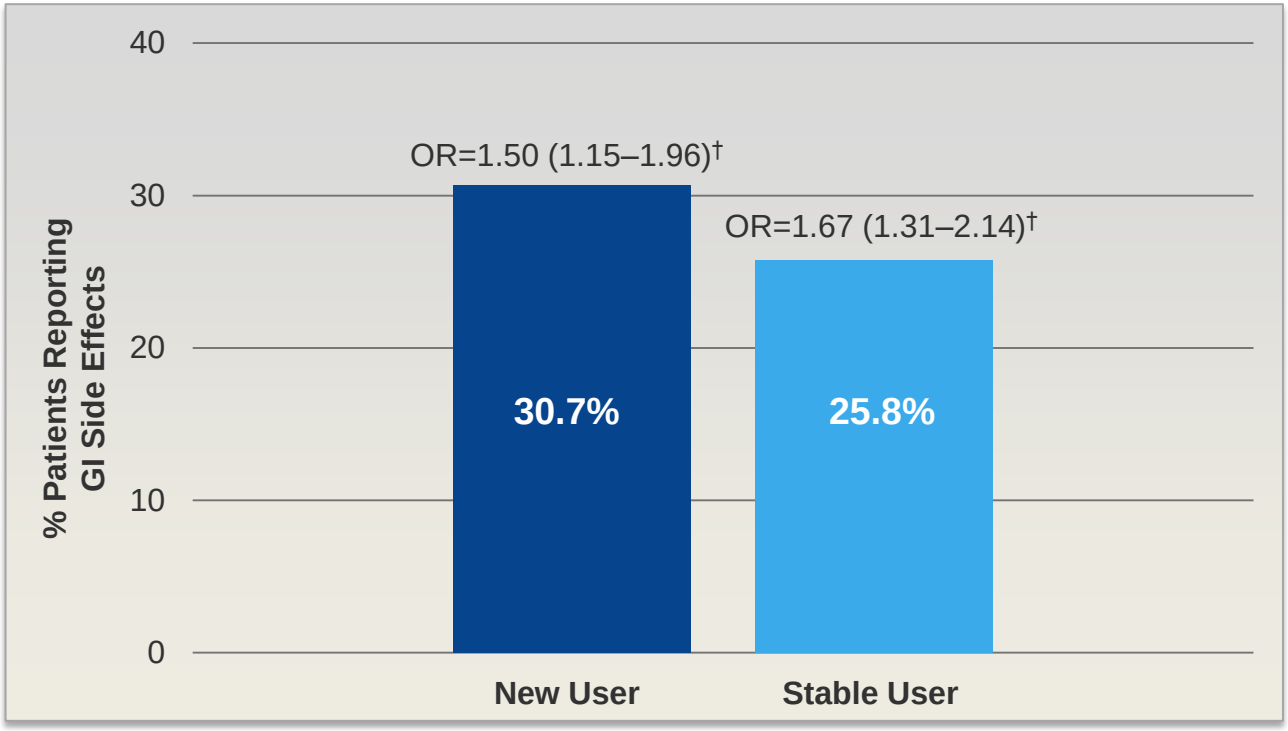
Is There a Link between Intolerance and Fracture Risk?



Papaioannou A, et al. CMAJ. 2010;182:1864-1873.
Brown JP, et al. Can Fam Physician. 2014;60:324-333.

Bisphosphonate Users, New or Stable, Are More Likely to Report GI Side Effects which May Impact Adherence

Reported GI SEs (%) at Month 6* among Patients in the POSSIBLE US Study Who Are New to and Stable on Osteoporosis Therapies[1]



Generic agents also may not be as well tolerated as the branded version[2]

* % reporting GI side effects at baseline: New=20%; Stable=21.5%
† Odds ratio for reporting a GI side effect among BP users compared to non-BP users

1. Woo C, et al. Curr Med Res Opin. 2010;26:1003-9.
2. Kanis JA, et al. Osteoporos Int. 2012;23(1):213-21.
3. Steering Group Communications. Mar. 5, 2012.

Patients with GI Problems Have Poorer Treatment Adherence to Osteoporosis Medications, Lower Treatment Satisfaction and Quality of Life

At baseline:

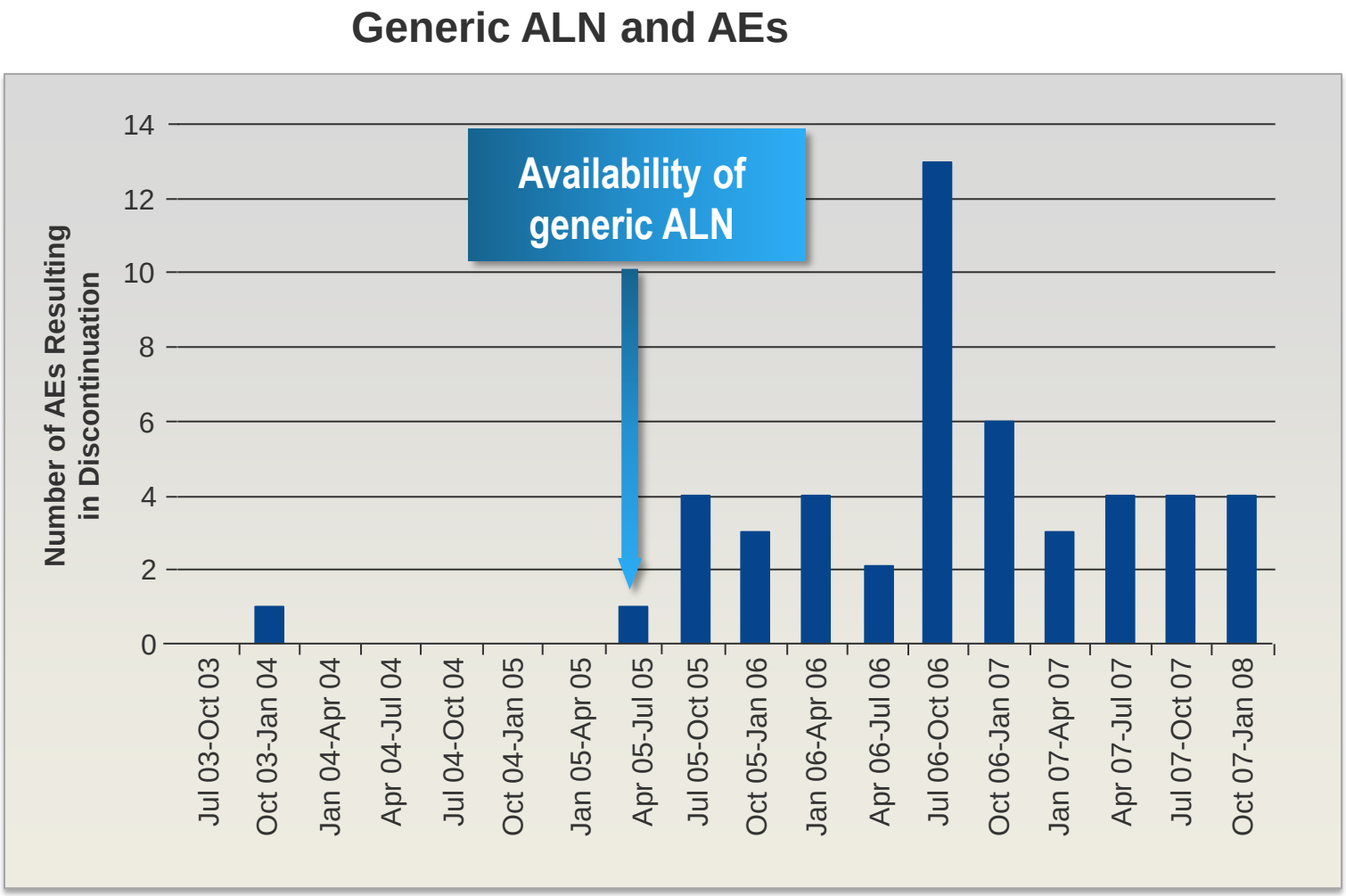
- GI problems prevalent in 69.4% of patients on BP treatment

Patients with GI problems consistently showed a lower medication adherence, QoL and treatment satisfaction, as measured by patient surveys (ADEOS, EQ-5D, OPSAT-Q) †

MUSIC-OS: Multi-objective prospective observational international study survey in 2,959 treated patients. Survey administered at study enrolment (baseline), and 3, 6 and 12 months after enrolment.
†ADEOS measure of adherence; EQ-5D measure of QoL; OPSAT-Q measures treatment satisfaction.

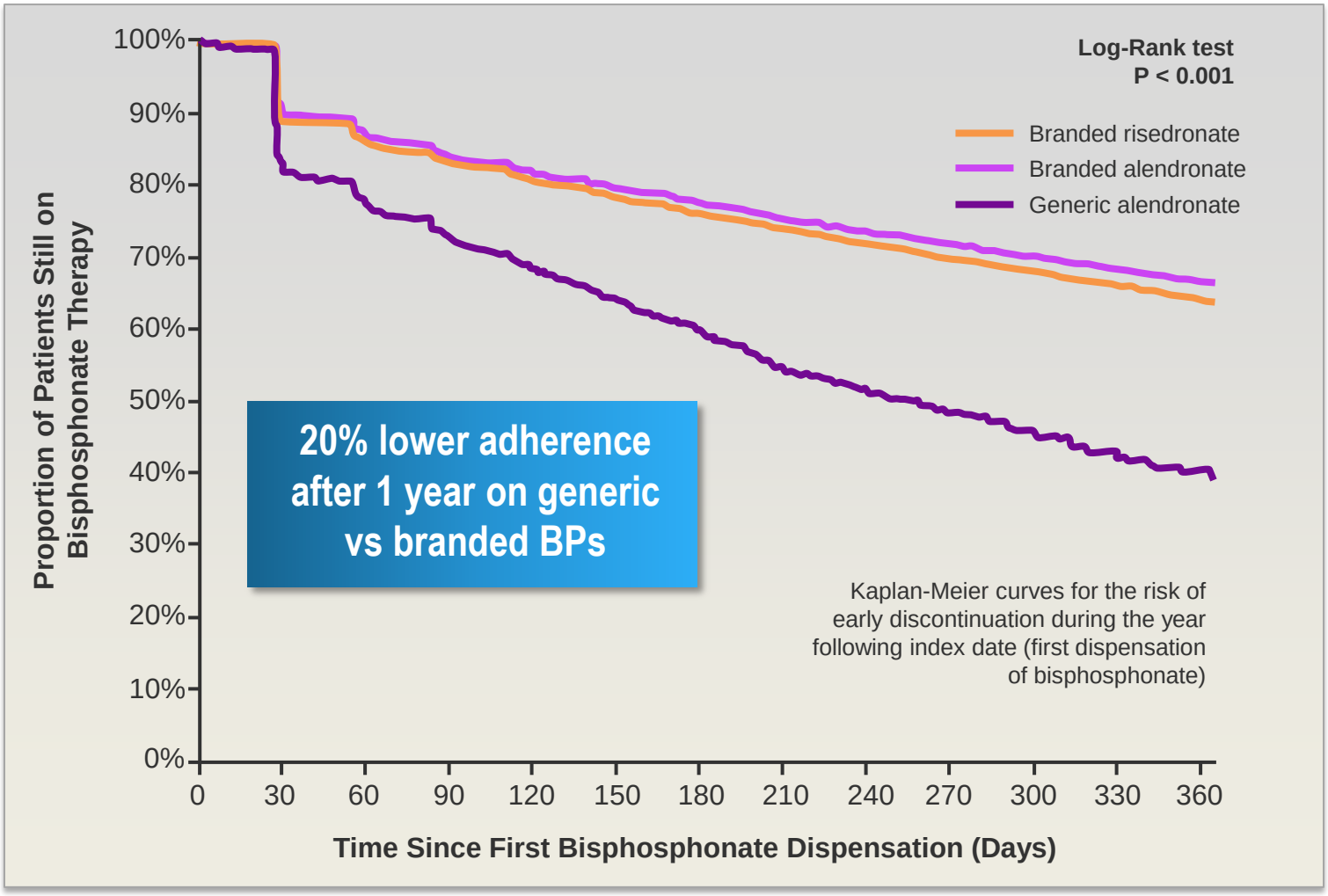
Adachi J, et al. ECTS. 2014;PP303.

Possible Reasons for OP Medication Intolerance



Grima DT, et al. BMC Musculoskelet Disord. 2010;11:68.

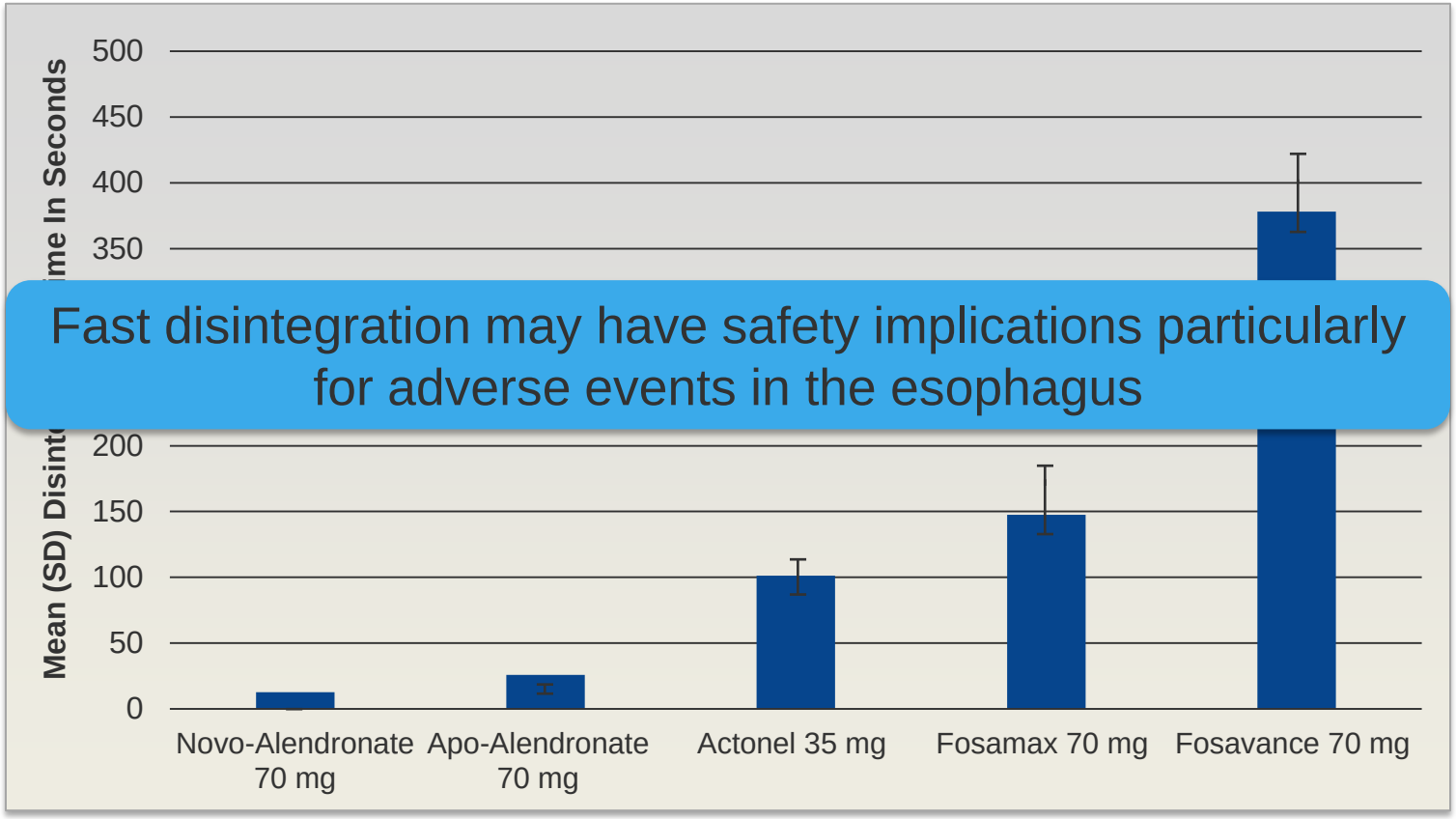
Persistence to Oral vs Generic Bisphosphonates



Kanis JA, et al. Osteoporos Int. 2012;23:213-221.

