Osteoporosis Screening and Treatment Guidelines

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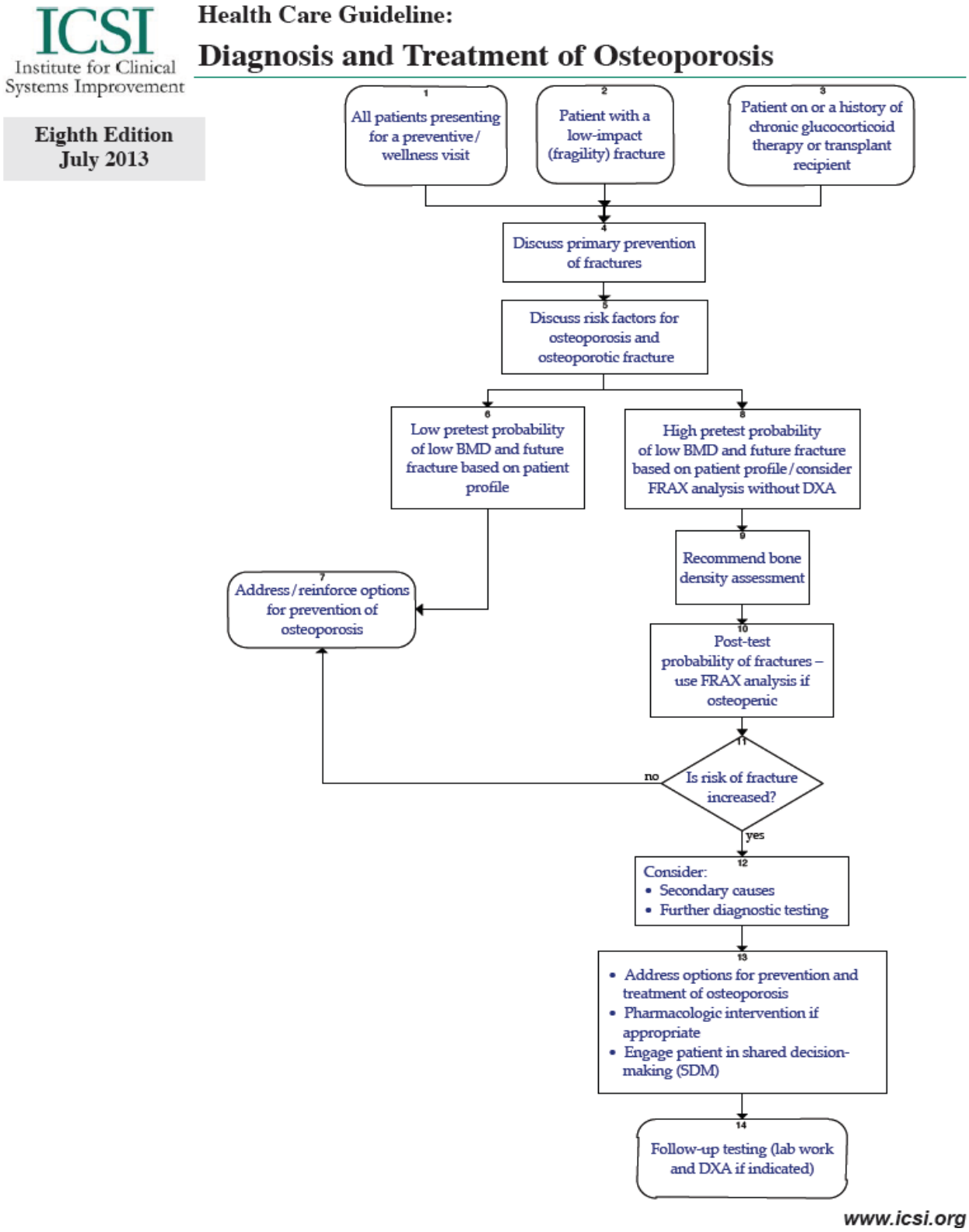
ICSI 2013 Algorithm for the Diagnosis and Treatment of Osteoporosis
***For Screening and Treatment Guideline Algorithm for Postmenopausal Women, see **Appendix Figure 1**



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to meet the special needs of a specific customer-owner as determined by the customer-owner's provider

Osteoporosis Screening and Treatment Guideline

A summary of clinical recommendations for screening, repeat scanning and treatment options is provided in this guideline.

