

# Osteoporosis Screening, Diagnosis, and Treatment Guideline

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**Guidelines** are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

# Major Changes as of April 2019

Following scheduled review, the KP Washington Osteoporosis Guideline team determined that there were no outstanding evidence gaps and re-approved the guideline with only minor changes to content. The KPWA guideline is in alignment with current KP National clinical guidance. A new shared decision-making section for talking with patients about the risks and benefits of oral bisphosphonate treatment is now included.

# Definitions

*Fragility fracture* is one caused by a degree of trauma not expected to cause a fracture; for example, a fall from standing height or lower. Fragility fractures, such as vertebral compression fractures and distal forearm fractures, are common in the elderly but can occur at any age.

*Major osteoporotic fracture* is a fracture of the hip, spine (clinical), wrist, or humerus.

**Osteoporosis** is defined as a history of fragility fracture and/or a T-score of -2.5 or lower on dual energy X-ray absorptiometry (DEXA).

Low bone mass (or osteopenia) is defined as a T-score between -1.0 and -2.5 on DEXA.

# **Primary Prevention**

The following are effective strategies for preventing osteoporosis:

### Fall prevention

- For all adults, recommend regular weight bearing and muscle building exercises for prevention of
  osteoporosis and falls.
- Discuss fall prevention strategies with your patient. Tools include the <u>Home Fall Prevention and</u> <u>Safety Checklist</u>, <u>Preventing falls in your home</u>, and the KP Washington Health Research Institute article <u>10 things you can do to prevent devastating falls</u>.
- Encourage patients to take their time when ambulating outside, especially around the curb and on rainy days.
- If a patient is unsteady, consider doing a fall risk assessment using the Timed Get Up and Go or other tool and/or referring the patient to Physical Therapy for fall risk assessment and walking aid recommendations.
- If appropriate, assess your patient for <u>unhealthy alcohol use</u>. Also assess for polypharmacy, including any medications that may cause sedation, dizziness or drowsiness
- If your patient has frequent falls, consider Physical Therapy referral to develop a personalized plan for improving balance and strength. Don't exclude patients who reside in a nursing home or similar setting – they can also benefit from PT services.

### Calcium and vitamin D

- Do not screen for vitamin D deficiency in adults age 50 or over without osteoporosis.
- If the recommended daily allowance is not achieved through diet alone, consider over-the-counter supplementation with:
  - Calcium 1200 mg a day in two divided doses; the body can only absorb about 600–800 mg elemental calcium in one sitting. For patients on acid-reducing agents like PPI or antacid, calcium citrate is the preferred form, as calcium carbonate needs acidity in the stomach to be absorbed. Calcium carbonate is best absorbed when taken after meals.
  - Vitamin D 1000–2000 IU a day (2000 IU a day in cloudier months of the year) for maintenance dose.

### Tobacco use

For all adults who are current smokers, recommend <u>smoking cessation</u>.

# Screening Recommendations and Tests

Table 1. Recommendations for osteoporosis screening with DEXA scan <sup>1, 2</sup>			
Population	Preliminary FRAX?	DEXA Frequency <sup>3</sup>	Comments
All women aged 65 years and older	No	Every 2–10 years depending on initial T-score	No upper age limit.
<ul> <li>Postmenopausal women under</li> <li>65 years with at least one of the following: <ul> <li>Parent with hip fracture</li> <li>Current smoking</li> <li>Excessive alcohol intake (3 or more servings/day)</li> <li>Low body weight</li> </ul> </li> </ul>	Yes If 10-year risk of major osteoporotic fracture 9.3% or higher, proceed to DEXA.	Every 2–10 years depending on initial T-score	
Men and women of any age with fragility fracture	No	Every 2–10 years depending on initial T-score	History of fragility fracture is diagnostic for osteoporosis. Assess for secondary causes of osteoporosis (see p. 5).
Men and women of any age with conditions known to be secondary causes of osteoporosis	No	Every 2–10 years depending on initial T-score	See p. 5 for secondary causes of osteoporosis.
osteoporosis           1         While there is limited direct ev	d 65 years and old	screening for osteoporosister because of strong evic	s to reduce fracture risk, DEXA is lence that bisphosphonates significantly

reduce hip-fracture risk for older women who have met the diagnostic T score criteria of lower than -2.5.

