

بنام خداوند جان و خرد

Osteoporosis Review

screening, diagnosis and management

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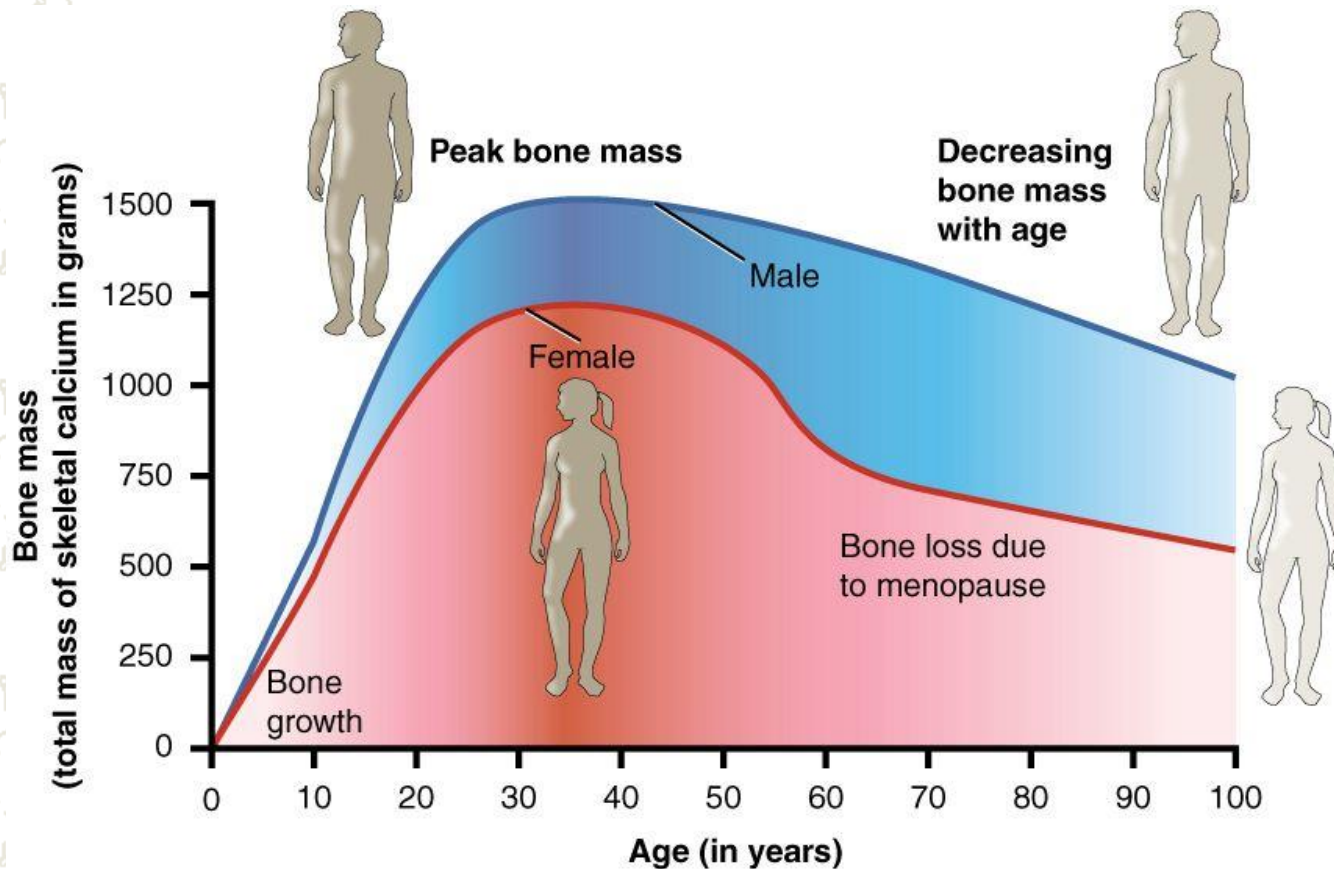
Introduction

- ✱ Osteoporosis is a prevalent metabolic bone disease characterized by low bone mass and microarchitectural deterioration, leading to increased bone fragility and fracture risk.
- ✱ It is often a "silent" condition until a fracture occurs.
- ✱ These fractures, particularly of the hip, spine, and wrist, cause significant morbidity, disability, loss of independence, and increased mortality.
- ✱ The personal and economic burden is enormous, with annual costs projected to exceed \$95 billion in the US by 2040.
- ✱ A major crisis in patient care is the "treatment gap," where the majority of high-risk patients are not diagnosed or treated after an initial fracture.

