

Guidelines on Management of Osteoporosis

Introduction

These guidelines take into account recommendations from the DH Guidance on Falls and Fractures (Jul 2009), NICE Technology appraisals for Primary and Secondary Prevention (updated January 2011) and interpreted locally, National Osteoporosis Guideline Group (NOGG) and local decisions on choice of drug treatment.

The recommendations in the guideline should be used to aid management decisions but do not replace the need for clinical judgement in the care of individual patients in clinical practice.

Diagnosis of osteoporosis

The diagnosis of osteoporosis relies on the quantitative assessment of bone mineral density (BMD), usually by central dual energy X-ray absorptiometry (DXA). BMD at the femoral neck provides the reference site. It is defined as a value for BMD 2.5 SD or more below the young female adult mean (T-score less than or equal to -2.5 SD). Severe osteoporosis (established osteoporosis) describes osteoporosis in the presence of 1 or more fragility fracture. Diagnostic thresholds differ from intervention thresholds for several reasons. Firstly, the fracture risk varies at different ages, even with the same T-score. Other factors that determine intervention thresholds include the presence of clinical risk factors and the cost and benefits of treatment.

Investigation of osteoporosis

The range of tests will depend on the severity of the disease, age at presentation and the presence or absence of fractures. The aims of the clinical history, physical examination and clinical tests are to:

- Exclude diseases that mimic osteoporosis (e.g. osteomalacia, myeloma).
- Identify the cause of osteoporosis and contributory factors.
- Assess the risk of subsequent fractures.
- Select the most appropriate form of treatment.

Procedures that may be relevant to the investigation of osteoporosis are shown in Table 1.

Table 1 Procedures proposed in the investigation of osteoporosis

All patients

- History and physical examination
- FBC
- ESR (if raised measure serum paraproteins and urine Bence Jones protein)
- Bone and liver function tests (Ca, P, Alk phos, albumin, ALT/GGT)
- Serum creatinine

Additional tests if indicated from the history

- TFT
- Serum 25OH Vit D and PTH
- Serum testosterone, LH, FSH and SHBG, PSA (men)
- 24 hour urinary cortisol/dexamethasone suppression test
- Endomysial and/or tissue transglutaminase antibodies (coeliac disease)
- Lateral radiographs of lumbar and thoracic spine/DXA-based vertebral imaging
- Isotope bone scan
- Bone densitometry (DXA)

SHBG – sex-hormone binding globulin

FSH – follicle stimulating hormone

LH – luteinising hormone

Other investigations, for example bone biopsy and genetic testing for osteogenesis imperfecta, are restricted to specialist centres.

Clinical risk factors

At present there is no universally accepted policy for population screening in the UK to identify individuals with osteoporosis or those at high risk of fracture. Patients are identified opportunistically using a case-finding strategy on the finding of a previous fragility fracture or the presence of significant clinical risk factors (CRFs). Some of these risk factors act independently of BMD to increase fracture risk (Table 2) whereas others increase fracture risk through their association with low BMD (e.g. some of the secondary causes of osteoporosis in Table 2).

Table 2 Clinical risk factors used for the assessment of fracture probability

Previous fragility fracture, particularly of the hip, wrist and spine including morphometric vertebral fracture

Current glucocorticoid treatment (any dose, by mouth for 3 months or more)

Parental history of hip fracture

Female hypogonadism

- post menopause
- untreated premature menopause
- drug or surgically induced menopause
- premenopausal amenorrhoea (>6months, exclude pregnancy)

Low body mass index (<19kg/m²)

Caucasian/Asian origin

Current smoking

Alcohol intake of 3 or more units daily

Male hypogonadism

Drugs associated with osteoporosis:

- Long term heparin
- Anticonvulsants
- Antipsychotics
- Depo-provera > 2yrs treatment
- Aromatase inhibitors, GnRH analogues

Secondary causes of osteoporosis including:

- Rheumatoid arthritis
- Untreated hypogonadism in men and women
- Prolonged immobility
- Organ transplantation
- Type I diabetes
- Hyperthyroidism
- Gastrointestinal disease
- Chronic liver disease
- Chronic obstructive pulmonary disease

Falls*

* Not presently accommodated in the FRAX algorithm

DEXA eligibility criteria

Either: One key risk factor:

- Low trauma fracture (clinical fractures or radiological evidence of vertebral fractures) in:
 - all men
 - women aged 75 or less (in women over 75 years treat diagnostic dexamethasone not needed)
- Patients in intermediate risk factor group as outlined by NOGG (FRAX®/WHO algorithms see below)
- Planned or past systemic steroid (any dose >3 months) in patients below the age of 65 (treat over 65 yr olds without dexamethasone)

Or: For patients < 75yrs without these key risk factors at least 2 other risk factors:

(NB: women >75yrs with 2 other risk factors can be treated for osteoporosis without need for diagnostic dexamethasone. For men > 75 do FRAX analysis as may still be at intermediate risk and needing a dexamethasone).

- Family history especially parental hip fracture <75 Years
- Premature menopause (<45 yrs)
- Hypogonadism
- >6 months amenorrhoea
- Low BMI (< 19 kg/m²)
- Prolonged immobility
- Excess alcohol intake
- Radiological osteopenia
- Diseases associated with osteoporosis
 - Chronic Inflammatory Diseases such as rheumatoid arthritis and inflammatory bowel disease; Malabsorption e.g. coeliac disease; Chronic liver disease; Anorexia Nervosa; Endocrine diseases, Hyperthyroidism, Cushing's syndrome, type 1 diabetes; Metabolic bone disease- Hyperparathyroidism
- Prolonged use of drugs with bone thinning effects e.g. heparin, anticonvulsants, depo-provera > 2yrs treatment, aromatase inhibitors*, GnRH analogues**

*** Aromatase inhibitor guidance available as algorithms in Appendix B to this guideline (taken from NOGG). NB: Only treatments approved in this document should be prescribed. Ibandronic acid is NOT a recommended treatment.**

**** The use of GnRH analogues in men is associated with bone loss and fractures but there is no official guideline to date on its management.**

Case finding, assessment of fracture risk and intervention thresholds for pharmacotherapy

Algorithms that integrate the weight of CRFs for fracture risk with or without information on BMD have been developed - FRAX[®]. The FRAX[®] tool (www.shef.ac.uk/FRAX) computes the 10-year probability of hip fracture or a major osteoporotic fracture (clinical spine, hip, forearm or humerus).^{5,6} Probabilities can be computed for several European countries, including the UK.