<sup>2</sup> KPWA recommends screening only those who will be willing to initiate treatment

<sup>3</sup> Because of limitations in the precision of DEXA testing, a minimum of 2 years may be needed to reliably measure a change in bone density; however, longer intervals may be adequate for repeated screening to identify new cases of osteoporosis.

# The FRAX calculator

This tool estimates the 10-year probability of osteoporotic fracture for postmenopausal women and men aged 50 years and older who have **not** been previously treated for osteoporosis. Risk factors included in the FRAX are: age, gender, low body weight, height, previous fracture, parent with hip fracture, smoking status, glucocorticoid use, history of rheumatoid arthritis, menopausal status, and excessive alcohol consumption.

The FRAX calculator is available online at <a href="http://www.shef.ac.uk/FRAX/">http://www.shef.ac.uk/FRAX/</a> . Use the drop-down list under "Calculation Tool."

*Limitations:* The FRAX calculator may underestimate fracture risk in patients with a history of a vertebral fracture, a hip fracture, or multiple fractures. Some risk factors, such as frailty and dementia, cannot be readily quantified and are not included in the calculation.

# Diagnosis

#### History of fragility fracture is diagnostic for osteoporosis.

For patients *without* a fragility fracture, interpret DEXA results as follows:

Table 2. Interpretation of bone density test results				
Test	Results <sup>2</sup>	Interpretation <sup>3</sup>		
Bone density by DEXA <sup>1</sup>	T-score <sup>4</sup>			
	T-score -2.5 and lower	Osteoporosis		
	T-score between -1.0 and -2.5	Low bone mass		
	T-score -1.0 and higher	Normal		
	Z-score <sup>5</sup>			
	Z-score -2.0 and lower	Below expected range for age		
	Z-score above -2.0	Within expected range for age		

- <sup>1</sup> May be measured and reported as a total hip score, the femoral neck score, and/or the L1 to L4 total lumbar score. Occasionally the distal radius is used if other sites are not practical or as an early indicator in hyperparathyroidism.
- <sup>2</sup> DEXA result is based on the worst score of the individual scores of the spine, total hip, femoral neck, and when applicable, the one-third radius (forearm). Premenopausal women and men younger than 50 will only have Z-scores.
- <sup>3</sup> Although these definitions are necessary to establish the presence of osteoporosis, they should not be used as the sole determinant of treatment decisions.
- <sup>4</sup> The T-score represents the number of standard deviations a patient's bone density differs from the average bone density of a healthy 30-year-old of the same sex and ethnicity.
- <sup>5</sup> The Z-score represents the number of standard deviations a patient's bone density is from the average bone density of people their same age, sex, and ethnicity.

# Evaluation for Secondary Causes of Osteoporosis

For patients diagnosed with osteoporosis or low bone mass, assess for secondary causes as follows:

# Initial lab testing

Order the following tests (can be done before office visit). Selection of lab testing may be individualized as appropriate.

- Complete blood count
- 25-OH vitamin D
- In men: 8 a.m. total testosterone
- 24-hour urine for calcium and creatinine
- TSH

- PTH
- TTG and serum IgA
- Calcium with GFR
- Creatinine

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Hepatic function

If any conditions emerge from testing, work up and treat findings appropriately.

