



Revolutionizing Osteoporosis Care: The Latest Advances in Goal-Directed Therapy

Updates to the 2017 Guidelines

Kayla Groen, PharmD PGY1 Pharmacy Resident

Advocate Good Samaritan Hospital

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Disclosures

The following faculty speakers and/or planning committee members have disclosed the following:

Faculty Name	Name of Ineligible Companies	Nature of Relationship
Megan Corrigan	WG Critical	Consultant, Relationship ended 12/31/25

The other planners and speaker have indicated that there are no relevant financial relationships with any ineligible companies to disclose. All of the relevant financial relationships listed for this individual have been mitigated.

Learning Objectives

At the end of this session, learners should be able to:

- 1. Outline the pharmaceutical classes used in osteoporosis treatment**
- 2. Describe treatment targets for treating osteoporosis**
- 3. Identify potential opportunities for pharmacist intervention in osteoporosis management**
- 4. Apply new goal-directed treatment strategies to a patient case**

Outline

Pathology

Screening

Pharmacotherapy

Diagnosis

Treatment Guidelines

Role of pharmacists/future practice

Patient Case

Abbreviation Key

- AACE = American Association of Clinical Endocrinologists
- ACE = American College of Endocrinology
- AFF = Atypical femoral fracture
- ASBMR = American Society for Bone and Mineral Research
- BMD = Bone Mineral Density
- BTM = Bone Turnover Marker
- CI = Confidence interval
- DXA/DEXA = Dual-energy X-ray absorptiometry
- FN = Femoral Neck
- FRAX® = Fracture Risk Assessment Tool
- GIO= Glucocorticoid induced Osteoporosis
- IU = International units
- IV = Intravenous
- LS = Lumbar spine
- NOF = National Osteoporosis Foundation
- ONJ = Osteonecrosis of the jaw
- PTH = Parathyroid hormone
- PO = By mouth
- TBS = Trabecular Bone Scores
- TH= Total hip
- TSH = Thyroid Stimulating Hormone
- RANKL = Receptor Activator of Nuclear factor Kappa-B Ligand
- VFA = Vertebral fracture assessment
- VTE = Venous thromboembolism

Osteoporosis Statistics

50%

All adults age
50+ at risk of
breaking a bone

10 million

Americans have
osteoporosis

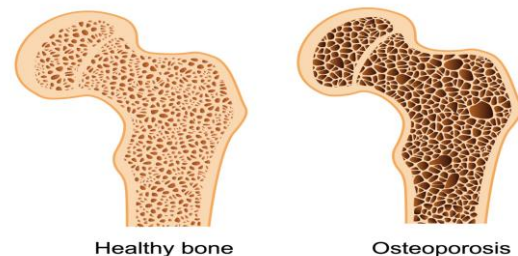
18%

Increased risk of
new fractures
within 2 years of
initial fracture

What is Osteoporosis?

Skeletal disorder characterized by deteriorated bone structure predisposing patients to an increased risk of fracture

- Primary osteoporosis:
 - Associated with age
 - Sex hormone deficiency
- Secondary osteoporosis:
 - Caused by several comorbidities & medications
 - Ex: glucocorticoid use

