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Optimizing Osteoporosis Prevention and Treatment: The Bone Health and Osteoporosis Foundation's Clinician's Guide 2022

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Larry Raisz Plenary Lecture
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Lawrence G. Raisz, M.D. Memorial Lecture Award

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CONSENSUS STATEMENT

The clinician's guide to prevention and treatment of osteoporosis

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Abstract
Osteoporosis is the most common metabolic bone disease in the USA and the world. It is a subclinical condition until complicated by fracture(s). These fractures place an enormous medical and personal burden on individuals who suffer from them and take a significant economic toll. Any new fracture in an adult aged 50 years or older signifies important elevated risk for subsequent fractures, particularly in the year following the initial fracture. What a patient perceives as an unfortunate accident may be seen as a sentinel event indicative of bone fragility and increased future fracture risk even when the result of considerable trauma (Leslie et al. Osteoporos Int 31(6): 1059–1067, 2009; Mackey et al. JAMA 298(20): 2381–388, 2007). Clinical or subclinical vertebral fractures, the most common type of osteoporotic fractures, are associated with a 5-fold increased risk for additional vertebral fractures and a 2- to 3-fold increased risk for fractures at other sites. Untreated osteoporosis can lead to a vicious cycle of recurrent fracture(s), often resulting in disability and premature death. In appropriate patients, treatment with effective antifracture medication prevents fractures and improves outcomes. Primary care providers and medical specialists are critical gatekeepers who can identify fractures and initiate proven osteoporosis interventions. Osteoporosis detection, diagnosis, and treatment should be routine practice in all adult healthcare settings. The National Osteoporosis Foundation (NOF) first published the *Clinician's Guide* in 1999 to provide accurate information on osteoporosis prevention and treatment. Since that time, significant improvements have been made in diagnostic technologies and treatments for osteoporosis. Despite these advances, a disturbing gap persists in patient care. At-risk patients are often not screened to establish fracture probability and *not* educated about fracture prevention. Most concerning, the majority of highest risk women and men who have a fracture(s) are *not* diagnosed and *do not* receive effective, FDA-approved therapies. Even those prescribed appropriate therapy are unlikely to take the medication as prescribed. The *Clinician's Guide* offers concise recommendations regarding prevention, risk assessment, diagnosis, and treatment of osteoporosis in postmenopausal women and men aged 50 years and older. It includes indications for bone densitometry as well as fracture risk thresholds for pharmacologic intervention. Current medications build bone and/or decrease bone breakdown and dramatically reduce incident fractures. All antifracture therapeutics treat but do not cure the disease. Skeletal deterioration resumes sooner or later when a medication is discontinued—sooner for non-bisphosphonates and latter for bisphosphonates. Even if normal BMD is achieved, osteoporosis and elevated risk for fracture are still present (Lewiecki *et al.*

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LeBoff MS, Greenspan SL, Insogna KL, et al. *Osteo Int.* In Press 2022

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Bone Health and Osteoporosis Foundation (BHOF) Clinician's Guide: Comprehensive Review of All Aspects of the Care of Patients with Low Bone Mass and Osteoporosis

- Osteoporosis Impact and review
- How to diagnose low bone mass and osteoporosis
- Treatment considerations and new therapeutic approaches
- Rehabilitation and pain management following fragility fractures
- Importance of Secondary Fracture Prevention

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Osteoporosis is a Prevalent Disease

- **1 out of 2** women and **1 out of 5** men ≥50 years will suffer an osteoporotic fracture
- **2 million fractures** each year in U.S..... projected to increase to 3.2 million in 2040
- Fractures result in >432,000 hospital admissions, ~2.5 million office visits, and ~180,000 nursing home admissions
- Costs are expected to increase from $57 billion to over $95 billion by 2040
- This heavy personal and economic toll could be reduced by routine evaluation and treatment

Lewiecki EM et al. *JBMR* 2019
Burge R et al. *JBMR* 2007

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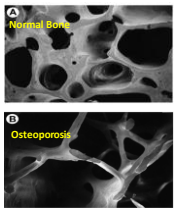
What is Osteoporosis?

