Adult Osteoporosis Screening and Treatment Guidelines

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Date: **10/15/2022**

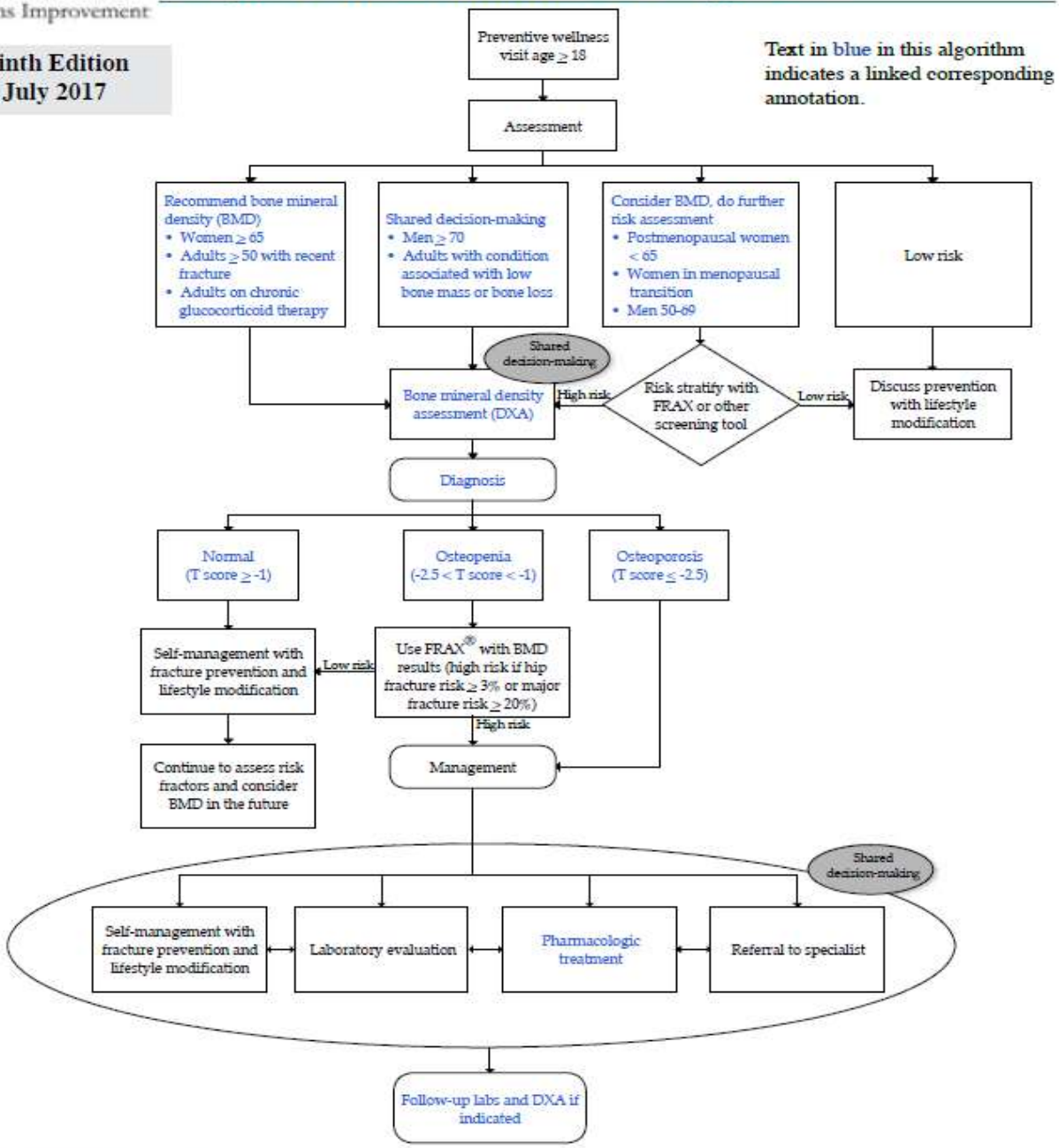
MCH CCBG Approval Date: **3/2/11**

ICSI
Institute for Clinical Systems Improvement

Ninth Edition
July 2017

Health Care Guideline:

Diagnosis and Treatment of Osteoporosis



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Osteoporosis Screening and Treatment Guideline

Figure 1: A summary of clinical recommendations from the ICSI for screening, repeat scanning and treatment options is provided in this guideline.

SECTION 1. Lifestyle Modification Recommendations for Bone Health Maintenance

1. Adequate Calcium Intake

- Recommended in all patients of both genders (Appendix Table 2)
- Dietary intake is preferable but supplementation is often needed to accomplish goals. At least half of daily calcium should come from dietary sources. (UpToDate)
- Calcium supplementation should not exceed 500-600 mg per dose, regardless of the preparation. If customer-owner is taking more than 600 mg of calcium daily, the dose should be divided. (AACE)

Daily Recommendations for Elemental Calcium (BHOF, IOM)	
Females	***Males***
19-50 Years of Age: 1000 mg	**19-70 Years of Age**: 1000 mg
>50 Years of Age: 1200 mg	**>70 Years of Age**: 1200 mg

*Daily intake above 1200-1500 mg can increase risk for developing kidney stones in at-risk individuals

2. Adequate Vitamin D Intake

Daily Recommendations for Vitamin D (BHOF ENDO)
Both Genders
19-49 Years of Age: 400-800 IU
≥50 Years of Age: 800-1000 IU

- *Oral Vit D regimens should be taken with food.*
- *Calcium and Vit D are best given together rather than separately to increase absorption.*

Addressing Vitamin D Deficiency (BHOF)

A desirable 25(OH)D level is approximately **30 ng/mL**.