Disintegration Rates Differ Between Generic and Branded Therapies

Generic compounds disintegrated significantly faster than branded versions – at a rate similar to that for tablets designed for disintegration in the mouth (<30 seconds)



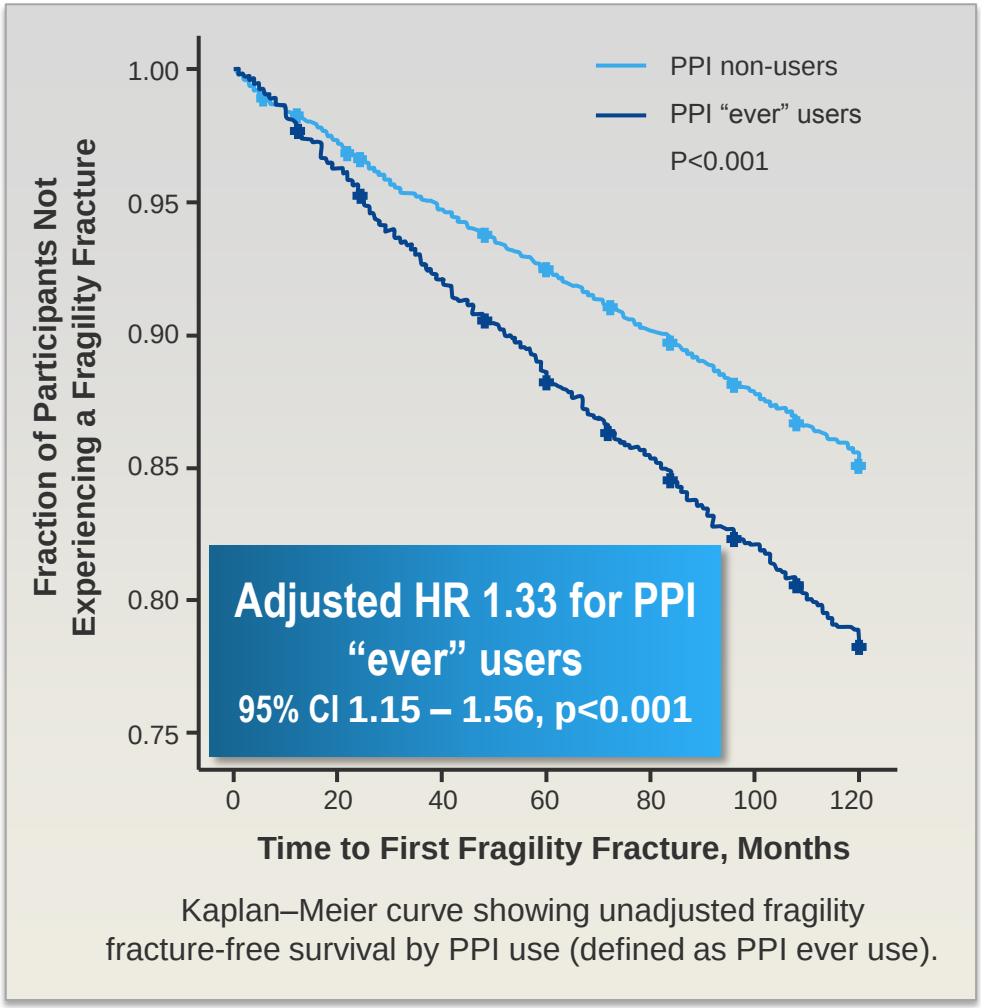
Fosavance (ALN+vit D) had a significantly slower disintegration time than all other tablets

Olszynski WP, et al. J Bone Miner Res. 2010;25;S124.

Managing BP Intolerance with PPIs May Increase Fracture Risk

Potential mechanisms by which PPI therapy causes an increase in fracture risk include:†

- Interference with Ca^{2+} absorption
- Direct action of PPI in skeletal cells (osteoclasts)



Kaplan–Meier curve showing unadjusted fragility fracture-free survival by PPI use (defined as PPI ever use).

PPI=proton pump inhibitor. P-value from the log rank test.
†Exact mechanism is not understood

Fraser LA, et al. Osteoporos Int. 2013;24:1161-1168.

Medications Known to Cause/Accelerate Bone Loss*

- Proton pump inhibitors (PPI)
- Selective serotonin reuptake inhibitors (SSRIs)
- Glucocorticoids (GCs), past or present use
- Aromatase inhibitors
- Antipsychotic drugs
- Hormonal/endocrine therapies - (GnRH, agonists, LHRH analogs)

* Note: Not an exhaustive list

1. Lee RH, et al. Am J Geriatr Pharmacother. 2010 Feb;8(1):34-46. 2. Crews MP, et al. Hum Psychopharmacol. 2012 Jan; 27(1):15-23. 3. Papaioannou A, et al. CMAJ. 2010;182:1864-1873. 4. Mayer EL. Am Soc Clin Oncol Educ Book. 2013:9-14. 5. Drinka PJ, et al. J Am Med Dir Assoc. 2007 Jun; 8(5):328-31. 6. Targownik LE, et al. CMAJ. 2008;179(4):319-326. 7. Wu Q, et al. Osteoporos Int. 2012 Jan; 23(1):365-75. 8. Ruddock B. CPJ/RPC. 2004;137:17-18.

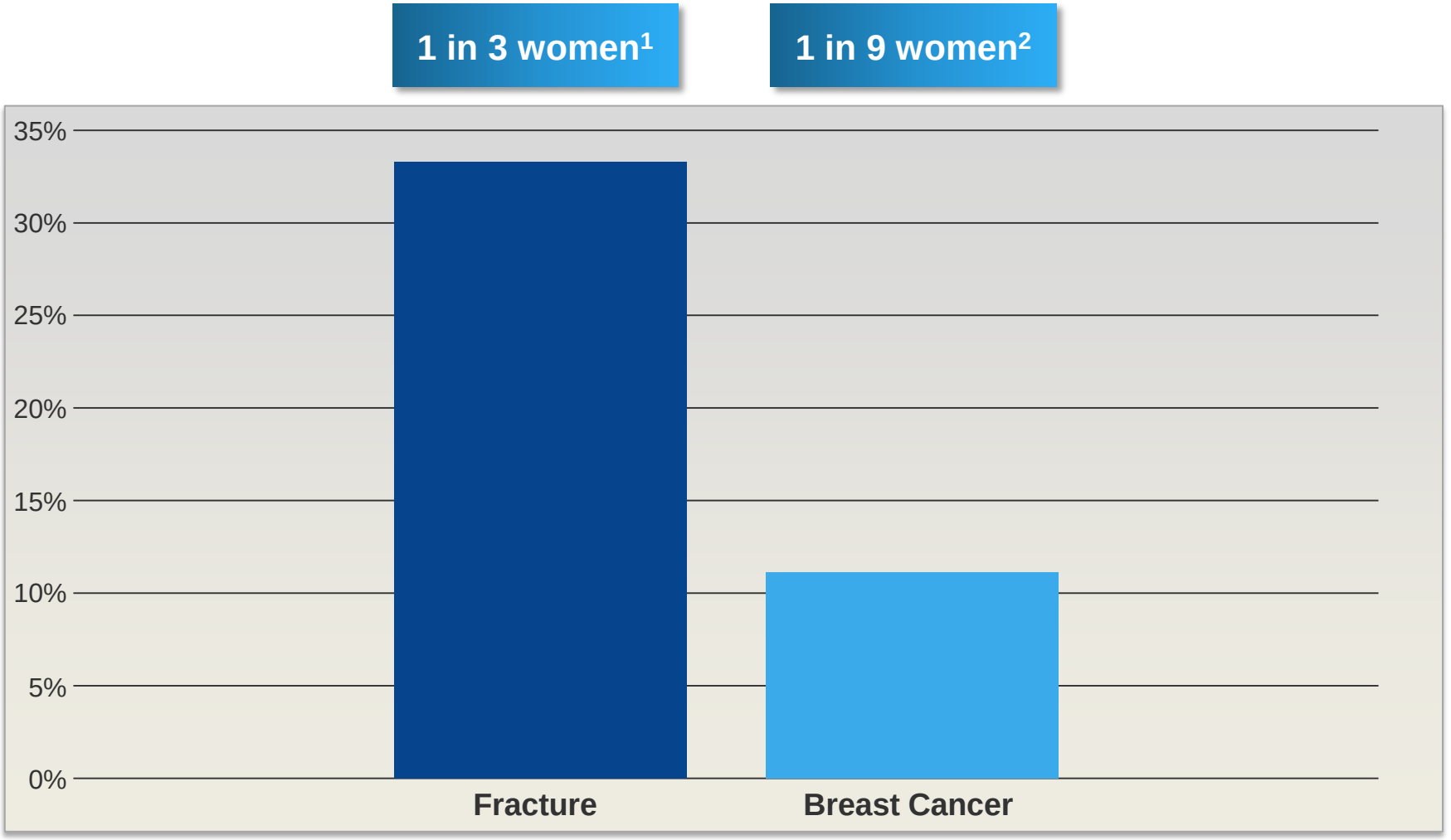
Alice 5 Years Earlier

Why is it important to ask about fractures in women after the age 50?

Over 80% of all fractures in people 50 years and older are caused by osteoporosis.

Osteoporosis Canada Facts & Statistics. www.osteoporosis.ca. Accessed: October 5, 2013.

Osteoporosis in Perspective: Lifetime Risk of Fracture in Women is High

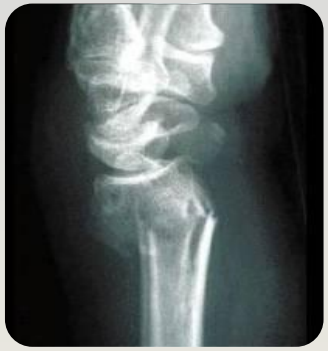


1. Osteoporosis Canada Facts & Statistics. http://www.osteoporosis.ca/osteoporosis-and-you/osteoporosis-facts-and-statistics/. Accessed July 3, 2014.
2. Breast Cancer Society of Canada Statistics. http://www.bcsc.ca/p/46/l/105/t. Accessed July 3, 2014.

What Are the Consequences of Underdiagnosing and Undertreating Osteoporosis?

In women with hip fracture:

Fracture begets future fracture



40% had prior fracture[1]

Deteriorated quality of life

40% need assistance walking[2]

Long-term care admission

18% enter LTC[3]

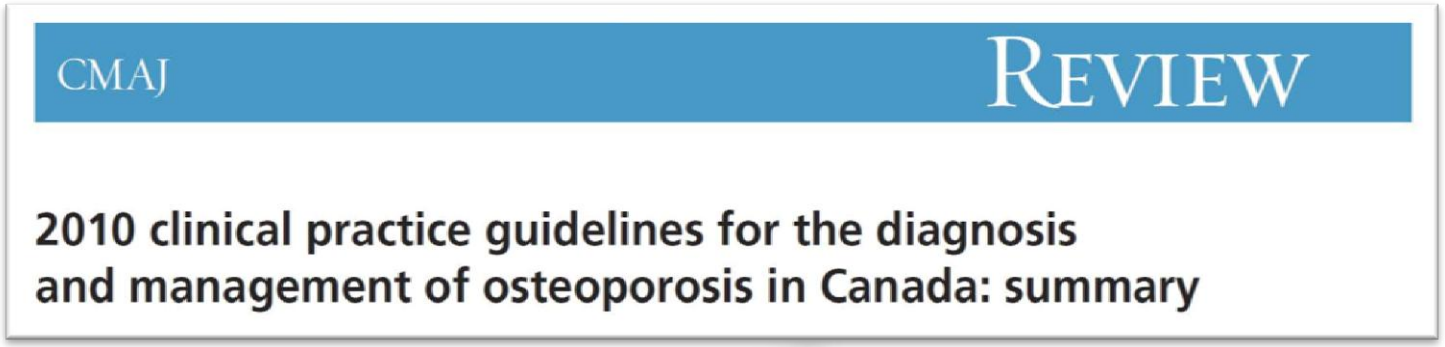
Mortality

23% die within 1 year[4]

Lifetime risk of hip fracture in women > 50 years is 12.1%[5]

1. Hajcsar EE, et al. CMAJ. 2000;163:819-822. 2. Cooper C, et al. Am J Med.1997;103:12S-19S. 3. Jean S, et al. JBMR. 2012; Available from: September 2012. 4. Ioannidis G, et al. CMAJ. 2009;181:265-271. 5. Hopkins RB, et al. Osteoporos Int. 2012;23:921-927.

Focus on Fractures



"Fragility fracture increases the risk of further fractures and should be considered in the assessment."