Low bone mass and microarchitectural changes that lead to reduced bone strength and increased fractures



Dempster DW, et al. *J Bone Miner Res.* 2000
NIH Consensus Development Panel. *JAMA.* 2001
LeBoff MS, Greenspan SL, Insogna KL, et al. *Oxteo Int.* In Press 2022

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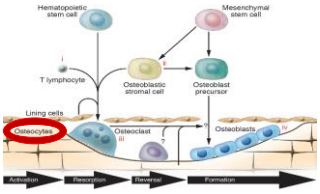
Bone is a Dynamic Organ: Osteoporosis Results from a Net Increase in Bone Breakdown Relative to Bone Formation



Raisz, LG. *The Journal of Clinical Investigation*, 2005

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A Fracture is A Sign of Osteoporosis

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Vertebral Fractures: Only 1/3 are Clinically Diagnosed

- Patients with spine fractures have a 5-fold increased risk of another spine and 2-fold risk of a hip fracture
- Predict future fractures *independent* of BMD
- Associated with increased morbidity and mortality
- Importance of spine imaging

Bliuc et al. *JAMA*. 2009
Ross et al. *Ann Intern Med*. 1991
Cooper et al. *Bone*. 1993

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A Spot Light on Wrist Fractures

- Most common fracture of the upper extremity and five times greater risk in women than men
- Early fracture with increased incidence with age
- In women and men recent data show that a wrist fracture is associated with *an increased* risk of other fragility fractures

Crandall CJ, Hovey KM, Cauley JA, ..LeBoff, MS. *JBMR*. 2015
Crandall CJ, Hovey KM, Andrews CA, ... LeBoff MS. *JCEM*. 2015
Sim, E.S., et al. *Osteo Int*. 2014
Edwards, B et al. *BMJ*. 2010
Burge R et. al. *J Bone Min Res*. 2007
Litwic A et al. *Orthopedic Muscul System*. 2014
Wright, N., Hooker, C., Nielson, *Osteo Int*. 2018

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Associations Between Incident **Wrist Fracture** (n=8,792)and **Subsequent Fracture(s):** Hazard Ratios

Fracture	Event	Hazard Ratio	95%CI
Any Non-Wrist	33,596	1.40	1.33-1.48
Spine	5,301	1.48	1.32-1.66
Humerus	4,309	1.78	1.57-2.02
Upper Extremity	7,228	1.88	1.70-2.07
Lower Extremity	14,867	1.36	1.26-1.48
Hip	3,801	1.50	1.32-1.71

Model: Adjusted for age, race and BMI

Crandall CJ, Hovey KM, Cauley JA et. al.. LeBoff, MS *JBMR 2015*

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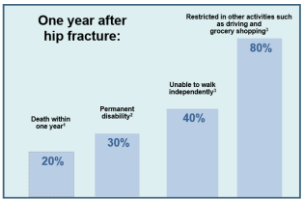
Hip Fractures: The Most serious Fractures



Leibson CL, et al. *Journal of the American Geriatric Society*. 2002
Magaziner, et al. *American Journal of Epidemiology*. 2003
Cooper *CAm J Med*. 1997
National Osteoporosis Foundation

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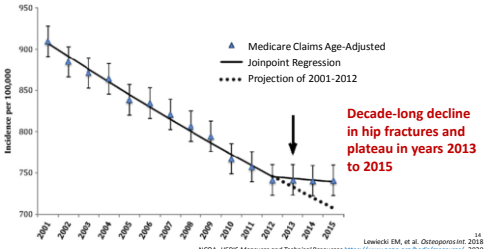
Decline in Hip Fractures Has Plateaued: Only *35% to 40% Medicare patients with fractures are evaluated and treated for their underlying osteoporosis*



Lewiecki EM, et al. *Osteoporos Int*. 2018
NCQA, *HEDIS Measures and Technical Resources https://www.ncqa.org/hedis/measures/*, 2020

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Diagnostic considerations

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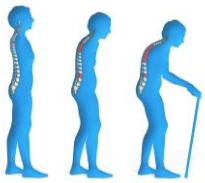
Why is Important to Diagnose Secondary Causes of Osteoporosis?