# Medical history and clinical exam

Assess the patient's medical history for the following conditions associated with osteoporosis:

#### Endocrine or metabolic disease (history, signs, or symptoms)

- Hyperparathyroidism/hypercalcemia
- Hypogonadism
- Hypopituitarism
- Hyperprolactinemia
- Cushing syndrome

#### Bone marrow-related disorders

- Multiple myeloma or myelodysplasia
- Thalassemia
- Systemic mastocytosis

#### Other conditions

- Rheumatoid arthritis
- History of organ transplantation
- Chronic kidney disease
- Secondary hyperparathyroidism due to renal disease
- Immobilization (paraplegia, quadriplegia, muscular dystrophy)
- Vitamin D deficiency

Hyperthyroidism

Anorexia nervosa

Acromegaly

Diabetes mellitus type 1

- Malabsorption (can be due to PPI therapy, celiac disease)
- Hypercalciuria
- Inadequate calcium intake

### Medication review

Assess the patient's medication list for the following medications associated with osteoporosis:

- Glucocorticoids (See Pharmacologic options for patients on long-term corticosteroid therapy, p. 10)
- Aromatase inhibitors
- Androgen deprivation therapy
- Anti-epileptics (e.g., phenytoin, phenobarbital)
- Excess thyroid replacement
- GnRH agonists (e.g., Lupron)
- Depo-Provera (medroxyprogesterone acetate)

# **Treatment Overview**

Eligible population	Fragility fracture?	Secondary cause of osteoporosis?	FRAX score	Recommendation
Patients diagnosed with osteoporosis by DEXA (T-score of -2.5 or lower) or presence of fragility fracture	Yes	No	N/A	Offer pharmacologic treatment for primary osteoporosis.
	Yes	Yes	N/A	Offer pharmacologic treatment for primary osteoporosis, and Treat the secondary cause or consider an e-consult with Endocrinology.
	No	Yes	N/A	Treat the secondary cause and re- check DEXA in 2–3 years, or consider an e-consult with Endocrinology.
	No	No	N/A	Offer pharmacologic treatment for primary osteoporosis.
Patients diagnosed with low bone mass by DEXA (T- score between -1.0 and -2.5)	N/A	No	High 10-year fracture risk <sup>1</sup>	Consider offering pharmacologic treatment.
	N/A	Yes	High 10-year fracture risk <sup>1</sup>	Treat the secondary cause and re- check DEXA in 2–3 years, or consider an e-consult with Endocrinology. Consider offering pharmacologic treatment.
	N/A	Yes	Lower 10-year fracture risk <sup>1</sup>	Treat the secondary cause and re- check DEXA in 2–3 years, or consider an e-consult with Endocrinology.

# Goal

Prevent fracture by decreasing risk factors and improving bone density to a T-score higher than -2.5. (The T-score target may be higher or lower in high-risk patients).

# Lifestyle modifications/non-pharmacologic options

Consuming adequate calcium and vitamin D, taking fall prevention precautions, and performing weightbearing exercise should be continued when initiating pharmacologic treatment for osteoporosis.

# Pharmacologic Options for Osteoporosis

# Shared decision-making: bisphosphonates

#### Key points

- Fractures can have a tremendous negative impact on a patient's quality of life.
- The benefits of bisphosphonates outweigh their potential risks.

Table 4. Adverse effects associated with bisphosphonates			
Adverse effect	Symptoms	Risk	Counseling points
Gastrointestinal	Abdominal pain Dyspepsia Nausea Flatulence Gastritis	12.6%	<ul> <li>Take the medication in the morning at least 30 minutes before food with a full glass (8 oz.) of plain water.</li> <li>Do not lie down for at least 30 minutes after taking the medication.</li> <li>Zoledronic acid (IV bisphosphonate) is an alternative option for those who have difficulty tolerating the oral formulation.</li> </ul>
Musculoskeletal pain	Bone, joint, and/or muscle pain	3.1%	In those who develop severe pain, bisphosphonates should be discontinued.
Osteonecrosis of the jaw	Pain, swelling, or redness of gums Loose teeth Jaw numbness Visible bone in the mouth	0.03–4.3%	• Very <b>rare</b> and, if seen, typically in patients with cancer or compromised immune system who are treated with high doses of IV bisphosphonates.
Atypical femur fracture (AFF)	Dull or aching groin pain from minimal trauma that moves to the thigh over time Subtrochanteric or femoral shaft location Should be diagnosed by specialist following specific criteria	0.002–0.1%	<ul> <li>Very rare. Risk increases somewhat with prolonged use (&gt; 5 years) but is still quite low, and can be mitigated by encouraging a drug holiday after 5 years.</li> </ul>

