

AME Regionale

“Approccio terapeutico all’osteoporosi”

Alfredo Scillitani

Unità di Endocrinologia

Ospedale “Casa Sollievo della Sofferenza”

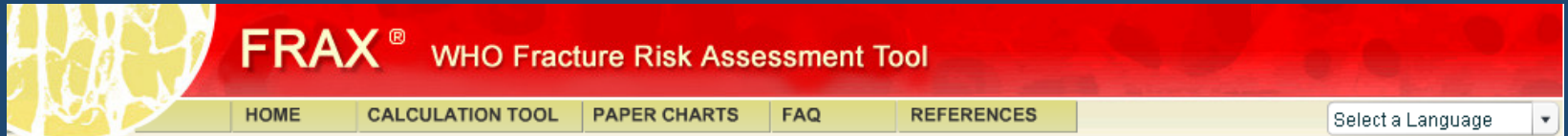
San Giovanni Rotondo

Matera, 9 Maggio 2014

“Il principale scopo della terapia dell’osteoporosi è quello di ridurre il rischio di fratture”

Cooper C. et al. *Lancet* 1995; 345: 743-744

FRAX[®] WHO Fracture Risk Assessment Tool



Calculation Tool



Weight Conversion:

pound:

Height Conversion:

inch:

Country : **UK** Name / ID : [About the risk factors](#)

Questionnaire:

1. Age (between 40-90 years) or Date of birth
Age: Date of birth: Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

5. Previous fracture No Yes

6. Parent fractured hip No Yes

7. Current smoking No Yes

8. Glucocorticoids No Yes

9. Rheumatoid arthritis No Yes

10. Secondary osteoporosis No Yes

11. Alcohol 3 more units per day No Yes

12. Femoral neck BMD

FRAX[®] WHO Fracture Risk Assessment Tool

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Select ▼

DeFRA: una via italiana alla predizione del rischio

Fattoriali di rischio DeFRA

	<i>Frattura di femore</i>	<i>Fratture Cliniche</i>
Storia familiare Frattura femore	1.6	1.2
Fuma <10 sigarette	1.3	1.0
Fuma >10 sigarette	1.9	1.5
Cortisonici (>5 mg Prednisone EQ)*	4.5	4.0
Immunosoppressori e Ipertiroidismo iatrogeno	1.3	1.3
Cortisonici <5 mg >2 mg Prednisone Eq	2	1.7
Alcool (>3 unità die)	1.5	1.2
Una pregressa frattura vertebrale o di femore	2.2	2.2
Più pregresse fratture vertebrali o di femore	4.0	4.0
Pregresse fratture non traumatiche (non femore o vertebre*)	1.4	1.4
Artrite Reumatoide e altre connettiviti	1.3	1.2

*Algoritmo non applicabile; *= connettiviti, terapie immunosoppressive, ipertiroidismo iatrogeno.

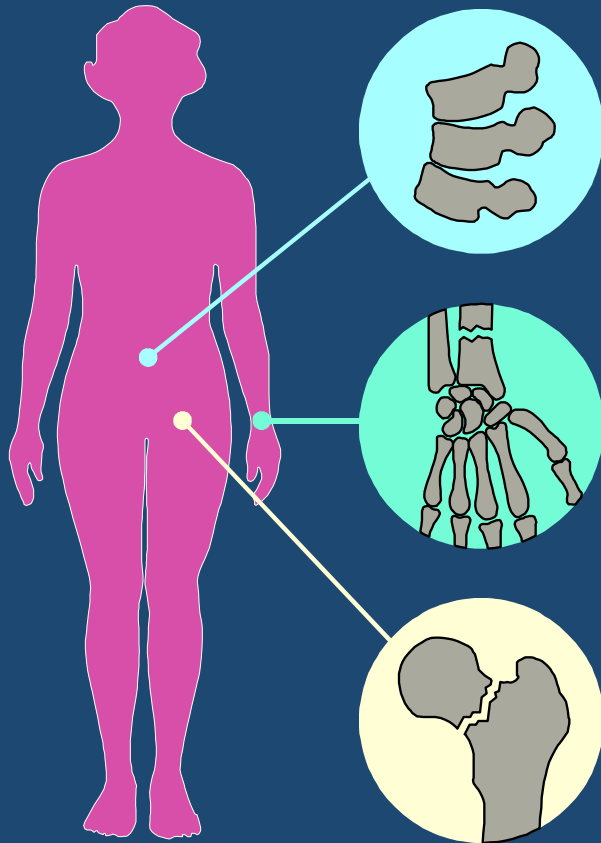
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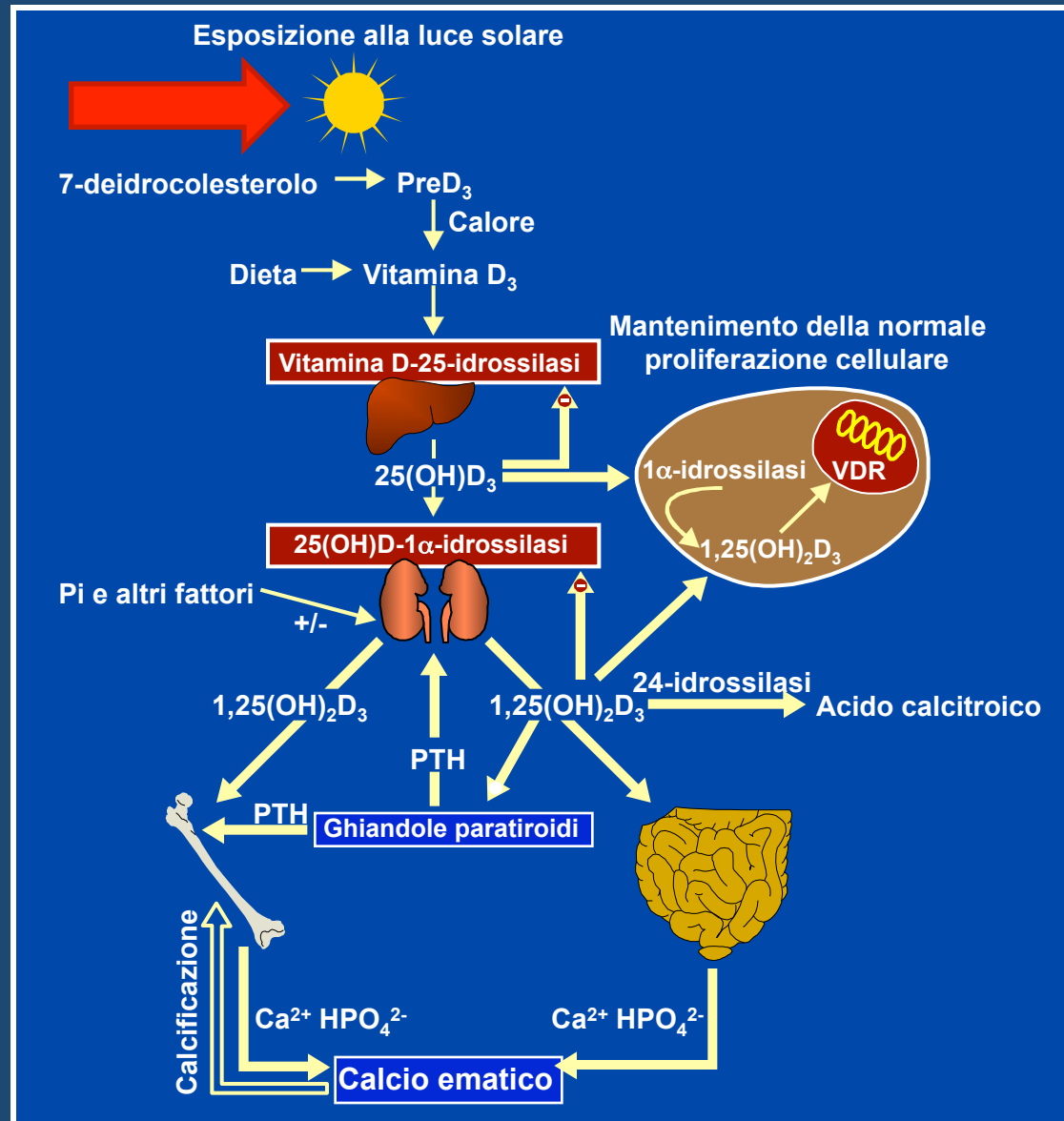
*Algoritmo non applicabile; *= connettiviti, terapie immunosoppressive, ipertiroidismo iatrogeno.

Terapia dell'osteoporosi e delle fratture ad essa conseguenti

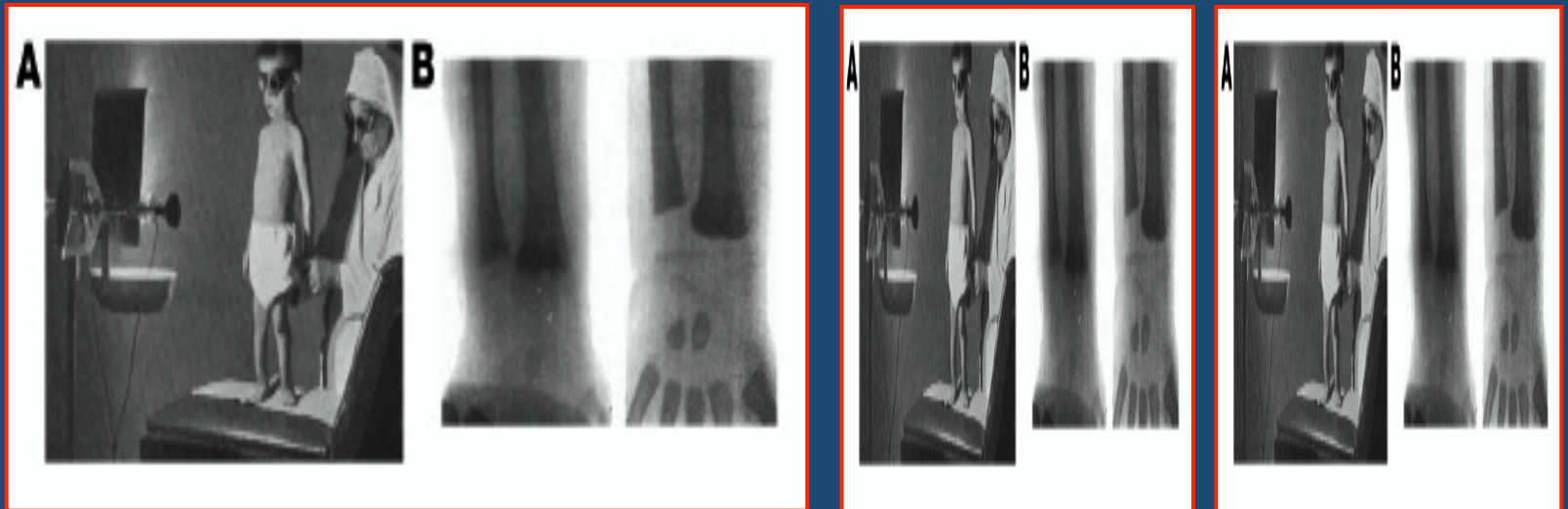


- Correggere eventuali errori dello stile di vita (fumo, eccessivo introito di alcol)
- Consigliare una adeguata attività fisica
- Fornire un adeguato apporto di calcio e vitamina D
- Aumentare la resistenza scheletrica, somministrando farmaci in grado di prevenire l'insorgenza di fratture
- Migliorare la qualità di vita

Metabolismo della vitamina D

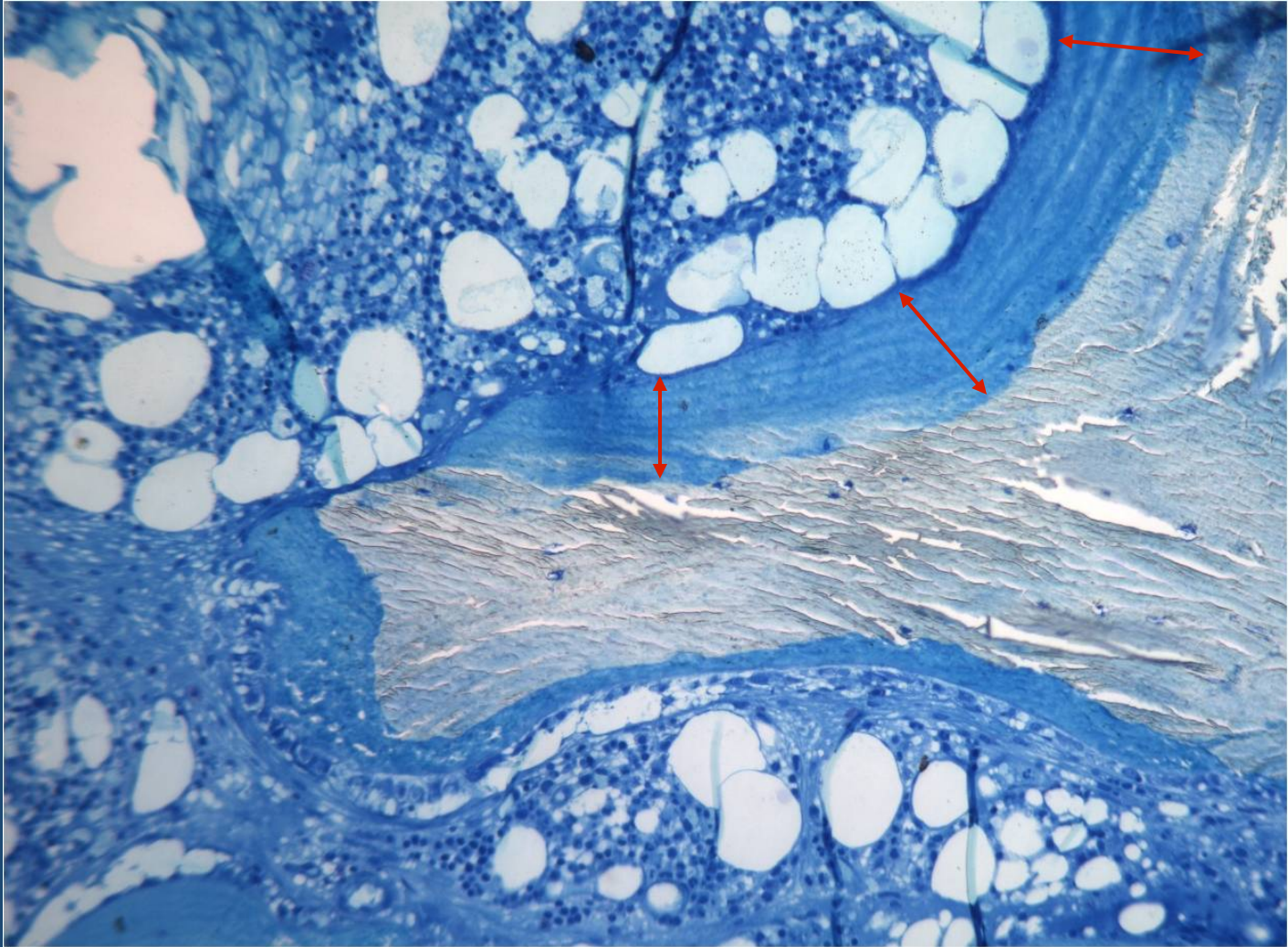


UV radiation therapy for rickets



Gamgee K.L.M., 1927. The Artificial light treatment of children in rickets, anaemia and malnutrition. P.B. Hoeber Inc. New York, New York, USA 172 pp.

