



## Osteoporosis treatment for post-menopausal women

### Clinical Question: How effective are bisphosphonates and denosumab in preventing fractures in post-menopausal women?

**Bottom Line: Bisphosphonates and denosumab are similarly effective at reducing risk of fracture in post-menopausal women. Over 1-4 years, bisphosphonates or denosumab provide an absolute reduction of ~0.5-1.0% for hip fractures, ~1.5-3% for non-vertebral fractures and ~3-6% for vertebral fractures compared to placebo.**

#### Evidence:

- Differences statistically significant unless noted.
  - Bisphosphonates:
    - 11 systematic reviews<sup>1-11</sup> compared alendronate, risedronate, or zoledronate to placebo:
      - Systematic reviews with best quality/reporting: over 1-4 years, bisphosphonates reduce:
        - Hip fracture [4-7 randomized controlled trials (RCTs), 9,863-11,859 patients]:<sup>1,2,3</sup>
          - 0.5-2.0% versus 1-3% placebo, number needed to treat (NNT)=100-200.
        - Non-vertebral fracture (4-6 RCTs, 9,625-12,397 patients):<sup>1,2,4</sup>
          - ~9% versus ~11% placebo, NNT=35-65.
        - Vertebral fracture (2-6 RCTs, 3139-7802 patients):<sup>1,2,3</sup>
          - 3-8% versus 7-13% placebo, NNT=16-33.
      - Consistent with other systematic reviews.<sup>3,5,7,8,10</sup>
      - Systematic reviews rarely distinguish true primary and secondary prevention.<sup>1-2</sup> Best available data<sup>12</sup> suggests similar relative benefits in primary and secondary prevention. Example alendronate:
        - Non-vertebral fracture: Relative risk 0.74 versus 0.81.
        - Vertebral fracture: Relative risk 0.60 versus 0.53.
    - Denosumab:
      - Five systematic reviews<sup>5,6,10,13,14</sup> compared denosumab versus placebo: Absolute event rates by fracture type not reported.
      - Largest RCT<sup>15</sup> (7868 post-menopausal women, T-score ≤-2.5) compared denosumab and placebo over 3 years:
        - Hip fracture: 0.7% versus 1.1% placebo, NNT=230.
        - Non-vertebral fracture: 6.1% versus 7.5% placebo, NNT=72.
        - Vertebral fracture: 2.3% versus 7.1% placebo, NNT=21.

- Bisphosphonates versus denosumab:
  - 6 systematic reviews<sup>6,10,16-19</sup> compared bisphosphonates and denosumab:
    - One systematic review<sup>10</sup> reported no difference in hip, non-vertebral and vertebral fractures.
    - Four systematic reviews<sup>16-19</sup> (4-11 RCTs, 1942-5446 patients) reported no difference in clinical fracture risk.
- Overall limitations: Event rates infrequently reported, variable outcome definitions, industry funding of RCTs.

### **Context:**

- Previous articles provide guidance for screening osteoporosis<sup>20</sup> and treatment duration.<sup>21</sup>
  - Atypical fracture risk with bisphosphonates increases with duration of therapy, particularly beyond 5 years.<sup>22</sup>
    - Fractures prevented outnumber atypical fractures at ~14-100:1 with 5 years of treatment.
- Decision aids<sup>23</sup> assess fracture risk and describe potential benefit to patients.
- Drug cost only (per year):<sup>24</sup>
  - Risedronate and alendronate: ~\$480.
  - Zoledronate IV infusion: ~\$350.
  - Denosumab SC injection: ~\$800.

### **Authors:**

Samantha Moe PharmD, G Michael Allan MD CCFP

### **Disclosures:**

Authors do not have any conflicts of interest to declare.

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