Identification and Treatment of Osteoporosis in Fractures

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Patients who present with osteoporotic fracture are at highest risk of further fractures and their associated morbidity. Despite the availability of several evidence-based therapeutic options, which have the potential to reduce the incidence of fractures by up to 50%, it is paradoxical that these high-risk patients are seldom assessed for osteoporosis and offered treatment. Secondary prevention of osteoporotic fractures should now be the priority for osteoporosis services; the challenge that remains is to devise new models of patient care that can deliver strategies for the secondary prevention of osteoporotic fractures in different healthcare settings.

Introduction

Opportunities to prevent further fractures in women and men who have sustained a fracture are usually neglected; to do so, however, is to preside over the natural history of osteoporosis and deny patients the opportunity of avoiding the morbidity [1–3] and, possibly, mortality [1,4•,5] associated with fractures. Low bone mineral density (BMD), which is common in women and men over 50 years of age with fractures, is amenable to intervention and has been an effective target for treatment (including alendronate [6••,7,8••,9,10], risedronate [11••,12•,13••], cyclical etidronate [14], raloxifene [15••], and calcitonin [16]) to achieve the prevention of further osteoporotic fractures (secondary prevention of osteoporotic fractures). Despite the recommendation in national guidelines that patients with fractures should be assessed for osteoporosis [17,18], this practice has rarely been adopted. In this review, recent evidence supporting strategies for the secondary prevention of osteoporotic fractures will be reviewed; the key challenge for researchers is translating this evidence into clinical practice.

Implication of Nonvertebral Fracture for Future Fracture Risk

History of fracture is associated with a two- to eightfold higher risk of fracture at the same anatomical site and also at other sites [19]. A study by van Staa *et al.* [20•] confirmed that the occurrence of a fracture at a nonvertebral or vertebral site in postmenopausal women is associated with a 1.6- to 5.8-fold increased risk (expressed as standardized incidence ratio) of subsequent fractures at vertebral and nonvertebral sites. Among the sites of fracture that carry predictive value for future fracture risk are fractures of wrist and hip, as previously reported, but also fractures at a range of other sites, such as lower leg (tibia/fibula and ankle), humerus, and even ribs (Table 1).

Three recent studies have shown that fracture events have a predictive value for future fractures, even if the original fracture occurred long before menopause (in women over 20 years of age) [20•,21,22]. Hosmer *et al.* [21] in their prospective 12-year follow-up of 9704 postmenopausal white women over the age of 65 demonstrated that a fracture occurring at any nonvertebral site in a premenopausal woman is associated with approximately a 35% increased risk of postmenopausal fracture at any nonvertebral site (hazard ratio 1.33; 95% confidence interval [CI] 1.14 to 1.56, $P<0.001$) (Table 1). Although women with a history of premenopausal fracture did tend to have slightly lower BMD, the increased risk of postmenopausal fracture persists even after adjustment for BMD (and also after adjustment for medication and history of maternal fracture). Fractures in men at any age are associated with even greater relative increase in risk of further fractures than is seen in women, although the absolute risk remains less [20•].

Implication of Vertebral Fracture for Future Fracture Risk

Clinically apparent vertebral fractures are associated with increased risk of fractures at vertebral and nonvertebral sites [23]. Asymptomatic vertebral fractures have been associated with an approximately twofold increase in risk of hip fractures [24]. Recent evidence has confirmed this observation. For example, Ismail *et al.* [25], in their further evaluation of fracture outcomes in the European Prospective Osteoporosis Study group, which comprises around 6300 men and 6788 women observed for a median of 3 years, have confirmed that hip fracture risk is increased by approximately four- to fivefold in women, but not in men, with asymptomatic vertebral fractures. Hip fracture risk rises in proportion to the number of prevalent vertebral fractures; the presence of two or more asymptomatic vertebral fractures is associated with a sevenfold increase in hip fracture risk. Although less dramatic, the

Table 1. Standardized incidence ratio of subsequent fractures stratified by fracture type in patients aged 20 years or older in the UK General Practice Research Database*

