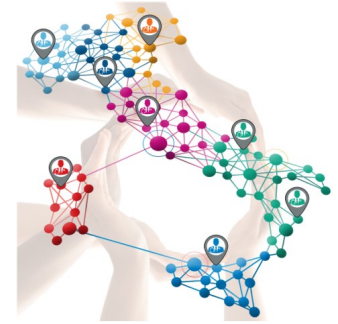




4° CONGRESSO NAZIONALE FRAGILITY FRACTURE NETWORK - ITALIA

*Appropriatezza, Qualità e Sostenibilità delle
Cure nel Percorso Ortogeriatrico*



**LA PREVENZIONE SECONDARIA DELLE FRATTURE DA FRAGILITA'
CURARE L'OSTEOPOROSI E PREVENIRE LE RIFRATTURE**

Efficacia del denosumab nella prevenzione secondaria delle fratture

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Stemmi dell'Ospedale di S. Maria della Misericordia di Perugia





CONFLICT OF INTEREST

Astra Zeneca

Pfizer

Pharmacological treatment of osteoporosis

Treatment

Action

Estrogen replacement therapy →
Selective estrogen receptor modulators (SERMs) →
Calcitonin →
Bisphosphonates →
Denosumab →
Strontium ranelate (?) - - - - - →

Inhibit bone turnover

Maintain or increase bone mass

Reduce fracture risk

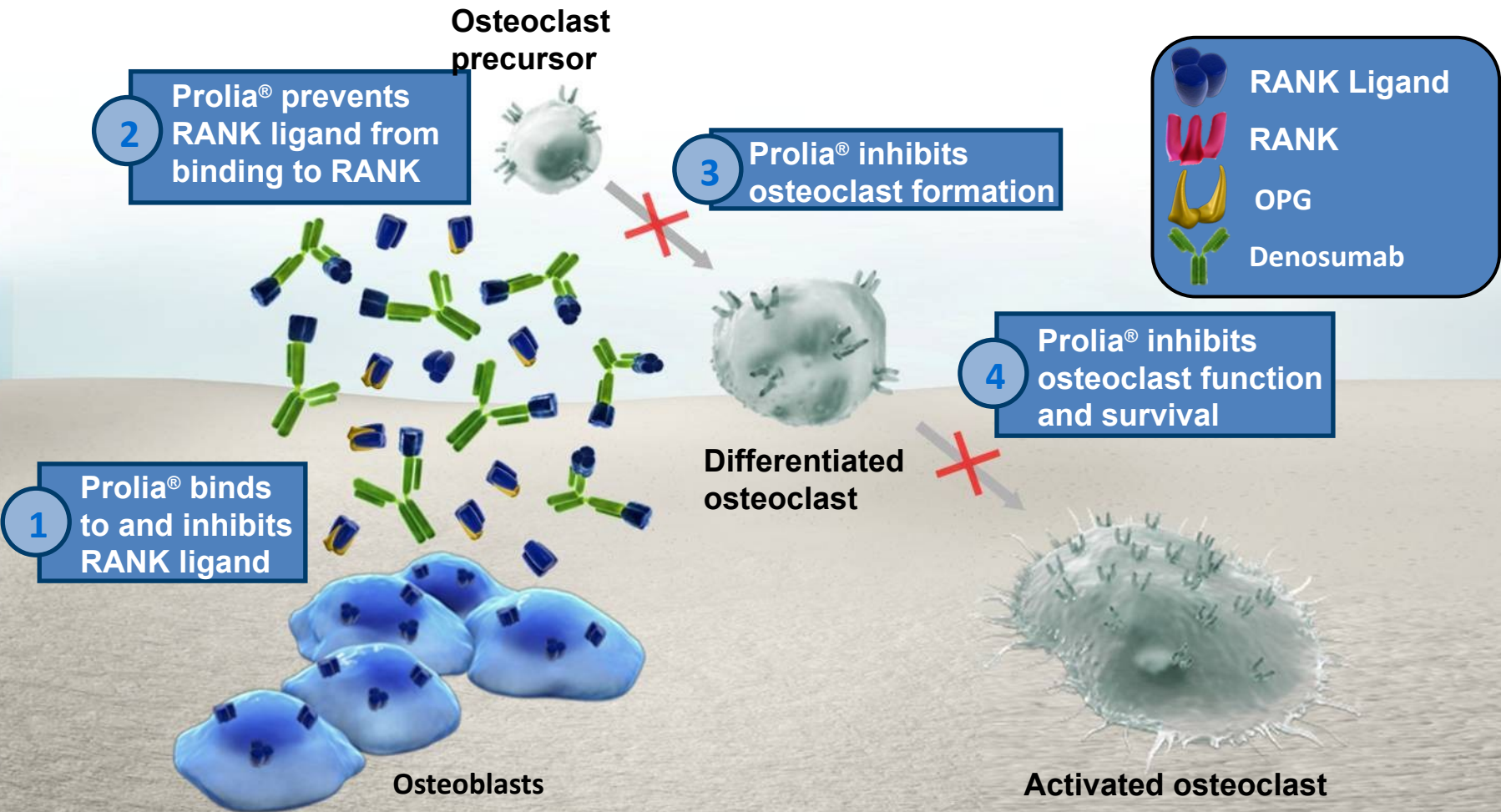
PTH (1–34) →
Romosozumab →
Abaloparatide →