- The normal serum vitamin D range is 20-50 ng/mL, but levels of approximate 30 ng/mL are an indicator of optimal calcium absorption.
- Adults who are vitamin D deficient are typically treated with 50,000 units once a week for 5-8 weeks until vitamin D serum levels are approximately 30 ng/mL.
- A maintenance period of 1000-2000 units/day should follow.
- Adults with malabsorption issues may require higher replacement doses of vitamin D to reach and sustain efficiency.
- **Alternative**: Some patients may have issues with adhering to a once weekly regiment. In these cases, the provider may consider a daily regimen of 5,000 IU of vitamin D3 until the patient reaches the desired 25(OH)D serum level.

3. Physical Activity

- Recommended lifelong exercise for all ages (ICSI)

- Regular weight-based and muscle-strengthening exercise reduces risk of falls and fractures by improving agility, strength, posture, and balance
- May modestly increase bone density
- Regular weight-bearing exercise, such as walking 30 to 40 minutes per session plus back and posture exercises 3 to 4 days per week, should be advocated. (CDC)
- Low-impact weight-bearing exercises are a safe alternative to high-impact exercises. Examples include: (BHOF)
    - Using elliptical training machines
    - Doing low-impact aerobics
    - Using stair-step machines
    - Fast walking on a treadmill or outside
- Individuals with severe osteoporosis should exercise caution when participating in activities that involve forward spine flexion and rotation, lifting heavy weights, or side bending of the trunk. These maneuvers may lead to fracture. For frail elderly, multicomponent physical activity of at least moderate intensity that is performed 3 or more times a week for a duration of 30 to 45 minutes per session, over at least 3 to 5 months, appears most effective to increase functional ability. (ENDO)
- Strengthening back extension (may include weighted and unweighted prone position), extension exercises, isometric contraction of the paraspinal muscles and careful loading of the upper extremities. (ICSI)

4. Achieve Healthy BMI

- Achieve and maintain normal BMI of 20-25 kg/m (ICSI)
- Low body mass (< 20 kg/m^2) is strong risk factor for osteoporosis and fracture (ICSI)

5. Fall Prevention

- Falls are the leading cause of both fatal and nonfatal injuries among adults 65 and older. They are also responsible for over 90% of hip fractures. (BHOF)
- All patients should be counseled on fall prevention. Especially those who are older or frail, have a stroke history, or are on medications that decrease alertness. (AACE)

Fall Prevention Interventions (ICSF, BHOF, AACE)	
Home safety assessment and modification Consider discontinuing the following medications if possible: o Psychotropic drugs o Drugs that induce dizziness or disorientation Correction of visual impairments Consider hip protectors in those with high risk of falling Targeted exercise (see "Section 3- Physical Activity" above)	Addressing severe Vitamin D deficiency Anchor rugs Minimize clutter Remove loose wires Use nonskid mats Install handrails in bathrooms, halls, and long stairways Light hallways, stairwells, and entrances Encourage patient to wear sturdy, low-heeled shoes

6. Cessation of Tobacco and Avoidance of Excessive Alcohol Intake

- Tobacco use is detrimental to skeleton and overall health; address cessation at every visit. Discussion may include nicotine replacement therapy with available options. (ICSI)
- Smokers do not absorb dietary or supplemental calcium as efficiently as their non-smoking counterparts. They are also at risk of early menopause, increased bone remodeling, and increased bone resorption. (ICSI)
- Excessive alcohol may be detrimental to bone health and increases fall and fracture risk (NOF): limit alcohol use to no more than 1 drink/day for women, no more than 2 drinks/day for men (ICSI)
- Decreased calcium absorption has been associated with alcohol intake levels above these. (BHOF)

7. Treat/Modify Secondary Causes of Osteoporosis

It is vital to treat secondary causes of osteoporosis, whenever possible. These include conditions such as: (ICSC, BHOF)

- Type 1 diabetes
- Osteogenesis imperfecta in adults
- Untreated long-standing hyperthyroidism
- Hypogonadism
- Premature menopause (onset <40 years old)
- Chronic malnutrition or malabsorption
- Chronic liver disease

Table 1: Medications Associated with an Increased Risk of Osteoporosis in Adults

Aluminum	Phenothiazine derivatives
Anticonvulsants	Pioglitazone and rosiglitazone
Aromatase inhibitors	Proton Pump Inhibitors
Barbiturates	Provera depo (chronic)
Caffeine (in excess)	SSRIs
Chemotherapeutic drugs	Tacrolimus
Cyclosporine A	Tamoxifen (premenopausal)
Diuretics causing hypercalciuria	Thyroid hormone (supra-therapeutic)
Glucocorticosteroids > 5mg/day of prednisone or equivalent for ≥3 months	Tenofovir
Gonadotropin-releasing hormone agonists	Tetracycline (extended use)
Heparin (long-term)	Total Parenteral Nutrition
Lithium	Vitamin A (excess)
Methotrexate	Warfarin (long term)

SECTION 2: Recommendations for Baseline BMD Screening

Assess fracture risk with the Fracture Risk Assessment Tool (FRAX) during initial evaluation for low bone mineral density (BMD). The below recommendations are performed using a central dual energy X-ray absorptiometry (DEXA).