Original fracture	Later fracture Any fracture SIR (95% CI)	Radius/ulna SIR (95% CI)	Tibia/fibula/ ankle SIR (95% CI)	Femur/hip SIR (95% CI)	Humerus SIR (95% CI)	Ribs SIR (95% CI)	Vertebral SIR (95% CI)
Any fracture		2.5 (2.4 to 2.6)	2.3 (2.2 to 2.4)	2.2 (2.1 to 2.2)	3.5 (3.3 to 3.6)	2.3 (2.2 to 2.4)	2.2 (2.0 to 3.3)
Radius/ulna	3.0 (2.9 to 3.1)		2.1 (1.9 to 2.2)	2.0 (1.8 to 2.1)	5.8 (5.5 to 6.1)	1.8 (1.6 to 2.1)	1.5 (1.3 to 1.8)
Tibia/fibula/ ankle	2.7 (2.6 to 2.8)	1.6 (1.5 to 1.8)		2.1 (1.9 to 2.4)	1.8 (1.5 to 2.1)	1.7 (1.4 to 2.0)	1.6 (1.3 to 1.8)
Femur/hip	2.6 (2.5 to 2.7)	2.0 (1.8 to 2.1)	2.8 (2.5 to 3.1)		2.7 (2.5 to 3.1)	1.8 (1.5 to 2.2)	2.1 (1.8 to 2.5)
Humerus	3.8 (3.6 to 3.9)	5.6 (5.2 to 5.9)	2.1 (1.8 to 2.4)	2.8 (2.5 to3.0)		2.6 (2.2 to 3.2)	2.8 (2.3 to 3.4)
Ribs	2.6 (2.4 to 2.7)	2.1 (1.9 to 2.4)	2.2 (1.9 to 2.6)	2.1 (1.8 to 2.4)	2.7 (2.3 to 3.2)		4.3 (3.7 to 5.2)
Vertebral	2.9 (2.8 to 3.1)	1.8 (1.6 to 2.1)	2.2 (1.8 to 2.7)	2.9 (2.6 to 3.3)	3.0 (2.5 to 3.6)	5.1 (4.3 to 6.0)	

*Note that fractures at nonvertebral and vertebral sites, even in young adults, are associated with increased risk of future fractures at any site. This study was not able to assess later fracture risk at the same anatomical site. Vertebral fractures were clinically apparent fractures.
CI—confidence interval; SIR—standardized incidence ratio.

Table 2. Observed 5-year risk of subsequent fracture from the UK General Practice Research Database applied to lifetables to provide an actual fracture risk by gender and after fracture at any given age

Original fracture	Later fracture	65 to 74 years		75 to 84 years		85 years or older	
		Men	Women	Men	Women	Men	Women
Radius/ulna	Femur/hip	2.5%	3.0%	2.9%	9.4%	6.3%	17.0%
	Vertebral	0.6%	0.9%	0.7%	1.4%	—	1.8%
Femur/hip	Radius/ulna	2.8%	5.8%	2.6%	7.4%	0.6%	5.8%
	Vertebral	1.1%	1.5%	1.3%	2.2%	3.2%	1.5%
Vertebral	Radius/ulna	1.0%	4.5%	1.5%	6.4%	0.8%	3.1%
	Femur/hip	5.7%	6.2%	7.4%	15.5%	8.8%	23.9%

risk of "any limb" fracture is also increased by a factor of 1.8, but only in women. This relationship has persisted even after correction for low BMD.

Further fractures can occur early after the initial fracture event. Johnell *et al.* [26•] have assessed the timing of subsequent fractures that require hospitalization after hospital admission for low-trauma vertebral fracture; only 8% to 20% of vertebral fractures necessitate hospitalization [27]. Six (95% CI 4.2 to 8.4) per 1000 women and 7.1 (95% CI 5.8 to 8.8) per 1000 men aged 50 to 54 are subsequently readmitted with hip fracture within 6 months of hospitalization for vertebral fracture. This represents a 20.9- and 16.7-fold increase, respectively, in the risk of hip fracture over that seen in the general population. The risk rises with age, and if the vertebral fracture that necessitates admission occurs in women and men over 85, their risk of hip fracture within 6 months is, respectively, 70.3 (61.1 to 80.9) and 85.7 (80.5 to 91.2) times higher than expected. The subsequent fracture risk is greatest early on, after the initial vertebral fracture. Hip fracture risk decreases with increasing time after the original vertebral fracture and 4 years later is approximately 30% to 40% less than the risk at 6 months, which emphasizes the need for early intervention. To achieve optimal reduction in fracture risk, it is clear that strategies for secondary prevention need to be implemented early.

