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Original Article

The Burden of Osteoporotic Fractures: A Method for Setting Intervention Thresholds

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Abstract. The aim of this study was to assess the relationship between morbidity from hip fracture and that from other osteoporotic fractures by age and sex based on the population of Sweden. Osteoporotic fractures were designated as those associated with low bone mineral density (BMD) and those that increased in incidence with age after the age of 50 years. Severity of fractures was weighted according to their morbidity using utility values based on those derived by the National Osteoporosis Foundation. Morbidity from fractures other than hip fracture was converted to hip fracture equivalents according to their disutility weights. Excess morbidity was 3.34 and 4.75 in men and women at the age of 50 years, i.e. the morbidity associated with osteoporotic fractures was 3–5 times that accounted for by hip fracture. Excess moribidity decreased with age to approximately 1.25 between the ages of 85 and 89 years. On the assumption that the age- and sex-specific pattern of fractures due to osteoporosis is similar in different communities, the computation of excess morbidity can be utilized to determine the total morbidity from osteoporotic fractures from knowledge of hip fracture rates alone. Such data can be used to weight probabilities of hip fracture in different countries in order to take into account the morbidity from fractures other than hip fracture, and to modify intervention thresholds based on hip fracture risk alone. If, for example, a 10-year probability of hip fracture of 10% was considered an intervention threshold, this would be exceeded in women with osteoporosis aged 65 years and more, but when weighted for other osteoporotic fractures would be exceeded in all women (and men) with osteoporosis.

Keywords: Absolute risk; Hip fracture equivalents; Intervention thresholds; Quality of life; Osteoporotic fracture

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Introduction

The development of intervention thresholds for osteoporosis requires a consideration of the threshold of fracture risk at which intervention is appropriate. Much attention has focused on hip fractures in women because of their high cost to individuals and to healthcare agencies. Indeed, health economic assessments in osteoporosis have mainly focused on this fracture [1–5]. However, intervention thresholds determined on hip fracture risk alone would neglect the many other fractures that occur, particularly in younger age groups where the pattern of fractures differs from the elderly. Even in the elderly, hip fractures represent less than 50% of all fractures in men and women aged 80 years or more [6,7]. Thus, public health measures that focus on hip fracture underestimate considerably the burden of other fractures.

Consideration of other fractures requires a detailed evaluation not only of the pattern of fracture types with age, but also their morbidity. For example, an intervention that prevented 10 fractures per 100 treated

patients (NNT = 10) would have a different significance at the age of 50 years where hip fractures are rare, than at the age of 70 years where they form a much higher proportion of fractures. A further consideration is that not all fractures are due to osteoporosis. Fractures not due to osteoporosis may not be prevented by pharmacologic intervention, at least not to the same extent as fractures associated with osteoporosis. For example, the efficacy of bisphosphonates on appendicular fractures appears to be less marked in women without osteoporosis [8], or in women with risk factors for falls rather than in women with osteoporosis [9]. Thus, nonosteoporotic fractures should be excluded in the context of setting intervention thresholds.

There are few detailed assessments of the pattern of fracture types with age in different parts of the world. This poses problems in the development of intervention thresholds that take account of all fractures due to osteoporosis. There is, however, more complete information on the incidence of hip fracture worldwide. The aim of this paper is to characterize the pattern and burden of osteoporotic fracture by age in men and women in order to provide a methodology to develop intervention thresholds that take account of the differing significance of different fractures at different ages. A further aim is to provide algorithms so that intervention thresholds might be applied internationally from knowledge of the risk of hip fracture alone.

Methods

The calculation of incidence of fractures attributed to osteoporosis was based where possible on the population of Sweden or if not, on regional figures from Malmo. Admissions to hospital for fracture in Sweden were examined to identify fractures in 1996 (National Bureau of Statistics, Stockholm). Where there was insufficient information (rib, clavicular, scapular and sternal fractures), rates were imputed from the distribution of fractures observed in Olmsted County, Rochester [7]. Fractures were considered to be osteoporotic where the fracture type is known to be associated with a decreased bone mineral density (BMD) [10]. In additon, fractures that showed no increase in incidence with age were excluded.

The following fractures were considered to be due to osteoporosis:

Vertebral fractures. There is an established relationship between bone mass and vertebral fracture [10] and between vertebral fracture and other osteoporotic fractures [11]. Because a minority of vertebral fractures are admitted to hospital, we utilized data from Malmo [12] documenting vertebral fractures that came to clinical attention. They do not include, therefore, those morphometric deformities that are asymptomatic or otherwise subclinical. Fractures known to be associated with metastases to the spine were excluded.

Rib fractures. These were considered to be osteoporotic because they are associated with low BMD. A large prospective study showed that the risk of rib fractures increased 1.8-fold for each SD decrease in BMD at the distal radius [10]. They increase in frequency with age in both men and women [6,10,11]. A limitation of the Swedish hospital data is that they are derived from inpatient admissions and therefore omit an uncertain but large proportion treated as outpatients only.

There are few data on the incidence of rib fracture in both men and women that span the relevant age range. The most complete are from Olmsted County, which document radiographically verified rib fractures [7]. The pattern of the classical osteoporotic fractures (hip, distal forearm, proximal humerus) is similar comparing Olmsted County and Sweden (reviewed in the Discussion), although there are appreciable differences in incidence. We assumed that the pattern of incidence of rib fracture was similar in Sweden and Olmsted County compared with the pattern of other osteoporotic fractures, and from this estimated the incidence of rib fractures in Sweden. Comparison of these estimates with the reported rates for hospital admission suggest that 8.6% of rib fractures in men aged 50 years or more and 9.8% of women are hospitalized.