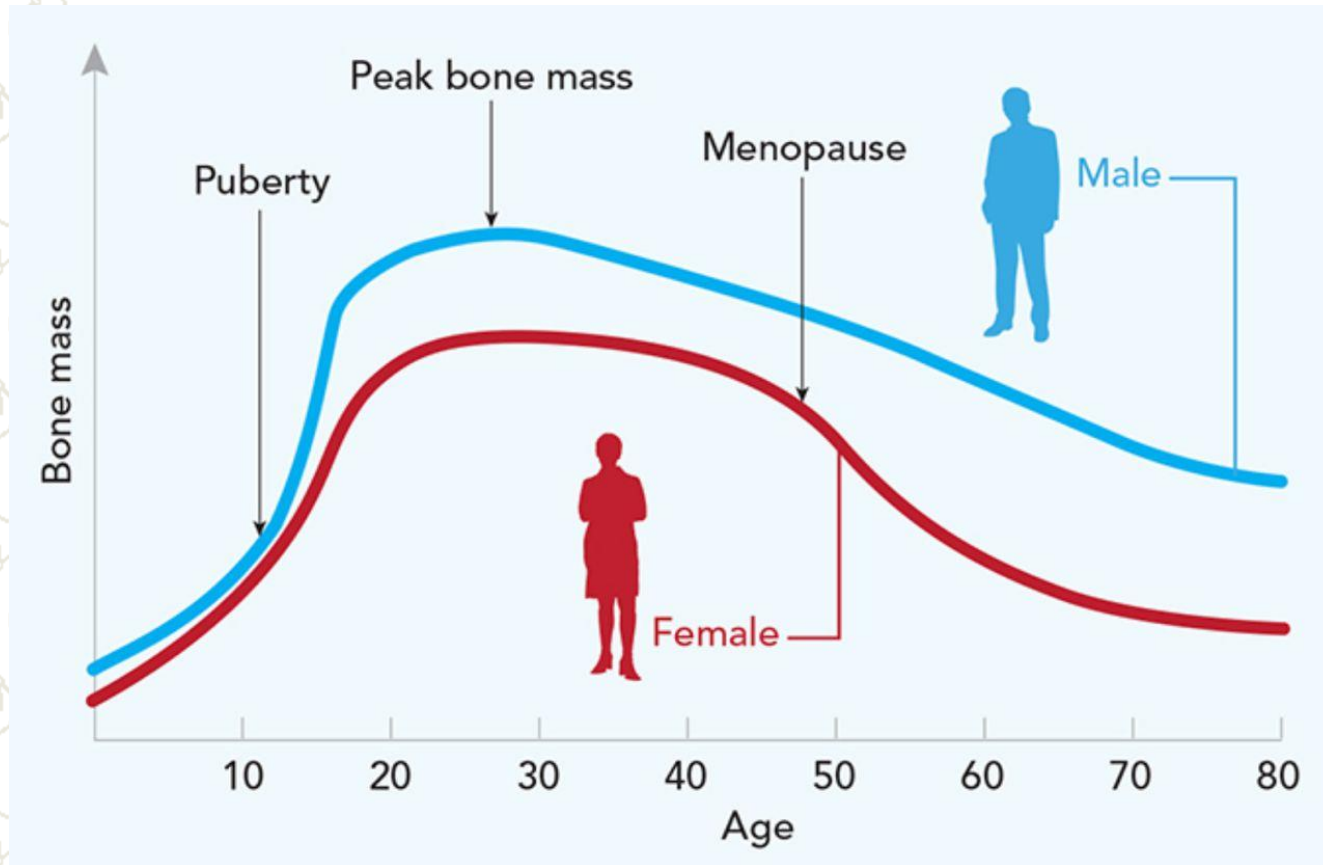
Failure To Diagnose and Treat

- ✱ Studies show failure to diagnosis and treat osteoporosis in older patients who have suffered a fracture
- ✱ In study of 4 Midwestern health systems:
 - 1/8 – 1/4 of hip fracture pts received BMD testing
 - $< \frac{1}{4}$ were given calcium/D supplements
 - $< \frac{1}{10}$ treated with antiresorptive medications

Bone physiology



Bone physiology



Risk Factors

- ✱ Inadequate bone strength reflects a failure to achieve optimal peak bone mass during early adulthood, excessive bone loss at later ages, or both.
- ✱ Peak bone mass typically occurs in early adulthood by the end of the first 2 decades of life.
- ✱ Peak bone mass and subsequent rate of bone loss are influenced by multiple genes.
- ✱ Genomic-wide association studies have identified loci associated with BMD, bone strength, and fracture risk factors.
- ✱ Nutrition(such as adequate calcium intake); physical activity; and levels of estrogen, progesterone, testosterone, growth hormone, and other hormones are also major regulators of peak bone mass.
- ✱ History of fracture as an adult
- ✱ Fragility fracture in first degree relative

Risk Factors

- ✱ Premature menopause (before 40 years of age),
- ✱ hypogonadism,
- ✱ Nutritional deficiencies (eg, vitamin D or calcium),
- ✱ Low body mass index (BMI) of less than 20,
- ✱ Weight loss,
- ✱ Immobility, **Impaired vision, Dementia, Poor health/frailty, Recent falls**
- ✱ Presence of certain comorbidities (eg, inflammatory bowel disease, rheumatoid arthritis, chronic liver or kidney disease), and
- ✱ Use of certain medications (eg, glucocorticoid, aromatase inhibitors such as anastrozole and letrozole, androgen deprivation agents such as leuprolide and bicalutamide) contribute to accelerated bone loss.
- ✱ Current smoking and high alcohol consumption (≥ 3 drinks daily) are also risk factors for bone loss.

Medical Conditions Associated with Increased Risk of Osteoporosis

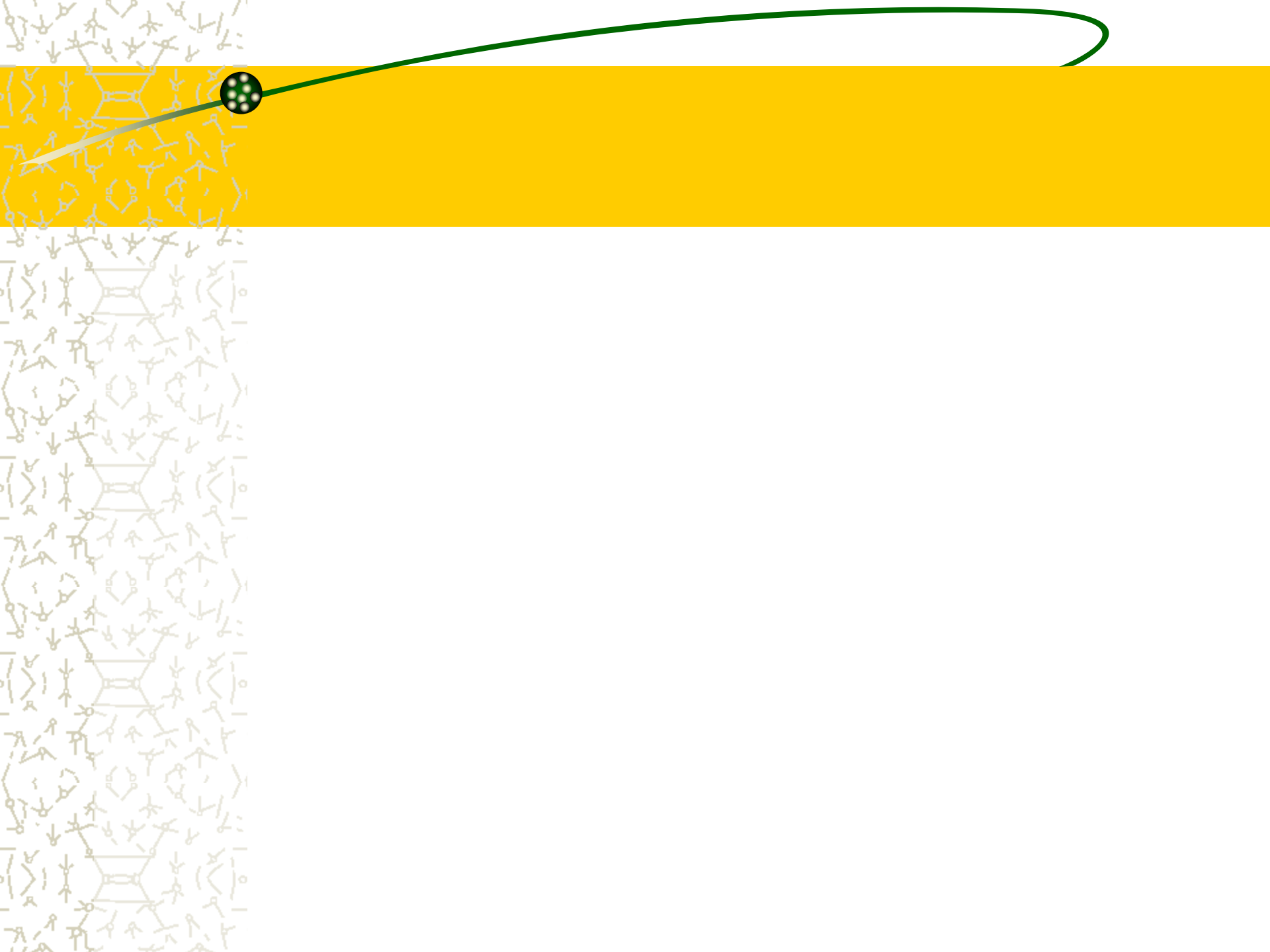
- ✱ COPD
- ✱ Cushing's syndrome
- ✱ Eating disorders
- ✱ Hyperparathyroidism
- ✱ Hypophosphatasia
- ✱ IBS
- ✱ RA, other autoimmune connective tissue disorders
- ✱ Type 1 and 2 DM
- ✱ Multiple sclerosis
- ✱ Multiple myeloma
- ✱ Stroke (CVA)
- ✱ Thyrotoxicosis
- ✱ Vitamin D deficiency
- ✱ Liver diseases

