E16. Pharmacological Management of Osteoporosis in Postmenopausal Women:
An Endocrine Society Clinical Practice Guideline

Read the guideline and associated resources by navigating to:
endocrine.org/2019Osteoporosis

ENDO2019

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Plenary Panel Members

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- Nelson B. Watts, MD
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Panel:

- Clifford J. Rosen, MD
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- Richard Eastell, MBChB, MD
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Disclosures

Nelson B. Watts, MD – Consultant: Amgen Speaker: Amgen, Radius

Clifford J. Rosen, MD – No conflicts of interest

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Dolores Shoback, MD – No conflicts of interest

Access Guideline and Other Resources

Guideline

J Clin Endocrinol Metab 2019; 104(5): 1595–1622

Guideline Resource Page

endocrine.org/2019Osteoporosis

Includes access to:

- Full published guideline and systematic review papers
- Patient resources
- Pocket Card
- Interview with the Guideline Writing Committee Chair

Overview of Guideline

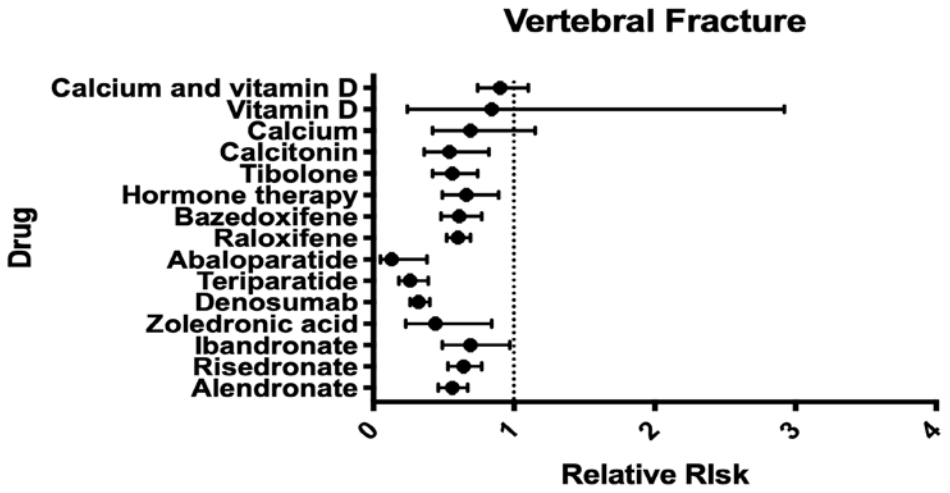
Clifford J. Rosen, MD

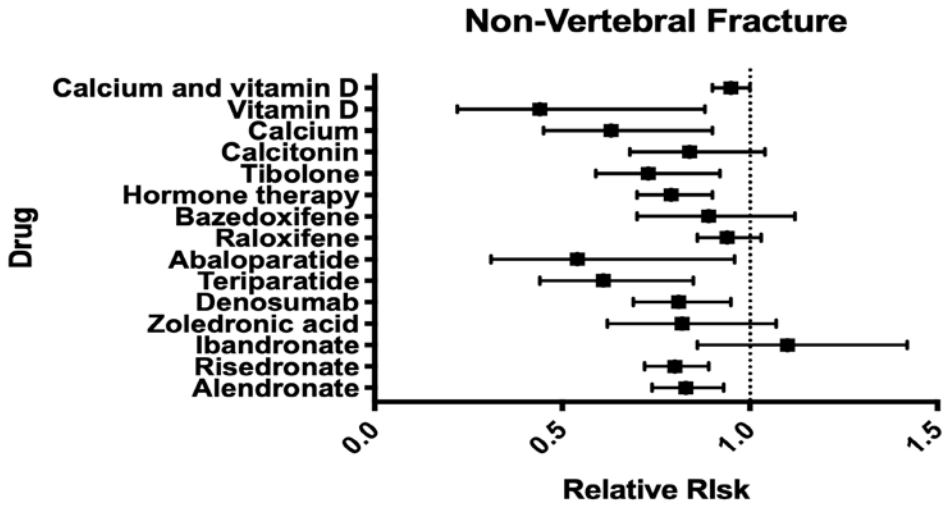
Senior Scientist, Director, Maine Medical Center Research Institute, ME