Stimulates bone turnover

Maintain or increase bone mass

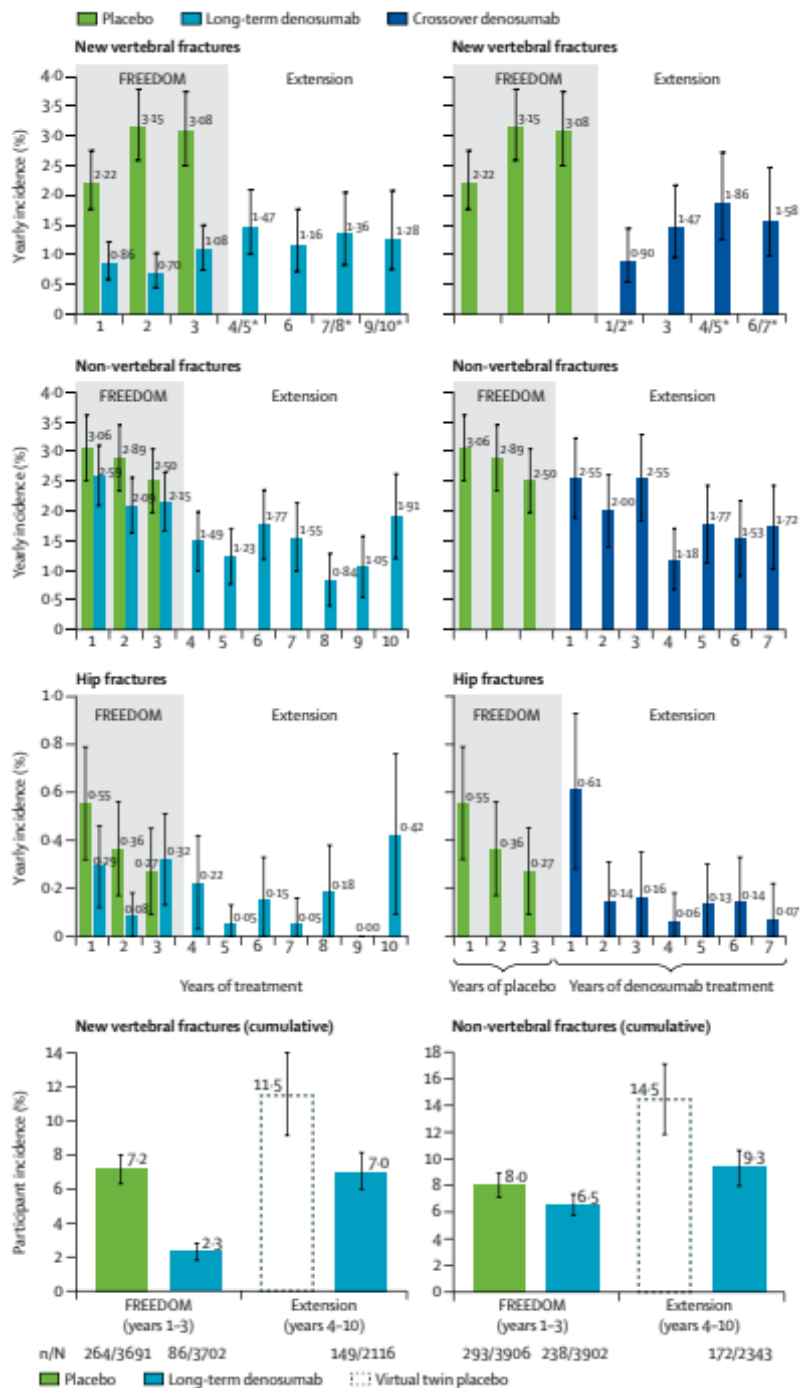
Reduce fracture risk

Denosumab, a RANK Ligand Inhibitor, Inhibits Osteoclast Formation, Function, and Survival



Phase 3 randomised FREEDOM trial and open-label extension

22-24% of patients with vertebral fracture at baseline



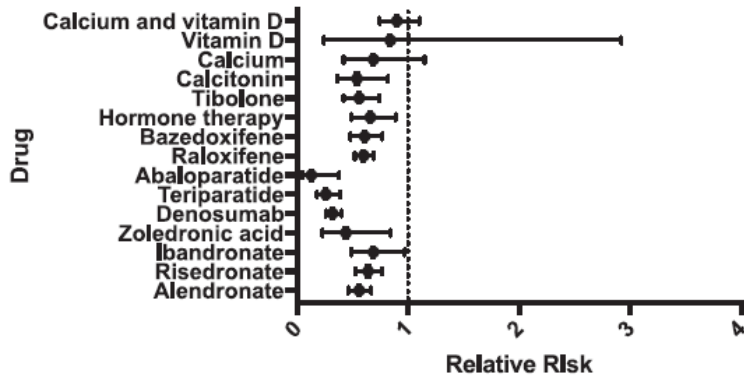
Bone HG et al, Lancet Diab Endocrinol 2017

Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society* Clinical Practice Guideline

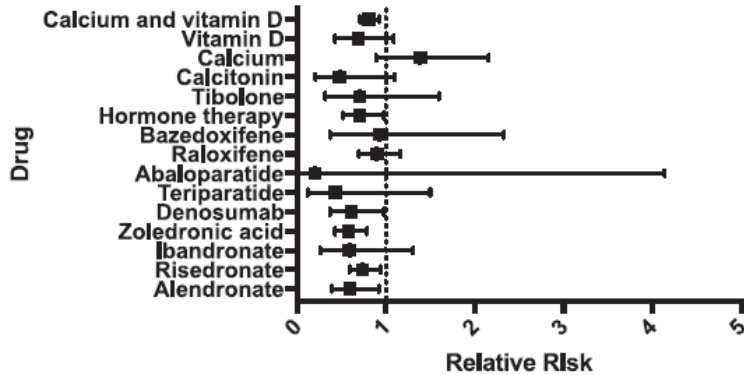
Richard Eastell,¹ Clifford J. Rosen,² Dennis M. Black,³ Angela M. Cheung,⁴ M. Hassan Murad,⁵ and Dolores Shoback^{6,7}

(*J Clin Endocrinol Metab* 104: 1595–1622, 2019)

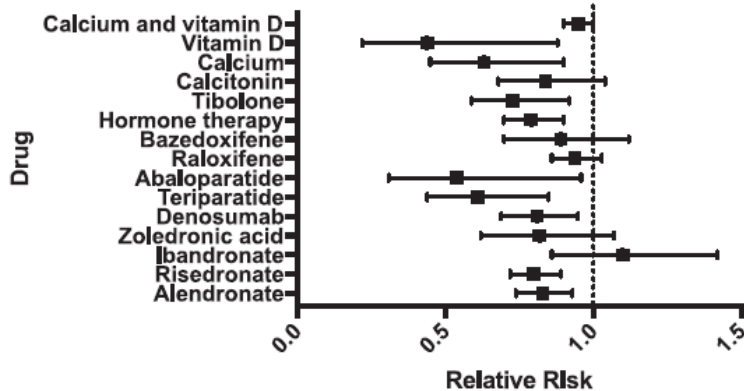
Vertebral Fracture



Hip Fracture



Non-Vertebral Fracture



Riduzione del rischio di frattura osteoporotica post-menopausale (trattamento vs placebo)

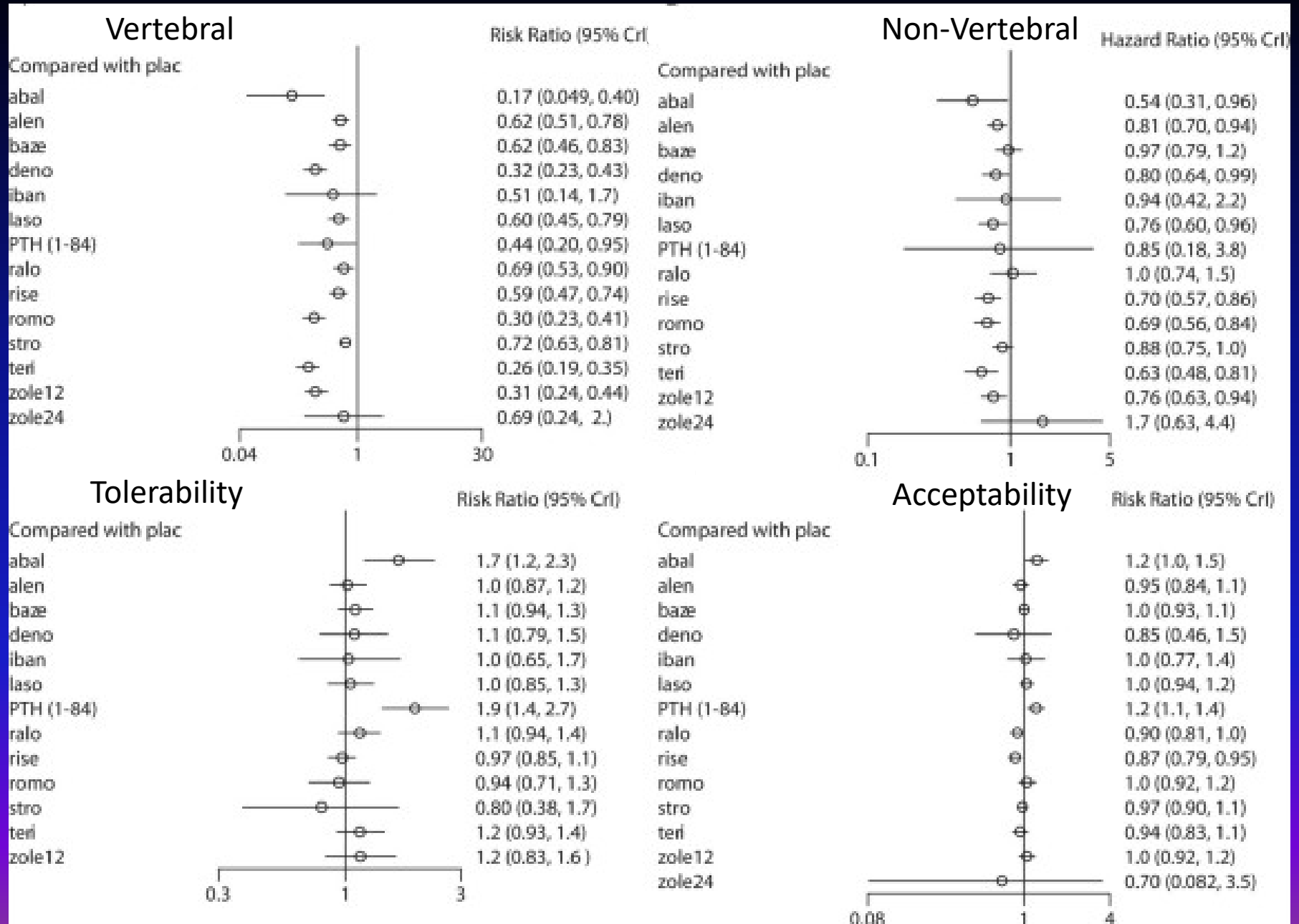
	Vertebrale	Femorale	Non-vertebrale
Alendronato	-44%	-40%	-17%
Risedronato	-36%	-26%	-20%
Ibandronato	-31%	NS	NS
Zoledronato ev	-56%	-42%	-21%
Denosumab	-68%	-39%	-19%
Teriparatide	-74%	NS	-39%

Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society* Clinical Practice Guideline

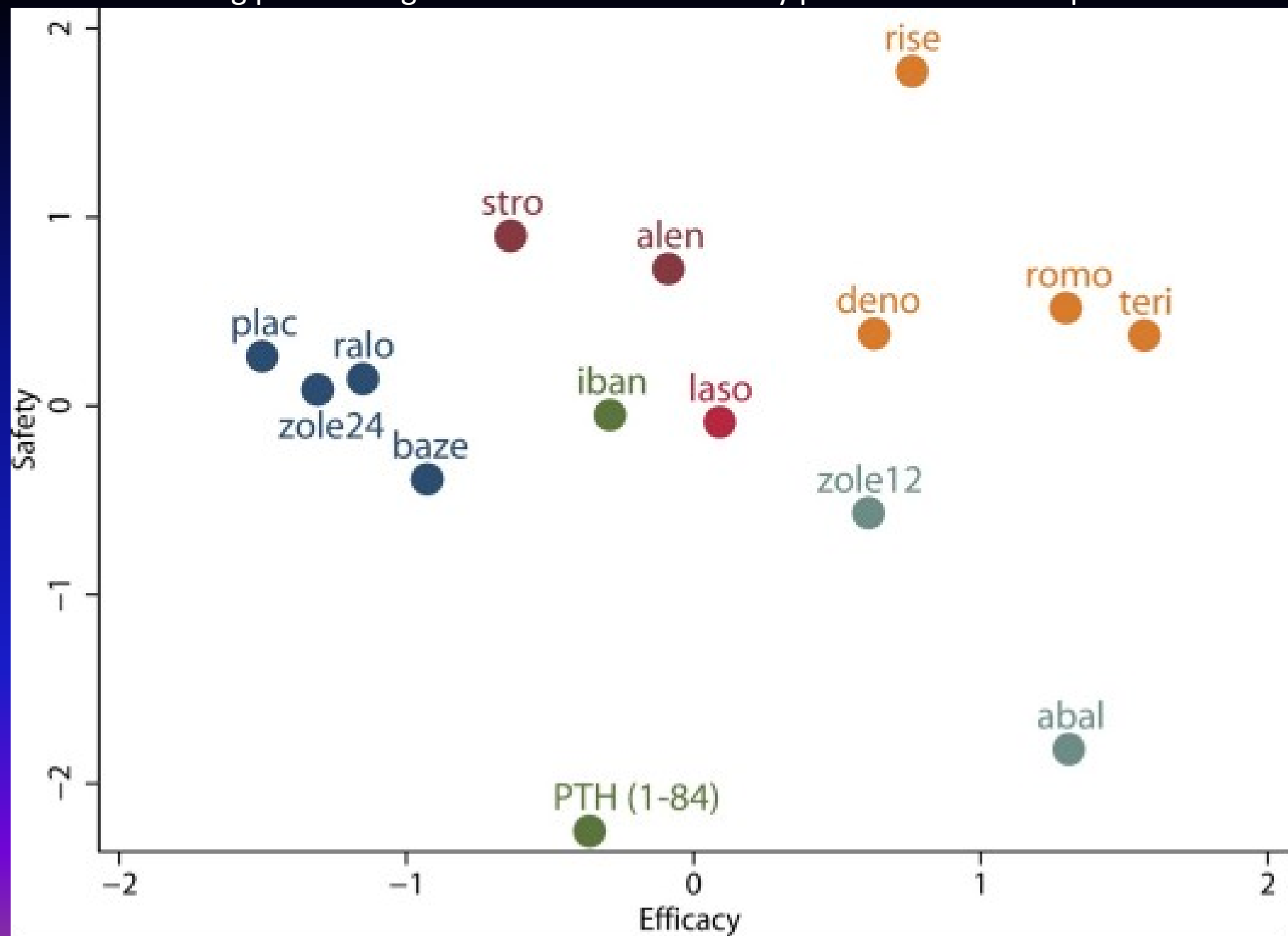
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(*J Clin Endocrinol Metab* 104: 1595–1622, 2019)

Network meta-analysis for secondary prevention with active drugs vs. placebo



Clustered ranking plot of drug intervention for secondary prevention of osteoporotic fractures



Secondary Fracture Prevention: Consensus Clinical Recommendations from a Multistakeholder Coalition

Robert B Conley,¹ Gemma Adib,² Robert A Adler,³ Kristina E Åkesson,⁴ Ivy M Alexander,⁵ Kelly C Amenta,⁶ Robert D Blank,^{7,8} William Timothy Brox,⁹ Emily E Carmody,¹⁰ Karen Chapman-Novakofski,¹¹ Bart L Clarke,¹² Kathleen M Cody,¹³ Cyrus Cooper,¹⁴ Carolyn J Crandall,¹⁵ Douglas R Dirschl,¹⁶ Thomas J Eagen,¹⁷ Ann L Elderkin,¹⁸ Masaki Fujita,¹⁹ Susan L Greenspan,²⁰ Philippe Halbout,²¹ Marc C Hochberg,²² Muhammad Javaid,²³ Kyle J Jeray,²⁴ Ann E Kearns,¹² Toby King,²⁵ Thomas F Koinis,²⁶ Jennifer Scott Koontz,^{27,28} Martin Kužma,²⁹ Carleen Lindsey,³⁰ Mattias Lorentzon,^{31,32,33} George P Lyritis,³⁴ Laura Boehnke Michaud,³⁵ Armando Miciano,³⁶ Suzanne N Morin,³⁷ Nadia Mujahid,³⁸ Nicola Napoli,^{39,40} Thomas P Olinginski,⁴¹ J Edward Puzas,¹⁰ Stavroula Rizou,³⁴ Clifford J Rosen,^{42,43} Kenneth Saag,⁴⁴ Elizabeth Thompson,⁴⁵ Laura L Tosi,⁴⁶ Howard Tracer,⁴⁷ Sundeep Khosla,¹² and Douglas P Kiel⁴⁸

2020

Recommendation 11: First-line pharmacologic therapy options for people aged 65 years or older with a hip or vertebral fracture include:

- The oral bisphosphonates alendronate and risedronate, which are generally well tolerated, familiar to health care professionals, and available at low cost; and
- Intravenous zoledronic acid and subcutaneous denosumab, if oral bisphosphonates pose difficulties.

