

GUIDELINES FOR THE PREVENTION AND MANAGEMENT OF OSTEOPOROSIS IN ADULTS*

Dr R H Hyatt MB FRCP

Consultant Physician and Orthogeriatrician

Dr Y Demssie MD, FRCP

Consultant Physician in Diabetes & Endocrinology

Mr A Foster MPharm, MGPPhC

Clinical Pharmacist

Dr J Ruddlesdin MSc MRCP

Specialty Registrar in Geriatrics and General Medicine

**These guidelines are intended for use in both primary and secondary care; they will
be revised and updated in January 2015*

CONTENTS	Pages
DEFINITIONS AND EPIDEMIOLOGY	3
WHO TO TREAT?	5
HOW TO TREAT?	7
HOW LONG TO TREAT?	10
WHAT ARE THE RISKS OF TREATMENT?	12
REFERENCES	18
APPENDICES	19
- TREATMENT ALGORITHMS	19
- FRAX [®] WHO FRACTURE RISK ASSESMENT TOOL	22
LOCAL RESOURCES	27

Osteoporosis: Definitions and Epidemiology

Osteoporosis is a progressive, systemic skeletal disorder characterised by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.

The World Health Organization (WHO) has established diagnostic criteria for osteoporosis based on the measurement of bone mineral density (BMD) on dual energy X-ray absorptiometry (DXA) scan, expressed as the T-score, which is the number of standard deviations (SD) below the mean BMD of young adults at their peak bone mass:

- **normal BMD:** T-score of -1 SD or above
- **osteopenia:** T-score of between -1 and -2.5 SD
- **osteoporosis:** T-score of -2.5 SD or below
- **established (severe) osteoporosis:** T-score of -2.5 SD or below with one or more associated fractures ⁽¹⁾.

Fragility fracture (osteoporotic or low trauma fracture) is defined as a fracture sustained as the result of a force equivalent to the force of a fall from a standing height or less ⁽²⁾.

Fragility fractures occur most commonly in the hip, wrist, and vertebrae; and are associated with substantial mortality and morbidity. Fractures of other long bones (eg. humerus, shaft of femur), are also often associated with osteoporosis.

In women aged over 50 years, the lifetime risk of a vertebral fracture is estimated to be one in three, and that of hip fracture one in five.

It is estimated that annually there are 180,000 osteoporosis-related symptomatic fractures in England and Wales. Of these, 70,000 are hip fractures, 41,000 are wrist fractures, and 25,000 are clinical vertebral fractures; current projections indicate that numbers of hip fracture patients will double by 2050.

Postmenopausal women with an initial fracture are at substantially greater risk of subsequent fractures. For instance, a woman with a vertebral fracture has a relative risk (RR) of 4.4 for a further vertebral fracture, 2.3 for a hip fracture, and 1.4 for a wrist fracture ⁽³⁾.

Given that cost-effective, evidence based treatments are available for osteoporosis; this provides the opportunity to help prevent fractures and the associated mortality and morbidity.

These brief guidelines are devised to assist local clinicians in these treatment decisions.

The terms primary and secondary prevention are often used in the context of osteoporosis. In this context, these can be defined as:

Primary prevention: “opportunistic identification of patients at risk of osteoporotic fragility fractures and who would benefit from drug treatment”.

Secondary prevention: “treatment for further prevention of fragility fractures in patients who have osteoporosis and/or have sustained a clinically apparent osteoporotic fragility fracture.”

Some key questions for clinicians are:

Who to treat?

How to treat?

How long to treat?

What are the risks of treatment?

All of these are covered in outline in the algorithms on pages 19 and 20. The following pages and appendices provide more detail which may also be of assistance.

WHO TO TREAT?

Risk (of osteoporotic fracture) stratification can be applied with or without a DXA scan.

Patients at risk can be identified opportunistically using a case-finding strategy based on the finding of a previous fragility fracture (most powerful clinical risk factor for further fracture); or the presence of other significant clinical risk factors (see appendix 4). Case finding can take place in either primary or secondary care.

Patients can be considered as at low (<10% 10 year risk of major osteoporotic fracture), intermediate (10-20% 10 year risk of major osteoporotic fracture), or high risk (>20% 10 year risk of major osteoporotic fracture); (see appendix 1) ⁽⁵⁾.

Probabilities of a major osteoporotic fracture (as well as hip fracture probabilities) can now also be plotted at the National Osteoporosis Guideline Group (NOGG) web site (www.shef.ac.uk/NOGG) available through FRAX[®],

which is an online fracture risk assessment tool developed by the WHO ⁽⁴⁾ (see also appendix 3).

Assessment of the patient includes history (including drug history: see appendix 4,5); and examination. Given the clinical risk factors and secondary causes previously alluded to; further tests will be indicated (see appendix 6).

Corticosteroid induced osteoporosis – An important subcategory of patients who may be at risk of osteoporosis are patients on long-term corticosteroids.

To reduce the risk of osteoporosis doses of oral corticosteroids should be as low as possible, and courses of treatment as short as possible. The risk of osteoporosis may be related to cumulative dose of corticosteroids; even intermittent courses can therefore increase the risk. The greatest rate of bone loss occurs during the first 6–12 months of corticosteroid use and so early steps to prevent the development of osteoporosis are important. Long-term use of high-dose inhaled corticosteroids may also contribute to corticosteroid-induced osteoporosis ⁽⁶⁾.