Calculation of absolute risk of fracture is more useful than relative risk for identifying and prioritizing those who are at sufficiently great short-term risk to benefit from the inconvenience and cost of treatment for the secondary prevention of fractures. van Staa *et al.* [20•] applied their fracture incidence data to UK lifetables (Table 2) to provide estimates of absolute fracture risk. In a 65-year-old person, the 5-year risk of suffering a nonvertebral fracture after a fracture at radius/ulna, femur/hip, or vertebra ranges from 3% to 6.2% in women and from 1% to 5.7% in men (Table 2). Five-year post-fracture, nonvertebral fracture risk increases with age and, in those over the age of 85, is between 3.1% and 23.9% for women and between 0.6% and 8.8% for men. In general, nonvertebral fractures are less predictive of vertebral fracture occurrence, although this may be a consequence of including only those patients who had symptomatic vertebral fractures with a confirmatory radiograph. For men, forearm fracture risk is lower and is less influenced by fracture history. Similar trends, but higher predicted subsequent 5-year fracture rates, were reported in a study of postmenopausal women with fractures in Australia. The subsequent 5-year fracture risk in a 65-year-old woman with a fracture at spine, hip, or other site ranged from 0.9% to 14.3%; at age 85, the risk rises to between 18.4% and 40.2% [28•].

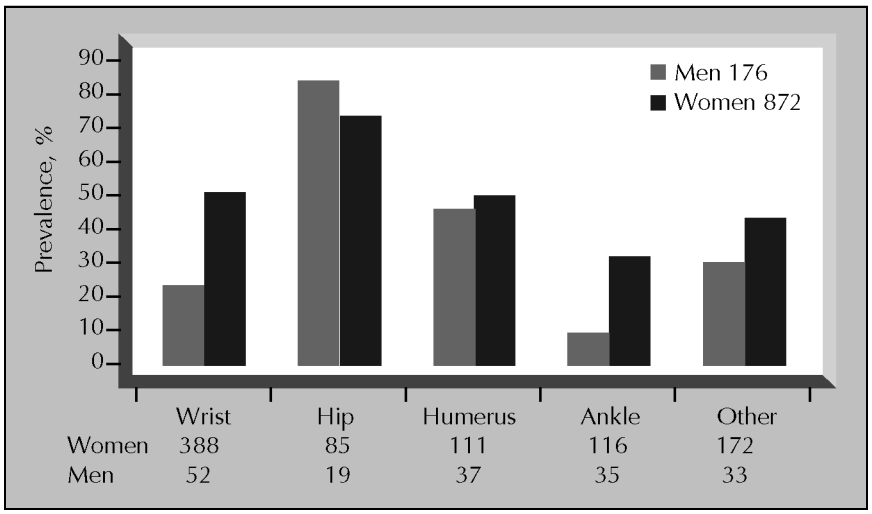

Figure 1. The prevalence of osteoporosis by fracture site and by gender in 1048 patients assessed by dual radiograph absorptiometry through the Fracture Liaison Service.

Are All Fractures Osteoporotic Fractures?

The factors that contribute to fracture risk can be broadly divided into those that relate to the integrity of the skeleton and those that relate primarily to risk of falling. Low BMD carries the greatest implication for fracture risk. Because low BMD provides an opportunity to target treatment to reduce fracture risk, it is helpful to review the prevalence of osteoporosis in different fracture groups. It should be emphasized that there is an inverse relationship between BMD and fracture risk; the risk of fracture rises approximately 2.5-fold per standard deviation reduction in BMD.

Osteoporosis has been shown to be present in 73.5% of low trauma symptomatic vertebral fractures (defined as loss of height of one vertebral dimension of 20% or more) in women; the prevalence rises with age, and 87% of those aged 70 to 79 with clinical vertebral fracture have osteoporosis at hip or spine [29•]. The author's data (Fig. 1) show that, depending on the site of fracture, between 32% (ankle) and 74% (hip) of women and 10% (ankle) and 85% (hip) of men over the age of 50 with low trauma fractures have osteoporosis.

In Fracture Cases, Does Assessment for Osteoporosis Take Place?

