A burden of illness study commissioned by Merck Sharp & Dohme

C. de Laet, M.D.¹ B.A. van Hout, Ph.D.² H.A.P. Pols, Ph.D.³

- 1) Department of Epidemiology and Biostatistics, Erasmus University Rotterdam.
- 2) Institute for Medical Technology Assessment, Erasmus University Rotterdam.
- 3) Department of Internal Medicine III, University Hospital Rotterdam.

Correspondence: institute for Medical Technology Assessment Erasmus University Rotterdam P.O. Box 1738 3000 DR Rotterdam The Netherlands

Tel: + 31 10 408 85 33 Fax: + 31 10 408 90 94 E-mail: <u>delaet@bmg.eur.nl</u>

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1. Introduction

This report provides an overview of the currently available quantitative information about osteoporosis in the Netherlands, and of the cost associated with it. We present information relevant for this country, making as few assumptions as possible. When assumptions are made, they are clearly stated in the text.

Although the main subject is osteoporosis, the focus in this report is on fractures, as these are the most relevant outcome events of this condition.

The data were collected from publicly available data sources and from international literature. Information is mostly about the year 1993, but sometimes we are forced to use information from other years. No primary data collection has been carried out.

The reader finds detailed information about the occurrence of osteoporosis and fractures, the utilisation of health care, mortality, and the costs in the results' section of this report. In the conclusions, we present a synthesis of the most important findings.

2. Background and rationale

Osteoporosis is, by consensus, defined as a systemic skeletal disease, characterised by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture. There is an important age-related decrease in bone mass and bone strength. Osteoporosis is primarily described in post-menopausal women but men are not free from it; they also reach high fracture incidence rates at an older age. Combined with the longer survival of women, this leads to the observation that most osteoporotic fractures are encountered in females.

Osteoporosis and its direct consequences, fractures, are a major concern for public health, as they are responsible for death and for substantial disability. Moreover, they represent an important cost for the public health budget. In the US, it was estimated that osteoporotic fractures cost US\$ 7 - 10 billion each year, and that this cost will inevitably rise as the population continues to age.²

Osteoporosis, defined as a reduction in bone mass below a specified threshold, has been shown to be a major determinant of fracture risk.³ Bone mass can be measured with sufficient accuracy and precision, so that it is nowadays the best readily available indicator of fracture risk, other than age and sex. There is however a considerable overlap of bone density values between people who develop fractures and people who do not.

Bone mineral density (BMD) is however not the only element involved in fractures. There is of course the trauma, that is the direct cause of the fracture. Propensity to fall increases with age due to disturbances of equilibrium, decrease in mobility, dementia, cardiovascular morbidity, etc. The impact of those, non bone density related factors, is commonly measured by using age as a surrogate for predicting fractures. Bone strength is not only determined by bone mass, but also dependent upon the properties of the bone tissue and upon its spatial arrangement. This is often referred to as bone quality. It has been suggested that the relative contributions of bone mass, bone quality, and trauma to the aetiology of fractures might be different for different parts of the skeleton.²

3. Data sources

In each of the following chapters the data sources used are mentioned. Here, a general description of the data sources is given. Were possible, data for 1993 (the 'reference year') are used. Where this is not possible, it is clearly indicated in the text.

3.1. Central Bureau for Statistics (CBS)

The CBS (Centraal Bureau voor de Statistiek) is the official Dutch organisation that covers the national registration of a wide variety of statistics, including demography, registration of causes of death, etc. Some of this information is published in yearly and monthly publications. Other information, such as causes of death related to osteoporosis was specifically obtained for this study.

3.2. Foundation for Health Care Information (SIG)

The SIG (Stichting Informatiecentrum voor de Gezondheidszorg) is a national registry collecting various health care related data. All of the hospitalisations in academic and general hospitals within the Netherlands are included in this registration as is most of the nursing home information. Both published information and files specifically obtained for the purpose of this study are used in this report.

3.3. Institute for Medical Statistics (IMS)

IMS is a company that collects data on health care by sampling GP's and specialists. These data provide an indication about the patient contacts they had within a given week. The reason for encounter, diagnosis, patient demographics, and therapy is recorded. Furthermore, data from pharmacies are sampled to calculate the actual sales of drugs. In the latter registration, no medical indication is recorded.

3.4. Home Health Care Service Rotterdam

The Home Health Care Service Rotterdam (Thuiszorg Rotterdam) collects information on all home health care activities in the city of Rotterdam. This registration is used to estimate the use of home health care in the Netherlands.

3.5. Literature

An effort is made to use information directly relevant for the Netherlands. Where specific data for the Netherlands are lacking, international data were used, and this is clearly indicated in the text.

3.6. Expert opinion

Where available data needed more explanation and clinical common sense was required, expert opinion was obtained from specialists at the Rotterdam Academic Hospital.

4. Results

4.1. Evaluation of the prevalence of osteoporosis

Age and sex distribution of the population

Demographic trends

As in most Western countries, the population of the Netherlands is ageing. The size of the population increased from 10 million to 15 million in the period 1950-1990 mainly due to the post-war baby boom. At the same time there was a gradual increase in the proportion of old people. Over the next decades this latter trend will continue. The Dutch population is primarily white Caucasian, and the incidence of osteoporosis is known to be different in other races. No ethnic specific information about osteoporosis is available for the Netherlands. The Netherlands Central Bureau of Statistics (CBS) produces on a regular basis forecasts to predict the future composition of the population. Those forecasts are known as the high, medium and low variant, but their basic assumption is that there are no drastic changes in neither behaviour, policy, (medical) technology and that there are no major catastrophes. It is what is called a *surprise-free forecast*. The forecasts are based on the trends from the near past. The CBS forecasts are updated each year, on the basis of the latest developments. For this report, we use the 1994-2050 forecast.

The Dutch population by age and sex in 1993

Age and sex distribution on January 1, 1993⁵

Age class	Men	Women	Total
0-4	497136	474951	972087
5-9	466268	446458	912726
10-14	463287	442961	906248
15-19	487831	467578	955409
20-24	634632	612174	1246806
25-29	671772	636212	1307984
30-34	652018	624608	1276626
35-39	602068	581178	1183246
40-44	589866	564605	1154471
45-49	556623	530227	1086850
50-54	422624	406733	829357
55-59	364725	365343	730068
60-64	333548	358229	691777
65-69	283457	337536	620993
70-74	222178	298242	520420
75-79	148868	238855	387723
80-84	86591	176009	262600
≥85	51776	142015	193791
Total	7535268	7703914	15239182

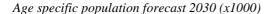
Age and sex distribution on January 1, 1993 (grouped by broader age classes)

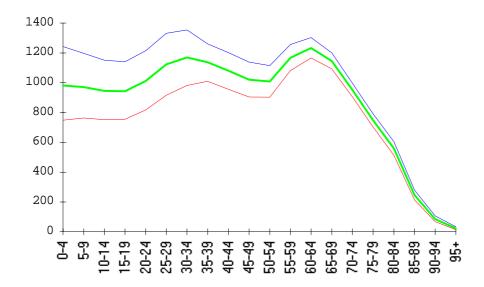
Age class	Men	Women	Total
0-44	5064878	4850725	9915603
45-54	979247	936960	1916207
55-64	698273	723572	1421845
65-74	505635	635778	1141413
75-84	235459	414864	650323
≥85	51776	142015	193791
Total	7535268	7703914	15239182

Population forecast

Different variants are published. The medium variant is the most likely development. In the low variant birth rates as well as immigration and divorce rates are lower, while mortality, emigration and marriage rates are higher. The opposite is done in the high variant.

In the elderly population of interest in this report, the differences between the several variants are relatively small in the coming decades. Those persons are born already, and only mortality and migration will influence their numbers. As an illustration the age specific population forecast for 2030 is shown with the low, medium and high variant.





The data shown in the next table are the medium variant of the forecast. Those data show a slight increase of the total population until around the year 2035 when a maximum of 17.5 million Dutch will be reached. Thereafter a slight decrease of the total population is predicted.

Census projection, medium variant (x1000)

census project	iion, meainm	variani (x10	00)				
Prediction 200	00			Prediction 201	10		
Age class	Men	Women	Total	Age class	Men	Women	Total
0-19	2008	1914	3922	0-19	2083	1976	4059
20-39	2457	2341	4798	20-39	2176	2056	4232
40-59	2220	2153	4373	40-59	2515	2440	4955
60-79	1088	1298	2386	60-79	1403	1546	2949
≥80	151	352	503	≥80	195	420	615
Total	7924	8058	15982	Total	8372	8438	16810

Prediction 2020				Prediction 203	0		
Age class	Men	Women	Total	Age class	Men	Women	Total
0-19	1978	1874	3852	0-19	1972	1869	3841
20-39	2222	2082	4304	20-39	2297	2144	4441
40-59	2460	2366	4826	40-59	2187	2088	4275
60-79	1719	1891	3610	60-79	1942	2136	4078
≥80	229	449	678	≥80	322	590	912
Total	8608	8662	17270	Total	8720	8827	17547

Prediction 2040				Prediction 205	50		
Age class	Men	Women	Total	Age class	Men	Women	Total
0-19	2021	1915	3936	0-19	1958	1856	3814
20-39	2192	2042	4234	20-39	2186	2036	4222
40-59	2238	2115	4353	40-59	2308	2175	4483
60-79	1856	2051	3907	60-79	1655	1814	3469
≥80	363	687	1050	≥80	406	759	1165
Total	8670	8810	17480	Total	8513	8640	17153

Age and sex distribution of the population meeting BMD definition of osteoporosis

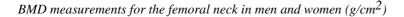
The BMD reference data for the Netherlands come from a cross-sectional, population based study, where baseline BMD measurements were performed in 1762 ambulatory subjects (678 men and 1084 women) aged 55 years and more. This study is part of *the Rotterdam study*, a prospective follow-up study of the occurrence and determinants of disease and disability in the elderly that also will provide, over time, follow-up data on BMD evolution and fractures.

