8th National Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Diseases
Antalya November 2024

Osteoporosis in Men: Update of a European Perspective

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nature reviews rheumatology

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Evidence-based guidelines

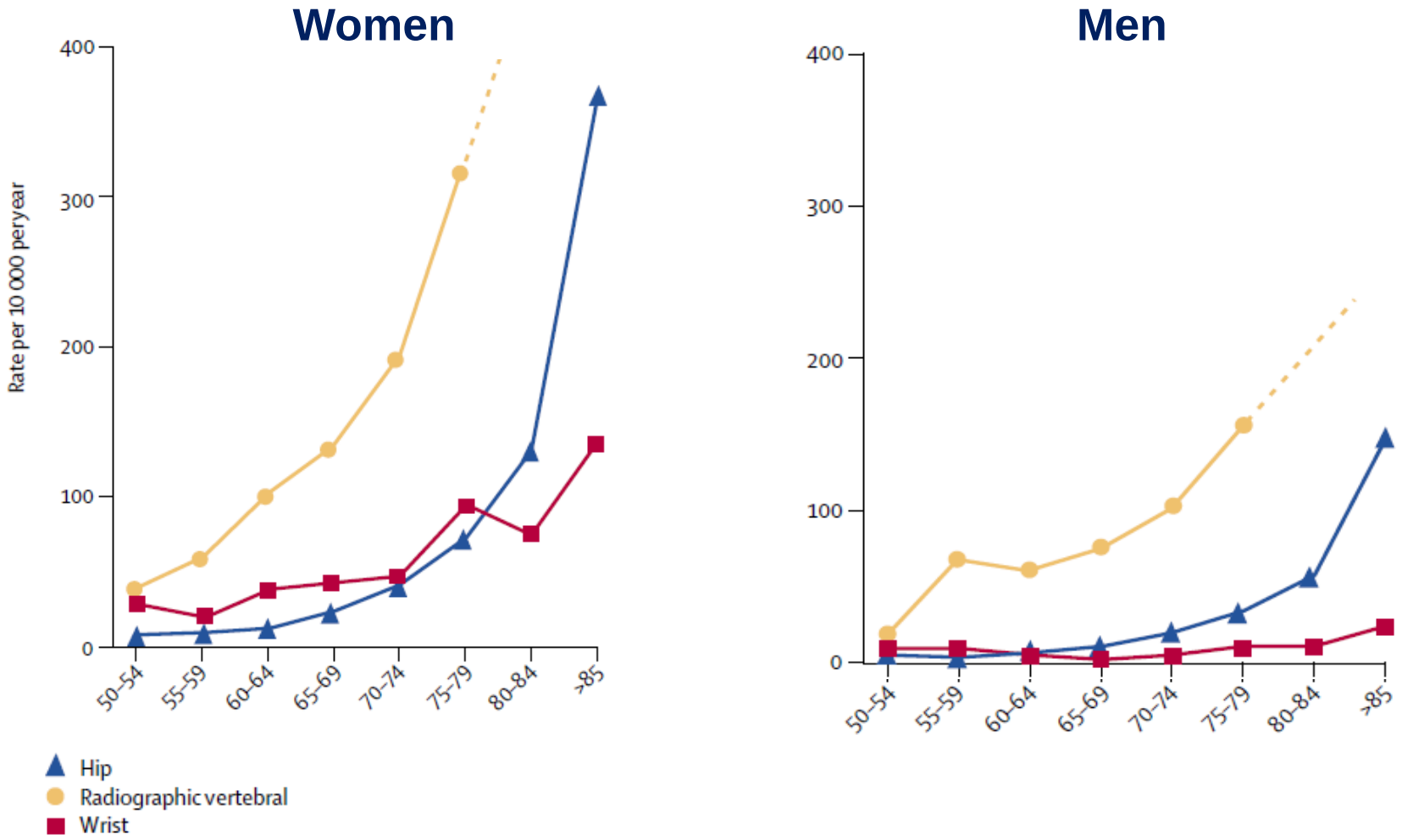
Check for updates

Evidence-Based Guideline for the management of osteoporosis in men

Nicholas R. Fuggle[1], Charlotte Beaudart[2,3], Olivier Bruyère[3], Bo Abrahamsen[4], Nasser Al-Daghri[5], Nansa Burlet[3,6], Manju Chandran[7], Mario M. Rosa[8], Bernard Cortet[9], Céline Demonceau[3], Willard Dere[10], Philippe Halbout[11], Mickaël Hiligsmann[12], John A. Kanis[13,14], Jean-Marc Kaufman[15], Andreas Kurth[16], Olivier Lamy[17], Andrea Laslop[18], Stefania Maggi[19], Radmila Matijevic[20], Eugene McCloskey[13], Ali Mobasheri[21], Maria C. Prieto Yerro[22], Régis P. Radermecker[23], Shaun Sabico[5], Yousef Al-Saleh[4,24], Stuart Silverman[25], Nicola Veronese[26], René Rizzoli[27], Cyrus Cooper[1,28,29], Jean-Yves Reginster[3,30,31] & Nicholas C. Harvey[1,28,31]

Fuggle et al Nature Rev Rheumatol 2024

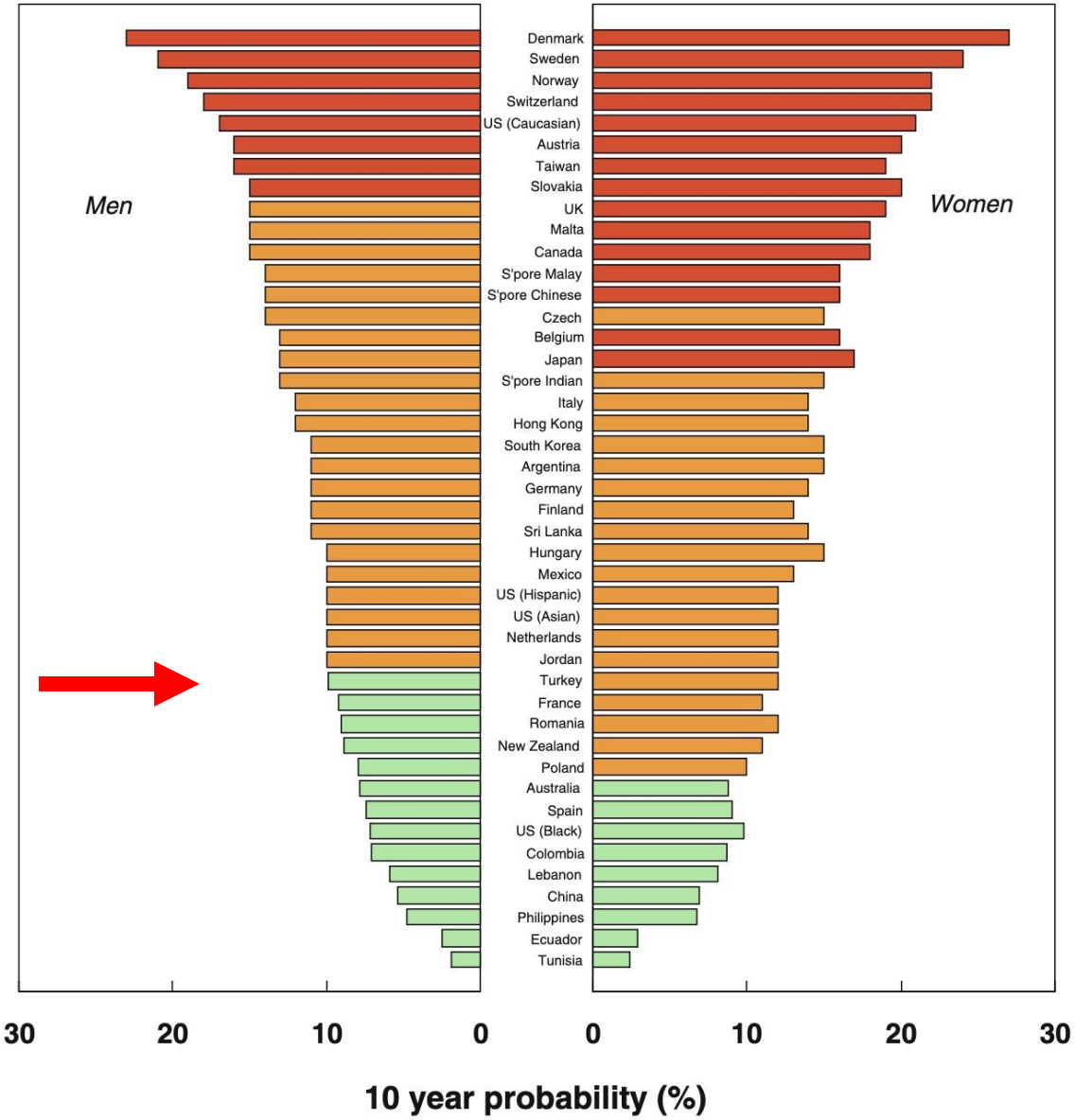
Age- and sex-specific incidence of radiographic vertebral, hip and distal forearm fractures



Sambrook et al Lancet 2006

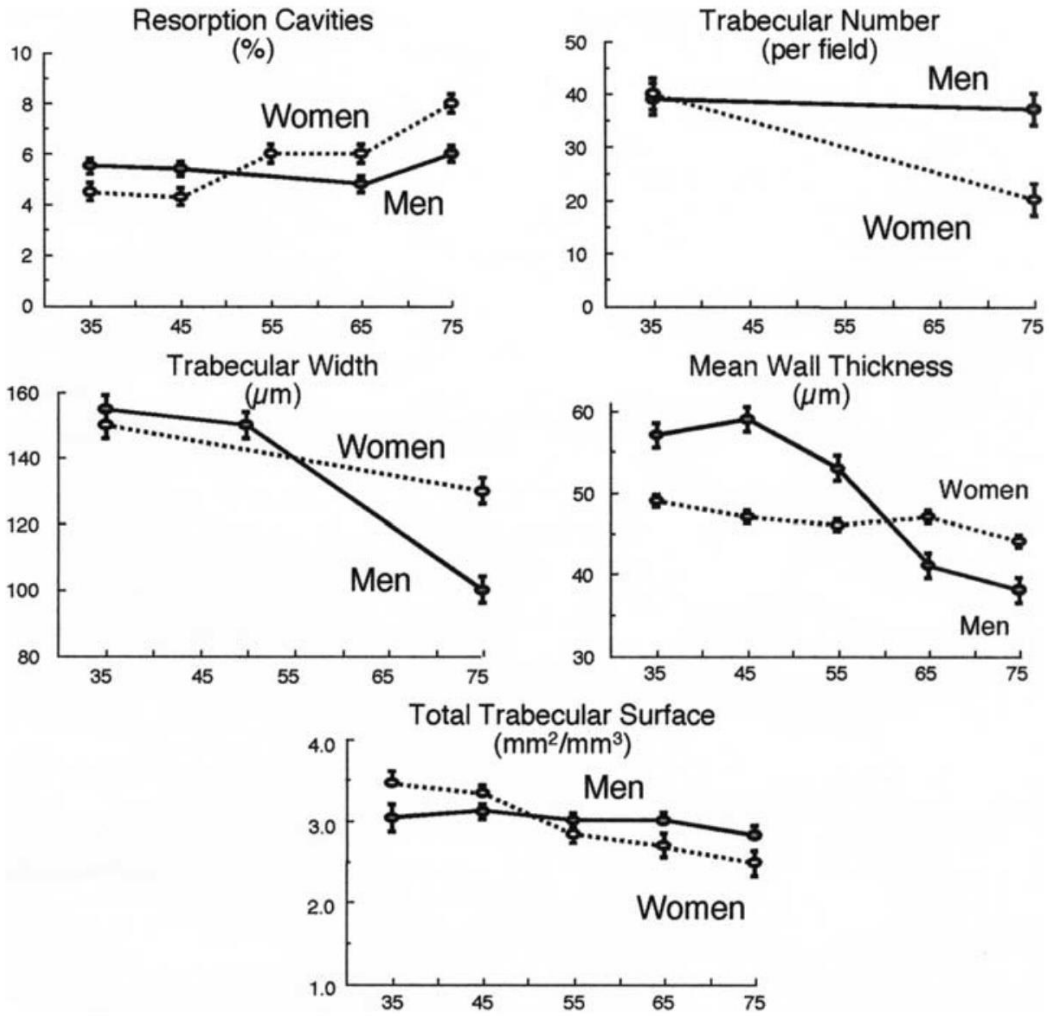
A systematic review of hip fracture incidence and probability of fracture worldwide