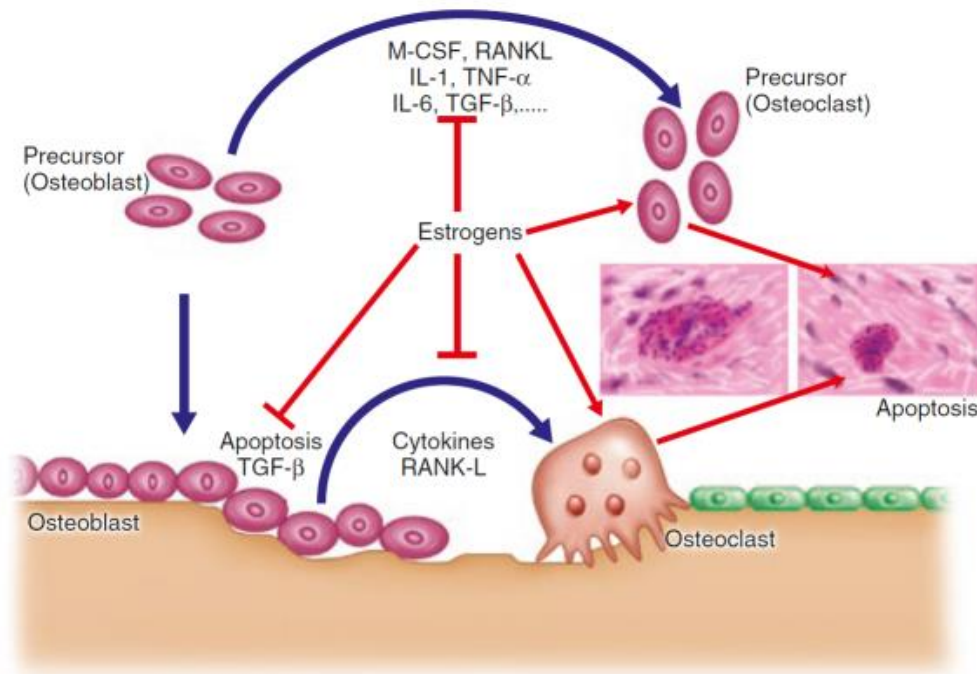


Pathophysiology

Bone undergoing constant remodeling

Osteoblasts: bone builders

Osteoclasts: responsible for bone resorption



Risk Factors

Non-modifiable:

- Age
- Height loss
- Female gender
- Family history
- Previous fractures
- Ethnicity
- Estrogen deficiency and amenorrhea
- Menopause and hysterectomy

Modifiable:

- Alcohol
- Smoking
- Low body mass index
- Inadequate calcium intake
- Vitamin D deficiency
- Eating disorders
- Insufficient exercise
- Frequent falls

Assessment Question #1

KJ is a 59-year-old Caucasian female who lives in Chicago. She has a past medical history of hypertension, diabetes, and is a current smoker. Six months ago, she tripped over her rug in her kitchen and was seen in the Emergency Department. Imaging was performed and revealed a fracture to her pelvis.

What are KJ's risk factors for osteoporosis?

- A. Smoking
- B. Diabetes
- C. Caucasian
- D. Vitamin D deficiency
- E. All of the above

Fundamental Measures for Bone Health

Ensure adequate:

- Calcium intake
- Vitamin D intake
- Regular, weight-bearing or resistance exercise
- Protein intake

Limit:

- Excessive vitamin A intake
- Alcohol intake
- Caffeine intake

Consider:

- Smoking cessation
- Fall prevention
- Physical Therapy

Screening

Recommendations from ACP (2017) and AACE/ACE Guidelines (2020):

1. Men and women 50+ with fragility fractures
2. Postmenopausal women < 65 years with 1 or more risk factors for osteoporosis
3. Men 70+ and women 65+ with no additional risk factors

Clinical Fracture Risk Assessment

FRAX[®]: Fracture Risk Assessment Tool

- Estimates 10-year fracture risk
- Risk Factors included:
 - Country of residence
 - Ethnicity
 - Age
 - Sex
 - Height and weight
 - Personal or family history of fractures
 - Rheumatoid arthritis
 - Alcohol use
 - Secondary osteoporosis
- Considerations: can underestimate risk in certain patient populations, only reports hip fracture and major fracture risk

