Danish Osteoporosis Outcome Model (DOOM)

Palle Mark Christensen[1], Kim Brixen[2] and Ivar Sønbø Kristiansen[3]

1. Research Unit of Clinical Pharmacology
University of Southern Denmark

2. Department of Endocrinology
Odense University Hospital

3. Research Unit of Health Economics
University of Southern Denmark

Health Economics Paper 2003:2

Foreword

Osteoporosis is a condition characterised by bone-loss, fragility of bones, and increased risk of bone fractures, in particular of the hips, forearm and spine. Osteoporosis is most often seen in postmenopausal women, but also in younger women and older men.

Osteoporosis is in itself asymptomatic, but the consequent fractures represent a considerable burden to patients, their relatives and to the health care system. During the first year of a hip fracture, the mortality risk is 5-10% up to 50% depending on age. In old people the prognosis of a hip fracture is just as serious as of a heart attack or a cancer. It should be noted however, that a considerable proportion of the excess mortality risk may be caused by underlying factors such as dementia or cancer, and the excess mortality will not be eliminated even if osteoporosis is successfully treated. In addition to the excess mortality, osteoporotic fractures may cause severe pain and loss of function. A considerable proportion of patients will therefore have their need for medical care permanently increased, and several will require nursing home care. Swedish and Norwegian cost estimates indicate that medical for care osteoporotic fractures represent 1-2% of total health care expenditure.

While osteoporosis is an important health policy issue, the burden of it does ***not*** imply that any intervention is justified. Rather, the use of resources to avoid or reduce osteoporosis may have alternative uses and may create more benefit elsewhere. The use of osteoporosis interventions should therefore undergo critical scrutiny of costs as well as benefits.

The Danish Osteoporosis Outcome Model (DOOM) was developed to explore an array of issues related to fractures. The first aim was to undertake economic evaluation of. It should be noted that DOOM only accounts for fractures and mortality, and it is therefore not useful for interventions with more health effects than reduced fracture risk. A model that accounts for other outcomes would need additional modelling, and this is beyond the scope of the current project. The second aim was to explore issues related to epidemiology and the concept of risk.

DOOM is one of the first, if not the first, model to account for the ***partial*** reversibility of the excess mortality after hip fracture. The model is described in detail in order to make it transparent for those interested. We hope the model will be useful for policy makers as well as scientists.

Ivar Sønbø Kristiansen
Associate professor
Institute of Public Health
Health Economics Research Unit
University of Southern Denmark

Introduction

Osteoporosis is a medical condition in which the bone mass is decreased leading to an increased risk of fractures, primarily of the hip, forearm and spine[1]. Sustaining any of these fractures will have a great negative impact on the quality of life[2]. In the last decade a number of interventions aiming at preventing or treating osteoporosis have emerged[3]. In order to justify allocating scarce health care resources to the field of osteoporosis it is essential to weigh the change in cost to the gain in health[4]. These types of considerations are analysed in cost-effectiveness and cost-utility analysis[4;5]. Model-based economic evaluation is crucial in the field of osteoporosis as an array of assumptions on and integration of economic, epidemiological and clinical data have to be made[5].

Aim

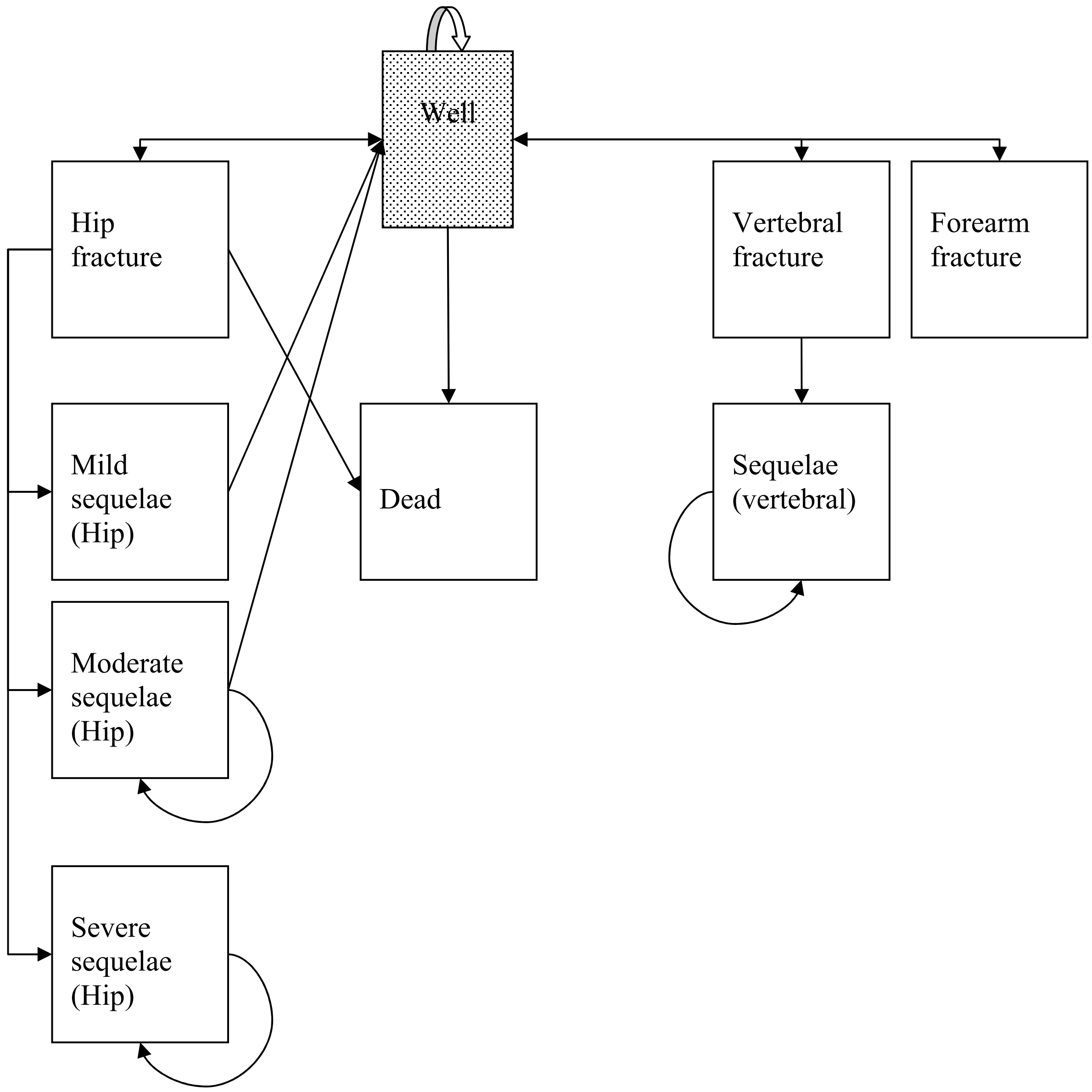
From a broad health-care sector perspective to estimate the cost-effectiveness (expressed in cost per quality adjusted life year gained, cost per life year gained, cost per hip fracture gained, cost per vertebral fracture gained, cost per forearm fracture gained) of an intervention that specifically and solely reduces the risk fractures in women.

General model

The model follows a cohort of 10,000 women from age 50 years until age 100. The model encompasses of 5 health states (figure 1). Sets of age-dependent transitions probabilities determine how simulated patients move from state to state. The transitions occur in 1-year cycles. These transitions are described in more detail in the following sections.

Throughout this paper "(#)" denotes that the model parameter can be varied at the discretion of the analyst.

Figure 1. Depiction of one cycle (first year) in the Markov state transition model.



