BREAKING FREE FROM OSTEOPOROSIS

AN INTERDISCIPLINARY APPROACH TO BONE HEALTH

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LEARNING OBJECTIVES

1. Describe the pathophysiology of osteoporosis and ways to prevent and diagnosis this disease.
2. Assess and screen for vertebral compression fractures.
3. Recognize the various non-pharmacological and pharmacological options for the treatment of osteoporosis.
4. Identify the different therapeutic classes, mechanisms of action, dosages, side effects and contraindications associated with approved drug therapy for the treatment of osteoporosis.
5. Instruct others on safe movement and strengthening options for the frail patient to optimize health and minimize risk of future fractures.

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OSTEOPOROSIS DIAGNOSIS AND TREATMENT GUIDELINES AND EDUCATIONAL RESOURCES

- AACE/ACE (American Assoc Clinical Endo) May 2020
- ACP (American College Physicians) endorsed by AAFP: May 2017
- Bone Health and Osteoporosis Foundation (BHOF, prior NOF) 2022
- The Clinician's Guide to the prevention and treatment of osteoporosis
- FRAX: http://www.shef.ac.uk/FRAX
- University New Mexico. Telementoring Bone Health TeleECHO Clinic. http://www.ofnm.org/project-echo
- Mayo Clinic Shared Decision-Making National Resource Center https://osteoporosisdecisionaid.mayoclinic.org

Complete references in bibliography

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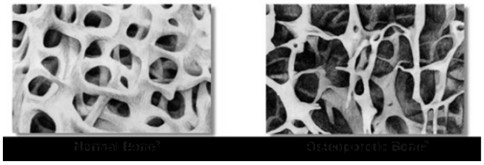
OSTEOPOROSIS

Bone disease marked by reduced bone strength leading to an increased risk of fractures.



Bone Strength = Bone Mass (density) + Bone Quality (microarchitecture)

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IMPACT OF OSTEOPOROTIC FRACTURES

Over age 50 up to

1/2 women

1/4 men

will break bone due to osteoporosis

300,000 hip fx/yr

1/4 will die within a year

1/4 **end up in nursing homes**

1/2 will need a walking aid

Annual fracture related cost

$57 billion

After a fracture, **Only 1/5** women over 67 **are tested or treated for** osteoporosis

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VERTEBRAL FRACTURES : ONLY 1/3 ARE CLINICALLY DIAGNOSED

- Most common osteoporotic fractures
- Wedge fractures are the most common
- Patients with a spine fracture have a 5-fold future risk of another spine fracture and 2-fold risk of a hip fracture
- Pulmonary: 9% decrease in lung capacity per vertebral fracture
- GI: Constipation, early satiety, wt loss
- Psychosocial: depression, social isolation

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WRIST FRACTURES – EARLY WARNING SIGN

- The most common fracture of the upper extremity
- 5 times more common in women than men
- Increased incidence with age
- Associated with an increased risk of additional fragility fractures

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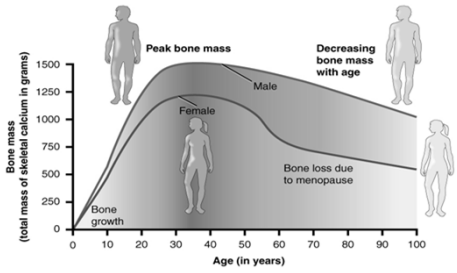
STRONG BONES BEGIN IN CHILDHOOD



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BONE MINERAL DENSITY TEST (BMD, DEXA) SCREENING RECOMMENDATIONS

USPSTF 2018:

- All women ≥ 65 y (B rec.)
- Younger postmenopausal women at increased risk as determined by a formal clinical risk assessment tool (B rec.)
- Men: Evidence is insufficient to recommend screening in men to prevent osteoporotic fractures (I statement)

Bone Health and Osteoporosis Foundation (BHOF) additionally recommends screening:

- Men ≥ 70 y and younger men with risk factors
- Men and women with a fracture after age 50
- Steroids (≥ 5.0 mg/day ≥ 3 months)