Appendix A shows the current recommended case finding strategy based on calculation of 10 year fracture risk using the FRAX[®]/WHO algorithms. Treatment intervention charts for men and women based on clinical risk factors (as detailed above), age and bone density are included. Where densitometry results are not available charts using the BMI are also shown.

Treatment of Osteoporosis

General management includes assessment of the risk of falls and their prevention. Maintenance of mobility and correction of nutritional deficiencies, particularly of calcium, vitamin D and protein, should be advised. Intakes of at least 1000 mg/day of calcium, 800 IU of vitamin D and of 1 g/kg body weight of protein can be recommended. Advise patients to avoid tobacco and alcohol abuse (government recommendations). Maintain body weight. Recommend regular weight bearing exercise (the equivalent of 30mins walk 3 times per week. Intensive exercise regimes have not been shown to be of greater benefit and may result in excessive weight loss or amenorrhoea).

Major pharmacological interventions are the bisphosphonates, strontium ranelate, denosumab, raloxifene and parathyroid hormone peptides. All these interventions have been shown to reduce the risk of vertebral fracture when given with calcium and vitamin D supplements. Some have been shown to also reduce the risk of non-vertebral fractures, in some cases specifically at the hip (see Table 3).

The low cost of generic alendronate, which has a broad spectrum of anti-fracture efficacy, makes this the first line treatment in the majority of cases. In individuals who are intolerant of alendronate or in whom it is contraindicated, other bisphosphonates, denosumab or raloxifene may provide appropriate treatment options. Strontium ranelate use is restricted to high risk patients where no other treatment option is available (due to safety concerns). The high cost of parathyroid hormone peptides restricts their use to those at very high risk, particularly for vertebral fractures.

TABLE 3
Antifracture Efficacy Of Pharmacological Interventions For Osteoporosis
(when given with calcium and colecalciferol)

| Intervention | Vertebral | Non-vertebral | Hip |
|--------------------|-----------|---------------|-----|
| Alendronate | + | + | + |
| Risedronate | + | + | + |
| Zoledronic acid | + | + | + |
| Etidronate | + | - | - |
| Ibandronate | + | + | - |
| Raloxifene | + | - | - |
| PTH (1-84) | + | - | - |
| Teriparatide | + | + | - |
| Strontium ranelate | + | + | + |
| Denosumab | + | + | + |

* post-hoc analysis in high risk group

Information on the Therapeutic Agents Available For The Management Of Osteoporosis

(See **Table 3 for evidence of impact on fractures**)

- Refer to the latest data sheet for full prescribing details about use in elderly, renal and hepatic impairment, contraindications, precautions etc <http://www.medicines.org.uk/emc/> .
- Refer to BNF for advice on using eGFR / calculated creatinine clearance to adjust doses for patients with renal impairment.

CALCIUM AND VITAMIN D₃ (Use current formulary choice)

Adequate levels of calcium and vitamin D₃ (colecalfiferol) are required to ensure optimum effects of all the treatments for osteoporosis. Unless the clinician is confident that the patient has adequate calcium intake and is vitamin D replete, calcium and colecalciferol supplementation at a dose of calcium 1 – 1.2 gram (equivalent to 2.5 – 3.0g calcium carbonate) and colecalciferol 20 micrograms (800 IU) daily should be prescribed.

Recheck serum calcium within three months of commencing calcium and vitamin D supplements unless primary hyperparathyroidism has been previously excluded.

Avoid colecalciferol in severe renal impairment as it cannot be converted to its active form.

BISPHOSPHONATES

- **Alendronate is the first choice bisphosphonate.**
- Risedronate (where patients unable to comply with the special instructions for the administration of alendronate OR have a contra-indication to or are intolerant of alendronate i.e. latter defined as symptoms resulting in discontinuation of alendronate despite correct administration)
- For other bisphosphonates choices see Table 3 for site specific anti-fracture efficacy
- The intravenous bisphosphonate, zoledronic acid 5mg IV annually, may be used as an alternative

Oral bisphosphonates should be swallowed whole with a glass of water 30-60 minutes before the first food or drink (other than water) of the day. Patients should stand or sit upright (not lie down) for at least 30 minutes post dose.

Discontinue treatment if oesophageal ulceration, erosion, stricture, or severe lower gastrointestinal symptoms occur.

Bisphosphonates should be avoided in patients with moderate to severe renal impairment. (Calculated creatinine clearance <35ml/minute for alendronate, <30ml/minute for risedronate).

Atypical stress fractures may occur after 'long-term' use (18 months to 10 years) of alendronate. An increased risk with other bisphosphonates cannot be excluded, as limited data may simply reflect their lower usage and more limited long term data. Some patients experienced thigh pain weeks to months before presenting with a completed femoral fracture which were frequently bilateral. Patients who develop atypical stress fractures should discontinue therapy and receive no further bisphosphonate treatment unless the benefits of continued treatment are thought to clearly outweigh the risks to the individual.

Osteonecrosis of the jaw has been reported rarely with IV bisphosphonate use and very rarely with oral use. Adequate oral hygiene should be maintained during and after bisphosphonate treatment. Ideally in patients with concomitant risk factors e.g. cancer, chemotherapy treatment, glucocorticoid treatment, or poor oral hygiene, remedial dental work should be completed before starting bisphosphonates.

For patients treated with bisphosphonates check serum calcium and creatinine at 3/12 & yearly thereafter.

Bisphosphonates should be used with great caution in women of childbearing potential due to possible teratogenicity and prolonged bone binding. If absolutely necessary use agent with shorter bone half life and stop 1 year prior to planned pregnancy (seek guidance from secondary care).