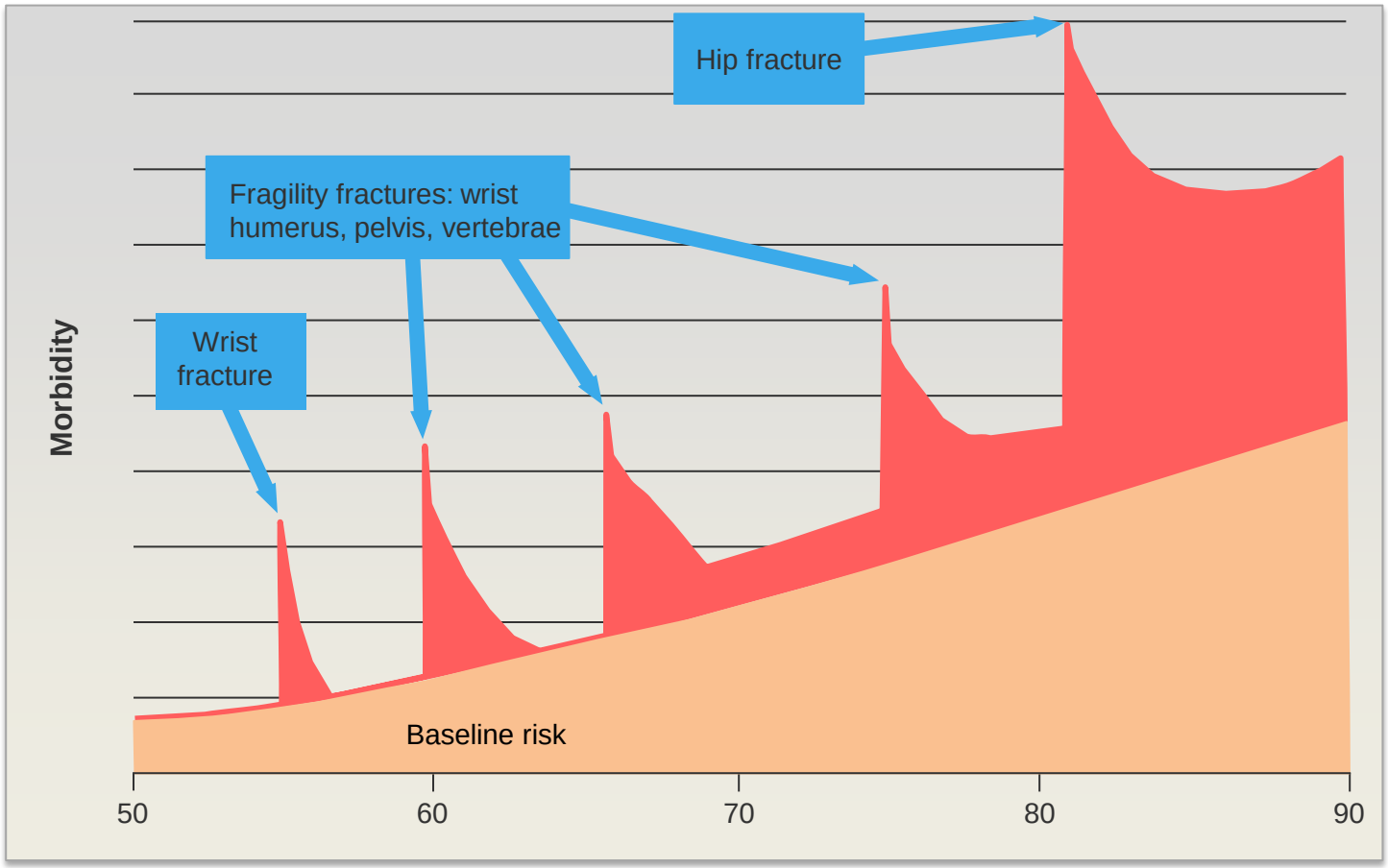
Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

Fracture Continuum: Several Fragility Fractures May Precede the Hip Fracture

Wrist Fracture Most Likely Related to OP

Fragility Fracture Increases Risk of Hip Fracture

40% of Hip Fractures Are Preceded by a Fragility Fracture



Adapted from: Kanis JA, Johnell O. J Endocrinol Invest. 1999;22(8):583-8.

Are We Missing Patients at High Risk of Fracture in Our Practice?

Ask your patient at each visit:

1. Have you fallen?
2. Have you had a fracture?

- Supplementary questions:
  - Are you taking medication that increases fracture risk?
  - Do you smoke?
  - Do you consume excess alcohol?
  - Do you have a chronic inflammatory disorder?
  - Do you have other conditions that may make you fall, such as dizziness, Parkinson’s, hypotension, nocturia, osteoarthritis?
  - Have you lost height in the last year or more?

Closing the Care Gap

"Worldwide, there is a large care gap that is leaving millions of fracture patients at serious risk of future fractures. Capture the Fracture hopes to close this gap and make secondary fracture prevention a reality."

John A. Kanis, President, International Osteoporosis Foundation

Capture the Fracture promotes secondary fracture prevention by facilitating the development of:

- Standards for best practice (framework)
- Change at the national level (guides/toolkits)
- Awareness

Adapted from: http://www.capturethefracture.org. Accessed June 18, 2014.

What if Alice…

broke her wrist at age 50?

had a risk assessment based on BMD alone?

What if Alice was not treated for osteoporosis after she broke her wrist at age 50?

Efforts of Key Osteoporosis Organizations Are Focusing on High Risk Patients and Secondary Fracture Prevention…

ASBMR Task Force Report on Secondary Fracture Prevention

John A Eisman,[1] Earl R Bogoch,[2] Rick Dell,[3] J Timothy Harrington,[4] Ross E McKinney Jr.,[5] Alastair McLellan,[6] Paul J Mitchell,[7] Stuart Silverman,[8] Rick Singleton,[9] and Ethel Siris[10] for the ASBMR Task Force on Secondary Fracture Prevention

"Making the First Fracture the Last Fracture."

"*The occurrence of a fragility fracture needs to be linked automatically with provision of post fracture assessment for osteoporosis, future fracture risk, and need for treatment to prevent secondary fractures.*"

ASBMR: American Society for Bone and Mineral Research

Eisman JA, et al. for the ASBMR Task Force on Secondary Fracture Prevention. J Bone Miner Res. 2012;27(9):1-9.

Previous Fractures Increase the Risk for Subsequent Fractures

- Having one prior fracture (wrist) doubles the risk of sustaining a second incident fracture
- Compared with women with no previous fractures, women with 1, 2, or 3 prior fractures were 1.8-, 3.0-, and 4.8-fold more likely to have any incident fracture
- Based on previous fracture, risk of fracturing at hip and spine is twice as high

Gehlbach S, et al. J Bone Miner Res. 2012;27:645-653.

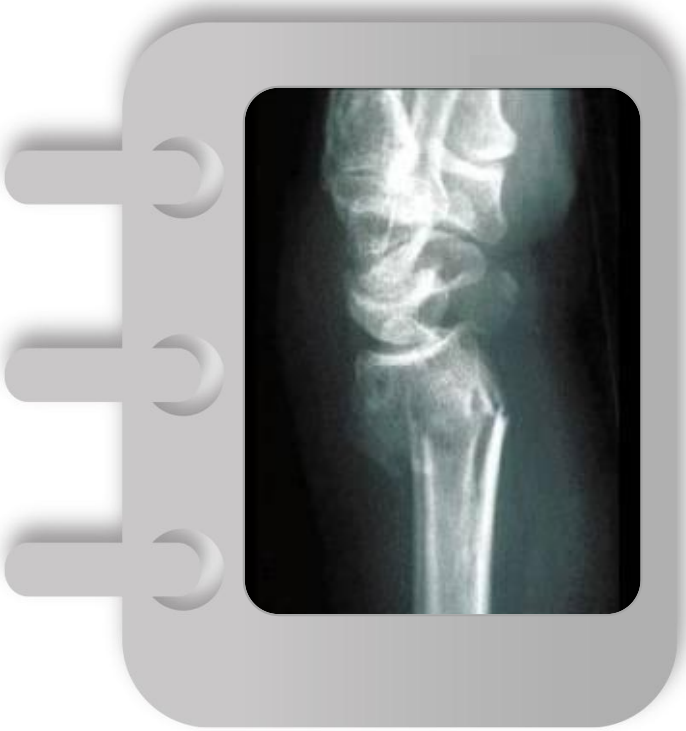
Data based on n=51,296

Understanding a Fragility Fracture Is Critical

Definition of a fragility fracture*:

A fracture that occurs spontaneously or following a minor trauma such as:

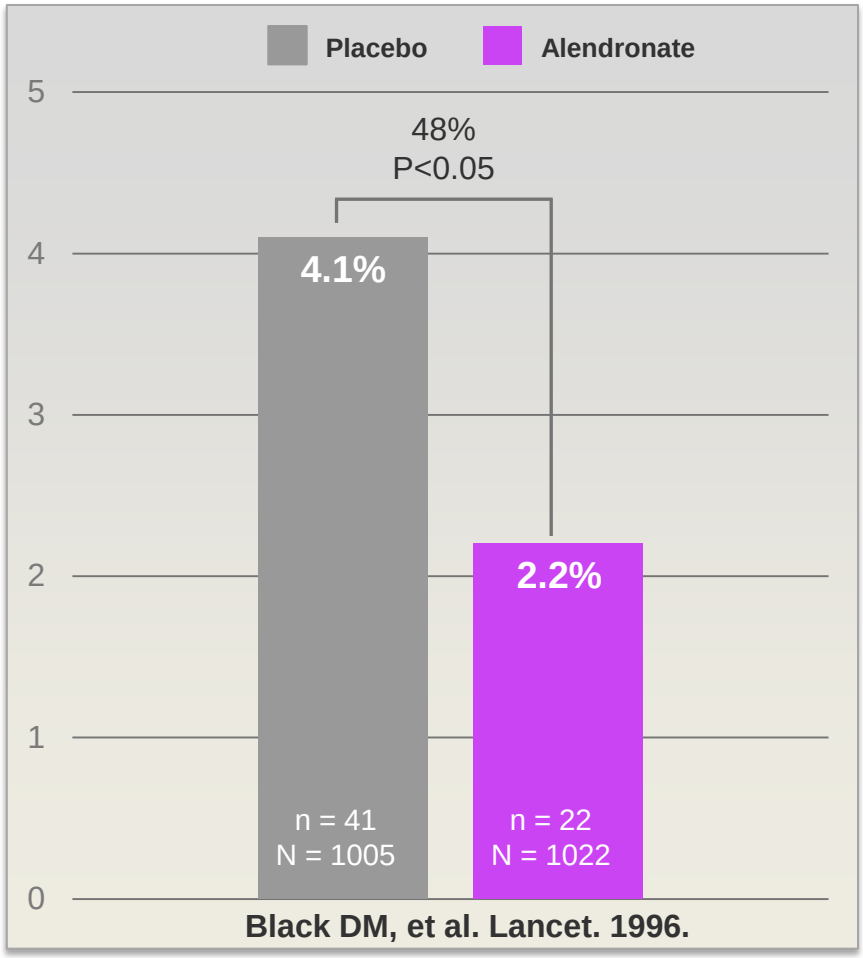
- Fall from a standing height (i.e. on the ice)
- Fall from a sitting position
- Fall from a supine position (bed or reclining deck chair < 1 metre high)
- Fall after having missed 1 to 3 steps in a staircase
- After a movement outside of the typical plane of motion or coughing



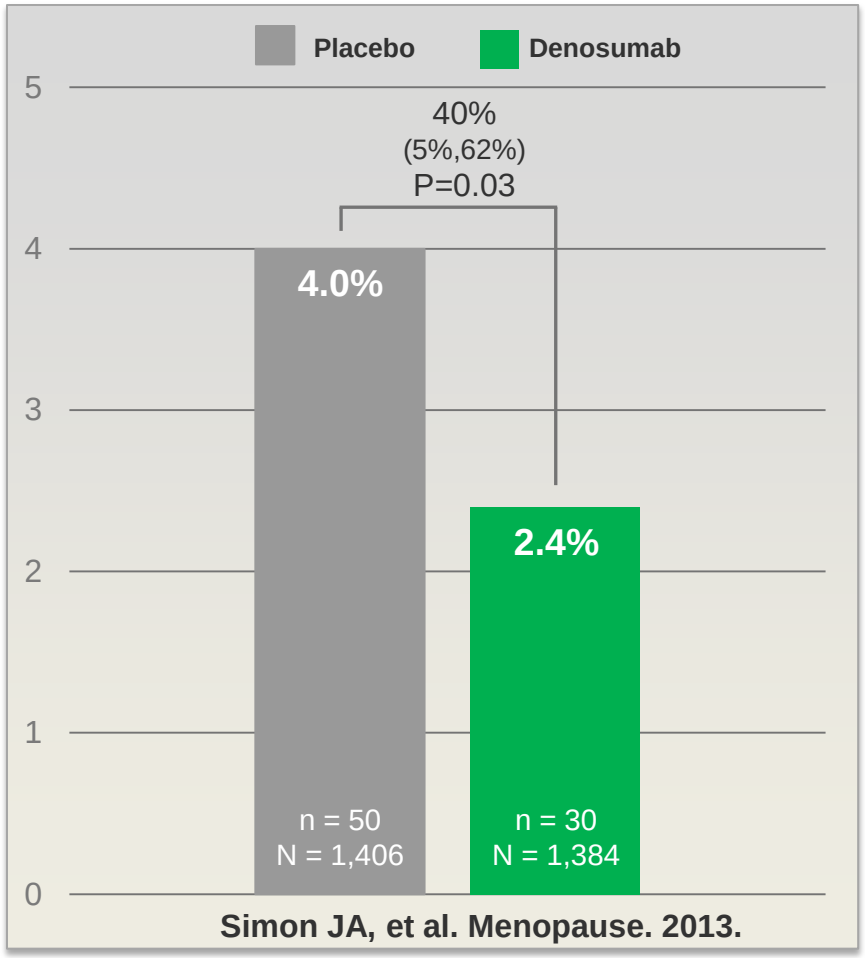
* Fragility fracture includes all bones, except skull and face, patella, hands and feet, cervical spine

1. Bessette L, et al. Contemp Clin Trials. 2008; 29:194-210.
2. Brown JP, et al. J Bone Miner Res. 2007;23(Suppl 1):M350.

Decrease in Incidence of Wrist Fractures in High Risk‡ Patients at Month 36



Black DM, et al. Lancet. 1996.



Simon JA, et al. Menopause. 2013.

‡ At baseline, patients had femoral neck BMD ≤-2.5; Relative risk reduction (95% CI)
n=number of patients with ≥ 1 wrist fracture; N=number of randomized patients; CI=confidence interval
Studies are not head-to-head comparisons and thus cannot be directly compared. Simon et al. is a post-hoc analysis.

1. Black DM, et al. Lancet. 1996;348:1535-1541.
2. Simon JA, et al. Menopause. 2013:20;130-137.

What if Alice was not considered high risk based on BMD alone?

