

GUIDELINES & PROTOCOLS

ADVISORY COMMITTEE

Osteoporosis: Diagnosis, Treatment and Fracture Prevention

Effective Date: May 1, 2011

Scope

Osteoporosis (OP) is a significant risk factor for fragility fracture. This guideline summarizes current recommendations for risk estimation, diagnosis, prevention, and treatment of osteoporosis and related fractures in a general adult population (age 19+ years).

Diagnostic Code: 733.0: Osteoporosis

The following steps are outlined in this guideline (See *Algorithm 1: Recommendations for evaluation and management of osteoporotic and fragility fracture risk*):

1. Assessment of Risk
2. Risk Stratification
3. Lifestyle Advice (regardless of risk level)
4. Therapy
5. Monitoring

STEP 1: ASSESSMENT OF RISKS OF OSTEOPOROSIS OR FRACTURE

There are two aspects of risk that can be explored by identifying known risk factors:

- Risk of developing OP (Section 1.1); and
- Risk of fracture within 10 years (Section 1.2).

1.1 Risk of developing osteoporosis

Family history	Parental history of hip fracture
Medical history	<ul style="list-style-type: none">• Advanced age• Frailty*• Hyperthyroidism (including iatrogenic) or hyperparathyroidism• Celiac and other malabsorption syndromes• BMI < 20 kg/m² or weight loss• Medication history, particularly chronic glucocorticoid use** (see <i>Appendix A</i>)• Rheumatoid arthritis• Chronic liver or kidney disease
For men	Androgen deficiency (primary or secondary)
For women	<ul style="list-style-type: none">• Estrogen deficiency (primary or secondary)• Early menopause (< 45 years), including surgical• Cessation of menstruation for 6-12 consecutive months (excluding pregnancy, menopause or hysterectomy)
Lifestyle	<ul style="list-style-type: none">• Smoking (current or former)• Daily alcohol consumption > 3 units (1 unit = 5 oz wine, 1.5 oz spirits, 12 oz beer)• Caffeine intake > 4 cups/day• Inadequate calcium and vitamin D intake• Lack of sunlight exposure (may cause vitamin D deficiency)• Prolonged immobility and lack of weight-bearing exercise

* See www.BCGuidelines.ca – *Frailty in Older Adults – Early Identification and Management for definition*

** i.e., ≥ 3 months (consecutive) therapy at a dose of prednisone ≥ 7.5 mg per day or equivalent

1.2 Calculate the 10-year fragility fracture risk

The fracture risk of a patient can be estimated as Low (< 10% in next 10 years), Moderate (10 - 20% in next 10 years), or High (> 20% in next 10 years) using known risk factors and a clinical assessment tool. There are two tools available to calculate 10-year fracture risk. One is the FRAX® (see *Appendix C - Using the FRAX® Calculator to Assess Absolute Fracture Risk*), developed by the World Health Organization (WHO), and the other is produced by the Canadian Association of Radiologists and Osteoporosis Canada (CAROC).¹⁻³

FRAX® * employs a web-based (www.shef.ac.uk/FRAX) calculator that includes a number of risk factors; including bone mineral density (BMD) which is optional. The CAROC paper-based risk table takes into account age, sex, fracture history and glucocorticoid use to determine a ten-year absolute risk of all osteoporotic fractures but BMD is required to calculate risk.

1.3 Falls and the risk of fracture (also see “Falls prevention strategies” in Section 4.1)

Over and above the risk of OP, other clinical factors predict those at increased risk of fracture, including:⁴

Previous fragility fracture:

- Fractures sustained in falls from standing height or less, in which bone damage is disproportional to the degree of trauma. Includes vertebral compression fractures not attributable to previous major trauma, which may be suggested by height loss.
- Where other disease has been ruled out, patients with low trauma fragility fractures may have OP and are at **high** risk of other fragility fractures within 10 years.
- Fractures of the hip, vertebra, humerus, and wrist are most closely associated with OP and increased future fracture risk whereas those of the skull, fingers, toes, and patella fractures are not.