Age: 85

BMI: 25

without BMD

THE TEN-YEAR PROBABILITY OF FRACTURE

Major osteoporotic 56 %

Hip Fracture 34 %

Testing and Evaluation

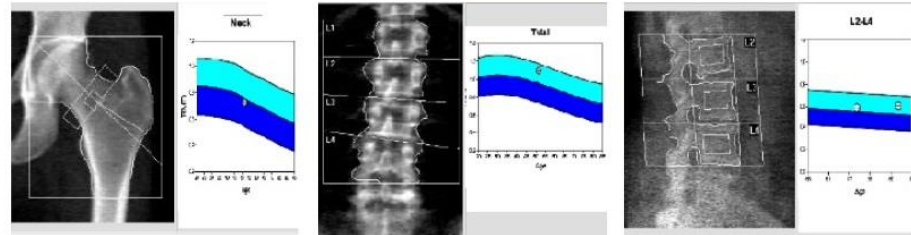
Calcaneal Ultrasonography

- more useful for ruling in osteoporosis than ruling out

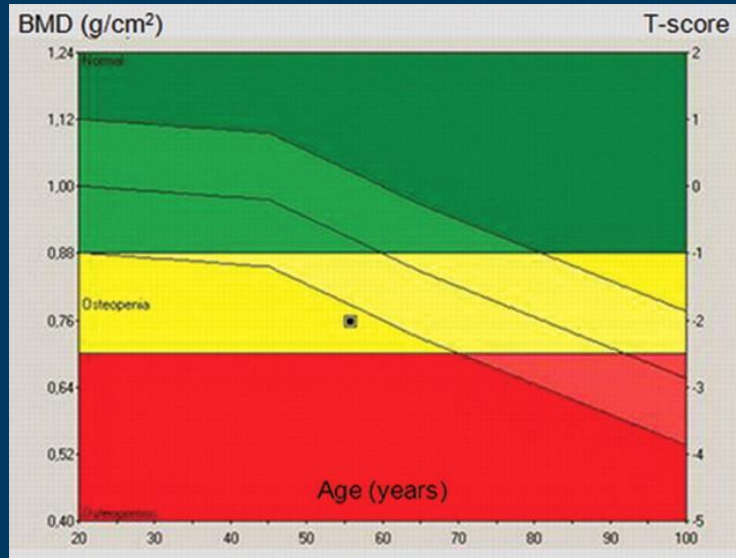
DXA scan: Dual Energy X-Ray Absorptiometry

- measures bone mineral density at lumbar spine, hip (femoral neck or total hip), and forearm
- reported as gram of mineral per cm^2 and converted to t- and z-scores
- used to calculate vertebral fracture assessment and trabecular bone score

DXA (DEXA) Scan



Interpreting the DXA



Z-score: how many standard deviations from the population mean

(how does this patient compare to others their own age)

T-score: how many standard deviations from the mean

(how does this patient compare to the average 30-year-old)

Gaps in Care

Early screening in
at-risk individuals

Prompt diagnosis

Starting
appropriate
pharmacotherapy

Specialist
availability

Patient adherence
"silent disease"

Osteoporosis care
in men

Pharmacotherapy Review

Overview of Pharmacotherapy

Antiresorptive agents

Bisphosphonates

Denosumab

Selective estrogen receptor modifiers

Hormonal therapies

Calcitonin

Anabolic agents

Parathyroid hormone

Parathyroid hormone related protein
analogue

Sclerostin inhibitor

Antiresorptive Agents

Bisphosphonates

Drugs:	alendronate (Fosamax®), risedronate (Atelvia®), ibandronate (Boniva®), zoledronic acid (Zolmigra®)		
Mechanism	Bind with high affinity to mineral matrix of the bone to inhibit osteoclast resorption		
Indications	First line for prevention/treatment of osteoporosis in postmenopausal women, men, and GIO patients (excluding ibandronate)		
Dosing	Bisphosphonate	Treatment dose	CrCl Recommendation
	Alendronate	10 mg PO daily or 70 mg PO weekly	≥ 35 mL/min
	Risedronate	5 mg PO daily, 35 mg PO weekly, or 150 mg once monthly	≥ 30 mL/min
	Zoledronic acid	5 mg IV yearly	≥ 35 mL/min
	Ibandronate	2.5 mg PO daily, 150 mg PO monthly, or 3 mg IV every 3 months	≥ 30 mL/min
Administration	Take with glass of water in the morning prior to a meal and remain upright for at least 30 minutes		
Length of therapy	Moderate to low fracture risk: drug holiday after 3-5 years High fracture risk: drug holiday after 6-10 years		
Contraindications	Hypocalcemia, CrCl < 30-35 mL/min, esophageal disorders, history of bariatric surgery		
Monitoring	BMD at baseline and every 1-2 years on treatment		
Adverse Effects	Upper gastrointestinal discomfort, osteonecrosis of the jaw, atypical femoral fractures		

GIO: Glucocorticoid induced osteoporosis

Ganesan K, Goyal A, Roane D. Bisphosphonate. StatPearls [Internet] 2025.