Ten-year probability of a major fracture (in percent) in men and women aged 65 years with a prior fragility fracture (and no other clinical risk factors) at the threshold of osteoporosis as judged by BMD at the femoral neck (i.e. a T- score of −2.5 SD). The body mass index was set at 24 kg/m2



Kanis et al Osteoporos Int 2012

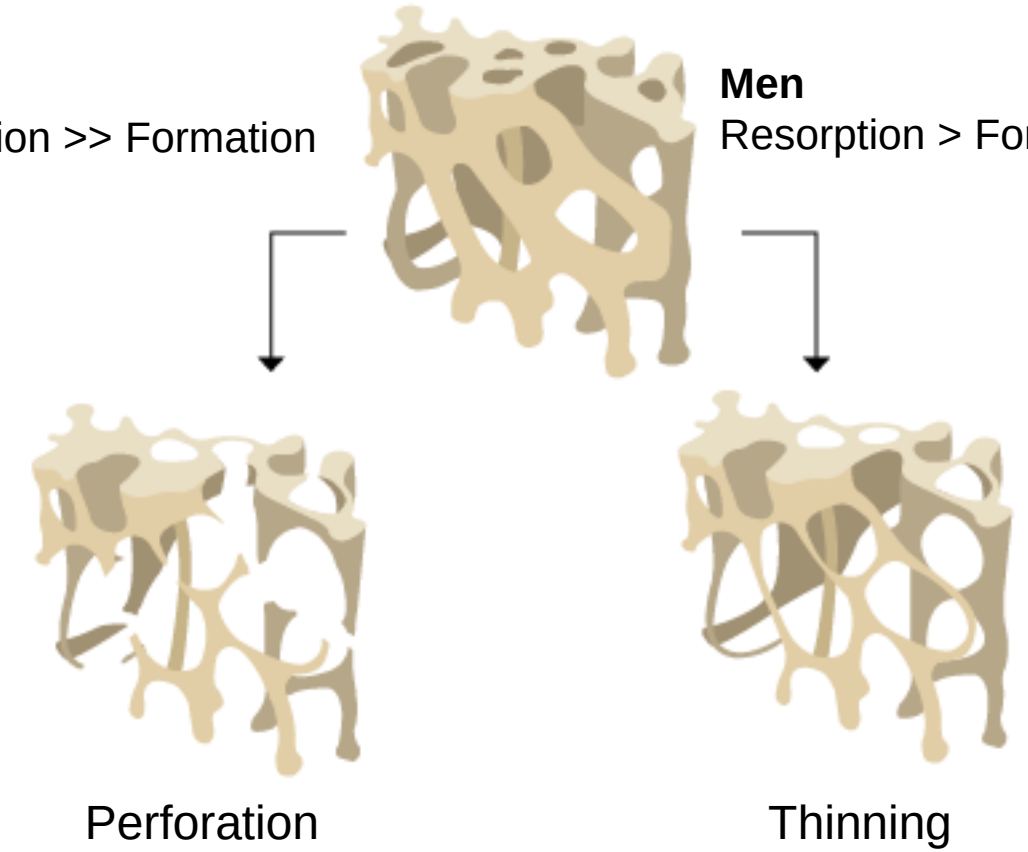
Trabecular Bone – Age Related Loss Differs Between Men and Women



Aaron et al Clin Orthop Rel Res 1987

Women
Resorption >> Formation

Men
Resorption > Formation



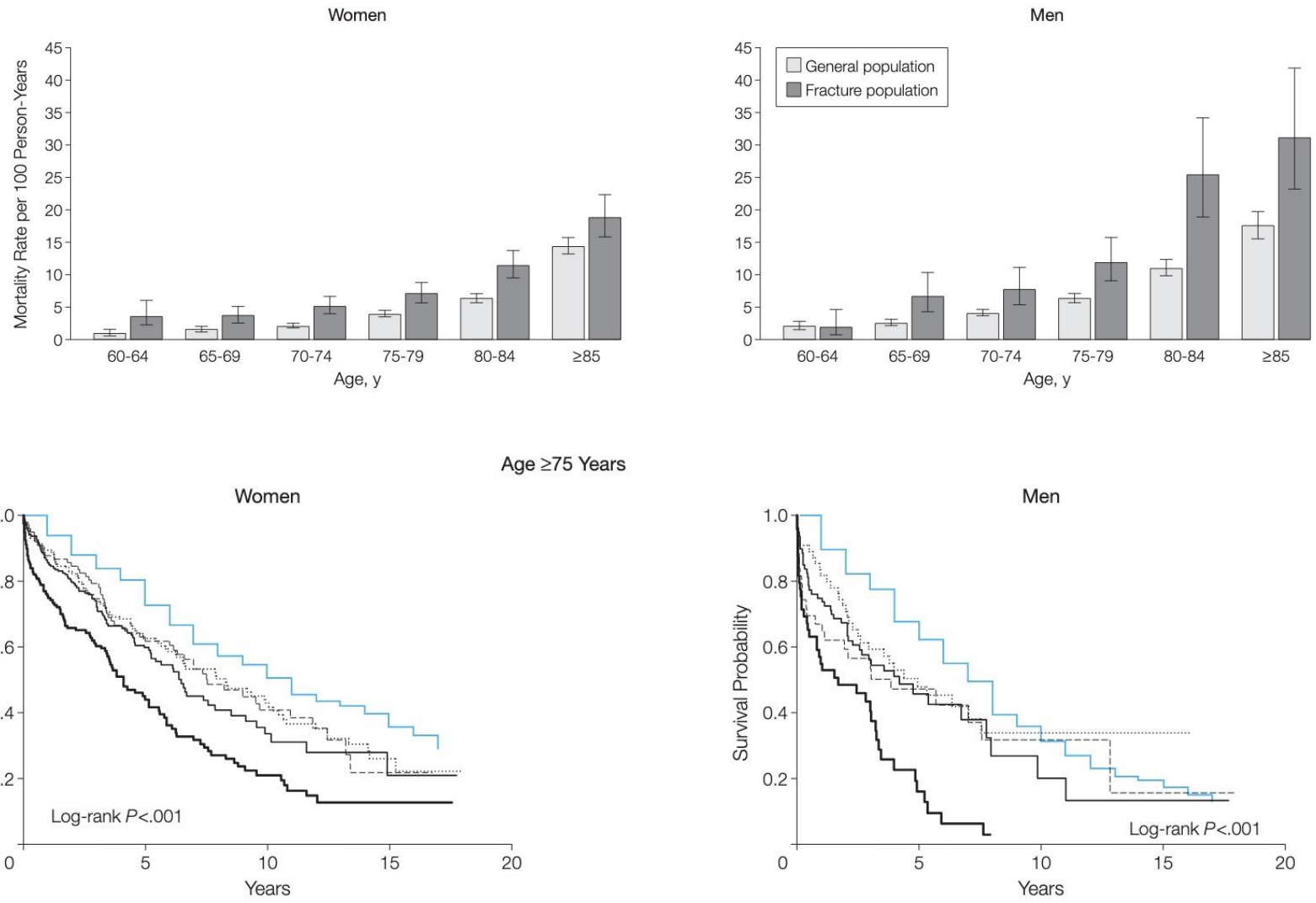
Perforation

Thinning

Adapted from Seeman E., J Appl Physiol 2003

Mortality Risk Associated With Low-Trauma Osteoporotic Fracture and Subsequent Fracture in Men and Women

Figure 2. Mortality Rates for the General Population and Fracture Participants According to Age



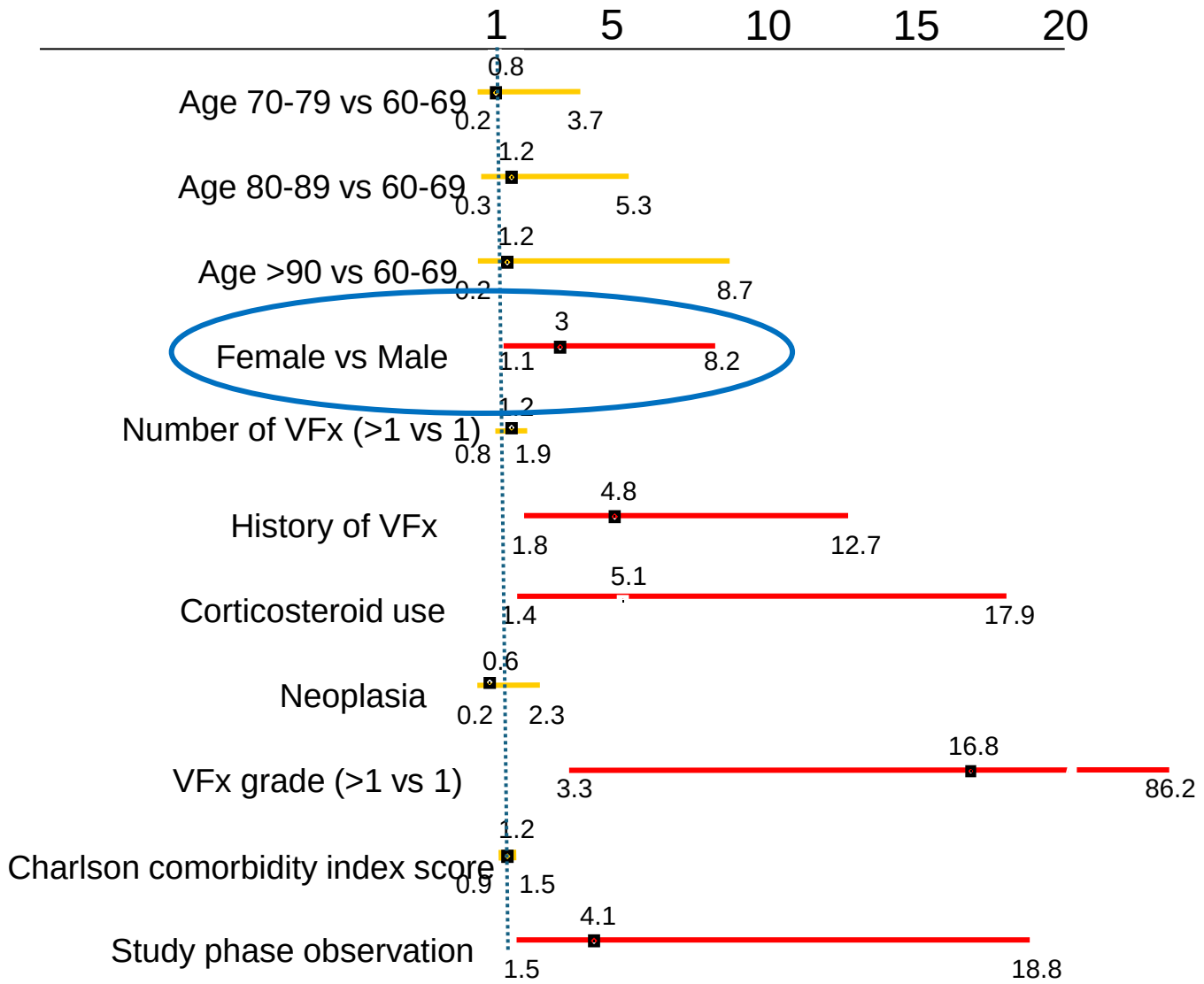
Bliuc et al JAMA 2009

A Prospective Study on Socioeconomic Aspects of Fracture of the Proximal Femur

	Odds ratio	
Patients returned to private housing 1 year after fracture[d]		
age (per 10 years)	0.37	(0.25–0.55)
male gender	0.39	(0.17–0.91)
living circumstances (alone vs. couple or family)	0.47	(0.25–0.90)
general health condition (bad vs. good)	0.22	(0.10–0.49)

