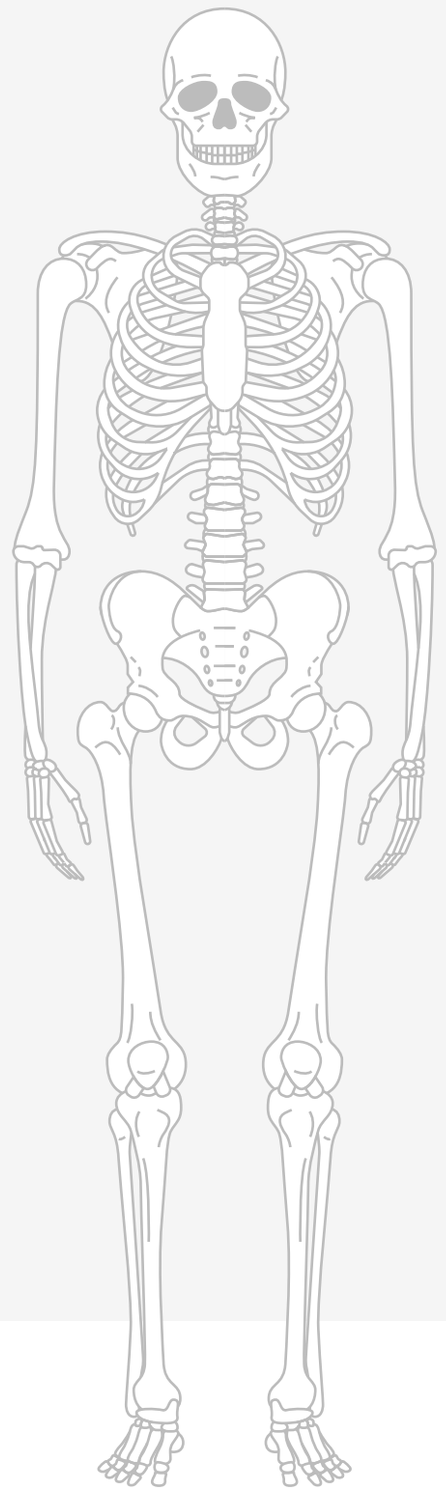
Drug therapy for osteoporosis

Osteoporosis is a process of bone loss, present in almost all individuals older than 50–60 years



Assess:

Age | *Ethnicity* | *Fracture history* | *Bodyweight* | *Bone mineral density (BMD)*

Conditions associated with increased risk of fractures include:

- **Hypogonadism**
- **Increased frequency of falls**
- **Chronic inflammation** causing high levels of osteoclast stimulating cytokines
- **Weight loss** with reduced amounts of anabolic hormones
- **Glucocorticoids reducing bone formation** via apoptosis of osteoblasts and osteocytes