- Reduced acquisition of peak bone mass, a determinant of osteoporosis later in life
- Increased bone loss and elevated fracture risk
- Skeletal changes that may be reversible



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Risk Factors: Medical Disorders

Gastrointestinal disorders:
- Celiac disease
- Inflammatory bowel disease
- Pancreatic disease
- Primary biliary cirrhosis
- Gastric bypass

Hematologic disorders:
- Multiple myeloma
- Sickle cell disease
- Leukemia/lymphoma
- Systemic mastocytosis

Rheumatologic diseases
- Rheumatoid arthritis
- Systemic lupus
- Ankylosing spondylitis

Genetic diseases
- Cystic fibrosis
- Ehlers-Danlos
- Hemochromatosis
- Hypophosphatasia
- Marfan syndrome
- Osteogenesis imperfecta

Neurologic disorders:
- Epilepsy
- Multiple sclerosis
- Parkinson's disease
- Spinal cord injury
- Muscular dystrophy
- Stroke

Misc:
- Acquired Immune Deficiency Syndrome
- Chronic Obstructive Pulmonary Disease
- End-Stage Renal Failure
- Post-transplant bone disease
- Hypercalciuria and nephrolithiasis
- Congestive Heart Failure

Urticaria Pigmentosa

LeBoff MS, Greenspan SL, Insogna KL, et al. *Osteo Int*. In Press 2022 17

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Risk Factors: Medications

Medications:
- **Glucocorticoids**
- Thyroid hormone (excess)
- Depo-medroxyprogesterone
- Tamoxifen (premenopausal use)
- Aromatase inhibitors
- Androgen suppression
- GnRH agonists
- *Proton pump inhibitors*
- Selective serotonin reuptake inhibitors
- Thiazolidinediones
- Lithium
- Methotrexate
- Cyclosporine A& tacrolimus
- Chemotherapy agents
- Anticoagulants (heparin)
- Anticonvulsants (e.g. phenobarbital, phenytoin, valproate)

LeBoff MS, Greenspan SL, Insogna KL, et al. *Osteo Int*. In Press 2022 18

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How Do You Evaluate a Patient with Osteoporosis?

- Detailed history, calculated calcium intake, and physical examination
- Family History
- Falls History
- Height Measurement (with stadiometer)
- Bone Density testing
- Laboratory Tests

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Dual-energy X-ray Absorptiometry (DXA)

- Measures areal BMD (aBMD) spine, hip, forearm and VFA
- Low radiation
- Utility of DXA
  - Diagnose osteoporosis and monitor treatment
  - Predict fracture risk

FNIH Bone Quality Study: Meta-regression Analysis showed larger Improvements in BMD associated with **greater reductions in fracture risk** (e.g., 4% increase in lumbar spine BMD associated with 62% decrease in vertebral fracture and a 38% reduction in hip fracture

Vertebral Fracture Assessment

Bousseïn ML, et al. JBMR 2019

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How are Low Bone Mass and Osteoporosis Diagnosed?

World Health Organization Criteria	
Category	**T-Score**
Normal	-1.0 or above
Low Bone Mass (Osteopenia)	-1.1 to -2.4
Osteoporosis	-2.5 or below

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Who Should Have A Bone Density Test?

- Postmenopausal women and men ≥50 with >**1 risk factor***[+]
- **Women: ≥Age 65 yrs** [+]
- **Men: ≥ Age 70 yrs***
- Fracture ≥50 years
- Vertebral Deformity
- Hyperparathyroidism
- Glucocorticoid therapy(≥ 5.0 mg/d ≥3 months)
- Monitor response to therapy
- Medical necessity

Medicare Mandate 1998
*LeBoff MS, Greenspan SL, Insogna KL, et al. *Osteo Int*. In Press 2022
*Watts N, et al. *JCEM* 2012
[+]US Preventive Services Task Force JAMA 2018

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Consider Bone Density Test at the 33% Radius in the Following Patients

- BMD cannot be measured at the spine or hip (e.g, bilateral hip replacements or obesity)
- Hyperparathyroidism
- Hyperthyroidism
- Androgen deprivation therapy for prostate cancer (metastatic disease)
- Those undergoing Orthopedic Surgery

LeBoff MS, Greenspan SL, Insogna KL, et al. *Osteo Int*. In Press 2022

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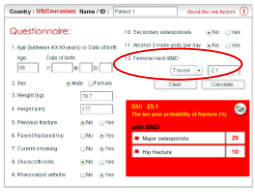
Risk Factors and Bone Density: FRAX®



