Is Osteoporosis Cutting Edge?

What's New in Fracture Prevention

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1

MEET OUR OSTEOPOROSIS TEAM

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2

DISCLOSURES

I, Victoria Reinhartz, am a licensed consultant pharmacist who currently and has previously received financial compensation for consulting expertise relevant to clinical services, continuing education, workflow, and technology systems within both the pharmacy and mobile integrated health industries.

I, Victoria Reinhartz, currently serve as CEO of Mobile Health Consultants, Inc., a business specializing in clinical education, disease management, and consulting services for interprofessional and mobile health teams.

I do NOT have any of the following:

- a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity
- any affiliation with an organization whose philosophy could potentially bias my presentation

I, Sabrina Alahmad, a licensed pharmacist, hereby declares having no vested interest in any corporate organization that could create a conflict of interest. Specifically, I do not have any financial or ownership interest in any corporate entity that may influence her professional judgment or decision-making.

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This presentation does not constitute professional advice, and individuals are encouraged to seek appropriate guidance for their specific circumstances.

3

LEARNING OBJECTIVES

By the end of this course, learners will be able to:

Pharmacist	Technician
• Identify the impact of osteoporosis on health outcomes and cost of care	• Identify the impact of osteoporosis on health outcomes and cost of care
• Interpret study results and key pharmacotherapeutic updates within the arena of fracture prevention	• Interpret study results and key pharmacotherapeutic updates within the arena of fracture prevention
• Evaluate key elements of biologics and other antiosteoporotic medications to identify critical counseling needs and changes in pharmacy practice	• Understand which biologics and other antiosteoporotic medications will require patient counseling and changes in pharmacy practice
• Apply concepts to patient case scenarios, illustrating appropriate osteoporosis pharmacotherapeutic care	• Apply concepts to patient case scenarios, illustrating appropriate osteoporosis pharmacotherapeutic care

4

Assessment Question 1

According to the 2023 ACP guidelines, which of the following drugs is NO LONGER considered first line treatment for osteoporosis?

A. Alendronate
B. Teriparatide
C. Denosumab
D. Romosozumab

5

Assessment Question 2

Which of the following are risks of bisphosphonate therapy that become more likely with longer duration of therapy?

A. Osteonecrosis of the jaw
B. Infusion reactions (with IV zoledronic acid)
C. Atypical fractures
D. Both A & B
E. Both A & C

6

Assessment Question 3

Which of the following drugs is most likely to LOWER bone mineral density and WORSEN osteoporosis?

A. Prednisone
B. Alendronate
C. Hydrocodone
D. Rosuvastatin

7

Assessment Question 4

Which of the following drugs is limited to a maximum therapeutic course of 24 months of use?

A. Denosumab
B. Zoledronic Acid
C. Teriparatide
D. Alendronate

8

Assessment Question 5

LR is a 66 YOF currently on bisphosphonates for osteoporosis. Her provider is considering lab monitoring. Which of the following is TRUE regarding bone turnover markers (BTM)?

A. BTM monitoring plays no role in disease management
B. BTM monitoring may serve as a key element in the future of individualized management of osteoporosis
C. BTM is routinely done with biologics like denosumab
D. BTM is only useful after hip fracture

9

Assessment Question 6

SK is a 73 YOF with severe osteoporosis and multiple hip and vertebral fractures. She is at very high risk for future fractures and is started on ORAL bisphosphonates. When do the AACE guidelines recommend a drug holiday for this patient?

A. After 1 year
B. After 3 years
C. After 10 years
D. Never; should be continued indefinitely

10

Interactive Case

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PMH: Diabetes Mellitus, hypertension, COPD, macular degeneration, peripheral neuropathy, and Transient Ischemic Attack (TIA) 3 years ago

Medications:
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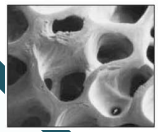
- carvedilol 25 mg twice daily
- zolpidem 10mg at bedtime
- gabapentin 800mg four times daily
- Metformin 500 mg twice daily
- amitriptyline 100mg at bedtime
- pantoprazole 40mg daily

11

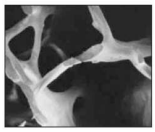
DEFINITION: OSTEOPOROSIS

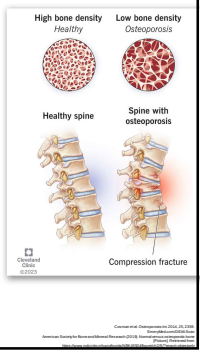
- Bone disorder characterized by:
  - Osteopenia: low bone mineral density (BMD)
  - Impaired bone architecture
  - Compromised bone strength
- Predisposes a person to increased fracture risk

Normal Bone



Osteoporotic Bone





12

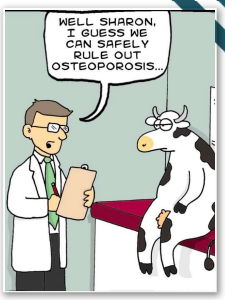
EPIDEMIOLOGY

Woman's lifetime risk 50%

Man's lifetime risk 20%

- Most common bone disease
- Osteoporosis & Osteopenia
  - 53 million Americans
  - More common in White & Hispanic
  - Osteoporosis risk increases with age
    - 50% of women >75 years old
    - <30% treated after fracture

Challenges:
<30% treated after fracture
75% discontinued within one year



13

FIGURE 92-1 Etiology of osteoporosis and osteoporotic fractures

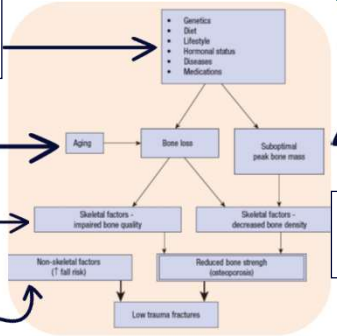
Peri- and post-menopausal: bone resorption 2° to estrogen deficiency

Bone loss starts in 3rd/4th decade

Bone quality affects bone strength more than bone mass

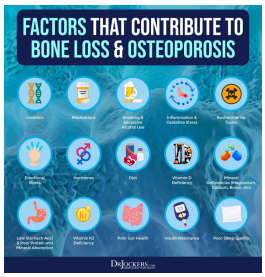
Up to 50% of older adults ≥1 fall/year

By age 21: 60-80% genetic



14

Risk Factors



- Female
- Advanced age
- Race/Ethnicity
- History of a previous fracture as an adult
- Osteoporotic fracture
- Low body weight or body mass index
- Premature menopause (<45 yrs old)
- Secondary arthritis (especially rheumatoid arthritis)
- Past or current systemic oral glucocorticoid therapy
- Cigarette smoking
- Alcohol intake (>3 drinks/day)
- Low calcium/vitamin D
- Cognitive impairment
- Impaired vision

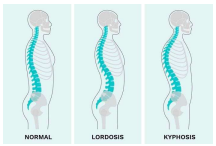
15

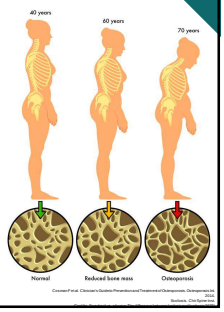
Clinical Presentation

Types of Osteoporosis

- Postmenopausal Osteoporosis
- Age-Related Osteoporosis
- Male Osteoporosis
- Drug-Induced Osteoporosis

- Pain
  - Lower back pain
    - May radiate
  - "old age"
- Immobility
- Loss of height
  - ≥1.5 inches
- Kyphosis or lordosis
- May be asymptomatic





16

Secondary Causes

- Type 1 Diabetes Mellitus
- Untreated Hyperthyroidism
- Chronic malnutrion or malabsorption
- Hypogonadism
- Smoking
- Premature menopause (<45 yo)
- Genetic Causes
- Chronic liver disease

