

Objective one

Asses the osteoporosis risk of all adult patients as part of periodic health examinations.

Check also the CCFP 105 Topics: Periodic Health Assessment Part One and Two episodes.

So, first things first: Who should be assessed for osteoporosis and fracture risk?

There are three categories:

- 1. All women and men aged 65 or more;
- 2. Adults aged 50-64 who are at high risk of fracture or have already experienced a fragility fracture;
- 3. Younger adults under the age of 50 who are at high risk of fractures.

We know who, let's see "How?"

Objective two

Use bone mineral density testing judiciously (e.g., don't test everybody, follow a guideline)

The cornerstone is bone mineral density (BMD) testing using dual-energy x-ray absorptiometry (DEXA scan). However, it should be used wisely.

Let's follow the 2010 guidelines' recommendations and jump directly to BMD testing with DEXA scans just for people aged 65 or more. Below that threshold, prioritize the risk factors assessments before BMD testing.

The Canadian Task Force recommends prioritizing risk assessment—first screening (FRAX tool without BMD testing) for women aged 65 or older to prevent fragility fractures while considering patients' values and preferences.



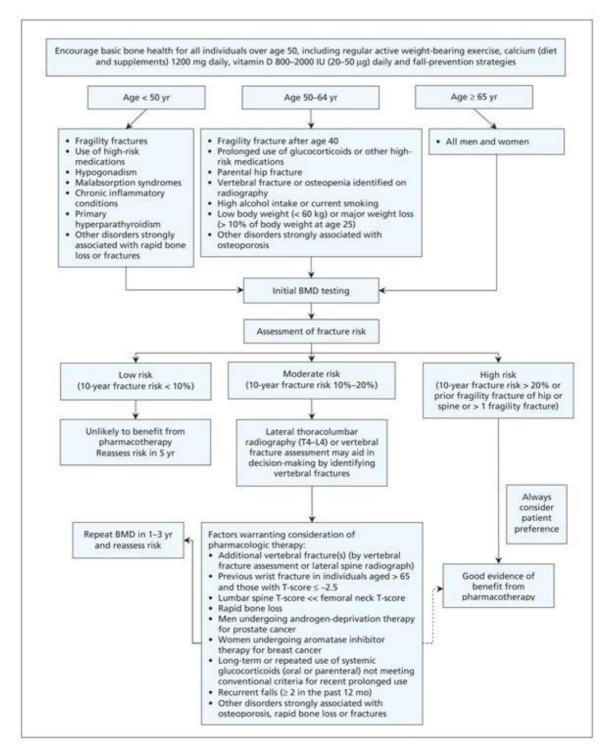


Fig. 2. Integrated approach to the management of patients who are at risk for fracture.

BMD = bone mineral density. The dashed arrow indicates that evidence for benefit from pharmacotherapy is not as strong in this instance as for other recommendations. (from CMAJ 2010;182:1864-1873)

Osteoporosis, the "silent thief", has no clinical manifestations until a fracture occurs. Many fractures are discovered by chance on the chest or abdominal X-rays. Conducting a focused history and detailed physical examination looking for risk factors for low bone mineral density, falls and fractures is crucial.



So, let's look at what's important to consider.

Before 50 we look for:

<u>Current or previous fragility fractures</u>. We keep mentioning fragility fractures.
 What's this?

They are fractures caused by low trauma or minor impact (falls from standing height, own height or less) as well as daily activities (bending, twisting, coughing or sneezing). Therefore, when looking for them, ask about pain, especially back pain – we all have it, but focus on the pain with its characteristic features.

Hip, vertebra, proximal humerus and wrist fractures are most frequently associated with osteoporosis and increased future fracture risk.

During the physical examination, you may find some warning signs for different types of fractures. Measure height annually and check for vertebral fractures as they are the most common ones and can lead to height loss due to collapsed vertebra.

o Screen for use of high-risk medications: The most important are glucocorticoids, which interfere with bone formation. Check for at least three months of use in the last year at a prednisone-equivalent dose of ≥ 7.5 mg daily (don't forget about COPD's treatment).

Here comes the men's part, prostate cancer therapy, and check for <u>androgen</u> <u>deprivation therapy</u>. Androgens are required for developing peak bone mass and maintaining bone mass.

o <u>Other conditions</u> and <u>high-risk medications</u> strongly associated with rapid bone loss or fractures should be considered as well and they are listed below.