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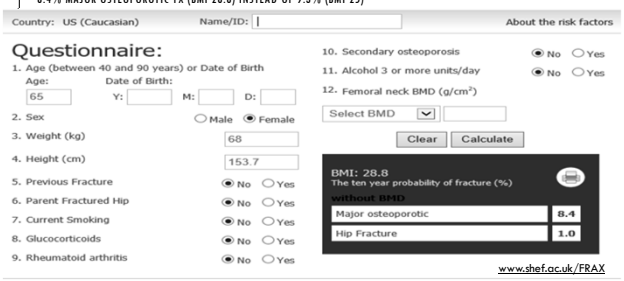
UPDATED FRAX ® RISK ESTIMATE
65 YO WHITE FEMALE W/O MAJOR RISK FACTORS IN U.S.
8.4% MAJOR OSTEOPOROTIC FX (BMI 28.8) INSTEAD OF 9.3% (BMI 25)



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DEXA INTERVAL FOR SCREENING:
SERIAL DEXA INTERVALS FOR OSTEOPOROSIS SCREENING BASED ON INITIAL DEXA AND FRAX 10 YR FRACTURE RISK

Suggested testing interval, years	Initial BMD T score	Initial major osteoporosis fracture risk, %	Initial hip fracture risk, %
<3	-2.0 to -2.4	20+	2.3 to 2.9
3-5	-1.5 to -1.9	15 to 19	1.5 to 2.2
5-10	-1.0 to -1.4	10 to 14	0.8 to 1.4
>10	> 1.0	<10	< 0.8

Leslie WD, Crandal J. Serial Bone Measurement for Osteoporosis Screening. *JAMA*. 2021;326(16):1622-1623. doi:10.1001/jama.2021.9858

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WHO Diagnosis of Low Bone Mass and Osteoporosis by DEXA

	T- score
Normal	Equal to -1.0 or higher
Low Bone Mass (Osteopenia)	Between -1.0 and -2.5
Osteoporosis	Equal to -2.5 or lower
Severe Osteoporosis	Equal to -2.5 or lower with fracture

BHOF Clinician's Guide to Prevention and Treatment of Osteoporosis. 2022

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2020 AACE/ACE DIAGNOSTIC CRITERIA FOR OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN (PMW)

T-score -2.5 or below	→	Lumbar spine, femoral neck, total proximal femur, or 1/3 radius
Low-trauma spine or Hip fracture	→	Regardless of bone mineral density
T-score between -1.0 and -2.5	+	Fragility fracture of proximal humerus, distal forearm, pelvis
T-score between -1.0 and -2.5	+	High FRAX ® fracture probability based on country-specific thresholds.

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Secondary causes (1 of 4)

Lifestyle Factors		
Alcohol abuse	Excessive thinness	Excessive vitamin A
Frequent falling	High salt intake	Immobilization
Inadequate physical activity	Low calcium intake	Smoking (active or passive)
Vitamin D insufficiency/deficiency		
Genetic Diseases		
Cystic fibrosis	Ehlers-Danlos	Gaucher's disease
Hemochromatosis	Hypophosphatasia	Hypophosphatemia
Marfan syndrome	Menkes steely hair syndrome	Osteogenesis imperfecta
Parental hip fracture	Porphyria	Homocystinuria

Note: items in bold are the most commonly undiagnosed disorders

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Secondary causes (2 of 4)

Hypogonadal states		
Anorexia nervosa	Androgen insensitivity	Female athlete triad
Hyperprolactinemia	Hypogonadism	Panhypopituitarism
Premature menopause (<40)	Turner's & Klinefelter's syndromes	
Endocrine disorders		
Cushing's syndrome	Diabetes mellitus (type 1 & 2)	**Hyperparathyroidism**
Obesity	Thyrotoxicosis	
Gastrointestinal disorders – malabsorption syndromes		
Celiac disease	Bariatric surgery / Gastric bypass	Gastrointestinal surgery
Inflammatory bowel disease (e.g. Crohn's, ulcerative colitis)	Pancreatic disease	Primary biliary cirrhosis
Hematologic disorders		
Hemophilia	Leukemia and lymphomas	Monoclonal gammopathies
Multiple myeloma	Sickle cell disease / thalassemia	Systemic mastocytosis

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Secondary causes (3 of 4)

Rheumatologic and autoimmune diseases		
Ankylosing spondylitis	Rheumatoid arthritis	Systemic lupus
Other rheumatic and autoimmune diseases		
Neurological and musculoskeletal risk factors		
Epilepsy	Muscular dystrophy	Multiple sclerosis
Parkinson disease	Spinal cord injury	Stroke
Miscellaneous conditions and disease		
HIV / AIDS	Amyloidosis	Chronic metabolic acidosis
Chronic obstructive lung disease	Congestive heart failure	Depression
Renal disease (CKD 3 – ESRD)	**Hypercalciuria**	Hyponatremia
Idiopathic scoliosis	Post-transplant bone disease	Sarcoidosis
Weight loss		