#### Tools

- Mayo Clinic Osteoporosis Decision Aid: <u>https://shareddecisions.mayoclinic.org/decision-aid-information/decision-aids-for-chronic-disease/other-decision-aids/</u>
- The Health Dialog patient decision aid, titled <u>Should I Take a Bisphosphonate?</u> is available at <u>https://wa.kaiserpermanente.org/kbase/topic.jhtml?docId=te7592</u> (Requires log-in.)
- Osteoporosis Shared Decision-Making Tool by Health Decision. Org <u>https://www.healthdecision.org/tool#/tool/osteoporosis</u>

### Recommended pharmacologic options

Table 5. Recommended pharmacologic options for osteoporosis treatment				
Eligible population	Line	Medication <sup>1</sup>	Initial dose	Therapeutic/goal dose/ duration of treatment
Patients with osteoporosis	1 <sup>st</sup>	Alendronate	70 mg once weekly or 10 mg daily	5 years.
	or	Risedronate [F/ST] <sup>2</sup> for intolerance to alendronate	35 mg once weekly or 5 mg daily	
	Or 1 <sup>st</sup>	Zoledronic acid for GI intolerance to oral bisphosphonates	5 mg IV infused over at least 15 minutes every 12 months	3 years
	2nd	Denosumab [PA— consult with Endocrinology] <sup>3</sup>	60 mg as a single dose, once every 6 months	No studies have evaluated the optimal duration of treatment.
consult with once every 6 months optimal duration of treatment				

bisphosphonate use.<sup>2</sup> F/ST = Formulary/Specialty Tier

<sup>3</sup> Denosumab may be considered only after failed trial of oral and IV bisphosphonates. See PA criteria.

#### **Baseline tests**

Before initiating therapy, order these baseline tests: 25(OH) vitamin D level, serum calcium, and creatinine.

#### Considerations while taking osteoporosis medication

- To ensure absorption, advise the patient to take oral bisphosphonates with water only and not with food or other medications.
- **Calcium supplementation:** Use calcium citrate in patients taking proton pump inhibitors (PPIs) or H2 blockers.
- Vitamin D: Optimize 25 OH vitamin D > 30 and ensure that hypocalcemia is not present.
- **Dental hygiene:** Educate patients starting a bisphosphonate about the importance of regular dental cleanings and good dental hygiene. For those patients who have a planned tooth extraction or dental implant surgery, consider delaying the start of bisphosphonate therapy until 3 months after completion of the dental procedure, or until maxillofacial bone healing is complete. Both considerations are based upon the moderate evidence for association of osteonecrosis of the jaw (ONJ) with bisphosphonate use (0.001% to 0.069% per year increased incidence over non-bisphosphonate users).

#### Interventions to reduce side effects

- If the patient has **GI intolerance with oral bisphosphonates**, try risedronate or switch to IV zoledronic acid. Some patients tolerate one better than the other. If the patient can't tolerate either option, refer to Endocrinology to discuss denosumab (Prolia).
- There is strong evidence for an **acute phase reaction within 3 days of zoledronic acid administration** (up to 25% increased risk over placebo of any of the following symptoms: pyrexia, myalgia, headache, arthralgia, chills). A 650 mg dose of acetaminophen initiated 45 minutes before zoledronic acid infusion and continuing every 6 hours for 3 days has been shown to reduce severity of symptoms. It is common practice also to ensure the patient is well hydrated prior to infusion.