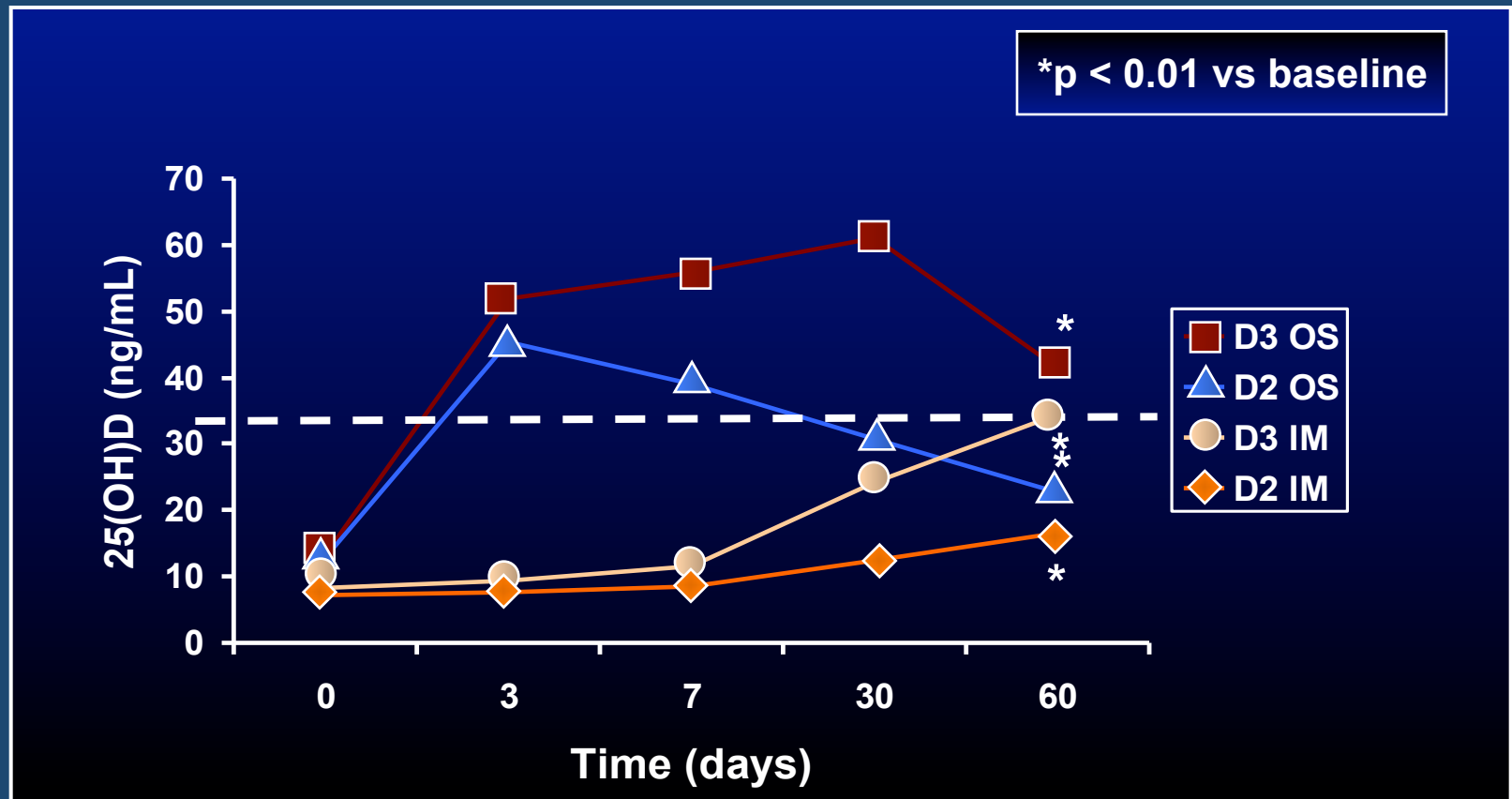
Severe vitamin D deficiency



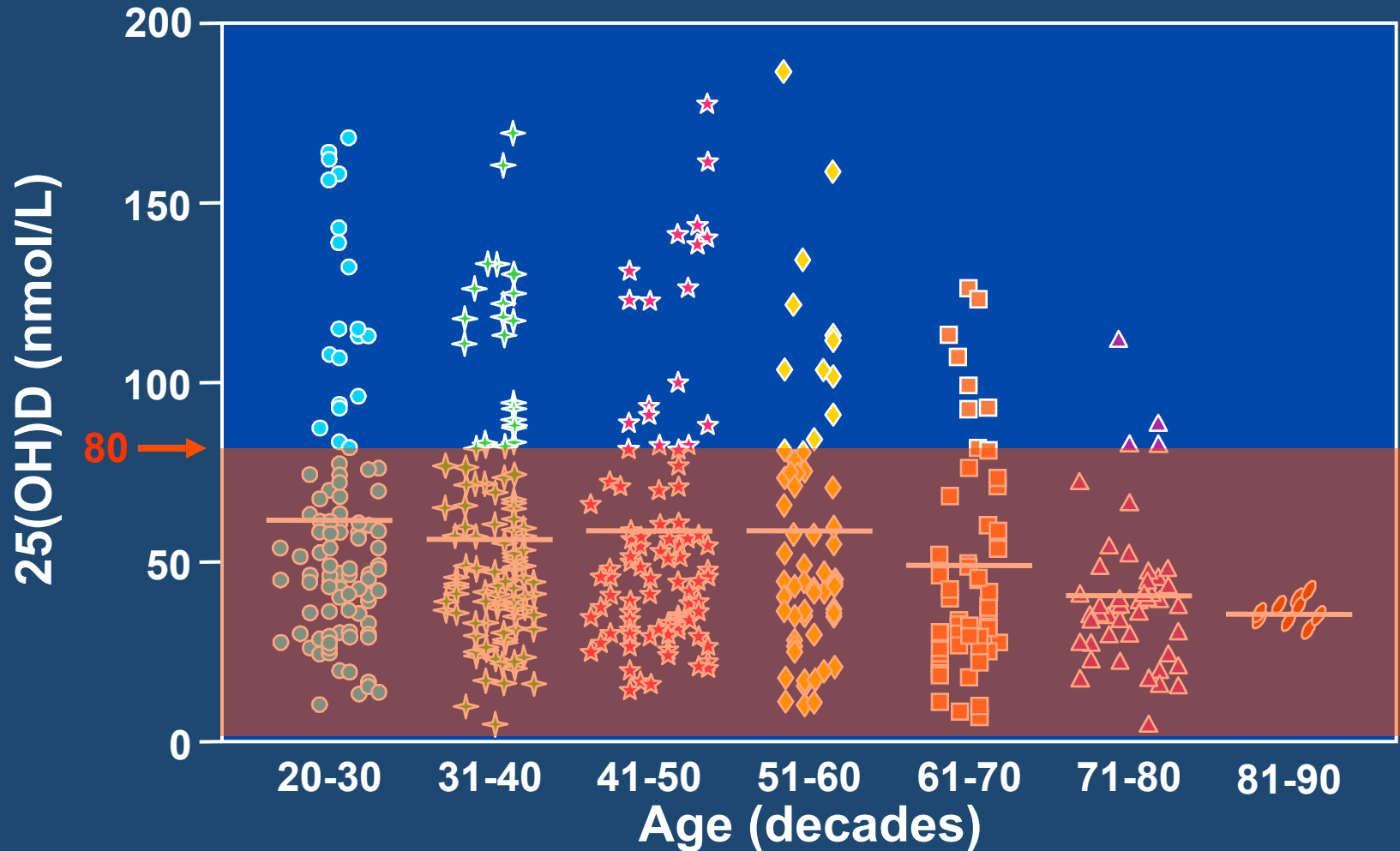
Courtesy of P. Ballanti

Effect of a single large dose of cholecalciferol and ergocalciferol (300,000 IU) on 25(OH)D serum changes

(the dashed line represents the threshold level for vitamin D sufficiency, settled at 32 ng/mL)

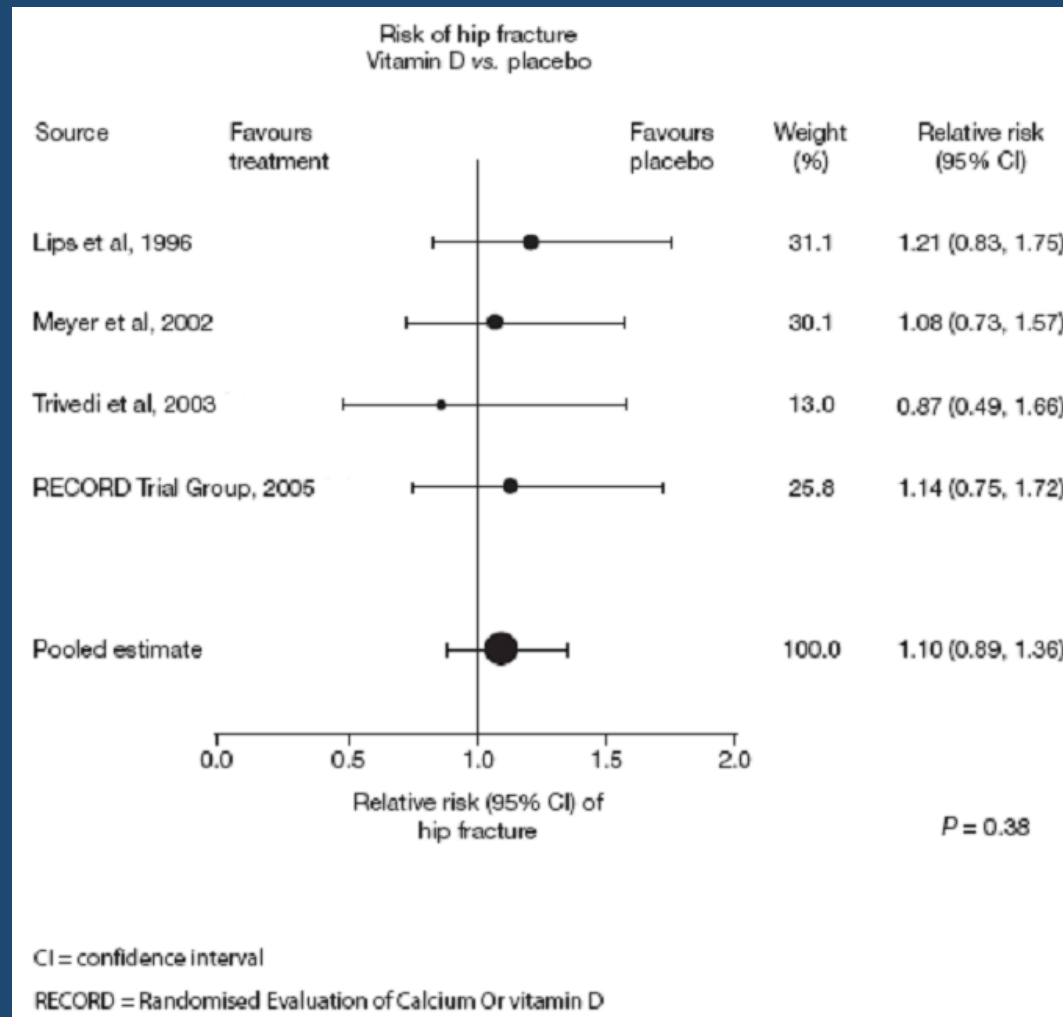


Serum vitamin D levels according to age in healthy subjects (n=487)