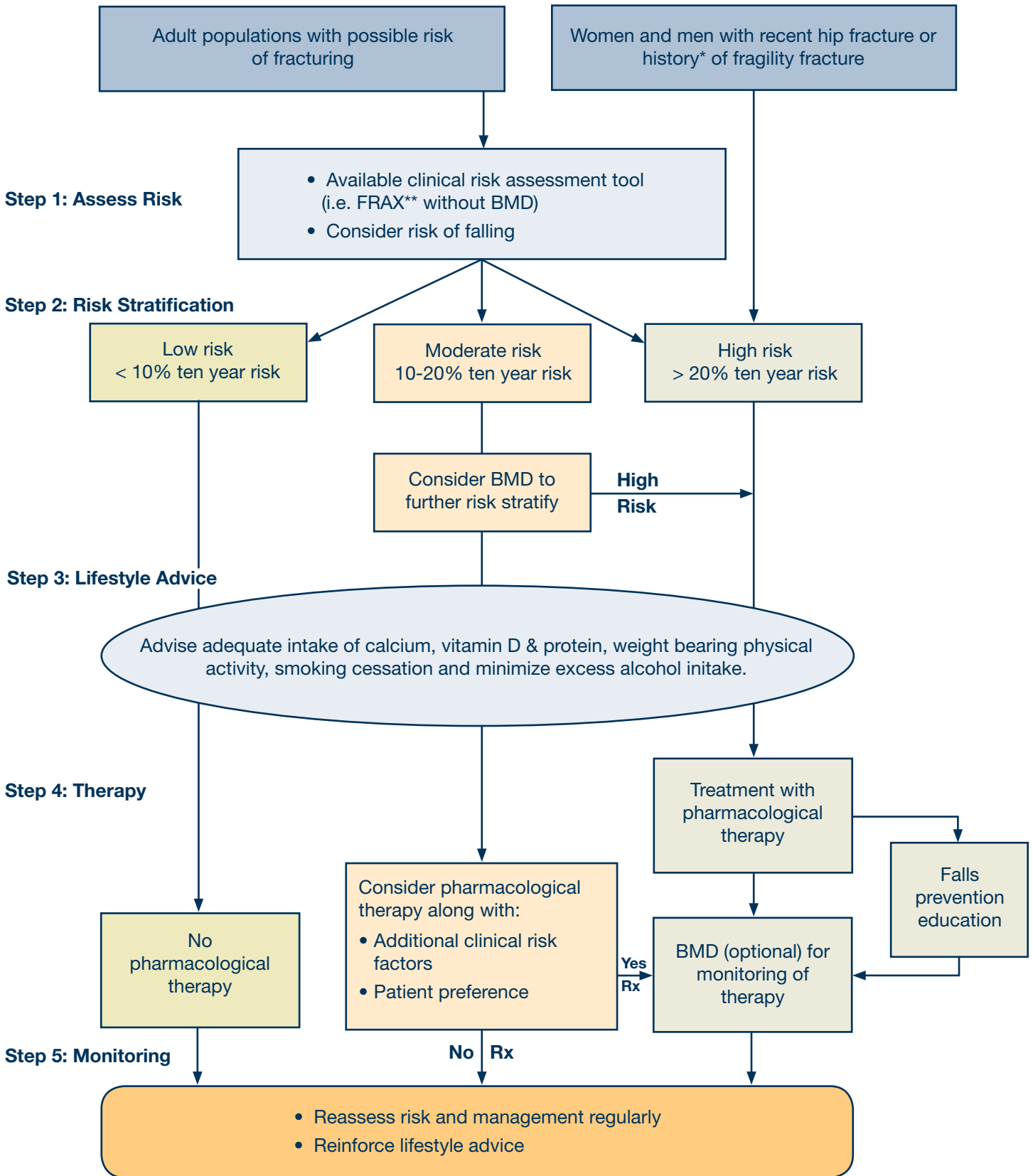
A fall in the last year

High risk of falling as determined by:

- Physical frailty or significant weight loss (loss of muscle mass). Refer to *BCGuidelines.ca - Frailty in Older Adults – Early Identification and Management*
- A global assessment of functional mobility like the timed ‘Up and Go’ test⁵
- Poor strength
- Balance problems
- Gait problems
- Dizziness
- Poor vision
- Psychotropic medications
- Cardiac insufficiency
- Urinary frequency and toileting issues
- Other validated tests⁶

*Although the FRAX® tool has been developed for prognosis and is not prescriptive, this guideline suggests the use of a tool to identify all risk groups for whom treatment will depend on individual clinical parameters and specific therapeutic indications listed in Steps 3 and 4 (e.g., age, previous vertebral fracture, T score, where appropriate).

