Guidance on the Diagnosis and Management of Osteoporosis in New Zealand

OSTEOPOROSIS NEW ZEALAND
Better bones, fewer fractures

Presentation

No fracture AND ≥1 risk factor[a] for osteoporosis

Any fracture not involving major trauma[b]

Consider referral to Fracture Liaison Service

Key note item

To preserve bone health throughout life, encourage all patients to:

- Perform regular weight-bearing exercise
- Eat a balanced diet
- Limit alcohol (≤2 drinks/day; ≥2 alcohol-free days/week)
- Stop smoking
- Maintain healthy weight (BMI 20–25 kg/m²)
- Have adequate sun exposure

Lifestyle modifications

- Address modifiable risk factors
- Falls risk assessment and prevention programme if appropriate
- Vitamin D supplementation if appropriate[c]

Clinical risk assessment

- BMD assessment if appropriate/available[d] (DXA)
- Fracture risk assessment (FRAX®/Garvan ± DXA[e])
- Consider lateral DXA of the spine or spinal x-ray to identify vertebral fracture

Exclude secondary osteoporosis in individuals with low BMD for age (i.e. Z-score <-2)[f]

Risk stratification

10-year FRAX®/Garvan hip fracture risk ≥3%[g] OR T-score ≤-2.5

NO → Re-assess fracture risk at appropriate interval

YES → First-line therapy

First-line therapy

Oral bisphosphonate[h]

IV zoledronate[h]

Monitoring

6-month post-treatment PINP <35 µg/L

NO → Review oral dosing practices or switch to IV zoledronate

YES → Treat for 4–5 years

Administer 3 doses at 18 to 24 month intervals[i]

Perform/repeat DXA

T-score ≤-2.5 OR new/recurrent fracture

NO → No treatment for 4–5 years

YES → Continue treatment for 4–5 years[j] but, if on oral bisphosphonates, consider a 1- to 2-year drug holiday in this period

New/recurrent fracture → Consider teriparatide and/or discuss with secondary care colleague

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BMD: *bone mineral density* **BMI:** *body mass index* **DXA:** *dual-energy x-ray absorptiometry* **PINP:** *procollagen type I N-terminal propeptide*

Key notes

a Risk factors:

- Age ≥65 years (women); ≥75 years (men)
- BMI <20 kg/m^2
- Family history of osteoporosis
- Smoking (current)
- Glucocorticoid use (current)
- Early menopause
- >2 alcoholic drinks daily
- History of falls
- Rheumatoid arthritis
- History of eating disorders

b The most common **osteoporotic fractures** are those of the vertebrae, proximal femur, distal forearm, humerus and pelvis; however, any recent fracture at a major skeletal site in older adults should prompt further assessment for osteoporosis. Exceptions are fractures of the digits, face and skull.

c Individuals at risk of **vitamin D deficiency** include the frail/institutionalised elderly, veiled women and those with dark skin living at higher latitudes.

d Although **DXA** is recommended after fracture, treatment must **not** be delayed if DXA is unavailable.

e **FRAX®** or **Garvan** fracture risk can be calculated without BMD if DXA is not available.

f Search for **contributory factors** as appropriate through a clinical history and examination and through measurement of relevant biomarkers.

g A **10-year hip fracture risk** of ≥3% as the threshold for initiating treatment is indicative, based on pharmacoeconomic analyses. Individuals with a 10-year hip fracture risk of 3% have a 10-year major osteoporotic fracture risk of ~20% and a total fracture risk of ~40%.

h As an alternative to bisphosphonates, **oestrogen therapy** may be considered as first-line therapy for women within 10 years of menopause.

i **Zoledronate** is an **IV bisphosphonate** that **reduces risk** of hip, vertebral and non-vertebral fractures[6]. In the pivotal clinical trials, zoledronate was administered annually for three years. However, zoledronate's duration of action is **considerably longer** than one year; therefore, it is common practice to administer the three initial doses at intervals of 18 or 24 months.

j There is limited evidence to guide **treatment beyond 10 years.** Individuals with a persistently increased fracture risk should be considered for long-term intervention, with **drug holidays** every few years. Guidance from a secondary care colleague should be considered.

Presentation

Fracture Liaison Service (FLS)

The FLS systematically identifies individuals who have sustained a fragility fracture, with the intention of preventing subsequent fractures. Fragility fracture sufferers will be offered an assessment for future fracture risk including bone health (i.e. osteoporosis) and falls risk.