1. BMD testing is recommended for: (AACE, BHOF, NAMS)

a. All women 65 years of age or older
b. All postmenopausal women:
    a. With a history of fracture(s) without major trauma
    b. With osteopenia identified radiographically
    c. Starting or taking long-term systemic glucocorticoid therapy (≥3 months)
    d. Discontinuing estrogen with additional risk factors for fracture
c. All men ≥ 70 years of age
d. Men aged 50 to 69 years with clinical risk factors for fracture
e. Other perimenopausal or postmenopausal women with risk factors for osteoporosis if willing to consider pharmacologic interventions
    a. Low body weight (<127 lb or body mass index <20 kg/m2)
    b. Long-term systemic glucocorticoid therapy (≥3 months)
    c. Family history of osteoporotic fracture
    d. Early menopause
    e. Current smoking
    f. Excessive consumption of alcohol
f. Secondary osteoporosis
g. Adults who have a fracture at age 50 years and older
h. Adults with a condition (e.g., rheumatoid arthritis, organ transplant) or taking a medication (e.g., glucocorticoids, aromatase inhibitors, androgen deprivation therapy) associated with low bone mass or bone loss

2. Indications for vertebral imaging: (BHOF, AACE)

Vertebral fractures are the most common osteoporotic fracture and indicates a high risk for future fractures, when the T-score does not meet the threshold for an osteoporosis diagnosis. (AACE) A vertebral fracture assessment should be considered in some cases.

- All women aged ≥ 65 years and all men aged ≥ 80 years if T-score at the lumbar spine, total hip, or femoral neck is ≤ − 1.0.
- Men aged 70 to 79 years if T-score at the lumbar spine, total hip, or femoral neck is ≤ − 1.5
- Postmenopausal women and men age ≥ 50 years with specific risk factors:
    - Fracture during adulthood (age ≥ 50 years)
    - Historical height loss of 1.5 in. or more
    - Prospective height loss of 0.8 in. or more
    - Recent or ongoing long-term glucocorticoid treatment
    - Medical conditions associated with bone loss such as hyperparathyroidism
- T-score is less than -1.0 and one or more of the following is present:

- Women aged ≥70 years or men aged ≥80 years
- Historical height loss of >4 cm (>1.5 inches)
- Self-reported but undocumented prior vertebral fracture
- Glucocorticoid therapy equivalent to ≥5 mg of prednisone or equivalent per day for ≥3 months

SECTION 3: Diagnosis via DEXA Scan Interpretation

Diagnosis is obtained by DEXA measurement of bone density at hip and lumbar spine. The resulting T-scores measure the number of standard deviations from the mean level for a young adult population. In pre-menopausal women and men <50 years, an ethnic or race-adjusted Z-score should be used for diagnosis. Diagnosis and decision to treat is further clarified by calculation of the FRAX score. (ICSI)

FRAX®; www.shef.ac.uk/FRAX

NOTE: The FRAX® tool has not been validated in patients currently or previously treated with pharmacotherapy for osteoporosis. Patients not on medication for two to three years might be considered untreated for FRAX purposes.

DEXA scores:

DEXA Scores and Interpretations	
Normal*	T-score > -1
Osteopenia (low bone mass)**	T-score between -1 and -2.5
Osteoporosis	T-score ≤ -2.5

*Normal and osteopenic DEXA scores in patients with a history of fragility fracture, including asymptomatic vertebral fracture may also qualify as diagnosis of osteoporosis (ACOG)
**A T-score between –1.0 and –2.5 and increased risk of fracture, as determined by a formal clinical risk assessment tool (such as FRAX), is consistent with a diagnosis of postmenopausal osteoporosis (ACOG)

In some patients it is reasonable to make a presumptive diagnosis and start treating despite absence of BMD assessment (ICSI).

SECTION 4: Recommendations for Repeat BMD Scanning

Repeat DEXA scanning should ideally be performed at same testing center as original scan to improve accuracy of data. (AACE) The frequency will depend upon the clinical situation. Generally, repeat DEXA should be done no more than every 12-24 months (ICSI), may consider more often in steroid-treated patients or other high-risk individuals.

- AACE recommends a repeat DXA 1 to 2 years after initiation of therapy until bone density is stable.
- Obtain a baseline axial (lumbar spine and hip; 1/3 radius) dual-energy X-ray absorptiometry (DXA) and repeat DXA every 1 to 2 years until findings are stable. (AACE)The BHOF recommends repeating BMD assessments every 2 years in adults ages 65 and older, with the understanding that testing less or more frequently may be warranted in individual patients.

- In patients at risk of substantial short-term decreases in demineralization, such as those receiving glucocorticoid therapy, 1-year follow up is recommended (ACOG)
- In healthy postmenopausal women without osteoporosis, repeat BMD testing after 3 years does not enhance fracture risk prediction. For postmenopausal women aged 50 to 64 years with baseline T-scores greater than 1.5, retesting could be deferred to age 65, the age at which routine BMD screening is recommended for all women. Earlier retesting should be considered in women within 5 years of menopause whose initial BMD T-score was lower than 1.5 or in those with other important risk factors such as prior fracture or with medical problems or medications predisposing to bone loss. (NAMS)

SECTION 5: Recommendations for Initiation of Therapy

Drug therapy is recommended to prevent bone loss in postmenopausal women with (NAMS)

- Premature menopause, at least until the average age of natural menopause.
- Low BMD (T-score< 1.0) and experiencing relatively rapid bone loss because of acute estrogen deficiency in the menopause transition or on discontinuing estrogen therapy.
- Low BMD (T-score < 1.0) and other risk factors for fracture (eg, family history) but who do not meet the criteria for osteoporosis treatment.