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Secondary causes (4 of 4)

Medications		
Aluminum-containing antacids	Androgen deprivation therapy	Anticoagulants (unfractionated heparin)
Anticonvulsants (e.g. phenobarbital, phenytoin, valproate)	Aromatase inhibitors	Barbiturates
Chemotherapeutic drugs	Cyclosporine A and tacrolimus	Glucocorticoids (≥ 5 mg/day prednisone or equivalent for ≥ 3 months)
GnRH (Gonadotropin releasing hormone) agonists and antagonists	Depot medroxyprogesterone acetate (Depo-Provera)	Methotrexate
Parenteral nutrition	Proton pump inhibitors	SSRIs
Tamoxifen (premenopausal use)	Thiazolidinediones (e.g. pioglitazone and rosiglitazone)	
Thyroid replacement hormone (in excess)		

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LABS TO CONSIDER FOR SECONDARY CAUSES

- Chemistry (calcium, renal, phosphorus)
- Liver function tests
- CBC
- TSH, iPTH
- 25(OH)Vitamin D
- Testosterone younger men
- 24-hour urine
  - calcium, Na, creatinine

Selected cases:

- SPEP/UPEP
- Celiac disease (tTG)
- Iron and ferritin
- Homocysteine
- Tryptase
- Prolactin
- Bone turnover markers

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ADVISE UNIVERSAL RECOMMENDATIONS FOR BONE HEALTH REGARDLESS OF BONE DENSITY

- Recommend daily calcium (ideally from diet)
- Vitamin D 800-1000 IU daily
- Advocate smoking cessation and limited alcohol intake
- Advocate regular exercise for strength, posture and balance
- Fall Prevention

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VITAMIN D REPLENISHMENT AND SUPPLEMENTATION

- If serum 25[OH]D ≤ 20, replenish with Vitamin D 5000 units daily for 8-12 weeks to achieve level ≥ 30

- Ancillary VITAL study – no significant improvement in fracture rate with vit D supplementation in generally healthy older adults (did NOT include institutionalized adults)

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CONSENSUS RECOMMENDATIONS FOR RESIDENTS IN CARE FACILITIES

- Fall risk assessment
- Multifactorial interventions to prevent falls
  - Medication review
  - Environment/assistive devices or technology
  - Exercise to include strength, balance, and functional components
  - Staff and caregiver education
- Vitamin D supplementation should be considered
- Adequate calcium intake

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EXERCISE AND PHYSICAL THERAPY FOR BONE HEALTH

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EXERCISE & AGING: THE PROBLEM…

Tendency for increased sedentary behaviors with increase in age

Comorbidities: Sarcopenia, osteopenia developing into osteoporosis, obesity, diabetes etc.

Lack of healthcare resources, underserved communities

Lack of structured exercise programs in long term care settings

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POSTURE & AGING: ANOTHER PROBLEM…

20-40% of older adults with hyperkyphosis
= **At least** a 40-degree curve

Effects of Vertebral Compression Fractures (VCFs)

Increased (abnormal) loading on lumbar vertebral bodies

Slower gait, impaired balance, increased postural sway

= increased risk for fall

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WOLFF'S LAW

Bones naturally will respond and remodel to the stresses and demands applied to them*

- Stimulus **has** to be above and beyond status quo

Bone remodeling: resistance or compression

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RESISTANCE

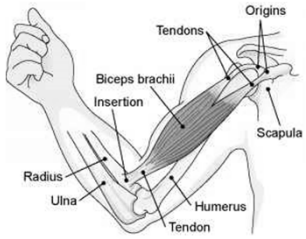
Greater resistance applied

=

Greater tendon pull on bone

Weights, bands

(body weight) sit to stands/active range of motion



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COMPRESSION

Weight-bearing/impact on bones

Stepping, walking, aerobics classes, stairs

Sitting upright/standing (if highly frail)

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PHYSICAL THERAPY: FOR SPINE SAFETY AND BONE HEALTH

Exercise
- Resistance training
- Aerobic
- Impact

Posture – protect spine during ADLs and exercise

Balance – Fall prevention

Home exercise program/Wellness Program

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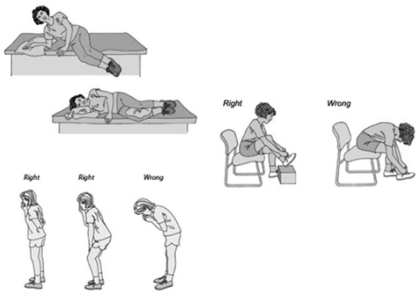
EXAMPLES OF POSTURE TRAINING



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EXAMPLE EXERCISES FOR HIGH LEVEL

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EXAMPLE EXERCISE FOR FRAIL

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LET'S MOVE FOR POSTURE!
PRACTICE SCAPULAR RETRACTION

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LET'S MOVE FOR POSTURE!
PRACTICE THORACIC EXTENSION

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HOW DO I REFER TO PHYSICAL THERAPY?