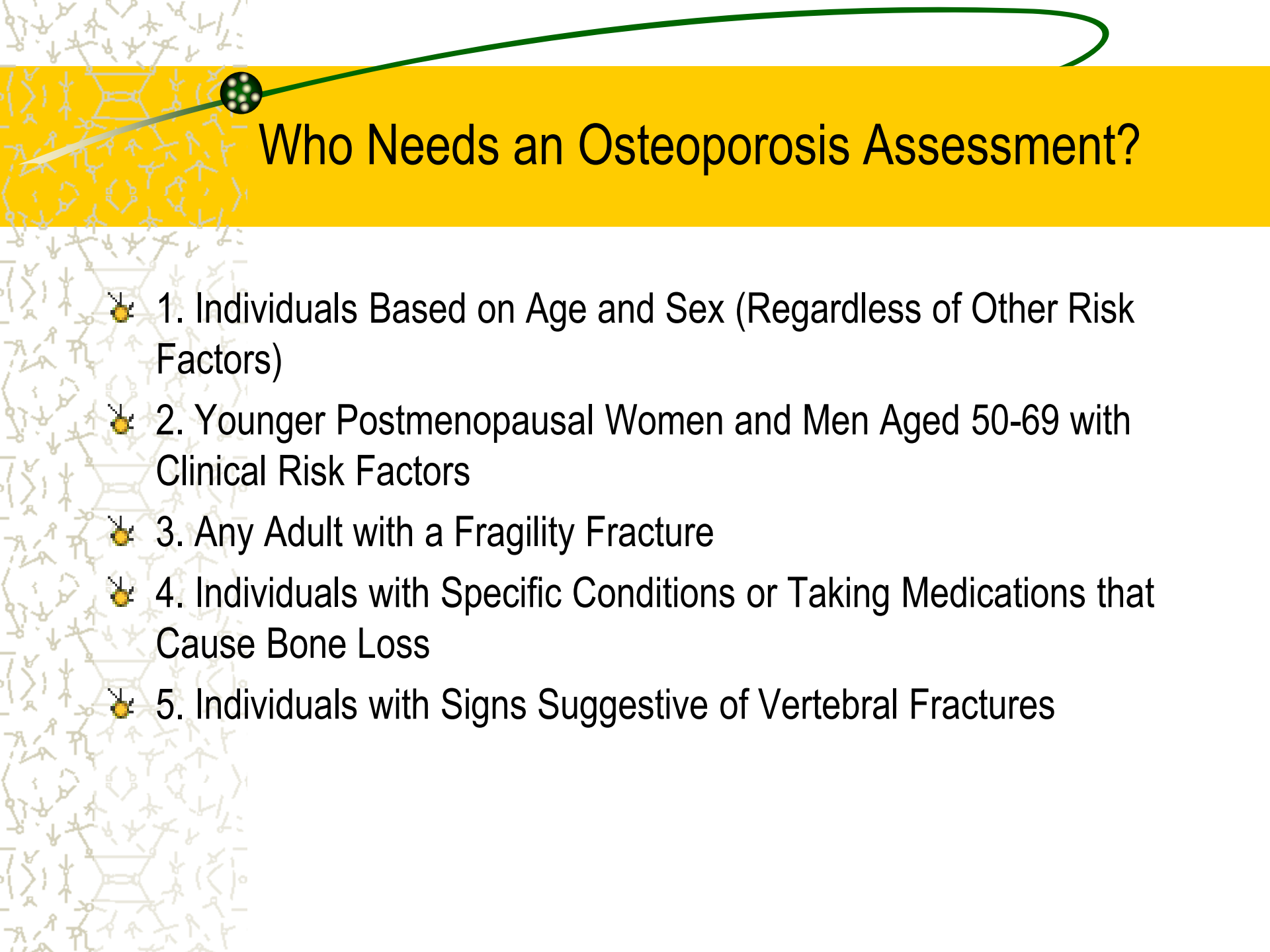
Not an inclusive list

Drugs Associated with reduced Bone Mass

- ☼ Aluminum
- ☼ Anticonvulsants
- ☼ Cytotoxic drugs
- ☼ Glucocorticosteroids (oral/high dose inhaled)
- ☼ Immunosuppressants
- ☼ Gonadotropin-releasing hormone (e.g. Lupron)
- ☼ Lithium
- ☼ Heparin (chronic use)
- ☼ Supraphysiologic thyroxine doses
- ☼ Aromatase inhibitors
- ☼ Depo-Provera

Not an inclusive list





Who Needs an Osteoporosis Assessment?

- ✿ 1. Individuals Based on Age and Sex (Regardless of Other Risk Factors)
- ✿ 2. Younger Postmenopausal Women and Men Aged 50-69 with Clinical Risk Factors
- ✿ 3. Any Adult with a Fragility Fracture
- ✿ 4. Individuals with Specific Conditions or Taking Medications that Cause Bone Loss
- ✿ 5. Individuals with Signs Suggestive of Vertebral Fractures

🦋 1. Individuals Based on Age and Sex (Regardless of Other Risk Factors)

- Women aged 65 and older.
- Men aged 70 and older.

🦋 2. Younger Postmenopausal Women and Men Aged 50-69 with Clinical Risk Factors

- This includes factors such as:
- **A previous fracture** as an adult (after age 50), especially a hip, vertebral, or wrist fracture.
- **Prolonged use of glucocorticoids** (e.g., prednisone ≥ 5 mg/day for ≥ 3 months).
- **A parent has had a hip fracture.**
- **Current smoking.**
- **High alcohol intake** (more than 2-3 drinks per day).
- **Low body weight** or body mass index (BMI).
- **Medical conditions associated with bone loss** (see list below). 🦋

🦋 3. Any Adult with a Fragility Fracture

- **This is a major red flag.** Any broken bone in an adult aged 50 or older from a minor trauma (e.g., a fall from standing height or less) should be considered a "sentinel event" and warrants immediate assessment for osteoporosis. This includes fractures of the hip, spine, wrist, pelvis, and proximal humerus.

🦋 4. Individuals with Specific Conditions or Taking Medications that Cause Bone Loss

- **Medical Conditions:**

- Type 1 and Type 2 diabetes
- Hyperparathyroidism
- Hyperthyroidism
- Chronic kidney or liver disease
- Malabsorption syndromes (e.g., Celiac disease, IBD)
- Early menopause (before age 40) or hypogonadism in men
- Some cancers and their treatments (e.g., aromatase inhibitors for breast cancer, androgen deprivation therapy for prostate cancer)
- Prolonged immobilization
- **Medications:**
- Glucocorticoids (most common cause of drug-induced osteoporosis)
- Aromatase inhibitors
- Androgen deprivation therapy
- Certain anti-seizure medications
- Long-term use of proton pump inhibitors (PPIs)
- Selective serotonin reuptake inhibitors (SSRIs)
- Excessive thyroid hormone replacement

5. Individuals with Signs Suggestive of Vertebral Fractures

- Even without a known injury, the following signs can indicate silent spinal fractures and warrant vertebral imaging (X-ray or DXA-VFA):
- **Documented height loss** of 1.5 inches (4 cm) or more from their young adult height.
- **Prospective height loss** of 0.8 inches (2 cm) or more measured between clinical visits.
- **Development of a stooped posture (kyphosis).**
- **Unexplained chronic back pain.**

Which DM patient Needs BMD?

