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Management of osteoporosis

A national clinical guideline

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KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1 ⁺⁺	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1 ⁺	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 ⁻	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2 ⁺⁺	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2 ⁺	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 ⁻	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1 ⁺⁺ and directly applicable to the target population; <i>or</i> A body of evidence consisting principally of studies rated as 1 ⁺ , directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2 ⁺⁺ , directly applicable to the target population, and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 1 ⁺⁺ or 1 ⁺
C	A body of evidence including studies rated as 2 ⁺ , directly applicable to the target population and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 2 ⁺⁺
D	Evidence level 3 or 4; <i>or</i> Extrapolated evidence from studies rated as 2 ⁺

GOOD PRACTICE POINTS

☒	Recommended best practice based on the clinical experience of the guideline development group
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1 Introduction

1.1 THE NEED FOR A GUIDELINE

Osteoporosis affects both men and women. Its prevalence increases with age, and it is particularly common in postmenopausal women. One in three women and one in twelve men over the age of 50 will suffer an osteoporotic fracture, affecting around 200,000 women and 40,000 men in Scotland.¹ Given the increasingly sedentary lifestyle followed by many people, particularly children,² and an increasing elderly population,³ the number of men and women suffering an osteoporotic fracture is likely to grow.

The significance of osteoporosis lies in the increased risk of fracture as the disease progressively reduces bone mineral density (BMD). In Scotland there are over 20,000 cases of osteoporotic fractures annually. More than 20% of orthopaedic bed days are taken up by patients who have suffered hip fractures.

Figure 1: Presentations with low impact fracture

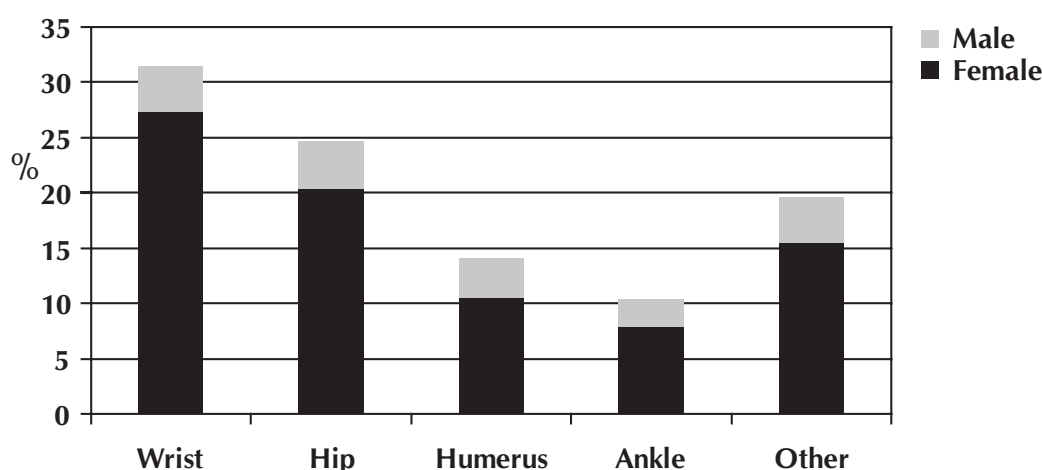


Figure 1 shows presentations with fracture (sustained in the absence of major trauma) in men and women over the age of 50 as a percentage of approximately 2,600 fracture events presenting over a two year period at a Scottish teaching hospital serving a catchment population of around 250,000 people.

There is a personal cost to each patient in addition to the £1.7 billion annual cost to the UK exchequer of treating osteoporotic fractures.⁴

Fifty per cent of hip fracture patients are no longer able to live independently and 20% die within 6 months. In addition there is the pain, deformity and disability associated with vertebral fracture.

It is difficult to tease out the risk factors for osteoporosis, falls, and fracture. Osteoporosis is itself a risk factor for fracture while, for example, a sedentary lifestyle contributes to osteoporosis risk and also to the risk of falling. The three are inextricably linked and this complicates the review of the evidence.

A wide range of diagnostic and monitoring tools are available to identify those at risk of, or suffering from, osteoporosis, and it is important to identify the most effective of these. Across Scotland there is significant variation in the availability of physicians with an interest in osteoporosis, in availability of diagnostic equipment, and in referral and treatment rates.¹ A guideline to inform the public, clinicians, and those who allocate funding within NHSScotland is required to minimise variation and provide an evidence base for commissioning services.

1.2 REMIT OF THE GUIDELINE

This guideline explores the selection of patients for referral or further investigation and monitoring, and treatment options. The objective is to ensure the timely identification of those individuals at highest risk of osteoporosis, as well as those who already have the disease. Patients who have already suffered a low impact fracture, including those who have just been admitted to hospital with such a fracture, are at highest risk.^{5,6}

Women and men over 50 who present with fractures (that occur in the absence of major trauma, such as road traffic accidents) have a high prevalence of osteoporosis, which can be readily identified and treated either within an orthopaedic setting or by liaison between orthopaedic and other secondary or primary care services. NHS Quality Improvement Scotland (formerly CEPS) have funded an audit of existing models of care for the secondary prevention of osteoporotic fractures. This will report in 2004 and may inform future service development.

This guideline pays particular attention to the treatment options that can be used in these patients to reduce their increased risk of further fractures with the aim of achieving "secondary prevention of fracture". Further information on the specific management of hip fracture can be found in SIGN Guideline 56.⁷

Specifically excluded from the remit are population screening, primary prevention of osteoporosis, and osteoporosis in children or adolescents.

1.3 DEFINITIONS

A World Health Organisation (WHO) working group and consensus conference have defined osteoporosis as "A disease characterised by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk".⁸

Osteoporosis is a systemic skeletal disease and osteoporotic fractures can occur at any site, though the fractures classically associated with this disorder are those involving the thoracic and lumbar spine, distal radius, and proximal femur. The definition does not imply that all fractures at sites associated with osteoporosis are due to the disorder. The interaction between bone geometry and the dynamics of the fall or the traumatic event, happening in a given environment, are also important factors in causing fracture. These can happen independently of, or in association with, low bone density.

1.3.1 BONE MINERAL DENSITY (BMD)

The risk of falls and the resultant trauma are difficult to assess and predict. The WHO definition of osteoporosis therefore captures only the bone-specific estimate of fracture risk. This is best captured by bone mineral density. The WHO working group used this technique to stratify risk as follows:

<i>Normal</i>	Bone mineral density less than 1 standard deviation below the young normal mean ($T > -1$)
<i>Osteopaenia</i>	Bone mineral density between 1 standard deviation and 2.5 standard deviations below the young normal mean (T between -1 and -2.5)
<i>Osteoporosis</i>	Bone mineral density more than 2.5 standard deviations below the young normal mean ($T < -2.5$)

This definition only applies to women. Recent reviews have suggested that applying the same definition to men, based on a male normative range, would have the same utility⁹ although this is not universally accepted.¹⁰

1.3.2 T-SCORES AND Z-SCORES

Measurements of bone mineral density are often cited in terms of a **T-score**, which is the number of standard deviations by which the patient's BMD differs from the mean peak BMD for young normal subjects of the same gender. Another measure of BMD is the **Z-score**, which is the number of standard deviations by which the patient's BMD differs from the mean BMD for subjects of the same age

1.4 PATIENT CONCERNS AND HOW THEY INFLUENCED THE GUIDELINE

Patient concerns regarding osteoporosis were identified through contact with patients themselves and via the published literature. A review of the literature highlighted issues that are of concern to people suffering from, or concerned about their risk of suffering from, osteoporosis. Similar concerns were also identified from calls received by the National Osteoporosis Society (NOS) helpline (managed by a team of osteoporosis nurse advisers). The concerns raised by patients are summarised below.

1.4.1 AM I AT RISK OF DEVELOPING OSTEOPOROSIS?

Lack of awareness of risk factors or lack of visibility of osteoporosis as a health problem means that women may not perceive themselves to be at risk of developing the disease.¹¹⁻¹⁵

Patients may be aware of the importance of some risk factors, such as family history, and seek out advice and treatment. Men tend to be less aware of the risk and what it implies for their health and lifestyle.

"I knew I was at risk of it because my mum and auntie both had... you know.. the hump back. ... am quite happy now on my HRT and I do plenty walking."

Risk factors are discussed in section 2

1.4.2 DO I NEED A BONE SCAN?

Patients are concerned that they do not have access to bone scans. Current provision in Scotland is variable.

Some patients report anxiety if they are not offered a repeat bone scan following treatment.

"It really helps to have a bone scan every now and then as I feel I am doing the right thing and carrying on with the treatment- my bones have not got any worse - I don't want to end up like my mother - she really suffered an awful lot of pain."

Bone densitometry is discussed in sections 3 and 6

1.4.3 WHAT CAN I DO TO MAKE THINGS BETTER FOR MYSELF?

The majority of people with osteoporosis, if given appropriate information, are very keen to do what they can to influence their bone health and protect themselves from (further) fractures. This means not just taking medication but also having a calcium rich diet and being able to take regular exercise without the fear of having a fall and/or fracture.¹⁶⁻¹⁸

"How much calcium should be taken? Do I take tablets, or rely on calcium rich foods?"

"I have been told not to have too much fat because of my heart problems – so what do I eat when I am not allowed too much cheese or milk?"

"For the last three months I have attended exercise classes twice weekly and now attend a maintenance class which I find very beneficial ... I was too frightened to do much on my own before ... I kept thinking I would do myself some damage."

"Getting some exercise has really helped my confidence."

Diet and exercise are discussed in section 4

1.4.4 ARE THERE ANY RISKS ASSOCIATED WITH MY MEDICATION?

Many patients report feeling confused and anxious about the type of medication they have been prescribed. Women express concern about taking hormone replacement therapy (HRT), and the fear of breast cancer is very real.¹⁹

Undesirable side effects mean that some patients do not continue with their medication.^{12,13,20-22} Some experience gastric discomfort that they attribute to bisphosphonates.¹⁷

Pharmacological treatments are discussed in section 6.

1.4.5 HOW CAN I MANAGE THIS PAIN?

Patients report the pain following a vertebral fracture as excruciating. Everyday activities such as going to the hairdresser or on an outing to the theatre or cinema can be very painful, and many women are depressed by the difficulty they have in finding clothes that fit comfortably and also look good. It would be immensely helpful to know that health professionals *understood* these problems and could take them into account when assessing the impact on patients and their families.²³⁻²⁵

"I slept in a chair for three months ... or crawled about the floor ... couldn't even wash my hair ... there seemed no end to the pain ... the painkillers didn't really work ... I became very depressed... I have lost all my confidence."

Pain management is discussed in section 6.11.

1.4.6 OTHER CONCERNS

Calls made to the NOS helpline indicate that many patients diagnosed with osteoporosis do not receive enough information and support from the health professionals looking after them. Patients are often told that they have osteoporosis but are not given an adequate explanation of what this means or the implications of the disease, and this can be a bewildering and frightening experience for them.

As the patient with osteoporosis makes his or her journey from being identified as at risk, then through diagnosis and treatment, studies suggest that good communication, support and explanation is important at all stages. Good communication between patients, their families, carers, and health professionals alleviates some of the anxieties and concerns and improves compliance with long term treatments.^{26,27} Practical information on such things as diet and exercise, and on adjunct methods of pain relief empowers patients to contribute to the management of their condition.²⁴

Going into hospital for any reason can be alarming for people with osteoporosis, especially if it is severe and they have already experienced fractures.^{28,29}

"I had terrible toothache... and abscess...I needed more treatment and he wanted me to go for a general anaesthetic in the hospital but I couldn't ...I might get broken when asleep!"

1.5 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of medical care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor in light of the clinical data presented by the patient and the diagnostic and treatment options available. However, it is advised that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

1.6 REVIEW AND UPDATING

This guideline was issued in 2003 and will be considered for review in 2007, or sooner if new evidence becomes available. Any updates to the guideline in the interim period will be noted on the SIGN website: www.sign.ac.uk

2 Risk Factors for Osteoporosis

2.1 INTRODUCTION

This chapter summarises the evidence for the major risk factors that act as predictors for osteoporosis. Many other factors have been proposed as conveying risk of osteoporosis, but there is no consistent evidence for any risk factors other than those discussed below.

2.2 FALLS

Not all fractures are associated with osteoporosis. Clinical risk factors related to physical function and falls are not a risk factor for osteoporosis *per se*, but are powerful predictors of fracture risk. This guideline, however, does not address the important issue of falls and their prevention. SIGN 56 on hip fracture briefly documents identifiable risk factors for falls,⁷ and NHS Health Scotland has conducted qualitative research into lay and professional attitudes to falling and how they can influence fall prevention programmes.³⁰ A much fuller review of this topic can be found in the guidelines developed by the American and British Geriatrics Societies.³¹

2.3 HISTORY OF PREVIOUS FRACTURE

Women who have suffered a previous fragility fracture (defined as a fracture occurring after a fall from standing height or less) are at increased risk of further fractures, independent of BMD.³² Women who develop a vertebral fracture have a 19.2% (95% CI 13-6-24.8%) risk of a further vertebral fracture within one year.³³ Men and women aged 65 years or older with a vertebral fracture have a five year risk of femur or hip fracture of 6.7% and 13.3% respectively.³⁴ In women, the presence of one or two vertebral fractures increases the risk of further fracture 7.4 fold.³⁵

2++

Those at highest risk of fracture are those who have already fractured including those with loss of height or kyphosis which can indicate (what may have been painless) vertebral fractures.^{36,37}

1++

B

Patients who have suffered one or more fragility fractures should be priority targets for investigation and treatment of osteoporosis.

