Guide to osteoporosis evaluation and management in primary care

Li Song, MD

University of Texas Southwestern Medical Center
Division of Endocrinology
Charles and Jane Pak Center for Mineral Metabolism and Clinical Research

2026

Disclosure

I have nothing to disclose.

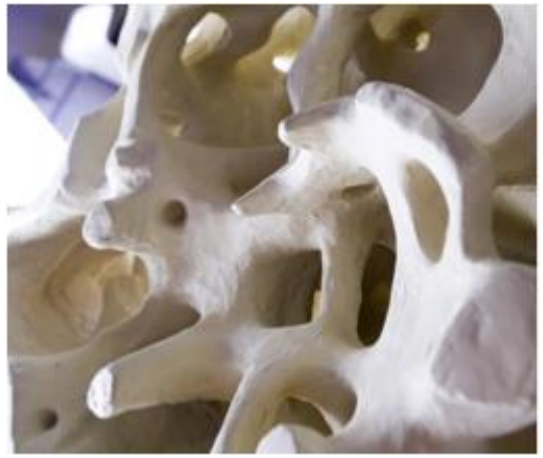
Osteoporosis: definition

Reduced bone mass (*quantity*)
Deteriorated microarchitecture (*quality*)

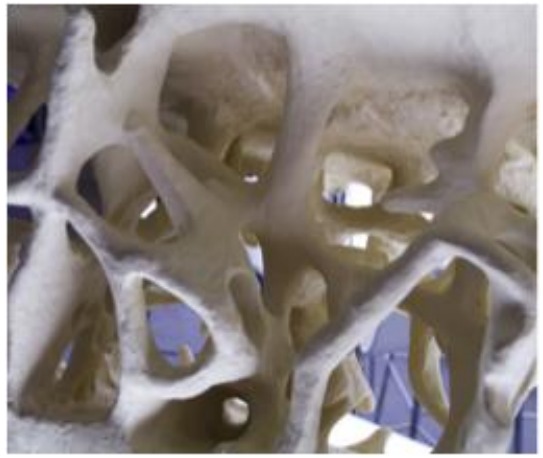
→

Decreased bone strength
Increased bone fragility

Normal

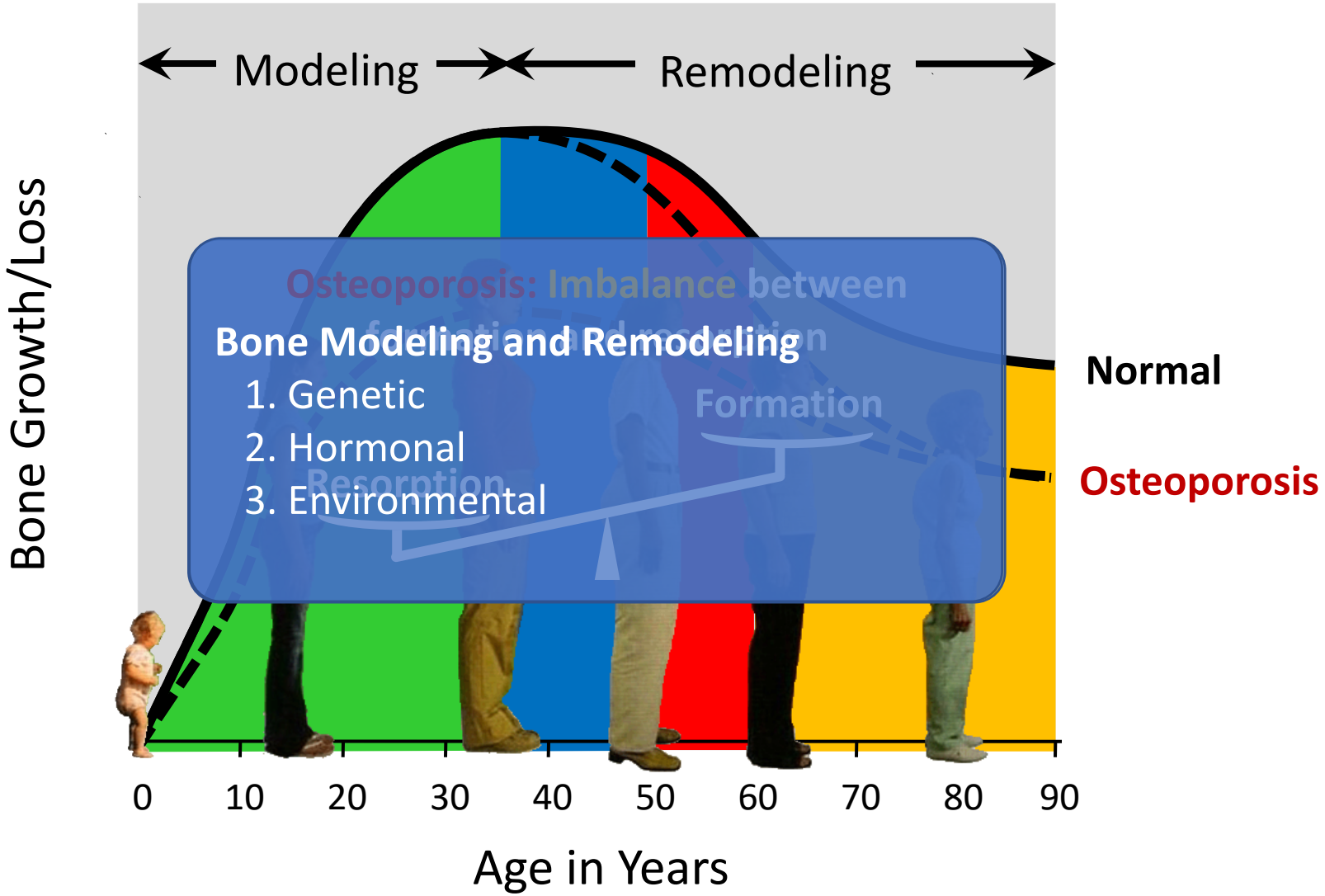


Osteoporosis



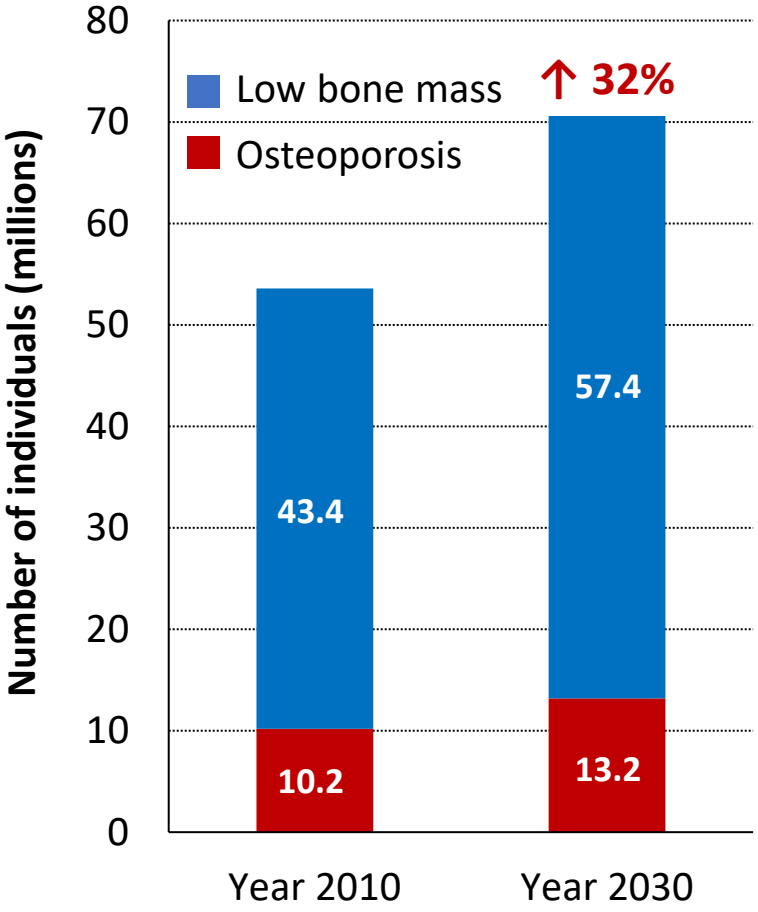
JA Kanis *et al*. *Osteoporos Int* 2001 and IOF The Breaking Spine 2020

Pathophysiology of Osteoporosis



Health and Economic Burden of Osteoporotic Fractures

Prevalence of osteoporosis and low bone mass among adults age ≥ 50 years in the U.S.



Fractures: annual incidence: **2 million**

Mortality and Morbidity

1-year mortality after hip fracture: **> 20% (higher in men)**

Needing long-term care: **20-50%**

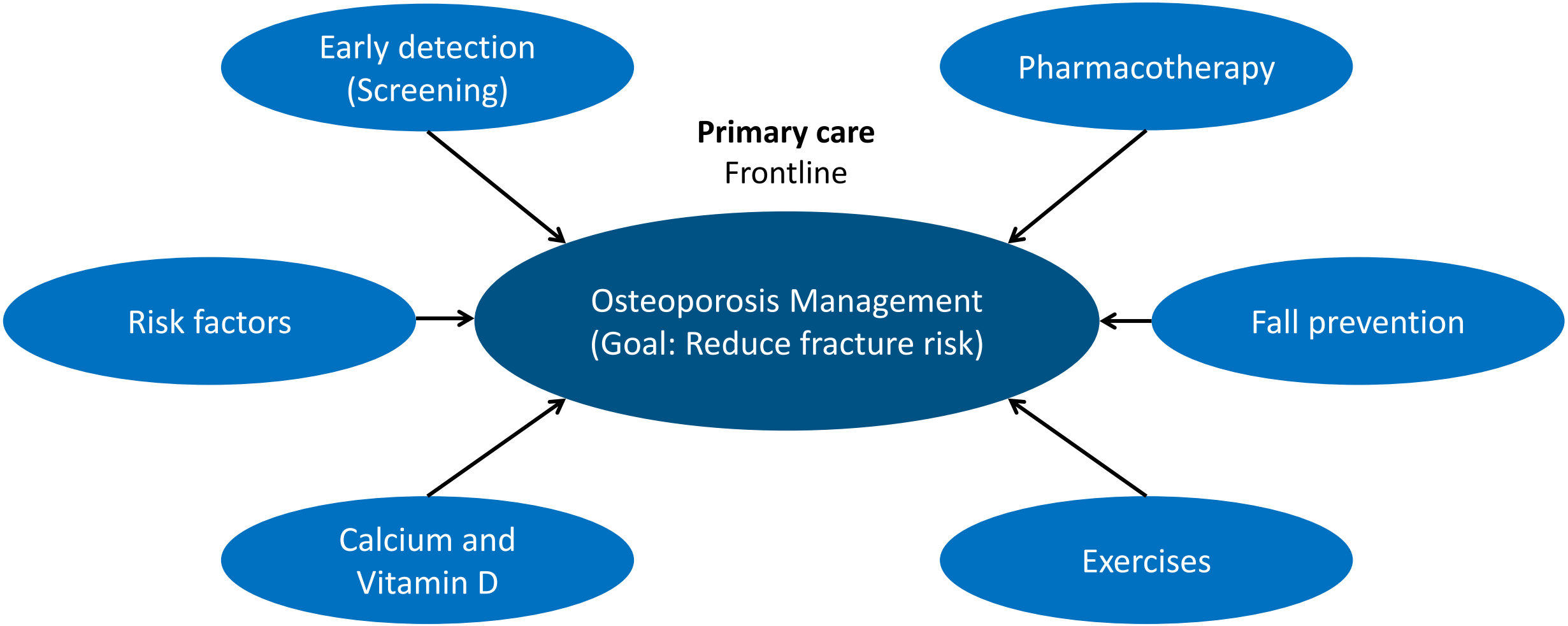
Annual cost: $17 billion

Gap in care:

- Under screened: **< 20%** women age ≥ 65 years had DXA
- Under treated: **< 10%** patients age ≥ 50 years receive osteoporosis mediations within 6 months after a hip fracture

NC Wright et al. JBMR 2014; Burg. JBMR 2007; EM Lewicki et al. Osteoporos Int. 2017; RJ Desai et al. JAMA 2018

Approach to Management of Osteoporosis



Screening

The US Preventive Services Task Force (USPSTF) recommends screening:

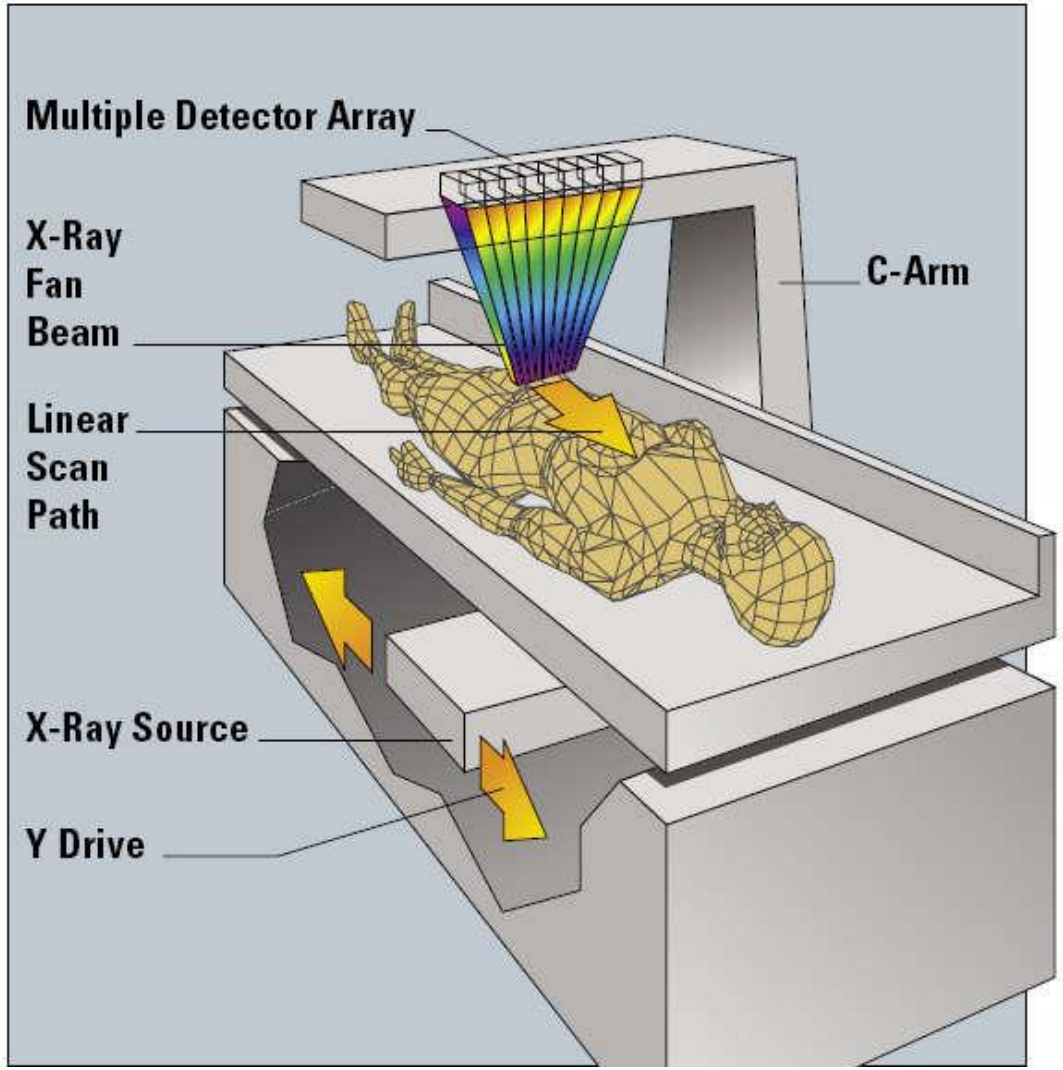
- Postmenopausal Women:
  - Age ≥ 65 years
  - Age < 65 year if at increased risk of fractures (*i.e.* additional risk factors)

- Men: evidence of benefits for screening is lacking *

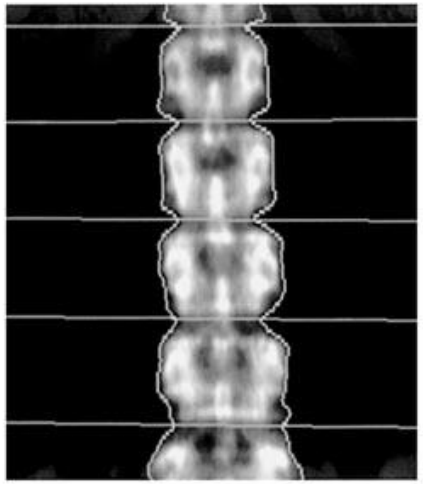
* Men get osteoporosis too and have a higher mortality after fractures than women. Some guidelines suggest screening men at age ≥ 70 years and younger if at risk

USPSTF, JAMA, 2025

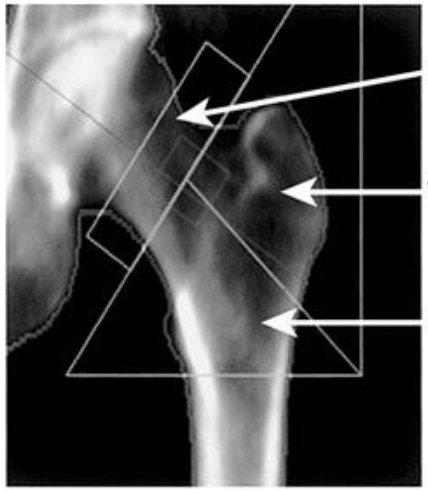
BMD Assessment by Dual X-ray Absorptiometry (DXA)



- Measure BMD at spine and hip in all patients



Lumbar spine



Proximal femur

Total hip = FN + troch + intertroch

- Measure Forearm BMD if:
  - Hyperparathyroidism
  - Hip and/or spine BMD cannot be measured
  - Very obese patient (> weight limit for table)

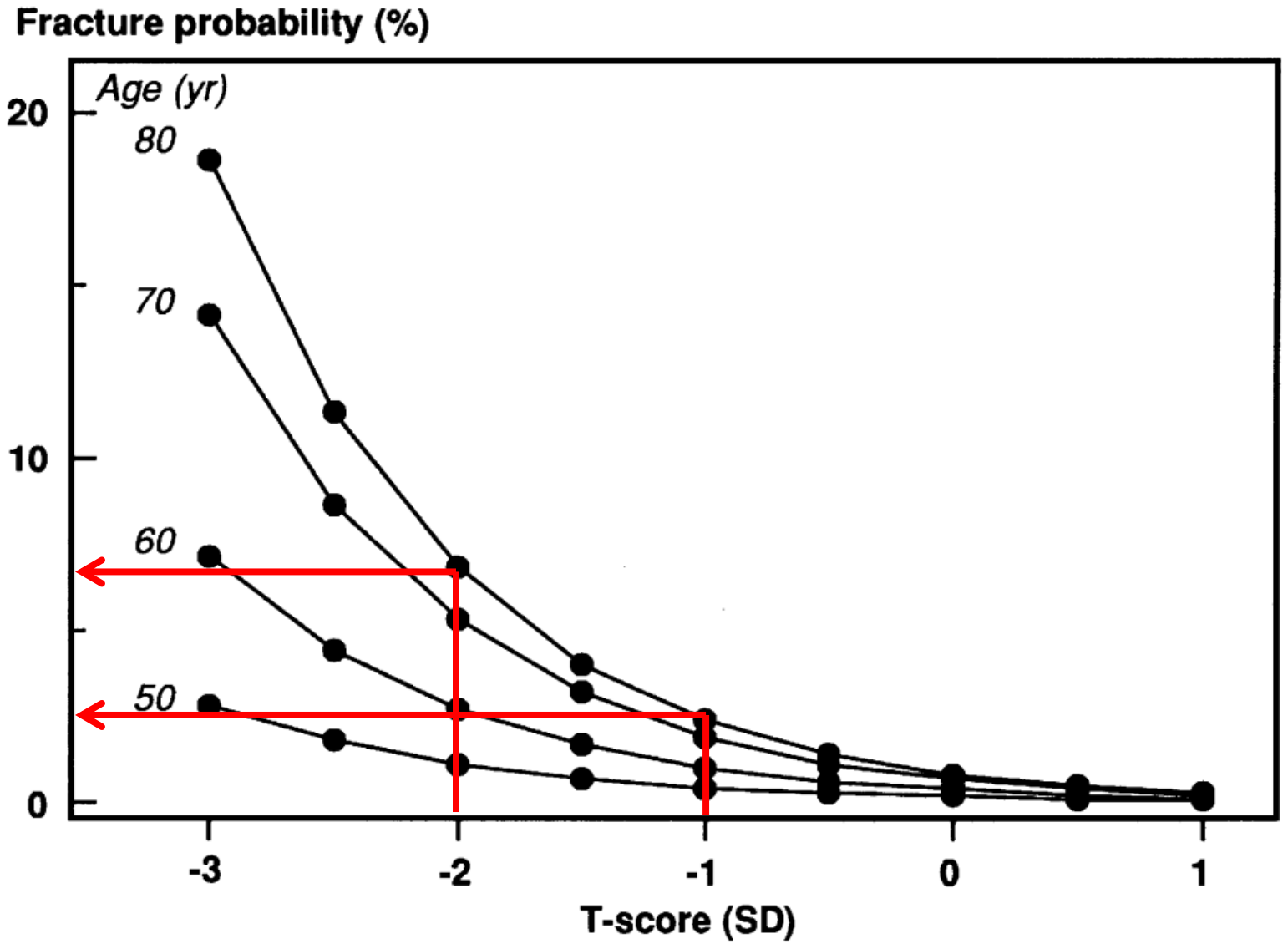
Osteoporosis: diagnosis by DXA

WHO diagnostic threshold in **postmenopausal women** and **men ≥ age 50:**

	T-score
Normal	≥ - 1.0
Low bone mass (osteopenia)	Between -1.0 and -2.5
Osteoporosis	≤ -2.5
Severe osteoporosis	≤ -2.5 with fragility fracture

2023 ISCD Official Positions: Adult

Femoral neck T-score and Hip Fracture Incidence



Kanis JA, Osteoporosis Int, 2001

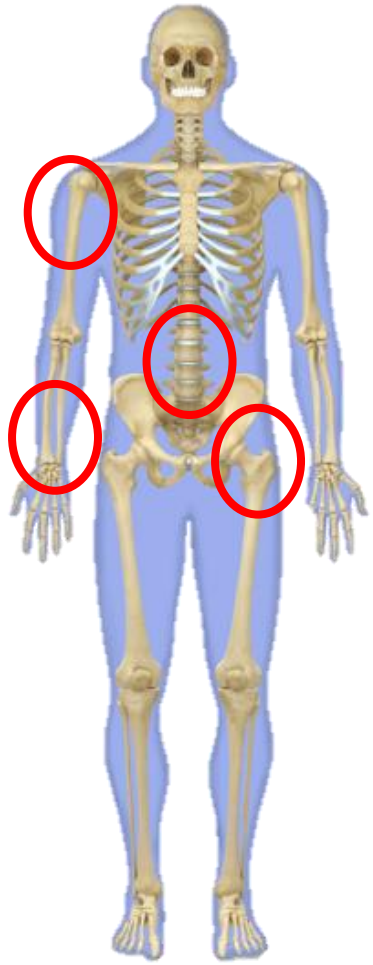
Osteoporosis: diagnosis by fragility fractures

Fragility fracture:

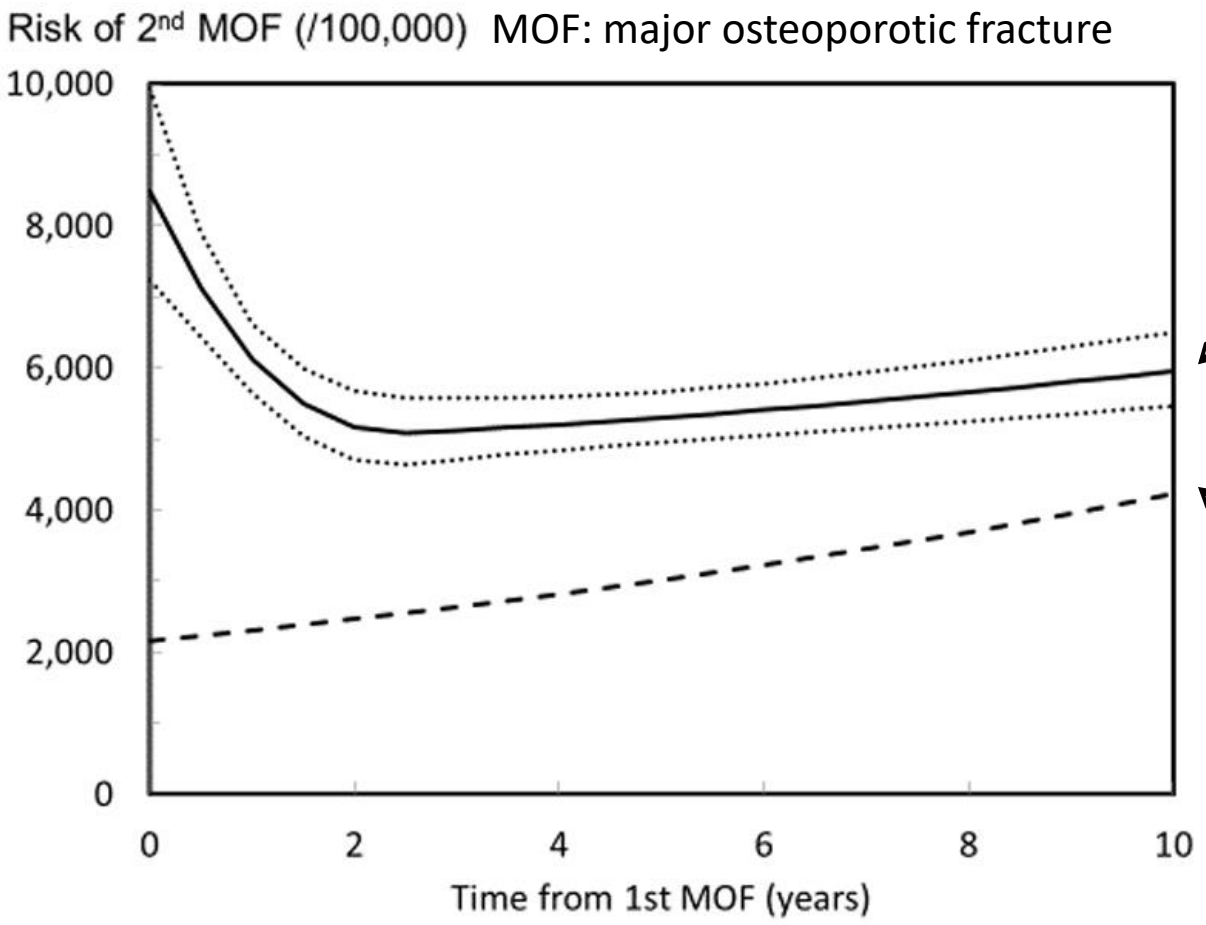
- Low energy trauma (fall from standing height or less)

- Classic sites:
  - Vertebral, proximal femur, distal forearm, proximal humerus

- Not considered osteoporotic fractures:
  - Skull, face, hands, feet, patella



Imminent Risk of Fracture after a Fracture



Risk of 2nd MOF after a 1st MOF for a woman at age 75 years at her 1st MOF

Risk of 1st MOF in whole population for a woman 75 years at baseline

Cummings SR. *et al. JBMR* 2016 , Johansson H. *et al. Osteoporos Int.* 2017

Case 1: Ms. A

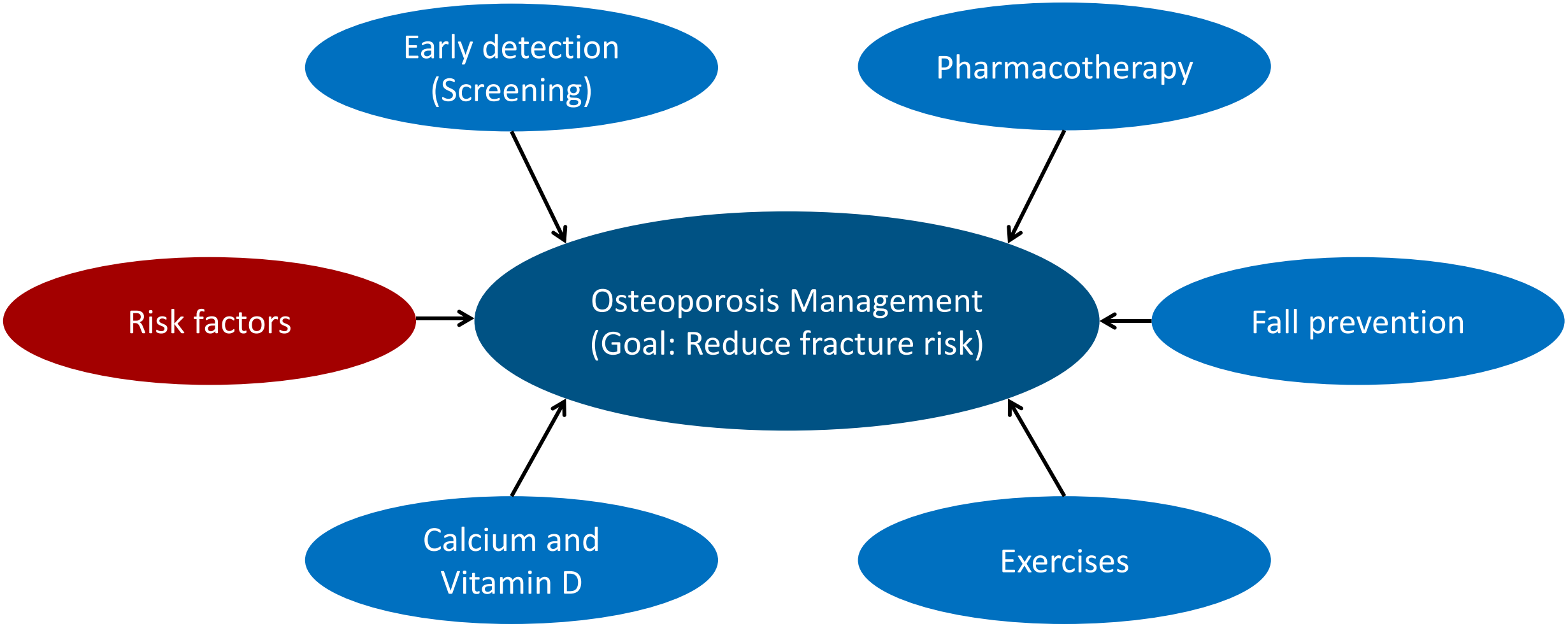
60-year-old Caucasian woman with a history of rheumatoid arthritis (RA) and breast cancer who presents for primary care visit. For RA, she took prednisone for 4 weeks in her 40s and currently takes methotrexate. For breast cancer, she underwent lumpectomy, chemotherapy, radiation and 5 years of anastrozole (last use at age 55). Family history is significant for her mother with osteoporosis and hip fracture. She has no prior fractures.

Region	BMD (g/cm^2)	T-score	Z-score
Lumbar spine	0.905	-1.5	-1.3
Left femoral neck	0.792	-1.1	-0.2
Left total hip	0.820	-0.5	+0.3

Impression: Osteopenia

What's next?

Approach to Management of Osteoporosis



Evaluation: Risk factors and secondary causes

Why is evaluation important?

- Prevalence of secondary osteoporosis:
  - Postmenopausal women: 20-30%
  - Premenopausal women: > 50%
  - Men: 30-60%

- Bone loss may be reversible
- Response to therapy may be incomplete
- Impact on choice of therapy

Ebeling PR, *et al*, *Endocrine Reviews*, 2022

Risk factors

Non-modifiable	**Modifiable**
• Age	• Current smoking
• Sex	• Excessive alcohol use
• Race	• Low body weight
• Prior fractures	• Calcium and vitamin D intake
• Family history	• Physical activity
• Early menopause	• Fall risk

Secondary causes

GI
- Celiac disease
- IBD
- Primary biliary cholangitis
- Chronic hepatitis
- Hemochromatosis
- Liver transplant

Rheumatology
- Rheumatoid arthritis
- Ankylosing spondylitis

Infectious diseases:
- HIV

Psychiatry:
- Anorexia nervosa

Cardiology
- Heart transplant

Endocrine
- Hypogonadism
- Hyperparathyroidism
- Cortisol excess
- Hyperthyroidism
- T1DM
- T2DM
- Post-bariatric surgery

Hematology / oncology:
- Multiple myeloma
- MGUS
- Mastocytosis
- Thalassemia
- Stem cell transplant
- Prostate cancer
- Breast cancer

Osteoporosis / Osteopenia

Screening

Nephrology
- CKD-MBD
- Hypercalciuria
- Distal RTA
- Renal transplant

Pulmonary
- Cystic fibrosis
- COPD
- Lung transplant

Neurology
- Cerebral palsy
- Duchenne muscular dystrophy
- Multiple sclerosis
- Parkinson disease
- Post stroke

Medications:
- Glucocorticoid
- Anti-convulsant
- Depo-Provera
- Aromatase inhibitor
- GnRH agonists
- Androgen deprivation therapy
- Pioglitazone
- Tenofovir disoproxil fumarate
- Calcineurin inhibitors
- SSRI
- PPI

PR Ebeling, *et al. Endocrine Reviews*, 2022

Laboratory studies

For all:

- **Blood:** CMP, Phos, CBC, 25(OH)D, PTH
- **24-hour urine:** calcium, creatinine

Consider:

- **Blood:** Mg, TSH, testosterone, SPEP, celiac screen
- **24-hour urine:** UPEP, cortisol

F Cosman *et al. Osteoporo Int* 2014 and PM Camacho *et al. Endocrine Practice* 2020

Case 1: Ms. A has osteopenia

60-year-old Caucasian woman with a history of RA and breast cancer. For RA, she took prednisone for 4 weeks in her 40s. For breast cancer, she received 5 years of anastrozole. Family history is significant for her mother with osteoporosis and hip fracture. No prior fragility fractures.

Additional risk factors from H&P:

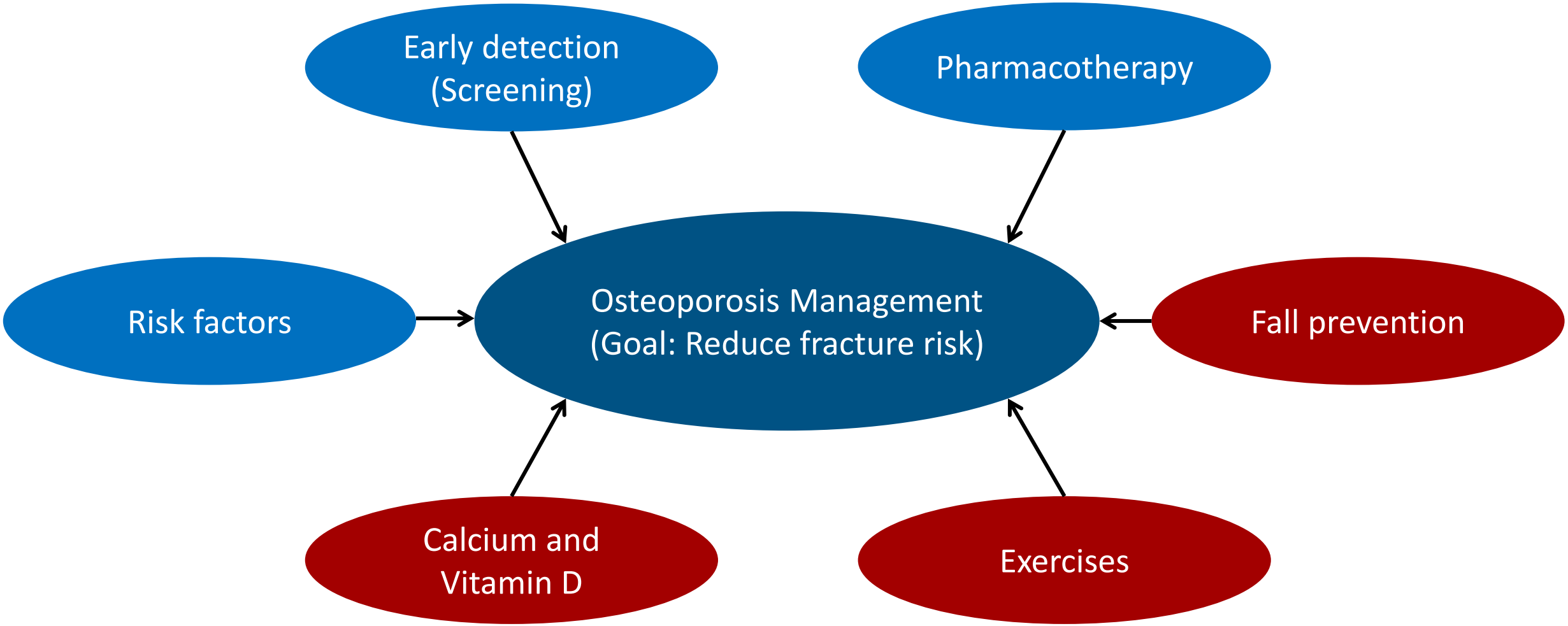
- Menopause: age 50
- No calcium or vitamin D supplement
- 1 glass of milk per day
- Sedentary

Laboratory studies:

- CMP, Phos, PTH, CBC, and SPEP: normal
- 25(OH)D: 25 ng/mL (ref range: 30-80 ng/mL)
- 24-hour U_{Ca}: 88 mg/day (ref range: 100-250 mg/day)
- 24-hour U_{Cr}: 990 mg/day

Therapy plan?