Algorithm 1: Recommendations for evaluation and management of osteoporotic and fragility fracture risk



* Review available lateral thoracolumbar x-ray for evidence of fragility fracture

** FRAX not applicable at < 40 years

STEP 2: RISK STRATIFICATION

2.1 Levels of risk

Fracture risk estimation, using known risk factors and a clinical assessment tool, can be used to categorize patients as Low (< 10% in next 10 years), Moderate (10 – 20% in next 10 years) or High (> 20% in 10 years) fracture risk.

2.2 Risk stratification using Dual-Energy X-Ray Absorptiometry (DXA) BMD

BMD is not indicated unless patients (men and women) are age > 65 years, at moderate risk of fracture (10 - 20% 10-year risk), and results are likely to alter patient care.^{7,8,9} There has been a shift away from BMD and towards emphasizing multivariate fracture risk using a risk calculation model (FRAX[®] or CAROC). BMD is not recommended to be used alone as it explains only a portion of fracture risk. If a clinical risk assessment tool suggests moderate fracture risk category, consider BMD testing to further stratify risk and guide treatment; if high risk, consider treatment.

BMD is NOT indicated for:

- Investigation of chronic back pain
- Investigation of exaggerated dorsal kyphosis (fractures are best excluded by radiography)
- Screening women aged < 65 years, unless significant clinical risk factors have been identified
- Part of a routine evaluation around the time of menopause
- Confirmation of OP when a fragility fracture occurs

T-score classification (number of standard deviations above or below the mean peak BMD):⁶

- *Normal*: T is -1 and above
- *Osteopenia*: T is -1.1 to -2.4
- *Osteoporosis*: T -2.5 and below
- *Established or severe OP*: T is -2.5 or below and one or more prevalent low-trauma fractures

DXA is a quantitative test and it requires careful quality assurance. Structural abnormalities, positioning, artifacts (e.g., body weight), and analysis can significantly affect results.⁹

2.3 Laboratory testing (bone turnover markers and vitamin D)

Indications: Blood tests are not indicated to make an OP diagnosis or determine risk. Blood tests are only useful to establish or to rule out secondary causes of OP. Refer to *Appendix B - Testing for Suspected Secondary Causes of OP in Selected Patients*.

Bone turnover markers: At present no single or combined assay is recommended except in specific circumstances.¹⁰ Assays have a proven use in research studies involving large samples but they are complex and variation is too great to be useful at the individual level.

Vitamin D: Routine testing is not required to diagnose OP or before/after starting vitamin D supplementation. Refer to *BCGuidelines.ca - Vitamin D Testing Protocol*.

STEP 3: LIFESTYLE ADVICE (REGARDLESS OF RISK LEVEL)

Nutrition: Help reduce fracture risk via adequate daily calcium and vitamin D. Note: doses recommended below for calcium and vitamin D represent total intake from diet and supplements.

- Calcium: Recommend 1000-1200 mg elemental calcium per day including supplements, if necessary.¹¹⁻¹³ See *OP Patient Guide*. Advise patients not to exceed recommended amounts, as evidence does not support higher doses of calcium supplementation.¹⁴ In addition, a 2010 meta-analysis reported an increase in myocardial infarction in men and women given calcium supplementation (i.e., ≥ 500 mg elemental calcium per day) versus placebo. Note: this meta-analysis studied calcium supplementation alone and not in combination with vitamin D and the increased risk was associated with dietary intakes of greater than 800 mg (approximately) elemental calcium per day.¹⁵
- Vitamin D: Recommend 800-1000 IU per day of vitamin D₃, including supplements if necessary, to adults over the age of 50.¹⁷ Higher doses (i.e., 2000 IU per day) may be needed in some cases and are considered safe.¹⁶ See *Patient Guide and BCGuidelines.ca - Vitamin D Testing Protocol*.
- Protein: Recommend an adequate intake of dietary protein (1g/kg/day).²¹

Exercise: Regular weight-bearing and muscle-strengthening reduce the risk of falls and fractures by improving agility, strength, posture, and balance, as well as general health benefit.