17

Drugs Associated with Low BMD

Medications	Comments
Anticonvulsant Therapy (phenytoin, carbamazepine, phenobarbital, valproic acid)	↓BMD and ↑ fracture risk; ↑ vitamin D metabolism leading to low 25 (OH) vitamin D conc.
Aromatase inhibitors (letrozole, anastrozole)	↓BMD and ↑ fracture risk; ↓estrogen conc.
Furosemide	↑ fracture risk; ↑calcium renal elimination
Glucocorticoids (chronic oral therapy)	↓BMD and ↑ fracture risk; dose and duration dependent
Gonadotropin-releasing hormone agonists or analogs (leuprolide, goserelin)	↓BMD and ↑ fracture risk; ↓sex hormone production
Heparin (unfractionated) or low-molecular-weight heparin	↓BMD and ↑ fracture risk; (unfractionated>>>low molecular weight) with long-term use (>6 m); ↓osteoblast function and ↑osteoclast function

30% to 50% of patients taking chronic oral glucocorticoids will experience a fracture

18

Drugs Associated with Low BMD

Medications	Comments
HIV (nucleoside reverse transcriptase inhibitors, protease inhibitors)	↓BMD (ART>PI), no fracture data; ↑ osteoclast activity and ↓osteoblast activity
Medroxyprogesterone acetate depot administration	↓BMD, no fracture data; possible BMD recovery from discontinuation; central DXA monitoring of BMD recommended with ≥2 years of use; ↓estrogen conc.
PPI	↑ Vertebral and hip fracture risk; possible calcium malabsorption secondary to acid suppression for carbonate salts
SSRI	↑ Hip fracture risk; ↓osteoblast activity
Thyroid hormone; excessive supplementation	↓BMD and ↑ fracture risk (>in men); ↑ risk with TSH conc <0.1 mIU/L; possible ↑in bone resorption
Vitamin A: excessive intake (≥1.5mg of retinol form)	↓BMD and ↑ fracture risk; ↓osteoblast activity and ↑osteoclast activity

Modified from Dipiro et al. Pharmacotherapy: A Pathophysiologic Approach, 11th Ed.

19

Over-The-Counter (OTC) Drugs Increased Fall Risk

Allergy Cough & Cold Medications	• Diphenhydramine (Benadryl) • Cetirizine (Zyrtec) • Chlorpheniramine (Chlor-Trimeton) • Brompheniramine (Dimetapp) • Dextromethorphan (Delsym, Robitussin DM) • Guaifenessin (Mucinex) • Phenylephrine (Sudafed PE) • Pseudoephedrine (Sudafed)
Motion Sickness, Nausea, Sleep Aids and "PM" Medications	• Dimenhydrinate (Dramamine) • Meclizine (Bonine) • Acetaminophen/diphenhydramine (Tylenol PM) • Ibuprofen/diphenhydramine (Advil PM) • Aspirin/diphenhydramine (Bayer PM) • Naproxen/diphenhydramine (Aleve PM) • Doxylamine (Unisom)

Beers Criteria for Inappropriate Medication Use 2023 Update. Am Fam Physician. 2023;
AGS BGC. Postmenopausal Osteoporosis CPG. Endocr Pract. 2020;26(Suppl 1)
Dipiro et al. Pharmacotherapy: A Pathophysiologic Approach 11th Ed.

20

Prescription Drugs Increased Fall Risk

NOT ALL INCLUSIVE

PAIN RELIEF
- Hydrocodone/APAP (Norco)
- Oxycodone (Oxycontin)
- Hydromorphone (Dilaudid)
- Fentanyl (Duragesic)
- Methadone

SEIZURE CONTROL
- Phenytoin (Dilantin)
- Valproic acid (Depakote)
- Carbamazepine (Tegretol)
- Phenobarbital

CARDIAC & ANTIHYPERTENSIVES
- Furosemide (Lasix)
- HCTZ (Microzide)
- Bumetanide (Bumex)
- Torsemide (Demadex)
- Nifedipine IR (Procardia)
- Carvedilol (Coreg)
- Clonidine (Catapres)
- Digoxin (Lanoxin, Digox)

HEART RHYTHM CONTROL
- Amiodarone (Pacerone)
- Flecainide (Tambocor)
- Propafenone (Rhythmol)
- Sotalol (Betapace)

URINARY & PROSTATE HEALTH
- Doxazosin (Cardura)
- Prazosin (Minipress)
- Terazosin (Hytrin)
- Oxybutynin (Ditropan)
- Tolterodine (Detrol)

MUSCLE RELAXERS, SPASMS, & SLEEP AIDS
- Zolpidem (Ambien)
- Eszopiclone (Lunesta) Gabapentin (Neurontin)
- Pregabalin (Lyrica)
- Tizanidine (Zanaflex)
- Carisoprodol (Soma)
- Cyclobenzaprine (Flexeril)
- Baclofen

MOOD AND MENTAL HEALTH
- Haloperidol (Haldol)
- Ziprasidone (Geodon)
- Quetiapine (Seroquel)
- Risperidone (Risperdal)
- Olanzapine (Zyprexa)
- Amitriptyline and combos
- Chlordiazepoxide
- Doxepin (Silenor)
- Triazolam (Halcion)
- Alprazolam (Xanax)
- Lorazepam (Ativan)
- Temazepam (Restoril)

PARKINSONS & NEUROLOGY
- Ropinirole (Requip)
- Pramipexole (Mirapex)
- Carbidopa/Levodopa (Sinemet)
- Benztropine (Cogentin)

Beers Criteria for Inappropriate Medication Use 2023 Update. Am Fam Physician. 2023;

21

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22

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Which medications may be contributing to fall risk?

23

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Which medications may be contributing to losses in BMD?

24

DIAGNOSIS & CLINICAL PRESENTATION

25

Imaging

DEXA Scan

- Dual-energy X-ray absroptometry (DEXA)
  - Gold standard for measuring bone mineral density
  - Used to scan lumbar, spine, femur, and hip
    - lowest BMD value used for diagnosis
  - Measures: Actual BMD, T-score, Z-score
    - T- and Z-scores are measures of standard deviation

T-Score
Comparison of the pt's measured BMD to the mean BMD of a sex-matched healthy 20-29 yo caucasian
Typically used for diagnosis

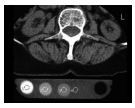
Johansson H et al. Osteoporos Int. 2017 Nov; 28(11): 3095–3103.

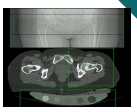
26

Imaging - Cutting Edge

QCT

- Quantitive Computed Tomography
  - More sensitive than DEXA
    - Reduced overestimation of BMD
  - Developed to evaluate bone loss
  - In-scan calibration phantom is used to calculate BMD from the measured CT values
  - True 3D method
- May be useful for:
  - Risk of osteopenia
  - Monitoring treatment for diagnosis of osteoporosis
  - Receiving steroid therapy
  - Hyperparathyroidism
  - Vertebral abnormalities
- Limitations
  - Bulky machine and limited accessibility
  - High cost





Advantages	Contraindications
• Arthritis • Scoliosis • Disc space narrowing • Spinal degenerative diseases • Aortic calcification • Osteophytes • Obesity	• Anyone who recently had a test that involved barium, iodine, or other contrast materials • Women who are or may be pregnant

Engelke K. Journal of Clinical Densitometry 2017.

