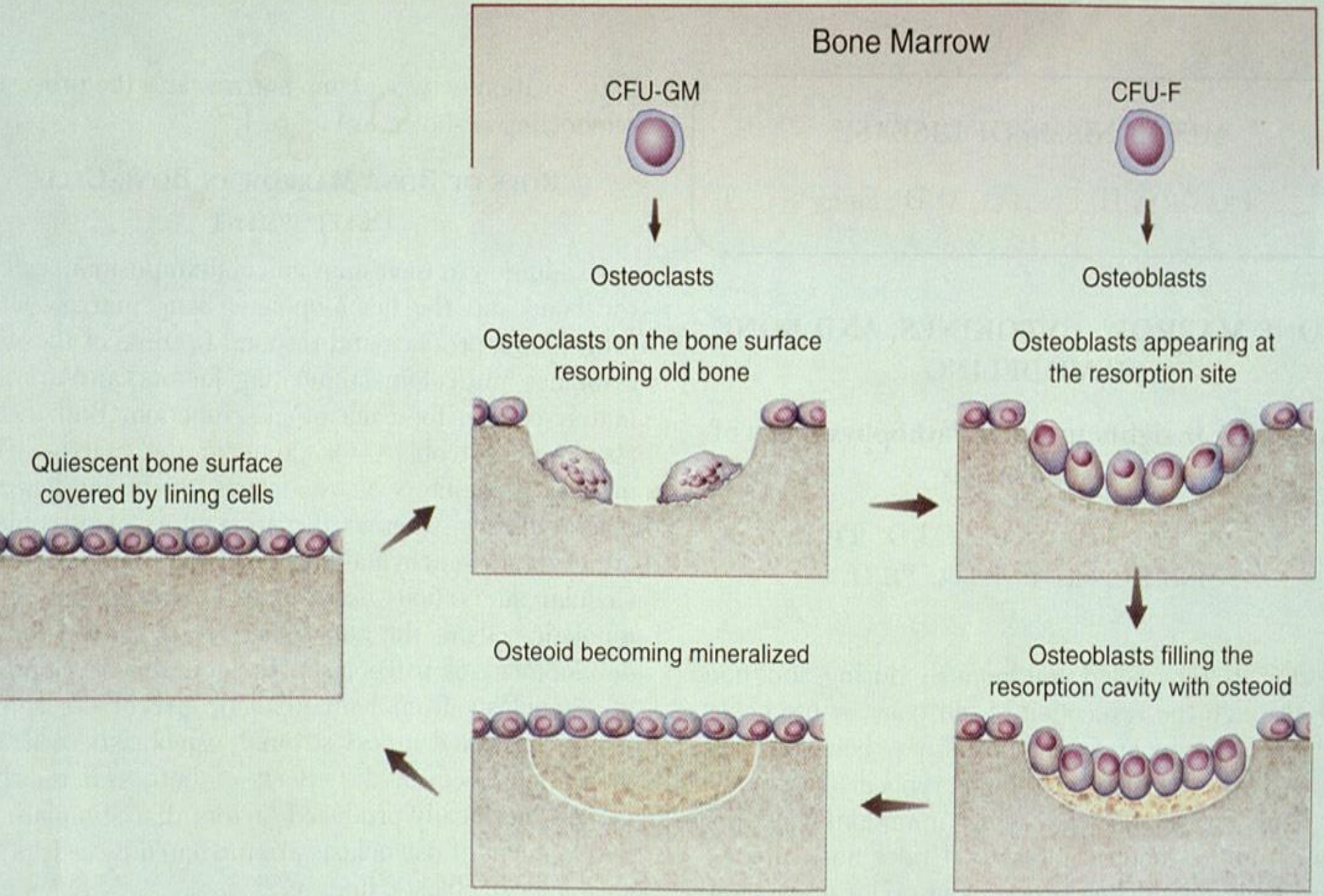
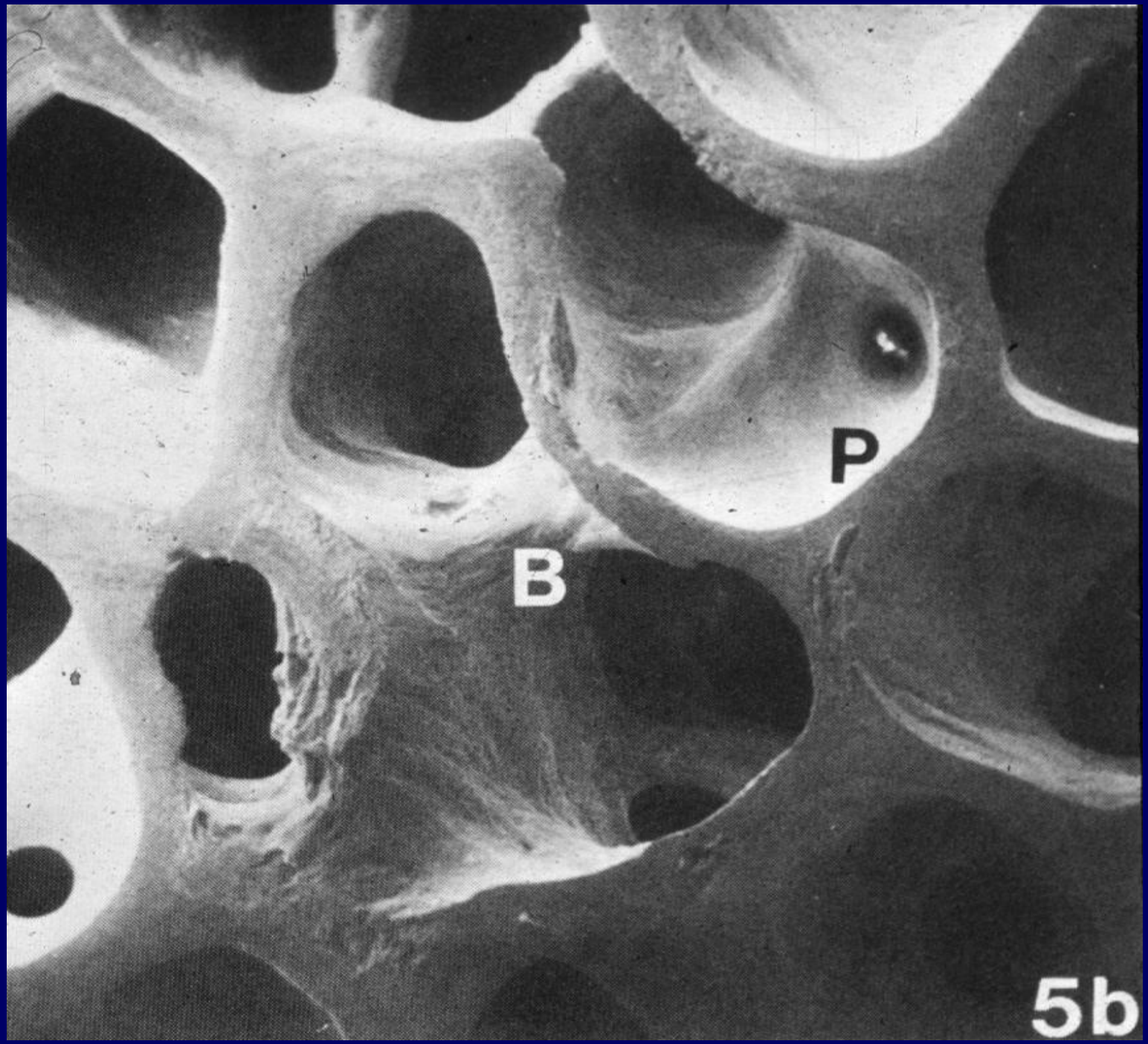
Current Osteoporosis Therapies and Their Long-term Use

Ian Reid

University of Auckland


Bone Marrow
CFU-GM
CFU-F
Osteoclasts
Osteoblasts
Osteoclasts on the bone surface resorbing old bone
Osteoblasts appearing at the resorption site
Quiescent bone surface covered by lining cells
Osteoid becoming mineralized
Osteoblasts filling the resorption cavity with osteoid


P
B
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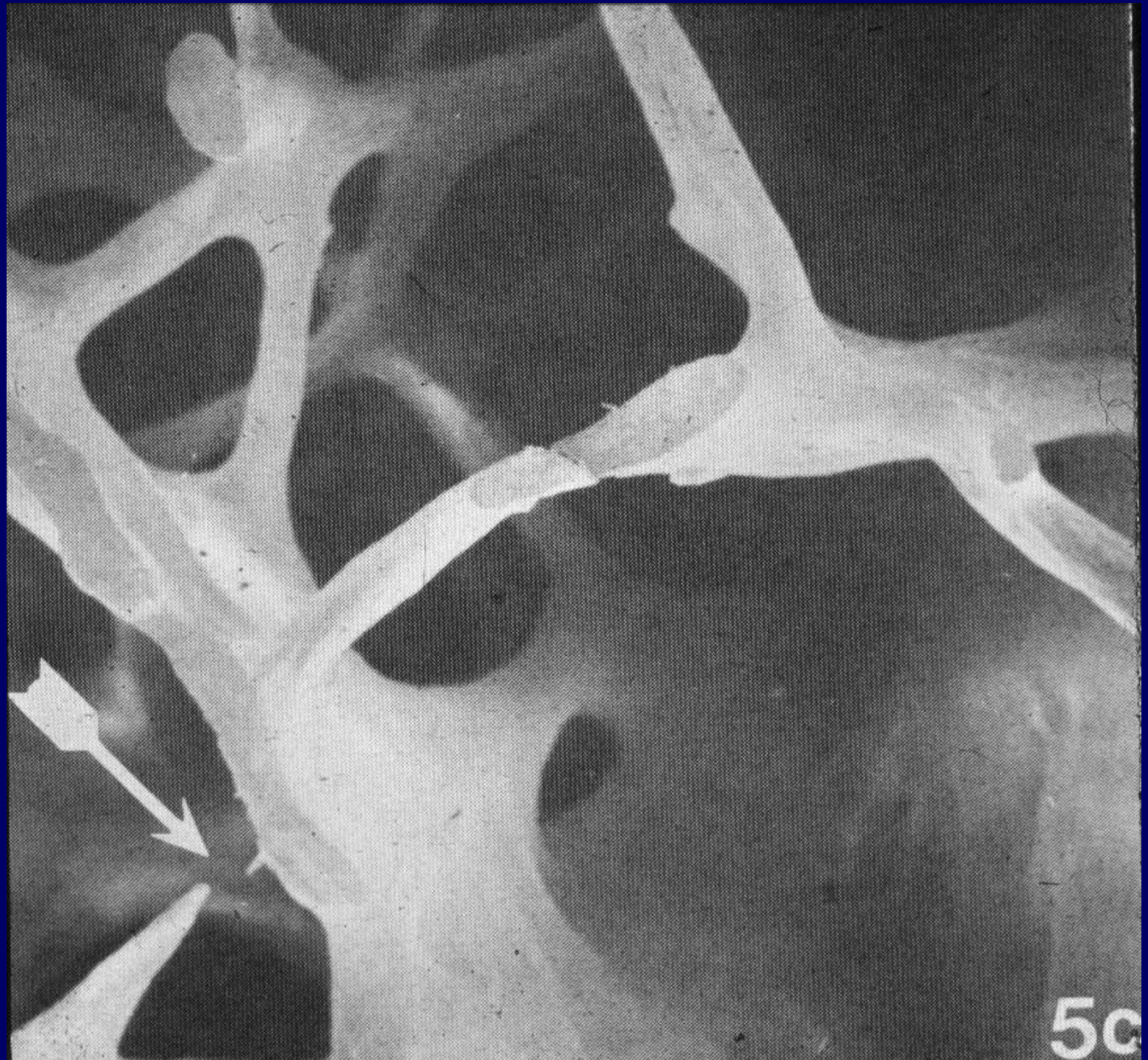
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Treatment Approach