Schürch et al JBMR 1996

Factors which influence vertebral fracture detection on X-ray



Casez et al, Osteoporos Int 2006

Vertebral fractures predict subsequent fractures

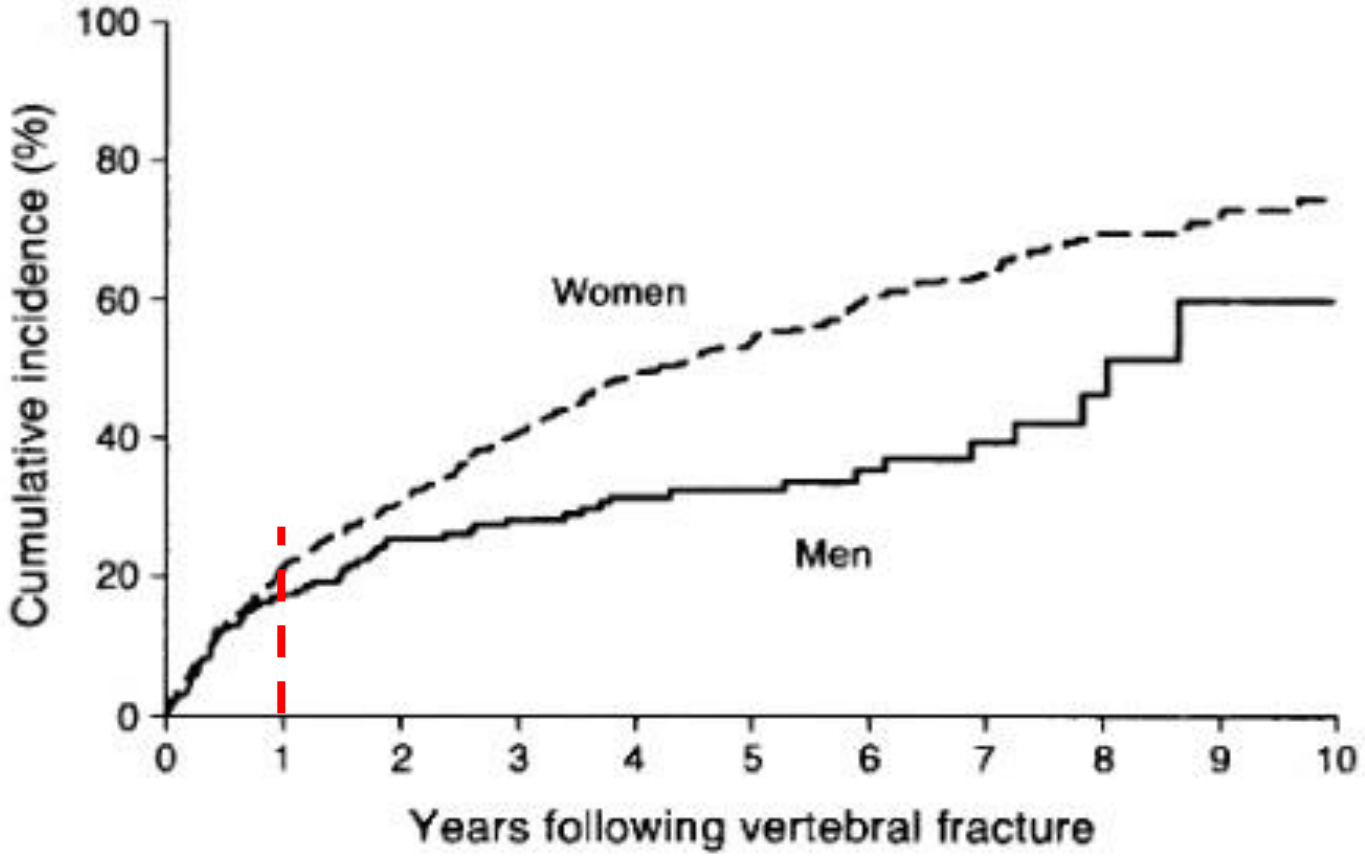
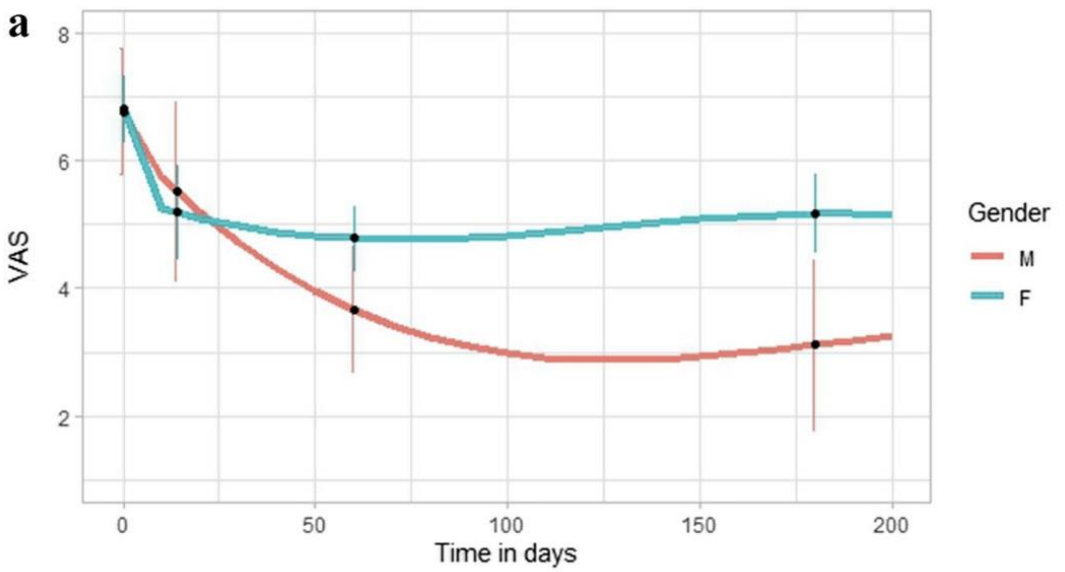
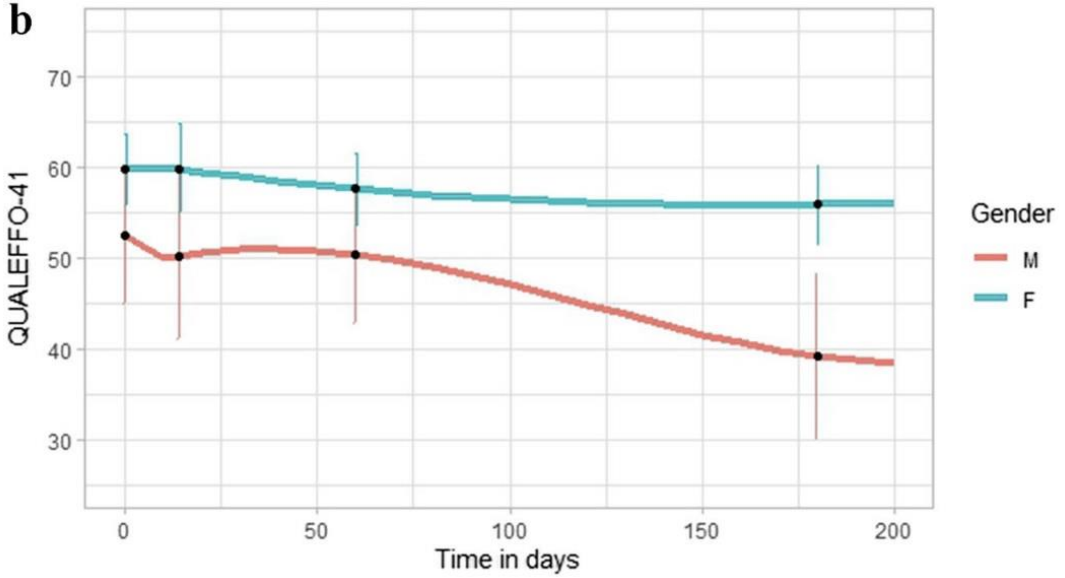


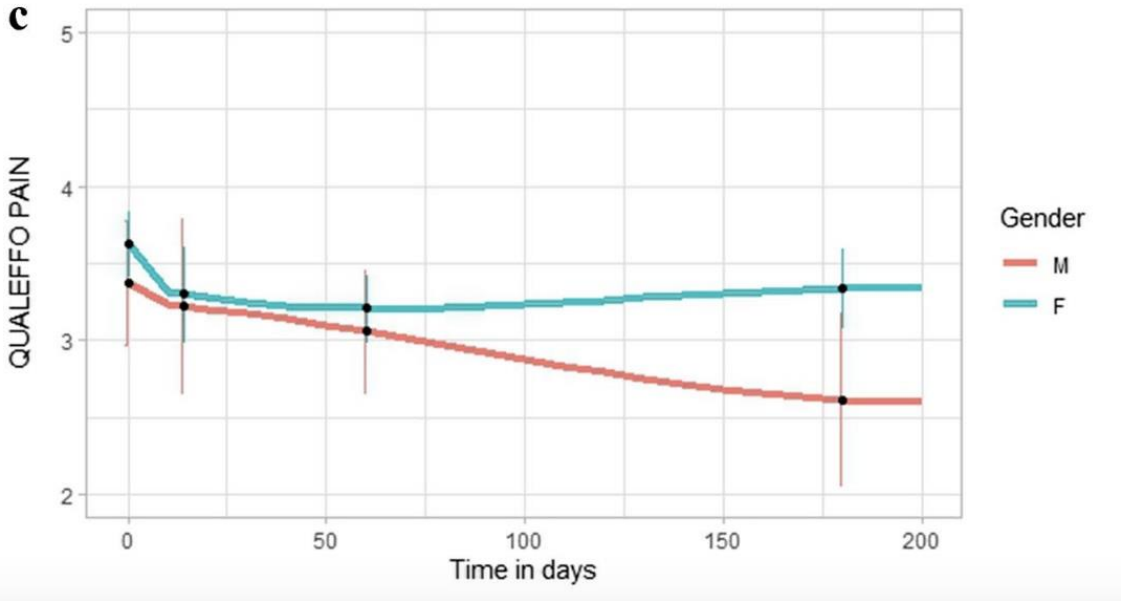
Fig. 1. Cumulative incidence of any subsequent fracture following the initial vertebral fracture among Rochester, Minnesota, women and men in 1985–94.