The FLS works with the fragility fracture sufferer and their GP to develop a long-term plan aimed at reducing risk of falls and fractures, and promoting long-term management.

In New Zealand, this service is provided by health professionals who are employed by District Health Boards or Primary Health Organisations. While respective FLS may have slight variations in target population, generally any individual with an age-related low impact (or non-traumatic) fracture involving the proximal femur, wrist, humerus, vertebrae or pelvis is considered appropriate for FLS assessment.

Clinical standards for FLS* in New Zealand are available that detail the evidence-based standards of post-fracture care that health professionals and patients should expect. *www.osteoporosis.org.nz/resources/health-professionals/clinical-standards-for-fls/

Lifestyle modifications

Modifiable risk factors

Modifiable risk factors include:

- Limiting alcohol to no more than two standard drinks per day, with at least two alcohol-free days per week
- Maintaining a body mass index 20–25 kg/m^2
- Stopping smoking
- Regular exercise, including ≥30 minutes of weight-bearing physical activity each day

Falls risk assessment and prevention programme *(Ask, Assess, Act)*

Ask, Assess, Act* is an initiative of the Health Quality and Safety Commission of New Zealand.
*www.hqsc.govt.nz/assets/Falls/PR/AAA-pocket-card-read-Apr-2014.pdf

It requires the health practitioner to:

1. ASK the person three simple screening questions:
   (i) Have you slipped, tripped or fallen in the last year?
   (ii) Can you get out of a chair without using your hands?
   (iii) Have you avoided some activities because you are afraid you might lose your balance?
2. ASSESS the person to identify their particular falls risk
3. ACT by putting individualised intervention and supports in place

A falls prevention programme* may include education on the risk of falling, medication review, evidence-based exercise programmes**, use of appropriate assistive devices, treatment of postural hypotension and cardiovascular disorders, reduction of environmental hazards, eyesight examinations and correction of vitamin D deficiency.

*www.acc.co.nz/preventing-injuries/falls/older-people/information-for-health-professionals/index.htm

***There is evidence that completion of structured programs with progressive lower-limb strengthening and balance exercises can reduce falls rates by up to 30%.*

Vitamin D supplementation

Vitamin D is mainly important for the prevention of osteomalacia; treatment of mild vitamin D deficiency does not seem to confer significant benefits in terms of bone mineral density (BMD)[1] or fracture risk.[2]

The best source of vitamin D is sunlight. For most people, vitamin D deficiency can be prevented by 5 to 10 minutes' exposure of face, arms and hands to sunlight 4 to 6 times per week. In New Zealand, exposure should be restricted at high UV times.[3]

Most healthy European New Zealand adults living independently do not require vitamin D supplements. Individuals at risk of vitamin D deficiency include the frail/institutionalised elderly, veiled women and those with dark skin living at higher latitudes. If vitamin D supplementation is required, doses of 400–800 IU/day or 1.25 mg/month are usually sufficient.

Calcium supplementation

Calcium supplementation is no longer routinely recommended to improve bone health because it lacks fracture reduction efficacy and potentially increases cardiovascular events.[4]

A dietary calcium intake of 500 mg/day (2–3 servings of calcium-rich foods such as dairy products [milk, yoghurt, cheese], calcium-fortified products [fortified soy and rice milks, fortified cereals and fortified orange juice], tofu, calcium-rich vegetables, tinned sardines/salmon [including the bones] or calcium-rich nuts and fruits) is sufficient for an adult.

Clinical Risk Assessment

Bone mineral density (BMD) assessment

BMD is one predictor of fracture risk and should be measured using dual energy x-ray absorptiometry (DXA) performed at two sites, preferably anteroposterior spine and hip. With advancing age, degenerative changes in the spine may result in falsely elevated BMD levels at that site; therefore, DXA of the hip is more reliable.

BMD results are reported as a T-score (number of standard deviations that BMD is above or below the mean of healthy young adults) or a Z-score (number of standard deviations that BMD is above or below the mean of normal controls matched for age).

The World Health Organization defines osteoporosis as a T-score ≤-2.5 and osteopenia as a T-score between -1 and -2.5.