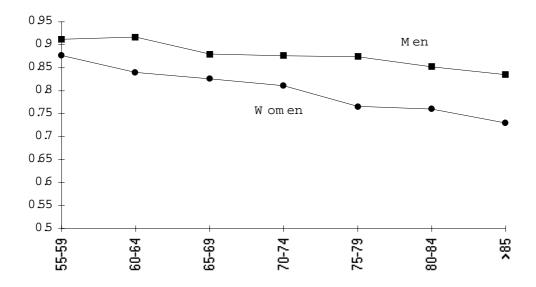
For densitometry, institutionalised persons (10%) were not eligible in this study. Densitometry was performed using dual energy X-ray absorptiometry (DXA) of the lumbar spine and proximal femur (femoral neck, Ward's triangle and trochanter). BMD measurements were performed using a Lunar DPX-L densitometer (Lunar Radiation Corporation, Madison, WI).

Men				
Age class	Neck g/cm ²	Ward g/cm ²	Trochanter g/cm ²	L2-L4 g/cm ²
	(SD)	(SD)	(SD)	(SD)
55-59	0.912 (0.108)	0.771 (0.129)	0.882 (0.115)	1.138 (0.193)
60-64	0.917 (0.124)	0.755 (0.143)	0.883 (0.122)	1.179 (0.186)
65-69	0.880 (0.131)	0.713 (0.157)	0.836 (0.150)	1.140 (0.203)
70-74	0.876 (0.142)	0.705 (0.154)	0.836 (0.139)	1.171 (0.213)
75-79	0.874 (0.140)	0.708 (0.156)	0.835 (0.138)	1.165 (0.214)
80-84	0.852 (0.157)	0.690 (0.193)	0.828 (0.167)	1.193 (0.249)
≥85	0.835 (0.147)	0.675 (0.172)	0.838 (0.191)	1.344 (0.278)
Total	0.886 (0.134)	0.724 (0.156)	0.851 (0.140)	1.166 (0.211)
Adjusted ^a	0.892 (0.121)	0.730 (0.139)	0.860 (0.122)	1.176 (0.183)

Women				
Age class	Neck g/cm ²	Ward g/cm ²	Trochanter g/cm ²	L2-L4 g/cm ²
	(SD)	(SD)	(SD)	(SD)
55-59	0.877 (0.131)	0.749 (0.150)	0.758 (0.128)	1.062 (0.141)
60-64	0.840 (0.120)	0.695 (0.144)	0.746 (0.128)	1.007 (0.174)
65-69	0.826 (0.128)	0.680 (0.143)	0.735 (0.128)	1.042 (0.184)
70-74	0.811 (0.124)	0.668 (0.141)	0.734 (0.131)	1.040 (0.183)
75-79	0.766 (0.132)	0.615 (0.143)	0.694 (0.144)	0.996 (0.193)
80-84	0.760 (0.110)	0.613 (0.127)	0.696 (0.152)	1.038 (0.201)
≥85	0.730 (0.125)	0.580 (0.145)	0.655 (0.140)	1.077 (0.224)
Total	0.814 (0.131)	0.670 (0.149)	0.727 (0.136)	1.032 (0.183)
Adjusted ^a	0.812 (0.120)	0.664 (0.139)	0.720 (0.122)	1.026 (0.183)

^a Adjusted for age and body mass index.





The main conclusion from this cross-sectional study is that the apparent rate of bone loss is significantly different between men and women at all femoral sites. The rate of decline of the BMD in women at the femoral neck is almost twice as high as that in men. The observed absolute rates of decline in the proximal femur of women are equal to the results of the Framingham Osteoporosis Study. It is also observed that the mean bone reduction due to early menopause is relatively small compared to the effect of age. In this study, it is estimated that 1 year of age-related bone reduction in the Ward's triangle could be compensated by a 3 year later onset of menopause. This last finding seems to be contradicted in another study on BMD and age in Dutch women by Erdtsieck et al. From this relatively small and highly selected group of 260 healthy women aged 20-80 they conclude that a 1 year later onset of the menopause compensates for 2 years of age-related BMD loss.

At the lumbar spine no significant age-related decrease in BMD is found. It is suggested that this could be explained by age-related local factors such as the presence of marked spinal osteoarthritis in the region of interest.

Finally, caution is expressed for the fact that this study concerns cross-sectional data, and that the results may have been influenced by age-dependent selection and also by cohort effects.

Age and sex-specific incidence of fractures

Hip fractures

In the Netherlands, virtually all persons with hip fractures are treated clinically. Therefore, it is felt that hospital data give an accurate view of the incidence of hip fractures.

Data for hip fractures in 1993 were collected from SIG hospital registration data as described in the chapter on data sources. A specific file of all hospital admissions for hip fracture was obtained and analysed. Trend data since 1972 are collected from literature, ¹⁰ and are based on the same (SIG) hospital registration source.

To make the comparison with available trend data possible, a first analysis was made including all patients with hospital admission due to hip fracture (ICD-9 code 820xx). In the subsequent analysis, patients with codes for high energy trauma or cancer were omitted, as specified in the MSD study protocol.

Absolute numbers of hip fractures in 1993

Age class	Men	Women	Total
0-4	14	15	29
5-9	13	5	18
10-14	27	17	44
15-19	32	5	37
20-24	38	9	47
25-29	48	9	57
30-34	46	10	56
35-39	50	22	72
40-44	84	34	118
45-49	123	72	195
50-54	100	125	225
55-59	149	194	343
60-64	203	385	588
65-69	307	702	1009
70-74	470	1256	1726
75-79	649	1862	2511
80-84	689	2532	3221
≥85	840	3971	4811
Total	3882	11225	15107

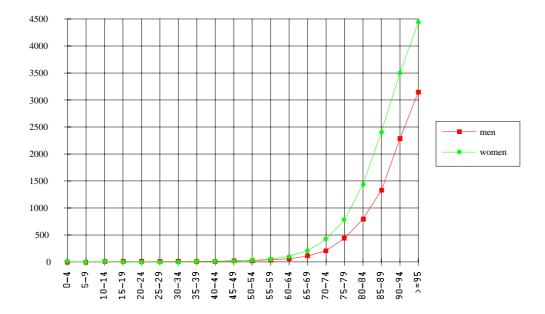
Age and sex-specific hip fracture incidence in 1993

The absolute numbers of fractures were combined with the age and sex distribution of the 1993 Dutch population to estimate the hip fracture incidences.

In the next table, the incidences per 100.000 person years are given in the standard CBS 5 year age classes. The figure additionally displays the incidences of 85-89, 90-94 and \geq 95. At those ages, hip fracture incidences become very high.

Age class	Men	Women
0-4	2.82	3.16
5-9	2.79	1.12
10-14	5.83	3.84
15-19	6.56	1.07
20-24	5.99	1.47
25-29	7.15	1.41
30-34	7.06	1.60
35-39	8.30	3.79
40-44	14.24	6.02
45-49	22.10	13.58
50-54	23.66	30.73
55-59	40.85	53.10
60-64	60.86	107.47
65-69	108.31	207.98
70-74	211.54	421.13
75-79	435.96	779.55
80-84	795.69	1438.56
≥85	1622.37	2796.18

Hip fracture incidence in the Netherlands in 1993 per 100.000



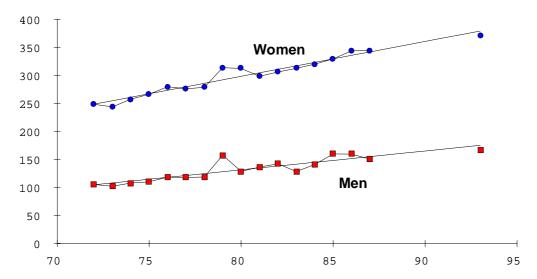
1993 Hip fracture incidence (per 100.000) in the broader age classes

Age class	Men	Women
0-44	6.95	2.60
45-54	22.77	21.03
55-64	50.41	80.02
65-74	153.67	307.97
75-84	568.25	1059.14
≥85	1622.37	2796.18

Trend data

Trend data from 1972 till 1987 for the Netherlands are published for men and women aged 50 years and older. ¹⁰ Hip fracture incidence was age-adjusted by direct standardisation. To be able to compare the 1993 data with the published data, we obtain the standard population for the standardisation in the same way as in the study by Boereboom et al (summation of the Dutch population for the calendar years 1972-1987). When we add the 1993 data to the previous analysis the significant upward trend that is described previously is confirmed. In women, age standardised hip fracture incidence that increased from 249/100.000 in 1972 to 345/100.000 in 1987 reached 371/100.000 in 1993. For men, the increase was from 105/100.000 in 1972 over 150/100.000 in 1978 to 168/100.000 in 1993. This trend is highly significant in both men and women (p<0.001). The strange peak in the 1979 data remains unexplained. A data artefact in that year may have occurred.

Trend in age-adjusted hip fracture incidence in the Netherlands in men and women aged 50 years and older (incidence/100.000)

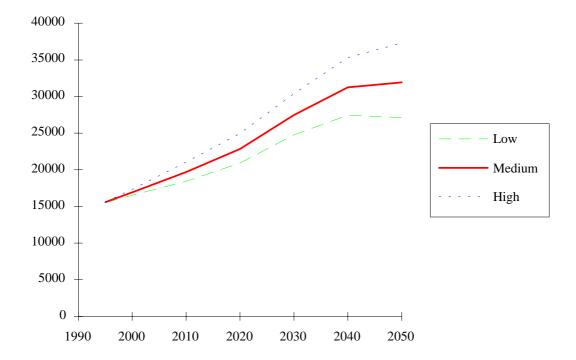


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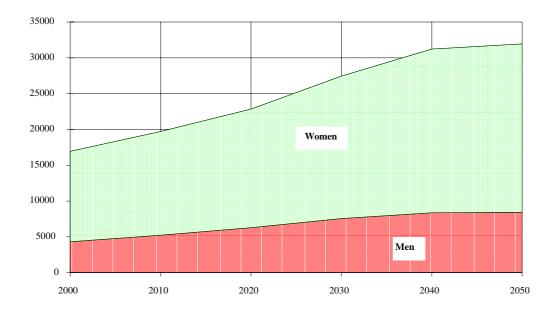
Effect of demography on hip fractures

Apart from this important age-adjusted upward trend, the total number of hip fractures in the Netherlands in the next decades will also increase due to the demographic changes with the ageing of the population. If the current age specific hip fracture rates are applied to the population forecast figures, the total number of hip fractures will double by the year 2050 due to demography alone.