Write **"Eval and Treat"** on referral for physical therapy

Common ICD 10 Codes:

- **M81.0 Age-related osteoporosis without current pathological fracture**
- **M85.8 Other specified disorders of bone density and structure (osteopenia)**
- R26.8 Other abnormalities of gait and mobility
- R26.9 Unspecified abnormalities of gait and mobility
- M62.81 Muscle weakness (generalized)

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HOW DO I REFER TO PHYSICAL THERAPY CONT'D

- Medicare covers physical therapy for ICD 10 diagnoses of:
- Osteopenia (M85.80) or Osteoporosis (M81.0)

- Order: Physical Therapy to evaluate and treat, instruct in spine safe posture and exercises to optimize strength and balance and minimize fall risk.

- Vertebral fractures - physical therapy decreases risk of subsequent vertebral fractures

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THE PT EVALUATION

One-on-one session with patient

Reviews medical intake, including past medical history, meds, co-morbidities with subjective questioning

Motivational interviewing, assessing for yellow flags including fear of falling & kinesiophobia

- Systems-level & neuro-screen for red flags

Balance, strength/power and posture assessment

Differential MSK evaluation for addt'l ortho. Complaints as needed

Home environment & safe assistive device use

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FYI…ON THE PLAN OF CARE (POC)

Following PT evaluation, POC will be faxed to you for signature
- **Must be signed** for Medicare
- 2022 Medicare = $2,150 for PT and Speech combined
- Approx. ~ 25-28 sessions
- No longer a hard cap – but must be medically necessary

Typically 2x/week for 4-6 weeks
- ~45min to 1 hour
- Average of 10-12 visits for bone health
- More visits allowed for addt'l ortho complaints or more complex

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HELPFUL PATIENT RESOURCES

- Bone Health Osteoporosis Foundation (BHOF)
  Osteoporosis exercise for strong bones
- CDC.Gov
  Osteoporosis or low bone mass in older adults
- Harvard Health
  Effective Exercise for osteoporosis
- Bones.NIH.gov
  Exercise for Your Bone Health

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https://bonehealthandosteoporosis.org/wp-content/uploads/2016/05/Safe-Yoga-NOF-Flyer-2016.pdf

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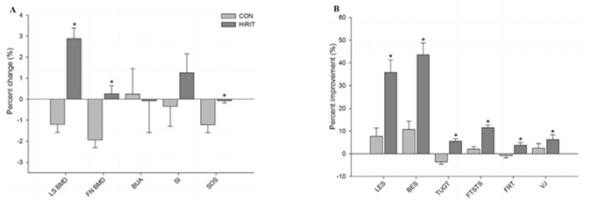

THE LIFTMOR RANDOMIZED CONTROLLED TRIAL (2017, 2018)
BACK TO EXERCISE: THE RESEARCH

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Exercise interventions	Mean difference between groups for change from baseline (95% CI), g/cm^2		
	Lumbar spine BMD (79 trials, n = 6912)	Femoral neck BMD (49 trials, n = 4768)	Total hip BMD (22 trials, n = 1793)
Aerobic	0.05 (0.02 to 0.07)	0.05 (0.02 to 0.08)	0.03 (0.00 to 0.07)
Resistance	0.07 (0.03 to 0.11)	0.05 (0.00 to 0.09)	0.08 (0.03 to 0.12)
Combination†	0.04 (0.01 to 0.07)	0.04 (0.00 to 0.07)	0.02 (−0.02 to 0.06)
Whole-body vibration	0.03 (−0.02 to 0.08)	0.06 (0.02 to 0.10)	0.02 (−0.05 to 0.09)
Mind-body‡	0.12 (0.08 to 0.16)§	0.11 (0.08 to 0.15)‖	0.01 (−0.10 to 0.11)

Mind-body exercise had the highest probability of being the best intervention for improving lumbar spine BMD (94%) and femoral neck BMD (95%); resistance exercise had the highest probability of being the best intervention for improving total hip BMD (81%).