2.4 NON-MODIFIABLE RISK FACTORS

2.4.1 AGE

BMD decreases, and consequently the risk of osteoporosis increases with age. A significant increase in prevalence with each decade after age 60 has been demonstrated. The United States National Health and Nutrition Survey (NHANES) III survey of postmenopausal women showed that the prevalence of osteoporosis in non-Hispanic white American women was 27% (50-59 years), 32% (60-69 years) and 41% for those ≥70 years.³⁸ A previous estimate based on data from Rochester, Minnesota indicated a lower (though still high) prevalence – 14.8% (age 50-59 years), 21.6% (aged 60-69 years), 38.5% (70-79 years) and 70% (≥80 years).³⁹ A Yorkshire based study showed a prevalence of 24% in women aged 60-69 years.⁴⁰

2.4.2 SEX

Women are at greater risk of osteoporosis as they have smaller bones and hence lower total bone mass. Additionally, women lose bone more quickly following the menopause, and typically live longer. Osteoporosis is less common in men but is still a significant problem.

The rate of bone loss in men is less than that in women. In the Framingham Osteoporosis Study annualised percent bone loss for women was 0.86% to 1.21% at different sites and for men, 0.04% to 0.90%.⁴¹ Secondary causes of osteoporosis are, however, more common in men, affecting approximately 40% of cases.^{42,43}

Excepting reproductive factors and taking into account the increased influence of secondary factors in men, the risk factors in women also apply to men.

2.4.3 ETHNICITY

Afro-Caribbean women have a higher BMD than white women at all ages due to a higher peak bone mass and slower rate of loss.^{38,44} White women have a 2.5-fold greater risk of getting osteoporosis.³⁸

2.4.4 REPRODUCTIVE FACTORS

A late menopause or short time from menopause to BMD measurement are associated with higher BMD. There is consistent evidence that low BMD is associated with early menopause.⁴⁵ Consequently, women with an early menopause should be considered at higher risk of osteoporosis than others at a similar age.

BMD decreases most rapidly in the early postmenopausal years.⁴⁶

There is no consistent evidence that tubal ligation, parity, number of previous miscarriages, or breast feeding affect BMD.

Current use of oestrogen replacement therapy is associated with a higher BMD.⁴¹ Those currently taking oestrogen therapy should therefore be considered as being at lower risk than others at a similar age, unless the therapy was prescribed for osteoporosis.

2.4.5 FAMILY HISTORY OF OSTEOPOROSIS

Lower BMD is found in women and men with a family history of osteoporosis, a family history being defined as a history of osteoporosis or brittle bones, kyphosis ("dowager's hump"), or low trauma fracture after age 50 years as reported by the offspring.

Individual BMD decreases as the number of family members with osteoporosis increases. Overall family history is a more sensitive predictor of osteoporosis risk than maternal or paternal history alone.⁴⁷ Prevalence of a positive history in sisters is similar to prevalence reported for mothers.^{47,38}

In one epidemiological study the greatest risk of categoric osteopaenia (RR 2.16, CI = 1.38-3.37) was in patients whose father had a history of osteoporosis.⁴⁷

C Use of family history in assessing risk of osteoporosis should include maternal, paternal and sister history.

C Family history should include not only a given diagnosis of osteoporosis but also kyphosis and low trauma fracture after age 50.

2⁺

2.5 MODIFIABLE RISK FACTORS

2.5.1 WEIGHT

Weight loss or low body mass index (BMI) is an indicator of lower BMD.⁴⁸ In addition, those in the lowest tertile of BMI have a two-fold greater bone loss than those in the highest tertile over two years. Post menopausal women with below average BMI should be considered as being at increased risk of osteoporosis.⁴⁶

2.5.2 SMOKING

A meta-analysis of studies looking at the effect of smoking found that BMD in smokers was 2% lower with each increasing decade after the menopause than in non-smokers, with a 6% difference at 80 years.⁴⁹ Men who smoke show greater bone loss at the trochanter.⁴¹ Female smokers have been shown to be at greater risk of hip fracture than non-smokers, with the risk increasing in line with cigarette consumption. The level of risk declines on giving up smoking, but is not significantly reduced until 10 years after cessation.⁵⁰

2⁺

B Smokers should be considered at greater risk of osteoporosis than non-smokers, and advised to stop, for this and other reasons.

2.5.3 ALCOHOL

Evidence for alcohol as a risk factor for low BMD is inconsistent, as the majority of studies do not include subjects with excessive alcohol intake.

2.5.4 EXERCISE

A positive relationship between both current physical activity, physical activity in adolescence and BMD has been shown in young female Canadians (18-35 years)⁵¹ and in Italian middle aged women.⁵² Current exercise has been associated with higher bone density in postmenopausal English women⁵³ and in Norwegian women aged 50-75 years with fractures.⁴⁸ However a study of an Australian population has shown that current physical activity was positively associated with BMD but that after adjustment for age, BMI, calcium intake, and quadriceps strength the relationship did not remain statistically significant.⁵⁴ Consequently, individuals with a sedentary adolescent lifestyle should be considered at higher risk of osteoporosis. Those who currently have a sedentary lifestyle may also be at higher risk.

2.5.5 DIET

Past dietary intake of milk in adult premenopausal women (45-49 years) has been positively associated with BMD.⁵⁵ Evidence of association between current calcium intake and low BMD is inconsistent. Vitamin D levels have been shown to be positively correlated with BMD in independent living men and women aged >80 years in Stockholm.⁵⁶ No consistent association has been found between other dietary factors and BMD.

2.6 SECONDARY CAUSES OF OSTEOPOROSIS

A large number of clinical conditions and some categories of drugs have been associated with osteoporosis in adults. The most common conditions associated with osteoporosis are:

- Anorexia nervosa
- Chronic liver disease
- Coeliac disease
- Hyperparathyroidism
- Inflammatory bowel disease
- Male hypogonadism
- Renal disease
- Rheumatoid arthritis
- Long term corticosteroid use
- Vitamin D deficiency

☒ The possibility of osteoporosis should be considered in patients with the conditions listed above.

Osteoporosis is also associated with the contraceptive Depo-Provera®. At the present time, there is no 'evidence based' answer to the concerns about adverse effects of Depo-Provera® on bone density as the available data are conflicting.⁵⁷⁻⁵⁹

2.7 ASSESSING RISK OF OSTEOPOROSIS

2.7.1 RISK SCORES

Although there have been attempts to develop risk scores for osteoporosis most are not of satisfactory quality and have not been validated. One tool⁶⁰ was evaluated in 1,013 white American women and had a sensitivity of 98% and a specificity of 12% in that group. The positive predictive value was 69% and the negative predictive value was 75%. Other risk tools have assessed fracture risk. The best performing has a receiver operating characteristic (ROC) curve (graph indicating specificity and sensitivity at all possible cut-off points) of 0.88 (values >0.8 are generally required to indicate effectiveness of a test) but this has not been validated in a separate population.⁶¹

The development of a validated tool of this kind would be a useful addition to the diagnosis of osteoporosis.

2.7.2 WHO IS AT HIGHEST RISK?

It must be clear which risk is being considered: the risk of osteoporosis, or the risk of falling or fracturing. Each of these is linked and osteoporosis is only one risk factor for fracture.

Priority should be given to finding and managing patients at the highest risk of falling and experiencing a fracture. Those who have already experienced a fracture are at high risk of a further fracture. Thus patients with a previous fracture are a key target group.

The next group to target are those with osteoporosis risk who have not yet sustained a fracture. The risk factors that have best evidence for increasing risk for this group are shown in Table 1. Although many are not modifiable, these factors contribute to a threshold for diagnostic testing, which helps prioritise which patients should be sent for a DXA scan (See section 3.5).

Table 1: Risk factors for osteoporosis (when no history of fracture)

Strongest risk factors	Other significant risk factors
Female sex	Caucasian origin
Age >60 years	Early menopause
Family history of osteoporosis	Low BMI
	Smoking
	Sedentary lifestyle
	Long term (≥ 3 months) corticosteroid use

It is difficult to offer evidence based advice about particular combinations of risk factors which justify further investigation since the evidence is lacking, but there seems to be an additive effect of risk factors – more present means greater risk.⁶⁰ A systematic approach to offering osteoporosis assessment to all such patients should be developed, though scarce resources should be targeted at those at highest risk to ensure the most efficient use of these resources.

3 Measurement, Diagnosis and Monitoring

3.1 INTRODUCTION

Bone mineral density is the major criterion used for the diagnosis and monitoring of osteoporosis. BMD differs between different sites around the body and there is only a moderate correlation between BMD at different sites.⁶² BMD of a specific site is the best predictor of fracture at that particular site.⁶³ Techniques available for measuring BMD are shown in Table 2.

Table 2: Techniques for measuring BMD

Technique	Appropriate sites
Dual-energy X-ray Absorptiometry (DEXA or DXA)	Anteroposterior (AP) spine, lateral spine, proximal femur, total body, forearm, heel
Quantitative Computed Tomography (QCT)	Spine
Peripheral Dual-energy X-ray Absorptiometry (pDXA)	Forearm
Peripheral Quantitative Computed Tomography (pQCT)	Forearm
Single Photon Absorptiometry (SPA)	Forearm
Single-energy X-ray Absorptiometry (SEXA or SXA)	Forearm
Radiographic Absorptiometry (RA)	Phalanges

Other techniques are available that measure properties related to bone density. Quantitative Ultrasound (QUS) can be used to measure properties of the calcaneus related to bone quality and structure, though it cannot be used to diagnose osteoporosis or to target treatment. Biochemical markers such as resorption markers can be used to assess bone turnover.

This section focuses on the techniques of DXA, QCT, and QUS, and the use of biochemical markers for the diagnosis and monitoring of osteoporosis.

3.2 PLAIN RADIOGRAPHS

Assessment of bone density from plain radiographs is not appropriate as it is open to marked observer variation and apparently normal density does not reliably exclude osteoporosis.⁶⁴ Although severe osteopaenia on plain films correlates reasonably with low BMD measured by DXA, there is a wide overlap.⁶⁵ Treatment should not be instituted on the basis of plain film findings as this could lead to many patients being treated unnecessarily. Similarly, many patients with osteoporosis would be missed. The use of digital radiography, which allows the image to be manipulated electronically, has introduced a degree of uncertainty that makes it even more difficult to reliably assess bone density.

1 +

B Conventional radiographs should not be used for the diagnosis or exclusion of osteoporosis.

B When plain films are interpreted as "severe osteopaenia" it is appropriate to suggest referral for DXA.

Grading of vertebral fractures and the number of fractures will influence management. Standardisation of reporting of vertebral fractures identified on plain radiographs would be helpful. There is an established method for such reporting.⁶⁶

☒ The presence of vertebral fractures should be included in reports on conventional radiographs along with a recommendation for further action. (See Section 6.2)

3.3 PERIPHERAL TECHNIQUES

DXA scanning is the current standard technique for the diagnosis of osteoporosis due to its ability to measure BMD at a variety of sites. Peripheral imaging techniques such as pQCT, pDEXA, SXA, RA, phalangeal ultrasound, and peripheral radiographic fractal analysis are often used as screening methods for subsequent DXA, for diagnosis of osteoporosis, or the monitoring of treatment. Their principal advantages compared to DXA are their relatively modest cost and the portability of the equipment. Few studies have been done to compare these techniques against the current standard of DXA.

It has been suggested that patients with a forearm T-score of less than -2.5 on DXA should begin treatment, while those with a score greater than -1 should simply be reassured that fracture risk is low.⁶⁷ This, however, only applies to the diagnosis of fracture risk in postmenopausal women. A significant proportion of women with T-scores between -1 and -2.5 would still have to be referred for subsequent axial DXA. It should also be noted that there is only a moderate correlation between forearm or heel and axial BMD and therefore forearm or heel BMD is not appropriate for making treatment decisions. In addition the forearm is not a suitable site for monitoring response to treatment.⁶⁸

- ☒ There is no role for forearm or heel scanning in the diagnosis of osteoporosis in targeting therapy to reduce fracture risk. In remote or rural areas provision of a mobile DXA service is a viable alternative.

3.3.1 QUANTITATIVE ULTRASOUND

Quantitative ultrasound equipment is available that measures a range of parameters using several different methods. Most systems measure speed of sound (SOS) and broadband ultrasound attenuation (BUA) of the calcaneus. Different systems produce different values both in absolute terms and in relation to age-matched subjects. It is not possible to extrapolate the findings from one instrument or technique and apply it to another, and this limits the amount of generally applicable evidence.

This complexity is reflected in the literature, where there is a considerable variation in the design of studies and the presentation of conclusions.

Some studies are based on populations of elderly patients living in sheltered or supervised accommodation. Conclusions from these studies may not be generalisable to populations living independently, particularly when looking at the development of new fractures where protection from falls may have a bearing on fracture incidence.

There is evidence³² that QUS of the heel can predict fracture risk of hip and spine independently of BMD measurements. There is also some evidence that QUS in addition to BMD evaluation by DXA may give a better estimate of fracture risk than DXA scanning alone.³² The precision of QUS is generally poor and changes in QUS of the heel may not reflect changes in BMD at the spine or hip.

The ultimate conclusion must be that though QUS may have a role in improving estimates of fracture risk, this is at best a proxy for the assessment of bone density. QUS of the heel cannot, therefore, be recommended for the investigation or monitoring of patients suspected of being at risk for osteoporosis or to justify initiation of treatment.

There is insufficient evidence to support the use of any of these techniques for population screening, or for pre-screening for DXA.