Moving forward, assessing the risk of developing osteoporosis for individuals aged 50 to 64 implies screening for:

Family History – parental history of hip fracture **Medical History**

- o fragility fractures again, now after the age of 40;
- o <u>ask specifically about vertebral fractures or osteopenia</u> identified on the x-ray. Canadian Task Force has a strong recommendation that states to perform lateral thoracolumbar x-ray (T4-L4) or vertebral fracture assessment by DEXA scan if clinical evidence is suggestive of a vertebral fracture. Therefore, check for sudden onset of back pain and its specific features. *Go check* CCFP 105 Topics: Low Back pain episode for more details about back pain.
- Check for prolonged glucocorticoid use again and the other high-risk medications use mentioned earlier:



- o look for <u>low body weight</u> (less than 60 kg or BMI less than 20 kg/m2) or <u>major body weight loss</u> (>10% of weight at age 25 years old);
- o other conditions strongly associated with osteoporosis are listed below.

Lifestyle

o current smoking, high daily alcohol intake (more than 3 units per day) or high daily caffeine intake (more than 4 cups per day).

Medi	cations
Medications causing bone loss	
Aromatase inhibitors	Glucocorticoids for >3 mo
Thyroid hormone in excess	Immunosuppressive agents (eg, cyclosporine)
Gonadotropin-releasing hormone agonists or antagonists	Some anticonvulsants (eg, phenytoin)
Cytotoxic agents	Intramuscular medroxyprogesterone
Medications associated with increased fracture risk	
Proton pump inhibitors	Thiazolidinediones
SGLT2-inhibitors	Insulin with hypoglycemia
Selective serotonin-reuptake inhibitors	Selective norepinephrine-reuptake inhibitors
Medical	conditions
Genetic disorders	
Osteogenesis imperfecta	Hypophosphatasia
Thalassemia	Hemochromatosis
Endocrinopathies	
Gonadal insufficiency (primary and secondary)	Type 1 and type 2 diabetes mellitus
Hyperthyroidism	Primary hyperparathyroidism
Hypercortisolism, including Cushing syndrome	
Nutritional disorders	
Eating disorders	Obesity
Disorders of calcium balance	•
Vitamin D deficiency	Hypercalciuria
Gastrointestinal diseases	
Malabsorption syndromes (eg, celiac disease)	Inflammatory bowel disease
Gastrectomy	Chronic liver disease
Other disorders and conditions	
Chronic renal disease	Systemic mastocytosis
Rheumatologic diseases (eg, rheumatoid arthritis)	Hematologic malignancies (eg, leukemia, multiple myeloma
Frailty	Neuromuscular or visual impairment

SGLT2, sodium glucose cotransporter 2. Cosman F, et al⁴; Camacho PM, et al.⁷

 $Fig. 1\ Common\ or\ important\ medications\ and\ medical\ conditions\ that\ can\ adversely\ affect\ bone\ health\ \ (North\ American\ Menopause\ Society\ DOI:\ 10.1097/GME.000000000001831)$

To rule out secondary causes for osteoporosis Canadian Task Force recommends performing additional investigations based on the clinical assessment. Keep in mind that blood tests are not indicated to make an osteoporosis diagnosis or determine the risk category.

Measure serum levels of 25 hydroxyvitamin D for patients who will receive pharmacologic therapy for osteoporosis and in other circumstances after three to four months of adequate supplementation and do not repeat it if an optimal level (≥ 75 nmol/L) is achieved.

We know the risk, more or less a cause, then we go for initial BMD testing. Now let's move on to risk stratification and see how we assess 10-year fragility fracture risk by combining BMD results and risk factors.

Two tools are available in Canada and validated in the Canadian population:

- o the fracture Risk Assessment tool (FRAX) uses several risk factors and optionally bone mineral density of the femoral neck. Most of the osteoporosis risk factors listed in the notes are assessed for FRAX as well.
- o the 2010 version of the Canadian Association of Radiologists and Osteoporosis Canada (CAROC) considers age, sex, fracture history and glucocorticoid use to determine a ten-year absolute risk of all osteoporotic fractures, BMD is required to calculate risk. This tool stratifies women and men over the age of 50 into three zones of risk for major osteoporotic fracture within 10 years: low (< 10%), moderate (10%–20%) and high (> 20%).