Fracture Risk Assessment

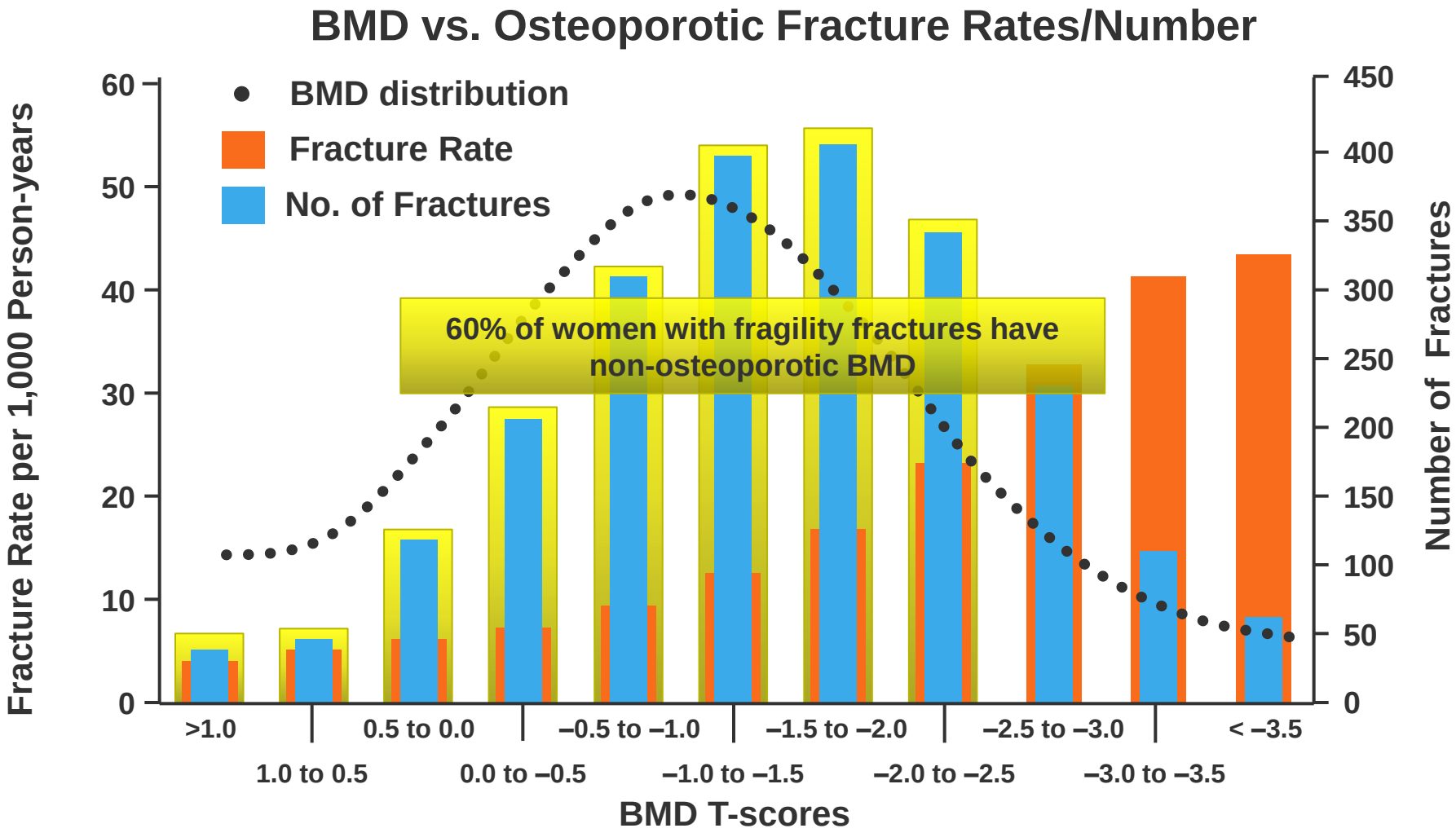
CMAJ REVIEW

2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary

"To address this care gap for high-risk patients, the 2010 guidelines concentrate on the assessment and management of women and men over age 50 who are at high risk of fragility fractures and the integration of new tools for ***assessing the 10-year risk of fracture*** *into overall management."*

Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

Other Risk Factors Must Be Considered as BMD Alone Does Not Explain Fracture Risk



Adapted from Siris ES, et al. JAMA. 2001;286:2815-22.

Risk Factors for Fracture Risk Assessment

CAROC*	FRAX®‡
Risk Factors: • Sex • Age • BMD • **Fragility fracture after 40** • Systemic glucocorticoid use (≥3 months)†	**Additional Risk Factors:** • Low BMI • Parental history of fracture (especially hip) • Current smoking • Alcohol intake ≥ 3 units/day • Rheumatoid arthritis, or other secondary causes of osteoporosis

- Both tools are recognized by Osteoporosis Canada as validated methods for the prediction of fracture risk, with 90% concordance between results
- CAROC may add simplicity, requiring only 5 parameters
- FRAX® can be used in the absence of BMD
- Evidence supports that FRAX® can be used to assess fracture risk in patients on treatment[2]
- FRAX® has country-specific tools; ensure the Canadian version is used

*Canadian Association of Radiologists and Osteoporosis Canada, 2010
† ≥3 months in the prior year of a prednisone equivalent dose ≥ 7.5 mg daily
‡ Fracture Risk Assessment Tool of the World Health Organization

1 Papaioannou A, et al. CMAJ. 2010;182:1864-1873; 2. Leslie WD, et al. J Bone Miner Res. 2012;27:1243-1251.

Clinical Risk Factors that Identify Patients at High 10-year Fracture Risk without Use of CAROC/FRAX®

Patients with:

- Hip fractures
- Vertebral fractures
- ≥1 fragility fractures
- 1 fragility fracture + steroid use†

†At least three months cumulative therapy in the previous year at a prednisone-equivalent dose ≥ 7.5 mg daily.

Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

5 Years Earlier: Fracture Risk Assessment

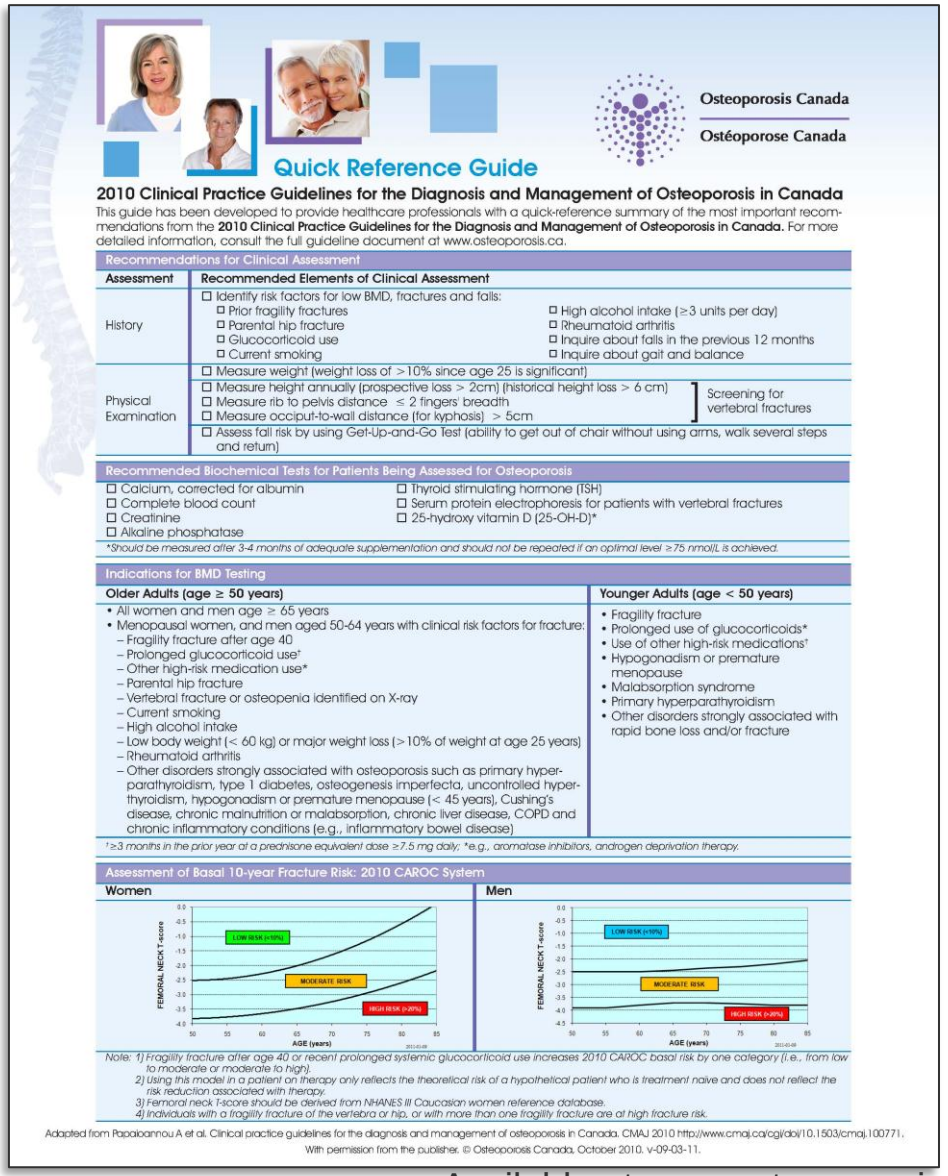
Key Aspects of Fracture Risk Assessment

- Ask about broken bones, falls, back pain and corticosteroid use
- Look for kyphosis and evidence of height loss
- Imaging and labs

1. Siminoski K, et al. Osteoporos Int. 2006;17:290-6.
2. Papaioannou A, et al. CMAJ. 2010;182:1864-1873.
3. Timed up-and-go test. Available at: http://www.saskatoonhealthregion.ca/pdf/03_Timed%20Up%20and%20Go%20procedure.pdf

Existing Tools Are Available from Osteoporosis Canada

Quick Reference Guide for Diagnosis and Management of Osteoporosis in Canada: 2010 Clinical Practice Guidelines



Osteoporosis Canada
Ostéoporose Canada

Quick Reference Guide

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

This guide has been developed to provide healthcare professionals with a quick-reference summary of the most important recommendations from the **2010 Clinical Practice Guidelines for the Diagnosis and Management of Osteoporosis in Canada.** For more detailed information, consult the full guideline document at www.osteoporosis.ca.

Recommendations for Clinical Assessment

Assessment	Recommended Elements of Clinical Assessment
History	☐ Identify risk factors for low BMD, fractures and falls: ☐ Prior fragility fractures ☐ Parental hip fracture ☐ Glucocorticoid use ☐ Current smoking ☐ High alcohol intake (≥3 units per day) ☐ Rheumatoid arthritis ☐ Inquire about falls in the previous 12 months ☐ Inquire about gait and balance
Physical Examination	☐ Measure weight (weight loss of >10% since age 25 is significant) ☐ Measure height annually (prospective loss > 2cm) (historical height loss > 6 cm) ☐ Measure rib to pelvis distance ≤ 2 fingers' breadth ☐ Measure occiput-to-wall distance (for kyphosis) > 5cm (Screening for vertebral fractures) ☐ Assess fall risk by using Get-Up-and-Go Test (ability to get out of chair without using arms, walk several steps and return)

Recommended Biochemical Tests for Patients Being Assessed for Osteoporosis

- ☐ Calcium, corrected for albumin
- ☐ Complete blood count
- ☐ Creatinine
- ☐ Alkaline phosphatase
- ☐ Thyroid stimulating hormone (TSH)
- ☐ Serum protein electrophoresis for patients with vertebral fractures
- ☐ 25-hydroxy vitamin D (25-OH-D)*

*Should be measured after 3-4 months of adequate supplementation and should not be repeated if an optimal level ≥75 nmol/L is achieved.

Indications for BMD Testing

Older Adults (age ≥ 50 years)

- All women and men age ≥ 65 years
- Menopausal women, and men aged 50-64 years 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 (< 60 kg) or major weight loss (>10% of weight at age 25 years)
  - Rheumatoid arthritis
  - Other disorders strongly associated with osteoporosis such as primary hyperparathyroidism, type 1 diabetes, osteogenesis imperfecta, uncontrolled hyperthyroidism, hypogonadism or premature menopause (< 45 years), Cushing's disease, chronic malnutrition or malabsorption, chronic liver disease, COPD and chronic inflammatory conditions (e.g., inflammatory bowel disease)

Younger Adults (age < 50 years)

- Fragility fracture
- Prolonged use of glucocorticoids*
- Use of other high-risk medications†
- Hypogonadism or premature menopause
- Malabsorption syndrome
- Primary hyperparathyroidism
- Other disorders strongly associated with rapid bone loss and/or fracture

†≥3 months in the prior year at a prednisone equivalent dose ≥7.5 mg daily; *e.g., aromatase inhibitors, androgen deprivation therapy.

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

Women

Men

Note: 1) Fragility fracture after age 40 or recent prolonged systemic glucocorticoid use increases 2010 CAROC basal risk by one category (i.e., from low to moderate or moderate to high).
2) Using this model in a patient on therapy only reflects the theoretical risk of a hypothetical patient who is treatment naive and does not reflect the risk reduction associated with therapy.
3) Femoral neck T-score should be derived from NHANES III Caucasian women reference database.
4) Individuals with a fragility fracture of the vertebra or hip, or with more than one fragility fracture are at high fracture risk.

Adapted from Papaioannou A et al. Clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. CMAJ 2010 http://www.cmaj.ca/cgi/doi/10.1503/cmaj.100771.
With permission from the publisher. © Osteoporosis Canada, October 2010. v-09-03-11.

Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

Available at www.osteoporosis.ca

Clinical Decisions:
The Challenge of the Moderate Risk Patient

Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

Top 5 Reasons to Consider Treatment in the Moderate Risk Patient[1]

1. Fracture: vertebral (asymptomatic vertebral fracture identified on lateral spine X-ray) or wrist fracture (in patient >65 or BMD ≤ -2.5)
2. Lumbar spine T-score << femoral neck T-score (by > 1SD)[2]
3. Concurrent high risk disorder or medications, including:
   - Hypogonadism or premature menopause (age <45 yr)
   - Primary hyperparathyroidism
   - Hyperthyroidism
   - Rheumatoid arthritis
   - Glucocorticoids (long-term or repeated use)
   - Aromatase inhibitor therapy
4. Falls (≥2 in the past year)
5. Patient preference to be treated

1. Steering Group Communications. Feb. 9, 2012 based on Osteoporosis Canada Guidelines: Papaioannou A, et al. CMAJ. 2010;182:1864-1873.
2. Leslie WD, et al. Osteoporos Int. 2011;22:839-847.

What if Alice…

- has experienced falls since increasing her anti-hypertensive medication?
- has multiple issues leaving insufficient time for OP assessment?
- is on an SSRI?

What if Alice has experienced falls since increasing her anti-hypertensive medication?

Risk of Falls Associated with Antihypertensive Medication

- Antihypertensive medications have long been implicated as a potential cause of falls in older people due to orthostatic hypotension
- Thiazides appear to be associated with an increased risk of first falls[1]

1. Gribbin J, et al. Age Ageing. 2010 Sep;39(5):592-7.
2. Tinetti ME, et al. JAMA Intern Med. 2014;174(4):588-595.

Medications that Increase the Risk of Falling, Potential Fracturing

Medications	Symptoms causing potential to fracture or associated with fracture risk
Benzodiazepines, narcotics, neuroleptics, any anticholinergic	Cognitive impairment, confusion, sedation, drowsiness
Anticonvulsants, antidepressants, antihypertensives, benzodiazepines, narcotics	Dizziness, orthostatic hypotension
Antidepressants, metoclopramide, neuroleptics	Gait abnormalities
Beta-blockers, nitrates, vasodilators	Syncope
Neuroleptics, anticholinergics	Visual disturbances (blurring)

Ruddock B. CPJ/RPC. 2004;137:17-18.

