



# General Management

- **Treatment of any Disease Causing Bone Loss**
- **Ensure Dietary Calcium Intake  $\geq 1000$  mg /d**
- **Ensure Adequate Dietary Protein Intake**
- **Correct or Prevent Vitamin D Insufficiency (800 IU/d)**
- **Promote Weight-Bearing Physical Exercise**
- **Reduce Falling Risk**
- **Reduce Fall Consequences (Hip Protectors)**



# Risk Factors Associated with Falls

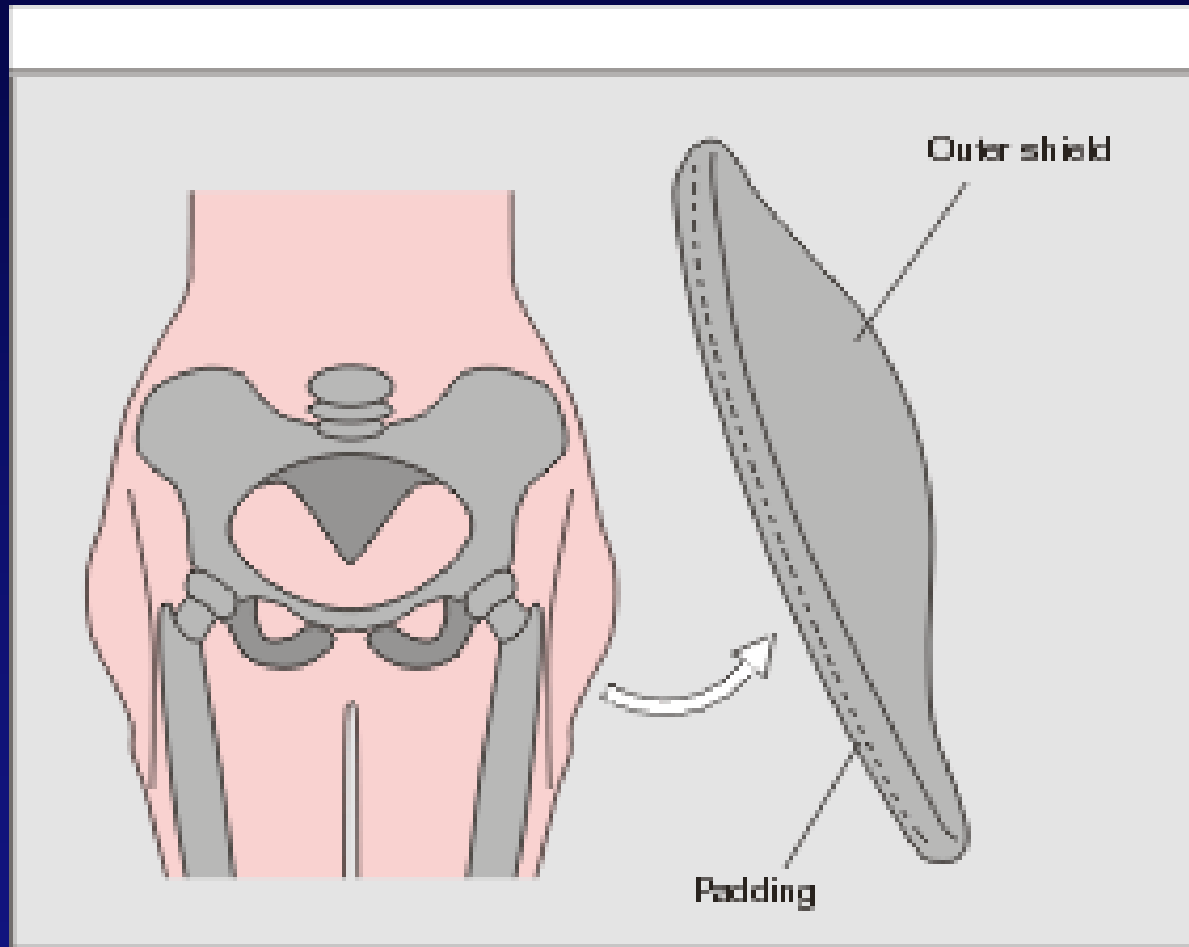
- 1. Impaired Mobility, Disability**
- 2. Impaired Gait and Balance**
- 3. Neuromuscular or Musculoskeletal Disorders**
- 4. Age**
- 5. Impaired Vision**
- 6. Neurological, Heart Disorders**
- 7. History of Falls**
- 8. Medication**
- 9. Cognitive Impairment**