LeBoff, M S et al. Osteoporosis international. 2022;33(10):2049-2102.

Denosumab

Drugs:	denosumab (Prolia™)
Mechanism	Monoclonal antibody that inhibits RANKL to decrease bone resorption
Indications	<ul style="list-style-type: none">• First line for patients at high risk of fracture or who are unable to take oral therapy• Approved in men and women
Dosing	60 mg subcutaneously every 6 months
Administration	<ul style="list-style-type: none">• Do not administer intravenously or intramuscularly• Injection sites include upper arm, upper thigh, or abdomen• No premedications required• Administer vitamin D and calcium as necessary to treat or prevent hypocalcemia
Contraindications	CKD Stage 5 or dialysis
Monitoring	Calcium levels
Adverse Effects	Serious infection, dermatological reactions, fatigue, peripheral edema, musculoskeletal pain, hypophosphatemia, hypercholesterolemia, ONJ, AFF

Selective Estrogen Receptor Modifiers (SERMs)

Drugs:	raloxifene (Evista®)
Mechanism	Agonistic estrogenic activity on bone, decreases bone resorption and bone turnover Antagonistic estrogenic activity on breast and uterine tissue
Indications	<ul style="list-style-type: none">• First-line therapy only in women requiring reduced risk of spine fracture• Weaker antiresorptive therapy for higher risk patients during bisphosphonate drug holiday• Not approved in men
Dosing	60 mg PO daily
Contraindications	Women with history or active venous thromboembolism (VTE), premenopausal women, pregnant women
Monitoring	BMD at baseline and every 1-2 years on treatment
Adverse Effects	Vaginal bleeding, hot flashes, worsening of hypertriglyceridemia, VTE, death due to stroke, cardiovascular disease

Hormonal Therapies

Drugs:	conjugated estrogens with bazedoxifene, estrogen therapy (Duavee®)
MOA	<ul style="list-style-type: none">• Agonistic estrogenic activity on bone, decreases bone resorption and bone turnover• Antagonistic estrogenic activity on breast and uterine tissue
Indications	Prevention of osteoporosis in women while treating vasomotor symptoms
Dosing	Conjugated estrogens 0.45 mg & bazedoxifene 20 mg PO once daily
Contraindications	Women with history or active VTE, premenopausal women, pregnant women
Monitoring	Baseline risk for breast cancer and cardiovascular disease, age-appropriate breast and pelvic exams, blood pressure, serum triglycerides, thyroid stimulating hormone (TSH), BMD
Adverse Effects	Vaginal bleeding, hot flashes, worsening of hypertriglyceridemia, venous thromboembolism, death due to stroke, cardiovascular disease

Calcitonin

Drugs:	calcitonin-salmon (Miacalcin®)
Mechanism	Calcitonin receptors found on osteoclasts and osteoblasts
Indications	<ul style="list-style-type: none">• Osteoporosis in women postmenopausal 5+ years when alternative therapies not feasible• Paget's disease in men and women• Short term for hypercalcemia in men and women
Dosing	200 units daily intranasally or 100 units subcutaneously daily
Contraindications	Anaphylactic reaction to calcitonin
Monitoring	Calcium levels
Adverse Effects	Nausea, vomiting, rhinitis, nasal irritation, back pain, arthralgia, nosebleed, headache, hypocalcemic tetany

Anabolic Agents

Parathyroid Hormone

Drugs:	teriparatide (Forteo®, Bonsity®)
Mechanism	Synthetic fragment of human parathyroid hormone
Indications	<ul style="list-style-type: none">• Treatment of osteoporosis in men and women at high risk for fracture• Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy
Dosing	20 mcg subcutaneous injection daily
Contraindications	Increased risk for osteosarcoma: Paget's disease of the bone, prior radiation therapy involving the skeleton, open epiphyses, history of bone metastases or malignancies, unexplained elevated alkaline phosphatase
Monitoring	Calcium levels
Adverse Effects	Transient orthostatic hypotension, leg cramps, and nausea
Notes	<ul style="list-style-type: none">• When discontinued, bone loss can be rapid• Use cautiously in patients with active or recent kidney stones, hypercalcemia and hypercalcemic disorders