**PREVENZIONE SECONDARIA IN PAZIENTI CON
PREGRESSE FRATTURE OSTEOPOROTICHE**

Non vertebrali, non di femore

vertebrali o di femore

T score BMD colonna o femore ≤ -3

1 o 2 fratture

≥ 3 fratture

Nuova frattura nonostante trattamento in nota 79 da almeno 1 anno

≥ 1 frattura + trattamento > 12 mesi con dosi di prednisone o equivalenti ≥ 5 mg/die

≥ 1 frattura + Tscore BMD colonna o femore < -4

I scelta: alendronato \pm vitD, risedronato, zoledronato,

II scelta: denosumab, ibandronato, Raloxifene, Bazedoxifene

III scelta: stronzio ranelato

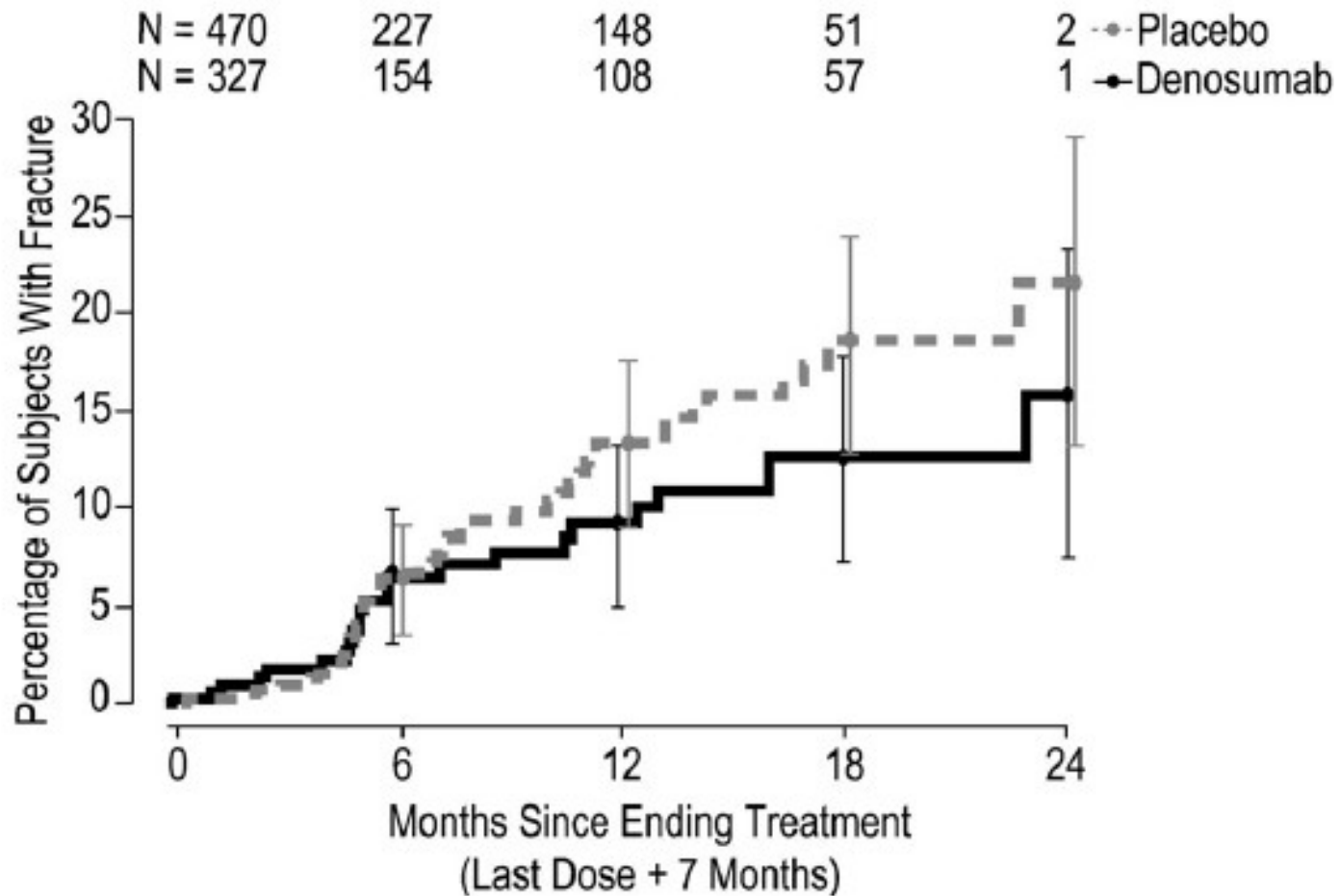
I scelta: teriparatide

II scelta; denosumab, zoledronato

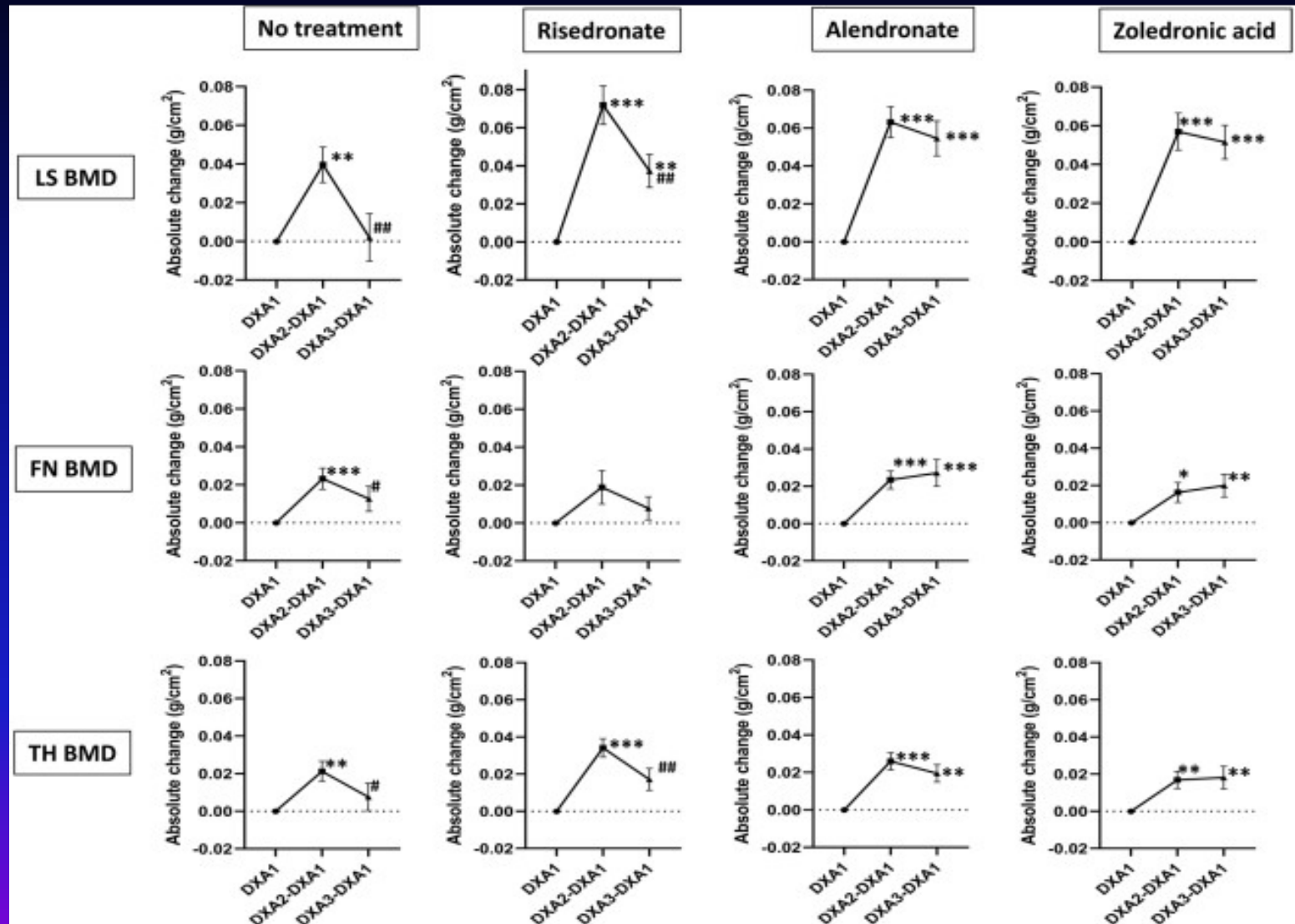
III scelta: alendronato \pm vitD, risedronato, ibandronato