- Indicated for those with BMD in low bone mass (osteopenia range)
  - Postmenopausal women and men age ≥50
- Treatment thresholds in U.S.:
  - 10-year probability of hip fracture **≥3%**
  - 10-year probability of major osteoporosis-related fracture **≥20%**

www.shef.ac.uk/FRAX

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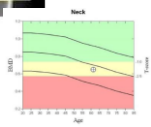
Hip BMD showing Low Bone Mass and a History of Fracture: FRAX® score indicates an elevated absolute risk



Sex: Female	Height: 64.5 in
Ethnicity: White	Weight: 115.0 lb
	Age 61

DXA Results Summary:

Region	Area (cm2)	BMC (g)	BMD (g/cm2)	T-score	PR(%)	Z-score	AM(%)
Neck	**5.14**	**3.34**	**0.649**	**-1.8**	**76**	**-0.5**	**93**
Troch	11.79	6.68	0.567	-1.4	81	-0.4	93
Inter	11.92	15.03	0.839	-1.7	76	-0.9	85
Total	34.85	25.04	0.719	-1.8	76	-0.8	88
Ward's	1.14	0.56	0.493	-2.1	67	0.0	100

Total BMD CV 1.0%
WHO Classification: Osteopenia

10-year Fracture Risk1	Without Prior Fracture	With Prior Fracture
Major Osteoporotic Fracture	19%	30%
Hip Fracture	2.3%	4.0%

Reported Risk Factors: US (Caucasian), Neck BMD = 0.649, BMI = 19.4, Parental fracture, smoking rheumatoid arthritis

1 FRAX® Version 3.08. Fracture probability calculated for an untreated patient. Fracture probability may be lower if the patient has received treatment

Kanis JA, et al. *Osteo Int*. 2011

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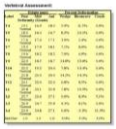
Who Should Have a Vertebral Imaging/Vertebral Fracture Assessment (VFA)?



Measured height loss
- Historical height loss of ≥ 1.5 inches
- Prospective height loss of ≥ 0.8inches

In all **women ≥70 yrs.** and all **men ≥80 yrs.** if T-score is ≤ -1.0

In **women aged 65-69 yrs.** and **men aged 75-79 yrs.** if T-score is ≤ -1.5

Postmenopausal women and men ≥ 50 yrs. with **Risk Factors:**
- Fractures
- Glucocorticoids
- Hyperparathyroidism

International Society for Clinical Densitometry (ISCD) Official Positions – Adult 2019
LeBoff MS, Greenspan SL, Insogna KL, et al. *Osteo Int*. In Press 2022

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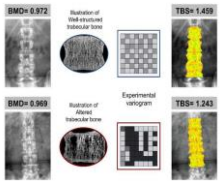
Trabecular Bone Score (TBS) in Patients with Low Bone Mass

- Textural measure of spine DXA images to estimate structural characteristics
- *Predicts fracture risk* independent of BMD and FRAX®
- Higher TBS associated with better bone ***microarchitecture***
- TBS-adjusted FRAX



Hans D, et al. *Journal of clinical densitometry*. 2011
Roux JP et al. *Osteoporosis Int*. 2013
Silva BC et al. *J Bone Miner Res*. 2013
Krieg MA, et al. *Osteoporosis*. 2014
Goldman A et al. *Osteoporosis Int*. 2018

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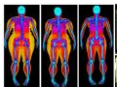
Other Imaging Technologies: Used in Research

DXA for Body Composition: aBMD (whole body) and body composition (total and regional fat and lean tissue and VAT)

Peripheral Quantitative Computed Tomography (pQCT) at Radius and Tibia: Total, trabecular, and cortical volumetric (v)BMD and strength indices at the radius and tibia

High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) at Radius and Tibia: Microarchitecture, cortical and trabecular bone vBMD, trabecular number, thickness, and separation and strength indices



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Other Imaging Technologies (Cont)

Computed Tomography (QCT): vBMD of the spine or proximal femur using calibration approaches. Finite Element Analyses provide estimates of bone strength. Higher radiation exposure than DXA. Opportunistic QCT uses tests performed for other reasons with a synchronous calibration to assess vBMD

Magnetic Resonance Imaging (MRI): MRI imaging to estimate bone geometry and trabecular bone structure of the radius, tibia, femur and calcaneus. No ionizing radiation

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Universal bone health recommendations