Several recent reports suggest that, despite the availability of several agents with potential to achieve secondary prevention of osteoporotic fractures, little progress has been made in applying this knowledge to patients who present with a fracture. In a recent retrospective assessment of outcome after distal forearm fracture in 343 postmenopausal women from Minnesota, only 28% had received treatment or treatment advice regarding osteoporosis 12 months after the fracture [30]. Repeated presentations with fractures do not guarantee that patients will be assessed or treated for osteoporosis; only 33% of women presenting with their second fracture received treatment or treatment advice regarding osteoporosis. Similarly, poor treatment rates are seen in the UK; 5% of wrist fractures patients, 4% of hip fracture patients, and 39% of vertebral fracture patients identified through the UK General Practice Research Database were given treatment within 12 months of their fracture [31]. Osteoporosis assessment and treatment rates are low, which is reflected in discharge medication, whether fracture patients are discharged from acute care or from rehabilitation facilities [32]. Assessment and treatment rates are similarly low, even when there are open- or direct-access dual radiograph absorptiometry (DXA) services to which primary care clinicians can refer fracture cases; the author's experience suggests that only 2.7% of Colles' fracture and 11.6% of hip fracture cases are referred for assessment by DXA.

The Fracture Liaison Service: A Service Model that Achieves Secondary Prevention of Osteoporotic Fractures

Understanding the pathway of care of fracture patients is essential for the identification of opportunities to target effort to offer osteoporosis assessment. Most fracture cases are readily identifiable through the Accident and Emergency or Orthopaedic Services, which routinely deal with the acute fracture management. It is clear that, despite the ease of identification of patients with fractures, with the possible exception of vertebral fractures, osteoporosis assessment and management are seldom offered by the services that provide acute fracture care or by their primary care clinicians.

The Fracture Liaison Service (FLS) was established in 1999 to deliver a strategic approach to secondary prevention for the author's hospital's fracture cases. Before this, osteoporosis assessment in fracture patients was available through secondary care-based osteoporosis clinics and through a direct-access DXA service, which could refer fracture patients directly for DXA via their primary care clinician. Having confirmed that osteoporosis assessment was rarely offered, it was agreed with primary care and orthopedic colleagues that the solution lay in taking the expertise of the

existing osteoporosis service directly to the patients where their acute fracture care was being provided (*ie*, in the orthopaedic wards or at the orthopaedic fracture clinics). This was achieved through creation of a novel service within secondary care, the FLS, in which a new nurse practitioner role, the Fracture Liaison Nurse (FLN), would effect delivery of osteoporosis assessment and protocol-based treatment, where necessary, for the secondary prevention of fractures. All men and women over the age of 50 with fractures (apart from those sustained in road traffic accident or in fall from above head height) are now offered osteoporosis assessment or treatment. The FLS is based on the principle of maximizing personal contact with fracture cases when they are inpatients or when, as outpatients, they attend the orthopedic fracture clinics—fracture patients who do not meet with the FLN personally are contacted via letter. The purpose of initial contact is to advise patients that their fracture is associated with possible risk of underlying osteoporosis and of further fracture, and to offer assessment for osteoporosis by DXA. Dual radiograph absorptiometry assessment is provided through a one-stop DXA/FLN clinic (two sessions per week) at which DXA is performed; the result is discussed in the context of other risk factors for fracture, and the optimal management plan (defined by protocol, and tailored to the individual's need) is agreed on.

If DXA is not perceived to be necessary in determining treatment selection, for example, if the patient is assessed to be unsuitable for bisphosphonates (perhaps because of dementia and the lack of someone to supervise medication), then 1000 mg of calcium carbonate and 800 IU of vitamin D are started without further assessment.

The FLS, which is described in detail elsewhere, achieves assessment (by DXA) or treatment in 71% to 81% of patients with fractures at all sites in women and men; the remainder only fail to undergo assessment because they decline the opportunity [33].