Individuals at high risk, for example those aged 65 years or over and those with a prior fragility fracture, should be advised to commence bone-protective therapy at the time of starting corticosteroids. Measurement of bone density is not required before starting treatment.

In other individuals, measurement of bone mineral density using dual energy X-ray absorptiometry is recommended for assessment of fracture risk in individuals treated with corticosteroids. Antiresorptive treatment is advised for individuals less than 65 years with a T-score of less than -1.5 who are

commenced on long-term steroids Other secondary causes of osteoporosis should be excluded in individuals with a prior fracture ^(7,8), (see also appendix 6).

Alendronate, risedronate, zoledronic acid and teriparatide are all licensed treatments for corticosteroid-induced osteoporosis ⁽⁸⁾.

Other important subcategories of patients who have or may be at risk of osteoporosis who may not easily fall into the risk stratification model because of the nature of their disease and/or other characteristics.

These include:

- Males
- Pregnant women
- Children
- Patients with CKD
- Patients with malignant disease on chemotherapy
- Patients with coeliac disease and inflammatory bowel disease
- Patients with Downs' Syndrome
- Patients with osteogenesis imperfecta

Management of such patients' osteoporosis may be complex; and should always involve the appropriate sub-speciality.

Bone Mineral Density (BMD) measurement with DXA scan will usually assist complex treatment decisions. Indications for DXA are listed in appendix 7.

HOW TO TREAT?

General management

- Assessment of falls risk; and falls prevention where possible ⁽⁹⁾
- Maintenance of mobility and prescription of appropriate exercise (particularly balance, strength and gait training)
- Identification and correction of nutritional deficiencies, particularly of calcium, vitamin D and protein. Intakes of at least 1000 mg/day of calcium, 800 units of vitamin D and of 1g/kg body weight of protein are recommended.
- Advice on smoking cessation and alcohol intake where applicable.

Pharmacological Treatment

Commonly used agents are listed in appendix 8; as is the strength of evidence to support their use.

The cost of one month's treatment to the local health economy for each of these treatments is listed in appendix 9, along with each drug's licenced indication.

The low cost of generic alendronic acid, which has a broad spectrum of anti-fracture efficacy, makes this the first line treatment in the majority of cases.

Risedronate is now also available generically.

For individuals who are intolerant of alendronic acid or in whom it is contraindicated, other bisphosphonates including annual zoledronate; and other agents such as denosumab, strontium ranelate* or raloxifene may provide appropriate treatment options ⁽¹⁰⁾. The high cost of parathyroid hormone peptides (eg teriparatide) restricts their use to those at very high risk ⁽¹¹⁾.

Alendronate, risedronate, zoledronic acid and teriparatide are also approved for treatment of men at high risk of osteoporotic fracture.

Alendronate, risedronate and teriparatide are also approved for the prevention and treatment of glucocorticoid induced osteoporosis; risedronate for postmenopausal women only.

Use of injectable medications to treat osteoporosis (zoledronic acid, denosumab and ibandronic acid), can be particularly useful for patients for whom adherence to treatment is problematic ⁽¹²⁾.

Other pharmacological interventions for postmenopausal women at risk of fragility fracture include calcitonin, calcitriol, etidronate, raloxifene and hormone replacement therapy.

*Strontium ranelate is restricted to treatment of severe osteoporosis in postmenopausal women at *high risk* of fracture or in men at *increased risk* of fracture. This is because of an increased risk of serious cardiac disorders, including myocardial infarction. Prescribers should assess the patient's cardiovascular risk before commencing treatment ²⁹.

Vitamin D supplementation

Vitamin D is essential for musculoskeletal health as it promotes calcium absorption from the bowel, enables mineralisation of newly formed osteoid tissue in bone and plays an important role in muscle function ⁽³¹⁾. Vitamin D levels should be measured in patients with osteoporosis or suspected osteoporosis and levels should be corrected. Further guidance on the measurement and treatment of vitamin D can be found on the East Lancashire Medicines Management Board (ELMMB) website (<http://www.elmmb.nhs.uk/guidelines/disease-specific-guidelines>) under 'East Lancashire Health Economy Guideline on Diagnosis and Management of Vitamin D Deficiency for Non-Specialists.'

HOW LONG TO TREAT?

It is known that bisphosphonates have a long half life and remain in the skeleton for significant periods of time after administration has ceased. However concerns of side-effects of bisphosphonates (discussed below) have also raised the question of optimum duration of treatment.

Evidence is restricted to longer term (> 3-5 years) treatment with alendronic acid, risedronate and zoledronic acid. Current evidence suggests that 3 years off zoledronic acid therapy (after 3 years of treatment), results in only mild reductions in BMD; though with slight increase in radiological vertebral

fractures in the group who had ceased treatment. These findings were more marked in similar data looking at withdrawal of alendronic acid after 5 years of treatment. More rapid declines in BMD were reported in patients stopping treatment with risedronate and denosumab ⁽¹²⁾.

Patients likely to benefit from treatment beyond this time-frame are those with the lowest BMD (< -2.5 on DXA); and/or patients at high risk of fracture for other reasons.

