

OSTEOPOROSIS CANADA 2023 UPDATE: PRACTICAL PEARLS FOR EVERYDAY USE

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1

DISCLOSURES

- Honorarium – 2nd Annual Sunnybrook Updates in Endocrinology and Diabetes – received educational grants/support from: Abbott, Boehringer Ingelheim, Dexcom, Eli Lilly, Janssen, Novo Nordisk, and Sanofi

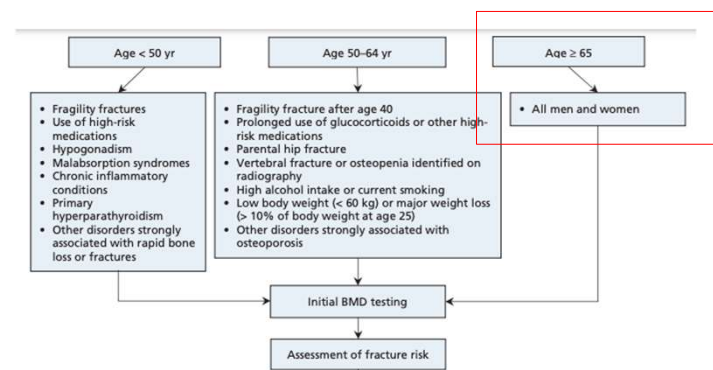
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OUTLINE

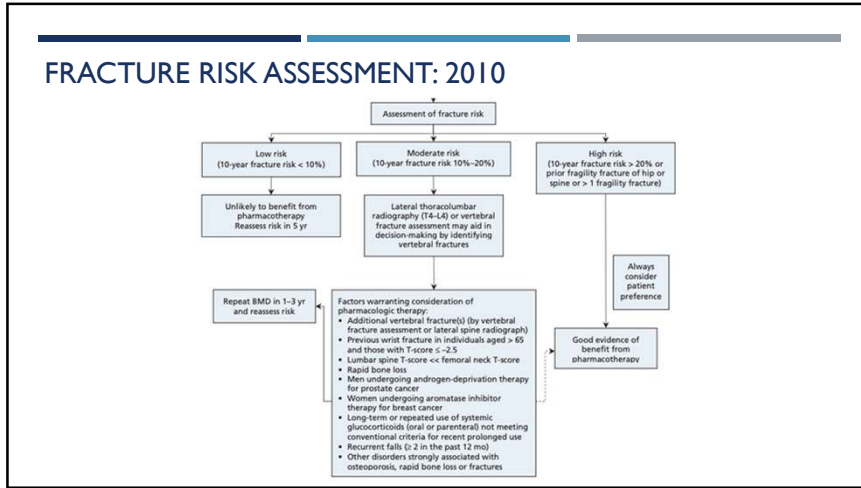
1. Compare and contrast important differences between 2010 and 2023 guidelines
2. Discuss practical pearls for everyday use including decision around drug holiday, denosumab interruption and discontinuation

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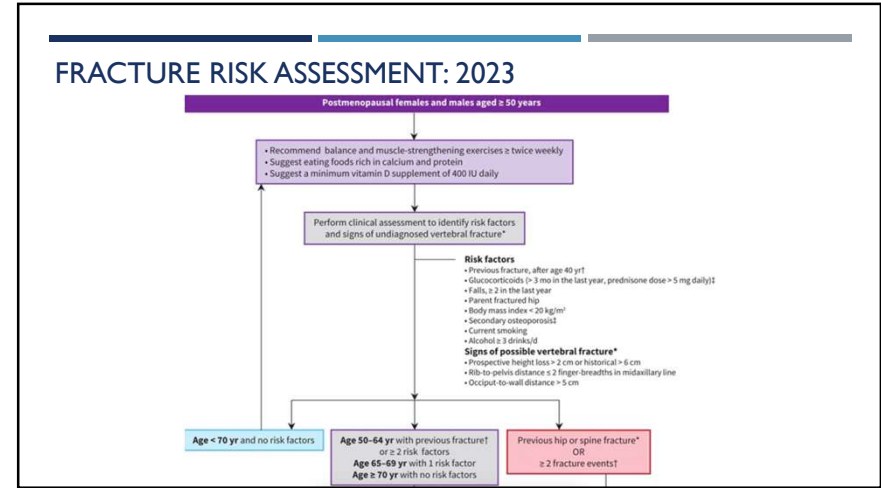
FRACTURE RISK ASSESSMENT: 2010