3.4 QUANTITATIVE COMPUTED TOMOGRAPHY

Quantitative Computed Tomography has been widely used to measure BMD, particularly in the spine. It can be performed on conventional CT scanners by purchasing special software. An advantage of QCT is that it can measure cortical and trabecular bone separately. Disadvantages are the relatively high radiation dose involved and the high cost of scans.

Given the limited availability of CT scanners in Scotland and the competing demands for their use, it would not be appropriate to use QCT for the routine diagnosis or monitoring of osteoporosis in NHSScotland.

3.5 DUAL ENERGY X-RAY ABSORPTIOMETRY

DXA can measure BMD at the spine, hip, forearm, heel, and in the total body. The diagnosis of osteoporosis varies greatly depending on the measurement site, and on the number of sites measured. It is not possible to exclude a diagnosis of osteoporosis on the basis of a DXA measurement at only one site.³²

Bone mineral density measurement at the hip provides the best prediction of hip fracture risk⁶⁹ but does not exclude the possibility of osteoporosis at the spine. As scans are not analysed while the patient is still lying on the scanner, it is normal to acquire both hip and spine scans at the one visit. The spine is the preferred site for monitoring the response to treatment. Careful interpretation of the spine image, and comparison of the T-scores of individual vertebrae is required as the measured BMD may be affected by factors such as vertebral fracture or degenerative changes.

A well conducted systematic review on the diagnosis and monitoring of osteoporosis in postmenopausal women has demonstrated the effectiveness and usefulness of DXA.³²

1++

A

BMD should normally be measured by DXA scanning performed on two sites, preferably anteroposterior spine and hip.

3.5.1 MONITORING

The precision of DXA varies with BMD and the measurement site. In this context, precision is a measure of how reproducible BMD is if it is measured several times during the same patient visit, with the patient re-positioned on the scanner between measurements. This determines how large the change in BMD must be between successive patient visits before it can be confidently interpreted as a genuine change.

In the spine precision can be affected by artefacts associated with degenerative changes. When outliers were removed, long term precisions of 1.1, 2.2 and 1.3% were achieved for the lumbar spine, femoral neck and total hip BMD respectively.⁷⁰ To detect changes at the 95% confidence level they must be at least 2.8 times the precision error. Changes in BMD of the spine, femoral neck and total femur cannot therefore be detected with confidence unless they are around 3, 6 and 4% respectively.

Careful examination of DXA spine images is required to ensure that apparent changes in BMD are not due to artefacts. Misleading changes have been reported in the monitoring of osteoporosis therapy where it has been shown that women who lose BMD during the first year of treatment can gain BMD if the same treatment is continued for a second year. Effective treatments for osteoporosis should not normally be changed because of loss of BMD during the first year of use.⁷¹ There is insufficient evidence to determine whether repeating BMD measurements two years after starting treatment is useful.^{4,32}

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B

Repeat measurements should only be performed if they influence treatment.

3.5.2 RISK

The radiation dose from DXA scans varies depending on the scanner type and the site measured. The combined effective dose from AP spine, lateral spine, and hip scans is typically less than 30 µSv, which corresponds to only a few days natural background radiation or a single transatlantic flight.

☒

Patients should be reassured that the radiation dose from DXA is extremely small.

There is no significant difference in accuracy or precision between older generation pencil beam and newer fan beam DXA scanners. Fan beam systems offer shorter scanning times leading to a high patient throughput. Some models of fan beam DXA scanners also offer high resolution lateral spine imaging.

Spinal degenerative disease is prevalent among the elderly and may result in an artefactual increase in spine BMD measured in the AP view. Lateral spine DXA selectively measures the trabecular rich vertebral bodies and is less affected by spinal degenerative disease. Lateral spine DXA identifies more osteoporotic patients and is more sensitive to age related bone loss than AP spine DXA.⁷² Lateral spine DXA is, however, less precise and a greater treatment effect for lateral spine rather than AP spine DXA may be offset by greater precision errors.⁷³ The lateral spine view is not available on many DXA systems.

2+
3

C If DXA investigations are repeated, AP spine and total hip measurements should be used to follow response to treatment.

☒ Although the greatest treatment effect is often observed in the spine, it is often also helpful to monitor changes in hip BMD because spinal images may be affected by artefacts.

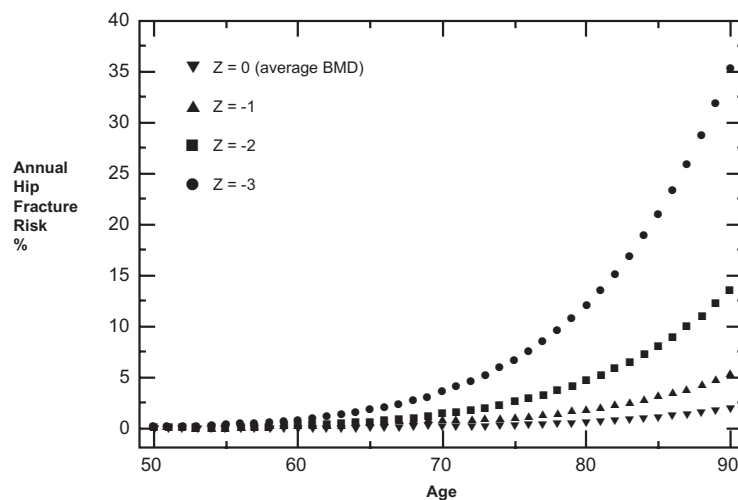
A model DXA report is included in Annex 2.

3.6 FRACTURE PREDICTION

Annual hip fracture risk can be estimated from age, sex and femoral neck BMD⁷⁴⁻⁷⁷. An example of the annual hip fracture risk for females as a function of age and Z-score is shown in Figure 2. To extend the annual fracture risk to a 10 year fracture risk requires the assumption that the patient's Z-score will remain constant.

2+
2+

Figure 2: Annual hip fracture risk for women as a function of age and femoral neck BMD



BMD has been converted to Z-score to make the data independent of the particular DEXA system.
Calculated from De Laet et al JBMR 13 (1998) 1587-93.

C Following a DXA scan of the hip, the annual hip fracture risk (or 10 year fracture risk) should be included in the DXA report.

Existing vertebral fractures increase the risk of a subsequent vertebral fracture by a factor of four, and double the risk of a subsequent hip fracture.⁷⁸ Identification of existing vertebral fractures is therefore an important factor in the assessment of future fracture risk. Lateral spine DXA can detect vertebral deformity. Visual assessment of lateral spine images from high resolution fan beam DXA agrees as well with lateral radiographs as radiographs interpreted by different radiologists.^{79,80} Fan beam DXA results in a radiation dose of only 1% of a lateral radiograph. In addition to its role in identifying existing fractures, lateral DXA can identify artefacts such as aortic calcification and degenerative changes that affect BMD measured in the AP view.

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2+
4

C Where lateral spine scans acquired with fan-beam DXA are available, visual assessment should be used to assess prevalent vertebral fractures.

B Evidence of existing vertebral deformity should be used to modify the hip fracture risk estimated from age, sex, and BMD.

3.7 COST OF DXA SCANNING

Provision of, and access to, DXA scanners is variable across Scotland. As a consequence, not all patients suspected of having osteoporosis are scanned. Without scans, patients may be treated inappropriately or not at all. Annex 3 provides an example annual costing of a DXA service. Once a service has been established, the cost per scan is relatively low.

Since some of the costs are fixed it is clear that increased use of a scanner reduces the unit cost. We do not, however, have sufficient evidence to draw conclusions about the impact of DXA on treatment costs, or the effect on healthcare expenditure that may arise from a reduction in fracture incidence.

A complete DXA investigation, including patient preparation, image acquisitions, analysis, printouts and report generation, is typically performed in 20 to 25 minutes, making each DXA system capable of a throughput of approximately 4,000 patients per year. Assuming an annual referral rate of 1% of the population,⁸¹ a minimum of 13 DXA scanners would be required for the Scottish population. Taking into account geographical factors and the distribution of population density, however, a larger number would be required if all communities were to be given equal access.

☒ DXA should be available in all Health Board areas.

☒ When new DXA scanners are purchased these should be high resolution systems with fast acquisition times. Consideration should be given to purchasing a system that is capable of lateral spine imaging. Where this is available a typical study should consist of quantitative measurements of AP lumbar spine and hip, and visual assessment of the lateral spine.

3.8 BIOCHEMICAL MARKERS

Biochemical markers of bone turnover have the potential to have a major clinical impact on the investigation and management of osteoporosis in Scotland. Individual marker assays are simple and inexpensive to perform and modern laboratory technology has the capacity to cope with the maximum likely workload.

By definition, the diagnosis of osteoporosis is directly linked to the measurement of BMD. Several studies have sought to use biochemical markers to select patients at risk of rapid bone loss for subsequent BMD measurement, but have failed to demonstrate a consistent relationship between marker results and bone loss. The sensitivity and specificity of the bone marker assays were too low to be useful.³²

1⁺⁺

A Biochemical markers of bone turnover should have no role in the diagnosis of osteoporosis or in the selection of patients for BMD measurement.

There is evidence from recent studies that resorption markers measured in urine or more recently in serum, can predict increased fracture risk (OR ~ 2) independently of BMD. However, there is no conclusive evidence that has demonstrated the value of one or more specific markers, either alone or in combination with other factors, in the prediction of fracture risk in the individual patient.⁸² At the present time biochemical markers of bone turnover have not been proven to have clinical value in the prediction of fracture risk in individual subjects.

Changes in biochemical marker concentrations alter with therapy and these changes may be used to predict subsequent changes in BMD. It has been suggested that regular monitoring of biochemical markers can increase patient compliance with therapy and/or assist with the alteration of therapy to achieve optimal effect on improving BMD. Although several original studies support this view,^{83,84} they have used different markers and different study protocols resulting in variable outcomes.³² A recent meta-analysis shows that the greater the increase in BMD at the spine and hip, or decrease in bone markers at one year, the greater the reduction in the risk of non-vertebral fracture.⁸⁵

There is currently no agreement on the marker(s) of choice for this application or on the preferred strategy for optimal use. Currently there is insufficient evidence to support a recommendation for the routine use of a specific panel of biochemical markers of bone turnover in monitoring and adjusting the treatment being given to patients with osteoporosis. However, this position will change in the foreseeable future and there is every likelihood that evidence will emerge to establish a definite role for biochemical markers in this application.

4 Non-pharmacological interventions

4.1 INTRODUCTION

A number of non-pharmacological factors have been implicated in the prevention of fractures in patients with osteoporosis either independently of, or in combination with, positive effects on bone density. Many anecdotal and non-peer reviewed comments suggest that a number of diet-related factors may have a positive influence on bone density. This guideline focusses on exercise, calcium, the fluoridation of water, and non-soy derived isoflavone as areas where a body of evidence does exist.

- ☒ Everyone with osteoporosis will benefit from a good calcium intake and weight-bearing exercise.

4.2 EXERCISE

There is mounting evidence to suggest that physical exercise reduces the risk of falling in older people. Gait training, appropriate use of assistive devices, and exercise programmes with balance training have emerged as key components of exercise programmes for community dwelling older people.³¹

1 +

A number of systematic reviews and meta-analyses⁸⁶⁻⁸⁸ have suggested that an exercise programme combining low impact weight bearing exercise and high-intensity strength training maintains bone density in men and postmenopausal women.

- B** High intensity strength training is recommended as part of a management strategy for osteoporosis.

- B** Low impact weight bearing exercise is recommended as part of a management strategy for osteoporosis.

Resistance training refers to training where an overload resistance is applied. The resistance can be low, usually referred to as muscular endurance training, or moderate to high, called strength training. Strength training needs to be of a high intensity to produce gains in strength and BMD. Any form of strength training should be site specific i.e. targeting areas such as the muscle groups around the hip, the quadriceps, dorsi/plantar flexors, rhomboids, wrist extensors and back extensors.

Weight-bearing activity is carried out when standing. Low impact weight-bearing activity is characterised by always having one foot on the floor. Jumping (both feet off floor) is termed high impact training. High impact training is not suitable for patients with osteoporosis.

Weight bearing exercises should be targeted to loading bone sites predominantly affected by osteoporotic change – ie hip and spine.

To be effective all exercise programmes need to be progressive in terms of impact and intensity as fitness and strength levels improve.⁸⁹ Programmes should begin at a low level that is comfortable for the patient. An initial assessment by a suitably trained individual such as a physiotherapist will give the patient a reference point from which to start the exercise programme. Patients and healthcare professionals should refer to the guidelines produced by the Chartered Society of Physiotherapists for an indication as to the kind of exercise that could be recommended to different patient groups.⁹⁰

- ☒ All healthcare professionals should encourage regular exercise, such as walking, to promote good bone and general health.

4.3 CALCIUM

4.3.1 DIETARY DERIVED CALCIUM

Two systematic reviews^{91,92} suggest that dietary derived calcium is as effective as pharmacologically derived sources at maintaining adequate calcium balance in postmenopausal Caucasian women. A well conducted meta-analysis⁹³ suggests that 1000 mg per day of dietary calcium leads to a 24% reduction in hip fractures.

1++

A Postmenopausal women should aim for a dietary intake of 1,000 mg calcium per day.

As a treatment for osteoporosis, this is higher than the 700mg recommended nutrient intake advised by the Committee on Medical Aspects of Food and Nutrition Policy (COMA) for maintenance of bone health.⁹⁴

Milk, including skimmed or semiskimmed, offers a very cheap source of calcium with no associated risk for the majority of the population. A calcium intake of up to 2,500 mg per day does not promote hypercalciuria or stone formation in the absence of renal dysfunction. Patients with impaired renal function should avoid excessive calcium intake ($\geq 2,500$ mg per day) and consult with their doctor. An average daily intake of 1000 mg of calcium can most easily be obtained from 600 ml (1 pint) of milk with either 50 g (2 oz) hard cheese (eg Cheddar or Edam), one pot of yoghurt, or 50 g (2 oz) sardines.