DENOSUMAB (Prolia®)

Denosumab subcutaneous injection (every 6 months) is recommended as an osteoporosis treatment option for post menopausal women and for men in the following situations:

- 1st line in patients with severe renal impairment (eGFR<35ml/min)

OR

Alternative treatment in the following groups:

- patients unable to comply with administration instructions for oral bisphosphonates

OR

- where oral/IV bisphosphonates are contraindicated or not tolerated

Initiation, prescribing and administration of the initial dose should be undertaken by secondary care specialists. Responsibility for **ongoing prescribing may be transferred to primary care** under the **transfer of care guidelines**. A **template letter** is available to ensure that relevant prescribing information for safe management is provided at the point of transfer of care. **Patients with eGFR<15ml/min must remain under the care of the specialist.**

NB: Prescribers must ensure that patients are capable of remembering to administer treatment every six months. Compliance to this regimen is very important. **

** Unlike other osteoporosis agents (such as the bisphosphonates and strontium) which have appreciable long term efficacy long after cessation, studies of denosumab suggest a rapid loss of gain in bone density and anti-fracture efficacy upon withdrawal. Therefore treatment needs to be long term and measures to ensure compliant usage must be in place.

The following drug safety advice has been issued in Drug Safety Update Oct 2012, with monitoring advice provided in Drug Safety Update September 2014:

The following precautions should be followed to minimise the risk of hypocalcaemia with denosumab in osteoporosis:

Contraindications:

- Denosumab 60 mg (for osteoporosis indications) should not be used in patients with hypocalcaemia, regardless of severity*

Warnings and recommendations:

- Pre-existing hypocalcaemia must be corrected prior to initiating denosumab.
- Patients with severe renal impairment (creatinine clearance <30 mL/min; eGFR 15–29 mL/min/1.73m²) or receiving dialysis are at greater risk of developing hypocalcaemia.
- Adequate intake of calcium and vitamin D is important in all patients receiving 60 mg denosumab
- Check calcium levels before each dose and within 2 weeks of initial dose in patients with eGFR<30/ml/min/1.73m². Recheck calcium if suspected symptoms of hypocalcaemia occur. **Note that local guidance recommends checking calcium level before each dose for all patients, and within 2 weeks of each dose in patients with eGFR<30/ml/min/1.73m².**
- Patients should be advised to report symptoms of hypocalcaemia to their doctor (muscle spasms, twitches, cramps, numbness or tingling of the fingers, toes or around the mouth).

The following safety advice has been issued in Drug Safety Update Feb 2013:

- During denosumab treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Patients presenting with such symptoms should be evaluated for an incomplete femoral fracture.
- Atypical femoral fractures may occur with little or no trauma in the subtrochanteric and diaphyseal regions of the femur.
- The contralateral femur should be examined in denosumab-treated patients who have sustained a femoral shaft fracture, as atypical femoral fractures are often bilateral (as noted from the bisphosphonates assessment).

Discontinuation of denosumab treatment should be considered if an atypical femur fracture is suspected, while the patient is evaluated. An individual assessment of the benefits and risks should be performed.

The following safety advice has been issued in Drug Safety Update Sept 2014:

Osteonecrosis of the jaw (ONJ) is a well-known and common side effect in patients receiving denosumab 120 mg for cancer. Risk factors for ONJ include:

- smoking

- old age
- poor oral hygiene
- invasive dental procedures (eg, tooth extractions, dental implants, oral surgery)
- comorbidity (eg, dental disease, anaemia, coagulopathy, infection)
- advanced cancer
- previous treatment with bisphosphonates
- concomitant treatments (eg, chemotherapy, antiangiogenic biologics, corticosteroids, radiotherapy to head and neck)

The following precautions are now recommended for denosumab 60mg (osteoporosis indication) to reduce the risk of ONJ:

- Check for ONJ risk factors before starting denosumab 60 mg. A dental examination and appropriate preventive dentistry are now recommended for patients with risk factors.
- Tell all patients to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain, or swelling to a doctor and dentist.

RALOXIFENE

As a treatment option for postmenopausal women with vertebral osteoporosis ONLY with a contraindication to, or intolerance of, bisphosphonates. **Avoid in severe renal impairment.**

STRONTIUM RANELATE

In February 2014, the European Medicines Agency recommended restrictions on the group of patients for whom strontium be prescribed. The advice issued in February 2014 supersedes the advice issued in March 2012 and April 2013:

- **Strontium ranelate is restricted to the treatment of severe osteoporosis in postmenopausal women and adult men at high risk of fracture who cannot use other osteoporosis treatments due to contraindications or intolerance.**
- Treatment should only be started by a physician with experience of treating osteoporosis (this may be in primary or secondary care).
- The risk of developing cardiovascular disease should be assessed before starting treatment. Treatment should not be started in people who have or have had
 - Ischaemic heart disease
 - Peripheral arterial disease
 - Cerebrovascular disease
 - Uncontrolled hypertension
- Cardiovascular risk should be monitored every 6-12 months.
- Treatment should be stopped if the individual develops ischaemic heart disease, peripheral arterial disease or cerebrovascular disease, or if hypertension is uncontrolled.

Strontium should be taken at bedtime at least 2 hours after food and /or milk.

Other contraindications:

- **Avoid in severe renal impairment (calculated creatinine clearance of <30ml/min).**
- Strontium ranelate should not be used in patients with current or previous venous thromboembolic events (VTE), including deep vein thrombosis and pulmonary embolism and/or patients with temporary or permanent immobilisation (e.g. post-surgical recovery or prolonged bed rest).

Warnings and other recommendations:

- The need for continued treatment with strontium ranelate should be re-evaluated in patients over 80 years who have been diagnosed at risk of VTE.
- Patients with significant risk factors for cardiovascular events (eg, hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with strontium ranelate after careful consideration
- Skin reactions: **The following safety advice (Drug Safety Update May 2012) regarding skin**

reactions has been issued to healthcare professionals:

- Patients should be advised of the likely time-to-onset and signs and symptoms of severe skin reactions such as DRESS, Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN). The highest risk for occurrence of SJS or TEN is within the first few weeks of treatment and usually around 3-6 weeks for DRESS. Symptoms or signs of SJS or TEN include progressive skin rash, often with blisters or mucosal lesions; symptoms of DRESS include rash, fever, eosinophilia and systemic involvement (eg, adenopathy, hepatitis, interstitial nephropathy, interstitial lung disease).
- Patients should be made aware of the symptoms and likely time-to-onset of severe allergic reactions, including skin rash, and should be advised to stop taking the medicine and seek medical advice immediately. In these patients, strontium ranelate should not be re-introduced

ZOLEDRONIC ACID

Zoledronic acid is a potent intravenous bisphosphonate.