Pelvic fractures. These are associated with low bone mass [10] and incidence rises steeply with age comparable to the incidence of hip fractures [13]. We assumed that all pelvic fractures were hospitalized, an assumption that is likely to understimate fractures. For example, institutionalized individuals in Holland are not consistently admitted [C. DeLaet, personal communication, 2000]. The underestimate is, however, offset to some degree by the inclusion of pelvic fractures due to severe trauma, which account for approximately 25% of pelvic fractures in men and women aged 55 years or more [14].

Humeral fractures. There is an established relationship between low BMD and fractures of the proximal humerus [10]. Since many such fractures are not hospitalised, we utilized data from raidology records of Malmo [12]. The data do not include fractures of the humeral shaft and distal humerus. These increase in frequency with age [11,15,16]. In these series they accounted for approximately 20% of all humeral fractures and we estimated these from the rates of fracture of the proximal humerus at Malmo.

Forearm fractures. There is an established relationship between low bone mass and forearm fractures [10]. Forearm fractures are also significantly associated with other types of osteoporotic fracture [17,18]. Since not all patients are admitted to hospital, we utilized the data from Malmo outpatient records [12]. This would exclude diaphyseal fractures, but there is no increase in these fractures with age in either men or women [7,15].

Hip fracture. There is a well-established relationship between hip fracture and low BMD. There is also a strong association between hip fracture and other osteoporotic fractures. Incidence was taken from the

Swedish National database and assumed that all hip fractures were admitted to hospital. We included cervical and trochanteric fractures, though trochanteric fractures appear to be more closely related to low BMD [10]. Readmissions to hospital for the same fracture were included.

Other femoral fractures. These were included as osteoporotic but they will include fractures of the shaft as well as subtrochanteric and supracondylar fractures. Fractures of the diaphyseal shaft account for 25% of such fractures [19]. Their association with low BMD is uncertain, but they show a steep gradient of risk with age similar to that seen for hip fracture [13,14,19].

Tibia and fibula. Fractures of the leg have been associated with low BMD in women and their incidence increases with age. However, the risk in men does not increase consistently with age [14,20; this study] so that these fractures were excluded as being osteoporotic in men.

Clavicle, scapula and sternum. These fractures are rarely admitted to hospital. Although data on clavicular fractures are available from Malmo [21], none is available for scapular and sternal fractures. We used data from Rochester [7] adjusted to the pattern of fracture in Sweden as for rib fractures. The incidence of clavicular fractures rises with age and they are strongly associated with low appendicular BMD [10].

Fractures at the following sites were classified as not due to osteoporosis.

(a) Skull and face. No increase in either sex with age was observed in Sweden, nor in other series [7].
(b) Tibia and fibula in men.
(c) Hands and fingers. No increase in self-reported fractures are reported in women with age [7,10] nor in men [7,22]. They are not significantly associated with low BMD in women [10].
(d) Feet and toes. The incidence of fractures of the hands, fingers, feet and toes showed no increase with age in a large survey from Cardiff based on Accident and emergency attendances [22] and are only weakly and not significantly associated with low BMD in women [10]. Others have also observed no increase in incidence with age for fractures of the feet [7].
(e) Ankle. Fractures of the ankle are not associated with low BMD in elderly women [10]. However, they appear to be associated with low peak bone mass, which is lower in patients than controls at the time of menopause [23]. There is, however, no age-related increase in risk from the age of 50 years in men nor in women [7,15,20,22,24], although a modest increase was observed in men (but not women) in one survey [22]. It is relevant that the risk factors for ankle fractures in the postmenopause differ from those for other osteoporotic fractures. For example, high body weight, but not early menopause are risk factors for ankle fractures, whereas low body weight and early menopause are risk factors for wrist fractures [25].
(f) Patella. These fractures are rare and the increase in risk with low BMD was not significant [10]. The increase in risk with age is small in women and there is no increase with age in men [15].

Weighting of Fractures

The severity of fractures considered to be osteoporotic was weighted according to their morbidity. For this purpose we used utility values derived by the National Osteoporosis Foundation of the USA [26] (Table 1). Utilities describe health states that range between 1 (perfect health) and 0. The utilities that were used to characterize osteoporotic fractures were based on expert opinion rather than on patient or populations opinion. They were chosen since weights by the same panel of experts were given to all fracture types, whereas utilities derived from healthy populations or patients have generally examined one fracture type, and the methodologies used have varied. We modified the utility for rib fractures since we considered that the long-term morbidity after the event is low. We assumed that the utility lost in the second and subsequent years would be comparable to that of a forearm fracture (rather than a vertebral fracture). Loss of utilities after the second and subsequent years were assumed to decrease by 10% per annum (termed utility discount rate). The cumulative loss of utility over time (disutility) was calculated in men and women for each fracture and at each age interval over the remaining lifetime. For these calculations we assumed that improvements in mortality would continue over the life expectancy [27]. We also examined the effects of variable utility discount rates. Since the health of the general population decreases with age, disutility values (i.e. total utility lost) for each fracture were adjusted by multiplying each disutility value by the average utility value of the age- and sex-matched general population of the UK [based on data given in references 28 and 29].