BMD = bone mineral density; other abbreviations defined in Glossary.
*Includes direct and indirect treatment comparisons.
†≥2 types of exercise.
‡For example, tai chi, yoga, and dance.
§Mind-body exercise improved lumbar spine BMD vs. combination exercise, aerobic exercise, and whole-body vibration.
‖Mind-body exercise improved femoral neck BMD vs. combination, resistance, and aerobic exercise.

IN OSTEOPOROSIS OR OSTEOPENIA, EXERCISE INTERVENTIONS IMPROVE BMD; EFFECTS VARY BY EXERCISE TYPE AND BMD SITE (2022)
THE RESEARCH CONT'D

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EFFECT OF EXERCISE ON BONE MINERAL DENSITY AMONG PATIENTS WITH OSTEOPOROSIS AND OSTEOPENIA: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS (2022)
THE RESEARCH CONT'D

N= 97 studies (8502 participants with osteopenia or osteoporosis)

Comparing aerobic, resistance, combined, whole body vibration or mind-body exercise on BMD of lumbar, femoral neck, and total hip to groups without exercise

Mind-body exercise = #1 improving lumbar and femoral neck BMD
- Eg: Tai Chi, wuqinxi, qigong. Half squat posture, stability – slow movements including arms

Resistance = #1 improving total hip BMD (significant improvement in all groups compared to no exercise)

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N= 21 studies
(1840 participants with primary osteoporosis)

Significantly greater lumbar & hip BMD gains in groups undergoing kinesitherapy + antiosteoporosis meds vs. meds alone

THE EFFECT OF KINESITHERAPY ON BONE MINERAL DENSITY IN PRIMARY OSTEOPOROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS (2020)
THE RESEARCH CONT'D

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PHARMACOLOGY

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CALCIUM

- Good for treatment or prevention of osteoporosis and healthy bone lifestyle at any age
- Used when dietary intake is poor or insufficient
- Helps achieve higher bone mass index in adulthood
- Slightly increases BMD
- Constipation, bloating, kidney stones
- Upper daily limit is 2000 mg
- Calcium RDA
  - >70 years & women 51-70 years – 1200 mg
  - 19-70 years – 1000 mg
  - <19 years – 1300 mg

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CALCIUM SUPPLEMENTATION

- Calcium carbonate
  - 40% of elemental calcium
  - Require stomach acid for absorption should be taken with food
- Calcium citrate
  - 20% of elemental calcium
  - Absorbed equally well on an empty stomach
  - Alternative for patients with achlorhydria, IBS, absorption disorders, and on PPIs
- Daily doses should be divided into 2-3 doses
- Maximum single dose of 600 mg of elemental calcium – more will not be absorbed
- Cardiovascular disease risk linked with calcium supplementation
  - Conflicting data

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DRUG INTERACTIONS WITH CALCIUM

Drug/micronutrient	Effect	Recommendation
Iron, Zinc, Magnesium	Calcium inhibits nutrients absorption	Separate dose at least 2 hours
Corticosteroids	Inhibits calcium absorption from intestine	Consider calcium supplementation
H2RAs & PPI's	Decrease absorption of calcium carbonate	Consider using calcium citrate
Tetracycline's & Fluroquinolones	Calcium decreases antibiotic absorption	Take 2 hrs before or 6 hrs after antibiotic
Phenytoin, carbamazepine, phenobarbital	Decreases calcium absorption by increasing metabolism of vitamin D	Consider calcium and vitamin D supplementation

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VITAMIN D

- Facilitates calcium absorption
- Best choice of vitamin D intake is increasing dietary vitamin D
- Vitamin D RDA
  - >70 years – 800 IU (20 mcg)
  - 14-20 years – 600 IU (15 mcg)
- Supplements
  - Vitamin D3 (Cholecalciferol)
    - Form produced in humans
  - Vitamin D2 (Ergocalciferol)
    - Derived from plant sources
- Upper limits for vitamin D intake is 4000 units/day for adults

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VITAMIN D LEVELS

- Best index of vitamin D in our body
- Low levels of vitamin D is associated with a high risk of fractures
- Vitamin D2 or D3 50,000 units weekly or 7000 units daily x 5-8 weeks to raise serum 25-hydroxyvitamin D to 30 ng/mL
- Vitamin D2 or D3 1000 to 2000 units/day maintenance