Identification of Osteoporosis and Fracture Risk: When to Treat

Assessment of fracture risk in individual patients requires consideration of factors that reflect skeletal integrity and factors that determine risk of falling. For some patients, attention to the latter may achieve more in modifying fracture risk. However, pharmaceutical intervention primarily modifies the skeleton's contribution to fracture risk, and of the three key risk factors for fracture, BMD, age, and previous fracture, it is BMD or previous fracture that are appropriate criteria for targeting treatment to reduce fracture risk. Confirmation that a patient's fracture risk is high is insufficient to assure that antiresorptive therapy can potentially reduce the incidence of fractures, if that risk assessment is not primarily determined by BMD as assessment by axial DXA. For example, targeting antiresorptive therapy to patients whose risk is primarily based on risk factors other than BMD has not reduced the incidence of fractures [13••]. Although ultrasound, peripheral DXA, and markers of bone turnover have a role in predicting future fracture risk, none of these has been an effective means of targeting treatment to patients to reduce their fracture risk.

The aim of treatment of osteoporosis in fracture patients is to reduce the incidence of further fractures. Treatments can be categorized into those that, in double blind, randomized, placebo-controlled trials, have reduced risk of fractures at vertebral and nonvertebral sites (Table 3) (alendronate [7], risedronate [11••,12•], and hormone replacement therapy [34]), and those whose fracture efficacy is restricted to reduction in risk of vertebral fractures only (cyclical etidronate [14], calcitonin [16], and raloxifene [15••]). Clearly, for most patients, treatments with potential to achieve secondary prevention of fractures at all sites would be preferable to those treatments that can only reduce risk of vertebral fracture.

Table 3 summarizes the key double blind, randomized, placebo-controlled trials that have been performed in osteoporotic women, and allows comparison of trial size, the incidence of fractures (vertebral and non-vertebral) in the trials' placebo groups, which is an indicator of the actual fracture risk that may be experienced when applying similar BMD and fracture inclusion criteria in clinical practice. Table 3 also summarizes the efficacy of these treatments in reducing the incidence of fractures at vertebral and nonvertebral sites. Three broad strategies for targeting antiresorptive treatments, based on ascertainment of prevalent fractures with or without BMD measurement, can be inferred from clinical trials (Table 3). In the first strategy, ascertainment of potential risk is based on the presence of at least one vertebral fracture coupled with BMD measurement by axial DXA. Alendronate, at 10 mg per day (with calcium and vitamin D), has reduced incident fracture rate by approximately 50% at spine and hip when targeted on basis of vertebral fracture coupled with a femoral neck T score of -1.6 or less (using the National Health and Nutrition Examination Survey reference dataset for calculation of T scores). The number needed to treat (NNT) to prevent one vertebral fracture is 15, whereas the NNT to prevent one hip fracture is 90.

Schnitzer *et al.* [35] compared 70 mg once weekly with the 10 mg daily alendronate regimen and showed equivalent BMD increments for these different regimens for administration of alendronate. This clinical trial was not designed to establish equivalent fracture risk reduction.

The only double blind, randomized, placebo-controlled trial of the efficacy of hormone replacement therapy in the secondary prevention of fractures in osteoporotic women was based on use of transdermal estrogen [34]. Although a very small study and flawed because the number of incident vertebral fractures was used to define efficacy rather than the number of patients with new vertebral fractures, the incidence of vertebral fractures was reduced after just 1 year of treatment. This relationship is likely to be causal and is supported by The Women's Health Initiative, which is the largest double blind placebo-controlled clinical trial of estrogen (and progester-

Table 3. Summary of key double blind, randomized, placebo-controlled clinical trials demonstrating efficacy in reducing the incidence of vertebral and nonvertebral fractures

