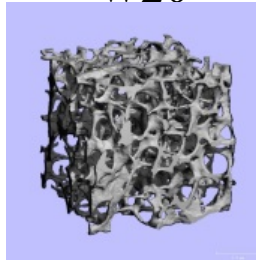


Osteoporosis

A systemic **skeletal disease** characterized by **low bone mass** and **microarchitecture deterioration** of bone tissue, with a counterpart increase in bone fragility and susceptibility to **fracture** (Am J Med 94: 646-50,1993)

Ageing is the major culprit

W20



W80



With the increase of life expectancy, it has become a **major public health** problem because fractures may **increase dramatically mortality, morbidity and dependence**, particularly in the elderly, with high costs for the social security budget

Safe and efficient treatments are available for fracture prevention: it is important to **select** patients who will benefit the most of these treatments, and therefore to **diagnose osteoporosis and evaluate fracture risk**

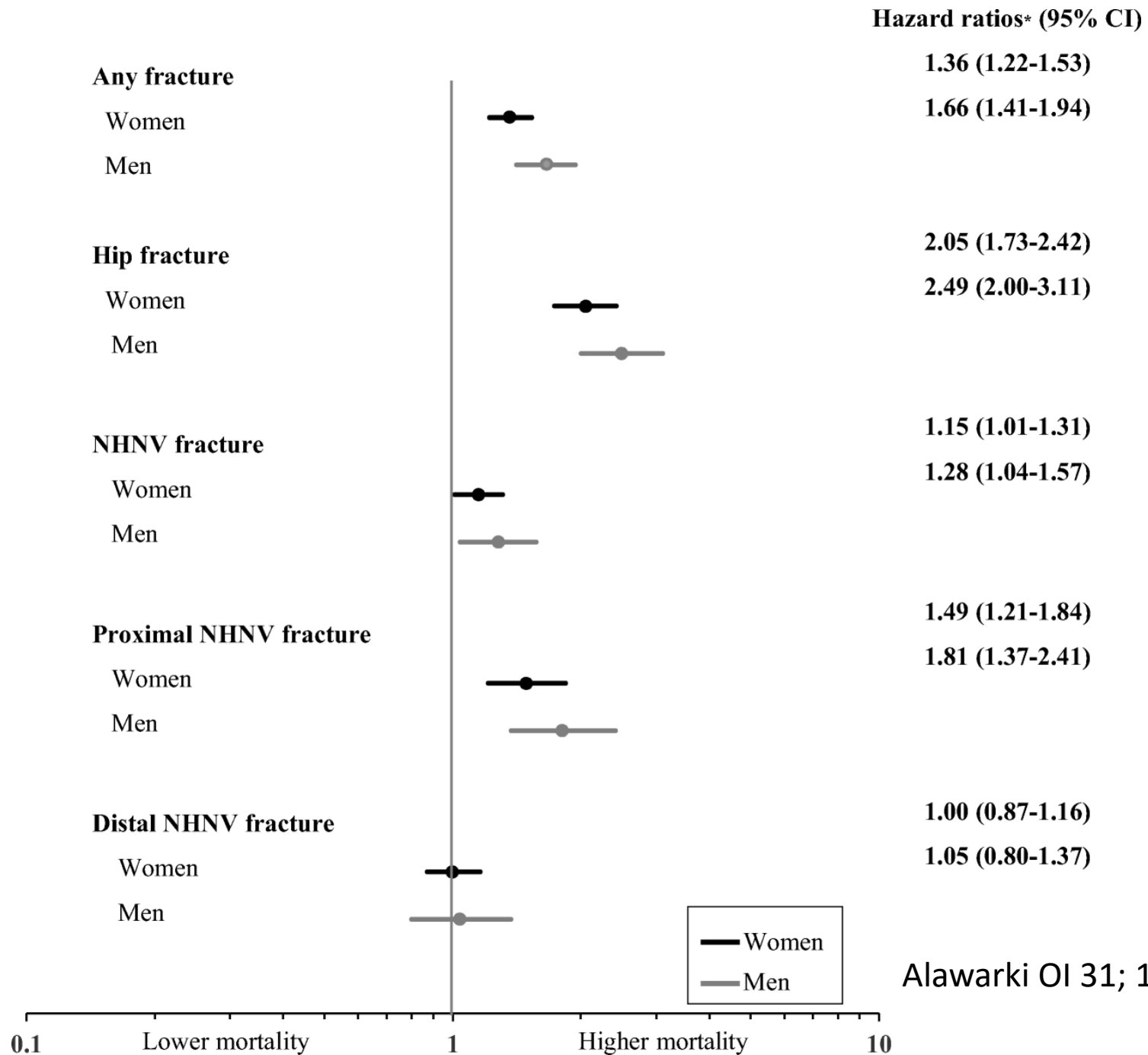
- Fractures as a public health problem
- Pathophysiology
- Diagnosis
 - Fragility fractures
 - Low BMD at DXA
 - High fracture risk
- Treatments
 - Non-pharmacological
 - Anti-resorptives
 - Pro-anabolic
- Take home messages
- Perspectives

Remaining Lifetime Fracture Risk (%) in Caucasian Population at the Age of 50

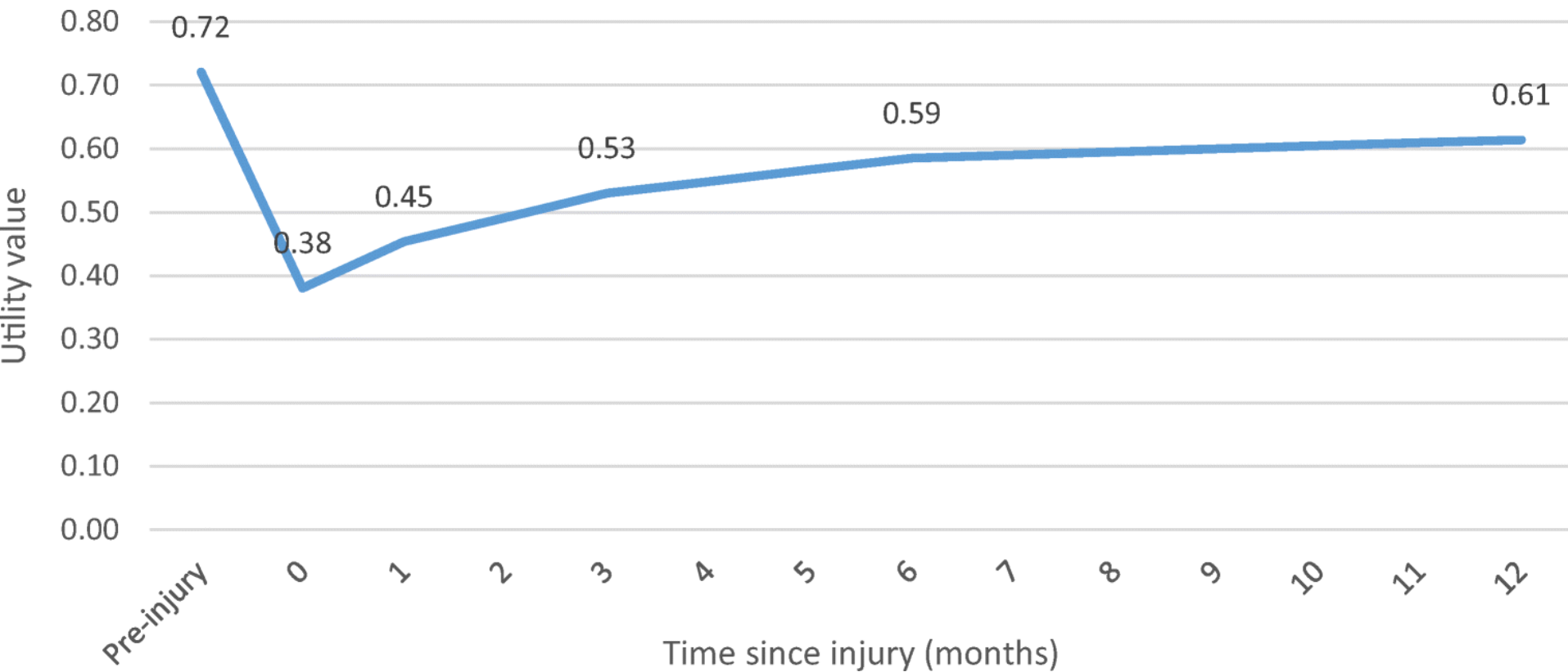
Type of Fracture	Men	Women
Forearm	4.6	20.8
Hip	10.7	22.9
Spine	8.3	15.1
Proximal Humerus	4.1	12.9
Other	22.4	46.4