27

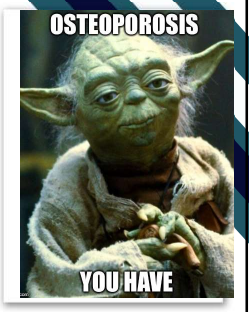
DIAGNOSIS

Osteoporosis

T-score at or below -2.5

Low bone mass or Osteopenia

T-score between -1 and -2.5

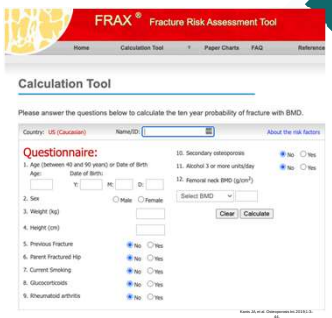


28

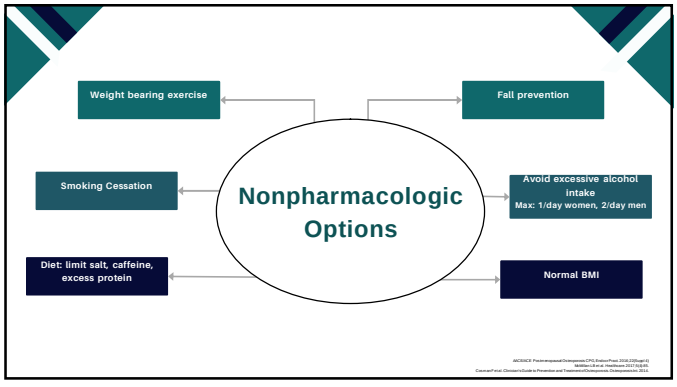
Assessment Tool

FRAX

- Fracture Risk Assessment Tool
- Tool is country specific (USA only)
- Prediction model
  - Centre for Metabolic Bone Disease, Sheffield University
- Probability of hip/major osteo fracture in next 10 years
- Should NOT be used if already on therapy for osteoprososis
- Does NOT accomodate all risk factors
  - Ex: fall risk



29



30

CONSEQUENCES

- After a hip fracture:
  - **Less than 50%** of patients regain basic ADL
  - 20% become nonambulatory
  - Up to 33% totally dependent (or nursing home)
- Age 50 and over:
  - **20-24% die within a year -- up to 36%**
  - Men have a two-fold higher mortality rate

31

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PMH: Diabetes Mellitus, hypertension, COPD, macular degeneration, peripheral neuropathy, and Transient Ischemic Attack (TIA) 3 years ago

FJ visits your pharmacy with an update after her most recent appointment with her physician. Scan results are as follows:

T-Score (hip) -3.3
T-Score (spine) -2.9
T-score (femoral neck) -3.4

32

Assessment Question

Which of the following are TRUE?

T-Score (hip) -3.3
T-Score (spine) -2.9
T-score (femoral neck) -3.4

A. This patient has osteoporosis
B. This patient has osteopenia
C. This patient is eligible for medication
D. Not enough information without FRAX score

33

IDEAL OUTCOMES

PREVENT

- PREVENTION
- Adolescence and early adulthood
  - optimize skeletal development & mass accrual

STABALIZE

- After diagnosis
  - Stabilize or improve bone mass and prevent fractures

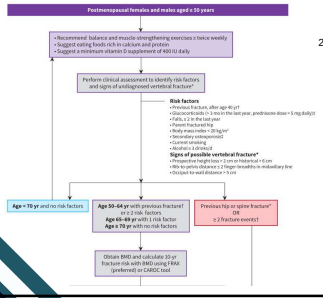
TREAT

- Post-osteoporotic fracture
  - Reduce pain and deformity
  - Improve function, QOL
  - Reduce risk of future fractures

34

FRACTURE PREVENTION

Vitamin K regulates calcium promoting calcium and bone binding



2023 Canadian Guideline Updates highlight fracture prevention

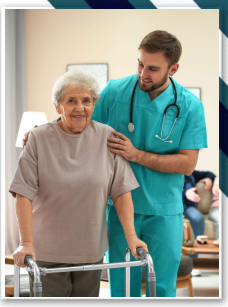
- Movement:
  - Balance and functional training ≥ 2x weekly to ↓ fall risk
  - Progressive resistance training 2x weekly targeting back and abdominal extensor muscles
  - Participate in activities (yoga, walking, pilates, impact exercise) for enjoyment
- Nutrition:
  - No supplement if meeting required dietary allowance
  - Calcium and Vitamin D supplement for >50 yrs
- Fracture Assessment:
  - Identify risk factors
  - Assess undiagnosed fractures
  - BMD testing or utilization of FRAX tool (or CAROC)

Moon RM, Feldman S, Funnell L, et al. CMAJ. 2023;195(38): E1333-E1348. doi:10.1503/cmaj.221637
Hu, L., Ji, J., Li, D. et al. J Orthop Surg Res 16, 540 (2021). doi.org/10.1186/s13018-021-02720-4

35

ELDERLY PATIENTS

- Up to 80% not receiving therapy after fracture!
- Think about it!
  - Often indoors ⍰ lack of vitamin D
  - Digestion issues ⍰ diet?
  - Mobility issues ⍰ exercise?
  - Bisphosphonate therapy?
    - Bedbound?
    - Difficulty swallowing?
    - Fluid restrictions?
- Appropriate OTC supplementation
- Fall prevention



36

CALCIUM & VITAMIN D

37

CALCIUM

- Dietary sources preferred
- Supplementation
  - Premenopausal (or < 50yo): 1000mg daily
  - Postmenopausal (or > 50yo): 1200mg daily
- Efficacy
  - Greater ↑ or maintenance of BMD vs placebo
  - Role for fracture prevention?
  - Notable: clinical trials for anti-osteoporosis meds include calcium supplementation

ACOG/ACP. Postmenopausal Osteoporosis. CPG. Endocr Pract. 2020;26 (Suppl 1).
Bridgeman CJE, et al. Handbook of Nonprescription Drugs. 19th Ed.
Ozma et al. Pharmacokinetics: A Pathophysiologic Approach. 1:26-54.
NIH Office of Dietary Supplements. Calcium Fact Sheet. 2020.

38

CALCIUM-COUNSELING

- Divide doses (≤500mg per dose)
  - Give with meals
- Side effects
  - GI (constipation, gas): how do we fix this?
  - Kidney stones (rare)
  - Risk of MI and cardiovascular death with doses >3g/day
  - Risk of prostate cancer suggested at >1.5g/day

Consider recommending <1,500 mg/day supplemental

Institute of Medicine recommends max 2g – 2.5 g/day

NIH Office of Dietary Supplements. Calcium Fact Sheet. 2020.
Chiodini I et al. European Journal of Endocrinology. 2018; 178(4):313-320.
Han Q et al. JAMA. 2013;173(8):639.
U.S. Department of Health and Human Services. Systematic review of health ... 2017.
Prentice RL et al. Osteoporosis Int. 2017;28(6):1907.

39

CALCIUM SALTS & DRUG INTERACTIONS

- Which salt is better?
  - Calcium carbonate
  - Calcium citrate
  - Calcium gluconate
  - Calcium lactate + several others
- Which formulation is better?
  - Chews
  - Tablets
  - Gummies
  - Solution
- Interactions
  - PPIs may make ↓ carbonate
  - Fiber/cholestyramine ↓ absorption
  - Calcium ↓ absorption of drugs
  - Bisphosphonates, Iron, Thyroid hormones, Quinolones, Tetracyclines

40

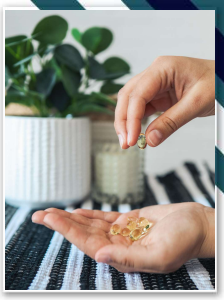
VITAMIN D

- In liver:
  - Cholecalciferol & ergocalciferol → 25 (OH) vitamin D (calcidiol)
  - In kidney: calcidiol → calcitriol
- Calcitriol ↑ calcium binding proteins in the gut = ↑ Ca absorb
  - Effect maxes at 25 (OH) vitamin D levels of 29-32 ng/mL
- Vitamin D deficiency is <20 ng/mL
  - Ergocalciferol (vitamin D2)
    - Greater ↑ or maintenance of BMD vs placebo
  - Role for fracture prevention?
  - Notable: clinical trials for anti-osteoporosis meds include calcium supplementation

41

VITAMIN D

- Treatment (deficiency): Ergocalciferol (vitamin D2)
  - 50,000 units once to twice weekly for 8-12 wks, repeat prn until therapeutic
- Guidelines suggest **30-50 ng/mL** necessary to maximize intestinal calcium absorption
  - New evidence (other diseases) promotes ≥ 60 ng/mL



42

VITAMIN D

- Maintenance Supplementation: cholecalciferol (D3)
  - 800-1,000 units daily (2mcg-25mcg)
  - 2020 Guidelines
    - 1000-2000 units daily (25mcg-50mcg)
- Megadoses (>300,000 units/yr)
  - NOT recommended

43

INITIATING MEDICATIONS

44

When to Initiate Pharmacotherapy?