Study	Treatment	Average age, y	Patients, *n*	Target BMD	Non-VFxR and hip FxR in PBO (y)	RR non-VFxR	VFxR in PBO (y)	RR VFx
Targeting treatment at low BMD plus at least one VFx and showing reduction in VFx and non-VFx								
[7]	Alendronate 5 to 10 mg per day*	71	2077	FN T score -1.6	14.7% (3); hip Fx 2.2% (3)	0.8 (0.63 to 1.01 (NS)	15% (3)†	0.53 (0.41, 0.68)
Targeting treatment at low BMD plus at least one VFx and showing reduction in VFx								
[34]	Estrogen and progesterone*	66	75	T score -1 or less (DPA)				0.4 (0.21, 0.78)‡
[15••]	Raloxifene 60 to 120 mg per day*	67	2304	FN T score -2.5 or less	9% (3)	0.9 (0.8, 1.1) NS	21.2% (3)†	0.7 (0.6, 0.9)
[16]	Calcitonin 100, 200, 400 IU per day*	68	1255	LS T score -2 or less		NS	26% (5)†	0.67 (0.47, 0.97)
Targeting treatment at low BMD and showing reduction in VFx or non-VFx								
[9]	Alendronate 5 to 10 mg per day*	68	4432	FN T score -2.5 or less (N)§	19.6% (4.2); hip Fx 2.2% (4.2)	Hip 0.44 (0.18, 0.97)	5.8% (4.2)†	0.5 (0.31, 0.82)
[8•]	Alendronate 10 mg per day	63	1908	LS T score -2 or less	3.9% (1)	0.5 (0.3, 0.9)		
[13••]	Risedronate 2.5 to 5 mg per day*	74	5445	FN T score -2.7 to -2.9 (N)	10.7% (3); 3.2% hip Fx (3)	0.8 (0.7, 1.0)		
Targeting treatment at low BMD and showing reduction in VFx								
[15••]	Raloxifene 60 to 120 mg per day*	67	4524	FN T score -2.5 or less or LS T score -2.5 or less	9% (3)	0.9 (0.8, 1.1) NS	4.5% (3)†	0.5 (0.4, 0.8)
Targeting treatment at two or more VFx and showing reduction in VFx and non-VFx								
[11••]	Risedronate 2.5 to 5 mg per day*	68	2458		8.4% (3)	0.6 (0.39, 0.94)	16.3% (3)¶	0.59 (0.43, 0.82)
Targeting treatment at two or more VFx and showing reduction in VFx								
[14]	Cyclical etidronate*	66	423				6.3% (2)†	0.44 (0.2, 1.0)
[12•]	Risedronate 2.5 to 5 mg per day*	71	1225		16% (3)	0.69 (0.44, 1.04) NS	29% (3)¶	0.51 (0.36, 0.73)

*In conjunction with calcium or vitamin D.
†Vertebral fracture is defined as loss of vertebral height of 20% or greater.
‡Refers to number of VFx and not patients with new VFx.
§Subgroup analysis.
¶Vertebral fracture is defined as a loss of vertebral height of 15% or greater.
BMD—bone mineral density; DPA—dual photon absorptiometry; FN—femoral neck; Fx—fracture; LS—lumbar spine; NS—not significant; PBO—placebo; RR—relative risk; VFx—vertebral fracture; VFxR—vertebral fracture response.

one) that confirmed that, even when used in healthy postmenopausal women (whose BMD status was unknown), hormone replacement therapy is associated with significant fracture risk reduction including fracture at the hip [36••]. This trial was, however, designed to assess the overall risks and benefits of hormone replacement therapy and was stopped prematurely because, after approximately 5 years of use, the adverse risks (increased risk of breast cancer, myocardial infarction, and stroke) outweighed the benefits (fracture risk reduction and reduction in the incidence of colonic cancer).

Vertebral fracture, but not nonvertebral fracture, risk reduction has been shown with raloxifene at 60 mg per day [15••] and also with 200 IU per day intranasal calcitonin [16] (used in conjunction with calcium and vitamin D) when administered to women whose fracture risk is defined by low axial BMD with at least one vertebral fracture.

In the second strategy (Table 3), fracture risk reduction can be achieved by targeting antiresorptive treatments at thresholds of BMD that are sufficiently reduced to result in increased fracture risk, but are, nevertheless, modifiable with intervention. It is these treatment thresholds that can be applied to patients presenting with nonvertebral fractures. A nonvertebral fracture doubles (at least) the patients' future fracture risk at that and other skeletal sites, and when used in conjunction with evidence-based thresholds of BMD defined by clinical trials, treatments are likely to confer greater benefit in terms of the absolute fracture risk reduction in those with fracture (and low BMD) than would be seen in patients with similarly reduced BMD without a nonvertebral fracture.

Alendronate at 10 mg per day with calcium and vitamin D administered to patients with femoral neck T scores of -2.5 or lower can significantly reduce the incidence of vertebral (NNT 35) and nonvertebral fractures (hip fracture NNT 81) [9]. Similar efficacy in nonvertebral fractures risk reduction (NNT 54) has been reported in the Foxamax International Trial Study Group trial [8•], also of alendronate, in which treatment was given of the basis of lumbar spine BMD T score of -2 or under.