Examples of dietary sources of calcium and their calcium content are provided in Annex 4.

4.3.2 CALCIUM AND VITAMIN D SUPPLEMENTATION

Calcium supplementation using tablets is one means of ensuring an adequate calcium intake in those unwilling or unable to do so by dietary means. A daily calcium intake of 1,000 mg or more taken in tablet form is likely to reduce fracture rates by a similar rate to that seen with dietary derived sources of calcium. There is no evidence that a vitamin D supplement is needed for active people under 65 years of age. However, everyone over 65 years of age should aim to take 10 μ g (400 IU) daily of vitamin D. For the majority of people this can only be achieved by vitamin D supplementation.⁹⁴ Where vitamin D deficiency has been confirmed or is likely, such as in the case of housebound individuals, a vitamin D supplement of 20 μ g (800 IU) is the recommended dose.

The role of calcium and vitamin D supplementation in conjunction with pharmacological therapy is dealt with in Section 6.8.

4.4 WATER FLUORIDATION

Studies relating the fluoridation of drinking water to fracture rates in women with a low BMD consistently show no effect in patients with low bone density or osteoporosis,^{95,96} although the duration of the studies may be too short to demonstrate such an effect. There is some evidence to support a modest effect of water fluoridation on improving axial BMD.^{97,98} However, a well conducted meta-analysis has concluded that water fluoridation has no net effect on fracture rates.⁹⁶ Although these studies do not support water fluoridation for the prevention of osteoporosis, neither do they suggest any detrimental effect in relation to fracture rates.

4.5 OTHER DIETARY INTERVENTIONS

Natural progesterone, magnesium, boron, and homeopathic remedies have all been proposed as treatments for osteoporosis. Again, no evidence was identified regarding any role they may have in the management of osteoporosis and fracture prevention.

4.5.1 IPRIFLAVONE

Ipriflavone is a flavinoid found in large amounts in soy-rich foods. It has been suggested that it may prevent fractures in patients with osteoporosis.

There is no consistent evidence of a beneficial effect of isoflavone on BMD or fracture rates in patients with low bone density or osteoporosis. Two RCTs report a small beneficial effect on radial and vertebral BMD at two years,^{99,100} whereas a recent well conducted RCT¹⁰¹ showed no effect on BMD at three sites or on biochemical markers of bone resorption.

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B **Isoflavone should not be used as a sole therapy for fracture reduction in patients with osteoporosis.**

The effects of soy-rich foods containing isoflavone or other flavonoids has not been tested in a rigorous enough manner to allow further consideration. Similarly, there are no data to address the role of flavonoids as adjuncts to other pharmacological agents to treat osteoporosis.

4.5.2 CAFFEINE

It is frequently suggested that carbonated drinks or beverages containing alcohol or caffeine are detrimental to bone health. Available evidence regarding their intake by patients with low bone density or osteoporosis is, however, inconclusive and does not support any recommendation in relation to fracture prevention.

5 Hormone Replacement Therapy and Osteoporosis

The majority of women in the UK use HRT for the relief of menopausal symptoms that may be very unpleasant and affect quality of life and wellbeing. HRT tends to be used for relatively short durations in the perimenopausal period.¹⁰² It is generally prescribed for women at an age when fracture risk is low.

5.1 USE OF HRT IN THE MANAGEMENT OF OSTEOPOROSIS

Primary prevention of osteoporosis is outwith the scope of this guideline, but the Women's Health Initiative Study (WHI) has added greatly to knowledge in this area.¹⁰³ It is simply not known whether data from primary prevention studies can be extrapolated to treatment of osteoporosis. The WHI study looked at 16,608 normal, healthy women aged 50 to 79 taking a combination of conjugated equine oestrogens 0.625 mg and medroxyprogesterone acetate 2.5 mg. A secondary end point of the study looked at incidence of fractures. This confirmed the long held assumption that HRT prevents osteoporotic fractures. (Table 3)

Table 3: Reduction in osteoporotic fractures with HRT: WHI study data¹⁰³

Fracture site	HRT (n=8506)	Placebo (n=8102)	Hazard ratio	95% CI
Hip	44	62	0.66	0.45– 0.98
Spine	41	60	0.66	0.44– 0.98
Other osteoporotic	579	701	0.77	0.69– 0.86
Total	650	788	0.76	0.69– 0.85

There are limited data available from other randomised controlled trials on the use of HRT to prevent fractures. Recent meta-analyses^{4,104} have been mainly influenced by two large trials, one of which (the HERS study) produced a negative result.¹⁰⁵

When assessing the role of HRT in the treatment of osteoporosis, there is only one small (75 patients) double blind randomised placebo-controlled trial assessing the efficacy of HRT (transdermal oestrogen with progestogen) in the secondary prevention of (vertebral) fractures.¹⁰⁶ When analysed on the basis of the number of vertebral fractures that occurred in the two groups, the oestrogen treated group had a significant reduction in vertebral fracture incidence. However, analysis based on the numbers of *women* with new vertebral fractures (the usual end point of more recent studies) did not show a statistically significant reduction.

A number of relatively small randomised controlled trials gauging the efficacy of oestrogen replacement (HRT) in treating low BMD have been conducted. One study¹⁰⁷ has compared the BMD benefits of HRT against alendronate and placebo and shows that with use of HRT over two to three years significant BMD gains occur at the lumbar spine and femur and are at least as great as those seen with bisphosphonates. These studies have not been of sufficient power to provide an insight into the antifracture efficacy of HRT. In the light of the WHI data on normal women where bone density was not known but HRT demonstrated overall fracture reduction, it seems highly likely that current use of HRT will also reduce fracture risk in women with known low BMD.

5.2 BENEFITS VERSUS RISKS OF HORMONE REPLACEMENT THERAPY

The risks and benefits of HRT are complex and require the individual assessment of each woman considering taking HRT, especially for more than five years. The increase in risk of breast cancer associated with HRT is small, but related to duration of use and is the major reason why most women opt not to continue HRT in the long term. The large re-analysis by Beral and colleagues

of the world wide data on HRT and breast cancer estimated that 45 women in every 1,000 who do not use HRT will have breast cancer diagnosed between the ages of 50 and 70.¹⁰⁸ For women who start to use HRT at age 50, the extra number of breast cancers that are diagnosed has been estimated as follows:

Table 4: Breast cancer incidence in women starting HRT at age 50

Length of time on HRT	Extra breast cancers found to age 70 (per 1,000 women) in excess of the 45 which would occur in non-HRT users
5 years	2
10 years	6
15 years	12

Other considerations in the risk benefit analysis include an increased risk of venous thromboembolism, with a relative risk between two and four with an absolute risk of around three per 10,000 users per year.¹⁰⁹ Raloxifene (a Selective Estrogen Receptor Modulator or SERM) carries a similar increased risk of venous thromboembolism (VTE).¹¹⁰ Previous history of VTE contraindicates oral HRT or raloxifene.¹¹¹

Use of unopposed oestrogen in women increases the risk of endometrial cancer by around six-fold after more than five years of use.¹¹² Progestogens should be added to reduce risk of endometrial cancer. Recent data make it clear that an increase in risk of endometrial cancer still remains with longer term use of sequential combined HRT (RR 1.5) and prescribers should be aware of this possibility after more than five years of therapy.¹¹³ This increasing risk is not found in women using continuous combined oestrogen and progestogen regimens.¹³⁹

Recently conducted randomised controlled trials have failed to show any benefit in coronary heart disease (CHD).^{109,114,103} The WHI data confirmed this and, in addition, demonstrated excess risk of both myocardial infarction and stroke in HRT users (Table 5). A more recent analysis of evidence from RCTs on the long term effects of HRT provides further support for the lack of effect on CHD and increased risk of stroke.¹¹⁵

Further data from the WHI study¹⁰³ confirm increased risks of breast cancer and thromboembolism with HRT (Table 5). As yet, there are no data from the oestrogen-only versus placebo arm of the same study. Endometrial cancer rates were not affected, in keeping with previous data. Colorectal cancers appear to have a lower incidence. Overall there were no differences in mortality between the HRT and placebo groups.

Table 5: Absolute risk reduction/excess risk attributed to continuous combined HRT in 10,000 users over one year¹⁰³

Outcome	HRT versus placebo per 10,000 person-years
Cardiovascular disease	+ 7 (37 versus 30 cases)
Stroke	+ 8 (29 versus 21 cases)
DVT/PE	+ 18 (34 versus 16 cases)
Breast cancer	+ 8 (38 versus 30 cases)
Colon cancer	- 6 (10 versus 16 cases)
Hip fracture	- 5 (10 versus 15 cases)

- ☒ Use of HRT can be considered as a treatment option for osteoporosis but the risks and benefits should be discussed with each individual woman before starting treatment.

Perimenopausal women at risk of osteoporosis could consider taking HRT and can be reassured that current usage of HRT reduces risk of osteoporotic fracture. Duration of usage should be based on regular reassessment of the risks and benefits of continuing HRT for each individual woman.

6 Pharmacological Management

This section describes the following treatment scenarios:

- **Postmenopausal women with multiple vertebral fractures (DXA not essential but other destructive diseases should be excluded)**
- **Postmenopausal women with osteoporosis determined by axial DXA and a history of at least one vertebral fracture**
- **Postmenopausal women with osteoporosis (determined by axial DXA) with or without a previous non-vertebral fracture**
- **Frail, elderly women with a diagnosis of osteoporosis, with or without previous osteoporotic fracture**
- **Men with a diagnosis of osteoporosis determined by axial DXA with or without previous osteoporotic fractures**

HRT is discussed within each scenario, and further information about HRT is also given in section 5.

The quick reference guide accompanying this guideline summarises the decision making process for each of these scenarios (except for men).

6.1 THE AIMS OF TREATMENT

6.1.1 REDUCTION IN THE INCIDENCE OF FRACTURES

The prime objective of treatment for osteoporosis is to reduce the incidence of fractures. Patients with a history of previous fracture are two to eight times more likely to have a fracture at any skeletal site. These patients are readily identifiable and should be prioritised for treatment. Patients with vertebral fractures, whether painful or painless, share the same or possibly greater future fracture risk but only a minority of these are currently recognised and treated.

6.1.2 ALLEVIATION OF FRACTURE RELATED MORBIDITY

The priority from the patient's perspective may be the provision of an effective analgesic regimen - to reduce the pain associated with vertebral fracture, for example. Treatment of osteoporosis to achieve the secondary prevention of fractures will not influence pain that is currently being experienced by a patient as a result of a fracture. Advice on pain management is given in Section 6.11.

6.1.3 WHICH SUBSEQUENT FRACTURES CAN BE PREVENTED?

The treatments reviewed in this section can broadly be divided into those that have been shown to have potential to reduce the incidence of vertebral fractures only and those with wider potential efficacy in reducing fractures at any skeletal site (ie vertebral and non-vertebral sites). Some therapies have been shown to reduce the incidence of hip fractures as part of their efficacy in reducing the risk of non-vertebral fractures. In general, the first choice therapeutic option would be a treatment that is effective in reducing both vertebral and non-vertebral fracture risk.

6.1.4 RISK FACTORS FOR FRACTURE AND THEIR USE IN TARGETING TREATMENT

The key risk factors for fracture are low BMD, past history of fracture, age, and the risk of falling (see Section 2).^{35,78} Together these define the baseline fracture risk and ultimately are useful in defining who should be treated. Women aged over 60 with osteoporosis and a history of osteoporotic fracture are at greatest risk of vertebral and non-vertebral fractures.³² Assessment of BMD by axial DXA is a prerequisite for targeting treatment in the vast majority of cases. The notable exception is patients who have had at least two vertebral fractures and are known not to have underlying metastatic tumours, myeloma or other destructive disease, when clinical trials have shown that the bisphosphonates are capable of achieving the secondary prevention of vertebral fractures. In all other situations, BMD assessment by axial DXA would be essential to define a

level of fracture risk at which treatment is likely to be effective in reducing the patient's risk of fracturing. Targeting treatment to reduce fracture risk on the basis of clinical risk factors for falling (without measurement of BMD) has been shown to be ineffective as a means of reducing the incidence of fractures.¹¹⁶

Efficacy of therapies in reducing fracture risk has most frequently been assessed in terms of the impact on vertebral fracture risk. The majority of studies have specifically assessed potential reduction in incidence of "morphometric" (ie non-clinical) vertebral fractures. These are usually defined on the basis of reductions in posterior, mid, or anterior vertebral body dimensions and these may be accompanied by a semiquantitative grading of fracture severity. The clinical trials differ in the thresholds of height loss that define incident morphometric vertebral fracture. Studies of risedronate^{117,118} and HRT¹⁰⁶ have based the definition of incident vertebral fractures on a decrease of at least 15% in one of these vertebral dimensions, albeit in association with changes in the semiquantitative grading system. In other clinical trials of etidronate,¹¹⁹ alendronate,^{36,37,120} raloxifene,¹¹⁰ and calcitonin¹²¹ incident vertebral fractures have been defined on the basis of loss of at least 20% of vertebral body height. This has a key influence on the placebo vertebral fracture rates. Results of the main placebo controlled RCTs of drug treatments to reduce fracture risk are summarised in Table 6.

Selection of specific drug therapy for an individual patient is ultimately at the discretion of the prescribing clinician and should take into account the risk versus benefit of therapy in the context of the patient's health record and their individual concerns. Similarly, therapeutic regimens should be reviewed periodically as the risk/benefit ratio may change over time.