Transitions in the Markov cohort simulation model

Starting in the “well” state a woman can experience a forearm fracture, a vertebral fracture or a hip fracture or remain “well” (unfractured). If a woman sustains a forearm fracture, she returns to the “well” state at the end of the cycle. If a woman sustains a vertebral fracture, she will either move to “sequelae vertebral” or “well” states at the end of the cycle. If a woman sustains a hip fracture, she will end up (i) “dead”; (ii) having “mild sequelae” and subsequently return to “well”; (iii) having “moderate sequelae hip” and then remain in this state or become “well”; or (iv) having “severe sequelae hip”. Women not sustaining a fracture can either remain “well” or “die”. In the next cycle a woman can begin in one of the following cycles: “well”; “sequelae vertebral”; “moderate sequelae hip” or “severe sequelae hip”. For those women who are “well” the possible transitions are those described above (i.e. fracture/not fracture etc.). Patients starting in a “sequelae” health state can either remain in this specific state or “die”.
We assumed that the fractures all occurred on January 1st each year whereas deaths occurred mid cycle.

Transition probabilities data

Annual mortality rates
We used age and sex specific mortality rates, for Denmark[6](#).

Hip fracture risks
We searched MEDLINE from 1980 through December 2002 using the MESH terms, “hip fractures”, and “incidence” and combined this with “Denmark” or “Sweden” or “Norway”, which resulted in 45 hits of which 9 were relevant. Other papers were identified by checking the reference lists of the identified studies. In total, we identified twenty-four studies describing the incidence of hip fractures in Scandinavia[7-30]. In this model the risk of sustaining a hip fracture was based on a

Norwegian study[7], because data seemed valid in that more than 99% of the identified fractures were verified by reviewing the corresponding medical records and the remainder by examining X-rays, thus the potential source of error by using electronic registers was not an issue (table 1) (#). Preliminary Danish data indicate that the incidence of hip fracture is in the same order of magnitude in Denmark[31].

Table 1. Annual sex and age-specific incidence of hip fractures in Norway, Oslo in 1996/97

Gender	**Age group**	**Population (01/0197)**	**Number of fractures**	**Annual incidence per 10,000**
Women	50-	15,107	8	5.3
	55-	10,502	12	11.4
	60-	9,335	15	16.1
	65-	10,373	42	40.5
	70-	11,810	91	77.1
	75-	11,721	167	142.5
	80-	8,987	254	282.6
	85-	5,489	261	475.5
	90-	2,670	165	618.0

Vertebral fracture risks

We searched MEDLINE from 1980 through December 2002 using the MESH terms, “Denmark” or “Sweden”or “Norway” and “spinal fractures” which resulted in 17 hits of which none were relevant. Beside this we undertook a free text search with “vertebral” and “fractures” combined with the MESH terms for the countries in Scandinavia, which resulted in 15 hits, but none of these hits were relevant, either. We also searched the reference list of some of the papers reporting prevalence data. We identified one register study describing the incidence of vertebral fractures in Scandinavia[32]. We believe, however, that incidence data based on registers may be biased. The only study we have been able to identify in which incident clinical diagnosed fractures were the endpoint was a U.S.-population-based study[33]. We chose to use data from this study in our model (table 2) (#).

Table 2. Annual sex and age-specific incidence of clinically diagnosed vertebral compression fractures among Rcochester, MN, US residents, 1985-1989

Gender	**Age group**	**Population (n=238)***	**Number of fractures after moderate trauma**	**Annual incidence per 100,000**
Women	45-54	mangler noe her???	7	44
	55-64		30	241
	65-74		58	536
	75-84		85	975
	85+		50	1167

*50 of those 238 were asymptomatic (26%).

Forearm fracture risks

We searched MEDLINE from 1980 through December 2002 using the MESH terms, "Colles'-fracture" combined with "Denmark" or "Sweden" or "Norway", which resulted in 12 hits of which 3 were relevant. Beside this we undertook a free text search using "forearm" and "fractures" combined with MESH terms for the three countries in Scandinavia, which resulted in 10 hits of which 2 were not identified by the first search history 10. Other papers were identified through the reference lists of the identified papers. In total, we identified 7 studies describing the incidence of forearm fractures in Scandinavia[34-40]. We chose to use data from Solgaard et al. as this was based on Danish patients[39] (table 3) (#).

Table 3. Annual sex and age-specific incidence of distal radius fracture in the county of Frederiksborg, Denmark 1981.

Gender	**Age group**	**Population at risk in thousands**	**Number of fractures after moderate trauma**	**Annual incidence per 10,000**
Women	50-	15	77	50
	60-	12	101	81
	70-	8.2	95	115
	80-	3.5	47	133
	90-	0.74	5	68

Post-fracture probabilities

We have not been able to identify any studies concerning the long-term (1 year and beyond) effects after sustaining a forearm fracture in Scandinavia. We searched

MEDLINE from 1980 through December 2002 combing the MESH terms, "Colles'-fracture-complications" and "Denmark" or "Sweden", or "Norway", which gave no hits. We also undertook a free text search on "forearm" and "fractures" combined with "functional outcome" combined with the MESH terms for the three countries in Scandinavia, which also produced no hits. We ended up assuming that after sustaining a forearm fracture all (100%) women ended up well(#).

We have not been able to identify any studies concerning the long-term (1 year and beyond) effects after sustaining a vertebral fracture in Scandinavia. We searched MEDLINE from 1980 through December 2002 using the MESH terms, "Denmark" or "Sweden" or "Norway" in combination with "spinal fractures" which resulted in 2 hits, but none of these hits were relevant, either. We also undertook a free text search using "vertebral" and "fractures" and "functional outcome" combined with the MESH terms for the three countries in Scandinavia, which resulted in 0 hits. We ended up assuming that after sustaining a vertebral fracture 25%(#) would have sequelae and the rest would end up being well after one year. This assumption was based on a study by Chrischilles et al. [41] in which the authors have been told ("personal communication") that 25% of the incident clinically diagnosed vertebral fractures were admitted to hospital.

To identify studies on the mortality in the year after a hip fracture we searched MEDLINE from 1980 through December 2002 using the MESH terms, "hip fractures-mortality" or "femoral neck fractures-mortality", in combination with "Denmark" or "Sweden" or "Norway", which resulted in 26 hits of which 6 were relevant. We also undertook a free text search using the terms "hip fracture" and "mortality" combined with the MESH terms for the three countries in Scandinavia, which resulted in 21 hits of which 2 were not identified in the first search strategy. We also checked the reference lists of the identified studies for further studies. In total, this search strategy resulted in 8 studies on the mortality in the year after sustaining a hip fracture in Scandinavia fracture[17;42-48]. We chose to use the study which was based on Danish data, in which it was found that the mortality in the year after the hip fracture varied from 10-30%(#) depending on age [46].

