Secondary prevention of osteoporosis: when should a non-vertebral fracture be a trigger for action?


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Summary

The burden of non-vertebral fractures is enormous. Hip fractures account for nearly 10% of all fractures (and a much greater proportion in the elderly), while wrist fractures may account for up to 23% of all limb fractures. The best available predictors of non-vertebral fracture risk are low BMD and a tendency to fall. Hip, forearm, proximal humerus and rib fractures have all been associated with low BMD, though ankle fracture is not strongly related to osteoporosis. Although clinical risk factors identify only about one-third of postmenopausal women at increased risk of osteoporotic fracture, the occurrence of one fracture commonly predicts a second fracture. Guidelines are presented for identifying and treating patients at risk of non-vertebral osteoporotic fractures, especially those with a previous fracture, based on the algorithm recently published by the Royal College of Physicians and the Bone and Tooth Society. Prevention of falls and use of external hip protectors may reduce the occurrence of hip fracture. Treatment options for patients presenting with hip fracture include HRT, bisphosphonates, and calcium plus vitamin D, and for Colles’ fracture include general measures, HRT, bisphosphonates, or calcitonin plus calcium.

Introduction

The burden of non-vertebral fractures on the National Health Service is enormous. Hip fractures alone account for nearly 10% of all fractures, and for a much higher proportion in the elderly. However, most orthopaedic surgeons do not see the need to investigate or treat osteoporosis in patients presenting with hip fracture. Over 180 000 osteoporosis-related fractures occur each year in the UK, of which about 70 000 are hip fractures, 25 000 are symptomatic vertebral fractures, and 41 000

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are wrist fractures. The direct cost (health plus social services) to the nation of these osteoporotic fractures is estimated as £1.7 billion/year, with hip fractures accounting for the greater part. Hospital resources are used to a disproportionate extent by patients with hip fractures. In a series in Rochester, Minnesota, hip fractures accounted for only 7% of all fractures, but for nearly 29% of those hospitalized and for 52% of hospital bed-days used. In contrast, fractures of the radius and ulna accounted for 27% of all fractures, but only for 8% of hospital bed-days. Targeting therapy to patients at high risk of sustaining hip fracture in particular, but also other non-vertebral fractures that may increase the risk of hip or other fractures, may provide substantial costs savings and improve patient management.

Decreased BMD at various skeletal sites has been associated with the occurrence of vertebral, hip, and wrist fracture in many studies, and evidence is beginning to accumulate that other fractures, e.g., humerus and rib fractures, may be related to osteoporosis. In view of this evidence, a UK Consensus Group recently reviewed the literature on non-vertebral osteoporosis-related fractures. This was not a systematic review, but all relevant English-language articles on issues relating to patients with non-vertebral fractures were identified and discussed by the group of experts, followed by a further discussion meeting to review the draft manuscript. The aim was to identify the risk factors for non-vertebral fractures, and specifically when such fractures should be considered as the trigger for initiating secondary prevention of osteoporosis, in order to improve the overall management of osteoporosis-related fractures. Adequate follow-up is particularly important for patients with these fractures, who are at risk of future fractures, but may only present to orthopaedic or fracture clinics.

Epidemiology of fracture

Hip fracture

In the West, the incidence of hip fracture rises exponentially with advancing age in men and women over 75-years-old (Figure 1). Overall, in the UK, hip fractures may account for up to 9% of all limb fractures (4% of fractures in men and 15% in women) (Table 1). In African populations, however, no marked increase in the incidence of hip fracture with increasing age up to 74 years was found in either men or women.

Regional variations in the incidence of hip fracture in the UK have been noted, and rates also vary between countries. A low incidence of osteoporotic fractures in West Africa is observed despite low BMD being common. Seasonal variations in the incidence of hip fracture have been reported in both northern and southern temperate regions of the world, possibly related to lower levels of vitamin D in winter.

Wrist fracture

The lifetime risk of a fracture of the lower end of the radius and ulna is 16% for women, and this makes it as common as hip fracture. Overall, such
fractures account for about 23% of all limb fractures in the UK (18% of fractures in men and 30% in women) (Table 1). The incidence of wrist fractures peaks during childhood, then declines before rising steadily from age 45 years in women but not in men (Figure 1). Over the last 50 years, the incidence of forearm fractures in children has increased, though the reason for this is unclear.

The incidence of wrist fracture also varies with geographical location in a pattern similar to that for hip fracture but different from that reported for vertebral deformity, for which prevalence rates are more similar. Seasonal variations in the incidence of Colles' fracture have been reported.

Other fractures

Less epidemiological information is available than for hip, vertebral and wrist fractures, but fractures of the foot, ankle, humerus, ribs, pelvis, hand and clavicle generally appear to be more common in elderly White Caucasians, particularly women, than in Black populations. Fractures in the elderly tend to occur at the ends of the long bones, particularly at the proximal ends, and are mainly associated with moderate trauma. Fractures of the proximal humerus show a marked age-related increase in incidence in White women, particularly after the age of 65 years (Figure 2). Fractures of the shaft and distal humerus are less common than proximal fractures, but show similar trends. The incidence of fractures of the ankle and foot are less common than proximal fractures, but show similar trends. The incidence of fractures of the foot, ankle, humerus, ribs, pelvis, hand and clavicle generally appear to be more common in elderly White Caucasians, particularly women, than in Black populations. Fractures in the elderly tend to occur at the ends of the long bones, particularly at the proximal ends, and are mainly associated with moderate trauma. Fractures of the clavicle and scapula gradually increased in incidence to mid-life and then steadily declined; these fractures tend to be associated with moderate or severe trauma. Fractures of the ribs and sternum had a relatively high incidence, and showed a gentle increase in the elderly.

In a longitudinal study in White Caucasian subjects aged > 60 years, non-hip fractures accounted for 90% of total fractures up to age 80 years, and after 80 years accounted for 59%. Rib fractures and humerus fractures were more common than previously thought (300/100 000 woman years and 400/100 000 woman years, respectively) compared with distal radial fracture (600/100 000 woman years) and hip fracture (700/100 000 woman years) in the same group. Focusing on hip fractures may thus underestimate the resource implications of osteoporosis. This incidence of humerus fractures, however, is higher than that reported elsewhere in the UK (annual incidence of 70/100 000 population for all humerus fractures). A study based on Accident and Emergency admissions has also indicated that non-hip fractures account for over 90% of all fractures. The overall annual incidence of non-hip fractures in this study was 1964/100 000, which is substantially greater than previous reports.

Increasing trends in fracture rates

The incidence rates and absolute numbers of vertebral, hip and limb fractures appear to be increasing in Western populations. This may be partly due to an increase in the proportion of elderly people, but also arises from a pronounced increase in the age-adjusted incidence, particularly in the population > 75-years-old, after 1980/1981. In the same study, the age-specific incidence of

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Figure 2. Incidence of fracture of the proximal humerus by age, race and sex. US Medicare population, 1986–1989. From Baron et al.26
vertebral fractures in the elderly showed a steady increase after age 60–69 years in 1982/1983 that had not been evident in the early 1950s. Between 1950/1954 and 1983, the prevalence of vertebral fracture in normal lateral chest radiographs increased about fivefold. In women, the incidences of fragility fractures of the distal radius, proximal humerus, ankle, tibial condyle and patella increased between the 1950s and the 1980s, particularly in women over 55–60-years-old. This increasing trend seems to have continued for fractures of the proximal humerus in elderly people up to 1993. Age-adjusted hip fracture rates in the UK and USA rose through earlier decades of this century, but appear to have now reached a plateau; numbers of fractures continue to increase because of the ageing of the population.