Drug therapy is recommended to treat osteoporosis in these populations: (NAMS)

- Pharmacologic therapy is strongly recommended for patients with osteopenia or low bone mass and a history of fragility fracture of the hip or spine. (AACE)
- Pharmacologic therapy is strongly recommended for patients with a T-score of − 2.5 or lower in the spine, femoral neck, total hip, or 1/3 radius. (AACE)
- All postmenopausal women who have had a vertebral or hip fracture.
- All postmenopausal women who have T-scores from 1.0 to 2.5 and any one of the following:
    - History of fracture of proximal humerus, pelvis, or distal forearm.
    - History of multiple fractures at other sites (excluding face, feet, and hands).
    - Increased fracture risk according to country-specific thresholds using FRAX. In the United States, those thresholds are a 10-year risk of major osteoporotic fracture (spine, hip, shoulder, and wrist) of at least 20% or of hip fracture of at least 3%.

SECTION 6: Duration of Treatments

- No pharmacologic treatment should be considered indefinite; duration decisions need to be individualized. (NOF)

1. Bisphosphonates

- Low to Moderate Risk Patients (ACOG)
    a. Consider a drug holiday for low-to-moderate risk patients who are stable after 5 years of treatment with oral bisphosphonates or after 3 years of treatment with intravenous zoledronic acid.
- High Risk Patients (ACOG)

a. Longer treatment, of up to 10 years for oral bisphosphonates or up to 6 years for intravenous zoledronic acid, is suggested for patients at high risk of fracture.

- Resumption of treatment should be considered in patients with new fractures, additional risk factors for fractures, or significant decreases in BMD. (ACOG) Another recommendation is switching to denosumab or an osteoanabolic agent. (NAMS)

2. Denosumab

- A drug holiday is not recommended for denosumab because of the increased risk of rapid bone loss and vertebral fractures within a few months of treatment cessation. The duration of continued treatment will depend on clinical factors, such as the patient's individual risk of fracture, as well as the antiresorptive agent used. Clinical data are available for up to 10 years of denosumab use. (ACOG)
    a. Administration of denosumab should not be delayed or stopped beyond 7 months without subsequent therapy to prevent bone loss and vertebral fractures. (NAMS)
    b. Do not stop denosumab treatment without a plan for subsequent anti-resorptive therapy, where renal function permits. (NAMS)

3. Teriparatide

- Treatment with teriparatide should be limited to 2 years
- After stopping treatment, bone loss is rapid; Anabolic therapy needs to be followed by treatment with an antiresorptive agent such as a bisphosphonate or denosumab to preserve the BMD gains (ACOG)
- Ensure patient is dedicated to therapy and adherence
- The teriparatide label changed (November 2020) to allow a repeat teriparatide course in appropriate patients. (NAMS) Continued teriparatide use can be considered in:[7]
    a. Very high fracture risk, unable to come off glucocorticoid therapy
    b. High fracture risk, with P1NP(procollagen type 1 N-terminal propeptide) level that remains high after 2 years on teriparatide
    c. High fracture risk, with multiple vertebral compression fractures at baseline but none while on teriparatide
    d. Adynamic renal bone disease
    e. Severe chronic obstructive pulmonary disease and vertebral compression fractures

3. Hormone Therapy

- The use of hormone therapy should be limited to the lowest effective dose for the shortest duration necessary. Relatively rapid bone loss and loss of protection from fracture occurs after discontinuation of hormone therapy. This can be prevented by switching to a bisphosphonate or another antiresorptive agent. (ACOG)

SECTION 7: Recommended Pharmacologic Agents for Osteoporosis

Table 2. Pharmacologic Therapies for Osteoporosis

Medication	Drug Efficacy (BHOF)	Dose Administration	Place in Therapy
Bisphosphonates			
Alendronate (Fosamax)	**Spine**: Reduces fracture incidence by about 50% over 3 years in patients with	70 mg tablet by mouth once weekly	• **First line** in majority of cases for osteoporosis treatment in men and women • Should be considered if no contraindication

	prior vertebral fracture and 48% over 3 years in patients without a prior vertebral fracture. **Hip**: Reduces hip fractures by about 50% in patients with hip T-scores -2.5 or below.	Must be taken at least 30 minutes before first meal of the day with a full glass of plain water only. Individual should remain upright and not eat/drink for 30 minutes after taking medication.	• Increases BMD in patients who require long-term glucocorticoid therapy • Preventive therapy for men undergoing androgen-deprivation tx for prostate cancer

Adverse Events/Contraindications

Common Adverse Events:
- Abdominal pain
- Dyspepsia
- Diarrhea
- Musculoskeletal pain
- Acid regurgitation
- Dysphagia
- Flu-like symptoms (rare post market experience)
- Nausea
- Constipation

Serious Adverse Events:
- Osteonecrosis of the jaw (ONJ) (rare)
- Gastric ulcer
- Esophageal ulcer
- Esophagitis
- Dysphagia
- Atypical fractures

Contraindications:
- Abnormalities of the esophagus that delay esophageal emptying
- Inability to sit/stand for 30 minutes
- Hypersensitivity
- Uncorrected hypocalcemia
- **CrCl ≤ 35 ml/min**