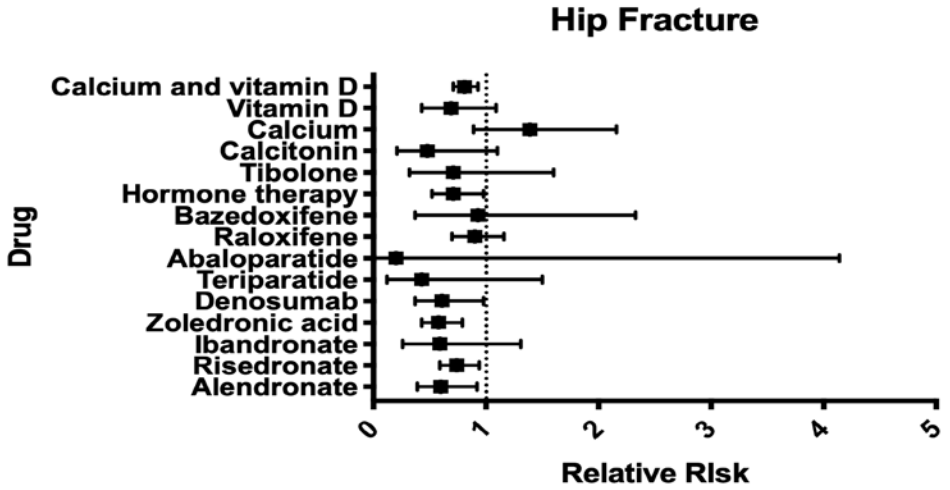
Introduction: Guideline Development

- Guideline Writing Committee and the Chair consisted of five content experts and a methodologist
- Recommendations were evidence-based; classified using the *GRADE* approach
- 2 systematic reviews and 1 meta-analysis:
  i. Synthesized the evidence derived from RCTs in postmenopausal women with primary osteoporosis
  ii. Evaluated values and preferences relevant to the management of osteoporosis

Risk of Fracture in Response to Treatment







Relative Risk and 95% CI
Effect of treatment compared to placebo
Direct calculation

Eastell R, Rosen CJ, Black DM, Cheung AM, Murad H, Shoback D. JCEM, 2019; 104(5)