Individuals with a lumbar spine or total hip T-score of ≤ -2.5 should be considered at least at moderate risk.

Therefore, if a clinical risk assessment tool suggests:

- o a low fracture risk, then encourage lifestyle changes and reassess the risk in 3-5 years
- o a moderate fracture risk, consider lateral thoracolumbar x-ray (T4-L4) or fracture assessment by DEXA scan to rule out compression vertebral fracture, further stratify risk based on additional risk factors and guide the treatment. Go for the treatment if one or more additional risk factors from the notes are present. Repeat BMD testing and reassess the risk every 1-3 years.
- o <u>if high fracture risk</u> or prior fragility fracture of hip or spine or more than 1 fragility fracture are present consider treatment based on the patient's preference and continue it without a drug holiday

To wrap up, BMD testing with a DEXA scan is not indicated unless patients (men and women) are aged 65 or more, at moderate risk of fracture (10 - 20% 10-year risk) and results are likely to alter patient care.

Remember that, starting in May 2023, Task Force recommends prioritizing risk assessment—first screening (FRAX tool without BMD testing) for women aged 65 or older to prevent fragility fractures while considering patients' values and preferences.

Objective three

Counsel all patients about primary prevention of osteoporosis (i.e., dietary calcium, physical activity, smoking cessation), especially those at higher risk (e.g., young female athletes, and patients with eating disorders).

In general, if there are no risk factors for rapid loss of bone mineral density, lifestyle changes are enough to prevent osteoporosis. For those at higher risk such as young premenopausal female athletes and patients with eating disorders focus on preventing caloric deficit by improving nutritional aport.

Encourage weight-bearing and resistance exercises 30 to 60 minutes per day, 3 times per week to reduce the risk of falls and fractures and improves the quality of life for those with osteoporosis.

Weight-bearing exercises could be as simple as walking, climbing stairs or anything else that implies using your weight, resistance exercises imply muscle-strengthening and lifting weights or using resistance machines. Osteoporosis Canada has a programme called "Too Fit to Fracture" that includes exercise recommendations for people impacted by osteoporosis.



Too Fit to Fall or Fracture

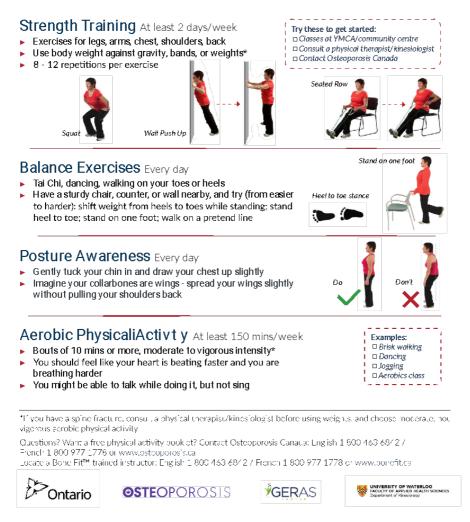


Fig. 3. "Too Fit to Fracture" one-page guide packed with useful information to get you started thinking about ways you can safely and effectively exercise from Osteoporosis Canda

Bone health is important at every age and a healthy diet benefits may help with this. Total daily elemental <u>calcium</u> intake (through diet and supplements) over the age of 50 should be 1200 mg according to Canadian Task Force.

Patients with malabsorption syndromes (such as celiac disease, inflammatory bowel disease, etc) may require more than 1200 mg of calcium per day. Certain medications change the amount of calcium that is absorbed and/or excreted. Loop diuretics, furosemide (Lasix) increase the amount of calcium excreted in the urine.

Calcium supplements interfere with the absorption of iron and thyroid hormone, therefore,



these medications should be taken at different times. Examples of foods that contain Calcium are listed below:

Examples of Foods That Contain Calcium				
Type of Food	Estimated Elemental Calcium Content (Approximate Content)			
Canned salmon (with bones)	181 mg per 85 g, or 3 oz			
Sardines in oil, with bones	324 mg per 85 g, or 3 oz			
Turnip greens (boiled)	99 mg per 120 ml, or ½ cup			
Broccoli (raw)	21 mg per 120 ml, or ½ cup			
Cow's milk (skim, 2%, homo)	291-302 mg per 240 ml, or 1 cup			
Soy or rice milk	80 IU per 240 ml, or 1 cup			
Some orange juices	100 IU per 240 ml, or 1 cup			
Tofu (firm, made with calcium sulfate)	204 mg per 120 ml, or ½ cup			
Yogurt (plain, low-fat)	415 mg per 228 g, or 8 oz			
Yogurt (fruit, low-fat)	245–384 mg per 228 g, or 8 oz			
Cheddar cheese	306 mg per 42.5 g, or 1.5 oz			
Cottage cheese (1% milk fat)	138 mg per 240 ml, or 1 cup			
Ice cream (vanilla)	21 mg per 120 ml, or ½ cup			

Fig 4.. Examples of Foods That Contain Calcium from BC Guidelines - Osteoporosis and Fracture Prevention A Guide for Patients

The amount of sunlight we get in Canada is insufficient to produce enough "sunshine vitamin", <u>Vitamin D</u>. In addition, as we become older we produce less vitamin D. Moreover, there are few food sources of vitamin D. Hence, year-round vitamin D supplementation is advised for Canadian adults.

Healthy Canadians over the age of 50 should consume 400-1000 IU (10-25 g) of vitamin D3 (cholecalciferol) daily. To achieve optimal vitamin D levels, people with <u>osteoporosis</u>, <u>multiple fractures or conditions affecting vitamin D absorption</u> should take more than 1000 IU (25 g) per day. Daily doses of up to 2000 IU (50 g) are considered safe and do not require monitoring.

According to a 2022 study supplementing with 2000 IU of vitamin D3 daily did not significantly reduce the risk of fractures among the generally healthy population compared to a placebo. In Canada, margarine, infant formula, cow's milk and substitutes, egg products, meal replacements and nutritional supplements are required to be vitamin D fortified. Other Vitamin D food sources are listed below:



FOOD	SERVING SIZE	IU'S PER SERVING
Orange Juice, Fortified	1/2 c/125 mL	50
Margarine, fortified	5 mL/1 tsp	25-36
Mushrooms, white	125 mL/ 1/2 c	4
Swordfish, Baked or Broiled	75 g	761
Salmon, pink, Canned, Drained with solids and bones	75 g	435
Cod Liver Oil	5 mL/1 tsp	426
Salmon (Sockeye), Baked or Broiled	75 g	394
Snapper, Baked or Broiled	75 g	392
Milk (all types)	1 c/250 mL	103-105
Soy Beverage, Enriched	1 c/250 mL	86
Yogurt, Plain, Vitamin D Added	175 g	50
Egg Yolk, cooked	2 Large	64
Tuna, canned in water, drained unsalted	75 g	60

Fig. 5. Vitamin D food sources from Osteoporosis Canada

<u>Protein</u> intake is recommended to be adequate as well (1g/kg/day). In fall-prone older adults who were losing weight, higher protein intake was associated with fewer falls.

Of note here, a validated assessment for risk of falls in the frail adults is known as the Timed-Up-And-Go test – a link to the BC guidelines cited approach is here https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/frailty-TUG.pdf

<u>Smoking cessation</u> has benefits for both the bones and general health as well as <u>alcohol consumption</u> limitation.

Objective four

In menopausal or peri-menopausal women, provide advice about fracture prevention that includes improving their physical fitness, reducing alcohol, smoking cessation, risks of physical abuse, and environmental factors that may contribute to falls (e.g., don't stop at suggesting calcium and vitamin D).

The North American Menopause Society reinforces the importance of nonpharmacologic measures and lifestyle modifications for all women, regardless of their BMD, clinical risk factors or fracture risk, to support general and bone health.



These general approaches, however, will not prevent bone loss in early menopause, will not significantly increase BMD in postmenopausal women and are certainly not adequate treatment for women with osteoporosis. The daily intake of <u>calcium recommendation</u> for both postmenopausal women and women with normal BMD is 1000 mg to 1200 mg, with an upper limit of 2000 mg.

The current recommendation is that postmenopausal women consume at least 800 international units (20 micrograms) of <u>vitamin D</u> per day. Although the optimal intake has not been established in premenopausal women, 600 international units (15 micrograms) of vitamin D daily is generally suggested.

There are lots of misconceptions regarding supplements that may be beneficial to women's bone health. However, studies have shown that only a few supplements may have a positive effect and I'll mention two of them.