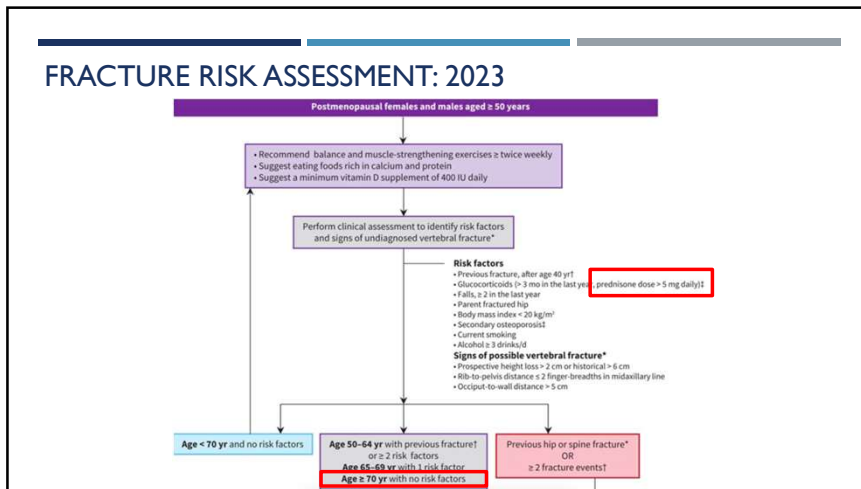
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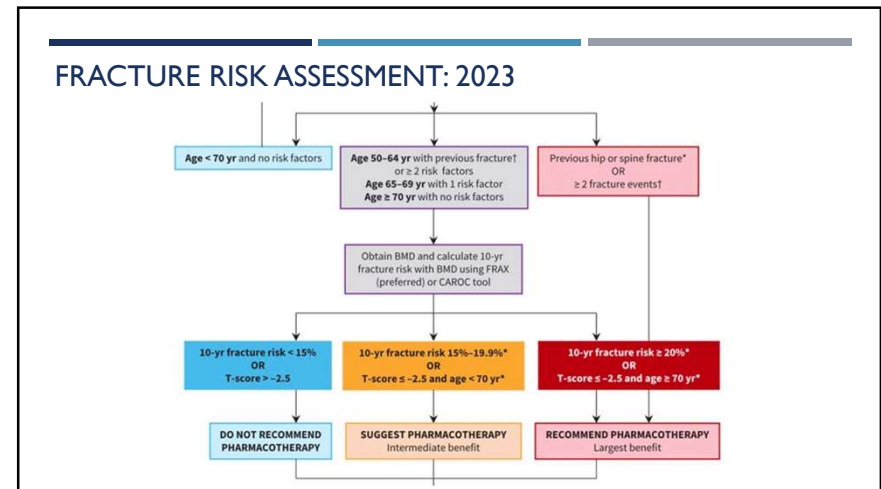
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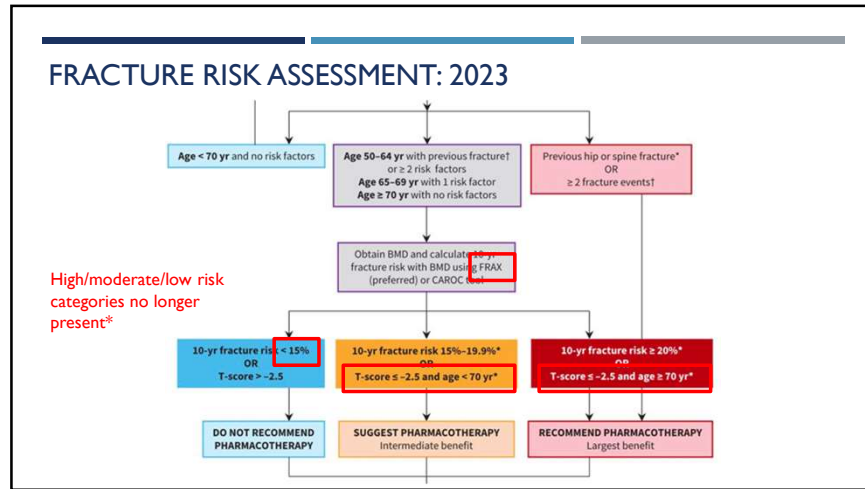