Management: Non-pharmacological



Management: Non-pharmacological

Recommend for **all** patients with osteoporosis or osteopenia

- **A** Alcohol / Smoking
- **B** BMD by DXA
- **C** Calcium intake
- **D** Vitamin D intake
- **E** Exercise
- **F** Fall prevention

Rx

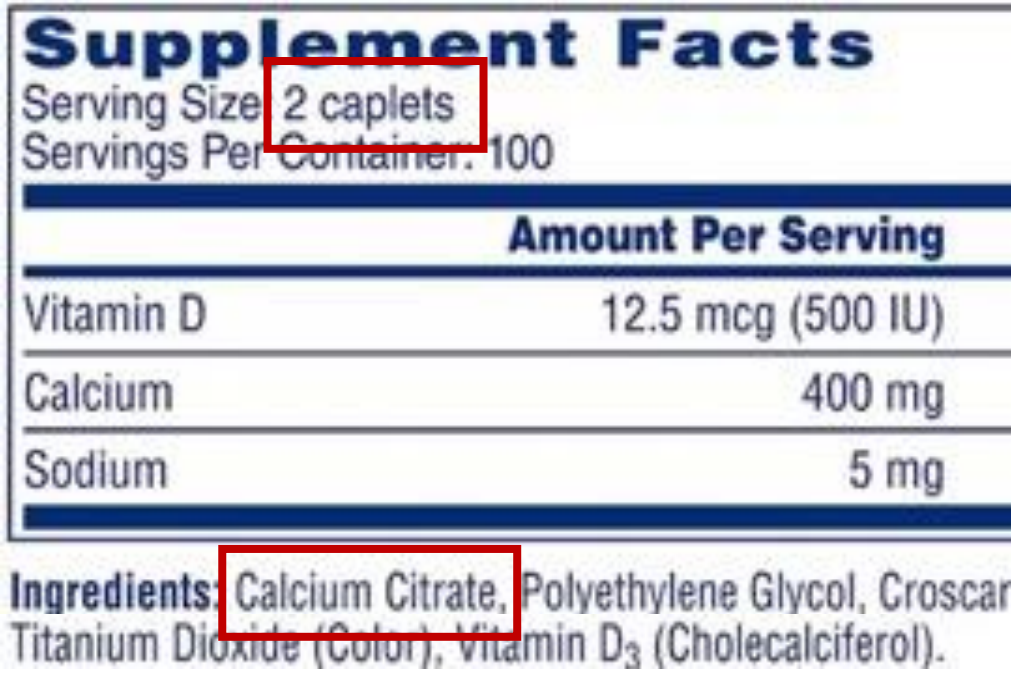
Provide specifics

Calcium

Age (years)	Calcium intake (mg/day)
Men > 70 and Women > 50	1200
Younger adults	1000

Estimate daily calcium intake

Non-dairy sources	250mg
Dairies (1 serving)	300mg
Calcium fortified	Varies
Calcium supplement	Varies
Total	1200mg



Supplement Facts

Serving Size 2 caplets

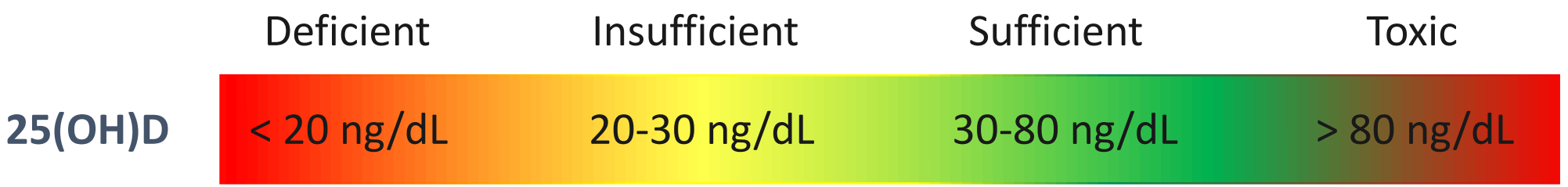
Servings Per Container: 100

	Amount Per Serving
Vitamin D	12.5 mcg (500 IU)
Calcium	400 mg
Sodium	5 mg

Ingredients: Calcium Citrate, Polyethylene Glycol, Croscar
Titanium Dioxide (Color), Vitamin D_3 (Cholecalciferol).

F Cosman *et al. Osteoporo Int* 2014, PM Camacho *et al. Endocrine Practice* 2020, and AC Ross *et al. JCEM* 2011

Vitamin D



? Optimal: 30-50 ng/dL

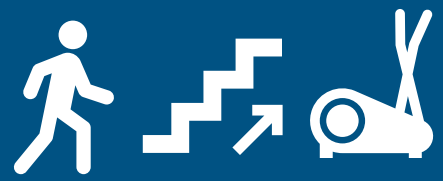
Cholecalciferol (vitamin D3) is better at raising and maintaining 25(OH)D than ergocalciferol (vitamin D2)

Cholecalciferol 1000 IU daily will typically raise 25(OH)D by 10 ng/dL (some may need more)

L Tripkovic *et al. Am J Clin Nutr* 2012

Exercise

Weight-bearing



30 minutes / day
5 days / week
Moderate intensity

Resistance

8-10 reps x 1-2 sets
2-3 days / week
Can do > 10 reps: too light
Cannot do > 8 reps: too heavy

CAUTION

Forward bending
Twisting
High impact loading
Abrupt movements

Balance

Daily

Posture

5-10 minutes daily

Physical therapy

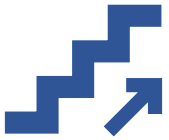
Balance and gait
Muscle strength and function
Posture
Coordination
Functional exercises (ADL)

NOF. IOF, Osteoporosis Canada, and UK Royal Osteoporosis Society

Fall prevention

Declutter

Non-slip mats



Handrail

Shower chair

Lighting

Medications

Alcohol

Nutrition

Vision

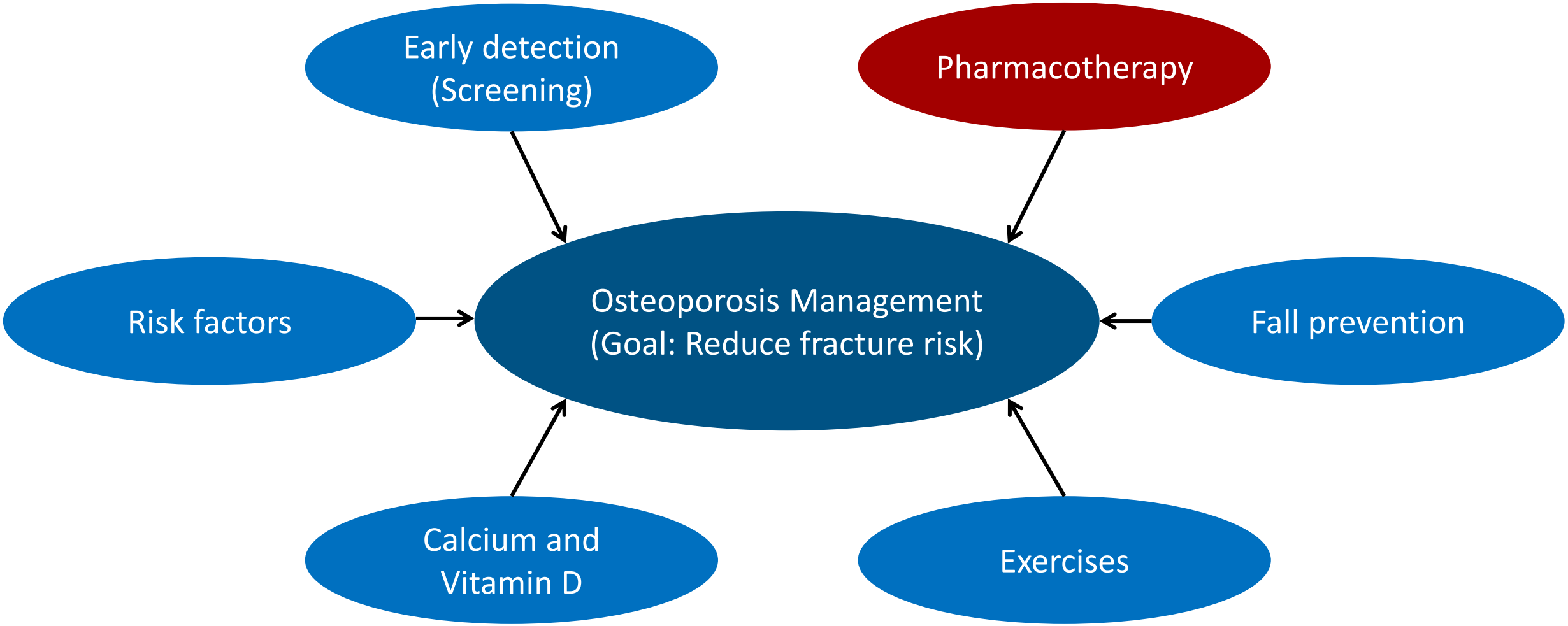
Shoes

Exercise

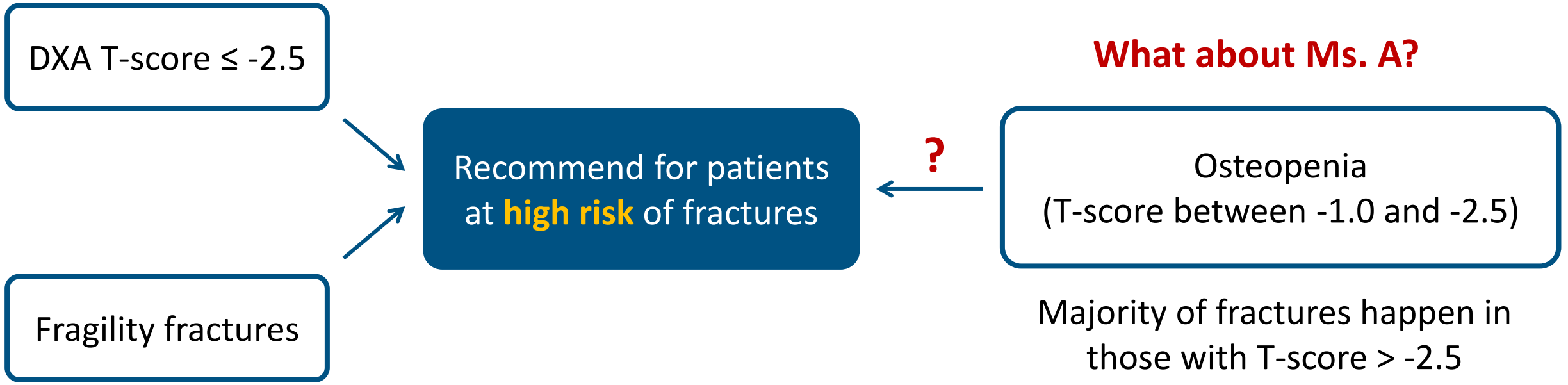
Case 1: Ms. A's "prescription"

	Ms. A: current lifestyle	We recommended
A Alcohol / Smoking		Rx
B BMD by DXA		
C Calcium intake	8oz milk, no supplement	Additional 600-650mg
D Vitamin D intake	25(OH)D: 25 ng/mL	Cholecalciferol 1000 IU daily
E Exercise	Sedentary	Walk 30 minutes/day x 5 days/week
F Fall prevention		Resistance exercises 2-3 days/week

Management: Pharmacotherapy



Management: Pharmacotherapy



How do we capture the high-risk patients when T-score > -2.5?