Melton et al Osteoporos Int 1999

Effect of gender on the evolution of pain and quality of life after treatment of symptomatic vertebral fragility fractures



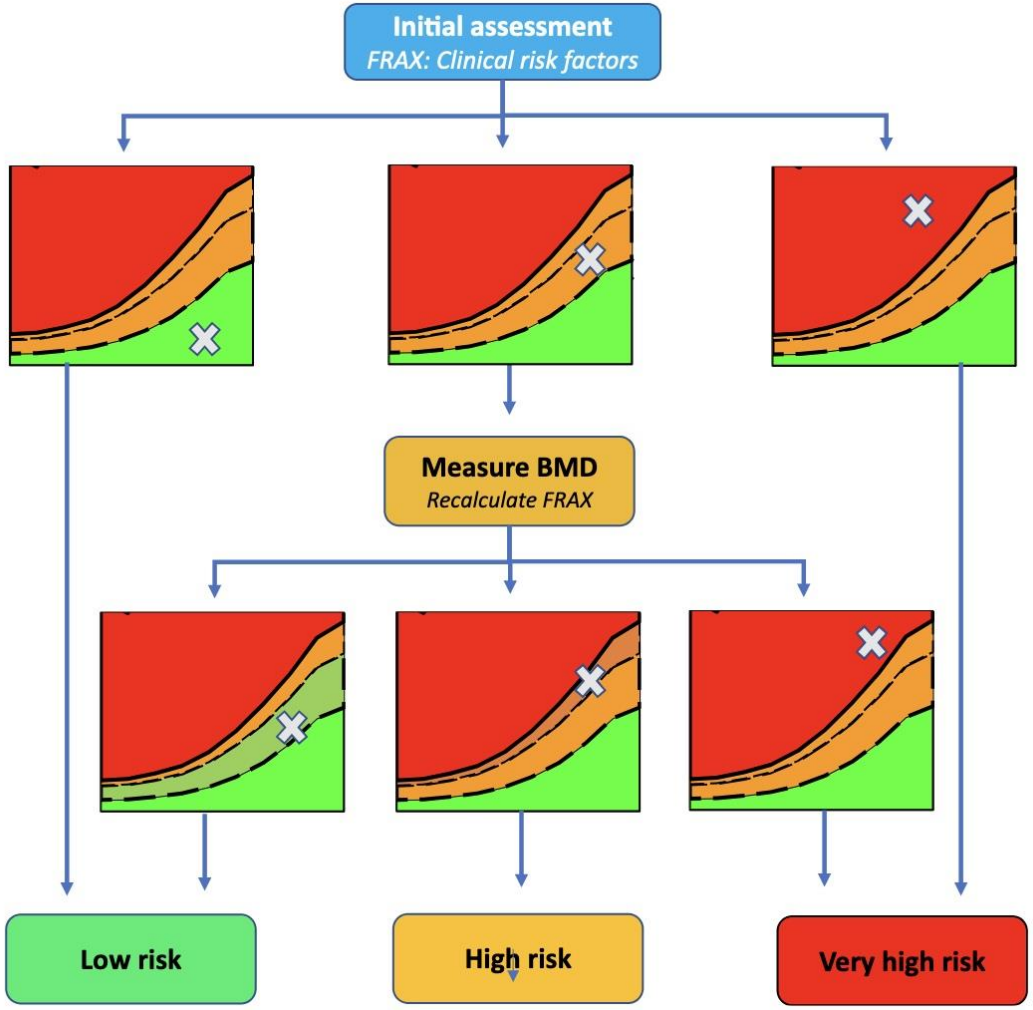


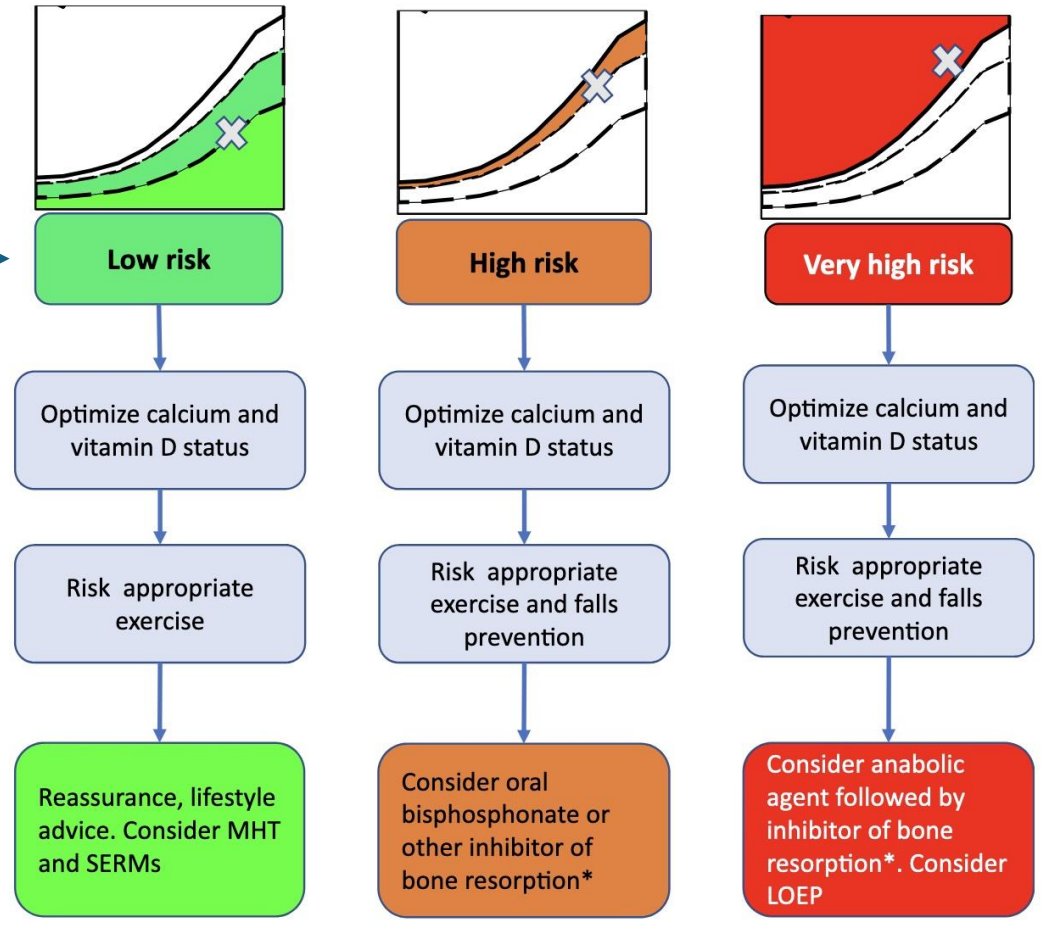


Conservative therapy ± vertebroplasty

Peris et al Osteoporos Int 2024

Algorithm for the management of patients at low, high and very high risk of osteoporotic fractures



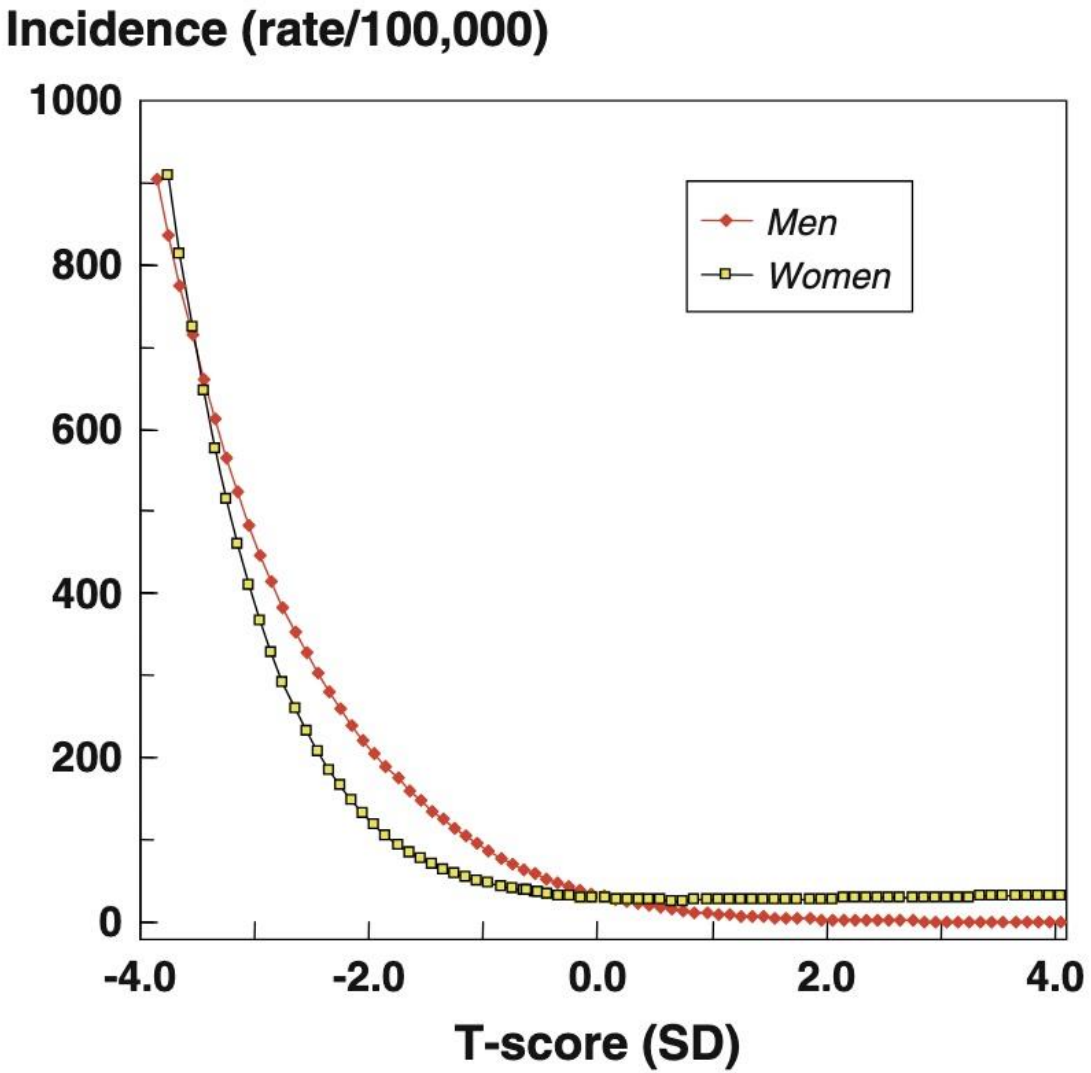


MHT, menopausal hormone therapy;
SERM, selective estrogen receptor modulator;
LOEP, local osteo-enhancement procedure