Yearly predicted number of hip fractures in the Netherlands due to demographic changes



Yearly predicted number of hip fractures in the Netherlands due to demographic changes by sex



1993 hip fractures, excluding trauma or cancer

When applying the exclusion criteria from the MSD Study Protocol, only a few of the total hip fracture cases have to be excluded:

Elimination of old fractures or non-osteoporotic fractures

ICD 9-CM	Description	Number
733.42	Aseptic Necrosis of head and neck of femur	8
733.81-733.82	Non-union of fractures	12
198.5	Sec. malignant neoplasm of bone and bone marrow	22
199.0	Disseminated malignant neoplasm	9
199.1	Cancer, site unspecified	7
733.1	Pathologic fracture	8
Total		66
Total potential e	exclusions (a few double exclusions)	64
733.0x	Osteoporosis (not to be excluded)	- 3
Number of exclu	usions	61

After excluding those cases, the age-adjusted incidences barely change. It is however uncertain whether the registration of secondary diagnosis is as accurate as that of primary diagnosis. These exclusions might thus be underestimated.

1993 Hip fracture incidence (per 100.000) in broader age classes after exclusions

Age class	Men	Women
0-44	6.91	2.60
45-54	22.77	20.71
55-64	50.27	79.61
65-74	153.07	307.03
75-84	563.58	1055.29
≥85	1604.99	2791.25

Absolute numbers of hip fractures after exclusions

Age class	Men	Women	Total
0-4	14	15	29
5-9	13	5	18
10-14	27	17	44
15-19	31	5	36
20-24	38	9	47
25-29	47	9	56
30-34	46	10	56
35-39	50	22	72
40-44	84	34	118
45-49	123	71	194
50-54	100	123	223
55-59	149	192	341
60-64	202	384	586
65-69	306	701	1007
70-74	468	1251	1719
75-79	644	1855	2499
80-84	683	2523	3206
≥85	831	3964	4795
Total	3856	11190	15046

In the analyses hereafter, the above numbers, after exclusions, will be used.

Non-hip fractures

Dutch data for non-hip fractures

Although hip fractures are the most serious consequences of osteoporosis, other fractures do occur. Those are mainly fractures of the vertebrae and the forearm. Most frequently, those fractures do not require a hospital admission and are treated either in the outpatient clinic or, in the case of vertebral fractures, often not treated at all. When looking at the hospital admissions for fractures other than the hip, we observe smaller numbers and also the absence of the typically high percentage of persons over 65 years of age. We equally do not observe the typically high female/male ratio of fractures. Therefore, it seems that the hospitalisation data are not reflecting the osteoporosis related fractures, and that they cannot be used to estimate the incidence of osteoporosis related non-hip fractures.

Hospital admissions for vertebral and forearm fractures in the Netherlands in 1992¹¹

	Total	≥65 years	≥65 year (%)	female/male ratio
Vertebrae	2586	977	37.8%	1.1
Forearm	4180	902	21.6%	1.0
Hip	14467	12583	87.0%	2.8

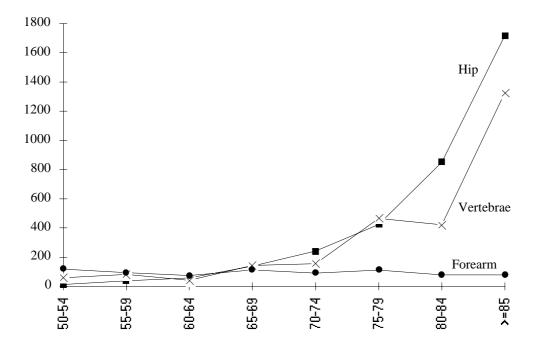
No data are available yet for osteoporosis related non-hip fractures in the Netherlands. In the absence of those data, data from the international literature are taken. In the future, incidence data for fractures in the Netherlands will be available from the Rotterdam study.

International data for non-hip fractures

Melton et al., in an 1992 overview article, ¹² present the following incidence figures for men and women in Rochester, Minnesota. Those data should be used with caution since the incidences refer to different time periods and the vertebral fractures only refer to clinically diagnosed fractures. We choose to use clinically diagnosed vertebral fractures, since there is some debate about the definition of radiographic vertebral deformities. Different techniques of measurement and different criteria can produce varying results and varying fracture rates. On the other hand, clinically diagnosed vertebral fractures are more directly relevant to the cost. These incidence rates appear to be the best available estimate.

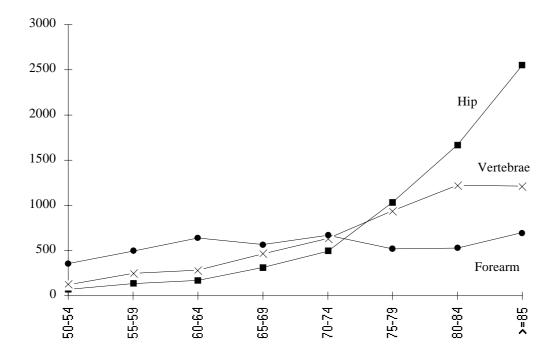
First fracture incidence rates per 100.000 person-years in men

Men	Hip	Vertebrae	Forearm
50-54	12.5	58.6	118.4
55-59	36.9	82.4	92.9
60-64	58.0	40.8	74.3
65-69	139.7	143.2	113.3
70-74	241.7	154.8	90.6
75-79	423.2	466.1	111.8
80-84	850.6	421.0	78.3
≥85	1719.5	1326.7	78.3



First fracture incidence rates per 100.000 person-years in women

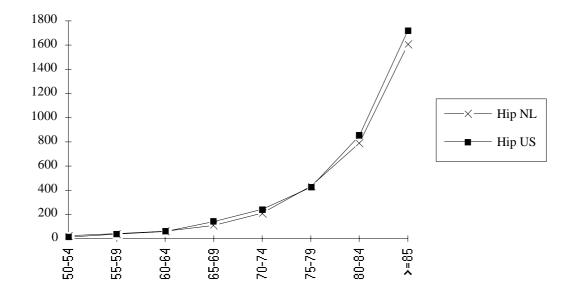
Women	Hip	Vertebrae	Forearm
50-54	69.5	123.0	355.4
55-59	135.4	248.2	494.9
60-64	169.6	283.3	639.8
65-69	314.2	463.5	567.6
70-74	493.5	634.0	669.8
75-79	1033.2	938.7	517.8
80-84	1669.3	1224.2	526.9
≥85	2552.5	1213.5	699.2



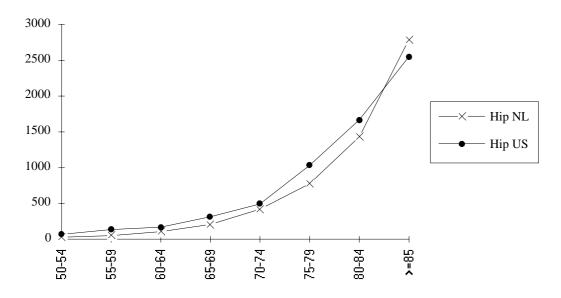
Extrapolation of international data to Dutch non-hip fractures

When comparing the Rochester incidences of hip fractures with the ones for the Netherlands in 1993, they appear to be remarkably similar.

Age specific hip fracture incidence in men.



Age specific hip fracture incidence in women.



Since the incidence rates of hip fractures are very comparable, we assume we can also use the Rochester data to estimate the number of non-hip fractures in the Netherlands, although we are aware that time trends and incidences might be different. The upward time trend in the hip fracture incidence for example appears to have stopped in several countries, including the US. 13

Estimated yearly number of (first) non-hip fractures in the Netherlands in men

Age class	Vertebrae	Forearm
50-54	248	500
55-59	301	339
60-64	136	248
65-69	406	321
70-74	344	201
75-79	694	166
80-84	365	68
≥85	687	41
Total	3181	1884

Estimated yearly number of (first) non-hip fractures in the Netherlands in women

Age class	Vertebrae	Forearm
50-54	500	1446
55-59	907	1808
60-64	1015	2292
65-69	1564	1916
70-74	1891	1998
75-79	2242	1237
80-84	2155	927
≥85	1723	993
Total	11997	12617

4.2. Evaluation of the health care utilisation associated with osteoporosis

Pharmacotherapy

The use of drugs in the treatment or prevention of osteoporosis is estimated based on IMS data. The total figures are adjusted for the estimated proportion of the drug that is used for osteoporosis.

Presentation and dosage can differ from one prescription to another. Therefore, date are recalculated to estimate patient-years of treatment for the leading products.

Patient years in 1993 for the leading osteoporosis products in the Netherlands (x 1000)

	1993	Share
	patient years	
Didrokit	18.6	30.7%
Calcium Forte	11.7	19.3%
Calcium Fortissimum	5.8	9.6%
Cacit 500	5.0	8.3%
Etalpha	0.9	1.5%
Didronel	0.2	0.3%
Progynova	1.2	2.0%
Decadurabolin	0.4	0.7%
Devaron	5.3	8.8%
Premarin	0.3	0.5%
Procal	0.5	0.8%
Zumenon	0.2	0.3%
Estraderm TTS	1.3	2.2%
Dohyfral AD 3	9.1	15.0%
Calc. gluc-2	0.0	0.0%
Calcii lactas-2	0.0	0.0%
Total	60.6	100.0%

Hospitalisations

Hip fractures

Hospitalisation data are collected from the SIG hospital registration data. We use the same file of hospital admissions as used for the estimation of hip fracture incidence.