Fracture Risk Assessment Tool (**FRAX**)

FRAX (Fracture Risk Assessment Tool)

Predicts 10-year probability of a major osteoporotic fracture (MOF) and hip fracture

Pros	Limitation
• Better predicts risk than using BMD alone	• Use limited to treatment-naïve patients
• Capture high risk patients with T-score > -2.5	• Does not capture dose response or some risk factors (*e.g.* falls, T2DM, recency of fracture, *etc*)
• Yes / no responses (simple to use)	• Underestimates risk in those with low BMD at spine

2008: FRAX → **2014: TBS-adjusted FRAX**

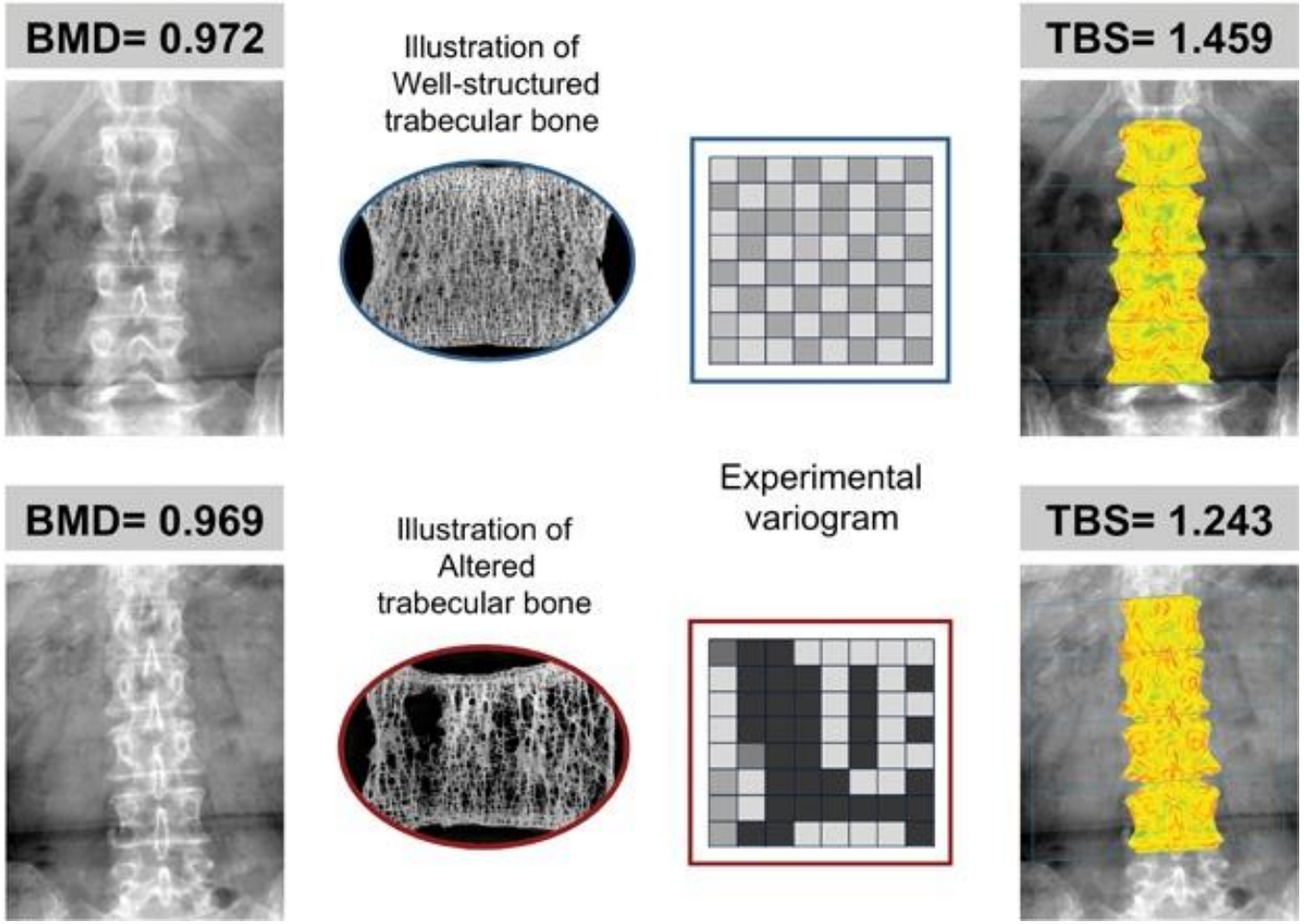
2025: FRAXplus®

TBS: trabecular bone score

BMD: *quantity* of bone

TBS: *quality* of bone (indirect measure)

TBS predicts fractures: independently from BMD, FRAX and clinical risk factors



BC Silva *et al. JBMR* 2014 and G Shafiee *et al. J Diabetes Metab Disord.* 2020

FRAXplus®

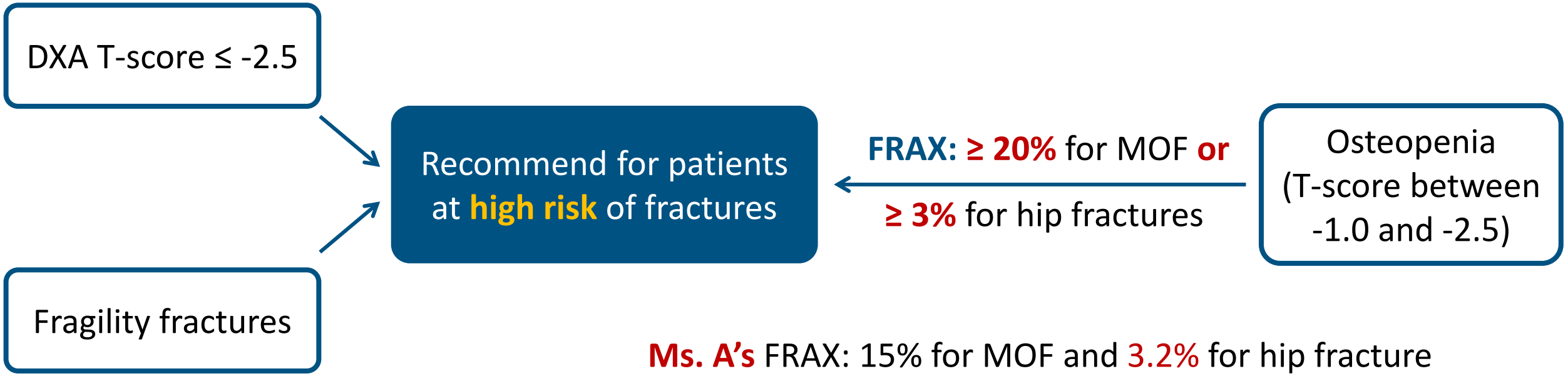
Further adjusts fracture risk by the following:

- TBS
- Fractures (number, recency, sites)
- Falls within the previous year
- Glucocorticoid dose
- Duration of T2DM
- Primary hyperparathyroidism
- Lumbar spine BMD
- Hip axis length

Limitations:

- No evidence base available on the accuracy of multiple adjustments.
- Cost

What about pharmacotherapy?



Ms. A's FRAX: 15% for MOF and 3.2% for hip fracture

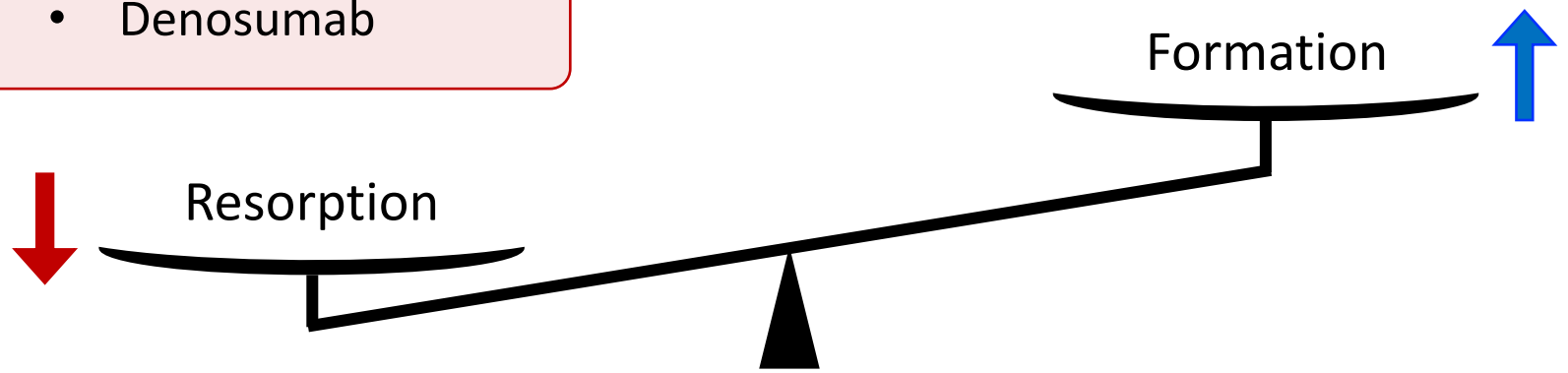
Pharmacotherapy is indicated

MOF: major osteoporotic fractures

Pharmacotherapy: what drugs are available?

Anti-resorptive:
- HRT
- SERMs
- Bisphosphonates
- Denosumab

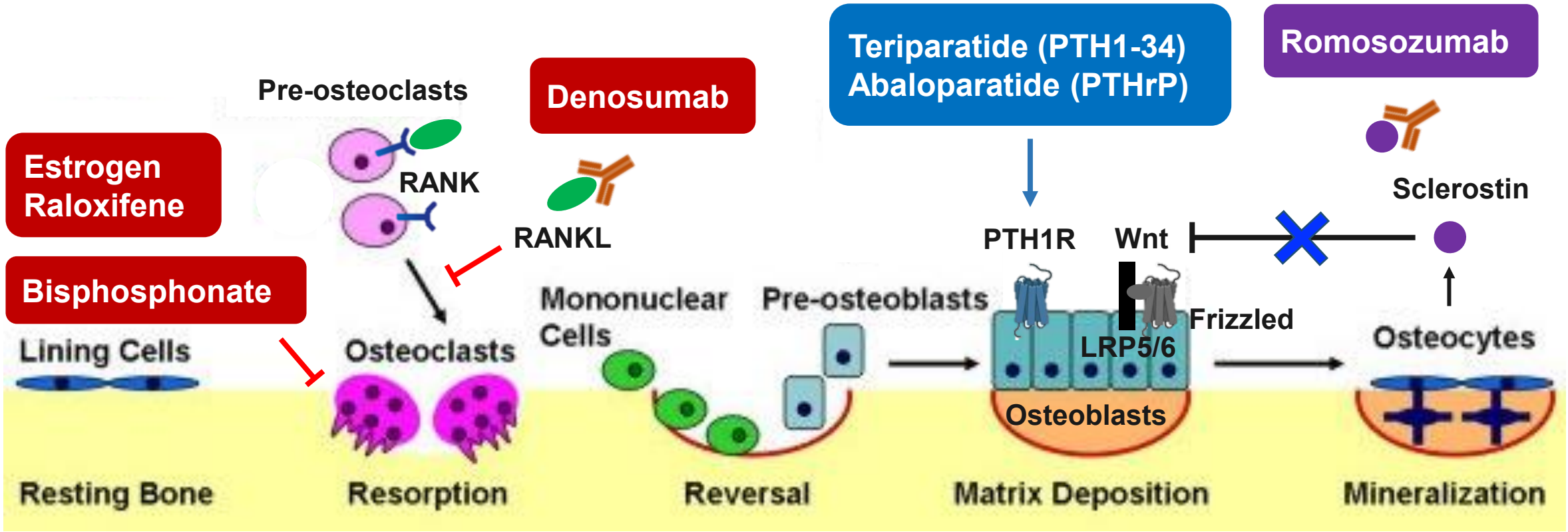
Anabolic:
- Teriparatide
- Abaloparatide
- Romosozumab*



An Imbalance in Bone Remodeling

*Dual action: increase formation and decrease resorption

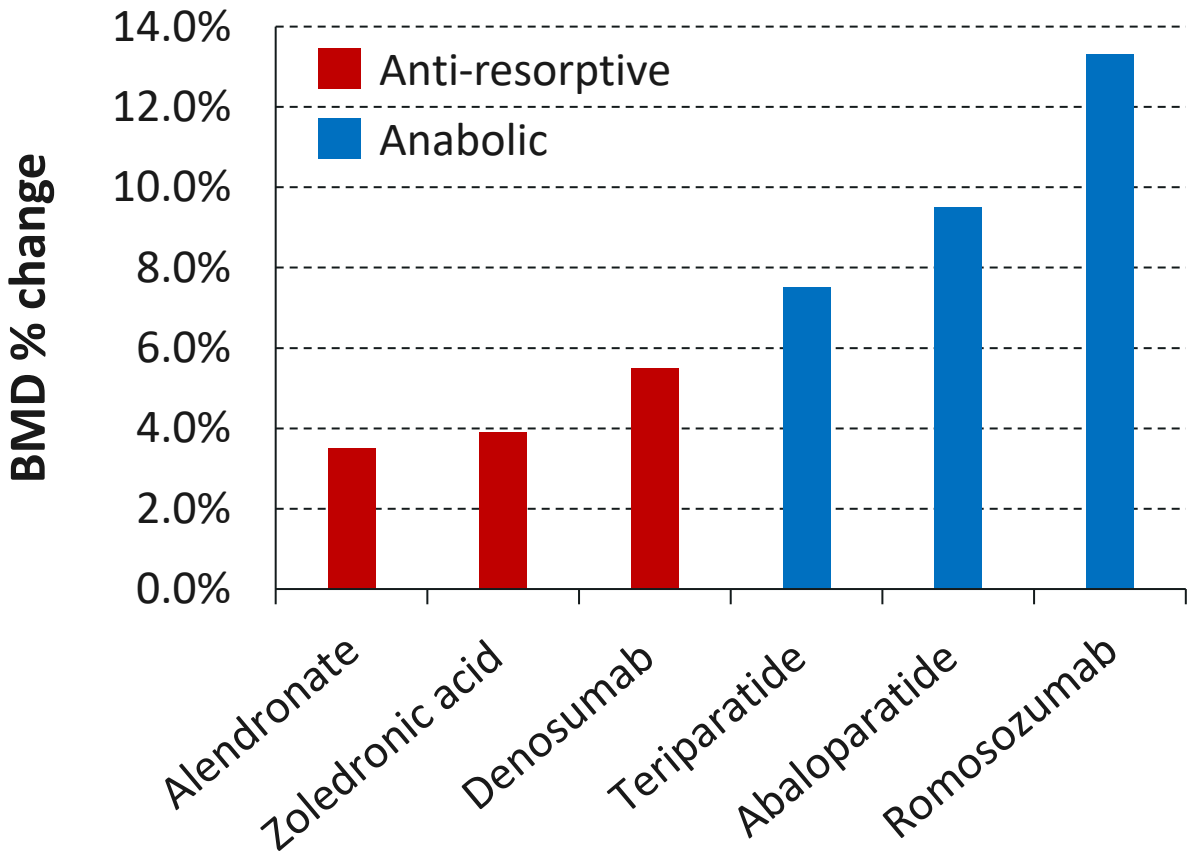
How do they work?