After Myers et al., Bone 1996



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# The Hip Protector





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# Therapeutic Agents Used in Osteoporosis

## *Anticatabolic Agents*

- *Estrogens ± Progestagens*
- *SERMs*
- *Bisphosphonates*
- *Calcitonin*
- *Calcium*

## *Complex Action*

- *Vitamin D and Derivatives*
- *Anabolic Steroids*
- *(Ipriflavone)*
- *Tibolone*

## *Anabolic Agents*

- *(Fluoride)*
- *Parathyroid Hormone*

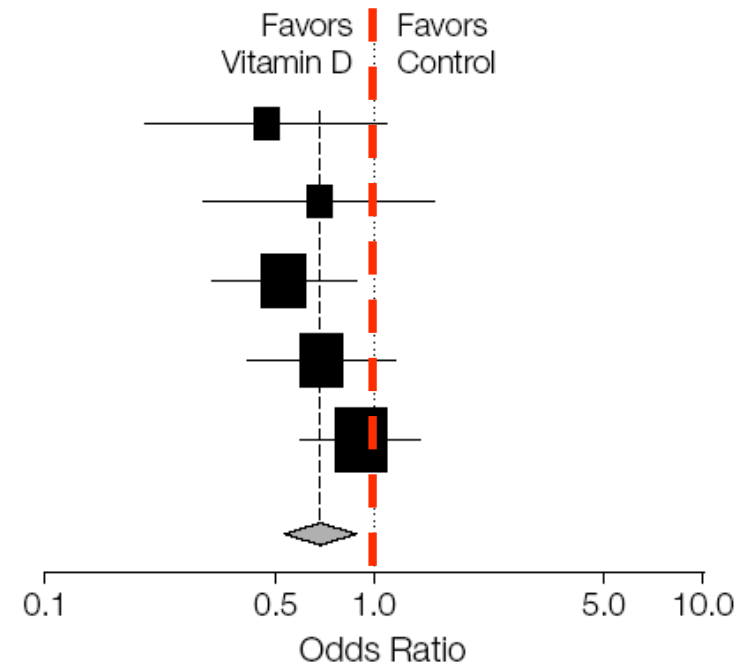


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# Vitamin D and Risk of Falling

## Primary Analysis

| Source                              | Odds Ratio<br>(95% CI) |
|-------------------------------------|------------------------|
| Pfeifer et al, <sup>11</sup> 2000   | 0.47 (0.20-1.10)       |
| Bischoff et al, <sup>12</sup> 2003  | 0.68 (0.30-1.54)       |
| Gallagher et al, <sup>17</sup> 2001 | 0.53 (0.32-0.88)       |
| Dukas et al, <sup>18</sup> 2004     | 0.69 (0.41-1.16)       |
| Graafmans et al, <sup>19</sup> 1996 | 0.91 (0.59-1.40)       |
| Pooled (Uncorrected)                | 0.69 (0.53-0.88)       |



H. Bischoff-Ferrari et al JAMA 2004



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# Hormone Replacement Therapy and Fracture Risk