#### Pharmacologic options not recommended for osteoporosis

Tamoxifen, estrogen, nasal calcitonin

# Stopping bisphosphonate therapy/drug holidays

#### Higher-risk patients

Patients with a history of fragility fracture or a T score lower than -3.5 may benefit from up to 10 years of oral bisphosphonate or 6 years of IV bisphosphonate.

#### Lower-risk patients

Patients with mild to moderate osteoporosis and no fragility fracture while on therapy may be considered for a drug holiday after 5 years of therapy. There is insufficient evidence to guide treatment for more than 5 years.

If bone density is measured and:

- The patient has **achieved goal density**, the bisphosphonate may be stopped, and dietary and lifestyle modifications continued.
- The patient has a **T-score lower than -2.5**, explore adherence to treatment. If adherence is not an issue, consider one of the following:
  - Continue bisphosphonates for an additional 2–5 years. (The safety of long-term [more than 10-year] use of osteoporosis medications is not known.)
  - o Recommend a "drug holiday" for 2 years, followed by 3 more years of therapy.
  - o Consider switching to another class of medication.
  - o Consider stopping bisphosphonate treatment and continuing dietary and lifestyle modifications.
- The patient has **decreased bone density from baseline**, consider consultation with an endocrinologist or rheumatologist.

Table 6. Additional considerations for drug holiday in patients at low risk for fragility fracture			
	Factors favoring continuing therapy <sup>1</sup>	Factors favoring drug holiday with monitoring	
Fall risk/fracture	Increased fall risk or history of osteoporotic fracture while on bisphosphonate therapy for 6 months or more	Not at high risk for falls	
High-risk medications	Taking high-risk medications	Not taking high-risk medications	
Thyroid, parathyroid, rheumatoid arthritis	Prolonged suppressed TSH or history of hyperparathyroidism or rheumatoid arthritis that is not reversed by treatment	Normal thyroid and parathyroid function, no history of rheumatoid arthritis	
Change in bone density while consistently taking bisphosphonates	Absolute reduction of 5% or more between two successive BMD measurements at the same site	Absolute reduction of less than 5% between two successive BMD measurements at the same site	
T-score/Z-score	T-score lower than -3.5 at any site or Z-score -2.0 or lower	T-score higher than -2.5	
probable cause of mala	e factors favoring continuing therapy, has t absorption (e.g., PPI therapy, celiac disea to IV zoledronate and repeat DEXA after	se, Crohn's disease, gastric bypass, or	
	a probable cause of malabsorption, has		

or more factors favoring continuing therapy, evaluate for secondary causes of osteoporosis (see p. 5).

#### During continuing therapy

Ensure adherence to bisphosphonate therapy and repeat DEXA after 2 years of therapy. E-consult with Endocrinology if considering prolonged therapy for 5–10 years (oral) or > 5 years (IV).

#### During drug holiday

Measure bone density in 2 years or upon occurrence of new fragility fracture.

# Pharmacologic options for patients on long-term corticosteroid therapy

Because long-term use of corticosteroids—defined as 5 mg/day prednisone for 3 consecutive months is associated with increased risk of osteoporosis, it is reasonable to consider starting prophylactic therapy in patients on chronic steroids. The dose of steroid treatment for which the benefit of treatment with bisphosphonates is thought to outweigh the risk ranges from 5 to 7.5 mg/day.

To decrease the risk of developing osteoporosis, assess patients on corticosteroids to see if it would be appropriate to:

- Reduce the dose
- Switch to a topical or inhaled form
- Switch to an alternative drug

#### Prevention of steroid-induced osteoporosis

Medications for the prevention of steroid-induced osteoporosis are appropriate for men and women who are taking oral corticosteroid medication at a dose of  $\geq$  5 mg/day prednisone or equivalent for a duration of 3 months or more and have a FRAX 10-year risk of hip fracture  $\geq$  3%. Risedronate and zoledronic acid are FDA-approved for both the treatment and prevention of steroid-induced osteoporosis. Alendronate is not FDA-approved for the prevention of steroid-induced osteoporosis.