The studies describing the probabilities of hip fracture outcome were found by searching MEDLINE from 1980 through December 2002 using the MESH terms, “hip fractures-complications” or “femoral neck fracture-complications” in combination with “Denmark” or “Sweden” or “Norway”, which resulted in 12 hits of which 1 were relevant. We also undertook a free text search using the terms “hip fracture” and “complications” and “functional outcome” combined with the MESH terms for the three countries in Scandinavia, which resulted in one more paper that was not found by the first search strategy. The rest of the papers were identified by checking the reference lists of the identified studies. In total, this search strategy resulted in 7 different Danish/Scandinavian publications[49-55]. Finsen et al[51] found that, one year after the fracture, 30% of the patients needed no aids, 48% needed either one or two sticks or a walking frame, while 21% were bedridden. These percentages changed very little during the next two years of follow up. In a resent Swedish study[53] 12% of those living independently before the hip fracture ended up in institutions and 71% needed no walking before the fracture compared to 34% after the fracture and finally 59% needed household help after the fracture compared to 38% before the fracture. Jensen et al[49] found that 8% were discharged permanently to nursing home among 383 Danish patients admitted from their own home to hospital for hip fracture. In another Danish study[52] of 180 patients admitted to hospital from their own home 5% were discharged to a nursing home. We assumed that 30%(#) ended up in “mild sequelae hip”, 60%(#) ended up in “moderate sequelae hip” and 10%(#) ended up in “server sequelae hip” in the basic estimates. Of those with “mild sequelae hip” 100%(#) were well at the end of the cycle (assumption without any empirical data). Of those “moderate sequelae hip” we assumed that 50%(#) ended up being “well” and the rest remained “moderate sequelae hip”. Of those “sever sequelae hip” we assumed that all remained in this health state.

For those starting the next cycle in a sequelae health state it was assumed that their mortality was increased by 25%(#) compared to the background mortality (assumption without any empirical data).

Table 4 summarises the transitions in the Markov model and the sources used for the transitions probabilities.

Table 4 Transitions in Markov cohort simulation and source of transitions probabilities

Transitions from	**Transition to**	**Source of transition probabilities**
Well	Forearm fracture	Falch et al[56]
Well	Vertebral fracture	Cooper et al[33]
Well	Hip fracture	Lofthus et al[7]
Well	Dead	Statistics Demark[6]
Well	Well	
Forearm fracture	Well (forearm fracture)	Expert judgement
Vertebral fracture	Well (vertebral fracture)	Expert judgement
Vertebral fracture	Sequelae vertebral	Expert judgement
Hip fracture	Dead (hip fracture)	Eiskjaer et al[46]
Hip fracture	Mild sequelae hip	Finsen et al[51] and Jensen et al[50]
Hip fracture	Moderate sequelae hip	Finsen et al[51] and Jensen et al[50]
Hip fracture	Server sequelae hip	Finsen et al[51] and Jensen et al[50]
Mild sequelae hip	Well (mild hip)	Expert judgement
Moderate sequelae hip	Well (moderate hip)	Expert judgement
Moderate sequelae hip	Moderate sequelae hip	Expert judgement
Server seuelae hip	Server sequelae hip	Expert judgement
	Second year	
Sequelae vertebral	Dead	Expert judgement
Sequelae vertebral	Sequelae vertebral	Expert judgement
Moderate sequelae hip	Dead	Expert judgement
Moderate sequelae hip	Moderate sequelae hip	Expert judgement
Server sequelae hip	Dead	Expert judgement
Server sequelae hip	Server sequelae hip	Expert judgement

Intervention

The model allows simulating the consequences of a fracture-specific intervention. The model is designed to simulate any intervention, pharmaceutical and non-pharmaceutical, that influences the risk of hip, vertebral and/or forearm fracture. Since the model does not encompass malignant diseases or cardiovascular diseases, it is inappropriate for model hormone replacement therapy.. The intervention can be initiated at any age between 50 and 100 years and any length of time up til the age of 100. The effect of the intervention can be assumed to stop directly upon discontinuation of the intervention or vane gradually over a specified number of years. The compliance to the intervention can be varied from 0% to a 100% per year.

The risk of fracture in the intervention group compared to the background population can be varied from zero to infinitive. The risk of fracture in the intervention group compared to the background population can be expressed in terms of bone mineral density (BMD). BMD is measured in terms of *t*-scores and *z*-scores. A *t*-score indicates how many standard deviations the BMD differs from the mean BMD of a young individual. A *z*-score indicates how many standard deviations the BMD differs from the age specific mean BMD, e.g. a *z*-score of -3 indicates that the BMD was three standard deviations below the age specific mean BMD. A study group working for WHO suggested that osteoporosis should be defined based on BMD and that osteoporosis is present when the *t*-score is below -2.5[57]. This definition of osteoporosis has been has been used in almost all studies using pharmaceuticals as the intervention. Thus, when modelling an intervention in our model the risk in the intervention group can be converted into a BMD value. The association between fracture risk and BMD has been analysed in meta-analysis that indicate that the risk of all types of fracture (forearm, hip, spine) increase by a factor of 1.5 (relative risk 1.5) for each standard deviation decrease in BMD[58]. In a later study by Scott et al. the relative risk 1.9 for each standard deviation decrease in BMD [59]. We choose to use the estimate(#) presented by Scott, as this was based on a European population. An intervention used for a 71-year-old woman who has twice the risk of sustaining a fracture compared to the background risk may illustrate how z and *t*-scores works. This woman will have a z-score of -1.1 (ln(2)/ln(1.9)) which is approximately equivalent to a *t*-score of -2.9 in femur [60]. In line with this we also assumed that each standard deviation decrease in BMD was associated with a 1.19(#) increase in mortality [61]. Finally we assumed that only

14%(#) of the deaths following a hip fracture were caused by or hastened by the hip fracture [62] and thus preventable by intervention.

Health related quality of life data.

We searched MEDLINE from 1980 through December 2002 using the MESH terms, “osteoporosis” and “quality-adjusted-life-years”, which resulted in 11 hits of which only one was relevant. We also undertook a free text search using the terms “osteoporosis” and “utility”, which resulted in 179 hits of which 3 hits were relevant and not found by the first search strategy. Other papers were identified by checking the reference lists of the identified studies. Thus in total, we identified seven published papers[2;53;63-65] on HRQOL values, for one or more of the osteoporosis related conditions (established osteoporosis, hip, vertebral and forearm fracture). All HRQOL values were based on generic preference based instruments. Based on a systematic review a set of “multipliers” for the proportionate effect of fracture on HRQOL in first year after a fracture have been published[2] (table 5).

Table 5. Reference set of health state values for osteoporotic fractures.

Health state	Value (95% confidence interval)	Source
Hip fracture	0.797 (0.651-1.012)	Brazier et al[2]
Vertebral fracture	0.909 (0.84-0.97)	Oleksik et al[64]
Forearm fracture	0.981 (0.978-0.986)	Dolan et al[65]

We chose to use the estimates presented in table 5 in our model.

These “multipliers” should then be applied to sex and age- HRQOL values of patients without a fracture. We used Danish data(#) for the general population[66] as norms for pre-fracture HRQOL (table 3). These values have been used in the model accounting for the fact that patients’ health states are somewhat reduced due to age even before the fracture (table 6).

Table 6. Danish population norms for health state values.

Age	Health state value			
	EQ-5D		15D	
	Score	Number of persons interviewed	Score	Number of persons interviewed
45-49	0.9086	157	0.9249	159
50-54	0.8753	154	0.9170	153
55-59	0.8830	144	0.9199	144
60-64	0.8600	127	0.8992	122
65-69	0.8605	121	0.8882	111
70-74	0.8625	80	0.8939	72
75-79	0.8219	80	0.8630	65
80-84	0.8055	30	0.8529	17
85+	0.6961	18	0.8339	13

It has been found that the utility scores are higher for 15D than EQ-5D[67], which also is confirmed by the Danish data. We chose to use the estimates produced by 15D(#).

Using the above mentioned literature search strategy no empirical data describing the health state values for the subsequent years after a fracture have been published. In previous economic models[2] it has been assumed that vertebral and hip fractures have half the impact in the following years, whereas a forearm fracture has no impact beyond the first year. We used the same assumption and thus used a value of 0.9 for hip fracture (moderate) and 0.85 for a hip fracture (severe) and a value of 0.955 for a vertebral fracture.