		Criteria 1	Criteria 2
TREATMENT DOSES	1	History of hip or vertebral (clinical or asymptomatic) fractures	
	2	T-scores ≤ -2.5	
PREVENTION DOSES	3	Postmenopausal W + M age 50+ WITH Osteopenia (T-score -1 to -2.5)	AND 10-year hip fracture probability
	4	Postmenopausal W + M age 50+	AND FRAX 10-year fracture probab

45

Assessment Question

Which of the following patients should be initiated on osteoporosis therapy? (Select all that apply)

- **A** 66 YOF with a T-score of -3.9
- **B** 75 YOM with hip fracture after a fall
- **C** 80 YOF with an asymptomatic vertebral fracture
- **D** 61 YOF with a T-score of -1.1 and low FRAX risk

46

Drug Therapies by Mechanism

Place in Therapy	Osteoporosis Strategy	MOA	Agents
First Line	Antiresorptive	Nutritional Supplement	Calcium & Vitamin D
		Prevent osteoclast activity	Bisphosphonates
		RANK Ligand Inhibitor	Denosumab
High Risk	Bone Formation	Recombinant Human Parathyroid Hormone (PTH 1-34 units)	Teriparatide
		Recombinant Human Parathyroid Hormone-related Peptide (PTHrP 1-34)	Abaloparatide
	Antiresorptive & Bone Formation	Sclerostin Inhibitor	Romosozumab
Special Considerations	Antiresorptive	Selective Estrogen Receptor ModulatorBone ProtectiveInhibits osteoclast activity	Raloxifene Estrogen Calcitonin

AACE/ACE Postmenopausal Osteoporosis CPG, Endocr Pract. 2020;26(Suppl 1)
Barnett M, et al. Journal of Clinical Endocrinology & Metabolism. May 2019; 104(5):1595-1622

47

Comparative Efficacy

	Medication	↓ Vertebral Fractures	↓ Nonvertebral Fracture	↓ Hip Fracture	% ↑ Spine BMD	% ↑ Hip BMD
First Line	**Bisphosphonates***	41-70%	25-39%	40-51%	4.3-6.7%	2.8-6%
	Denosumab	68%	20%	40%	9.2%	6%
High Risk	**Abloparatide**	86%	43%	No significant change	10.4%	4.3%
	Teriparatide	35-65%	47-53%	No significant change	8.6-9.7%	3.5%
	Romosozumab	73%	25%	No data	13.3%	6.8%
Special Considerations	Estrogen +/- Progestin	33-40%	13.27%	30-50%	3.5-7%	1.7-5%
	Raloxifene	30-68%	No significant change	No significant change	2.6%	2.1%
	Calcitonin	33%	No significant change	No significant change	3%	No significant change

*risedronate and zoledronic acid only; alendronate and ibandronate nonsignificant

Modified from Dyno et al. Pharmacotherapy: A Pathophysiologic Approach. 11th Ed.
Barnett M, et al. Journal of Clinical Endocrinology & Metabolism. May 2019; 104(5):1595-1622

48

Bisphosphonates

- Mimic pyrophosphate (bone resorption inhibitor)
  - *zoledronic acid (Reclast®)—IV
  - *alendronate (Fosamax®)—tab & sol
  - *risedronate (Actonel ®)
  - ibandronate (Boniva ®)—tab & IV
- PK
  - Bioavailability <1%
  - Half lives: up to ~10 years (Incorporated into bone)
  - Renally eliminated

- Dosage varies depending on indication
- Prevention in postmenopausal women
  - alendronate 35 mg once weekly
  - zoledronic acid: 5 mg IV over 15 min once every 2 years
- Treatment for M + W with osteoporosis
  - alendronate 70 mg once weekly
  - zoledronic acid: 5 mg IV over at least 15 min once yearly

*FDA indicated for postmenopausal, male, and glucocorticoid-induced osteoporosis

Greater Bone Absorption & retention

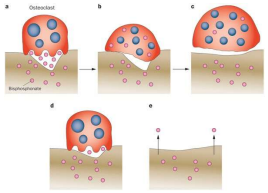
AACE/ACE. Postmenopausal Osteoporosis CPG. Endocr Pract. 2020;26(Suppl

Dipiro et al. Pharmacotherapy: A Pathophysiologic Approach. 11th Ed.

49

Bisphosphonates - Efficacy

- High fracture risk reductions
  - Seen as early as 6 months
- Increases in BMD
  - Dose-dependent, greatest in first 6-12 months
  - Plateaus in hip after 2-5 years
  - Weekly alendronate > weekly risedronate
  - Weekly alendronate ≈ monthly ibandronate



Vertebral Fracture (%)	Nonvertebral Fracture (%)	Hip Fracture (%)	Change in Spine BMD (%)	Change in Hip BMD (%)
41-70 ↓	25-39 ↓	40-51 ↓	4.3-6.7 ↑	2.8-6.0 ↑

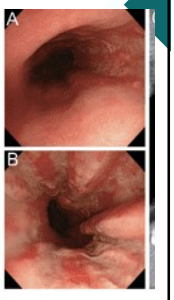
AACE/ACE. Postmenopausal Osteoporosis CPG. Endocr Pract. 2020;26(Suppl

Dipiro et al. Pharmacotherapy: A Pathophysiologic Approach. 11th Ed.

50

Bisphosphonates - AE

- GI effects
  - abd pain, nausea, C/D, dyspepsia
  - Post-marketing: ulceration, perforation, bleeding
  - Switch drug or consider IV zoledronic acid
- Esophageal AEs: esophagitis, esophageal erosions
- Hypocalcemia
  - Calcium levels must be normal before starting

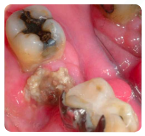


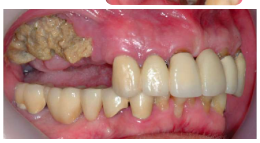
Nemec, Tóth et al. "Alendronate-induced esophagitis: possible pathogenic role of hypersensitivity to alendronate." Internal medicine 47 23 (2008): 2063

51

Bisphosphonates - AE

BRONJ



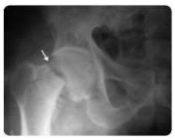


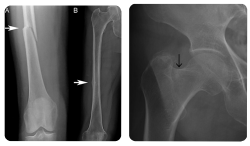
- Bisphosphonate-Related Osteonecrosis of Jaw (BRONJ)
  - Incidence range 0.01% to 0.35%
  - About 1 in 100,000 patients
  - **Avoid major dental work**
- More common in high dose IV bisphosphonates
  - Cancer patients (1-8% incidence)
  - Chemo, radiation, glucocorticoids, genetic predisposition

Gupta M, et al. Bisphosphonate-Related Jaw Osteonecrosis. StatPearls. 2020
Owosho A et al. Oral Surg. 2016 Feb 14; pii: S2231-6450(16)30010-0
Ruggiero, S.L., & Mehrotra, B. (2006). Bisphosphonate-related osteonecrosis of the jaw: diagnosis, prevention, and

52

Bisphosphonates - AE





- Subtrochanteric (Atypical) femoral fractures (AFF)
  - Incidence: 1-2/1000 patients per year
  - Mortality impact unclear
  - For every 1 AFF
    - >1200 fractures prevented

Holiday required: Should NOT be on bisphosphonates forever!!