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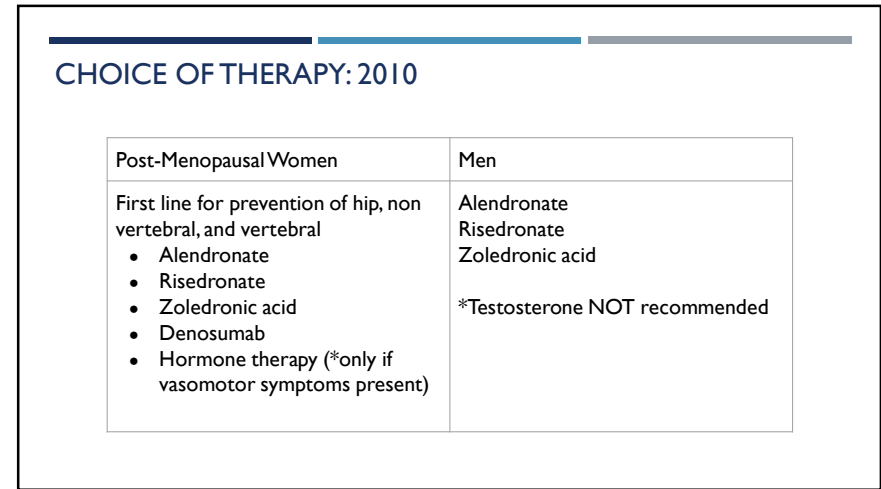
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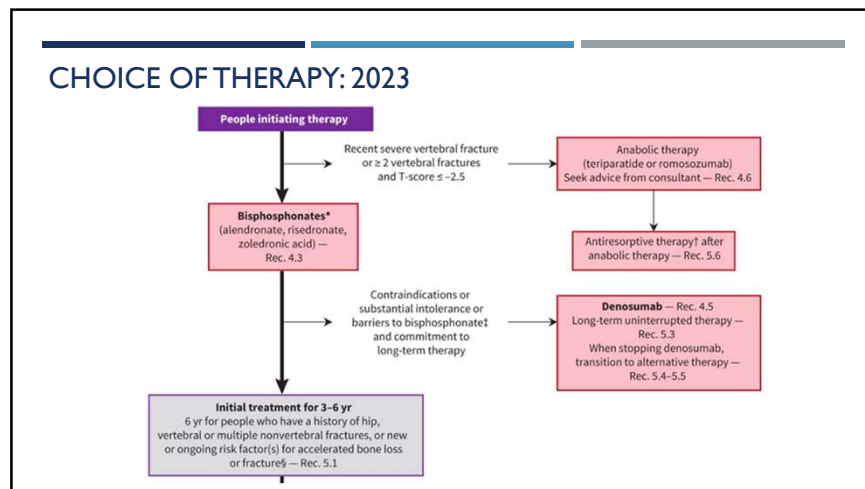
