Reducing fracture risk in osteoporosis

Building healthy bones and preventing fractures are key to managing osteoporosis. Identifying fracture risk using a multifaceted approach will help target interventions to those most at risk. This NPS News outlines ways to detect men and women at risk of osteoporotic fracture, and interventions to reduce the risk of new or further fractures.

Identifying risk factors for fractures, bone loss and falls

Assess each person’s individual risk of osteoporotic fracture taking into account the many factors that contribute to this risk. The presence of one major risk factor (such as low bone mineral density [BMD]) does not reliably predict overall fracture risk.¹ Box 1 outlines risk factors: showing which may be modified, which are partly independent of BMD, and which indicate the need for BMD testing.

Some risk factors can be modified (e.g. reducing the risk of falls) while others cannot (e.g. previous fracture). Address modifiable risk factors wherever possible (e.g. remove falls hazards in the home, such as loose rugs or poor lighting). Take into account the person’s medical conditions and/or medicines being taken, and lifestyle factors (such as smoking, alcohol intake and sedentary lifestyle). Medicines can increase fracture risk by weakening bone (e.g. by reducing BMD) or their adverse effects can increase falls risk (see page 2).

Box 1: Risk factors for osteoporotic fractures²⁻⁷

<table>
<thead>
<tr>
<th>Major risk factors</th>
<th>Other significant risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Modifiable</strong></td>
<td><strong>Non-modifiable</strong></td>
</tr>
<tr>
<td>Low BMD</td>
<td>Advanced age (&gt; 65 years)*⁻⁷</td>
</tr>
<tr>
<td>Low body weight*⁻⁷</td>
<td>Female gender</td>
</tr>
<tr>
<td>Oral glucocorticoid therapy*⁻⁷</td>
<td>Early menopause (&lt; 45 years of age)*⁻¹</td>
</tr>
<tr>
<td>Increased risk of falls*⁻⁷</td>
<td>Amenorrhoea (&gt; 6–12 months)*⁻¹</td>
</tr>
<tr>
<td>Cigarette smoking*</td>
<td>Primary hypogonadism¹</td>
</tr>
<tr>
<td></td>
<td>Previous fragility fracture*⁻¹</td>
</tr>
<tr>
<td></td>
<td>Family history of fragility fracture*⁻¹</td>
</tr>
<tr>
<td></td>
<td>Slim build*⁻¹</td>
</tr>
<tr>
<td><strong>Non-modifiable</strong></td>
<td><strong>Modifiable</strong></td>
</tr>
<tr>
<td>Asian or Caucasian race</td>
<td>Regular excessive alcohol intake*</td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td>Prolonged immobilisation</td>
</tr>
<tr>
<td>Inadequate calcium intake</td>
<td>Vitamin D deficiency</td>
</tr>
<tr>
<td>High bone turnover*</td>
<td>Other secondary causes of osteoporosis*⁻¹⁻³</td>
</tr>
</tbody>
</table>

* At least partly independent of BMD.
† Important risk factors that indicate the need for BMD testing in men and women.
‡ For example, rheumatoid arthritis, malabsorption syndromes, primary hyperparathyroidism, clinical hyperthyroidism, chronic renal or hepatic disease, long-term anticonvulsant therapy.
Two internet-based fracture risk calculators

Consider using a fracture risk calculator as part of the overall assessment of individual fracture risk. Two fracture risk calculators are available online which provide estimates of fracture risk in the next 5–10 years. They can be used in men and women with or without a BMD measurement or previous fracture and both incorporate data from the long-running Dubbo study (this was started in 1989 and includes more than 2,500 men and women from Dubbo, NSW, Australia). Neither indicates when to start drug therapy. They differ in:

- which risk factors are assessed (see Box 2).
  For example, FRAX specifies the type of BMD measurement required but does not ask about falls.
- what types of fracture risks are calculated. FRAX estimates the 10-year probability of major osteoporotic fracture (clinical spine [vertebral], forearm, hip or shoulder) while the Garvan Institute fracture risk calculator estimates the 5 and 10-year fracture risk for any osteoporotic fracture.