Factors which can therefore assist in decision making regarding cessation of therapy after 3-5 years are: current BMD, history of recent fracture, existence of other clinical risk factors, compliance, tolerability and history of side-effects. Bone turnover makers may also help; though are currently not routinely available.

For lower risk patients; cautious cessation of therapy after 3 years for zoledronic acid; and five years for alendronic acid seems warranted; with ongoing re-assessment of fracture risk ^(12,13). There are no current data to guide optimum duration of therapy of other agents.

It is very important that the patient is actively involved in the above decision; and the considerable uncertainties frankly discussed.

Duration of bisphosphonate therapy ⁽³⁰⁾

For *postmenopausal women and osteoporosis in men*, generally oral bisphosphonates should be continued for 5 years, with a repeat DXA scan done to re-assess BMD (unless there are vertebral fractures, where bisphosphonate therapy should continue for 10 years). If the repeat DXA scan in the hip or spine shows BMD values in the osteoporotic range (T-score

<-2.5), then continue bisphosphonate therapy for a further 5 years, and then repeat DXA scan. If the BMD values are not in the osteoporotic range (T-score >-2.5), and there have been no further fragility fractures then discontinue the bisphosphonate and repeat the DXA scan in 5 years.

For *glucocorticoid induced osteoporosis*, oral bisphosphonates should be continued while the patient is on glucocorticoid therapy. When the treatment has stopped, a DXA scan then may be considered to assess the need to continue on a bisphosphonate as the treatment threshold for glucocorticoid induced osteoporosis (T-score <-1.5) is lower than that of postmenopausal osteoporosis. A further DXA scan should then be done after 5 years.

WHAT ARE THE RISKS OF TREATMENT?

Full details of side-effects of bisphosphonates and other medications licensed for the prevention and treatment of osteoporosis are listed in the BNF; and can also be found on www.medicines.org.uk; and also the medicines and healthcare products regulatory agency (MHRA) website (www.mhra.gov.uk).

Some additional specific potential side-effects of treatments for osteoporosis have more recently been reported; and warrant addressing in more detail.

Osteonecrosis of the jaw (ONJ) – is defined as exposed bone in the maxillofacial region that is present for at least 8 weeks in patients who have not received radiation to that area. It is reported in patients on bisphosphonates and also denosumab; with an incidence of 1.5-2% in

patients on high doses for skeletal malignancy. It is much less common in patients treated (with oral bisphosphonates) for osteoporosis, the estimated incidence being 1:10,000-100,000 patient years of exposure; which is comparable to that in the general population; though a recent review noted a prevalence of 0.5% (1 patient) in 201 patients treated with IV zoledronic acid for osteoporosis.

Dental disease and trauma are known risk factors for ONJ; therefore significant dental disease should be treated before initiation of bisphosphonate (particularly IV bisphosphonate) or denosumab therapy. It is also recommended that patients are advised to maintain good oral hygiene with regular check-ups; and report any oral symptoms such as dental pain and swelling ^(14,15,16).

Atypical Femoral Fractures (AFF) – In 2008, a Europe-wide review of bisphosphonates and atypical stress fractures concluded that alendronic acid use was associated with an increased risk of atypical stress fractures of the proximal femoral shaft and a warning was subsequently added to alendronic acid product information. A further Europe-wide review concluded:

Atypical femoral fractures have been reported rarely with bisphosphonate therapy, mainly in patients receiving long-term treatment for osteoporosis. Atypical femoral fractures are considered a class effect of bisphosphonates. They can occur after minimal or no trauma, and are often bilateral. They have also recently been reported with denosumab ⁽¹⁷⁾. Some patients experience thigh or groin pain, often associated with features of stress fractures on radiograph, weeks to months before presenting with a completed femoral

fracture. Poor healing of these fractures has been reported. Radiologically; these fractures present as simple transverse or oblique fractures with diffuse cortical thickening and medial beaking.

The overall balance of risks and benefits of individual bisphosphonates in their authorised indications remains favourable. The absolute number of atypical fractures reported is far lower than the number of osteoporotic fractures prevented.

Discontinuation of therapy in patients suspected to have an atypical femur fracture should be considered while they are evaluated, and should be based on an assessment of the benefits and risks of treatment for the individual.

During treatment, patients should be advised to report any thigh, hip, or groin pain. Any patient who presents with such symptoms should be evaluated for an incomplete atypical femoral fracture.

The optimum duration of bisphosphonate/denosumab treatment for osteoporosis has not been established. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of bisphosphonate therapy for individual patients, particularly after 5 or more years of use with oral agents; and 3 or more years of use with parenteral agents (zoledronic acid/denosumab).

To date; these fractures have not been reported with other antiresorptive treatments (eg denosumab) ^(9,18).

Oesophageal cancer – In 1994, erosive oesophagitis was reported in five patients. Subsequently a range of oesophageal lesions related to oral bisphosphonates was reported including ulcerative oesophagitis; oesophageal

stricture and also perforation. Patient information now reflects this; encouraging patients to take oral bisphosphonates with a glass of water in a sitting; not lying position.

These side-effects prompted concerns over risk of oesophageal and other cancers. Data from the US in 2009 suggested an association between bisphosphonate prescriptions and oesophageal cancer rates. A study conducted in the UK's General Practice Research Database, which compared the incidence of oesophageal and gastric cancer in patients who were exposed or not exposed to oral bisphosphonates, however found no increase in the risk of either cancer; and a recently published series of nested case control studies also showed no association with gastro-intestinal cancers.