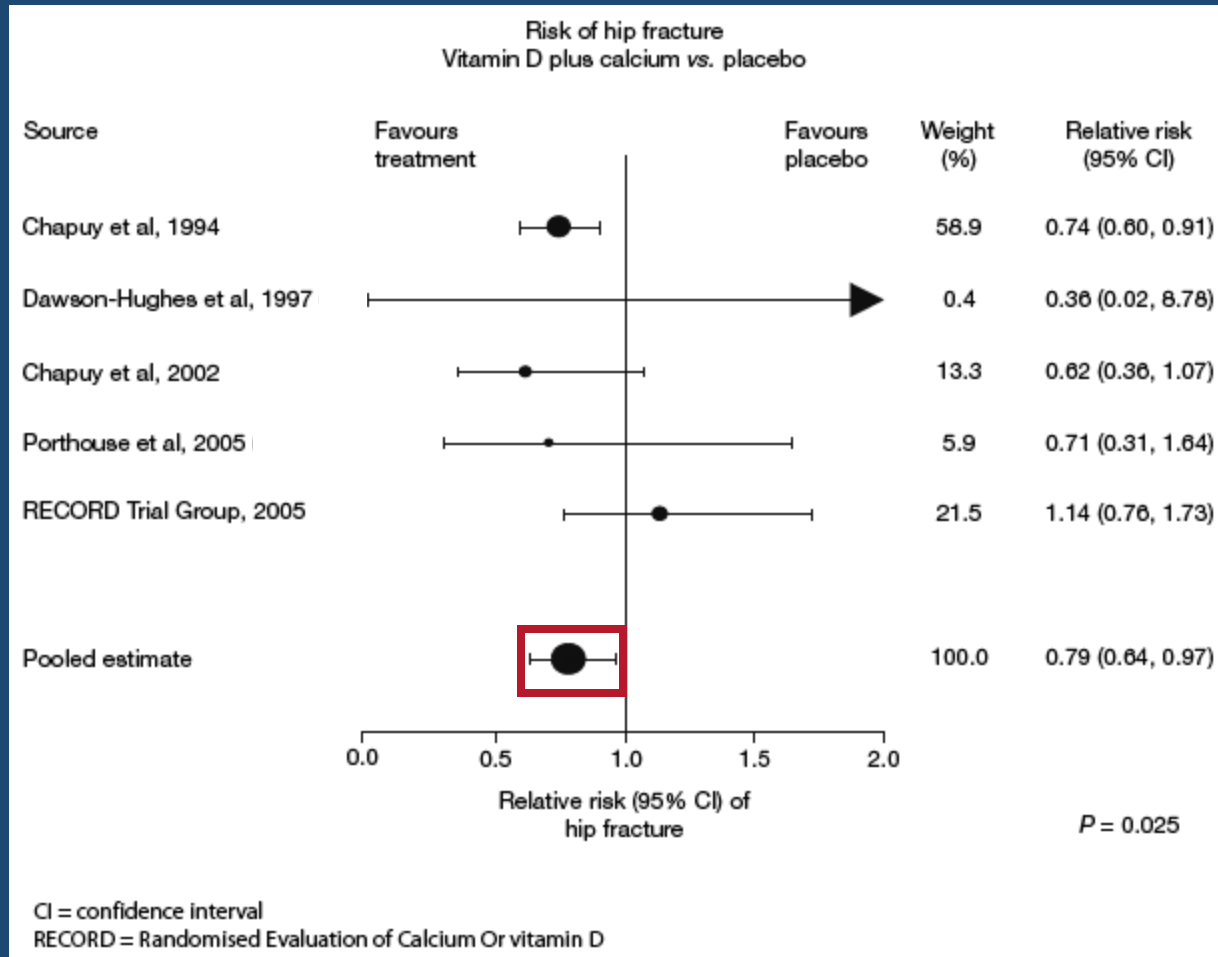


Data from: Romagnoli E. et al., Br. J. Nutr., 1999
Carnevale V. et al., Osteoporos. Int., 2001
Pepe J. et al., Osteoporos. Int., 2005

Forest plot of the risk of hip fracture between vitamin D and placebo/no-treatment groups

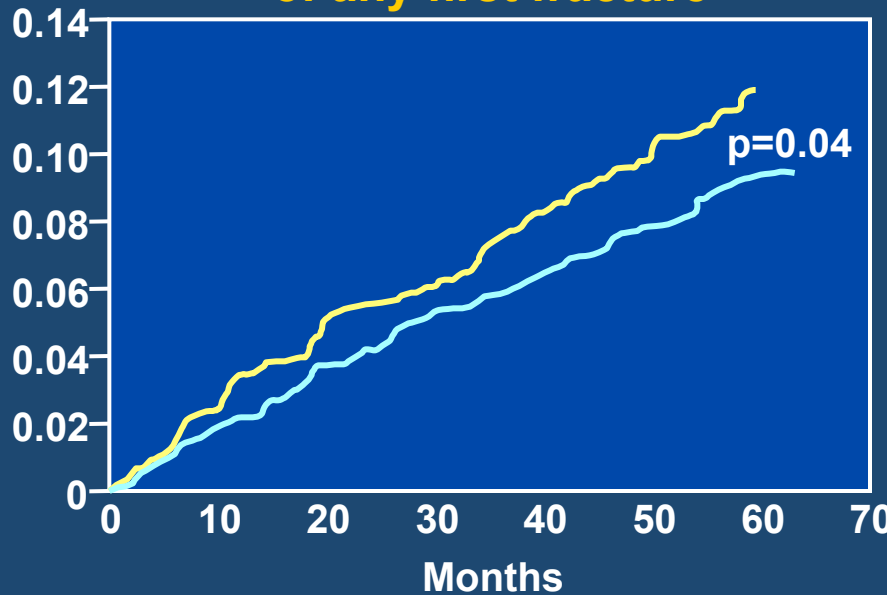


Forest plot comparing the risk of hip fracture between vitamin D and calcium and placebo/no-treatment groups

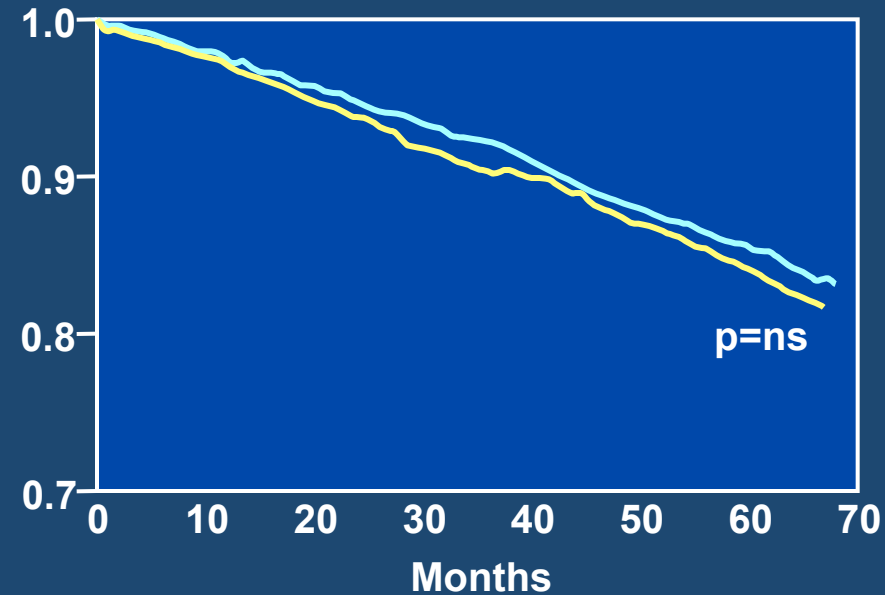


Vitamin D therapy, fractures and survival

Cumulative probability of any first fracture



Cumulative survival



— Vitamin D (n=1345) — Placebo (n=1341)

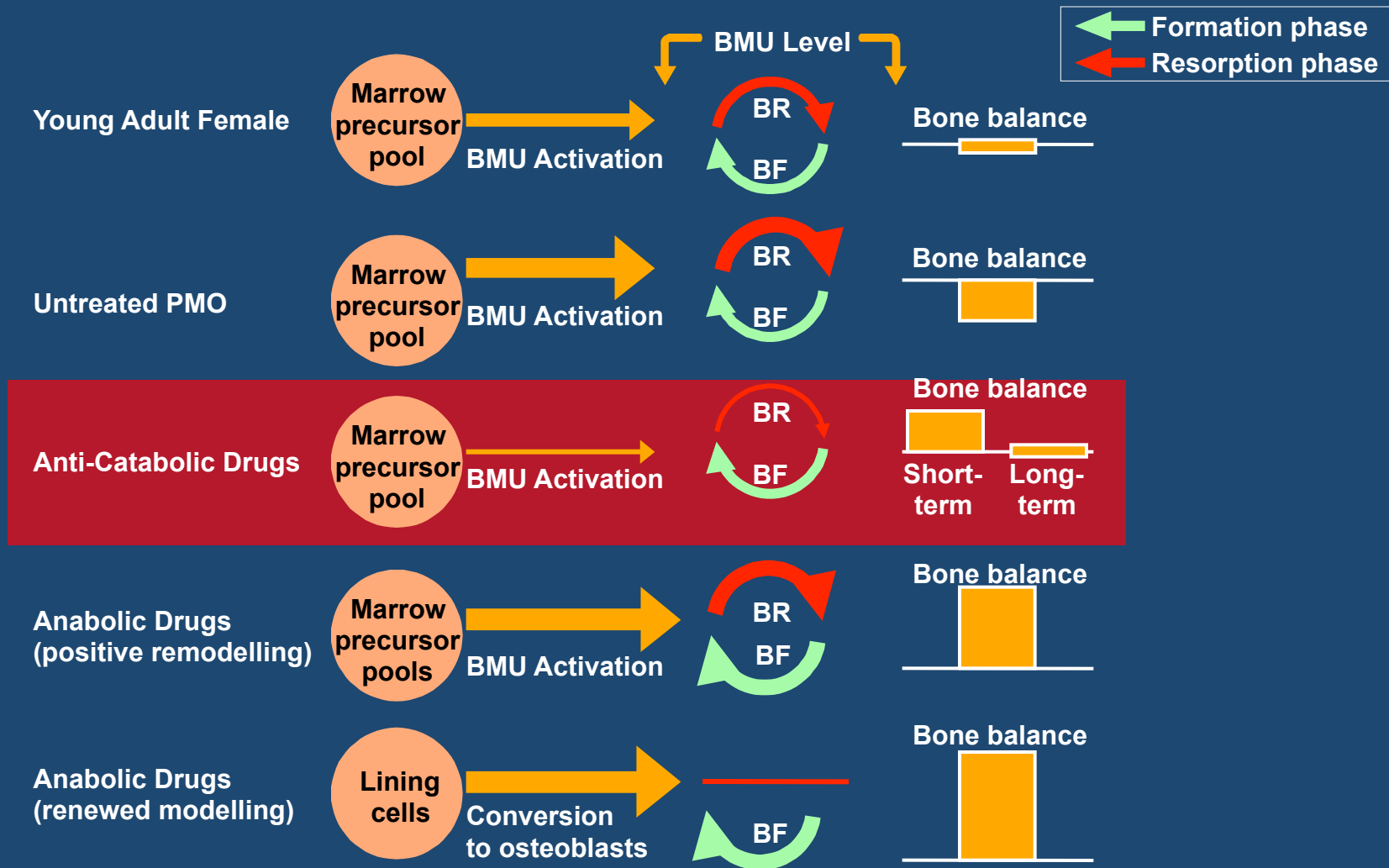
Farmaci più frequentemente impiegati nella terapia dell'osteoporosi

- Alendronato
- Calcitonina
- Clodronato
- Denosumab
- Estrogeni ed Estroprogestinici
- Etidronato
- Ibandronato
- Ipriflavone
- Neridronato
- Ormoni anabolizzanti
- Pamidronato
- Paratormone
- Raloxifene
- Risedronato
- Sali di calcio
- Sali di fluoro
- Sali di stronzio
- Tibolone
- Vitamina D e suoi metaboliti
- Zoledronato

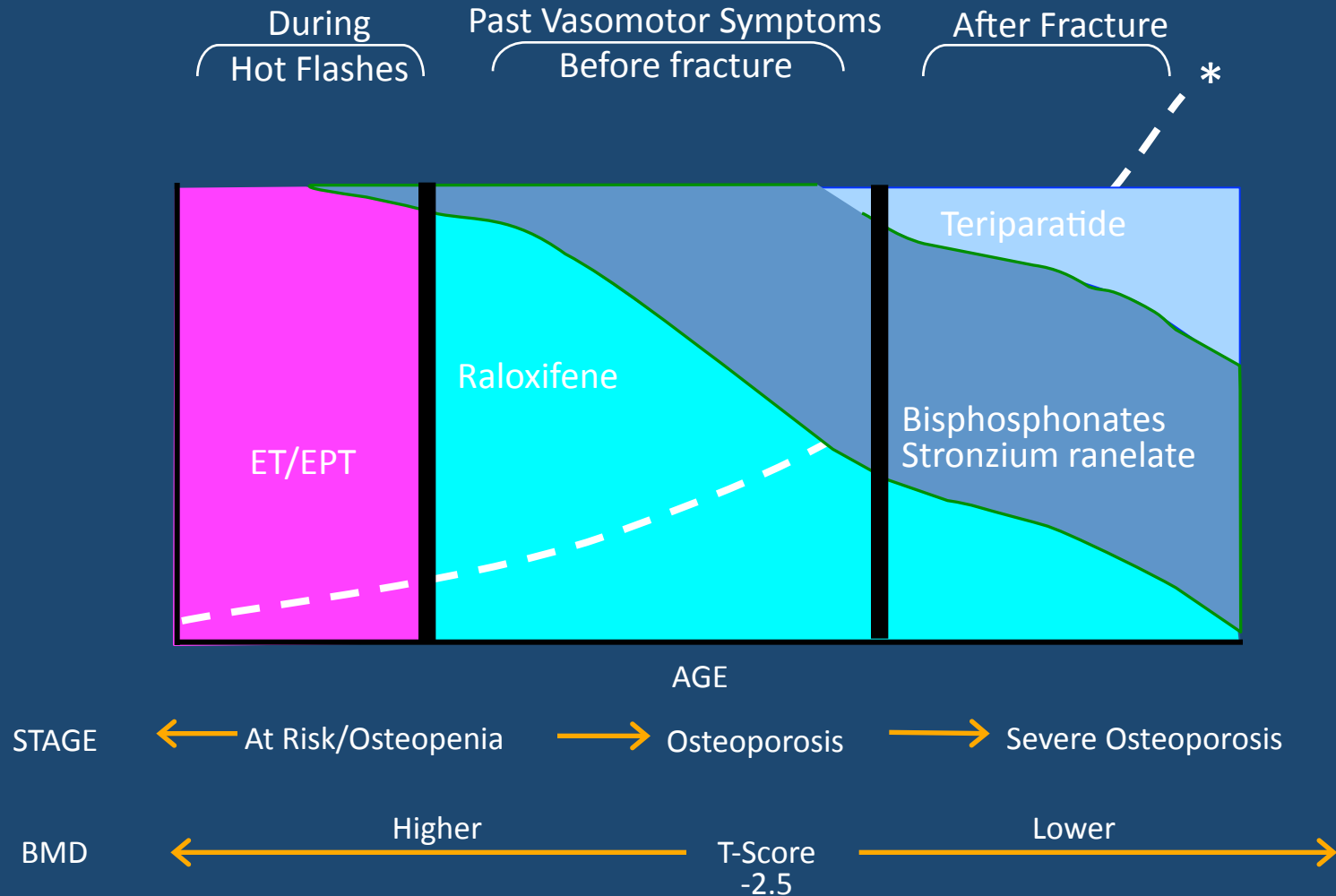
In fase sperimentale

- Ormone della crescita
- Terapie sequenziali?
- Terapie d'associazione?