Box 2: Risk factors assessed by the FRAX and Garvan Institute fracture risk calculators

<table>
<thead>
<tr>
<th>FRAX — WHO fracture risk assessment tool</th>
<th><a href="http://www.sheffield.ac.uk/FRAX/tool.jsp?country=31">www.sheffield.ac.uk/FRAX/tool.jsp?country=31</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age or date of birth (accepts age 40–90 years)</td>
<td>Gender</td>
</tr>
<tr>
<td>Weight (kg) and height (cm) — calculates BMI if no BMD result</td>
<td>Femoral neck BMD (g/cm²) if available*</td>
</tr>
<tr>
<td>Previous minimal trauma fracture</td>
<td>History of hip fracture for either parent</td>
</tr>
<tr>
<td>Current tobacco smoker</td>
<td>Glucocorticoids use</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>Secondary osteoporosis†</td>
</tr>
<tr>
<td>Alcohol (&gt; 3 units/day)</td>
<td>Garvan Institute fracture risk calculator</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (accepts age 60–96 years)</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg) (if no BMD result)</td>
<td>BMD T-score or BMD (g/cm²) if available*</td>
</tr>
<tr>
<td>Minimal trauma fracture since age 50 years‡</td>
<td>Falls over the last 12 months‡</td>
</tr>
</tbody>
</table>

Medicines can increase fracture risk

When assessing fracture risk, consider all current medicines: some may directly act on bone, while others may increase fracture risk by increasing falls risk.

Which medicines weaken bone?

Some medicines can cause bone weakening (see Box 3) by reducing BMD or interfering with calcium and/or vitamin D metabolism. It is not always possible to separate the effect of the medicine from that of the underlying disease for which it has been prescribed.

Box 3: Some medicines which may weaken bone academics

- Glucocorticoids (oral or injectable) (e.g. prednisolone)
- Thyroid hormone (e.g. thyroxine) in excessive doses
- Heparin — with long-term use
- Antiepileptic drugs — only some (e.g. carbamazepine)
- Gonadotrophin-releasing hormone agonists or analogues (e.g. goserelin)
- Aromatase inhibitors (e.g. anastrozole)
- Thiazolidinediones (‘glitazones’)

Which adverse effects increase risk of falls?

Preventing falls is one of the most important strategies for reducing fracture risk. Be alert for people taking medicines known to be associated with increased risk of falls (Table 1) or who are taking > 4 medicines. Both contribute to fracture risk. Consider whether it is possible to stop or decrease the dose of these medicines.

Table 1: Common adverse effects associated with increased risk of falls

<table>
<thead>
<tr>
<th>Class of medicine</th>
<th>Common adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>anticholinergics</td>
<td>blurred vision, dizziness, drowsiness</td>
</tr>
<tr>
<td>antidepressants</td>
<td>blurred vision, dizziness, drowsiness, hypotension, sedation</td>
</tr>
<tr>
<td>antihypertensives</td>
<td>dizziness, hypotension</td>
</tr>
<tr>
<td>antipsychotics</td>
<td>blurred vision, hypotension, sedation</td>
</tr>
<tr>
<td>benzodiazepines</td>
<td>drowsiness, light-headedness, sedation</td>
</tr>
</tbody>
</table>

* Also select the make of DXA scanning equipment used.
† Caused by a disease strongly associated with osteoporosis (e.g. type I diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition, or malabsorption and chronic liver disease).
‡ Indicate 0, 1, 2, 3 or more.
Maintaining bone health throughout the lifespan

Adequate calcium and vitamin D intake, and exercise are important for reaching and maintaining optimal peak bone mass. Calcium and vitamin D absorption decrease with ageing.

Average dietary calcium intake in Australia is well below recommended levels. Enough calcium for most adults can be provided by 3 serves of dairy food per day. The recommended daily intake of calcium for various age groups, as well as the calcium content of dairy products and other foods is available at the Osteoporosis Australia website (www.osteoporosis.org.au). Calcium supplements are only needed when dietary intake is not enough. For more information about calcium supplements, refer to NPS News 53 (available at www.nps.org.au/news_53).

Vitamin D is essential for calcium absorption: ensure adequate vitamin D in people at risk of deficiency, particularly those with osteoporosis. In frail residents of aged care facilities with inadequate calcium and/or vitamin D intake, providing adequate calcium and vitamin D supplementation reduced the risk of hip and other non-vertebral fractures (adequate vitamin D supplementation alone did not achieve this). For more information about vitamin D, refer to NPS News 72 (available at www.nps.org.au/news_72).