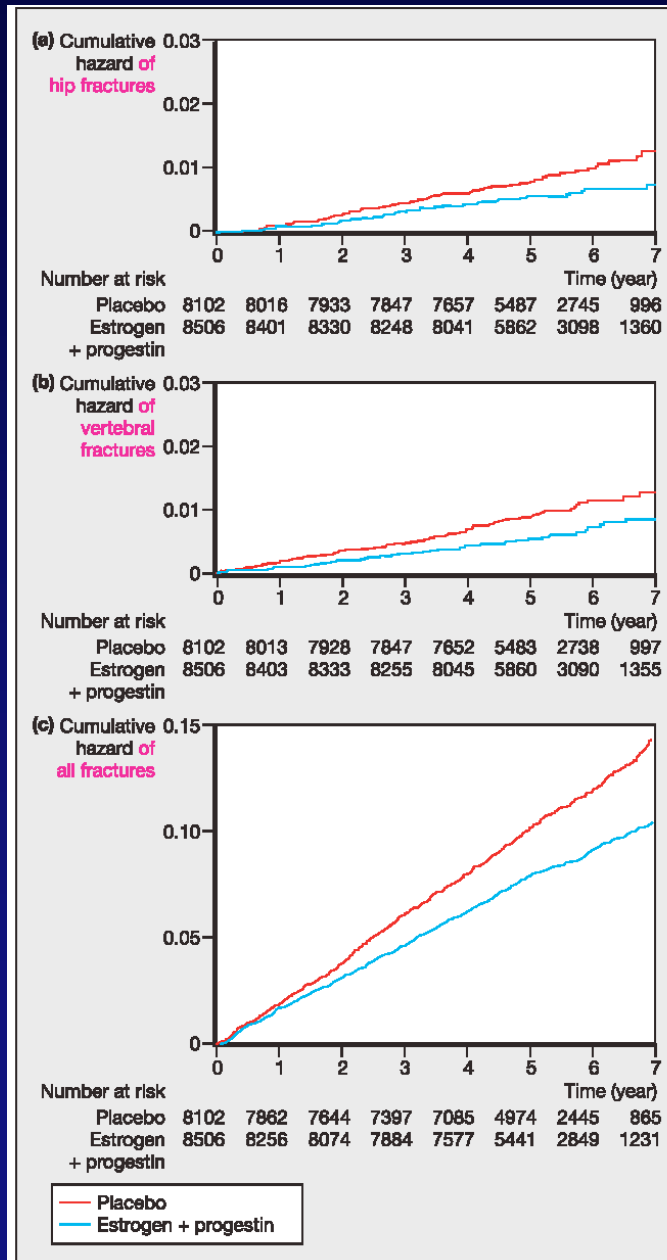
Hip

Vertebral

All Fractures

Placebo  
HRT

WHI Study,  
Cauley et al, 2003

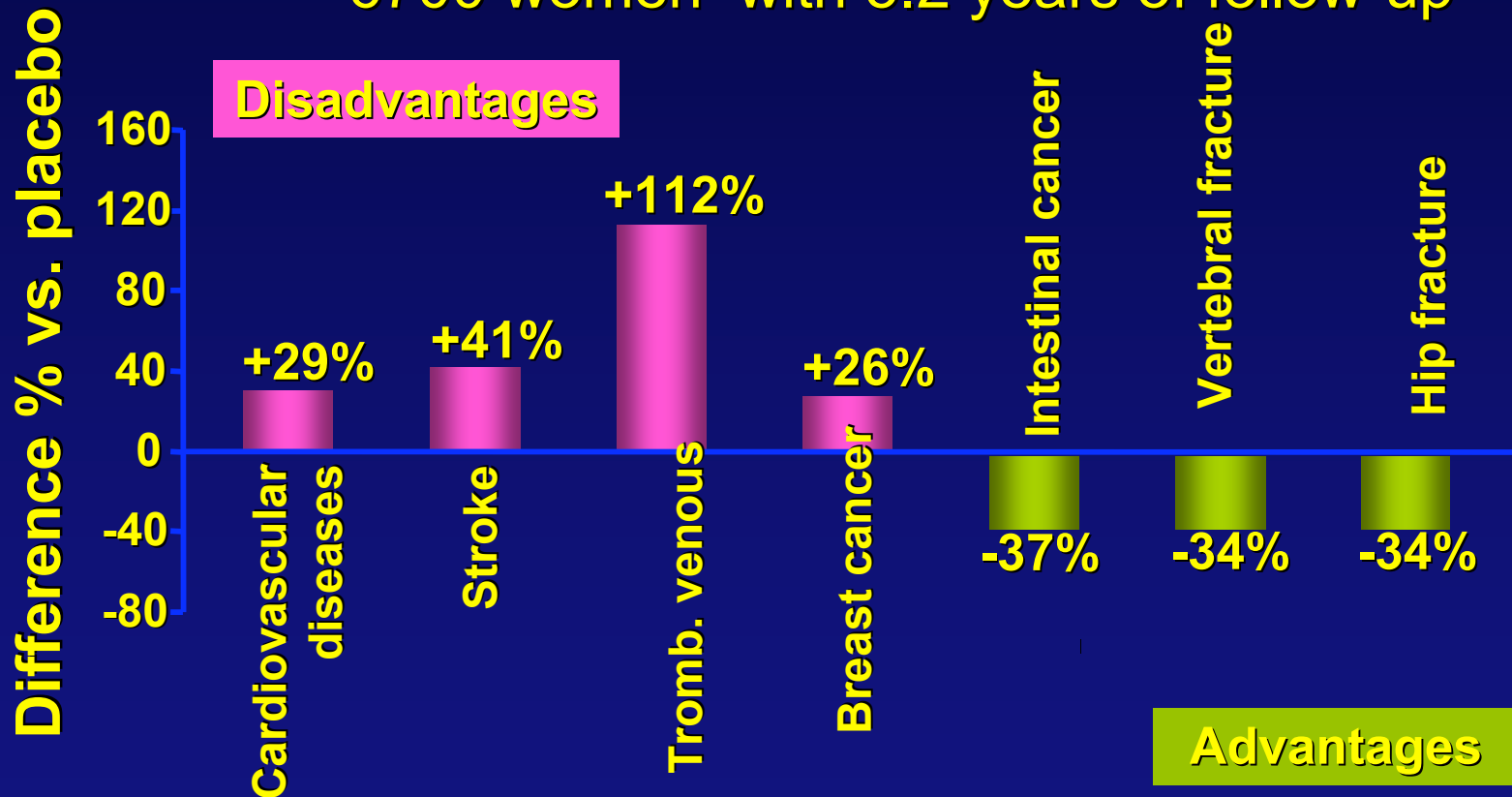




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# Women's Health Initiative - First randomized, controlled trial in women (50-79 years) treated with HRT