Health and economic consequences

- Cost
 - 600.000 hip fractures in EU in 2010 (cost +/- 20.000€ per fracture > 12×10^9 €) (Hernlund Arch Osteoporosis 8:136)
 - 15.000 hip fractures in Belgium (300×10^6 €)
- Mortality, morbidity, QUALY



Health related QOL after hip fracture (Dutch study: 821 patients >65)

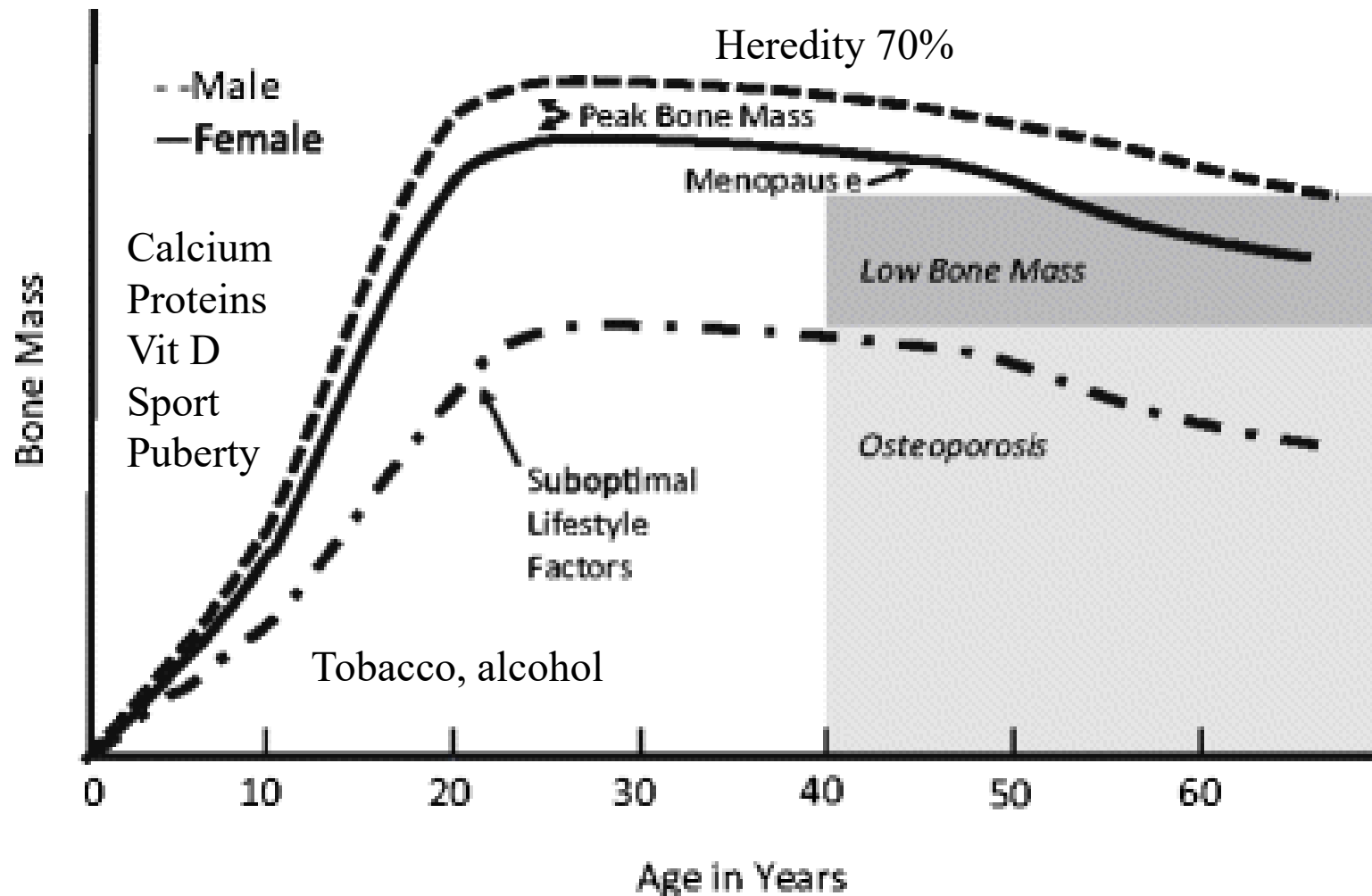


Utilities: mobility, self-care, usual activities, pain/discomfort and anxiety/depression

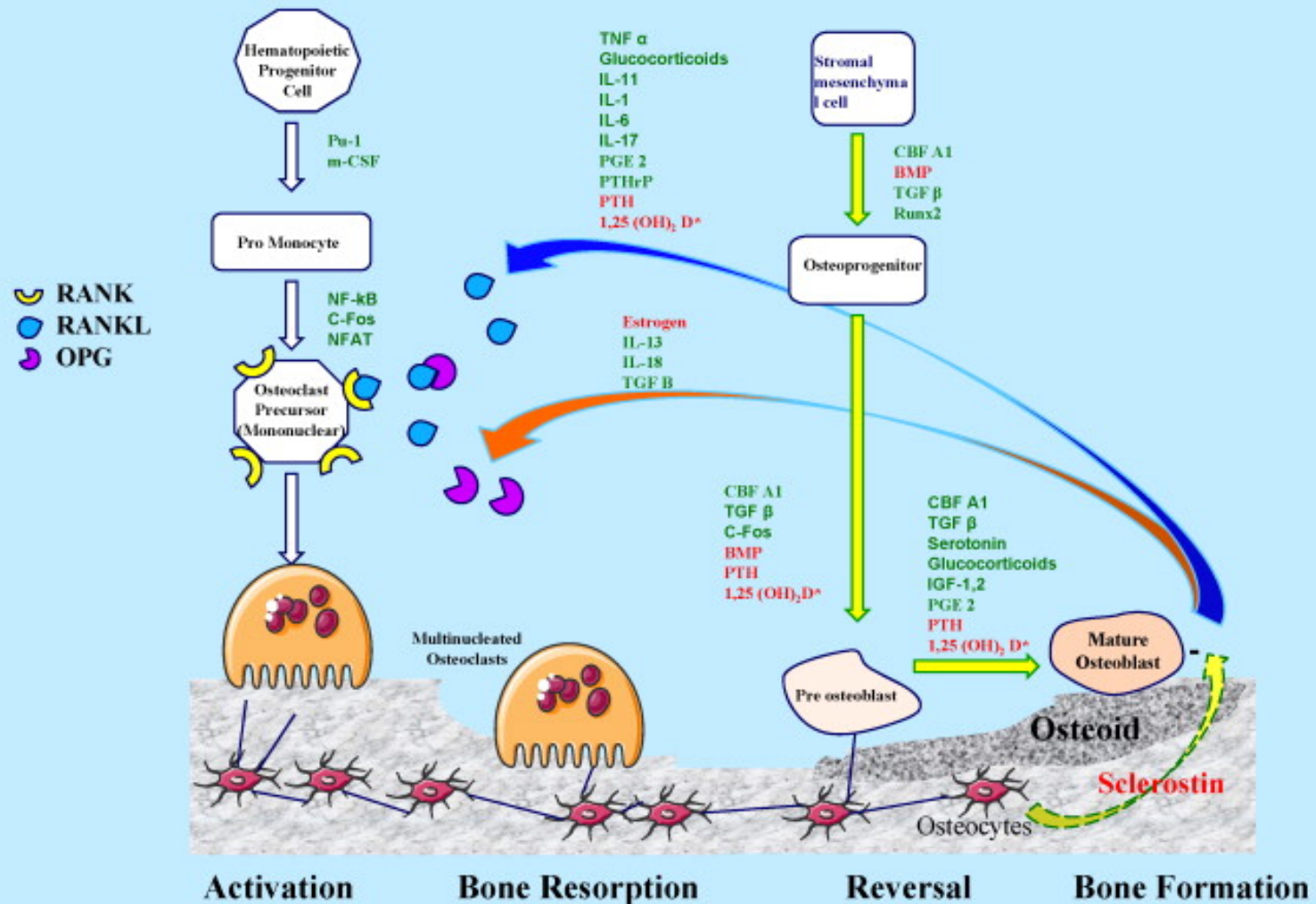
Kanters, Archives of Osteoporosis volume 15, Article number: 11 (2020)

