Osteoporosis in postmenopausal women

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Clinical question

How effective are bisphosphonates and denosumab for preventing fractures in postmenopausal women?

Bottom line

Bisphosphonates and denosumab are similarly effective. Over 1 to 4 years, bisphosphonates or denosumab provide an absolute reduction of about 0.5% to 1.0% for hip fractures, 1.5% to 3% for nonvertebral fractures, and 3% to 6% for vertebral fractures, compared with placebo.

Evidence

Differences are statistically significant unless noted.

Bisphosphonates

- Eleven systematic reviews[1] compared alendronate, risedronate, or zoledronate with placebo.
- The systematic reviews with the best quality and reporting found that over 1 to 4 years, bisphosphonates reduced the following.
  - -Hip fracture (4-7 RCTs, 9863-11 859 patients)[2-4]: 0.5% to 2.0% vs 1% to 3% with placebo (NNT = 100-200).
  - -Nonvertebral fracture (4-6 RCTs, 9625-12 397 patients)[2,3,5]: about 9% vs about 11% with placebo (NNT = 35-65).
  - -Vertebral fracture (2-6 RCTs, 3139-7802 patients)[2-4]: 3% to 8% vs 7% to 13% with placebo (NNT = 16-33).
- Results are consistent with other systematic reviews.[1]
- Systematic reviews rarely distinguish true primary and secondary prevention.[2,3] The best data[6] suggest similar relative benefit in primary and secondary prevention (eg, alendronate: relative risk is 0.74 vs 0.81 for nonvertebral fracture and 0.60 vs 0.53 for vertebral fracture).

Denosumab

- Five systematic reviews[1] compared denosumab with placebo; absolute event rates by fracture type not reported.
- The largest RCT[7] (7868 postmenopausal women, T-score ≤-2.5) compared denosumab with placebo over 3 years.
  - -Hip fracture: 0.7% vs 1.1% placebo (NNT = 230).
  - -Nonvertebral fracture: 6.1% vs 7.5% placebo (NNT = 72).
  - -Vertebral fracture: 2.3% vs 7.1% placebo (NNT = 21).

Bisphosphonates versus denosumab

- One systematic review[1] reported no difference in hip, nonvertebral, and vertebral fractures.
- Four systematic reviews[1] (4-11 RCTs, 1942-5446 patients) reported no difference in clinical fracture risk.

Context

- Overall limitations: event rates infrequently reported, variable outcome definitions, industry funding of RCTs.
- Atypical fracture risk with bisphosphonates increases with duration of therapy, particularly beyond 5 years.[8]
  - -Fractures prevented outnumber atypical fractures at about 14-100:1 with 5 years of treatment.
- Approximate drug cost (per year)[9]: $480 for risedronate and alendronate, $350 for zoledronate intravenous infusion, $800 for denosumab subcutaneous injection.

Implementation

The osteoporosis screening tool is a simplified tool that reliably predicts osteoporosis and identifies those who would benefit from bone mineral density testing.[10] Before starting a bisphosphonate or denosumab, discuss fracture risk and potential risks and benefits with the patient. The Mayo Clinic's Bone Health Choice Decision Aid provides information to support that discussion.[11] When prescribing, consider duration of therapy. Evidence suggests that after 5 years of treatment, discontinuation of bisphosphonates carries little to no increased future fracture risk,[12] and atypical fracture risk increases with duration of therapy beyond 5 years.[8]

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Competing interests
None declared

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