6700 women with 5.2 years of follow-up

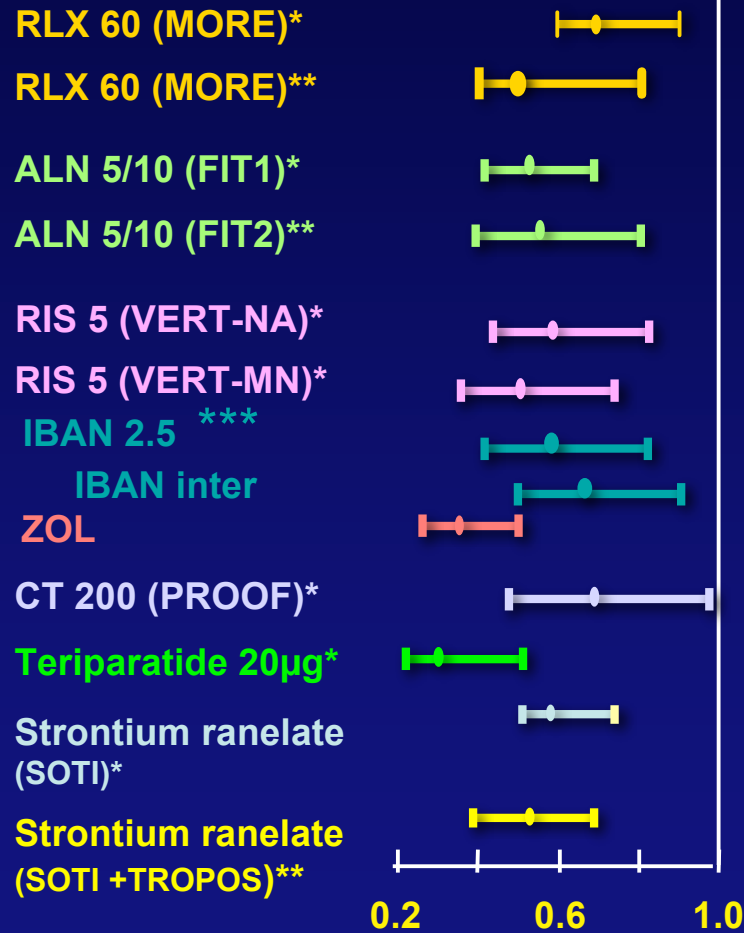


Manson JE et al, N Engl J Med, 2002;347:523-534



# Anti -fracture efficacy (RR $\pm$ 95% CI)

## Vertebral Fx



\* with prev vert fracture(s) \*\* without prev vert fractures

\*\*\* with or without prev vert fractures



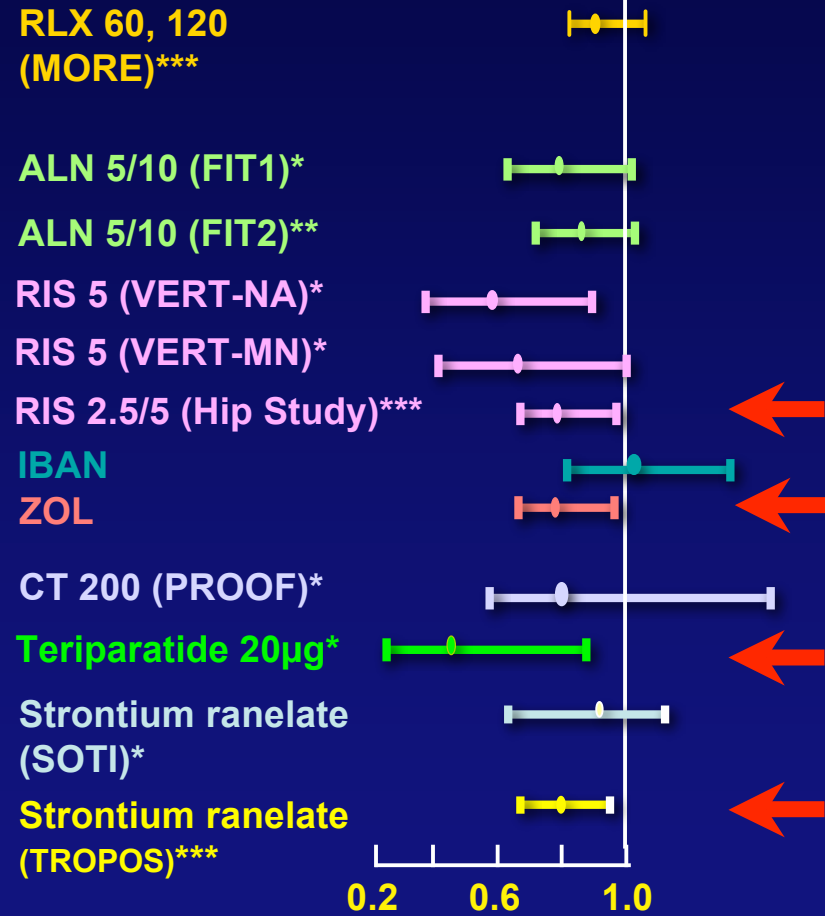


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# Anti -fracture efficacy (RR ± 95% CI)

## Vertebral Fx

## Non-Vertebral Fx



\* with prev vert fracture(s) \*\* without prev vert fractures

\*\*\* with or without prev vert fractures



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# Anti -fracture efficacy (RR $\pm$ 95% CI)

## Hip Fx

Significant hip fracture risk  
Reduction: 3 studies

Only studies with  
preplanned analysis:  
RIS 2.5/5 (Hip Study)  
ZOL 5 mg (Horizon Study)