Different drugs and conditions on the components of bone remodelling



Therapeutic Management of Postmenopausal Osteoporosis




ET = Estrogen therapy
 EPT = Estrogen plus progestin therapy

*Increasing risk of fracture with age

Women's Health Initiative

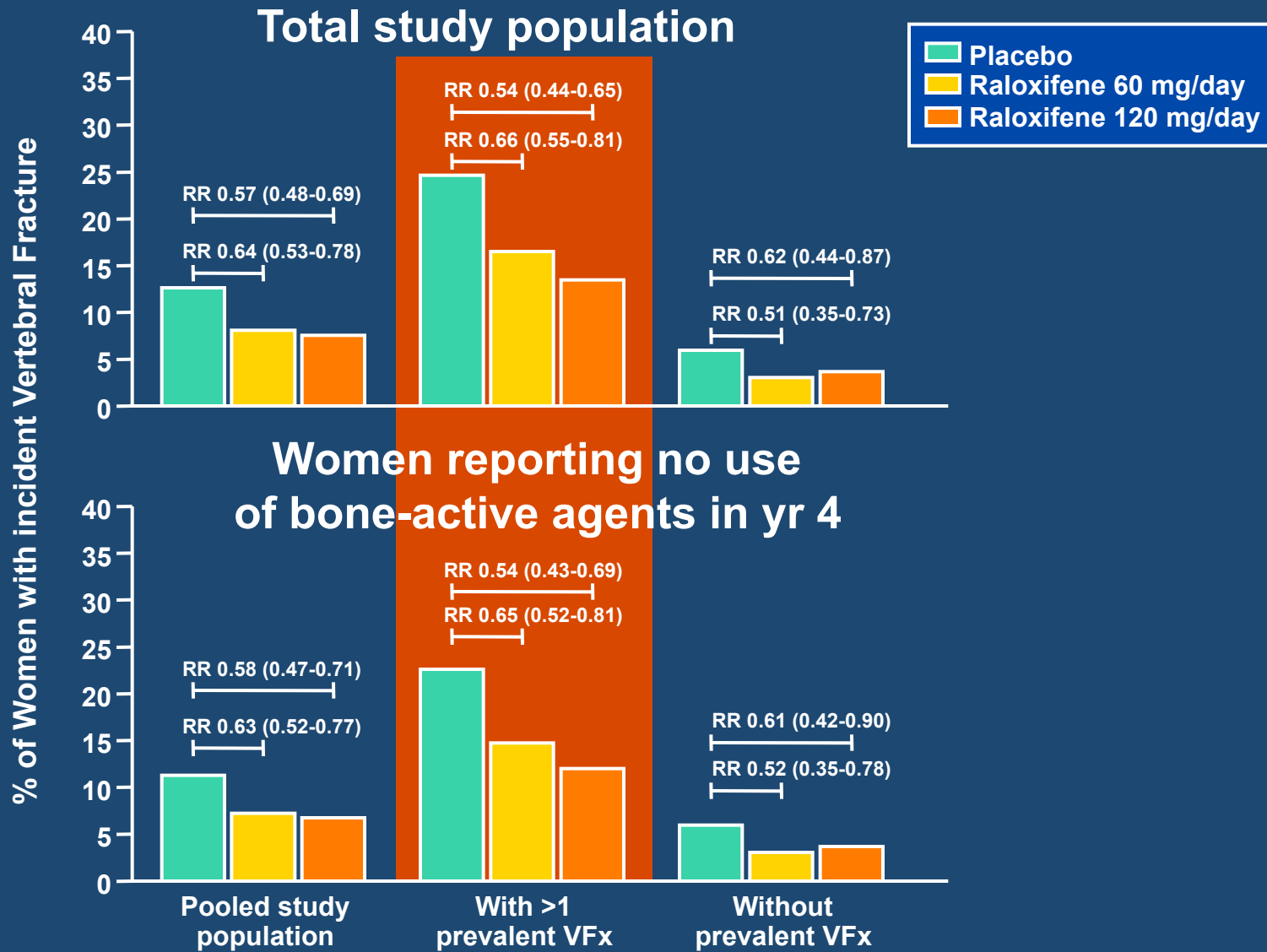
8506 donne
Estroprogestinici

8102 donne Placebo

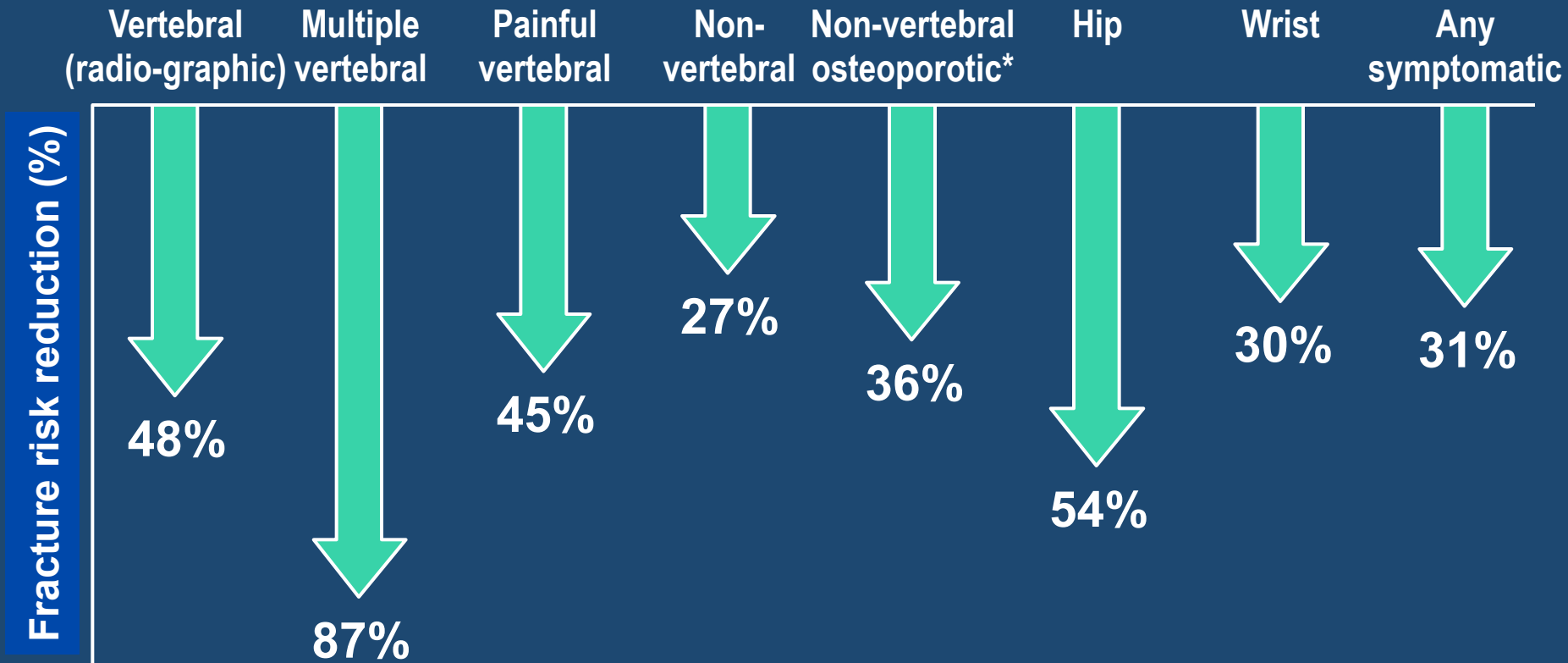
 **Neoplasia mammaria invasiva**
Malattia cardiaca coronarica
Stroke
Embolia polmonare

 **Fratture femorali**
Neoplasie coloretali

Four-year results from MORE

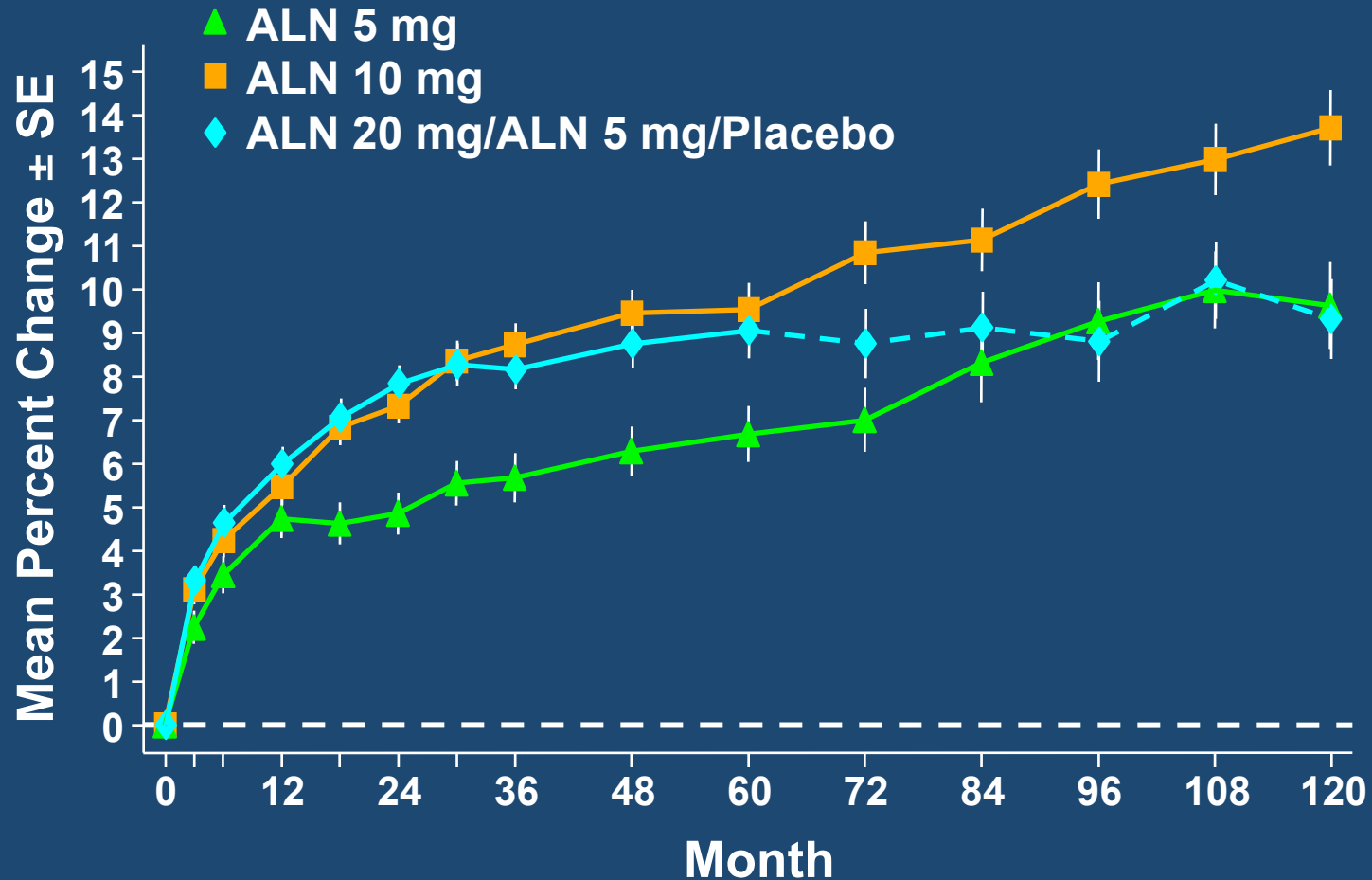


Alendronate reduced the risk of fractures at all key sites in women with osteoporosis



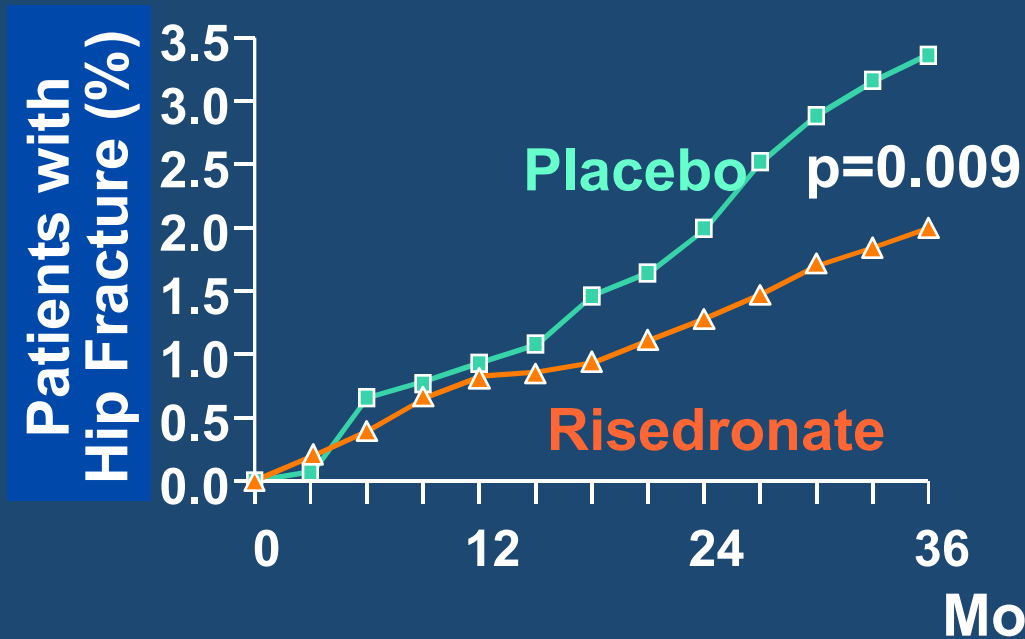
*fracture of the clavicle, humerus, pelvis, hip or leg