Smoking: Tobacco products are detrimental to the skeleton as well as to overall health.

Alcohol: Intake of 3 or more units (5oz wine, 1.5oz spirits, 12oz beer) per day is detrimental to bone health and increases the risk of falling.

STEP 4: THERAPY

4.1 Falls prevention strategies

Falls prevention is the first line of treatment (versus OP medications) for those at high risk for falling.

Table 2: Items to identify falls risk and reduce falls (review with patient at least annually)

- | | |
|---|---|
| <ul style="list-style-type: none">• Ask about falls in the past year• Assess the time taken to stand from sitting• Assess muscle strength, balance, and gait by watching the patient walk and move• Check and correct postural hypotension and cardiac arrhythmias | <ul style="list-style-type: none">• Evaluate any neurological problems• Review prescription meds that may affect balance• Provide a checklist for improving safety at home, i.e., <i>The Safe Living Guide-A Guide to Home Safety for Seniors</i>, www.phac-aspc.gc.ca |
|---|---|

Consider referral to geriatric medicine, a falls prevention program, homecare, occupational therapy or physical therapy.

4.2 Pharmacological therapy

(See also *Appendix D - Prescription Medication Table for Osteoporosis*)

Medications may be recommended, depending on fracture risk assessment. Manage based on degree of risk:

- **Low risk:** Generally require lifestyle advice and daily intake of calcium and vitamin D.²²
- **Moderate risk:** Medication is usually not necessary but can be considered in addition to lifestyle advice and adequate daily intake of calcium and vitamin D. When considering medications, take into account patient preference and additional clinical risk factors (Table 3).²²

Table 3: Additional clinical risk factors

- | | |
|---|---|
| <ul style="list-style-type: none">• Vertebral fractures (> 25% height loss with end-plate disruption)• Lumbar spine BMD T-score that is significantly worse than hip BMD T-score• Men receiving androgen deprivation therapy for prostate cancer• Women receiving aromatase inhibitor therapy for breast cancer | <ul style="list-style-type: none">• Long-term or repeated systemic corticosteroid use (oral or parenteral) that does not meet the conventional criteria for recent prolonged systemic corticosteroid use (i.e., ≥ 3 consecutive months) therapy at a dose of prednisone ≥ 7.5 mg per day or equivalent)• Recurrent falls |
|---|---|

- **High risk:** Consider medication in addition to lifestyle advice and adequate daily intake of calcium and vitamin D.²³ Patients with hip and other fragility fractures are considered to be high risk. Individuals can be considered as candidates for medication after implementing fall prevention strategies and providing lifestyle advice (see Step 3).

OP medications available in Canada include (alphabetically): alendronate, calcitonin, denosumab, estrogens (with or without progesterone), etidronate, raloxifene, risedronate, teriparatide, and zoledronic acid.²³ Data are insufficient to determine if one drug class is superior to another for fracture prevention.²² Medication adherence (compliance and persistence) is required for fracture reduction, yet rates of adherence to OP treatments are low.²⁴

- Consider barriers to adherence including mode of administration, dosing regimens, side effects, and cost (see *Appendix D - Prescription Medication Table for Osteoporosis*).
- Combine adequate calcium and vitamin D with all pharmacological treatments. (See Step 3: Lifestyle Advice) For information regarding PharmaCare coverage of these medications please refer to *Appendix D*.

4.2.1 Bisphosphonates: These drugs preserve bone by decreasing rate of bone turnover and enhancing bone mineralization. ^{22,23,25,26,30} To date, this class of drugs (specifically alendronate, risedronate, and zoledronic acid) has the largest body of randomized controlled trial evidence for osteoporosis. Superiority of one bisphosphonate over another has not been conclusively shown. Most studies have been in post-menopausal women and the optimal duration of therapy is unknown (to date most studies, with fractures as an endpoint, have had an average five years duration).