Parathyroid Hormone-Related Protein Analogue

New
Agent!
2017

Drugs:	abaloparatide (Tymlos®)
Mechanism	Synthetic peptide analogue of human parathyroid related protein
Indications	<ul style="list-style-type: none">• Osteoporosis in women and men at high risk for fracture• Patients who have failed or are intolerant to other available therapies
Dosing	80 mcg subcutaneously daily
Administration	<ul style="list-style-type: none">• Administer into periumbilical region of abdomen• Duration of therapy limited to 2 years
Contraindications	Pre-existing hypercalcemia, underlying hypercalcemic disorder
Monitoring	Urine calcium if pre-existing hypercalciuria or active urolithiasis, blood pressure
Adverse Effects	Dizziness, nausea, headache, palpitations, fatigue, upper abdominal pain, vertigo risk of orthostatic hypotension, hypercalcemia, urolithiasis

Sclerostin Inhibitor

New
Agent!
2019

Drugs:	romosozumab (Evenity®)
Mechanism	Monoclonal antibody directed against sclerostin
Indications	<ul style="list-style-type: none">• Osteoporosis in postmenopausal women at high risk for fracture• Not yet approved in men
Dosing	Two 105 mg subcutaneous injections give one after another monthly for 12 months
Contraindications	Women with history or active VTE, premenopausal women, pregnant women
Monitoring	Calcium levels
Adverse Effects	<ul style="list-style-type: none">• Boxed Warning: myocardial infarction, stroke, and cardiovascular (CV) death• Rhinitis, nasal irritation, back pain, arthralgia, nosebleed, headache• Few cases of AFF and ONJ
Notes	Use limited to 1 year

Treatment Targets

Diagnosis

BMD Diagnosis

Classification	BMD	T-score
Normal	Within 1 standard deviation of mean level for young, healthy adult	≥ 1
Osteopenia	Between 1.0 and 2.5 standard deviations of mean level for young, healthy adult	Between -2.5 to -1.0
Osteoporosis	2.5 standard deviations or more from the mean level for young, healthy adult	≤ -2.5

Clinical Diagnosis:

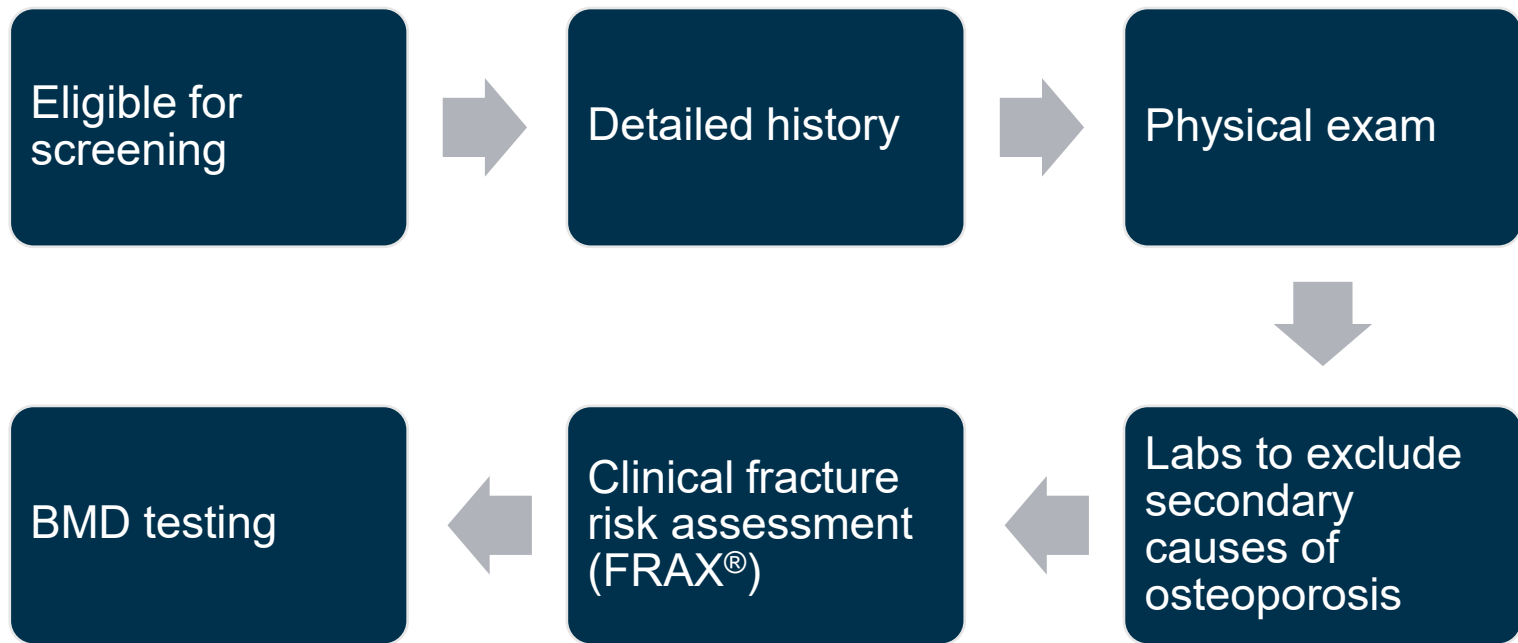
1. Incidence Fractures: presence of fragility fractures in the absence of other metabolic bone disorders
2. T- score between -1.0 and -2.5 at femoral neck or total hip with FRAX® risk score $\geq 3\%$ for hip fracture and $\geq 20\%$ major fracture