Evolution of bone mass with age

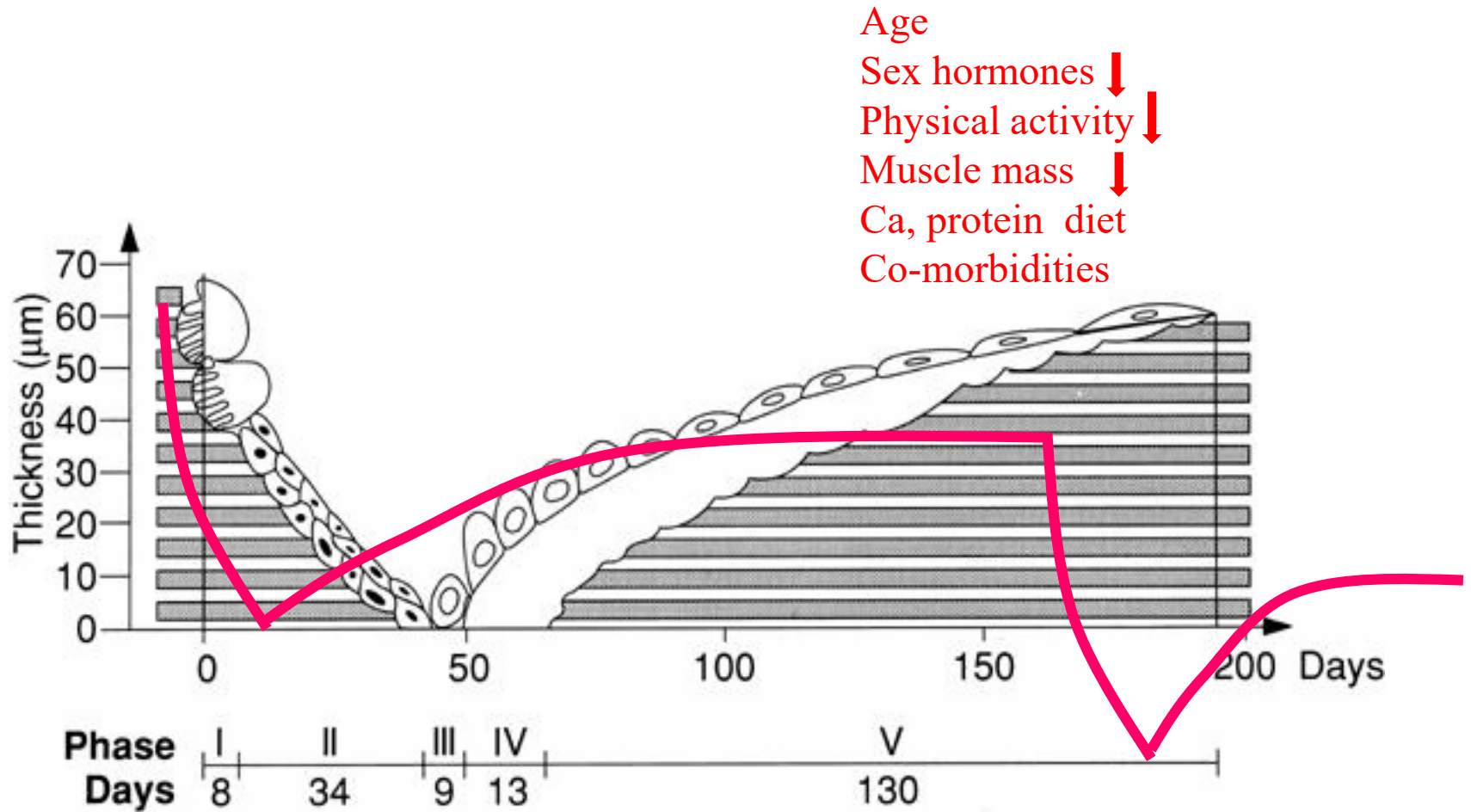
Weaver CM, OI 2016



Bone remodeling



Bone remodeling before and after 50 (—)



Secondary osteoporosis

- Endocrine diseases: HPT1°, thyrotoxicosis, hypercortisolism, gonadal insufficiency,
- Nutrition: vitamin D deficiency (HPT2°), poor calcium and protein diet
- Inflammatory diseases (RA, IBD)
- Neurological diseases (disuse)
- Renal failure (besides CKD-MBD)
- Drugs: corticosteroids, thyroid hormones (excess), aromatase inhibitors, androgen deprivation treatment