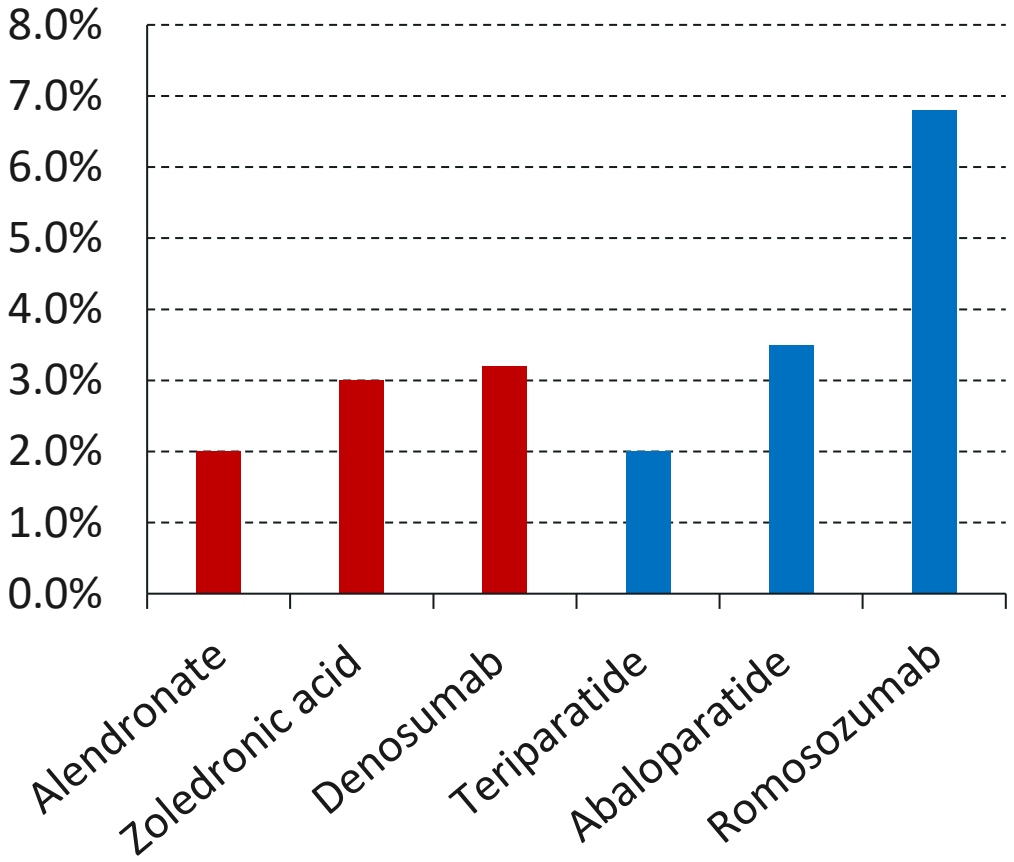
Picture adopted from K Kapinas *et al. Arthritis Research &Thera*py 2011 with modifications

Efficacy: effects on BMD*

BMD % change from baseline at 12 months at lumbar spine

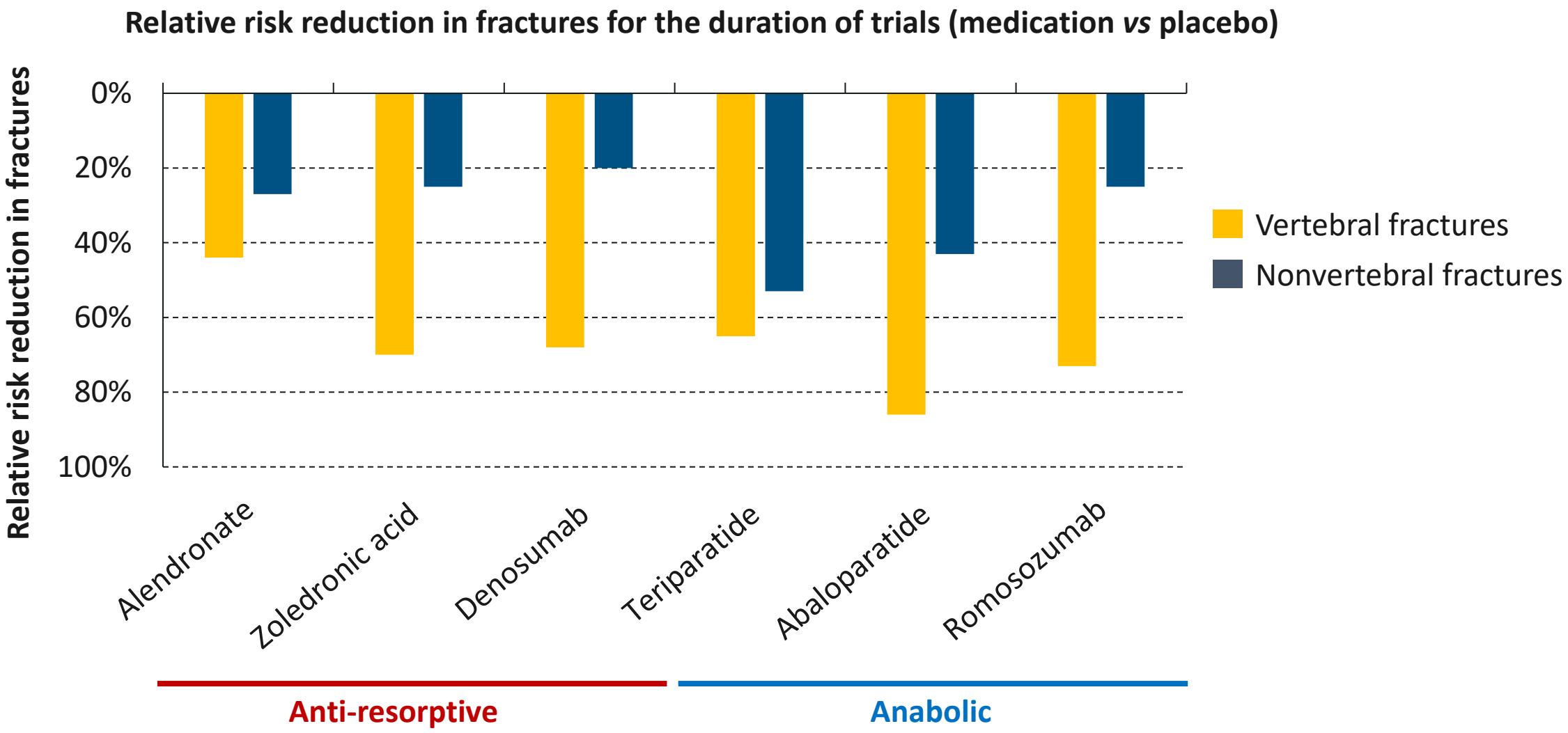


BMD % change from baseline at 12 months at total hip



* **Not directly comparable due to from different trials:** FIT, HORIZON, FREEDOM, Neer *et al*., ACTIVE, and FRAME trials

Efficacy: effects on fracture reduction*



* **Not directly comparable due to from different trials:** FIT, HORIZON, FREEDOM, Neer *et al*., ACTIVE, and FRAME trials

FDA approved indications

	Postmenopausal osteoporosis prevention	Postmenopausal osteoporosis	Osteoporosis in men	Glucocorticoid induced osteoporosis
Raloxifene	✓	✓		
Oral bisphosphonate	✓	✓	✓	✓
IV Zoledronic acid (Reclast)	✓	✓	✓	✓
SC Denosumab (Prolia)		✓	✓	✓
SC Teriparatide*		✓	✓	✓
SC Abaloparatide*		✓	✓	
SC Romosozumab*		✓		

* Osteoporosis at high risk for fracture (history of fragility fracture or multiple risk factors for fractures) or who have failed or are intolerant to other osteoporosis therapy.

Choice of pharmacotherapy: treatment strategies

Standard (stepwise) therapy

First line: **bisphosphonate**

↓ Poor response / Intolerance

Alternative therapy

Treat to target (personalized)

Start with: **Anabolic / injectable therapies**

↓ **Very high-risk patients**
High imminent fracture risk
Very low T-score < -3.0

Rapidly reduce fracture risk
Target T-score > -2.5 (or > -2.0)

Camacho PM *et al* Endocrine Practice 2020 and Shoback D *et al* JCEM 2020

Other considerations: side effects / contraindications

	Contraindications / Caution
Oral bisphosphonate *	• Active esophageal disease • Inability to stand/sit upright for ≥ 30 to 60 minutes • Renal dysfunction • Hypocalcemia
IV zoledronic acid *	• Renal dysfunction • Hypocalcemia
SC denosumab *	• **Blackbox warning:** severe hypocalcemia in advanced CKD • Poor compliance (rapid bone loss with missing / delayed doses)

Oral bisphosphonate:
Empty stomach
Alone with 6-8oz water (cannot combine with other medications)
Wait for 30 (or 60) minutes before taking other medications or eating breakfast
Stay upright for 30 (or 60) minutes after taking it

* For patients with chronically low alkaline phosphatase, hypophosphatasia should be ruled out BEFORE starting anti-resorptive therapy.

Other considerations: side effects / contraindications

	Contraindications / Caution

SC teriparatide/ abaloparatide	• Avoid in patients with increased risk of osteosarcoma
	  • Open epiphyses
	  • Paget's disease of bone
	  • Osteosarcoma / bone metastases
	  • Radiation therapy involving skeleton
	• Avoid in patients with hypercalcemia

SC romosozumab	• **Blackbox warning:** avoid in patients with MI / Stroke within the past year

Other considerations: cost, compliance, convenience

	Annual cost
Alendronate	$48*
Risedronate	$360*
Ibandronate	$96*
Zoledronic acid	$130
Denosumab (Prolia)	$3,070
Teriparatide	$35,640
Abaloparatide (Tymlos)	$30,552
Romosozumab (Evenity)	$26,280

Lowest listed average wholesale price from Red Book Online®

*Cost from GoodRx

Patient compliance:

- If non-compliant, the following may not be ideal:
  - Denosumab
  - Oral bisphosphonate

Patient preference:

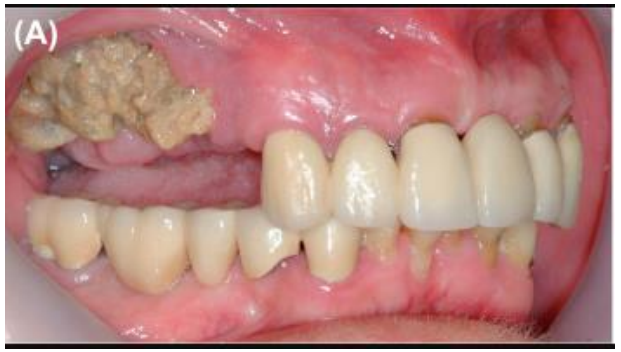
- Oral and less frequency preferred

Assess response to therapy

	Good Response	Poor Response
BMD by DXA:	BMD stabilizes or increases (over LSC*)	BMD decreases (over LSC*)
Fragility fracture:	≤ 1 fragility fracture	≥ 2 fragility fractures

Least significant change (LSC): Expected normal inter-measurement variation
Important to do DXA at the same facility on the same machine

Risks of long-term bisphosphonate: Osteonecrosis of Jaw (ONJ)