What if you did not see Alice for an OP specific visit?

Making the Next Visit OP Focussed

- Ask the patient to book a follow-up appointment to address how multiple complex issues may be managed
- Tell them at that visit you will be focussed on fracture risk assessment and include a targeted musculoskeletal exam

Ask your patient at each visit:

- Have you had a fracture?
- Have you had any falls since your last visit?

What if Alice is on an SSRI?

Depression Is the Most Common Mental Health Problem in the Elderly

- Data suggests 14% to 20% of the elderly living in the community experience depressive symptoms[1]
- Rates are highest among those in hospital (12% to 45%) and in long-term care facilities (approximately 40%)[2,3]
- ~ 20% of older adults with depressive symptoms receive antidepressant medication[4]
- Awareness and monitoring for side effects is low including increased fracture risk[4]

1. Blazer D, Williams CD. Am J Psychiatry. 1980;137:439-444. 2. Koenig HG, et al. J Am Geriatr Soc. 1988;36:699-706.
3. Ames D, Br J Psychiatry. 1990;156:667-675. 4. Lindsey PL. J Gerontol Nurs. 2009;35:28-38.

Be Aware that Patients on SSRIs Are at Increased Fracture Risk

- CaMos data shows an association between SSRI use and fragility fractures
  - Controlling for multiple risk factors* adjusted HR for current SSRI use remained elevated (HR, 1.68; 95% CI, 1.32-2.14)[1]
- Meta-analysis of 13 studies showed over 72% increase in risk of fracture with SSRI users vs. nonuser[2]

Medication Use	SSRI
Any fracture	
Odds ratio 95% CI P-value	1.66 (1.31-2.11) <0.0001
Hip fracture	
Odd ratio 95% CI P-value	0.65 (0.20-2.09) 0.47
Spine fracture	
Odd ratio 95% CI P-value	2.18 (1.12-2.26) 0.02
NHNV fracture	
Odd ratio 95% CI P-value	1.66 (1.29-2.15) <0.0001

Multivariate regression analysis predicting year 3/year 5 fracture based on medication use vs. no medication use[3]

*Charlson score, previous falls, and BMD hip and lumbar bone density
NHNV: non-hip, non-vert

1. Moura C, et al. Osteoporos Int. 2014 May;25(5):1473-81.
2. Wu Q, et al. Osteoporos Int. 2012 Jan;23(1):365-75.
3. Adapted from Adachi JD, et al. Osteoporos Int. 2013.

Tomorrow:
What Will You Change in Your Practice?

- What systems/pathways are in place in your office to capture patient fractures?
  - How can these be adapted to better identify those at high risk of fracture?
- How does your office flag patient OP risk factors?
  - Is there an opportunity to streamline this process?

Key Messages

- Ensure adequate screening of all patients for fracture risk
- Use BMD with CAROC/FRAX® tool to stratify risk to prevent the first fracture
- For patient at high risk, initiate therapy immediately making the first fracture the last one!
- Assess compliance and satisfaction on osteoporosis therapy
- Choose the appropriate treatment, from among different options, to best meet patient need

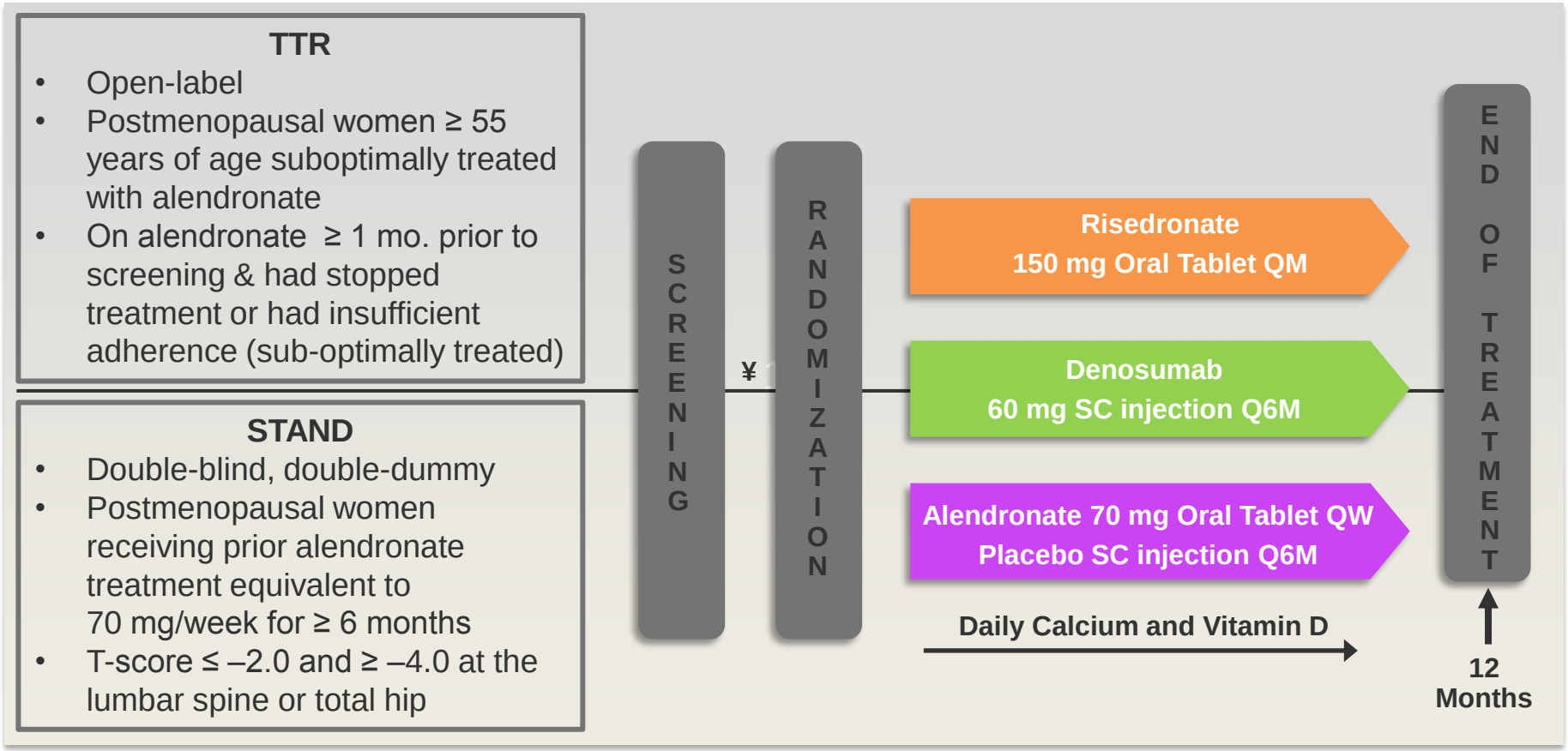
Electronic Parking Lot & FAQs

- What is the effect of changing antiresorptive treatment?
- Should a drug holiday be considered for your patients?
- When should BMDs be done?
- What is a fragility fracture?
- How do you calculate a patient's 10-year fracture risk?
- What medications impact fracture risk?
- Is there a concern with ONJ and anti-resorptive therapy?
- Is there a concern with atypical fractures and anti-resorptive therapy?
- How long should patients stay on therapy?
- How do you improve patient adherence to anti-resorptive medications?
- How much calcium and vitamin D should be recommended?

What is the effect of changing antiresorptive treatment?

TTR/STAND* Study Designs

Multi-centre, Randomized, Parallel Studies

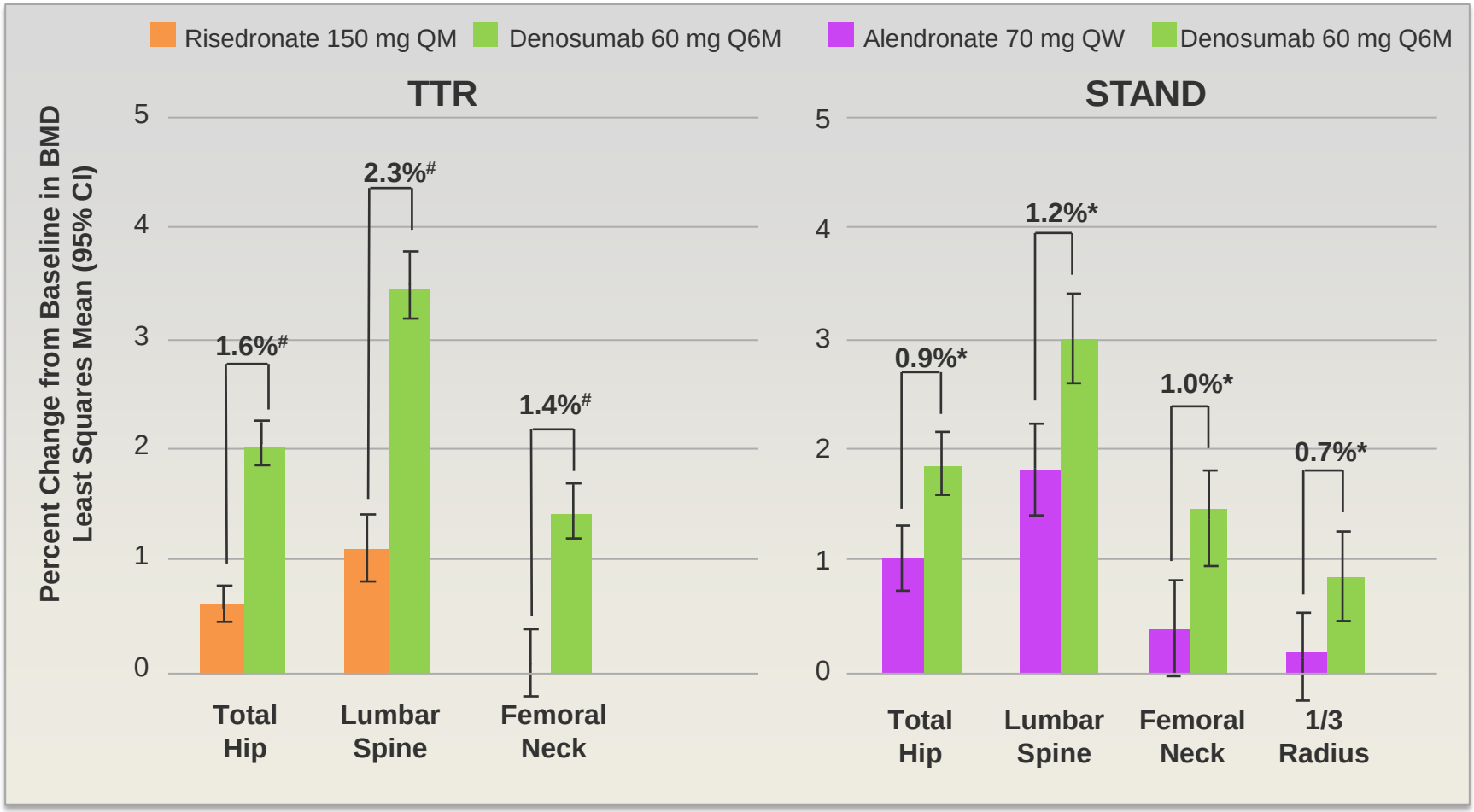


¥ In the STAND trial, all subjects received branded alendronate 70 mg QW during a 1-month run-in period before randomization.
*TTR=Transition to risedronate, STAND= Study of Transitioning from Alendronate to Denosumab

1. Roux C, et al. Bone. 2014;58:48-54.
2. Kendler DL, et al. J Bone Miner Res. 2010;25:72-81.

Percent Changes in BMD at Month 12

TTR/STAND Studies



#P ≤ 0.0001, *P≤0.05

1. Roux C, et al. Bone. 2014;58:48-54.
2. Kendler DL, et al. J Bone Miner Res. 2010;25:72-81.

Summary of Adverse Events

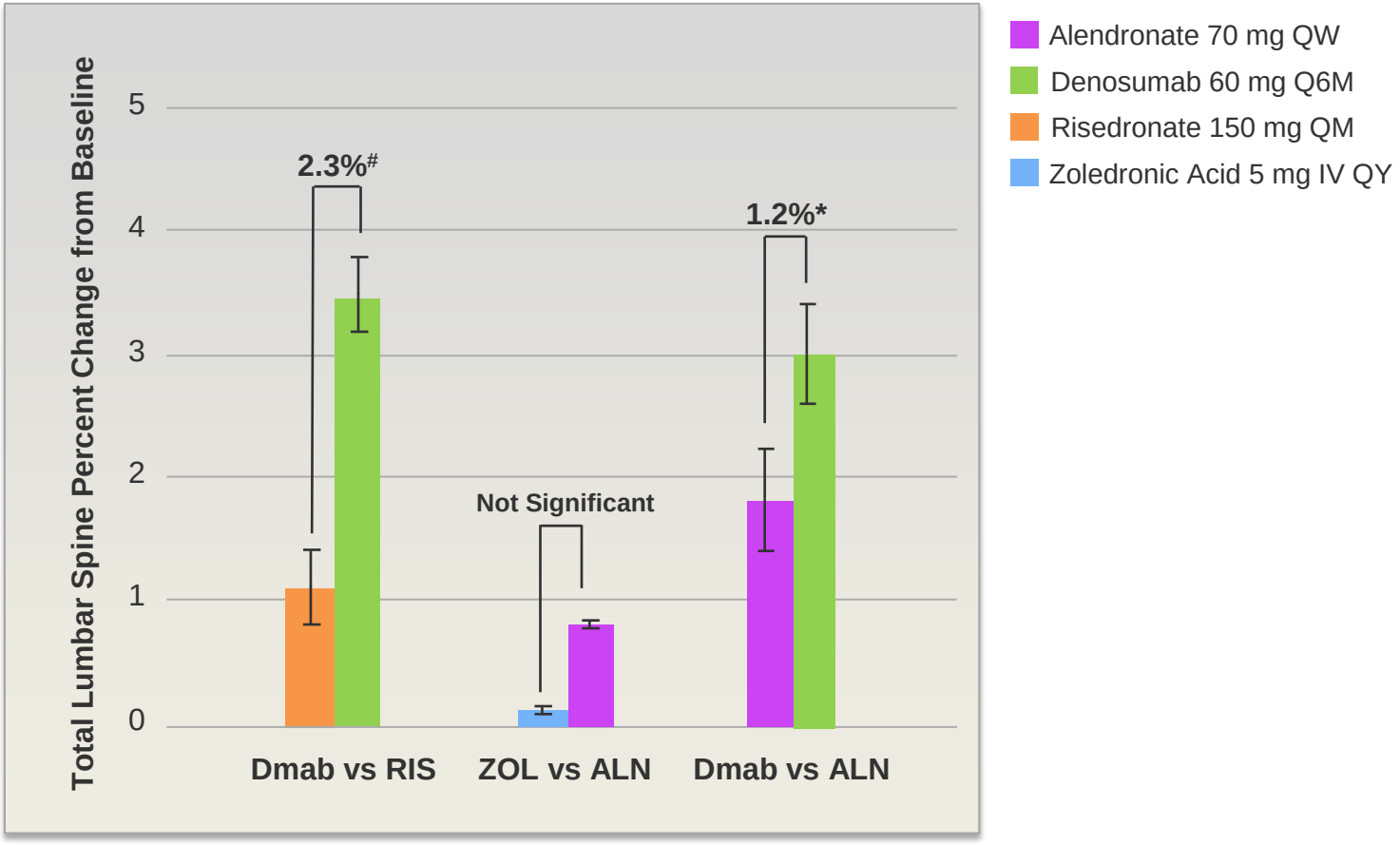
TTR/STAND Study

n (%)	TTR		STAND	
	Risedronate 150 mg QM (n=429)	Denosumab 60 mg Q6M (n=429)	Alendronate 70 mg QW (n=249)	Denosumab 60 mg Q6M (n=253)
Any adverse event	293 (68.3)	269 (62.7)	196 (79.0)	197 (77.9)
Serious adverse events	35 (8.2)	33 (7.7)	16 (6.4)	15 (5.9)
Adverse events leading to study discontinuation	19 (4.4)	10 (2.3)	2 (0.8)	3 (1.2)
Deaths	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.4)
Fractures*	17 (4.0)	23 (5.4)	4 (1.6)	8 (3.2)
Serious infections	5 (1.2)	5 (1.2)	3 (1.2)	1 (0.4)

