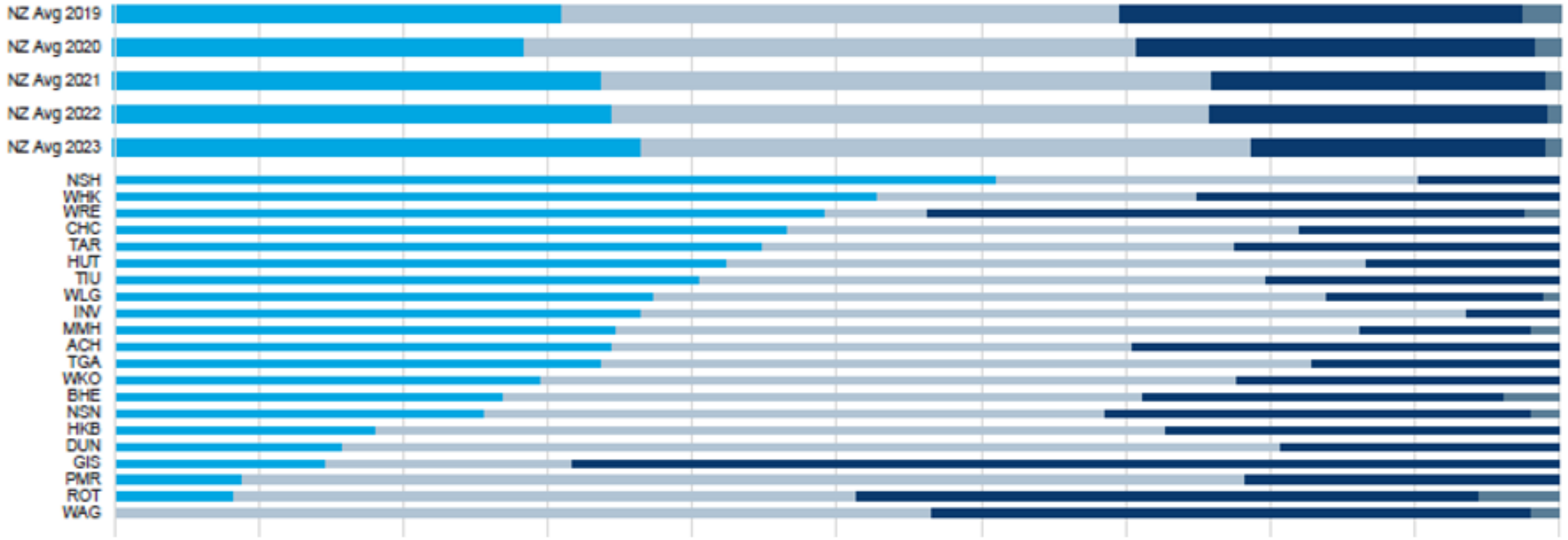
Hip fest 2024. The Bare bones

How are you doing?

Figure 116 – Bone protection medication on discharge

There continues to be an improvement in the proportion of people leaving hospital on a bisphosphonate, denosumab or teriparatide. Figure 116 shows that in New Zealand, 38% of hip fracture patients left hospital on bone protection medicine. In Australia, 32% of patients left hospital on a bisphosphonate, denosumab or teriparatide.



Proportion leaving hospital on bone protection

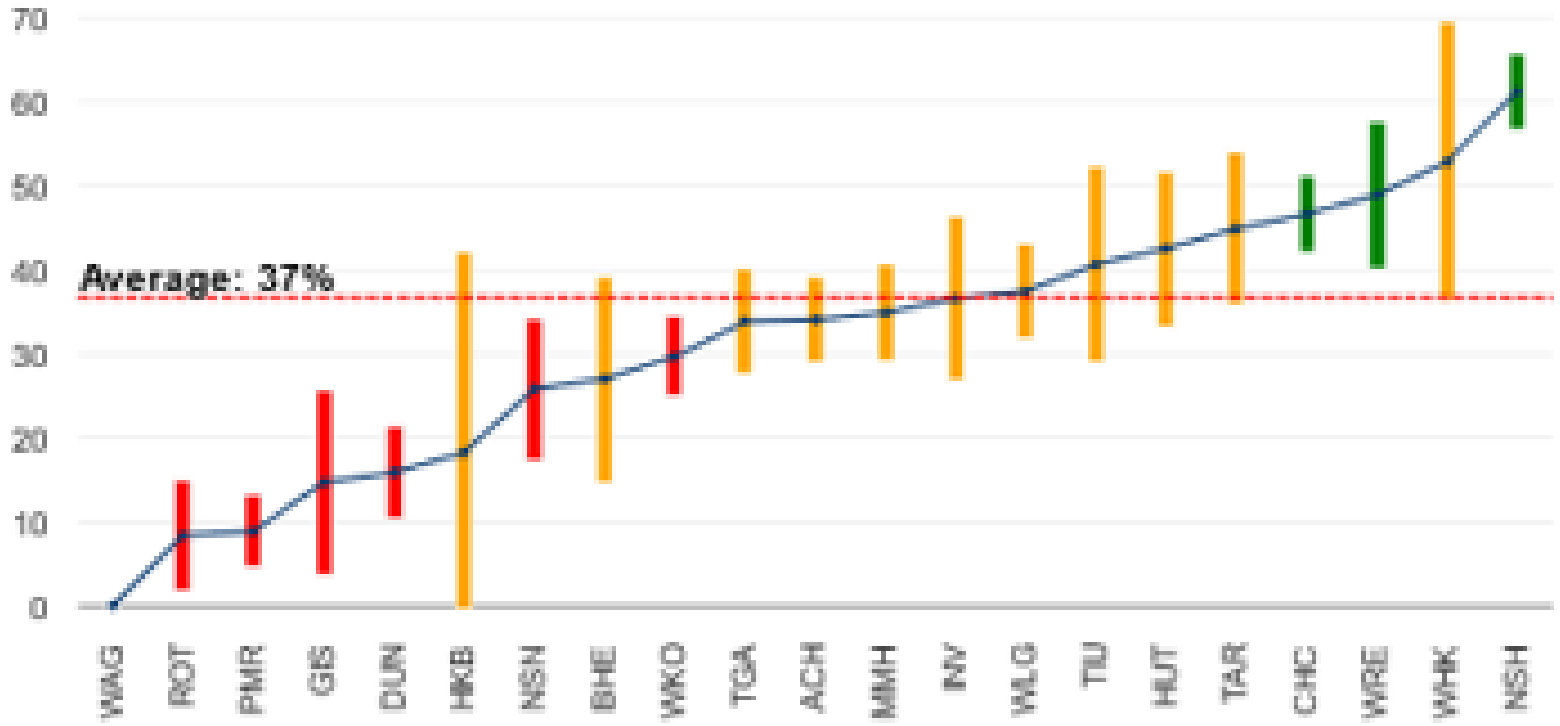
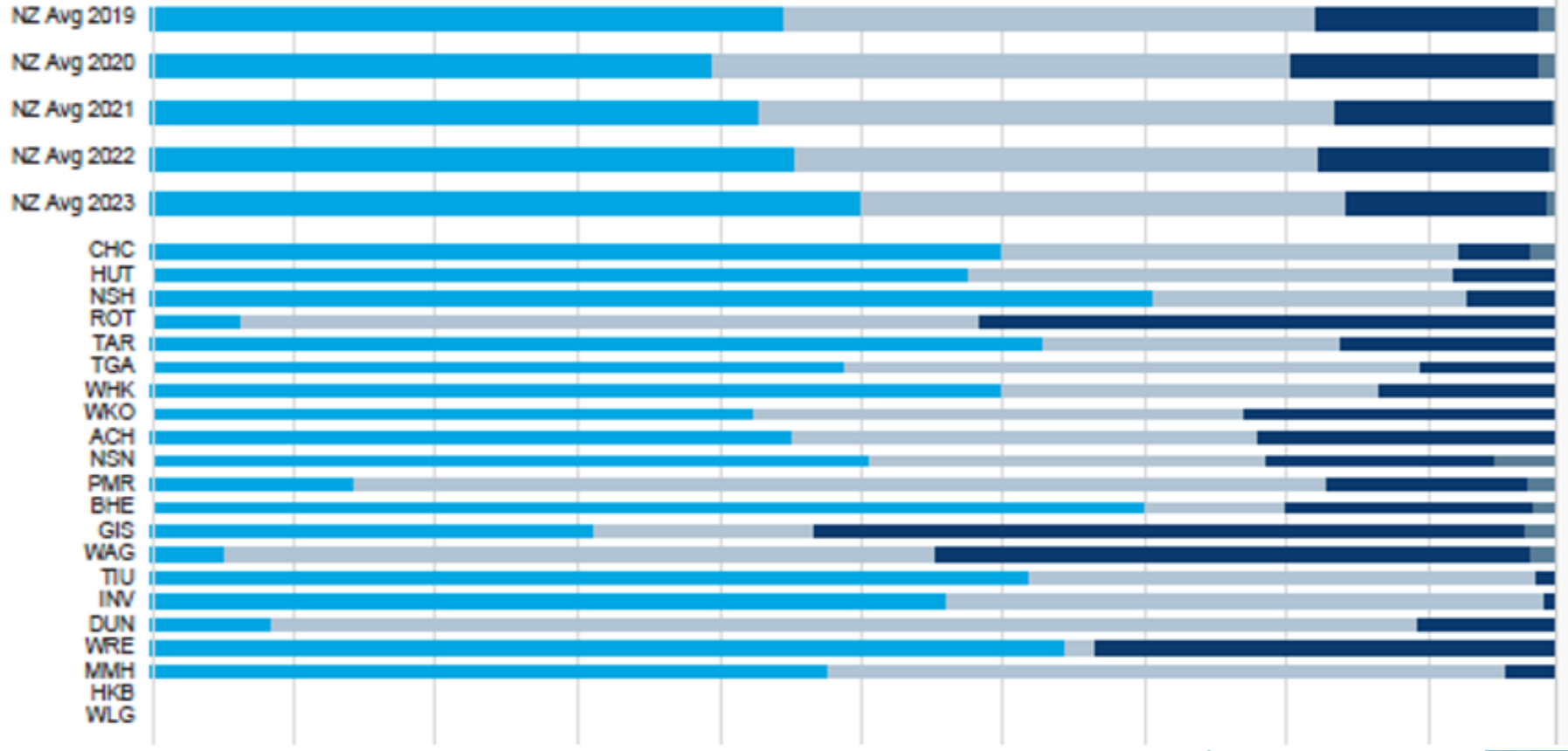


Figure 127 – Bone protection medication at 120 days



In NZ our system makes it simple

- Cant get a bone density scan
- Can only get bisphosphonates and zol is better than alendronate