Table 4.4—Diagnostic assessment

Individuals who should receive BMD testing

People aged ≥ 65 years

Postmenopausal women and men aged ≥ 50 years with history of adult-age fracture or with diabetes-specific risk factors:

- Frequent hypoglycemic events
 - Diabetes duration >10 years
 - Diabetes medications: insulin, thiazolidinediones, sulfonylureas
 - A1C $>8\%$
 - Peripheral or autonomic neuropathy, retinopathy, nephropathy
 - Frequent falls
 - Glucocorticoid use
-

Assessments Used in the Evaluation and Management of Osteoporosis

	Description	When should this test be used?	Other considerations
Laboratory investigations			
Blood testing	Measure serum calcium, phosphate, alkaline phosphatase, and creatinine levels and assess thyroid function	Prior to initiating therapy to assess for - Potential secondary causes of osteoporosis (eg, hyperparathyroidism or chronic liver disease) - Potential contraindications to treatment when considering pharmacotherapy (eg, kidney dysfunction) in individuals with osteoporosis (if levels were not measured within prior year)	Clinical guidelines vary in the extent of testing recommended
Test individuals at risk for vitamin D deficiency	Measure serum 25-hydroxyvitamin D (25[OH]D) level	When treating individuals at risk for vitamin D deficiency, including those with malabsorption, liver disease, chronic kidney disease, reduced sun exposure, and after gastric bypass surgery	Routine follow-up (3 mo after initiation of supplementation) is not recommended for those without risk factors for vitamin D deficiency
Fracture risk assessment tools			
Fracture Risk Assessment Tool (FRAX) ^a	All 3 tools predict probability of fracture over 1-10 y (depending on the tool used) based on clinical risk factors (with or without measurement of femoral neck for bone mineral density)	- All 3 tools assess absolute fracture risk in adults who are not currently receiving treatment for osteoporosis - Most guidelines recommend assessing fracture risk when ≥50 y of age in both postmenopausal females and in males	- Takes into consideration competing risk of mortality - Bone mineral density is an optional input variable - Bone mineral density is not an input variable
QFracture (assesses the risk of osteoporotic fracture)			
Garvan Fracture Risk Calculator			
			- Includes the number of falls and prior fractures - Bone mineral density is an optional input variable

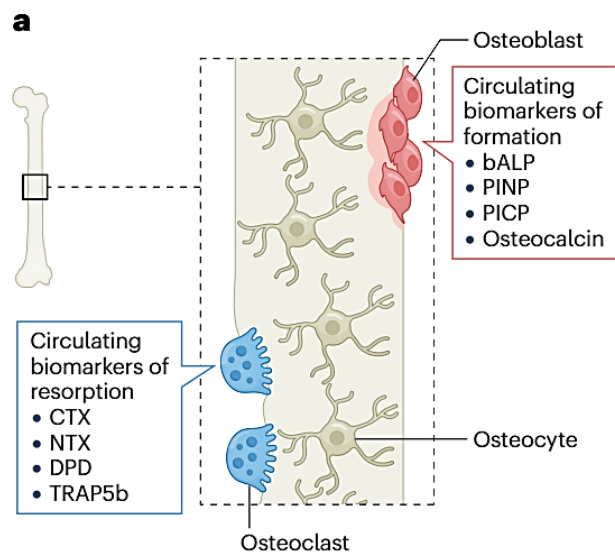
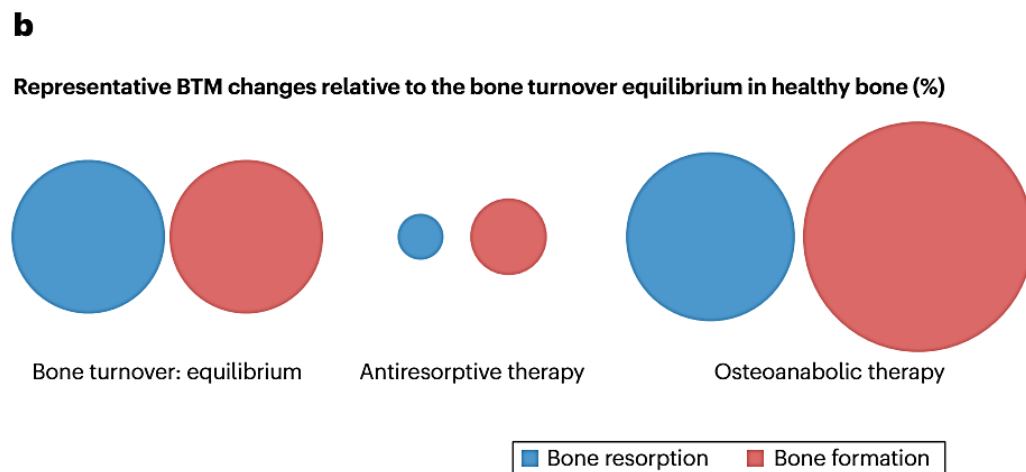


Fig. 2 | BTMs during physiological equilibrium of bone metabolism, antiresorptive therapy and osteoanabolic therapy. a, Bone turnover markers (BTMs), including resorption and formation, are shown. Additional lab markers in general can include calcium, phosphate, parathyroid hormone, calcitriol, liver and kidney parameters and many others depending on clinical questions. Levels of BTMs are preferably determined in serum or plasma. **b,** The equilibrium state of levels of BTMs is shown (left); with antiresorptive therapy,



levels of both formation and resorption BTMs are reduced (centre), with higher reductions in resorption markers; osteoanabolic therapy increases the levels of both BTM types, with the emphasis on bone formation markers^{115,233,234}. bALP, bone-specific alkaline phosphatase; CTX, crosslinks (C-terminal telopeptide of collagen type I); DPD, deoxypyridinoline; NTX, N-terminal telopeptide of collagen type I; PINP, procollagen I N-terminal propeptide; PICP, procollagen I C-terminal propeptide; TRAP5b, tartrate-resistant acid phosphatase 5b.

FRAX Iran

Calculation Tool

Please answer the questions below to calculate the ten-year probability of fracture with or without BMD.

Continent Country

Local Reference

About the risk factors ?