Probiotics may help prevent bone loss caused by estrogen deficiency because gut microbiota can affect several aspects of bone health, including calcium and vitamin D absorption and immune response. Phytoestrogens, including isoflavones, are plant-derived compounds with weak estrogenic activity that may have a moderately beneficial effect against estrogendeficiency bone loss according to some studies.

Regular weight-bearing and resistance exercises should be encouraged for bone health and overall health. Lifting or pulling with forward spine flexion or rotation should be avoided by women with osteoporosis, especially those who have vertebral fractures.

Encouraging smoking cessation and alcohol intake limitation and avoiding any harmful event that puts too much pressure on the osteoporotic body (eg, physical abuse, etc). Every year, at least one-third of women 65 and over fall, and as people age, their chance of falling and breaking a bone increases. Since falls are the primary cause of fractures, efforts to prevent them should be encouraged too.

Objective five

In patients with osteoporosis, avoid prescribing medications that may increase the risk of falls.

Conduct a focused history to identify a fall in the last year and do a physical examination to assess fall risk by using the Get-Up-and-Go Test (check the ability to get out of a chair without using arms and walk several steps and return). Postural hypotension, cardiac arrhythmias and any neurological problems should also be assessed.

Review the medication list, including over-the-counter medications. Think about medications that can cause drowsiness, dizziness, hypotension, parkinsonian effects, ataxia and other gait disturbance, vision disturbance, osteoporosis and bleeding. A never-ending list, right?

To make things a little easier, consider medications that suppress the central nervous system, such as those that reduce alertness and cause slower reactions and movements. These include anxiolytics (benzodiazepines – diazepam, lorazepam, etc), antidepressants (especially



tricyclic antidepressant – amitryptiline), antiepileptics, alpha-adrenergic blockers (benign prostatic hyperplasia and pheochromocytoma medications) and painkillers (narcotics/opioids – codeine, etc). More examples are listed below.

Examples of drugs that can increase the risk of falling, or of a serious outcome if a fall occurs (and possible mechanisms)

ACE Inhibitors (3) Benazepril Captopril Cilazapril Enalapril/enalaprilat Fosinopril Lisinopril Perindopril Quinapril Ramipril Trandolapril	Methsuximide (1,2,5) Oxcarbazepine (1,2,5,6) Phenobarbital (1,2) Phenytoin (1,2,5,7) Primidone (1,2) Topiramate (1,2) Valproic acid (1,2,5) Vigabatrin (1,2)	Cyproheptadine Diphenhydramine Hydroxyzine Meclizine Promethazine Trimeprazine Antipsychotics (1,3,4) Chlorpromazine	Digoxin (mechanism unknown) Eye drops (6) Herbal and Natural health products Natural sleep aids	Fentanyl Hydromorphone Meperidine Methadone Morphine Oxycodone Oxymorphone Nalbuphine Pentazocine Propoxyphene Sufentanil
Alcohol (1,5)	Antidepressants	Clozapine Flupenthixol	Natural products for sexual	Proton Pump
Alpha Receptor Blockers (2,3, especially initial doses)	(1,2,3,6) Amitriptyine Bupropion Citalopram Clomipramine	Fluphenazine Haloperidol Loxapine Methotrimeprazine Olanzapine	enhancement (possible adulteration with undeclared drugs)	Inhibitors (9) Esomeprazole Lansoprazole Omeprazole Pantoprazole
Alfuzosin Doxazosin Prazosin Tamsulosin	Desipramine Doxepin Escitalopram Fluoxetine	Paliperidone Perphenazine Pimozide Pipotiazine	Metoclopramide (1,2,4)	Rabeprazole Sedative/ hypnotics
Terazosin	Fluvoxamine Imipramine Maprotiline	Prochlorperazine Quetiapine Risperidone	Muscle Relaxants (1,2) Baclofen	Benzodiazepines Barbiturates (1,2,5)
Anticoagulants (8) Dalteparin Danaparoid Enoxaparin Heparin Nadroparin	Mirtazapine Moclobemide Nortriptyline Paroxetine Phenelzine 1,2,3 Sertraline	Thioproperazine Thiothixene Trifluoperazine Zuclopenthixol	Carisoprodol Chlorzoxazone Cyclobenzaprine Dantrolene Methocarbamol Orphenadrine	Alprazolam Bromazepam Chloral hydrate Clorazepate Diazepam Diphenhydramine
Nicoumalone Tinzaparin	Tranylcypromine 2,3 Trazodone	Corticosteroids, oral (7)	Tizanidine	Doxylamine Flurazepam
Warfarin	Trimipramine Venlafaxine	Corticosteroids, inhaled, high-dose (7)	Nitrates (2,3) Isosorbide dinitrate Isosorbide	Lorazepam Midazolam Nitrazepam
Anticonvulsants (1,2,5,6,7) Carbamazepine	Antihistamines, sedating (1)	Beclomethasone Betamethasone Budesonide	mononitrate Nitroglycerin	Oxazepam Pentobarbital Phenobarbital
(1,2,6) Ethosuximide (1,2,5) Fosphenytoin (1,2,5,7)	Cold Medications that contain sedating antihistamines (1)	Cortisone Dexamethasone Fludrocortisone Fluticasone	NSAIDs ASA/acetylsalicylic acid (8)	Temazepam Triazolam Zopiclone
Gabapentin (1,2,5,6) Lamotrigine (1,2,6) Levetiracetam (1,2,5)	Azatadine Brompheniramine Cetirizine Chlorpheniramine Clemastine	Hydrocortisone Methylprednisolone Prednisolone Prednisone Triamcinolone	Opiates/narcotics (1,2,3) Alfentanil Butorphanol Codeine	Thiazolidinediones (7) Pioglitazone Rosiglit