IV scelta: stronzio ranelato

Fractures after discontinuation of denosumab



Absolute change in BMD during denosumab treatment and after discontinuation



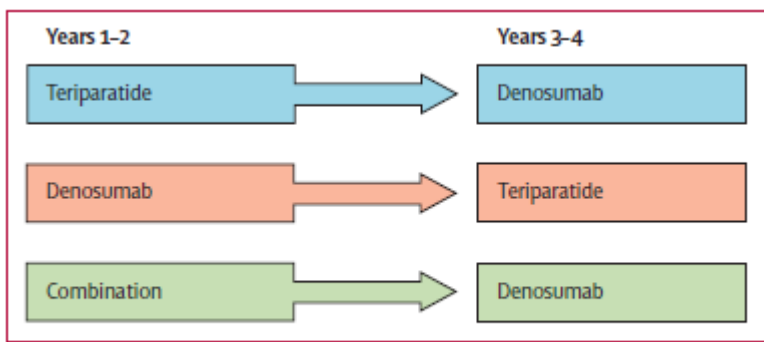
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2020

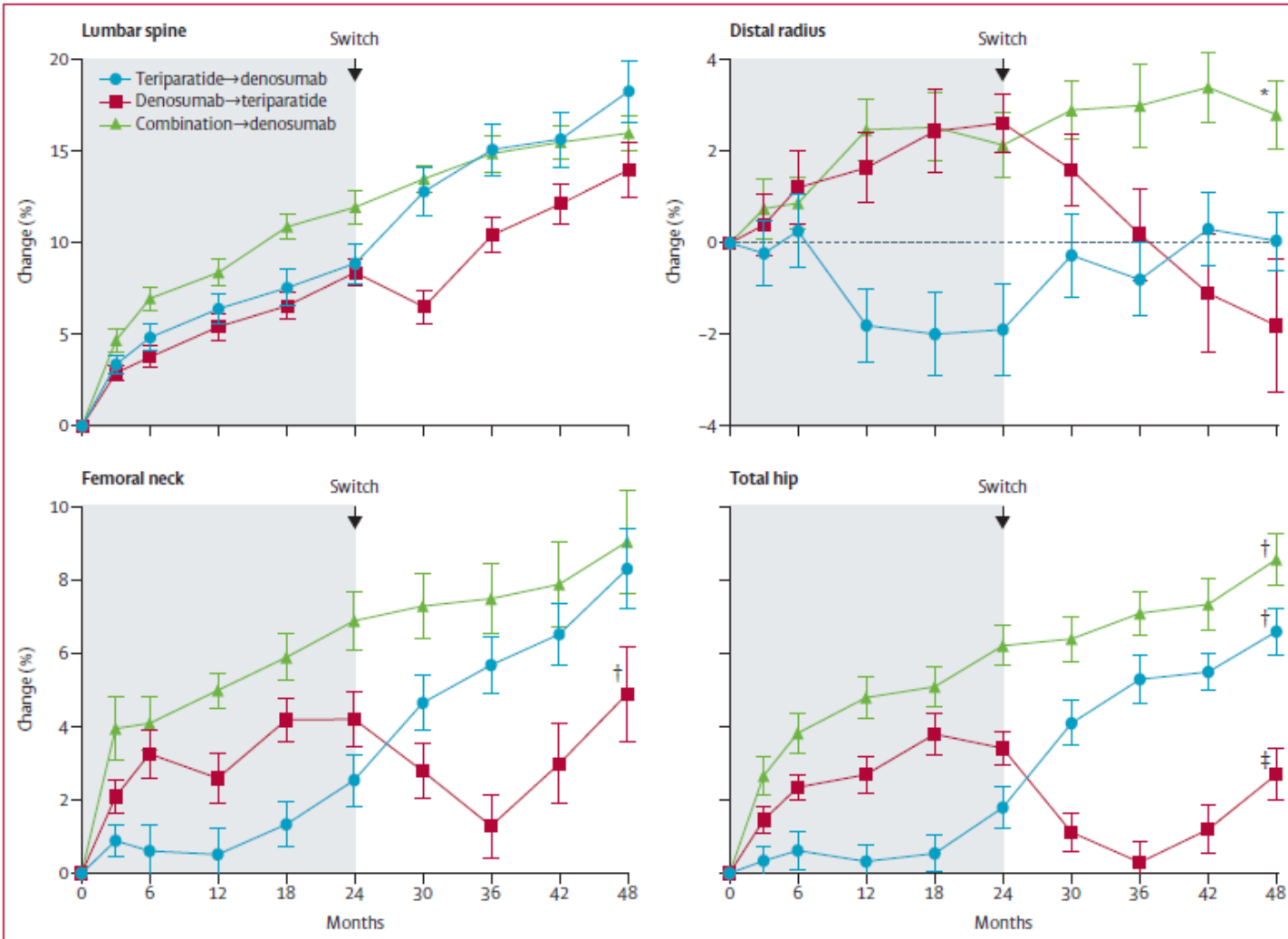
Recommendation 12: The optimal duration of pharmacologic therapy for people aged 65 years and older with a hip or vertebral fracture is not known.

- General recommendations on stopping and restarting anti-osteoporosis drugs are available to individualize treatment for each patient.
- Most published guidelines recommend that the need for therapy with bisphosphonates be reassessed after 3 to 5 years, based on their long half-life in bone and evidence suggesting that the risk of certain rare adverse events may increase with longer duration of treatment.
- Stopping denosumab without starting another antiresorptive drug should be avoided because of the possibility of rapid bone loss and increased fracture risk. Similarly, patients stopping anabolic agents also should be placed on an antiresorptive therapy.