For the purpose of weighting, the total morbidity in each sex and at each 5-year interval of age was computed from the incidence of each fracture type multiplied by the disutility for that fracture. The sum of the incidence-adjusted morbidity provided an index of the morbidity. The morbidity accounted for by all

Table 1. Utility loss associated with different osteoporotic fractures

Fracture site	Utility in first year	Utility in subsequent years
Vertebra	0.0502	0.0490
Ribs	0.0502	0.006
Pelvis	0.0502	0.0490
Humerus	0.0464	0.006
Clavicle, scapula, sternum	0.0464	0.006
Hip	0.4681	0.1695
Other femoral fractures	0.4681	0.1695
Tibia and fibula	0.4681	0.1695
Distal forearm	0.0464	0.006

fractures divided by the morbidity assigned to hip fracture at each age provided an index of the excess morbidity from other osteoporotic fractures in hip fracture equivalents (termed excess morbidity). The average morbidity for a fracture at each age range was computed from the total morbidity divided by the total numbers of fractures.

Results

The annual rates of fracture by age and sex are given in Table 2 and the proportion of all osteoporotic fractures according to fracture site is shown in Table 3. There was a marked variation in the pattern of fractures with age in both men and women. For example, hip fractures accounted for a minority of fractures at age 50 years (4.7% and 3.8%, respectively in men and women), but was the most common fracture after the age of 70 years in women and 85 years in men.

The cumulative loss of utility (disutility) due to fractures of different types is shown in Table 4 by age and sex. As expected, disutility was greatest in the case of hip fractures over all ages, intermediate for vertebral fractures and lowest for rib and Colles' fracture. Disutility values were higher in the younger age groups due to the higher life expectancy.

The effect of different utility discount rates is shown in Fig. 1 for hip fracture. Discount rates of 20% or 25% showed no appreciable increment in disutility after 10 years. The higher utility discount rates (15–25%) would imply therefore that there was on average no residual morbidity 10–15 years after hip fracture. In contrast, annual discount rates of less than 10% showed progressive increments with time after fracture suggest-

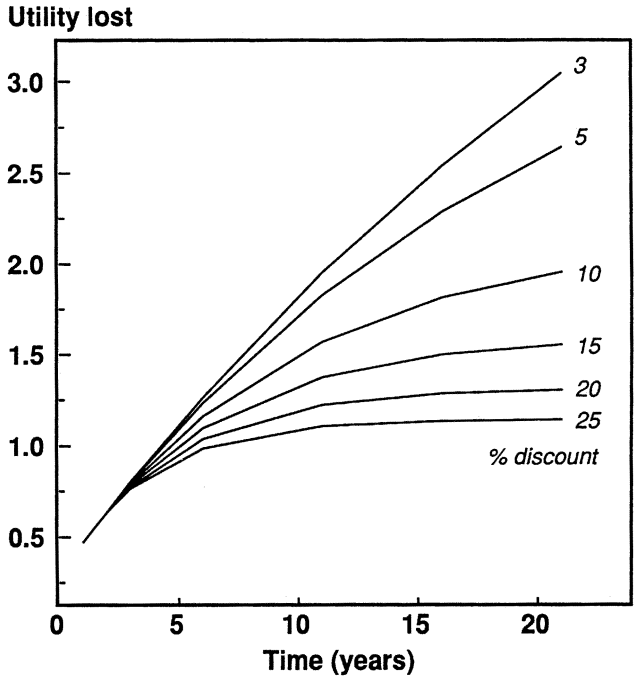

Fig. 1. Cumulative disutility after hip fracture using variable annual rates for the attenuation of disutility.

Table 2. Incidence of fractures (per 100 000 per year) by age and site in men and women

Site of fracture	Age range (years)							
	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85–89
Men								
Vertebra	195	119	226	242	499	619	933	1194
Ribs	324	750	399	790	855	805	3072	3007
Pelvis	12	16	21	31	51	80	179	288
Humeral shaft	22	10	20	31	69	60	78	168
Proximal humerus	65	31	60	92	207	179	235	505
Clavicle, scapula, sternum	116	139	89	216	198	81	659	859
Hip	42	68	134	274	495	940	1923	3241
Other femoral fractures	15	18	24	41	43	51	88	128
Tibia and fibula[a]	–	–	–	–	–	–	–	–
Distal forearm	101	151	140	282	89	175	259	323
Total	892	1302	1113	1999	2506	2990	7430	9713
Women								
Vertebra	161	158	303	439	778	1111	1163	1641
Ribs	126	162	167	340	433	903	1400	3194
Pelvis	9	16	29	47	125	203	436	698
Humeral shaft	41	42	42	117	128	210	195	373
Proximal humerus	124	127	126	352	384	629	585	1120
Clavicle, scapula, sternum	77	97	42	145	121	362	415	356
Hip	41	91	181	387	817	1689	3364	5183
Other femoral fractures	11	17	36	52	89	150	239	404
Tibia and fibula	60	79	88	98	106	145	146	207
Distal forearm	417	456	568	691	904	1032	1208	1387
Total	1067	1245	1582	2668	3885	6434	9151	14563

[a] Excluded in men.