Morbidity and mortality of hip fracture

At 1 year after a hip fracture, about 40% of patients are unable to walk independently, 60% are limited in at least one class 1 activity of daily living (e.g. feeding, dressing, toileting), and 80% are limited in a class 2 activity of daily living (e.g. shopping, gardening, climbing stairs). In the first year, about 27% of hip fracture patients will require nursing home care; after 1 year this figure falls to 14%, though 30% will still require home support. Of the patients who were independent before a hip fracture, 18% become dependent and 8% require nursing home care. Life expectancy is reduced by hip fracture, and this increase in mortality is greater in older women than in younger women. Mortality in men is greater than in women at all ages over 50 years. This excess mortality is restricted to patients with reduced mental status, reduced somatic health and low physical ability.

The epidemiology of non-vertebral fractures is summarized in Table 2.

Risk factors for fracture

To avoid the development of osteoporosis-related fractures in later life, it is particularly important to identify perimenopausal or early postmenopausal women at increased risk of such fractures. Several factors contribute to the development of osteoporosis-related fractures, including bone mineral density (BMD), bone architecture, and other factors associated with physical frailty and an increased risk of falls. The best available predictor is BMD, but methods of measurement are expensive and not always available. Attempts to identify clinical predictors have met with only limited success, and in general clinical risk factors are poor at predicting low BMD or fractures. Only about 17–27% of postmenopausal women at risk of hip fracture, 18–35% of those at risk of vertebral fracture, and 37–47% of those at risk of radial fracture because of low BMD are identified by assessing clinical risk factors. The clinical risk factors that have been associated with a small increase in the risk of hip fractures include excess caffeine (but not tea), age, benzodiazepines, falls in the previous year, being on the feet for <4 h/day, maternal hip fractures, inability to rise from a chair, current smoking, and anticonvulsants. It appears that no single factor is responsible for the pathogenesis of osteoporosis-related fractures, but a combination of factors, which may differ between individuals.

BMD as a predictor

BMD is determined by several factors, including peak bone mass, genetic influences and environmental factors, in addition to disease states.

Table 2 The epidemiology of non-vertebral fractures

<table>
<thead>
<tr>
<th>Fracture Type</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip fractures</td>
<td>10% of all fractures, but a much greater proportion in the elderly. Lifetime risk of hip fracture from age 50 years in the UK is 3% in men and 14% in women.</td>
</tr>
<tr>
<td>Wrist fractures</td>
<td>Lifetime risk of a wrist fracture is higher than for any other type of fracture, and may account for up to 23% of all limb fractures. Incidence rises in women over age 45 years, but not in men.</td>
</tr>
<tr>
<td>Non-hip fractures</td>
<td>Overall incidence of proximal humerus fractures in UK women is 400/100,000 woman years, and these fractures show a marked age-related increase in incidence in women.</td>
</tr>
<tr>
<td>Rib fractures</td>
<td>Overall incidence of rib fractures in UK women is 300/100,000 woman years, and these fractures show a gentle increase in the elderly.</td>
</tr>
<tr>
<td>Vertebral fractures</td>
<td>Incidence in the elderly people, and secondly and more importantly, a pronounced increase in the age-adjusted incidence of fractures, particularly in elderly women.</td>
</tr>
<tr>
<td>Focusing on hip fractures</td>
<td>Has probably underestimated the resource implications of osteoporosis.</td>
</tr>
</tbody>
</table>
**Hip fracture and BMD**

In patients with hip fracture, BMD is low in the hip, radius, and lumbar spine, and calcaneus. Hip fractures, particularly intertrochanteric fractures, have also been associated with low bone mass measured by quantitative ultrasonography. Women over 65 years of age with hip BMD in the lowest quartile had an 8.5-fold greater risk of hip fracture than those in the highest quartile, and low hip BMD was a stronger predictor of hip fracture than BMD at other sites. A low hip BMD in a patient with hip fracture increases the risk of subsequent hip fracture.

**Forearm fracture and BMD**

In most studies, BMD of the non-fractured forearm was decreased in patients with forearm fractures, although there have been exceptions. Most forearm fractures occur about 2.5 cm from the radial styloid, in the ultradistal radius, where at least two-thirds of the bone is cancellous and less than one-third is cortical. In 119 normal women aged 30–75 years and 40 women aged 53–80 years with women Colles’ fracture, the risk of Colles’ fracture rose sharply as ultradistal radial BMD fell below 0.4 g/cm² (Figure 3). The association was at least as strong between forearm ultradistal BMD and forearm fracture as it was between lumbar spine BMD and vertebral fracture and between hip BMD and hip fracture. In a prospective study, the incidence of distal forearm fractures was 4.1 times greater and that of proximal humerus fracture 7.5 times greater in women in the lowest quintile of distal radial BMD compared with those in the highest quintile. Forearm BMD does not decrease with age in men, nor does the incidence of forearm fracture increase.

Spinal BMD is 5–7% lower in women following a Colles’ fracture, although this lowering is less than in the ultradistal radius in these patients (Figure 4). Low spinal BMD could result from a low BMD at the time of the menopause and/or from an increased rate of bone loss, but this latter finding has not been confirmed. In a series of 1288 men and women with distal forearm fracture, there was a fivefold increase in risk among women and a 10-fold increase among men in the risk of vertebral fracture.

Colles’ fracture is also associated with a 1–8% lower hip BMD, although a recent study has suggested that in women over 65 years of age, hip BMD following Colles’ fracture was not lower than the age-matched normal value. The risk of hip fracture following Colles’ fracture is higher in older people.

In a study of postmenopausal women with vertebral, Colles’, or both fractures, ultradistal radial BMD was a significantly better indicator of Colles’ fracture than spinal BMD; the converse was also true. Colles’ fractures tend to occur in postmenopausal women with low metacarpal BMD and in women under 65-years-old with low hip BMD. In a meta-analysis of prospective cohort studies with about 90,000 person years of observation and over 2000 fractures, the relative risk of forearm fracture was 1.7–1.8 for each decrease of 1 SD in BMD at the site, compared with a relative risk of 2.6 for hip fracture with each...
1 SD decrease in hip BMD. The predictive ability of a decrease of 1 SD in BMD was similar to (or for hip and spine measurements better than) that of a 1 SD increase in blood pressure for stroke and better than a 1 SD increase in serum cholesterol level for cardiovascular disease.

Predictions of the incidence of Colles' fracture in the general population based on BMD alone are very close to the observed incidence, which suggests that in addition to falling, low BMD is a major determinant of Colles' fracture, and that Colles' fracture is strongly related to osteoporosis. In particular, it is a useful indicator of an increased risk of hip fracture, in addition to an increased risk of vertebral fracture. Colles' fracture occurs relatively commonly, and is a diagnosis that is unlikely to be missed.

