What's new in osteoporosis management?

Leading the fight in primary care

Ashley Hawarden, Zoe Paskins and Faraz Mughal

Why is osteoporosis important?

Osteoporosis has been defined as a *'progressive systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk'*.[1] However, because microarchitectural deterioration of bone tissue cannot be measured clinically, the description of osteoporosis based on T-score has been accepted as the clinical definition.

The World Health Organization defines osteoporosis as a T-score value for bone mineral density (BMD), measured by dual-energy X-ray absorptiometry (DXA) at the femoral neck, of ≥2.5 standard deviations below the young adult female mean (T-score ≤–2.5).[2] Using this definition, it is estimated that 5.2% of the UK population (approximately 3 755 000 people) are affected.[3] The clinical significance of osteoporosis is fragility fracture, of which there are 527 000 annually in the UK, projected to rise to 665 000 annually by 2034.[3] Fragility fractures impact on individuals and may lead to pain, disability, and reduced quality of life. Osteoporotic fragility fractures are associated with reduced relative survival and, at 12 months post-hip fracture, mortality in the UK is approximately 28%.[4,5] Fragility fractures also impose a significant economic burden on the NHS, costing the UK *c.* £4.5 billion annually, representing approximately 2.4% of total healthcare expenditure.[3]

This clinical practice article provides general practice teams with guidance on fracture risk assessment and osteoporosis drug management informed by the latest evidence, the current authors' experience and expertise, and the National Institute for Health and Care Excellence (NICE)-accredited 2021 National Osteoporosis Guideline Group (NOGG) clinical guideline.[5]

Why has the approach to treatment changed?

Over the past 15 years, there has been a step change in the management of osteoporosis to make treatment decisions based on the concept of fracture risk rather than BMD readings in isolation. This is because most people who sustain fragility fractures do not have osteoporotic range BMD,[6] osteoporosis treatments are effective in people without osteoporotic range BMD,[7] and algorithms that aggregate risk factors (for example, FRAX®) are more effective at predicting a subsequent fracture than BMD alone.[8] This is a nationally endorsed approach that advocates treatment based on high fracture risk even in the absence of BMD measurement.[5]

What does a bone health assessment involve?

A bone health assessment consists of an assessment of lifestyle factors and falls and fracture risk. Blood tests to exclude secondary causes of osteoporosis may also be performed where appropriate.

The purpose of the fracture risk assessment is to guide BMD measurement and prompt timely referral and/or drug treatment. There is a strong recommendation to perform a fracture risk assessment on any postmenopausal female or any male aged ≥50 years with a clinical risk factor for fragility fracture. Important clinical risk factors include low body mass index (BMI), history of fracture, parental history of hip fracture, behavioural factors (smoking, excess alcohol intake, recurrent falls, and inadequate physical activity), medications that increase bone loss (glucocorticoids, aromatase inhibitors, and androgen deprivation therapy), and secondary causes of osteoporosis such as diabetes mellitus, untreated hyperthyroidism, hypogonadism, premature menopause, chronic liver disease, chronic malabsorption, and chronic kidney disease.

Table 1. Summary of oral bisphosphonate therapy

Oral bisphosphonates (co-prescribe with vitamin D[a] +/– calcium[b])		
Evidence for fracture risk reduction	**Side effects**	**Cautions**
Alendronate: vertebral fracture, non-vertebral fracture, hip fracture **Risedronate**: vertebral fracture, non-vertebral fracture **Ibandronate**:[c] vertebral fracture, non-vertebral fracture	**Common** • Reflux, oesophagitis, sore throat (<1 in 10) • Bone, joint, or muscle pain (<1 in 10) • Diarrhoea/constipation (<1 in 10) • Eye inflammation (<1 in 100) • Headache (<1 in 100) **Rare** • Atypical femoral fracture (<1 in 1000) • Osteonecrosis of the jaw (<1 in 1000)	• Renal impairment: avoid alendronate if CrCl <35 mL/minute; avoid risedronate and ibandronate if CrCl <30 mL/minute • Gastrointestinal bleeding • Seek specialist advice if history of osteonecrosis of the jaw or atypical femoral fracture

[a]Supplement vitamin D in all patients aged ≥65 years. If <65 years, test and replace as required. [b]If dietary intake of calcium is inadequate (<700 mg per day) then supplement. A calcium calculator may be helpful. [c]Not licensed in men. CrCl = creatinine clearance.