Costs data

As a large proportion of the target population in this study will be retired from the labour force and productivity losses incurred are negligible, indirect costs are not included. However, in the sensitivity analysis the effect of including indirect cost can be analysed. All costs are expressed in 2002 Danish kroner (DKK)(1 Euro = 7.5 DKK).

Cost of intervention

As the model can simulate the consequences of a fracture-specific intervention (e.g. pharmaceutical drugs, lifestyle) the costs will depend on the intervention chosen. In general it is a matter of identifying the cost components, quantifying them and then valuing them in monetary terms.

Costs of hip fractures

First year

In order to find studies on costs of hip fractures we searched MEDLINE from 1980 through December 2002 using the MESH terms, "hip fractures-economics" and, "health-care-costs" combined with "Denmark"or "Sweden"or"Norway", which resulted in 13 hits of which 2 were relevant. We also undertook a free text search using the terms "cost" and "hip fracture" which resulted in 9 hits without adding any new papers compared to the first search strategy. The rest of the papers were identified by checking the reference lists of the identified studies. Thus in total, we found two studies from Scandinavia, in which the patient was used as his or her own control [68;69]. Beside the two Scandinavian studies we are aware of, two other studies used this type of design[70;71]. This design accounts for the crucial fact that hip fracture patients tend to be frail and would probably consume a substantial amount of health care resources and other services even without the fracture. We chose to use empirical costs estimates from a Swedish study [69](#). This study compares the direct costs during the year before the fracture with the direct costs during the year after the fracture. For women in different age group surviving the first year the extracted costs estimates can be seen in table 7.

Table 7 Annual cost of hip fracture in the first year [69]

Age	Costs in 1994 in Swedish kroner	Costs in 1994 in Danish kroner	Inflation rate since 1994		Adjusted for inflation
50	107,000	87,740	1994	2	107,346
51	110,000	90,200	1995	2.1	110,356
52	112,000	91,840	1996	2.1	112,362

53	116,000	95,120	1997	2.2	116,375
54	120,000	98,400	1998	1.8	120,388
55	125,000	102,500	1999	2.5	125,405
56	128,000	104,960	2000	2.9	128,414
57	131,000	107,420	2001	2.4	131,424
58	134,000	109,880	2002	2.4	134,434
59	137,000	112,340			137,443
60	139,000	113,980			139,450
61	141,000	115,620			141,456
62	143,000	117,260			143,463
63	145,000	118,900			145,469
64	148,000	121,360			148,479
65	150,000	123,000			150,485
66	152,000	124,640			152,492
67	154,000	126,280			154,498
68	156,000	127,920			156,505
69	158,000	129,560			158,511
70	162,000	132,840			162,524
71	168,000	137,760			168,544
72	175,000	143,500			175,566
73	179,000	146,780			179,579
74	183,000	150,060			183,592
75	187,000	153,340			187,605
76	190,000	155,800			190,615
77	193,000	158,260			193,625
78	196,000	160,720			196,634
79	200,000	164,000			200,647
80	206,000	168,920			206,667
81	212,000	173,840			212,686
82	218,000	178,760			218,706
83	225,000	184,500			225,728
84	231,000	189,420			231,748
85	237,000	194,340			237,767
86	241,000	197,620			241,780
87	245,000	200,900			245,793
88	250,000	205,000			250,809
89	262,000	214,840			262,848
90	268,000	219,760			268,867
91	275,000	225,500			275,890
92	281,000	230,420			281,909
93	287,000	235,340			287,929
94	293,000	240,260			293,948
95	300,000	246,000			300,971
96	312,000	255,840			313,010
97	318,000	260,760			319,029
98	325,000	266,500			326,052
99	337,000	276,340			338,091
100	346,000	283,720			347,120

Subsequent years

By using the same literature search strategy as mentioned above no studies using patients as their own controls were identified. Therefore the cost estimates mentioned below are based on a combination of empirical data and clinical judgement.

For those ending up with severe sequelae after a hip fracture we assumed that they all ended up in a nursing home. The costs of a stay in a nursing home in Denmark have been reported to vary from DKK 890 to 1,380 per day[72;73]. We chose to use a cost of DKK 1,000 per day(#). Thus, the total average costs the following years for those ending with severe sequelae after a hip fracture was 365,000 DKK (table 8).

Table 8. Annual cost estimates in the subsequent years for a woman ending up having server sequelae after a hip fracture.

Type of cost	Unit cost	Quantity of units consumed per year	Proportion consuming this unit	Total average costs in the subsequent years
Nursing home	365,000 DKK/year	1	100%	365,000 DKK
			total	***365,500 DKK***

For those having moderate sequelae after a hip fracture we assumed that they all had two visits to a GP per year (assumption without any empirical data) at a cost of DKK 103[74] each time. We also assumed that 20%(#) (assumption without any empirical data) will have a series of 12(#) treatments (assumption without any empirical data) at a physiotherapist at a total cost of DKK 2,539.20 and 10%(#) (assumption without any empirical data) need qualified home service. A Danish study[75] reported that after 6 month observation the number of visits of qualified home service raised from 12 before the hip fracture to 22 per month. We assumed that in the following years there was18(#) visits per month, thus an increase of 6 visits per months (assumption without any empirical data).We also assumed that on average each visit lasted for 30 minutes(#) (direct contact between patient and quailed home service). The marginal cost per hour for a qualified home service assuming 30 minutes of direct contact to the patient has been estimated to be DKK 236[75]. Thus, the costs per year for qualified home service are DKK 16,992. We also assumed that 75%[76](#) used painkillers (acetaminophen 1g twice a day) at a yearly cost of DKK 438.

Thus, the total average costs for those having moderate sequelae after a hip fracture the costs the following years was DKK 2742.08 (table 9), which was used in the base case of the model.

Table 9. Annual cost estimates in the subsequent years for a woman ending up having moderate sequelae after a hip fracture.

Type of cost	Unit cost	Quantity of units consumed per year	Proportion consuming this unit	Total average costs in the subsequent years
GP visit	103.09 DKK/per visit	2	100%	206 DKK
Physiotherapy	211.6 DKK/visit	12	20%	508 DKK
Qualified home service	236 DKK/hours	72	10%	1,699 DKK
Pain killers	438.48 DKK/year	1	75%	329 DKK
			total	***2,742 DKK***

Costs of forearm fractures

In order to find studies on costs of forearm fractures we searched MEDLINE from 1980 through December 2002 using the MESH terms, "Colles'-fracture-economics" combined with "Denmark" or "Sweden" or "Norway", which resulted in 2 hits, of which none were relevant. Beside this we undertook a free text search using the terms "forearm" and "fracture" and "cost" combined with MESH terms for the three countries in Scandinavia, which did not result in any hits. We also searched the reference lists of relevant papers. Thus, we did not identify any studies using patients as their own controls in Scandinavia. In lack of this type of studies we chose first to present costs estimates of a forearm fracture which we believe are realistic based on a combination of empirical data and clinical judgements and then at the end present data from the few empirical studies that have been published.

We assumed that all patients will be transported on average 10 km (#) (assumption without any empirical data) to hospital by private car or taxi to the emergency room at an average cost of DKK130[77]

A study performed in USA[41] found that 10% of patients with a distal forearm fracture needs further hospitalisation (assumption without any empirical data), a Norwegian study[78] assumed 15% (assumption without any empirical data) and a Danish study[79] assumed 25% (assumption without any empirical data). We ended up choosing 15%(#).

