

# Osteoporosis: Era of the bisphosphonates

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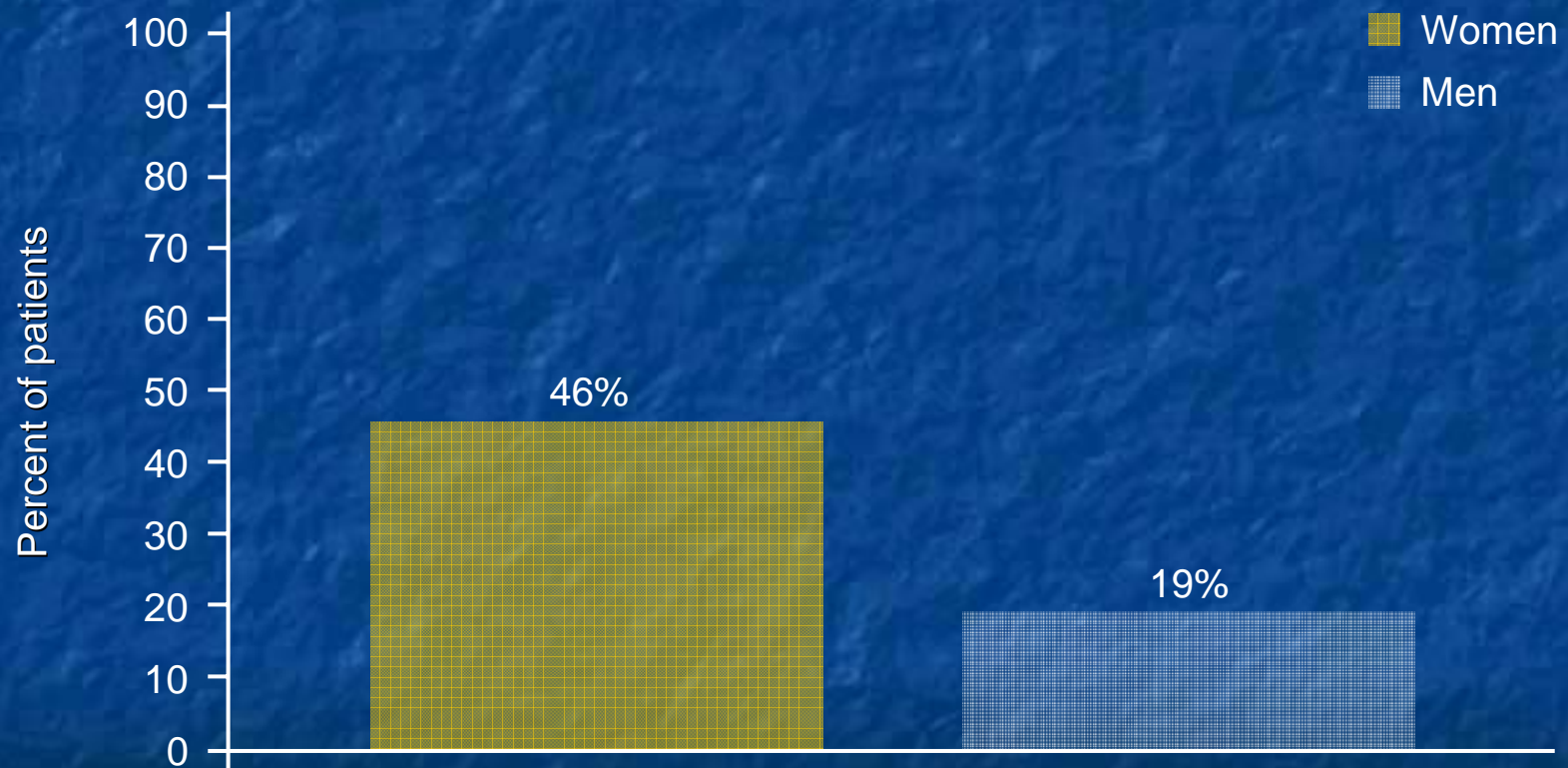
————— *Teaching Slides* —————