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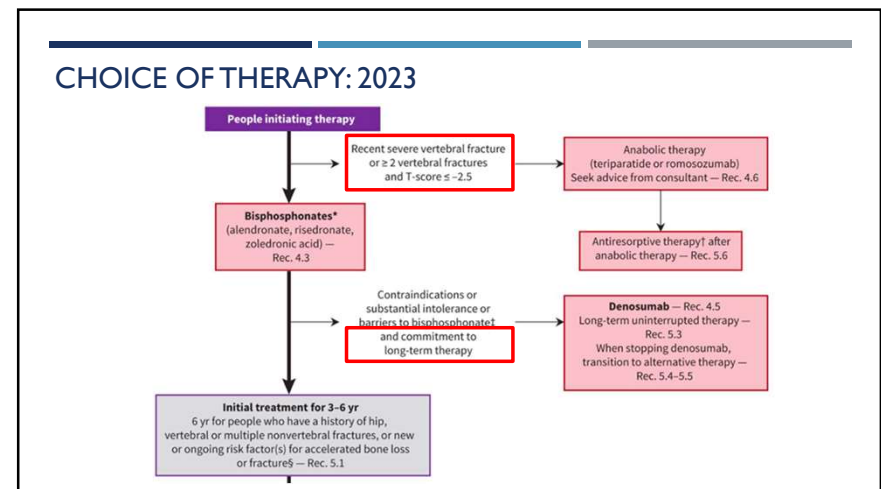
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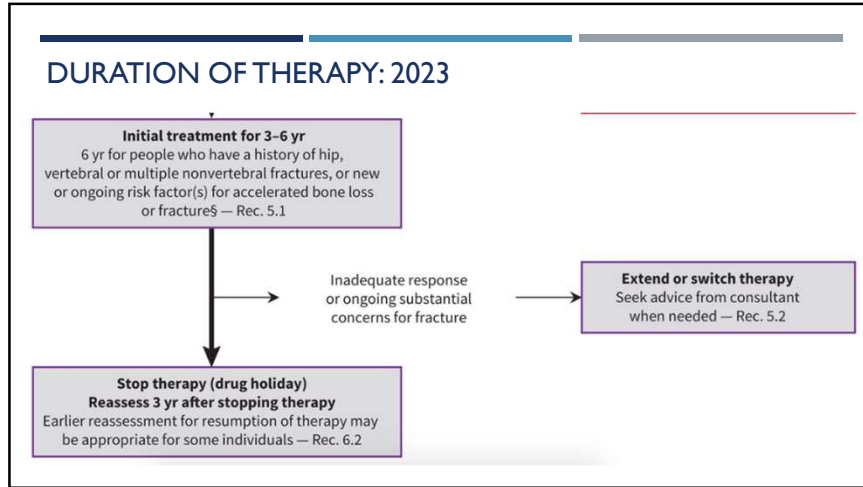
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13