Recommendations for Bone Health Maintenance

1. Advise all patients of both genders to consume adequate amounts of calcium and vitamin D (Appendix Table 2). Dietary intake is preferable but supplements are often needed to accomplish goals:
    a. Daily recommendations of calcium:
        i. Women ≥51 and Men >70: 1200 mg/day
        ii. Women 19-50 years, Men 50-70 years: 1000 mg/day
    b. Daily recommendations for vitamin D
        i. Adults <50: 400-800 IU daily
        ii. Adults ≥50: 800-1000 IU daily (NOF)
        iii. Obtained from a combination of dairy products, other calcium-rich foods, sunlight, vitamin D-fortified milk, cereals, egg yolks, fatty fish, and liver.
2. Treat vitamin D deficiency
    a. High prevalence of vitamin D deficiency in limited sun exposure, dark skin, and obese individuals
    b. Maintain serum 25-hydroxyvitamin D (25[OH]D)level to ≥30 ng/ml
        i. Treat with 50,000 IU once weekly for 8-12 weeks
        ii. Follow with maintenance dose of 1500-2000 IU daily
            1. Many will need more than general recommendations of vitamin D
            2. Safe upper limit of vitamin D intake is 4000 IU per day
3. Engage in regular weight-based and muscle-strengthening exercise
    a. Reduces risk of falls and fractures by improving agility, strength, posture, and balance
    b. May modestly increase bone density
    c. Recommended lifelong for all ages (ICSI)
    d. Achieve and maintain normal BMI of 20-25 (ICSI)
4. Fall Prevention
    a. Home safety assessment and modification
    b. Gradual withdrawal of psychotropic medication, if possible
    c. Correction of visual impairments
    d. Consider hip protectors in those with high risk of falling
5. Cessation of tobacco use and avoidance of excessive alcohol intake
    a. Tobacco use is detrimental to skeleton and overall health; address cessation at every visit (ICSI)
    b. Excess alcohol (>2 drinks/day for women, >3 drinks/day for men) may be detrimental to bone health; increases fall risk (NOF)
    c. Limit alcohol use to no more than 1 drink/day for women, no more than 2 drinks/day for men (ICSI)
6. Recommend baseline central DEXA scanning (AP spine and hip) to patients who meet the ANMC indications for baseline DEXA scan, detailed below.
7. All patients diagnosed with osteoporosis should be evaluated for secondary causes, such as other disease processes or medications which cause osteoporosis (see Table 2). Secondary causes should be modified/treated whenever possible.

Recommendations for Baseline Bone Mineral Density Screening (Central DEXA) - See Appendix Table 5

Assess fracture risk with the Fracture Risk Assessment Tool (**FRAX**) during initial evaluation for osteoporosis. Bone mineral density testing (BMD) by central dual-energy X-ray absorptiometry (DEXA) should be recommended for:

1. All postmenopausal women aged ≥65 years
2. Men aged ≥70 years (ICSI, NOF)
3. Women under 65 years whose fracture risk is ≥9.3% from FRAX analysis or are considered to be at fracture risk (NOF, USPSTF) (also list by ICSI of risk factors)

4. Post-menopausal women of any age with additional risk factors for osteoporosis or fracture. Pertinent additional risk factors include:
    a. Family history of osteoporosis with fractures (mother or sister)
    b. Weight <127 pounds or 58 kg or BMI <20 (ICSI)
    c. Alcoholism
    d. Current tobacco smoking
    e. History of premature menopause (prior to age 45)
    f. Frailty/high likelihood of falls
    g. Excessive caffeine intake
    h. Gonadal hormone deficiency
    i. Immobilization and inadequate activity
    j. Low calcium or vitamin D intake
    k. White or Asian race
5. Men aged 50-69 based on risk factor profile (NOF; but evidence is insufficient to access benefit/harm (USPSTF, See Table 5)
6. Adults (both women and men) who have a fracture (NOF) without major trauma (low-impact/fragility fracture)
7. Adults with significant acquired kyphosis and/or historical height loss >4 cm or measured height loss greater than 2 cm should have lateral vertebral assessment with DEXA or thoracic and lumbar spine radiographs and bone density testing (ICSI)
8. Consider in patients with fractures who are willing to accept treatment
9. Patients undergoing organ transplantation – recommend baseline BMD test at entrance to transplantation program, follow-up yearly prior to transplant (or every 6-12 months if on high-dose steroids), then yearly after transplant (ICSI)
10. May be recommended with exogenous (oral) glucocorticoid (source: ICSI – no studies on fracture rates with inhaled or nasal steroids) therapy (past, present, or ongoing) equivalent to prednisone 5 mg/day or more for 3 months. DEXA may be done at initiation of treatment if greater than 3-month course is anticipated.
11. May be recommended if peripheral screening is abnormal or inconclusive.
12. May be recommended medical conditions and medications associated with an increased risk of osteoporosis in adults. (Appendix Tables 3 and 4)