RLX 60, 120  
(MORE)\*\*\*

ALN 5/10 (FIT1)\*



ALN 5/10 (FIT2)\*\*

RIS 5 (VERT-NA)\*

RIS 5 (VERT-MN)\*

RIS 2.5/5 (Hip Study)\*\*\*

IBAN



ZOL



CT 200 (PROOF)\*

Teriparatide 20 $\mu$ g\*

Strontium ranelate

(SOTI)\*

Strontium ranelate

(TROPOS)\*\*\*

0.2 0.6 1.0



\* with prev vert

\*\*\* with or without prev vert fractures



## Bisphosphonate New Schedules of Administration

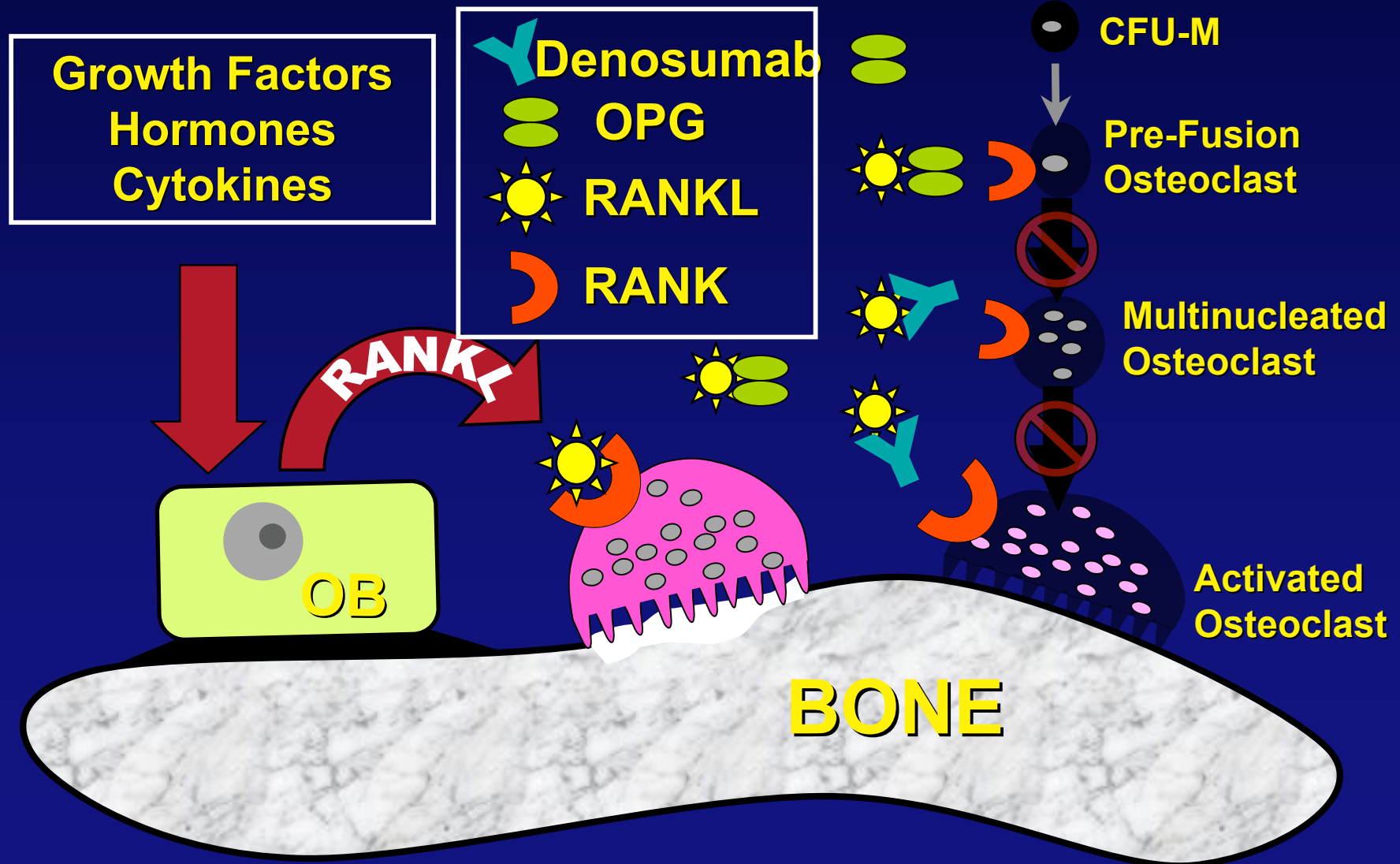
1. Weekly (**Alendronate, Risedronate**)  
-> Monthly Oral Administration - Ibandronate  
- Risedronate
2. Trimonthly Intravenous Administration - Ibandronate
3. Annual Intravenous Administration - Zoledronate \*
4. Sequential Regimen (PTH -> ALN, RIS or ALN -> PTH)

\*: Fracture Data



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# Mechanism of Action of Denosumab