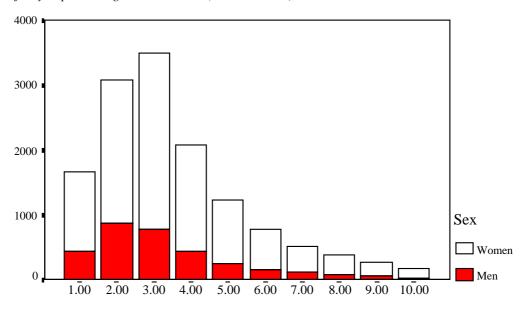
Age and sex specific length of stay (days) after hip fractures

The mean length of stay (LOS) is 26.03 days, with a standard deviation of 29 days. The distribution of the LOS is highly skewed and an association with age and sex is observed. Mean LOS in men is 23.7; mean LOS in women is 26.8 (p<0.001). Median LOS is 16 days for men and 19 days for women.

Age and sex specific mean length of stay (days)

Age class	Men	Women	Total
0-4	32.6	19.6	30.6
5-9	31.8	19.2	28.3
10-14	16.7	10.1	14.1
15-19	14.4	19.4	15.1
20-24	14.8	10.8	14.0
25-29	13.0	12.3	12.9
30-34	13.3	20.0	14.5
35-39	17.8	12.1	16.1
40-44	14.5	14.9	14.6
45-49	13.4	16.5	14.5
50-54	16.2	16.0	16.1
55-59	17.6	19.2	18.5
60-64	18.6	18.5	18.6
65-69	19.7	21.8	21.1
70-74	23.4	22.6	22.8
75-79	26.5	26.4	26.4
80-84	28.2	29.7	29.4
≥85	27.4	29.5	29.2

Length of stay in persons aged 50 and older (until 10 weeks)



Length of stay (weeks)

Age and sex specific number of hospitalisation days

Age class	Men	Women	Total
0-4	456	294	750
5-9	414	96	510
10-14	450	172	622
15-19	446	97	543
20-24	561	97	658
25-29	612	111	723
30-34	613	200	813
35-39	891	266	1157
40-44	1218	506	1724
45-49	1648	1173	2821
50-54	1618	1964	3582
55-59	2625	3683	6308
60-64	3759	7114	10873
65-69	6019	15275	21294
70-74	10944	28325	39269
75-79	17082	48988	66070
80-84	19248	74932	94180
≥85	22809	116983	139792
Total	91413	300276	391689

Discharge status after hospitalisation

Absolute numbers

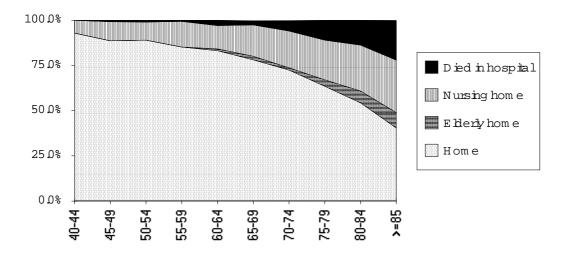
Discharge status	Men	Women	Total
home	2510	6643	9153
elderly home	153	840	993
nursing home	799	3044	3843
died in hospital	391	660	1051
left (own decision)	3	3	6
Total	3856	11190	15046

Percentages

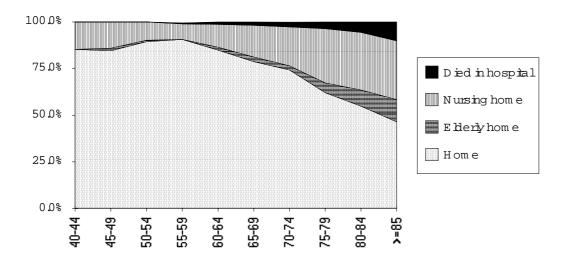
Discharge status	Men	Women	Total
home	65.1%	59.4%	60.8%
elderly home	4.0%	7.5%	6.6%
nursing home	20.7%	27.2%	25.5%
died in hospital	10.1%	5.9%	7.0%
left (own decision)	0.1%	0.0%	0.0%

After the acute episode, women go more often to a home for the elderly or to a nursing home than men, but in men the crude in-hospital mortality is almost twice that of women. The trends in discharge status are also strongly age dependent as can be seen in the next two figures.

Discharge status by age for men



Discharge status by age for women



Non-hip fractures

With respect to non-hip fractures, only the data for 1992 are readily available. As mentioned before, we need to be cautious while interpreting those data. These hospitalisations do not seem to reflect the typical osteoporosis related fracture pattern such as a high female/male ratio, and might be more related with high energy trauma. Most people with those fractures are indeed treated outside the hospital. The data are included here for the sake of completeness.

Hospital admissions for vertebral and forearm fractures in the Netherlands in 1992

	Total	≥65 years	≥65 year (%)	female/male ratio
Vertebrae	2586	977	37.8%	1.1
Forearm	4180	902	21.6%	1.0
Hip	14467	12583	87.0%	2.8

Non-hospital inpatient care (full care and day care)

Data for non-hospital inpatient care are obtained from the SIG data source. Data are collected for both full care as for day care in nursing homes. Data collection is relatively complete but less so than the hospitalisation data. Information is available for 89.9 % of nursing homes, corresponding to 92.8 % of the 'somatic' beds and 91.2 % of the 'psycho-geriatric' beds. Overall information is available from 92 % of the nursing home beds. ¹⁴ Patients with fractures are mainly (98%) treated in the somatic nursing home wards. To obtain a more accurate estimate of the absolute numbers for the Netherlands, we multiply the data from the SIG registration with a factor 1.08. For day care, the information is slightly less complete: information is available concerning 88.7% of 'somatic' beds and 89.5% of the 'psychogeriatric' beds. Overall information is available from 89.1% of the day care beds. For day care therefore, the multiplication factor used is 1.12.

In addition to the published data, files of all 1993 discharges (full care and day care) with admission diagnosis of hip- or other fractures were obtained and analysed. A complication here is that admission diagnosis is not coded with ICD-9 codes, but with a proprietary 'SIVIS' code. The codes that are of interest here are

- 17.01 Hip fracture
- 17.02 Other fractures (all other fractures that are reason for admission)
- 19.03 Status after hip fracture

 $\underline{Full\ care}$ Number of discharges in 1993 with admission diagnosis

Admission diagnosis	Men	Women	Total
Hip fracture	241	1013	1254
Other fractures	298	1091	1389
Status after hip fracture	521	2667	3188
Total	1060	4771	5831

Proportion of fracture patients vs. total population in nursing homes

When looking at the total population of people in nursing homes, the proportion of people with admission diagnose of fracture seems to be relatively stable. Two cross-sectional views at specific days are compared; one from our data analysis, the other from the published data.

Cross-sectional situation on December 31, 1993 (our analysis)

	Total po	pulation	Frac	ctures
Age class	Men	Women	Men	Women
0-44	425	373	9	13
45-54	386	394	5	15
55-64	960	957	35	41
65-74	2730	4270	99	295
75-84	5133	14750	227	1345
≥85	3156	15195	250	1914
Total	12790	35939	625	3623
	48729		42	248
Percentage of total			4.9%	10.1%
population			8.	7%

Cross-sectional situation on September 30, 1992 (published data)

Admission diagnosis	Total	Proportion of	Proportion of
		total population	all fractures
Hip fracture	1116	2.3%	26.9%
Other fractures	801	1.7%	19.3%
Status after hip fracture	2228	4.6%	53.8%
All fractures	4145	8.6%	100.0%
Hip fracture and status after	3344	6.9%	80.7%
Total population	48202	100.0%	

From those data we conclude that fractures account for about 8.7 % of the population of nursing homes. Over 80 % of these are admitted for hip fractures and its sequelae.

Applying the multiplication factor (1.08) described above, it is estimated that in 1993, respectively **4588** persons (4248*1.08), and **3702** (4248*1.08*80.7 %) have been treated daily in nursing homes for respectively fractures or hip-fractures and its sequelae.

It is important however to estimate the proportion of nursing home admissions that are directly related to fractures. Some of the patients might also have been admitted without a hip fracture because of comorbidity, while the hip fracture event is only the precipitating factor. Therefore, we analyse length of stay and discharge status.

Age and sex specific length of stay (days)

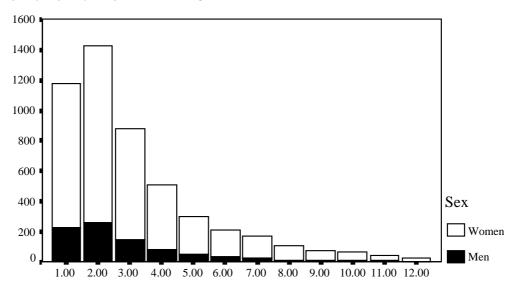
The average length of stay is approximately the same for both sexes: 238 (SD=553) for men and 241 (SD=553) for women (p=0.85). Median LOS is 67 days for men and 70 days for women. The high mean LOS and its high standard deviation are explained by the relatively large group of people that stay extremely long (up to 21 years). It is hypothesised that those long stays in nursing homes cannot solely be attributed to the hip-fracture but must largely be due to co-morbidity leading to a more dependent state.

Number of patients by length of stay and admission diagnosis (full care nursing home)

	0-3 months	4 months -	> 1 year	Total
		1 year		
Men				
Hip fracture	121	77	43	241
Other fractures	193	68	37	298
Status after hip fracture	329	116	76	521
Total men	643	261	156	1060
Women				
Hip fracture	512	299	202	1013
Other fractures	586	352	153	1091
Status after hip fracture	1744	612	311	2667
Total women	2842	1263	666	4771
Grand Total	3485	1524	822	5831

The majority of patients are discharged within 3 months. When those people that stay up to 3 months in the nursing home are considered separately, the average LOS are 41.6 days (SD=23.6) for men, and 44.0 days (SD=22.4) for women (p=0.02).

Length of stay in first year (full care nursing home)



Number of months

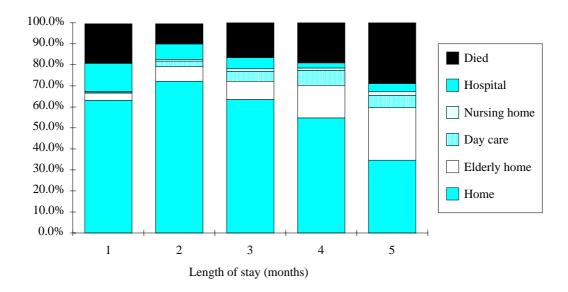
Discharge status

When looking at discharge status, we again treat those people that stay for a shorter period separately from those that stay longer. The majority of people that stay more than one year in a nursing home, stay there until they die (over 80 % in both men and women and for all diagnosis groups).