Assess fracture risk

↓

Correct reversible risk factors

↓

Treat if risk justifies

↓

Follow-up

FRAX™ WHO Fracture Risk Assessment Tool

HOME | CALCULATION TOOL | PAPER CHARTS | FAQ | REFERENCES | Select a Language

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Weight Conversion:

pound: convert

Height Conversion:

inch : convert

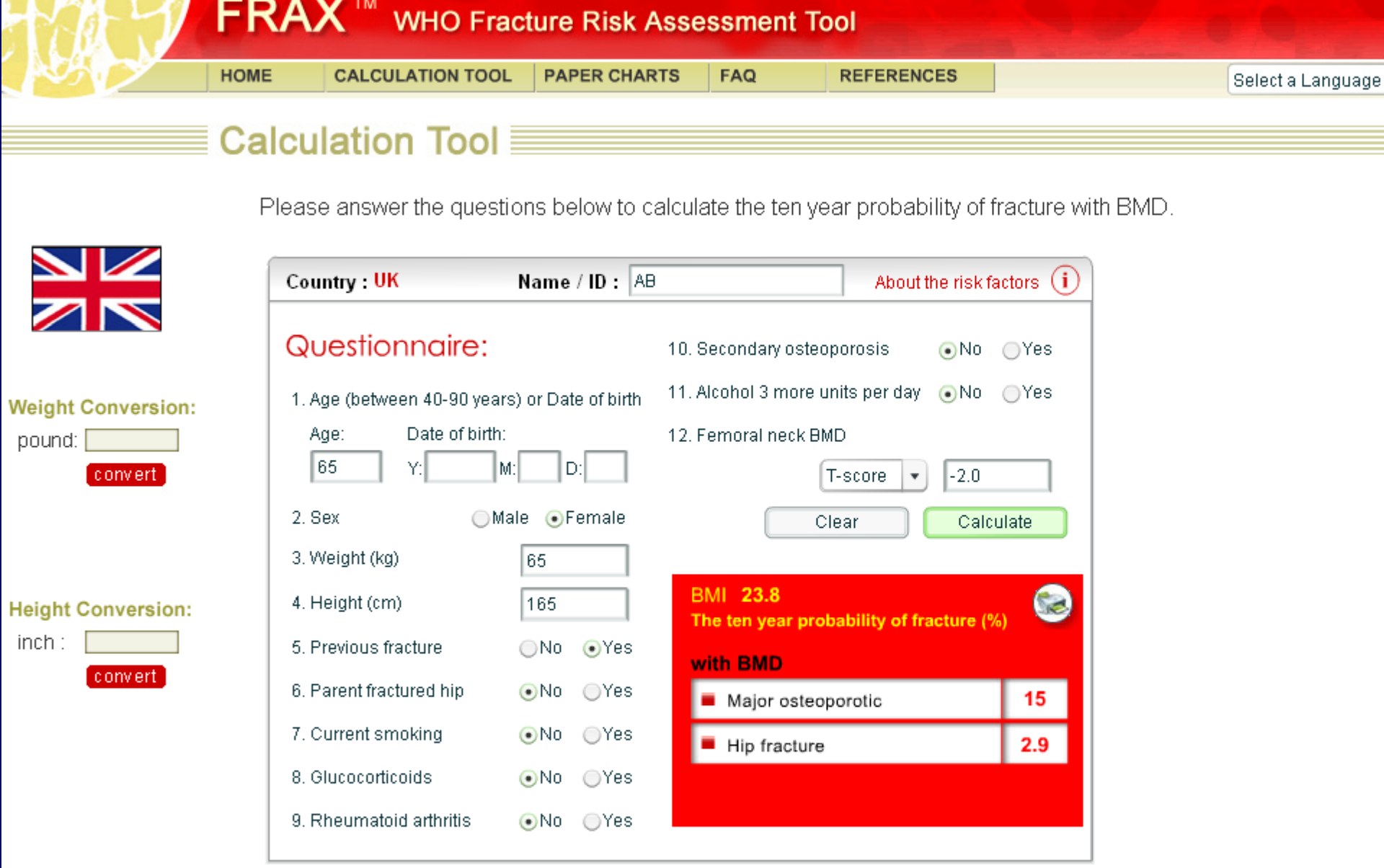
Country : UK **Name / ID :** About the risk factors

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
    Select

Clear Calculate

Risk factors



Major osteoporotic fracture is hip fracture, clinically evident vertebral fracture, proximal humerus fracture and distal forearm fracture. This is about half of total fractures (SOF, Stone JBMR 18:1947, 2003)

FRACTURE RISK CALCULATOR

GARVAN INSTITUTE

Fill out the following to estimate your fracture risk

Full Name (optional): Test

Sex?
- ○ Male
- ◉ Female

Age: 70

Fractures since the age of 50 (excluding major trauma, e.g. car accidents): 0

Falls over last 12 months: 0

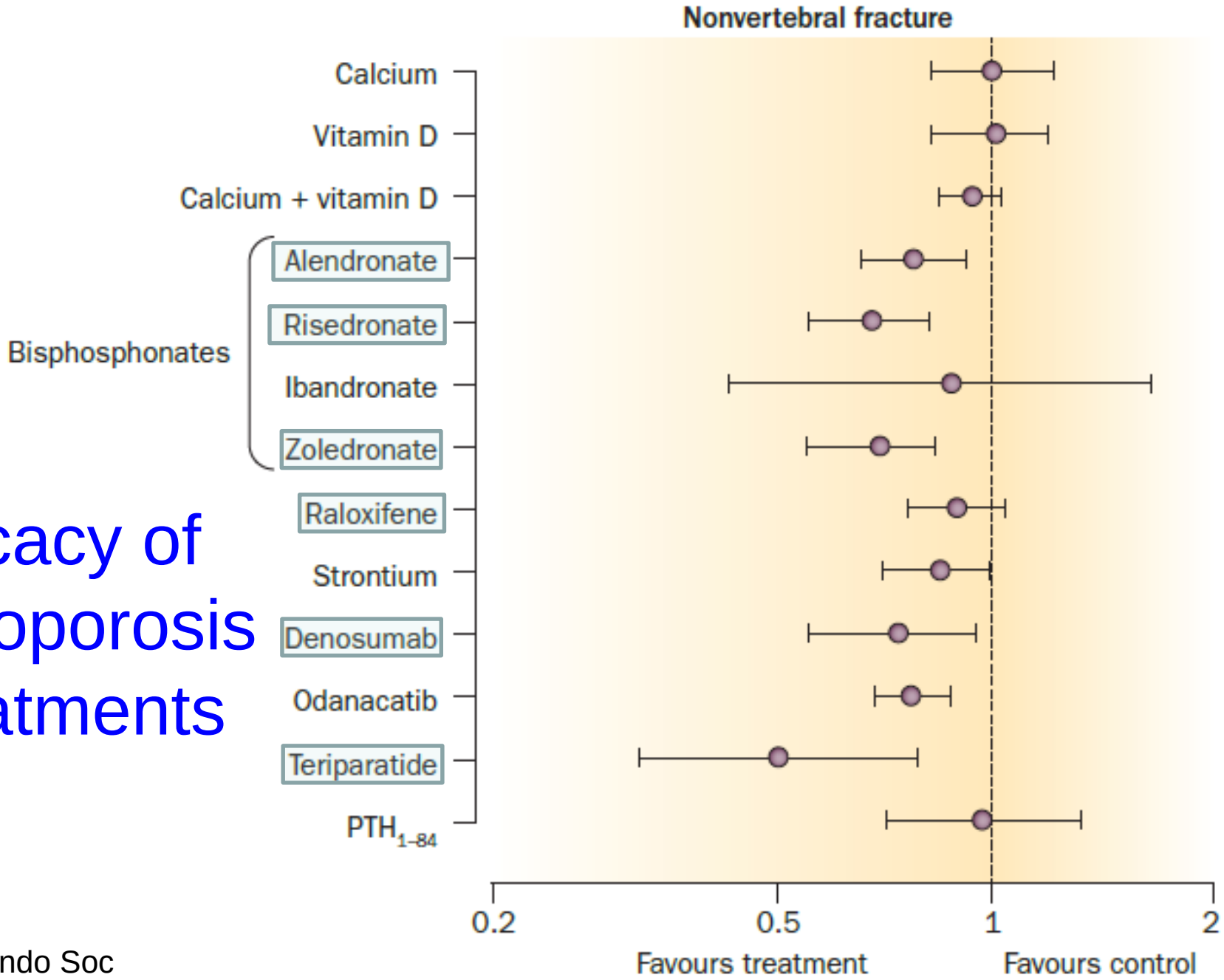
Do you have a Bone Mineral Density (BMD) measurement?
- ◉ Yes
- ○ No

-2.5

-3

?

Efficacy of Osteoporosis Treatments



Murad, Endo Soc
Reid, Nature Rev Endo 2015

Patient 1

- 58 year-old woman
- 2 forearm fractures
- 2 falls in the last year
- No osteoporosis treatment to-date
- Femoral neck T-score –1.8
- FRAX: hip 1.9%
  major osteoporotic 11%

- What do you recommend?