Black DM, et al. Endocrine Reviews. Apr 2015; 45(2): 333-368.
Eriksen E, et al. BMC Musculoskelet Disord. 2017; 18(29).
Khan AA, Kaiser S. CMAJ. 2017;189(24):E853. doi:10.1503/cmaj.160300

53

Bisphosphonates - AE

- Drug Holiday
  - Based on individual risk!
  - **Drug Holiday should be at least 1-2 years, up to 5 years**

	Oral Bisphosphonate	IV Bisphosphonate
High Risk	Holiday after 5-10 years of tx	Holiday after 6 years of tx
Low Risk	Holiday after 4-5 years of tx	Holiday after 3 years of tx

Holiday required: Should NOT be on bisphosphonates forever!!

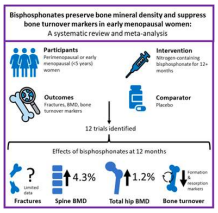
Black DM, et al. Endocrine Reviews. Apr 2015; 45(2): 333-368.
Eriksen E, et al. BMC Musculoskelet Disord. 2017; 18(29).
Khan AA, Kaiser S. CMAJ. 2017;189(24):E853. doi:10.1503/cmaj.160300

54

Bisphosphonates - Cutting Edge?

Cutting Edge Questions

- When to Start?
- Bisphosphonates improve BMD and reduce bone turnover markers compared to placebo in early menopausal women

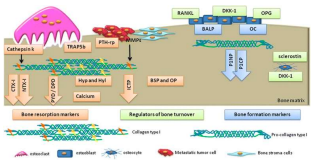


55

Bisphosphonates - Cutting Edge?

Cutting Edge Questions

- Should we monitor Bone Turnover Markers (BTMs)?
- 2020 Guidelines - Evidence?



56

Bisphosphonates

Counseling

- **Swallow WHOLE with 6-8 ounces of water**
  - **Oral solution "chased" with 2 oz water**
- **Take on empty stomach (≥30 minutes before food)**
- **Sit/stand upright 30-60 minutes**

CONTRAINDICATED in:

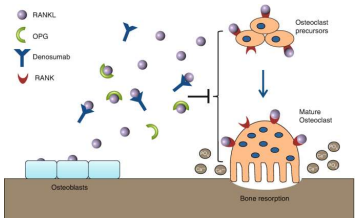
- **Esophageal abnormalities (stricture)**
- **Pregnant**
- **CrCl <35 mL/min**

57

BIOLOGICS

58

Denosumab (Prolia®)



- Fully human monoclonal antibody
  - Binds to RANKL
  - Blocks osteoclastogenesis (maturation process)
- Indicated for M & W with **high risk** of fracture
- Possible option in CKD patients
- Significant decreases in fracture risk
- ↑ in BMD similar to alendronate
  - Can ↑ BMD *after* alendronate therapy

AACE/ACE. Postmenopausal Osteoporosis CPG. Endocr Pract. 2020;26(Suppl 1). Clynes et al. Pharmacotherapy of Osteoporosis: Recommendations from the Consensus Panel of the Croatian Academy of Medical Sciences. Osteoporos Int. 2014.

59

Denosumab (Prolia®)

- 60 mg administered Subcutaneously q 6 months
  - Half life?
  - Protection thought to dissipate after discontinuatio
- Refrigerated
  - room temp up to 14 days
- Injected SQ
  - upper arm, upper thigh, abdomen
  - *By whom?*

Technician Role- When is the patient's appointment?

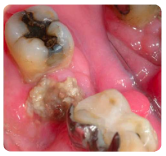
Vertebral Fracture (%)	Nonvertebral Fracture (%)	Hip Fracture (%)	Change in Spine BMD (%)	Change in Hip BMD (%)
68↓	20↓	40↓	9.2↑	6.0↑

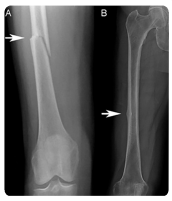
AACE/ACE. Postmenopausal Osteoporosis CPG. Endocr Pract. 2020;26(Suppl 1). Clynes et al. Pharmacotherapy of Osteoporosis: Recommendations from the Consensus Panel of the Croatian Academy of Medical Sciences. Osteoporos Int. 2014.

60

Denosumab - Adverse Effects

- Dermatologic rxns (not at injection site)
  - Eczema, dermatitis, or more severe
- Infection (respiratory & GI most common infection)
  - Report s/sx resp infection, cellulitis, cystitis, etc
- Arthralgias, musculoskeletal pain
- Hypocalcemia
  - More common in renal impairment
  - Correct before initiation
- Warnings: **ONJ, atypical fractures possible**
- Pancreatitis reported in clinical trials





61

Teriparatide (Forteo®)

- Parathyroid hormone analog (PTH 1-34)
- FDA indicated for M + W at high risk of fracture, glucocorticoid-induced osteoporosis
- Reserved for severe osteoporosis
  - Bisphosphonate failure, T<-3.5, hx of fracture, multiple risk factors
  - Given short term (18-24 months)
  - Followed by bisphosphonate
    - Why?

Vertebral Fracture (%)	Nonvertebral Fracture (%)	Hip Fracture (%)	Change in Spine BMD (%)	Change in Hip BMD (%)
65↓	65↓	↔	8.6↑	3.5↑

62

Teriparatide (Forteo®)

- Daily SQ injection, rotate sites (thigh, abdomen)
  - Refrigerated, good for 28 days
  - Orthostatic hypotension: 1st dose administration? CAREFUL HERE

- BBW: Osteosarcoma
  - approved for use up to 2 years ONLY
    - second therapeutic course?

- Ensure not used in:
  - Pts with hypercalcemia, other metabolic bone diseases, metastatic or skeletal cancers, or premenopausal women of child-bearing potential

63

Abaloparatide (Tymlos®)

- Analog of human parathyroid protein (PTHrP 1-34)
- FDA indicated for M + W at high risk of fracture, glucocorticoid-induced osteoporosis
- Reserved for severe osteoporosis
  - Bisphosphonate failure, T<-3.5, hx of fracture, multiple risk factors
- Given short term (18-24 months)
- Followed by bisphosphonate

64

Abaloparatide—ACTIVE Results

- Analog of human parathyroid protein (PTHrP 1-34)
- Abaloparatide Comparator Trial In Vertebral Endpoints (ACTIVE)
  - 18 month Phase 3, multicenter, multinational, blinded RCT
  - 2,463 women (avg 69 yrs) randomized
    - Postmenopausal with T< -2.5 or hx of vertebral fracture
    - Daily SQ injections of placebo, abaloparatide 80 ug, or teriparatide 20 ug
- Primary Endpoint: % with new vertebral fracture
- Secondary Endpoints: Change in BMD and time to first nonvertebral fracture

Relative Risk Reduction		
	Teriparatide	Abaloparatide
Vertebral Fracture	80% reduction	86% reduction
Nonvertebral Fracture	28% reduction	43% reduction

Absolute Risk (Fracture Incidence)			
	Placebo	Teriparatide	Abaloparatide
Vertebral p<0.0001	4.21%	0.84%	0.58%
Nonvertebral p<0.0318	4.01%	2.93%	2.18%