*In the STAND trial, 5 clinical fractures were also observed during the screening phase

1. Roux C, et al. Bone. 2014;58:48-54.
2. Kendler DL, et al. J Bone Miner Res. 2010;25:72-81.

Other Head-to-Head Studies Demonstrating Effects On BMD In Patients Changing Therapies



Denosumab data are least-squares means and 95% confidence intervals.
ZOL/ALN percent change from baseline with standard errors
#P ≤ 0.0001, *P≤0.05
For all studies, patients were previously on Alendronate

1. Roux C, et al. Bone. 2014;58:48-54. 2. McClung M, et al. Bone. 2007;41:122-128.
3. Kendler DL, et al. J Bone Miner Res. 2010;25:72-81

FAQ

Should a drug holiday be considered for your patients?

Bisphosphonate Drug Holidays May Be Considered for Certain Patients

Why can we consider a bisphosphonate drug holiday*?
Bisphosphonates are unique in that they may be bound to bone for many years with residual action following discontinuation

Canadian Recommendations:		
10-year Fracture Risk	**Can a drug holiday be considered?**	
Low (<10%)	Yes	• Monitor at 3-5 year intervals
Moderate (10-20%)	Maybe	• If no previous fragility fracture and femoral neck BMD >-2.5 • If vertebral fractures found, stratify patient as high risk & continue therapy
High (>20%)	No	• Ongoing therapy is recommended: continue BP therapy or switch to another proven agent (i.e. teriparatide or denosumab)

***Note:** this does not apply to other osteoporosis therapies (denosumab, estrogen, raloxifene, teriparatide) in which there is an offset of action following discontinuation

Adapted from: Brown JP, et al. Can Fam Physician. 2014;60:325-333.

FAQ

When should a BMD be done?

Screening for Osteoporosis: When to Do a BMD[1]

Aged ≥ 65 years

- Everyone

Aged 50-64 years

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

Aged <50 years

- 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 9, 2012.

BMD for Treatment Follow-up

- Existing Canadian guidelines recommend measuring BMD at regular intervals
  - 1-3 years after initiation of therapy and when treatment changes[1]
- Follow-up measurements should be done on the same machine as the first measurement

- The optimal interval of BMD monitoring is still under active investigation[2]
- A BMD that has improved or remains unchanged suggests a good response to therapy

1. Papaioannou A, Morin S. CMAJ. 2010;82:864-73. 2. Bell KJL, et al. BMJ. 2009;338:2266.

Current Reimbursement Criteria for BMD Testing in ON

Baseline BMD Testing

1 test in patient lifetime
All patients

Subsequent BMD Testing
by risk stratification category

Low Risk
1 test following baseline at ≥36 mo
Subsequent tests at ≥ 60 mo

Defined as:
- Not at risk for accelerated bone loss
- No osteoporosis or osteopenia on previous BMD testing
- Bone loss less than 1% per year by BMD testing

High Risk
1 test every 12 mo or more

Defined as:
- High risk for accelerated bone loss (in the absence of other risk factors - age not a risk factor)
- Osteopenia or osteoporosis on any previous BMD testing
- Bone loss in excess of 1% per year as demonstrated by previous BMD testing

1. Diagnostic Radiology Ontario Guidelines.
2. Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

Current Reimbursement Criteria For BMD Testing in BC

Baseline BMD Testing

Not indicated unless patients (men and women) are >65 years of age, at moderate or high risk for fracture (>10% 10-yr risk) and results are likely to alter patient care

Subsequent BMD Testing

For Patients Not Taking OP Medication

There is insufficient evidence to recommend a testing frequency for patients not taking OP medications. Based on a patient's risk profile, BMD retesting may be indicated in 3-10 years.

For Patients on OP Medication

- Repeat BMD not justified based on current evidence.
- Not considered medically necessary prior to 3 years after original measurement.
- Exceptions:
- Patients receiving > 7.5 mg prednisone/equivalent daily for 3 months consecutively who require a baseline examination and repeat scans at 6 month intervals while on treatment.
- Patients in whom an early exam may be indicated: moderate and high risk patients on OP medications with multiple risk factors and test is likely to alter patient management.

FAQ

What is a fragility fracture?

Understanding Fracture Risk Requires Recognizing a Fragility Fracture

Definition of a fragility fracture*:

A fracture that occurs spontaneously or following a minor trauma such as:

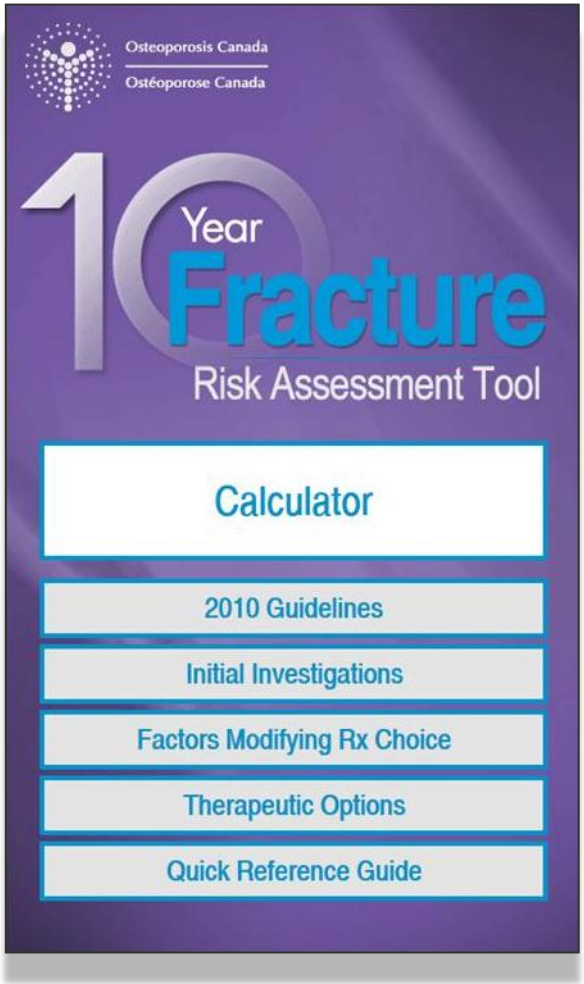
- Fall from a standing height (i.e. on the ice)
- Fall from a sitting position
- Fall from a supine position
  (bed or reclining deck chair < 1 metre high)
- Fall after having missed 1 to 3 steps in a staircase
- After a movement outside of the typical plane of motion or coughing

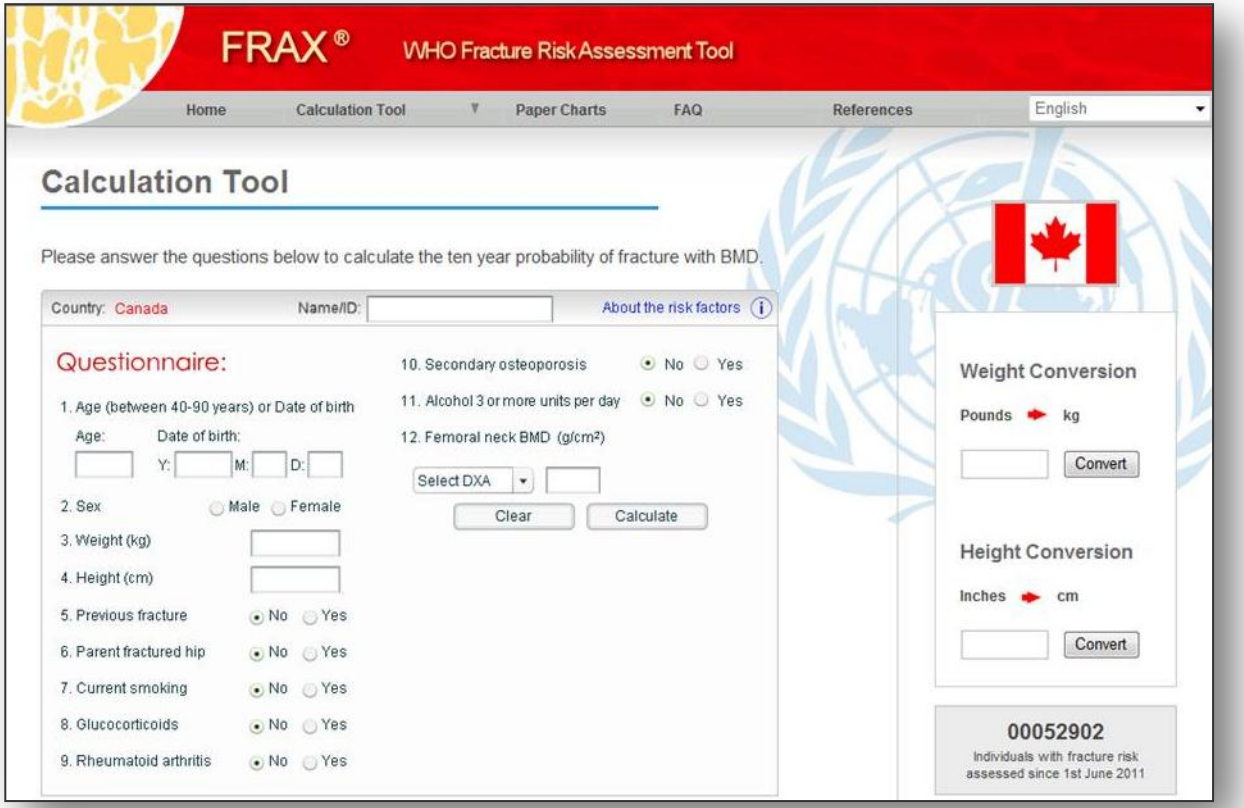
1.Bessette L, et al. Contemp Clin Trials. 2008; 29:194-210.
2.Brown JP, et al. J Bone Miner Res. 2007;23(Suppl. 1): M350.

FAQ

How do you calculate a patient's 10-year fracture risk?

Two Tools Are Available for Fracture Risk Assessment





1.OC Guidelines tool available at: http://www.osteoporosis.ca/multimedia/FractureRiskTool/index.html#/Home. Accessed July 3, 2014.
2.FRAX® tool available at: http://www.shef.ac.uk/FRAX/tool.jsp.

Risk Factors for Fracture Risk Assessment

CAROC*	FRAX®‡
Risk Factors: • Sex • Age • BMD • **Fragility fracture after 40** • Systemic glucocorticoid use (≥3 months)†	**Additional Risk Factors:** • Low BMI • Parental history of fracture (especially hip) • Current smoking • Alcohol intake ≥ 3 units/day • Rheumatoid arthritis, or other secondary causes of osteoporosis

- Both tools are recognized by Osteoporosis Canada as validated methods for the prediction of fracture risk, with 90% concordance between results
- CAROC may add simplicity, requiring only 5 parameters
- FRAX® can be used in the absence of BMD
- FRAX® has country-specific tools; ensure the Canadian version is used

*Canadian Association of Radiologists and Osteoporosis Canada, 2010
† ≥3 months in the prior year of a prednisone equivalent dose ≥ 7.5 mg daily
‡ Fracture Risk Assessment Tool of the World Health Organization

Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

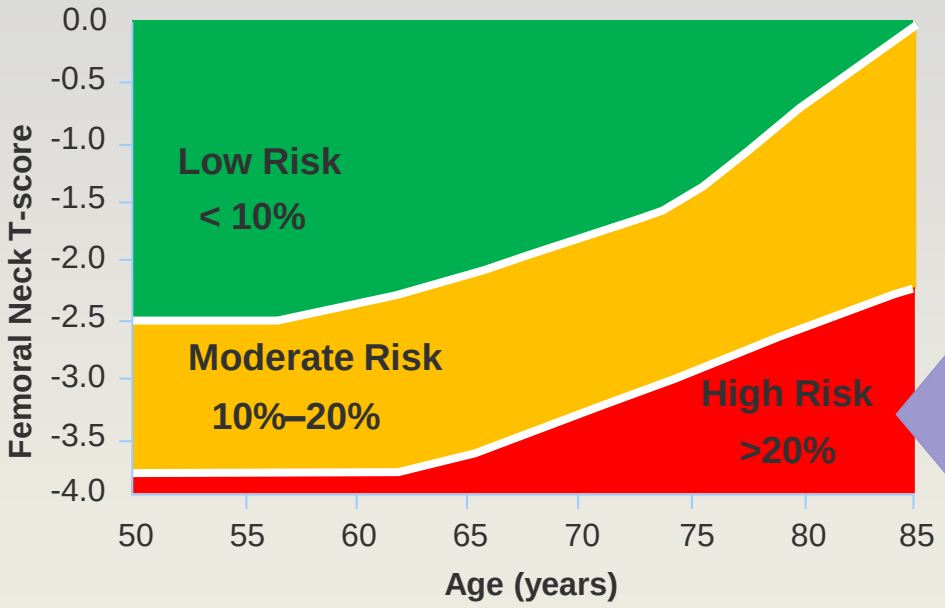
Calculating 10-year Absolute Fracture Risk for Postmenopausal Women: CAROC

Increases to the next risk category

Prior fragility fracture after age 40

Prolonged corticosteroid therapy*

10-year Absolute Fracture Risk in Treatment-naïve Women Combining Femoral Neck T-score and Age[1]



Prior hip or vertebral fracture, or >1 non-vertebral fragility fracture

Femoral neck T-score ≤ -2.5: Consider the individual to be at least at moderate risk

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

1. Papaioannou A, et al. CMAJ. 2010;182:1864-1873.
2. Leslie WD, et al. J Bone Miner Res. 2009;24:353-360.

FAQ

What medications impact fracture risk?