- SO
- Put them all on zol

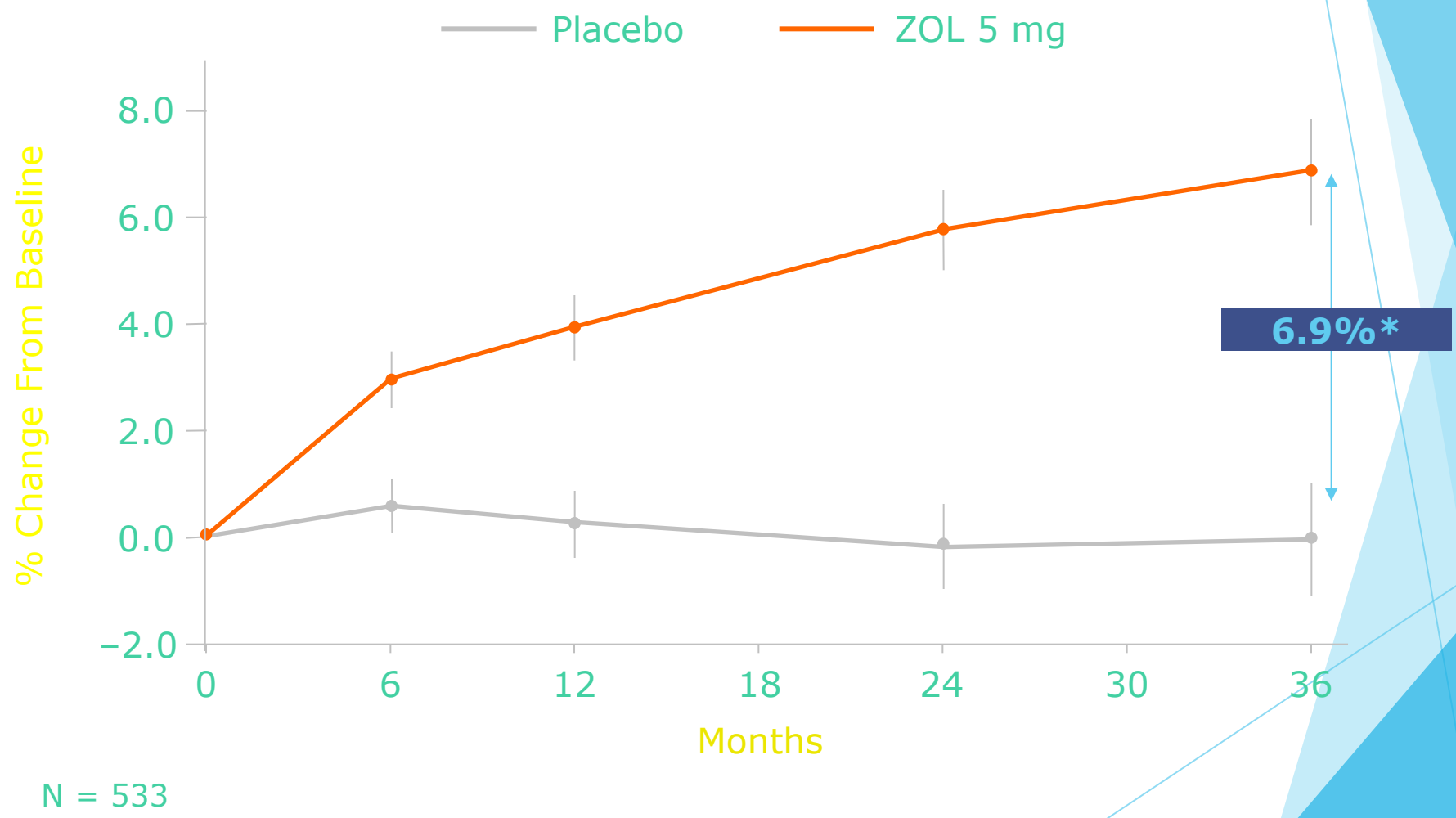
Oral alendronate/risedronate vs IV zoledronate

Compliance

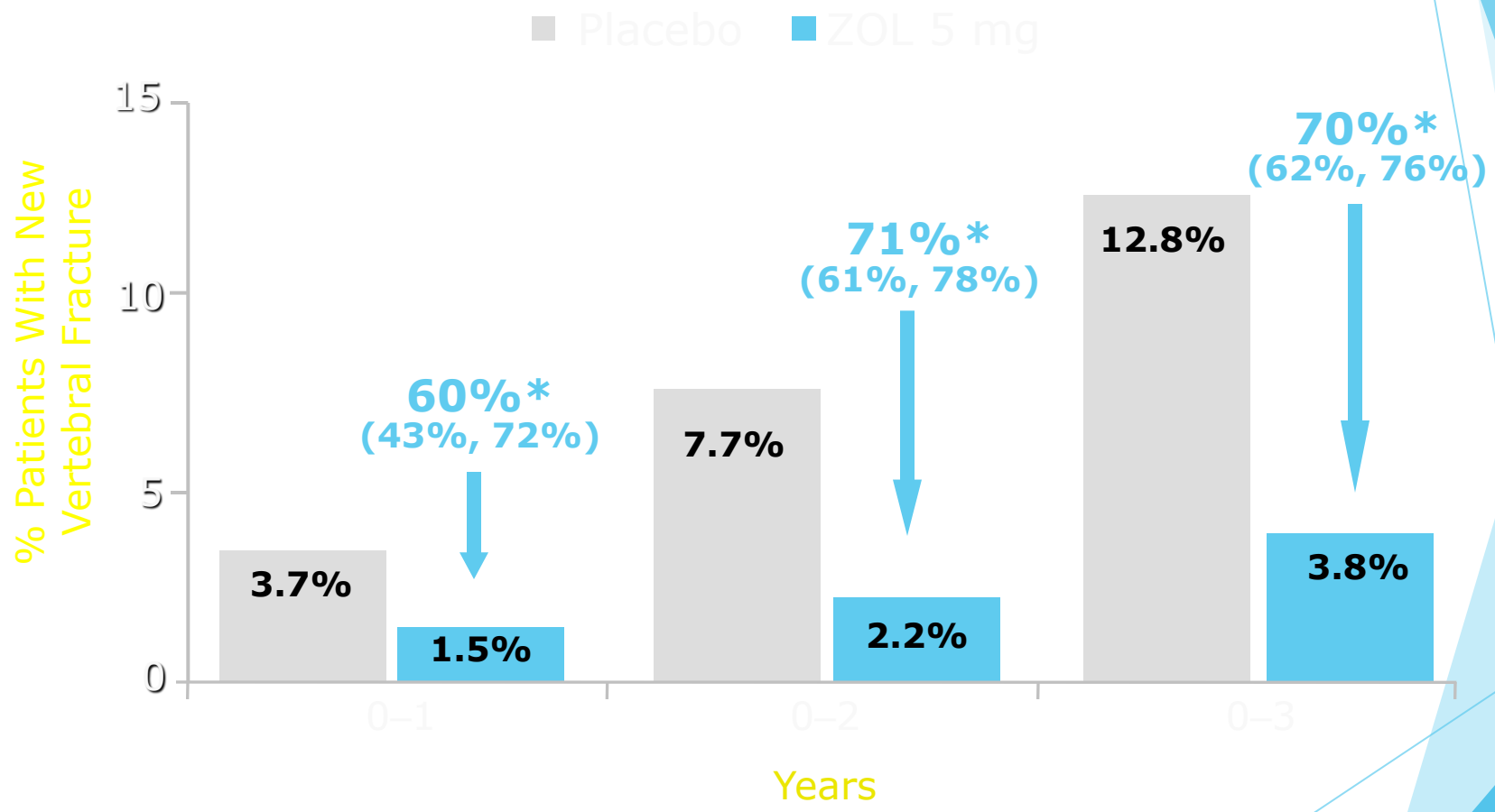
- **Take alendronate first thing in the morning, at least 30 minutes before you eat or drink anything or take any other medicine. take it on the same day each week and always first thing in the morning. Take with a full glass (6 to 8 ounces) of plain water. Remain upright after taking.**

- Perhaps 50% of patients persist with oral treatment
- Patients who do not adhere do not get fracture benefits
- Fasting (**only 0.65% absorbed**) GI side effects.
- Check P1NP on treatment

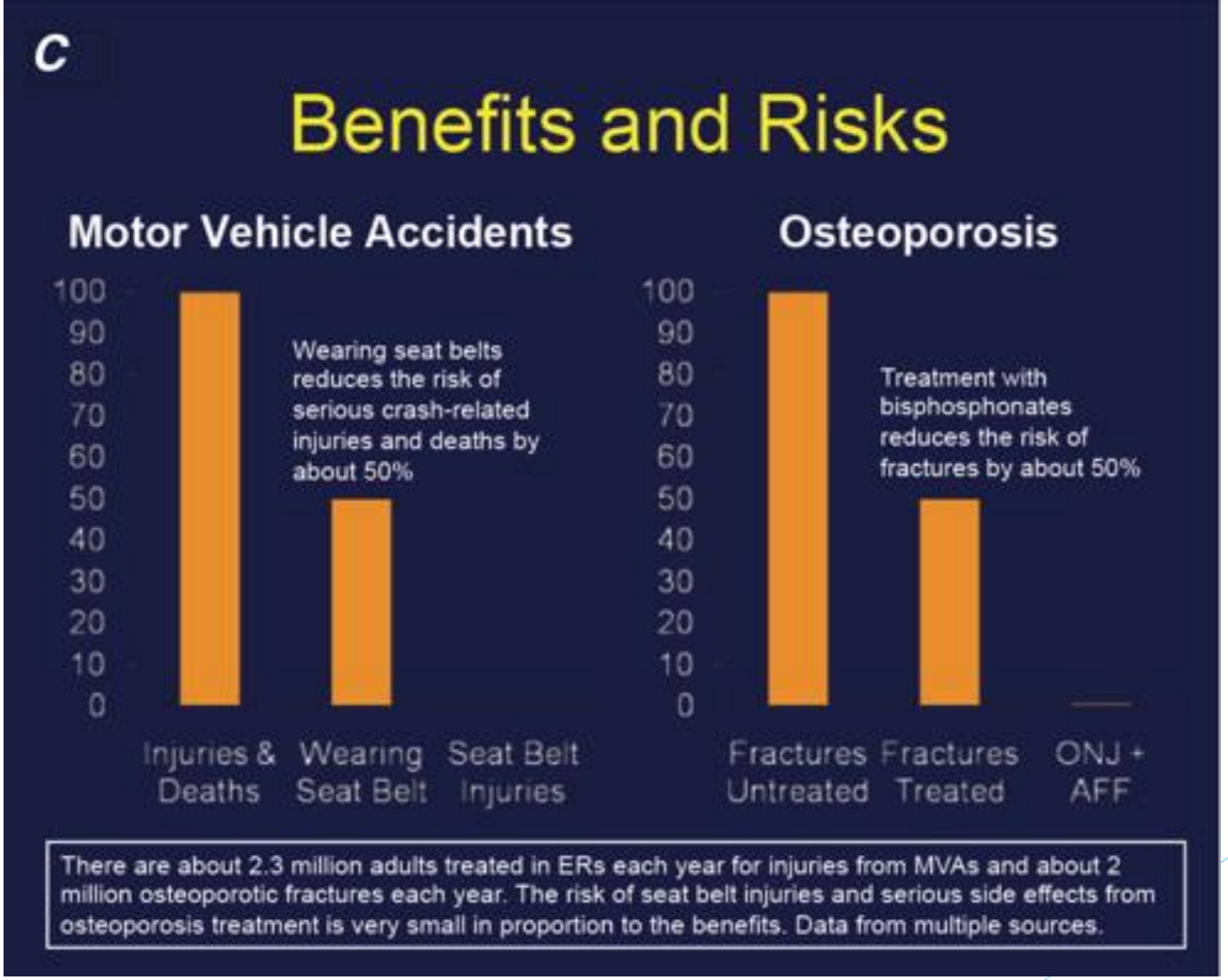
Mean Percentage Change in Lumbar Spine BMD Over Time



Morphometric Vertebral Fracture Results (Stratum I)



Relative risk reductions (95% confidence intervals) vs placebo
*$P < .0001$, based on logistic regression with treatment and baseline fracture status in the model using log-likelihood type approach


C
Benefits and Risks
Motor Vehicle Accidents
100
90
80
70
60
50
40
30
20
10
0
Wearing seat belts reduces the risk of serious crash-related injuries and deaths by about 50%
Injuries & Deaths
Wearing Seat Belt
Seat Belt Injuries
Osteoporosis
100
90
80
70
60
50
40
30
20
10
0
Treatment with bisphosphonates reduces the risk of fractures by about 50%
Fractures Untreated
Fractures Treated
ONJ + AFF
There are about 2.3 million adults treated in ERs each year for injuries from MVAs and about 2 million osteoporotic fractures each year. The risk of seat belt injuries and serious side effects from osteoporosis treatment is very small in proportion to the benefits. Data from multiple sources.