Those that stay for less then one year have a totally different discharge pattern. In general, about 60% of the people admitted to nursing home stay there for a maximum of 3 months. Over 70% of those return home afterwards, 8.6% die in the nursing home (men more then women, persons with hip fracture more then persons with other types of fracture). The rest goes primarily to homes for the elderly, or to a lesser degree to day care, hospital etc.

For longer stays, the discharge status changes: gradually more people are dying and less people are going home. At 4 months LOS the percentage going home drops to 54.8 %, after 5 months to 34.6 %. These persons with longer stays clearly represent a more dependent group of people, with more concomitant illnesses. On the basis of the length of stay and discharge patterns, we hypothesise that only the first few months of stay in a nursing home represent the direct effect of osteoporosis and fractures. Therefore, we include only the first three months of stay in the nursing home in the calculation of costs.

Discharge patterns in first 5 months of LOS (full care nursing home)



Discharges after 1 - 3 months (full care nursing home)

		N	Ien		Women					
Status	Hip fr.	Other fr.	Post hip fr.	Total	Hip fr.	Other fr.	Post hip fr.	Total		
Died	24	18	52	94	89	44	111	244		
Home	70	134	226	430	311	429	1365	2105		
Day care	6	4	5	15	5	9	31	45		
Hosp	7	24	27	58	25	23	71	119		
Nursing home	3	1	1	5	10	7	12	29		
Home for the elderly	11	10	18	39	71	72	151	294		
Other					1		1	2		
Unknown		2		2		2	2	4		
Total	121	193	329	643	512	586	1744	2842		

Discharges after 1 - 3 months (percentages - full care nursing home)

		N	Ien		Women				
Status	Hip fr.	Other fr.	Post hip fr.	Total	Hip fr.	Other fr.	Post hip fr.	Total	
Died	19.8%	9.3%	15.8%	14.6%	17.4%	7.5%	6.4%	8.6%	
Home	57.9%	69.4%	68.7%	66.9%	60.7%	73.2%	78.3%	74.1%	
Day care	5.0%	2.1%	1.5%	2.3%	1.0%	1.5%	1.8%	1.6%	
Hosp	5.8%	12.4%	8.2%	9.0%	4.9%	3.9%	4.1%	4.2%	
Nursing home	2.5%	0.5%	0.3%	0.8%	2.0%	1.2%	0.7%	1.0%	
Home for the elderly	9.1%	5.2%	5.5%	6.1%	13.9%	12.3%	8.7%	10.3%	
Other	0.0%	0.0%	0.0%	0.0%	0.2%	0.0%	0.1%	0.1%	
Unknown	0.0%	1.0%	0.0%	0.3%	0.0%	0.3%	0.1%	0.1%	

Discharges after 4 months - 1 year (full care nursing home)

		N	Ien			Wo	men	
Status	Hip fr.	Other fr.	Post hip fr.	Total	Hip fr.	Other fr.	Post hip fr.	Total
Died	28	13	35	76	71	64	118	253
Home	25	42	35	102	114	162	271	547
Day care	4	4	9	17	8	6	26	40
Hosp	4	2	7	13	4	8	22	34
Nursing home	1	1	4	6	10	8	11	29
Home for the elderly	15	6	26	47	90	104	162	356
Other							1	1
Unknown					2		1	3
Total	77	68	116	261	299	352	612	1263

Discharges after 4 months - 1 year (percentages - full care nursing home)

		N	I en		Women				
Status	Hip fr.	Other fr.	Post hip fr.	Total	Hip fr.	Other fr.	Post hip fr.	Total	
Died	36.4%	19.1%	30.2%	29.1%	23.7%	18.2%	19.3%	20.0%	
Home	32.5%	61.8%	30.2%	39.1%	38.1%	46.0%	44.3%	43.3%	
Day care	5.2%	5.9%	7.8%	6.5%	2.7%	1.7%	4.2%	3.2%	
Hosp	5.2%	2.9%	6.0%	5.0%	1.3%	2.3%	3.6%	2.7%	
Nursing home	1.3%	1.5%	3.4%	2.3%	3.3%	2.3%	1.8%	2.3%	
Home for the elderly	19.5%	8.8%	22.4%	18.0%	30.1%	29.5%	26.5%	28.2%	
Other	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.2%	0.1%	
Unknown	0.0%	0.0%	0.0%	0.0%	0.7%	0.0%	0.2%	0.2%	

Discharges after > 1 year (full care nursing home)

		M	I en		Women				
Status	Hip fr.	Other fr.	Post hip fr.	Total	Hip fr.	Other fr.	Post hip fr.	Total	
Died	35	28	64	127	171	117	267	555	
Home	3	4	4	11	3	8	9	20	
Day care		1	1	2				0	
Hosp	1		3	4	7	6	11	24	
Nursing home	0		2	2	7	4	6	17	
Home for the elderly	3	4	2	9	14	18	18	50	
Other				0				0	
Unknown	1			1				0	
Total	43	37	76	156	202	153	311	666	

Discharges after > 1 year (percentages - full care nursing home)

		M	Ien		Women					
Status	Hip fr.	Other fr.	Post hip fr.	Total	Hip fr.	Other fr.	Post hip fr.	Total		
Died	81.4%	75.7%	84.2%	81.4%	84.7%	76.5%	85.9%	83.3%		
Home	7.0%	10.8%	5.3%	7.1%	1.5%	5.2%	2.9%	3.0%		
Day care	0.0%	2.7%	1.3%	1.3%	0.0%	0.0%	0.0%	0.0%		
Hosp	2.3%	0.0%	3.9%	2.6%	3.5%	3.9%	3.5%	3.6%		
Nursing home	0.0%	0.0%	2.6%	1.3%	3.5%	2.6%	1.9%	2.6%		
Home for the elderly	7.0%	10.8%	2.6%	5.8%	6.9%	11.8%	5.8%	7.5%		
Other	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%		
Unknown	2.3%	0.0%	0.0%	0.6%	0.0%	0.0%	0.0%	0.0%		

Age and sex specific number of nursing home days

Here we assume that the total number of nursing home days can be estimated by including all registered nursing home days and applying the 1.08 correction coefficient for the nursing homes that were not registered.

Corrected number of nursing home days for men (full care nursing home)

		Hip 1	fracture			Other	fracture		Sta	Status post hip fracture			
Age	1-3	4-12	>1 year	Total	1-3	4-12	>1 year	Total	1-3	4-12	>1 year	Total	
class	Mo	Mo			Mo	Mo			Mo	Mo			
0-49	178	123	399	700	2253	1913	691	4857	402	0	1155	1556	
50-54	118	210	0	327	257	225	6312	6793	105	138	0	243	
55-59	117	318	8252	8686	383	1048	436	1867	384	302	0	687	
60-64	159	265	0	423	478	648	0	1126	699	400	0	1098	
65-69	488	808	433	1729	804	588	775	2166	1018	2177	4929	8125	
70-74	870	819	3618	5307	744	657	17301	18701	2257	2610	14386	19253	
75-79	1109	3167	13209	17485	1242	2382	1450	5075	2394	3078	14210	19682	
80-84	1536	3840	16011	21387	1105	3110	11789	16005	3198	4407	18642	26247	
≥85	1673	4268	22019	27960	1703	2289	11119	15110	3201	7753	28784	39739	
Total	6248	13816	63941	84006	8969	12858	49873	71701	13659	20867	82105	116630	

Corrected number of nursing home days for women (full care nursing home)

		Hip fracture				Other fracture S			St	tatus post hip fracture		
Age	1-3	4-12	>1 year	Total	1-3	4-12	>1 year	Total	1-3	4-12	>1 year	Total
class	Mo	Mo			Mo	Mo			Mo	Mo		
0-49	91	253	0	343	1004	805	0	1809	484	609	407	1500
50-54	53	0	0	53	387	828	0	1215	348	204	0	552
55-59	96	468	0	564	492	923	0	1416	950	740	970	2660
60-64	297	430	1241	1968	1143	2131	7667	10940	2739	2432	1732	6903
65-69	1385	1011	4103	6498	2885	3729	1783	8397	5800	3684	4801	14284
70-74	3373	5256	12923	21552	3734	6917	12369	23020	11758	9687	23872	45317
75-79	5307	10205	36988	52500	6803	10882	37648	55333	17551	21449	57036	96036
80-84	6687	15867	94698	117252	7158	16093	43242	66493	18835	30015	148240	197090
≥85	9199	22387	118526	150112	7384	20277	87482	115143	19037	37979	186786	243802
Total	26488	55877	268478	350843	30990	62586	190191	283767	77502	106799	423844	608145

<u>Day care</u>

Number of discharges from day care in 1993 with admission diagnosis

Admission diagnosis	Men	Women	Total
Hip fracture	24	82	106
Other fractures	16	47	63
Status after hip fracture	50	178	228
Total	90	307	397

Proportion of fracture patients vs. total population in day care

When looking at the total population of people in day care, the proportion of people with admission diagnose of fracture again seems to be relatively stable. Two cross-sectional views are compared; one from our data analysis, the other from published data.

Cross-sectional situation on 31 December 1993 (our analysis)

	Total p	opulation	Frac	ctures	
Age class	Men	Women	Men	Women	
0-44	56	57	2	0	
45-54	111	102	3	2	
55-64	365	251	3	5	
65-74	1045	888	18	37	
75-84	1257	1662	35	66	
>=85	345	781	10	32	
Total	3179	3741	71	142	
	69	920	213		
Percentage of total			2.2%	3.8%	
population			3.	1%	

Cross-sectional situation on 30 September 1992 (published data)

Admission diagnosis	Total		Proportion of	Proportion of
			total population	all fractures
Hip fracture		42	0.6%	20.8%
Other fractures		32	0.5%	15.8%
Status after hip fracture		128	1.9%	63.4%
All fractures		202	3.0%	100.0%
Hip fracture and status after		170	2.5%	84.2%
Total population		6682	100.0%	

From those data we conclude that fractures account for about 3.1 % of the population of day care. About 85 % of these fractures are hip fractures and its sequelae.