Individuals with fracture risk assessed since 1st June 2011: 231,606

Questionnaire

1. Age (between 40 and 90 years)

2. Sex

☒ Female ☐ Male

3. Weight

kg kg / cm

4. Height

cm

5. Previous Fracture

☐ X

6. Parent Fractured Hip

☐ X

7. Current smoking

☒ ✓

8. Glucocorticoids

☐ X

9. Rheumatoid arthritis

☐ X

10. Secondary osteoporosis

☐ X

11. Alcohol 3 or more units/day

☐ X

12. Femoral neck BMD

Hologic

Calculate

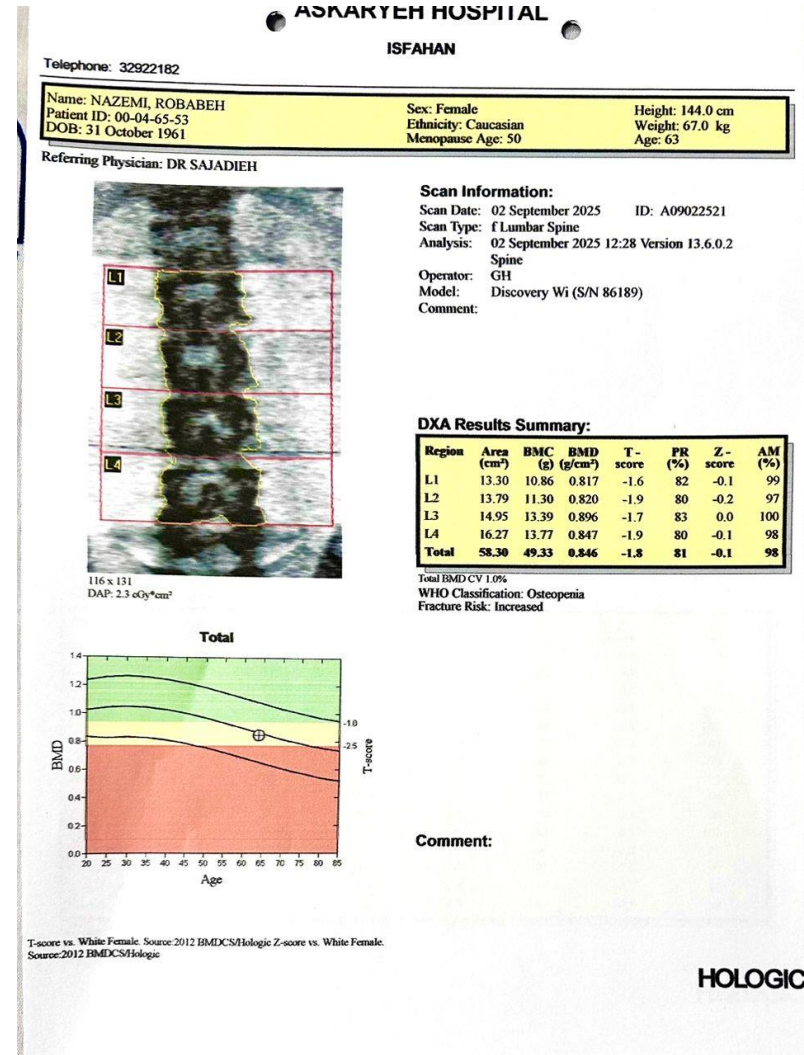
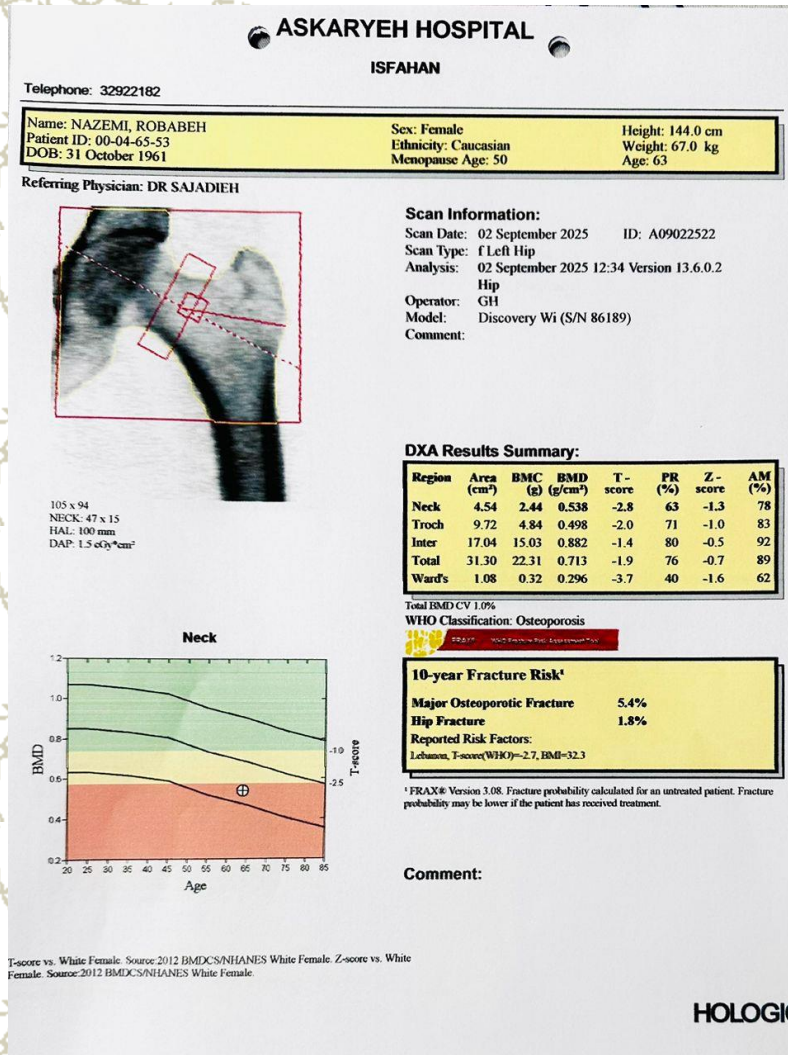
Clear

Assessments Used in the Evaluation and Management of Osteoporosis

Imaging			
Imaging of lateral spine	• Vertebral fracture assessment using conventional radiography or dual-energy x-ray absorptiometry	• To identify the presence of a vertebral fracture in individuals with signs or symptoms of acute vertebral fractures or of occult vertebral fractures (such as height loss and kyphosis)	• A confirmed vertebral fracture on imaging (even if the patient is asymptomatic or it is a remote fracture) is associated with a high fracture risk
Dual-energy x-ray absorptiometry	Areal bone mineral density assessment is • Expressed in g/cm^2 • Expressed as a T score (SDs above or below peak bone mass)	• To assess bone mineral density in both postmenopausal females and in males aged ≥ 50 y as part of the fracture risk assessment or for monitoring the response to osteoporosis therapy	• Patients are considered to have normal bone mass when the T score is ≥ -1.0 • Patients are considered to have low bone mass (osteopenia) when the T score is between -1.0 and -2.5 • Patients are considered to have osteoporosis when the T score is ≤ -2.5
Trabecular bone score	• Unitless texture measure derived from dual-energy x-ray absorptiometry images of the lumbar spine, which are only available when specific software is available for the densitometer	• The trabecular bone score can be entered in the FRAX prediction algorithm to assess fracture risk in adults • When available on the bone mineral density report, the trabecular bone score is useful in individuals close to the treatment threshold (indicates when the results are most likely to alter clinical management)	• Adding the trabecular bone score to FRAX improves fracture prediction

^a Calibrated using individual population-specific fracture and mortality data by country. The country-specific tool is available at <https://www.fraxplus.org>.