BMD should be assessed in individuals with suspicion of osteoporosis to establish a baseline reading that can be used to inform future management. Indications for BMD assessment include:

- Minimal trauma fracture
- Women aged <65 years with risk factors for osteoporosis
- Women aged ≥65 years and men aged ≥75 years considering specific measures to prevent osteoporosis
- All users of glucocorticoids for >6 months

However, fracture risk assessment and anti-osteoporotic treatment must not be withheld if DXA scanning is unavailable. It is acceptable to assess fracture risk with FRAX®/Garvan calculators without a BMD value if DXA is unavailable. Patients aged ≥75 years with a significant osteoporotic fracture demonstrated radiologically do not necessarily require a BMD assessment for PHARMAC medication access. *Refer - First-line Therapy section of this document.*

Note that Accident Compensation Corporation (ACC) can fund DXA scans in relation to an accepted ACC claim for a fragility fracture if the referral has been made by a vocationally-registered specialist. The request is subject to approval and must meet the following criteria:

1. There is an accepted ACC claim for a fracture AND
2. The fracture is likely to be a fragility fracture (fracture resulting from a fall from standing height or less) AND
3. The person is <75 years old and considered to be at reasonable risk of further fractures OR is between 50–75 years old and is receiving systemic glucocorticoid therapy (≥ 5 mg/day prednisone equivalent) for ≥3 months AND
4. The person has not had a DXA scan previously and is not known to be on bisphosphonates or other osteoporosis medication AND
5. The request for DXA must be part of an assessment in a comprehensive and integrated pathway to minimise harm from falls and fractures.

Fracture risk assessment

Absolute fracture risk is usually the basis of therapeutic shared decision making. This can be calculated using the Fracture Risk Assessment (FRAX®) tool* or Garvan Fracture Risk Calculator*. FRAX® and Garvan calculators include BMD as a risk factor; however, risk can be calculated in the absence of a BMD measurement.

Hip fracture risk calculated by FRAX® doubles every 5 to 6 years in postmenopausal women. This should be the basis for determining the time to follow-up BMD measurement in those not requiring intervention at the time of the present assessment. For example, if current hip fracture risk is 0.5%, reassessment is not likely to lead to a management change for approximately 15 years, whereas higher baseline fracture risk justifies earlier re-measurement.

*www.shef.ac.uk/FRAX/tool.aspx?country=23 *www.garvan.org.au/promotions/bone-fracture-risk/calculator

Secondary osteoporosis

Secondary causes of osteoporosis should be investigated in individuals with low BMD for age (i.e. a Z-score <-2).

The following conditions have been associated with increased risk of osteoporosis:

- Low body weight from any cause (including a past or current eating disorder)
- Chronic inflammatory disease (e.g. inflammatory bowel disease, rheumatoid arthritis, chronic obstructive pulmonary disease, inflammatory connective tissue disease/arthropathy, coeliac disease)
- Iatrogenic glucocorticoid excess or Cushing's disease
- Hypogonadism or premature menopause (<45 years)
- Excess alcohol use or smoking

Other conditions associated with low BMD include: type 1 diabetes mellitus, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hyperparathyroidism, chronic malnutrition or malabsorption, bariatric surgery and chronic liver disease.

Drug classes associated with major bone loss include glucocorticoids[5] and androgen deprivation therapy. Some bone loss has been reported with use of injectable medroxyprogesterone acetate and aromatase inhibitors.

Search for contributory factors as appropriate through a clinical history and examination and through measurement of:

- Serum calcium
- Serum phosphate
- Alkaline phosphatase
- Cortisol
- Thyroid-stimulating hormone
- Coeliac screen
- Liver and renal function tests
- Protein electrophoresis
- Full blood count
- C-reactive protein

In men aged <75 years with a Z-score <-2 and fractures, consider evaluating testosterone levels.

Note that a detailed screen for secondary causes of osteoporosis is not indicated in individuals with a BMD in the appropriate range for age (i.e. a Z-score ≥-2).

Treatment

Patients with any of the following characteristics should be offered treatment:

- 10-year FRAX®/Garvan hip fracture risk of ≥3%
- T-score ≤-2.5 (or ≤-1.5 for individuals on long-term glucocorticoid therapy)

First-line Therapy

Oral bisphosphonates

Alendronate* and risedronate are oral bisphosphonates shown to reduce the risk of hip, vertebral and non-vertebral fractures.[6] Risedronate is available for general prescription in New Zealand without Special Authority approval.