Zol 18 monthly for low bone mass in women >65 years

	placebo	zol
Serious adverse events	1017	820
death	41	27
ONJ	0	0
MI	43	25

Zoledronate after hip fracture

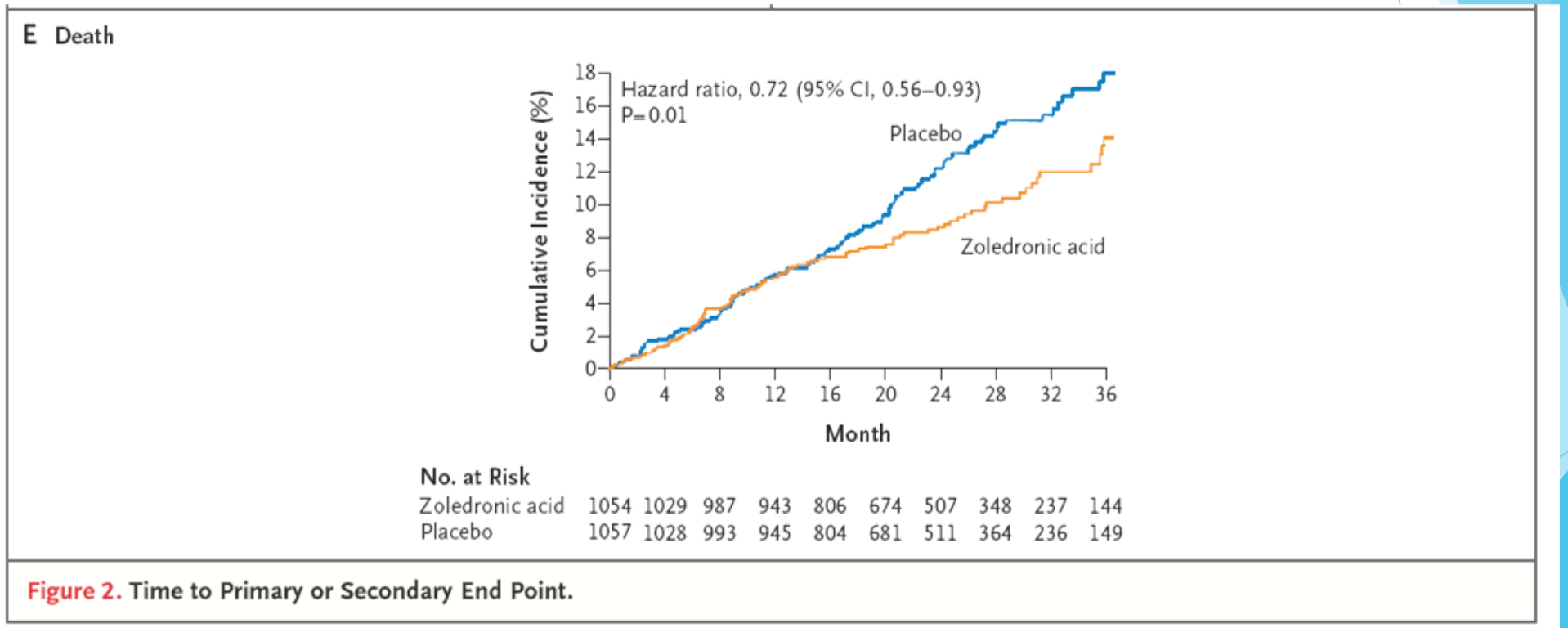
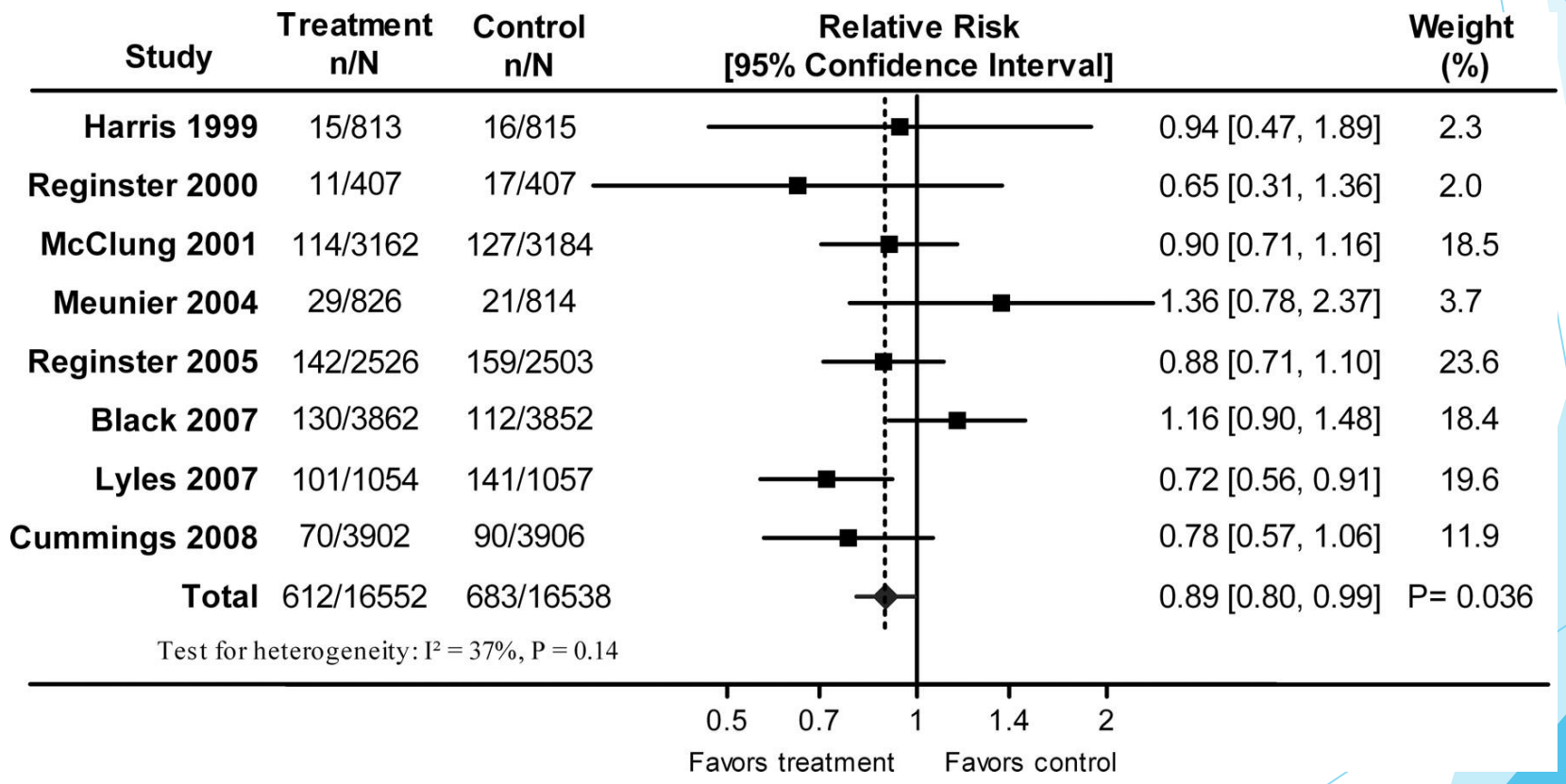


Figure 2. Time to Primary or Secondary End Point.

The effect of treatment of osteoporosis on mortality in eight studies included in the primary analysis.



Bolland M J et al. JCEM 2010;95:1174-1181

THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

The bad….

- 15% acute phase reaction
- Dexamethasone 4mg on day of infusion and next 2 days blocks APR
- Be aware of renal issues GFR >25(35)
- Make sure they are replete with D/calcium
- Make sure they are not unwell, not too much on
- Provide the data sheet, lots of rare stuff
- Panadol after, keep up fluids

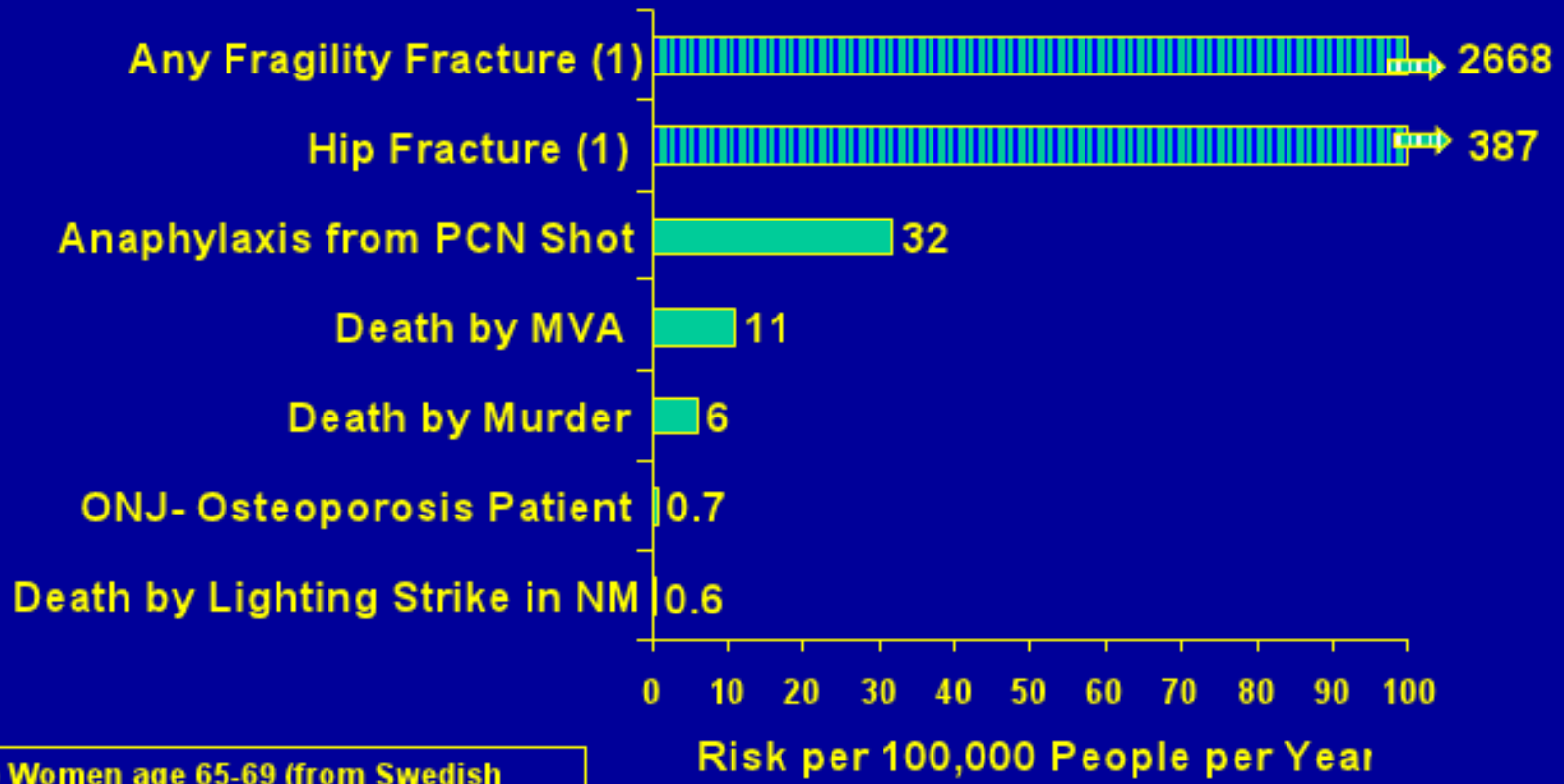
Creatinine clearance less than 35

- Sl controversial if you should check it
- Explain to patient that this is use off label
- Maybe use oral
- Optimise renal state hydration withhold meds
- Check cr after
- Maybe reduced dose
- Maybe extra saline load
- Actual risk is very low especially if they’ve had it before and no ADR