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TREATMENT OPTIONS

ANTIRESORPTIVE AGENTS	ANABOLIC AGENTS
• BISPHOSPHONATES • RANKL • CALCITONIN • ESTROGEN • SERMS • TSEC	• PTH ANALOGS • SCLEROSTIN INHBITOR

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FDA APPROVED DRUGS FOR OSTEOPOROSIS

Bisphosphonates
Alendronate
Ibandronate
Risedronate
Zoledronic acid
RANKL inhibitor
Denosumab
Estrogen-related therapies
Estrogen
Raloxifene
Conjugated estrogen/Bazedoxifene
Calcitonin Salmon
Calcitonin
Parathyroid hormone analog
Abaloparatide
Teriparatide
Sclerostin inhibitor
Romosozumab

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BISPHOSPHONATES

	Fracture Reduction		
	Hip	**Vertebral**	**Non-Vertebral**
Alendronate	Yes	Yes	Yes
Ibandronate	No	Yes	No
Risedronate	Yes	Yes	Yes
Zoledronic Acid	Yes	Yes	Yes

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BISPHOSPHONATES

Alendronate

Ibandronate

Risedronate

- 1st line therapy for treatment of osteoporosis
- Provides greatest fracture risk reduction and BMD increase
- Inhibit activity and shorten lifespan of osteoclasts
- Approved for:
  - Prevention and treatment of postmenopausal osteoporosis
  - Treatment to increase bone mass in men with osteoporosis
  - Treatment of osteoporosis in men and women taking glucocorticoids

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BISPHOSPHONATES

Alendronate

Ibandronate

Risedronate

- Administration
  - Must remain upright for at least 30 minutes (alendronate) - 60 minutes (ibandronate, risedronate) and before eating, drinking, or taking other medications

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BISPHOSPHONATES

Zoledronic Acid

- Approved for:
  - Prevention and treatment of postmenopausal osteoporosis
  - Treatment to increase bone mass in men with osteoporosis
  - Treatment of osteoporosis in men and women taking glucocorticoids
  - Prevention of new fractures in patient who have recently had a low trauma hip fracture
- 5 mg/100 mL IV yearly (over 15-30 minutes)

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BISPHOSPHONATES

- Contraindications
  - Estimated CrCL <35 mL/min
  - Low calcium and vitamin D levels – must be corrected
- Side effects
  - Gastrointestinal issues – difficulty swallowing, esophageal inflammation
  - Musculoskeletal pain
  - Hypocalcemia
  - Atypical femur fracture (AFF)
  - Osteonecrosis of the jaw (ONJ)
- Reevaluate duration of therapy after 5 years for those at <u>not</u> at very-high risk of fracture or after 10 years for those originally at very high risk but now at high risk

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OSTEONECROSIS OF THE JAW (ONJ)

- Considered a disruption of vascular supply or avascular necrosis with exposure of the jaw bones for >8 weeks
- More common with:
  - IV vs oral bisphosphonates
  - Longer duration of therapy (>2 years)
- Risk factors
  - Older age, cancer, concomitant corticosteroids, estrogen, chemotherapy, diabetes, anemia, smoking, poor oral hygiene, periodontitis, dentures, and invasive dental procedures
- American Dental Association recommends
  - Routine dental care and good oral hygiene
  - Major dental work should be done before starting treatment
  - If procedure is needed during treatment, use clinical judgement

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BROAD SPECTRUM BISPHOSPHONATES

Alendronate	
Osteoporosis treatment in women and to increase bone mass in men	70 mg weekly 10 mg daily
Prevention of osteoporosis in women	35 mg weekly 5 mg daily
Glucocorticoid induced osteoporosis	5 mg daily 10 mg daily for post menopausal women not receiving estrogen

Risedronate	
Osteoporosis treatment and prevention in women	150 mg monthly 35 mg weekly 5 mg daily
To increase bone mass in men	35 mg weekly
Glucocorticoid induced osteoporosis	5 mg daily

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IBANDRONATE

Osteoporosis treatment and prevention in women	150 mg monthly

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BISPHOSPHONATE HOLIDAY

- Bisphosphonate Holiday = temporary suspension of therapy up to 5 years
- Rationale
  - May reduce risk of ONJ or AFF
  - Antifracture benefits will be conferred for some period of time
- Modest fracture risk – T-score > -2.5 w/no fracture
  - After 3 years of IV therapy OR 5 years oral therapy
- High fracture risk – T-score < -2.5 and/or recent fracture
  - Consider continuation of treatment up to 10 years with oral therapy OR 6 years with annual IV zoledronic acid