Applying the multiplication factor (1.12) described above, it is estimated that in 1993, respectively **239** persons (213*1.12), and **201** (213*1.12*84.2 %) have been treated daily in day care for respectively fractures or hip-fractures and its sequelae.

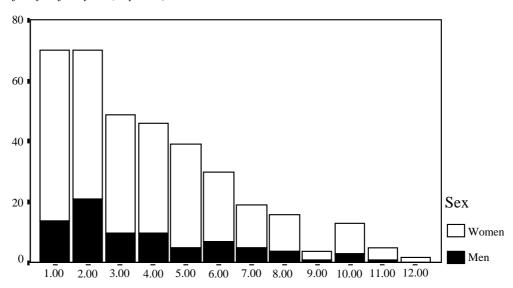
Age and sex specific length of stay (days)

The average length of stay is 201 (SD=416) for men and 151 (SD=215) for women (p=0.27). Median LOS is 86 days for men and 97 days for women. The high averages combined with a high standard deviation (especially in men), are explained by the relatively large group of people that stay long in day care.

Number of patients by length of stay and admission diagnosis (day care)

	0-3 months	4 months -	> 1 year	Total
		1 year		
Men	45	36	9	90
Women	144	138	25	307
Total	189	174	34	397

Length of stay in first year (day care)



Number of months

Age and sex specific number of day care days

We estimate the total number of day care days on the basis of the registered nursing home days and by applying the 1.12 correction coefficient for the nursing homes that were not registered.

Corrected number of day care days for men (day care)

		Hip f	racture			Other fracture				Status post hip fracture			
Age	1-3	4-12	>1 year	Total	1-3	4-12	>1 year	Total	1-3	4-12	>1 year	Total	
class	Mo	Mo			Mo	Mo			Mo	Mo			
0-49					80			80	56			56	
50-54									19			19	
55-59					36			36					
60-64		246		246						197	1472	1669	
65-69	161			161	43			43	116	146	6128	6390	
70-74	76	853		930	164			164	103	1191		1294	
75-79	78	472		550	157	300	1468	1925	234	1934	456	2624	
80-84	123	429	741	1294	48			48	304	479		783	
≥85	161	105		257	47			45	205	690	768	1604	
Total	600	2106	741	3438	573	300	1468	2340	1037	4637	8823	14438	

Corrected number of day care days for women (day care)

		Hip f	fracture			Other fracture			Status post hip fracture			
Age	1-3	4-12	>1 year	Total	1-3	4-12	>1 year	Total	1-3	4-12	>1 year	Total
class	Mo	Mo			Mo	Mo			Mo	Mo		
0-49						308		308				
50-54										159		159
55-59					73			73	27	151		178
60-64		307		307		457	1159	1616	131	890		1021
65-69	224	893		1117					146	691	3511	4348
70-74	109	1468	3249	4826	198	365	418	981	909	1432		2342
75-79	309	625	911	1845	460	2043	653	3156	840	4351	2140	7332
80-84	545	2262	684	3492	143	1173		1316	1095	2549	3464	7109
≥85	599	2126	627	3232	188	707	904	1734	727	3152	1303	4996
Total	1786	7681	5471	14819	1063	5052	3134	9185	3875	13376	10418	27485

Outpatient care

Outpatient care is not systematically registered in the Netherlands. For General Practitioners, there are a series of surveys, but those deal primarily with the typical GP pathology and they allow no estimate of fracture- or osteoporosis-related number of contacts. For the assessment of the direct cost of outpatient care, we use published cost estimates.

Home health care

The number of clients of home health care and the number of contacts is estimated on the basis of data available for the Rotterdam district. No specific information is available on clinical indication for home health care. To estimate the maximum possible home health care consumption for hip fractures in the Netherlands, we take the number of patients that go home after discharge from hospital. Next we assume that they all need home health care. We conclude that at the maximum about 5 % of the total home health care can be allocated to hip fractures.

Estimate of the maximum use of home health care after hip fracture in the Netherlands

Age	Nbr of clients in	Nbr of	Nbr of hip	Proportion	Returning home	Proportion
class	home health care	contacts	fractures		after hip fracture.	
60-64	12715	452584	586	4.6%	494	3.9%
65-69	20788	823545	1007	4.8%	791	3.8%
70-74	29699	1151326	1719	5.8%	1268	4.3%
75-79	34587	1501128	2499	7.2%	1560	4.5%
80-110	74612	1236997	8001	10.7%	3935	5.3%
Total	172401	5165580	13812	8.0%	8048	4.7%

4.3. Proportionate mortality

Total mortality, all cause by age and sex in the Netherlands

Absolute numbers (1992)⁵

· <u>·</u> /			
Age class	Men	Women	Total
0-44	4630	2805	7435
45-54	3736	2362	6098
55-64	8231	4526	12757
65-74	17132	10102	27234
75-84	20899	20384	41283
≥85	11636	23444	35080
Total	66264	63623	129887

Age specific mortality (mortality/1000)

Age class	Men	Women	Total
0-44	0.91	0.58	0.75
45-54	3.82	2.52	3.18
55-64	11.79	6.26	8.97
65-74	33.88	15.89	23.86
75-84	88.76	49.13	63.48
≥85	224.74	165.08	181.02
Total	8.79	8.26	8.52

Osteoporosis mortality by age and sex

Osteoporosis related mortality is due to fractures, mainly hip fractures. Mortality following hip fractures is high and age dependent. Attributing death to fractures however is not easy. Hip fractures may be associated with death in various ways and official death certification does not necessarily reflect the underlying cause. Therefore, it is felt that official death certification is in no way sufficient to indicate the real death toll of osteoporosis. Excess mortality after hip fracture needs to be looked upon. In addition of the official death certification data, mortality data from a follow-up study in the Netherlands (Utrecht) are included.

Official death certification data for 1993 with death due to an external cause associated with hip-fracture (and a few death with primary cause osteoporosis).

Men	and	women
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	Primary cause of death	0-44	45-54	55-64	65-74	75-84	≥85	Total
E826	Pedal cycle accident				1			1
E880	Fall on stairs or steps				1			1
E884	Other falls one level to other					1	4	5
E885	Fall on level-tripping					4	6	10
E887	Fracture, cause unspecified				33	244	563	840
E888	Fall unspecified /unclassifiable			1	5	26	45	77
Total ex	xternal causes of death		1	1	40	275	618	934
7330	Osteoporosis		1		1	10	14	26
Grand 7	Гotal		2	1	41	285	632	960

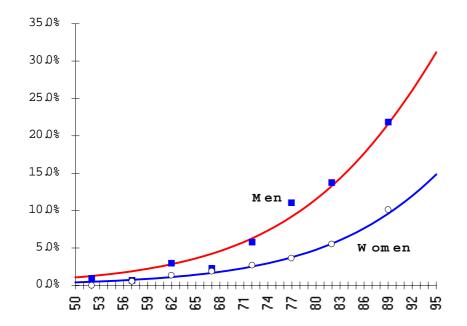
Men								
	Primary cause of death	0-44	45-54	55-64	65-74	75-84	≥85	Total
E826	Pedal cycle accident				1			1
E884	Other falls one level to other						2	2
E885	Fall on level-tripping					2	3	5
E887	Fracture, cause unspecified				16	91	136	243
E888	Fall unspecified /unclassifiable			1	3	9	17	30
Total e	xternal causes of death			1	20	102	158	281
7330	Osteoporosis					4	3	7
Grand '	Гotal			1	20	106	161	288
Women								
	Primary cause of death	0-44	45-54	55-64	65-74	75-84	≥85	Total
E880	Fall on stairs or steps				1			1
E884	Other falls one level to other					1	2	3
E885	Fall on level-tripping					2	3	5
E887	Fracture, cause unspecified				17	153	427	597
E888	Fall unspecified /unclassifiable				2	17	28	47
Total e	xternal causes of death		1		20	173	460	653
7330	Osteoporosis		1		1	6	11	19
Grand '	Total		2		21	179	471	672

Those numbers need to be interpreted with great care. As said before, they do not reflect the increased mortality after hip fracture. In fact, combined with the number of hip fractures in the Netherlands, they show lower mortality rates after hip fracture than in the population at large. Therefore, those data are insufficient to describe mortality associated with hip fractures.

Dutch follow-up data on mortality after hip fracture

In our data, we observe an overall in-hospital mortality of 10.1 % for men and 5.9 % for women. This in-hospital mortality is strongly age dependent, rising from almost non-existent at younger ages to 22% for men and 10 % for women in the highest age group. Mortality in men is twice as high as in women for all age groups.

In-hospital mortality after hip fracture (observed values in 5 year age classes, and calculated regression curves)



We cannot correctly assess mortality after hospitalisation from our data, although we do present some information on mortality in nursing homes. For a better idea of the mortality after hip fracture, we need follow-up data. Boereboom et al. studied 493 patients with a hip fracture during the period 1982-1984 in three hospitals in Utrecht. In-hospital mortality was similar to our findings with 9.1 % of the patients dying during hospitalisation. One year after the hip fracture, 23.6 % of the women and 33 % of the men had died.

Mortality was highest during the first 8 weeks after the hip fracture and strongly age and sex dependent. Relative risk of dying for men was 1.88 (95% CI 1.40-2.53) compared to women. Concomitant illness and hospital complications were also shown to be related with mortality. When looking at the official cause of death mentioned on the death certificate, it was found that in only 19 % of the women and 25 % of the men, hip fracture was mentioned as cause of death.

Mortality after hip fracture is strongly elevated in the months following the event, especially in men. One should be careful however not to attribute all of this excess mortality exclusively to the hip fractures. Patients with a hip fracture more often have concomitant illnesses and a poor general condition. This condition in itself can increase the risk of falling and the perioperative risk. This condition can also impair the rehabilitation after the treatment and hamper the mobilisation.