There are two important considerations that should be taken into account when using oral bisphosphonates.

- All bisphosphonates are poorly absorbed. Typically, only between one and five per cent of the ingested dose is actually absorbed. Optimal absorption requires all bisphosphonates to be ingested on an empty stomach, either first thing in the morning after overnight fasting with the subsequent avoidance of food for 30 minutes or in the middle of a four hour fast, and they should be washed down with a large glass of water.
- All bisphosphonates can potentially be associated with gastrointestinal side effects. For aminobisphosphonates such as alendronate this can on rare occasions present as oesophageal ulceration. The risk of these symptoms can be lessened by the avoidance of lying flat within 30 minutes of ingestion, or by using the once weekly preparations.

Given the complicated nature of the protocols for ingestion, it is doubtful if bisphosphonate therapy would be appropriate for patients who are unlikely to be able to comply with such a regimen. This may apply, for example, where the patient is confused and does not have a resident carer.

Table 6: Summary of RCTs evaluating the effectiveness of drug therapies in reducing fracture incidence in postmenopausal women

Fracture risk reduced	Therapy	Patients	BMD	Placebo fracture rate	Fracture rate with treatment	RR (95% CI)	NNT*
<i>Women with multiple vertebral fractures, but no DXA scan</i>							
Vertebral fracture	Etidronate ¹¹⁹	423	-	9.3% over 2 years	4.1% over 2 years	0.44 (0.2,1.0)	19
Vertebral fracture	Risedronate ¹¹⁷	2458	-	16.3% over 3 years	11.3% over 3 years	0.59 (0.43,0.82)	20
Non-vertebral fracture	Risedronate ¹¹⁷	2458	-	8.4% over 3 years	5.2% over 3 years	0.6 (0.39,0.94)	32
Vertebral fracture	Risedronate ¹¹⁸	1225	-	29% over 3 years	18.1% over 3 years	0.51 (0.36,0.73)	10
<i>Women with low BMD established by axial DXA, and with at least one vertebral fracture</i>							
Vertebral fracture	Alendronate ³⁶	2078	Femoral neck T≤-1.6	15% over 2.9 years	8% over 2.9 years	0.53 (0.41,0.68)	15
Hip fracture	Alendronate ³⁶	2078	Femoral neck T≤-1.6	2.2% over 2.9 years	1.1% over 2.9 years	0.49 (0.23,0.99)	90
Vertebral fracture	Calcitonin ¹²¹	1255	Lumbar spine T≤-2	26% over 5 years	18% over 5 years	0.67 (0.47,0.97)	12
Vertebral fracture	Raloxifene ¹¹⁰	2304	Femoral neck T≤-2.5	21.2% over 3 years	14.7% over 3 years	0.7 (0.6,0.9)	16
<i>Women with low BMD determined by axial DXA, with or without previous non-vertebral fracture</i>							
Vertebral fracture	Alendronate ³⁷	4432	Femoral neck T≤-1.6	3.8% over 4.2 years	2.1% over 4.2 years	0.56 (0.39,0.8)	60
Vertebral fracture	Alendronate ³⁷	1640	Femoral neck T≤-2.5	5.8% over 4.2 years	2.9% over 4.2 years	0.5 (0.31,0.82)	35
Hip fracture	Alendronate ³⁷	1640	Femoral neck T≤-2.5	2.2% over 4.2 years	1% over 4.2 years	0.44 (0.18,0.97)	81
Non-vertebral fracture	Alendronate ¹²²	1908	Lumbar spine T≤-2.5	4.4% over 1 year	2.4% over 1 year	0.53 (0.3,0.9)	54
Vertebral fracture	Raloxifene ¹¹⁰	4524	Femoral neck T≤-2.5	4.5% over 3 years	2.3% over 3 years	0.5 (0.4,0.8)	46
Hip fracture	Risedronate ¹¹⁶	5445	Femoral neck T≤-2.7	3.2% over 3 years	1.9% over 3 years	0.6 (0.4,0.9)	78
Non-vertebral fracture	Risedronate ¹¹⁶	5445	Femoral neck T≤-2.7	10.7% over 3 years	8.4% over 3 years	0.8 (0.7,1.0)	43

*NNT values are calculated, rather than quoted from the source references. The NNT is not only a function of the efficacy of the therapy but is significantly determined by the baseline risk as reflected in the incidence of fractures (vertebral and non-vertebral) observed in the placebo groups of these trials. As indicated in the Table, the placebo rate varies significantly between trials and direct comparison of the NNTs as a guide to relative efficacy is not appropriate.

6.2 POSTMENOPAUSAL WOMEN WITH MULTIPLE VERTEBRAL FRACTURES

Women with multiple vertebral fractures are at greatest risk of future fracture.³⁵ That future risk rises exponentially in association with increased number of prevalent fractures. Only a minority of vertebral fracture patients are ever diagnosed or treated for osteoporosis. Only 50% of vertebral fractures are associated with pain but the morbidity with regard to future potential fracture risk and mortality are the same whether a vertebral fracture has been associated with symptoms or not. Inconsistency in radiology reporting is a factor that contributes to low rates of identification and subsequent poor treatment of patients with osteoporotic vertebral fracture.¹²³

The efficacy of three years' risedronate 5 mg daily (with calcium $\pm$ vitamin D) was associated with significant reduction in morphometric vertebral fracture incidence among women with at least two vertebral fractures in two large clinical trials.^{117,118} The larger study¹¹⁷ also demonstrated reduction in non-vertebral fracture risk.

The alternative regimen of risedronate 35 mg once weekly is as effective as the 5 mg daily regimen in improving bone density¹²⁴ and by implication has similar efficacy in reducing fracture risk.

Intermittent cyclical etidronate (400 mg cyclical etidronate for 14 days followed by 76 days of 500 mg of calcium per day), is effective in the secondary prevention of vertebral fractures in women with at least two vertebral fractures and radiological osteopaenia but without targeting treatment using DXA.¹¹⁹

6.2.1 OPTIONS FOR THERAPY

Provided underlying destructive disease such as tumour (including myeloma), or infection, has been excluded as the cause of multiple vertebral fractures, there is evidence¹¹⁷⁻¹¹⁹ that targeting women with at least two vertebral fractures with bisphosphonates is associated with a significant reduction in vertebral fracture risk.

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Postmenopausal women who have suffered at least two vertebral fractures should be considered for one of the following options:

A To reduce fracture risk at all sites: treatment with oral risedronate (5 mg daily or 35 mg once weekly + calcium $\pm$ vitamin D).

Although not tested specifically in this scenario in clinical trials, it is likely that alendronate would have equal efficacy to risedronate.

A To reduce vertebral fracture risk: treatment with intermittent cyclical etidronate (400 mg daily for 14 days + 500 mg calcium daily for 76 days, repeating 3 monthly cyclical therapy).

In either of these cases treatment can be initiated without prior assessment by DXA scanning.

The selection of specific drug therapy for an individual patient is at the discretion of the prescribing clinician taking into account the patient's health record, but will also be influenced by formulation, cost, tolerability, and patient choice. Other things being equal, however, risedronate or alendronate should be the preferred option for this category of patient as they reduce fracture risk at all sites.

6.3 POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS DETERMINED BY AXIAL DXA AND WITH A HISTORY OF AT LEAST ONE VERTEBRAL FRACTURE

6.3.1 BISPHOSPHONATES

Alendronate 10 mg daily (with 500 mg calcium + 250 IU vitamin D per day) is effective in the secondary prevention of osteoporotic vertebral fractures when targeted at women with at least one vertebral fracture and with BMD at the femoral neck that is lower than a T-score of -1.6 .³⁶ Like other studies cited below, this trial used reference data from the independent National Health and Nutrition Survey (NHANES).¹²⁵ In this trial the incidence of morphometric vertebral fractures was significantly reduced. Although overall non-vertebral fracture risk was not reduced, specific fracture subtypes such as hip fracture were significantly reduced.

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The alternative regimen of alendronate 70 mg once weekly is as effective as the 10 mg daily regimen in increasing BMD (although there are currently no fracture data).¹²⁶

1++

6.3.2 HORMONE REPLACEMENT THERAPY

Only one small RCT of the efficacy of transdermal oestrogen in the secondary prevention of fractures has been identified.¹⁰⁶ Patients were recruited on the basis of low bone density and the number of incident vertebral fractures was used to define efficacy, rather than the number of women suffering a new vertebral fracture as used in most other trials.

1+

6.3.3 RALOXIFENE

60 mg raloxifene in association with 500 mg calcium and between 400 and 600 IU vitamin D per day has been shown to be effective in reducing the incidence of morphometric vertebral fractures in women with low BMD,¹¹⁰ and either one moderate or two mild vertebral fractures. Raloxifene has not been shown to reduce the incidence of non-vertebral fractures.

1++

6.3.4 CALCITONIN

200 IU calcitonin intranasally in association with 1000 mg calcium plus 400 IU vitamin D per day has been shown to reduce the incidence of vertebral fractures.¹²¹ Unusually, a dose response relationship was not seen: neither 100 IU per day nor 400 IU per day were associated with a change in the incidence of morphometric vertebral fractures. Calcitonin has not been shown to have efficacy in reducing the incidence of non-vertebral fractures in well conducted RCTs.

1++

6.3.5 OPTIONS FOR THERAPY

Postmenopausal women who have suffered at least one vertebral fracture and who have had osteoporosis confirmed by DXA scanning should be considered for one of the following options:

A To reduce fracture risk at all sites: treatment with oral alendronate (10 mg daily or 70 mg once weekly + calcium ± vitamin D).

Although not tested specifically in this scenario in clinical trials, it is likely that risedronate would have equal efficacy to alendronate

A To reduce vertebral fracture risk: treatment with oral raloxifene (60 mg daily + calcium ± vitamin D).

B To reduce vertebral fracture risk: treatment with intranasal calcitonin (200 IU daily + calcium ± vitamin D).

☒ Use of HRT can be considered as a treatment option for osteoporosis to reduce vertebral fracture risk, but the risks and benefits should be discussed with each individual woman before starting treatment (see section 5).

The selection of specific drug therapy for an individual patient is at the discretion of the prescribing clinician taking into account the patient's health record, but will also be influenced by formulation, cost, tolerability, and patient choice. Other things being equal, however, alendronate or risedronate should be the preferred option for this category of patient as it reduces fracture risk at all sites. Calcitonin has been shown to have some effectiveness as an analgesic for acute pain (*section 6.11.1*) and may be considered for patients suffering pain from vertebral fractures.

6.4 POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS DETERMINED BY AXIAL DXA, WITH OR WITHOUT PREVIOUS NON-VERTEBRAL FRACTURE

The importance of a non-vertebral fracture is that it at least doubles the potential fracture risk at that or other skeletal sites. The evidence base for treating this group of patients derives from studies that have targeted therapy on the basis of low BMD and have shown efficacy in reducing the risk of subsequent fracture. Treatment should be given on the basis of low BMD. If a patient

has a non-vertebral fracture they are at greater risk of future fracture.⁷⁸ It follows that there should be greater benefits from treating this high risk group (patients with low BMD and non-vertebral fracture) due to the higher number of fractures prevented.

6.4.1 BISPHOSPHONATES

Alendronate 10 mg per day (with 500 mg calcium + 250 IU vitamin D) has been studied in a large clinical trial³⁷ comprising over 4,400 patients where treatment was targeted on the basis of low BMD alone without previous fracture. During the trial, international standardisation of the hip BMD reference data occurred and this impacted significantly on the actual severity of reduction of BMD in the patients recruited to this trial. Subsequent analyses based on the NHANES reference database led to re-evaluation of the entire clinical trial group with re-categorisation of their bone densities by T-scores. The incidence of vertebral fractures is reduced in women treated at femoral neck T-score ≤ -1.6 . If, however, treatment is targeted at those patients with femoral neck T-score ≤ -2.5 , a reduction in incidence of vertebral and non-vertebral (including hip) fracture is seen.

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Similar efficacy in non-vertebral fracture risk reduction has been reported in another clinical trial of alendronate¹²² in which 1900 women were treated with alendronate 10mg daily with 500mg calcium per day on the basis that their lumbar spine BMD T-score was ≤ -2 .

Risedronate 5 mg per day (with 1,000 mg calcium plus up to 500 IU vitamin D per day) has been shown to be effective when targeted at elderly women with femoral neck T-scores of ≤ -4 (equates with NHANES T-scores of around -2.7 to -2.9) or with slightly higher bone density and other skeletal risk factors such as increased hip axis length.¹¹⁶ This study uniquely addressed the primary end point of hip fracture incidence and demonstrated efficacy in reducing non-vertebral fracture risk, and specifically hip fracture risk. The incidence of hip fractures was low at 3.2% in the placebo group over three years.

6.4.2 RALOXIFENE

Raloxifene 60 mg per day (with 500 mg calcium and up to 600 IU of vitamin D per day) has been studied in 4500 women who were treated on the basis of femoral neck T-score ≤ -2.5 .¹¹⁰ The relative risk of morphometric vertebral fractures in association with raloxifene was reduced. There was no significant reduction in the incidence of non-vertebral fractures.

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6.4.3 OPTIONS FOR THERAPY

Postmenopausal women who have had low BMD confirmed by DXA scanning should be considered for one of the following options:

A To reduce fracture risk at all sites: treatment with either oral alendronate (10 mg daily or 70 mg once weekly + calcium $\pm$ vitamin D) or oral risedronate (5 mg daily or 35 mg once weekly + calcium $\pm$ vitamin D).

A To reduce vertebral fracture risk: treatment with oral raloxifene (60 mg per day + calcium $\pm$ vitamin D).