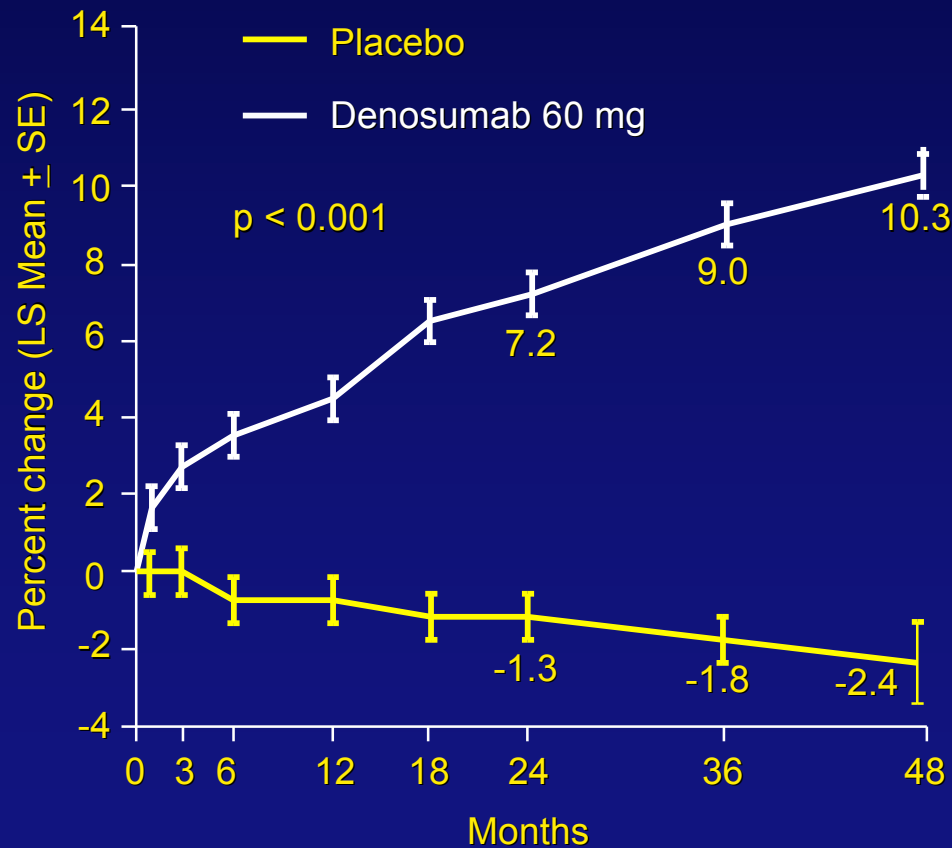




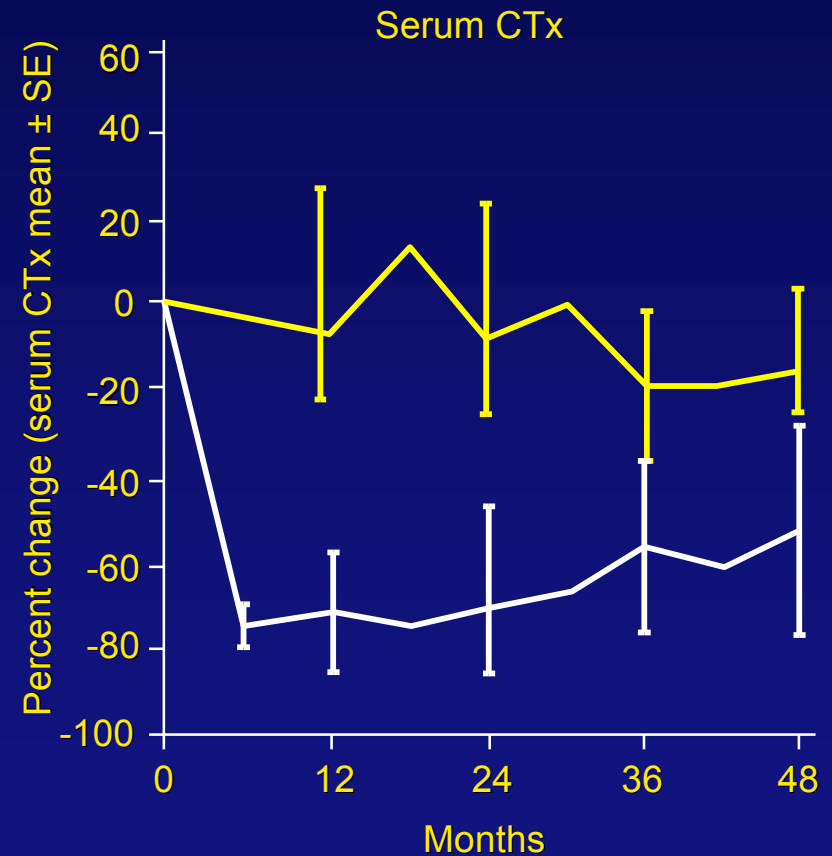
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# Effect of Denosumab on Bone Mineral Density and Bone Turnover Markers: 48-Month Results

Effect of 4 years of denosumab treatment on lumbar spine BMD



Effect of 4 years of denosumab treatment on serum CTX level





# Osteoporosis Treatment in 2008

## Summary

- HRT: ↓ spine fx; ↓ hip fx
- SERMS: ↓ spine fx; no effect on peripheral fx
- Calcitonin: possible ↓ spine fx; no hip data
- Alendronate: ↓ spine fx; ↓ hip fx
- Risedronate: ↓ spine fx; ↓ hip fx
- Ibandronate: ↓ spine fx; no effect on hip
- Zoledronate: ↓ spine fx; ↓ hip fx
- PTH: ↓ spine fx
- Strontium Ranelate: ↓ spine fx; ↓ hip fx