As binding of this agent to bone is sustained for long periods, the required dosage and frequency is 5mg once a year only (also see duration of treatment below).

TERIPARATIDE (Specialist use only)

Teriparatide is a parathyroid hormone analogue and is recommended as a treatment option in the following situation:

Patients with an unsatisfactory response/intolerance to the above therapies **AND**

- aged ≥ 65 yrs old who have a T score of -4 SD or below **OR**
- aged ≥ 65 yrs old who have a *T score of -3.5 SD or below **plus more than 2 fractures** **OR**
- aged 55 – 64 yrs old who have a *T score of -4 SD or below **plus more than 2 fractures**

*[Update Feb 2015]*Crushed vertebrae can result in falsely high BMD and therefore should be excluded from the T score calculation. In such cases, use the femoral neck BMD value **or** an average of the lowest individual vertebral T scores that are not fractured. Do not use the Ward's triangle or average spinal BMD. In the unusual event when all the lumbar vertebrae have fractured, then T-scores would not be relevant and teriparatide would be a recommended treatment option on the basis that there has been more than 2 fractures whilst the patient has been on active therapy.*

Use with caution in moderate renal impairment. Contraindicated in severe renal impairment.

DURATION OF TREATMENT (Specialist View)

Oral bisphosphonates, strontium ranelate and selective oestrogen receptor modulators are recommended for up to five years of treatment ***followed by re-evaluation of the individual patient.***

As many side effects such as osteonecrosis of the jaw, atypical stress fractures and oesophageal cancers are only seen with long term usage, a careful review of indications for ongoing treatment is recommended. This should involve:

- consideration of risk factors **and**
- may include repeat bone densitometry **or**
- evaluation of biochemical markers of bone turnover.

Preliminary data suggests a T score > -2 at five years indicates a favourable prognosis.

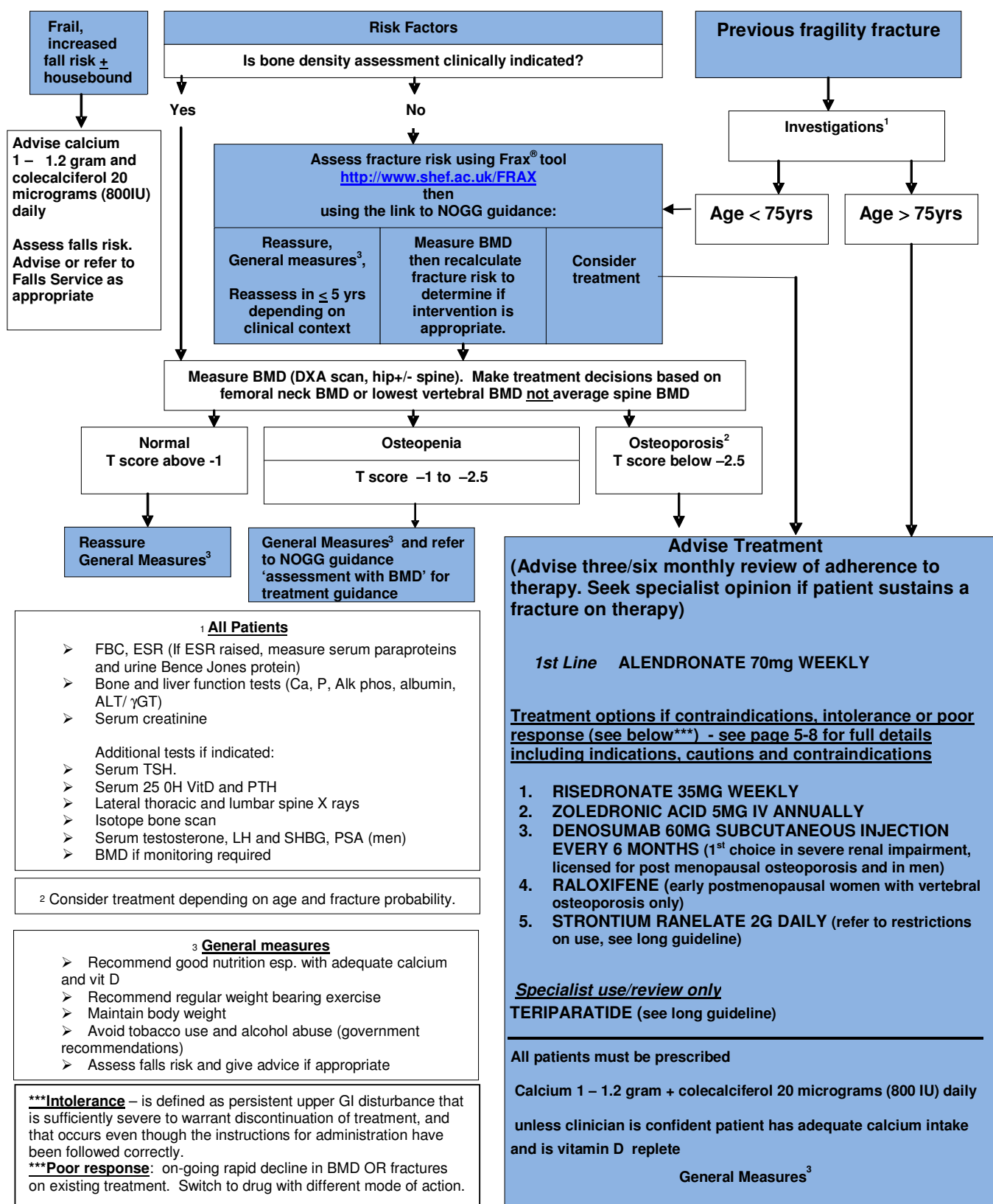
After five years of treatment, for patients not considered at high risk of fracture, a “drug holiday period” of up to three to five years without therapy can be considered. In other circumstances, it appears safe to continue for a further five years of treatment.