The selection of specific drug therapy for an individual patient is at the discretion of the prescribing clinician taking into account the patient's health record, but will also be influenced by formulation, cost, tolerability, and patient choice. Other things being equal, however, alendronate or risedronate should be the preferred options for this category of patient as they reduce fracture risk at all sites.

6.5 FRAIL, ELDERLY (AGED 80+ YEARS) WOMEN WITH A DIAGNOSIS OF OSTEOPOROSIS, WITH OR WITHOUT PREVIOUS OSTEOPOROTIC FRACTURES

Studies assessing the efficacy of the bisphosphonates etidronate, alendronate and risedronate and of the SERM raloxifene, have generally recruited women up to 80-85 years of age and one study¹¹⁶ included a study arm that recruited women of any age over 80 years. Age *per se* should not therefore preclude treatment with antiresorptive therapies. The same criteria for targeting treatment apply to the elderly. Axial DXA would be a prerequisite to establish that the BMD is sufficiently low before starting treatment with bisphosphonates, unless the patient has suffered multiple vertebral fractures.

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For such patients, and others who are perceived to be “frail” such as those who are housebound, another common treatable risk factor for hip fracture is vitamin D deficiency. This is a consequence of lack of exposure to ultraviolet light. There is evidence that treating these frail patients with calcium and vitamin D can reduce the incidence of hip fractures by 35% and non-vertebral fractures by 26% without the need to either measure vitamin D or target this therapy using DXA scanning.¹²⁷

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6.5.1 OPTIONS FOR THERAPY

A To reduce fracture risk at all sites elderly women who have suffered multiple vertebral fractures or who have had osteoporosis confirmed by DXA scanning, should be considered for treatment with either oral risedronate (5mg daily or 35 mg once weekly + calcium ± vitamin D) or oral alendronate (10 mg daily or 70 mg once weekly + calcium ± vitamin D).

It is clear that targeting bisphosphonate therapy (risedronate) to patients whose fracture risk is defined on the basis of risk factors for falling, will not reduce fracture risk.¹¹⁶ Bisphosphonates strengthen bone, they do not prevent falls.

☒ Falls risk reduction strategies should be employed to reduce fracture risk for elderly women who have suffered any form of previous fracture.

A To reduce hip fracture risk, frail elderly women who are housebound should receive oral calcium 1,000-1,200 mg daily + 800 IU vitamin D.

It is not necessary to measure vitamin D levels before commencing treatment.

6.6 MEN WITH A DIAGNOSIS OF OSTEOPOROSIS DETERMINED BY AXIAL DXA WITH OR WITHOUT PREVIOUS OSTEOPOROTIC FRACTURE

Although osteoporotic fractures are less common in men than women, men experience greater fracture-associated morbidity and mortality.¹²⁸⁻¹³¹ Men are also at increased risk of osteoporosis from secondary causes.^{42,43}

In women there is a clear relationship between BMD and fracture risk. Further studies are required to establish whether this is also true for men. It is therefore not certain whether women's and men's bones will fracture at similar BMD levels. There is some evidence that men and women may fracture at similar gender-specific T-scores of BMD,¹³² supporting the WHO criteria as being applicable to men using the average young adult male BMD at peak bone mass as the reference for comparison. There are few studies in males with osteoporosis and more studies are required to establish the efficacy of antiresorptive therapies in achieving primary and secondary prevention of osteoporotic fractures

There is one well conducted RCT¹³³ in men with low BMD and a history of one or more vertebral fractures or one non-vertebral osteoporotic fracture. Alendronate (10 mg daily + 500 mg calcium ± 400 IU vitamin D) was shown to significantly increase lumbar spine and femoral neck BMD and reduce morphometric vertebral fracture risk and height loss.

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The evidence relating to calcium + vitamin D supplementation in men is inconsistent. The efficacy of calcium + vitamin D in the absence of concurrent antiresorptive therapy in osteoporotic men is not known.

The efficacy of Calcitriol in reducing vertebral fracture risk or changing hip or spinal BMD in men has not been established.

The evidence base for the use of androgens is small and dominated by poor quality studies. Testosterone in hypogonadal men may increase spinal BMD but there are no trial data relating to fracture outcomes. There are no convincing data of efficacy in changing BMD in eugonadal men. No studies have targeted testosterone on the basis of low BMD.

6.6.1 OPTIONS FOR THERAPY

A To reduce fracture risk at all sites, men with low BMD and/or a history of one or more vertebral fractures or one non-vertebral osteoporotic fracture should be treated with oral alendronate (10mg + 500mg calcium $\pm$ 400 IU vitamin D daily).

70mg weekly oral alendronate has been shown to result in equivalent BMD changes to oral 10mg once daily in women.¹²⁶ It is not currently licensed for use in men. It is likely that both formulations share the same efficacy with regard to fracture risk in men.

6.7 CORTICOIDSTEROID INDUCED OSTEOPOROSIS

The guideline development group decided not to proceed with a detailed literature review of corticosteroid induced osteoporosis in view of the publication of an evidence based guideline published by the UK Bone and Tooth Society in association with the National Osteoporosis Society and the Royal College of Physicians of London in December 2002.¹³⁴ The clinical practice algorithm from that guideline is reproduced in Annex 5.

6.8 COMBINATION OF TREATMENTS

In clinical trials bisphosphonates (alendronate, etidronate, or risedronate), raloxifene and calcitonin have usually been assessed in conjunction with calcium +/- vitamin D. Doses of calcium have varied from 500 to 1,000 mg and vitamin D from 6.25 to 20 μ g (250 to 800 IU) per day. Where calcium intake is suboptimal (see section 4.3.2), daily doses of up to 1000mg calcium carbonate plus 20 μ g (800 IU) vitamin D are appropriate for use in association with these drugs (in the absence of conditions associated with hypercalcaemia).

Several clinical trials have reported that the addition of bisphosphonate to HRT¹³⁵⁻¹³⁷ or of bisphosphonate to raloxifene confers additional benefit regarding BMD compared with monotherapy. Further studies are required to elucidate whether such combinations achieve greater reductions in fracture incidence. Until data are available, combinations of HRT or raloxifene with bisphosphonates are not recommended.

6.9 DURATION OF TREATMENT

After initiating therapy on the basis of assessment of fracture risk defined using fracture history, usually together with axial DXA measurement in the context of the patient's age, it is likely that treatment would be required on a lifelong basis. Fracture efficacy data, however, exist only for between 1-4 years, the duration of the doubleblinded randomised placebo-controlled trials. Safety data do, however, exist for several years thereafter for bisphosphonates and suggest that there is unlikely to be any cumulative disadvantage to the skeleton even though they are likely to be retained in the skeleton for years. Few data exist regarding BMD or fracture risk after cessation of bisphosphonates, although one study¹³⁸ reported increases in markers of bone turnover, without changes in BMD two years after stopping alendronate and this may indicate reactivation of processes that may ultimately result in bone loss.

Identification of optimal longer term treatment patterns should be the subject of future research. Until such time as this has been clarified, it should be assumed that long term management is required. Further data on the benefit of intermittent regimens is awaited.

6.10 MONITORING TREATMENT EFFECT WITH DXA

There is evidence of a relationship between therapy associated increases in BMD and the extent of fracture risk reduction.^{139,140}

The efficacy of "monitoring" BMD responses by DXA has not been evaluated by clinical trial, although it has been a key end point in most clinical trials relating to osteoporosis management. Application of repeat DXA to individual patients requires consideration of the following:

- The lumbar spine trabecular bony site is the preferred site for follow up DXA.
- Increases of BMD of at least 3-4% are required as “the least significant difference” that is likely to exceed the error of the measurement.
- Follow-up should normally be undertaken only after at least two years of therapy. (Note that more frequent follow up is required to monitor the effects of bone-toxic drugs such as chemotherapy.)

There are circumstances in which follow up DXA can be helpful in managing individual patients. Until such time as this issue has been resolved by clinical trial, local policies relating to DXA follow up should be devised by agreement with the DXA service provider, primarily to ensure that allocation of scans for monitoring is feasible within the existing DXA service arrangements.

6.11 TREATMENT OF PAIN

From the patient’s perspective the pain of osteoporotic fracture in both the acute and chronic phase is often their most immediate concern. Osteoporotic vertebral fractures may be painless but progressive vertebral failure may give rise to worsening dorsal kyphosis with possible subsequent chronic pain and debility. The acute pain of fracture can vary widely and chronic pain is associated with significant physical dysfunction and decreased quality of life.

Treatment must involve an appreciation of both the need to prevent further progression of the osteoporosis and an assessment of analgesic needs. The use of the WHO Analgesic Ladder may be of value in logically achieving adequate analgesia and its use is validated outwith cancer care.¹⁴¹ Outwith conventional analgesic agents, the use of bisphosphonates has not been shown to alleviate pain.

6.11.1 ACUTE PAIN

General measures in the acute fracture phase should be undertaken as appropriate including rest, ice, compression and elevation. Conventional analgesics should be used regularly rather than on demand. Other specific measures such as splintage, reduction and plaster immobilisation or fracture fixation need to be utilised as appropriate to the fracture.

As acute pain can be debilitating, admission to hospital may be necessary, both for analgesia and mobilisation. Achieving adequate analgesia may be difficult and the involvement of a Pain Service may be of value. Opiates may be necessary. Care in their use in the elderly should not prevent their use.

Calcitonin, preferably intranasally rather than by injection, has been shown to be of value in difficult cases with unremitting pain due to acute vertebral fracture¹⁴² but it does not hold a product licence as an analgesic agent in the United Kingdom. It is licensed for the treatment of postmenopausal osteoporosis.

Successful analgesia in the acute phase should allow early mobilisation.

6.11.2 CHRONIC PAIN

Chronic pain should be identified and treated along accepted guidelines and analgesic scales. Recording of pain levels using, for example, a Visual Analogue Scale is of value in assessing achieved analgesia. Adequate control of chronic pain is often difficult and unsatisfactory. Analgesic agents, NSAIDs, and physiotherapy with physical activity programmes are all of value.^{90,143} Calcitonin has again been shown to be of value in control and treatment of chronic back pain.¹⁴²

Parathyroid hormone has been used therapeutically in an 18-month RCT which has shown benefit in reducing back pain in postmenopausal women.¹⁴⁴ It is not yet licensed for use in the United Kingdom and the evidence for its efficacy has not therefore been examined in this guideline.

The use of non-pharmacological measures such as acupuncture or Transcutaneous Electrical Nerve Stimulation (TENS) have been shown to be of value and should be considered. Back strengthening exercises are also valuable.

The psychological care of the osteoporotic patient with pain is important as depression and lack of sleep are commonplace. Clinical psychological intervention may be of benefit along with adjunctive therapy of antidepressants.

6.11.3 NEW DEVELOPMENTS

At present there is some suggestion that emerging technologies such as vertebroplasty and kyphoplasty¹⁴⁵ may offer a therapeutic role in acute vertebral fracture with significant pain reduction. Their role still needs to be defined through randomised controlled trials and until such evidence becomes available they cannot be recommended.

7 Economics and Service Provision

A review of the literature for evidence of cost effectiveness of diagnosis and treatment options covered by “A” grade recommendations was carried out. The evidence for diagnostic approaches is minimal but a recent Health Technology Assessment (HTA)¹⁴⁶ provides some evidence on the cost effectiveness of treatment options.

We also offer a considered economic perspective on some aspects of service provision as they relate to our guideline recommendations.

7.1 COST EFFECTIVENESS OF DIAGNOSTIC APPROACHES

Only three relevant economic papers on the use of DXA scanning were identified. These all involved modelling, rather than incorporation of economic evaluation into clinical trials.

There is some evidence that for relatively expensive medication, such as bisphosphonates, treatment programmes with prior bone density screening are likely to be more cost-effective than those without and, in some circumstances, become cost saving.^{147,148}

One recent paper concluded that diagnosis and treatment of women at risk of osteoporosis would be made more cost effective by targeting treatment to those with the lowest bone measurement results. Inclusion of another assessment, such as a risk profile, may improve the cost effectiveness of diagnosis.³²

7.2 COST EFFECTIVENESS OF TREATMENT

A recent Health Technology Assessment¹⁴⁶ examined the cost utility and cost effectiveness of different treatments for established osteoporosis. This study compared treatments using the cost per quality-adjusted life-year (QALY). It used a threshold of £30,000 or less per QALY to represent cost effectiveness. Using an economic model developed by the authors, at age 50 years only HRT and calcium plus vitamin D were likely to be considered cost-effective (assuming that the agent would decrease the risk of non-vertebral fractures at this age). In older age groups a wider range of treatments, including HRT, calcium with or without vitamin D and bisphosphonates were considered cost effective.

This HTA demonstrates that age is an important determinant of cost effectiveness since the risk of fractures increases with age. High costs of intervention are associated with poorer cost effectiveness since, in general, the variation in cost is greater than any proven variation in efficacy.

7.3 IMPLICATIONS FOR SERVICE PROVISION

The volume of evidence, though small, does indicate that a cost-effective way of providing a good service in terms of diagnosis and treatment of osteoporosis involves prior bone density measurement by DXA scanning of patients at highest risk. One model costing for providing such a service is offered in Annex 3.

8 Implementation, audit and research

8.1 LOCAL IMPLEMENTATION

Implementation of national clinical guidelines is the responsibility of each NHS Trust and is an essential part of clinical governance. It is acknowledged that every Trust cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

The National Osteoporosis Society has produced an Osteoporosis Framework⁸¹ setting out standards for osteoporosis services in Scotland. This framework has been endorsed by the Chief Medical Officer.