Study Completion Rates: 77% Placebo, 80% Teriparatide, 74% Abaloparatide

65

Abaloparatide—ACTIVExtend Results

- ACTIVExtend Trial: additional 6 months of alendronate

Change in BMD: Abaloparatide or Placebo, then Alendronate x 6 mo		
	Placebo + Alendronate	Abaloparatide + Alendronate
Lumbar Spine p<0.0001	3.5%	12.8%
Total Hip p<0.0001	1.4%	5.5%

- Teriparatide trials cortical remodeling & porosity
- Abaloparatide trials slightly greater cortical gain
- Less hypercalcemia, more hyperuricemia with abaloparatide

66

Abaloparatide (Tymlos®)

- Refrigerated
- Allow to come to room temp x 30 min before administering
- Good at room temp for up to 30 days

- Contraindicated: hypocalcemia
- Warning: Orthostatic hypotension, hypercalcemia, hypercalciuria and urolithiasis
- Hypercalciuria: 11%
- Elevation in uric acid levels
- Risk of osteosarcoma unknown

AACE/ACE Postmenopausal Osteoporosis CPG, Endocr Pract. 2020;26(Suppl 1)
FDA Tymlos Package Insert

67

Romosozumab (Evenity®)

- Inhibits sclerostin (a protein which blocks bone formation)
  - FDA indicated for postmenopausal women
- 210 mg subcut (2 separate injections) once monthly x 12 mo
- Reserved as alternative to 1st lines & high risk only

- Two large Phase 3 trials – not powered to show fracture reduction
- ARCH TRIAL- 4,093 women randomized
- Postmenopausal with T< -2.5 AND hx of vertebral fracture
- Monthly romosozumab (210 mg) or weekly alendronate (70mg)
- Followed by alendronate 70 mg x 1 year
- Primary Endpoint: new vertebral and nonvertebral fractures

ARCH Trial	Alendronate	Evenity then Alendronate	
Vertebral fractures	8%	4.1%	ARR 4% (2.5-5.6) p<0.001
Clinical fractures p<0.001	13%	9.7%	HR 0.73 (0.61-0.88) p<0.001

- BMD improved with Evenity at spine, total hip, femoral neck
- *BMD returns to baseline within 12 mo with Evenity alone

Buckley et al. Arthritis Rheumatol. 2017, 69, 152
AACE/ACE Postmenopausal Osteoporosis CPG, Endocr Pract. 2020;26(Suppl
Saag KG, et al. N Engl J Med. 2017;377:1417-142
Dipiro et al. Pharmacotherapy: A Pathophysiologic Approach. 11th E
Miller et al. JAMA. 2016 Aug 16; 316(7):72

68

Romosozumab (Evenity®) Adverse Effects

- Refrigerated
- Allow to come to room temp x 30 min before administering
- Good at room temp for up to 30 days

- Contraindicated: hypocalcemia
- Warning: Increased risk of heart attack, stroke, CVD death
- MACE: 2% vs 1.1% alendronate, HR 1.87 (1.11-3.14)
- Hypersensitivity reactions (Chinese hamster cell lines)

Buckley et al. Arthritis Rheumatol. 2017, 69, 1521
AACE/ACE Postmenopausal Osteoporosis CPG, Endocr Pract. 2020;26(Suppl 1)
Saag KG, et al. N Engl J Med. 2017;377:1417-1427.
Dipiro et al. Pharmacotherapy: A Pathophysiologic Approach. 11th Ed.
Miller et al. JAMA. 2016 Aug 16; 316(7):722.

69

Interactive Case

FJ is a 63 YOF with history of falls. She has a recent vertebral fracture, and had a hip fracture two years ago.
PMH: Diabetes Mellitus, hypertension, COPD, macular degeneration, peripheral neuropathy, and Transient Ischemic Attack (TIA) 3 years ago

Upon going through FJ's medical history with her, she mentions a previous issue with bleeding in her esophagus because of ulcers and stress. Her doctor no longer wishes to have her on bisphosphonate therapy. She also presents today with a new prescription, lisinopril, because her blood pressure continues to run high.

Which biologic options might be preferred?

A) Denosumab
B) Romosozumab
C) Abaloparatide
D) None of the above

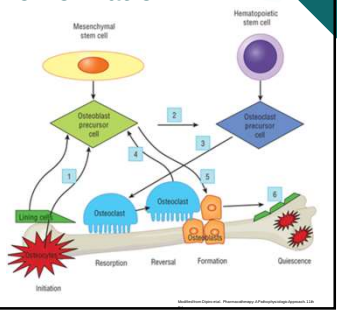
70

BONE TURNOVER MARKERS (BTM)

71

Stages of Bone Formation

1. **Resting:** Osteocytes trigger remodeling cycle
2. **Resting:** Stem cells differentiate into osteoclasts
3. **Resorption:** Osteoclasts remove bone
4. **Reversal:** Osteoclast activity halts, mesenchymal stem cells differentiate into osteoblasts
5. **Formation:** Osteoblasts make new bone by laying down protein matrix (osteoid)
6. **Quiescence:** Stable inactivity



72

Bone Turnover Markers (BTM)

Bone Turnover — Concept encompassing biological processes from bone resorption to bone formation

Bone Turnover Markers — Biological markers reflecting resorption or formation is occurring

Bone Resorption Markers

Breakdown products resulting from osteoclastic activity in the bone – released into the bloodstream

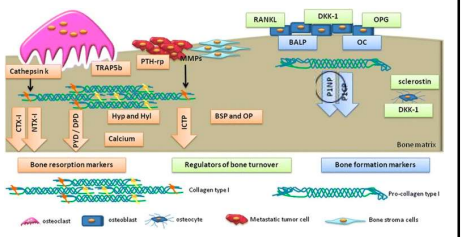
Bone Formation Markers

Byproducts resulting from osteoblast activity in the bone – released into the bloodstream when bone is formed

73

Bone Turnover Markers (BTM)

P1NP shown the greatest potential as a sensitive and stable bone biomarker for early detection



74

REVIEW

Bone turnover markers to monitor oral bisphosphonate therapy

Markers of Bone Formation

- Bone-specific alkaline phosphatase (BSAP)
- N-terminal propeptide of type I procollagen (PINP)
- Procollagen type I carboxyterminal propeptide (PICP)
- Osteocalcin

Markers of Bone Resorption

- C-terminal telopeptide of type I collagen (CTX)
- N-terminal telopeptide of type I collagen (NTX)
- Pyridinoline and Deoxypyridinoline
- Tartrate-resistant acid phosphatase 5b

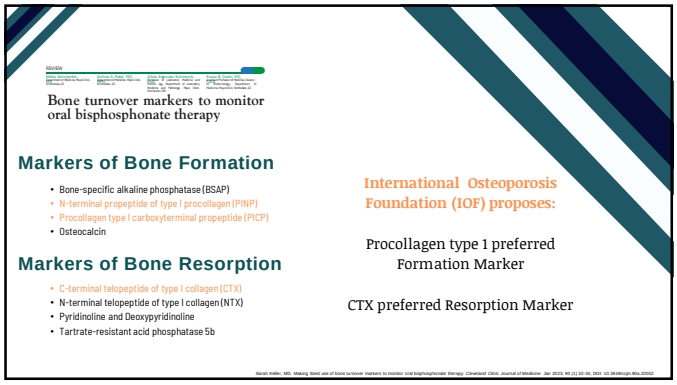
TABLE
Common bone turnover markers, their properties, and pros and cons