BMD: Bone mineral density

Cosman F, Lewiecki M, Eastell R, et al. *Journal of Bone and Mineral Research*. 2024;39(10):1393–1405.

LeBoff, M S et al. *Osteoporosis international*. 2022;33(10):2049-2102.

Assessing Fracture Risk



Risk Stratification

AACE/ACE 2020 Guidelines:



Low Risk:

- T-score > -2.5
- No history of fragility fractures
- Low FRAX® probability



High Risk:

- T-score ≤ -2.5
- History of fragility fractures
- High FRAX® probability



Very High Risk:

- Advanced Age
- Frailty
- Very low t-scores
- Increased fall risk



Imminent Risk:

- Recent fractures (within 2 years)
- Multiple fractures

Assessment Question #2

KJ is a 59-year-old Caucasian female who lives in Chicago. She has a past medical history of hypertension, diabetes, and is a current smoker. Six months ago, she tripped over her rug in her kitchen and was seen in the Emergency Department. Imaging was performed and revealed a fracture to her pelvis.

After the visit, she had an outpatient DEXA scan showing a t-score of -2.1 in the femoral neck and -2.4 at the total hip. **What risk category does KJ fall into for treatment?**

- A. Low risk, due to t-score between -1.0 and -2.5
- B. Moderate risk, due to t-score between -1.0 and -2.5
- C. Very High risk, due to t-score between -1.0 and -2.5 and history of fractures
- D. Imminent risk, due to recent pelvic fracture regardless of t-score

Treatment Targets

- Individualized, achievable goals
- Treat to target & beyond
- Goal based on risk of fracture:
 - Imminent risk: rapidly and maximally reduce fracture risk
 - BMD increase = greater reduction in fracture risk
 - Sustained treatment likely required
 - Not at imminent risk: consider baseline t-scores, fracture history, other major risk factors
 - Baseline T-score ≥ -2.5 : T-score level at least < -2.5 at respective skeletal sites
 - Baseline T-score < -2.5 : Increase BMD; T-score target not defined

Achieving Treatment Targets

1. Initiating appropriate treatment

- Probability of achieving treatment target
- Evaluating fracture risk, t-scores,
- Other factors: cost, adherence, etc.