The key recommendations from the NOS framework document are:

- Include prevention of osteoporotic fractures in the local Health Improvement Plan (HIP)
- Identify lead clinicians in primary and secondary care to develop a local osteoporosis programme based on this framework. Each Local Health Cooperative, Primary Care, and Acute Trust should have a lead clinician for osteoporosis.
- Each Health Board should have a consultant in Public Health to assist in coordinating this osteoporosis strategy between primary and secondary care.
- Establish a local osteoporosis advisory group to facilitate multidisciplinary implementation of this framework.
- Use a selective case-finding approach to target treatment at individuals at high risk.
- Provide access to adequate levels of diagnostic and specialist services – eg a Local Health Care Co-operative serving a population of 50,000 would require approximately 500 DXA scans per year.
- Promote the use of care pathways and audit to improve standards of care.
- Monitor performance to assess health impact.

8.2 KEY POINTS FOR AUDIT

Diagnosis

- Risk profile of those referred for investigation
- Proportion of low impact fractures in orthopaedic wards referred for investigation of osteoporosis
- Proportion of patients who are referred following identification of severe osteopaenia on plain X-ray
- Proportion of those sent for a DXA scan that are subsequently diagnosed with osteoporosis

Treatment

- Proportion of patients diagnosed with osteoporosis that are subsequently offered treatment.
- Proportion of patients referred for high-intensity strength training and low impact weight bearing exercise.
- Proportion of post-menopausal women achieving a dietary intake of 1000mg calcium per day

Follow-up

- Number of osteoporosis patients followed-up two years after first referral
- Extent of compliance with treatment.
- Increase in BMD following treatment.

Audit criteria for osteoporosis are expected to be developed by Scottish Programme for Improving Clinical Effectiveness in Primary Care (SPICEpc) based on this guideline.

8.3 RECOMMENDATIONS FOR RESEARCH

The following list of research topics represents the key areas where the guideline development group were unable to identify good existing evidence, and where there is a need for such evidence.

- Development of a validated risk scoring method that would allow primary care workers to prioritise patients for scanning or treatment.
- The role of DXA in monitoring the effectiveness of treatment over time.
- Identification of the most appropriate biochemical markers for monitoring the effectiveness of treatment, and the preferred strategy for their use.
- Investigation of the possible role of such techniques as vertebroplasty and kyphoplasty in the management of acute vertebral fracture and the associated pain.

9 Information for discussion with patients and carers

9.1 NOTES FOR DISCUSSION WITH PATIENTS AND CARERS

9.1.1 WHO IS AT RISK OF OSTEOPOROSIS?

There are a number of factors that can help identify individuals who are at risk of developing osteoporosis. Women are generally more at risk than men, particularly once they have passed the menopause. This does *not* mean that men should not consider their level of risk, particularly if they have been exposed to one or more of the secondary causes of osteoporosis (Section 2.6).

Those at highest risk of osteoporosis are people who have already suffered a broken bone, particularly in the spine or hip. Fractures that occur without an obvious cause, such as a fall or other accident, are particularly likely to be associated with osteoporosis. Osteoporotic spinal (vertebral) fractures may only be identified during investigation of pain or other symptoms.

Other factors that increase the risk of osteoporosis include:

- Family history
- Increasing age
- Caucasian ethnic origin
- Low BMI
- Sedentary lifestyle
- Smoking
- Long term use of corticosteroids

None of these factors positively indicate the presence of osteoporosis either on their own or in combination. As a general rule, however, the more risk factors that apply to an individual the more likely they are to develop osteoporosis.

9.1.2 WHO SHOULD BE SENT FOR A BONE SCAN?

The decision on whether to provide a bone scanning service, and at what level, is a complex one that depends on a range of clinical and economic factors. This guideline identifies DXA scanning as the most effective means of diagnosing osteoporosis, and advocates the availability of such scanners in all Health Board areas. Even when scanners are available, however, the decision on who to scan must be based on a balance between the level of risk for individual patients and the availability of local resources.

The use of other techniques based on measurements of bone density at the heel or forearm have been considered, but it has not been demonstrated that any of these techniques are sufficiently reliable to be used as diagnostic tools for osteoporosis.

There is no evidence that repeated scans are useful for monitoring progress or the success of treatments. There is evidence that scans carried out less than two years after commencing treatment can give misleading results. This guideline recommends that repeat scans should only be used where they are likely to influence future treatment.

9.1.3 WHAT CAN BE DONE TO MINIMISE RISK OF OSTEOPOROSIS?

Some risk factors, such as age or gender, cannot be altered. Many others can be modified, and the overall level of risk reduced accordingly. Chief among these are diet and exercise. A diet rich in calcium and vitamin D will help to reduce the level of risk, particularly if associated with weight control. A programme of exercise aimed at increasing strength and balance is also helpful, particularly as it can help reduce the risk of falling and causing further fractures.

Frail elderly women are at particular risk and should be offered assistance with fall risk reduction if they have already suffered any kind of fracture. If housebound or living in residential care, they should be offered calcium and vitamin D supplementation.

Further information and advice on the control of risk factors is available from the sources listed later in this section of the guideline, and from the Osteoporosis in Scotland website at www.osteoporosisinscotland.org (to be launched late summer 2003).

9.1.4 ARE THERE ANY RISKS ASSOCIATED WITH MEDICATIONS GIVEN FOR OSTEOPOROSIS?

Many of the medicines prescribed for osteoporosis have potential side effects. Some of these can be minimised by strictly adhering to the (sometimes fairly complicated) instructions for taking these drugs. The question of risk associated with HRT is particularly complex, and should be discussed with all patients being offered this option

Patients should be advised of the importance of continuing to take medication, and invited to discuss alternatives if a particular prescription is producing side effects or is otherwise giving them cause for concern. All medication prescribed for osteoporosis should be reviewed periodically to ensure its continued effectiveness.

9.1.5 MANAGING PAIN

Many of the consequences of osteoporosis, particularly vertebral fractures, are associated with severe pain. There are a number of ways, some involving painkillers and some non-pharmaceutical measures, in which this pain can be alleviated. Patients should be advised of all the options, and encouraged to try different approaches until they find one that works well for them. It is important to stress that patients do not need to put up with pain, but should discuss it and the problems it causes with their GP.

9.2 SOURCES OF FURTHER INFORMATION FOR PATIENTS AND CARERS

National Osteoporosis Society

Camerton, Bath BA2 0PJ

Tel: 01761 471771 (for general enquiries), Helpline: 0845 4500230 (for medical queries)

Fax: 01761 471104

E-mail: info@nos.org.uk, Website: www.nos.org.uk

The NOS is the only national charity dedicated to improving the diagnosis, prevention and treatment of osteoporosis. They provide a wide range of materials and support including access to a wide range of information and the organisation of support groups.

NHS Health Scotland

Woodburn House, Canaan Lane, Edinburgh EH10 4SG

Tel: 0131 536 5500, Textphone: 0131 536 5503, Fax: 0131 536 5501

NHS Health Scotland provides access to a wide range of health information resources relating to falls and fall prevention, as well as osteoporosis.

Contact Health Promotion Library Scotland to access library services and to get help with general health information enquiries.

Tel: 0845 912 5442, Textphone: 0131 536 5503, Fax: 0131 536 5502

Email: library.enquiries@hebs.scot.nhs.uk, Website: www.hebs.com/library

Age Concern Scotland

Leonard Small House, 113 Rose Street, Edinburgh EH2 3DT

Telephone: 0131 220 3345, Freephone: 0800 00 99 66 (7am - 7pm, 7 days a week)

Fax: 0131 220 2779

E-mail: enquiries@acscot.org.uk, Website: www.ageconcernscotland.org.uk/home.asp

Age Concern provides information on a wide range of topics that may be useful for those wishing to prevent or manage osteoporosis, including information on healthy eating and the prevention of falls.

10 Development of the guideline

10.1 INTRODUCTION

SIGN is a collaborative network of clinicians and other healthcare professionals, funded by NHS Quality Improvement Scotland. The overall direction of SIGN's development and SIGN's guideline programme is determined by members of SIGN Council. Guidelines are developed using a standard methodology, based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in "SIGN 50: A Guideline developer's handbook" available at www.sign.ac.uk

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Professor David Reid	<i>Consultant Rheumatologist, Foresterhill, Aberdeen</i>
Dr Mary Scott	<i>General Practitioner, Dunfermline</i>
Mrs Anne Simpson	<i>National Osteoporosis Society Co-ordinator for Scotland</i>

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. Declarations of interests were made by all members of the guideline development group. Further details are available from the SIGN Executive. In addition to the work done by Dr Krabshuis, guideline development and literature review expertise, support, and facilitation were provided by the SIGN Executive.

10.3 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out by Dr Justus Krabshuis using an explicit search strategy devised in collaboration with members of the guideline development group.

Searches were restricted to systematic reviews, meta-analyses, randomised controlled trials, and longitudinal studies. Internet searches were carried out on the websites of the Canadian Practice Guidelines Infobase, the UK Health Technology Assessment Programme, the US National Guidelines Clearinghouse, and the US Agency for Healthcare Research and Quality. Searches were also carried out on the search engines Google and OMNI, and all suitable links followed up. Database searches were carried out on Cochrane Library, Embase 1993 – 2000, and Medline 1990 - 2000. Searches were later updated to June 2001.

The main searches were supplemented by material identified by individual members of the development group. All selected papers were evaluated using standard methodological checklists before conclusions were considered as evidence.

10.4 CONSULTATION AND PEER REVIEW

10.4.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held in February 2002 and was attended by 328 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline. The comments received from the national open meeting were considered when the guideline was redrafted for peer review.

10.4.2 SPECIALIST REVIEW

The guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. SIGN is very grateful to all of these experts for their contribution to the guideline.

Dr Christine Bain	<i>Consultant Gynaecologist, Aberdeen</i>
Professor David Barlow	<i>Nuffield Professor of Obstetrics and Gynaecology, University of Oxford</i>
Dr Jane Bishop-Miller	<i>Consultant Physician in Care of the Elderly, Stirling</i>
Dr Juliet Compston	<i>Reader in Metabolic Bone Disease, University of Cambridge Clinical School</i>
Professor Cyrus Cooper	<i>Consultant in Rheumatology, Southampton General Hospital</i>
Dr Veena Dhillon	<i>Consultant Rheumatologist, Western General Hospital, Edinburgh</i>
Dr Roger Francis	<i>Consultant in General Medicine, Freeman Hospital, Newcastle upon Tyne</i>
Dr Anna Glasier	<i>Director, Family Planning and Well Woman Services, Edinburgh</i>
Professor James Hutchison	<i>Regius Professor of Surgery, Aberdeen</i>
Dr Elizabeth MacDonald	<i>Consultant Physician, Royal Victoria Hospital, Edinburgh</i>
Mr Phil Mackie	<i>Senior Specialist in Public Health, Edinburgh</i>
Dr Allan Merry	<i>General Practitioner, Ardrossan</i>
Mr Walter Newton	<i>Consultant in Orthopaedics, Hairmyres Hospital, East Kilbride</i>
Dr Patricia O'Connor	<i>Consultant in Accident & Emergency, Hairmyres Hospital, East Kilbride</i>
Dr Paul Padfield	<i>Consultant Physician/Reader in Medicine, Western General Hospital, Edinburgh</i>
Dr Andrew Power	<i>Medical Prescribing Adviser, Glasgow Royal Infirmary</i>
Professor David Purdie	<i>Consultant in Obstetrics & Gynaecology, Hull Royal Infirmary</i>

Dr Christine Roxburgh	<i>General Practitioner, Perth</i>
Professor Hamish Simpson	<i>Professor of Orthopaedics, Edinburgh</i>
Sister Anne Sutcliffe	<i>Osteoporosis Sister, Freeman Hospital, Newcastle upon Tyne</i>
Dr Peter Tothill	<i>Honorary Fellow of the University of Edinburgh, Department of Medical Physics</i>
Dr Sally Voice	<i>General Practitioner, Montrose</i>

10.4.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an Editorial Group comprising the relevant specialty representatives on SIGN Council to ensure that the peer reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The Editorial Group for this guideline was as follows:

Dr David Alexander	<i>British Medical Association Scottish General Practice Committee</i>
Professor Gordon Lowe	<i>Chairman of SIGN; Co-Editor</i>
Miss Tracy Nairn	<i>Senior Professional Adviser, Care Commission, Glasgow</i>
Dr Sara Twaddle	<i>Director of SIGN; Co-Editor</i>
Dr Peter Wimpenny	<i>School of Nursing and Midwifery, The Robert Gordon University</i>

Each member of the guideline development group then approved the final guideline for publication.