It does however seem appropriate to alert patients to the need to take oral bisphosphonates as prescribed and when prescribing to carefully consider the balance of risk and benefit; particularly in patients with upper gastro-intestinal problems ^(19,20).

Calcium supplements and cardiovascular disease -

Two papers published in the BMJ in 2010 and 2011 raised concerns about the safety of long term calcium and vitamin d supplements in the doses used to treat osteoporosis^(21,22); and suggested their use in osteoporosis management should be reassessed.

However a subsequent editorial in the same journal stated that the evidence for using calcium and vitamin D supplements as an adjunct to bisphosphonates in the treatment of osteoporosis was reassuring, both in terms of cardiovascular safety and improved survival ⁽²³⁾.

This remains a controversial area therefore. A further editorial suggested that there is no role for calcium and vitamin D supplements in fitter post-menopausal women; and that they should be used in older; frailer people; particularly those who are housebound and/or institutionalised; based on previously documented reduction in hip fracture in this situation and the increasing prevalence of calcium and vitamin D subnutrition in this situation. Correction of vitamin D deficiency prior to parenteral administration of antiresorptives (eg zoledronic acid and denosumab) was also advised ⁽²⁴⁾.

Other side-effects – Renal toxicity is reported with intravenous zoledronic acid; with reports of renal impairment and renal failure, especially in patients with pre-existing renal dysfunction or other risk factors. It is advised that renal function be measured before each dose, and patients should be adequately hydrated before treatment. Oral bisphosphonates are not recommended to be given to patients with creatinine clearance less than 30-35 ml/min; though reports of adverse renal outcomes with oral bisphosphonates are sparse ^(25,26).

Hypocalcemia has been reported after treatment with IV zoledronic acid and denosumab. Severe symptomatic hypocalcaemia has been reported in patients receiving denosumab 120 mg (used for skeletal metastases); or 60 mg (used for osteoporosis). Some of these cases were fatal in patients receiving the 120 mg dose; and were more common in patients with severe renal impairment. Although hypocalcaemia most commonly occurs within the first 6 months of treatment, it may occur at any time during treatment. It is

strongly recommended that hypocalcaemia and vitamin D deficiency are corrected before initiating treatment with these agents ⁽²⁷⁾.

Other reported side-effects with bisphosphonates include gastro-intestinal symptoms, musculo-skeletal pains and an acute phase reaction after zoledronic acid infusion. These are usually not severe; and do not usually limit prescribing.

The benefits of antiresorptive treatment for fractures prevention in patients at high risk have been confirmed in many large trials recruiting thousands of patients ⁽²⁸⁾.

The above potential side-effects emphasise the importance of targeting treatment to high risk individuals and avoiding long-term treatment in individuals at low risk.