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Universal Recommendations

- Recommend daily calcium (ideally from diet)
- Vitamin D 800-1000 IU/daily
- Counsel on fall prevention
- Advocate regular weight-bearing exercises
- Advocate smoking cessation and limited alcohol intake

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Estimate Dietary Calcium Intake from Calcium-Rich foods

Product	# of Servings/d	Estimated calcium/ serving, in mg	Calcium in mg
Milk (8 oz.)	_____	X 300	= _____
Almond/soy milk (8 oz.)	_____	X450	= _____
Yogurt (6 oz.)	_____	X 300	= _____
Cheese (1 oz. or 1 cubic in.)	_____	X 200	= _____
Fortified foods or juices	_____	X 80 to 1,000**	= _____
Tofu, firm (8 oz.)	_____	X 250	= _____
		Subtotal	= _____
STEP 2: Add 250 mg for non-dairy sources to subtotal			+ 250
		TOTAL Calcium, in mg	= _____

*About 75 to 80% of the calcium consumed in American diets is from dairy products
**Calcium content of fortified foods varies, and it is important to review individual labels

LeBoff MS, Greenspan SL, Insogna KL, et al. *Osteo Int*. 2022

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Recommended Calcium and Vitamin D Intakes for Women and Men

LIFE STAGE GROUP	CALCIUM IOM/BHOF (mg/day)	CALCIUM Safe upper limit (mg/day)	VITAMIN D IOM/BHOF (units/day)	VITAMIN D Safe upper limit (units/day)
51+ year old women	1,200	2500	600/800-1000	4000
51–70-year-old men	1,000	2000	600/800-1000	4000
71+ years old men and women	1,200	2000	800/800-1000	4000

LeBoff MS, Greenspan SL, Insogna KL, et al. *Osteo Int.* 2022
Ross AC, Manson JE, Abrams SA, et al. *JCEM.* 2011

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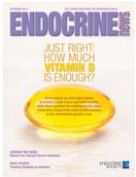
How Much Vitamin D For Bone?

- Deficiency: < 20 ng/ml
- **Goal for 25(OH)D level: ≥ 30 ng/ml**
- Reference Range **20-50** ng/ml



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Large Population-Based, Primary Prevention Study in Generally Healthy Adults: VITamin D and OmegA-3 TriaL (VITAL)

- *VITAL* is a research study in 25,874 **men and women** enrolled from 50 states that investigated whether daily supplemental **vitamin D_3 (2000 IU)** and/or omega-3 fatty acids (fish oil; 1g) reduced the risk of **cancer, heart disease, and stroke**.
- **VITAL** Effects of vitamin D and/or fish oil on **fractures** and **bone health measures** (R01 AR 60574 and R01 AR 059775
  PI: MS LeBoff)

Supported by the NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases

JoAnn Manson, MD Julie Buring, ScD JoAnn E. Manson, MD, DrPH

BWH Division of Preventive Medicine and Endocrinology, Diabetes and Hypertension

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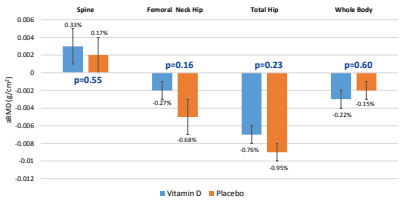
No Effect of Supplemental Vitamin D3 vs. Placebo on Absolute or Percent changes in aBMD (n = 771) In Adults Not Selected for Vitamin D Deficiency or Low Bone Mass



DXA

*Analyses adjusted for age, sex and race

LeBoff MS et al. *J Bone Miner Res.* 2020.

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How much Exercise for Adults with Low Bone Mass and Osteoporosis? BHOF Guide

• **Weight-bearing activities**	• 30 min on most days of the week in a single 30-min session or in multiple sessions spread throughout the day
• **Muscle strengthening activities**	• 2-3 days per week. Can be done all at once or in multiple short sessions, full body or one body part per day (For example, arms one day, legs the next and trunk the next)
• **Balance, posture, and functional activities**	• Every day or as often as needed. Focus on area of most need: If patient has fallen, balance activities should be emphasized. If patient has trouble climbing stairs or getting up from the couch, he/she should do more functional exercises

LeBoff MS, Greenspan SL, Insogna KL, et al. *Osteo Int*. In Press 2022
BHOF Health Professional's Guide to Rehabilitation of the Patient with Osteoporosis, 2003
BHOF Boning up on osteoporosis, 2019