- Teriparatide should be used for up to 24 months.
- Present data is limited regarding the long term use of denosumab but it should be noted that a rapid rebound loss of efficacy is seen with this agent and long term usage seems necessary.
- Most patients can be given a drug holiday after three years therapy with IV zoledronic acid.

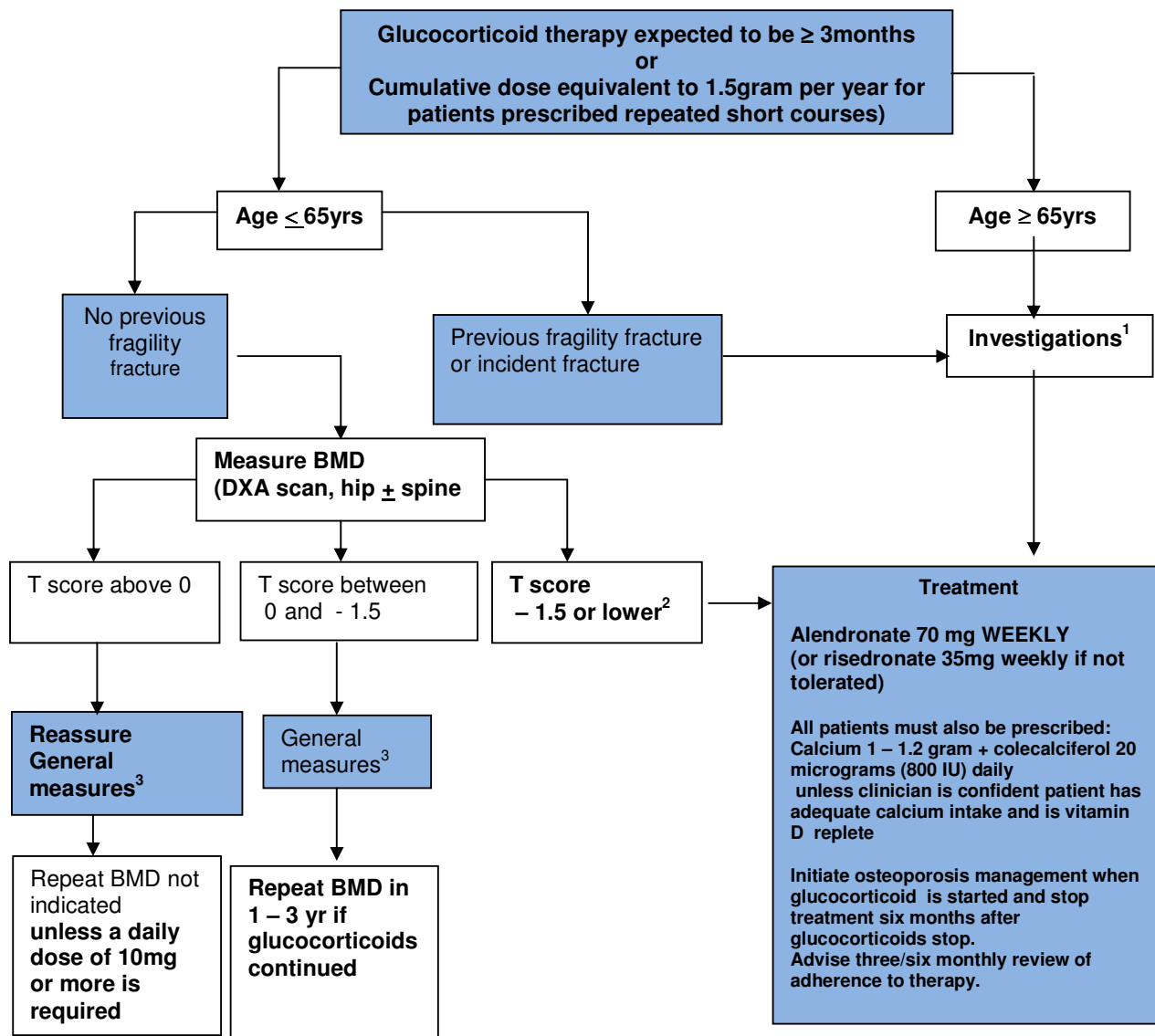
Refer to Summaries of Product Characteristics for full prescribing information

<http://www.medicines.org.uk/emc/>

Medical Management of Men and Women over 45yrs with OP or at risk of Osteoporosis (OP)



ALGORITHM FOR THE MEDICAL MANAGEMENT OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS IN ADULTS



¹All Patients

- FBC, ESR (If ESR raised, measure serum paraproteins and urine Bence Jones protein)
- Bone and liver function tests (Ca, P, Alk phos, albumin, ALT/γGT)
- Serum creatinine

Additional tests if indicated:

- Serum TSH.
- Serum 25 OH VitD and PTH
- Lateral thoracic and lumbar spine X rays
- Isotope bone scan
- Serum testosterone, LH and SHBG, PSA (men)
- BMD if monitoring required

²Consider treatment depending on age and fracture probability

³General measures

- Reduce dose of glucocorticoid when possible,
- Consider glucocorticoid sparing therapy if appropriate or consider alternative route of administration
- Recommend good nutrition esp. with adequate calcium and vit D
- Recommend regular weight bearing exercise
- Maintain body weight
- Avoid tobacco use and alcohol abuse (> government recommendations)
- Assess falls risk and give advice if appropriate

Notes

- It is not advisable to request DEXA for patients < 20 years or > 85 years as there is no reference population.
- In high risk patients dexta may be used to monitor response. Minimum recommended interval between follow-up dexta should be 24-36 months due to insensitivity of this test. Once a satisfactory response is observed, further testing is not required. If an early assessment of response is required (eg in very high risk cases), an alternative is a urinary marker of bone turnover (referral to secondary care required).
- Only part of the anti-fracture efficacy of bisphosphonates is due to changes in BMD, the remainder being due to effects on bone micro architecture and mineralisation.
- As the waiting list for DEXA scans may be long, commence bisphosphonates in all patients in whom corticosteroid treatment is anticipated to continue for greater than 3 months while the result is awaited.
- For Hypogonadal men-
 - Refer to Consultant Endocrinologist for investigation/testosterone replacement therapy