Women's Values & Preferences of Treatment

Equally Ranked

- Efficacy/effectiveness
- Adverse effects

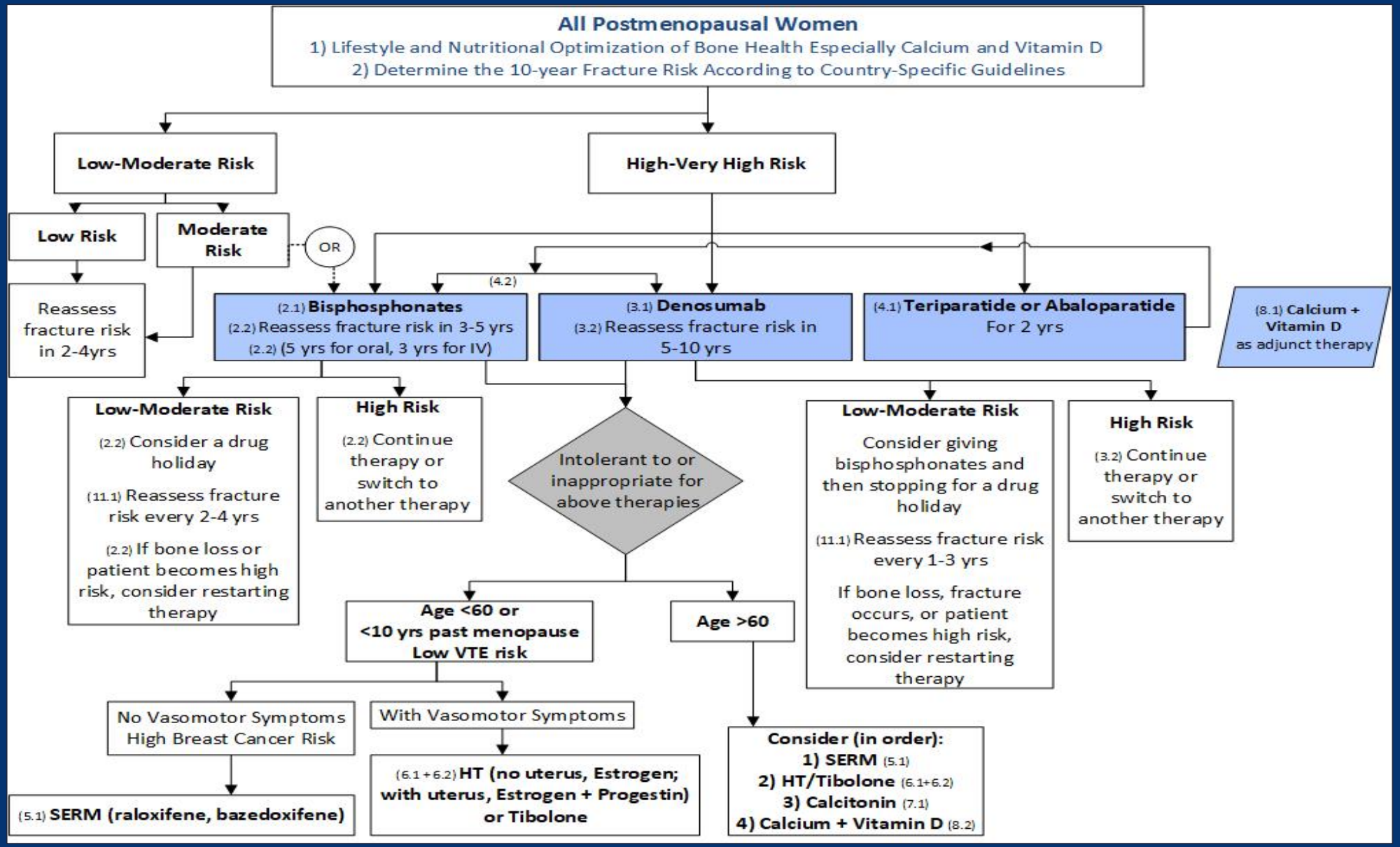
Convenient Administ-ration

- Oral preferred over injectable
- Less frequent dosing preferred over more frequent
- Injectable acceptable if less frequent doses

Other Decisional Factors

- Cost (out of pocket)
- Duration of treatment
- Drug time on the market
- Less drug-drug interactions
- Natural drug, doesn't cause hormonal effects

Algorithm for the Management of Postmenopausal Osteoporosis



Eastell R, Rosen CJ, Black DM, Cheung AM, Murad H, Shoback D. JCEM, 2019; 104(5)

Key Points

- Treat high risk individuals - particularly those with previous fracture.
- For risk-assessment follow country-specific risk assessment and intervention thresholds.
- Bisphosphonates and denosumab should be the first therapeutic choices for postmenopausal women at high risk of fracture.
- Reassess fracture risk after being on bisphosphonates for 3 – 5 years.

Key Points *(cont.)*

- Women who are on bisphosphonates and low-to-moderate risk of fractures should be considered for a bisphosphonate holiday after being reassessed.
- Prescribe anabolic therapy for women at very high risk of fractures, including those with multiple fractures.
- Supplement calcium and vitamin D in the diet or via supplements in all women undergoing treatment with other osteoporosis therapies.
- Monitor the BMD of high risk individuals with a low BMD every 1 to 3 years.

Cases, Panel Discussion & Audience Questions

Nelson B. Watts, MD

Director, Mercy Health Osteoporosis and Bone Health Services, Cincinnati, OH

Case discussions to focus on:

1. Selecting Initial Treatment
2. Bisphosphonate Holidays
3. Denosumab: Why would you stop? What would you do?
4. Anabolic Agent for Initial Treatment
5. Combination Therapy
6. If you consider teriparatide for a denosumab user, would you add or switch?

Case 1: Selecting Initial Treatment

Presentation:

Helen is a 74-year old woman who has been well all her life. Her weights is 105 pounds (47.6 Kgs) and is 5'8" (1.7 m) tall. BMI is 16 kg/m^2. Menopause was age 53. Her mother had a hip fracture at age 82.

T- scores:

Spine -3.2; Femoral neck -2.7

Z-scores:

Spine -1.0; Femoral neck -0.9

Other Labs:

Calcium and creatinine - normal;
25-OH D -satisfactory

Follow country-specific risk assessment, and intervention thresholds, in countries that do not include T-score.

Question: What pharmacologic treatment would you recommend?

A. An oral bisphosphonate
B. An IV bisphosphonate
C. Raloxifene
D. Denosumab

Selecting Initial Treatment

Panel Discussion
Audience Questions

Guideline:

- She is at high risk as she has BMD T-score of -2.5 or less.
- Thus, the guidelines would recommend bisphosphonate (oral or iv) or denosumab, taking into account patient preference.
- We would have recommended raloxifene (or menopausal hormone therapy) had the patient been intolerant of the above treatments.

Case 2: Bisphosphonate Holidays

Presentation:

Teresa is a 60-year old woman with a history of facial neuralgia and acid reflux. She is known to have osteoporosis and had fractures at spine (T6 in 2013 - fell down the stairs), clavicle, and humerus.

Treatment:

Received 3 annual infusions of zoledronic acid, last in March 2017. Now on vitamin D and calcium.

T- scores:

Spine -2.4 (-4.4% since 2016)
Total hip -1.0 (-3.5% since 2016)

Other Labs:

P1NP - 39 µg/L (previous 13 in 2015)

Question: What is the next best step?