Zoledronic Acid (Reclast)	**Spine**: Reduces vertebral fractures by 62-70% with significant reduction at 1 year. **Hip**: Reduces incidence of hip fractures by 41% **Non-vertebral**: Reduces incidence of fractures by 21-25% over 3 years.	**TREATMENT:** A single 5mg infusion once a year given intravenously (IV) over no less than 15 minutes. **PREVENTION:** 5mg infusion given IV once every 2 years over no less than 15 minutes *Must adequately supplement calcium and vitamin D if dietary intake is not sufficient to avoid hypocalcemia. *Make sure patient is well-hydrated *Pre-treat with acetaminophen to prevent acute phase reaction	• Approved for increasing BMD in men and postmenopausal women • Preventative therapy after a hip fracture as well as once every 2 years for prevention of first fracture • Should be considered in men undergoing androgen deprivation therapy for prostate cancer (ICSI) • Supported for reducing bone loss in patients diagnosed with glucocorticoid-induced bone loss • May prevent bone loss after organ transplantation • Intravenous bisphosphonates **should be offered to patients with contraindications for oral bisphosphonates**, which include esophageal disorders (eg, achalasia, esophageal stricture, esophageal varices, Barrett's esophagus), hypocalcemia, an inability to follow the dosing requirements, and conditions associated with gastrointestinal malabsorption (eg, gastric bypass) (ACOG)

Adverse Events/Contraindications

FDA warning 2011: CI in patients with renal impairment CrCl<35ml/min

	Adverse Effects: • Acute phase reaction: fever, flu-like symptoms, HA, arthralgia/myalgia; (may pre-treat with acetaminophen) • Jaw osteonecrosis (rare); recommend routine oral exam prior to initiation • Transient increase in creatinine • Atrial fibrillation • Hypocalcemia • Nausea/ vomiting/ diarrhea • Eye inflammation • Atypical femur fractures (rare) with long use (>5 years)	**Contraindications**: • Hypersensitivity • Uncorrected hypocalcemia • **CrCl < 35 ml/min** • Evidence of acute renal impairment

RANK Ligand (RANKL) Inhibitor/Human Monoclonal Antibody			
Denosumab (Prolia)	**Spine**: Reduces incidence of vertebral fractures by about 68% at year 1. **Hip**: Reduces hip fractures by about 40% **Non-vertebral**: Reduces fractures by about 20% at 3 years. Longer term use results in a 48% reduction in the risk of all upper limb fractures. *Does not reduce the risk of non-vertebral fractures. (BHOF)*	60 mg subcutaneously (SQ) once every 6 months, administered by a health professional Taken with calcium 1000 mg daily and at least 400 IU vitamin D daily *When stopped, bone loss is rapid; use another agent to maintain BMD	• **Initial therapy for postmenopausal patients at increased risk of fracture who prefer every 6-month subcutaneous administration.** • Option for those at high risk of fracture • Option for those with contraindications to bisphosphonates (renal function) • Approved for men treated with androgen-deprivation therapy and women receiving adjunctive aromatase inhibitor therapy for breast cancer, and at high risk for fracture • **Must correct hypocalcemia and VitD deficiency prior to initiation** • If discontinuing, it is advised to switch to an alternative therapy (typically a bisphosphonate) to prevent rapid bone loss.
	Adverse Events/Contraindications		
	Common: • Hypertriglyceridemia • Vomiting • Anemia • Pain (back, extremity, and musculoskeletal) • Rash • Cystitis • Nasopharyngitis • Upper respiratory infection (URI) • Fatigue • Infections	**Serious**: • Endocarditis • Cellulitis • Dermatitis • Hypocalcemia • Anaphylaxis • Aseptic necrosis of the jaw (rare) • Atypical femoral fracture • Cancer	**Contraindications**: • Hypersensitivity • Hypocalcemia (must correct prior to initiation) • Pregnancy

Anabolic Agents: Parathyroid Hormone (PTH)			
Teriparatide (Forteo)	**Spine**: Reduces risk of vertebral fractures by 65-77% **Non-vertebral**: Reduces risk of fractures by 35-53% in osteoporotic patients	20mcg subcutaneously daily for not more than 2 years *Not to be used for more than 2 years. Duration may be increased if patient is high risk. *When stopped, bone loss is rapid; use another agent such as bisphosphonate or denosumab to maintain BMD	• For the treatment of **postmenopausal osteoporosis for up to 2 years in patients who are at very high risk of fracture or who continue to sustain fractures or have significant bone loss while taking antiresorptive therapy**. (ACOG) • Approved by the FDA for initial treatment of women with postmenopausal osteoporosis who are at high risk of fracture or have failed or been intolerant of previous osteoporosis therapy. • Consider treating patients concurrently with bisphosphonates while on teriparatide therapy.

			• Teriparatide is also approved for treatment of glucocorticoid-induced osteoporosis and treatment of osteoporosis in men. • Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture

Adverse Events/Contraindications

BLACK BOX WARNING:
Show to cause an increase in the incidence of osteosarcoma in male and female rats, dependent on dose and duration of treatment.