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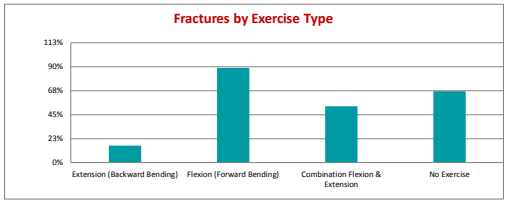
Activities that Require Spinal Flexion Increase Risk of Spine Fractures and Spinal Extension Exercises Decrease Risk



Sinaki M, Mikkelsen BA. *Arch Phys Med Rehab*. 1984

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US FDA-Approved Drugs for Osteoporosis

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FDA-Approved Drug Therapies on Fracture Reductions

	Vertebral fracture	Hip fracture	Non-spine
Alendronate	X	X	X
Risedronate	X	X	X
Ibandronate	X	No	No
Zoledronic acid	X	X	X
Hormone therapy (prevention)	X	X	X
Raloxifene	X	No	No
Denosumab	X	X	X
Teriparatide	X	N/A	X
Abaloparatide	X	N/A	X
Romosozumab	X	Post ALN	X

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Consider osteoporosis treatment in postmenopausal women and men ≥50 yrs. for:

Primary Fracture Prevention*:*

- **T-Score ≤ -2.5** at **femoral neck, total hip, lumbar spine, *33% radius***
- **Low bone mass** (**osteopenia: T-score between -1.0 and -2.5)** by DXA **with FRAX score and** 10-year hip fracture risk ≥3% or a 10-year major osteoporosis-related fracture risk ≥20%

Secondary Fracture Prevention:

- **Fracture of the hip or vertebra** regardless of BMD
- **Fracture of *distal forearm,* proximal humerus, or pelvis in persons with low bone mass**

LeBoff MS, Greenspan SL, Insogna KL et al *Osteo Intern* 2022 In Press

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Inhibitors of Bone Breakdown: Bisphosphonates

- **Oral bisphosphonates**: alendronate, risedronate given once weekly
  - FDA approved for Prevention and Treatment of Osteoporosis and other indications
- **Intravenous bisphosphonate**: Zoledronic Acid given once a year.
  - Approved with post-hip fracture with vitamin D
  - In women aged ≥ 65 years with l**ow hip BMD**, zoledronic acid administered every 18 months for 6 years reduced vertebral and nonvertebral fractures
- Rare risk of osteonecrosis of the jaw and atypical femur fractures and flu-like symptoms with zoledronic acid
- Meta-analysis of RCTs found *no delay* in fracture healing with bisphosphonates

Xue D, et al. *J Orthop Surg Res.* 2014

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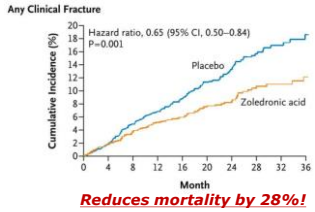
Zoledronate and Vitamin D Post-hip Fracture: Reduced Clinical, Spine, and Non-spine Fractures



Reduces mortality by 28%!

Lyles et al. *N Engl J Med.* 2007

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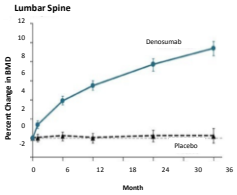
Other Inhibitors of Bone Breakdown: Denosumab

- Denosumab is a fully human monoclonal antibody against RANKL
- Administered as a SQ injection every 6 months
- Rare skin and other infections, rare risk of osteonecrosis of the jaw and atypical femur fractures
- If not given every 6 months rebound bone breakdown and spine fractures. When stopping start another antiresorptive medication

Effects of 3 Years of Denosumab on Spine BMD



Cummings S et al. *N Engl J Med 2009*

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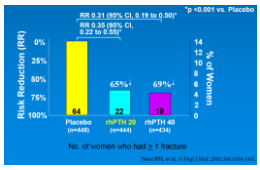
Stimulators of Bone Formation

- Teriparatide (PTH1-34) or **Abaloparatide (PTHrP 1-34)**
- Administered as a daily SQ injection (abaloparatide injected peri-umbilically)
- Optimally started before an inhibitor of bone breakdown
- Follow treatment with an antiresorptive agent, usually a bisphosphonate or denosumab, to maintain or further increase BMD

Effect of rhPTH(1-34) on the Risk of New Vertebral Fractures



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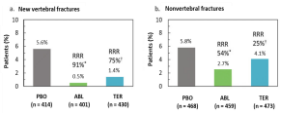
Who is a candidate for Teriparatide (1-34 PTH) or Abaloparatide (PTHrp 1-34).