A. Nothing; follow up
B. Give another 3 infusions of zoledronic acid
C. Give 1 infusion of zoledronic acid
D. Switch to another treatment
E. Discharge; she no longer has osteoporosis according to BMD criteria

Bisphosphonate Holidays

Panel Discussion
Audience Questions

➢ Guideline

- A bisphosphonate drug holiday is considered after 3 years of treatment with zoledronic acid if the BMD T-scores is above -2.5.
- Bisphosphonate (or other treatment) should be resumed within 5 years of stopping it or when there is evidence that the treatment is no longer working.
- Here, the PINP level has increased significantly (by more than 10 mcg/L) and the BMD decreased significantly, the treatment is no longer working.

Case 3: Denosumab

Presentation:

Denise is a 71-year old woman who has been receiving denosumab every 6 months without side effects, started 5 years ago. Cost is not an issue.

T- scores:

Spine -3.2 ➔ -1.1
Total hip -2.7 ➔ -0.9

Question: What is the next best step?

A. Stop treatment
B. Carry on with denosumab
C. Change to zoledronic acid
D. Change to an oral bisphosphonate

Denosumab
Why would you stop? What would you do?

Panel Discussion
Audience Questions

Guideline:

- Denosumab should not be stopped without subsequent anti-resorptive therapy (bisphosphonate, HT or SERM).
- Follow-on treatment prevents the rebound in bone turnover, rapid bone loss and increased risk of vertebral fracture that may occur after stopping denosumab.

Case 4: Anabolic Agent for Initial Rx

Presentation:

Joan is 70 year-old woman, menopausal for 25 years, referred for osteoporosis management. No prior therapy. No prior radiation therapy. Recent painful T12 compression fracture.

T-scores:

Spine -3.5; Femoral neck -2.9

Z-scores:

Spine -1.3; Femoral neck -1.1

Other Labs:

Calcium, creatinine, PTH, ALP, SPEP, UPEP normal
25-OH D satisfactory

Question: What therapy would you initiate?

A. An oral bisphosphonate
B. An IV bisphosphonate
C. Denosumab
D. Teriparatide or abaloparatide

Anabolic Agent for Initial Rx

Panel Discussion
Audience Questions

➢ Guideline:

- She is at very high risk of fracture as she has a recent vertebral fracture as well as BMD T-score of -2.5 or less.
- She could be considered for an anabolic treatment (teriparatide or abaloparatide) or for an anti-resorptive treatment.
- If she receives an anabolic treatment this should be followed by an anti-resorptive treatment to maintain bone density gains.

Case 5: Combination Therapy

Presentation:

Rebecca is a 58-year old woman. Natural menopause was age 52. Wrist fracture age 57 (fell while fly fishing) – “worst the orthopedist had ever seen”. Calcium intake and exercise are OK. Father - hip fracture age 79. Mother - may have had osteoporosis (stroke age 62).

T- scores:

Spine -3.2 Femoral neck -3.0

Z-scores:

Spine -1.8 Femoral neck -1.9

Other Labs:

Calcium, creatinine, SPEP, kappa and lambda light chains, PTH, 24-h urine calcium normal.
25-OH D satisfactory.

She says cost is no problem and wants whatever will increase her bone density fastest and greatest.

Question: What do you tell her that would be?

A. Teriparatide
B. Abaloparatide
C. Denosumab
D. Combination teriparatide + denosumab

Combination Therapy

Panel Discussion
Audience Questions

Guideline:

- She is at high risk as she has BMD T-score of -2.5 or less. Thus, the guidelines would recommend bisphosphonate (oral or iv) or denosumab, taking into account patient preference.
- We would have recommended teriparatide or abaloparatide had the fracture risk been very high.

Case 6: Teriparatide for Denosumab User - Add or Switch?

Presentation:

Jane is a 67-year old white woman. She had a remote vertebral fracture discovered one year ago. She has been otherwise healthy; no history of radiation therapy. Treatment with denosumab was started (2 doses so far). She fell last week and sustained a fracture of her proximal humerus.

T-scores:

Spine -3.5; Femoral neck -2.7

Other Labs:

Calcium and creatinine are normal, 25-OH D is satisfactory.

You are considering teriparatide.

Question: What would you do?

A. Continue denosumab and not add teriparatide

B. Continue denosumab and add teriparatide

C. Stop denosumab and begin teriparatide

Teriparatide For A Denosumab User - Add Or Switch?

Panel Discussion
Audience Questions

Guideline:

- In clinical practice, the occurrence of one fracture while on effective therapy and in a compliant patient will raise the consideration of changing therapy.
- We would recommend consideration for teriparatide of abaloparatide treatment.

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