Patient 1

- 58 year-old woman
- 2 forearm fractures
- 2 falls in the last year
- No osteoporosis treatment to-date
- Femoral neck T-score –1.8
- FRAX: hip 1.9%
  major osteoporotic 11%
- Garvan: hip 17%
  osteoporotic 43%
- What do you recommend?

Patient 2

- 68 year-old woman
- Previous forearm fracture, 6 years ago
- On alendronate 70 mg/week for 5 years
- T-score 5 years ago -3.6
- Current T-score -2.9

What do you recommend?

1. Stop alendronate
2. Continue alendronate 70 mg/week
3. Change to alendronate 70 mg/2 weeks
4. Change to parenteral therapy
5. Carry out investigations

Patient 3

- 68 year-old woman
- Previous forearm fracture, 6 years ago
- On alendronate 70 mg/week for 5 years
- T-score 5 years ago -3.6
- Current T-score -2.3

What do you recommend?

1. Stop alendronate
2. Continue alendronate 70 mg/week
3. Change to alendronate 70 mg/2 weeks
4. Change to parenteral therapy
5. Carry out investigations

Patient 4

- 68 year-old woman
- Previous forearm fracture, 6 years ago
- On alendronate 70 mg/week for 5 years
- T-score 5 years ago -3.6
- Current T-score -3.7

What do you recommend?

1. Stop alendronate
2. Continue alendronate 70 mg/week
3. Change to alendronate 70 mg/2 weeks
4. Change to parenteral therapy
5. Carry out investigations

Patients 2 - 4: Questions to Consider

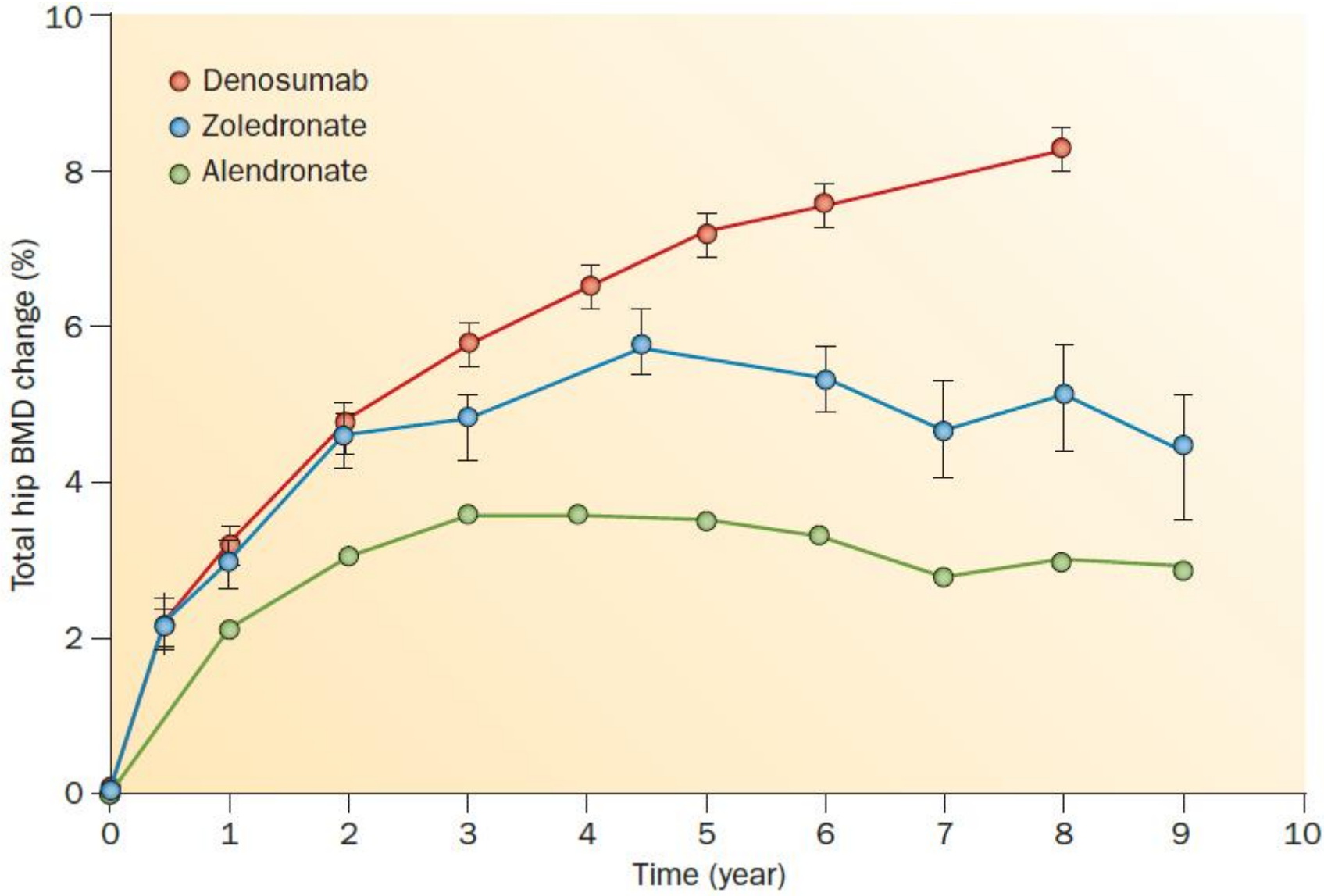
- Has patient responded appropriately to therapy?
- If not, what tests might be helpful?
- Is continued therapy needed?
- If so, what?

Patient 2

- 68 year-old woman
- Previous forearm fracture, 6 years ago
- On alendronate 70 mg/week for 5 years
- T-score 5 years ago -3.6
- Current T-score -2.9

Has patient responded appropriately to therapy?

Long-Term Effects of Anti-Resorptives on Total Hip BMD



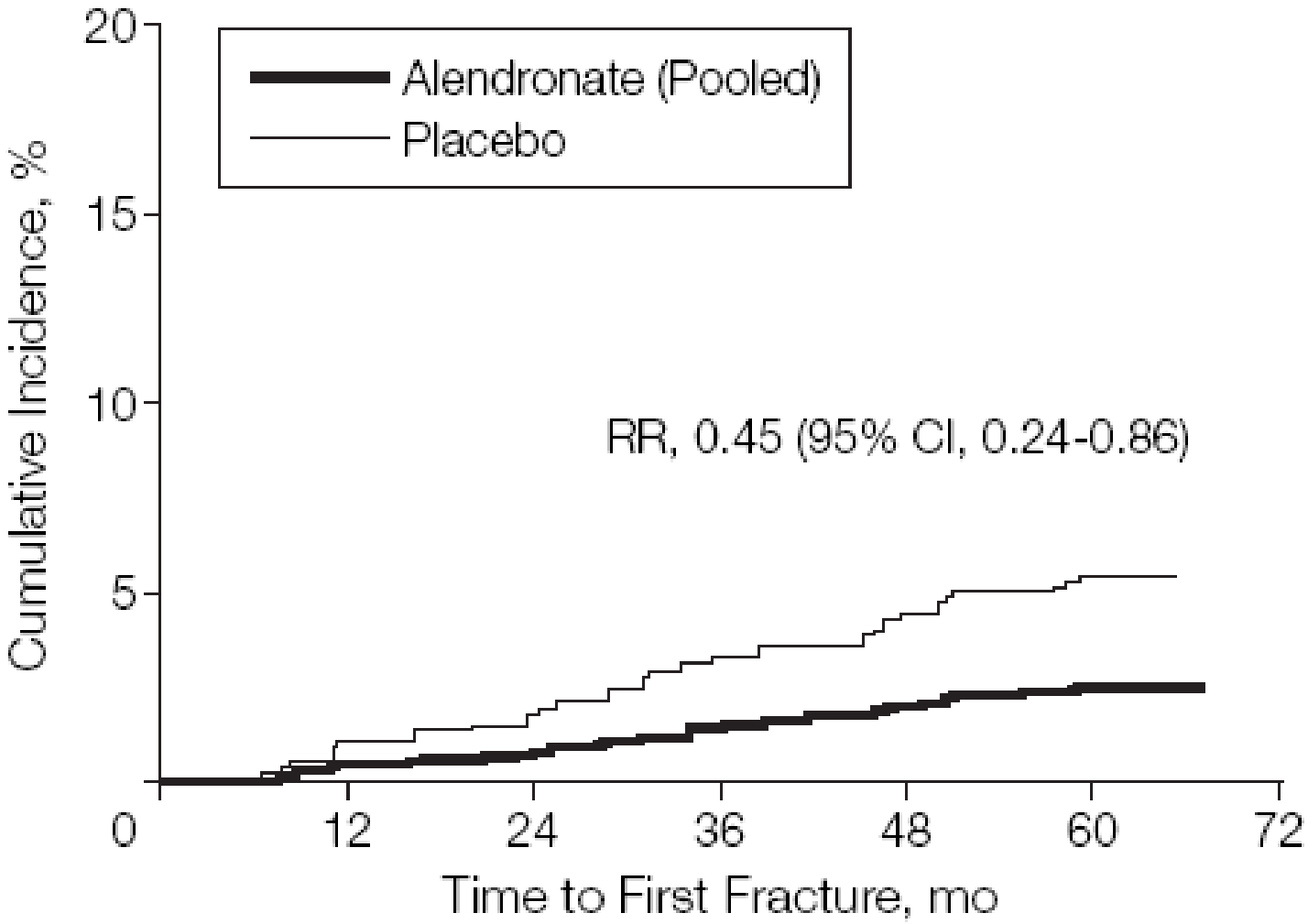
Reid, Nature Rev Endocrinol, 2015

Patient 2

- 68 year-old woman
- Previous forearm fracture, 6 years ago
- On alendronate 70 mg/week for 5 years
- T-score 5 years ago -3.6
- Current T-score -2.9