^{*}Possible mechanisms (often unclear): (1) Drowsiness; (2) Dizziness; (3) Hypotension; (4) Parkinsonian effects; (5) Ataxia/gait disturbance; (6) Vision disturbance; (7) Osteoporosis or reduced bone mineral density increases the fracture risk if a fall occurs; (8) Risk of serious bleeding if a fall occurs. Drugs are listed by generic (chemical) name under each drug group. For Brand (manufacturer's) names, check in the CPS to find the generic name. This list includes only those drugs for which there is evidence of increased risk of falls or their consequences. There may be other drugs that increase this risk in certain patients.

Fig. 6. Barbara Cadario and BC Falls and Injury Prevention Coalition. Drugs and the Risk of Falling: Guidance Document. Revised August 2011 from BC Guidelines

Objective six



Provide advice and counselling about fracture prevention to older men, as they too are at risk for osteoporosis.

Osteoporosis is commonly thought to be a woman's disease, but older men are also susceptible to bone loss. Men have fewer research studies on osteoporosis than women. According to Osteoporosis Canada, at least one in five men will break a bone as a result of osteoporosis and men account for one-quarter of the 30,000 hip fractures caused by osteoporosis in Canada.

Everyone (men and women) should take the same steps to prevent fractures and promote bone health. Therefore, encourage the men to engage in weight-bearing and resistance activities, eat a healthy balanced diet rich in dairy products, avoid smoking and limit alcohol consumption.

Objective seven

Treat patients with established osteoporosis regardless of their gender (e.g., use bisphosphonates in men).

Treatment adherence to osteoporosis pharmacotherapy is quite low. Therefore, individualized management plans (lifestyle changes and pharmacologic therapy) should be used to improve adherence. In general, pharmacotherapy reduces the risk of vertebral fracture by 30% to 70%, depending on the agent and level of adherence.

Before starting therapy, the potential benefits and risks should be discussed to support informed decision-making. Bisphosphonates have been shown to reduce hip, nonvertebral and vertebral fractures for both women (perimenopausal or postmenopausal) and men. There is no evidence that testosterone reduces fractures in men.

When prescribed wisely, women will benefit from hormone replacement therapy (estrogen with or without progesterone) when it's already being used for managing menopausal symptoms or raloxifene, a selective estrogen receptor modulator. Synthetic parathyroid hormone prevents bone loss and increases lumbar spinal BMD.

Gains in BMD decline once treatment is discontinued, therefore it should be followed by long-term anti-resorptive therapy with a bisphosphonate or receptor activator for nuclear factor ligand inhibitor after completing the treatment course. In almost a decade, Romosozumab, a sclerotin inhibitor, is the first new treatment approach for osteoporosis and fracture risk.

It significantly and rapidly (over 12 months) increases bone formation and decreases bone resorption in both the lumbar spine and hip. Calcitonin Salmon is no longer used in Canada. For information regarding the PharmaCare plan's coverage rules check with local services.



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