Recommendations for Repeat Bone Mineral Density Scanning (Central DEXA)

Repeat DEXA scanning frequency will depend upon the clinical situation. Generally repeat DEXA should be done no more than every 12-24 months (ICSI), may consider every 6-12 months in steroid-treated patients or those on suppressive doses of thyroid hormones. Some common examples:

1. Baseline T scores > -1.0, no new risk factors: repeat in 5 - 10 years.
2. Baseline T scores < -1.0, not on therapy, with ongoing risk factors: repeat in 2-4 years.
3. Baseline T scores < -1.5, monitoring therapy: repeat in 5 years. (ACP)
4. Aggressive disease progression suspected, based on clinical situation: may repeat in 6-12 months, but this should be fairly uncommon.
5. Note: The Z-score, and not the T-score, should be used in premenopausal women, men <50 years, and in children (ICSI)

Recommendations for Initiation of Therapy (Appendix Table 4)

Postmenopausal women and men age 50 and older presenting with the following should be considered for treatment:

1. A hip or vertebral (clinical or morphometric) fracture (fragility fracture)
2. T-score $\leq$ -2.5 at the femoral neck, lumbar spine (anteroposterior), or hip after appropriate evaluation to exclude secondary causes
3. Low bone mass:

a. T-score between -1.0 and -2.5 at the femoral neck or spine and a 10-year probability of a hip fracture ≥ 3%
b. OR a 10-year probability of a major osteoporosis-related fracture ≥20% based on the US-adapted WHO absolute fracture risk model (FRAX)
    i. FRAX®; www.NOF.org and www.shef.ac.uk/FRAX

4. Consider all men and postmenopausal women with low-impact (fragility fractures as potential candidates for pharmacologic intervention, and women and men over 70 with prior fragility fracture as candidates for osteoporosis therapy even without bone density testing
5. Steroid use
    a. Have been shown to cause bone loss with extended use
    b. No studies have been done on increased rates of fracture after inhaled or nasal glucocorticoids (ICSI)
6. ALL patients should also receive adequate calcium and vitamin D, participate in weight bearing exercise, and avoid additional risk factors.
7. ALL modifiable lifestyle changes should be in place
8. Evaluate any secondary causes of osteoporosis (Tables 3 and 4)

Table 1: Recommended Pharmacological Agents for Osteoporosis (latest 5/2017)