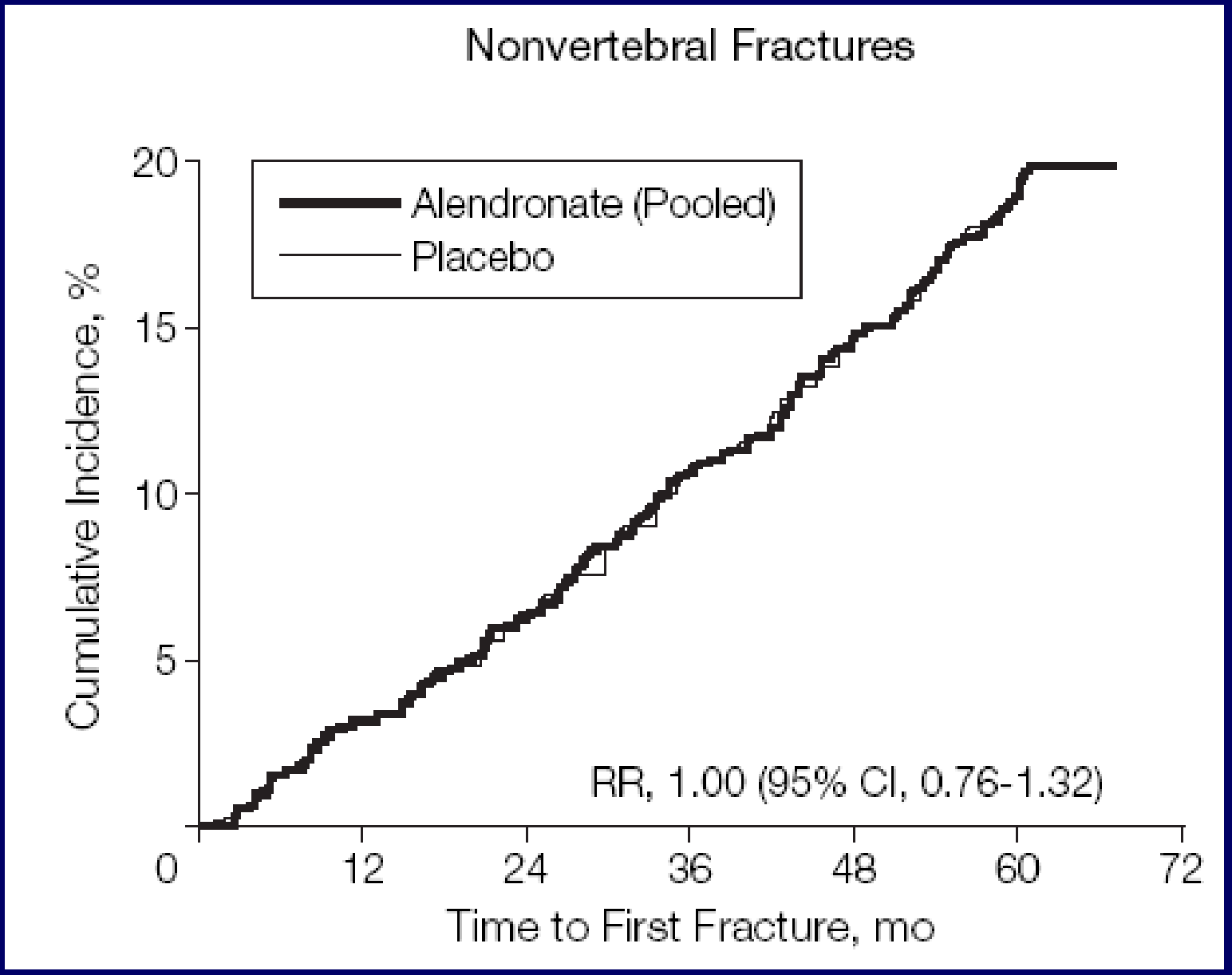
Is continued therapy needed?

FLEX



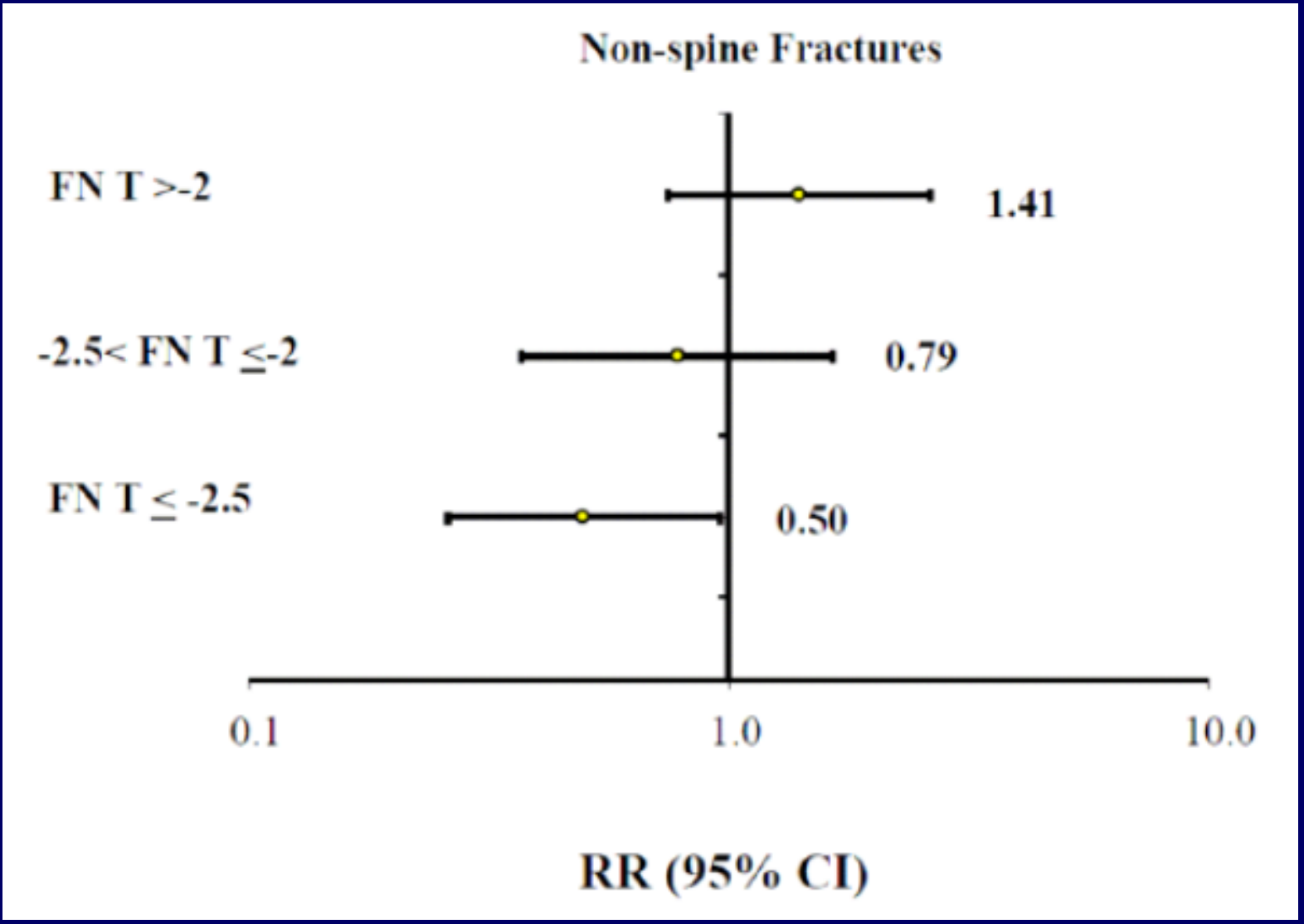
Black JAMA 296:2927, 2006

FLEX



Black JAMA 296:2927, 2006

Nonvertebral Fracture by FLEX Baseline T-Score



Schwartz, JBMR 25:976, 2010

Patient 2

- 68 year-old woman
- Previous forearm fracture, 6 years ago
- On alendronate 70 mg/week for 5 years
- T-score 5 years ago -3.6
- Current T-score -2.9

Is continued therapy needed?

If so, what?

Patient 3

- 68 year-old woman
- Previous forearm fracture, 6 years ago
- On alendronate 70 mg/week for 5 years
- T-score 5 years ago -3.6
- Current T-score -2.3
  - Has patient responded appropriately to therapy?
  - Is continued therapy needed?

How long is a drug holiday?

Alendronate – 1-5 years

Risedronate – 6-12 months

Long-Term Zoledronate

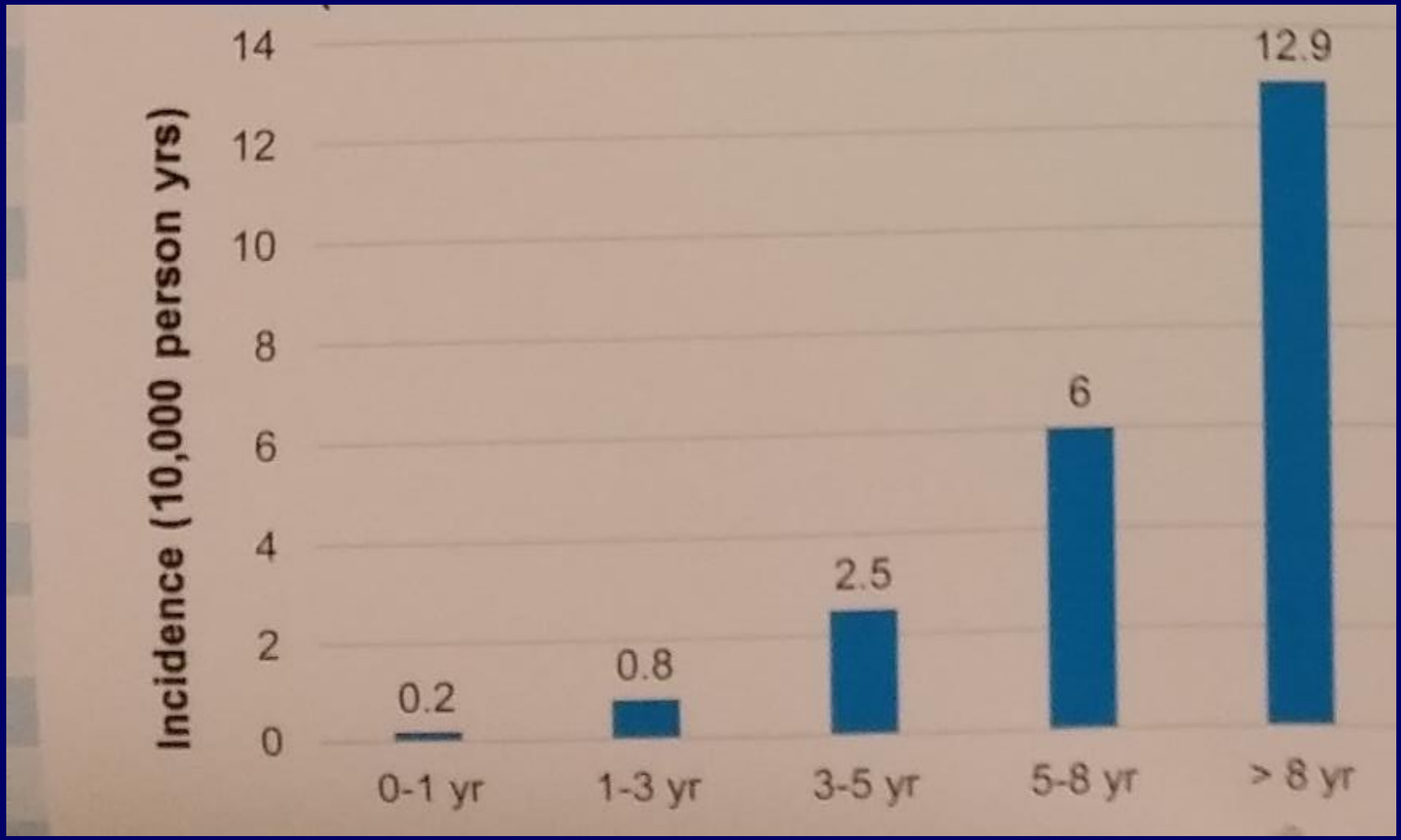
- Dose every 18 months initially
- With satisfactory BMD response at 3-5 years, extend inter-dose interval to 24-36 months

Why minimise the duration of anti-resorptive treatment?