2. Following appropriate sequence

- Sequence matters
 - Anabolic --> anti-resorptive = greater increases in BMD
 - Therapy "escalation" to osteoanabolic agents showed lower increases in BMD

Assessment Question #3

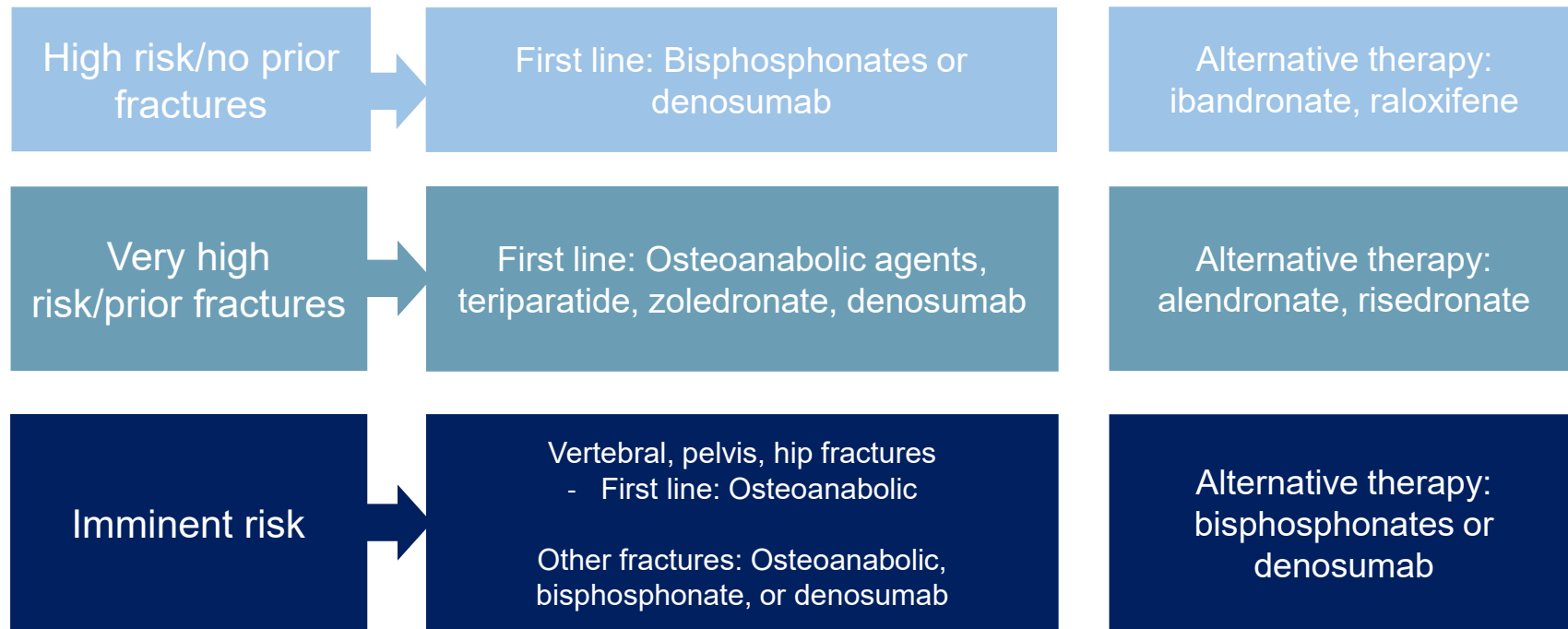
KJ is seen by her primary care provider who recommends supplementing with vitamin D and calcium, smoking cessation, and educates on fall prevention. She also wants to start pharmacotherapy and asks for your recommendation. **What treatment target is appropriate for KJ?**

Reminder: Six months ago, she had a stable pelvic fracture. Her DEXA scan showed a t-score of -2.1 in the femoral neck and -2.4 at the total hip. She is risk-stratified as "imminent risk".

- A. Treat to target a t-score of -1.0
- B. Treat to maintain a t-score of > -2.5
- C. Treat to target bone mineral density increases, no t-score goal
- D. Treat to target a bone mineral density goal $> 1 \text{ g/cm}^2$

Initiating Pharmacotherapy

ASBMR/BHOF Task Force Position Statement (2024)



Achieving Targets

- Unsuccessful:
 - As indicated by new fractures
 - Reassess adherence, fall risk interventions, address secondary causes
 - Start/continue the most potent medication or sequence for 2 years
- Successful:
 - BMD expected to decrease once discontinued
 - Transition to bisphosphonates?
 - Recommendations to continue bisphosphonates after denosumab therapy
 - IV zoledronic acid?