Adverse Events:
- Orthostatic hypotension
- Nausea
- Increase in serum calcium
- May increase risk of digoxin toxicity
- Increase in urinary calcium
- Arthralgia
- Pain
- Leg cramps

Contraindications:
- Hypersensitivity
- Avoid in patients with increased risk of osteosarcoma (including Paget's disease, prior radiation, unexplained elevation of alkaline phosphatase, or in patients with open epiphyses)
- Do not use in patients with a history of skeletal metastases, hyperparathyroidism or pre-existing hypercalcemia
- Not for use in patients with metabolic bone disease other than osteoporosis.
- Should not be administered to pregnant or breastfeeding women

Medications for SELECT Patient Populations

Selective Estrogen Receptor Modulator (SERM) Raloxifene	**Spine**: Reduces incidence of vertebral fractures by about 30-40% in those with a prior vertebral fracture and about 55% in those without a prior fracture. *Does not reduce the risk of non-vertebral fractures.*	60 mg PO daily	• Approved for prevention and treatment of postmenopausal osteoporosis • **Option for women with an elevated risk of breast cancer who are at low risk of venous thromboembolism and do not have significant vasomotor symptoms.**

Adverse Events/Contraindications

BLACK BOX WARNING: Risk of deep vein thrombosis and pulmonary embolism

Common:
- Hot sweats
- Leg cramps

Serious:
- VTE
- Cerebrovascular accident
- Thromboembolism

Contraindications:
- History of venous thromboembolism
- Pregnant or nursing women

Female Menopausal Hormone Therapy: Estrogen +/- Progestin	**Spine**: Reduced incidence of clinical vertebral fractures by 34% over 5 years **Hip**: Reduced fractures of hip by 28-34% over 5 years. **Non-vertebral**: Reduced incidence of fractures by 23%	Strengths and dosages vary	• NOT recommended first line in management or prevention of osteoporosis • **Option for women at increased risk who:** ○ Are younger than 60 years or within 10 years of menopause ○ Are at low risk of venous thromboembolism, breast cancer, and cardiovascular disease ○ Have bothersome menopausal symptoms

			○ For whom other therapies such as bisphosphonates or denosumab are not appropriate ● **For women at significant risk who cannot take non-estrogen therapies**

Adverse Effects/Contraindications

BLACK BOX WARNING: Endometrial cancer, Cardiovascular disease, Breast Cancer, Dementia

Adverse Reactions: (reactions depend on dose formulation)

- Cerebrovascular accident, edema, hypertension, MI, PE
- Dementia exacerbation, depression, dizziness, headache, irritability
- Pruritus, urticaria
- Change in libido, hirsutism, weight changes, hypocalcemia
- Abdominal cramps, nausea, vomiting

Contraindications:

- Undiagnosed abnormal genital bleeding
- DVT or PE (current or history)
- Active or recent arterial thromboembolic disease (stroke, MI)
- Carcinoma of breast
- Estrogen-dependent tumor
- Hepatic dysfunction or disease
- Pregnancy

Male Hormone Therapy: Testosterone	N/A	Dose and administration vary by agent	• NOT FDA approved for osteoporosis, but may be and **option for men symptomatic with hypogonadism** • Bone loss associated with male hypogonadism is reversed by testosterone therapy (partly via aromatization to estrogen) ● ONLY administered for hypogonadism caused by disorders of the testicles, pituitary gland or brain in adult males; <u>not for treatment of low testosterone due to aging</u> (ICSI)

Adverse Events/Contraindications

BLACK BOX WARNING: Blood pressure increases (oral testosterone undecanoate; subcutaneous testosterone enanthate

Adverse Reactions: (reactions depend on dose formulation)

- Skin reactions, pruritus
- BPH, PSA increase
- Increased hematocrit
- Peripheral edema, vascular disease
- Emotional lability, depression, anxiety, fatigue,
- Acne vulgaris
- Hyperlipidemia, decrease HDL, increased triglycerides,
- Increase TSH, increased estradiol
- Decreased libido, gynecomastia, hot flash, weight gain
- Sleep apnea

Contraindications:

- Breast cancer
- Prostate cancer (known or suspected)
- Pregnancy
- Serious cardiac, hepatic, or renal disease

No Longer Recommended			
Calcitonin	**Spine**: Reduces vertebral fracture occurrence by about 30% in those with prior vertebral fractures. *Does not reduce the risk of non-vertebral fractures*.	200 units (1 spray) in one nostril daily; alternate nostrils daily	• **No longer recommended** • FDA concludes that benefits **<u>DO NOT</u>** outweigh the risks • Use should be limited to those with no possible alternatives ● Short-term use may provide analgesic effect for acute pain from a compression fracture

Adverse Events/Contraindications

Common:

- Rhinitis
- Flushing, rash

Common:

- Hypersensitivity reactions: Salmon-derived products
- Hypocalcemia (correct prior to therapy)

- Depression, dizziness, paresthesia
- Nausea, abdominal pain
- Infection
- Back pain, myalgia, osteoarthritis
- Conjunctivitis
- Bronchospasm, flu-like symptoms, sinusitis, URI

Concerns of cancer risk

- Neoplasm
- Lymphadenopathy

TABLE 8. *Drugs approved in North America for treating women with postmenopausal osteoporosis*