Atypical Sub-Trochanteric Fractures

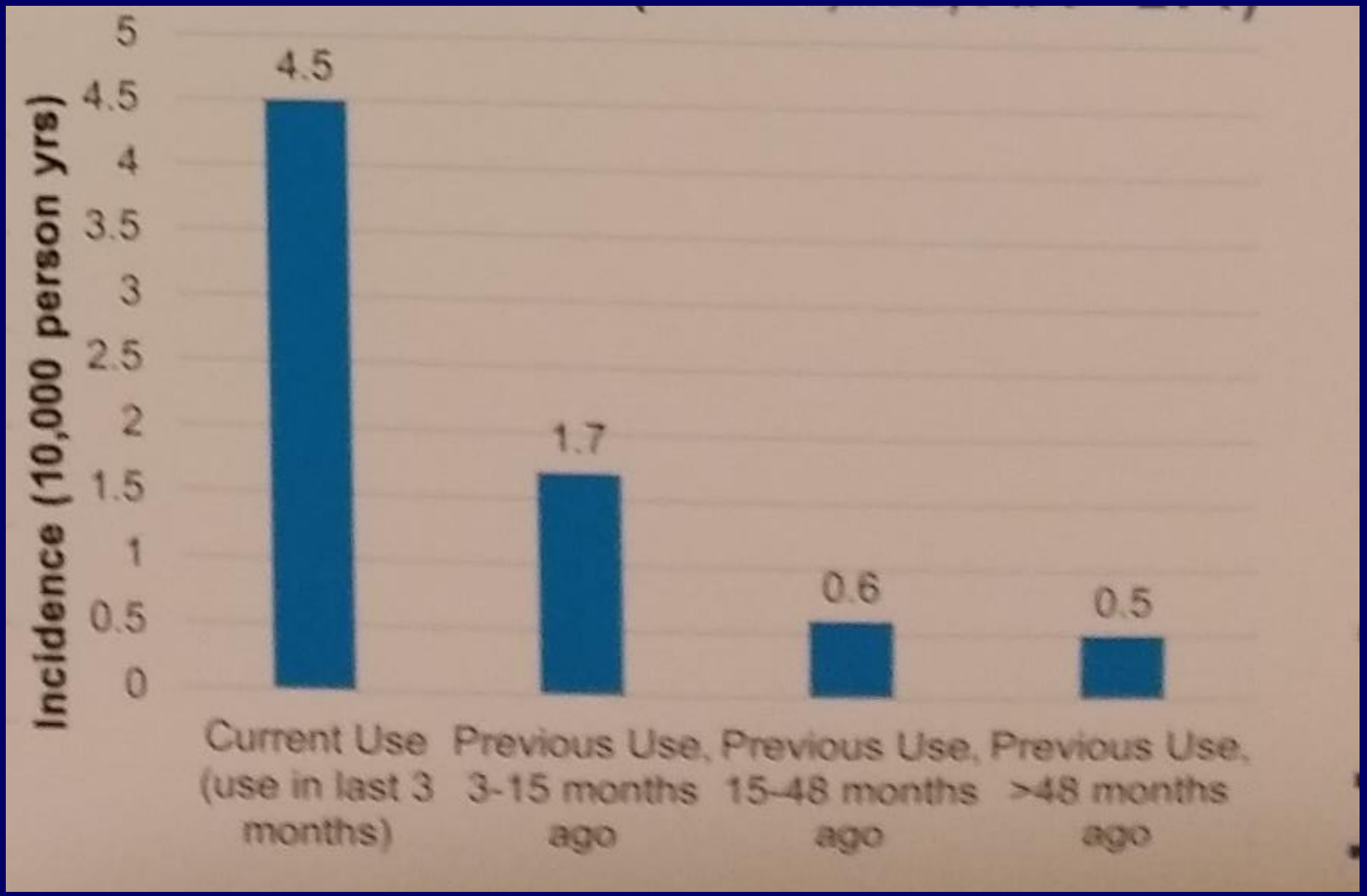
Kwek, Injury 39:224, 2008

AFF Rates by Duration of Use



Geiger et al, ASBMR 2018

AFF Rates by Time Since Discontinuation



Geiger et al, ASBMR 2018

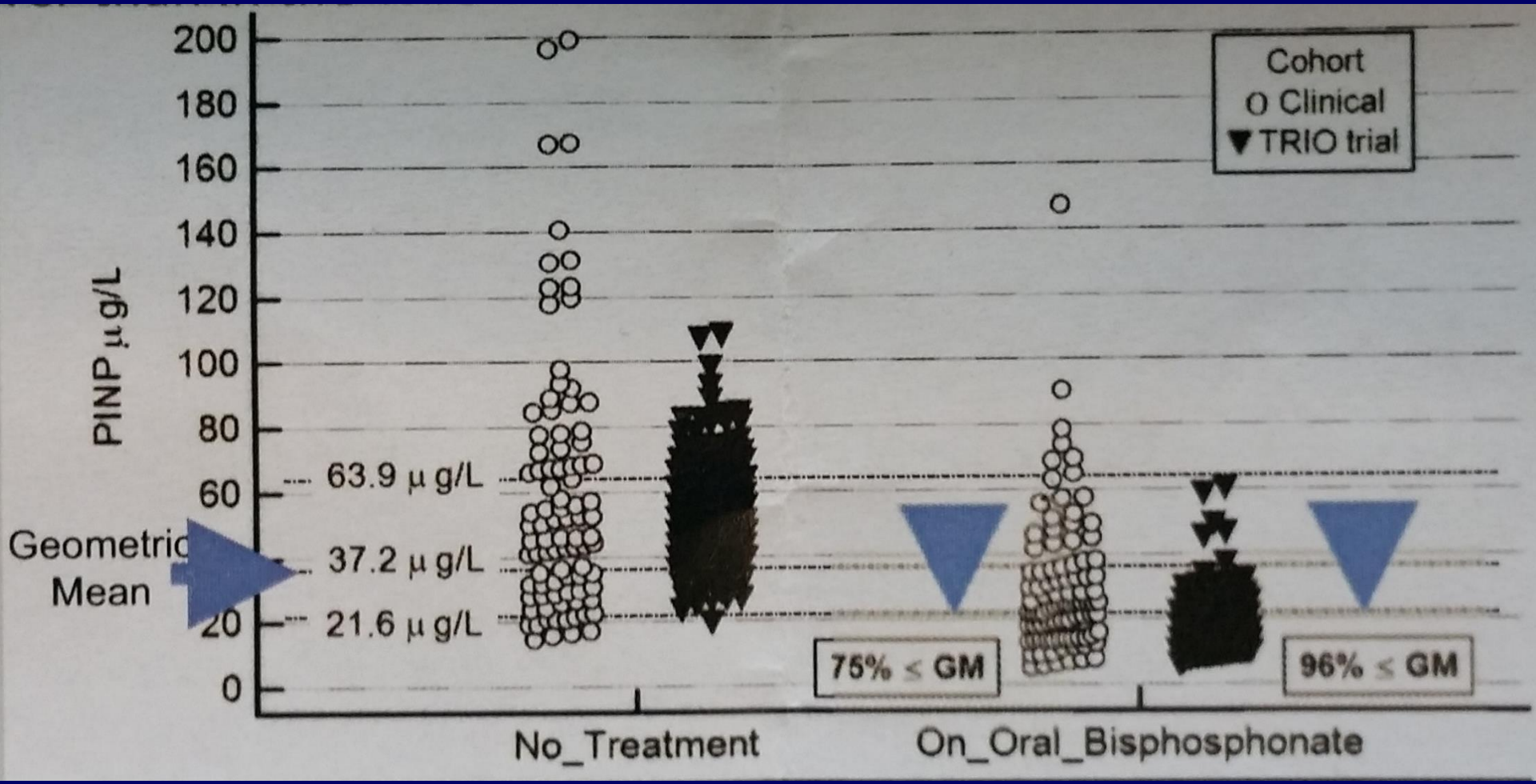
Patient 4

- 68 year-old woman
- Previous forearm fracture, 6 years ago
- On alendronate 70 mg/week for 5 years
- T-score 5 years ago -3.6
- Current T-score -3.7
  - Has patient responded appropriately to therapy?
  - If not, what tests might be helpful?
  - Is continued therapy needed?
  - If so, what?