Table 3. Proportion (%) of osteoporotic fractures at different sites in men and women by age

Fracture type	Age range (years)							
	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85–89
Men								
Vertebra	21.9	9.1	20.3	12.1	19.9	20.7	12.6	12.3
Ribs	36.3	57.6	35.8	39.5	34.1	26.9	41.3	31.0
Pelvis	1.3	1.2	1.9	1.6	2.0	2.7	2.4	3.0
Humeral shaft	2.5	0.8	1.8	1.6	2.8	2.0	1.0	1.7
Proximal humerus	7.3	2.4	5.4	4.6	8.2	6.0	3.2	5.1
Clavicle, scapula, sternum	13.0	10.7	8.0	10.8	7.9	8.7	8.9	8.8
Hip	4.7	5.2	12.0	13.7	19.8	31.4	25.9	33.3
Other femoral	1.7	1.4	2.1	2.1	1.7	1.7	1.2	1.3
Tibia and fibula[a]	–	–	–	–	–	–	–	–
Distal forearm	11.3	11.6	12.6	14.1	3.6	5.9	3.5	3.3
Women								
Vertebra	15.1	12.7	19.2	16.4	20.0	17.3	12.7	11.3
Ribs	11.8	13.0	10.6	12.7	11.1	14.0	15.3	21.9
Pelvis	0.8	1.3	1.8	1.8	3.2	3.2	4.8	4.8
Humeral shaft	3.8	3.4	2.7	4.4	3.3	3.3	2.1	2.6
Proximal humerus	11.6	10.2	8.0	13.2	9.9	9.8	6.4	7.7
Clavicle, scapula, sternum	7.2	7.8	2.7	5.4	3.1	5.6	4.5	2.4
Hip	3.8	7.3	11.4	14.5	21.0	26.3	36.8	35.6
Other femoral	1.0	1.4	2.3	1.9	2.3	2.3	2.6	2.8
Tibia and fibula	5.6	6.3	5.6	3.7	2.7	2.3	1.6	1.4
Distal forearm	39.1	36.6	35.9	25.9	23.2	16.0	13.2	9.5

Table 4. Disutility for different fracture types by age adjusted for the population tariffs using a discount of 10% per annum

Fracture type	Age range (years)							
	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
Men								
Vertebra[a]	0.341	0.318	0.296	0.267	0.232	0.194	0.155	0.124
Rib	0.077	0.072	0.069	0.066	0.060	0.055	0.048	0.045
Forearm[b]	0.074	0.069	0.066	0.063	0.057	0.052	0.045	0.042
Hip[c]	1.411	1.319	1.243	1.144	1.015	0.881	0.730	0.626
Women								
Vertebra[a]	0.356	0.338	0.318	0.286	0.247	0.207	0.165	0.125
Rib	0.079	0.075	0.073	0.069	0.061	0.056	0.049	0.042
Forearm[b]	0.076	0.072	0.070	0.066	0.059	0.053	0.046	0.040
Hip[c]	1.467	1.395	1.331	1.215	1.062	0.918	0.761	0.610

[a] Same values used for pelvic fractures.
[b] Same values used for humeral, clavicular, scapular and sternal fractures.
[c] Same values used for other femoral fractures and leg fractures in women.

ing on average continued morbidity throughout life. For this reason a discount rate of 10% was considered appropriate.

The impact of adjusting fracture frequency by morbidity is shown in Fig. 2. In men, fractures other than those at the spine, forearm and hip accounted for the majority of fractures. They accounted for a minority of the morbidity. The inequality between fracture incidence and morbidity was greatest in the case of hip fracture. In men aged 50–55 years hip fracture accounted for 5% of the total number of osteoporotic fractures but gave rise to 30% of the morbidity. The corresponding values for women were 4% and 21%. The impact of hip fracture rose with age and accounted for 50% or more of the total morbidity in men and women after the age of 60 and 65 years, respectively.

The total morbidity (disutility-adjusted incidence) rose, as expected, with age (Table 5), but the increase with age was less steep than that accounted for by hip fracture due to the large number of osteoporotic fracture in the younger age groups. In women, for example, morbidity rose 7.8-fold between the age ranges of 50–54 years and 85–89 years, whereas there was a 126-fold rise in hip fracture incidence (see Table 2).

The average morbidity from an osteoporotic fracture remained relatively stable with age. This reflected the