BMD REASSESSMENT

2010	2023
If pharmacotherapy initiated: <ul style="list-style-type: none"> • 1-3 years Low risk: 5-10 years Moderate risk: 1-3 years High risk: no mention	If pharmacotherapy initiated: <ul style="list-style-type: none"> • 3 years If pharmacotherapy not initiated: <ul style="list-style-type: none"> • Risk < 10% → 5-10 years • Risk between 10-15% → 5 years • Risk ≥ 15% → 3 years

14

MONITORING THERAPY

6.4. We suggest against using a fracture risk assessment tool (FRAX or CAROC) for monitoring response to pharmacotherapy. Conditional recommendation; very low-certainty evidence

Remark: Inadequate response to treatment should be considered when > 1 fracture or substantial bone density decline (e.g., ≥ 5%) occurs despite adherence to an adequate course of treatment (typically > 1 yr). However, fractures or bone density decline during therapy do not always indicate inadequate response to treatment (e.g., secondary causes of osteoporosis, falls, BMD imprecision errors).

15

CALCIUM, VITAMIN D3, AND OTHER

	2010	2023 → all based on RDA
Calcium	Individuals > 50 → 1200mg	Men <ul style="list-style-type: none"> • 51-70 → 1000mg • > 70 → 1200mg Women <ul style="list-style-type: none"> • > 50 → 1200mg
Vitamin D3	Adults above 50 with risk of vit D insufficiency: 800-1000 IU daily, up to 2000 IU safe and does not need monitoring Target 25 OHD ≥ 75 nmol/l	≤ 70 → 600 IU > 70 → 800 IU *to meet RDA, Health Canada recommends supplementation of 400 IU/d on top of vit D-rich foods Target 25 OHD ≥ 50 nmol/l
Protein, vit K, Mg	No mention	For ppl following Canada's food guide, no supplementation required

16

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Vitamin D3	Adults above 50 with risk of vit D insufficiency: 800-1000 IU daily, up to 2000 IU safe and does not need monitoring Target 25 OHD ≥ 75 nmol/l	≤ 70 → 600 IU > 70 → 800 IU *to meet RDA, Health Canada recommends supplementation of 400 IU/d on top of vit D-rich foods Target 25 OHD ≥ 50 nmol/l
Protein, vit K, Mg	No mention	For ppl following Canada's food guide, no supplementation required

17

PRACTICAL PEARLS 101

18

HOW CAN I ACCESS ZOLEDRONIC ACID (IV BISPSPHONATE)?

Dose: 5 mg IV once a year → 3-6 years

For the treatment of osteoporosis in postmenopausal females who meet the following criteria:

- High risk* for fracture; and **In men: code = 523, same criteria**
- For whom oral bisphosphonates are contraindicated due to abnormalities of the esophagus (e.g. esophageal stricture or achalasia) OR inability to stand or sit upright for at least 30 minutes.

*High fracture risk is defined as either:

- 436
- a prior fragility fracture AND a moderate 10-year fracture risk (10% to 20%) based on the Canadian Association of Radiologists and Osteoporosis Canada (CAROC) tool or the Fracture Risk Assessment (FRAX) tool; OR
 - a high 10-year fracture risk (greater than or equal to 20%) based on the CAROC or FRAX tool; OR
 - where a patient's 10-year fracture risk based on the CAROC or FRAX tool, is less than the thresholds defined above, a high fracture risk based on evaluation of clinical risk factors for fracture

19

HOW CAN I ACCESS ZOLEDRONIC ACID (IV BISPSPHONATE)?

If you have hospital privileges → check your medical day care centre/day unit

If you have a private office exclusively → check private infusion clinics (e.g., Bayshore, Oshawa Clinic Group Infusion clinic, etc.)

20

WHEN SHOULD I CONSIDER DRUG HOLIDAY?

- Long term use of bisphosphonates and denosumab are associated with risk of atypical femoral fracture and osteonecrosis of the jaw; AFF and ONJ have also been associated with use of romosozumab



Papioannou et al. (2010) - 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. CMAJ Review DOI:10.1503/cmaj.100771
 Khan and Kaiser (2017). Atypical femoral fracture. CMAJ. 189 (14): E542. doi:https://doi.org/10.1503/cmaj.140450
 Image left: Hwang et al. (2023) Journal of Clinical Medicine. https://doi.org/10.3390/jcm12031038; right: Kharazmi, Nilsson, & Hallberg. (2017) British Dental Journal 222, 645

21

RISK FACTORS FOR AFF

ORIGINAL ARTICLE

Atypical Femur Fracture Risk versus Fragility Fracture Prevention with Bisphosphonates

Dennis M. Black, Ph.D., Erik J. Geiger, M.D., Richard Eastell, M.D., Eric Vittinghoff, Ph.D., Bonnie H. Li, M.S., Denison S. Ryan, M.P.H., Richard M. Dell, M.D., and Annette L. Adams, Ph.D.