4.4. Assessment of direct medical cost for osteoporosis and fractures

To assess the medical cost of osteoporosis and fractures, we use two separate approaches. In the first (global approach) we use published Dutch cost estimates for hip, forearm and vertebral fractures. Those estimates are combined with our incidence figures. In a second approach, the detailed costs of medical consumption related to osteoporosis and fractures are calculated, based on the medical consumption described in this report.

Global approach

In a 1993 iMTA report, Al et al. estimate the cost of hip, vertebral and forearm fractures. ¹⁷ Costs for hospital treatment, complications, home care, physiotherapy and GP visits are estimated. Nursing home care was not included in this iMTA estimate, since it was argued that the fracture very often is but the trigger, rather than the cause of the entrance into a nursing home. The demand for home health care was used as a proxy for the additional help needed. For vertebral fractures, we use the cost for clinically diagnosed fractures, since the incidence figures only reflect this category of vertebral fractures.

Costs for fractures

Hip fracture	f 22919
Vertebral fracture	f 2295
Forearm fracture	f 1859

We apply those costs to the (partly estimated) 1993 incidence figures for the Netherlands. For this part of the analysis, we consider only fractures at the age of 50 and older, the age of 50 being an arbitrary cut-off point for osteoporotic fractures.

Hip fractures (million f)

Age class	Men	Women	Total
50-54	2.29	2.82	5.11
55-59	3.41	4.40	7.82
60-64	4.63	8.80	13.43
65-69	7.01	16.07	23.08
70-74	10.73	28.67	39.40
75-79	14.76	42.52	57.28
80-84	15.65	57.83	73.48
≥85	19.05	90.85	109.90
Total	77.54	251.95	329.49

Vertebral fractures (million f)

Age class	Men	Women	Total
50-54	0.57	1.15	1.72
55-59	0.69	2.08	2.77
60-64	0.31	2.33	2.64
65-69	0.93	3.59	4.52
70-74	0.79	4.34	5.13
75-79	1.59	5.15	6.74
80-84	0.84	4.95	5.78
≥85	1.58	3.95	5.53
Total	7.30	27.53	34.83

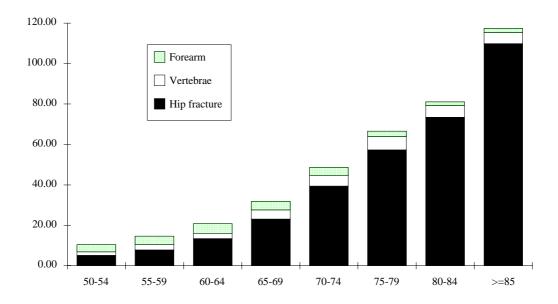
Forearm fractures (million f)

Age class	Men	Women	Total
50-54	0.93	2.69	3.62
55-59	0.63	3.36	3.99
60-64	0.46	4.26	4.72
65-69	0.60	3.56	4.16
70-74	0.37	3.71	4.09
75-79	0.31	2.30	2.61
80-84	0.13	1.72	1.85
≥85	0.08	1.85	1.92
Total	3.50	23.46	26.96

Global estimated costs for hip, vertebral and forearm fractures (million f)

329.49
34.83
26.96
391.28

Global age-specific estimated costs for hip, vertebral and forearm fractures (million f)



Detailed approach

In this detailed approach, the analysis is again limited to persons 50 years of age and older. It is clear that not all of those fractures are osteoporosis related, and that even those that are, can not all be prevented. The next section gives an overview of total cost; the preventable cost will evidently depend on the effectiveness of the proposed preventive measures.

The choice of the costs corresponding with one day of hospitalisation, one contact, etc. are based on the Dutch guidelines for cost calculations in health care.¹⁸ The costs per person-year of pharmacotherapy are calculated based on cost information in the *Pharmacotherapeutisch kompas* ¹⁹ and on the recommended dosage.

Pharmacotherapy

	1993 person years	Price (f) per	1993 total cost
	(x1000)	person year	(million f)
Didrokit	18.6	543.2	10.11
Calcium Forte	11.7	173.2	2.03
Calcium	5.8	169.3	0.98
Fortissimum			
Cacit 500	5.0	173.2	0.87
Etalpha	0.9	559.9	0.51
Didronel	0.2	414.7	0.08
Progynova	1.2	164.8	0.20
Decadurabolin	0.4	203.9	0.09
Devaron	5.3	32.9	0.18
Premarin	0.3	259.8	0.08
Procal	0.5	19.7	0.01
Zumenon	0.2	195.4	0.03
Estraderm TTS	1.3	242.2	0.32
Dohyfral AD3	9.1	16.2	0.15
Total	60.6		15.63

Hospitalisations for hip fractures

To assess the direct cost of hip fracture hospitalisation, the number of hospitalisation days for persons over age 50, are combined with an average daily price for hospitalisation of f 773.

Direct cost of hip fracture hospitalisation (million f)

Age class	Men	Women	Total cost
50-54	1.25	1.52	2.77
55-59	2.03	2.85	4.88
60-64	2.91	5.50	8.40
65-69	4.65	11.81	16.46
70-74	8.46	21.90	30.35
75-79	13.2	37.87	51.07
80-84	14.88	57.92	72.80
≥85	17.63	90.43	108.06
Total	65.01	229.79	294.80

Hospitalisations for non-hip fractures

Hospitalisation for non-hip fractures can be estimated from 1992 figures. We only have the proportion of persons aged 65 and older. This means we disregard the patients aged between 50 and 64 which probably leads to an underestimation. On the other hand, those fractures will also include non-osteoporosis related fractures, leading to an overestimation.

For the reasons mentioned in the corresponding chapter, it is unclear whether or not those figures should be included in an estimate of the cost of osteoporosis. We include them here for the sake of completeness in the maximum cost estimate.

Average length of stay in 1992 was 5.7 for forearm fractures and 17.2 for vertebral fractures. 11

Direct cost of non-hip hospitalisations (patients ≥65 years) in 1992

	Total	≥65 years	days	Total cost
Vertebrae	2586	977	16804	12.99
Forearm	4180	902	5141	3.97
Total	6766	1879	21945	16.96

Non-hospital inpatient care (full care)

It would be an overestimation to include all nursing home patient days. Fracture can be the trigger that changes a borderline independent state into a dependent state of life, for people who would anyhow arrive in a nursing home. As argued in the chapter on nursing homes, we only consider the first three months of stay in a nursing home, in the calculation of the cost. It should be clear that using the cut-off point of 3 months is an arbitrary choice, but a choice that is based upon the arguments developed in the discussion on length of stay and discharge status.

An average daily price for nursing home care of f 209 is used.

Direct cost of nursing home care for fractures (million f)

	Men			Women			Total cost			Grand Total
	Hip	Other	Post	Hip	Other	Post	Hip	Other	Post	All fractures
Age class	fr.	fr.	hip fr.	fr.	fr.	hip fr.	fr.	fr.	hip fr.	
50-54	0.07	0.12	0.04	0.01	0.18	0.11	0.08	0.30	0.16	0.53
55-59	0.09	0.20	0.12	0.06	0.19	0.32	0.15	0.39	0.44	0.98
60-64	0.05	0.16	0.19	0.14	0.57	0.88	0.20	0.73	1.07	2.00
65-69	0.23	0.25	0.50	0.52	1.12	1.79	0.74	1.37	2.29	4.40
70-74	0.33	0.42	0.95	1.45	1.83	3.92	1.77	2.25	4.87	8.89
75-79	0.75	0.51	1.14	2.82	3.19	7.05	3.57	3.70	8.19	15.46
80-84	1.02	0.83	1.55	4.39	4.22	9.42	5.41	5.05	10.97	21.43
≥85	1.17	0.81	2.21	6.42	5.29	11.50	7.59	6.10	13.72	27.41
Total	3.70	3.30	6.71	15.80	16.59	35.00	19.50	19.89	41.70	81.10

Non-hospital inpatient care (day care)

For the same reason as with the nursing homes, only the first 3 months of day care are included in the calculation of the cost. An average daily price for day care of f 122 is used.

Direct cost of day care for fractures (million f)

	Men			Women			Total			Grand Total
	Hip	Other	Post	Hip	Other	Post	Hip	Other	Post	All fractures
Age class	fr.	fr.	hip fr.	fr.	fr.	hip fr.	fr.	fr.	hip fr.	
50-54	0.000	0.000	0.002	0.000	0.000	0.012	0.000	0.000	0.015	0.015
55-59	0.000	0.004	0.000	0.000	0.009	0.016	0.000	0.013	0.016	0.029
60-64	0.012	0.000	0.037	0.025	0.037	0.066	0.037	0.037	0.103	0.178
65-69	0.020	0.005	0.064	0.065	0.000	0.105	0.084	0.005	0.169	0.259
70-74	0.059	0.020	0.087	0.138	0.062	0.223	0.197	0.082	0.311	0.589
75-79	0.047	0.057	0.166	0.113	0.181	0.389	0.160	0.237	0.555	0.952
80-84	0.052	0.006	0.074	0.216	0.080	0.408	0.269	0.086	0.483	0.837
≥85	0.032	0.006	0.062	0.248	0.098	0.351	0.280	0.104	0.413	0.797
Total	0.223	0.098	0.494	0.804	0.467	1.571	1.027	0.564	2.065	3.656

Outpatient care

No hard data on the outpatient care for osteoporosis related fractures are available for the Netherlands. In the absence of those data we use the assumptions for outpatient care from Al et al. ¹⁷ that are also used in the global approach.

For *hip fractures*, they assume that patients have on the average 2 GP visits after the discharge from hospital and that 50 % of the patients have an average of 12 treatment sessions by a physiotherapist. This leads to a global outpatient care price of f 319 per hip fracture.

For *vertebral fractures*, they assume that 5 out of 6 of the total number of clinically diagnosed patients are treated by the GP. 5 GP visits, one specialist visit (including an X ray) and 12 treatment sessions by a physiotherapist are assumed with a total cost of f 1204, leading to an outpatient cost of f 1003 per vertebral fracture.