BMD and other fractures

Fractures of the foot, ankle, humerus, ribs, pelvis, hand and clavicle have all been related to low BMD. In a retrospective study of 621 patients, foot and rib fractures were associated with low femoral neck BMD, though BMD at both the lumbar spine and the femoral neck was normal in subjects who had suffered ankle fractures. In another retrospective study of 3222 women (mostly postmenopausal), earlier fractures of the rib, ankle, clavicle and patella were related to reduced spinal BMD, and fractures of the clavicle, tibia, patella and foot were related to reduced femoral neck BMD. This study is difficult to interpret, however, because most of the fractures occurred when the women were premenopausal. In the prospective Study of Osteoporotic Fractures, which enrolled 9704 patients over 65 years old, the incidence of most fracture types (including wrist, foot, humerus, hip, rib, toe, leg, hand, pelvis and clavicle, but excluding ankle, elbow, fingers and face) was significantly increased in elderly women with low BMD at the distal or proximal radius, or the calcaneus. In a follow-up study, neither ankle nor foot fractures were related to age or to femoral neck or lumbar spine BMD, though they were related to low distal radial BMD. Other studies have shown that ankle fracture is related to significantly increased weight and body mass index, but is largely independent of low bone mass.

The body of evidence does not, therefore, support the view that ankle fracture is strongly related to osteoporosis. Of fractures other than vertebral, hip or wrist, fractures of the humerus, rib and pelvis are the most likely to be related to osteoporosis. Fracture of the humerus is potentially the most useful indicator, being related to low BMD and showing a marked age-related increase in women over 65 years old. It also occurs relatively commonly and is a diagnosis that is unlikely to be missed. Although the incidence of rib fracture increases in the elderly, and it is at least as common as proximal humerus fracture with increasing age, patients often tolerate a rib fracture without seeking medical attention. When a patient with a low or moderate trauma rib fracture does present, however, osteoporosis should be considered.

Bone architecture

Bone structure is related to bone composition and turnover, skeletal geometry and body habitus. The femoral neck and the mid-shaft radius consist predominantly of cortical bone, whereas the distal radius and vertebrae are mainly cancellous in content. The proximal humerus is mainly metaphyseal bone, which is predominantly cancellous, while the ribs are mainly diaphyseal bone, which is predominantly cortical.

Changes in bone composition have been linked with osteoporosis. With increasing age, marked loss of osteocytes in the femoral head occurs without any change in vertebral osteocyte numbers, and this bone death may contribute to hip fracture in the elderly, though it is similar in cases of hip fracture and age-matched controls. The
connectivity of osteoporotic cancellous bone, which reflects its strength, is also significantly decreased compared with normal bone, independently of bone volume. Differences in connectivity have been linked with ethnic differences in fracture rates. Bone turnover may be lower in Black subjects, which may increase trabecular strength, though this is not a universal finding. The Black femoral neck, though not the shaft, has a distribution of bone which gives it intrinsically greater strength. The geometric characteristics of bone have been implicated in the risk of hip fracture. The risk of osteoporotic hip fractures is significantly higher in White women than in Asian or Black women, who have a significantly shorter hip axis length. Hip axis length was also significantly longer in women with osteoporosis and hip fracture than in those with osteoporosis and vertebral fracture, though femoral neck BMD was reduced to a similar extent below control values in both groups. This probably reflects differences in mechanical loading, with a shorter femoral neck intrinsically stronger and less susceptible to fracture. Hip strength analysis may provide a better prediction of recent contralateral hip fracture than conventional BMD, even though as subjects grow older their apparent hip strength may fall less rapidly than BMD due to apparent expansion of the periosteal envelope. Hip axis length may have been growing over recent generations in White patients.

Falls and muscle strength

The considerable increase in incidence of wrist fractures in perimenopausal women has been related to the increasing incidence of falls in these women. In contrast, the risk of falling does not increase in middle-aged men, which is reflected in the stable incidence of wrist fractures in men throughout life. The incidence of falls increases in the elderly in both sexes, but is generally lower in men than in women. Falling is the major cause of a first hip fracture in women, and an increased incidence of falling also increases the risk of a second hip fracture. Muscle weakness, postural instability (e.g. in menopausal women) and incoordination, and possibly drug treatment (e.g. with long-acting benzodiazepines or anti-convulsants) all increase the risk of falling, and as a result increase the risk of hip fracture. In a comprehensive study of over 8000 women >65-years-old who suffered 203 hip fractures and 321 wrist fractures during 4.1 years of follow-up, the nature of the fall determined the type of fracture. Whether a fracture actually occurred when the faller landed on a particular bone, however, was determined by BMD and factors that attenuated the force of impact of the fall. For direct falls on the hip, the odds ratio for the risk of hip fracture was 32.5, while for falls on the hand or wrist, the odds ratio for wrist fracture was 20.4. This suggests that one approach to prevention of these fractures may be modification of the trauma, e.g. hip protection devices. In women who had one or more falls in the year before baseline, the relative risk of Colles’ fracture was 1.31; good visual acuity, which reduces the risk of falling, reduced the relative risk of distal forearm fracture to 0.83. Ankle fractures have also been associated with a history of falls.

The importance of muscle strength is indicated by a study of 3270 healthy elderly women, in whom the risk of hip and other non-vertebral fractures was reduced significantly by giving calcium and vitamin D. The reduction became evident within 6 months, and was probably due to reversal of secondary hyperparathyroidism and an increase in muscle strength. Physical activity and muscle strength both protect against hip fracture, and the risk of fracture is lower in subjects with greater grip strength (which correlates with activity). Decreased quadriceps strength and postural instability may increase the risk of osteoporosis-related fracture.

Previous fracture

The risk of hip fracture is increased by a previous fracture. In patients over 35-years-old, the relative risk of hip fracture increased significantly and almost immediately following a Colles’ fracture, the increase being most marked in men (Table 3). The odds ratio of hip fracture was increased by 2.3 in men and women with a previous wrist fracture. In women >60-years-old, fractures of the lumbar spine, olecranon, knee or ankle increased the risk of a subsequent hip fracture, but this increased risk tended to level off 3 years after the primary fracture. In a retrospective, population-based cohort study, the risk of hip fracture following an index forearm fracture was increased 1.4-fold in women and 2.7-fold in men, and the risk of subsequent vertebral fracture increased 5.2-fold in women and 10.7-fold in men. A previous hip fracture also increased the odds ratio of a later, second hip fracture by 6–8-fold, though second hip fractures usually occur in the
A previous spine fracture increases the risk of a subsequent hip fracture 2.4-fold. The risk of wrist fracture may also be increased by a previous fracture. Women who had sustained a fracture at any site since the age of 50 years had a slightly increased risk (relative risk 1.26) of suffering a Colles’ fracture, as did women who had one or more falls in the year before baseline (relative risk 1.31). Women with vertebral fractures also have an increased incidence of forearm fractures. An overview of the risk factors for non-vertebral fractures is presented in Table 4.