OSTEONECROSIS

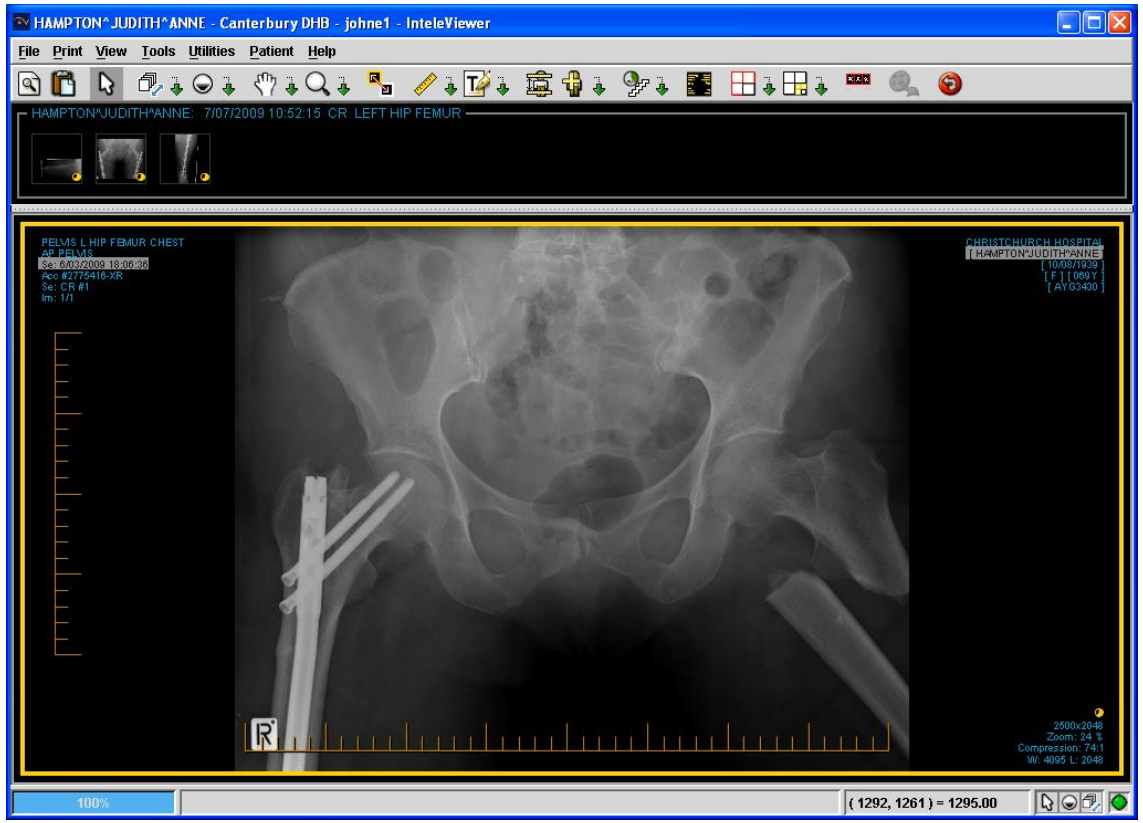
- RARE IN OSTEOPOROSIS PATIENTS
- 1 in 10,000 to 100,000
- Poor oral hygiene, smoking, alcohol, steroids, ill health
- Usually follows dental extraction/procedure
- (Zol trial 2 cases, 1each treatment and control)
- COMMON IN CANCER PATIENTS ON HIGH DOSE BISPHOSPHONATES

Comparative Risks



(1) Women age 65-69 (from Swedish National Bureau of Statistics and database of Olmsted County, MN, USA.)

Atypical femoral shaft fractures



Atypical fractures, require all
look for bisphosphonates

- Major features
- Located anywhere along the femur from just distal to the lesser trochanter to just proximal to the supracondylar flare
- Associated with no trauma or minimal trauma, as in a fall from a standing height or less
- Transverse or short oblique configuration
- Noncomminuted
- Complete fractures extend through both cortices and may be associated with a medial spike; incomplete fractures involve only the lateral cortex

Atypical fractures, requires none

- Minor features
- Localized periosteal reaction of the lateral cortex
- Generalized increase in cortical thickness of the diaphysis
- Prodromal symptoms such as dull or aching pain in the groin or thigh
- Bilateral fractures and symptoms
- Delayed healing
- Comorbid conditions (eg, vitamin D deficiency, rheumatoid arthritis, hypophosphatasia)
- **Use of pharmaceutical agents (eg, BPs**, glucocorticoids, proton pump inhibitors)

Sub-Trochanteric Fractures in FIT, FLEX & Horizon

14195 women → 284 femoral fractures → 12 fractures in 10 patients subtrochanteric

RH (95% CI): FIT 1.0 (0.06-17)

FLEX 1.3 (0.1-15)

Horizon 1.5 (0.3-9.0)

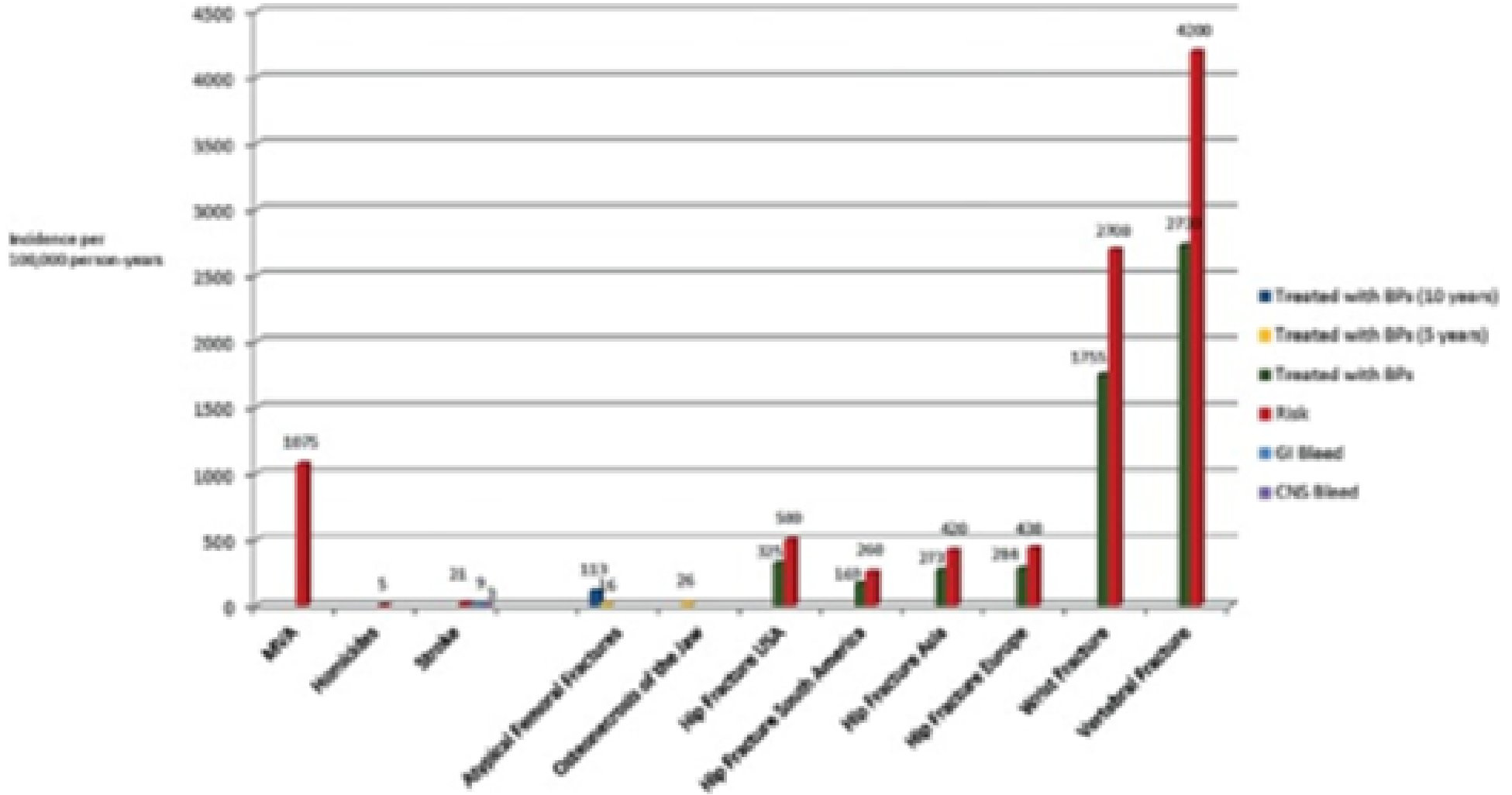
Treat 1000 patients for 3 years:

Prevent: 71 vertebral, 11 hip, 16 other #s

Cause: 0.3 subtrochanteric #s (if RR 1.5)

Black, NEJM 2010

Managing Osteoporosis in Patients on Long-Term Bisphosphonate Treatment: Report of a Task Force of the American Society for Bone and Mineral Research



Maintainance approach with Fosamax or Aclasta

- Most benefit is in the first 5 yrs/3 yrs
- Long term use is probably safe, but risk of atypicals increases with time likely 5+years
- Risk of atypical fractures reset by 1-2 years off treatment?
- More concern in the young

- **Consider 2- years off (seems to reset atypical risk) or Zol 2-3 yearly:**
- Those who normalise BMD, are not having fractures(particularly vertebral), younger.
- **follow up 2-3yearly**.

Who shouldn’t you treat

- Died in hospital
- 15% discharged to hospital care
- 15% discharged resthome
- 70% home
- Alendronate withheld while in collar due to swallowing difficulties
- Not able to contact EPOA to administer
- Single fracture and good bone density, not fragility fracture
- 10 of the 11 patients not administered additional treatment due to frailty/comorbidity have subsequently died.

Denosumab

- Given 6monthly injection
- Adverse Reponses similar to placebo except slight increase in eczema, low calcium(especially if renal impairment and high PTH), cellulitis, ONJ, atypical fractures
- $800 NZD per year
- Pharmac requires new fracture after 1 year Rx, cr cl <35
- Cant be stopped, must transition
- I think you should do a phone consult at 5.5 months if you put someone on this

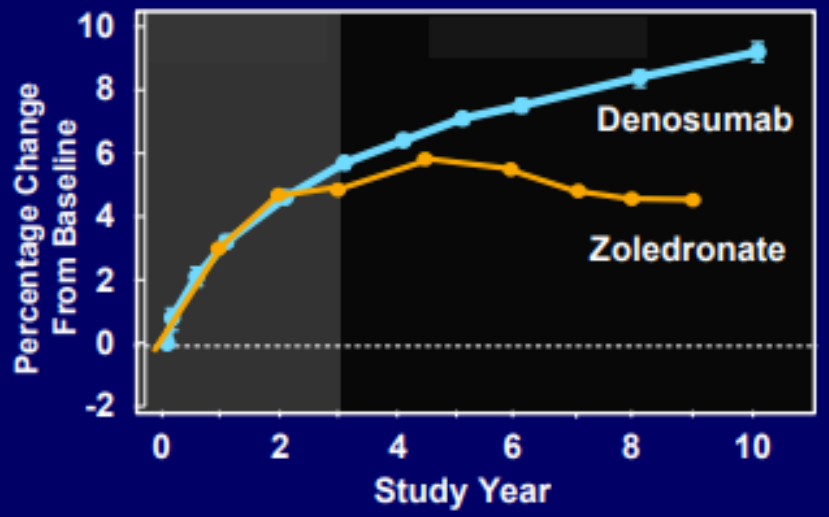
Adverse events in Freedom

Table 3. Adverse Events.*

Event	Denosumab (N = 3886)	Placebo (N = 3876)	P Value†
	no. (%)		
All	3605 (92.8)	3607 (93.1)	0.91
Serious	1004 (25.8)	972 (25.1)	0.61
Fatal	70 (1.8)	90 (2.3)	0.08
Leading to study discontinuation	93 (2.4)	81 (2.1)	0.39
Leading to discontinuation of a study drug	192 (4.9)	202 (5.2)	0.55

Switching Osteoporosis Therapies:
Bisphosphonate to Denosumab

- **BMD gain plateaus after 5 years of bisphosphonate therapy but not with denosumab**



Bone HG et al. *Lancet Diabetes Endocrinol* 2017 2017;5:513-23
Black DM et al. J Bone Miner Res 2015;30:934-44

Transition from bisphosphonate to denosumab

Patients who had previously been treated with bisphosphonates were randomly assigned to a bisphosphonate or denosumab.