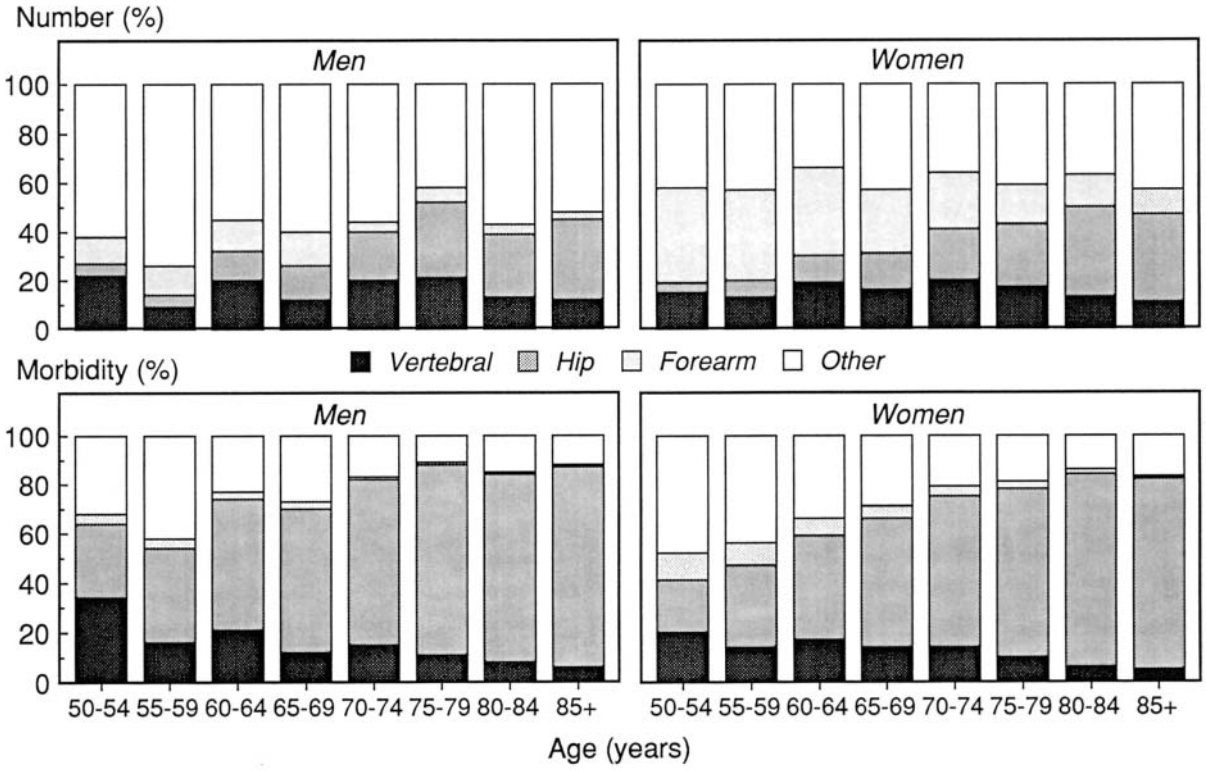

Fig. 2. The proportion (%) of osteoporotic fractures by age and sex at different sites (*upper panels*) and their proportional morbidity (*lower panels*).

Table 5. Morbidity (quality-adjusted life years per 100 000) associated with fractures due to osteoporosis by age and sex (discount rate 10%)

Fracture type	Age range (years)							
	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85–89
Men								
Vertebra	66	38	67	65	116	120	145	148
Ribs	25	54	28	52	51	44	147	135
Pelvis	4	5	6	8	12	15	28	36
Humerus	6	3	4	6	16	12	14	28
Clavicle, scapula, sternum	9	10	6	14	11	4	30	36
Hip	59	90	167	312	502	828	1404	2029
Other femoral	21	24	30	47	44	45	64	80
Tiba and fibula[a]	–	–	–	–	–	–	–	–
Distal forearm	7	10	9	18	5	9	12	14
Total	197	234	317	522	757	1077	1844	2506
Excess morbidity	3.34	2.60	1.90	1.67	1.51	1.30	1.31	1.23
Average morbidity	0.22	0.18	0.28	0.26	0.30	0.36	0.25	0.26
Women								
Vertebra	57	53	96	126	192	230	192	205
Ribs	10	12	12	23	26	51	69	134
Pelvis	3	5	9	13	31	42	72	87
Humerus	13	12	12	31	30	44	36	60
Clavicle, scapula, sternum	6	7	3	10	7	19	19	14
Hip	60	127	241	470	868	1550	2560	3162
Other femoral	16	24	48	63	95	138	182	246
Tiba and fibula	88	110	117	119	113	133	111	126
Distal forearm	32	33	40	46	53	75	56	55
Total	285	383	578	901	1415	2282	3279	4089
Excess morbidity	4.75	3.02	2.40	1.92	1.63	1.47	1.28	1.29
Average morbidity	0.27	0.31	0.37	0.34	0.36	0.35	0.36	0.28

[a] Excluded in men.

competing effects of a rise in fractures with high morbidity and the lower disutility with advancing age from a lower life expectancy. The average morbidity was lower in men compared with women at most ages.

The morbidity of fractures in hip fracture equivalents (excess morbidity) is shown by age and sex in Table 5. Excess morbidity was higher in women than in men and decreased, as expected, with age.

Application

Table 6 gives the average 10-year probabilities of hip fracture in men and women from Sweden and the probability according to BMD thresholds for osteoporosis [12]. The excess morbidity can be used to adjust these 10-year risks of hip fracture to provide morbidity-adjusted risks in hip fracture equivalents (Table 6). The effect of this in increasing risks is most marked in the younger age groups due to the greater number of non-hip fractures. This has a marked effect on treatment thresholds. Assume for the sake of argument that a 10-year probability of hip fracture of more than 10% was considered to be an unacceptable risk and merited treatment. This threshold would be exceeded in women aged 75 years or more, and in women with a *T*-score of <-2.5 SD at the age of 65 years or more. When account is taken of the burden of other fractures, the threshold is exceeded in the general population of women aged 70 years or more, and in all women with osteoporosis irrespective of age. In men, the average population risk never exceeds this threshold when hip fracture risk alone is used. The threshold is exceeded in men with osteoporosis at the age of 70 years or more. By contrast, when account is taken of other fractures, all men with osteoporosis exceed the threshold.