Kanis et al Osteoporos Int 2020

BMD and Fracture in Women and Men

Age-adjusted incidence of hip fracture in men and women according to the T-score for femoral neck BMD



Kanis et al Osteoporos Int 2011

Evidence-Based Guideline for the management of osteoporosis in men

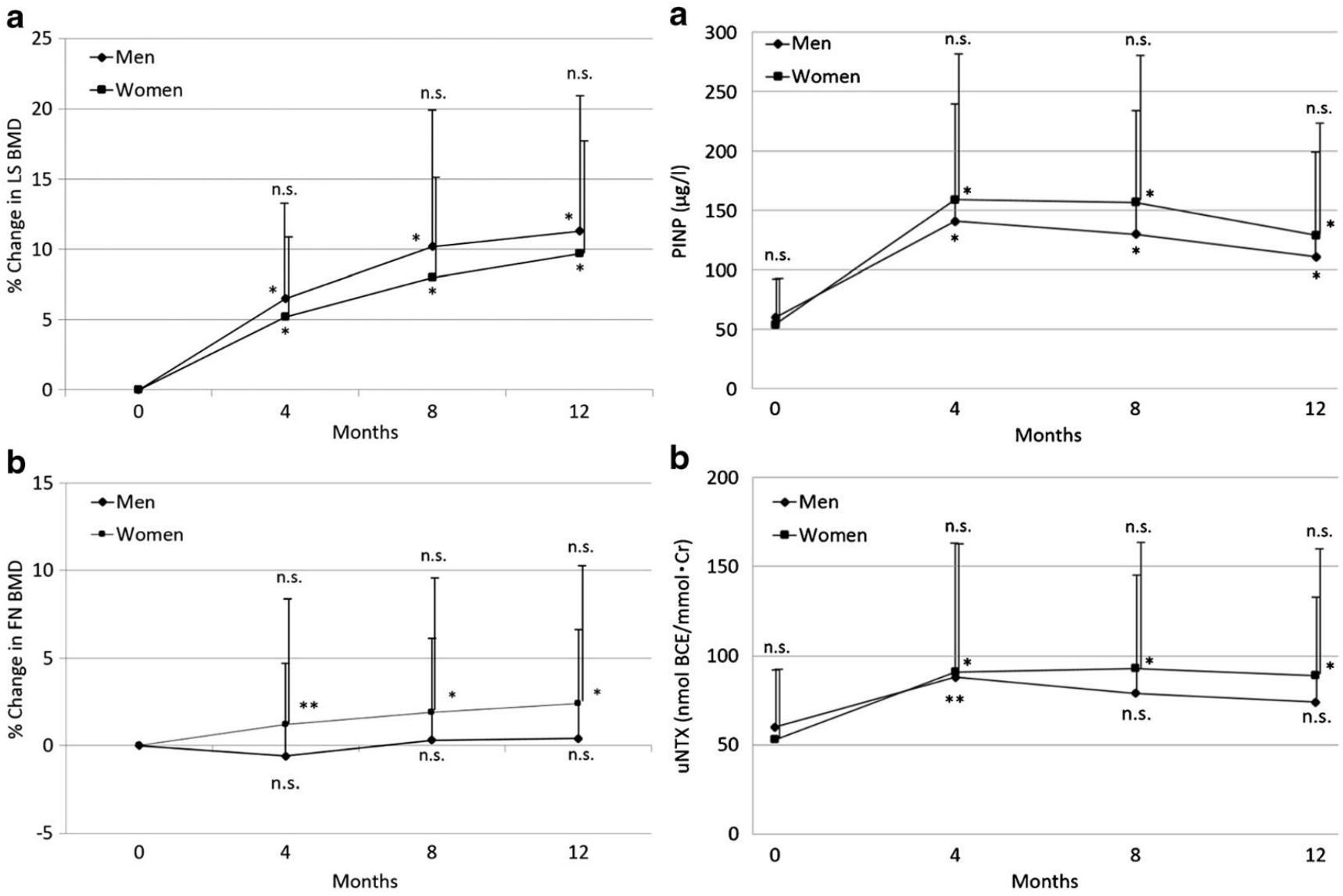
Recommendation:

• A female reference database should be used for the densitometric diagnosis of osteoporosis in men.	**Strong**
• FRAX is the appropriate tool for the assessment of fracture risk and as the basis for setting intervention thresholds in men with osteoporosis.	**Strong**
• FRAX-based intervention thresholds should be age dependent in men with osteoporosis.	**Strong**
• All men with a prior fragility fracture should be considered for treatment with anti-osteoporosis medications.	**Strong**

Strong: ≥ 75% voters (n=28)

Fuggle et al Nature Rev Rheumatol 2024

Analysis of daily **teriparatide** treatment for osteoporosis in men



Niimi et al
Osteoporos Int 2015

Osteoporosis treatment prevents hip fracture similarly in both sexes: the FOCUS observational study

Healthcare system to compare the reduction in hip fractures associated with standard-of-care osteoporosis treatment in men versus women. n=271’389 patients aged ≥65 yrs

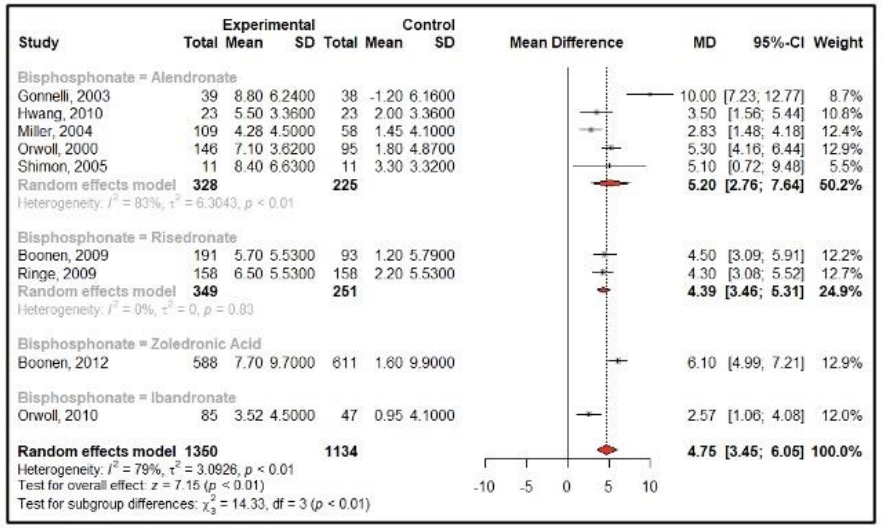
Table 3. Odds ratio (adjusted and crude) of hip fracture associated with osteoporosis treatment (treated vs not-treated patients; and partially-treated vs not-treated patients) for each sex at two-year follow-up.

		Adjusted odds ratio (95% CI)		Crude odds ratio (95% CI)	
Treated vs not-treated					
	Women	0.26	0.21–0.33	0.25	0.19–0.31
	Men	0.21	0.13–0.34	0.25	0.16–0.39
	Men:Women[a]	0.81	0.47–1.37	1.00	0.60–1.66
Partially-treated vs not-treated					
	Women	0.90	0.69–1.18	0.99	0.77–1.27
	Men	0.69	0.40–1.21	0.85	0.51–1.42
	Men:Women[a]	0.77	0.41–1.42	0.86	0.49–1.52

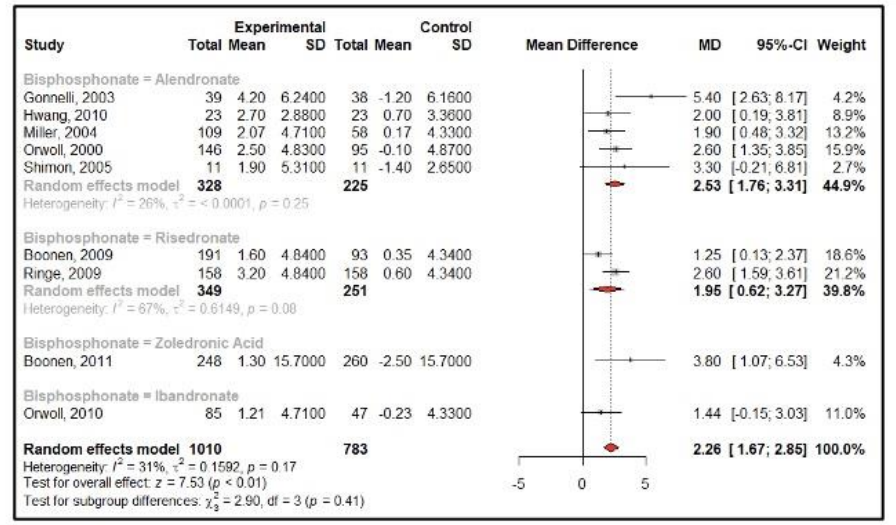
Keaveny et al JBMR 2024

Efficacy of osteoporosis pharmacological treatments in men: a systematic review and meta-analysis

Lumbar spine



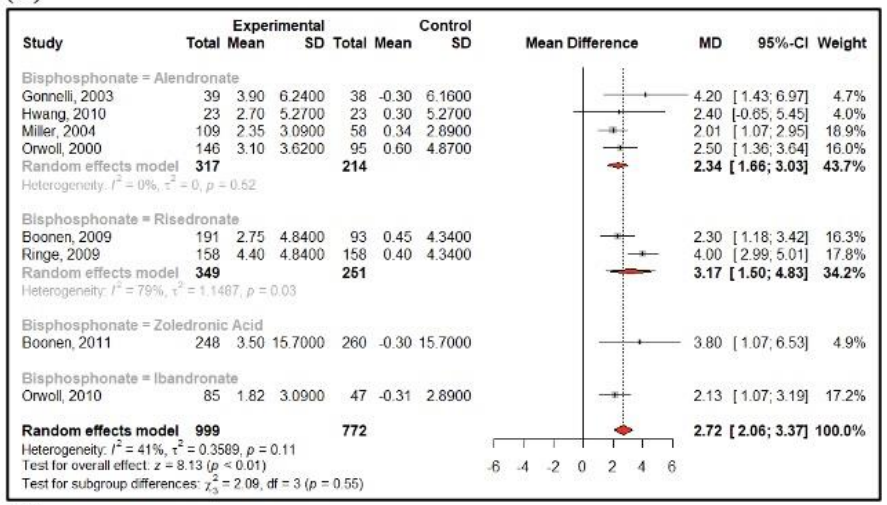
(A)



(B)