Successful Treatment

- Goal: prevent fractures
 - Improve BMD
 - Decrease t-scores
 - Reduce fracture risk
- Cannot eliminate risk of fracture
 - Fracture \neq treatment failure
 - Need to assess secondary causes, adherence, etc
- Does not reverse diagnosis

Latest Research

Infrequent IV zoledronic acid after fracture

Study	Population	Intervention	Comparison	Outcome
Bolland M et al. <i>NEJM</i> . 2025;392(3):239-248.	1054 female patients	<ul style="list-style-type: none">1:1:1 infusion at baseline and 5 yearsZoledronate-zoledronateZoledronate-placeboPlacebo-placebo	Presence of new vertebral fractures	Zoledronate-zoledronate compared to placebo showed hazard ratio of: 0.56 (95% CI (0.34-0.92)) for vertebral fracture 0.72 (95% CI (0.55-0.93)) for fragility fracture

BRIDGE Study

Study	Population	Intervention	Comparison	Outcome
Lewiecki E et al. <i>JECM</i> . 2018;103(9):3183-3193.	245 male patients aged 55-90 years	Randomized 2:1 to receive romosozumab 210 mg monthly or placebo for 12 months	Percent change from baseline in LS BMD at 12 months	Romosozumab group had greater increases from baseline in LS and TH BMD (LS: 12.1% vs 1.2%; $p < 0.001$; TH: 2.5% vs -0.5%; $p < 0.001$)

The Pharmacist's Role

Gaps in Care

Early screening in
at-risk individuals

Prompt diagnosis

Starting
appropriate
pharmacotherapy

Specialist
availability

Patient adherence
"silent disease"

Osteoporosis care
in men

Referrals

Who should be referred?

- Normal BMD and nontraumatic fracture
- Recurrent fractures despite treatment
- Less common secondary causes
- Osteoporosis with severe or unusual features
- Condition that complicates management

Pharmacist's Role

- Initial treatment with appropriate pharmacotherapy
- Ambulatory Care Pharmacist roles
 - Bone clinics
 - Endocrinology clinics
 - Family medicine
- Pharmacist led screening & education
 - Counseling
 - Administration of medications
 - Monitoring therapy

Fracture Liaison Model

Multidisciplinary model of post-fracture care

- Incorporates patient needs, goals, values, habits, abilities, and living conditions
- Evidence based diagnostic and treatment protocols
- Goal: evaluate and treat patients while optimizing provider time



Examples:

- Kaiser Permanente "Healthy Bones"
- American Orthopedic Association's "Own the Bone" program

Assessment Question #4

KJ is a 59-year-old Caucasian female who lives in Chicago. She has a past medical history of hypertension, diabetes, and is a current smoker. Six months ago, she tripped over her rug in her kitchen and was seen in the Emergency Department. Imaging was performed and revealed a fracture to her pelvis.

In addition to the pharmacist's recommendation for an agent to start pharmacotherapy, what other ways can pharmacists play a role in osteoporosis care?

- A. Counseling on medication side effects and monitoring
- B. Assisting providers in preparing and following up on prior authorizations
- C. Awareness on the latest literature and guideline updates in osteoporosis care
- D. All of the above

Key Takeaways



Osteoporosis can be diagnosed clinically and based on bone density on DEXA scans

Patients should be initiated on appropriate pharmacotherapy based on their risk stratification and treatment goals

Treatment targets should be individualized and achievable

There are many opportunities for pharmacists to address gaps in osteoporosis management

Future Research

- Novel Targets
 - NELL-1: International Space Station testing new NELL-1 modified protein on rats
 - Anti-Basigin therapy: UC Davis Health showed inhibition of basigin protein prevented bone loss and increased strength in mice
- New drug delivery systems: oral robotic delivery of teriparatide (RT-102)
 - Rani Therapeutics
 - Currently in Phase 2 Trials
 - Phase 1 trials showed 3 times higher bioavailability when orally delivered compared to subcutaneous delivery

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Questions?

Kayla Groen
kayla.groen@aah.org



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