Exclude Secondary Osteoporosis (e.g. if Z < -2)

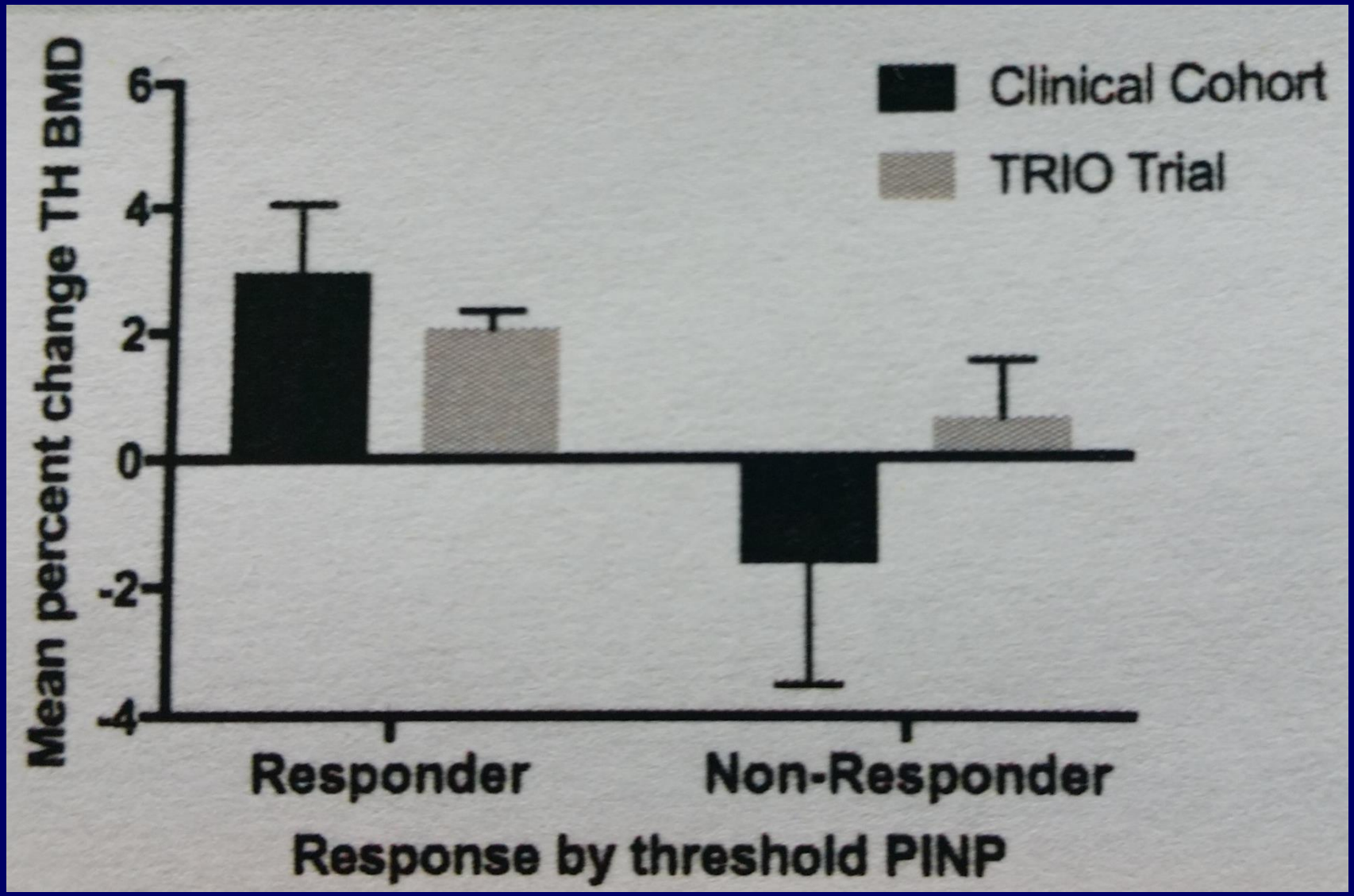
- Clinical history and examination
- Serum calcium
- Serum phosphate
- Alkaline phosphatase
- Cortisol
- TSH
- Coeliac screen
- Liver function tests
- Creatinine
- Protein electrophoresis
- Full blood count
- C-reactive protein
- Testosterone
- 25(OH)D