Data are least-squares means and 95% confidence intervals. *$p < 0.0001$ denosumab vs bisphosphonate

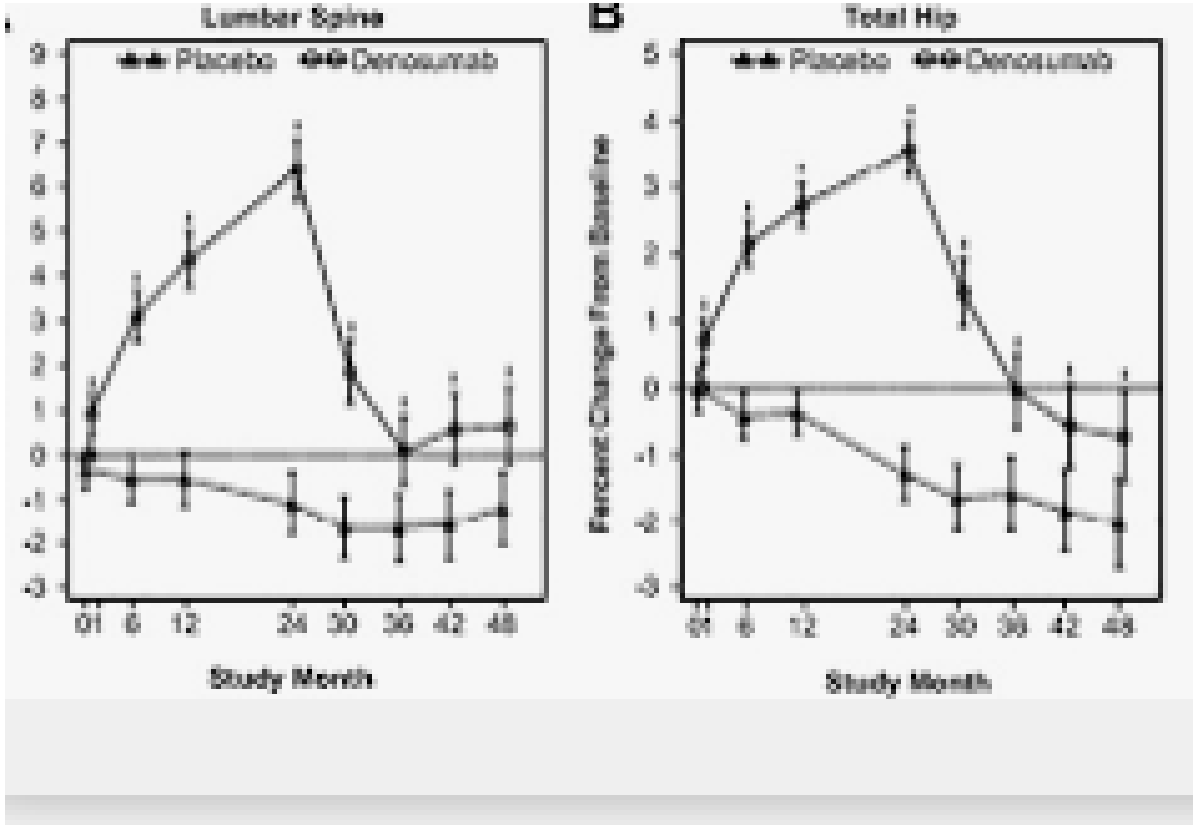
1. Roux C et al. Bone. 2014;58:48-54. 2. Recknor C et al. Obstet Gynec 2013;121:1291-9.
2. 3. Kendler DL et al. *J Bone Miner Res*. 2010;25:72-81. 4.Miller PD et al. *J Clin Endo Metab*. 2016;101:3163-70.

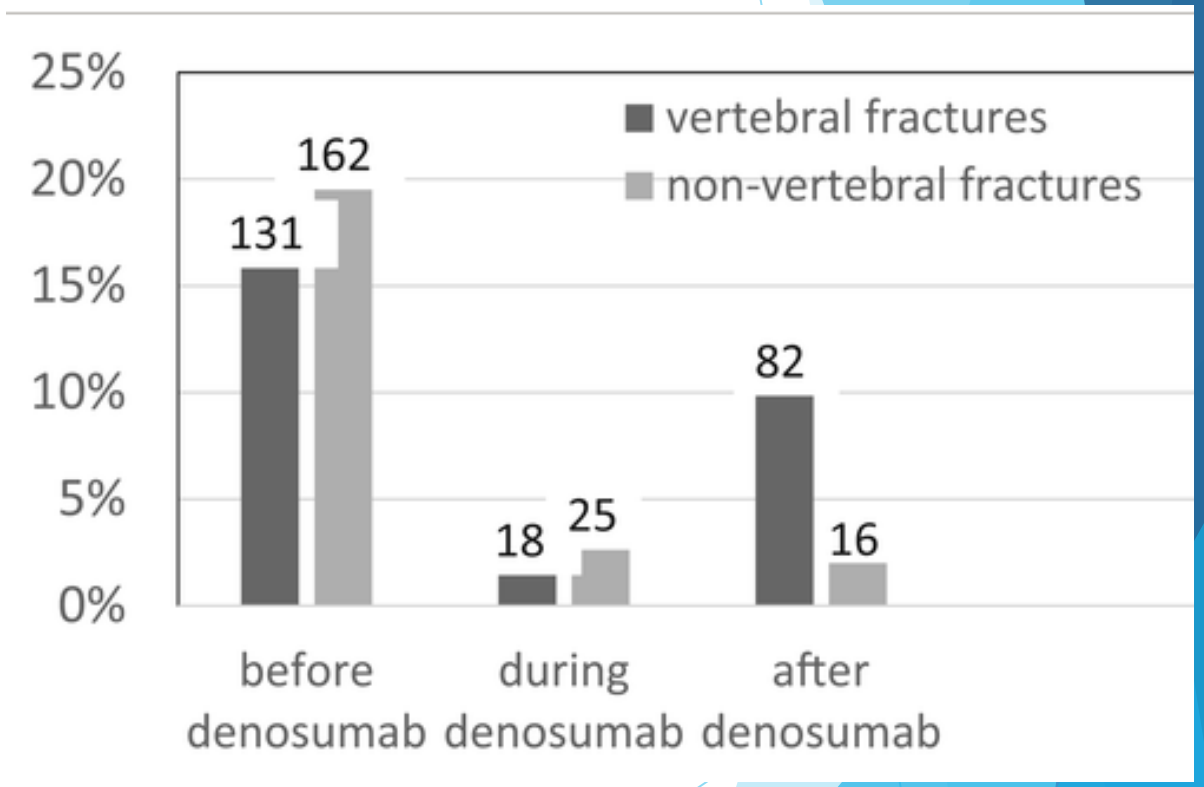
Switching Osteoporosis Therapies:

After 5 Years of Bisphosphonate Therapy

- For patients remaining at high risk of fracture after 5 years of bisphosphonate therapy, there is no justification for continuing the bisphosphonate.
- Switching to either denosumab or an anabolic agent is recommended, the choice being driven by the patients current risk of fracture.
- It appears that the BMD response when switching to romosozumab is greater than occurs with a switch to teriparatide
- However, we have no data about fracture risk with any of these transitions

Stopping denosumab





Highlights

Recent PMO Guidelines Have Evolved, Share Common Themes and Are More Actionable

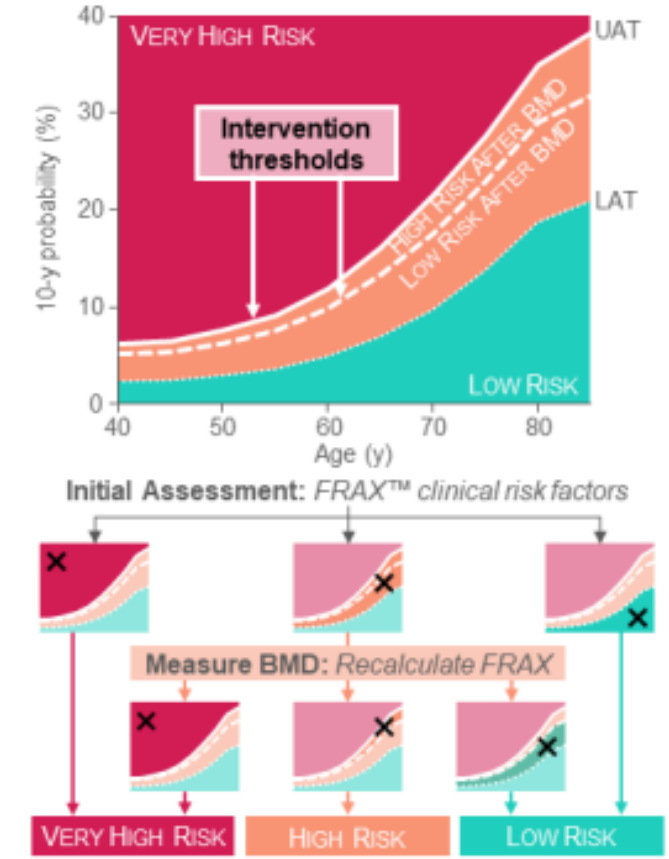
Risk of subsequent fracture	… is **highest** immediately after the index fracture[1-6]
Fracture risk assessment	… is **simplified** and made clearer, helping sort patients into distinct categories, including **very high, high & low risk**[1-5,7]
Early intervention	… is **warranted** in patients at highest risk, using agents with a **rapid effect** on reducing fracture risk[1-5,7]
Individualized treatment strategies	… are recommended **based on risk category**, so treatment can be matched to the patient's need[1-7]
Long-term treatment strategies	… should be considered, including **sequencing**, at time of initial therapy selection[1-5,7]

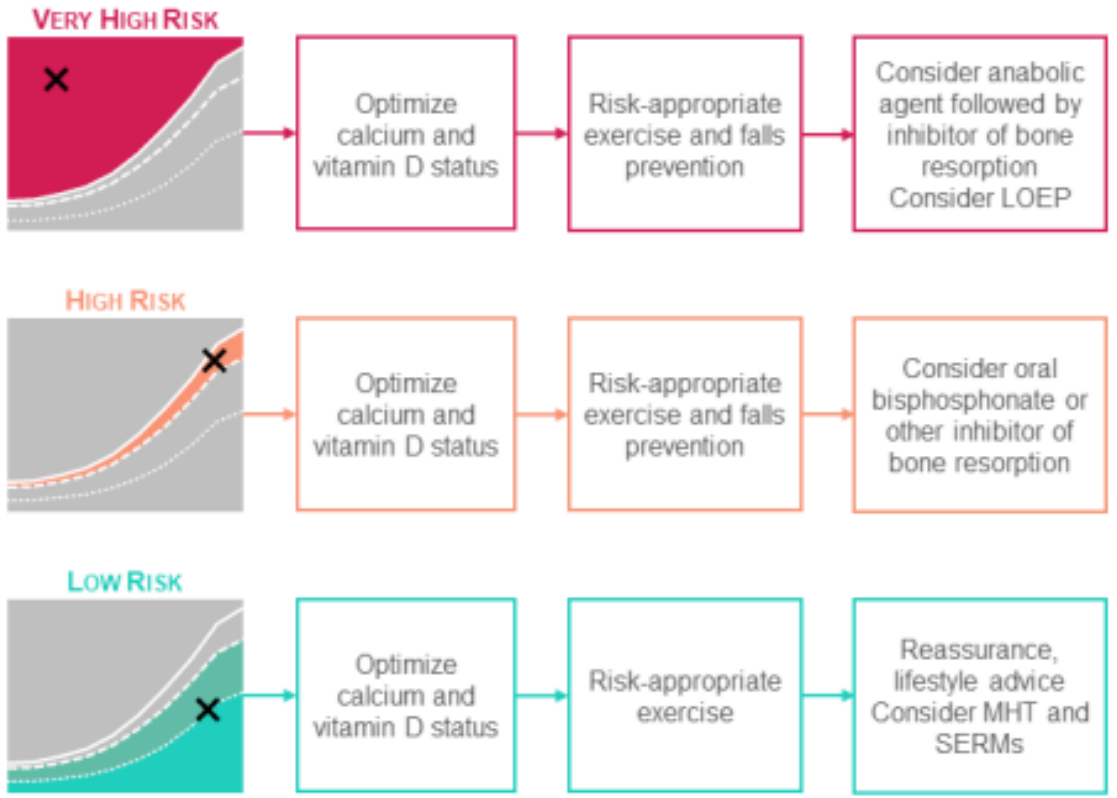
PMO = postmenopausal osteoporosis.