- Adult-motivated to take daily injection
- Women and men at high risk for fractures
- Do not use in patients with: hypercalcemia, XRT, skeletal malignancy, elevated alkaline phosphatase, Paget's Disease,
- BLACK BOX warning concerning osteosarcoma risk in rodents recently removed for both
- Teriparatide but not abaloparatide is currently approved for use beyond 2 years

Effect of Abaloparatide and Teriparatide on Fracture Risk



Miller PD, et al. *JAMA* 2016
McCloskey EV, et al. Arch Osteo. 2019

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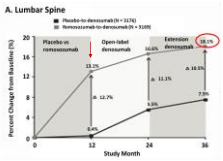
Romosozumab: Anabolic Therapy

- A fully human monoclonal antibody to sclerostin
- FDA-approved for treatment of osteoporosis in postmenopausal women at high risk for fracture
- Administered as monthly injections for 1 year
- Black Box warning - Major cardiac events: should not be initiated if had a myocardial infarction or stroke within preceding year
- Follow-up therapy with denosumab and, to a lesser degree, alendronate preserve or continue to accrue BMD benefits



Lewiecki EM. *JBMR*. 2018
Cosman F, et al. *JBMR*. 2018
McClung MR, et al. *JBMR*. 2018
Saag KG, et al. *NEJM*. 2017

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Osteoporosis Treatments are Effective

	VERTEBRAL FRACTURE	HIP FRACTURE
Inhibitors of Bone Breakdown		
Alendronate	↓44%	↓53%
Zoledronate	**↓70%**	**↓41%**
Denosumab	↓68%	↓40%
Stimulators of Bone Formation		
Teriparatide	↓65%	Not assessed. (Non-Vert Fractures by 53%
Abaloparatide	↓86%	Not assessed; Non-Vert Fractures by 43%
Romosozumab	**↓73%**	No; ↓38%* (ROMO Followed by ALN vs ALN followed by ALN)

Cummings, et al. *JAMA* 1998
Black, et al. *JCEM* 2000
Black, et al. *NEJM* 2007
Cummings, et al. *NEJM* 2009
Neer RM, et al. *N Engl J Med*. 2001
Miller, et al. *JAMA*. 2016
Cosman F et al. *NEJM* 2016
Saag KG et al., *NEJM* 2017

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What Medications Reduce Wrist Fractures?

- Alendronate-in women with low bone mass and an existing vertebral fracture (HR=0.52; p=0.013)
- Zoledronic Acid- in older women with osteopenia [HR=0.56 (0.37-0.85)]
- Denosumab- in patients with T-score ≤ -2.5 (40% absolute risk reduction p=0.03)
- Estrogen and Progesterone-women enrolled in WHI [HR=0.71(0.69-0.85)]
- Abaloparatide- HR=0.77; p = 0.051, trend was greater than teriparatide

Black, D. M., Cummings, S. R., Karpf, D. B, et al. *The Lancet* 1996
Reid, I.R., Horne, A.M., Mihov, B, et al. *NEJM* 2018
Simon, J.A., Recknor, C., Moffett Jr, A.H., et al. *Menopause* 2013
Watts NB,Dore RK, Baim S ... LeBoff MS. *Osteo Int* 2021
Cauley JA, Robbins J, Chen Z, Cummings SR,... LeBoff MS et al. *JAMA:* 2003

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Treatment considerations: Pharmacologic Therapies

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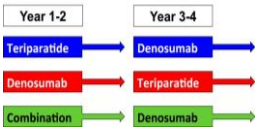
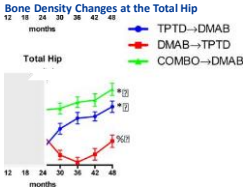
Importance of Sequence of Therapies: Anabolic followed by Anti-resorptive