Markers of bone formation	Measured in	Diurnal variation	Renal function variation	Pro	Con
Bone-specific alkaline phosphatase (BSAP)	Serum	No	No	No postprandial changes Stable sample due to half-life of 1–2 days Widely available	Roughly 20% cross-reaction with other types of alkaline phosphatase
N-terminal propeptide of type I procollagen (PINP)	Serum	Yes	Yes	Well studied in clinical trials Relatively low intra-individual variability PINP measures response to therapy more effectively than BSAP	Hepatic function can affect levels depending on the assay and form of propeptide being measured Increased in patients on hemodialysis
Procollagen type I carboxy-terminal propeptide (PICP)	Serum	Yes	Renal variation unknown		Less studied than other bone formation markers
Osteocalcin	Serum and urine	Yes	Yes	Correlates well with bone turnover	Less stable; must process within hours Production is dependent upon vitamin K and can decrease in response to vitamin K antagonists (eg, warfarin)

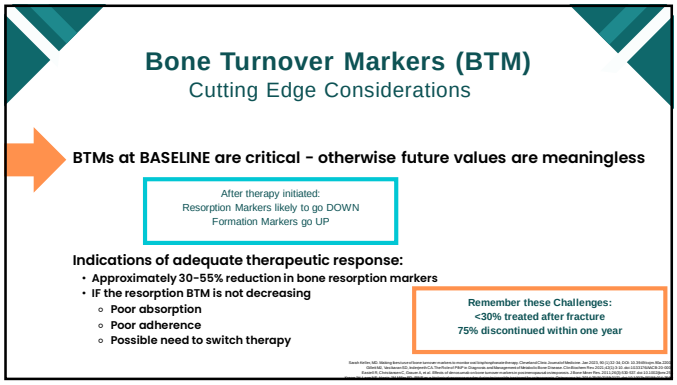
Markers of bone resorption	Measured in	Diurnal variation	Renal function variation	Pro	Con
C-terminal telopeptide of type I collagen (CTX)	Serum and urine	Yes	Yes	Stable biomarker Rapidly decreases with antiresorptive therapy	Postprandial variability Can be impacted by hepatic function
N-terminal telopeptide of type I collagen (NTX)	Serum and urine (24-hour urine collection or second morning void)	Yes	Yes	Minimal postprandial variability	Fasting measurements recommended Impacted by hepatic function
Pyridinoline and deoxy-pyridinoline	Urine (24-hour urine collection or second morning void with creatinine correction)	Yes	Yes	Can be renally adjusted	Impacted by hepatic function
Tartrate-resistant acid phosphatase 5b	Serum	Yes	No	No change with renal function	Predominately from but not exclusive to bone Unstable at room temperature Increases immediately after exercise

Nikita Ashcherkin, Archna A. Patel, Alicia Algeciras-Schimnich, Kruga B. Dooki. Bone turnover markers to monitor bisphosphonate therapy. *Cleveland Clinic Journal of Medicine*. Jan 2020, 90 (1) 26-31; DOI: 10.3949/ccjm.87a.22002

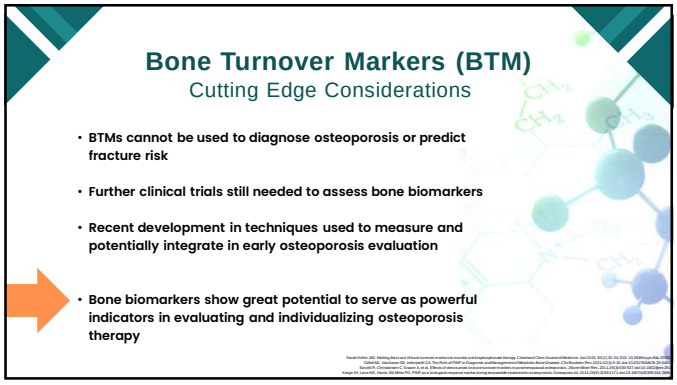
75


REVIEW
Bone turnover markers to monitor oral bisphosphonate therapy
Markers of Bone Formation
Bone-specific alkaline phosphatase (BSAP)
N-terminal propeptide of type I procollagen (PINP)
Procollagen type I carboxyterminal propeptide (PICP)
Osteocalcin
Markers of Bone Resorption
C-terminal telopeptide of type I collagen (CTX)
N-terminal telopeptide of type I collagen (NTX)
Pyridinoline and Deoxypyridinoline
Tartrate-resistant acid phosphatase 5b
International Osteoporosis Foundation (IOF) proposes:
Procollagen type 1 preferred Formation Marker
CTX preferred Resorption Marker

76


Bone Turnover Markers (BTM)
Cutting Edge Considerations
BTMs at BASELINE are critical - otherwise future values are meaningless
After therapy initiated:
Resorption Markers likely to go DOWN
Formation Markers go UP
Indications of adequate therapeutic response:
Approximately 30–55% reduction in bone resorption markers
IF the resorption BTM is not decreasing
Poor absorption
Poor adherence
Possible need to switch therapy
Remember these Challenges:
<30% treated after fracture
75% discontinued within one year

77


Bone Turnover Markers (BTM)
Cutting Edge Considerations
BTMs cannot be used to diagnose osteoporosis or predict fracture risk
Further clinical trials still needed to assess bone biomarkers
Recent development in techniques used to measure and potentially integrate in early osteoporosis evaluation
Bone biomarkers show great potential to serve as powerful indicators in evaluating and individualizing osteoporosis therapy

78

Interactive Case

FJ is a 63 YOF with history of falls. She has a recent vertebral fracture, and had a hip fracture two years ago.
PMH: Diabetes Mellitus, hypertension, COPD, macular degeneration, peripheral neuropathy, and Transient Ischemic Attack (TIA) 3 years ago

After having an allergic reaction to an injectable biologic for osteoporosis, the physician decides to initiate IV zoledronic acid.

Which impact on bone turnover markers might be seen?

A) Bisphosphonates would cause a reduction in resorption markers
B) Bisphosphonates would cause an increase in resorption markers
C) Bisphosphonates will not impact bone turnover markers
D) Only biologics will impact bone turnover markers

79

2020 AACE/ACP GUIDELINES

American Association of Clinical Endocrinologists
American College of Endocrinology
Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis

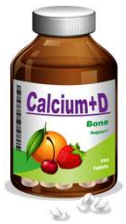
Endocrine Practice
Volume 26; Suppl 1
May 2020

80

2020 AACE/ACP Guidelines

Nutritional Support

- Calcium & Vitamin D
  - Target calcium intake of 1,200 mg/day
  - Target vitamin D3 intake of 1000 – 2000 units daily
  - Maintain 25-hydroxyvitamin D 25-OH of 30-50 ng/mL
- Initiate pharmacotherapy if T < -2.5 or fracture
- Initiate pharmacotherapy if T-score -1 to -2.5 and elevated FRAX Score



81

2020 AACE/ACP Guidelines

First Line Therapy

- **Bisphosphonates – Dose appropriately per indication**
  - **Alendronate, Risedronate, Zoledronic acid**
  - **Consider holiday after:**
    - **5-10 years (oral)**
    - **3-6 years (IV)**
- **Denosumab**
  - **Transition to another antiresorptive as clinically appropriate**
- **No combination of therapies recommended**

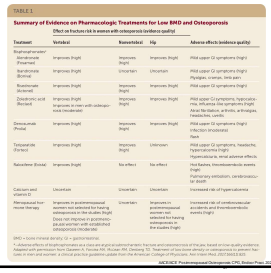


TABLE 1

Summary of Evidence on Pharmacologic Treatments for Low BMD and Osteoporosis

Effect on fracture risk in women with osteoporosis (evidence quality)