ADVICE ON WHAT TO DO IF A PATIENT HAS AN ACUTE LOW TRAUMA VERTEBRAL FRACTURE WITH SEVERE PAIN (Specialist View)

- Pain relief (analgesics/ TENS etc)
- Calcitonin sc injection 100 iu sc 3x weekly for 1 month (titrate up dose to max 100iu sc 5x week) to control pain, then initiate bisphosphonate treatment. In line with the MHRA Drug Safety Update, August 2012, warning of an increased risk of cancer with long term use of calcitonin-containing medicines, calcitonin must not be used in the treatment of osteoporosis.
- IV bisphosphonate therapy (specialist referral to metabolic bone clinic, endocrinology, CoE)
- Kyphoplasty (specialist referral to spinal surgeons)
- If fracture occurs on bisphosphonate patient may be eligible for teriparatide. (specialist referral as above)
- Investigate aetiology (A DEXA will not exclude bony metastases)

Glossary

| | |
|---------|--|
| BMD | Bone mineral density |
| BMI | Body mass index; weight (kg)/height ² (m) |
| CRF | Clinical risk factor for fractures due to osteoporosis |
| DXA | Dual energy x-ray absorptiometry |
| FRAX® | The WHO fracture risk assessment tool |
| SD | Standard deviation (of BMD measurements) |
| T-score | The number of standard deviations that a BMD measurement lays above or below the average value for young healthy women |

DEXA Scanning:

West Herts Hospitals NHS Trust – Use the agreed DEXA scanning form.

East and North Herts NHS Trust – Apply for DEXA scanning via Radiology Department.

Guidelines written by:

Dr Sundeep Bhalara, Consultant Rheumatologist, West Hertfordshire Hospitals NHS Trust
6th April 2011 [updated with new strontium contra-indications and cautions (04/2012, 06/2013 and 04/2014), new calcitonin MHRA warning (September 2012), denosumab MHRA advice (November 2012), denosumab transfer of care guidance (September 2013), extended license indications for denosumab (Sept 2014) and rewording of teriparatide T score initiation criteria (Feb 2015)]

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Appendix A

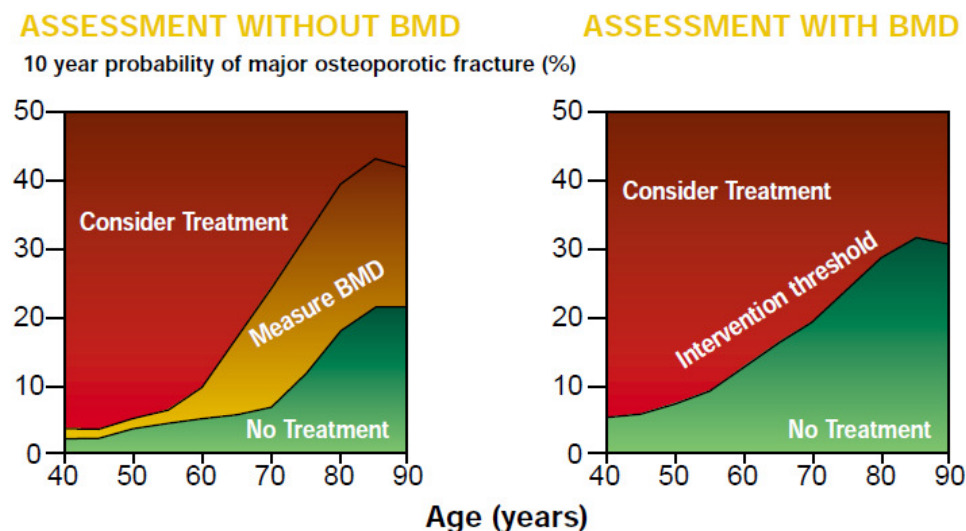
Case finding

Fracture risk should be assessed in postmenopausal women and in men aged 50 years or more with the risk factors outlined where assessment would influence management.

- Women with a prior fragility fracture should be considered for treatment without the need for further risk assessment although BMD measurement may sometimes be appropriate, particularly in younger postmenopausal women.
- In the presence of other CRFs, the ten year probability of a major osteoporotic fracture (clinical spine, hip, forearm or humerus) should be determined using FRAX® (www.shef.ac.uk/FRAX). Men and women with probabilities below the lower assessment threshold can be reassured. Those with probabilities above the lower assessment threshold but below the upper assessment threshold can be considered for testing with BMD using DXA and their fracture probability reassessed. Men and women with probabilities above the intervention threshold should be considered for treatment.
- In men and women who require a BMD test, fracture probabilities should be recomputed with FRAX®. Treatment can be considered in those in whom fracture probabilities lie above the intervention threshold.
- There are a number of other indications for bone densitometry including monitoring of treatment, determination of the extent of bone loss and assessment of suitability for certain treatments

The intervention threshold at each age is set at a risk equivalent to that associated with a prior fracture and, therefore rises with age. The proportion of women in the UK potentially eligible for treatment rises from 20 to 40% with age.⁷

Figure 1 Assessment and treatment thresholds in the absence of a BMD test (left) and with a BMD test to compute fracture probability (right) for men and women