<i>Bisphosphonates</i>	<i>Points to consider</i>
Alendronate (oral) & Risedronate (oral)	<ul style="list-style-type: none"> • Post-menopausal women: prevents vertebral, non-vertebral, and hip fractures^{31,32} • Men: Some evidence of decreased risk of vertebral fractures;^{27,28} some evidence of increased hip bone density, but no significant hip fracture reduction • Glucocorticoid induced osteoporosis (GIO): Some evidence of decreased vertebral fracture risk
Etidronate (oral)	<ul style="list-style-type: none"> • Post-menopausal women: prevents vertebral fractures³³ • GIO: maintains BMD in GIO although data is limited; Health Canada approved indication is for GIO prevention only (not treatment)²⁹
Zoledronic acid (intravenous)	<ul style="list-style-type: none"> • Post-menopausal women: prevents vertebral, non-vertebral, and hip fractures³⁴ • Men: Data is limited; Some evidence of decreased risk of vertebral and non-vertebral fractures (study included those with prior hip fracture and only 24% men);³¹ • GIO: maintains BMD • Cost effectiveness may limit use • Consider for high-risk patients who are unable to tolerate oral therapy or have poor adherence

4.2.2 Selective Estrogen Receptor Modulators [SERMs]: Raloxifene SERMs can act as estrogen agonists or antagonists. Raloxifene acts as an estrogen agonist on bone tissue. The estrogenic effects of raloxifene on bone in postmenopausal women decrease bone turnover. ^{22,25,26,35}

<i>Drug</i>	<i>Points to consider</i>
Raloxifene (oral)	<ul style="list-style-type: none"> • Post-menopausal women: reduces the incidence of vertebral fractures • May be considered in post-menopausal women who are unable to tolerate bisphosphonates and have no history of thromboembolic disease • Caution: Significantly increases the risk of venous thromboembolic disease and stroke

4.2.3 RANK Ligand Inhibitor: Denosumab is an injectable monoclonal antibody to the receptor activator of nuclear factor- κ B ligand (RANKL). It inhibits bone resorption by osteoclasts by blocking the interaction between RANKL and its receptor RANK on the surface of osteoblasts. ^{35,39,40}

<i>Drug</i>	<i>Points to consider</i>
Denosumab (subcutaneous)	<ul style="list-style-type: none"> • Postmenopausal women: prevents vertebral, non-vertebral, and hip fractures • Cost and lack of long term safety data may limit use

4.2.4 Synthetic Parathyroid Hormone: Teriparatide is an anabolic agent that improves bone quality, quantity, and increases bone strength. ^{22-24,30,36}

Drug	Points to consider
Teriparatide (subcutaneous)	<ul style="list-style-type: none"> • Post-menopausal women: prevents vertebral and non-vertebral fractures in postmenopausal women with severe OP • Men: increases BMD; currently no fracture data available • GIO: Some evidence of benefit in the treatment of GIO • Cost and need for daily subcutaneous injection may limit use • Consider for patients at increased risk of fracture or lack of response to other therapies • Maximum lifetime exposure is 24 months • Bisphosphonates must be discontinued prior to treatment • Gains in BMD decline once treatment with teriparatide is discontinued; consider anti-resorptive therapy after completing treatment course

4.2.5 Calcitonin Peptides: Calcitonin Salmon is an inhibitor of bone resorption; available in parenteral and nasal spray formulations. Although calcitonin does not build bone, in women > 5 years beyond menopause, it appears to slow bone loss and increase spinal bone density. ^{26,37,38}

Drug	Points to consider
Calcitonin (nasal)	<ul style="list-style-type: none"> • Post-menopausal women: Reduces incidence of vertebral fractures however evidence for benefit is limited • Consider as an alternative when other more effective drugs cannot be used • Effective in decreasing acute pain associated with vertebral osteoporotic fractures • Calcitonin injection is currently not approved for the treatment of OP; it is sometimes prescribed for patients who have pain due to acute vertebral fractures (See <i>Appendix D - Prescription Medication Table for Osteoporosis</i>) • Nasal route of administration has the most data for use in OP and is more commonly used due to convenience and tolerability

4.2.6 Hormone Replacement Therapy [HRT] (estrogen with or without progesterone): HRT is primarily indicated for the management of moderate to severe menopausal symptoms in women. ^{22,24-26,35} A beneficial effect has been seen on BMD and fracture risk due to the significant anti-resorptive activity of estrogen.