Annex 1

Glossary

AP spine	Anteroposterior spine
Biochemical marker of bone turnover	Chemical compounds that can be identified in blood or urine that are known to indicate either formation of new bone, or bone resorption
BMD	Bone Mineral Density
DEXA	See Dual-energy X-ray Absorptiometry
Dowager's hump	An abnormal outward curvature of the vertebrae of the upper back. Compression of the anterior portion of the involved vertebrae leads to forward bending of the spine (kyphosis) and creates a hump at the upper back.
Dual-energy X-ray Absorptiometry	A technique for measuring BMD using a specially designed scanner based on the use of two X-ray beams at different energy levels.
DXA	See Dual-energy X-ray Absorptiometry
Kyphosis	Outward curvature of the spine, causing a humped back (See <i>also</i> Dowager's hump)
Low impact fracture	A fracture occurring in the absence of major trauma.
Morphometric fracture	Fracture identified by a change in shape of a bone, rather than from pain or other symptoms
NHANES	National Health and Nutrition Survey
Osteopaenia	Bone mineral density between 1 standard deviation and 2.5 standard deviations below the young normal mean
Osteoporosis	Bone mineral density more than 2.5 standard deviations below the young normal mean
pDXA	Peripheral Dual-energy X-ray Absorptiometry
pQCT	Peripheral Quantitative Computed Tomography
Quantitative Computed Tomography	A technique for assessing BMD using a standard CT scanner
QCT	See Quantitative Computed Tomography
Secondary prevention of fracture	Prevention of further fractures in a patient who has sustained a low impact fracture
SERM	Selective Estrogen-Receptor Modulator
SEXA	See Single-energy X-ray Absorptiometry
Single-energy X-ray Absorptiometry	A technique for measuring BMD based on the use of a single-energy X-ray beam.
Single Photon Absorptiometry	A technique for measuring BMD based on the use of a radioactive source.
SPA	See Single Photon Absorptiometry
SXA	See Single-energy X-ray Absorptiometry
T-score	The number of standard deviations by which a patients BMD differs from the mean peak BMD for young normal subjects of the same gender.
Z-score	The number of standard deviations by which a patients BMD differs from the mean for subjects of the same age.

Annex 2

Model DXA Report

DXA Unit,
Hospital,
Address

GP
ADDRESS

Dear Dr

Re: Patient's Name
Address

Sex:

DOB:

Thank you for referring your patient for DXA which was performed on

Risk Factors for osteoporosis:

Early menopause; long term corticosteroid use.

Risk factors for fracture:

Previous Colles' fracture; current use of anticonvulsants; impaired visual acuity.

DXA Results:

Site	BMD g cm ⁻²	T-score	WHO Diagnosis	% of age-matched population with lower BMD
Spine (L1-L3)	0.503	- 4.9	Osteoporosis	<1
L Hip	0.596	- 2.3	Osteopenia	10

For diagnostic purposes it is normal to consider the site with the lowest T-score. For the sites measured the WHO category is: OSTEOPOROSIS.

L4 was excluded because BMD cannot be measured accurately due to an artifact.

Hip Fracture Risk:

Ten year risk – VERY LOW. Lifetime risk – EXTREME

{Very Low <5%, Low 5-10%, Moderate 10-15%, High 15-20%, Extreme >25%}

Note: For an age- and sex-matched patient of average BMD, the Ten Year risk is VERY LOW and the Lifetime risk is LOW.

The estimated hip fracture risks are based only on hip BMD and age.

Lateral Spine DXA:

The lateral spine DXA image shows a moderate wedge deformity of L4 and a severe wedge compression fracture of T6. These existing vertebral fractures significantly increase the risk of subsequent spine and hip fractures.

Life Style Advice:

Avoid smoking and excessive alcohol intake.

Advise adequate calcium intake.

Advise regular weight bearing exercise.

Recommended Treatment:

Bisphosphonate (Didronel PMO, Alendronate or Risedronate).

Follow up:

Please refer patient for repeat DXA in 2 years.

Yours sincerely,

Annex 3

Estimated annual cost of providing a DXA Service

Operating costs vary depending on the type of service provided but an example of typical annual operating costs is given below:

- Capital depreciation = £15,000
- Service contract = £6,500 (full contract covering all parts, labour and upgrades)
- 1.5 FTE Radiographer or Technologist = £43,000 (including overheads)
- 1 FTE Secretary / Receptionist = £14,000 (including overheads)
- 0.5 FTE Consultant = £37,500 (including overheads)
- Disposables = £4,000 (paper, discs, print cartridges etc)

Total = £120,000

Provided the scanners are fully utilised (4000 patients per annum), this corresponds to a cost of around £30 per patient.

If the workload is reduced to 2000 patients per annum, only 1 FTE Radiographer or Technologist and only 0.3 FTE consultant may be required but the cost increases to around £45 per patient.

Annex 4

Calculate your calcium¹⁴⁹

It is recommended that you take 1000 mg of dietary calcium daily to help to prevent loss of calcium from your bones. The richest natural sources of calcium are milk, yoghurt and hard cheeses. White bread, sardines and calcium fortified soya milk are also good sources of calcium. (Butter, cream and soft cheeses are poor sources of calcium).

Aim to take 3-4 portions of the following calcium rich foods daily (200-300 mg per portion):

- 200 ml glass milk
- 200 g bowl milk pudding
- 1 pot yoghurt
- 30 g/1oz hard cheese
- 200 g portion Macaroni cheese
- 170 g/6 oz Cheese & Tomato Pizza
- 200 ml glass soya milk + added calcium
- 60 g/2 oz sardines or fish paste
- 4 slices of white bread
- 1 bowl calcium rich cereal with milk
- 30 g/1 oz Tahini (sesame) paste

More detailed information on the calcium content of food is given in the table below. Also try to include a selection of foods with a more moderate amount of calcium, such as baked beans, spinach, orange juice and milk chocolate to ensure an adequate intake.

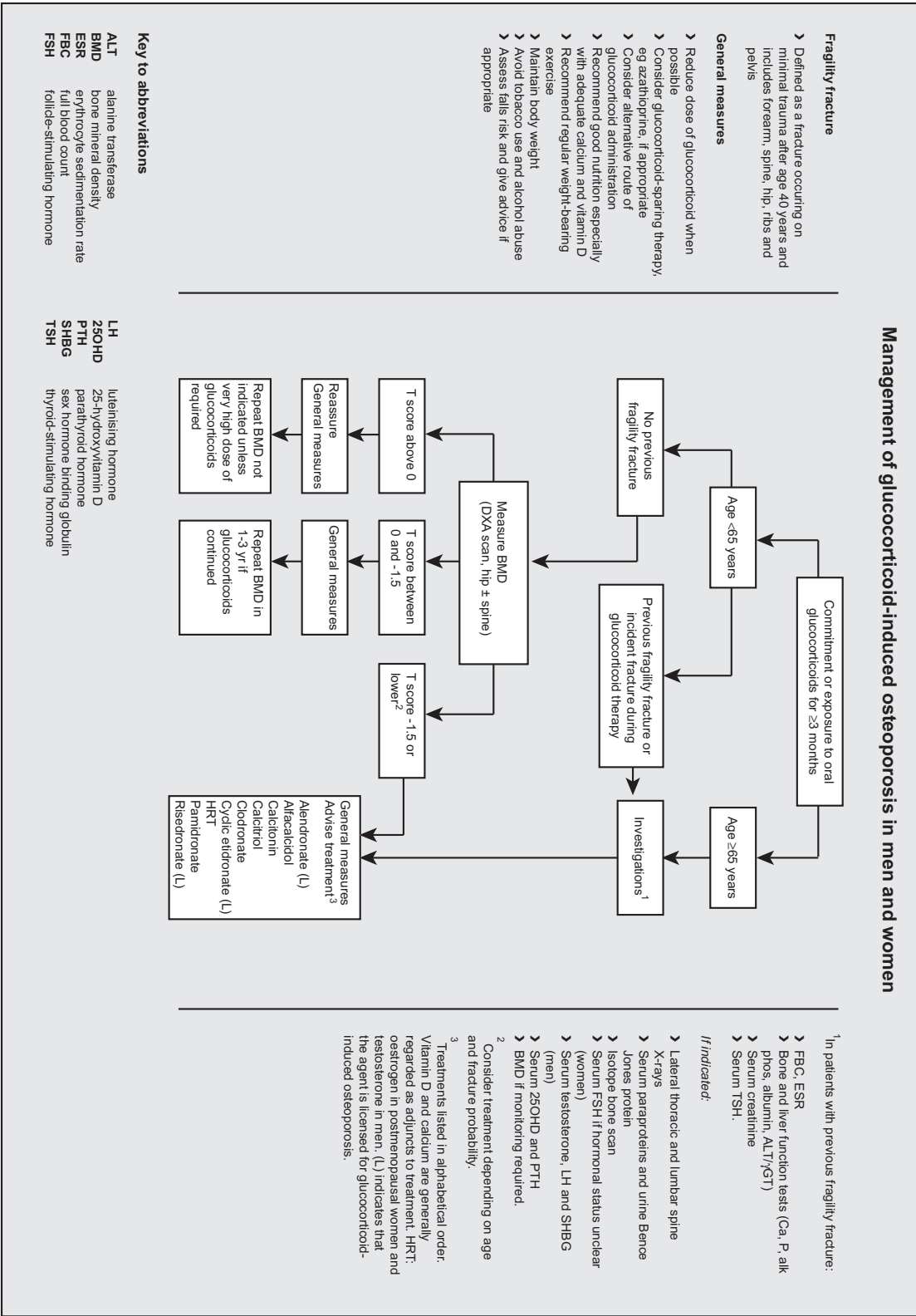
	Portion	Calcium (mg)
Dairy milk		
Milk (all types)	200 ml glass	240
Milk pudding	200 g bowl	260
Ice-cream (dairy)	60 g/2 oz	60
Cheese & yoghurt		
Plain yoghurt	125 g pot	250
Fruit yoghurt	125 g pot	170
Hard cheese e.g. Cheddar, Edam	30g/1 oz	225
Softer cheese e.g. Brie	30g/1 oz	80
Macaroni cheese	200 g/7 oz	340
Cheese & Tomato Pizza	170 g/6 oz	450
Confectionery		
White chocolate	50 g bar	140
Milk chocolate	50 g bar	110
Liquorice allsorts	50 g pkt	90
Bread & Cereals		
White bread (sliced)	4 x 30 g slices	200
Wholemeal bread	4 x 30 g slices	120
Nutrigrain	40 g bowl	220
Calcium fortified cereals e.g. Coco-pops; Rice Krispies; Cheerios	30 g bowl	140
Soya-milk products		
Soya milk (plain)	200 ml glass	26
Soya milk + calcium	200 ml glass	180
Soya fruit drink + calc*	330 ml	400
Soya yoghurt + calc*	125 g pot	126
Fish		
Sardines in oil	60 g/2 oz	300
Pilchards (canned)	60 g/2 oz	150
Fish paste	60 g/2 oz	170
Salmon (canned)	60 g/2 oz	50
Vegetables		
Tofu (steamed)	60 g/2 oz	300
Spinach (boiled)	90 g/3 oz	130
Baked beans	150 g/5 oz	80
Nuts & Seeds		
Tahini (sesame) paste	30 g/1 oz	200
Almonds	30 g/1 oz	70
Fruit & Fruit Juice		
Concentrated orange juice (unsweetened)	200 ml cup	70
Oranges	1 average	70
Figs (ready to eat)	30 g/1 oz	70

Note* Information on soya products with added calcium has been derived from manufacturers data.

Annex 5

Management of glucocorticoid-induced osteoporosis in men and women

Extracted with permission from *Glucocorticoid-induced osteoporosis: guidelines for prevention and treatment*.
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Update to printed guideline

7 Apr 2004

Section 4.3.2 changed from

Calcium supplementation using tablets is one means of ensuring an adequate calcium intake in those unwilling or unable to do so by dietary means. A daily calcium intake of 1,000 mg or more taken in tablet form is likely to reduce fracture rates by a similar rate to that seen with dietary derived sources of calcium. There is no evidence that a vitamin D supplement is needed for active people under 65 years of age. However, everyone over 65 years of age should aim to take 10 mg (400 IU) daily of vitamin D. For the majority of people this can only be achieved by vitamin D supplementation.⁹⁴ Where vitamin D deficiency has been confirmed or is likely, such as in the case of housebound individuals, a vitamin D supplement of 20 μ g (800 IU) is the recommended dose.

to

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22 Oct 2003

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Section 6.8 changed from

In clinical trials bisphosphonates (alendronate, etidronate, or risedronate), raloxifene and calcitonin have usually been assessed in conjunction with calcium +/- vitamin D. Doses of calcium have varied from 500 to 1,000 mg and vitamin D from 6.25 to 20 mg (250 to 800 IU) per day. Where calcium intake is suboptimal (see section 4.3.2), daily doses of up to 1000mg calcium carbonate plus 20 mg (800 IU) vitamin D are appropriate for use in association with these drugs (in the absence of conditions associated with hypercalcaemia).

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4 Jul 2003

Amendments to Table 6

Row 4 changed from –

Vertebral fracture	Risedronate ¹¹⁸	1225	-	8.4% over 3 years	18.1% over 3 years	0.51 (0.36,0.73)	10
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to

Vertebral fracture	Risedronate ¹¹⁸	1225	-	29% over 3 years	18.1% over 3 years	0.51 (0.36,0.73)	10
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Row 10 changed from –

Hip fracture	Alendronate ³⁷	1640	Femoral neck T≤-2.5	2.2% over 4.2 years	1% over 4.2 years	0.44 (0.18,0.97)	81
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to

Hip fracture	Alendronate ³⁷	1640	Femoral neck T≤-2.5	2.2% over 4.2 years	1% over 4.2 years	0.44 (0.18,0.97)	81
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1. **Calcium** and **vitamin D** supplements

2. **Biphosphonates**

3. **Teriparatide**

4. **Denosumab**

5. **Strontium ranelate**

6. **Calcitonin**

7. **Estrogen**

8. **Testosterone**

9. **Parathyroid hormone**

10. **Parathyroid hormone-related protein**

11. **Calcitonin receptor-related protein**

12. **Calcitonin receptor**

13. **Calcitonin receptor-like receptor**

14. **Calcitonin receptor-like receptor**

15. **Calcitonin receptor-like receptor**

16. **Calcitonin receptor-like receptor**

17. **Calcitonin receptor-like receptor**

18. **Calcitonin receptor-like receptor**

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27. **Calcitonin receptor-like receptor**

28. **Calcitonin receptor-like receptor**