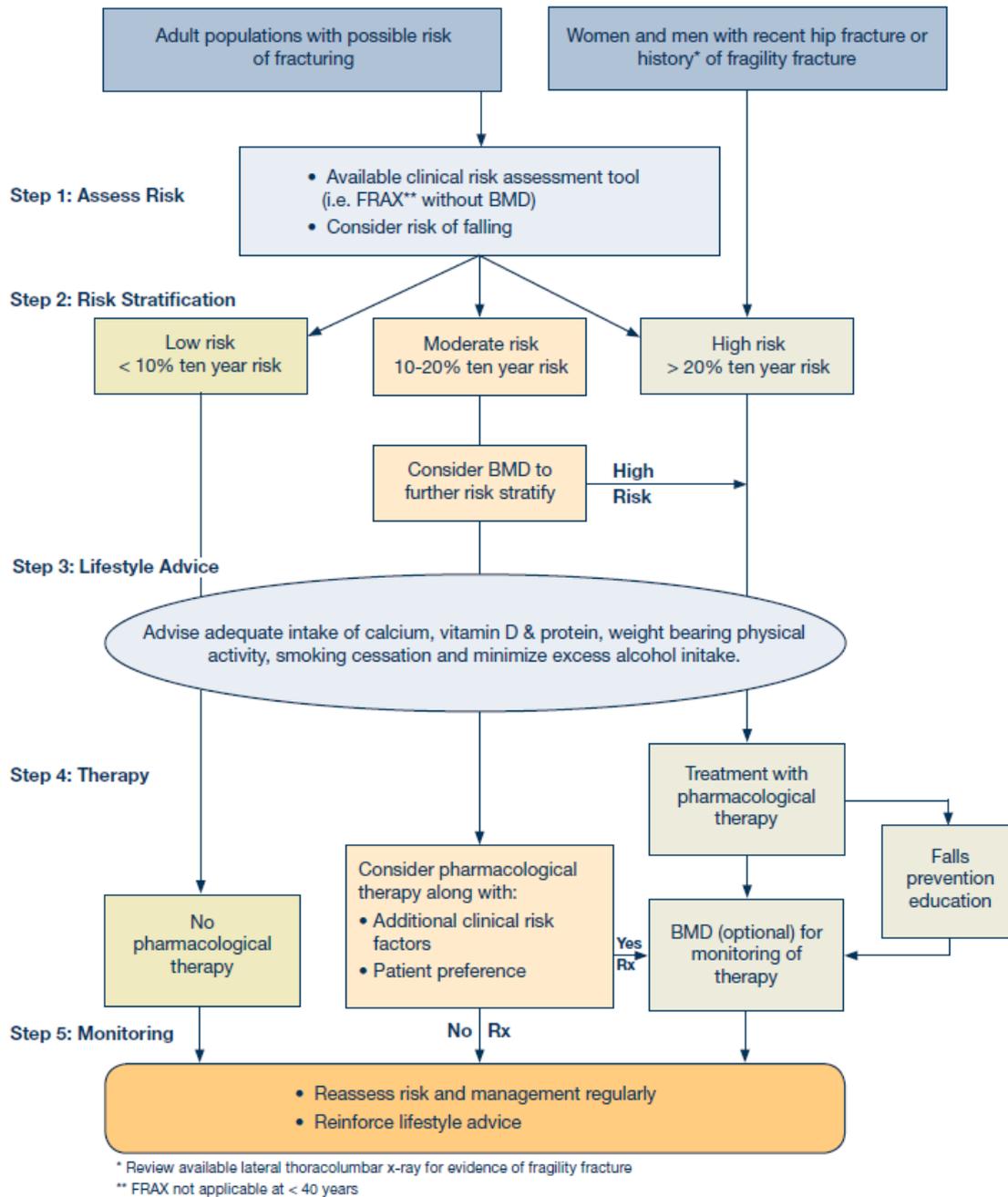
References

1. Assessment of Fracture Risk and its Application to Screening for postmenopausal Osteoporosis. Report of a WHO Study Group. Geneva: WHO; 1994.(Technical Report Series 843).
2. Management of Osteoporosis: A National Clinical Guideline. SIGN 71; 2003
3. NICE technology appraisal guidance 160/161 (amended) Jan 2011
4. NOGG/FRAX; (www.shef.ac.uk/NOGG)
5. Osteoporosis: Diagnosis, Treatment and Fracture Prevention; British Columbia Medical Association; 2011
6. BNF Jan 2013
7. Glucocorticoid-induced osteoporosis. A concise guide to prevention and treatment. BTS/NOS/RCP 2002
8. Osteoporosis: advances in assessment and drug therapy; ARC UK; 2012
9. AGS/BGS Clinical Practice Guideline 2010
10. NICE technology appraisal guidance 204, Oct 2010
11. Clinical practice guidelines for the use of parathyroid hormone in the treatment of osteoporosis. Hodsmann et al; CMAJ, 2006; 175(1), 48
12. Risk Assessment and Treatment of Osteoporosis, Compston J; Clin Med 2012, vol12, 6: s2-5
13. Continuing Bisphosphonate Treatment for Osteoporosis: for whom and for how long? Black D et al; NEJM 366; 22, 2051-2054; 2012
14. Osteonecrosis of the Jaw; Ryan et al, Postgrad Med J 2009; 85: 674-677
15. Incidence of Serious Side-effects of IV Bisphosphonate: A Clinical Audit; Powell D et al; QJM 2012; 105: 965-971
16. MHRA/ Drug Safety Update; Nov 2009
17. MHRA/ Drug Safety Update; Feb 2013
18. MHRA/Drug Safety Update; Jun 2011
19. Oral bisphosphonates and oesophageal cancer; Wysovsky D, BMJ 2010;341:c4805
20. Exposure to bisphosphonates and risk of GI cancers. Vinogradova et al; BMJ 2013; 356:f114
21. Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis. Bolland MJ, et al. BMJ 2010;341:c3691
22. Calcium supplements with or without vitamin D and risk of cardiovascular events. Bolland MJ, et al., BMJ 2011;342:d2040
23. Do calcium plus Vitamin D supplements increase the risk of cardiovascular disease? Abrahamson B, Sahota O; BMJ 2011;342:d2080
24. Aspray TJ, Francis RM; Calcium and Vitamin D supplementation and cardiovascular risk. Maturitas 69 (2011) 285-286
25. MHRA/Drug Safety Update; April 2010
26. Long-Term Use of Bisphosphonates in Osteoporosis; Watts N, Diab D; J Clin Endocrinol Metab, April 2010, 95(4):1555–1565
27. MHRA/ Drug Safety Update; Oct 2012
28. Anti-Hip Fracture Efficacy of Bisphosphonates, Nguyen N et al; JBMR, vol 21,1,2006
29. MHRA Drug Safety update volume 6, issue 9, April 2013. Strontium ranelate (Protelos): risk of serious cardiac disorders – restricted indications, new contraindications, and warnings.
30. East Lancashire Medicines Management Board – Guidelines for management of patients taking long term bisphosphonate therapy. March 2013.
31. National Osteoporosis Society - Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. April 2013.