Drug	Points to consider
HRT (oral or transdermal)	<ul style="list-style-type: none"> • Post-menopausal women: Shown to prevent vertebral, hip and non-vertebral fractures • Is not recommended for the sole indication of OP prevention and for long term use for this indication; consider benefits versus risks (See <i>Appendix D - Prescription Medication Table for Osteoporosis</i>) • May be appropriate for OP prevention when it is already being used for the management of menopausal symptoms

STEP 5: MONITORING

5.1 Clinical re-assessment

Re-assess patients as clinically indicated to monitor side effects, compliance, height loss, incident fractures, and risk of falls, which may alter patient management.

5.2 Follow-up BMD measurements

There is insufficient evidence to recommend a testing frequency for patients not taking OP medications. Based on a patient's risk profile, BMD retesting may be indicated in 3-10 years.

For patients on OP medication, repeat BMD examinations are not justified based on current evidence. If a BMD is to be done, any changes would be difficult to detect prior to 3 years.⁴¹ Consider more frequent testing in specific high risk situations (e.g., multiple risk factors, or receiving ≥ 7.5 mg prednisone daily or its equivalent for 3 months consecutively who require a baseline examination and repeat scans at 6-month intervals while on treatment).

Women > 65 years will usually lose bone. A stable BMD value on treatment may reflect successful treatment and appreciable decreases in fracture risk may accompany minor increases in BMD. Minor increases in BMD may also be due to testing variance. Ideally, any follow-up BMD testing is recommended to be done on the same DXA machine and at the same time of year.

Patient Education

A patient guide to OP is included with this guideline. Further information for patients about OP is available at Health Link BC (www.healthlinkbc.ca).

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Resources

- BC Guidelines: www.bcguidelines.ca
 - Frailty in Older Adults – Early Identification and Management
 - Vitamin D Testing Protocol
- BC Health and Seniors Information Line 1-800-465-4911, Victoria 250-952-1742 and website www.seniorsbc.ca/healthcare/
- Injury Prevention and Mobility Laboratory, Simon Fraser University www.sfu.ca/ipml
- Centre for Hip Health and Mobility, University of British Columbia www.hiphealth.ca
- Public Health Agency of Canada, Falls Prevention www.phac-aspc.gc.ca/seniors-aines/
- BC Ministry of Health, Seniors' Falls Prevention www.health.gov.bc.ca/prevention/fallprevention.html

Abbreviations

BMD	bone mineral density
BMI	body mass index
CAROC	Canadian Association of Radiologists and Osteoporosis Canada
DXA	dual-energy x-ray absorptiometry
FDA	Food & Drug Administration (U.S.A)
GIO	glucocorticoid induced osteoporosis
HRT	hormone replacement therapy
IU	international units
OP	osteoporosis
RANKL	receptor activator of nuclear factor kappa-B ligand
SERMs	selective estrogen receptor modulators

Appendices

- Appendix A: Examples of Medications that May Contribute to Bone Loss
- Appendix B: Testing for Suspected Secondary Causes of OP in Selected Patients
- Appendix C: Using the FRAX® Calculator to Assess Absolute Fracture Risk

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

A mobile version of this and other guidelines, is also available at www.BCGuidelines.ca

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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DISCLAIMER

The Clinical Practice Guidelines (the "Guidelines") have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problems.

Appendix A - Examples of Medications that May Contribute to Bone Loss*

ANTICOAGULANTS - <i>heparin, warfarin</i>	GONADOTROPIN RELEASING HORMONE AGONISTS - <i>buserelin, goserelin, leuprolide acetate</i>
ANTICONVULSANTS - <i>carbamazepine, phenytoin</i>	LITHIUM
AROMATASE INHIBITORS - <i>anastazole, letrozole, exemestane</i>	PROTON PUMP INHIBITORS
BARBITUATES - <i>phenobarbital</i>	SELECTIVE SEROTONIN REUPTAKE INHIBITORS - <i>various</i>
CHEMOTHERAPEUTIC/CYTOTOXIC AGENTS - <i>various</i>	TACROLIMUS
CYCLOSPORINE	THIAZOLIDINEDIONES - <i>pioglitazone, rosiglitazone</i>
DEPO-MEDROXYPROGESTERONE	THYROID HORMONES IN EXCESS
GLUCOCORTICOIDS** - <i>various</i>	

*This is not a complete list of medications.