DATA-Switch STUDY

Leder BJ et al, Lancet 2015

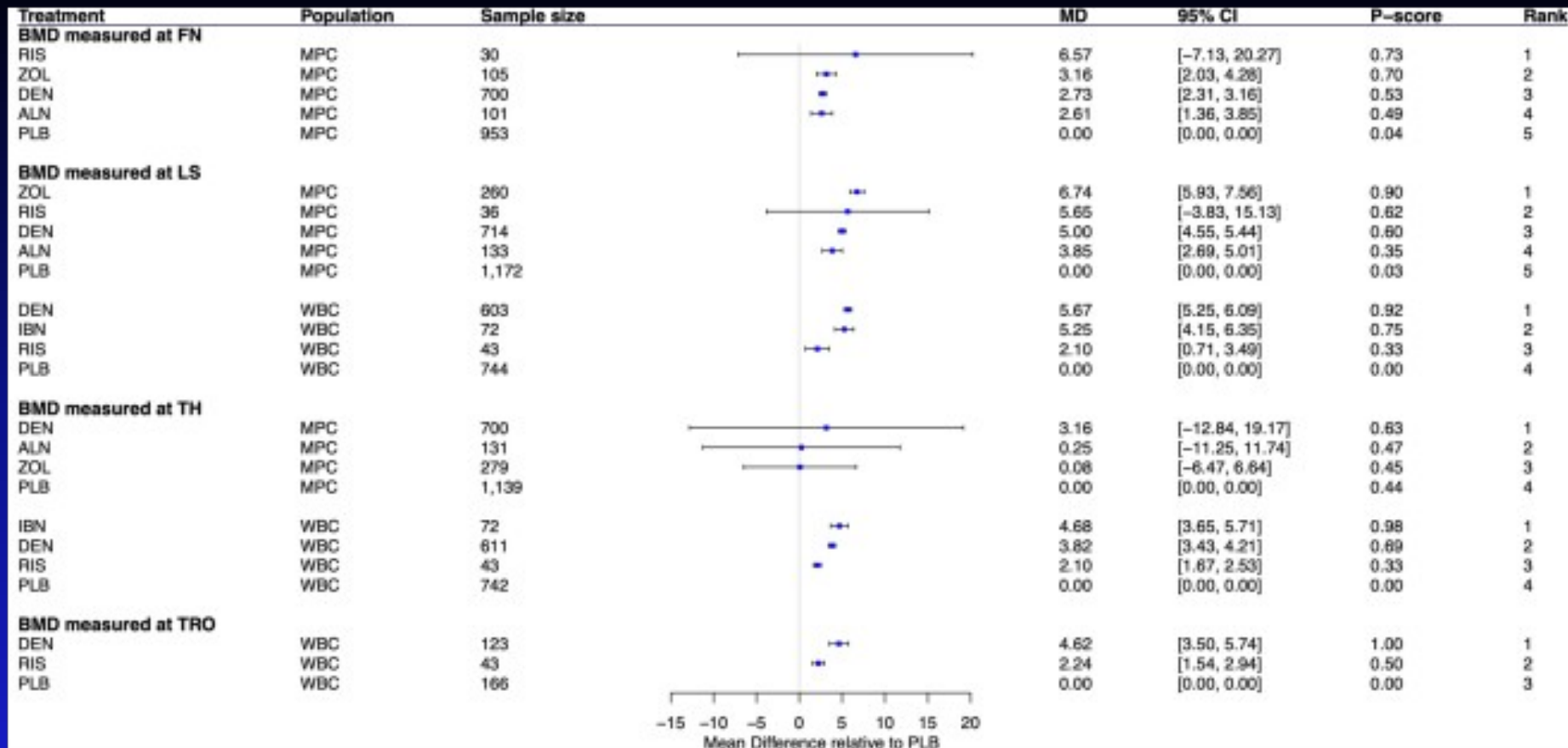


Prevention and Treatment of Glucocorticoid-Induced Osteoporosis in Adults: Consensus Recommendations From the Belgian Bone Club

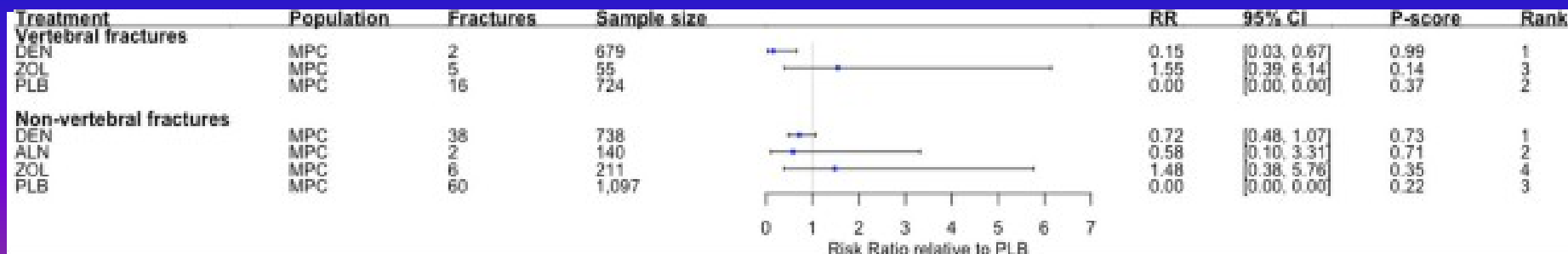
Michaël R. Laurent^{1,2*}, Stefan Goemaere³, Charlotte Verroken^{3,4}, Pierre Bergmann⁵, Jean-Jacques Body⁶, Olivier Bruyère⁷, Etienne Cavalier⁸, Serge Rozenberg⁹, Bruno Lapauw^{3,4} and Evelien Gielen^{1,10}

- *Recommendation 14: We recommend alendronate, risedronate, zoledronate, denosumab or teriparatide for GIOP prevention (strong recommendation, high-quality evidence).*
- *Recommendation 15: We suggest considering oral bisphosphonates in GIOP patients at high fracture risk, and teriparatide, denosumab or zoledronate in GIOP patients at very high fracture risk. Nevertheless, we suggest tailoring the choice between treatments not only according to the risk of fractures, but also according to contraindications, patient preference, cost and the possibility of poor compliance (weak recommendation, moderate quality evidence).*