Medication	Indications	Dose Administration	Reduction in fracture risk	Adverse drug reactions	Contraindications
Bisphosphonates					
Alendronate (Fosamax) *1st line agent majority of cases	PREVENTION • Postmenopausal osteoporosis • Glucocorticoid-induced osteoporosis • Men undergoing androgen-deprivation tx for prostate cancer (ICSI) • TREATMENT • Postmenopausal osteoporosis • Osteoporosis in men • Glucocorticoid-induced osteoporosis in men and women	PREVENTION 35 mg tab po weekly TREATMENT Postmenopausal: 70 mg tab po weekly *Glucocorticoid induced: 35 mg po weekly; 70mg po weekly in postmenopausal women not receiving estrogen	Vert: +++ Nonvert: ++ Hip: +++	• Esophagitis • abdominal pain • Diarrhea • Jaw osteonecrosis (rare) • Musculoskeletal pain • Dyspepsia • Acid regurgitation • Esophageal ulcer • Dysphagia • Flu-like symptoms (rare postmarket experience) • Nausea • Constipation	• Abnormalities of the esophagus that delay esophageal emptying • Inability to sit/stand for 30 minutes • Hypersensitivity • Uncorrected hypocalcemia • CI: patients with CrCl ≤ 35 ml/min
Zoledronic Acid (Reclast)	PREVENTION • Osteoporosis in postmenopausal women • Glucocorticoid-induced osteoporosis TREATMENT • Osteoporosis in men and postmenopausal women • Glucocorticoid-induced osteoporosis • Osteoporosis, secondary prophylaxis in patients with recent low-trauma hip fracture (Shown to decrease mortality in high risk patients suffering from hip fx (only bisphosphonate to do this) • Men undergoing androgen-deprivation tx for prostate cancer	**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 - average of at least 1,200 mg of calcium and 800 to 1,000 units of vitamin D daily is recommended *Make sure well-hydrated *Pre-treat with APAP to prevent acute phase	Vert: +++ Non-vert: ++ Hip: ++	**FDA warning 2011: CI in patients with renal impairment CrCl<35ml/min** • Acute phase reaction: fever, flu-like symptoms, HA, arthralgia/myalgia; (may pre-treat with APAP) • 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	• Hypersensitivity • Uncorrected hypocalcemia • CI in CrCl < 35 ml/min

	(ICSI)	reaction (NOF)		years)	
Human Monoclonal Antibody					
Denosumab (Prolia) *Option for those at high risk of fracture *Often an option for those who can no longer use bis-phosphonates (renal function)	TREATMENT • Postmenopausal women with osteoporosis at high risk for fracture • Increase bone mass in men with osteoporosis • Treatment of bone loss in men receiving androgen deprivation treatment for prostate cancer (vertebral fracture reduction) • Treatment of bone loss in women receiving adjuvant aromatase inhibitor therapy for breast cancer	60 mg SQ once every 6 months, Taken with calcium 1000 mg daily and at least 400 IU vitamin D daily	Vert: +++, Non-vert: + Hip: ++	• Pain (back, extremity, and muscoskeletal) • Hypertriglyceridemia • Infections (skin, subdominal, urinary, ear) • Rash • Hypocalcemia • Aseptic necrosis of jaw (rare) • Atypical femoral fracture	• Hypersensitivity • Hypocalcemia (must correct prior to initiation) • Pregnancy
Parathyroid Hormone (PTH)					
Teriparatide (Forteo) *Typically reserved for (women) with severe osteoporosis or who have had fractures (NOF) *Generally not first line because no data on reduction of all fracture types (ACP)	TREATMENT • Postmenopausal osteoporosis with high risk of fracture • Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture • Osteoporosis associated with glucocorticoid therapy at high risk for fractures (women and men) • Osteoporosis primary or hypogonadal	20mcg SubQ daily for not more than 2 years *When stopped, bone loss is rapid; use another agent to maintain BMD	Vert: +++ Non-vert: +++ Hip: N/A	**BLACK BOXED WARNING:** **Show to cause an increase in the incidence of osteosarcoma in male and female rats, dependent on dose and duration of treatment.** • Orthostatic hypotension • Nausea • Increase in serum calcium • May increase risk of digoxin toxicity • Increase in urinary calcium • Arthralgia • Pain • Leg cramps	• 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
Testosterone	*Not FDA approved for osteoporosis, "seems a reasonable first line therapeutic intervention in men symptomatic with hypogonadism who do not have contraindications to the use of testosterone therapy"… the bone loss associated with male hypogonadism is reversed by testosterone therapy at least partly via aromatization to estrogen (ICSI)				

Vert = vertebral; nonvert = nonvertebral; +++ > 50% reduction; ++ 40-50% reduction; + < 40% reduction; - unable to show reduced risk; N/A No data available from RCT

Duration of Treatments

1. No pharmacologic treatment should be considered indefinite; duration decisions need to be individualized. (NOF)
2. Assuming renal function remains adequate, recommended bisphosphonate therapy duration is
    a. 5 years in moderate-risk patients
    b. 6-10 years in higher-risk patients
    c. 3 annual doses of IV zoledronic acid in moderate-risk patients
    d. 6 annual doses in higher-risk patients on IV zoledronic acid
        i. after 5 years of stability in moderate-risk patients taking oral bisphosphonates
        ii. after 6-10 years of stability in higher-risk patients taking oral bisphosphonates
    e. Benefits of bisphosphonates may continue after discontinuation (NOOG, NOF)
    f. May use teriparatide or denosumab during the "bisphosphonate holiday" period for higher-risk patients
3. Treatment with teriparatide should be limited to 2 years
    a. After stopping treatment, bone loss is rapid; treatment should be switched to another agent (NOF)