Discussion

The diagnosis of osteoporosis is based on the assessment of BMD, preferably at the hip [30]. Osteoporosis is defined as a BMD that falls below a threshold *T*-score of -2.5 SD. The significance of osteoporosis differs, however, with age. For example the 10-year risk of hip fracture in a 50-year-old woman with a *T*-score of <-2.5 SD is 2.7% but is less than the risk of the population average at the age of 65 years (4.0%). In 65-year-old women with a *T*-score of -2.5 SD the 10-year probability is 11% (see Table 6). This emphasizes the importance of age as a determinant of risk, but also indicates that diagnostic thresholds cannot be used as intervention thresholds. In this paper we have developed the concept of using absolute risks to determine intervention thresholds without specifying what that threshold might be. The strength of this approach is that it takes account of fractures other than hip fracture as well as recognizing that not all fractures are equal in terms of the morbidity induced. A further feature is that morbidity weighting to hip fracture incidence can be undertaken on an international basis where the risk of hip fracture is known.

There are a large number of assumptions made that relate to the definition of osteoporotic fracture, the burden of fracture in Sweden and elsewhere, the pattern of fracture types with age, and the way in which incidence is weighted by disutility and their applicability elsewhere.

Table 6. Ten year probability (%) of hip fracture and hip fracture equivalents by age and sex according to World Health Organization diagnostic categories for low bone mass and osteoporosis

Age (years)	Hip fracture			Hip fracture equivalents[a]		
	$T=-1$	$T=-2.5$	$T<-2.5$	$T=-1$	$T=-2.5$	$T<-2.5$
Men						
50	0.6	2.2	3.4	1.9	6.3	9.5
55	1.1	3.7	5.7	2.3	7.8	12.0
60	1.9	5.7	9.1	3.3	9.8	15.3
65	3.0	8.2	13.3	4.7	12.5	20.0
70	4.5	13.5	21.5	6.3	18.1	28.2
75	6.8	21.8	32.8	8.8	26.5	39.0
80	8.7	23.2	36.2	10.9	28.2	42.8
85+	7.6	19.2	33.3	9.3	23.0	38.8
Women						
50	0.5	1.9	3.1	1.8	6.5	11.0
55	0.8	3.1	5.3	2.0	8.0	13.3
60	1.3	5.1	8.9	2.7	10.2	17.5
65	2.2	8.1	15.0	3.7	13.5	24.4
70	3.1	12.4	24.0	4.6	18.3	34.1
75	4.0	17.4	33.9	5.4	22.7	42.6
80	4.7	19.4	39.6	5.9	24.1	46.9
85+	3.8	16.7	36.0	4.9	20.8	43.0

[a] Includes hip fracture and other fractures.

Ascertainment of Fracture

There are well-recognised problems in fracture ascertainment from all sources. The strength of this study is that it is based primarily on a large sample size (the population of Sweden) and coding errors are infrequent. We did not take account of multiple admissions in the estimates of incidence since multiple admissions capture additional morbidity. The major difficulty with the primary data base is that hospitalization is not invariable for all fracture sites, and in particular for the classical osteoporotic fractures – forearm, proximal humeral and vertebral fracture. For these purposes we utilized data from Malmo. The rates for these fractures were similar to that of other regional estimates in Scandinavia [12].

No recent estimates from Scandinavia were available for rib, sternal, scapular or clavicular fractures and we derived esimates from the USA [7]. The estimates suggest that rib fractures occur somewhat more frequently than shoulder fractures and are consistent with the findings of several other surveys [6,10,20,25,31]. Where comparisons between sexes are available rates of rib fractures are consistently higher in men than in women [7,20].

The Pattern of Fracture

Despite a large number of studies that have examined the incidence of fractures by age and sex, there are problems in defining the pattern of fractures in different countries. There are differences in the population studied. Some studies have been from random samples of the general population [23,25], from self-selected populations [10], from accident departments [20], radiology departments [6] fracture clinics [15,32] or inpatient records [13]. These different sampling frames give rise to large differences in the pattern of fractures reported. Moreover, several surveys do not study or report all fracture types relevant to osteoporosis [22] have small samples [6], an age range not relevant to osteoporosis or do not include men [6]. A further problem is that the incidence and therefore the pattern of fracture changes with time, so that historical data may not be relevant [33–36]. The most complete recent information comes from the present study based in Sweden and studies in Olmsted County [7] and Edinburgh [15].

Available information suggests that the pattern of fractures is similar in the Western world and Australia, despite differences in incidence [7,15,20,37]. In the USA, Sweden and the UK the incidence of forearm, proximal humeral and hip fracture varies. For example, in women aged 80–84 years the rates of these fractures are 3206, 5157 and 2558/100 000 in the USA, Sweden and UK, respectively [7,15; this paper], but the pattern of these fractures with age is remarkably similar (Fig. 3). The relationship between the incidence of hip, vertebral and forearm fracture is also similar between this series and in Australia [38]. Within the USA the pattern appears to be similar amongst blacks and whites. For example, amongst white women aged 65–79 years the ratio of frequency of hip, distal forearm and proximal humerus is 43%, 38% and 19%, respectively. For black women the ratio is 45%, 36% and 18% [39].