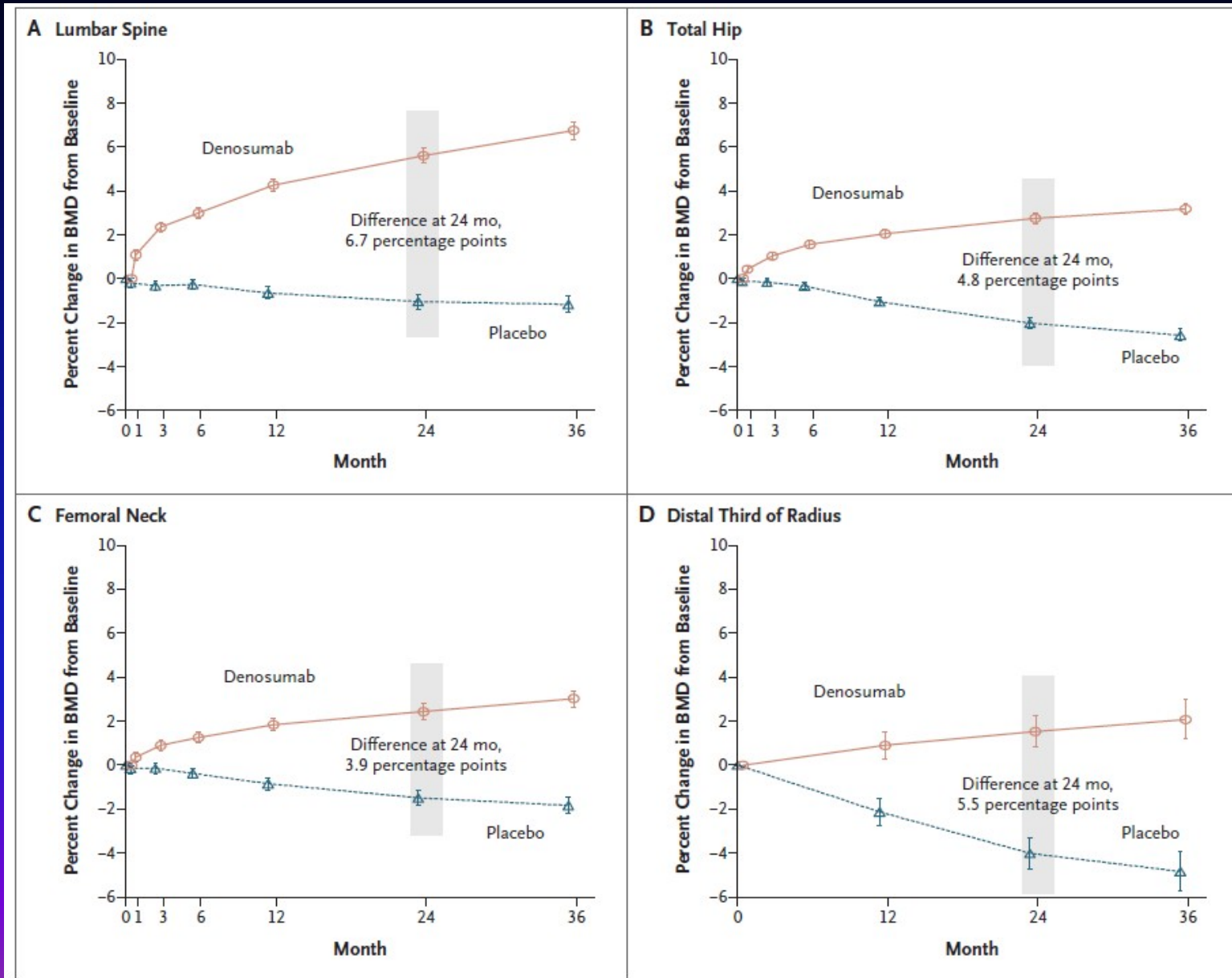
Network meta-analyses indicating the BMD in breast cancer



Network meta-analyses indicating the RR of vertebral fracture in breast cancer



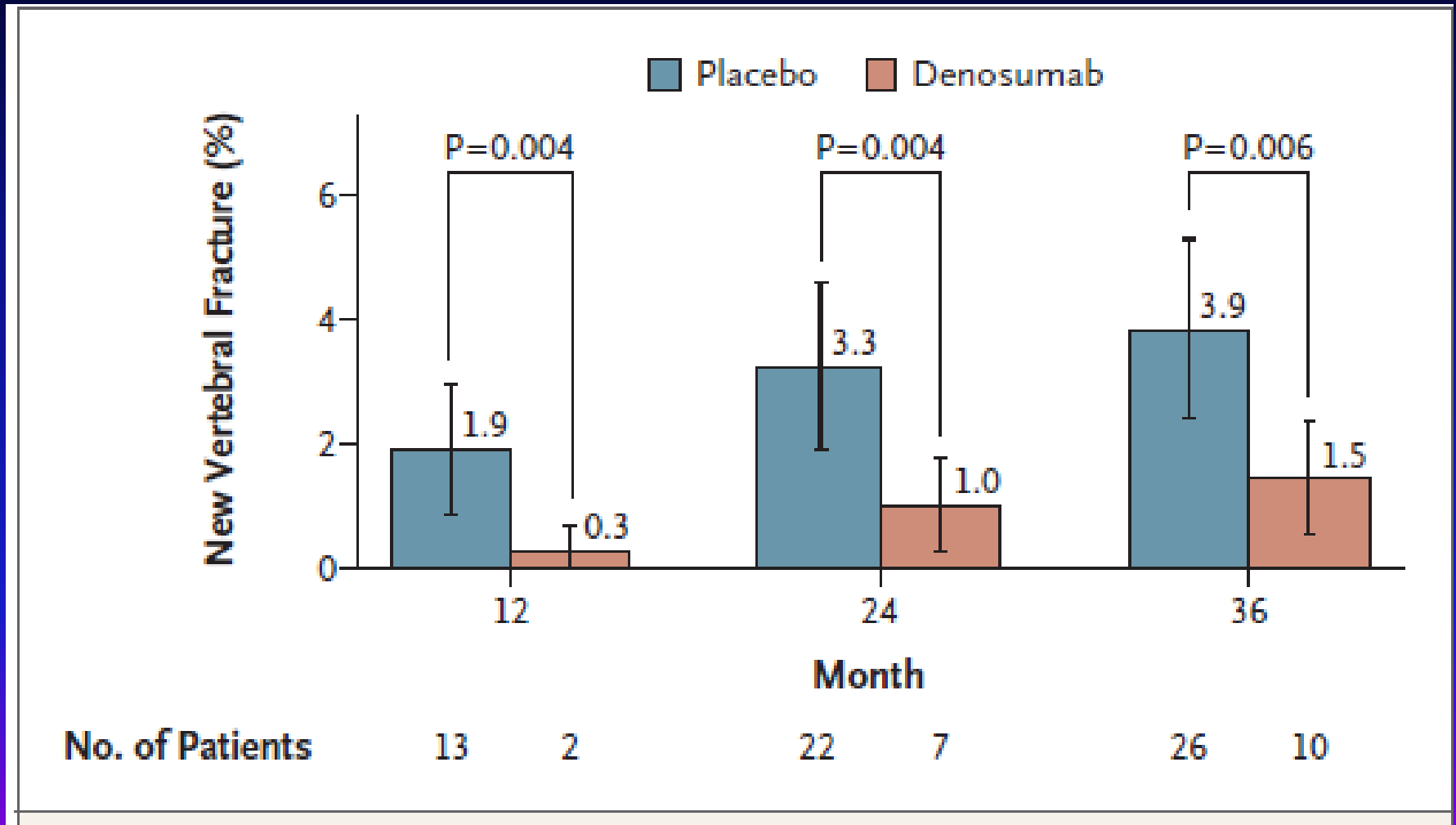
Mean percent changes from baseline of BMD in pts undergoing ADT for non-metastatic PC (treated independently of BMD and fracture risk)