**Particularly chronic glucocorticoid use i.e., ≥ 3 months of consecutive therapy at a dose of prednisone ≥ 7.5 mg per day or equivalent

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Appendix B - Testing for Suspected Secondary Causes of OP in Selected Patients*

<i>If Clinically Suspected:</i>	<i>Tests May Include:</i>
Bone marrow malignancy	CBC
Malabsorption	CBC, calcium (low), 25-hydroxyvitamin D
Hyperthyroidism	Thyroid-stimulating hormone, calcium (high)
Hypogonadism	FSH & total testosterone (men)
Hyperparathyroidism	Albumin-corrected serum calcium
Multiple myeloma	Serum protein electrophoresis
Celiac	Celiac serology

*This is not a complete list of etiology or tests.

Appendix C - Using the FRAX® Calculator to Assess Absolute Fracture Risk

Access online at: <http://www.shef.ac.uk/FRAX/>

FRAX® WHO Fracture Risk Assessment Tool

Home Calculation Tool Paper Charts FAQ References English

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **Canada** Name/ID: [About the risk factors](#)

Questionnaire:

1. Age (between 40-90 years) or Date of birth
Age: Date of birth: Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

5. Previous fracture No Yes

6. Parent fractured hip No Yes

7. Current smoking No Yes

8. Glucocorticoids No Yes

9. Rheumatoid arthritis No Yes

10. Secondary osteoporosis No Yes

11. Alcohol 3 or more units per day No Yes

12. Femoral neck BMD (g/cm²)
Select DXA

Weight Conversion
Pounds Kgs

Height Conversion
Inches Cms

- From “Calculation Tool” menu, choose “Canada ” model
- Enter patient’s age or date of birth
- Enter patient’s sex
- Enter patient’s weight
- Enter patient’s height
- Choose “no” or “yes” for risk factors 5-11
- If BMD score available (#12), select type of DXA scanner and enter femoral neck or total hip BMD as g/cm² (Note: A BMD test is not required to estimate fracture risk)
- Click on “Calculate”
- The 10-year hip fracture probability estimate to can be used to determine type of treatment based on level of risk

Appendix D - Pharmacological Therapy for Osteoporosis 21-23, 28

Generic Name	Strength (Brand name)	Route	Adult dose	Approximate annual cost of therapy ^A	PharmaCare coverage	Therapeutic considerations ^B
Bisphosphonates						
Alendronate	Tablets: 10 mg and 70 mg (Fosamax [®] , G)	Oral	10 mg once daily <hr/> 70 mg once weekly	\$393 (G) \$778 <hr/> \$249 (G) \$560	Limited Coverage	Administration: swallow whole with full glass of water 30 min before first food of day; patients must not lie down for at least 30 min after dose To enhance absorption and decrease gastrointestinal side effects emphasize proper administration Contraindications: renal impairment [i.e., CrCl < 30 mL/min], hypocalcemia Precautions: upper gastrointestinal problems Adverse effects: abdominal pain, dyspepsia, nausea, esophagitis, esophageal ulcers, joint/muscle pain [<i>may need to discontinue if persists</i>], ocular inflammation, osteonecrosis of the jaw (ONJ) [<i>more commonly reported with higher doses of bisphosphonates given intravenously i.e., as used in oncology</i>], atypical femoral fractures [<i>although rare, seems to be more common with long term bisphosphonate use and can present as thigh or groin pain</i>], esophageal cancer [<i>causality unknown</i>], atrial fibrillation [<i>data is conflicting, causality unknown</i>]
Alendronate plus cholecalciferol (Vitamin D ₂)	Tablets: 70 mg/5600 IU and 70 mg/2800 IU (Fosavance [®])	Oral	70 mg/ 5600 IU once weekly <hr/> 70 mg/ 2800 IU once weekly	\$249	Limited Coverage	Note: combination product containing vitamin D – adjust supplementation as needed See alendronate therapeutic considerations
Etidronate plus calcium carbonate	Tablets: 400 mg etidronate; 1250 mg calcium carbonate, (Didrocal [®] , G)	Oral	One tablet once daily	\$92 (G) \$182	Regular Coverage	Note: calcium carbonate 1250 mg = 500 mg elemental calcium Administration [etidronate]: swallow whole with full glass of water at bedtime 2 hours before or after eating; 90 day cycle: 400 mg etidronate once daily for 14 days followed by 1250 mg calcium carbonate daily for 76 days; then repeat See alendronate therapeutic considerations
Risedronate	Tablets: 5 mg, 35 mg, and 150 mg (Actonel [®] , G)	Oral	5 mg once daily <hr/> 35 mg once weekly <hr/> 150 mg once monthly	\$302 (G) \$711 <hr/> \$229 (G) \$541 <hr/> \$635	Limited Coverage ^C	See alendronate therapeutic considerations
Zoledronic Acid	Solution for injection: 5 mg/ 100 mL (Aclasta [®])	Intra-venous (IV)	5 mg once yearly	\$671	No coverage	Administration: IV infusion given over at least 15 minutes Precautions: ensure patient is well hydrated [at least 500 mL fluid prior to and following administration] Adverse effects: transient flu like syndrome, atrial fibrillation [<i>uncommon, data conflicting</i>], gastrointestinal effects [less than what is seen with oral bisphosphonates], renal dysfunction Also see alendronate therapeutic considerations for more information on contraindications, precautions and adverse effects