In the group admitted to hospital we assumed that 90%(#) (assumption without any empirical data) had uncomplicated surgery at a cost of DKK 10,918[80] (DRG 0826: operationer på hånd og handled, ekskl. større led u. kompl. bidiag) and 10%(#) (assumption without any empirical data) had complicated surgery at a cost of DKK 22,242[80] (DRG 0824: operationer på hånd og handled, ekskl. større led m. kompl. bidiag.) The distribution of complicated surgery versus non-complicated was calculated using the number of discharges for each DRG code[81], i.e. 2775/3090 (90%) vs. 315/3090 (10%).

Among those 85% who did not need surgery we used data from a Danish study[82] which found that 70%(#) had displacement and the others not. Among those with displacement we assumed that they needed reposition at a cost of DKK 1,337[80] (outpatient clinic visit) and closed reduction and plaster cast immobilization at a cost of DKK 3,740[80] (PG02D: indlæggelse af skinne el. Bandage, arthrocentese el. lukket reposition). Among those 30%(#) with no displacement we assumed that they had one visit to the emergency department including an X-ray at a cost of DKK 1,784[80] (Outpatient visit: DKK=1,337+ DKK 447 (PG014A: alm. Røntgenundersøgelse, inkl.mammografi)). We also assumed that 30%[76](#) visited their GP at a cost of DKK 103.09[74] for plaster check and prescription of painkillers acetaminophen 1g twice a day at a yearly cost of DKK 438.48 We assumed that all(#) (assumption without any empirical data) patients had a check up at the outpatient clinic including an X-ray at a cost of DKK 1,784[80] (Outpatient visit: DKK=1,337+ DKK 447 (PG014A: alm. Røntgenundersøgelse, inkl.mammografi)).

We also assumed that 30%(#) (assumption without any empirical data) were referred to a series of 5 treatments at a physiotherapist at a total cost of DKK 1,058[83].

In total, the average costs for treating a forearm fracture is DKK 7,645 (table 10).

Table 10. Annual cost estimates for a woman ending up having a forearm fracture.

Type of cost	Unit cost	Quantity of units consumed per year	Proportion consuming this unit	Total average costs in the following year
Transport	130 DKK/10 KM	1	100%	130 DKK
Emergency room (no displacement)	1784 DKK/visit	1	25%	455 DKK
Emergency room (displacement)	5077 DKK/visit	1	60%	3,046 DKK
Hospitalisation (uncomplicated surgery)	10,918 DKK/procedure	1	14%	1,528 DKK
Hospitalisation (complicated surgery)	22,242 DKK/procedure	1	1%	222 DKK
GP visit	103.09/visit	1	30%	31 DKK
Pain killers	438.48 DKK/year	1	30%	132 DKK
Outpatient check-up	1784 DKK/visit	1	100%	1,784 DKK
Physiotherapy	211.6 DKK/visit	5	30%	317 DKK
			total	***7,645 DKK***

This is roughly in accordance with a Norwegian study by Andersen et al[78]and a Danish study by Ankjær et al[79] which found the averages costs of a forearm fracture to be NOK 4,639 and DKK 7,188, respectively. However, all of these estimates have weak empirical basis. A Swedish study, based on empirical data found that the direct costs were SEK 19,362, the indirect costs to 3,312, thus in total SEK 22,674. This is considerably higher then the studies based primarily on guesstimates (including the costs which we calculated above). The study by Zethraeus et al[76] is preliminary in the sense that data have not been published in an international peer reviewed journal, the study had a relatively small sample size (n=50), a relatively low participation rate (42%), their was no information about the consumption of health care resources and other services in the year before the fracture. As a compromise between the non-empirical data and the empirical study we ended up choosing a mean cost of DKK15,000(#) where DKK 2,000(#) was indirect costs and DKK 13,000(#) where direct costs.

Cost of vertebral fractures

First year

In order to find studies on the costs of vertebral fractures We have not been able to identify any studies using patients as there own control in Scandinavia we searched MEDLINE from 1980 through December 2002 using the MESH terms, "Denmark", "Sweden", "Norway", "spinal fractures-economics" which resulted in 0 hits. Beside we undertook a free text search using the terms "vertebral" and "fracture" and "cost" combined with the MESH terms for the countries in Scandinavia, which resulted in 1 hit, which was not relevant. In lack of this type of studies we chose first to present costs of vertebral fracture, which we believe are realistic based on a combination of empirical data and clinical judgements and then at the end present data from the few empirical studies that have been published.

All(#) of these patients will have a GP visit at a cost of DKK 103.09[74] and an X-ray at a cost of DKK 1,784[80]((Outpatient visit: DKK=1,337+ DKK 447 (PG014A: alm. Røntgenundersøgelse, inkl.mammografi)). An American study assumed based on a personal communication that 25% of these incident fractures were admitted to hospital[41]. We chose to use the same distribution in our model. The costs of hospital care are DKK 11,710 (DRG 0843: symptomer fra muskel-skeletsystemet og bindevæv). All(#) these patients have an outpatient clinic follow up at a cost of DKK 1,137[80] and an X-ray at a cost of DKK 447[80](PG014A: alm. Røntgenundersøgelse, inkl.mammografi). 75%[76](#) used painkillers (acetaminophen 1gram twice a day) at a yearly cost of 438.48. Beside this we assumed that they will all(#) have a series of 12 treatments (assumption without any empirical data) at a physiotherapist at a total cost of DKK 2,539.20[83]. As mentioned earlier we assumed that this group represents those that are ending up in the health state chronic after vertebral fracture.

Among those 75%(#) (assumption without any empirical data) not admitted to hospital we assumed they had a series of 12 treatments (assumption without any empirical data) at a physiotherapist at a cost of DKK 2,539.20[83] and 100%(#) used painkillers at a yearly cost of 438.48. As mentioned earlier we assumed that this group represents those that are ending up in the health state well after vertebral fracture. Thus, the total average costs the first year after a vertebral fracture is DKK 6,901 (table 11).

Table 11 Annual cost estimates for a woman ending up having a vertebral fracture (first year)

Type of cost	Unit cost	Quantity of units consumed per year	Proportion consuming this unit	Total average costs in the following year
GP visit	103.09/visit	1	100%	103 DKK
X-ray+outpatient	1784 DKK/X-ray	1	100%	1784 DKK
Hospitalisation	11,710 DKK/procedure	1	25%	2,928 DKK
Outpatient check-up	1784 DKK/visit	1	25%	446 DKK
Pain killers	438.48 DKK/year	1	100%	438 DKK
Physiotherapy	211.6 DKK/visit	12	100%	2,539 DKK
			total	***8,238 DKK***

These costs are fairly comparable with a Danish study by Ankjær et al. [79] which found that the averages costs for a vertebral fracture to be DKK 3,790. A Norwegian study by Andersen et al[78] concluded that the average costs for a vertebral fracture to be NOK 24,784. However all of these estimates are weakly empirical based. A Swedish study by Zethraeus[76] from 2002 (prices were from year 2000) based on empirical data, estimated the direct costs to be SEK 30,470, the indirect costs to be 31,050, thus in total SEK 61,520 . This is considerably higher then the results based primarily on guesstimates (including the costs which we calculated above). The study by Zethraeus et al[76] is preliminary in the sense that data have not been published in an international peer reviewed journal, the study had a relatively small sample size (n=50), a relatively low participation rate (42%), their was no information about the consumption of health care resources and other services in the year before the fracture. As a compromise between the non-empirical data and the empirical study we ended choosing a mean cost of DKK40,000(#) where DKK 20,000(#) was indirect costs and DKK 20,000(#) was direct costs.

Subsequent years

Using the same search strategy as mentioned above, we have not been able to identify any studies using patients as their own controls in Scandinavia We therefore first present cost estimates that we believe are realistic based on a combination of empirical data and clinical judgement and at the end present published studies based on empirical data.