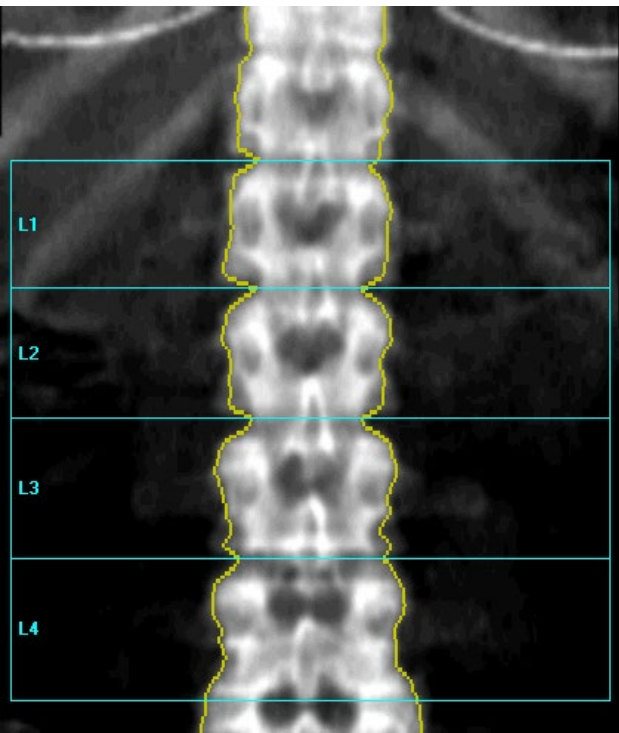
Diagnosis

- Fragility fracture
- Low BMD at DXA
- High Fracture risk

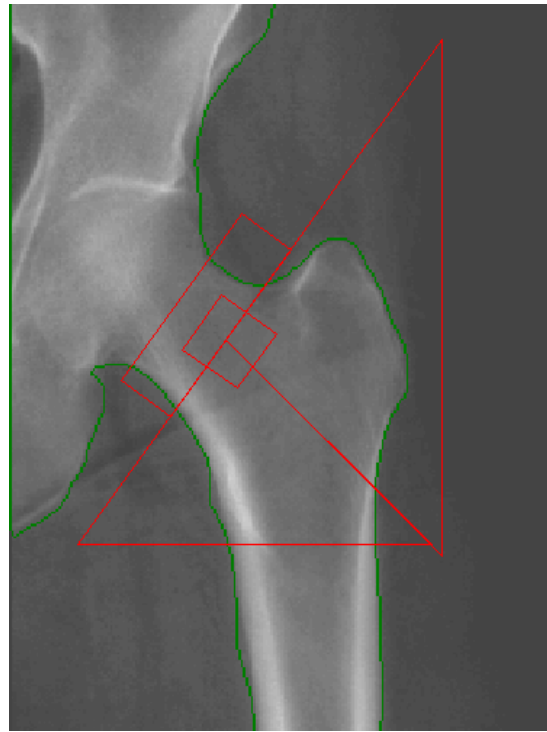
1. Fragility fractures

- MOF's
 - **Vertebral or hip fracture: treatment**
 - Proximal humerus, wrist: work up
- Non vertebral, non hip (NVNH) proximal: pelvis, shoulder, ribs
- NVNH distal: femur, tibia, elbow
- Mortality, morbidity
- All associated with an increased risk of subsequent fractures >the important role of **secondary prevention**

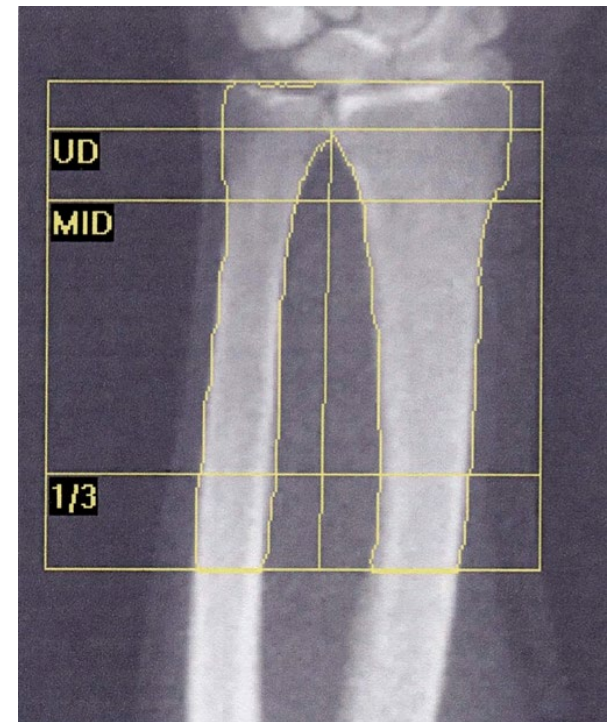
2. Bone Mineral Density (DXA)



Lumbar spine



Hip



Radius

BMD (DXA): results

- DXA = absorption of two X-rays with different energies (40 and 100 KeV) allows to separate bone and soft tissue compartments
- XRay absorption = f (amount of mineral in the tissue (g HA), bone mineral content, BMC)
- Algorithm (thresholding) to calculate bone area (A (cm²))
- BMD = bone mineral (areal) density (g of HA per cm²) = BMC/A
- Ex: spine BMD = 1,052 g/ cm²

A low BMD increases fracture risk

636

BLACK ET AL.

TABLE 3. ASSOCIATION BETWEEN BONE MINERAL DENSITY AND ALL FRACTURES IN 8134 WOMEN

Measurement (g/cm ³)	Standard deviation (SD)	Relative risk* (95% confidence interval)	
		Unadjusted	Adjusted for age
Proximal femur (total)	0.131	1.43 (1.23, 1.66)	1.40 (1.20, 1.63)
Femoral neck	0.111	1.44 (1.23, 1.69)	1.41 (1.20, 1.66)
Ward's triangle	0.110	1.45 (1.25, 1.69)	1.43 (1.22, 1.67)
Intertrochanteric	0.160	1.42 (1.22, 1.64)	1.39 (1.19, 1.62)
Trochanteric	0.102	1.41 (1.21, 1.64)	1.38 (1.18, 1.61)
Lumbar spine	0.169	1.36 (1.17, 1.60)	1.35 (1.15, 1.58)
Calcaneus	0.094	1.53 (1.31, 1.79)	1.51 (1.29, 1.77)
Distal radius	0.084	1.45 (1.24, 1.69)	1.42 (1.21, 1.67)
Proximal radius	0.103	1.35 (1.17, 1.56)	1.32 (1.14, 1.53)

*Relative hazards for bone mineral density (BMD) per standard deviation decrease in BMD.

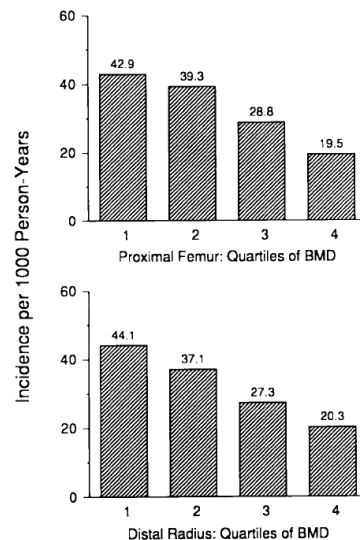


FIG. 1. Incidence of all fractures by age-adjusted quartile of bone mineral density (BMD).

We considered the possibility that the longer interval between SPA measurements and fractures may have weakened that association; however, the correlation between measurements of appendicular sites 2 years apart was $r \geq 0.89$, and thus the effect would be very small. For example, based on the observed relative risk of 1.42 for each standard deviation decrease in BMD of the distal radius, we estimate that the relative risk for measurements made 2 years later would not exceed 1.48.

DISCUSSION

We have demonstrated that reduced bone mineral density of the proximal femur and spine is strongly associated with an increased risk of all nonspine and of wrist fractures in older women. The strength of the relationship between BMD and all nonspine fractures in our cohort (range in relative risk from 1.3 to 1.5) appears to be similar to the relative risk of 1.5 reported by Hui et al.,⁽¹⁾ although somewhat lower than the range of values (1.5–1.9) reported by Wasnich et al.⁽¹⁰⁾ However, the Wasnich study was performed on a younger cohort of Asian-American women. The association between radial BMD and wrist fractures in our cohort is somewhat higher than that found by Hui et al.⁽¹⁾

We found that the magnitude of the association between BMD and all fractures or wrist fractures was similar, regardless of the site or method of measurement. This suggests that measurements of bone mass at the proximal femur, spine, and appendicular sites have similar predictive value for the overall risk of nonspine fracture in postmenopausal women. Our results differ somewhat from those of Eastell and colleagues,⁽¹¹⁾ who found that wrist fractures were somewhat more strongly associated with BMD of the distal radius than BMD of the spine by dual-photon absorptiometry. This difference might be due, in part, to differences in the methods of the two studies. Eastell and colleague's study was a retrospective case-con-