Appendix 1

Recommendations for evaluation and management of osteoporotic and fragility fracture risk

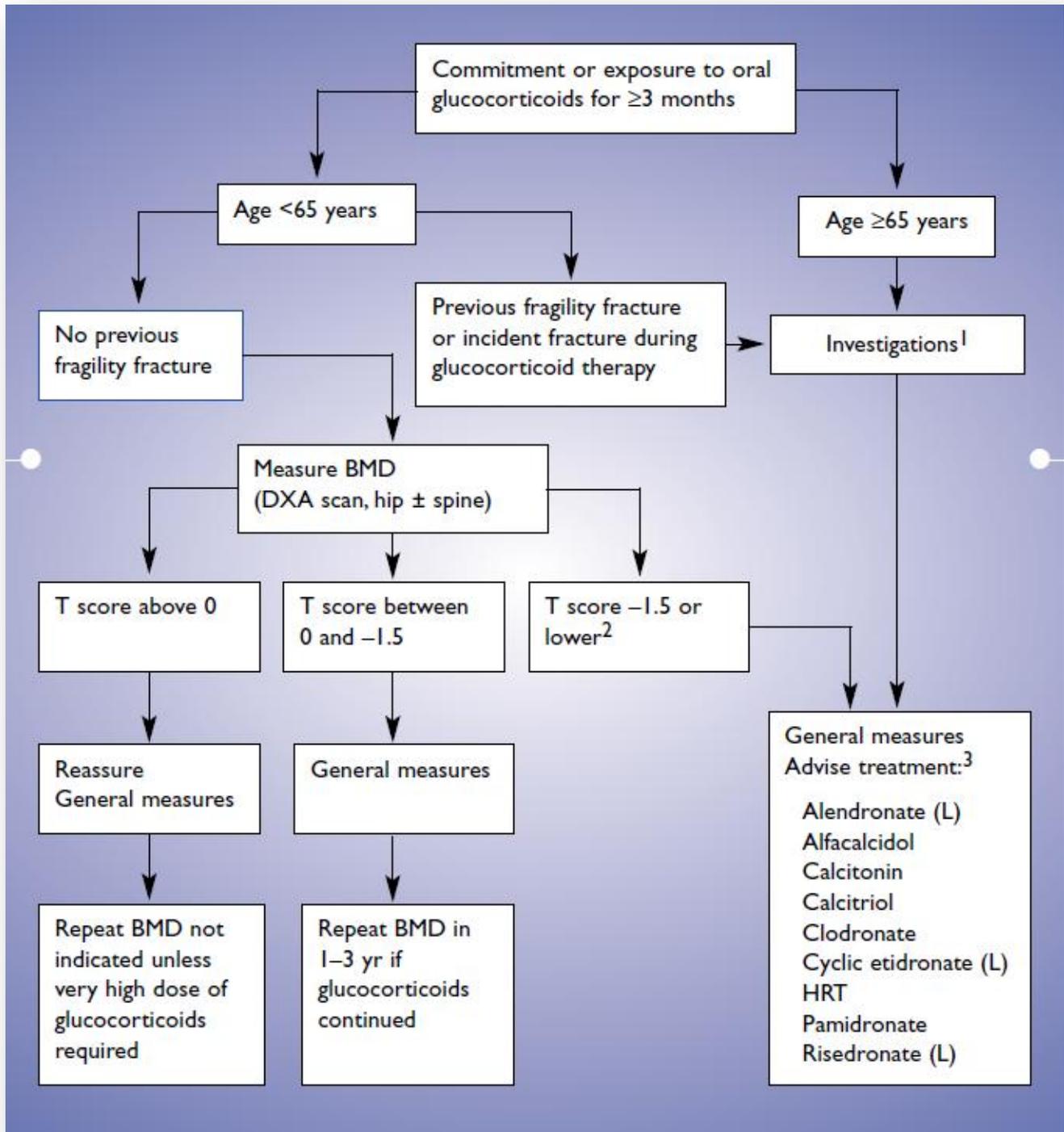
Taken from Osteoporosis: Diagnosis, Treatment and Fracture Prevention.
British Columbia Medical Association ⁽⁵⁾



Appendix 2

Management of glucocorticoid-induced osteoporosis in men and women

Taken from Glucocorticoid-induced osteoporosis. A concise guide to prevention and treatment by The Royal College of Physicians, December 2002 ⁽⁷⁾.



appendix 2, continued

Fragility fracture

- ▶ Defined as a fracture occurring on minimal trauma after age 40 years and includes forearm, spine, hip, ribs and pelvis

General measures

- ▶ Reduce dose of glucocorticoid when possible
- ▶ Consider glucocorticoid-sparing therapy, eg azathioprine, if appropriate
- ▶ Consider alternative route of glucocorticoid administration
- ▶ Recommend good nutrition especially with adequate calcium and vitamin D
- ▶ Recommend regular weight-bearing exercise
- ▶ Maintain body weight
- ▶ Avoid tobacco use and alcohol abuse
- ▶ Assess falls risk and give advice if appropriate

¹In patients with previous fragility fracture:

- ▶ FBC, ESR
- ▶ Bone and liver function tests (Ca, P, alk phos, albumin, ALT/γGT)
- ▶ Serum creatinine
- ▶ Serum TSH.

If indicated:

- ▶ Lateral thoracic and lumbar spine X-rays
- ▶ Serum paraproteins and urine Bence Jones protein
- ▶ Isotope bone scan
- ▶ Serum FSH if hormonal status unclear (women)
- ▶ Serum testosterone, LH and SHBG (men)
- ▶ Serum 25OHD and PTH
- ▶ BMD if monitoring required.

²Consider treatment depending on age and fracture probability.

³Treatments listed in alphabetical order. Vitamin D and calcium are generally regarded as adjuncts to treatment. HRT: oestrogen in postmenopausal women and testosterone in men. (L) indicates that the agent is licensed for glucocorticoid-induced osteoporosis.