**Bone turnover and calcium metabolism in patients with fracture**

**Bone turnover in hip fracture**

BMD may continue to decrease after hip fracture, by 4–5% at the uninjured hip in the first year, putting the patient at greater risk of a subsequent fracture. The loss in BMD at the femoral neck in the year after hip fracture may be five times that reported for the non-fractured population. In elderly patients with hip fracture, there was a 2.4% loss of BMD from the lumbar spine in the first year, and this correlated with 1,25-dihydroxy vitamin D status; the percentage loss of BMD was greatest in patients with a higher baseline BMD, reaching nearly 5% in those whose baseline lumbar spine BMD was >1 g/cm².

Direct, region-specific measurements of bone formation and resorption in the femoral neck are hard to perform and have seldom been attempted. In a small study, there was no significant difference in regional bone formation between women with previous contralateral hip fracture and controls. While bone formation measured in the femoral neck correlated well with bone formation in the whole body measured radioisotopically, no correlation has been demonstrated yet between whole body and femoral neck bone resorption. Therefore, what follows needs to be interpreted with a degree of caution.

Markers of both whole-body bone resorption and formation may be elevated in elderly people, and correlate inversely with bone loss. In the numerically robust EPIDOS study, the odds ratio for risk of hip fracture in elderly women with a hip BMD of 2 SD or more below the premenopausal mean, was about 2 in those with elevated bone resorption markers, compared with an odds ratio of 2.7 for low hip BMD. Combinations of hip BMD and resorption markers increased the relative risk to 4.1–4.8. In a nested, case-control analysis within the Rotterdam study, an increase of 1 SD in total and free deoxypyridinoline concentrations was associated with a substantially higher risk of hip fracture.

It was reported many years ago that patients with hip or vertebral fractures may have low vitamin K levels, and these findings have since been confirmed in controlled studies. In the EPIDOS study, femoral BMD was significantly lower in elderly women with under-carboxylated osteocalcin, which may be related to low vitamin K levels. High levels of under-carboxylated osteocalcin increased the relative risk of hip fracture to about 2, compared with 2.4 for low femoral neck BMD; again, combining these two risk factors raised the odds ratio to about 5. Levels of fully carboxylated osteocalcin can be restored to normal by vitamin K supplementation.

**Relationship of hip fractures to osteomalacia**

The causes of vitamin D deficiency in the elderly include reduced sunlight exposure, low dietary intake and reduced intestinal absorption of vitamin D. In Western Europe, many studies have also implicated low 1,25-dihydroxy vitamin D levels, which may result from reduced renal synthesis. In North America, however, vitamin D deficiency in elderly people is less common, though the incidence of hip fracture is similar to that in the UK. The elderly population groups at high risk of osteomalacia in the UK are those who suffer...
malabsorption or malnutrition, the housebound or institutionalized, and those of Asian ethnicity.

Bone disease due to vitamin D deficiency falls into two types, which differ in their underlying pathophysiological processes. Severe vitamin D deficiency is associated with defective mineralization of bone, resulting in rickets in children and osteomalacia in adults. Subclinical vitamin D deficiency, which gives rise to increased bone turnover as a result of secondary hyperparathyroidism. The main histological differences between osteomalacia and secondary hyperparathyroidism are shown in Table 5. The cardinal difference is that mineralization is defective in osteomalacia, with a low or even absent mineral apposition rate. The disproportionately low rate of mineral apposition, compared with osteoid apposition, produces an increase in osteoid seam width, which is limited to osteomalacia and some very rare metabolic bone diseases. In secondary hyperparathyroidism, in contrast, actively forming surfaces and bone turnover are increased, with a normal or increased mineral apposition rate, and probably also an increased osteoid apposition rate. The seam width is usually normal, however, because mineralization keeps pace with osteoid formation.

Secondary hyperparathyroidism is very common in the elderly, and perhaps more so in hip fracture patients. Many of the discrepancies in the literature regarding the reported prevalence of osteomalacia in hip fracture patients are due to a failure to distinguish between these two different types of bone disease. Studies that have examined the prevalence of osteomalacia in hip fracture patients have produced results varying from 0% to 37%. Studies based on measurement of osteoid surface rather than seam width have found much higher prevalences than those studies using more rigorous histomorphometric criteria, which have generally reported prevalences of less than 2%.

It thus appears that the prevalence of osteomalacia in hip fracture patients is similar to that seen in the elderly population in general, and that osteomalacia is not an important factor in the pathogenesis of hip fracture. Subclinical vitamin D deficiency, however, is likely to play an important role in the pathogenesis of hip fracture.

### Bone turnover in forearm fracture

Although considerable information on BMD in relation to forearm fractures is available, the data on bone turnover in forearm fractures are scarce.

Following a forearm fracture, an increase in the biochemical markers of bone turnover has been reported. Markers of bone formation increase rapidly after forearm fracture, possibly related to callus formation, and remain elevated for at least 1 year. Markers of bone resorption also increase rapidly, and with the exception of deoxypyridinoline remain elevated for at least 1 year. Based on these findings and BMD data, normal bone turnover is probably not restored for about 2 years after a fracture. Immobilization may...
increase bone resorption and decrease bone formation.\textsuperscript{119,144}

The rate of bone turnover may predict forearm bone loss,\textsuperscript{72} and rapid bone loss has been associated with fractures of the forearm and spine.\textsuperscript{73} In women with both Colles’ and vertebral fractures, bone loss was similar at the spine and the ultradistal radius, and it was concluded that differential bone loss at the two sites may be a major factor in determining which will fracture.\textsuperscript{6} More studies are needed to confirm these findings and assess their significance.

Current understanding of bone dynamics is indicated in Table 6.

### Management options for hip fracture

**Investigating patients with hip fracture**

Low serum calcium levels are consistent with osteomalacia, and high serum calcium levels with primary hyperparathyroidism, which is present in 1% of postmenopausal women. A low serum calcium level, however, lacks specificity or sensitivity for the diagnosis of osteomalacia. If vitamin D deficiency or osteomalacia is suspected as a cause of hip fracture, vitamin D and calcium can be given without further tests. Epidemiological studies suggest that a past history of hyperthyroidism or thyroidectomy is a risk factor for hip fracture,\textsuperscript{46,145} and thyroid function tests may discover covert hyperthyroidism in the elderly without the classical signs or symptoms of thyrotoxicosis. Several studies have now shown that elderly men with hip fractures have a higher prevalence of low testosterone levels than control subjects,\textsuperscript{146,147} though this may be a secondary event relating to the fracture or surgery. Longitudinal studies are needed to clarify this issue. In elderly men, however, it may be undesirable to give testosterone replacement because of the risk of prostate cancer, so measurement of testosterone and gonadotrophins may be unnecessary in many cases.

**Prevention of falls**

The risk factors associated with falling may be intrinsic, e.g. poor vision, neurological disease or cardiovascular disease, and medication, and/or extrinsic or environmental, e.g. trailing wires, loose carpets or rugs, and inappropriate footwear. There has been considerable interest, particularly in elderly care circles, in trying to modify the environment in which the elderly faller lives.