Appendix

Figure 1: Algorithm for Prevention, Screening, and Treatment in Postmenopausal Women

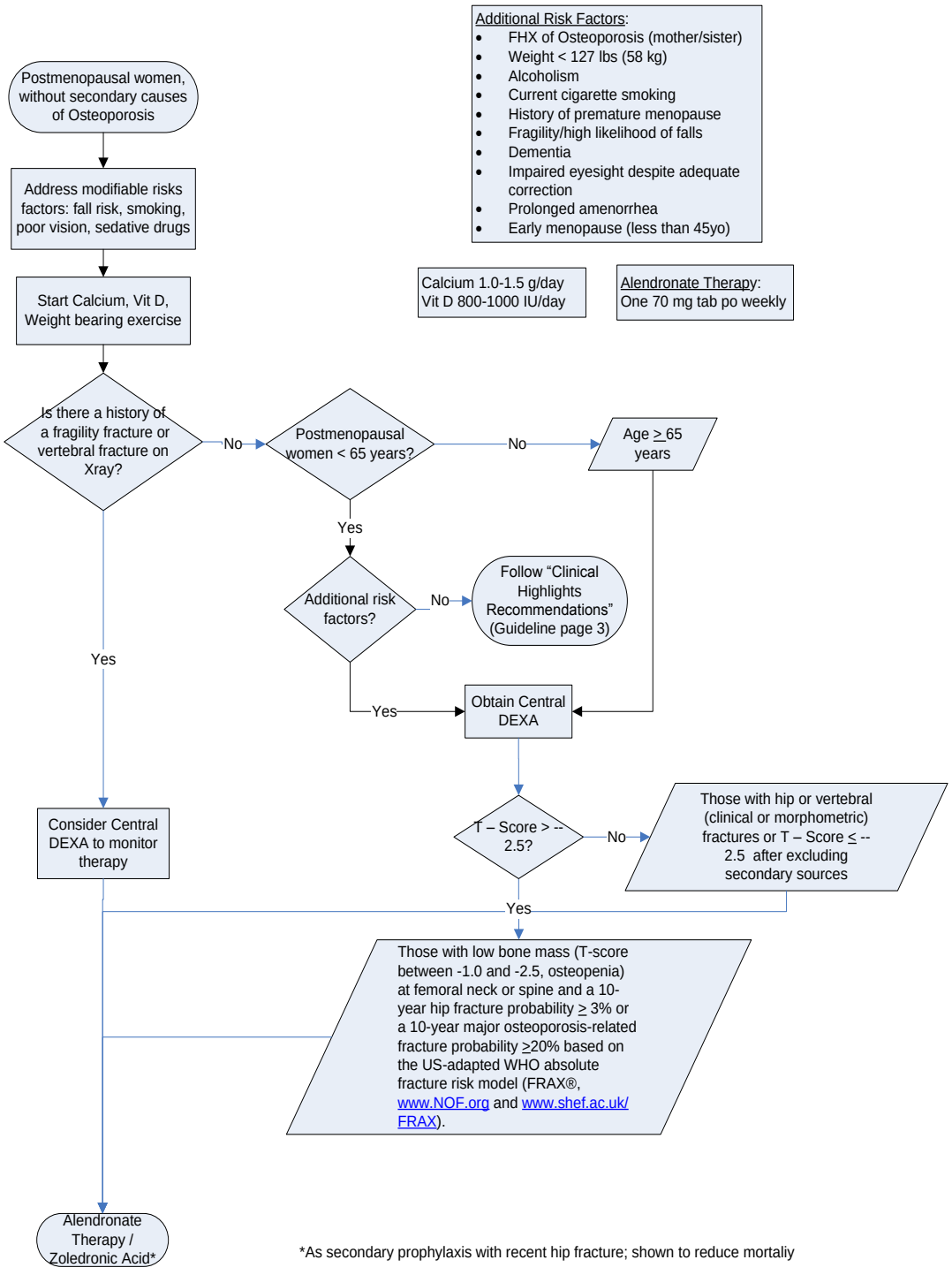

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Table 2: Common Sources of Calcium and Vitamin D