Drug	Trade names	Drug class	Dose, route of administration, and dosing interval	Fracture risk reduction (in primary analyses of registration trials)		
				Vertebral fracture	Nonvertebral fracture	Hip fracture
Raloxifene[151]	Evista; generics	EAA	60 mg/d PO	✓		
Alendronate[170-172,184]	Fosamax; Binosto; generics	Bisphosphonate	70 mg q wk PO	✓		✓
Risedronate[173-175,185-187]	Actonel; Atelvia; generics	Bisphosphonate	35 mg q wk PO; 150 mg q mo PO	✓	✓	✓
Ibandronate[176,188,189]	Boniva; generics	Bisphosphonate	150 mg PO q mo; 3 mg IV q 3 mo	✓		
Zoledronate[177]	Reclast; Aclasta; generics	Bisphosphonate	5 mg IV q y	✓	✓	✓
Denosumab[178,179]	Prolia	RANK ligand inhibitor	60 mg SQ q 6 mo	✓	✓	✓
Teriparatide[178,179]	Forteo; Teribone	PTH-receptor agonist	20 μg SQ daily	✓	✓	
Abaloparatide[179,180]	Tymlos	PTH-receptor agonist	80 μg SQ daily	✓	✓	
Romosozumab[181,182]	Evenity	Sclerostin inhibitor	210 mg SQ q mo	✓	✓	✓
Calcitonin-salmon[183]	Calcimar; Fortical; generics	Calcitonin	200 USP units by nasal spray daily	✓		

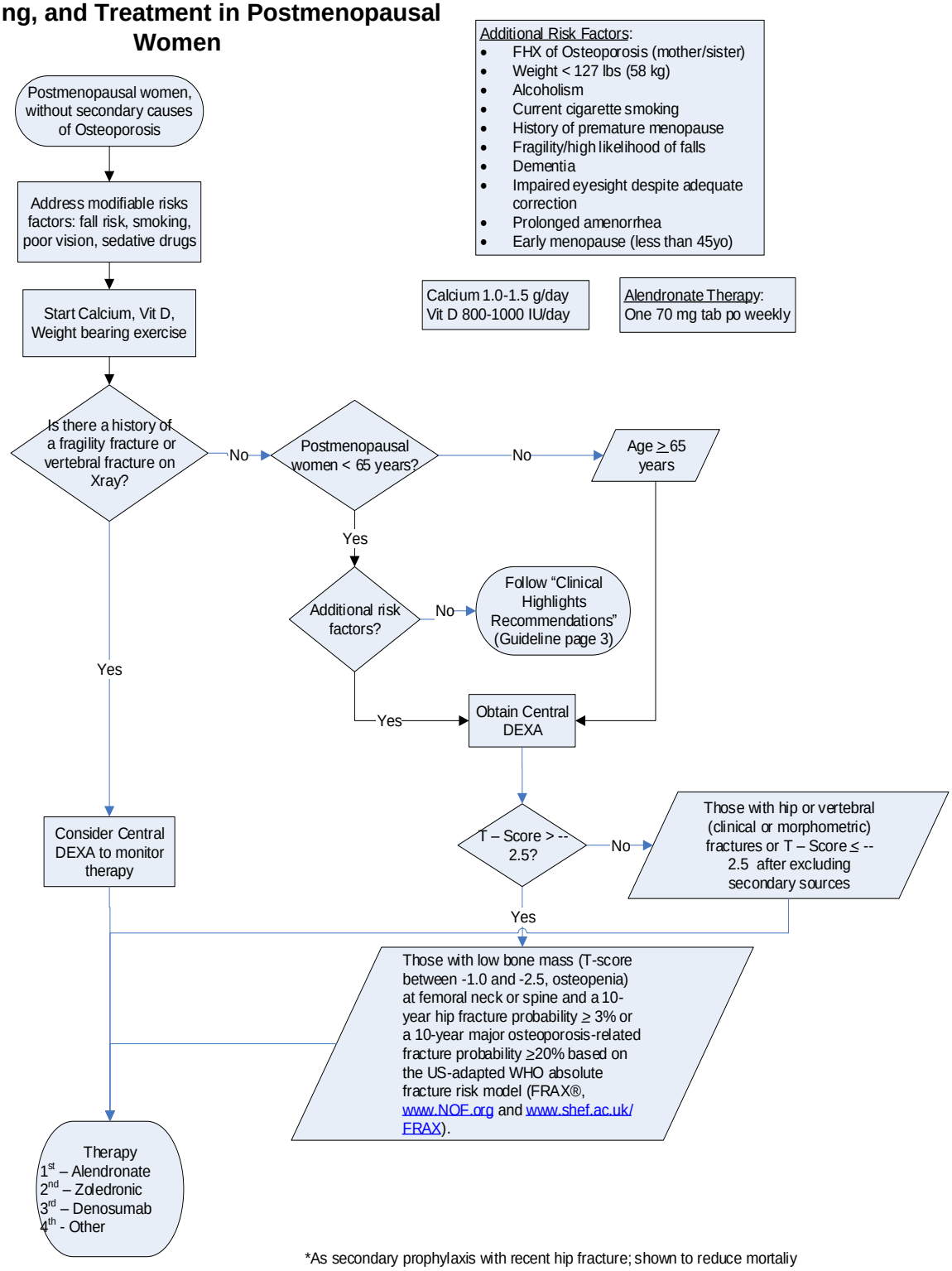
Available only in the United States.

EAA, estrogen agonist/antagonist; IV, intravenous; PTH, parathyroid hormone; SQ, subcutaneous.

Ettinger B, et al[151]; Liberman UA, et al[170]; Black DM, et al[171];Cummings SR, et al[172]; Harris ST, et al[173]; Reginster J, et al[174]; McClung MR, et al[175]; Chesnut CH 3rd, et al[176]; Black DM, et al[177]; Cummings SR, et al[178]; Neer RM, et al[179]; Miller PD, et al[180]; Cosman F, et al[181]; Saag KG, et al[182]; Chesnut CH 3rd, et al[183]; Schnitzer T, et al[184]; Brown JP, et al[185]; Delmas PD, et al[186]; McClung MR, et al[187]; Miller PD, et al[188]; Delmas PD, et al.[189]

Figure 2: A table taken from the NAMS guidelines that list drugs approved in North American for postmenopausal osteoporosis, dosing, and fracture risk reduction associated with each.