DATA-Switch Study Design



Bone Density Changes at the Total Hip



Leder BZ, Tsai JN, Uihlein AV et al. *Lancet* 2015

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Who Should have a Drug Holiday? ASBMR Task Force

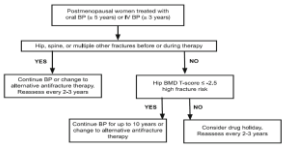
SUMMARY

Treatment duration: 5 years on oral (alendronate) or 3 years on intravenous (zoledronic acid). Then reassess fracture risk and consider *drug holiday* and reevaluate in 2 to 3 years

Those who remain at high risk should continue oral therapy for 10 years or intravenous bisphosphonate for 6 years or switch to new therapy

- ✓ Persistent osteoporosis at the hip
- ✓ Recent fracture(s) during therapy
- ✓ Multiple prevalent spine fractures

ASBMR TASK FORCE



Adler RA, El-Hajj Fuleihan G, Bauer DC, et al. *JBMR.* 2016

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Imminent Fracture Risk: Why it is Important

- Patient with a recent fracture and/or very low BMD (T-score <-3.0) are at elevated risk of fractures *one or two years after fracture*
- It is important to treat patients promptly after a fracture to reduce fracture risk
- Some osteoporosis medications reduce fracture in the first year (e.g., zoledronic acid, denosumab, romosozumab)
- Speed of effect onset of osteoporosis medications should be considered in relation to a patient's imminent fracture risk

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Pharmacologic Treatment Considerations Reviewed in the Clinician's Guide 2022

- Improving patient adherence with prescribed treatment; assess compliance and persistence at least yearly
- Treat-to-target management recommendations
- Endocrine Society's treatment algorithms on the management of postmenopausal osteoporosis according to fracture risk
- Antifracture treatment in men with osteoporosis
- Antifracture treatment in patients treated with glucocorticoids
- Evidence for antifracture benefits for older-old adults

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Rehabilitation Following Fragility Fractures

- ✓ Hip
- ✓ Spine
- ✓ Wrist

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Pain Management Strategies and Interventions for Osteoporotic Fractures

Pain Management Measure	
Acetaminophen	Cognitive Behavioral Therapy
Acupuncture	Complementary Therapies
Antidepressants (Amitriptyline, Duloxetine)	Electric stimulation
Anti-inflammatories (NSAIDs)	Ice and heat
Antiepileptics	Massage
Antispasmodics	Nerve root block injection
Aspirin	Opioid Use
Bed rest	Topical pain relievers (Capsaicin, Lidocaine)
Bracing and spinal orthoses	Vertebroplasty/kyphoplasty
Calcitonin salmon	

Lelioff MS, Greenspan SL, Insogna KL, et al. *Osteo Int.* 2022
Paolucci T, et al. *J Pain Res.* 2018.
Catalano A, et al. *Drugs Aging.* 2017
Lange U, et al. *Rheumatol Int.* 2005
Finnerup NB, *NEJM.* 2019

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Secondary Fracture Prevention

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Fracture Liaison Service at Point of Care Summarized in the Clinician's Guide

- Better care (quality metrics)
- Lower costs
- Prevention of fractures
  - FLS vs routine care in 10,000 hip fracture patients resulted in: 153 fewer fractures (109 hip)
  - 37.43 more *quality-adjusted* life years
- Better patient outcomes

Solomon et al. *J Bone Miner Res.* 2014

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Summary

CONSENSUS STATEMENT

The clinician's guide to prevention and treatment of osteoporosis

M.S. LeBoff[1] ✉ · S.L. Greenspan[2] · K.L. Insogna[3] · E.M. Lewiecki[4] · K.G. Saag[5] · A.J. Singer[6] · E.S. Siris[7]

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Take Home Messages: Osteoporosis is a Prevalent Disease

- A fracture is a sign of osteoporosis that can lead to a vicious cycle of other fractures
- There are patient care gaps
- Bone density testing, FRAX® score, VFA and TBS can identify patients at increased fracture risk
- *Many* medical conditions and therapies can increase a patient's risk of osteoporosis… and some are reversible
- There are effective therapies to reduce fractures… and some reduce fracture risk within 1 year
- The sequence of therapies is important
- Clinicians across the healthcare spectrum can contribute to extending health and independent lives of their patients by evaluating and treating patients with low bone mass and osteoporosis

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Thank You!

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