Interventions and treatments

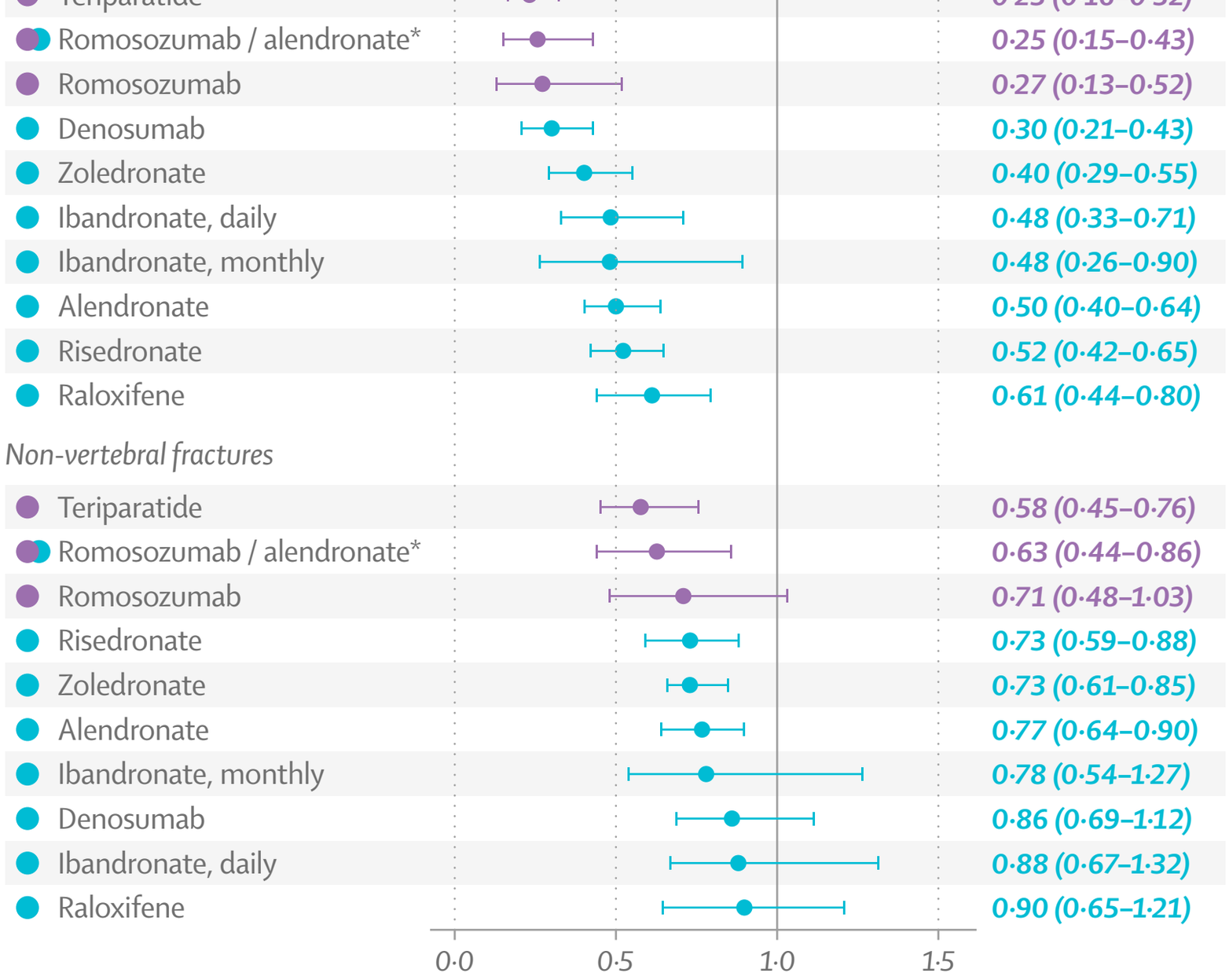
Lifestyle and environmental interventions include:

- **Correcting risk factor** – e.g. stop smoking, moderate alcohol intake, maintain body-mass index >20, minimise glucocorticoid dose where appropriate
- **Managing risk of falls** – e.g. optimise vision, modify home environment, minimise sedative use, prevent postural hypotension
- **Exercise programmes** – e.g. impact plus high-intensity resistance, balance training
- **Protein supplements if malnourished**
- **Preventing vitamin D deficiency**

Drug treatments fall in two main categories:

- **Anti-resorptive agents** – reduce bone resorption and preserve existing bone
- **Anabolic agents** – stimulate bone formation and replace lost bone

Risk of fractures compared with placebo, by treatment



*Romosozumab followed by alendronate

Read the full paper at www.thelancet.com

Reid IR, Billington EO. Drug therapy for osteoporosis in older adults. *The Lancet* 2022. Published online March 12