DXA



DXA

Askarieh Hospital

Askary St Esfahan
- Esfahan

Patient : NAZEMI, ROBABEH
Date of birth: 10/31/1961 63.8 years
Height / Weight: 144.0 cm / 67.0 kg
Gender / Ethnicity: Female / caucasian

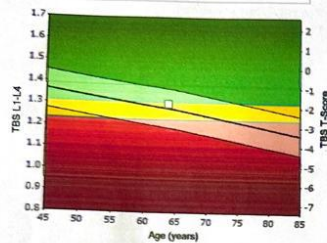
Patient ID: 00-04-65-53
Acquisition date: 09/02/2025
Prescribing doctor: DR SAJADIEH

SPINE TBS REPORT

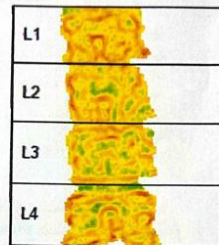
TBS reference graph

Reference population: European (Mediagap)

TBS T-Score L1-L4: -1.8



TBS Mapping



Non diagnostic image

Additional results

Region	TBS	TBS T-Score	TBS Z-Score	BMD
L1	1.145	—	—	0.817
L2	1.332	—	—	0.820
L3	1.432	—	—	0.896
L4	1.302	—	—	0.847
L1-L4	1.303	-1.8	0.2	0.846
L1-L3	1.303	-2.1	0.5	0.846
L1-L2	1.239	-2.7	0.2	0.818
L2-L3	1.382	-1.4	0.9	0.859
L2-L4	1.355	-1.3	0.6	0.855
L3-L4	1.367	-0.9	0.4	0.870

The TBS is derived from the texture of the DXA image and has been shown to be related to bone microarchitecture and fracture risk. This data provides information independent of BMD value; it is used as a complement to the data obtained from the DXA analysis and the clinical examination. The TBS score can assist the health care professional in assessment of fracture risk and in monitoring the effect of treatments on patients across time. Overall fracture risk will depend on many additional factors that should be considered before making diagnostic or therapeutic recommendations. The software does not diagnose disease or recommend treatment regimens. Only the health care professional can make these judgments. Date of analysis: 09/02/2025 - TBS version : 3.0.2.0 - DXA : Hologic Discovery Wi R6189 - DXA file: "PA258QZA.P21" Before accepting this report, the user is held accountable for ensuring that the DXA examination has been carried out: - by the osteodensitometer: Hologic Discovery Wi (R 86189) - scan mode "Fast array" - after the latest TBS height calibration, the 16/2020 10:46:11 AM.

ISFAHAN

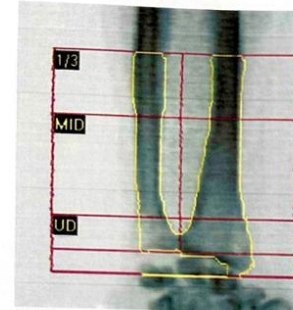
Telephone: 32922182

Name: NAZEMI, ROBABEH
Patient ID: 00-04-65-53
DOB: 31 October 1961

Sex: Female
Ethnicity: Caucasian
Menopause Age: 50

Height: 144.0 cm
Weight: 67.0 kg
Age: 63

Referring Physician: DR SAJADIEH



210 x 98
DAP: 1.4 cGy*cm²

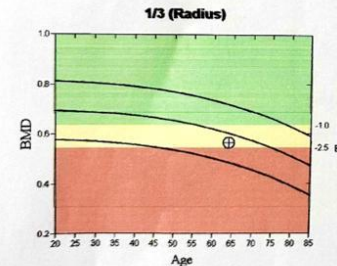
Scan Information:

Scan Date: 02 September 2025 ID: A09022524
Scan Type: a R. Forcann
Analysis: 02 September 2025 12:34 Version 13.6.0.2
Right Forearm
Operator: GH
Model: Discovery Wi (S/N 86189)
Comment:

DXA Results Summary:

Radius	Area (cm ²)	BMC (g)	BMD (g/cm ³)	T-score	PR (%)	Z-score	AM (%)
1/3	3.26	1.84	0.565	-2.2	81	-0.6	94
MID	6.22	2.76	0.443	-3.0	73	-1.5	85
UD	3.79	1.26	0.331	-1.9	75	-0.8	88
Total	13.27	5.86	0.441	-2.6	76	-1.1	88

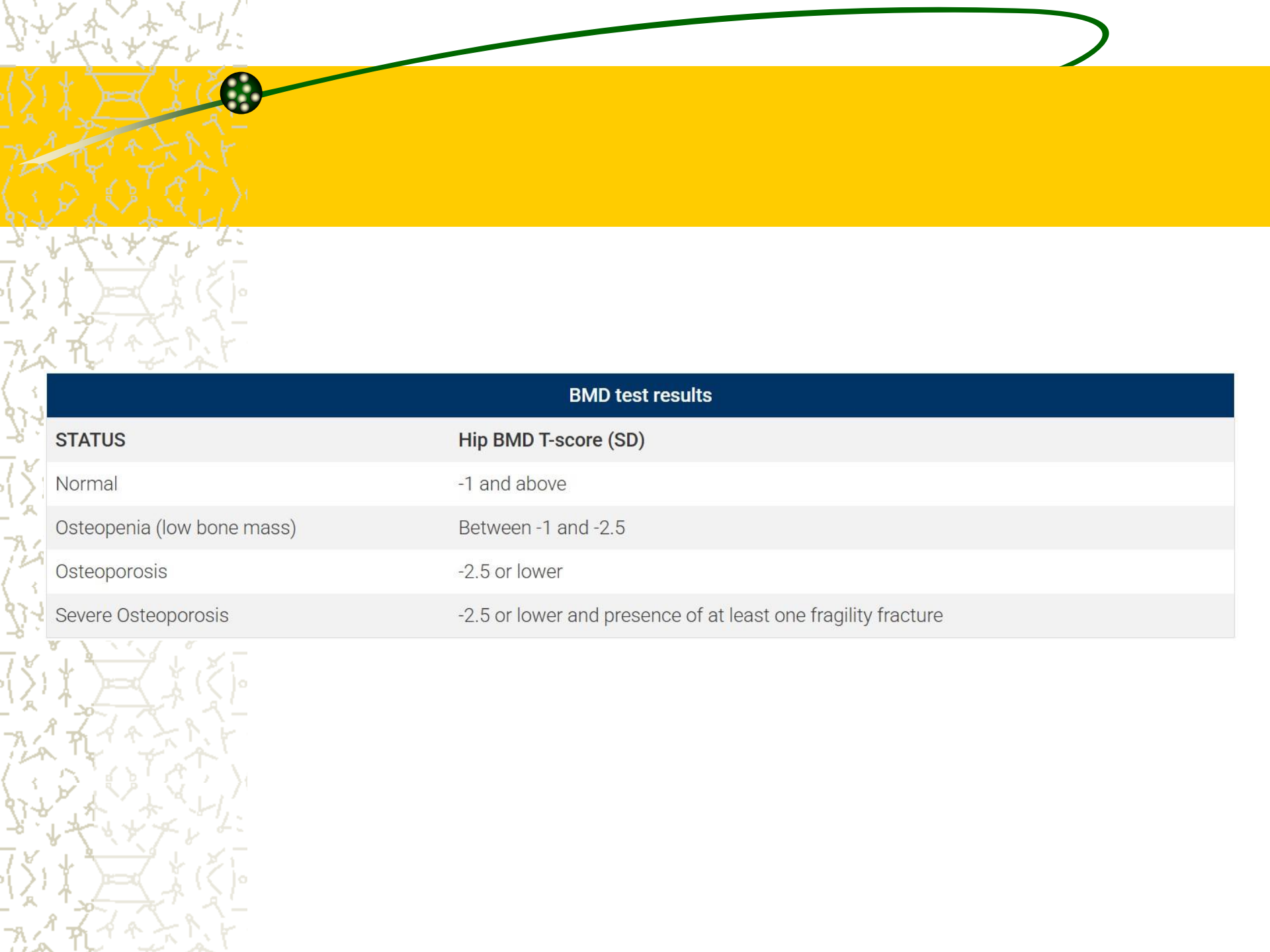
Total BMD CV 1.0%
WHO Classification: Osteopenia
Fracture Risk: Increased