Article Figures/Media Metrics August 20, 2020
 N Engl J Med 2020; 383:743-753
 DOI: 10.1056/NEJMoa1916525
 Chinese Translation 中文翻译

31 References 142 Citing Articles Letters

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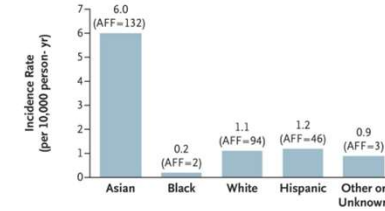
BLACK ET AL. (2020) NEJM

Caucasians	Asians
149 hip fractures prevented 2 AFF caused	91 hip fractures prevented 8 AFF caused

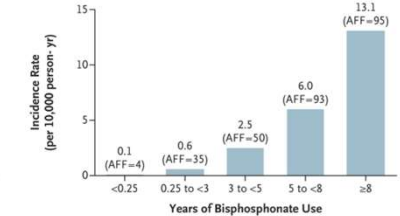
Black et al. (2020) Atypical femur fracture risk versus fragility fracture prevention with bisphosphonates. NEJM 383:743-753

23

B AFFs According to Race or Ethnic Group

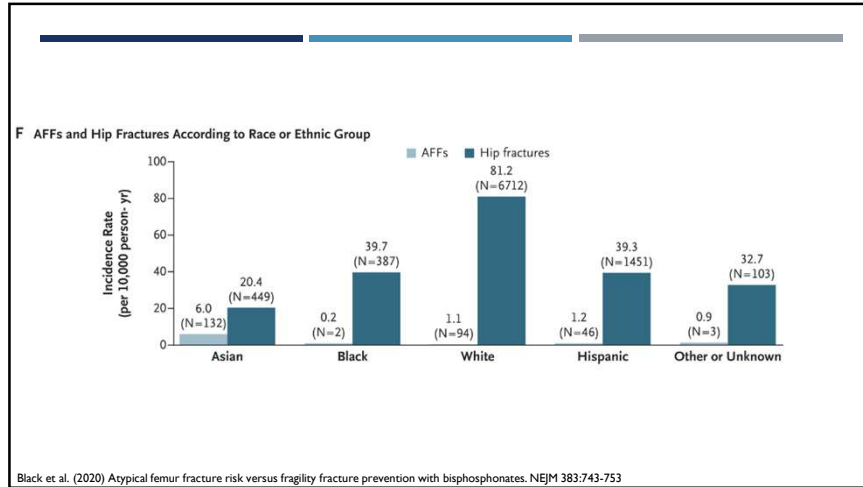


C AFFs According to Cumulative Bisphosphonate Exposure



Black et al. (2020) Atypical femur fracture risk versus fragility fracture prevention with bisphosphonates. NEJM 383:743-753

24



25

RISK FACTORS FOR FRACTURE WHILE ON DRUG HOLIDAY

- Poor adherence to meds initially
- Prior history of fracture
- Age >78 (compared to 50-60 years)
- Unit decrease in femoral neck T score during holiday
- Prior use of oral vs IV bisphosphonate

Wang, Wu, & Girgis (2022). Bisphosphonate drug holidays: evidence from clinical trials and real-world studies. JBMR Plus 6(6):1:17; doi: 10.1002/jbm4.10629

26

WHO SHOULD I CONSIDER BISPHOSPHONATE DRUG HOLIDAY FOR?

Bisphosphonate Drug Holiday

REDUCE the risk of Atypical Femoral Fracture

Individual factors:

- Treatment duration > 5-8 years
- Asian ethnicity
- Glucocorticoid use
- Femoral geometry
- Anthropomorphic features

INCREASE the risk of Fragility Fracture

Individual factors:

- Prevalent/incident fracture
- Low hip BMD ≤ -2.5 S.D. at end of treatment
- Older age
- Underweight
- Low adherence

Image: Hwang et al. (2023) Journal of Clinical Medicine, <https://doi.org/10.3390/jcm12031038>

27

WHAT TO DO IF DENOSUMAB IS INTERRUPTED?