# The Women's Health Initiative study results

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- HT increased BMD and reduced fracture risk
  - Data from estrogen/progestin arm showed increased risk of breast cancer and stroke with little or no CV benefit
  - With exception of breast cancer risk, these results are confirmed by estrogen-alone arm
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# The dilemma of diagnosis



Percent of patients with vertebral compression fracture who had osteoporosis diagnosed before their fracture

## Who should be treated? New NOF guidelines:

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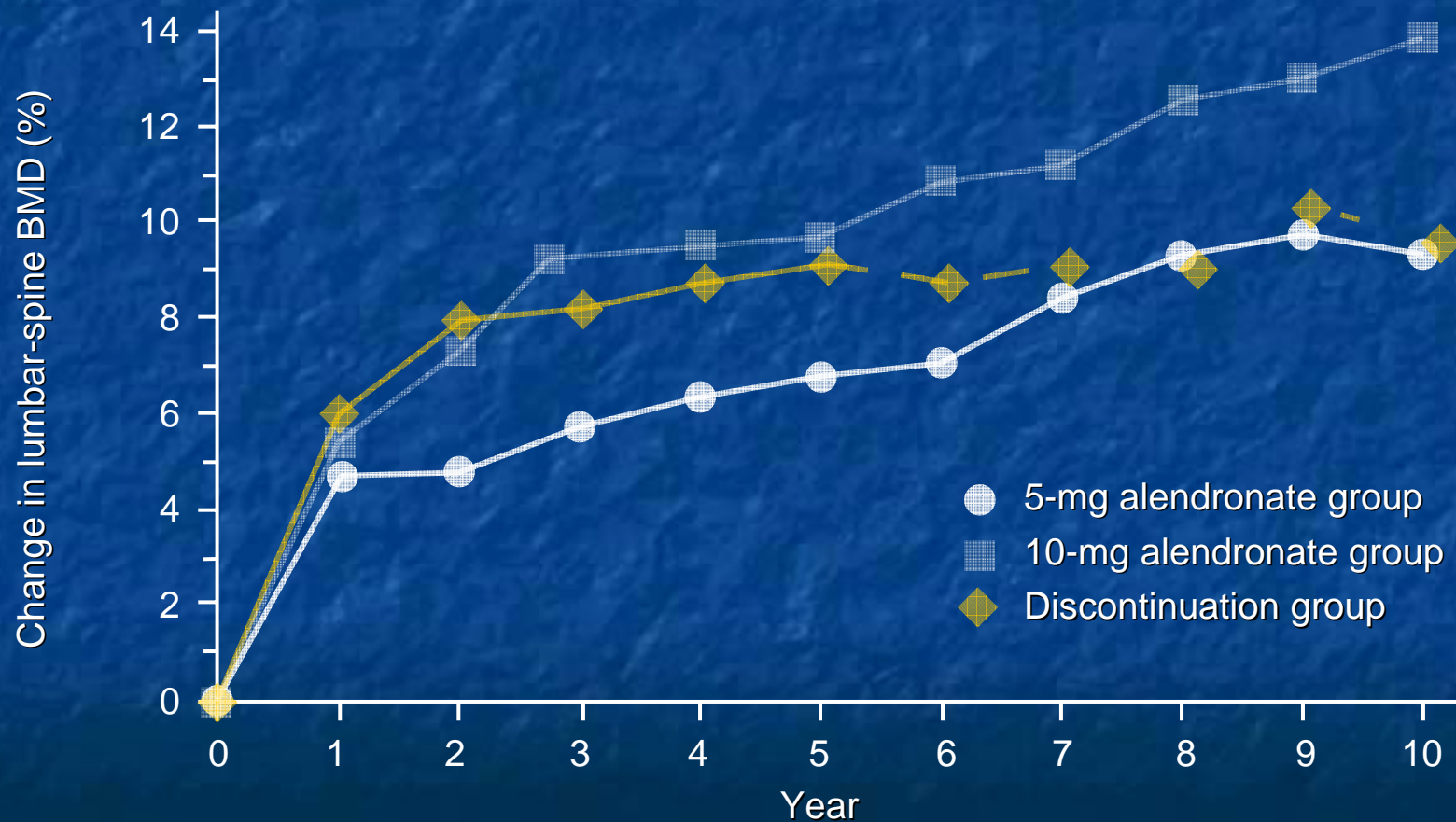
- BMD T-scores less than -2.0 and no other risk factors
  - BMD T-scores below -1.5 and one or more other risk factors
  - Patients with prior vertebral or hip fractures
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## Ten-year alendronate study (*N Engl J Med*)

