OSTEOPOROSIS: MOVING BEYOND BISPHOSPHONATES

Bisphosphonates are the mainstay of osteoporosis treatment but as more is elucidated about the underlying pathology of the condition, new drug targets are being investigated.

BY DAWN CONNELLY

8.9m

Worldwide, osteoporosis causes more than 8.9 million fractures annually, resulting in an osteoporotic fracture every three seconds.

Osteoporosis is estimated to affect 200 million women worldwide — approximately one-tenth of women aged 60 years, one-fifth of women aged 70 years, two-fifths of women aged 80 years and two-thirds of women aged 90 years.

£1.73bn

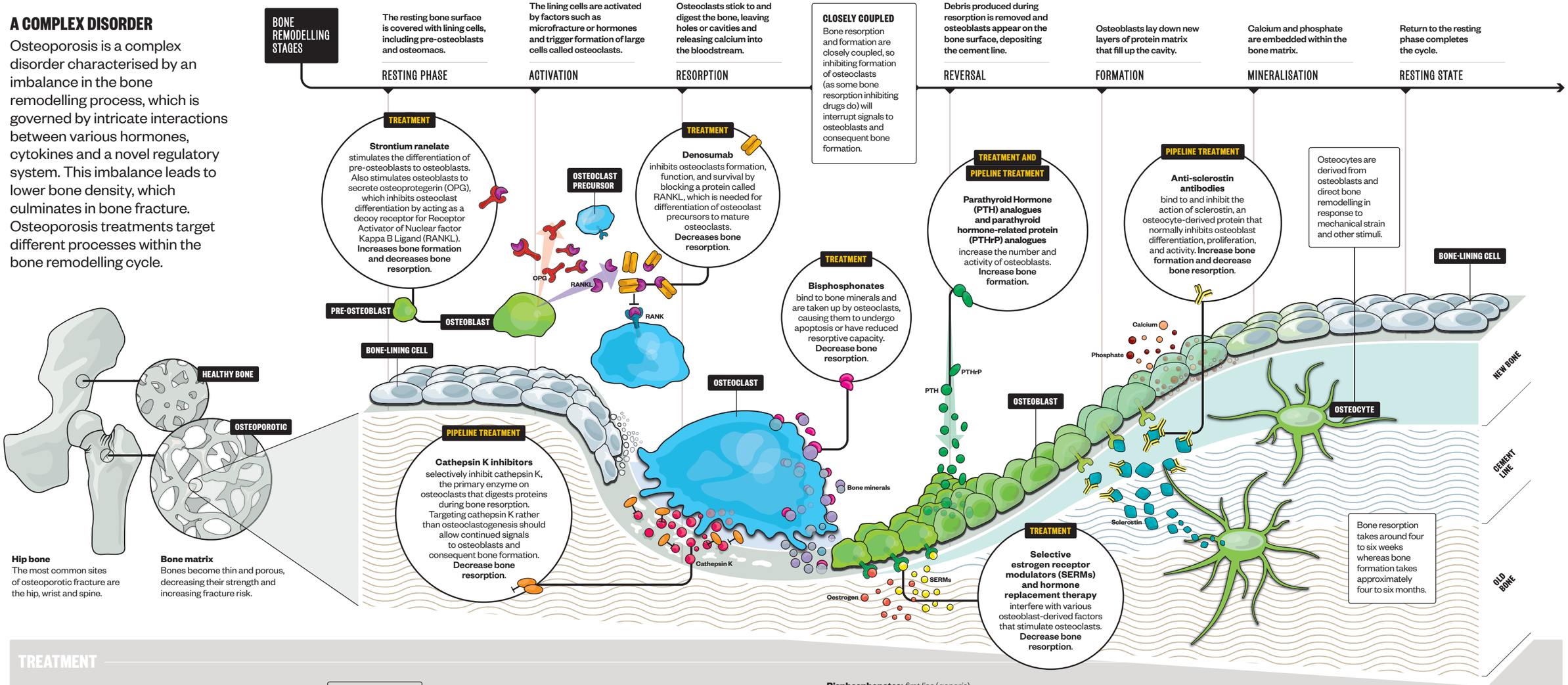
Osteoporosis results in over 200,000 fractures in the UK each year at an annual cost to the NHS of over £1.73bn.