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DENOSUMAB

- RANKL inhibitor – inhibits osteoclast formation, maintenance, and survival thereby reducing bone resorption and turnover
- Indicated for:
  - Treatment in men and women with or without osteoporosis at high risk for fracture
  - Treatment in patients who have failed or intolerant to other osteoporosis therapy
  - Treatment in glucocorticoid induced osteoporosis
  - To increase bone mass in men receiving androgen deprivation therapy for nonmetastatic prostate cancer and in women receiving adjuvant aromatase inhibitor therapy for breast cancer
- 60 mg SQ every 6 months
  - Discontinuation is associated with rapid bone loss
  - No dosage reductions in renal dysfunction

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DENOSUMAB

- Reduces vertebral fractures by 68% at 1 year, hip fractures by 40% at 3 years, and non vertebral fractures by 20% at 3 years
- Long-term 7-year risk fracture reduction:
  - 48% all upper limb fractures
  - 43% forearm and wrist
  - 58% humerus
- Side effects
  - Hypocalcemia
  - AFF
  - ONJ
  - Infection

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	Fracture Reduction		
	Hip	**Vertebral**	**Non-Vertebral**
Abaloparatide	No	Yes	Yes
Teriparatide	No	Yes	Yes
Romosozumab	Yes	Yes	Yes

ANABOLIC THERAPY

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ABALOPARATIDE

- PTH synthetic analog
- Stimulates bone formation
- Treatment of osteoporosis in postmenopausal women at high risk for fracture or failure/intolerance to other available osteoporosis therapy
- 80 mcg SQ daily in the periumbilical area not to exceed 24 months
  - Discontinuation results is associated with rapid bone loss
  - No dosage reductions in renal dysfunction
- Side effects
  - Leg cramps, nausea, and dizziness
  - Osteosarcoma
  - Hypercalcemia

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TERIPARATIDE

- PTH synthetic analog
- Stimulates bone formation
- Approved for the following:
  - Treatment of osteoporosis in men and postmenopausal women
  - Treatment of glucocorticoid induced osteoporosis in men and women
- 20 mcg SQ daily
  - Discontinuation results is associated with rapid bone loss
  - No dosage reductions in renal dysfunction
- Side effects
  - Transient orthostatic hypotension
  - Osteosarcoma
  - Hypercalcemia

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ROMOSOZUMAB

- Sclerostin inhibitor
- Increases new bone formation and decreasing bone resorption
- Approved for treatment for osteoporosis in postmenopausal women
- 210 mg (2 injections of 105 mg) SQ monthly x 12 months
  - No dosage reductions in renal dysfunction
- Side effects
  - Increased risk for MI, stroke, and CV death [Black Box]
  - Hypocalcemia
  - AFF
  - ONJ

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ESTROGEN-RELATED THERAPIES

Estrogen/Hormone Replacement Therapy

- Approved for prevention of osteoporosis
- Rapid bone loss after discontinuation
- Side effects – biliary issues, breast cancer, endometrial hyperplasia cancer, MI, stroke, PE, DVT

Raloxifene

- Estrogen agonist/antagonist (selective estrogen receptor modulator – SERM)
- Approved for prevention and treatment of osteoporosis in women
- 60 mg PO daily
  - No dosage adjustment in renal dysfunction
- Side effects – DVT, hot flashes, leg cramps

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OTHER AGENTS

Calcitonin

- Prevents bone breakdown
- Reduces vertebral fracture occurrence ~30% in those with prior vertebral fractures
- Reserved for women in whom alternative treatments are not suitable
- Approved for treatment of osteoporosis in postmenopausal women who are at least 5 years following menopause
- 1 spray (200 units) intranasally daily, alternate nostrils OR 100 units SQ/IM every day or every other day
- Side effects - rhinitis, epistaxis, cancer risk

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ESTROGEN-RELATED THERAPIES

Conjugated Estrogen/Bazedoxifene

- Approved the prevention of osteoporosis in women after menopause who have an intact uterus
- 0.45 mg/20 mg PO daily
- Rapid bone loss upon discontinuation
- Side effects – endometrial cancer, stroke, DVT, dementia [Black Box], muscle spasms, dyspepsia, upper abdominal pain, oropharyngeal pain