For *forearm fractures*, they assume that 95 % of patients are treated in the outpatient clinic with a total cost of f 1658. This lead to a cost per forearm fracture of f 1575.

Although those assumptions are arbitrary, they are thought to give a good approximation of the mean cost of the outpatient consumption. Furthermore, a sensitivity analysis showed that the impact of the outpatient care uncertainty on the total cost is limited.

Taking the same incidence figures as in the global approach, this leads to the following cost.

Global estimated costs for outpatient care for hip, vertebral and forearm fractures (million f)

Hip fracture	4.59
Vertebral fracture	15.23
Forearm fracture	22.84
Total	42.66

Home health care

Based on the assumptions made in the chapter on Home health care, we can calculate maximum possible cost for home health care related to hip fractures. In order to do so, we use a price of f 55 per contact.

Estimated maximum possible cost for home health care after hip fracture (million f)

	Nbr of	Max %	Maximum nbr. of hip	Cost
	contacts		fract. related contacts	
60-64	452584	3.9%	17584	0.97
65-69	823545	3.8%	31337	1.72
70-74	1151326	4.3%	49156	2.70
75-79	1501128	4.5%	67706	3.72
80-110	1236997	5.3%	65239	3.59
Total	5165580		231021	12.71

Overview of the detailed approach

Detailed overview of costs for osteoporosis treatment in the Netherlands in 1993 (million f)

	Estimated yearly cost
Pharmacotherapy	15.63
Hospitalisations hip fractures	294.80
Non-hospital inpatient care (full care)	81.10
Day care	3.66
Outpatient care	42.66
Total (excluding maximum estimates)	437.85
Hospitalisations non-hip fractures (max. est.)	16.96
Home health care (maximum estimate)	12.71
Total (including maximum estimates)	467.52

5. Conclusions

Prevalence and incidence

Osteoporosis and fractures are a major source of illness and health care costs in the Netherlands, both today as in the foreseeable future. Especially the most serious consequence, hip fracture, is frequent and the incidence is increasing. Both in men and women, the incidence increases exponentially with age. Men reach the same hip fracture incidence at an age 5-6 year older than women. An 80-year-old male has the same hip fracture risk as a 75-year-old female.

The total number of hip fractures will inevitable rise if no serious prevention efforts are undertaken. An upward time trend in age-adjusted hip fracture rates, as well as the ageing of the population are responsible for this. Several possible explanations for the upward trend have been suggested, such as the decreasing physical activity and sedentary live style, nutrition, or even the fact that people are growing taller than before. In the US, Sweden, and the UK, this upward trend of age-adjusted hip fractures seems to have levelled off. In other places such as Hong Kong and, as we show, also in the Netherlands, the rates are still increasing. While it is difficult to predict the evolution of this trend in this country, the ageing of the population is sure. Even when current incidence rates remain stable in the future, the total number of hip fractures will double by the year 2050 to over 30.000 per year.

Non-hip fracture incidence rates are more difficult to obtain and we derive them from international data. But, since we focus on cost and personal illness burden, non-hip fractures appear to be less relevant.

Prevention

For the prevention of osteoporotic fractures it is important to know who are at risk as well as which preventive strategy is effective for the different risk categories. The parameter that is most commonly used nowadays to determine fracture risk is bone mineral density (BMD). Cummings et al. found an age-adjusted relative risk for hip fracture of 2.6 per SD decrease in femoral neck bone density. Bone density at the hip is also more strongly related to the risk of hip fracture than bone density measured at other sites. A limitation of the follow-up studies carried out until today is the short follow-up time.

The observed and relatively modest decline in bone density with age can however not fully explain the exponential increase of hip fracture incidence with age. This suggests that also other factors are important contributors to the fracture risk, namely the previously mentioned bone quality and the propensity to fall.

Prevention only focussed on bone mineral density will thus do nothing to prevent the hip fractures caused by the above mentioned factors. An additional effect of therapy on bone quality can be important and the intervention should certainly not have adverse effects on bone quality, as suggested in some studies of high-dose sodium fluoride.²⁰

The cost-effectiveness of interventions is further influenced by other effects apart from the effect on bone strength, such as in the oestrogen supplementation scenarios. In a recent report from the Study of Osteoporotic Fractures Research Group, its authors conclude that estrogen prevents fractures not only by preserving bone mass but also by other additional mechanisms.²¹ Effects on muscle strength and neuromuscular function have been suggested, as well as effects on co-morbidity and cardiovascular function, but this is still under debate.^{22,23,24}

Reducing the frequency and severity of falls, and the use of external protective devices, together with physical exercise and other lifestyle interventions, have also been looked at as additional intervention possibilities.

Another problem of intervention solely focused on bone mineral density is the timing. Hip fractures incidence only rises above 1 % after the age of 80 for women and 85 for men. When the moment of intervention is at or soon after the menopause, we can expect that even with effective therapeutic strategies, the compliance with medication will be poor. If possible, it would be preferable to bring the preventive intervention nearer to the adverse outcome.

Mortality

Although hip fractures occur less frequently in men, their mortality after a hip fracture is more important. We found an in-hospital mortality that is twice that of women. Mortality is also strongly age dependent and related to concomitant illnesses and in-hospital complications. Published follow-up data show that mortality after hip fracture is strongly elevated in the first few months following the event, but the available data for the Netherlands do not allow a more precise estimate of the duration of the excess mortality.

One should be careful not to attribute exclusively all of this excess mortality to hip fractures. Patients with a hip fracture more often have concomitant illnesses and a poor general condition. This condition in itself can increase the risk of falling and the perioperative risk. This situation can also impair the rehabilitation after treatment and hamper mobilisation.

Health care utilisation

Osteoporosis and fractures are an important cause of health care consumption. Hip fractures as a rule lead to long hospitalisation with a mean length of stay of 26 days. Forearm and vertebral fractures are most frequently treated in an outpatient setting. People over age 85, representing less than 2 % of the population nevertheless cause over one third of the hospitalisation days for hip fractures. This is due both to the exponential increase of hip fracture with age, and to the longer length of stay. With an ageing population this will only deteriorate.

After the acute phase and the hospitalisation, nursing home care is often needed. Using *hospital data*, we see that 21 % of men and 27 % of women are discharged directly into nursing homes. This difference can partly be explained by the higher in-hospital mortality of men. In the *nursing home data* we see a similar number of men being admitted, but there are more women entering (about 33 % of the hip fractures). Apparently, some of the women return to their homes first, but are afterwards transferred to a nursing home. Nursing home stays can be very long, but the majority of patients leave the nursing home within 3 months. We presume that stays longer than 3 months are not related anymore to the hip fracture that leads to the admission. We use the same approach dealing with day care cost.

Other health care consumptions are home health care and outpatient care. Hard data about those activities are scarce and we make an attempt to estimate them using indirect information. Their contribution to the total cost of osteoporosis is substantial but secondary to hospital and nursing home cost. Drug use is also relatively unimportant for the total cost.

Cost

In this study we estimate the direct cost associated with fractures at older age. The majority of these fractures are osteoporosis related, but not all. A clear indication of the fact that most of these fractures are osteoporosis related is found in the observation that incidence increases exponentially with age. It is not possible to differentiate between osteoporotic fractures and non-osteoporotic fractures but we believe that the impact of the latter category is small.

The cost of osteoporosis is mainly the cost of hip fractures. It is this cost we could determine most accurately. In comparison, the cost of other fractures and the current cost of pharmacotherapy is low. We use two approaches to come to a global yearly cost of osteoporosis and fractures in the population aged 50 and over. The results of both the global and the detailed approach are comparable, and indicate a yearly cost between f 390 and f 470 million. The main difference between both approaches lies in the cost of nursing home care (non-hospital inpatient care). Nursing home care is not included in the global approach. In the detailed approach, we assume that only the first three months of nursing home care should be attributed to the fracture, the remainder being due to co-morbidity and frailty.

The medication cost of osteoporosis is difficult to ascertain, and the validity of the IMS data is not clear. It is however the only currently available source. It appears that the cost of medication is minor, compared to the cost of clinical treatment of the fractures.

We do not include indirect costs as osteoporosis mainly affects the elderly and their production losses can be neglected.

When comparing this cost with international figures, we find both higher and lower estimates. Several studies indicate a cost of US\$ 7 - 10 billion for the United States resulting in a yearly cost per capita of f 50 - 70 for osteoporosis and hip fractures. Our maximum global cost estimate of f 457 million is the equivalent of f 30 per head of the population. The US estimates however do include the indirect costs that we choose not to include. The estimates for France are lower, with a global cost of FF 3.5 billion and a per capita cost of f 20.

Further research

For this report, no primary data collection was done. Therefore, some of the fundamental questions will remain open, without additional research being done.

The bone mineral density data in this report are *cross-sectional*. Currently there are no prospective data about the predictive value of BMD measurements in the Netherlands. The *Rotterdam study* will, over time, provide these follow-up data on BMD evolution and fractures.

Osteoporosis is influenced by *various risk factors*, and it progresses silently for decades before fractures occur. Bone density can be measured directly, whereas other risk factors are measured by using age as a proxy. In general there are no symptoms prior to the fracture, making osteoporosis difficult to diagnose before an event occurs. In order to prevent them, we need to know who is most likely to experience a

major fracture and when this is most likely to occur. An additional problem is the fact that eventually all people are at high risk given they live long enough.

Clinical trials should not only focus on an intermediate outcome such as BMD, but must be designed to show the effect on the final outcome, even though this approach is limited by the long follow-up times needed. Current guidelines for clinical trials require evidence about the effect on bone density. In addition they also demand that there is no indication of detrimental effect on bone architecture or strength and that there is evidence for decreased fracture risk after at least three years.²⁵

In this report we assume that fractures at an older age are due to osteoporosis, and that they in turn have an impact on mortality, morbidity, and the quality of life. More research is needed to clarify this *chain of events* in order to evaluate whether prevention of osteoporosis and fractures will also influence those aspects of the disease. Only a better insight into this chain of events can lead to a proper cost-effectiveness analysis of suggested prevention strategies.

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