In a randomized controlled trial in a residential care setting, intervention to modify both intrinsic and extrinsic factors over 2 years resulted in a significant decrease (26%) in hospital admissions, and non-significant decreases in falls (9%) and deaths (17%) compared with a control group who had no intervention.\textsuperscript{148} A larger randomized controlled study found that nutritional, medical, environmental and fitness intervention did not reduce fracture incidence over 4 years.\textsuperscript{149} Two controlled trials have shown that intervention to modify identified risk factors in individual patients can significantly reduce the incidence of falls,\textsuperscript{150,151} and in one of these studies the incidence of falls over 1 year was reduced by 60% and the incidence of fracture by 50%, though this last decrease was not statistically significant.\textsuperscript{150} Nutritional support has been shown to reduce the risk of subsequent hip fracture.\textsuperscript{152,153} From an elderly care point of view, however, encouragement to take a better diet and provision of nutritional support is difficult in the presence of cognitive impairment.

In a randomized trial in 1801 frail elderly patients (mean age, 82 years), use of external hip protectors reduced the risk of hip fracture by 60% over 2 years.\textsuperscript{154} The mean compliance rate with the hip protector was 48%, and most fractures in the hip protector group occurred when patients were not using the protector. In another study lasting 11 months, the risk of hip fracture was highly significantly reduced in subjects using the hip protectors; the only subjects using hip protectors who suffered a fracture did so when they were not wearing the hip protectors.\textsuperscript{155} In a more recent controlled cohort study, the relative risk for hip fracture in elderly nursing home residents (men and

### Table 6  Current understanding of bone dynamics

Patients with hip fracture experience accelerated bone loss after the fracture. Following fracture of the distal forearm, an increase in markers of bone turnover is observed for at least 6 months. The prevalence of osteomalacia in patients with hip fracture is similar to that in the elderly general population. Osteomalacia is not an important factor in the pathogenesis of hip fracture, though subclinical vitamin D deficiency (giving rise to secondary hyperparathyroidism) may play an important role. Although it is now accepted that BMD predicts fracture risk, the usefulness of markers of bone turnover is still not clear.
women) using hip protectors was 0.33 compared with residents not using hip protectors.\textsuperscript{156} Use of hip protectors may be the most promising approach, because the motivation to take tablets in elderly frail patients is often very low, and many are in residential care. However, the current randomized controlled trials of their benefit are of only low to moderate quality.\textsuperscript{157}

**Treatment options**

There are currently no published studies on the secondary prevention of osteoporosis in the elderly presenting with hip fractures. The treatment options that can be extrapolated from other studies include HRT, bisphosphonates, and calcium plus vitamin D. The rationale for intervention with bone-active agents in elderly people presenting with hip fractures is derived from studies such as that of Jones \textit{et al.}, which showed that loss of BMD from the femoral neck continues into old age in both men and women.\textsuperscript{119}

Oestrogen replacement can effectively prevent further bone loss in postmenopausal women with established osteoporosis. In a study of women with established osteoporosis, further loss of BMD was significantly reduced at the spine and reduced at the hip.\textsuperscript{158} The mean age of the women in the study (68 years), however, was much less than the mean age of women presenting with hip fractures, and HRT might thus only have a role in younger women presenting with hip fracture. It has recently been demonstrated, however, that low-dose HRT together with calcium and vitamin D can be safely given to women over 65 years of age, producing bone-sparing changes similar to those that occur with higher doses of HRT in younger postmenopausal women.\textsuperscript{159} In a case-control study of 1327 women aged 50–81 years with hip fracture and 3262 randomly selected controls, the risk of hip fracture was decreased in both current users of HRT (OR 0.35) and in former users (OR 0.76) compared with those who had never used it.\textsuperscript{160} HRT thus appears to be protective against hip fracture, but this benefit ceases within 5 years of stopping. Intracapsular fracture risk reverts more quickly to that of never-users than does extracapsular (trochanteric) hip fracture risk.\textsuperscript{161}

Over a period of 3 years, cyclical etidronate produced an increase in femoral neck BMD of 1.4% compared with a decrease of 0.6% with placebo, which was a significant difference ($p<0.05$).\textsuperscript{162} Most studies with cyclical etidronate have only recruited women up to age 75 years, however, and so there are no data on efficacy in older women. In a recent study from the GP Research Database, about 30% of the patients were over the age of 75 years, and in these women the relative risk of hip fracture was significantly reduced by cyclical etidronate.\textsuperscript{163} Two studies with alendronate have recruited patients up to age 80 years, though neither of these included patients who already had a hip fracture.\textsuperscript{164,165} Nevertheless, the beneficial effect of alendronate on the incidence of hip fracture does not appear to decrease with age.\textsuperscript{166} Risedronate reduces the risk of hip fracture in patients with low BMD, but not in women at increased risk of falling. In a study of 9331 women, those who were under the age of 80 years and had a T score below $-3$, had a relative risk of hip fracture of 0.7 with risedronate therapy.\textsuperscript{167} Women over 80-years-old were selected primarily on the basis of non-skeletal risk factors, and in this group there was no change in the risk of hip fracture with risedronate treatment.

In the very frail or elderly, the most attractive option is vitamin D with calcium. In a study of very elderly (mean age 84 years), healthy and ambulatory women living in nursing homes or apartment houses for the elderly, calcium plus vitamin D significantly reduced the risk of hip and other non-vertebral fractures.\textsuperscript{106} Annual injections of vitamin D, 150 000 IU or 300 000 IU, reduced the risk of fracture by about 25% over 5 years in elderly patients either attending an elderly care outpatient clinic or living in a municipal home for the elderly, though the changes were not significant at any single site.\textsuperscript{168} Other data indicate that calcium plus vitamin D also has a beneficial effect on BMD in younger men and women and reduces the risk of non-vertebral fractures.\textsuperscript{169}

In contrast, although Lips \textit{et al.} were able to show a small but significant beneficial effect (2.2% after 2 years) of low-dose vitamin D on hip BMD, there was no effect on fracture rate at the hip or other appendicular sites.\textsuperscript{170} It thus appears that vitamin D and calcium may be beneficial, but there are no data in secondary prevention of hip fracture. A double-blind randomized controlled trial is currently in progress to enrol 6000 men and women over 70-years-old with osteoporosis-related fractures and investigate the effects of vitamin D or calcium over 3.5 years on various outcome measures, including fractures, BMD, and falls. Recruitment started in early 1999.

**Management options for Colles’ fracture**

Despite the clear indication that Colles’ fracture is an osteoporotic fracture, in the vast majority of cases no measures are initiated to protect patients
from subsequent, more serious fractures. The general approaches that could be considered are identification of those at increased risk and provision of appropriate treatment, either before or after the occurrence of a Colles’ fracture, depending on whether or not the patient has a coexisting vertebral fracture.

Investigating patients with Colles’ fracture

Although several factors increase the risk of Colles’ fracture, these do not identify individuals at risk, and any treatment offered on this basis would have to be generally appropriate. Investigations following a first Colles’ fracture can document the presence of osteoporosis, predict the risk of future fracture, and estimate the risk of future falling. About 21–42% of Colles’ fracture patients fulfil the WHO criteria for osteoporosis, depending on the site of measurement, representing 35% of those under 66 years of age and 64% of those over 66 years of age.