Medications that Impact Fracture Risk

Anticonvulsants[1]	Glucocorticoids[3]
Antipsychotic drugs[2]	Hormonal/endocrine therapies - (GnRH agonists, LHRH analogs)[3]
Aromatase inhibitors, androgen deprivation therapy[3]	Proton pump inhibitors (PPIs)[6]
Chemotherapeutic[4]/transplant drugs (i.e. glucocorticoids)[3]	Selective serotonin reuptake inhibitors (SSRIs)[7]
Furosemide[5]	Serotonin–norepinephrine reuptake inhibitors (SNRIs)[7]

1. Lee RH, et al. Am J Geriatr Pharmacother. 2010 Feb; 8(1):34-46. 2. Crews MP, et al. Hum Psychopharmacol. 2012 Jan; 27(1):15-23. 3. Papaioannou A, et al. CMAJ. 2010;182:1864-1873. 4. Mayer EL. Am Soc Clin Oncol Educ Book. 2013:9-14. 5. Drinka PJ, et al. J Am Med Dir Assoc. 2007 Jun; 8(5):328-31. 6. Targownik LE, et al. CMAJ. 2008;179(4):319-326. 7. Wu Q, et al. Osteoporos Int. 2012 Jan; 23(1):365-75.

FAQ

Is there a concern with osteonecrosis of the jaw (ONJ) and anti-resorptives?

ONJ is Exceedingly Rare, Occurring Most Often with Other Comorbidities or Concomitant Medication[1]

What is ONJ (Osteonecrosis of the jaw)?

A lesion in the oral cavity with exposed bone where mucosa is normally found, not healed after appropriate care by 8 weeks (no prior head, face or mouth radiation)[1,2]

Manifests as infection, inflammation, or erosion of the gums, tooth, or jaw bone, pain or slow healing after dental surgery[3]

- Risk factors include[1,2] cancer diagnosis, obesity, diabetes, oral infection, dental extractions, and co-morbid disorders
- **Absolute risk of bisphosphonate-associated ONJ is ~1 case per 100,000 person-years when BPs are administered for osteoporosis treatment**[4]
- Insufficient evidence for an anti-resorptive "drug holiday" or waiting periods for prevention of ONJ (Recommendations from *Canadian Consensus Guidelines* and *American Dental Association*)[1,5]

1.Hellstein JW, et al. American Dental Association. Available at: http://www.ada.org/sections/professionalResources/pdfs/topics_ARONJ_report.pdf. Accessed February 2012.
2.Khan AA, et al. J Rheumatol. 2009;36:478-90. 3. Ruggiero SL, et al. J Oral Maxillofac Surg. 2009;67:2-12.
4. Brown JP, et al. Can Fam Physician. 2014;60:325-333 ; 5.Khan AA, et al. J Rheumatol. 2008;35:1391-1397.

Summary of Main Recommendations of The Canadian Consensus Practice Guidelines of Bisphosphonate-associated ONJ[1]

Patient Group	Recommended Action by Dental Practitioner
All patients taking bisphosphonates	Stopping smoking, limiting alcohol intake, and maintaining good oral hygiene should be emphasized
All onco bisphos	A thorough dental examination including radiographs should be completed prior to the erapy
	ed bisphosphonate therapy
Osteoporosis patients taking oral/intravenous bisphosphonates	Dental examination not required prior to initiating therapy if there is appropriate dental care and good oral hygiene
Individuals with established ONJ	Best managed with supportive care including pain control, treatment of secondary infection, removal of necrotic debris, and mobile sequestrate
	Aggressive debridement is contraindicated

"Routine dental treatment generally should not be modified solely due to use of anti-resorptive agents." [2]

1. Khan AA, et al. J Rheumatol. 2008;35:1391-1397. 2. Hellstein JW, et al. American Dental Association. Available at: http://www.ada.org/sections/professionalResources/pdfs/topics_ARONJ_report.pdf. Accessed February 2012.

FAQ

Is there a concern with atypical fractures and anti-resorptive therapy?

Atypical Fractures Are Exceedingly Rare, Occurring Most Often with Other Comorbidities or Concomitant Medication[2]

What is an atypical fracture?

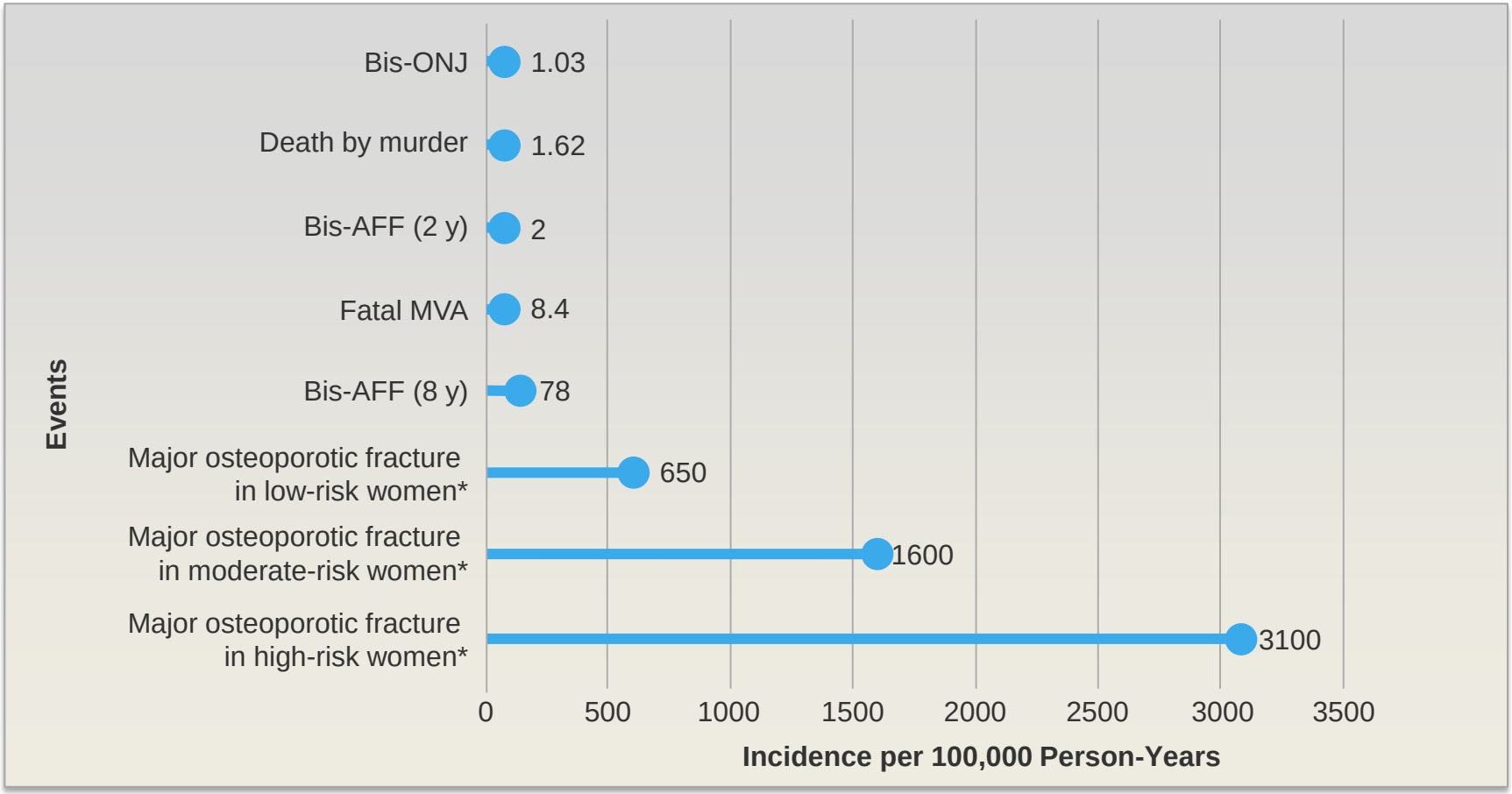
Fracture in the subtrochanteric region, with major features, as defined by the ASBMR Task Force[1]

- A causal association between anti-resorptives and atyp
- ***Aty***
  app
  frac
  evi
  type
- Absolute risk of bisphosphonate-associated atypical fractures is between 2 and 78 cases per 100,000 person-years[3]
- *The benefits of using bisphosphonate drugs in preventing fractures associated with osteoporosis outweigh the risk of an atypical femur fracture."*[2]

"One AFF may occur for every 100 fractures prevented." [1]

1. Shane E, et al. J Bone Miner Res. 2014;29(1):1-23.
2. www.hc-sc.gc.ca. Information Update. 2011(72):Accessed December 19, 2012.
3. Brown JP. et al. Can Fam Physician. 2014;60:325-333.

What Is the "Real-world" Risk of ONJ and Atypical Fractures?



Bis-AFF: Bisphosphonate-associated atypical subtrochanteric and diaphyseal femur fracture
Bis-ONJ: Bisphosphonate-associated osteonecrosis of the jaw
BMD=bone mineral density. FN=femoral neck. FRAX=fracture Risk Assessment Tool. MVA=motor vehicle accident
*10-year risk of major osteoporotic fracture by Canadian FRAX

Adapted from Brown JP, et al. Can Fam Physician. 2014;60:325-333.

FAQ

How long should patients stay on therapy?

For Patients at High Risk of Fracture, Antifracture Benefits Bisphosphonates Considerably Outweigh their Potential for Harm[1]

"***There is little evidence*** *to support any recommendation regarding duration of therapy or the use of drug holidays."*[1]

Individuals at high risk for fracture should continue osteoporosis therapy without a drug holiday.[2]

1. Brown JP, et al. Can Fam Physician. 2014;60:325-333.
2. Papaioannou A, et al. CMAJ. 2010;182:1864-1873.

For Patients on Long-term Anti-resorptive Treatment, What Are Some Things to Consider?

Consider	Supporting Evidence	Bisphosphonates	Denosumab
Will it still be safe?	Long-term data	AE profile at 5-6 years shows no significant difference in AEs from placebo[1-5]	AE profile through to 8 years similar to that seen in the initial pivotal trial[6]
What happens if my patient stops therapy?	Reversibility	Residual effect; depends on type & length of treatment[7]	Fully reversible[7]
	Duration of action	Slow offset of action[7]	Relatively rapid offset of action[7,8]
	Clearance	Renal; detectable in urine weeks, months or years after stopping[7]	Catabolized in reticuloendothelial system[7]; almost fully cleared by 6 months[9]

AE=Adverse event
BP=Bisphosphonate

1. Sorensen OH, et al. Bone. 2003;32:120-126. 2. Black D, et al. J Bone Miner Res. 2010;25(Suppl 1):S22-S23. Abstract 1070. 3. Black D, et al. J Bone Miner Res 2010;25 (Suppl 1):S22-S23. Abstract 1070. 4. Black DM. JAMA. 2006;296:2927-38. 5. Bone HG, et al. N Engl J Med. 2004;350:1189-99. 6. Papapoulos S. ASBMR 2013, Abstract LB-MO26. 7. Baron R, et al. Bone. 2011;48:677-692. 8. Miller PD. Curr Osteoporos Rep. 2009;7:18-22. 9. Bekker PJ, et al. J BoneMiner Res. 2004;19:1059-66.

Is Long-term Therapy Still Effective?

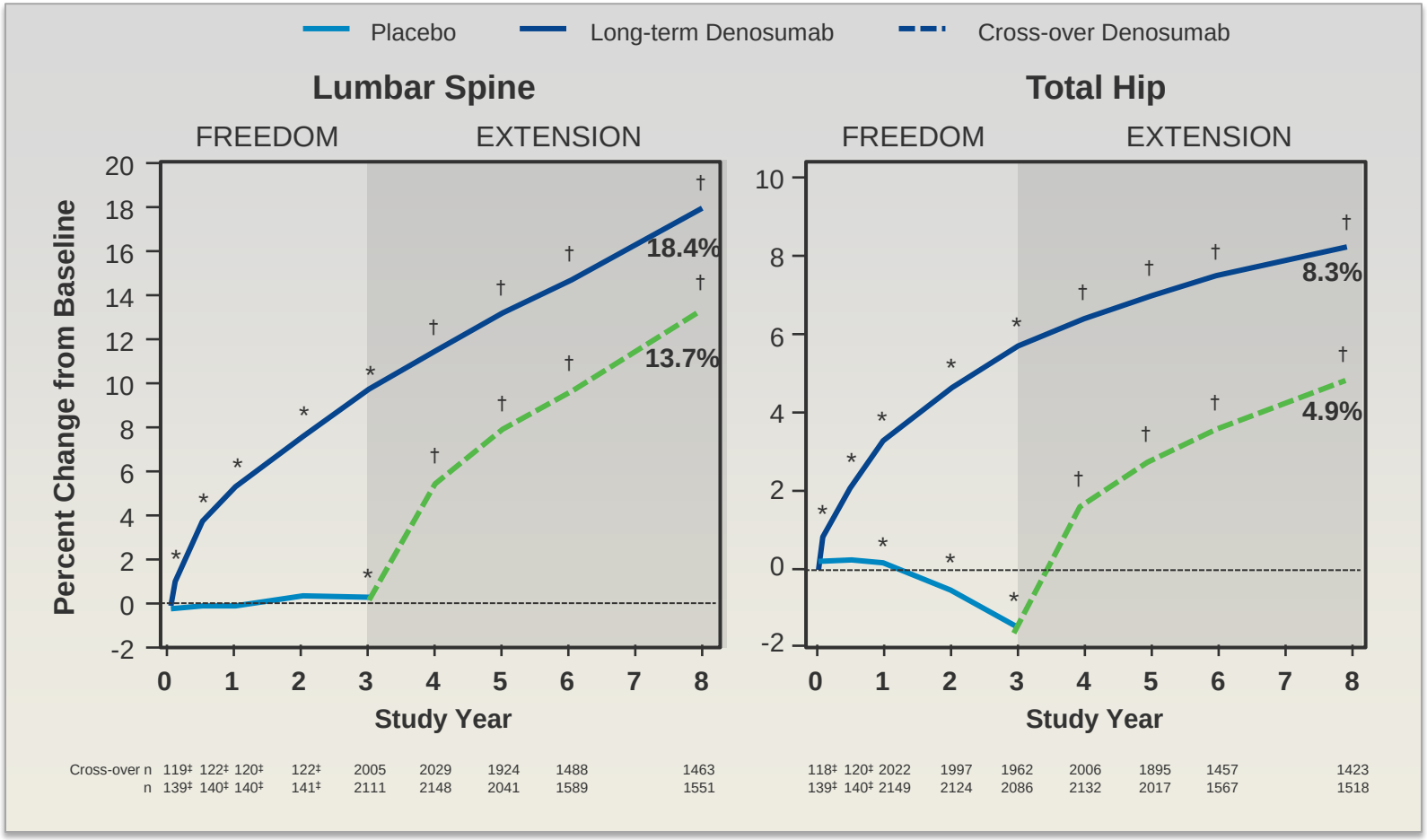
Medications	Pivotal Study Extension	Treatment Duration (yrs)	# of Participants	% Change Lumbar Spine BMD ∓	% Change Total Hip BMD∓	Hip Fracture Incidence (%)
Risedronate[1]	VERT-MN	7	68	11.5	3.9	‡Not measured
Acid[3†]	of 9-year study)					
Denosumab[4†]	FREEDOM (interim analysis of 10-year study)	8	2,343	18.4	8.3	0.2%

With long-term treatment BMD is maintained[1,2,3] or continues to increase[4]

* Not head-to-head analyses: Results cannot be compared due to differing study populations and methodologies.
∓ Represents % change from BL of Pivotal Trial
¥ Represents 10 mg dose only
‡Studies measured non-vertebral fracture incidence which included hip fractures. Non-vertebral fracture incidence: RIS 6.0%, ALN 8.5%.
†Interim Analyses, ZOL = 9 year study and DMAB = 10 year

1. Mellstrom, D et al. Calcif Tissue Int. 2004;75:462-468. 2. Bone HG, et al. N Engl J Med. 2004;350:1189-99. 3. Black DM, et al. J Bone Miner Res. 2012;27(2):243-254. 4. Papapoulos, S. ASBMR. 2013, Abstract LB-MO26.