Femoral neck

Total hip

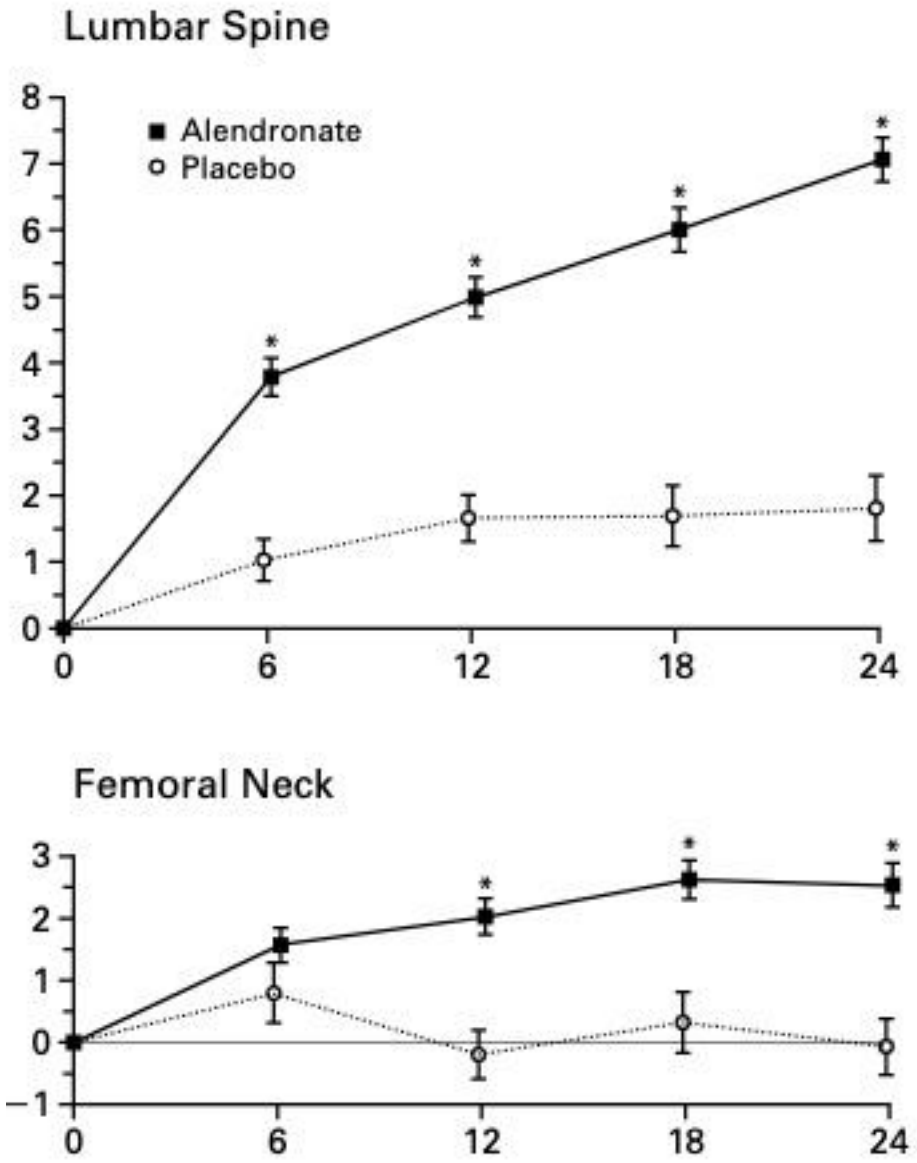


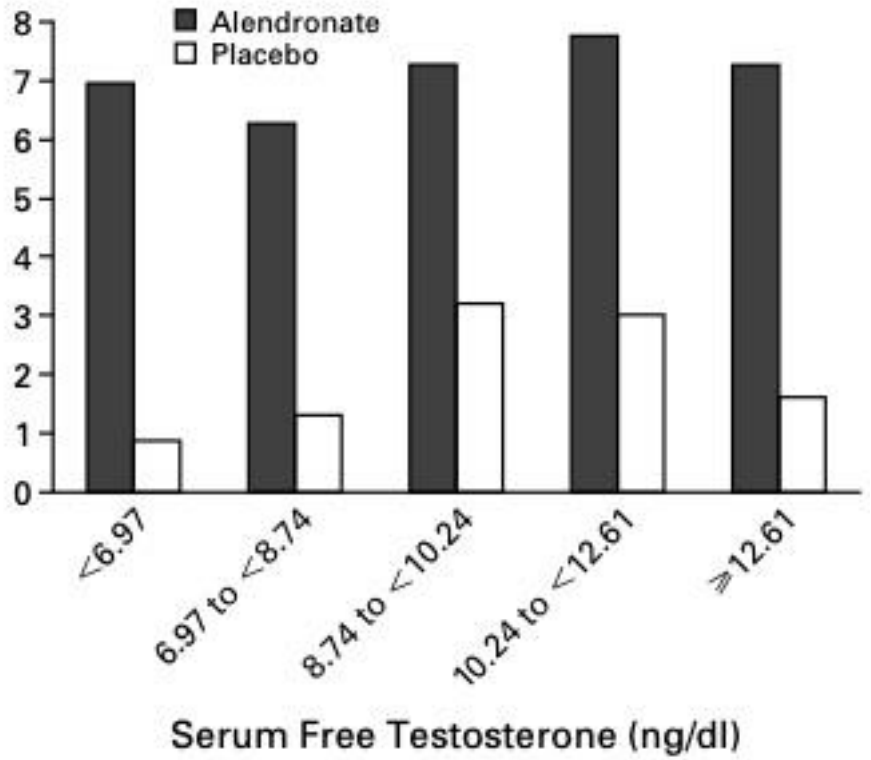
(C)

Bisphosphonates and BMD in men

Beaudart et al ACER 2023

ALENDRONATE FOR THE TREATMENT OF OSTEOPOROSIS IN MEN

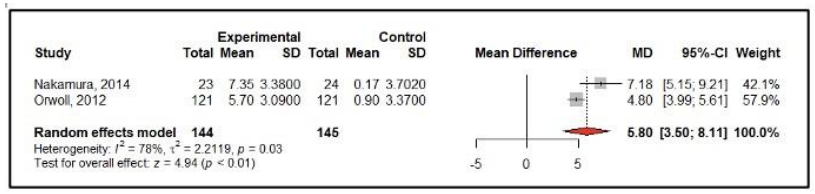




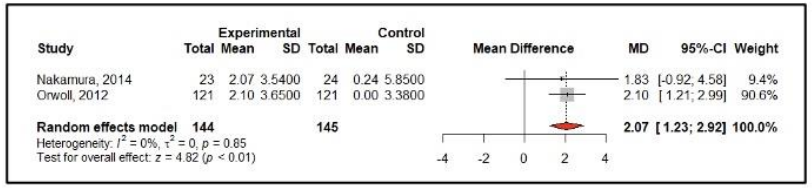
Orwoll et al NEJM 2000

Efficacy of osteoporosis pharmacological treatments in men: a systematic review and meta-analysis

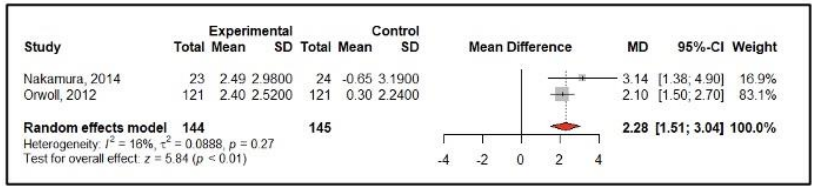
Denosumab



(A)

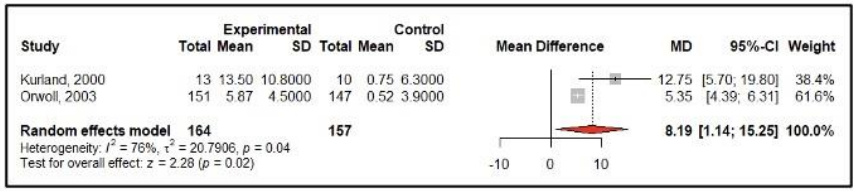


(B)

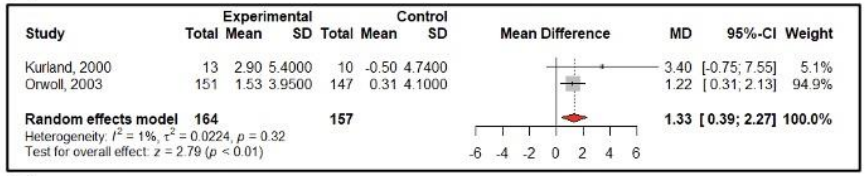


(C)

Teriparatide

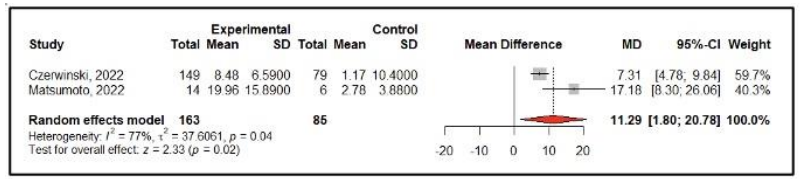


(A)

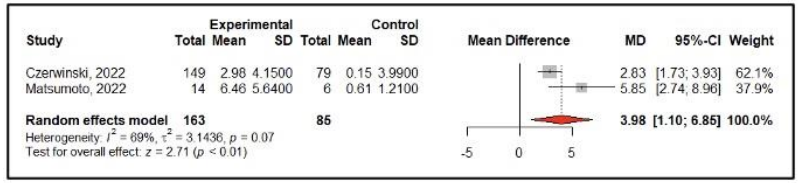


(B)

Abaloparatide



(A)



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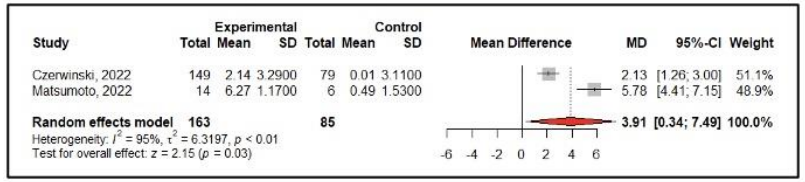
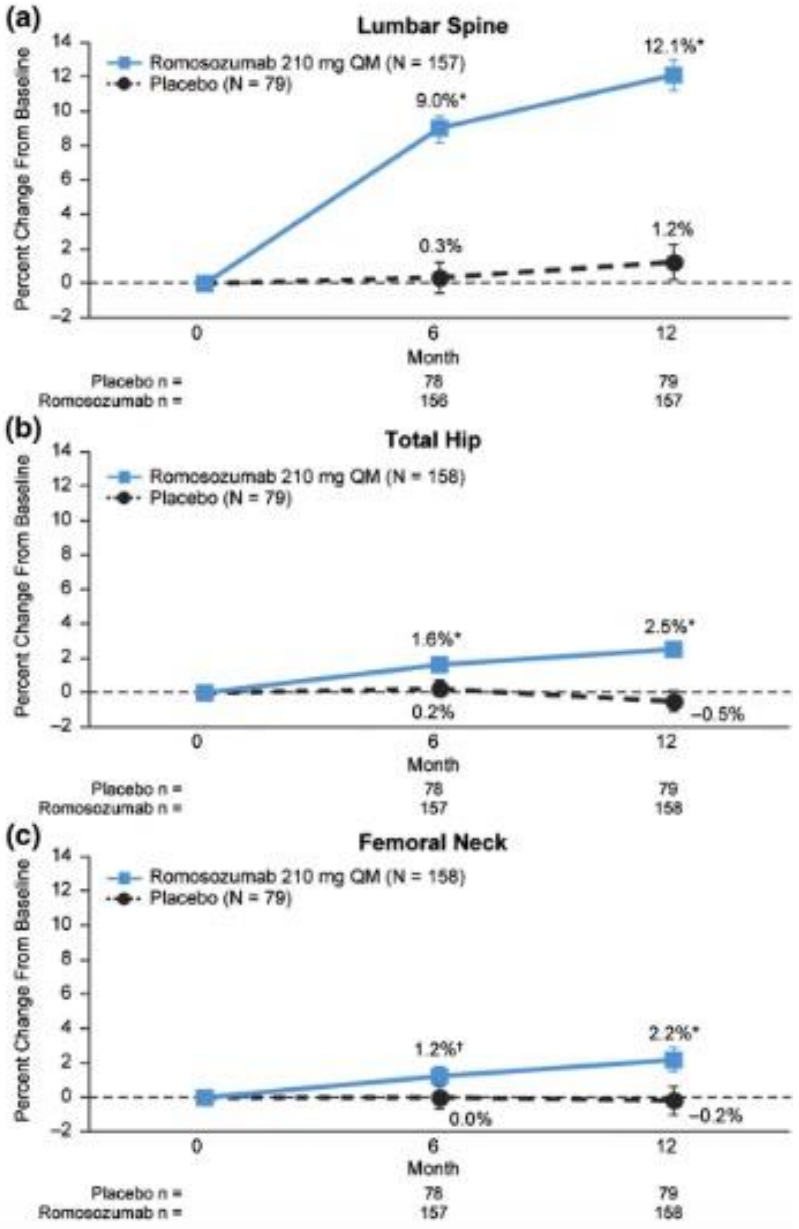