Generic Name	Strength (Brand name)	Route	Adult dose	Approximate annual cost of therapy ^A	PharmaCare coverage	Therapeutic considerations ^B
Synthetic Parathyroid Hormone						
Teriparatide	Solution for injection: 2.4 mL pre-filled pen; delivers 20 mcg per dose; 28 doses per pen (Forteo [®])	Sub-cutaneous	20 mcg once daily	\$9628	No coverage	Maximum lifetime exposure for an individual patient is 24 months. Administration: subcutaneous injection into the thigh or abdominal wall; administer initially under circumstances in which the patient can sit or lie down [may cause orthostatic hypotension] Contraindications: severe renal impairment, hypercalcemia, pregnancy Adverse effects: nausea, dizziness, leg cramps, transient hypercalcemia, syncope, osteosarcoma has been noted in rats receiving teriparatide (dose and duration dependent); the significance of this in humans is still unknown
Selective Estrogen Receptor Modulators (SERMS)						
Raloxifene	Tablet: 60mg (Evista [®] , G)	Oral	60 mg once daily	\$542(G) \$715	Limited Coverage	Note: bone loss often resumes once treatment is stopped Contraindications: pregnancy, history of venous thromboembolic events (VTE) Precautions: consider baseline cardiovascular risk (increased risk of stroke and VTE) Adverse effects: vasomotor symptoms, flushing, leg cramps, flu syndrome, thromboembolic events [see above]
Calcitonin Peptides						
Calcitonin salmon	Nasal Spray: 200 IU per metered dose; 14 doses per bottle (Miacalcin NS [®] , G)	Intra-nasal	200 IU intra-nasally once daily, alternate nostrils daily	\$614 (G) \$813	No coverage	Note: salmon calcitonin is also available in an injectable form^P Adverse effects: common adverse effects appear to be localized, transient nasal reactions
RANK Ligand Inhibitor						
Denosumab	Solution for injection: 60 mg/ mL pre-filled syringe or vial (Prolia [™])	Sub-cutaneous	60 mg sub-cutaneously once every 6 months	\$660	No Coverage	Administration: subcutaneous injection into the upper arm, upper thigh, or abdomen Contraindications: hypocalcemia Adverse effects: cellulitis, dermatitis, eczema, rashes, pancreatitis, osteonecrosis of the jaw (rare)
Hormone Replacement Therapy (HRT) ^{E,F}						
Conjugated estrogen	Tablets: 0.625 mg (Premarin (equine) [®] / C.E.S. [®])	Oral	0.625 mg once daily	\$38 (CES [®]) \$109.50 (Premarin [®])	Regular Coverage	Prescribe with progestin for women with an intact uterus Note: risk versus benefit needs to be taken into account when prescribing; consider using only in light of other available treatments Administration: use continuous or cyclical regimes and adjust dose as needed; topical – apply to skin, rotate sites Contraindications: history of thromboembolic events, breast cancer Adverse effects ^G : nausea, vomiting, abdominal discomfort, breast tenderness thromboembolic events, breast cancer; topical - skin irritation