Pitfalls for DXA

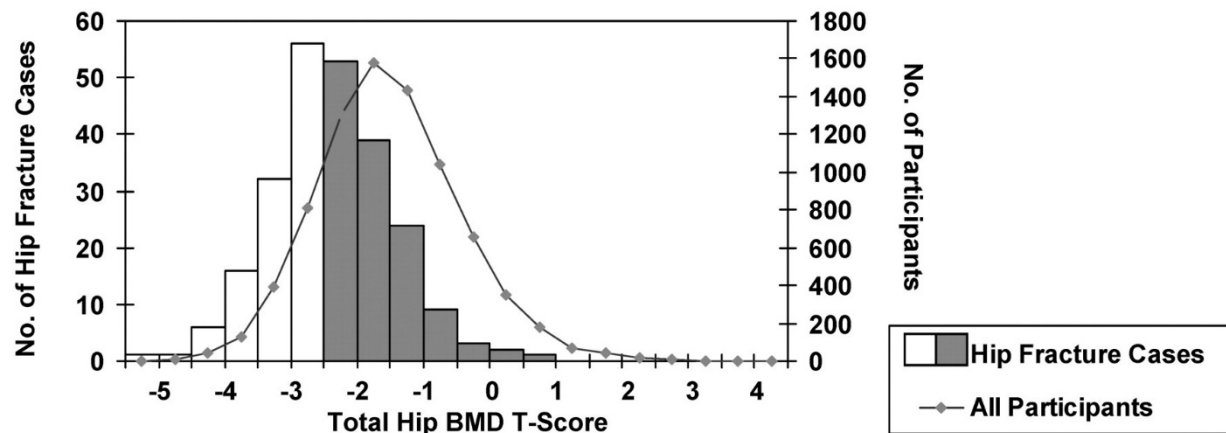
- Patient positioning
- Spondylarthrosis
- Scoliosis
- Vertebral fractures
- Aortic calcifications
- External artifacts
- Reference values

Osteoporosis diagnosis(WHO)

- BMD values converted in SD units : Z-score et T-score
- $Z\text{-score} = \frac{\text{observed value} - \text{mean reference value for age}}{\text{SD of reference values for age}}$
- $T\text{-score} = \frac{\text{observed value} - \text{mean reference value at peak (30y)}}{\text{SD of reference values at peak}}$
- **Osteoporosis : $T\text{-score} \leq -2,5$**

Limitations of the WHO definition based on T-scores

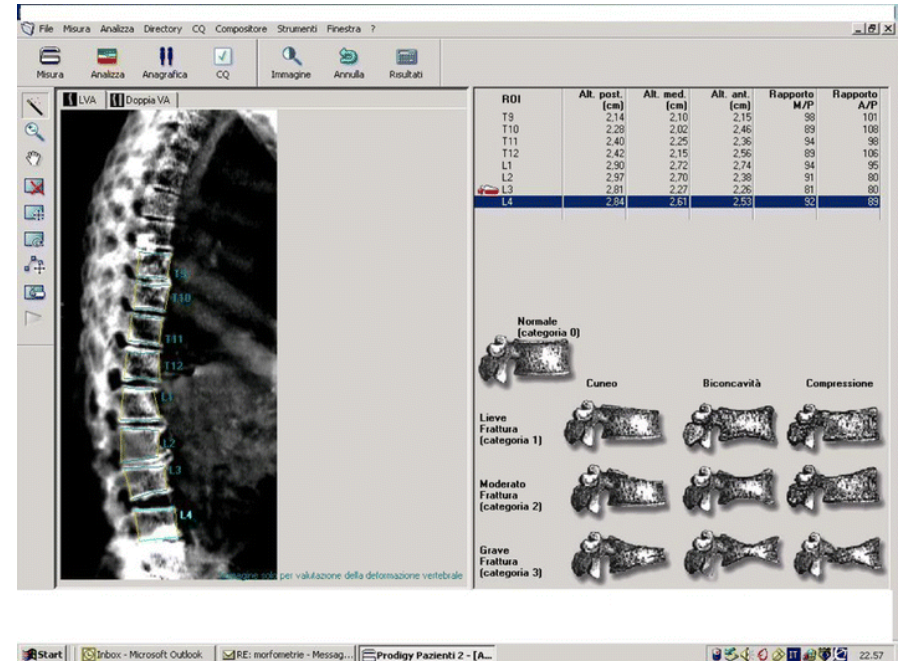
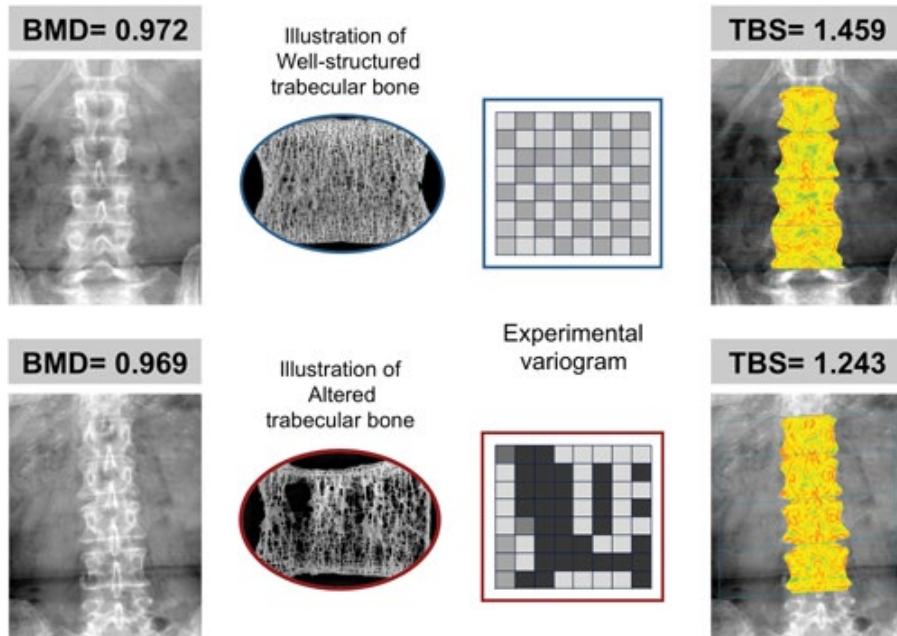
- Osteoporosis: T-score of BMD measured by DXA at the hip or spine $\leq -2,5$ was chosen for epidemiology, then adopted as a diagnostic criteria
- Continuous relation between BMD and fracture risk: more than 50% of the fragility fractures occur in patients with osteopenic ($-2,5 < T < -1,0$) or normal ($T \geq -1,0$) BMD values (Wainwright, OI, 2005)



- Other risk factors besides BMD: bone quality (architecture, material), risk of falls ...

TBS

VFA



3. Assessment of fracture risk



FRAX[®] Fracture Risk Assessment Tool

HomeCalculation Tool▼Paper ChartsFAQReferencesEnglish▼

Calculation Tool

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

Country: BelgiumName/ID:

About the risk factors

Questionnaire:

1. Age (between 40 and 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 or more units/day

☒ No ☐ Yes

12. Femoral neck BMD (g/cm²)

Select BMD ▼

Clear

Calculate



Weight Conversion

Pounds ➡ kg

Convert

Height Conversion

Inches ➡ cm

Convert

00404715

Individuals with fracture risk assessed since 1st June 2011



Q3: WHICH TOOLS should be used to diagnose osteoporosis and assess fracture risk in postmenopausal women?