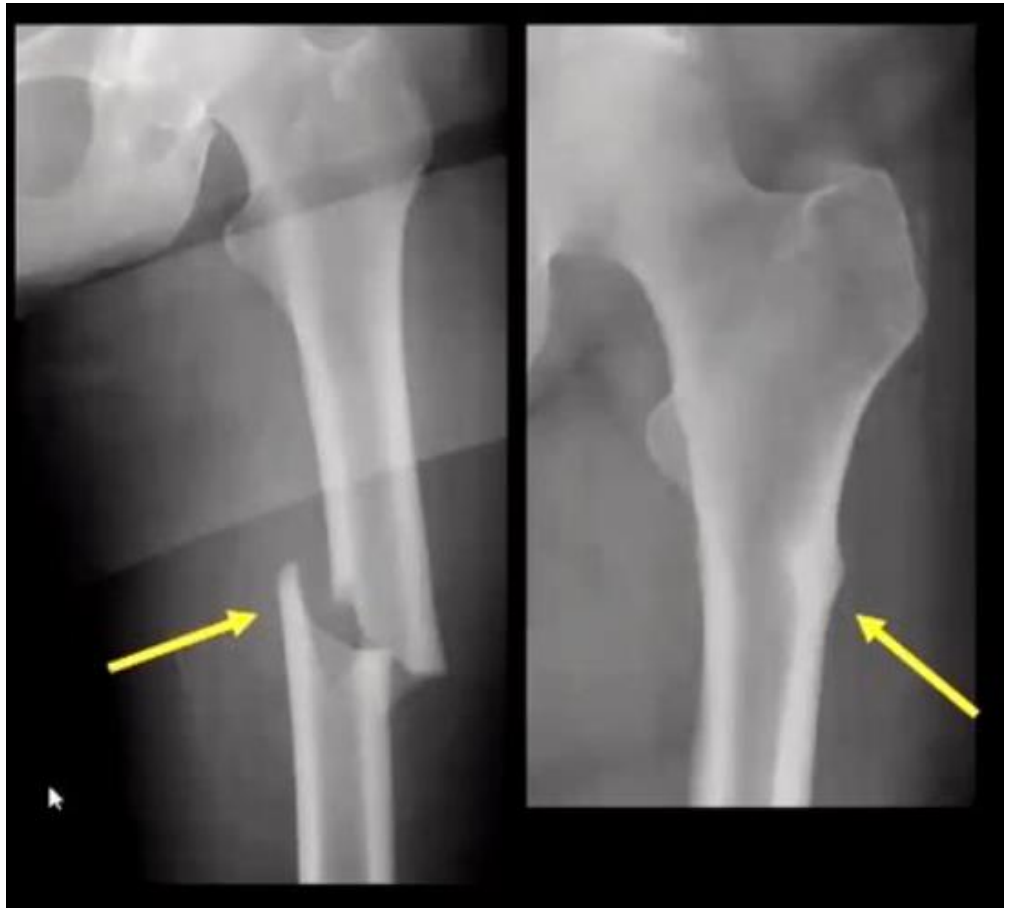
- **Incidence of ONJ:**
  - < 0.001% to 0.15% (osteoporosis use) *vs* 1-15% (oncologic use)
- **Risk factors:**
  - Dose, frequency and duration
  - Invasive dental procedures, poor oral hygiene, smoking, glucocorticoid, chemotherapy, radiation
- **Prevention is key:** Dental hygiene: baseline and routine dental care
- **What to do for dental procedures (extraction, implants)?**
  - Oral bisphosphonate: hold for 2 months prior to procedure
  - Denosumab: time procedure 4 months after denosumab dose to allow 2 months for healing before next dose

Ruggiero et al. AAOMS 2022 Update and ADA.org

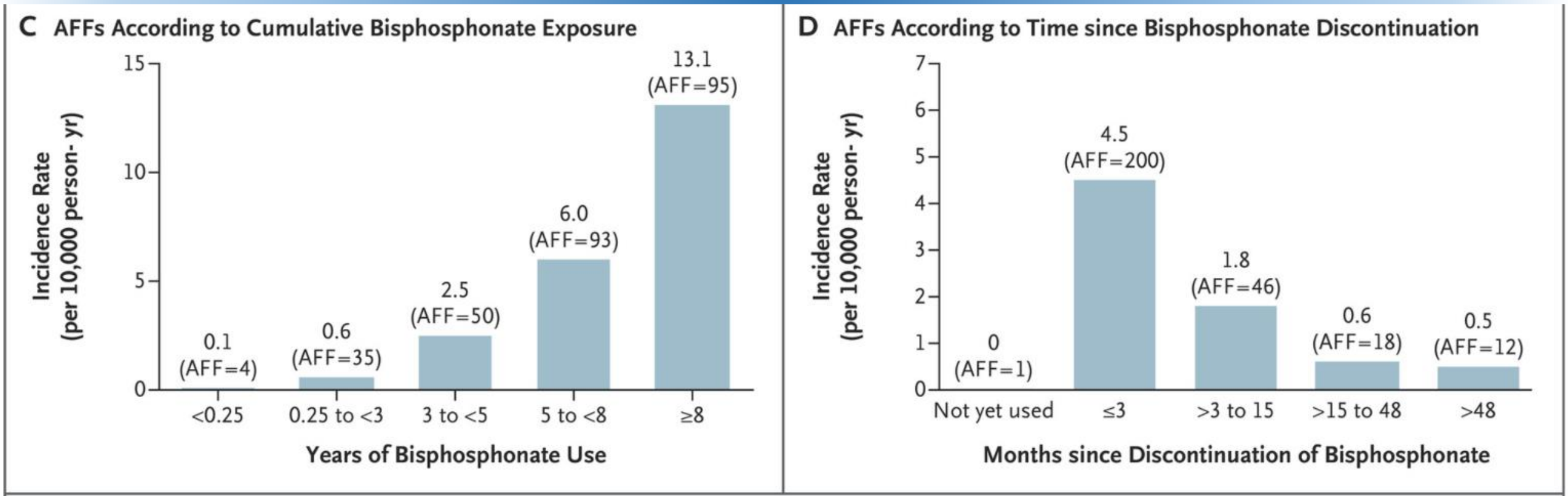
Risks of long-term bisphosphonate: Atypical femur fracture (AFF)

Prodromal: deep thigh or groin pain

Occurs spontaneously or with minimal trauma



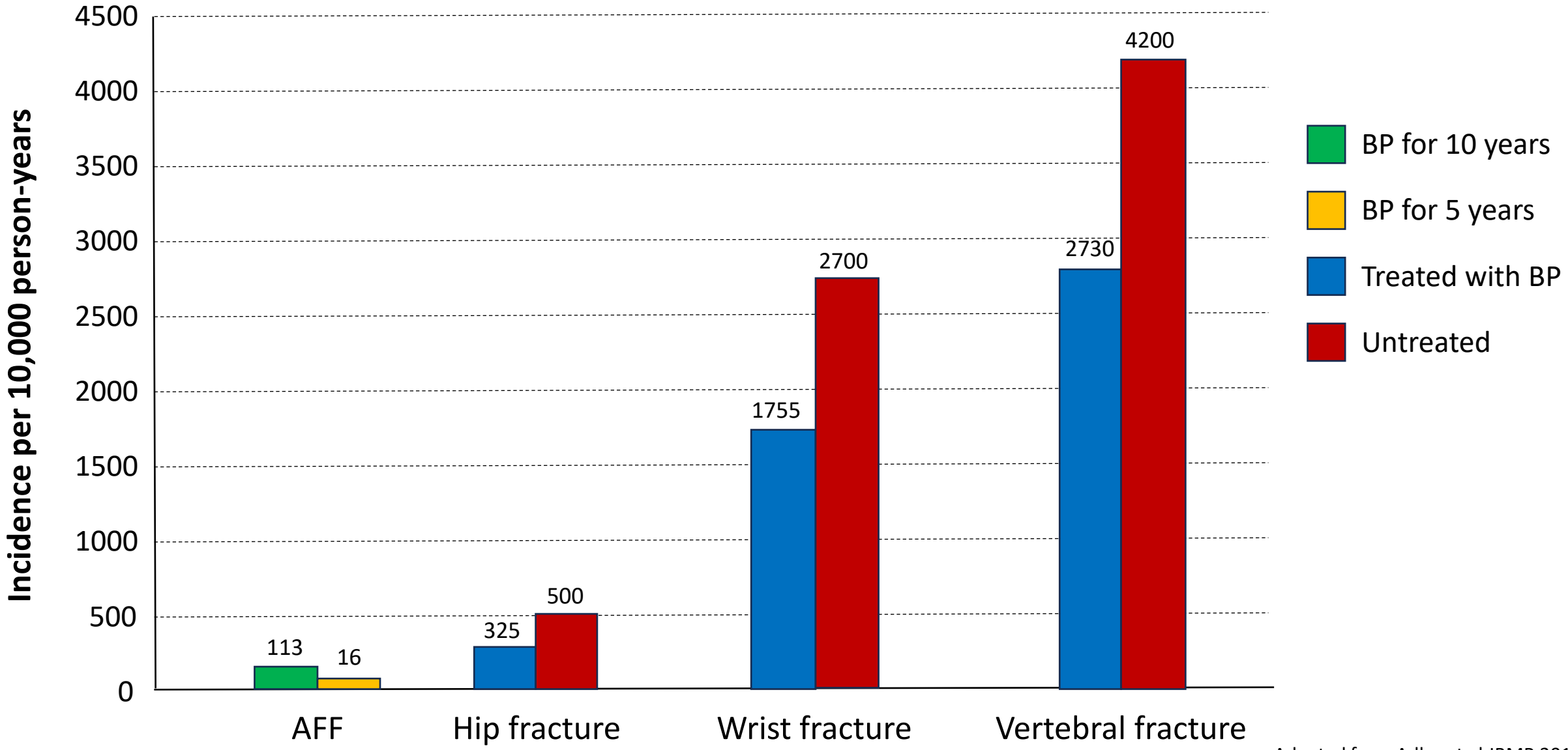
AFFs increase with BP duration



Risk of AFF significantly rises after 5 years of BP
Risk drops to near baseline after stopping BP for 15 months

Black D et al NEJM 2020

Risk of untreated osteoporosis *vs* AFF



Adapted from Adler et al JBMR 2016

Duration of bisphosphonate therapy

Oral bisphosphonate: 5 years
IV bisphosphonate: 3 years

↓

Reassess risk

↓

Low-moderate risk:
- Normal or osteopenia on DXA
- Lack of fragility fracture

↓

Bisphosphonate holiday

High-very high risk:
- Osteoporosis on DXA
- Fragility fracture

↓

Continue bisphosphonate
- Oral: additional 5 years
- IV: additional 3 years

Switch to alternative therapies

Monitoring during bisphosphonate holiday:
- ABCDEF
- Fragility fracture
- DXA every 1-2 years

Duration of non-bisphosphonate therapy

	Duration
Denosumab	Up to 10 years or longer
Teriparatide	Up to 2 years
Abaloparatide	Up to 2 years
Romosozumab	1 year

*Teriparatide and romosozumab: treatment course can be repeated if needed in the future