1. Shoback D, et al. *J Clin Endocrinol Metab*. 2020;105(3):1-8. 2. Kanis JA, et al. *Osteoporos Int*. 2020;31:1-12. 3. LeBoff MS, et al. *Osteoporos Int*. 2022;33(10):2049-2102. 4. Gregson CL, et al. *Arch Osteoporos*. 2022;17(1):58. 5. North American Menopause Society. *Menopause*. 2021;28(9):973-997. 6. Chandran, et al. *Osteoporos Int*. 2021;32(7):1249-1275. 7. Camacho PM, et al. *Endocr Pract*. 2020;26 (Suppl 1):1-46.

The greatest fracture risk is after a f

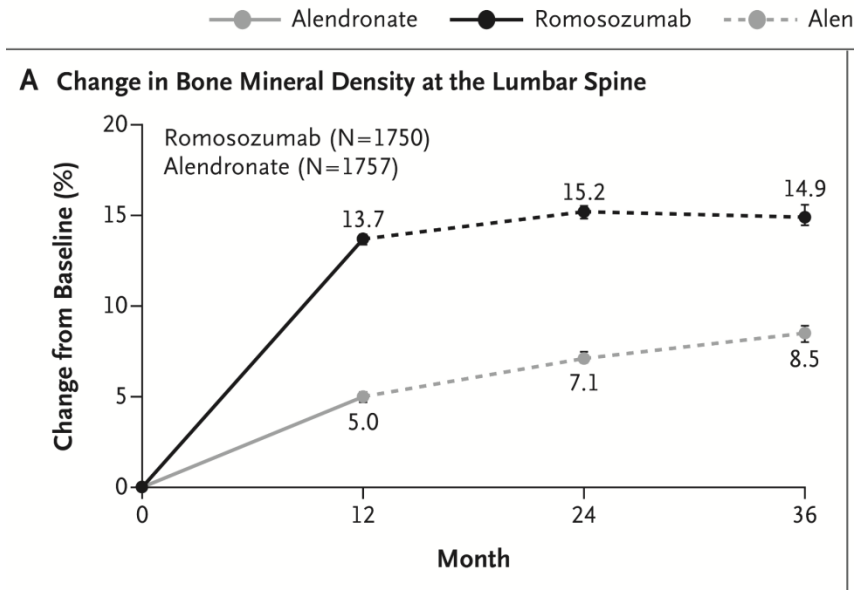
IOF-ESCEO (Global/Europe, updated 2019) Algorithm for Management of PMO

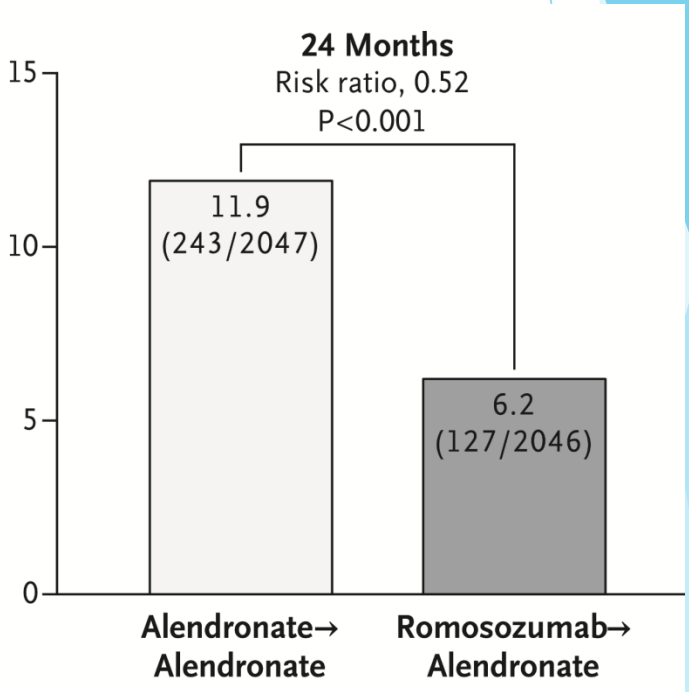




FRAX is a trademark owned by the International Osteoporosis Foundation.
ESCEO = European Society for Clinical and Economic Aspects of Osteoporosis; FRAX = Fracture Risk Assessment Tool; IOF = International Osteoporosis Foundation; LAT = lower assessment threshold; LOEP = local osteo-enhancement procedure; MHT = menopausal hormone therapy; PMO = postmenopausal osteoporosis; SERM = selective estrogen receptor modulator; UAT = upper assessment threshold.
Adapted from Kanis JA, et al. *Osteoporos Int*. 2020;31:1-12.

Romosuozumab vs alendronate





- Hip fracture 38% decrease
- Non vertebral fracture 19% decrease

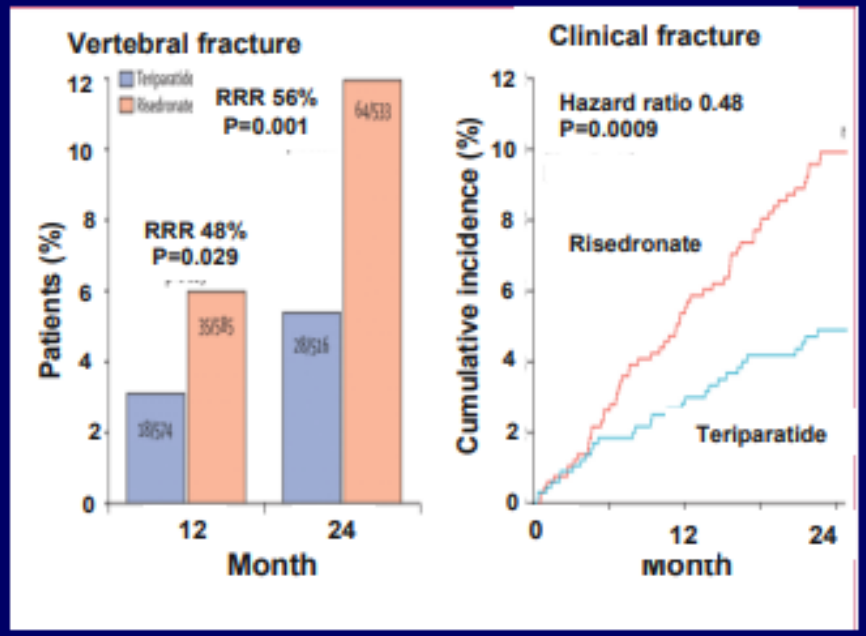
Saag NEJM Oct 2017

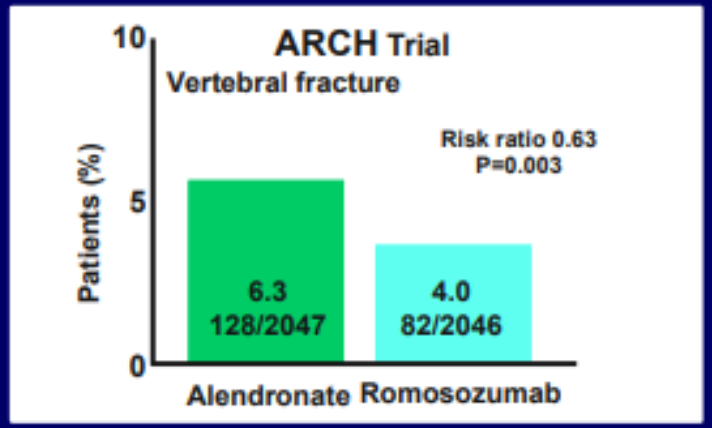
Osteoanabolic Therapy vs Bisphosphonates

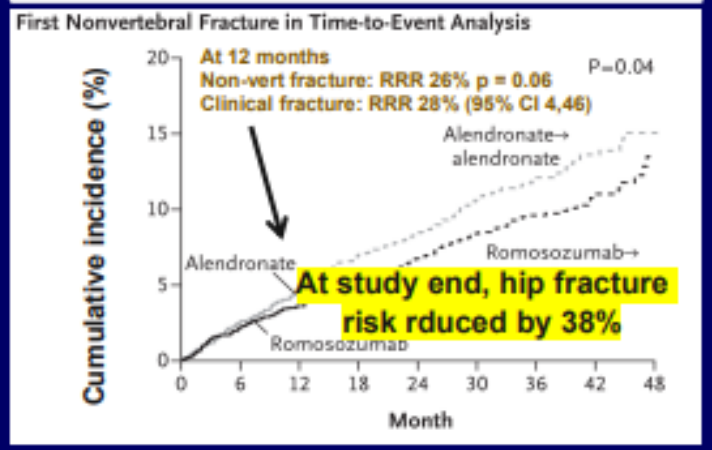
VERO Study and ARCH Trial

Key Point: Teriparatide and romosozumab reduce fracture risk better than do oral bisphosphonates

VERO Study







Kendler DL et al. *Lancet* 2017 Nov 9. pii: S0140-6736(17)32137-2

Saag K et al. *N Engl J Med* 2017;377:1417-27

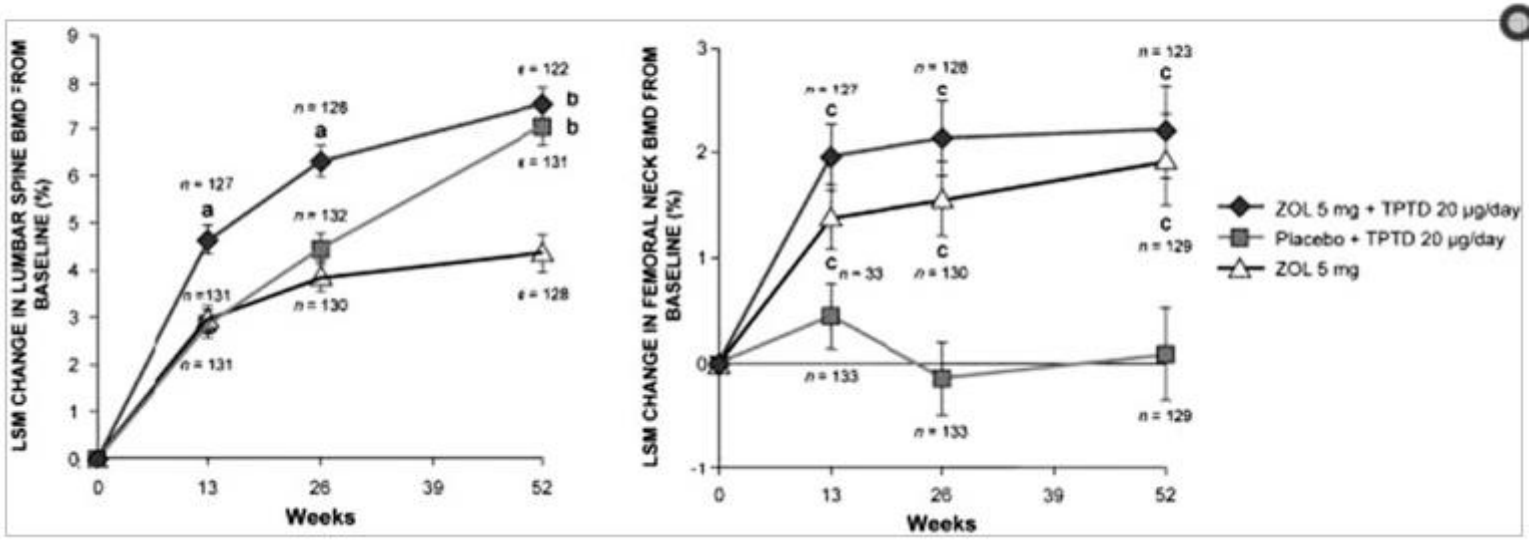
Teriparatide (Forteo)PTH analogue Abaloparatide PTHrp analogue

- The first truly anabolic agent.
- Given daily sc via a pre-filled pen device for 18 mths
- Funded access requires the patient to “fail” bisphosphonate therapy
- Fracture and T score <-3
- Have to transition after use
- Maybe improves fracture healing

Cosman F, et al.