Alendronate 10 Year Efficacy Data Lumbar Spine BMD

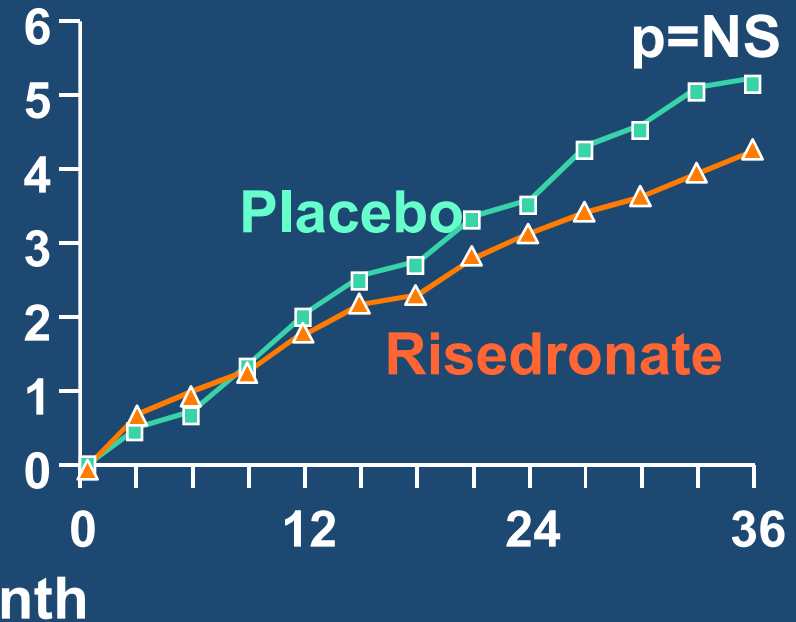


Incidence of Hip Fracture in the Younger Women (Left) and the Older Women (Right)

Women 70 to 79 Years Old *



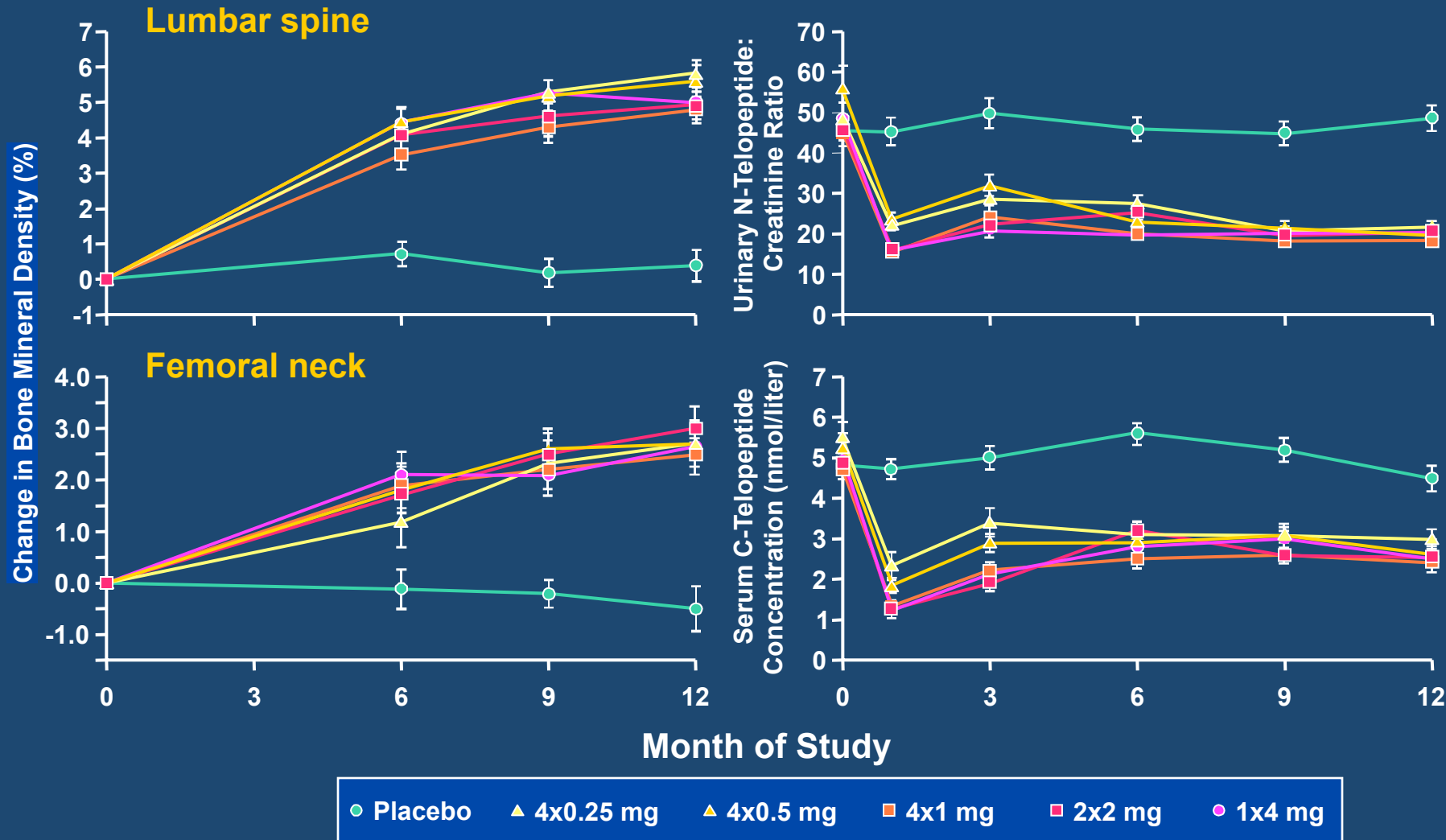
Women ≥ 80 Years Old **



* Enrolled if they had a low BMD at the femoral neck (T score, lower than -4 or lower than -3 with at least one nonskeletal risk factor for hip fracture).

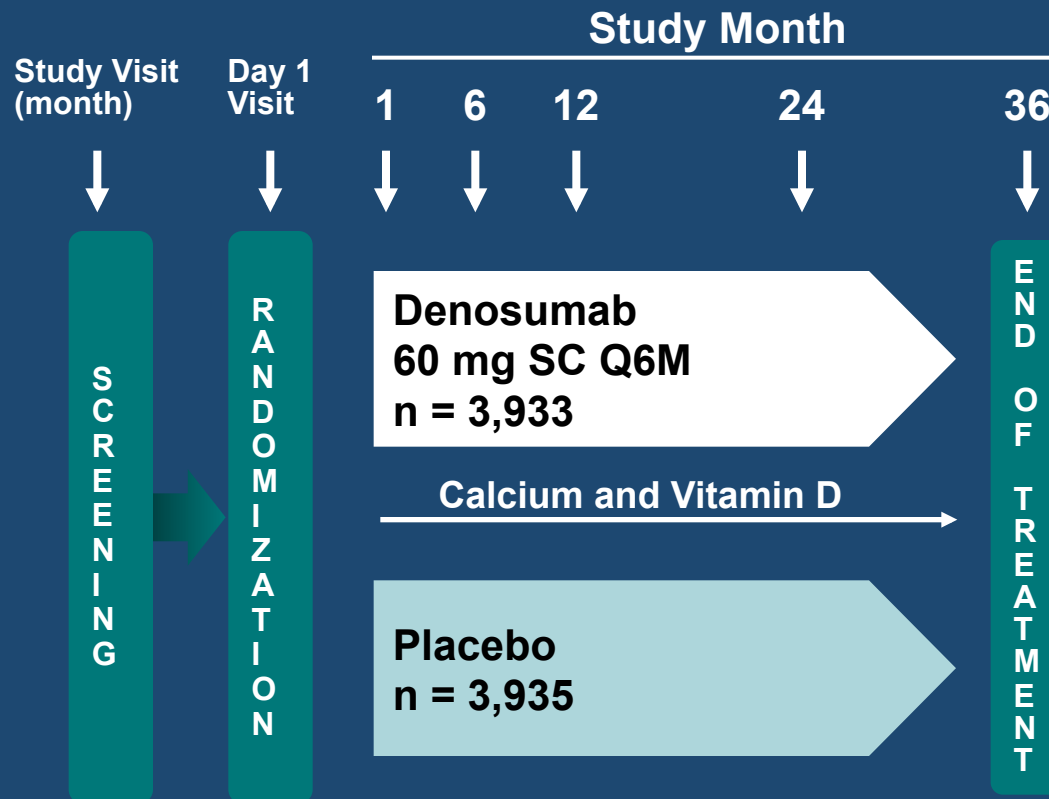
** Enrolled if they had at least one nonskeletal risk factor or low BMD at the femoral neck (T score, lower than -4 or lower than -3 with a hip-axis length ≥ 11.1 cm).

Various regimens of zoledronic acid, BMD and biomarkers



Study Design

Phase 3: The FREEDOM Trial



Enrolled study population

- 7,868 Postmenopausal women
- T-score < -2.5 at the lumbar spine or total hip and not < -4.0 at either site
- Exclusion any severe or > 2 moderate vertebral fractures

Primary endpoint

- New vertebral fracture* over 36 months

Secondary endpoints

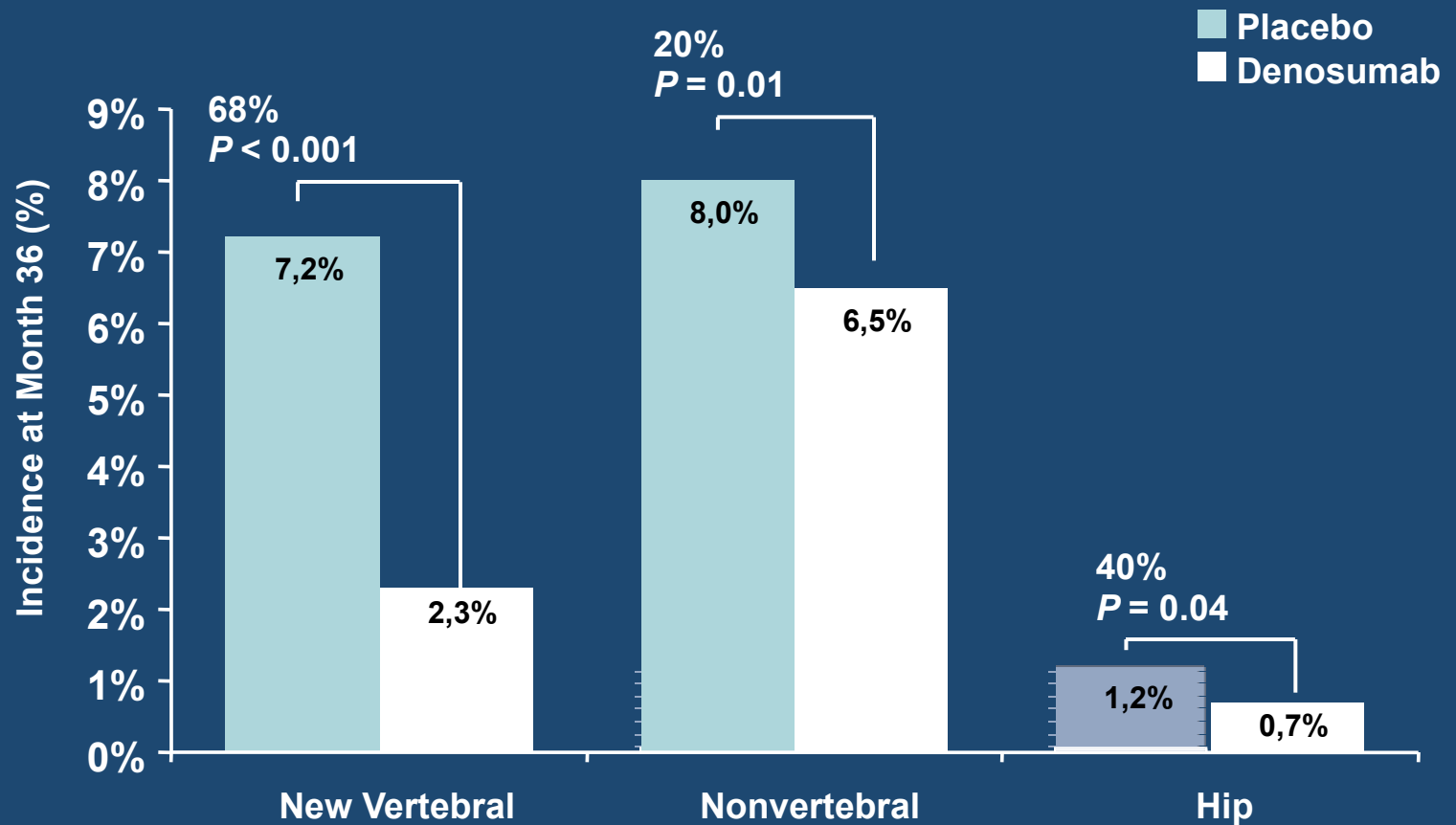
- Time to first nonvertebral fracture
- Time to first hip fracture

- International, placebo-controlled study

* Defined as an increase of at least one grade in a vertebral body that was normal at baseline
SC = subcutaneous; Q6M = once every 6 months