MORTALITY 20%

Approximately 33% of patients suffering a hip fracture are unable to live independently in the year following the fracture and up to 20% die, mainly owing to pre-existing conditions.

A COMPLEX DISORDER

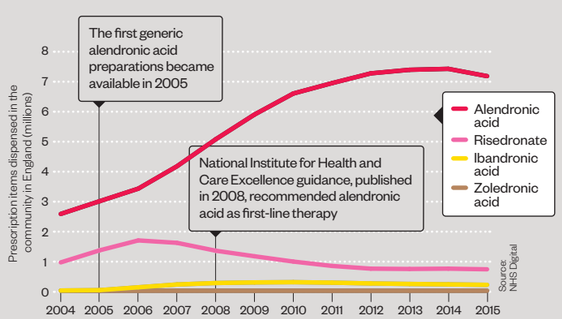
Osteoporosis is a complex disorder characterised by an imbalance in the bone remodelling process, which is governed by intricate interactions between various hormones, cytokines and a novel regulatory system. This imbalance leads to lower bone density, which culminates in bone fracture. Osteoporosis treatments target different processes within the bone remodelling cycle.



TREATMENT

Licensed treatments for osteoporosis reduce the risk of fractures, but are associated with various adverse effects — the risks and benefits should be weighed up for each patient. Several novel treatments are in the development pipeline.

Bisphosphonate usage
The prescribing of bisphosphonates has stagnated or declined following revised labelling for risk of osteonecrosis of the jaw in 2005 and subsequent reports of increased risk of atypical femoral fractures, with increasing publicity in the years thereafter. Better targeting of therapy may also be a factor.



Licensed treatments
Novel pipeline treatments

Reduces risk of:
Vertebral fractures
Non-vertebral fractures
Hip fractures

Bisphosphonates: *first line* (*generic*)

Alendronic acid (daily/weekly tablet)
Risedronate (daily/weekly tablet)
Ibandronic acid (monthly tablet or three-monthly injection)
Zoledronate (Aclasta; yearly injection). Difficult to take orally (patients have to stay upright for 30–60 minutes and cannot eat or drink during this time; they are only 1–5% absorbed so each dose needs to be taken). Associated with rare side effects, including osteonecrosis of the jaw (substantially greater risk with intravenous bisphosphonates) and external auditory canal, atypical fractures, oesophageal reactions (oral use) and hypocalcaemia.

Denosumab (Prolia; six-monthly injection). *Second line*. Human monoclonal antibody. Associated with rare side effects, including osteonecrosis of the jaw, atypical fractures and hypocalcaemia. Supplement with oral calcium and vitamin D.

Strontium ranelate (once-daily sachet). *Restricted to severe osteoporosis where other treatments are not possible*. Patients must avoid food for two hours before and after taking granules. Associated with an increased risk of heart attack and, very rarely, hypersensitivity reactions.

SERMs e.g. **raloxifene** (once-daily tablet). *Second line*. Associated with a small increase in the risk of venous thromboembolism and stroke.

Parathyroid hormone analogues *restricted to those at very high risk, particularly for vertebral fractures*, e.g. **teriparatide** (daily injection). Expensive and has to be given as a daily injection. Maximum treatment is two years (because of the risk of osteosarcoma).

Anti-sclerostin antibody e.g. **romosozumab** (phase III trials, monthly injection). Produced a greater increase in bone mineral density than alendronate and teriparatide.

Synthetic human parathyroid hormone-related protein e.g. **abaloparatide** (phase III trials, daily injection). Is less hypercalcaemic than teriparatide, according to initial trial results.

Cathepsin K inhibitors e.g. **odanacatib** (development discontinued at phase III trial stage in September 2016). Is associated with an increased risk of stroke.

Graphics: AlisdairMacdonald(alisdairmacdonald.co.uk) **Editorialadvisers:** JonTobias,ProfessorofRheumatology,UniversityofBristol;EbrahemJunaid,leadpharmacist medicinesinformation,CambridgeUniversityHospitalsNHSFoundationTrust; **Sources:** InternationalOsteoporosisFoundation;NationalOsteoporosisGuidelineGroup;NHSDigital.