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TREAT TO TARGET MANAGEMENT RECOMMENDATIONS

Risk stratification before initiating therapy

Site specific vulnerabilities

Speed of effect onset

Postmenopausal Osteoporosis Treatment Guidance	
Low Risk No previous spine/hip fracture Tscore >1 FRAX score below treatment threshold	Reassess fracture risk in 2-4 years
Moderate Risk No previous spine/hip fracture Tscore -1.0 and -2.5 FRAX score below treatment threshold	
High Risk Prior spine/hip fracture Tscore -2.5 or less FRAX 10 yr fracture risk above treatment threshold	Initial - Bisphosphonate (Alendronate, Risedronate, Zoledronic acid) Alternative - Denosumab Alternative - Raloxifene or Bazedoxifene (in women high risk of breast cancer) Alternative - Estrogen (in women with a low risk in DVT in which bisphosphonates and denosumab are not appropriate) Alternative - Calcitonin nasal spray (in those who cannot tolerate other therapies)
Very High Risk Multiple spine/hip fractures Tscore -2.5 or less	Teriparatide OR Abaloparatide x 2 years OR Romosozumab x 1 year Should be followed with antiresorptive therapy

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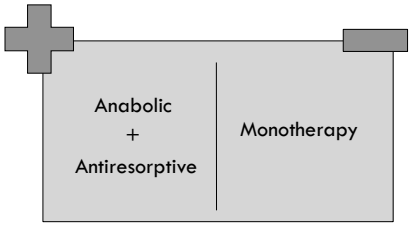
COMBINATION THERAPY



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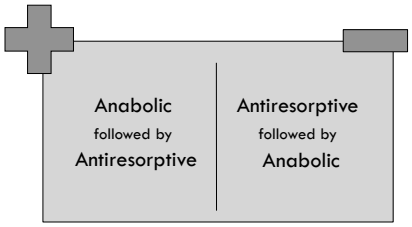
SEQUENTIAL THERAPY



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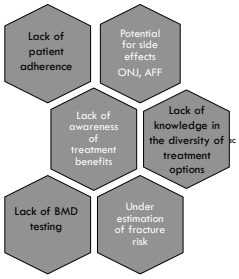
OSTEOPOROSIS TREATMENT GAP



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IMPROVING PATIENT ADHERENCE

- 25-30% of osteoporosis patients do not start taking their prescribed medication
- 50% or more do not continue treatment after 1 year
- 30% higher incidence of fracture in non adherent versus adherent patients
- Patients may unintentionally fail to initiate treatment:
  - Forgetfulness
  - Complexity of treatment regimen
  - Drug affordability
- Patients may intentionally fail to initiate treatment:
  - Limited knowledge of osteoporosis
  - Fear of side effects
  - General distrust of physician or medication
  - Lack of belief in the need for the medication and/or it's effectiveness (i.e. silent disease)

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CASE STUDY #1

SM is a 66-year-old white female who sustained a fall. Xray of right hip and leg note no fractures but reported signs of osteoporosis of hip. SM BMD T-score is -2.6 at the hip and -2 at the spine. FRAX score indicates she has a 10-year probability of a major osteoporotic fracture of 45% and hip fracture of 19%. SM has a medical history of HTN and RA for which she takes HCTZ 25 mg daily and MTX 20 mg qweekly. She also reports taking naproxen 500 mg bid but no other OTC medications.

What recommendations regarding pharmacologic treatment would you provide to SM to manage her osteoporosis?

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CASE STUDY #2

AP is a 77-year-old postmenopausal white female and has just received a diagnosis of osteoporosis by DEXA with a T-score of -2.69 at the spine and -2 at the femoral neck. She has a FRAX score indicating a 10-year probability of major osteoporotic fracture of 11% and hip fracture of 3.4%. AP has comorbid DM2, GERD, and HTN. She also has a history of severe chronic lower-back pain, which makes it difficult for her to stand or sit upright for extended periods. She is taking sitagliptin 50 mg daily, pantoprazole 40 mg bid, lisinopril 10 mg daily, celecoxib 100 mg bid, and pregabalin 150 mg daily. AP has normal renal and liver functions.

What recommendations would you provide to AP to manage her osteoporosis and reduce the risk of fractures?

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SUMMARY

- Actively counsel patients on the prevention of osteoporosis
- A fracture is a sign of osteoporosis, evaluate pts ≥ 50 with fracture
- Bone density testing and FRAX score can identify patients' fracture risk
- Medications reduce risk of fractures, some within 1 yr
- Encourage patients to exercise to decrease their fracture and fall risk

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THANK YOU!

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