PINP Off and On Bisphosphonates

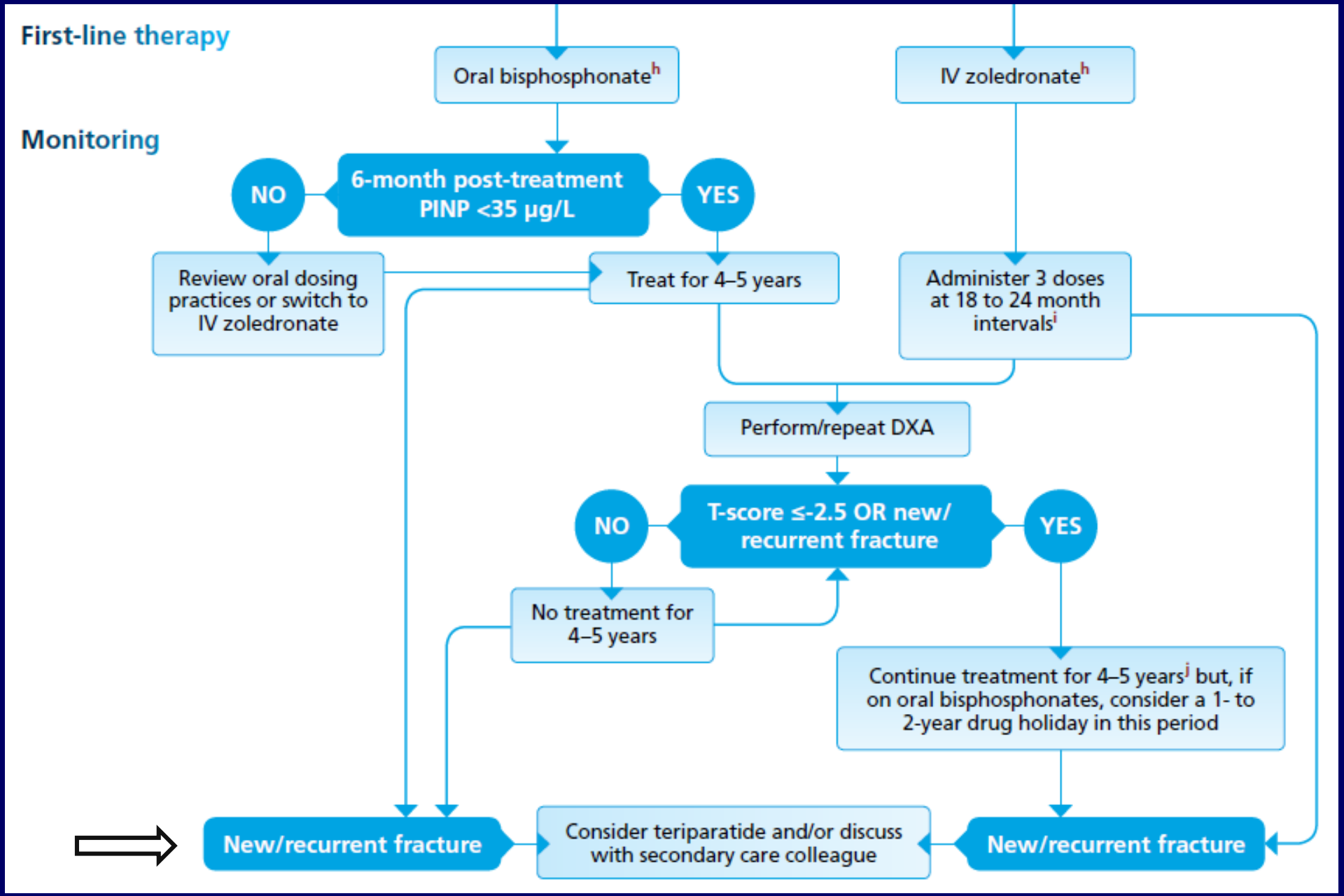


Ugur et al, ASBMR 2018

BMD Change in PINP Responders



Ugur et al, ASBMR 2018

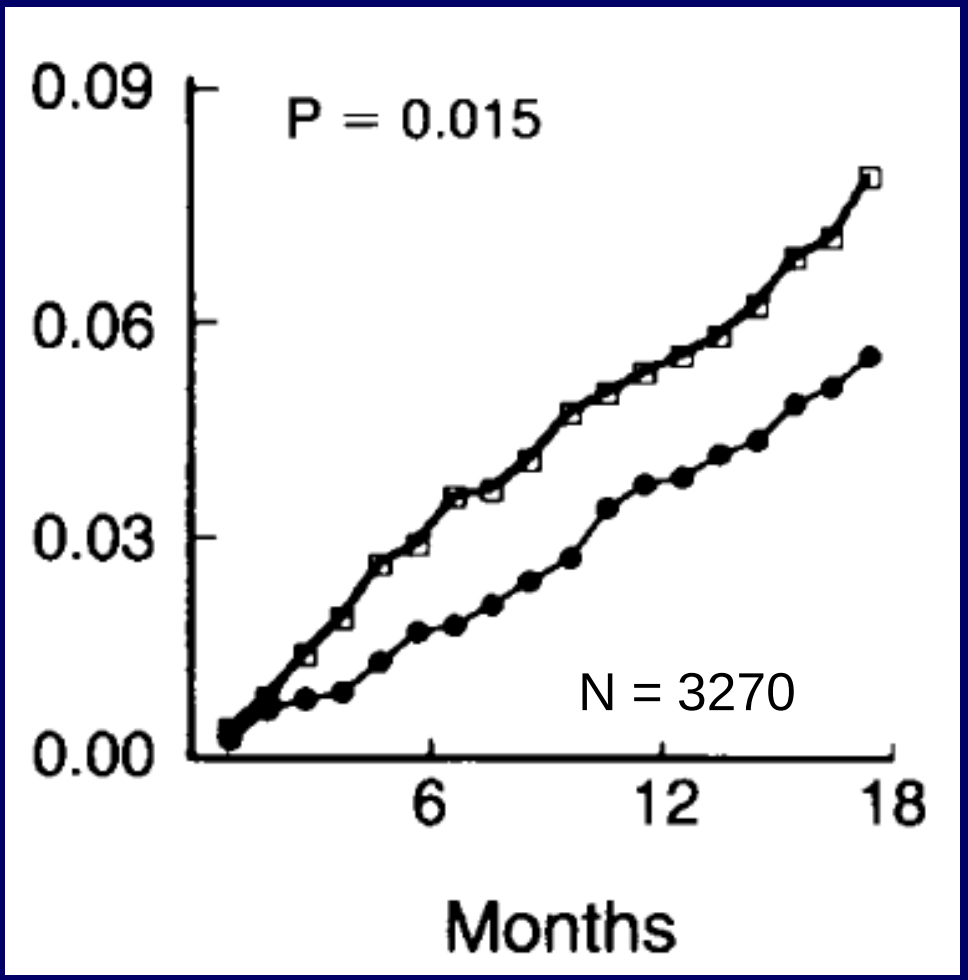


https://osteoporosis.org.nz/resources/health-professionals/clinical-guidance/

Teriparatide

- Have a plan for post-teriparatide treatment before starting teriparatide

Ca+D Effects on Non-Hip Non-Vert Fractures



Chapuy, NEJM 1992

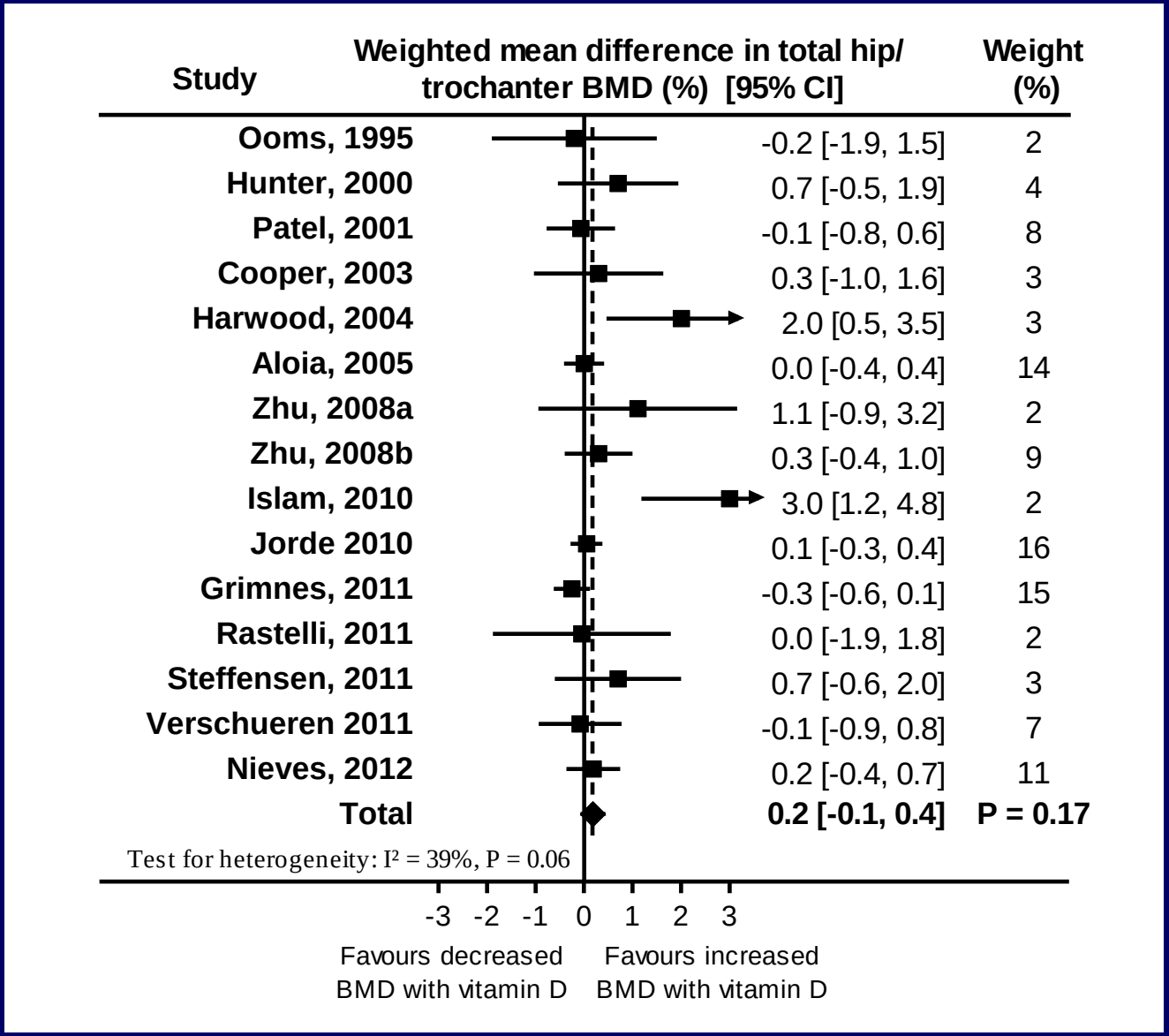
Women's Health Initiative

Total fractures

HR: 0.96 (0.91–1.02)
N = 36,282

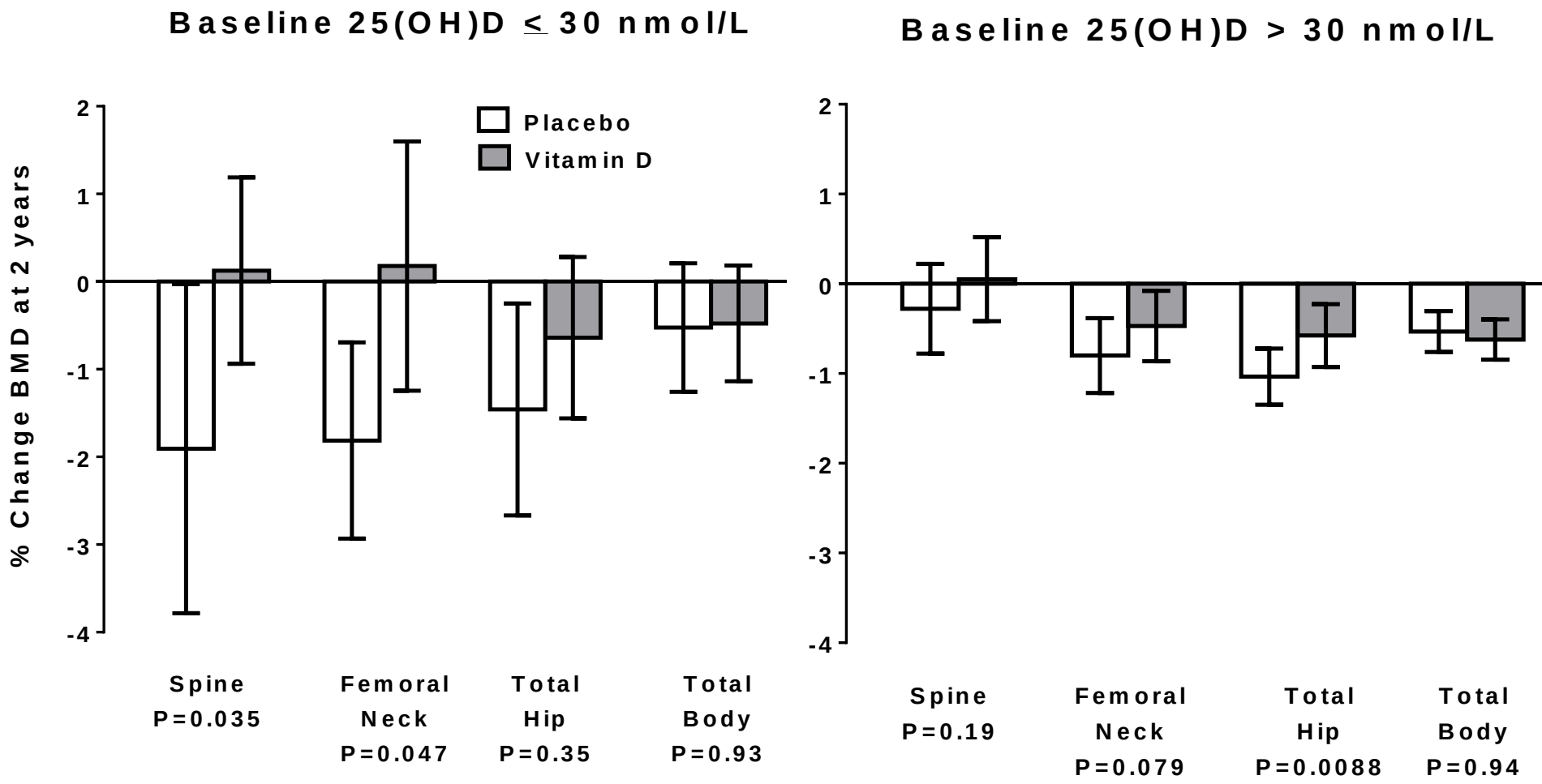
Jackson NEJM 354:669, 2006

Meta-Analysis of Vit D on Total Hip BMD



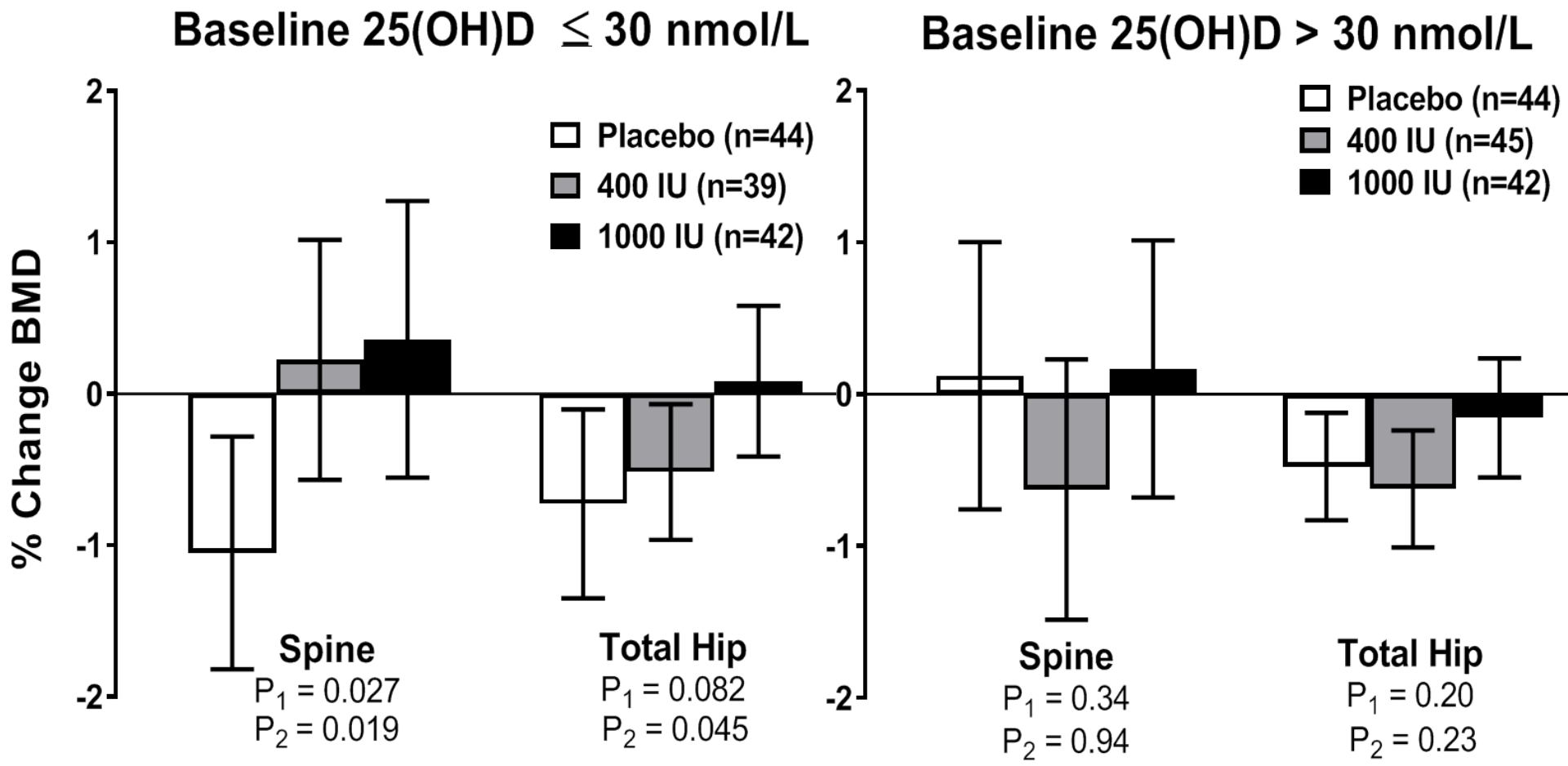
Reid et al, Lancet 2014

Vit D Effects on BMD Over 2 Years

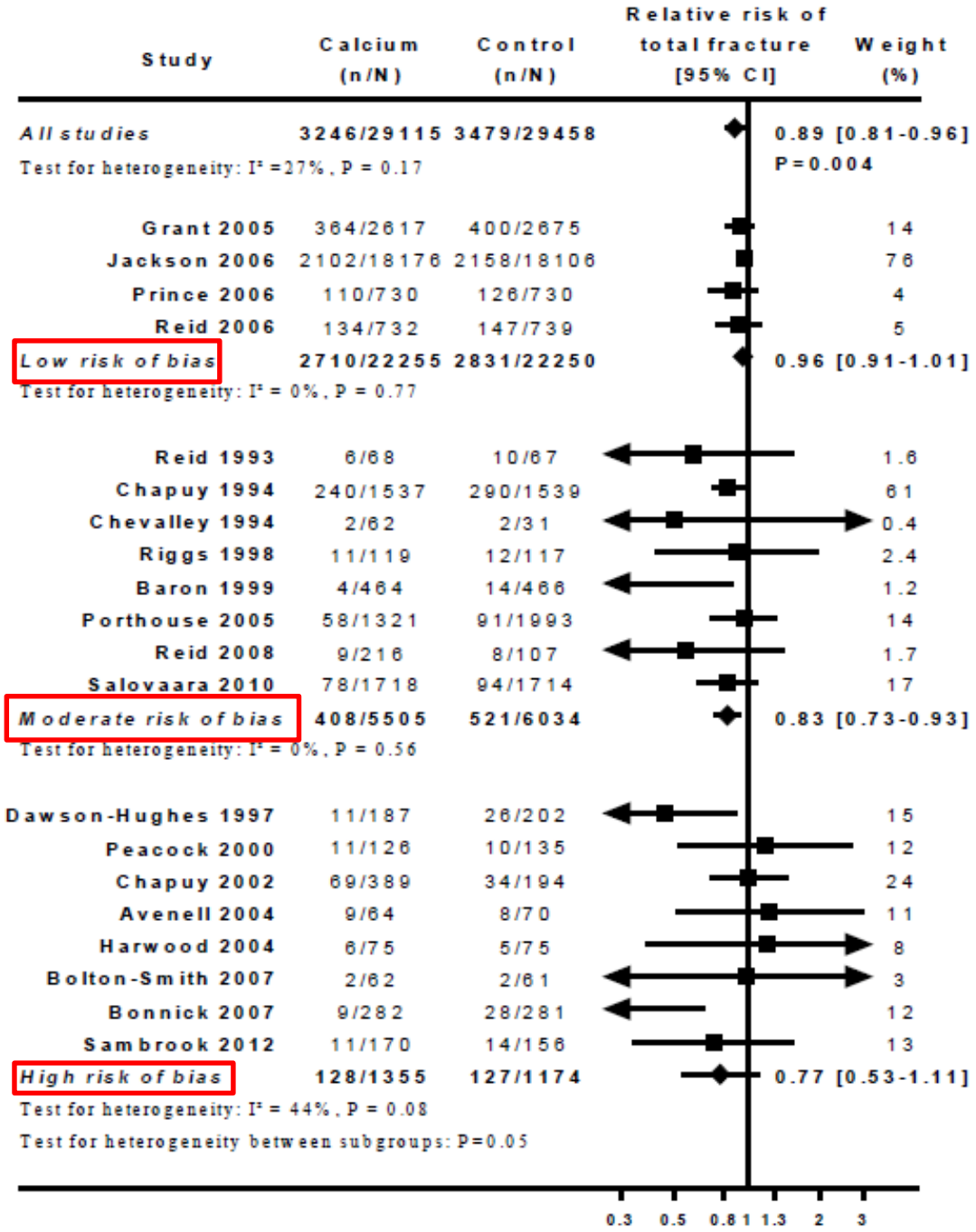


Reid, J Int Med 2017

Response to Daily Vitamin D Supplementation in Postmenopausal Women



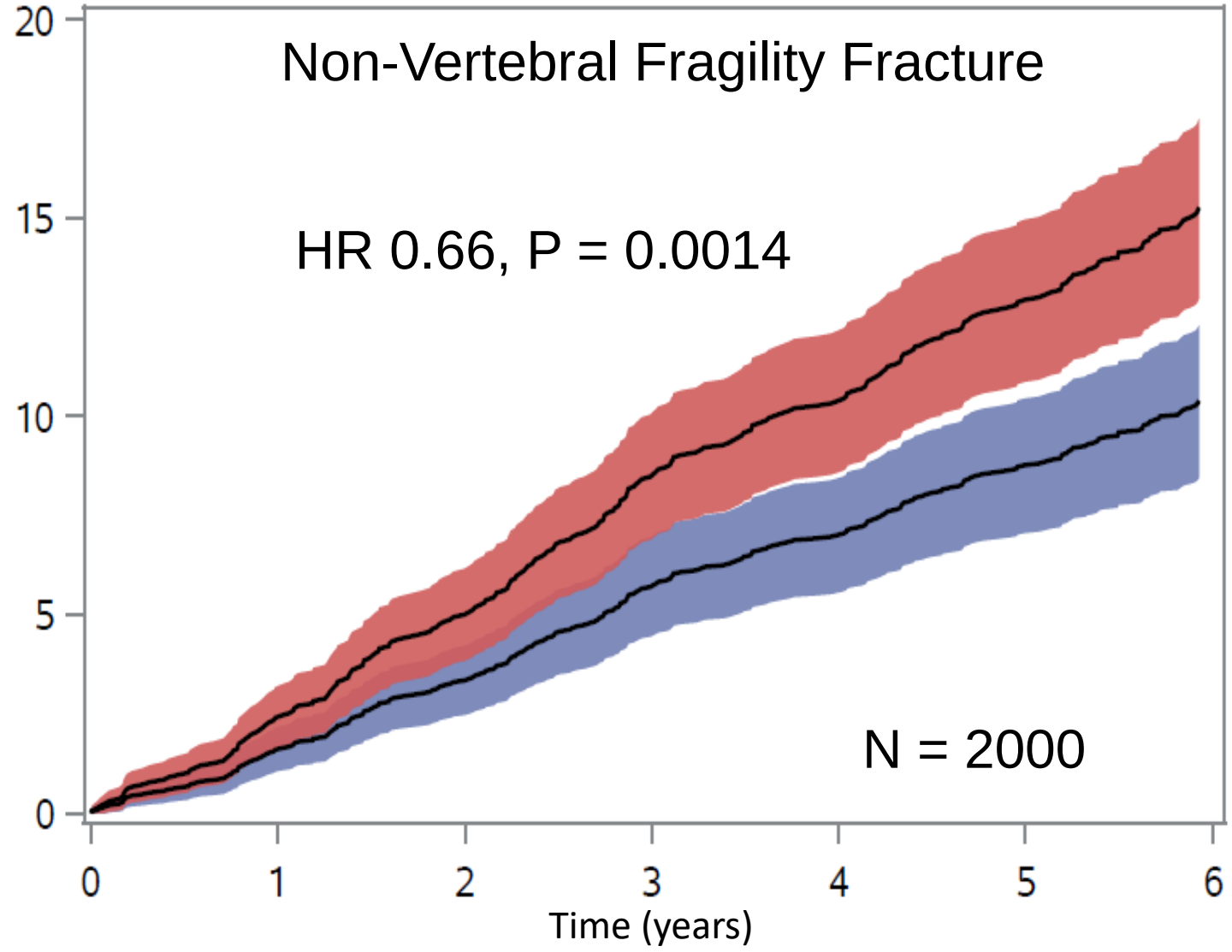
Macdonald et al, JBMR 2018



Effect of Calcium on Total Fracture, by Risk of Bias

Bolland, BMJ, 2015