(C)

BMD
(A) Lumbar spine
(B) Femoral neck
(C) Total hip

Beaudart et al ACER 2023

A Phase III Randomized Placebo-Controlled Trial to Evaluate Efficacy and Safety of Romosozumab in Men With Osteoporosis



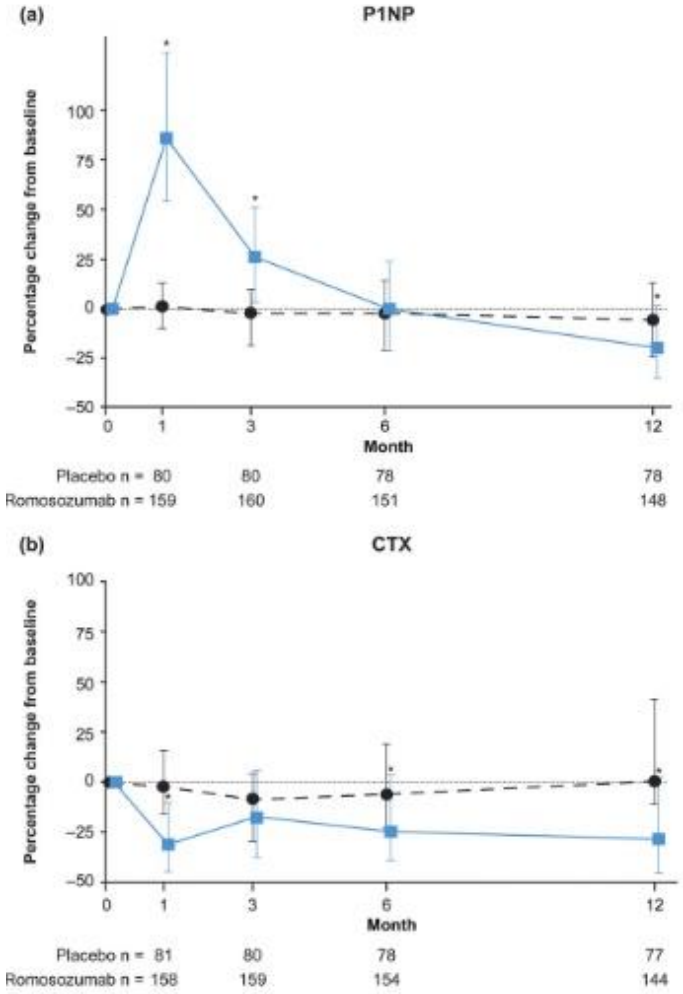


Table 2. Summary of Subject Incidence of Treatment-Emergent Adverse Events Through Month 12

Adverse event, n (%)	Romosozumab 210 mg QM (N = 163)	Placebo (N = 81)
Any adverse event	123 (75.5)	65 (80.2)
Serious adverse event	21 (12.9)	10 (12.3)
Adjudicated cardiovascular serious adverse event[a]	8[b] (4.9)	2 (2.5)
Cardiac ischemic event	3 (1.8)	0 (0.0)
Cerebrovascular event	3 (1.8)	1 (1.2)
Death[c,d]	2[e] (1.2)	1 (1.2)
Heart failure	1 (0.6)	0 (0.0)
Death	1 (0.6)	1 (1.2)
Leading to discontinuation of investigational product	5 (3.1)	1 (1.2)

Lewiecki et al JCEM 2018

Efficacy of osteoporosis pharmacological treatments in men: a systematic review and meta-analysis

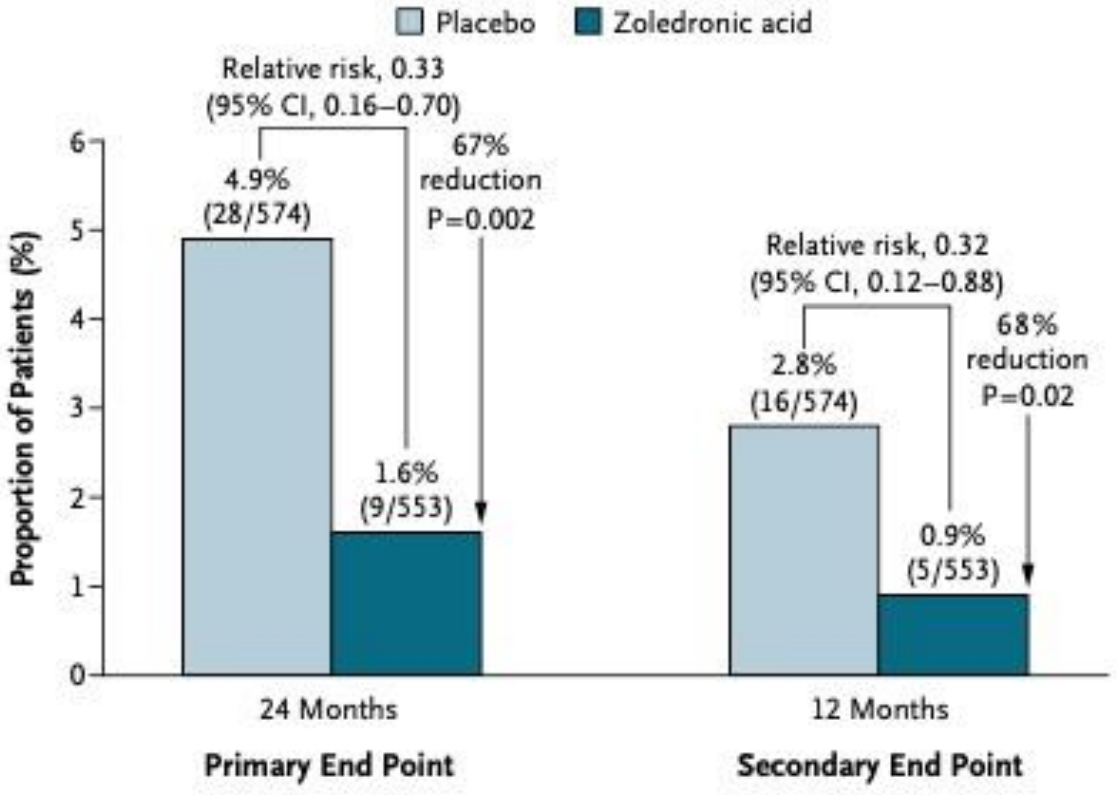
Summary of the incidence of fractures

First Author	Participants (n) and Treatment/comparator	Study duration	Primary/secondary endpoint	Type of fractures reported	Number of fractures treatment group	Number of fracture control group
Boonen, 2009[19]	Risedronate (n=191)/ Placebo (n=93)	24 months	Secondary endpoint	VF+ all clinical fractures	All clinical fractures: 7 VF: 2	NVF: 6 VF: 0
Boonen, 2011[6]	Zoledronic acid (n=248) / Placebo (n=260)	24 months	Primary endpoint	All fractures	Incident fractures: 16	Incident fractures: 20
Boonen, 2012[20]	Zoledronic acid (n=588) / Placebo (n=611)	24 months	Primary endpoint	VF	VF: 9	VF: 28
Czerwinski, 2022[18]	Abaloparatide (n=174)/ Placebo (n=64)	12 months	Secondary endpoint	VF+NVF	NVF: 1 VF: 0	NVF: 2 VF: 1
Kurland, 2000[21]	Teriparatide (n=13) / Control (n=10)	18 months*	Secondary endpoint	VF	VF: 1	VF: 2
Lewiecki, 2018[5]	Romosozumab (n=163)/ Placebo (n=82)	12 months	Safety	All fractures	Incident fractures: 3	Incident fractures: 2
Miller, 2004[8]	Alendronate (n=109)/ Placebo (n=58)	12 months	Safety	VF+NVF	NVF: 6 Morphometric VF: 6 Clinical VF: 5	NVF: 1 Morphometric VF: 3 Clinical VF: 3
Nakamura, 2014[7]	Denosumab (n=23)/ Placebo (n=24)	24 months	Primary endpoint	VF	VF: 0	VF: 2
Orwoll, 2000[10]	Alendronate (n=146)/ Placebo (n=95)	24 months	Secondary endpoint	VF+NVF	NVF: 6 VF: 1	NVF: 5 VF: 7
Orwoll, 2003[13]	Teriparatide (n=151) / Placebo (n=147)	12 months	Safety	NVF	NVF: 2	NVF: 3
Orwoll, 2010[11]	Zoledronic acid (n=154) / Alendronate (n=148)	24 months	Secondary endpoint	VF	VF: 4	VF: 6
Orwoll, 2010[9]	Ibandronate (n=85) / Placebo (n=47)	12 months	Safety	VF + Clinical fractures	VF: 1 Clinical fracture: 3	VF: 2 Clinical fracture: 0
Orwoll, 2012[14]	Denosumab (n=111)/ Placebo (n=117)	12 months	Secondary endpoint	VF+NVF	NVF: 1 VF: 0	NVF: 1 VF: 1
Ringe, 2009[15]	Risedronate (n=158) / Control (n=158)	24 months	Primary endpoint	VF+NVF	NVF: 18 VF: 14	NVF: 33 VF: 35
Shimon, 2005[16]	Alendronate (n=11) / Placebo (n=13)	12 months	Safety	VF+NVF	NVF:0 VF:0	NVF:1 VF:1
Walker, 2013[17]	Risedronate (n=10) / Teriparatide (n=9) / Combined (n=10)	18 months	VF: Secondary endpoint Clinical F: safety	VF + Clinical fractures	VF: 1 Clinical fracture (12 months): 0	Teriparatide: VF: 0; Clinical fracture (12 months) : 0 Combined: VF:1; Clinical fractures (12 months): 1

*fractures assessed at 12 months
VF= Vertebral fracture, NVF= Non vertebral fractures, F= fractures