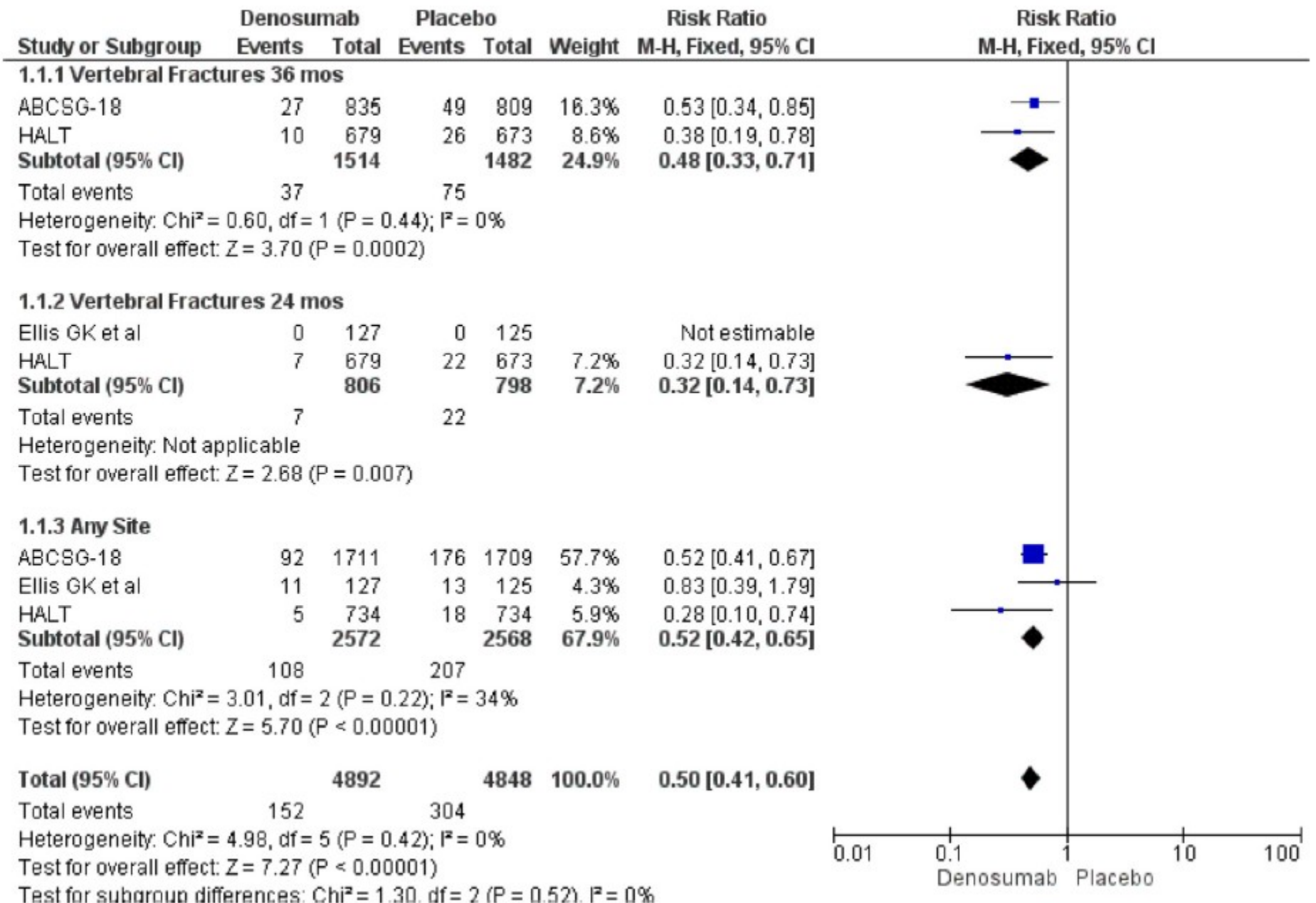
HALT study - 1468 patients enrolled

Smith MR et al, 2009

Cumulative incidence of new vertebral fractures at 12, 24 and 36 months of treatment in patients receiving ADT for non-metastatic prostatic cancer



Riduzione del rischio di frattura in pazienti in ADT trattati con denosumab



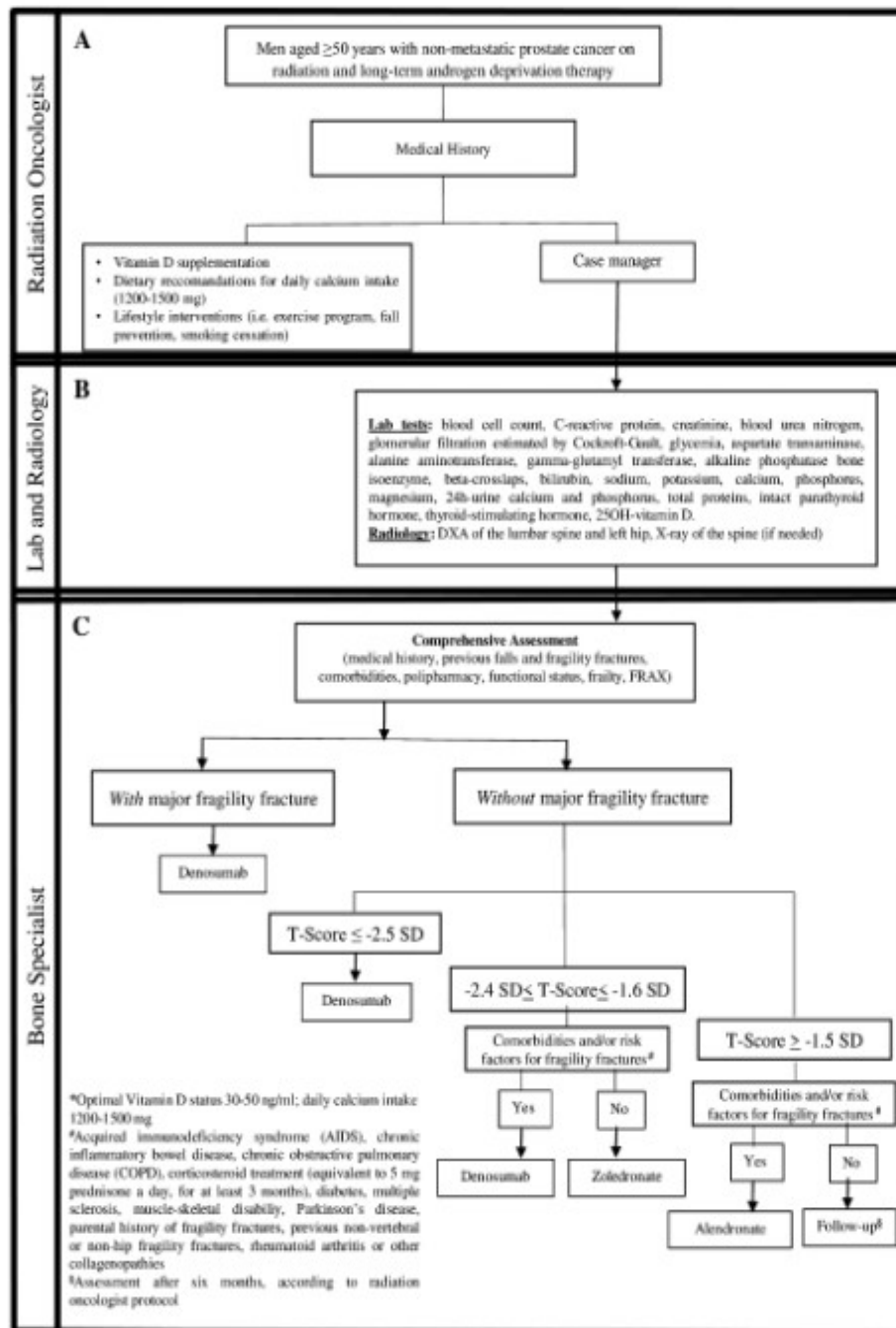


Figure 1. The diagnostic and therapeutic algorithm among services and specialists.