Figure 3: Algorithm for Prevention, Screening, and Treatment in Postmenopausal Women



*As secondary prophylaxis with recent hip fracture; shown to reduce mortaliy

This guideline is designed for general use for most patients but may need to be adapted to meet the special needs of a specific customer-owner as determined by the customer-owner's provider

SECTION 8: Common Sources of Calcium and Vitamin D

***ALL patients should be encouraged to get adequate amounts of elemental calcium and vitamin D first and foremost from their diet, and supplement only what is needed.**

	Dietary Sources *of* Elemental *Calcium*	Dietary Sources of *Vitamin D*
Milk (Vitamin D fortified)	300 mg Ca per 8 oz serving	400 IU per quart
Yogurt (Vitamin D fortified)	400 mg Ca per 8 oz serving	~65 IU
Cheese	200 mg Ca per 1 oz serving	
Fortified foods or juices	80-1000 mg Ca per serving, as per label	(Vitamin D fortified cereal) ≥40-50 IU per serving
Alaska Native chum, raw	7mg Ca/100grams (3.5ounces)	*Food sources of vitamin D are affected by the time of year they are harvested (ICSI)
Alaska Native red, smoked, canned	69mg Ca/100grams (3.5ounces)	

Common Supplements available at ANMC	
Calcium carbonate 1250 mg (Oscal)	500 mg elemental calcium per tab
Combination Calcium and vitamin D (Oyster Shell Calcium with Vitamin D)	500 mg elemental calcium plus 200 International Units vitamin D per tab
Vitamin D3 (cholecalciferal)	1,000 IU tablet
Vitamin D3 (cholecalciferal)	5,000 IU capsule
Vitamin D2 (ergocalciferal)	50,000 IU capsule

**Example: One tablet of Oyster shell Calcium with Vitamin D BID would provide 1000 mg calcium plus 400 IU vitamin D, appropriate for those who consume very little dairy or other calcium-rich food. One tablet daily would be appropriate for a person consuming two calcium-rich foods/day.

Table 3: Osteoporosis Screening Recommendations of Other Organizations

	Recommendations	
Organization	**Women**	**Men**
Bone Health and Osteoporosis Foundation **(BHOF 2022)**	BMD testing for all women ≥65 y and postmenopausal women 50-65 y with risk factors for osteoporosis	BMD testing for all men ≥70 y and men aged 50-69 y with risk factors for osteoporosis
	Consider BMD testing in the following individuals • Women ≥ 65 years of age and men ≥ 70 years of age, regardless of clinical risk factors • Younger postmenopausal women, women in the menopausal transition, and men aged 50 to 69 years with clinical risk factors for fracture • Adults who have a fracture at age 50 years and older • Adults with a condition (e.g., rheumatoid arthritis, organ transplant) or taking a medication (e.g., glucocorticoids, aromatase inhibitors, androgen deprivation therapy) associated with low bone mass or bone loss	
World Health Organization **(WHO)**	Indirect evidence supports screening women ≥65 y, but no direct evidence supports widespread screening programs using BMD testing	
American College of Physicians on Screening for Men **(ACP 2008)**		Clinicians should assess older men for osteoporosis risk factors and use DEXA to screen men at increased risk who are candidates for drug therapy for osteoporosis
American Congress of Obstetricians and Gynecologists **(ACOG 2021)**	Screening is recommended for osteoporosis in postmenopausal patients 65 years and older with BMD testing to prevent osteoporotic fractures. Screening is also recommended for osteoporosis with BMD testing to prevent osteoporotic fractures in postmenopausal patients younger than 65 years who are at increased risk of osteoporosis, as determined by a formal clinical risk assessment tool.	

U.S. Preventive Services Task Force **(USPSTF 2018)**	All women aged ≥ 65 years and younger women whose 10-year fracture risk is equal to or greater than that of a 65-year-old Caucasian woman with no additional risk factors (using FRAX algorithm)	No recommendation. Current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis in men.
American Association of Clinical Endocrinologists **(AACE 2020)**	Evaluate women aged 65 years and older and younger postmenopausal women at increased risk for bone loss and fracture, based on analysis of fracture risk.	

North American Menopause Society
 	
(NAMS 2021)
	Bone density should be measured in postmenopausal women with risk factors for low bone density where knowing the result will influence clinical management:
	
	- Those with a history of fracture since menopause
	- Those with known medical causes of bone loss or fracture
	- Those aged 65 years and older
	- Those aged 50 years and older with one or more of these additional risk factors:
	  o Body weight less than 127 lb (57.7 kg) or BMI less than 21 kg/m2
	  o History of hip fracture in a parent
	  o Current smoker
	  o Discontinuing estrogen with additional risk factors for fracture	

Endocrine Society (on osteoporosis in men) **(2012)**		Recommend testing men aged ≥70 and men aged 50-69 who have risk factors (e.g. low body weight, prior fracture as an adult, smoking, etc.)

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Revised 10/15/22njm

Revised 1/4/20njm

Revised 7/17/17njm

Revised 5/21/13njm

Revised 3/2/11njm

Approved 10/6/05njm