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- 247 postmenopausal women with osteoporosis
  - Subjects received alendronate for up to 10 years
  - Study design: randomized, double-blind, placebo-controlled
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# Ten-year alendronate study: change in lumbar-spine BMD (%)



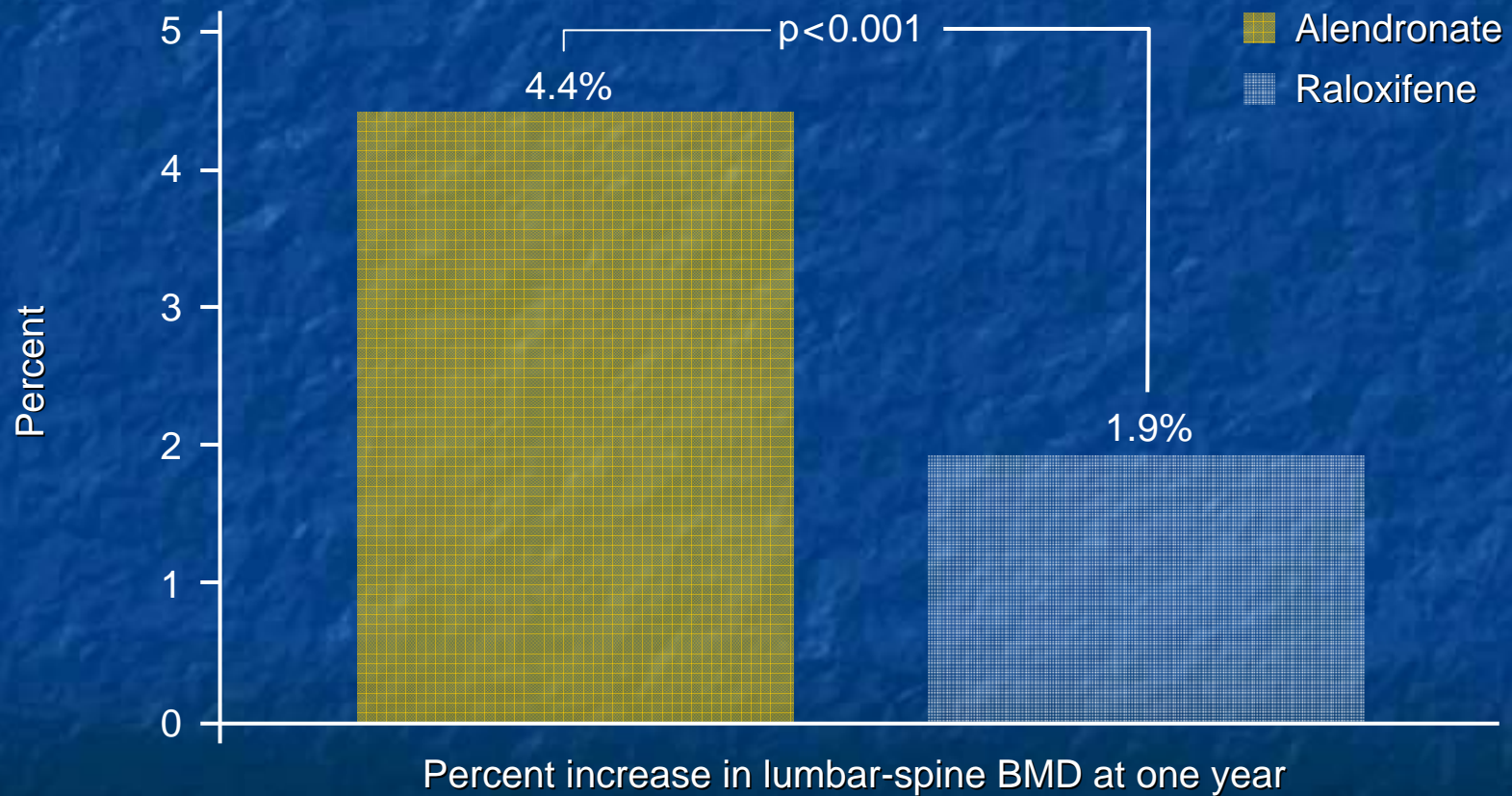
# Preliminary results of EFFECT

(the Efficacy of Fosamax vs Evista Comparison Trial)

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- 456 women with osteoporosis
  - Randomized to alendronate 70 mg once weekly or raloxifene 60 mg/day
  - BMD measured at baseline, at 6 months, and at 12 months
  - Primary end point: % change in lumbar-spine BMD at one year
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# EFFECT results: change in lumbar-spine BMD (%)



## Current treatment options: Estrogen

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- Ultralow-dose formulation recently approved for prevention of osteoporosis
  - Results of a controlled trial of very-low-dose transdermal estradiol in 417 women aged 60-80:
    - Lumbar-spine BMD increased 2.6% in estradiol group and 0.6% in placebo group ( $p < 0.001$ )
    - Mean total hip BMD increased 0.4% in the estradiol group and decreased 0.8% in the placebo group ( $p < 0.001$ )
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## Current treatment options: SERMs

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- Results of MORE trial:
    - Modest benefits on BMD
    - Reductions in bone turnover markers
    - Reduction in risk of vertebral fractures
    - Significant reductions seen in incidence of breast cancer and cardiovascular and cerebrovascular disease
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## Current treatment options: Calcitonin

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- Results of PROOF trial:
    - 200 IU/day reduced risk of vertebral fractures by 33% overall and by 36% in patients with existing vertebral fractures