Fracture risk assessment tools & treatment thresholds

BBC 2020 guidelines

To assess severity of osteoporosis and categorize patients at high vs. low risk of fractures by fracture risk assessment tool:

Threshold for individuals aged < 70 years:

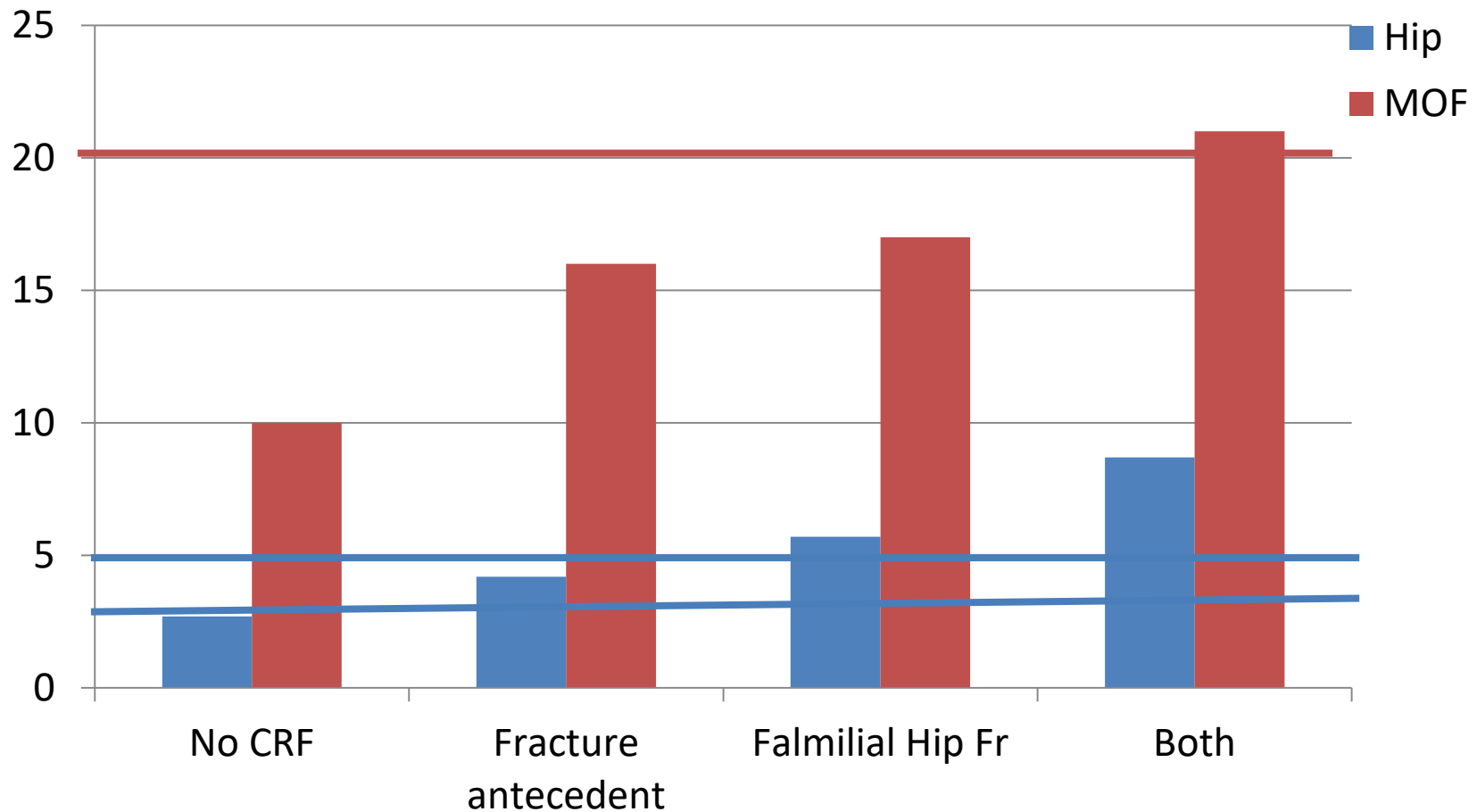
- 10-year risk of MOF $\geq 20\%$
- 10-year risk of hip fracture $\geq 3\%$

Threshold for individuals aged ≥ 70 years:

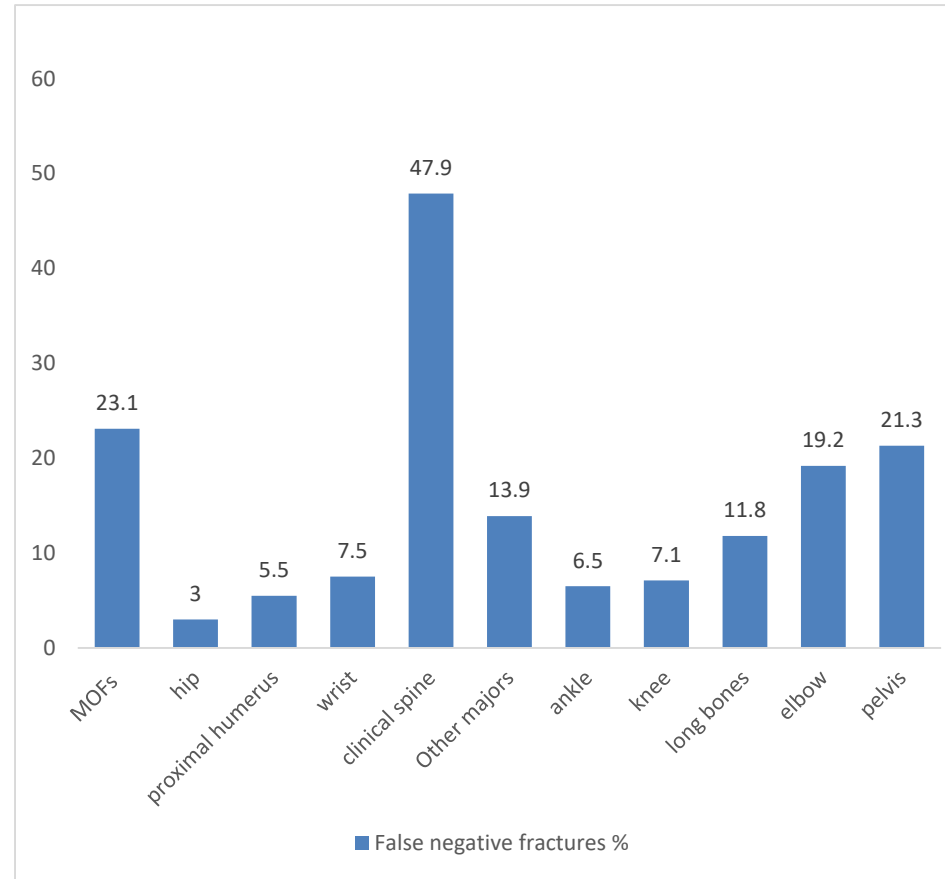
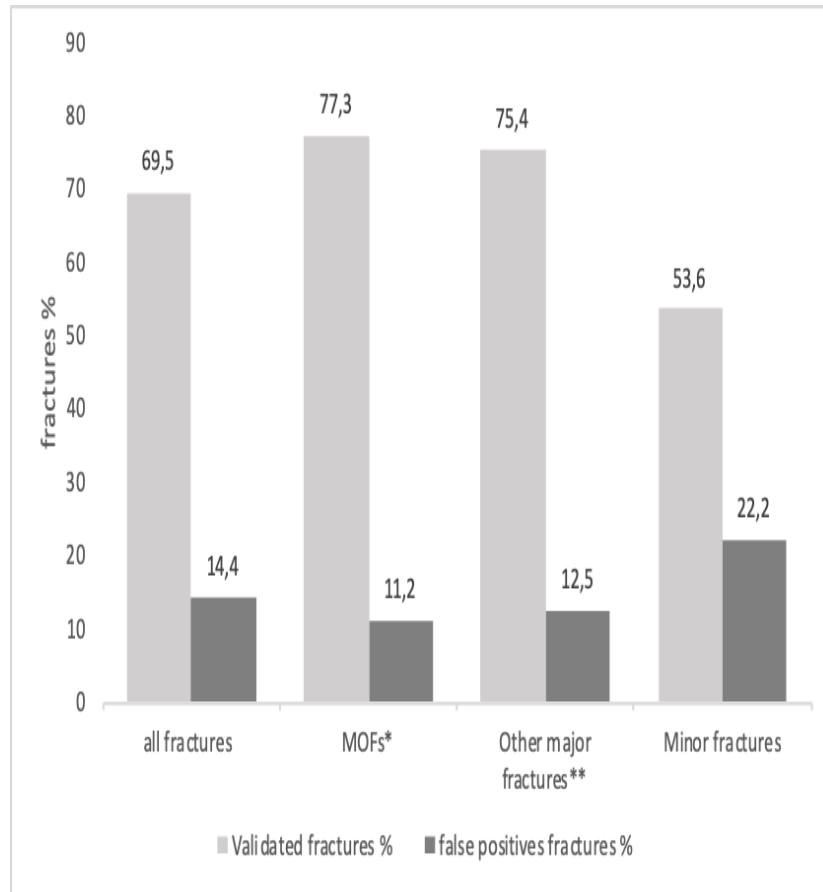
- 10-year risk of MOF $\geq 20\%$
- 10-year risk of a hip fracture $\geq 5\%$