We assumed that it is only those patients who are chronically disabled that incur costs in subsequent years(#). We assumed two(#) yearly visits to the GP (assumption without any empirical data) at a cost of DKK 103.09[74] per visit as well as a series of 6 treatments (assumption without any empirical data) at a physiotherapist at a total cost of DKK 1, 269[83] All (100%)(#) used painkillers (acetaminophen 1 gram twice a day) at a cost of DKK 438.48 per year.

Thus the total average costs the following years for those ending up having sequelae after a vertebral fracture is DKK 1,913.66 (table 12).

We have not been able to identify any empirical studies on the costs of vertebral fractures in the years beyond the first year.

Table 12. Annual costs estimates for the subsequent years in women ending up having sequelae after a vertebral fracture

Type of cost	Unit cost	Quantity of units consumed per year	Proportion consuming this unit	Total average costs in the subsequent years
GP visit	103.09/visit	2	100%	206 DKK
Pain killers	438.48 DKK/year	1	100%	438 DKK
Physiotherapy	211.6 DKK/visit	6	100%	1,270 DKK
			total	***1,914 DKK***

We therefore chose to use DKK1,914 as the average cost for the following years after a vertebral fracture.

Programming the model

The model was developed in Microsoft Excel. The total number of fractures was estimated by multiplying the incidences of fractures by the number of women entering the cycle each year. However, this number of fractures is distributed across too many patients, as our model does not account for the fact that having sustained one fracture increases the risk of sustaining a new fracture[84]

The yearly number of fatal outcomes was calculated by multiplying the age and sex specific deaths rates by the number of women entering the cycle each year. This total number is equivalent to the number of summary of deaths after hip fractures, deaths from permanently disabled, and deaths among non-fractured. The model does not allow for an individual to have more that one fracture per cycle.

Sensitivity analysis

The model allows for one- two- and three-way sensitivity analysis.

Discounting

The model allows for discounting both effect and costs. The discounting rate is flexible.

Output from the model

The model estimates the cost per life year gained, the cost per QALY gained; the cost per avoided hip fracture, the cost per avoided vertebral fracture; the cost per avoided forearm fracture.

Validating the model

The model will be validated according to "Principles of good practice for decision analytic modelling in health-care evaluation" published by Weinstein and colleagues:

Internal validity:

1. Thorough internal testing and "debugging": when using for example a drug called alendronate and assuming a risk reduction of 0.77 for three years in 71-year-old women the strategy was dominant but when assuming a risk reduction of 0.01 the cost per QALY gained was DKK 36,000,000.00

Between model validation:

1. Convergent validity will be very much appreciated however we have not actively contacted other modellers
2. The structure and assumptions made in other models make direct comparisons very difficult[5;85] .

3. Cross validity will be very much appreciated, however we have not actively contacted other modellers.

External and predictive validation

1. We have tried to base our model on the best available evidence for example by providing information about our literature search strategy.
2. The predictive validity of our model was assessed in terms of its ability to estimate life expectancy. To predict life expectancy 1 year mortality rates for Danish and 5 year Norwegian and Swedish mortality rates were entered and model based estimates of life expectancies for 50-, 60-, 70-, and 80-year-old women were compared with published sources[86;87] .

Table 13. Published and modelled life expectancies for Denmark and Norway

Start age (years)	Life expectancy (years)					
	Denmark			Norway		
	published (years)	modelled (years)	difference (%)	published (years)	modelled (years)	difference (%)
50	30.88	30.86	0.06	32.93	32.26	2.03
60	22.21	22.18	0.14	23.96	23.28	2.83
70	14.66	14.63	0.20	15.64	14.93	4.54
80	8.54	8.50	0.47	8.64	7.82	9.50

Table 14. Published and modelled life expectancies for Sweden

Start age (years)	Life expectancy (years)		
	Sweden		
	published (years)	modelled (years)	difference (%)
50	33.37	32.94	1.29
65	20.01	19.57	2.20

The reason for the increase in difference between the modelled and the published life expectancy with increasing age might be that the published life expectancies in Norway and Sweden are based on one-year mortality rates but we have only been able to get access to 5 year mortality rates. Norwegian health statistics even had collapsed all mortality rates over the age of 80 years to one estimate which might explain the difference of 9.5% in this age group (table 13). To explore this further we used Danish one-year mortality rates and found very little difference in modelled and published life expectancy. Other modellers[88] also found an increasing difference in published and modelled life expectancies with increasing age.

Discussion

This model is based on numerous assumptions. Firstly, we assumed that a patient could only sustain one fracture in one year. This is not realistic. The risk of having a new fracture is increased when a patient has sustained one already. If we should have included this in the model the number of health states would increase dramatically and making the model unnecessary complex. Our model overestimates the total number of individuals that sustain a fracture and underestimates the number of fractures in each individual. Theoretically, this will tend to make the cost-effective and cost-utility ratio lower. The reason is, that an individual already having sustained a fracture does not marginally loose as much quality of life and is not as costly compared to a healthy person sustaining a fracture.

When compared to other models ours is unique on two main aspects Firstly, it allows simulations of the extent to which an intervention reverses the excess mortality attributed to hip fractures. To our knowledge this has not been part of any of the previously published models in this field. Secondly, the health state values we used are based on empirical studies and the tariffs we used for the Danish population were also based on a large-scale population based study.

Reference List

1. Primer on the metabolic bone deseases and disorders of mineral metabolism. Lippincott Williams & Wilkins, 1999.

2. Brazier JE, Green C, Kanis JA. A systematic review of health state utility values for osteoporosis-related conditions. *Osteoporos.Int.* 2002;**13**:768-76.

3. Eastell R. Treatment of postmenopausal osteoporosis. *N.Engl.J.Med.* 1998;**338**:736-46.

4. Kanis JA,.Jonsson B. Economic evaluation of interventions for osteoporosis. *Osteoporos.Int.* 2002; **13**:765-7.

5. Zethraeus N, Ben Sedrine W, Caulin F, Corcaud S, Gathon HJ, Haim M *et al*. Models for assessing the cost-effectiveness of the treatment and prevention of osteoporosis. *Osteoporos.Int.* 2002;**13**:841-57.

6. Statistisk Årbog 2001 (www.dst.dk/dst/665). 2003.
Ref Type: Internet Communication

7. Lofthus CM, Osnes EK, Falch JA, Kaastad TS, Kristiansen IS, Nordsletten L *et al*. Epidemiology of hip fractures in Oslo, Norway. *Bone* 2001;**29**:413-8.

8. Cumming RG, Nevitt MC, Cummings SR. Epidemiology of hip fractures. *Epidemiol.Rev.* 1997;**19**:244-57.

9. Falch JA, Aho H, Berglund K, Duppe H, Finsen V, Hagstrom I *et al*. Hip fractures in Nordic cities: difference in incidence. *Ann.Chir Gynaecol.* 1995;**84**:286-90.

10. Baudoin C, Fardellone P, Potard V, Sebert JL. Fractures of the proximal femur in Picardy, France, in 1987. *Osteoporos.Int.* 1993;**3**:43-9.

11. Falch JA, Kaastad TS, Bohler G, Espeland J, Sundsvold OJ. Secular increase and geographical differences in hip fracture incidence in Norway. *Bone* 1993;**14**:643-5.

12. Falch JA, Ilebekk A, Slungaard U. Epidemiology of hip fractures in Norway. *Acta Orthop.Scand.* 1985;**56**:12-6.

13. Rogmark C, Sernbo I, Johnell O, Nilsson JA. Incidence of hip fractures in Malmo, Sweden, 1992-1995. A trend-break. *Acta Orthop.Scand.* 1999;**70**:19-22.