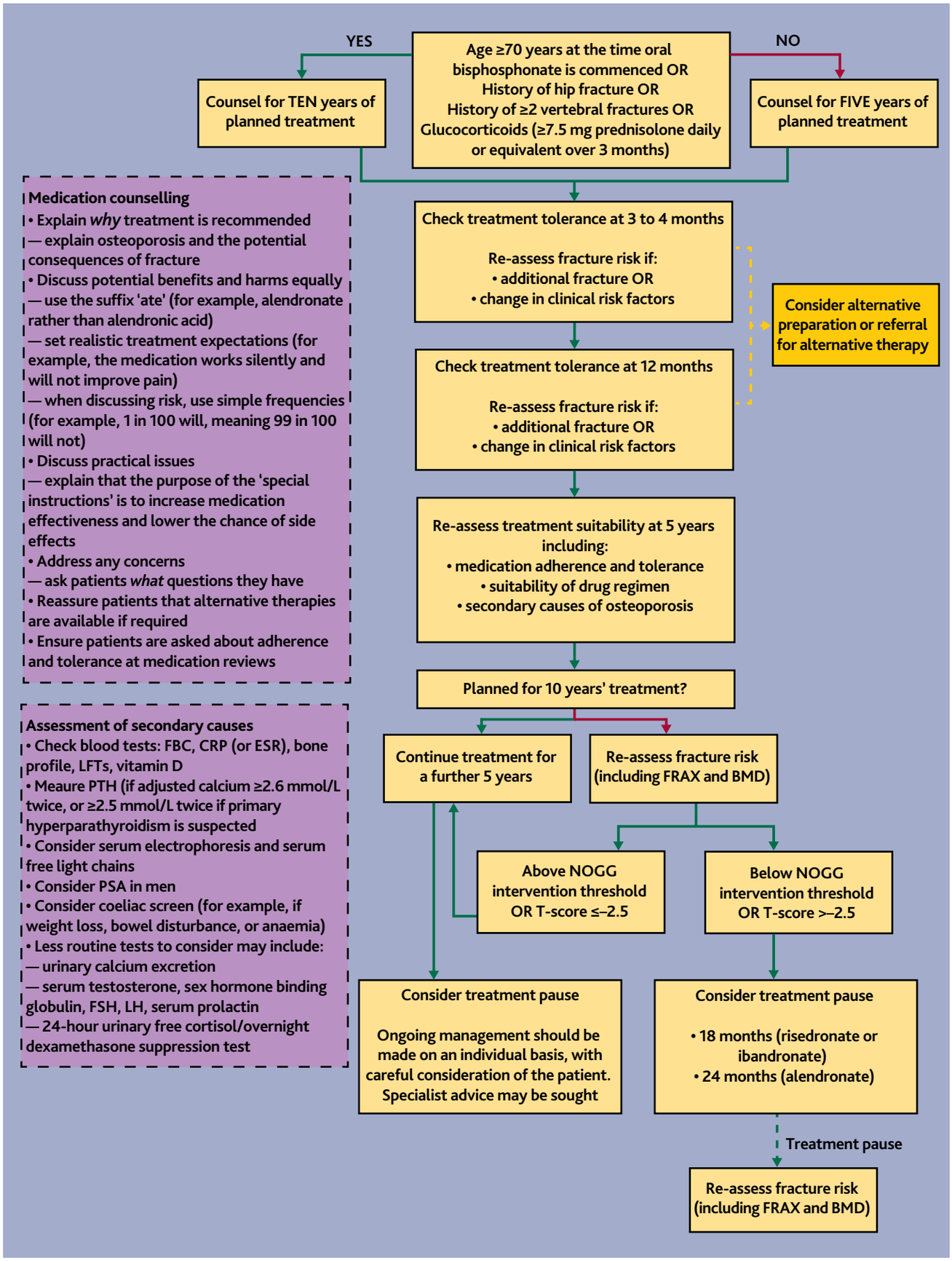

Figure 1. Flowchart for the long-term treatment and monitoring of oral bisphosphonates. Adapted from NOGG guidance.[5] BMD = bone mineral density. CRP = C-reactive protein. ESR = erythrocyte sedimentation rate. FBC = full blood count. FSH = follicle-stimulating hormone. LFT = liver function test. LH = luteinising hormone. NOGG = National Osteoporosis Guideline Group. PSA = prostate-specific antigen. PTH = parathyroid hormone.

