

Osteoporosis for the PCP: Breaking it Down ...

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Disclosures

- None

Background

- Osteoporosis is a major public health threat for 54 million Americans
- 1 in 2 postmenopausal women will have an osteoporotic fracture in her lifetime
- Concerns re: Atypical Femoral Fractures and Osteonecrosis of the Jaw
 - decline in treatment, higher incidence of hip fracture
- Focus will be on:
 - Postmenopausal Women
 - Treatment

Agenda

- Guidelines – Friend or Foe?
- Risk stratification – FRAX
- Therapies – Old and New
- Questions

Guidelines

USA

American College of Physicians (ACP): A clinical practice guideline on the treatment of low bone density or osteoporosis to prevent fractures in men and women, update (2017)

International

Endocrine Society (ES): Clinical practice guideline on the pharmacological management of osteoporosis in postmenopausal women (2019)

ACP Guidelines 2017

- Clinicians offer pharmacologic treatment with alendronate, risedronate, zoledronic acid, or denosumab to reduce the risk for hip and vertebral fractures in women who have known osteoporosis. (Grade: strong recommendation; high-quality evidence).
- Clinicians treat osteoporotic women with pharmacologic therapy for 5 years. (Grade: weak recommendation; low-quality evidence).
- Clinicians offer pharmacologic treatment with bisphosphonates to reduce the risk for vertebral fracture in men who have clinically recognized osteoporosis. (Grade: weak recommendation; low-quality evidence).
- Recommend against bone density monitoring during the 5-year pharmacologic treatment period for osteoporosis in women. (Grade: weak recommendation; low-quality evidence).

ACP Guideline 2017

- Recommend against using menopausal estrogen therapy or menopausal estrogen plus progestogen therapy or raloxifene for the treatment of osteoporosis in women. (Grade: strong recommendation; moderate-quality evidence)
- Clinicians should make the decision whether to treat osteopenic women 65 years of age or older who are at a high risk for fracture based on a discussion of patient preferences, fracture risk profile, and benefits, harms, and costs of medications. (Grade: weak recommendation; low-quality evidence)

Goal/Limitations of Guidelines

- Bring attention to importance of osteoporosis management and treatment
- Try to simplify for the busy primary care
- Oversimplification/loss of nuance
 - Pharmacokinetic differences between bisphosphonates/denosumab
- Missing some important therapeutic considerations
 - Anabolic agents

ES Guidelines- 1

- Who to treat?
 - High Risk Postmenopausal women (*Strong recommendation, high evidence*)
 - Defining High risk-
 - Previous Femoral Neck , Hip, or Vertebral Fracture (higher risk for recent fracture <2 years, than remote fracture >5 years)
 - T-score <-2.5 on DXA at Femoral Neck, Hip or Spine
 - T-score <1.5 on DXA with high fracture risk by calculator [FRAX >20% osteoporotic fx, 3% hip fx]

ES Guidelines-2

Bisphosphonates

- **Recommendations**

Initial treatment with bisphosphonates (alendronate, risedronate, zoledronic acid, and ibandronate) to reduce fracture risk. Ibandronate is not recommended to reduce nonvertebral or hip fracture risk. (*Strong recommendation; high-quality evidence.*)
- In postmenopausal women with osteoporosis who are taking bisphosphonates, recommends that fracture risk be reassessed after 3 to 5 years, and women who remain at high risk of fractures should continue therapy, whereas those who are at low-to-moderate risk of fractures should be considered for a “bisphosphonate holiday.” (*Strong recommendation; low quality evidence.*)

Reduction in Fracture risk with bisphosphonates versus placebo

| Bisphosphonate | Vertebral fracture risk | Hip fracture risk | Nonvertebral fracture risk |
|-----------------|-------------------------|-------------------|----------------------------|
| alendronate | 44% | 40% | 17% |
| risedronate | 36% | 26% | 20% |
| ibandronate | 31% | None | None |
| zoledronic acid | 56% | 42% | 18%* |

Drug Holiday

- Not automatic. Can be considered
 - after 5 years of oral therapy
 - 3 years of IV therapy
- Only if not at high risk
- On holiday fracture risk and BMD should continued to be assessed every 2-4 years