Comment:

T-score vs. White Female. Source: 2012 BMDCS/Hologic Z-score vs. White Female. Source: 2012 BMDCS/Hologic

HOLOGIC



BMD test results	
STATUS	Hip BMD T-score (SD)
Normal	-1 and above
Osteopenia (low bone mass)	Between -1 and -2.5
Osteoporosis	-2.5 or lower
Severe Osteoporosis	-2.5 or lower and presence of at least one fragility fracture

Pharmacological Fracture Prevention Therapies

Table 2. Pharmacological Fracture Prevention Therapies

	Drug	Dosage	Mechanism of action	Contraindications	Potential adverse effects
Antiresorptive agents					
Oral bisphosphonate	Alendronate	70 mg/wk	• Direct osteoclast inhibition	Creatinine clearance <30-35 mL/min, hypocalcemia, or esophageal abnormalities (eg, esophagitis or peptic ulcer disease)	Dyspepsia (20%-30% of patients), myalgia (4% of patients), osteonecrosis of the jaw (<0.1% of patients), and atypical femoral fracture (0.02%-0.1% of patients)
	Risedronate	35 mg/wk			
	Ibandronate	150 mg/mo			
Intravenous bisphosphonate	Zoledronic acid	5 mg every 12-18 mo (administered intravenously)	• Direct osteoclast inhibition	Creatinine clearance <30-35 mL/min or hypocalcemia	Headache, myalgia, or fever (30% of patients); transient elevated level of creatinine (2% of patients); kidney failure (rare); hypocalcemia (<1% of patients); osteonecrosis of the jaw (<0.1% of patients); and atypical femur fracture (0.02%-0.1% of patients)
	Ibandronate	3 mg every 3 mo (administered intravenously)			Esophageal abnormalities are not a consideration with the intravenous formulation
RANKL inhibitor	Denosumab	60 mg every 6 mo (administered subcutaneously)	• Reduces osteoclast differentiation and activity due to inhibition of RANKL	Hypocalcemia	Eczema (3% of patients), cellulitis (0.3% of patients), osteonecrosis of the jaw (<0.1% of patients), and atypical femur fracture (0.02%-0.1% of patients) Increased risk of vertebral fracture if denosumab dosing is delayed by >1 mo or interrupted
Selective estrogen receptor modulator	Raloxifene	60 mg/d (administered orally)	• Estrogen receptor agonist on bone	Venous thromboembolism, stroke, or cardiovascular disease	Hot flashes (10% of patients), leg cramps (7% of patients), peripheral edema (5% of patients), and deep vein thrombosis (0.9% of patients)
Anabolic agents					
Parathyroid hormone analog	Teriparatide	20 µg/d for 1.5-2 y (administered subcutaneously)	• Stimulation of parathyroid hormone receptor • Increases bone remodeling (formation is greater than resorption)	Creatinine clearance <30 mL/min, bone malignancy, increased risk for osteosarcoma, or hypercalcemia	Nausea (20% of patients), headache (13% of patients), hypercalcemia (3%-6% of patients), and leg cramps (3% of patients)
	Abaloparatide	80 µg/d for 1.5-2 y (administered subcutaneously)			
Sclerostin inhibitor	Romosozumab	210 mg/mo for 12 mo (administered subcutaneously)	• Inhibits the sclerostin-activating Wnt signaling pathways • Increases bone formation • Reduces bone resorption	Myocardial infarction or stroke (within past 12 mo) or hypocalcemia	Injection site reactions (5% of patients), serious cardiovascular events (2.5% of patients treated with romosozumab vs 1.9% treated with alendronate), osteonecrosis of the jaw (rare ^a), and atypical femur fracture (rare ^a)

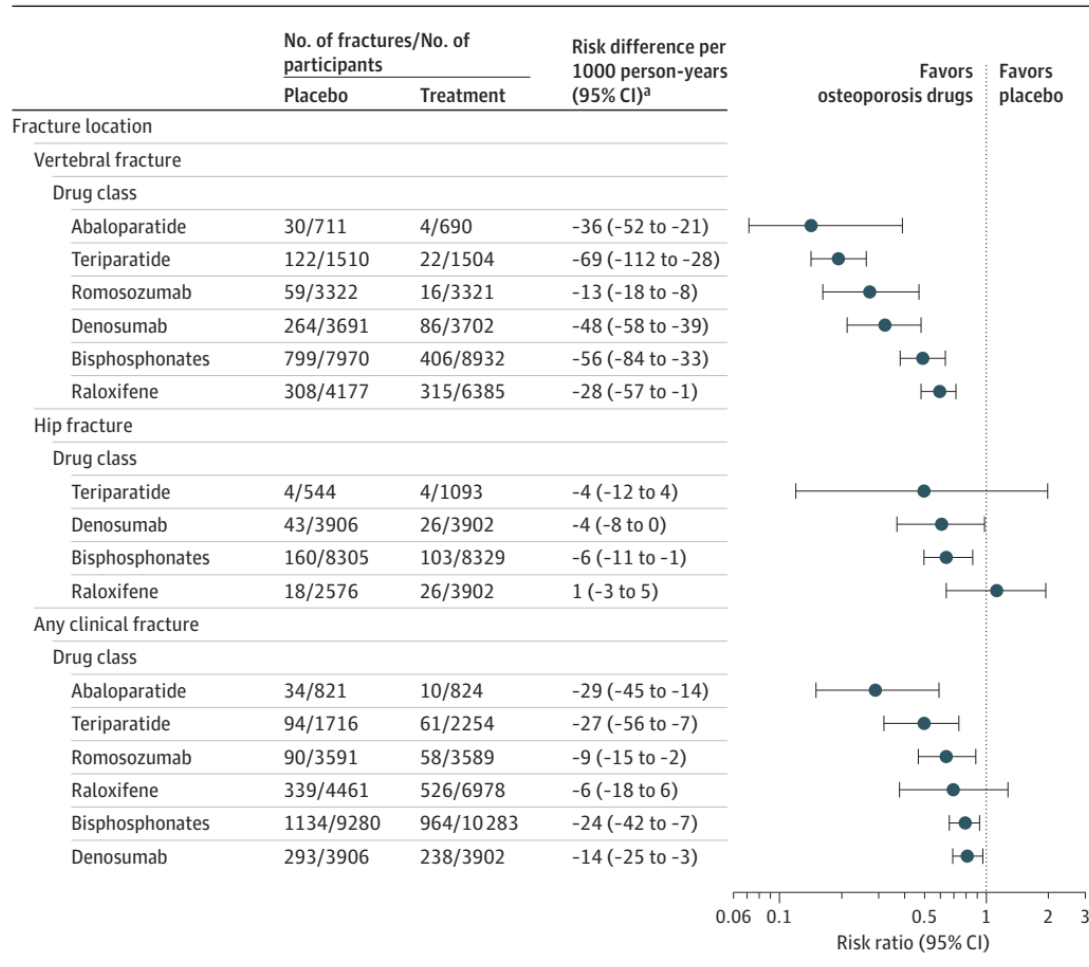
Abbreviation: RANKL, receptor activator of nuclear factor κB ligand.

participants who received romosozumab in the large romosozumab vs placebo trials.