Regular low-impact weight bearing exercise (e.g. walking) combined with high-intensity strength (resistance) training conserves BMD in people with osteoporosis. Strength and balance training — alone or as part of a multifaceted falls prevention program — reduces falls risk. A physiotherapist or exercise physiologist can create a program specific to the person’s needs, abilities and interests. Effective exercise programs should progress as fitness and strength levels improve. However, there is no clear evidence for a direct effect of exercise in preventing fractures.

Consider an anti-osteoporotic drug after an osteoporotic fracture

Reduce the risk of further fracture by using anti-osteoporotic drugs after an osteoporotic fracture. People with previous osteoporotic fractures are at increased risk of further fractures: the risk of vertebral fracture is about 4 times higher in women with a previous vertebral fracture than in those without.

Despite this increased risk, less than 30% of Australian postmenopausal women with a previous osteoporotic fracture were taking an anti-osteoporotic drug. Another study showed that only 10% of Australian men who were eligible for a PBS-subsidised bisphosphonate were taking (or had taken) one. Bisphosphonates are suitable for men and women; raloxifene, strontium or denosumab are also options for women.

All anti-osteoporotic drugs reduce fracture risk but differ in their specific data and adverse event profile. However, there are no comparative fracture prevention trials to guide drug choice: choose based on gender, age, medical history and the person’s preference. There are a range of routes and dose regimens (e.g. alendronate can be given daily, weekly or monthly; zoledronic acid is given as an annual intravenous infusion). Refer to NPS RADAR (www.nps.org.au/radar) or the Australian Medicines Handbook for more information.

Duration of therapy

The optimal duration of bisphosphonate therapy is uncertain. Their long-term effects on bones are yet to be determined. Effects such as delayed fracture healing or atypical femoral stress fractures have been rarely reported in long-term users although a causal relationship is unclear. Limited evidence suggests that oral bisphosphonates alendronate or risedronate can be stopped after 5 years in postmenopausal women (there are no data for men) who respond well and are not at high risk of vertebral fractures. Consider stopping if:

- there is a significant increase (≥ 5%) in BMD or no further bone loss
- no fractures occur during drug therapy

Measure BMD 1 year after stopping and assess falls risk. Restart if there is a significant decrease in BMD. Published evidence from randomised controlled studies supports the use of strontium for 5 years (with an additional 3 years’ data in an open label extension study), raloxifene for 4 years and, zoledronic acid or denosumab, each for 3 years. Limit lifetime exposure to teriparatide to 18 months as it has been shown to cause osteosarcoma in animal studies.

For online resources go to: nps.org.au/news_73
Reported long term adverse effects of bisphosphonates

Recent media reports linking bisphosphonates with atrial fibrillation (AF) and oesophageal cancer may have caused concern. The evidence weighs against an increased risk of AF.23,24

Two studies of oesophageal cancer rates using the same database had conflicting results: one found no increase among oral bisphosphonate users25; while the other, with longer follow-up, estimated that 5 years of treatment could increase the risk from about 1 in 1000 to 2 in 1000.26 A UK drug safety review found insufficient evidence to confirm a link, but emphasised the importance of taking bisphosphonates correctly to minimise oesophageal adverse events, and to use them with caution in people with upper gastrointestinal problems or oesophageal abnormalities.27

Osteonecrosis of the jaw is a rare but serious side effect of bisphosphonates. See the NPS fact sheet (www.nps.org.au/healthprof_factsheets) for more information.28

Keep in mind the established benefits of bisphosphonates for preventing fractures when discussing these possible adverse effects with patients. Newer drugs have less accumulated data on long-term adverse effects than bisphosphonates — so a true safety comparison is not possible.

Calcium supplements and MI: the jury is still out

Evidence is conflicting and further studies are needed to clarify whether calcium supplements increase the risk of myocardial infarction (MI). Two meta-analyses found an increased rate of MI among people taking calcium supplements29,30; the estimated number needed to treat with calcium, with or without vitamin D, for 5 years to cause 1 extra MI was 240.30 However, the first meta-analysis was criticised for including unverified patient reports of MI, and the second was questioned because of possible problems with confounding risk factors and the lack of a clear dose–response effect.31,32

Another meta-analysis, using only verified MI data, found no significant increase with calcium supplements, though its smaller dataset could explain this finding.33,34

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References
4. Poole KES, Compston JE. BMJ 2006;333:1251–6
34. Reid IR, Avenell A. J Bone Miner Res 2011;26:452–4.
Citations online at: www.nps.org.au/news/73

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