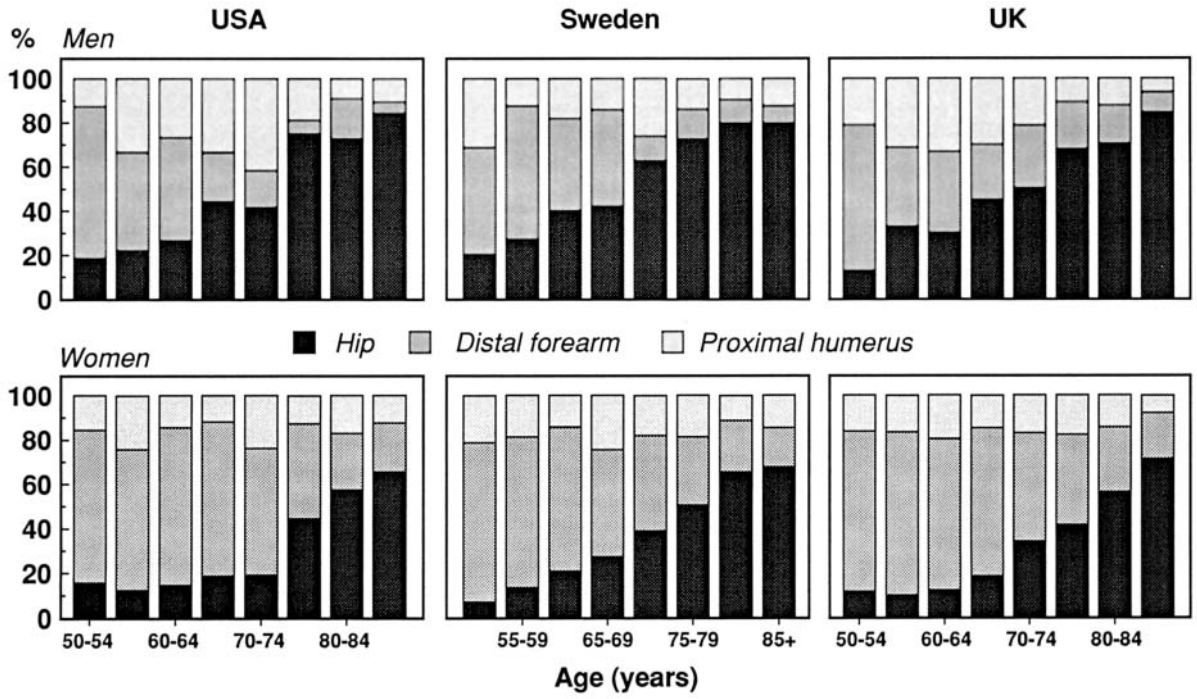

Fig. 3. Pattern of common osteoporotic fractures expressed as a proportion (%) of the total in the USA, Sweden and the UK. Data from the USA are from Melton et al. [7] and from the UK from Singer et al. [15].

This commonality of pattern is supported by register studies, which indicate that in those regions where hip fracture rates are high, so too is the risk of Colles' fracture and vertebral fractures (requiring hospital admission) [40,41].

Since the pattern of osteoporotic fractures appears to be broadly similar in the Western world, this suggests that the imputed rates for rib, scapular and clavicular fractures in Sweden are unlikely to be grossly over- or underestimated. The pattern of fractures elsewhere is, however, unknown and our approach would require validation, particularly in the Eastern world where information is presently wanting. It is also relevant that the pattern of forearm fractures in women is known to vary. In Scandinavia, forearm fractures increase progressively with age [12,17,36] whereas elsewhere rates appear to be flatten after the age of 65 years [7,32].

Osteoporotic Fractures

The definition of an osteoporotic fracture is not straightforward. An approach adopted widely is to consider low-energy fractures as being osteoporotic. This has the merit of recognizing the multifactorial causation of fracture. However, with high-energy trauma, osteoporotic individuals are more likely to fracture than those without osteoporosis [42]. There is also a disparity between low-energy fractures and fractures associated with reductions in BMD [10]. The classification is therefore incomplete.

An alternative approach is to designate an osteoporotic fracture as one sustained in an individual with osteoporosis as defined by the *T*-score and World Health Organization criteria, or to identify types of fracture that increase in frequency the lower the BMD. The association of several different fracture types with BMD has been investigated in the SOF study [10] and was the approach that we used to exclude some fracture types as not being due to osteoporosis. In addition we examined the pattern of fractures with age. A rising incidence of fractures with age does not provide evidence for osteoporosis, since a rising incidence of falls could also be a cause. By contrast, a lack of increase in incidence with age is reasonable presumptive evidence that a fracture type is unlikely to be osteoporosis related. An indirect arbiter of an osteoporotic fracture is the finding of a strong association between the fracture and the risk of classical osteoporotic fractures at other sites. Vertebral fractures, for example, are a very strong risk factor for subsequent hip and vertebral fracture [11,43,44].

Irrespective of the methods used, opinions would differ concerning the inclusion or exclusion of different sites of fracture. The fracture sites that we excluded were ankle, hands and feet, including the digits, and skull and face and kneecap. These did not fulfil our inclusion criteria and incur less morbidity than fractures at many other sites. They have, therefore, a small impact on the weighting. We also excluded fractures of the tibia in men. The inclusion critiera were, however, defined in this study and permit other estimates to be made with different criteria using the same approach.

A further assumption is that all fractures at a particular site included are due to osteoporosis. This is clearly an oversimplificatioin. Assuming that we mistakenly excluded some fracture sites (e.g. fingers), this may be offset by our assumptions that all fractures at an included site are due to osteoporosis. An alternative approach is to quantify by expert opinion the proportion of fractures at each site as due to osteoporosis, an approach used in Switzerland [37] and the USA [45,46], but this is also arbitrary and based on as many assumptions.