Anamnestic errors and risk estimation

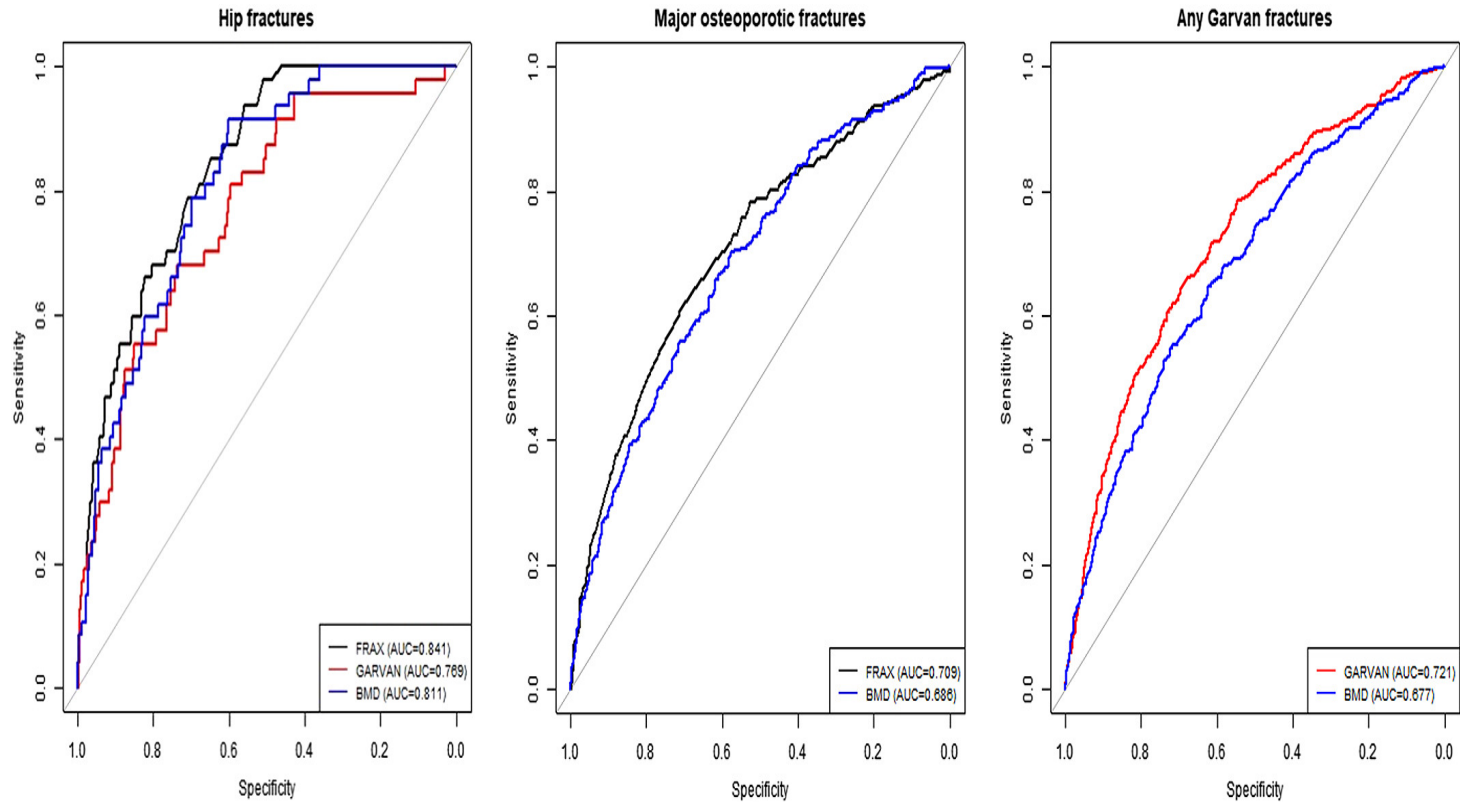
F 70 BMI 22;0 T-score FN -2;2



Validity of self reported fractures in prospective FRISBEE study (Baleanu F, Arch Osteoporosis 2020; Bone Reports 2020)



Independent External Validation of FRAX and Garvan Fracture Risk Calculators: A Sub-Study of the FRISBEE Cohort (Baleanu et al)