Effects of intravenous zoledronic acid plus subcutaneous teriparatide [rhPTH(1-34)] in postmenopausal osteoporosis. J Bone Miner Res 2011;26:503–511.

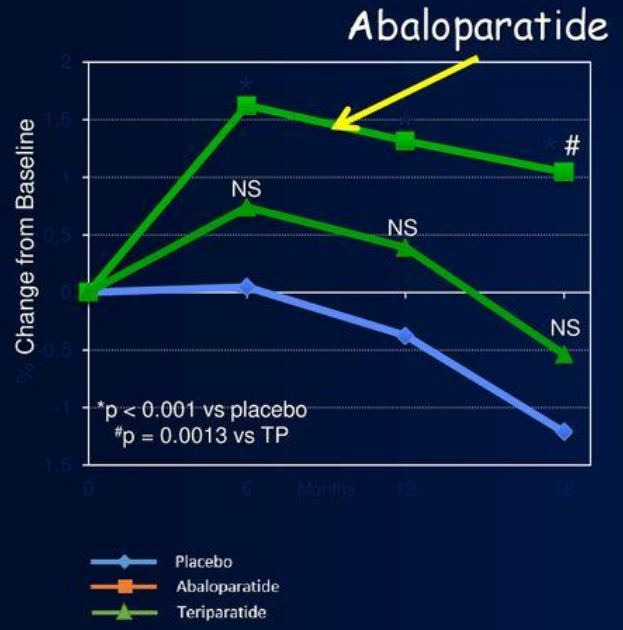
Figure 2



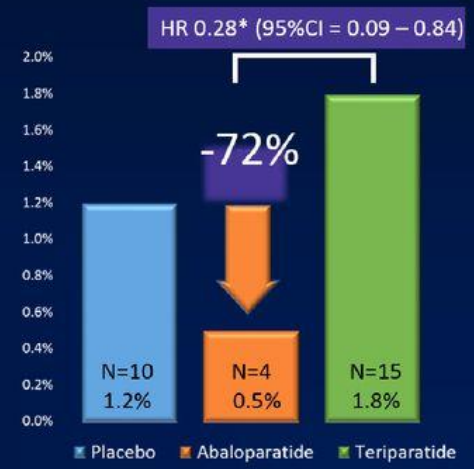
Changes in Wrist BMD and Wrist Fracture Reduction: Abaloparatide vs. Teriparatide vs. Placebo

(Miller et al. Endo Society 3-15)

Ultra-Distal Radius BMD



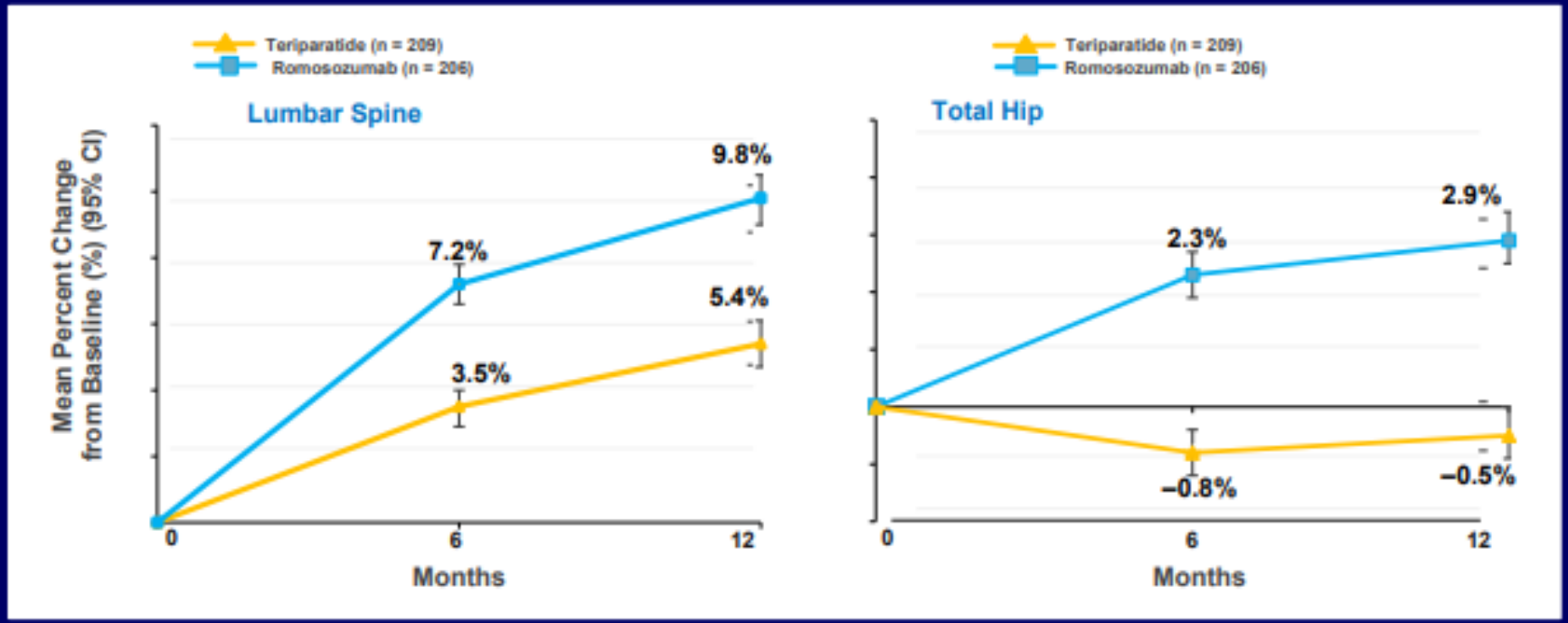
K-M Estimated Incidence Rate Wrist Fracture (ITT Population)



* Vs. TPTD, p=0.015

Switching Osteoporosis Therapies:
Alendronate to Osteoanabolic Agent

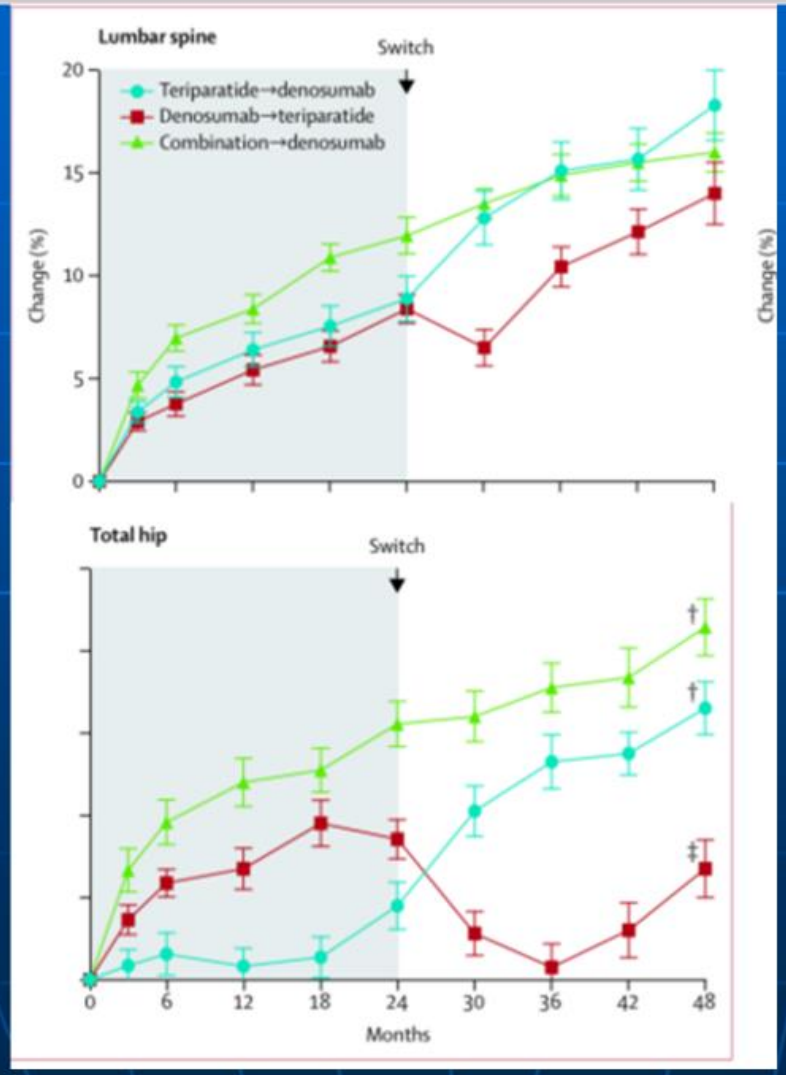
- In patients previous treated with alendronate, volumetric BMD and estimated hip strength increased significantly with romosozumab but not with teriparatide



Langdahl B et al. *Lancet* 2017;390:1585–94

Effect of Denosumab (DMAB) and Teriparatide (TPTD) Transitions on Peripheral Bone Mineral Density (BMD) and Microarchitecture: The DATA-Switch HR-pQCT Study

Joy Tsai, Padrig Tuck, Alexander Uihlein, Mary Bouxsein, Sherri-Ann Burnett-Bowie, Paul Wallace, Benjamin Leder, Robert Neer



There should be half as many admitted, and Every person admitted with a fracture should have had a bone density scan at age 65/70, the majority should be on treatment