Zoledronate Effect on Fractures in Osteopenic Women – No Calcium Supplements



Vertebral Fractures:
OR = 0.47
P = 0.0018

Reid, NEJM 2018

Pro's and Cons of Agents for Managing Osteoporosis - 1

Agent	Pro's	Con's
Calcium	Cheap	Low efficacy, ↑ GI, calculi, CVD
HRT	↓ all #s	↑breast ca, ↑DVT, ↑CVD
Raloxifene	↓vert #s, ↓breast ca	↑ DVT
Sr	↓ vert & nonvert #s	? Mechanism, skin AEs, ↑CVD

Pro's and Cons of Agents for Managing Osteoporosis - 2

Agent	Pro's	Con's
BPs	↓ vert/nonvert/hip #s	GI, APR
		Atypical #, ?ONJ
		IV BPs are nephrotoxic
D'mab	↓ vert/nonvert/hip #s	Very low turnover, atypical #, ?ONJ
		Rapid offset – multiple vert #s
PTH	↓ vert & nonvert #s	Expensive, daily injections
		Cortical bone loss
		Efficacy against hip fracture?

Maintain 25OHD > 40 nmol/L
Year round

Conclusions - Osteoporosis

- Screen with BMD measurements
- Calcium from diet
- Vitamin D supplementation in frail elderly
- Potent bisphosphonates are the mainstay of treatment
- PTH analogues in severe disease
- Denosumab well tolerated but rapid offset
- Anti-sclerostin drugs are coming?