Effects on BMD with Long-term Denosumab Therapy (Through 8 Years)

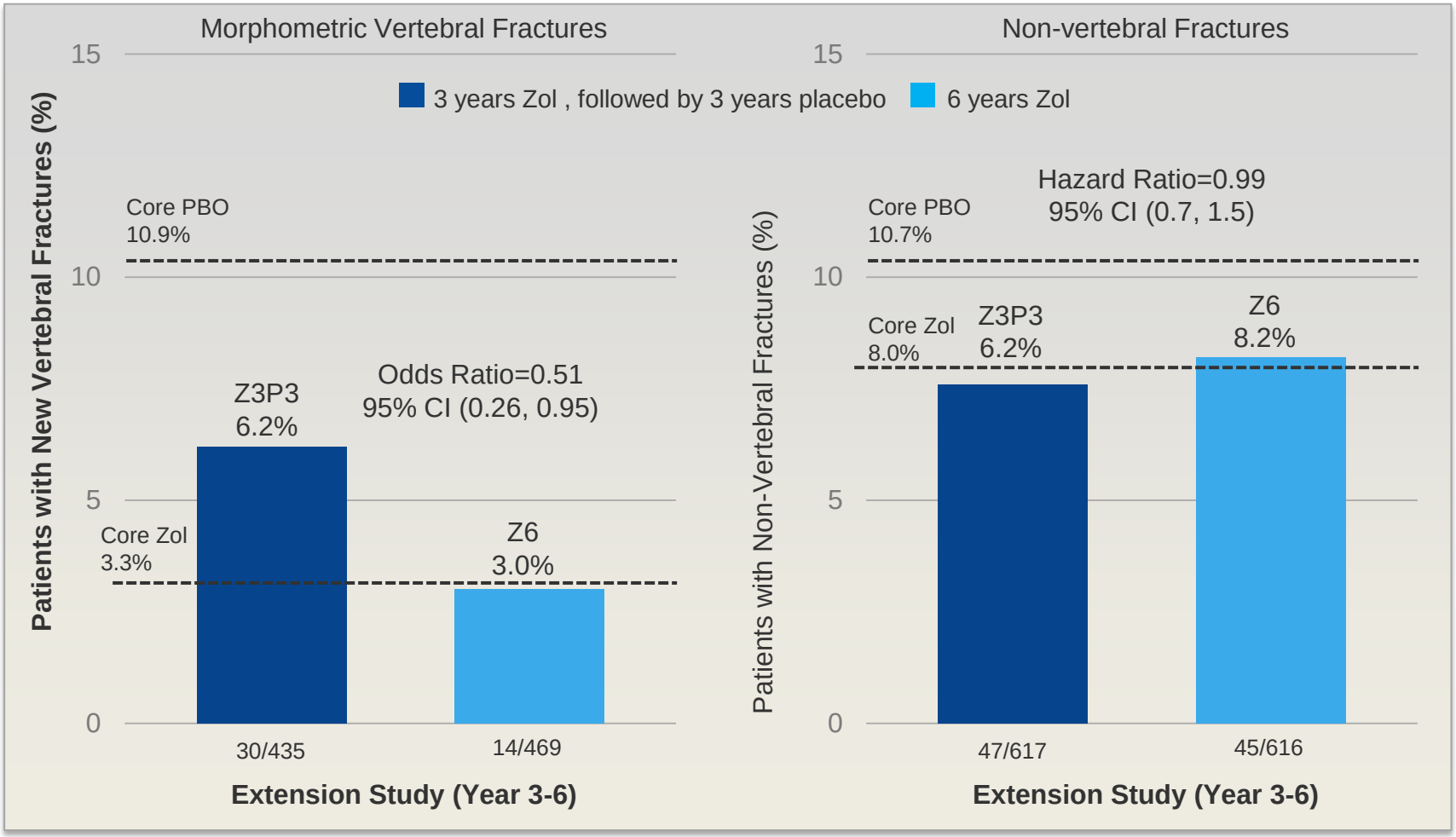


LS means and 95% confidence intervals. n=number of subjects with values at baseline and the time point of interest
*P < 0.05 vs FREEDOM baseline; †P < 0.0001 vs FREEDOM baseline and extension baseline
‡Represents subjects from the FREEDOM DXA substudy

Papapoulos S. ASBMR 2013, Abstract LB-MO26.

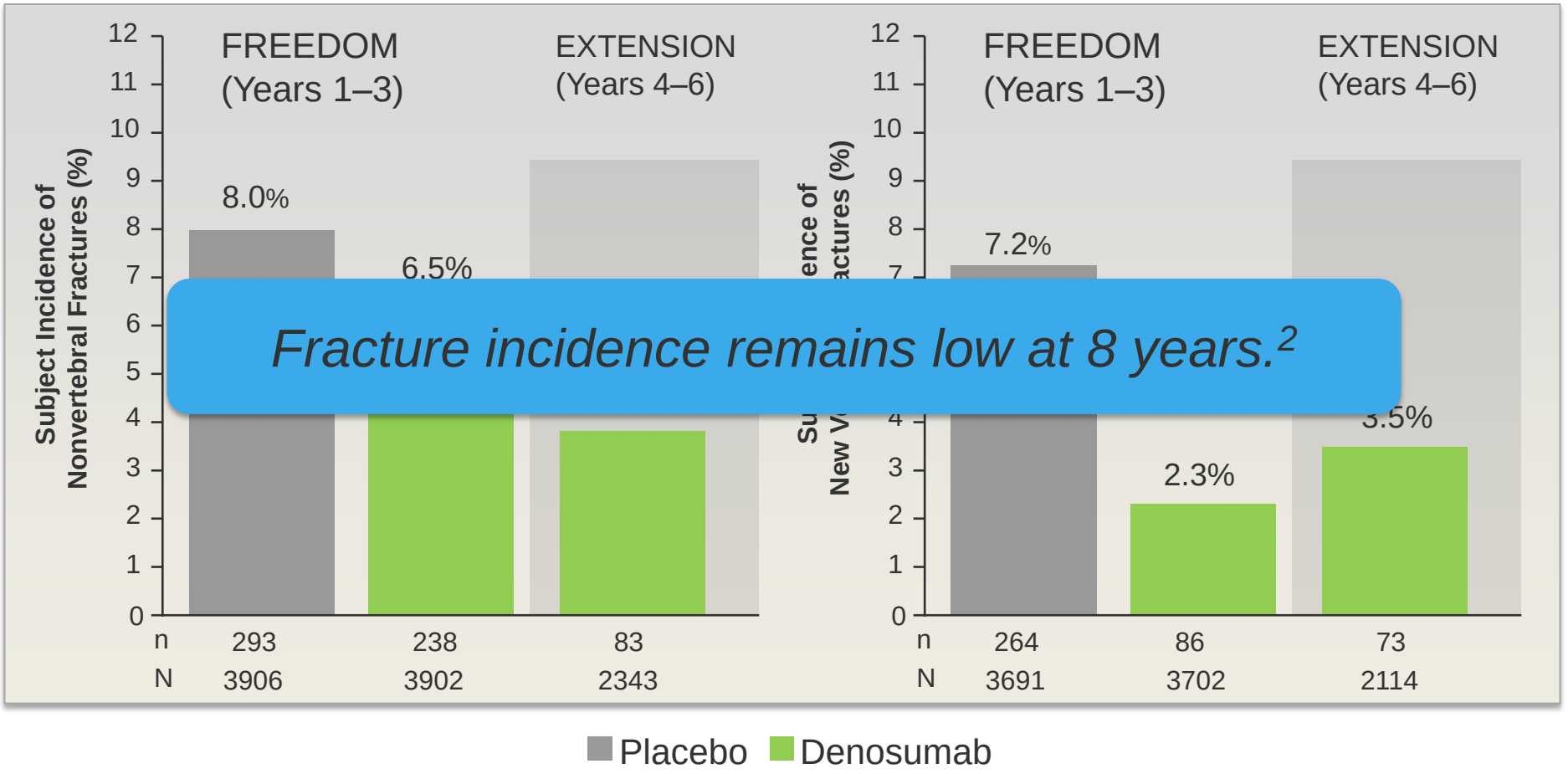
Significant Difference in Morphometric Vertebral Fractures between Year 3 and 6, With No Difference in Non-vertebral or Hip Fractures

Those at High Fracture Risk, Particularly Vertebral Fracture, May Benefit by Continued Treatment With Zoledronic Acid



Black DM, et al. J Bone Miner Res. 2012;27(2):243-54.

Low Incidence of New Vertebral and Non-vertebral Fractures through 6 Years of Denosumab Treatment[1]



Fracture incidence remains low at 8 years.[2]

n = number of subjects with ≥ 1 fracture. N = number of randomized (FREEDOM) or enrolled (Extension) **subjects.**
Percentages for nonvertebral fractures are Kaplan-Meier estimates.

1. Bone et al. J Clin Endocrinol Metab. 2013; 98: 4483-92.
2. Papapoulos S. ASBMR 2013, Abstract LB-MO26.

Safety of Long-term Anti-resorptive Treatment

Risedronate (VERT MN ext)[1] – 5 years	RIS (n=135)	Placebo (n=130)
Any serious AE	24.4%	30.0%

Zoledronic Acid (HORIZON ext)[2,3] – 6 years	Placebo (Years 1-3) (n=3,861)	Zoledronic Acid (Years 1-3) (n=3,875)	Zoledronic Acid (Years 3-6) (n=613)
Serious AEs	30.1%	29.2%	31.2%
Increase in serum creatine >0.5 mg/dL	0.4%	1.2%*	2.9%*
Atrial Fibrillation (Serious AE)	0.5%	1.3%*	2.0%

Alendronate (FLEX ext)[4,5] – Years 8-10 Incidence of AEs, %		
	Discontinuation (n=83)	ALN (10 mg) (n=86)
Serious AEs	21.7	20.9

p<0.05 compared to placebo

Denosumab (FREEDOM Ext)[6,7] Exposure-adjusted subject incidences of AEs (Rates per 100 subject-years)			
	Placebo Years 1-3 (n=3,883)	Denosumab Years 1-3 (n=3,879)	Denosumab Years 4-8 (n=2,343)
Serious AEs	10.4	10.6	10.7
Infections**	1.3	1.5	1.4

ONJ and atypical femoral fractures have been reported
**Incidence of cellulitis/erysipelas similar in extension to that seen in placebo group of pivotal trial

1. Sorensen OH, et al. Bone. 2003;32:120-126. 2. Black D, et al. N Eng J Med. 2007;356:1809-1822. 3. Black DM, et al. J Bone Miner Res. 2012;27(2):243-254. 4. Black DM. JAMA. 2006;296:2927-38. 5. Bone HG, et al. N Engl J Med. 2004;350:1189-99. 6. Papapoulos S, et al. J Bone Miner Res. 2012;27:694-701. 7. Papapoulos S. ASBMR 2013, Abstract LB-MO26.

FAQ

How do you improve patient adherence to anti-resorptive medications?

Patient Support Programs Can Improve Adherence

Consider patient support programs offering services such as nurse support, reimbursement information, dose reminders, and education[1,2]

Adherence in these programs has been shown to be as high as 94%[3]

Reputable websites on osteoporosis and therapies may also provide patients with valuable information

- **Osteoporosis Canada[4]:**
  - Patient and physician resources
  - Links to scientific references
- **HealthandBone.ca[5]:**
  - Educational website for patients
- **Drugcoverage.ca[6]:**
  - Search tool
  - Overview of private insurance plans and government drug benefit programs

1. For My Bones Program. Available at: https://www.formybones.ca/help_en.do. Accessed October 2010. 2. Patient Direct, ProVital™ Program. Available at: http://www.provital.ca. Accessed Nov. 30, 2011. 3. Patient Direct, ProVital™ Program, as at Nov. 30, 2011 report. 4. Osteoporosis Canada. Available at: http://www.osteoporosis.ca. Accessed November 2010. 5. Health and Bone. Available at: http://www.healthandbone.ca/en/home. Accessed November 2010. 6. Drug Coverage.ca Available at: http://www.drugcoverage.ca Accessed October 2010.

FAQ

How much calcium and vitamin D should be recommended?

Data Supports that Supplementation Does Not Cause Harm

CaMos:[1]

- Calcium supplements, up to 1,000 mg/d may be associated with reduced risk of mortality in women (HR 0.75-0.78)
- No evidence of vitamin D intake on mortality benefit or harm was observed

Women's Health Initiative:[2]

- Calcium and vitamin D supplementation were associated with a decrease in hip fracture risk, and an associated benefit on breast cancer and invasive cancer risk
- No impact on cardiovascular risk, colorectal cancer or total mortality

1. Langsetmo L, et al. J Clin Endocrinol Metab. 2013;98:3010-8. 2. Prentice RL, et al. Osteoporos Int. 2013;24:567-80.

Calcium and Vitamin D Recommendations from Osteoporosis Canada

Calcium	• Total daily intake through diet and supplements should be 1,200 mg
Vitamin D3 Supplementation	• 400 to 1,000 IU for adults under age 50 without osteoporosis or conditions affecting vitamin D absorption • 800 to 2,000 IU for adults over 50

1. Hanley DA, et al. CMAJ. September 7, 2010;182:E610-E618.
2. Papaioannou A, et al. CMAJ. 2010.

FAQ