Non-bisphosphonate: AVOID drug holiday

Non-bisphosphonate therapies

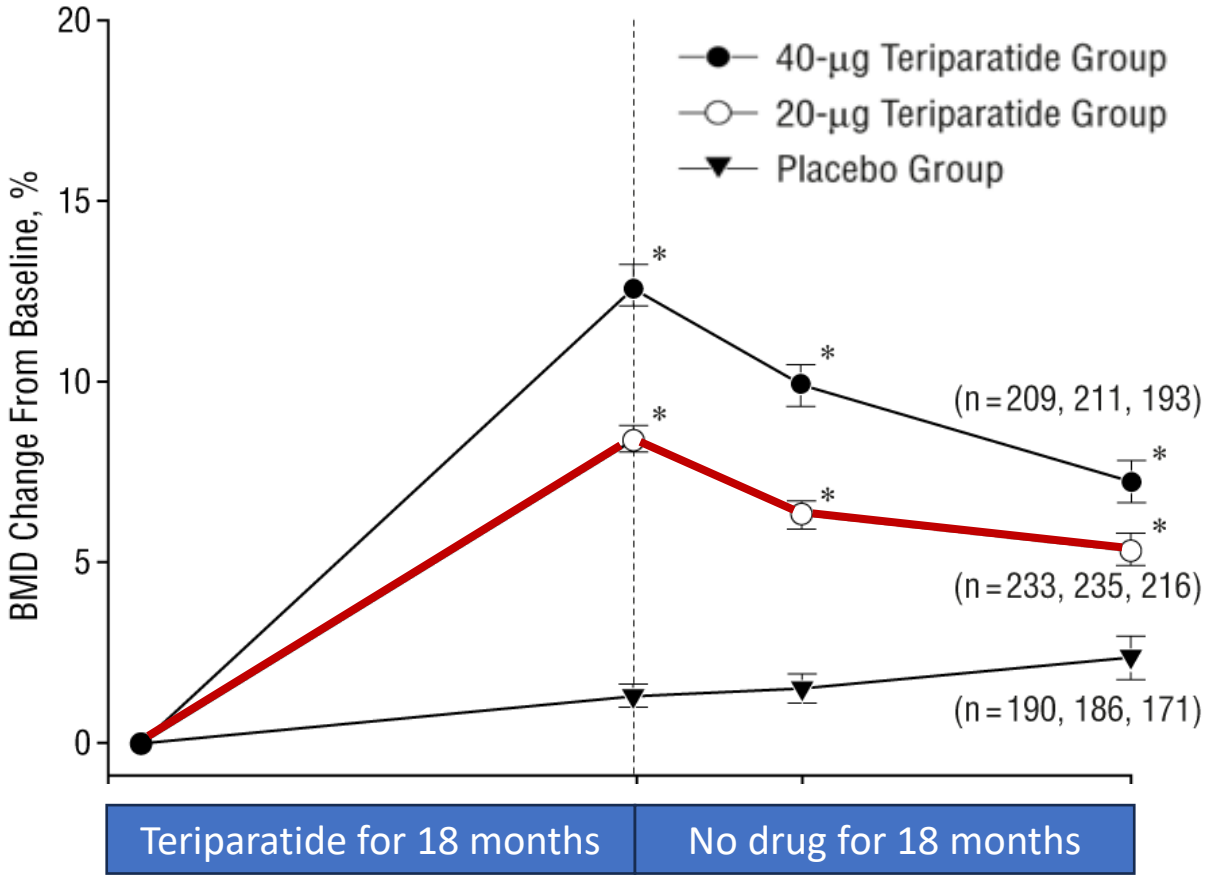
- Teriparatide
- Abaloparatide
- Romosozumab
- Denosumab

AVOID drug holiday →

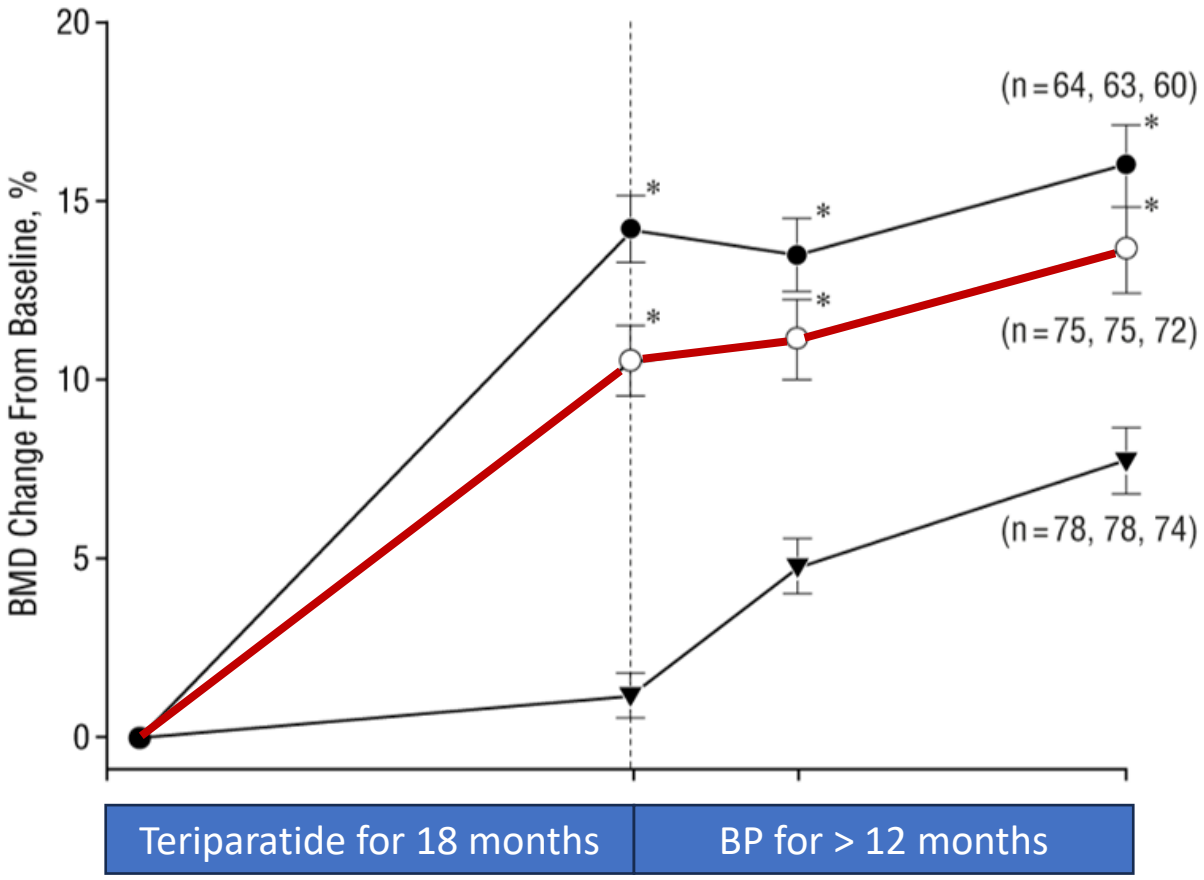
Anti-resorptive

BMD changes after teriparatide treatment

Teriparatide followed by no drugs

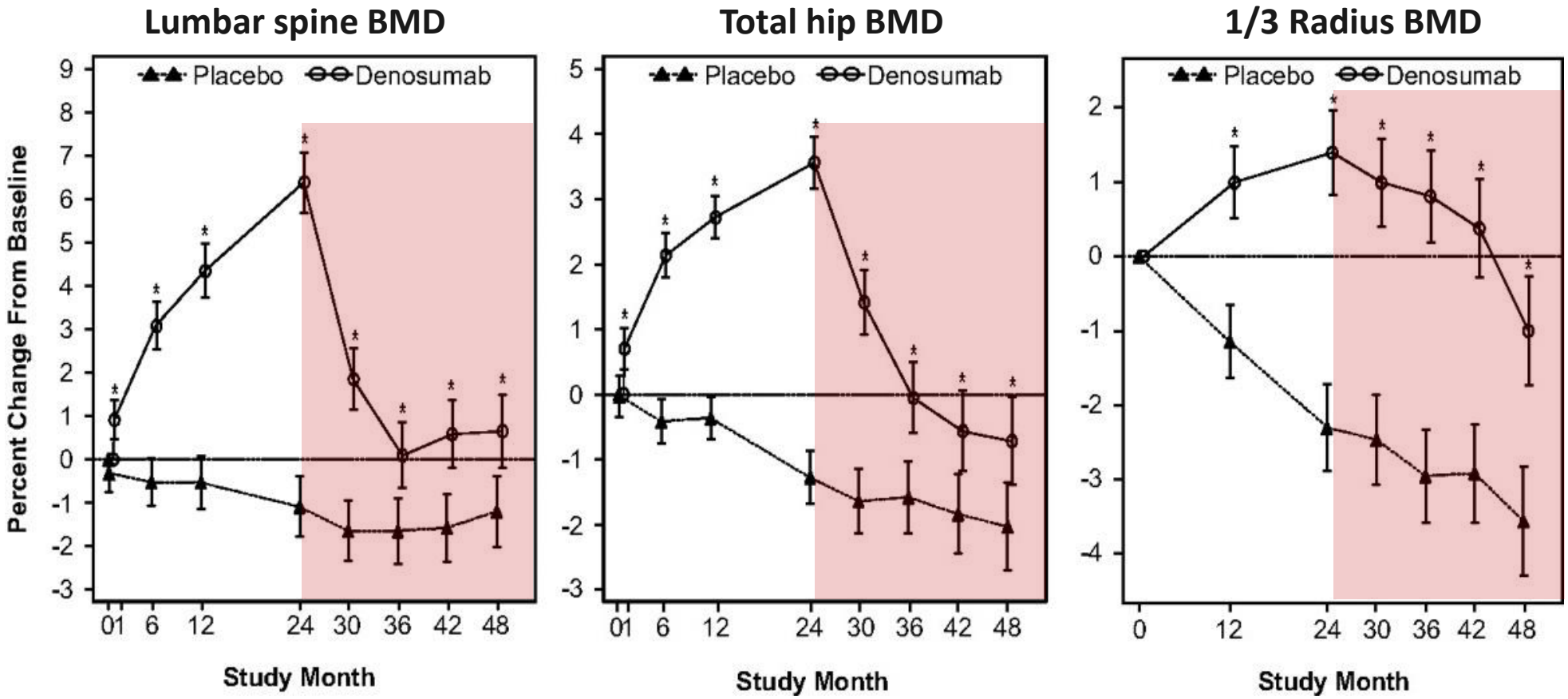


Teriparatide followed by bisphosphonate



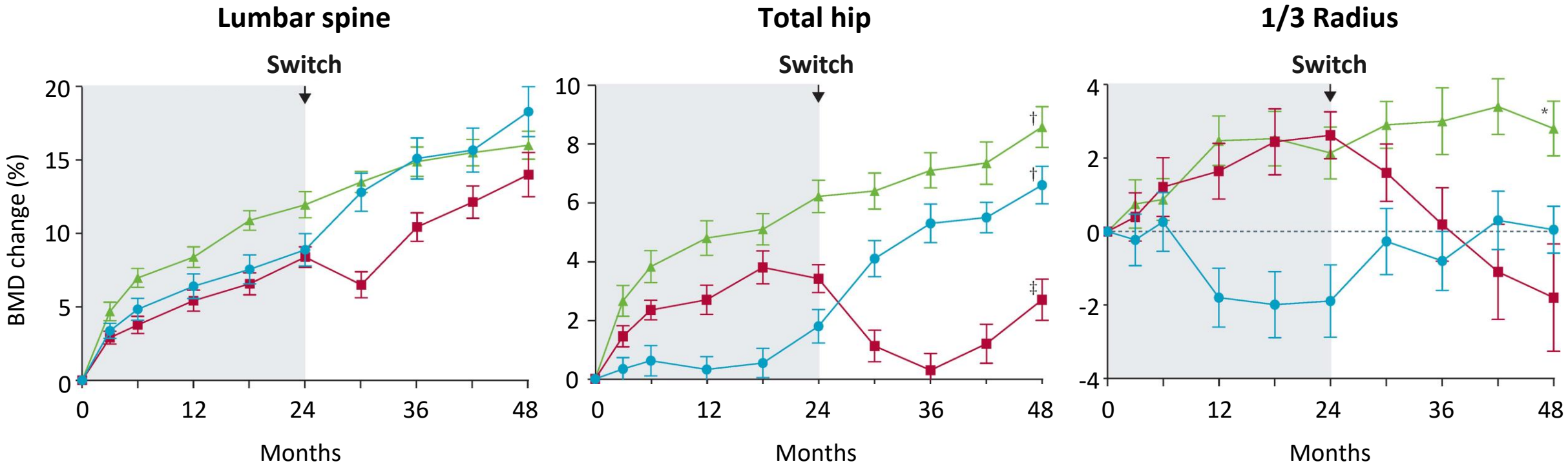
Lindsay R, Scheele WH, Neer R, *et al. Arch Intern Med.* 2004

AVOID abruptly stopping / delaying denosumab



Denosumab discontinuation → • Rapid ↓ in BMD • ↑ incidence of multiple vertebral fractures → Bisphosphonate Romosozumab

Transition of therapy: sequence matters



Denosumab → Teriparatide: **AVOID if possible**

Anabolic → Anti-resorptive = Greater BMD gain

Anti-resorptive → Anabolic = Blunting of BMD gain

Benjamin Z Leder *et al.* Lancet 2015

Take home points

Screening

Women age ≥ 65 and men age ≥ 70
Younger if at risk

For all

Workup / treat secondary causes
Non-pharmacologic: ABCDEF

A Alcohol / Smoking
B BMD by DXA
C Calcium intake
D Vitamin D intake
E Exercise
F Fall prevention

Pharmacotherapies

Osteoporosis by DXA
Fragility fractures
Osteopenia with high FRAX

↓

Assess every 1-2 years

↓

Duration of initial therapy

Bisphosphonate: 3-5 years
Non-bisphosphonate: variable

↓

Reassess fracture risk

Consider referral

Secondary causes: corresponding specialties

Physical therapy

Endocrinology / Mineral Metabolism:
- Considering injectable/anabolic
- Poor response to therapy
- Treatment transitions

Osteopenia and no fragility fractures

Bisphosphonate holiday
Non-bisphosphonate: **AVOID** holiday

Osteoporosis or fragility fractures

Continue bisphosphonate: 3-5 years
Switch to alternative therapies