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

	Dietary Sources *of 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 carbonate1250 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	
Vitamin D2 (ergocalciferal)	50,000 IU	

**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: Medications Associated with an Increased Risk of Osteoporosis in Adults

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

Table 4: Medical Conditions Associated with an Increased Risk of Osteoporosis in Adults

• Acromegaly • Acquired Immunodeficiency Syndrome • Addison's Disease • Adrenal insufficiency • Alcoholism • Amyloidosis • Androgen insufficiency • Ankylosing spondylitis • Anorexia nervosa and bulimia • Athletic amenorrhea • Celiac disease • Chronic metabolic acidosis • Chronic obstructive liver disease • COPD • Congenital porphyria • Congestive heart failure • Cushing's syndrome • Cystic fibrosis • Depression • Diabetes mellitus, type 1 • Eating disorders • Ehlers-Danlos • Emphysema • End stage renal disease • Epidermolysis bullosa • Epilepsy • Female athlete triad • Gastrectomy/Gastric bypass/G.I. surgery • Gaucher's disease • Glycogen storage diseasesHemochromatosis • Hemophilia • Homocystinuria • Hypophosphatasia	• Hypercalciuria • Hyperparathyroidism • Hyperprolactinemia • Hypogonadism, primary or secondary • Hypophosphatasia • Idiopathic hypercalciuria • Idiopathic scoliosis • Inadequate diet • Inflammatory bowel disease • Juvenile polyarticular arthritis • Lactose intolerance/lacto-vegetarian diet • Lupus • Lymphoma and leukemia • Malabsorptive syndromes • Malnutrition • Marphan syndrome • Mastocytosis • Menkes steely hair syndrome • Mitochondrial myopathies • Multiple myeloma • Multiple sclerosis • Muscular dystrophy • Osteogenesis imperfecta • Panhypopituitarism • Pancreatic disease • Parental history of hip fracture • Parkinson's disease (movement disorders) • Pernicious anemia • Porphyria	• Post-transplant disease • Pregnancy and lactation (reversible) • Premature ovarian failure • Primary biliary cirrhosis • Prior fracture as an adult • Prolonged bed rest/wheelchair-bound • Renal insufficiency or renal failure • Rheumatoid arthritis • Riley-Day syndrome • Sarcoidosis • Severe liver disease, especially primary biliary cirrhosis • Sickle cell disease • Smoking • Spinal cord transection • Sprue • Stroke • Systemic mastocytosis • Thalassemia • Thyrotoxicosis • Tumor secretion of parathyroid hormone related peptide • Turner's & Klinefelter's syndromes • Vitamin D deficiency • Weight loss

Table 5. Osteoporosis Screening Recommendations of Other Organizations

	Recommendations	
Organization	**Women**	**Men**
National Osteoporosis Foundation (NOF 2014)	BMD testing for all women ≥65 y and postmenopausal women <65 y, based on risk factor profile	BMD testing for all men ≥70 y and men aged 50-69 y, based on risk factor profile
	BMD testing in all adults (women and men) who have a fracture after age 50 and adults with a condition or taking a medication 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 2012)	BMD testing for all women ≥65 y and postmenopausal women <65 y who have 1 or more risk factors	
U.S. Preventive Services Task Force (USPST 2011)	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 2016)	Evaluate all postmenopausal women ≥50 years for risk through detailed history, physical exam, FRAX tool. Consider BMD testing based on clinical fracture risk profile	
North American Menopause Society (NAMS 2014)	BMD testing recommended for all women ≥65 years, with consideration for earlier testing in women with clinical risk factors for fracture (low body weight, history of prior fracture, family history of osteoporosis, smoking, excessive alcohol intake, or long-term use of high-risk medications)	N/A
Endocrine Society (on osteoporosis in men) (2011)		BMD in men at increased risk – age 70 is a sufficient risk factor. Younger men 50-69 years should be tested if additional risk factors are present

BMD = bone mineral density; DEXA = dual-energy x-ray absorptiometry

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