Treatment options

The options available at present are general measures (diet adequate in calcium and vitamin D, regular exercise, avoidance of smoking and excess alcohol consumption), hormone replacement therapy (HRT), calcitonin plus calcium, or a bisphosphonate, but very few studies have been published. In a prospective study of 245 women commencing HRT for reasons not related to osteoporosis, the risk of Colles’ and vertebral fracture was reduced overall compared with a matched control group not using HRT, but with a trend to diminishing protection with increasing age. In the Fracture Intervention Trial (FIT), postmenopausal women with a hip BMD T score of −2 SD or below and at least one prevalent vertebral fracture were randomized to receive either placebo or alendronate, 5 mg/day for 2 years, then 10 mg/day for 1 year. Both the alendronate-treated and the placebo groups received calcium and a supplemented intake of vitamin D where appropriate. About 4% of those who received placebo sustained a Colles’ fracture during the 3-year study, compared with 2% of those receiving alendronate (p=0.013), corresponding to a relative risk of 0.52. In women with the same BMD criteria but without a vertebral fracture, only about 4% sustained a Colles’ fracture during the 4.5 years of follow-up; this proportion was not significantly altered by the use of alendronate, 5 mg/day for 2 years, then 10 mg/day for at least 2 years, and there was little effect on forearm BMD. It thus appeared that in this latter study population, alendronate did not decrease the risk of a new Colles’ fracture.

In a study of 45 postmenopausal women with Colles’ fracture, treatment with salmon calcitonin, 100 IU/day, plus calcium, 1200 mg/day, for 10 days each month for 12 months significantly increased metacarpal index by 12.8%. Treatment with calcium alone also significantly increased metacarpal index, but to a lesser degree, whereas metacarpal index decreased in those receiving placebo. This study was too small to have a fracture end-point.

The management options for hip and Colles’ fracture are summarized in Table 7.

Table 7  Management options for hip and Colles’ fracture

Prevention of falls and use of external hip protectors may contribute to a reduction in the occurrence of hip fracture.

Treatment options for patients presenting with hip fracture include HRT, bisphosphonates, and calcium plus vitamin D. None of these has been assessed in the secondary prevention setting.

HRT can effectively prevent further bone loss, but may not be appropriate or acceptable in elderly women. Bisphosphonates significantly reduce the loss of femoral neck bone mass and the risk of hip fracture. Calcium plus vitamin D may significantly reduce the risk of hip and other non-vertebral fractures. Vitamin D can be given as an annual injection, with advantages for institutional care of the elderly.

The options for prevention of Colles’ fracture are general measures, HRT, bisphosphonates, or calcitonin plus calcium. General measures have not been assessed prospectively and are based on untested hypotheses.

HRT may reduce the risk of a first Colles’ fracture in women up to the age of 80 years. As with hip fracture, HRT may not be appropriate or acceptable in elderly women. Bisphosphonates may decrease the risk of Colles’ fracture in postmenopausal women with a prevalent vertebral fracture. Calcitonin plus calcium can increase metacarpal index in women after Colles’ fracture, but no effect on future fracture incidence has been shown.

Implementation in secondary care

Based on the epidemiological data presented in this review, and on the established relationship between BMD and prevalent and future fractures,
the Consensus Group believes that any patient who has suffered a Colles', hip, proximal humerus, pelvis, and/or rib fracture should undergo further investigation and/or treatment. Clinical experience suggests that this represents more than 250 patients/year in each General Hospital, who present at fracture or orthopaedic clinics or wards with these fractures, and would be considered at increased risk of subsequent osteoporosis-related fractures. The most cost-effective approach to this increased workload would be the use of specialists nurses, who could ensure appropriate follow-up of patients between orthopaedic and osteoporosis specialist departments, manage the appropriate diagnostic tests under the supervision of the interested physician, interpret test results and offer management advice to GPs via standard letters.

After considering the available data, the Consensus Group believes that the clinical approach to management of individual patients at risk should be differentiated according to the type of fracture sustained. The guidance offered below was therefore formulated for distal forearm fracture patients alone, and separately for patients with moderate-to-low trauma fractures of the hip, rib, proximal humerus and pelvis. The management algorithm shown in Figure 5, which is discussed in detail below, is based on that recently published by the Royal College of Physicians and represents the current judgement of the Consensus Group. The Group recognizes, however, that in view of the absence of data in some areas, not all of the measures are evidence-based. As far as possible, therapeutic recommendations are based on the published literature to date. The guidance has been formulated with practicality in mind.

**Moderate-to-low trauma fractures of the hip, rib, proximal humerus, or pelvis**

The management of patients with hip fracture involves a combined orthopaedic and elderly care approach, because both surgical fixation of the fracture and subsequent rehabilitation are necessary

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**Figure 5. Medical management of men and women aged over 45 years who have or are at risk of osteoporosis.**

*Recommended daily dose, 0.5–1 g 800 IU, respectively. †Major risk factors include untreated hypogonadism, high-dose glucocorticoid treatment, disease associated with increased prevalence of osteoporosis (e.g. gastrointestinal disease, chronic liver disease, hyperparathyroidism, hyperthyroidism). Other risk factors include tendency to falling, family history, low body weight, cigarette smoking, height loss, low bone mass measured by other techniques. ‡If not done within the previous 6 months: full blood count and erythrocyte sedimentation rate; serum calcium, phosphate and alkaline phosphatase; protein electrophoresis and urine screen for light chains; thyroid function tests; total testosterone or free androgen index (men); vitamin D and parathyroid hormone levels (if serum calcium and alkaline phosphatase are abnormal). §T score is the BMD result expressed in SD units where the mean value for a young person is 0. ¶Listed in alphabetical order. Vitamin D and calcium are generally regarded as adjuncts to treatment. HRT means oestrogen in women and testosterone in hypogonadal men. From the Royal College of Physicians and the Bone and Tooth Society. 174
in order to allow optimal recovery of functional capacity. Ideally, the risk of future fractures as a result of further falls should be reduced by minimizing further bone loss and falls, and by limiting the damage caused by any falls that do occur.

Clinical assessment
If secondary osteoporosis is suspected, the following diagnostic tests are recommended, if they have not been done within the previous 6 months, to exclude myeloma, hyperparathyroidism, osteomalacia, malabsorption, thyrotoxicosis and hypogonadism: full blood count and erythrocyte sedimentation rate; serum calcium, phosphate and alkaline phosphatase; protein electrophoresis and urine screen for light chains; thyroid function tests; total testosterone or free androgen index (men); vitamin D and parathyroid hormone levels (if serum calcium and alkaline phosphatase are abnormal). Any abnormalities detected in the work-up should be followed-up appropriately. Although men over 75 years old may benefit from testosterone treatment, the possibility that microscopic prostate cancer may be stimulated must be considered.

Therapeutic intervention
All patients with hip or low-trauma fractures of the rib, proximal humerus, or pelvis should be offered general advice on lifestyle measures to decrease bone loss, including eating a balanced diet rich in calcium, not smoking or drinking alcohol to excess, and maintaining regular exercise and adequate exposure to sunlight.