Weighting of the Severity of Fracture

The consequences of osteoporotic fractures vary according to the type of fracture. Since hip fracture accounts for the highest morbidity, and hip fracture rates increase with age, morbidity is expected to rise with age. However, other osteoporotic fractures contribute to morbidity and their consideration becomes important in younger individuals. Thus the distribution of fracture type can be weighted according to the morbidity that arises for each fracture type. In this study we have weighted fracture severity according to the disutility associated with each fracture type using a weighting system developed for adjusting life years according to quality of life. Quality-adjusted life years (QALYs) are the accepted parameter in the health economic assessment of interventions [26]. In order to estimate QALYs each year of life is valued according to its utility that ranges from zero, the least desirable health state, to 1 or perfect health. The decrement in utility (disutility) associated with each fracture is the cumulative loss of utility over time. The disutility times the incidence of fracture provides the estimate of morbidity from different fractures in the community.

There are few estimates of disutility in the literature. The assumptions that we use are listed in Table 1 which, with the exception of rib fractures, were based on expert opinion derived by the National Osteoporosis Foundation of the USA [26]. They have the merit that all relevant fractures were assesed by the same methodology. It should be noted that the disutility value we used for hip fracture was 0.4681 in the first year as calculated from the data and not 0.6183 as published by the National Osteoporosis Foundation. Other utility estimates have used time trade-off methods on patients or population samples or tariff values estimated from EQ-5D for Colles' facture [47], vertebral fracture [48,49] and hip fracture [2,5,48,50,51]. They are cross-sectional and cannot be used to compute utility losses over a lifetime for the most severe fractures.

Estimates of disutility also vary according to the technique used. Some studies in the health economic field have shown similar preferences by patients or nonpatients; others suggest that systemic differences occur when health states are assessed differently. In the

case of osteoporosis, patients accord significantly less disability to hip or vertebral fracture than that given by individuals without fracture [48], which in turn has a marked impact on assessments of cost-effectiveness. For example, in the case of disabling hip fracture, the disutility in the first year has been estimated at 0.35 by patients and 0.72 by non fracture subjects. The estimate that we used in this paper lay between these estimates (0.4681 in the first year). In the case of vertebral fracture, our estimates give smaller disutility weights than those directly assessed from patients or nonfracture subjects [48], but this study focused on patients with multiple vertebral fractures. Our estimate of utility loss is consistent with cross-sectional studies in women witih prevalent vertebral fractures randomized to an intervention study [49]. In the case of Colles' fracture, the utility loss assessed by time trade-off from patients has been estimated at approximately 2% [47], whereas we have used an estimate of 4%. The difference arises largely from differences in the perceived duration of disability, and the technique used by Dolan [47] (EQ-5D) would not be sensitive to algodystrophy, which affects approximately 30% of individuals after Colles' fracture [52]. There appear to be less marked differences between techniques used to estimate utilities (e.g. time trade-off or rating scale methods [48]). In the case of the utility weights that we chose the appropriate consideration is not the absolute weight used, but whether the relationship of these weights between fracture sites varies according to the technique used. There are no data to clarify this point.

Disutilities were assumed in the long term to be attenuated by 10% per annum and adjusted for the utilities expected for age and sex. Discount rates of 3–6% are widely used for health costs. We used a higher utility discount rates for several reasons. First, there are few estimates of long-term utility losses for any of the osteoporotic fractures so that the higher discount is conservative. Second, utility loss associated with osteoporotic fractures is lower when scored by patients than by the general population [48], suggesting that in the long term, patients adapt with time in terms of their perceived quality of life. In practice, rates of 3%, 5% or 10% per annum had no effect on the treatment threshold scenarios (data not shown). Higher utility discount rates would imply that no patients would have residual morbidity from fractures for longer than 10–15 years (see Fig. 1). Thus, the higher discount rates would decrease the impact of osteoporosis in the younger age groups with the longer life expectancy. The overall effect is, however, small since the vast majority of fractures with significant long-lasting morbidity occur in later life.

Application

The effect of adjusting fracture probabilities with morbidity has the advantage of enfranchising all fractures considered to be osteoporotic using a common currency, namely hip frcture equivalents. As such, it simplies the manner in which treatment thresholds of risk might be selected. The weighting itself affects all ages, but has a proportionately greater effect in the younger age groups in whom hip fractures are rare but morbidity will persist for longer. The accommodation of all relevant fractures also enfranchises a younger population than if hip fracture alone were used to derive treatment thresholds. In the example we used, we assumed that intervention might be justified where the 10-year probability of hip fracture exceeded 10%. In the osteoporotic population men at the age of 70 years or more and women over the age of 65 would surpass a treatment threshold (see Table 6). The consideration of other fractures expressed in hip fracture equivalents suggests that all men and women with osteoporosis should be eligible.

The methodology can also be used to derive treatment thresholds in countries other than Sweden. In many countries the risk of hip fracture is known, as too is the risk of death. This permits an esitmate of the long-term probability of hip fracture [27]. In the absence of data on other osteoporotic fractures the ''excess morbidity'' can be used to adjust these probabilities for the morbidity expected from other osteoporotic fractures. The use of this approach for intervention thresholds would depend on the assumption that treatment affects fracture risk at all chosen sites to a comparable degree. As mentioned, it also assumes that the pattern of fractures with age and their morbidity is similar in different countries despite the large variation in absolute risk.

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