Contraindications to oral bisphosphonates include: abnormalities of the oesophagus that delay oesophageal emptying such as stricture or achalasia; inability to stand/sit upright for ≥30 minutes; and hypocalcaemia.

The most common side effect of oral bisphosphonates is upper gastrointestinal irritation, which affects 20–30% of users. Patients should be advised to take their oral bisphosphonate on an empty stomach. They should swallow their oral bisphosphonate tablet with a full glass of water and stand/sit upright for ≥30 minutes and until after their first food of the day.

There is scant clinical evidence regarding use of oral bisphosphonates in patients with severe renal insufficiency. Consider a reduced dosing frequency in patients with estimated glomerular filtration rate (eGFR) ≤35 mL/min.

Atypical femoral fractures (AFFs) initially develop as stress fractures in the lateral cortex of the femoral shaft and can spontaneously progress to transverse fractures. The incidence of AFFs appears to increase steeply with duration of bisphosphonate use and drops dramatically in the 1–2 years after bisphosphonate discontinuation. For this reason, it is important to periodically review the need for continued bisphosphonate therapy and provide drug holidays for patients requiring therapy for >5 years.

Osteonecrosis of the jaw (ONJ) manifests as an area of exposed bone in the mouth that does not heal within 8 weeks. While ONJ has been associated with bisphosphonate use for the treatment of bone metastases, it is rarely seen in patients treated with oral or IV bisphosphonates for osteoporosis and appears to have an incidence similar to that found in patients with osteoporosis not treated with bisphosphonates. *www.pharmac.govt.nz/Schedule?osq=alendronate

Intravenous bisphosphonate

Zoledronate* is an IV bisphosphonate that reduces risk of hip, vertebral and non-vertebral fractures.[6] In the pivotal clinical trials, zoledronate was administered annually for three years. However, zoledronate's duration of action is considerably longer than one year; therefore, it is common practice to administer the three initial doses at intervals of 18 or 24 months.

Contraindications to zoledronate include: creatinine clearance or eGFR <35 mL/min; marked vitamin D deficiency; and hypocalcaemia.

The most common side effect of zoledronate is post-dose flu-like symptoms (affecting approximately 30% of patients), the majority of which occur within the first 3 days following zoledronate administration and resolve within 3 days. The incidence of these symptoms can be reduced with administration of paracetamol or ibuprofen shortly after the zoledronate dose. These symptoms decrease markedly with subsequent doses of zoledronate (incidence of 1–2%). Ensure adequate hydration.

Vitamin D deficiency should be corrected before the administration of zoledronate. In patients with suspicion of vitamin D deficiency, give oral supplementation (2 x cholecalciferol 50,000 IU) before infusion.

Consider a dose reduction (e.g. to 2.5 or 1 mg[7]) or slower infusion rate (e.g. to 30 to 60 mins) in patients with eGFR 35–50 mL/min.

*www.pharmac.govt.nz/Schedule?osq=zoledronic%20acid

Oestrogen therapy

In women with osteoporosis and within 10 years of menopause, oestrogen therapy may be an appropriate first-line intervention. Risks and benefits of therapy should be explored with the patient. Referral to a secondary care colleague may be helpful to help frame a long-term plan for the patient's osteoporosis management.

Contraindications to oestrogen therapy include: past or acute myocardial infarction or stroke, breast cancer or sex steroid hormone responsive tumours, liver tumours, past venous thromoembotic events (or a hereditary or acquired predisposition to venous thrombosis) and severe hepatic disease.

Common side effects of oestrogen therapy include: vaginal bleeding, fluid retention, breast tenderness, headaches and nausea.

Monitoring

Serum procollagen type I N-terminal propeptide (PINP) measurement

Bisphosphonates reduce bone turnover, which can be assessed by measuring serum PINP. With effective bisphosphonate therapy, PINP levels will decrease to <35 µg/L.

If PINP levels remain ≥35 µg/L after 6 months of oral bisphosphonate treatment, this indicates suboptimal adherence to the bisphosphonate or poor absorption of the bisphosphonate.[8] Switching to an IV bisphosphonate should be considered.

PINP measurement can be organised through the local laboratory, with no time-of-day restrictions for obtaining blood samples.

PINP levels do not usually need to be assessed in patients treated with IV bisphosphonate.