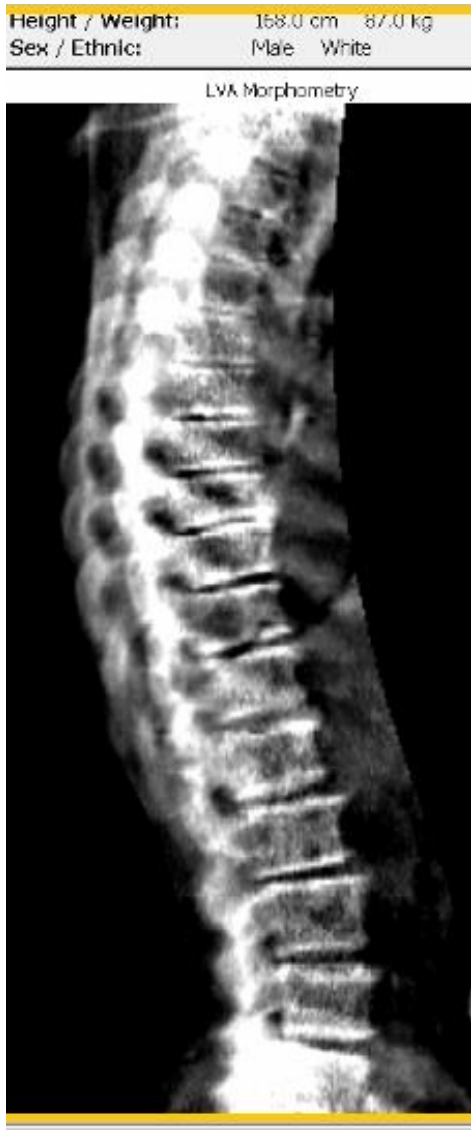
- Use both risk factors and frax
- FRAX
- Fracture liaison

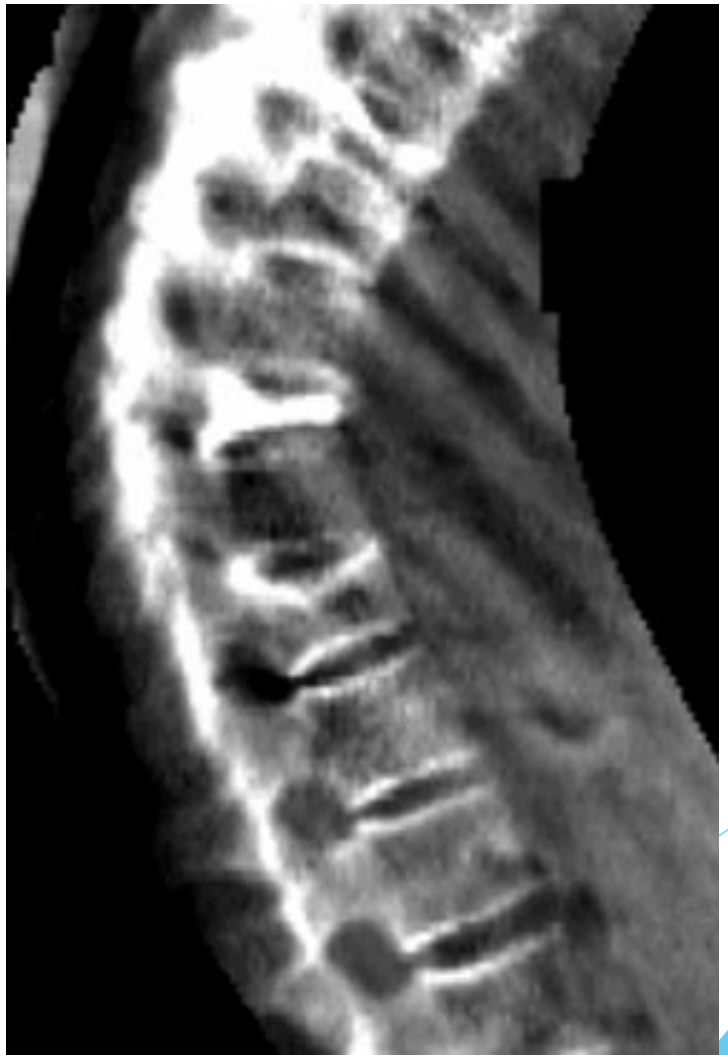
How do you diagnose

- Fractures (hypertension should only be diagnosed after a CVA,MI)
- All women at age 65, men age 70 get bone density scan
- Case finding Check if specific risk factors eg steroids aromatase inhibitors
- Frature risk predicition without bone density FRAX
- FRAX and bone density

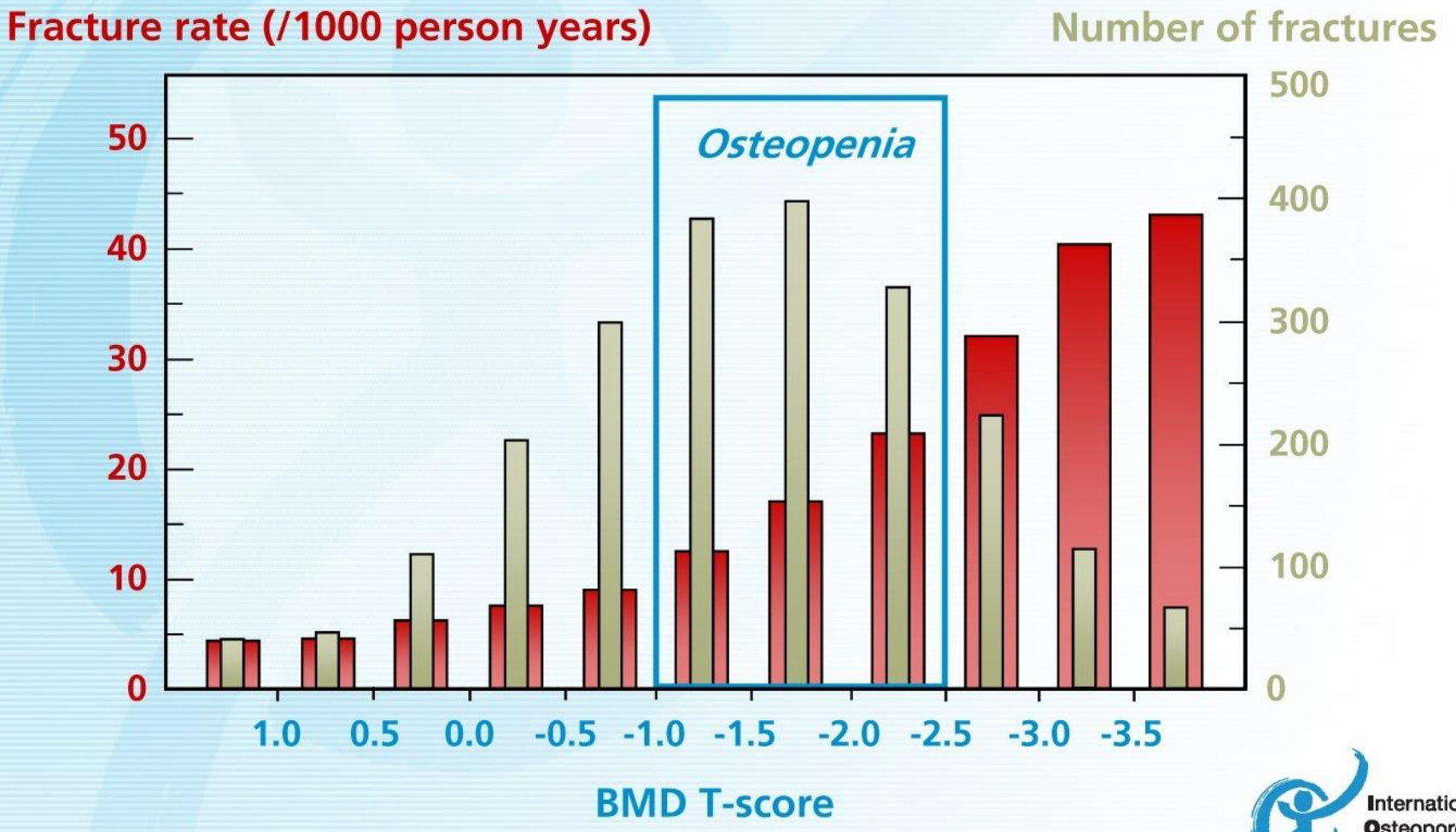
VFA

30% of vertebral fracture are not known





Osteoporotic fractures and bone mineral density (BMD)



Adapted from Siris et al., Arch Intern Med. 2004

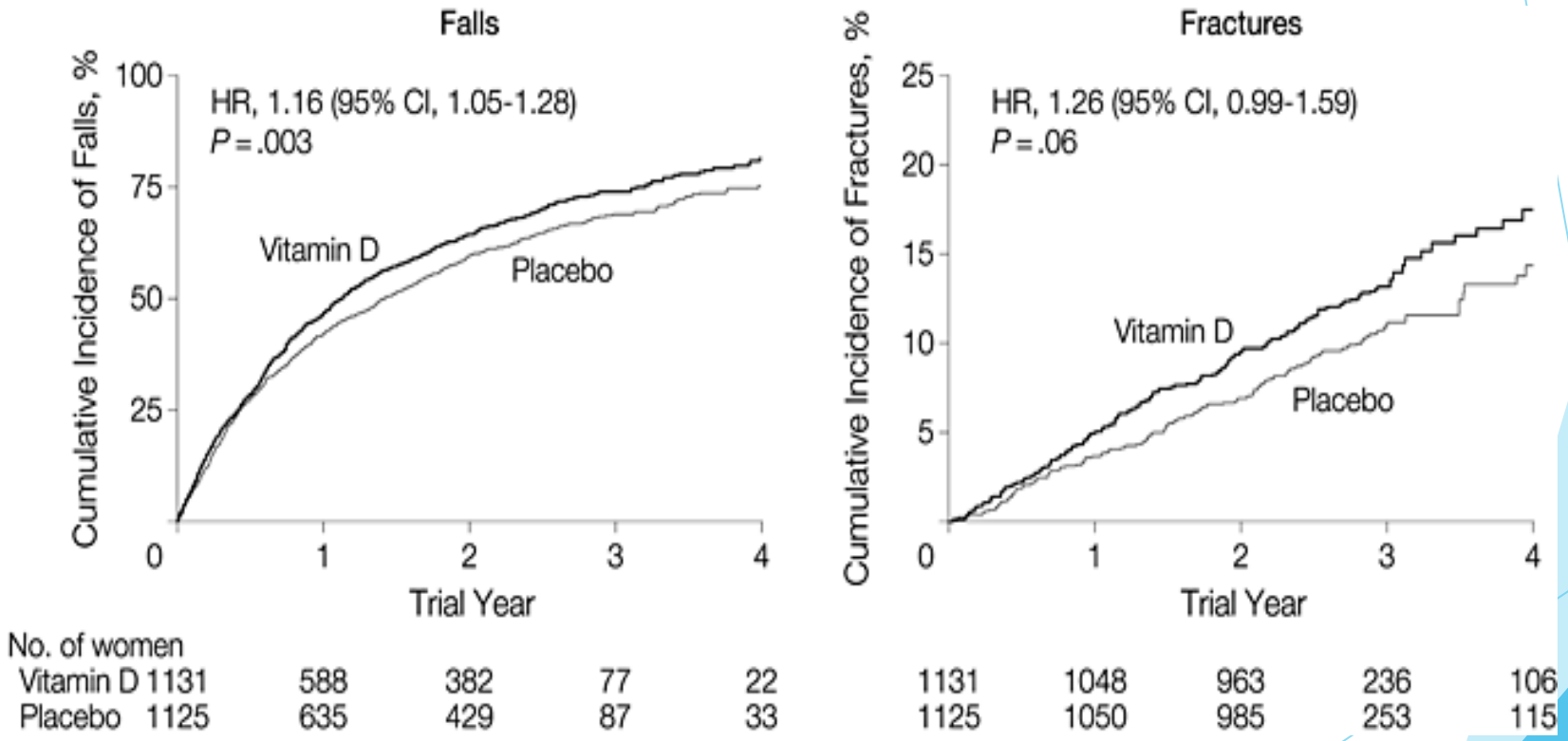
International Osteoporosis Foundation

Vitamin D

- Don’t routinely give calciferol 50,000 iu for 10 days, perhaps just 2 days

- Maintainance 50000iu per month for many, perhaps every 2 months
- Fosamax plus 5600 iu per week looks ok
- Zol 50000iu per month or 2.

Cumulative incidence of time to first fracture or fall



Sanders, K. M. *et al*. JAMA 2010;303:1815-1822.

Proportion leaving hospital on bone protection