    - 100 IU/day and 400 IU/day did not reach statistical significance
  - Results problematic because of 59% dropout rate and lack of blinding
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# Current treatment options: Bisphosphonates

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- Bind to sites where active bone resorption is taking place
  - Bone resorption is inhibited while bone formation continues, resulting in net increases in bone mass
  - Two available bisphosphonates: alendronate and risedronate
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# Current treatment options: Bisphosphonates (continued)

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## ■ Results of FIT:

- Alendronate increased spine BMD by 7-9% and hip BMD by 5-8%
- By year 4, the risk of fracture in women with osteoporosis but no prior hip fractures was reduced by 56%

## ■ Results of VERT trial:

- Approximately 40% reductions in risk of vertebral fractures with risedronate
  - These reductions were sustained for at least five years
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# Anabolic therapy (PTH)

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- Stimulates osteoblastic activity, resulting in increases in bone mass and strength
  - Results of a randomized, controlled study:
    - BMD increased overall and in lumbar spine and vertebral neck
    - New vertebral fractures in 14% (placebo), in 5% (20- $\mu$ g group), and 4% (40- $\mu$ g group)
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# Summary

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- Evidence supports the bisphosphonates as first-line therapy for the prevention and treatment of osteoporosis.
  - Comparison across trials of antiresorptive therapies suggested that alendronate is more effective than risedronate, calcitonin, raloxifene, or hormone therapy.
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