The Effect of Denosumab on Fracture Risks at 36 Months

Phase 3: The FREEDOM Trial



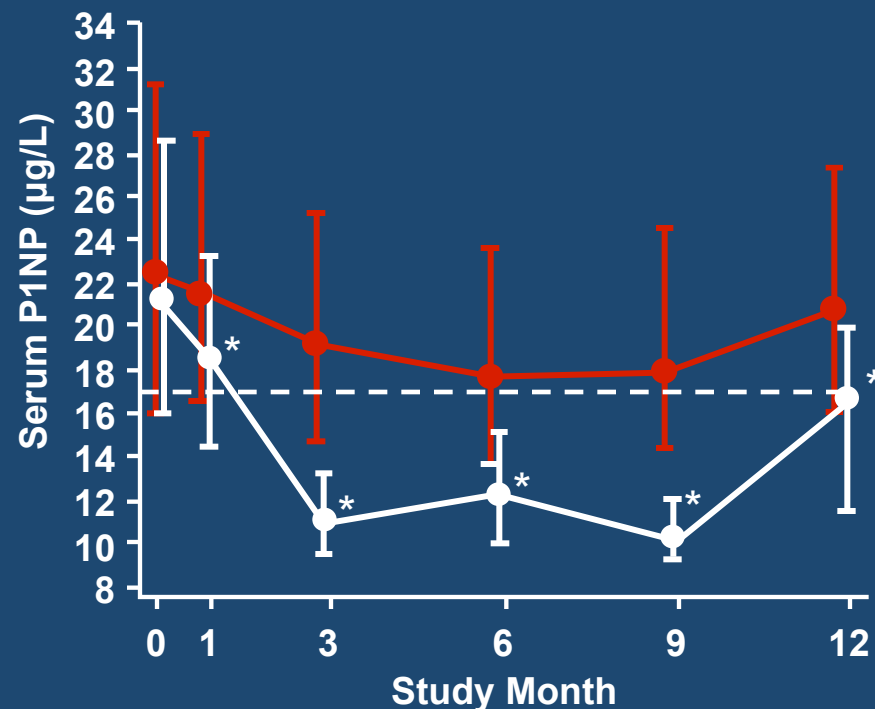
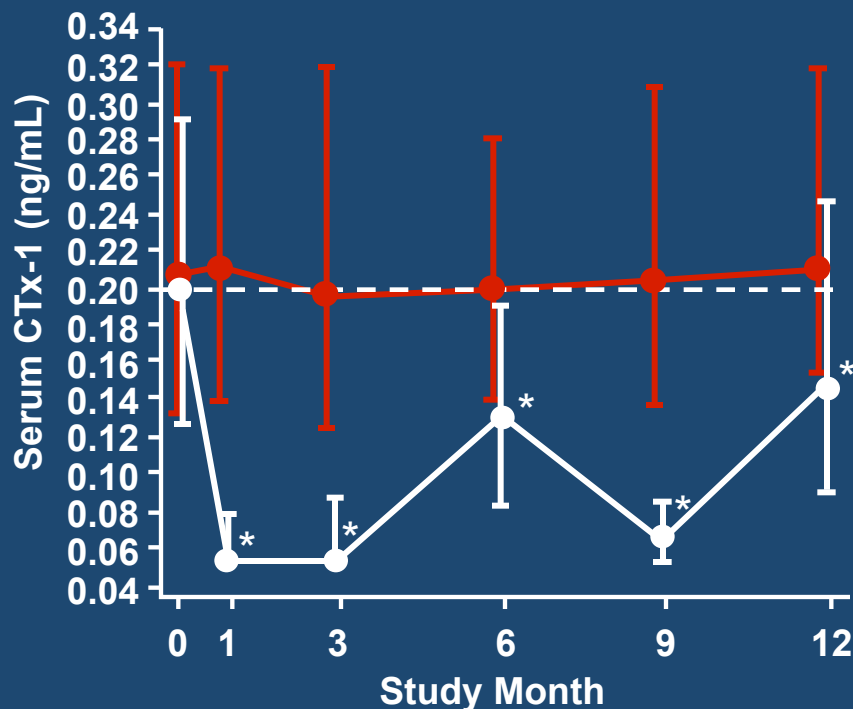
Effects of Treatment on Biochemical Markers of Bone Turnover Over 12 Months

Phase 3: The STAND Trial

● Alendronate 70 mg QW ● Denosumab 60 mg Q6M

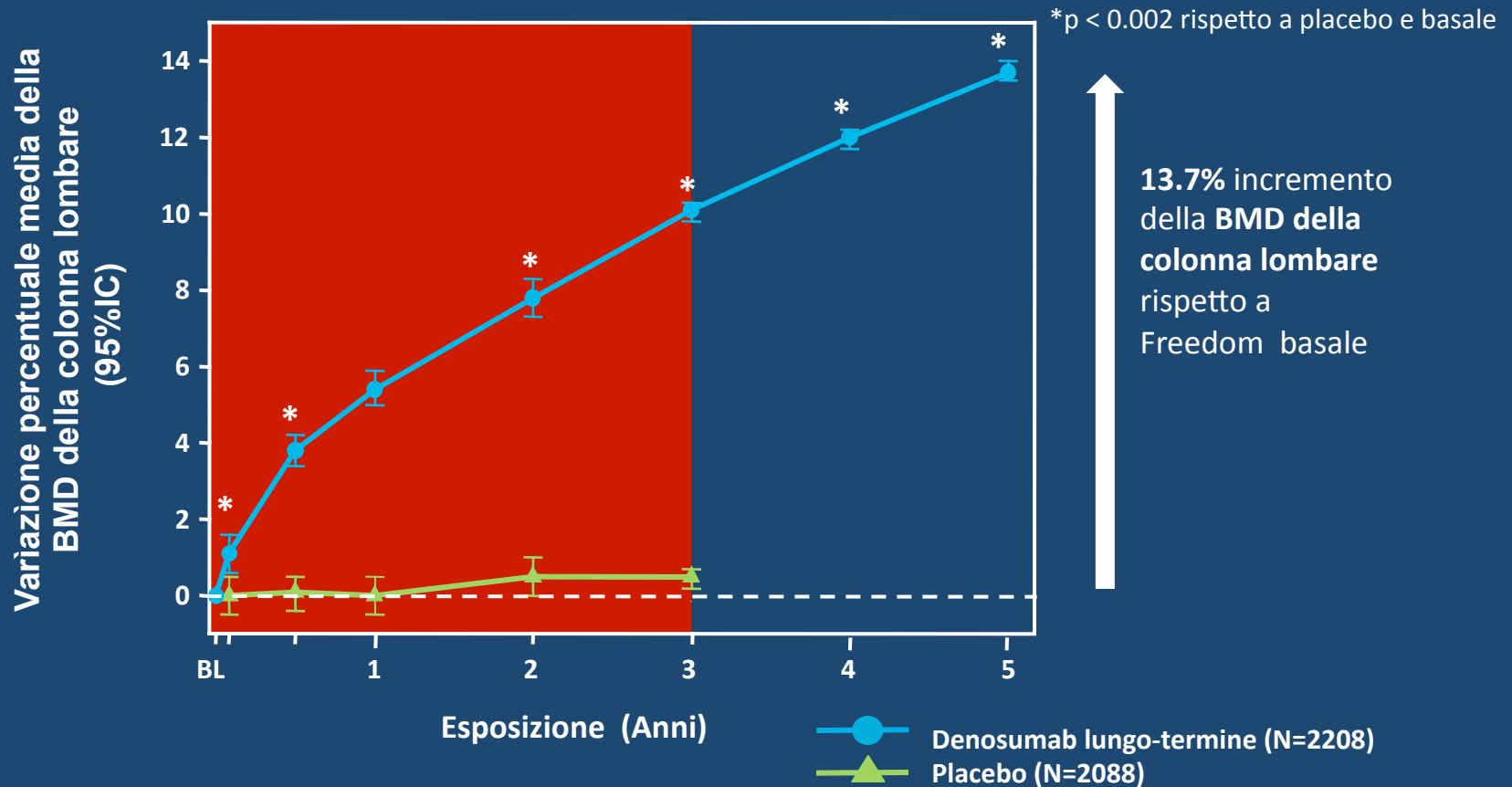
CTx-1

P1NP



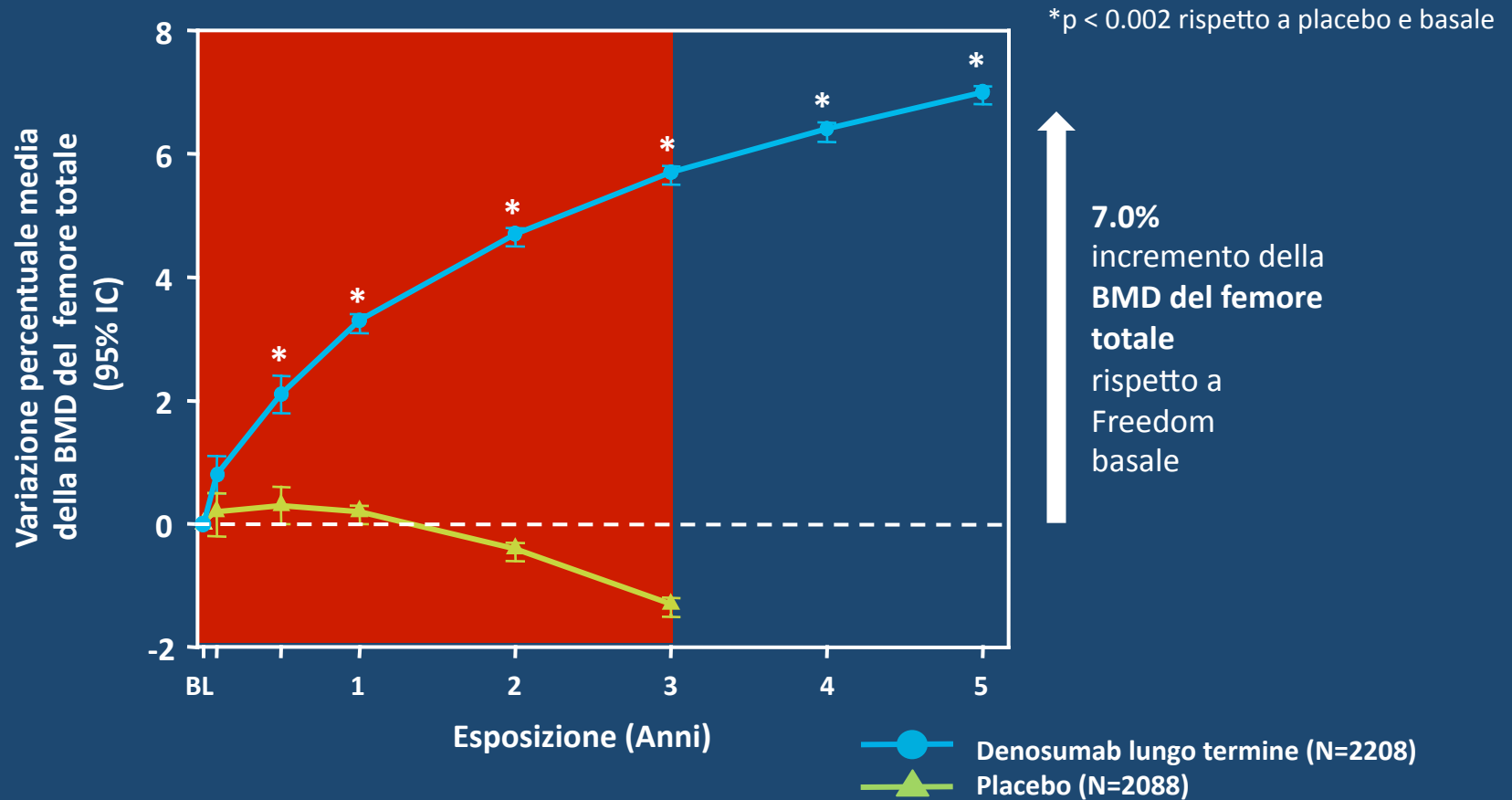
Dotted line is lower limit of premenopausal reference range.
Values are medians; error bars represent the interquartile range.
Analysis carried out in the observed data set; missing values were not imputed.
* $P < 0.0001$.

Variazione percentuale della BMD della colonna lombare



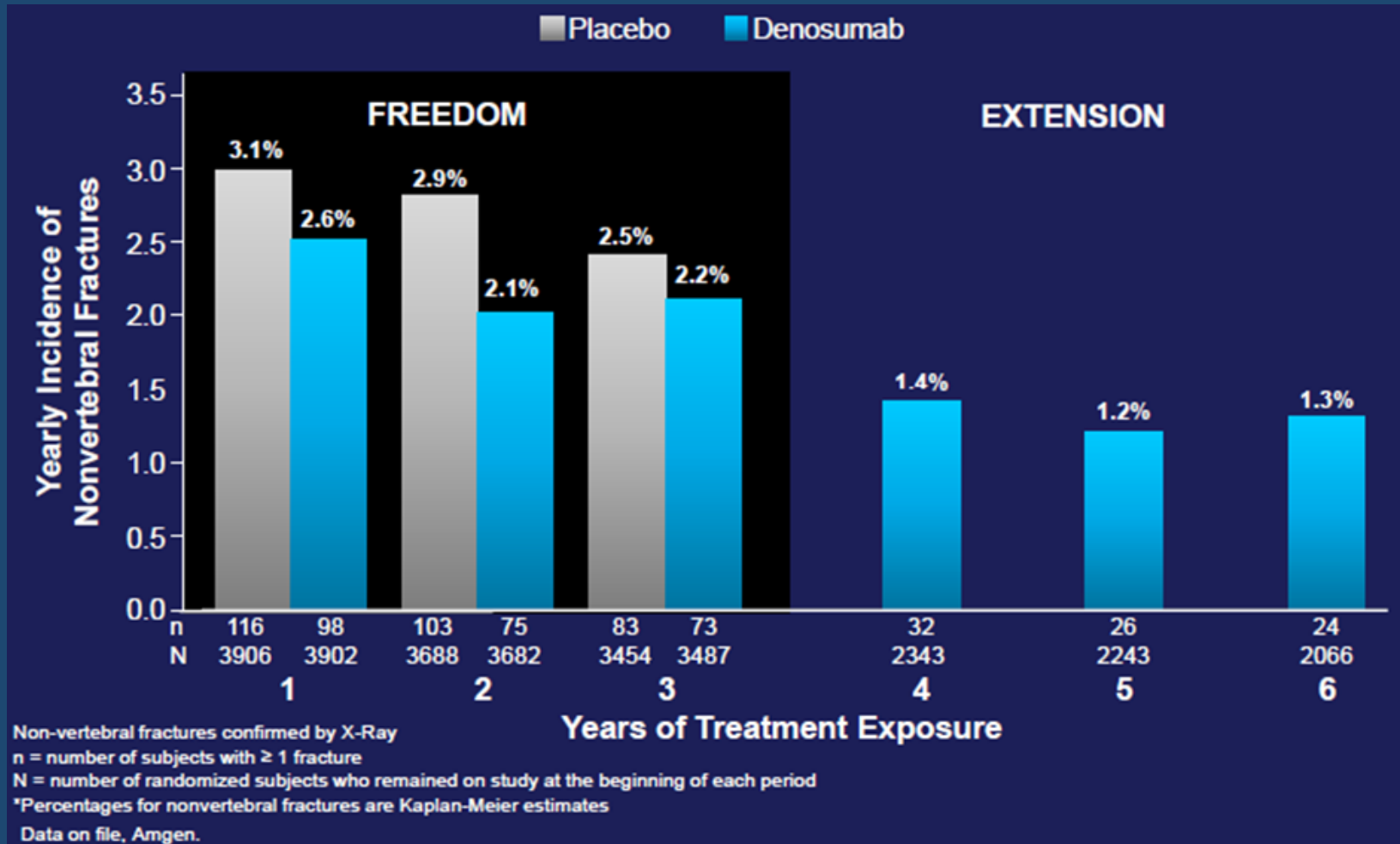
Continuo e significativo incremento della BMD nel 4° e 5° anno di trattamento a lungo termine con denosumab