Treatment	Vertebral	Nonvertebral	Hip	Adverse effects (evidence quality)
Bisphosphonates*				
Alendronate (Fosamax)	Improves (high)	Improves (high)	Improves (high)	Mild upper GI symptoms (high)
Ibandronate (Boniva)	Improves (high)	Uncertain	Uncertain	Mild upper GI symptoms (high) Myalgias, cramps, limb pain
Risedronate (Actonel)	Improves (high)	Improves (high)	Improves (high)	Mild upper GI symptoms (high)
Zoledronic acid (Reclast)	Improves (high) Improves in men with osteoporosis (moderate)	Improves (high)	Improves (high)	Mild upper GI symptoms; hypocalcemia; mild, influenza-like symptoms (high) Atrial fibrillation, arthritis, arthralgias, headaches, uveitis
Denosumab (Prolia)	Improves (high)	Improves (high)	Improves (high)	Mild upper GI symptoms (high) Infection (moderate) Rash
Teriparatide (Forteo)	Improves (high)	Improves (high)	Unknown	Mild upper GI symptoms, headache, hypercalcemia (high) Hypercalciuria, renal adverse effects
Raloxifene (Evista)	Improves (high)	No effect	No effect	Hot flashes, thromboembolic events (high) Pulmonary embolism, cerebrovascular death
Calcium and vitamin D	Uncertain	Uncertain	Uncertain	Increased risk of hypercalciuria
Menopausal hormone therapy	Improves in postmenopausal women not selected for having osteoporosis in the studies (high) Improves in postmenopausal women with osteoporosis (moderate)	Uncertain	Improves in postmenopausal women not selected for having osteoporosis in the studies (high)	Increased risk of cerebrovascular accidents and thromboembolic events (high)

GHG = bone mineral density; GI = gastrointestinal.

* Adverse effects of bisphosphonates as a class are atypical stress fractures and osteonecrosis of the jaw, based on low-quality evidence.

Adapted with permission from Qaseem A, Forciea MA, Mcclean RM, Denberg TD. Treatment of low bone density or osteoporosis to prevent fractures in men and women: a clinical practice guideline update from the American College of Physicians. Ann Intern Med. 2017;166(11):818.

82

2020 AACE/ACP Guidelines

Very High Risk

- **Zoledronic Acid**
- **Denosumab**
- **Abaloparatide or Teriparatide**
  - **Max of 2 years**
  - **Must follow with bisphosphonate or denosumab**
- **Romosozumab**
  - **Max of 1 year**
  - **Must follow with bisphosphonate or denosumab**

May be appropriate for:

- Patients unable to use oral therapy
- Patients with very high fracture risk

83

2023 ACP UPDATED GUIDELINES

American College of Physicians

Pharmacologic Treatment of Primary Osteoporosis or Low Bone Mass to Prevent Fractures in Adults

Annals of Internal Medicine
January 2023

84

2023 Guidelines
First Line Therapy

- Bisphosphonates - Dose appropriately per indication
  - Alendronate, Risedronate, Zoledronic acid
  - Longer than 3-5 years of use reduces risk for new vertebral fractures but no other fractures
  - Increases risk of long-term harms
  - Consider discontinuing unless strong indication for continuation
  - Holiday should be individualized and based on baseline risk for fractures, medications, benefits, harms, and half-life in bone

Antiresorptive agent should be initiated after use of anabolic agent

Second Line Therapy

Take individualized approach to start pharmacologic treatment with bisphosphonates to ↓risk of fractures in females >65 YO with osteopenia

- Use RANK ligand inhibitor as 2nd line pharmacologic treatment
  - Denosumab
    - Reduce risk of fractures in postmenopausal women and men diagnosed with primary osteoporosis who have contraindications to or experience AE of bisphosphonates

Person, ACP updates clinical recommendations on treatment of osteoporosis. 2023.

85

2023 Guidelines
Very High Risk

- Sclerostin inihibitor - Romosozumab
  - Max of 1 year
  - Must follow with bisphosphonate
  - Moderate certainty evidence
- Parathyroid hormone - Abaloparatide or Teriparatide
  - Max of 2 years
  - Must follow with bisphosphonate
  - Low certainty evidence
- Antiresorptive agent should be initiated after use of anabolic agent
  - To keep gains
  - Serious risk for rebound and multiple vertebral fractures

Person, ACP updates clinical recommendations on treatment of osteoporosis. 2023.

86

2023 Guidelines
Evidence Gaps and Research Needs

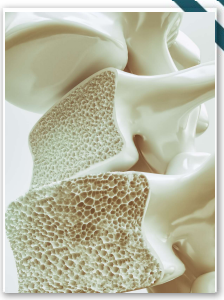
- **Long-term comparative benefits vs harms from all treatments with osteoporosis and osteopenia**
- **Focus on less studied populations**
  - **Premenopausal women**
  - **Males**
  - **Intersex persons**
  - **Transgender persons after transitioning treatment**
  - **Multimorbidity and/or polypharmacy**
- **Focus on baseline risk for fracture and prior treatment response**
- **Longer duration with biologic therapy**
- **Off-label treatment**

Person, ACP updates clinical recommendations on treatment of osteoporosis. 2023.

87

MONITORING

- Adherence
- Appropriate OTC supplementation
- Adverse Effects: Review individual drugs
- Drug therapy reassessment every 5 years



88

2020 AACE/ACP Guidelines

Response to Therapy

- **Bone Mineral Density (BMD)**
  - **DXA at same facility**
  - **No tx: Every 1-2 years, unless risk factors change**
  - **On tx: Every 5 years**
- **Labs**
  - **Serum calcium, vitamin D**
  - **Consider use of bone turnover markers (efficacy/adherence)**

TREATMENT SUCCESS	TREATMENT FAILURE
Stable or increasing BMD	2+ fractures while on therapy
Stable or reduced bone turnover markers (antiresorptive agent)	
Elevated bone turnover markers (anabolic/bone forming agent)	

89

The Cost

Medicare

- The Bone Health and Osteoporosis Foundation estimates:
  - 3 million fractures
  - $25.3 billion in direct healthcare costs per year by 2025
- Undertreatment and disease mismanagement osteoporosis and related fractures present cost burden to healthcare system
  - Osteoporotic fracture is more costly than breast cancer, myocardial infarction and stroke
  - Remains under-diagnosed
  - Poor medication adherence

Less than 50% of patients regain basic ADL
Up to 33% totally dependent (or nursing home)

90

Assessment Question 1

According to the 2023 ACP guidelines, which of the following drugs is NO LONGER considered first line treatment for osteoporosis?

A. Alendronate
B. Teriparatide
C. Denosumab
D. Romosozumab

91

Assessment Question 2

Which of the following are risks of bisphosphonate therapy that become more likely with longer duration of therapy?

A. Osteonecrosis of the jaw
B. Infusion reactions (with IV zoledronic acid)
C. Atypical fractures
D. Both A & B
E. Both A & C

92

Assessment Question 3

Which of the following drugs is most likely to LOWER bone mineral density and WORSEN osteoporosis?

A. Prednisone
B. Alendronate
C. Hydrocodone
D. Rosuvastatin

93

Assessment Question 4

Which of the following drugs is limited to a maximum therapeutic course of 24 months of use?

A. Denosumab
B. Zoledronic Acid
C. Teriparatide
D. Alendronate

94

Assessment Question 5

LR is a 66 YOF currently on bisphosphonates for osteoporosis. Her provider is considering lab monitoring. Which of the following is TRUE regarding bone turnover markers (BTM)?

A. BTM monitoring plays no role in disease management
B. BTM monitoring may serve as a key element in the future of individualized management of osteoporosis
C. BTM is routinely done with biologics like denosumab
D. BTM is only useful after hip fracture

95

Assessment Question 6

SK is a 73 YOF with severe osteoporosis and multiple hip and vertebral fractures. She is at very high risk for future fractures and is started on ORAL bisphosphonates. When do the AACE guidelines recommend a drug holiday for this patient?

A. After 1 year
B. After 3 years
C. After 10 years
D. Never; should be continued indefinitely

96

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100

Is Osteoporosis Cutting Edge?

What's New in Fracture Prevention

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101