Two tools exist, FRAX® and QFracture®, with which to calculate fracture risk; both tools yield different results and cannot therefore be used interchangeably. NOGG advocates using FRAX® because it can incorporate BMD results (which QFracture does not), and the intervention thresholds to guide treatment decisions, recommended in NICE quality standards, are calculated using FRAX® probabilities. However, it is worth noting that neither FRAX® nor QFracture® consider all risk factors and thus scores may underestimate fracture risk in some individuals. In this instance clinical judgement is required and discussion with a specialist (for example, via advice and guidance) may be appropriate.

What are the current drug treatments available for osteoporosis?

Drugs used in the management of osteoporosis are categorised based on their mechanism of action. Antiresorptive drugs are available in tablet (for example, oral bisphosphonates such as alendronate) or injectable (for example, intravenous bisphosphonates such as zoledronate) form and act by inhibiting bone resorption with secondary effects on bone formation. Anabolic drugs (for example, teriparatide) stimulate osteoblastic bone formation with variable effects on bone resorption. Injectable drugs are mostly prescribed in secondary care but denosumab (an antiresorptive) is sometimes prescribed in general practice under shared care agreements.

Historically, the first-line treatment to reduce fracture risk has been an oral bisphosphonate (Table 1). Recent guidance suggests that post-menopausal people with osteoporotic range BMD and a major osteoporotic fracture in the past 2 years would benefit from first-line injectable therapy with romosozumab (a dual anabolic and antiresorptive) to reduce their risk of future fractures.[9] This group of patients would therefore warrant early referral to access treatment with romosozumab.

Who should be considered for referral to specialist care?

Individuals with severe osteoporosis (T-score ≤–2.5 and fragility fracture), especially in the presence of vertebral fracture, and at very high risk of fragility fracture may benefit from anabolic therapy or other injectable treatment. The high-risk groups for which a *consideration* of referral is recommended are:[5]

- a recent (within the last 2 years) vertebral fracture;
- ≥2 vertebral fractures (whenever these have occurred);
- BMD T-score of ≤–3.5;
- treatment with high-dose glucocorticoids (≥7.5 mg/day of prednisolone or equivalent over 3 months); and
- presence of multiple clinical risk factors, particularly in the presence of recent fragility fracture.

In addition, groups that general practice teams may wish to refer for specialist assessment include:

- patients who sustain a fracture despite 2 years of treatment with oral therapy;
- patients who are intolerant of oral treatments;
- patients with contraindications to first-line treatment (for example, a patient with Stage 4 chronic kidney disease (CKD);
- women treated with aromatase inhibitors (for example, anastrozole [Arimidex]) and men treated with androgen deprivation therapy (for example, goserelin acetate (Zoladex)) who are at high risk of fracture; and
- younger men and women with osteoporosis and/or fragility fracture.

How long should treatment be continued?

One of the challenges for non-specialist clinicians has often been determining the duration of osteoporosis therapy. For most patients, oral bisphosphonates can be prescribed for a period of at least 10 years before a treatment pause (Figure 1). Intravenous bisphosphonates are initially prescribed for a period of 3 years and can be continued for up to 6 years in high-risk patients. Denosumab must not be discontinued without specialist consultation because of the risk of rebound vertebral fractures.

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Funding
Ashley Hawarden is funded by a Versus Arthritis Clinical Research Fellowship (ref: 22726). Zoe Paskins is funded by the National Institute for Health and Care Research (NIHR) (Clinician Scientist Award [CS-2018-18-ST2-010]/NIHR Academy). Faraz Mughal is funded by an NIHR Doctoral Fellowship (300957). The views expressed in this article are those of the authors and not necessarily those of the NHS, NIHR, or the Department of Health and Social Care.

Provenance
Freely submitted; externally peer reviewed.

Competing interests
Keele University has received sponsorship from Union Chimique Belge (UCB).

DOI: https://doi.org/10.3399/bjgp24X739641

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It is important to recognise that osteoporosis is a long-term condition for which regular review and monitoring is required. Following the prescription of oral bisphosphonates, it is suggested that adherence and tolerance be checked at 3 months post-initiation and to carry out an annual review thereafter.

Recommended resources

- FRAX® (https://www.fraxplus.org/).
- NOGG (https://www.nogg.org.uk/) — includes information for patients and frequently asked questions for health professionals.
- Royal Osteoporosis Society (https://theros.org.uk) — includes information for patients and healthcare professionals (including learning accredited by the Royal College of General Practitioners); and
- Evidence Based Resources for Osteoporosis (https://erohub.co.uk) — includes information for patients and healthcare professionals (including 'bitesize' clinical guides)

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