Variazione percentuale della BMD del femore totale

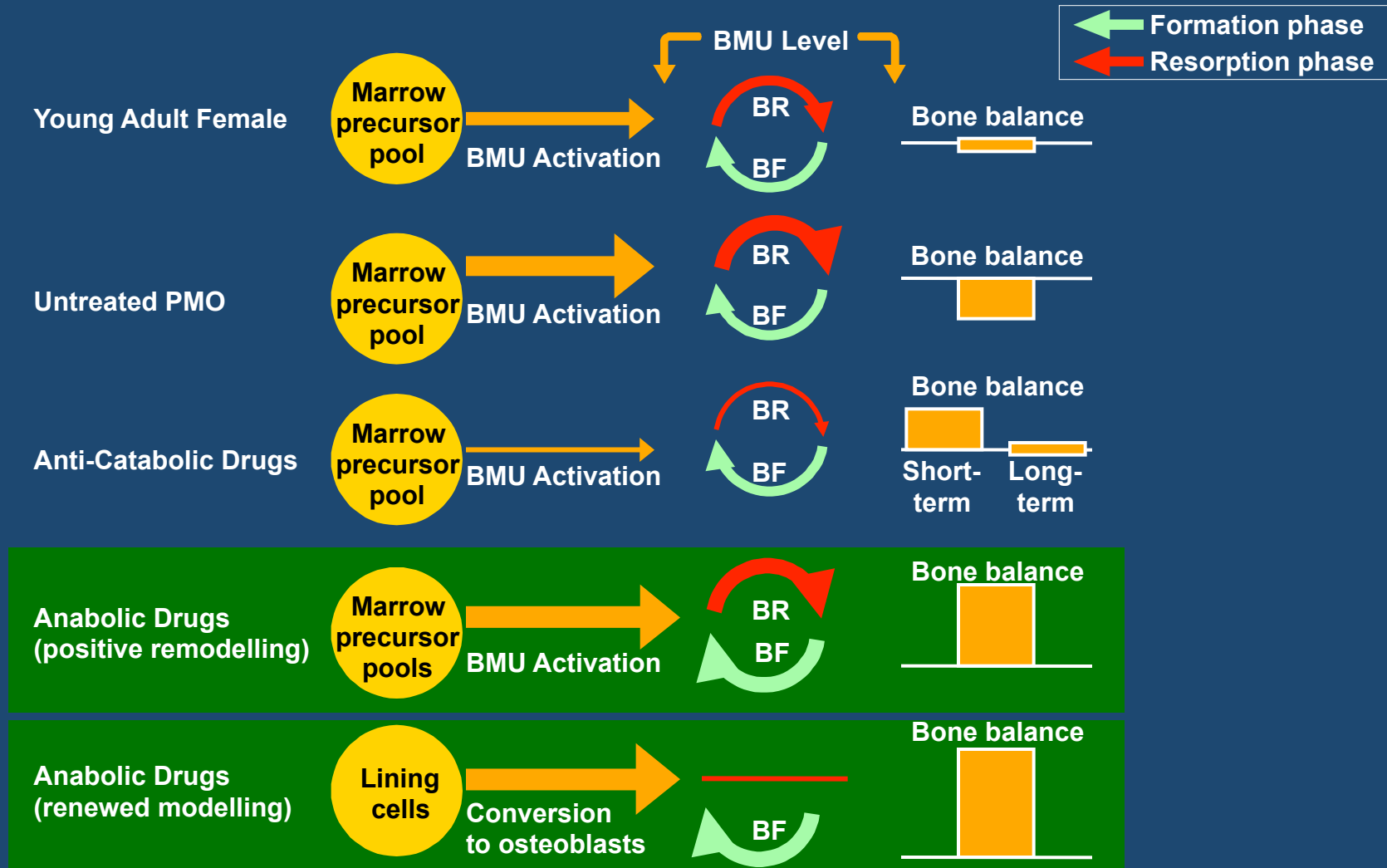


Continuo e significativo incremento della BMD nel 4° e 5° anno di trattamento a lungo termine con denosumab