After consideration of lifestyle and home environment factors, patients with hip or other low-trauma fractures can be divided into two main groups. The first group comprises those who are frail, elderly and/or in residential care, and who have a limited life expectancy or seldom venture outdoors. In these patients, who are often vitamin-D-deficient, it is probably inappropriate to perform substantial investigations to exclude secondary causes of osteoporosis or to confirm the diagnosis by bone densitometry. These patients are more likely to benefit from calcium plus vitamin D supplementation than from other therapeutic recommendations. The use of hip protectors to reduce the impact of any falls may also be considered. If a second fracture occurs, calcium plus vitamin D should be continued and a bisphosphonate added.

The second group comprises patients who are independent and were mobile before the fracture occurred. Those who are over 75 years of age may be treated with calcium plus vitamin D supplementation without further investigation. Those patients in this group who are under 75 years of age will benefit from more active investigation and intervention, as their life expectancy and quality of life can be improved by decreasing the risk of further fractures (Figure 5 and Table 8).

BMD has been considered to be of limited value in the diagnosis of osteoporosis in elderly patients with hip fracture, as most will have a reduced BMD and the results are unlikely to influence management. The recent results of the risedronate hip fracture studies, in which patients over 80 years old who were not documented to have reduced BMD benefited less than slightly younger patients who were known to have low BMD, will probably occasion a re-investigation of the value of BMD measurement in the over-80s. In younger independent patients, dual-energy X-ray absorptiometry (DXA) is useful to identify those with a low BMD. In the elderly the optimal measurement site is the proximal femur, as lumbar spine BMD may be artifactually elevated in the elderly due to degenerative changes. When DXA is not available, measurements such as single-energy X-ray

<table>
<thead>
<tr>
<th>Table 8</th>
<th>Anti-fracture efficacy of interventions in postmenopausal osteoporotic women: grades of recommendation</th>
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<tbody>
<tr>
<td></td>
<td>Spine</td>
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<tr>
<td>Alendronate</td>
<td>A</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>A</td>
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<tr>
<td>Calcitriol</td>
<td>A</td>
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<tr>
<td>Calcium</td>
<td>A</td>
</tr>
<tr>
<td>Calcium plus vitamin D</td>
<td>ND</td>
</tr>
<tr>
<td>Cyclical etidronate</td>
<td>A</td>
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<tr>
<td>Hip protectors</td>
<td>–</td>
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<tr>
<td>HRT</td>
<td>A</td>
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<tr>
<td>Physical exercise</td>
<td>ND</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>A</td>
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<td>Risedronate</td>
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<tr>
<td>Tibolone</td>
<td>ND</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>ND</td>
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</tbody>
</table>

Grade A, meta-analysis of randomized, controlled trials or from at least one randomized, controlled trial, or from at least one well designed, controlled study without randomization; grade B, from at least one other type of well designed, quasi-experimental study, or from well designed, non-experimental studies (e.g. comparative studies, correlation studies, case-control studies); grade C, from expert committee reports/opinions and/or clinical experience of authorities. ND, not demonstrated. Data from the Royal College of Physicians and the Bone and Tooth Society.\(^2\)
absorptiometry of the forearm and possibly ultrasound measurements of the heel may be considered as alternative methods for risk assessment, though there are limited data on their usefulness in a more elderly population. Moreover, BMD guidelines based on DXA may not be applicable to these other techniques.

Although no secondary prevention studies of the treatment of osteoporosis in elderly patients have yet been published, treatment with bisphosphonates and/or calcium plus vitamin D is recommended for independent patients under 75 years of age with low bone mass. Other treatments to consider are raloxifene, calcitriol, or HRT.

**Follow-up**

For those patients who have started therapy following diagnostic investigations, the response to therapy may be assessed with measurements of hip BMD after 2 years and then every 2–3 years as appropriate. If bone loss at the hip is >7%, an alternative therapy should be considered. This figure is based on, and is in excess of, the least significant change detectable at the hip. In the future, biochemical markers may be available as an alternative monitoring method.

**Distal forearm fracture**

Colles’ fracture alone is not sufficiently predictive of risk to warrant therapeutic intervention. A more detailed assessment of risk is required in women aged <75 years with forearm fracture (Figure 5). Recently, the risk factors specific to Colles’ fracture have been identified as a history of wrist fracture, low body weight, a low calcium intake, and non-use of HRT. In the presence of all four risk factors, risk was increased 12-fold (increasing to 30-fold in women who were postmenopausal), but the sensitivity and specificity of the risk factor score remained low because of the small number of women with more than one risk factor.

**Management approaches**

It has been proposed by a working group of the National Osteoporosis Foundation that a hip BMD T score of −3 to −1.5 SD should be used to make decisions about treatment, taking into account other risk factors. T score is the BMD result expressed in SD units, where the mean value for a young person is 0. A T score for hip BMD of −2.5 SD is found in 22% of women over 50 years old and in 40% of those over 80 years old. Between one-quarter and one-third of women over 65 years old have a T score of −2.5 SD, and 64% of women over the age of 66 years with forearm fractures have a T score below −2.5 SD when measured at the hip, spine, or ultradistal radius. Measurement of BMD is therefore of value if it is proposed to use a bisphosphonate, when appendicular anti-fracture efficacy may only be apparent in those with low BMD.

In patients aged 65–75 years with a low-impact Colles’ fracture, or in those under 65 years of age who are unwilling to take HRT, osteoporosis should be considered and BMD measured by DXA where possible (Figure 5). As discussed previously, DXA should be limited to the proximal femur in the more elderly group, or measured at the lumbar spine and proximal femur in younger patients.

In patients with a Colles’ fracture and T score for BMD below −2.5 SD, a cause for secondary bone loss should be excluded by appropriate diagnostic investigations (as outlined above for patients with moderate-to-low trauma fractures). Any abnormalities found during investigation should be treated as appropriate for the underlying condition.

Patients with a Colles’ fracture and a T score for BMD of −1 to −2.5 SD do not usually require further diagnostic tests. Their BMD should be assessed again after 5 years. Patients with BMD T scores greater than 0 SD should be reassured that they are at low risk of osteoporosis.

As with hip fracture, when DXA is not available, measurements such as single-energy X-ray absorptiometry of the forearm and possibly ultrasound measurements of the heel may be considered as alternative methods for risk assessment.

**Therapeutic interventions**

In most cases the GP can initiate treatment on the basis of the recommendations from the hospital. In some centres, a nurse specialist takes on the role of discussing treatment options with the patient, under the supervision of an interested clinician involved in osteoporosis. In this case, for the first year the clinician would review the decision process and countersign all the forms, but after that the nurse specialist would assume responsibility for informing the GP. It is essential that whoever makes the recommendations on long-term treatment understands the case thoroughly and presents all the necessary information to the GP.

All patients should be offered lifestyle advice (see Moderate-to-low trauma fractures, Therapeutic intervention). In patients over 75 years of age, calcium plus vitamin D supplementation or a bisphosphonate are the most appropriate active therapies, without the need for further investigation.