- × No clear evidence however consensus statement was drafted during height of COVID-19 pandemic to account for more limited access to care
- × Potential options:
 - + Bridge with oral bisphosphonate ASAP
 - + If patient has underlying GI disorder would choose risedronate over alendronate as lower potency

<https://www.asbmr.org/about/statement-detail/joint-guidance-on-osteoporosis-management-covid-19>

28

HOW TO PERMANENTLY DISCONTINUE DENOSUMAB?

- × Osteoporosis Canada 2023
 - + If 4 or fewer doses → transition to bisphosphonate 6 months after last dose and proceed with 1 year course
 - + If 5 or more doses → refer to specialist

29

HOW TO PERMANENTLY DISCONTINUE DENOSUMAB?

- × No consensus between international guideline societies
- × Potential options:
 - + Single dose zoledronic acid, 6-8 months after last dose of denosumab
 - + 1 year course of alendronate, 6 months after last dose of denosumab
 - + Selective estrogen receptor modulators or hormone therapy may be considered if bisphosphonate not tolerated

Tay & Tay (2022). Discontinuing Denosumab: Can It Be Done Safely? A Review of the Literature. Endocrinol Metab (Seoul).

30

WHEN SHOULD I CONSIDER SECONDARY WORK-UP?

- × Fragility fracture in:
 - + Pre-menopausal woman
 - + Man under age 50
- × Clinical/historical features suspicious for **osteomalacia**
- × Suspected disorder that can cause secondary osteoporosis
- × Prior to starting potent antiresorptive agent
- × Suspicion for inadequate response to therapy

Ganesan, K., Jandu, J. S., Anastasopoulou, C., Ahsun, S., & Roane, D. (2023). Secondary Osteoporosis. StatPearls.

31

Drugs	Endocrine disorders	Gastrointestinal & Nutritional disorders
Glucocorticoid steroids Aromatase inhibitors Anticonvulsants (particularly phenytoin, phenobarbital) GnRH agonists and antagonists Androgen-deprivation agents Cancer chemotherapy Immunosuppressants (eg. cyclosporine)	Hyperparathyroidism Hyperthyroidism Hypercortisolism/Cushing's syndrome Diabetes mellitus (Type 1 & Type 2) Prolonged premature hypogonadism Acromegaly	Inflammatory bowel disease Celiac disease Bariatric surgery Pancreatic insufficiency Other malabsorptive syndromes Primary biliary cholangitis Chronic liver disease Eating disorder Malnutrition Parenteral nutrition Vitamin D and/or calcium deficiency

32

Rheumatologic disorders	Genetic disorders	Other disorders
Rheumatoid arthritis Other inflammatory arthritis disorders Systemic lupus erythematosus	Osteogenesis imperfecta Hypophosphatasia Other genetic causes of osteomalacia	Multiple myeloma Other marrow-related disorders Idiopathic hypercalciuria Chronic kidney disease/renal failure Chronic obstructive pulmonary disease Organ transplantation Multiple sclerosis Parkinson's disease Other neuromuscular disorders Prolonged immobilization Paget's disease Acquired causes of osteomalacia

33

TAKE HOME POINTS

- Evaluate for risk factors fracture and clinical signs of undiagnosed vertebral fracture to help make decision regarding initial BMD testing
- Suggest or recommend pharmacotherapy if 10 year fracture risk is 15% or higher
- Bisphosphonates are first line therapy for most patients
- Consider your exit strategy prior to start denosumab
- Decision for drug holiday is nuanced and depends on a patient's individual risk factor for developing AFF versus developing a fracture on drug holiday

34

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35