Considerations and adverse effects of treatments

Anti-resorptive agents

	Registered indications	Cautions and adverse effects	Suggested duration, follow-up
Bisphosphonates			
Alendronate Oral	*70 mg/week:* treatment of postmenopausal, male, and glucocorticoid osteoporosis; *35 mg/week:* prevention of postmenopausal osteoporosis	Take fasting with glass of water, remain upright and fasting for 30 min. Gastrointestinal symptoms may develop in 20-30% (contraindicated in active upper gastrointestinal disease). Safety when eGFR <30–35 mL/min not established. Risk of AFF increases with duration of therapy (<2·5 cases per 10 000 patient-years for treatment duration <5 years). Incidence of ONJ <0·01%	Treat for 5 years followed by a drug holiday of 1–2 years
Risedronate Oral	Treatment or prevention of postmenopausal osteoporosis; treatment of male and glucocorticoid osteoporosis	Take fasting with glass of water, remain upright and fasting for 30 min. Gastrointestinal symptoms may develop in 20-30% (contraindicated in active upper gastrointestinal disease). Safety when eGFR <30–35 mL/min not established. Too few reports of AFF and ONJ to estimate incidence	Treat for 5 years followed by a drug holiday of 0·5–1 years
Ibandronate Oral or intravenous	*150 mg/month orally:* treatment or prevention of postmenopausal osteoporosis; *3 mg every 3 months intravenously:* treatment of postmenopausal osteoporosis	Requires eGFR >30 mL/min. Too few reports of AFF and ONJ to estimate incidence; *Oral:* take fasting with glass of water, remain upright and fasting for 60 min. Gastrointestinal symptoms may develop in 20-30% (contraindicated in active upper gastrointestinal disease); *Intravenous:* inject in 15–30 s. Ensure vitamin D-replete before infusion Self-limited flu-like illness in 30–40% of patients after first dose	Treat for 5 years followed by a drug holiday of 1–2 years
Zoledronate Intravenous	*5 mg/year:* treatment of postmenopausal, male, and glucocorticoid osteoporosis, and fracture prevention after hip fracture; *5 mg every 2 years:* prevention of postmenopausal osteoporosis	Intravenous infusion in 100 mL in at least 15 min. Requires eGFR >30–35 mL/min. Ensure vitamin D-replete before infusion. Self-limited "flu-like illness" in 30–40% of patients after first dose. Too few reports of AFF and ONJ to estimate incidence	With annual dosing, treat for 3–6 years followed by drug holiday of 3–5 years; alternative is to dose every 1·5 years initially, increasing the interval to 2–3 years over time
Selective oestrogen receptor modulator			
Raloxifene Oral	Prevention and treatment of postmenopausal osteoporosis	Venous thromboembolism risk increased up to 3x, but reduced risk of breast cancer	Bone benefit probably does not outlast treatment duration
Mixed steroid receptor agonist			
Tibolone Oral	Prevention of postmenopausal osteoporosis in patients for whom other treatments are contraindicated (UK)	Doubles stroke risk, conflicting evidence of its effects on breast cancer	Bone benefit probably does not outlast treatment duration
Monoclonal antibody against RANKL			
Denosumab Subcutaneous	Treatment of postmenopausal, male, and glucocorticoid osteoporosis, and patients at high fracture risk	Ensure vitamin D-replete before initiation. Have a plan for discontinuation before initiation. Do not delay dose by >1 month. Risk of hypocalcaemia, especially in renal dysfunction. Risk of rebound vertebral fractures. Too few reports of AFF to estimate incidence, probably similar to bisphosphonates	Treatment up to 10 years appears safe and effective; drug holidays are not appropriate; follow with another anti-resorptive agent or romosozumab

Read the full paper at www.thelancet.com

Reid IR, Billington EO. Drug therapy for osteoporosis in older adults. *The Lancet* 2022. Published online March 12

Considerations and adverse effects of treatments, continued

Anabolic agents

	Registered indications	Cautions and adverse effects	Suggested duration, follow-up
Parathyroid hormone analogue			
Teriparatide Subcutaneous	Treatment of postmenopausal, male, and glucocorticoid osteoporosis, and patients at high fracture risk	Mild hypercalcemia in 6–11%, might require dose adjustment; FDA recommends considering >2 years of cumulative use during a patient's lifetime only if fracture risk remains high	Treat for up to 2 years and follow with anti-resorptive agent
PTHrP analogue			
Abaloparatide Subcutaneous	Treatment of postmenopausal osteoporosis in patients at high fracture risk	Inject into the periumbilical region; administer initial doses where the patient can lie down if orthostatic hypotension occurs. Nausea, dizziness, and headache in up to 10% of patients; palpitations in 5%; mild hypercalcaemia in 3%; FDA recommends that cumulative use during a patient's lifetime is not >2 years	Treat for up to 2 years and follow with anti-resorptive agent
Monoclonal antibody against sclerostin			
Romosozumab Subcutaneous	Treatment of postmenopausal osteoporosis in patients at high fracture risk or those who have failed or are intolerant to other available osteoporosis therapy	Contraindicated if myocardial infarction or stroke within the preceding year. Possible increased risk of serious cardiovascular events compared with alendronate treatment; cases of AFF and ONJ reported in pivotal registration trial; real-world incidence unknown	Treat for 12 months and follow with anti-resorptive agent

Reid IR, Billington EO. Drug therapy for osteoporosis in older adults. *The Lancet* 2022. Published online March 12