Patients aged 65–75 years, or women aged <65 years but unwilling to take HRT, and with a low bone mass (T score of −2.5 SD or below), in whom secondary causes have been excluded or treated, should be treated with a bisphosphonate,
HRT, or raloxifene to increase bone mass. Calcium plus vitamin D supplementation (or calcitriol) is another option. HRT, alendronate and risedronate have all been shown to reduce the risk of non-vertebral fracture. Most studies using HRT are not randomized controlled trials and must be interpreted with caution. There is no evidence that raloxifene prevents fractures other than vertebral fractures.

Follow-up

The response to therapy of patients with Colles’ fractures may be monitored using DXA every 2 years. If bone loss at the hip is significant, then an alternative therapy should be considered.

Cost-benefit analysis of treatment of Colles’ hip and other fractures

The Advisory Group of Osteoporosis estimated in 1994 that the annual costs of osteoporosis in the UK were £742m (1992/1993 prices). A more recent cost assessment exercise included fracture costs for men as well as women, increasing the total estimate to £1.7 billion/year, of which over 20% was associated with the costs of treating hip fracture in men.

The costs of hip fracture comprise several components, including in-patient costs, post-fracture out-patient and GP care, and institutional care, and may reach £20 000. In a prospective assessment, the costs of hip fracture (Australian $15 984) were substantially greater than those for in-patient treatment of distal radial fractures (Australian $4075), upper or lower limb fractures (Australian $3057 and Australian $6211, respectively), and other fractures (Australian $9116). Fractures treated on an in-patient basis were more costly than those treated on an out-patient basis, as were fractures in hospitalized patients aged ≥75 years compared with those aged <75 years. In 1997, the US National Osteoporosis Foundation estimated the total costs for first year events in hip fracture patients to be US $28 242 for those aged 50–54 years, US $26 227 for those aged over 65 years, with nursing home costs of US $27 516. The lower costs in the older patients may reflect their earlier discharge to nursing homes. In the same analysis, the costs of acute treatment of both wrist fracture and vertebral fractures were US $1000. In the recent UK estimate, the total costs of hip fracture (£12 000) were also substantially greater than for wrist, vertebral and other fractures (£468, £479, and £1338, respectively).

Drug costs after fracture

The cost of the various therapeutic agents available for use after fracture vary from just over £7/30 days to just over £70/30 days. The National Osteoporosis Foundation analysis of the cost-effectiveness of treatment assumed that bisphosphonates typically produced a 50% overall reduction in the risk of further fracture for an annual cost of $740, that calcium and vitamin D produced a 10% reduction in all-site fracture risk for an annual cost of $50, and that calcitonin did not reduce the risk of hip or wrist fracture but reduced the risk of vertebral fracture by 75% for an annual cost of $740. The base analysis assumed 100% compliance with 5 years of treatment.

The discounted costs per vertebral fracture avoided by use of HRT, cyclical etidronate and salmon calcitonin were estimated at between £138 and £25 013 in 1995, with salmon calcitonin considerably the most expensive; the treatments were all considered to reduce the incidence of further fracture by 50–60%, so the costs reflect the medication costs. This indicates that although salmon calcitonin appears to be as effective as the other treatments, it should be reserved for situations in which HRT or bisphosphonates are inappropriate.

Costs of gaining quality-adjusted life years

The National Osteoporosis Foundation sets the value of a quality-adjusted life year (QALY) at US $30 000. This sum is simply the per capita Gross National Product of the USA in 1998; an equivalent figure in several large Western European countries would be $20 000–22 000. The number of QALYs lost following fracture depends on the type of fracture (Table 9). In a recent overview, the cost

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<th>Table 9</th>
<th>QALYs lost as a result of fractures. From the National Osteoporosis Foundation</th>
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</thead>
<tbody>
<tr>
<td>Hip fracture</td>
<td>0.0833</td>
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<tr>
<td>Acute care</td>
<td>0.6000</td>
</tr>
<tr>
<td>Discharge to nursing home &gt;1 year</td>
<td>0.3000</td>
</tr>
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<td>Moderate disability</td>
<td>0.0404</td>
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<tr>
<td>Wrist fracture</td>
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<tr>
<td>Acute treatment</td>
<td>0.2000</td>
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<tr>
<td>Dependency</td>
<td>0.5000</td>
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<tr>
<td>Vertebral fractures</td>
<td>0.2500</td>
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<tr>
<td>Acute treatment</td>
<td>0.0324</td>
</tr>
<tr>
<td>Pain every day</td>
<td>0.2000</td>
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<tr>
<td>Very severe pain</td>
<td>0.5000</td>
</tr>
<tr>
<td>Moderate deformity</td>
<td>0.2500</td>
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per QALY gained by HRT varied from about US $12 000 to about US $50 000 for symptomatic women, but was considerably more for asymptomatic women (US $28 000–US $73 000). The flaws of cost-utility analyses of HRT are that these studies assumed that HRT was required for only 5–10 years and that compliance was good. It is known that long-term compliance with HRT may be poor. The small increase in risk of breast cancer with long-term use of HRT would reduce the likely health gain, though the expected decrease in ischaemic heart disease would increase the likely health gain.

Based on their estimate of the monetary value of a QALY (US $30 000), the National Osteoporosis Foundation suggested that in relation to bisphosphonate treatment, BMD measurement is cost-effective for women without a previous fracture who are either 65 years old or who are 60 years old with one or more risk factors. For women with a previous non-vertebral or vertebral fracture who are either 60 years old or 50 years old with one or more risk factors, BMD screening is effective in relation to the monetary value of a QALY gained with bisphosphonate treatment:

- For women without a previous fracture who are either > 65 years old or who are > 60 years old with one or more risk factors.
- For women with a previous non-vertebral or vertebral fracture who are either > 60 years old or > 50 years old with one or more risk factors.

A descriptive cost-benefit analysis of treatment for non-vertebral fractures is presented in Table 10.

**Table 10** A descriptive cost-benefit analysis of treatment for non-vertebral fractures

The annual costs of osteoporosis in the UK are £1.7 billion. The total costs of hip fracture in the UK may reach £20 000 and are substantially higher than those for in-patient treatment of other fractures.

The drug costs per osteoporosis-related fracture avoided vary widely, depending on the preventive drug used. Salmon calcitonin is the most costly, and although it may be as effective as other treatments, it should be reserved for situations in which HRT or a bisphosphonate are inappropriate.

BMD screening is effective in relation to the monetary value of a QALY gained with bisphosphonate treatment:

- For women without a previous fracture who are either > 65 years old or who are > 60 years old with one or more risk factors.
- For women with a previous non-vertebral or vertebral fracture who are either > 60 years old or > 50 years old with one or more risk factors.

**Conclusion**

Non-vertebral fractures are common, affecting 1% of the population/year. One fracture commonly predicts a second fracture, e.g. the risk of vertebral fracture increases fivefold in patients with distal forearm fracture. Fracture patients are therefore a suitable target for treatments to prevent further fractures. This Consensus Group proposes a treatment algorithm based on that described by the joint report of the Royal College of Physicians and the Bone and Tooth Society. Preventive measures should be taken in patients who sustain non-vertebral fracture and whose bone density indicates osteopenia or osteoporosis.

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