Yearly incidence of **nonvertebral fractures** through 6 years: long-term group

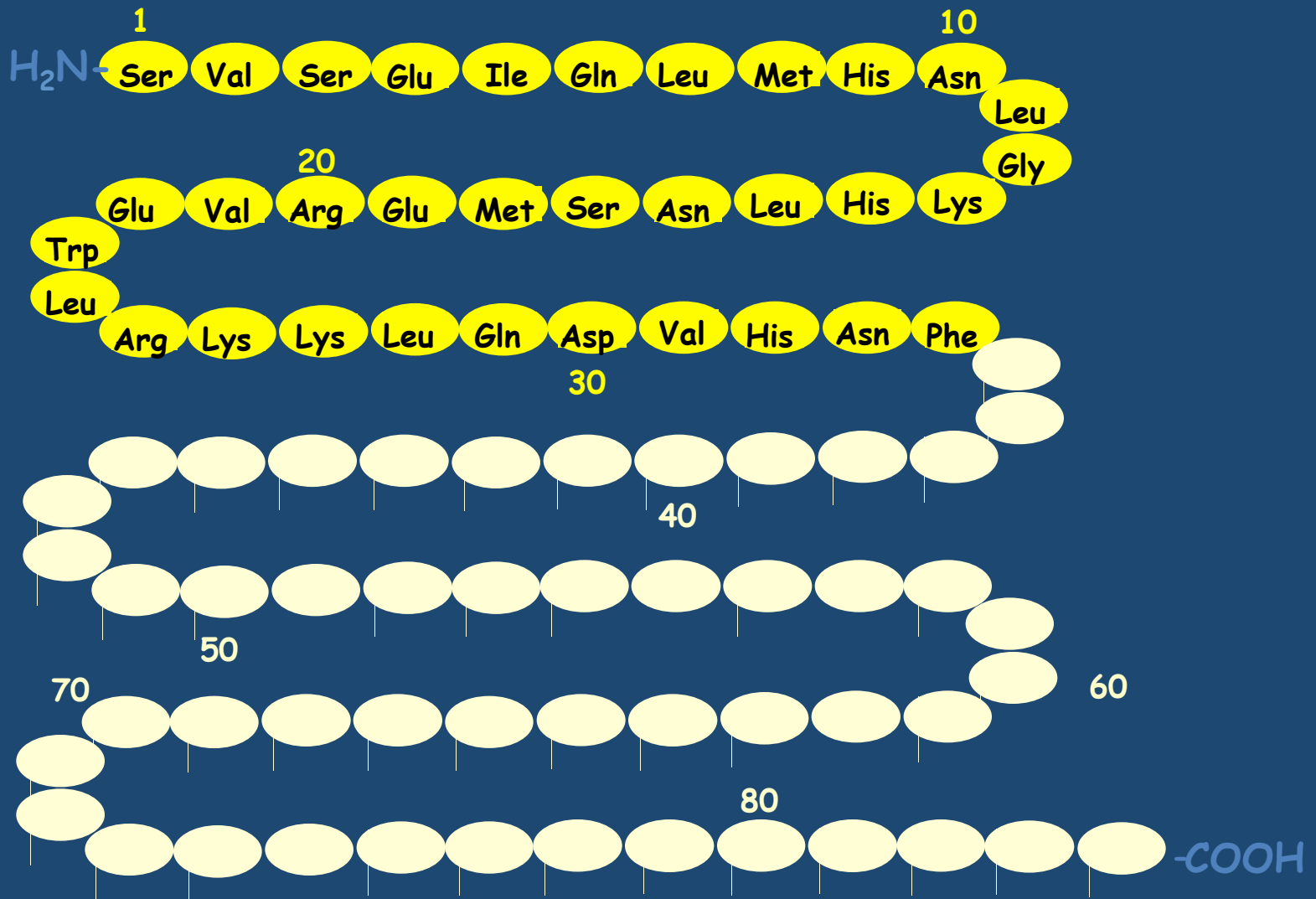


Different drugs and conditions on the components of bone remodelling

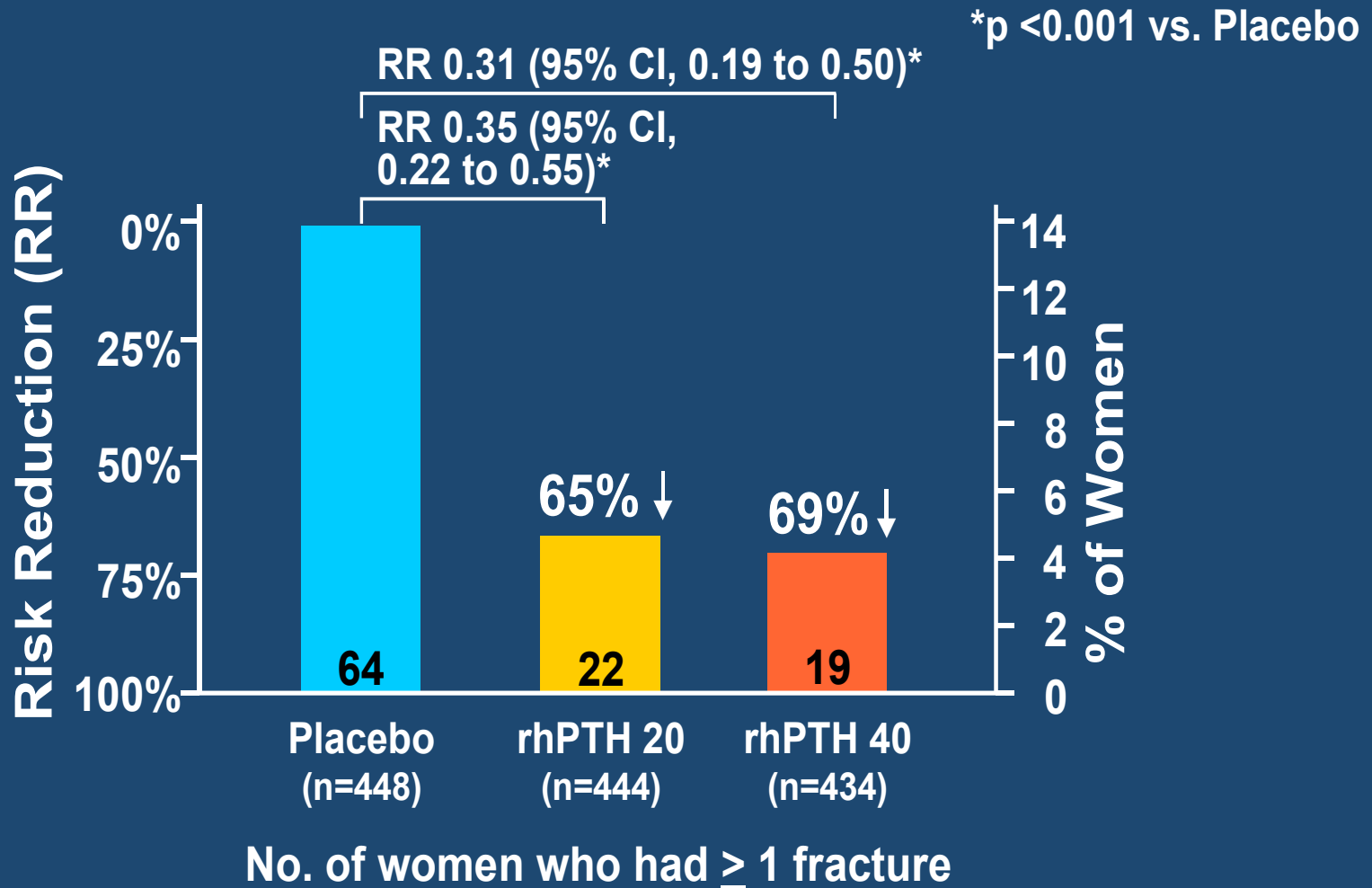


Ormone paratiroideo umano

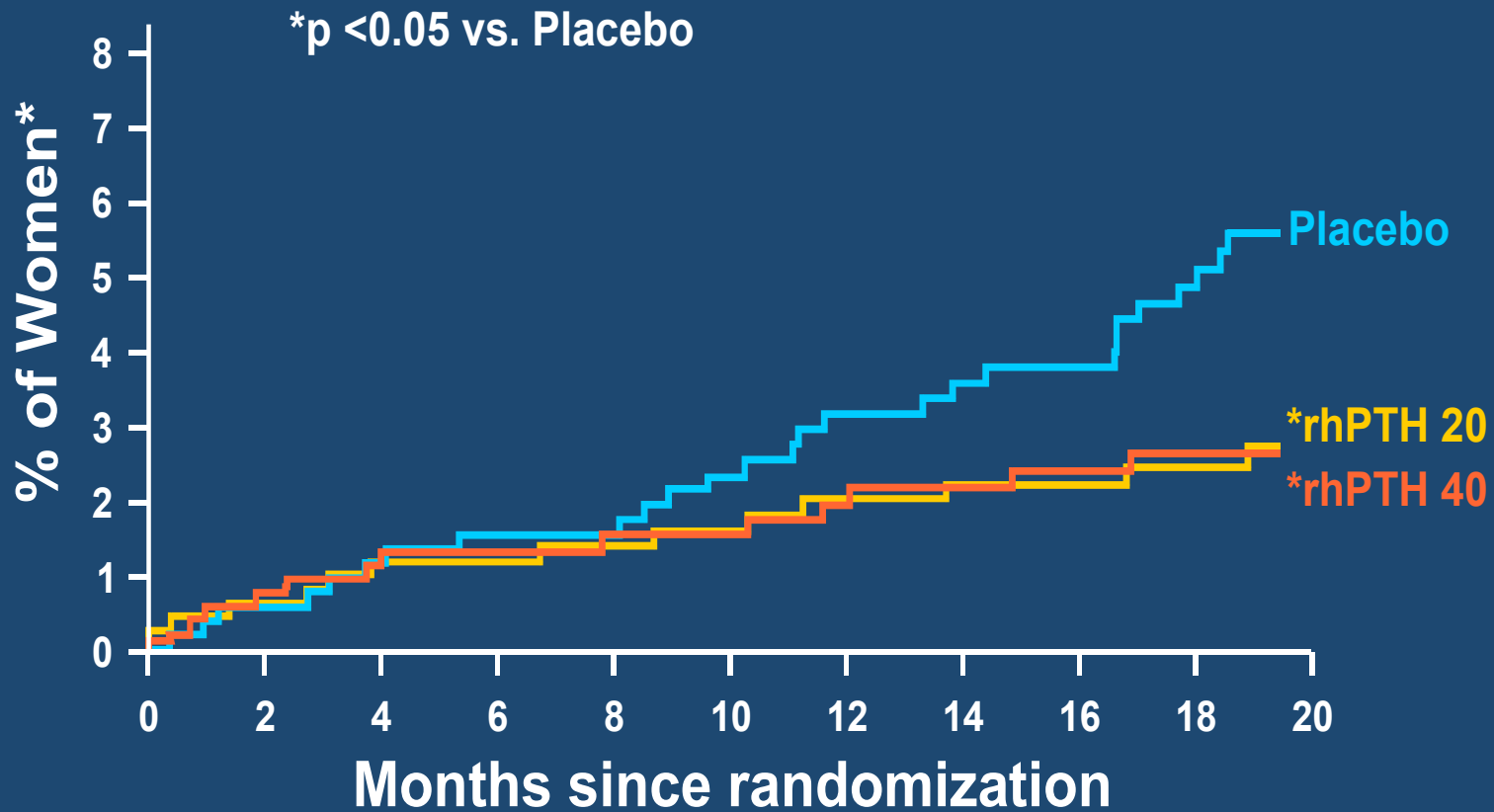
1-34 and 1-84



Effect of rhPTH (1-34) on the Risk of New Vertebral Fractures

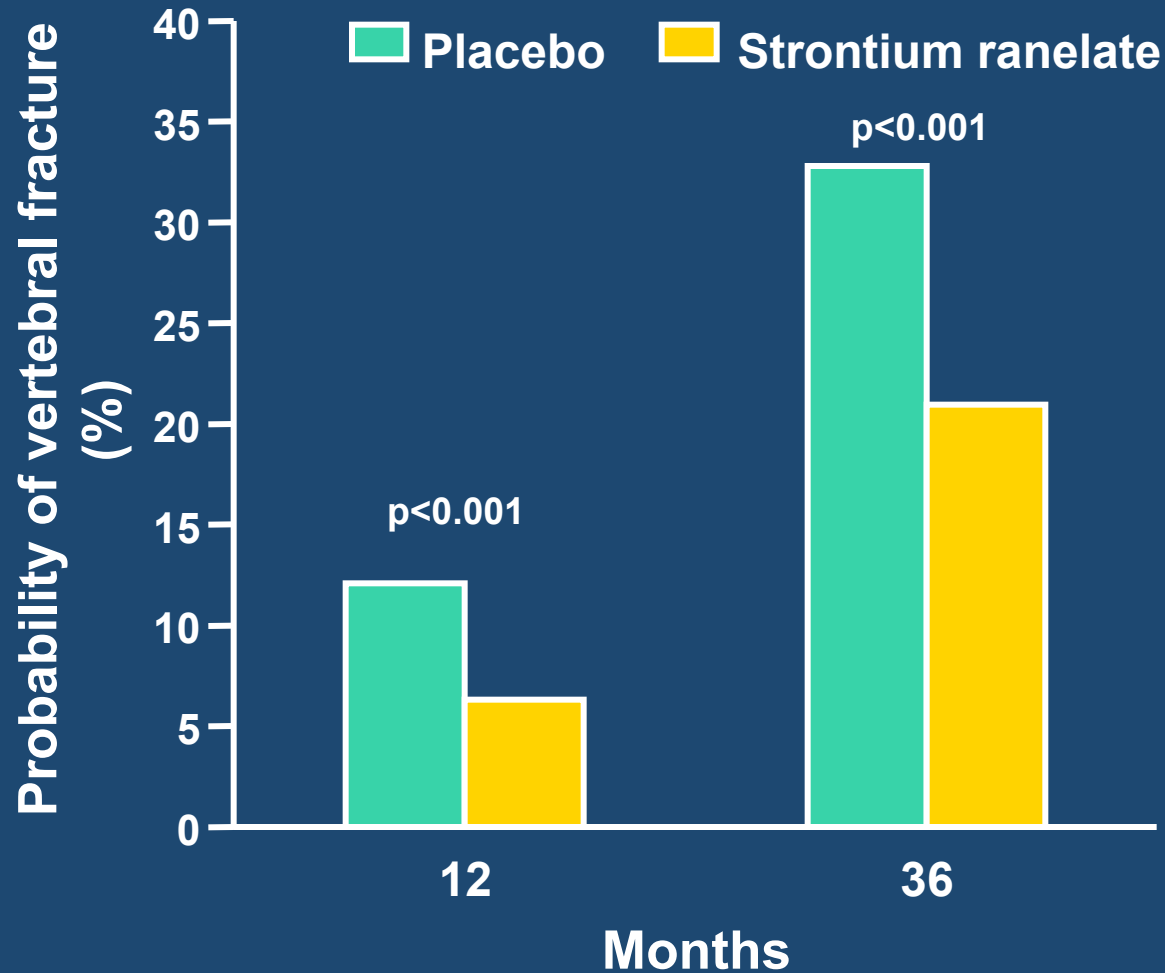


Effect of rhPTH (1-34) on the Risk of Nonvertebral Fragility Fractures (time to first fracture)

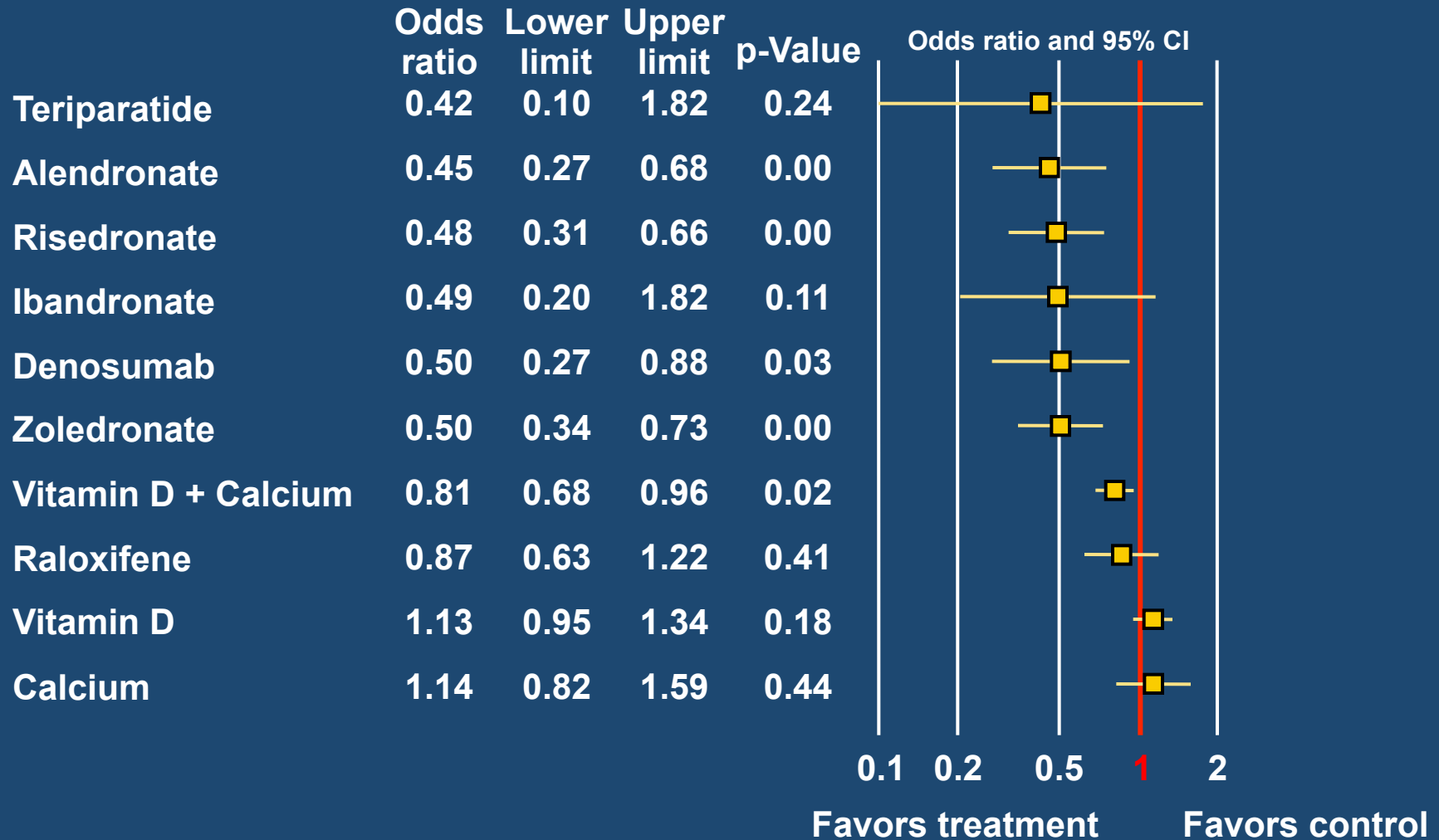


* Percent of women who had one or more nonvertebral fragility fractures during the study

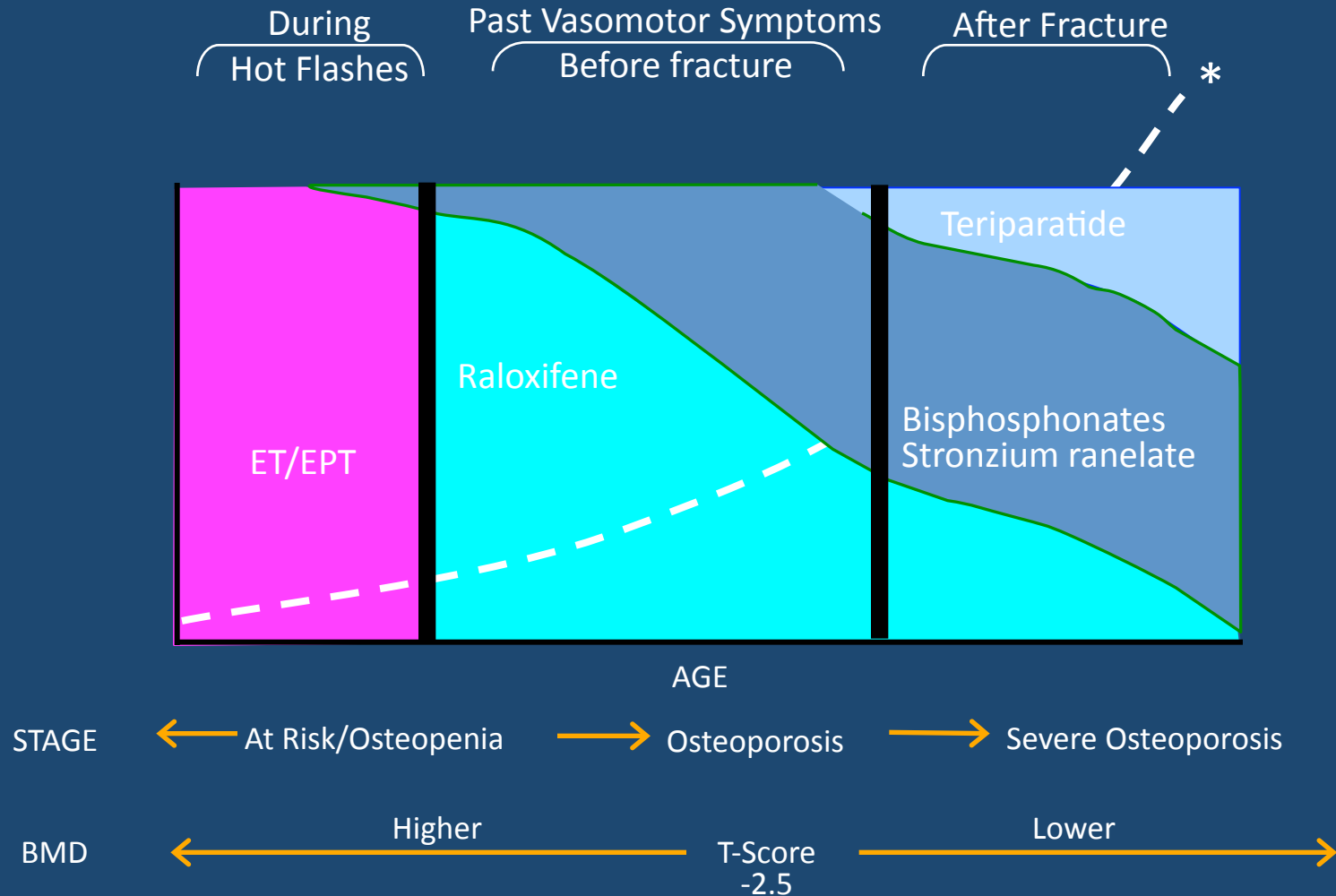
Strontium ranelate: the spinal osteoporosis therapeutic intervention (SOTI) study



Agents for the prevention of hip fractures compared against placebo (Comparative Effectiveness and Network Meta-Analysis)



Therapeutic Management of Postmenopausal Osteoporosis



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*Increasing risk of fracture with age

Treatment discontinuation following hip fracture