Hip fracture risk reduction has been reported with risedronate at 5 mg per day with calcium and vitamin D [13••] administered to elderly women with femoral neck T scores of -2.7 to -2.9 or with slightly higher bone density and other skeletal risk factors, such as increased hip axis length. This study uniquely addressed the primary endpoint of hip fracture incidence, and clearly established that hip fracture risk reduction with bisphosphonates could only be achieved by targeting treatment at low BMD, which is amenable to this treatment, and not by giving bisphosphonates to elderly women whose fracture risk is defined only by clinical risk factors for fracture (including fall-related factors).

Raloxifene at 60 mg per day with calcium and vitamin D has reduced the incidence of vertebral fractures (NNT 46) when given to patients with femoral neck T scores of -2.5 or less [15••].

In the third strategy (Table 3), fracture risk reduction can be achieved by targeting antiresorptive treatments in patients whose fracture risk is determined by the presence of multiple vertebral fractures (at least two), without the necessity to perform DXA. Risedronate at 5 mg daily, with calcium and vitamin D, has reduced the incidence of vertebral fractures (NNT 10 [12•] and NNT 20 [11••]), and nonvertebral fractures (NNT 32) [11••]). Intermittent cyclical etidronate [14] has reduced the incidence of vertebral fractures (NNT 19) when administered to patients with multiple vertebral fractures.

Although alendronate has not been evaluated in any study in where it was targeted on the basis of vertebral fractures without low BMD, subsequent analyses of Fracture Intervention Trials suggest that alendronate can reduce the incidence of vertebral fracture irrespective of original BMD. In practice, the key to targeting treatment is to define a level of risk that is sufficiently high that treatment is affordable and effective. For alendronate, as for risedronate, these options would be appropriate for treating patients with low BMD plus at least one vertebral fracture or with multiple vertebral fractures without DXA assessment.

Calcium and Vitamin D

Calcium and vitamin D, as discussed, have been used concurrently with active therapy and placebo during these key trials, and this practice is recommended in clinical practice. For patients in whom these treatment options are not appropriate, particularly those who are frail and elderly, 1000 mg of calcium carbonate and 800 IU of vitamin D per day are recommended. The evidence supporting this strategy derives not from a fracture secondary prevention trial, but form the study of French nursing home residents, who by virtue of lifestyle are vitamin D deficient; treatment has been shown to reduce the incidence of hip fractures by 35% [37].

Treatment of Men with Low Bone Mineral Density and with Previous Fracture

Although osteoporotic fractures are less common in men than women, almost 30% of hip fractures occur in men, and men experience greater fracture-related morbidity and mortality [4•,38,39]. 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, although there is some evidence that men and women may fracture at similar gender-specific T scores of BMD [40], which supports the World Health Organization criteria as being applicable to men using the average young adult male peak BMD as the reference for comparison. There has been only one fracture secondary prevention trial in men. Orwoll *et al.* [6••] recruited men with low BMD (femoral neck T score –2 or less, plus lumbar spine T score –1 or less, or femoral neck T score -1 or less, as well as a history of one or more vertebral fractures or one nonvertebral fracture). Alendronate at 10 mg per day with calcium and vitamin D was associated with significant reduction in vertebral fracture risk (0.8% vs 7.1%; $P<0.02$).

Conclusions

Women and men with osteoporotic fractures are at high risk of further fractures and their associated morbidity and even mortality. Fracture leads to fracture. Until now, healthcare systems have presided over the natural history of osteoporotic fracture and have failed to deliver strategies that can potentially reduce fracture morbidity by 50%. There is now a range of therapeutic options with evidence to support their role in secondary prevention of osteoporotic fractures. Targeting these treatments effectively requires an understanding of the magnitude of the individual patient's fracture risk, which is a function of BMD, previous fracture, and age. Treatment thresholds used to target treatment in the key clinical trials can be adopted in clinical practice. For patients with at least one previous vertebral fracture, hip T score of -1.6 or less should be considered. For patients with nonvertebral fracture, hip or spine T scores less than -2 to –2.5 should be considered. Where multiple vertebral fractures have occurred, DXA is not necessary for targeting treatment. The greater challenge, however, is how this knowledge can be deployed systematically to achieve the secondary prevention of osteoporotic fractures in the majority of these high-risk patients. The FLS model is a prime example of a service that is highly effective in delivering strategies for the prevention of osteoporosis.

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