14. Gullberg B, Duppe H, Nilsson B, Redlund-Johnell I, Sernbo I, Obrant K *et al*. Incidence of hip fractures in Malmo, Sweden (1950-1991). *Bone* 1993;**14 Suppl 1**:S23-S29.

15. Johnell O, Gullberg B, Allander E, Kanis JA. The apparent incidence of hip fracture in Europe: a study of national register sources. MEDOS Study Group. *Osteoporos.Int.* 1992;**2**:298-302.

16. Mannius S, Mellstrom D, Oden A, Rundgren A, Zetterberg C. Incidence of hip fracture in western Sweden 1974-1982. Comparison of rural and urban populations. *Acta Orthop.Scand.* 1987;**58**:38-42.

17. Kreutzfeldt J, Haim M, Bach E. Hip fracture among the elderly in a mixed urban and rural population. *Age Ageing* 1984;**13**:111-9.

18. Zain-Elabdien BS, Olerud S, Karlstrom G, Smedby B. Rising incidence of hip fracture in Uppsala, 1965-1980. *Acta Orthop.Scand.* 1984;**55**:284-9.

19. Johnell O, Nilsson B, Obrant K, Sernbo I. Age and sex patterns of hip fracture--changes in 30 years. *Acta Orthop.Scand.* 1984;**55**:290-2.

20. Zetterberg C, Elmerson S, Andersson GB. Epidemiology of hip fractures in Goteborg, Sweden, 1940-1983. *Clin Orthop.* 1984;43-52.

21. Swanson AJ,.Murdoch G. Fractured neck of femur. Pattern of incidence and implications. *Acta Orthop.Scand.* 1983;**54**:348-55.

22. Frandsen PA,.Kruse T. Hip fractures in the county of Funen, Denmark. Implications of demographic aging and changes in incidence rates. *Acta Orthop.Scand.* 1983;**54**:681-6.

23. Zetterberg C,.Andersson GB. Fractures of the proximal end of the femur in Goteborg, Sweden, 1940-1979. *Acta Orthop.Scand.* 1982;**53**:419-26.

24. Jensen JS. Incidence of hip fractures. *Acta Orthop.Scand.* 1980;**51**:511-3.

25. Lofman O, Berglund K, Larsson L, Toss G. Changes in hip fracture epidemiology: redistribution between ages, genders and fracture types. *Osteoporos.Int.* 2002;**13**:18-25.

26. Kaastad TS, Meyer HE, Falch JA. Incidence of hip fracture in Oslo, Norway: differences within the city. *Bone* 1998;**22**:175-8.

27. Laursen JO. Hoftenaere femurfrakturer--en epidemiologisk undersogelse i Sonderjyllands Amt. [Femoral fractures close to the hip--an epidemiological study in the county of Southern Jutland]. *Ugeskr Laeger* 1994;**156**:1107,1110-07,1111.

28. Nungu S, Olerud C, Rehnberg L. The incidence of hip fracture in Uppsala County. Change of time trend in women. *Acta Orthop.Scand.* 1993;**64**:75-8.

29. Lauritzen JB, Schwarz P, Lund B, McNair P, Transbol I. Changing incidence and residual lifetime risk of common osteoporosis-related fractures. *Osteoporos.Int.* 1993;**3**:127-32.

30. Rehnberg L,.Olerud C. Incidence of hip fractures in the elderly. Uppsala County 1980-1987. *Acta Orthop.Scand.* 1990;**61**:148-51.

31. Poulsen, T. K., Ovesen, O., Röck, N. D., Andersen-Ranber, F., Møller-Larsen, F., and Riis, J. Hip fractures in the county of Funen, Denmark. Incidences from 1973 ot 1978 compared with 1997 and 1998. 5th Congress o fthe European Federation of National Association of Orthopaedics and Traumatology, Rhodes-Greece, June 3-7: P137 . 2001.
Ref Type: Abstract

32. Bengner U, Johnell O, Redlund-Johnell I. Changes in incidence and prevalence of vertebral fractures during 30 years. *Calcif.Tissue Int.* 1988;**42**:293-6.

33. Cooper C, Atkinson EJ, O'Fallon WM, Melton LJ. Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985-1989. *J.Bone Miner.Res.* 1992;**7**:221-7.

34. Larsen CF,.Lauritsen J. Epidemiology of acute wrist trauma. *Int.J Epidemiol.* 1993;**22** :911-6.

35. Mallmin H,.Ljunghall S. Incidence of Colles' fracture in Uppsala. A prospective study of a quarter-million population. *Acta Orthop.Scand.* 1992;**63**:213-5.

36. Schmalholz A. Epidemiology of distal radius fracture in Stockholm 1981-82. *Acta Orthop.Scand.* 1988;**59**:701-3.

37. Jonsson B, Bengner U, Redlund-Johnell I, Johnell O. Forearm fractures in Malmo, Sweden. Changes in the incidence occurring during the 1950s, 1980s and 1990s. *Acta Orthop.Scand.* 1999;**70**:129-32.

38. Bengner U,.Johnell O. Increasing incidence of forearm fractures. A comparison of epidemiologic patterns 25 years apart. *Acta Orthop.Scand.* 1985;**56**:158-60.

39. Solgaard S,.Petersen VS. Epidemiology of distal radius fractures. *Acta Orthop.Scand.* 1985;**56**:391-3.

40. Falch JA. Epidemiology of fractures of the distal forearm in Oslo, Norway. *Acta Orthop.Scand.* 1983;**54**:291-5.

41. Chrischilles E, Shireman T, Wallace R. Costs and health effects of osteoporotic fractures. *Bone* 1994;**15**:377-86.

42. Meyer HE, Tverdal A, Falch JA, Pedersen JI. Factors associated with mortality after hip fracture. *Osteoporos.Int.* 2000;**11**:228-32.

43. Lund E. Dodeligheten av fractura colli femoris i Norge 1980-94. [Mortality resulting from femoral neck fractures in Norway 1980-94]. *Tidsskr.Nor Laegeforen.* 1998;**118**:2764-6.

44. Falch JA,.Meyer HE. Dodelighet av larhalsbrudd. [Hip fracture mortality]. *Tidsskr.Nor Laegeforen.* 1998;**118**:3674.

45. Elmerson S,.Zetterberg C. Endast var fjarde patient i livet tio ar efter hoftfrakturoperation. [Only every fourth patient is alive 10 years after hip fracture surgery]. *Lakartidningen* 1989;**86**:1903-4.

46. Eiskjaer S, Ostgard SE, Jakobsen BW, Jensen J, Lucht U. Years of potential life lost after hip fracture among postmenopausal women. *Acta Orthop.Scand.* 1992;**63**:293-6.

47. Berglund-Roden M, Swierstra BA, Wingstrand H, Thorngren KG. Prospective comparison of hip fracture treatment. 856 cases followed for 4 months in The Netherlands and Sweden. *Acta Orthop.Scand.* 1994;**65**:287-94.

48. Advocaat C,.Bautz-Holter E. Prognose ett ar etter hoftebrudd. [Prognosis one year after hip fracture]. *Tidsskr.Nor Laegeforen.* 1997;**117**:3801-3.

49. Jensen JS, Tondevold E, Sorensen PH. Social rehabilitation following hip fractures. *Acta Orthop.Scand.* 1979;**50**:777-85.

50. Jensen JS,.Tondevold E. Mortality after hip fractures. *Acta Orthop.Scand.* 1979;**50**:161-7.

51. Finsen V, Borset M, Rossvoll I. Mobility, survival and nursing-home requirements after hip fracture. *Ann.Chir Gynaecol.* 1995;**84**:291-4.