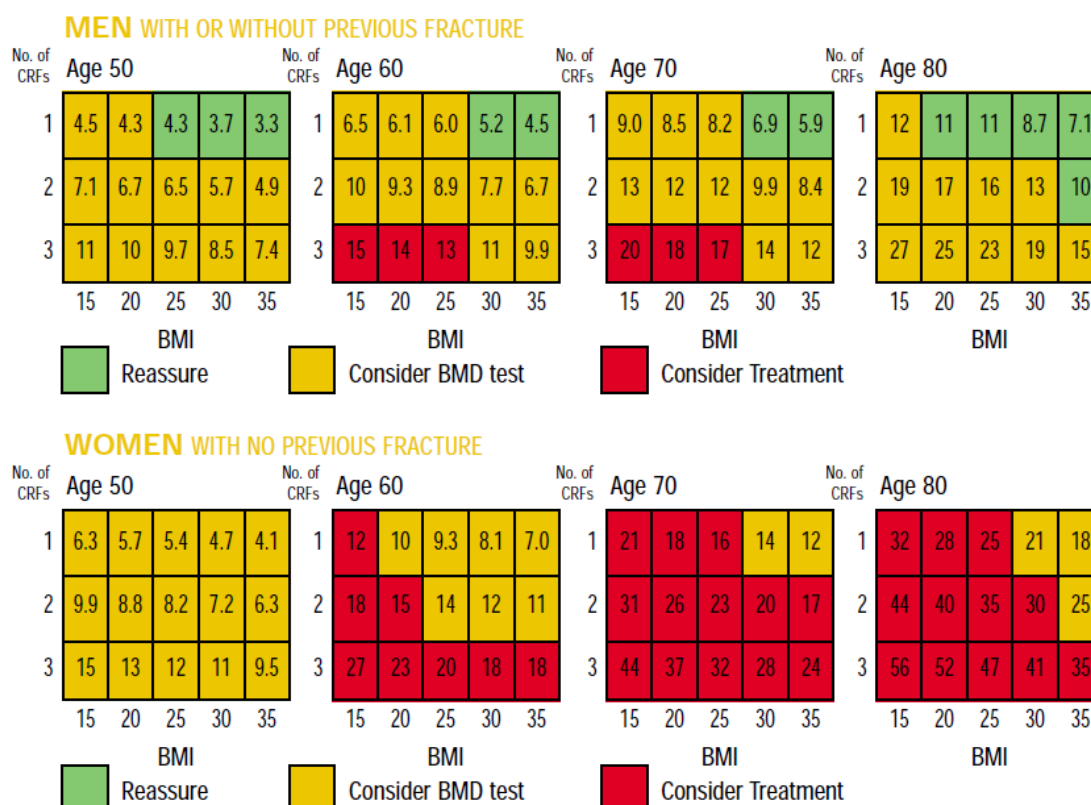
Probabilities of a major osteoporotic fracture (as well as hip fracture probabilities) can be plotted at the NOGG web site (www.shef.ac.uk/NOGG) available through FRAX®.

Without computer access, the following management algorithm can be used:

- Women with a prior fragility fracture should be considered for treatment without the need for further risk assessment, although BMD measurement may sometimes be appropriate, particularly in younger postmenopausal women.
- In women with other CRFs, and in men with any CRF, FRAX® probabilities should be approximated according to body mass index (weight/[height]² where weight is in kg and height is in metres).

The chart below (Fig. 2) gives average fracture probabilities according to BMI and the number of CRFs. The chart is colour coded. Green denotes that an individual's risk lies below the intervention threshold i.e. treatment is not indicated. Red denotes that the fracture probability is consistently above the upper assessment threshold, irrespective of the mix of CRFs, so that treatment can generally be strongly recommended. The intermediate category (orange) denotes that probabilities lie between these limits and that a BMD test should be considered to improve the estimate of fracture risk

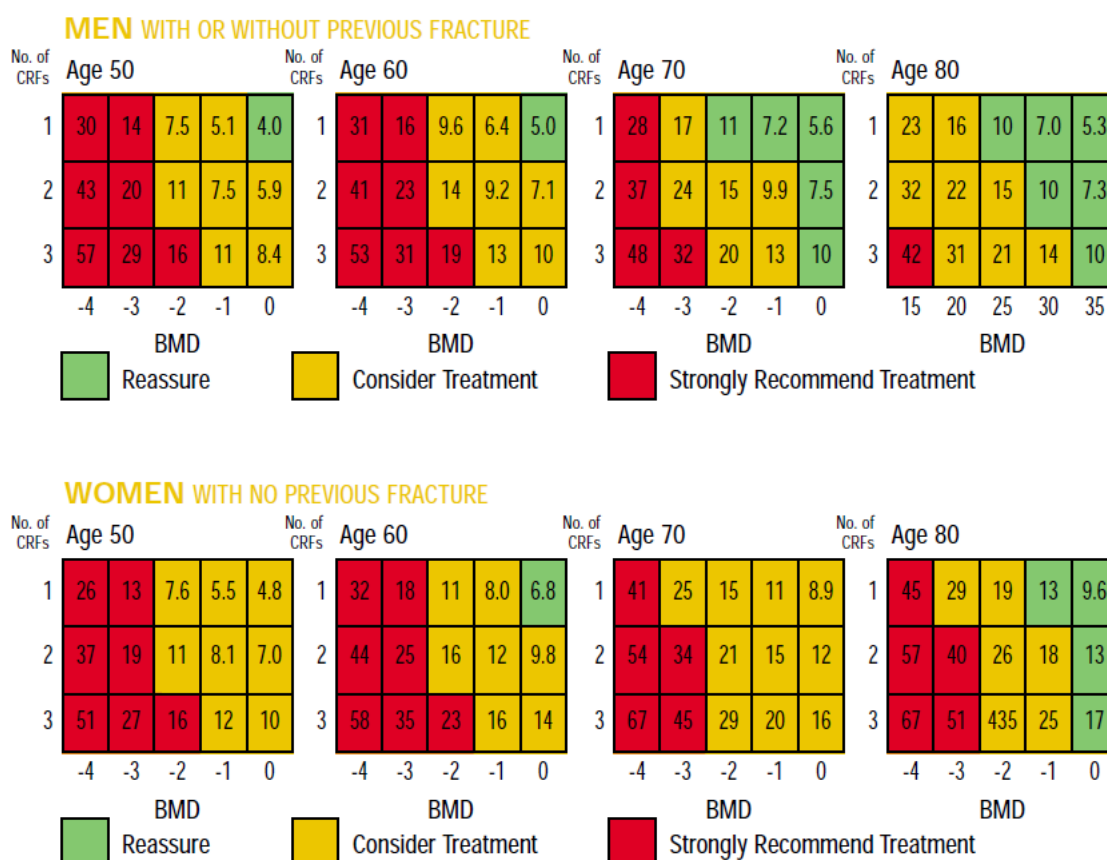
Figure 2 Assessment of men and assessment of women with no previous fracture according to body mass index (BMI) and the number of clinical risk factors (CRFs)



In men and women in whom BMD is available at the femoral neck, fracture probability can be approximated according to BMD T-score and the number of CRFs. The chart (Fig. 3) is colour coded. Green denotes that an individual's risk lies below the intervention threshold i.e. treatment is not indicated. Red denotes that the fracture probability is consistently above the upper assessment threshold, irrespective of the mix of CRFs, so that treatment can be strongly recommended in most cases. The intermediate category (orange) denotes that probabilities lie between these limits and that treatment can be recommended in those with the stronger risk factors. In general, smoking and alcohol are weak risk factors, glucocorticoids and secondary causes of osteoporosis are moderate risk factors, and a parental history of hip fracture is a strong risk factor.