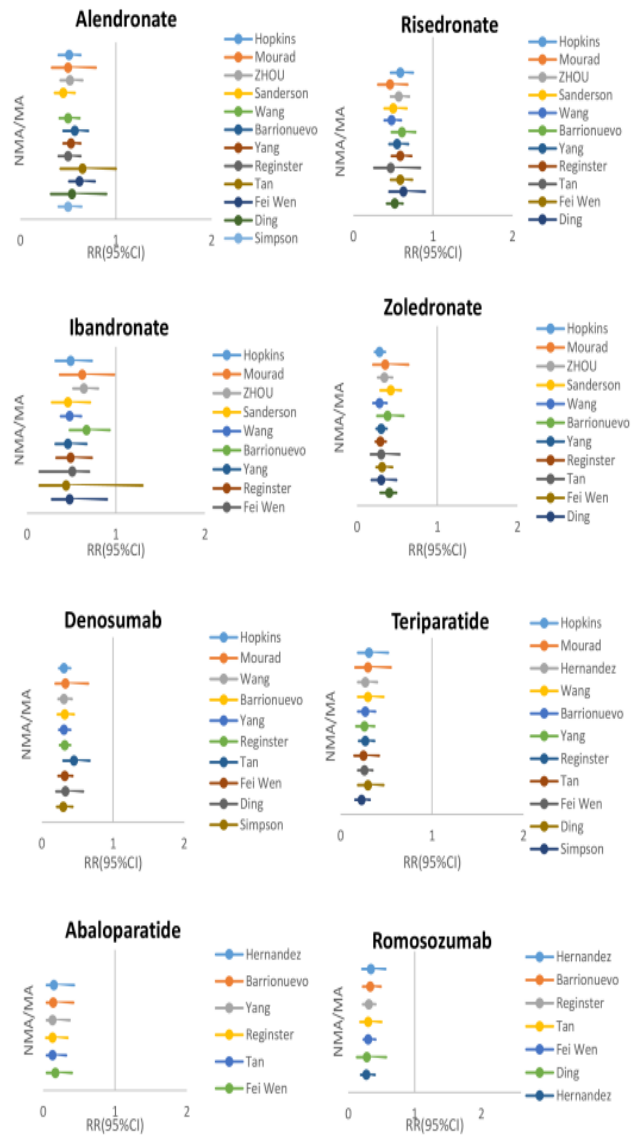
Pharmacologic treatments

Anti-resorptive

- Activate ER: MNP Hormone Therapy, SERM (Raloxifène=Evista)
- Intoxicate osteoclasts: Bisphosphonates (long acting)
 - Oral (Alendronate, Risedronate, Ibandronate)
 - IV (Ibandronate, Zoledronate)
- Block osteoclast differentiation: AntiRANK-Ligand (short acting) (Denosumab=Prolia)

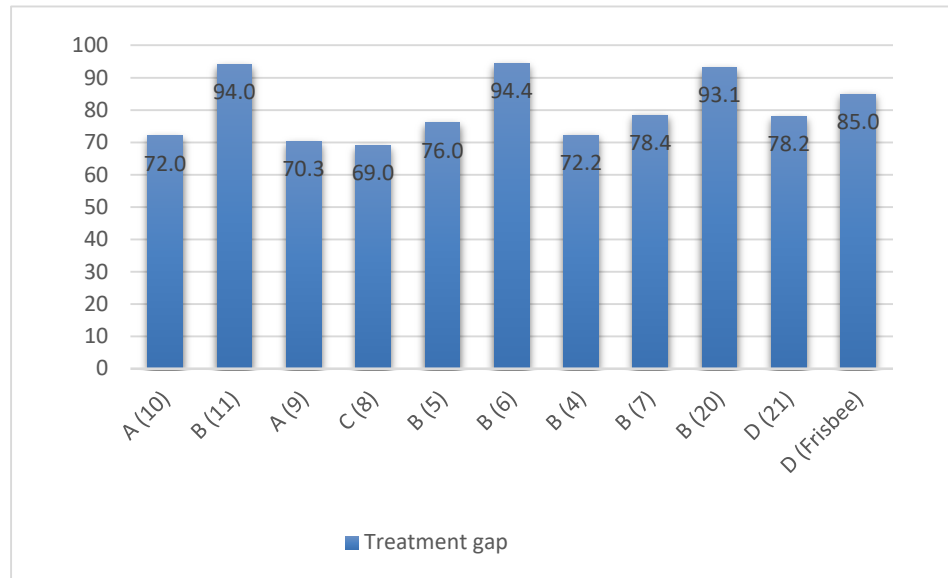
Anabolic

- Acting on PTH1 receptor
 - Teriparatide (PTH analog, Forsteo)
 - Abaloparatide (PTHrP analog)
- Inhibiting sclerostin (Romosozumab)



Treatment efficacy in real life

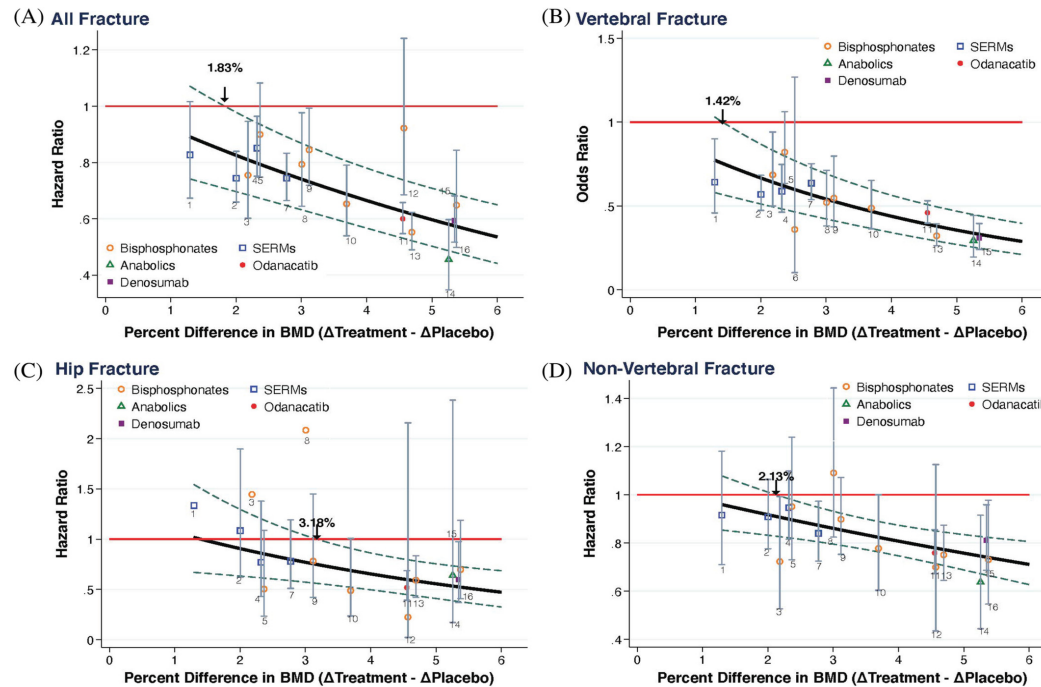
- Treatment gap after a first osteoporotic fracture
(Iconaru et al Osteoporos Int, 2020)



- Low adherence (<80%)

Follow up of treatment efficacy

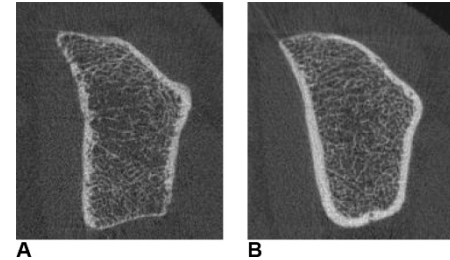
BMD: slow increase; long term reproducibility 1 to 2% > Least Significant Change (LSC) around 3-5%: min interval at follow up: 1 to 2 years



Take home messages

- Osteoporosis is a frequent condition, resulting from ageing, with major consequences for well being and public health because it increases the risk of fracture, and associated mortality, morbidity and dependence
- Any fracture not resulting from a major trauma is a risk factor for subsequent fractures and justifies a work up to diagnose osteoporosis (DXA, absolute fracture risk estimation)
- This diagnosis is essential because there are safe treatments which can reduce fracture risk by 30 to 70% and which are cost efficient when given to patients at high/very high risk
- DXA is central to osteoporosis diagnosis and management and thus it must be performed according to procedures which guarantee accuracy and reproducibility: errors in BMD measurement can result in over or undertreatment
- Fracture risk assessment tools like FRAX require that anamnesis over clinical risk factors is as precise as possible

Perspectives



– Diagnostic:

- Bone microarchitecture: HRpQCT (distal radius and tibia)
- Bone material quality:
 - » Matrix composition and mineralization, bone marrow fat (MRI spectroscopy)
 - » Reference Point Indentation (RPI)
 - » Bone turnover markers
- Other risk factors (quantification, falls, muscle performance, diabetes and metabolic bone diseases...)

– Treatment: drugs and factors acting on cellular senescence: senolytics?

THANK YOU

Questions? Vragen?