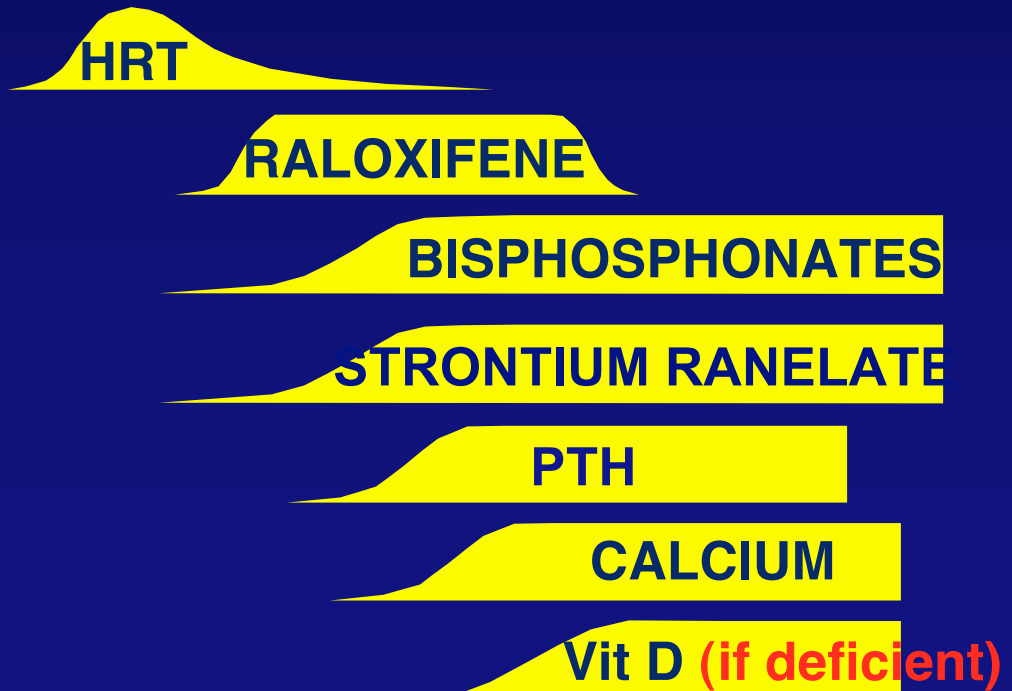
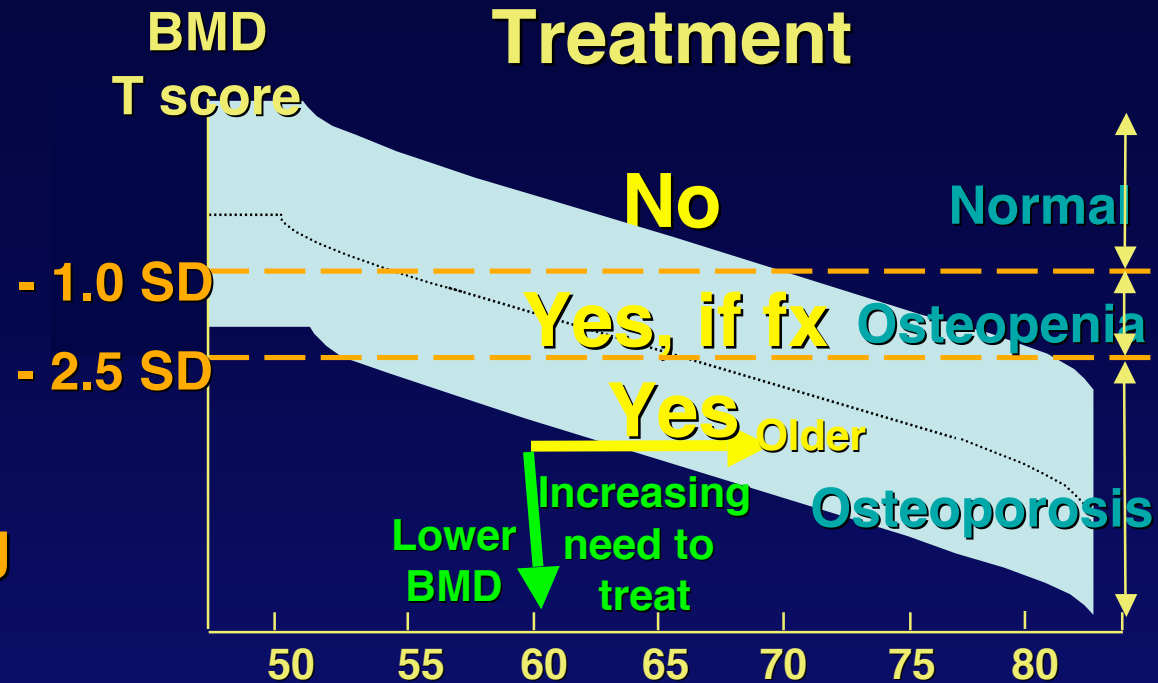


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Adapted from  
E. Seeman  
(2004)

## Factors Influencing Treatment Decision

- Advancing age
- Lower BMD
- Presence of Fracture
- Risk factors or disease causing continued bone loss
  - Leanness
  - Family history





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# 1. Aim of Therapy

**≠ Treatment of  
Osteoporosis**

**= Treatment of Patients  
with Osteoporosis**

## 2. Never Too Late