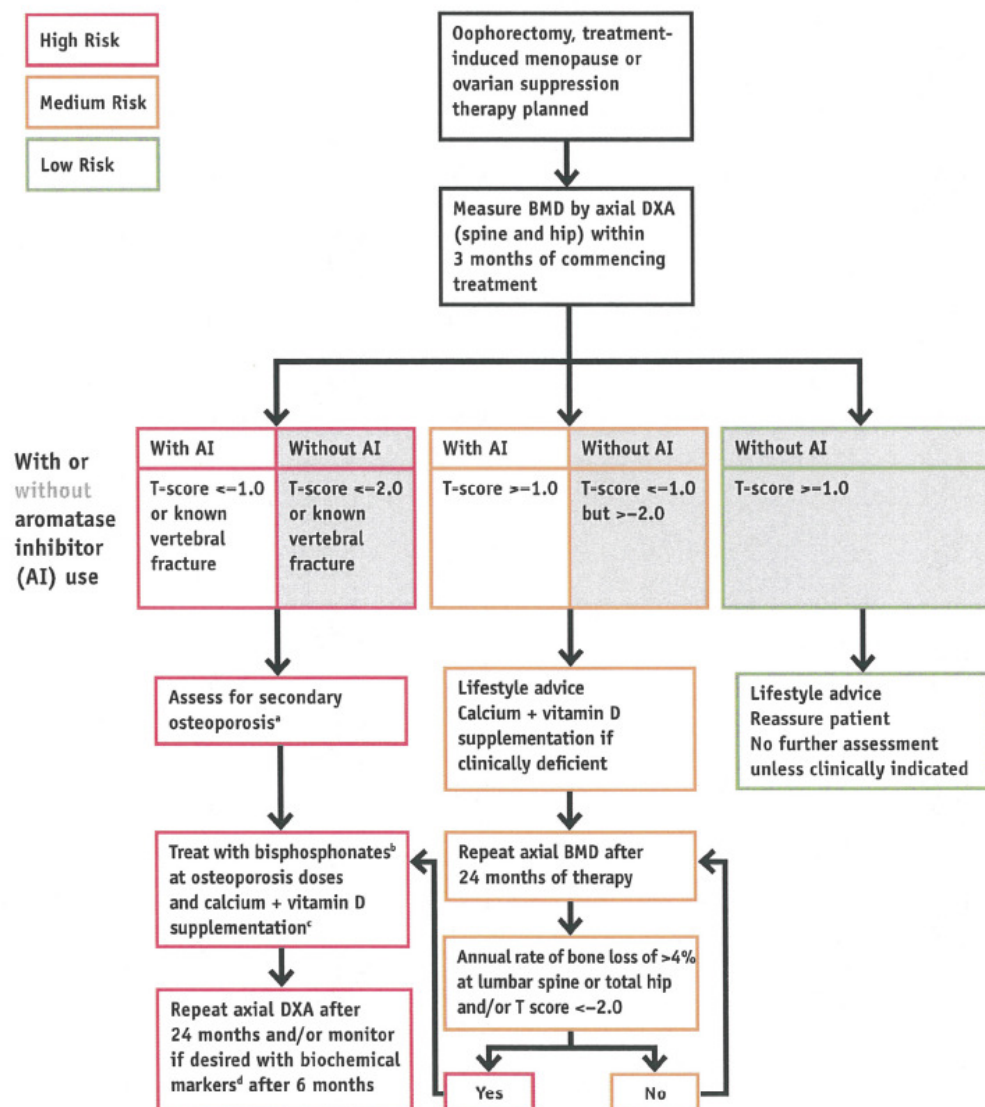
Note that the only secondary cause of osteoporosis that should be used with BMD is rheumatoid arthritis.

Figure 3 Assessment of men and assessment of women with no previous fracture according to femoral neck T-score for BMD and clinical risk factors (CRFs)



Appendix B

Algorithm 1: Adjuvant treatment associated with ovarian suppression/failure with or without concomitant aromatase inhibitor use in women who experience premature menopause



^a ESR, FBC, bone and liver function (calcium, phosphate, alkaline phosphatase, albumin, AST / γGT), serum creatinine, endomysial antibodies, serum thyroid-stimulating hormone

^b Alendronate 70 mg per week, risedronate 35 mg per week, ibandronate (150 mg po monthly or 3 mg iv 3-monthly), zoledronic acid 4 mg iv 6-monthly

^c To be given as ≥ 1 g of calcium + ≥ 800 IU of vitamin D

^d Biochemical markers such as serum C-terminal telopeptide of type I collagen or urinary N-telopeptide of type I collagen

Algorithm 2: Postmenopausal adjuvant treatment with aromatase inhibitors



^a Previous low-trauma fracture after age 50, parental history of hip fracture, alcohol intake of ≥ 4 units/day, diseases associated with secondary osteoporosis, prior corticosteroids for >6 months, low BMI (<22)

^b ESR, FBC, bone and liver function (calcium, phosphate, alkaline phosphatase, albumin, AST / γ GT), serum creatinine, endomysial antibodies, serum thyroid stimulating hormone

^c Alendronate 70 mg per week, risedronate 35 mg per week, ibandronate (150 mg po monthly or 3 mg iv 3-monthly), zoledronic acid 4 mg iv 6-monthly

^d To be given as ≥ 1 g of calcium + ≥ 800 IU of vitamin D

^e Biochemical markers such as serum C-terminal telopeptide of type I collagen or urinary N-telopeptide of type I collagen