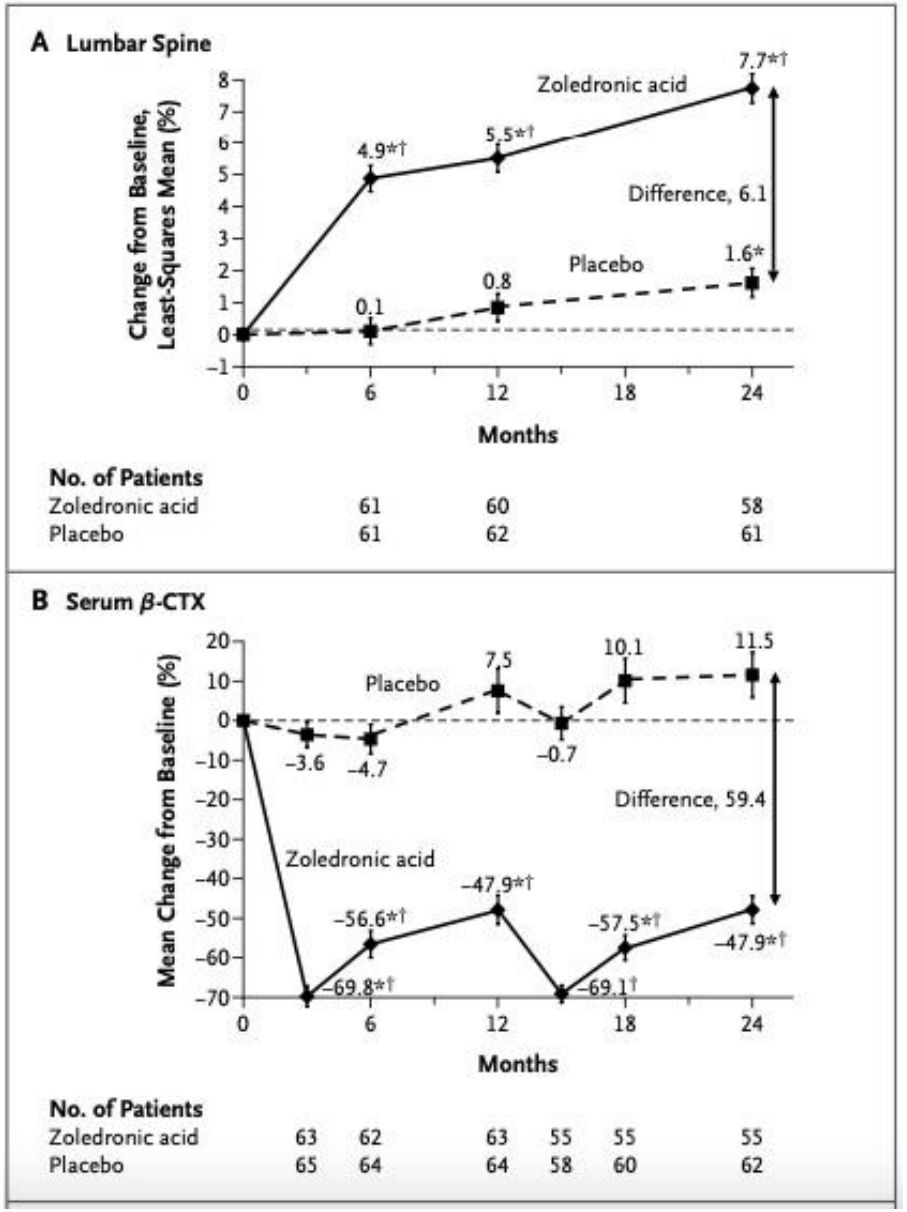
Beaudart et al ACER 2023

Fracture Risk and Zoledronic Acid Therapy in Men with Osteoporosis



(B) Incidence of clinical fractures (ITT population)

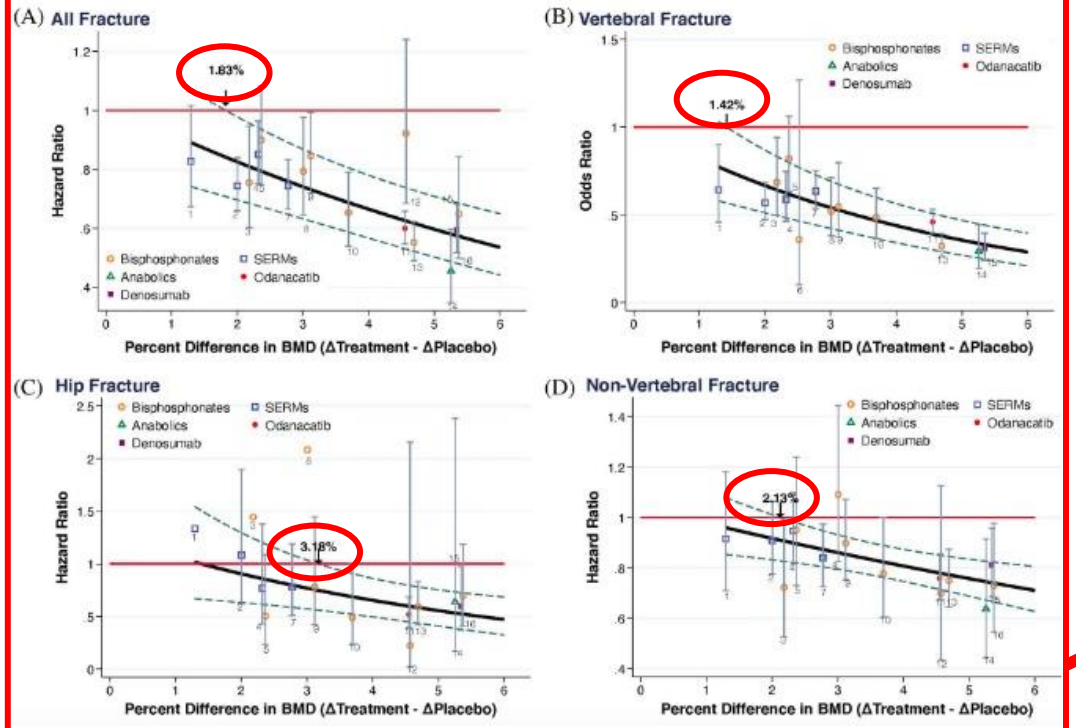
	Zoledronic acid, N=588	Placebo, N=611	Hazard ratio (95% CI)
Clinical fractures, n (%)	6 (1.0)	11 (1.8)	0.6 (0.2, 1.5)
Clinical vertebral fractures, n (%)	1 (0.2)	3 (0.5)	0.3 (0.0, 3.3)
Clinical nonvertebral fractures, n (%)	5 (0.9)	8 (1.3)	0.6 (0.2, 2.0)



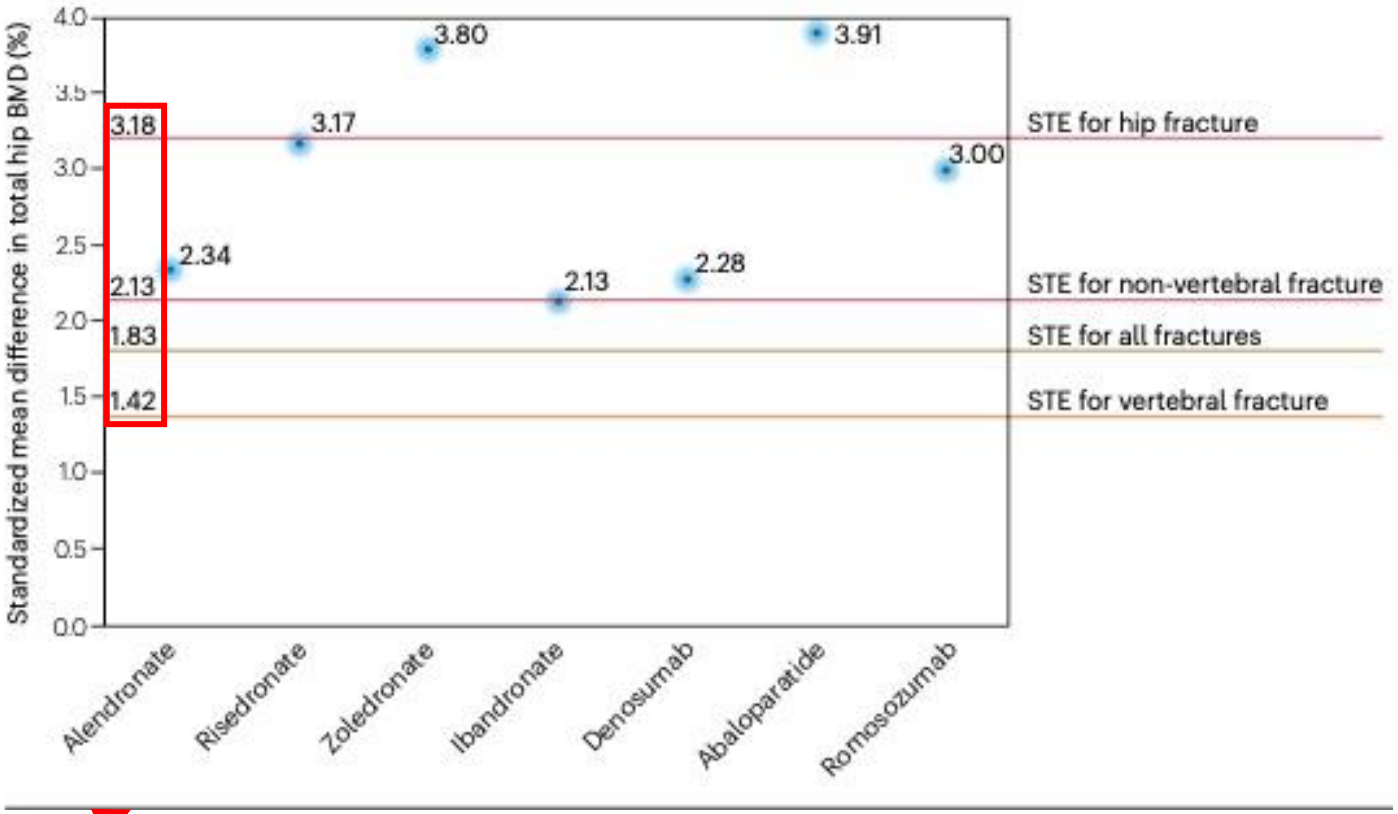
Boonen et al NEJM 2012

Evidence-Based Guideline for the management of osteoporosis in men

Validation of the Surrogate Threshold Effect for Change in Bone Mineral Density as a Surrogate Endpoint for Fracture Outcomes: The FNIH-ASBMR SABRE Project -> Total Hip



Eastell et al JBMR 2022



STE: Surrogate Threshold Effect

Fuggle et al Nature Rev Rheumatol 2024

Evidence-Based Guideline for the management of osteoporosis in men

	Recommendation:
• Vitamin D and calcium repletion should be ensured in **all men ≥ 65 years**.	**Strong**
• Oral bisphosphonates (alendronate or risedronate) are **first-line** treatments for men at a high risk of fracture	**Strong**
• Denosumab or zoledronate are **second-line** treatments for men at a high risk of fracture.	**Strong**
• A **sequential therapy** starting with a bone-forming agent followed by an anti-resorptive agent should be considered for men at a very high risk of fracture.	**Strong**
• Bone-forming agents should be used in accordance with the recommendations of the regulatory authorities.	**Strong**
• Physical exercise and a balanced diet should be recommended to all men with osteoporosis.	**Strong**

Strong: ≥ 75% voters (n=28)

Fuggle et al Nature Rev Rheumatol 2024

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