ES Guidelines

Denosumab

- In postmenopausal women with osteoporosis who are at high risk for osteoporotic fractures, the guideline recommends using denosumab as an alternative initial treatment. (*Strong recommendation; high quality evidence.*)
- 60 mg every 6 months subcutaneous injection
- Must be given every 6 months since effects reverses after 6 months- NO Drug Holidays with Denosumab

Reduction in fracture risk with denosumab versus placebo

| Medication | Vertebral fracture risk | Hip fracture risk | Nonvertebral fracture risk |
|------------|-------------------------|-------------------|----------------------------|
| denosumab | 68% | 39% | 19% |

ES Guidelines

- **Recommendation**

In postmenopausal women with osteoporosis at very high risk of fracture, such as those with severe or multiple vertebral fractures, the guideline recommends teriparatide or abaloparatide treatment for up to 2 years for the reduction of vertebral and nonvertebral fractures. (*Strong recommendation; moderate quality evidence.*)
- In postmenopausal women with osteoporosis who have completed a course of teriparatide or abaloparatide, the guideline recommends treatment with antiresorptive osteoporosis therapies to maintain bone density gains. (*Strong recommendation; low quality evidence.*)

Reduction in fracture risk for Anabolic agent versus placebo

| Medication | Vertebral fracture risk | Hip fracture risk | Nonvertebral fracture risk |
|---------------|-------------------------|----------------------------|----------------------------|
| teriparatide | 74% | Reduction not significant* | 39% |
| abaloparatide | 87% | Reduction not significant* | 46% |



FRAX

The screenshot shows the FRAX Fracture Risk Assessment Tool website. At the top, there is a logo of a yellow and white patterned circle, followed by the text "FRAX® Fracture Risk Assessment Tool". Below the logo is a navigation bar with links for "Home", "Calculation Tool", "Paper Charts", "FAQ", "References", and a language selector set to "English". The main content area is titled "Calculation Tool". It includes a section for "Country: US (Caucasian)" and "Name/ID: []". A link "About the risk factors" is also present. The "Questionnaire:" section contains 12 numbered questions. Questions 1 through 9 are dropdown menus for age, sex, weight, height, previous fractures, parent fractures, current smoking, glucocorticoids, and rheumatoid arthritis. Questions 10 through 12 are radio button groups for secondary osteoporosis, alcohol consumption, and femoral neck BMD. To the right of the questionnaire is a sidebar with an American flag icon, "Weight Conversion" (Pounds to kg), "Height Conversion" (Inches to cm), and a footer with the number "07713517" and the text "Individuals with fracture risk assessed since 1st June 2011".

- Only to be used in osteopenia
- Ages 40-90
- Race/country dependent

Therapy Threshold

- >3% hip fracture, >20% major osteoporotic fracture

Therapies- Old and New

- Calcium/VitaminD
 - Calcium 1200 mg /day. <1000 mg should be supplements, dietary calcium is preferred
 - Vitamin D – check level, treat to at least normal range >30
- Exercise
 - Strength training exercises-especially those for the upper back
 - Weight-bearing aerobic activities
 - Flexibility exercises
 - Stability and balance exercises
- Raloxifene
 - SERM
 - Low risk for DVT/history of Breast cancer
 - Can't
- Calcitonin
 - Not included in guidelines, not recommended

Therapies - Old and New

Anti Resorptives

- Bisphosphonates
 - Fosamax (Alendronate)
 - Actonel (Risedronate)
 - Boniva (Ibandronate)
 - Reclast (Zoledronic Acid)
- Prolia (Denosumab)
 - Biologic RankL –Inhibitor

Anabolics

- Forteo (teriparotide)
 - PTH analog
- Tymlos (abalaparotide)
 - PTHrP analog

Anti-Resorptive/Anabolic

- Evenity (romosozumab)
 - Sclerostin inhibitor

Question 1

A postmenopausal woman presents with thoracic back pain and found to have a vertebral compression fracture. The patient should

- a. Be instructed to take calcium and vitamin D and manage pain with calcitonin
- b. Start treatment with anabolic agent like teriparatide
- c. Obtain bone density and if normal do not need to treat
- d. Obtain bone density and start patient on therapy likely bisphosphonate

Question 2

A postmenopausal woman has been on bisphosphonate therapy for 5 years falls and fractures her hip. What do you do next?