- First-line: oral risedronate (5 mg/day)
- Second-line: IV zoledronic acid (5 mg IV infused over at least 15 minutes every 12 months)

#### Treatment of steroid-induced osteoporosis

- First-line: alendronate (5 mg/day) should be prescribed for most patients. Postmenopausal women not receiving estrogen should be prescribed 10 mg once daily.
- Second-line: risedronate (5 mg/day)
- Third-line: IV zoledronic acid (5 mg IV infused over at least 15 minutes every 12 months)

#### Monitoring/follow-up for patients with steroid-induced osteoporosis

- A DEXA scan within the first 6 months of starting steroids is recommended, due to the rapid bone loss that occurs during the first 3–6 months.
- If steroid use is continued, a DEXA scan is recommended every 2–3 years after the initiation scan.

# Follow-up/Monitoring

### Patients who have not sustained a fracture

Baseline or most recent DEXA score and/or clinical circumstances	Recommended screening interval
Patients <i>not</i> at high risk due to medications or chronic conditions and with a T-score of:	
Higher than -1.5	Repeat DEXA scan only if the number of risk factors increases or there is a clinical concern regarding osteoporosis. May choose to repeat DEXA scan in 10 years, or sooner if number of risk factors increases or there is a clinical concern.
-1.5 to -1.9	May choose to repeat DEXA scan in 5 years.
-2.0 to -2.4	May choose to repeat DEXA in 2 years.
-2.5 or lower, choosing no treatment	Repeat DEXA scan as clinically indicated but no more frequently than every 2 years.
-2.5 or lower, choosing bisphosphonates	May choose to repeat DEXA scan in 5 years
Patients <b>at high risk</b> due to comorbid conditions, and patients with fractures	Repeat DEXA scan after 2–3 years of treatment.

### Medication monitoring

Table 8. Recommended monitoring for medication side effects			
Eligible population— Test(s) Frequency patients taking:			
Alendronate	Creatinine, serum calcium, vitamin D	No studies have evaluated the optimal intervals for monitoring.	
Risedronate	Creatinine, serum calcium, vitamin D	No studies have evaluated the optimal intervals for monitoring.	
Zoledronic acid	Serum creatinine	Prior to each dose.	
	Serum calcium, vitamin D	At baseline and then as needed; no studies have evaluated the optimal intervals for monitoring.	

# When to consult with Endocrinology

Consider an e-consult with Endocrinology if:

- Patient has had 10 years of bisphosphonate and needs more therapy
- Patient with fragility fracture or osteoporosis has significant renal disease and may not be a candidate for bisphosphonate therapy
- Bisphosphonate therapy fails, as when a fracture occurs during active treatment
- Osteoporosis is unexplained, with no risk factors and negative workup
- Patient is intolerant of bisphosphonate therapy after trial
- Patient needs anabolic therapy (Forteo) because of multiple compression fracture, severe osteoporosis, or treatment failure

# **Evidence Summary/References**

To develop the Osteoporosis Screening, Diagnosis, and Treatment Guideline, the guideline team adapted recommendations from the following externally developed evidence-based guidelines:

- Kaiser Permanente. National Osteoporosis/Fracture Prevention Guideline. 2017.
- U.S. Preventive Services Task Force (USPSTF). Screening for Osteoporosis to Prevent Fractures Recommendation Statement. 2018.

# **Guideline Development Process and Team**

### **Development process**

To develop the Osteoporosis Guideline, the guideline team adapted recommendations from externally developed evidence-based guidelines and/or recommendations of organizations that establish community standards.

This edition of the guideline was approved for publication by the Guideline Oversight Group in April 2019.

### Team

The Osteoporosis Guideline development process included representatives from the following specialties: endocrinology, family medicine, geriatrics, nursing, and pharmacy.

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### Disclosure of conflict of interest

Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care–related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the Osteoporosis Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.