Key to abbreviations

ALT = alanine transferase; FBC = full blood count; 25OHD = 25-hydroxovitamin D; BMD = bone mineral density; FSH = follicle-stimulating hormone; PTH = parathyroid hormone; ESR = erythrocyte sedimentation rate; γGT = gamma glutamyl transferase; SHBG = sex hormone binding globulin; LH = lutenising hormone; TSH = thyroid-stimulating hormone

With regards to licenced bisphosphonates in the East Lancashire Health Economy, the first line drug is Alendronate, followed by Risedronate, then Etidronate (Didronel PMO).

Appendix 3:

FRAX[®] - World Health Organisation Fracture Risk Assessment Tool ⁽⁴⁾

Country: **UK** Name/ID: About the risk factors [i](#)

Questionnaire:

1. Age (between 40-90 years) or Date of birth
 Age: Date of birth: Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

5. Previous fracture No Yes

6. Parent fractured hip No Yes

7. Current smoking No Yes

8. Glucocorticoids No Yes

9. Rheumatoid arthritis No Yes

10. Secondary osteoporosis No Yes

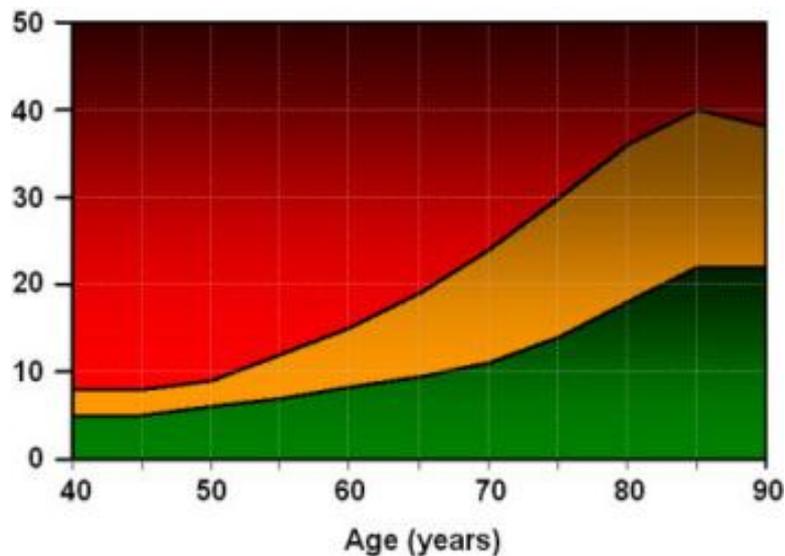
11. Alcohol 3 or more units per day No Yes

12. Femoral neck BMD (g/cm²)
 Select DXA

Weight Conversion
 Pounds kg

Height Conversion
 Inches cm

00848489
 Individuals with fracture risk assessed since 1st June 2011



NOGG treatment guidance: This is derived from data inputted in the calculation tool. A cross will appear in the relevant section of the above graph. Red = treat; Amber = Measure BMD; Green = lifestyle advice and reassurance. The Y axis plots the percentage 10 year risk of major osteoporotic fracture.

Appendix 4:

Clinical risk factors, medications, and medical conditions associated with osteoporosis ^(2,6)

Drugs	Conditions*	Clinical risk factors
Glucocorticoids*	RA/Ank.spondylitis/SLE	Age/female sex**
Cytotoxic drugs	Hypogonadism	Previous fragility fracture*
Phenobarbitone/Phenytoin	AIDS/HIV	Low-BMI*
GnRH agonists	Anorexia nervosa	Early menopause (<45yrs)
Long-term heparin	Organ transplantation	Recurrent falls
Excess Thyroxine	Multiple myeloma	Current smoking *
Total Parenteral Nutrition	Female athlete triad syndrome	Excess alcohol *
	COPD	Family history of fragility #
	Hyperparathyroidism	Long-term poor calcium intake
	Type 1 diabetes	
	Thyrotoxicosis	
	IBD	
	Chronic liver disease	
	Coeliac disease	
	Malabsorption	
	Previous gastrectomy	
	Haemachromatosis	
	Spinal cord injury/immobility	
	Multiple sclerosis	

BMI = body mass index; COPD = chronic obstructive pulmonary disease; DXA = dual X-ray absorptiometry; GnRH = gonadotrophin releasing hormone; IBD = inflammatory bowel disease; PBC = primary biliary cirrhosis; RA = rheumatoid arthritis; SLE = systemic lupus erythematosus.

** these risk factors are utilised by the FRAX tool; to derive 10 year fracture risk. DXA may be added but is optional.*

Appendix 5:

Other medications that may contribute to bone loss*

- Anticoagulants - heparin, warfarin
- Anticonvulsants - carbamazepine, phenytoin
- Aromatase inhibitors, anastrozole, letrozole, exemestane
- Depo Medroxyprogesterone Acetate
- Lithium
- Proton Pump Inhibitors
- Selective serotonin reuptake inhibitors
- Tacrolimus
- Thiazolidindiones - *pioglitazone, (rosiglitazone – discontinued)*

*This is not a complete list of medications.