- a. Put her on drug holiday since she has been on therapy 5 years
- b. Start treatment with anabolic agent like teriparatide
- c. Add calcium and vitamin D but continue the bisphosphonate
- d. Switch therapy to denosumab

Question 3

A postmenopausal woman has a bone density that shows T-score of -3.0 in the spine and -2.5 in the hip. She has not personally had a fracture but her mother had a hip fracture. She is terrified to take a bisphosphonate because she doesn't want "all these other fractures" and for "her jaw to hurt and her teeth to fall out". You advise her

- a. To continue weight bearing exercise, take calcium vitamin D and get a DXA every 2 years to monitor
- b. Start on teriparatide
- c. Start her on ibandronate
- d. Start on romosozumab

Conclusion

- Primary care physicians are pivotal in being gatekeepers for educating and treating patients with osteoporosis or at risk for it
- There are many more options than there used to be and so conversations need to be had to help reduce fracture risk
- Use specialists to help manage more complicated cases or if administration of certain drugs denosumab are not available







- *It is exceptionally laudable that the ACP took on the difficult task of developing osteoporosis guidelines at a time when there is a crisis in the field, as evidenced by a 50% reduction in the use of prescription bone therapy after hip fractures. Despite the clear value of the ACP guidelines to many patients and clinicians, these guidelines fall short in a number of important nuances and circumstances familiar to specialty providers. Our goal in presenting this critique is not to “pour cold water” on a good initial effort, but instead to “turn up the heat” on our colleagues in an effort to advance a more evidence-based approach where possible, to generate more evidence where needed, and to personalize care, particularly when there is a shortage of suitable evidence. We believe such an approach will yield the best outcomes in the care of the many patients with complex cases of osteoporosis seen by rheumatologists and other specialty practitioners.*

Response to the American College of Physicians Osteoporosis Guideline, 2017 Update.
[Arthritis Rheumatol.](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5667041/) 2017 Nov;69(11):2097-2101. doi: 10.1002/art.40305. Epub 2017 Oct 17.



US Preventive Services Task Force. Screening for osteoporosis to prevent fractures: US Preventive Services Task Force Recommendation Statement. 2018

- Women aged ≥ 65 years should be screened for osteoporosis with bone measurement. Postmenopausal women aged < 65 years and at increased risk should receive bone measurement
- Several clinical risk assessment tools are available:
 - Simple Calculated Osteoporosis Risk Estimation (SCORE)
 - Osteoporosis Risk Assessment Instrument (ORAI)
 - Osteoporosis Index of Risk (OSIRIS)
 - Osteoporosis Self-Assessment Tool (OST)

Recommendations from Other Societies

| Society | Recommendation |
|---|---|
| National Osteoporosis Foundation | BMD testing in all women aged ≥ 65 years, all men aged ≥ 70 years; also postmenopausal women aged < 65 years and men aged 50 to 69 years based on risk factors including fracture as an adult |
| International Society for Clinical Densitometry | BMD testing in all women aged ≥ 65 years, all men aged ≥ 70 years; also postmenopausal women aged < 65 years and men aged < 70 years based on risk factors for low bone mass |
| American Academy of Family Physicians | No DXA screening in women aged < 65 years and men aged < 70 years with no risk factors |
| American College of Obstetricians and Gynecologists | BMD testing with DXA beginning at age 65 years in all women and selective screening in postmenopausal women aged < 65 years who have osteoporosis risk factors or an adult fracture |
| American Association of Clinical Endocrinologists | Evaluating all women aged ≥ 50 years for osteoporosis risk and considering BMD testing based on clinical fracture risk profile |
| Endocrine Society | Screening men aged > 70 years and adults aged 50 to 69 years with significant risk factors or fracture after age 50 years |

Society Providing Recommendation

| Patient Category | USPSTF | NOF | AACE | ISCD |
|---------------------------------------|--------|-----|------|------|
| Women \geq 65 years of age | Yes | Yes | Yes | Yes |
| Women aged 60-64 with risk factors | Yes | Yes | Yes | Yes |
| All women \geq 65 with risk factors | | Yes | Yes | Yes |
| All women with a fragility fracture | | Yes | Yes | Yes |
| Anyone receiving treatment for OP | | | Yes | Yes |
| Men aged \geq 70 years | | | | Yes |
| All men with a fragility fracture | | | | Yes |
| Anyone considering therapy for OP | | Yes | | |
| Women on prolonged HRT | | Yes | | |





Executive Summary

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