^a There were 2 cases of osteonecrosis of the jaw and 3 cases of atypical femur fracture reported in 5621

Efficacy of Osteoporosis Medication Use for the Prevention of Vertebral, Hip, and Any Clinical Fractures

Figure 2. Efficacy of Osteoporosis Medication Use for the Prevention of Vertebral, Hip, and Any Clinical Fractures



Screening, Diagnosis, and Management of Osteoporosis and Fracture Prevention

Nonpharmacological interventions to prevent fractures^a

- Adequate intake of calcium and vitamin D (dietary and supplemental)
- Regular muscle resistance and balance exercises
- Fall assessment and prevention (if appropriate)
- Smoking cessation (if relevant)
- Alcohol intake reduction (≤ 2 drinks daily)
- Maintain body mass index (BMI) of $\geq 20^b$

Screening and evaluation^a

Assess for presence of clinical risk factors for fractures and physical examination

Risk factors for fracture

- History of fracture
- Glucocorticoid use (>3 mo in the last year) with prednisone dose ≥ 5 mg daily
- Falls (≥ 2 in the last year)
- Rheumatoid arthritis
- Parental history of hip fracture
- BMI $<20^b$
- Alcohol use (≥ 3 drinks daily)
- Current smoking
- Secondary osteoporosis (due to glucocorticoids, hyperparathyroidism, chronic kidney disease, vitamin D deficiency, or other conditions)

Physical examination findings suggesting vertebral fracture

- Height loss
- Increased occiput to wall distance^c

Clinical diagnosis of osteoporosis can be made in patients with a fall-related hip, vertebral, or multiple fracture events in the absence of another cause (eg, primary bone cancer or metabolic bone disease)

Estimate fracture risk as appropriate

Bone mineral density (BMD) screening; see Tables 1 and 3 for screening recommendations^d

If appropriate, measure BMD and include in FRAX risk estimation

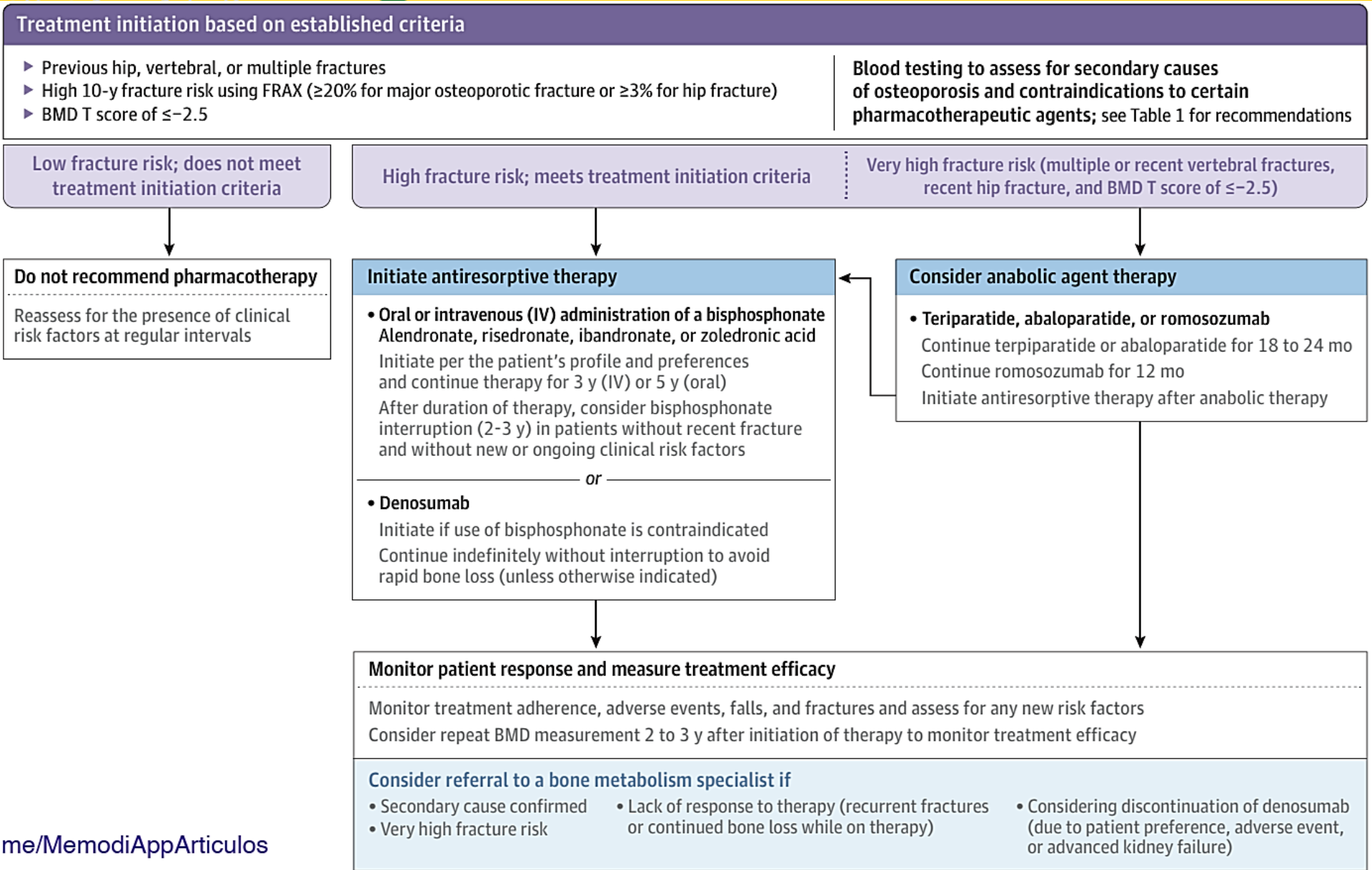
Spinal imaging; see Table 1 for screening guidelines

Perform lateral spinal radiograph or dual-energy x-ray absorptiometry-based vertebral fracture assessment to identify undiagnosed vertebral fractures

FRAX estimation

Estimate 10-y absolute fracture risk using country-specific Fracture Risk Assessment FRAX^e tool with previously collected clinical risk factors and BMD measurement (if available)

Previous hip, vertebral, or multiple fractures usually indicate high fracture risk regardless of FRAX or BMD





Goals and targets in long-term osteoporosis therapy

Treatment goals

- Keep the patient free of fragility fracture or at least reduce the fracture risk as much as possible
- Avoid long-term adverse effects of bone medication

Treatment targets

- Improve bone structure and density to a level associated with low fracture risk
- Preserve bone architecture and strength
- Control comorbidities and fall risk as well as individual risk factors

Thank you and hope for a good rain