Appendix 6:

Investigations for Secondary Causes of Osteoporosis*

- FBC, ESR, U&E, LFT, bone biochemistry,
- TSH
- Vitamin D and PTH levels
- Serum electrophoresis/ urine for Bence Jones protein
- Coeliac screen/ Duodenal biopsy
- Testosterone/LH/FSH, prolactin in men
- Oestradiol, LH/FSH, Prolactin in women
- Isotope Bone scans (for suspected malignancy)

* Referral to relevant speciality should be made when a secondary cause of osteoporosis is identified.

Appendix 7:

Indications for DXA scanning

- DEXA is **not** currently recommended for population screening.
- DEXA **is** recommended for individuals with clinical risk factors to confirm whether or not treatment is required.

DXA should be considered in the following groups of patients:

- Previous low trauma fracture – if uncertain of diagnosis
- Chronic oral corticosteroid use for 3 months or more
- Generalised radiographic osteopenia
- Low BMI (<19kg/m²)

- Loss of height
- Family history of osteoporotic fracture (esp. maternal hip)
- Untreated hypogonadism
- Premature menopause < 45 years
- Early hysterectomy < 45 years
- Prolonged amenorrhoea (natural or drug induced)

DXA may not be necessary or possible in the following categories of patients:

- Females over the age of 75 years; 70% will be diagnosed as osteoporotic by BMD measurement. If a patient over 75 has had a fragility fracture, they may be treated with anti-resorptive therapy (based on the advice in NICE TAG 161) (1).
- Patients receiving chronic oral corticosteroid therapy for >3 months if over 65yrs and/or pre-existing fragility fracture should receive prophylactic therapy.
- Severely cognitively impaired patients and/or severely physically frail patients may not be able to comply with the scan or with medication. This requires an individual assessment.
- It is generally not necessary to repeat a DXA at less than 3 year intervals.

Appendix 8:

Approved evidence based pharmacological interventions for fracture prevention when given with calcium and vitamin D in postmenopausal women with osteoporosis and/or increased fracture risk ⁽⁹⁾.

	Vertebral fracture	Non-vertebral fracture	Hip fracture
Alendronate	A	A	A
Risedronate	A	A	A
Zoledronate	A	A	A
Denosumab	A	A	A
Teriparatide	A	A	nae
Ibandronate	A	A ¹	nae
Raloxifene	A	nae	nae
Strontium Ranelate	A	A	A ¹

- A = approved
- nae = not adequately evaluated
- ¹ = evaluated in subsets of patients (post-hoc analysis)

Appendix 9:

Indications, licenced doses and approximate monthly cost of commonly prescribed medications (East Lancashire Health Economy)

Drug and licenced dose	Approximate monthly cost of medication	Licenced indication ¹		
		Post-menopausal women	Men at increased risk	Steroid-induced
Adcal D3 chewable tablets, 2 tablets daily	£3.65	A calcium and vitamin D supplement should always be co-prescribed		
Adcal D3 caplets, 4 caplets daily	£3.65			
Calcichew D3 Forte chewable tablets, 2 tablets daily	£4.24			
Calfovit D3 sachets, 1 sachet daily	£4.32			
Alendronate 70mg weekly	£0.91	Yes	No ²	No ²
Risedronate 35mg weekly	£1.20	Yes	Yes	No
Risedronate 5mg daily	£13.82	Yes	No	Yes ³
Ibandronic acid 150mg monthly	£7.92	Yes	No	No
Strontium Ranelate sachets 2g daily	£27.08	Yes	Yes	No
Raloxifene 60mg daily	£17.06	Yes	No	No
Teriparatide s/c injection 20mcg daily	£271.88	Yes	Yes	Yes
Zoledronic acid 5mg every 12 months	£11.92 ⁵	Yes	Yes	Yes
Denosumab 60mg every 6 months	£30.50 ⁶	Yes	No ⁴	No

- 1- It is however the case that sometimes these medications are prescribed off-licence, or not strictly according to licence; however the rationale for this should be carefully documented, and/or guidance from medicines management and/or specialists in secondary care should be sought under these circumstances.
- 2- The licenced dose of Alendronic acid for osteoporosis in men or corticosteroid induced osteoporosis is 10mg daily. This is non-formulary in the East Lancashire Health Economy.
- 3- Risedronate 5mg daily is licenced for corticosteroid induced osteoporosis in women only.
- 4- Denosumab is licenced for bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures.
- 5- Zoledronic acid cost calculated from £143 once yearly
- 6- Denosumab cost calculated from £183 twice yearly

Cost of drug data taken from Drug Tariff April 2013

ELHT hospital contract prices for Teriparatide, Zoledronic acid and Denosumab (April 2013)

Local Resources

Dr Hyatt's Secretary: Sheila Woolstencroft & Jennifer Ashworth
Tel: 01254 732853
e-mail: sheila.woolstencroft@elht.nhs.uk
e-mail: jennifer.ashworth@elht.nhs.uk

Dr Demssie's Secretary: Gemma Nutter
Tel: 01254
e-mail: gemma.nutter@elht.nhs.uk

East Lancs Hospitals NHS Trust Medicines Information: ext: 13004

FRAX/NOGG: <http://www.shef.ac.uk/FRAX/>

UK Electronic Medicines Compendium (EMC) www.medicines.org.uk:
this website contains a summary of product characteristics (SPC); and patient information leaflets (PIL), for all medications licensed in the UK

Medicines and Healthcare Products Regulatory Agency (MHRA)
www.mhra.gov.uk.