52. Ankjær-Jensen, A., Jacobsen, E. T., and Thomsen, I. S. Rehabilitering af ældre med hoftebrud - omkostninger og effekt (DSI 94.08). Dansk Sygehus Institut. 1994. Copenhagen, Dansk Sygehus Institut.
Ref Type: Report

53. Tidermark J, Zethraeus N, Svensson O, Tornkvist H, Ponzer S. Femoral neck fractures in the elderly: functional outcome and quality of life according to EuroQol. *Qual.Life Res.* 2002;**11**:473-81.

54. Cserhati P, Fekete K, Berglund-Roden M, Wingstrand H, Thorngren KG. Hip fractures in Hungary and Sweden - differences in treatment and rehabilitation. *Int.Orthop.* 2002;**26**:222-8.

55. Holmberg S, Kalen R, Thorngren KG. Treatment and outcome of femoral neck fractures. An analysis of 2418 patients admitted from their own homes. *Clin Orthop.* 1987;42-52.

56. Falch JA. Epidemiology of fractures of the distal forearm in Oslo, Norway. *Acta Orthop.Scand.* 1983;**54**:291-5.

57. Assesment of fracture risk and its application to screenign for postmenopausal osteoporosis: Reports of a WHO study group, Geneva: WHO Tecnical Report Series 843, 1994. WHO Tecnical Report Series 843, 1994 . 2001.
Ref Type: Report

58. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *BMJ* 1996;**312**:1254-9.

59. Schott AM, Cormier C, Hans D, Favier F, Hausherr E, Dargent-Molina P *et al*. How hip and whole-body bone mineral density predict hip fracture in elderly women: the EPIDOS Prospective Study. *Osteoporos.Int.* 1998;**8**:247-54.

60. Looker AC, Wahner HW, Dunn WL, Calvo MS, Harris TB, Heyse SP *et al.* Updated data on proximal femur bone mineral levels of US adults. *Osteoporos.Int.* 1998;**8**:468-89.

61. Browner WS, Seeley DG, Vogt TM, Cummings SR. Non-trauma mortality in elderly women with low bone mineral density. Study of Osteoporotic Fractures Research Group. *Lancet* 1991;**338**:355-8.

62. Browner WS, Pressman AR, Nevitt MC, Cummings SR. Mortality following fractures in older women. The study of osteoporotic fractures. *Arch.Intern.Med.* 1996;**156**:1521-5.

63. Salkeld G, Cameron ID, Cumming RG, Easter S, Seymour J, Kurrle SE *et al*. Quality of life related to fear of falling and hip fracture in older women: a time trade off study. *BMJ* 2000;**320**:341-6.

64. Oleksik A, Lips P, Dawson A, Minshall ME, Shen W, Cooper C *et al*. Health-related quality of life in postmenopausal women with low BMD with or without prevalent vertebral fractures. *J Bone Miner.Res.* 2000;**15**:1384-92.

65. Dolan P, Torgerson D, Kakarlapudi TK. Health-related quality of life of Colles' fracture patients. *Osteoporos.Int.* 1999;**9**:196-9.

66. Pedersen KM, Wittrup-Jensen K, Brooks R, Gudex C. Værdisætning af sundhed. Teorien om kvalitetsjusterede leveår og en dansk anvendelse [in Danish]. Syddansk Universitetsforlag, 2003.

67. Hawthorne G, Richardson J, Day NA. A comparison of the Assessment of Quality of Life (AQoL) with four other generic utility instruments. *Ann.Med.* 2001;**33**:358-70.

68. Zethraeus N, Stromberg L, Jonsson B, Svensson O, Ohlen G. The cost of a hip fracture. Estimates for 1,709 patients in Sweden. *Acta Orthop.Scand.* 1997;**68**:13-7.

69. Zethraeus N,.Gerdtham UG. Estimating the costs of hip fracture and potential savings. *Int.J Technol.Assess.Health Care* 1998;**14**:255-67.

70. Brainsky A, Glick H, Lydick E, Epstein R, Fox KM, Hawkes W *et al*. The economic cost of hip fractures in community-dwelling older adults: a prospective study. *J Am.Geriatr.Soc.* 1997;**45**:281-7.

71. De Laet CE, van Hout BA, Burger H, Weel AE, Hofman A, Pols HA. Incremental cost of medical care after hip fracture and first vertebral fracture: the Rotterdam study. *Osteoporos.Int.* 1999;**10**:66-72.

72. http://www.vestamt.dk. (accessed 20th December 2002) . 2002.
Ref Type: Internet Communication

73. http://www.holmegaard.dk/pages/borger/social/sotaks01.htm. (accessed 20th December 2002) . 2002.
Ref Type: Internet Communication

74. http://www.dadlnet.dk/plo/open/4overenskomster/horartabel/lok_okt02.htm. (accessed 20th December 2002) . 2003.
Ref Type: Internet Communication

75. Eeg, P. S. and Kristensen, K. H. Tal på tid - tale om tid. Standard for tidsregistrering i hjemmeplejen [In Danish]. ISBN 87-7848-604-1. 2001. Copenhagen, Kommunernes Landsforening.
Ref Type: Report

76. Zethraeus, N., Borgström, F, Johnell, O., Kanis, J., Önnby, K, and Jonsson, B. Costs and quality of life associated with osteoporosis related fractures - results from a Swedish survey. SSE/EFI working paper series in economics and finance, No 512, 1-18. 1-10-2002. Stockholm of Economics, Centre for Health Economics. SSE/EFI working paper series in economics and finance.
Ref Type: Report

77. http://www.odensetaxa.dk/Web/Home/Priser/Takstreglement (accessed 23.01.2003). 2003.
Ref Type: Internet Communication

78. Andersen, L., Kristiansen, I. S., Falch, J. A., and Aursnes I. Cost-effectiveness of alendronate for the prevention of osteoporotic fractures in Norwegian

women. Working paper 11/1995. 1995. Statens Institutt for Folkehelse.
Ref Type: Report

79. Ankjær-Jensen A,.Johnell O. Prevention of osteoporosis: cost-effectiveness of different pharmaceutical treatments. *Osteoporos.Int.* 1996;**6**:265-75.

80. Takstsytem 2002 - Vejledning (DRG). Sundhedsministeriet, 2002.

81. http://drg.sst.dk/info/takster_2002/dk_nd_ændr.XLS. (accessed 20th December 2002) . 2003.
Ref Type: Internet Communication

82. Solgaard S. Early displacement of distal radius fracture. *Acta Orthop.Scand.* 1986;**57** :229-31.

83. http://www.fysio.dk/sw501.asp. (accessed 20th December 2002) . 2003.
Ref Type: Internet Communication

84. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. *J Bone Miner.Res.* 2000;**15**:721-39.

85. Christensen PM, Brosen K, Brixen KT, Beck-Nielsen H, Sogaard J, Kristiansen IS. Farmakookonomiske evalueringer af medicinsk behandling af osteoporose. En litteraturoversigt. [Pharmaco-economic evaluation of drug therapy osteoporosis. A literature review]. *Ugeskr Laeger* 2002;**164**:1339-45.

86. www.scb.se. 2003.
Ref Type: Internet Communication

87. www.ssb.no. 2003.
Ref Type: Internet Communication

88. Tosteson AN, Jonsson B, Grima DT, O'Brien BJ, Black DM, Adachi JD. Challenges for model-based economic evaluations of postmenopausal osteoporosis interventions. *Osteoporos.Int.* 2001;**12**:849-57.