Repeat clinical risk assessment

Follow-up bone densitometry is not recommended at intervals of less than 3 years in most patients. In addition to reproducibility errors in results, a repeat scan in the first few years of therapy will not generally alter management. Repeat BMD assessment should be undertaken 4 to 5 years after initiating bisphosphonate treatment to determine whether treatment should continue.

Duration of treatment and drug holidays

Clinical trials have shown that after 3 to 5 years of bisphosphonate therapy, patients whose femoral T-score has risen above -2.5 and who have not had new fractures are able to discontinue bisphosphonate treatment for up to 5 years without an increase in their future fracture risk. Therefore, remaining off treatment for 4 to 5 years is appropriate for patients meeting these criteria.

Patients with a femoral T-score ≤-2.5 or with new/recurrent fractures should continue on treatment for a second 5-year period. However, there is concern that continuous, long-term bisphosphonate therapy progressively increases the risk of atypical femoral fractures, potentially neutralizing the benefit of ongoing treatment. To address this concern, many clinicians recommend a 1- to 2-year drug holiday at some time between years 5 and 10. Risedronate has a shorter duration of action than other bisphosphonates, so a 1-year break is likely appropriate for that medication.[9,10]

RNZCGP believes that use of PINP in monitoring osteoporosis treatment is not yet proven in clinical practice.

Second-line Therapy

Teriparatide

Teriparatide* is a fragment of parathyroid hormone, administered by once-daily subcutaneous injection, that may be used in patients with established osteoporosis and recurrent fracture and following at least 12 months of antiresorptive therapy.

*www.pharmac.govt.nz/Schedule?osq=teriparatide

Denosumab

Denosumab is a monoclonal antibody directed against RANK-ligand, administered by subcutaneous injection every 6 months, for treatment of osteoporosis. Denosumab is not yet reimbursed in New Zealand.

Other treatments:

Selective estrogen receptor modulators (SERMS)
SERMS (e.g. raloxifene) could be considered as an alternative to oestrogen therapy in postmenopausal women, although raloxifene does not prevent hip or other non-vertebral fractures.

Strontium ranelate
Strontium ranelate is not recommended because of its adverse cardiovascular profile.

References

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Development of the Guidance

The primary objective for the development of Diagnosis and Management of Osteoporosis for New Zealand was to provide clinicians working in both primary and secondary care settings with a user-friendly and highly practical tool to support evidence-based practice. The guidance provides a distillation of the current evidence base and makes practical recommendations on identification of high-risk individuals, diagnostics and treatment for both patients with fragility fractures and those at high-risk of suffering their first fragility fracture.

The guidance development process has been funded by ACC. The criteria for development was outlined in an agreement between ACC and Osteoporosis New Zealand.

To expedite the development process, the following Expert Panel from disciplines central to the management of osteoporosis were invited to join the group. Dr Nigel Gilchrist accepted the position of Chair.

Name	Title
Dr Nigel Gilchrist	Specialist Consultant Physician
Prof Ian Reid	Distinguished Professor of Medicine
Dr Shankar Sankaran	Consultant Geriatrician
Dr David Kim	Consultant Endocrinologist
Dr Alison Drewry	Senior Medical Advisor, ACC
Prof Les Toop	Professor and Head of Department of General Practice
Dr Frances McClure	General Practitioner

Osteoporosis New Zealand provided project management support to assist the Expert Panel wherever possible to develop this guidance.

Medical writer, Juliette Allport of Syntax Scientific Writing Ltd provided excellent freelance medical writing.

This Guidance will be reviewed in 2020 unless new therapeutic options become available prior to that date.

Endorsing organisations

The following learned societies and organisations endorse the Guidance on the Diagnosis and Management of Osteoporosis in New Zealand.

ACC
PREVENTION. CARE. RECOVERY.
Te Kaporeihana Āwhina Hunga Whara

ANZONA
Australia New Zealand Orthopaedic Nurses Association

Australian & New Zealand Society for Geriatric Medicine

ENSA

Fracture Liaison Network New Zealand

Health Quality & Safety Commission New Zealand
Kupu Taurangi Hauora o Aotearoa

The New Zealand Association of Musculoskeletal Medicine

NZOA
New Zealand Orthopaedic Association

New Zealand Rheumatology Association

NEW ZEALAND SOCIETY OF ENDOCRINOLOGY

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