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ORIGINAL RESEARCH

Assessing the Impact of Osteoporosis on the Burden of Hip Fractures

Anders Odén · Eugene V. McCloskey · Helena Johansson · John A. Kanis

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Abstract The aim of the study was to determine the number of hip fractures within defined countries for 2010 and the proportion attributable to osteoporosis. The number of incident hip fractures in one year in countries for which data were available was calculated from the population demography in 2010 and the age- and sex-specific risk of hip fracture. The number of hip fractures attributed to osteoporosis was computed as the number of hip fractures that would be saved assuming that no individual could have a femoral neck T-score of less than −2.5 SD (i.e., the lowest attainable T-score was that at the threshold of osteoporosis (=−2.5 SD). The total number of new hip fractures for 58 countries was 2.32 million (741,005 in men and 1,578,809 in women) with a female-to-male ratio of 2.13. Of these 1,159,727 (50 %) would be saved if bone mineral density in individuals with osteoporosis were set at a T-score of −2.5 SD. The majority (83 %) of these "prevented" hip fractures were found in men and women at the age of 70 years or more. The 58 countries assessed accounted for 83.5 % of the world population aged 50 years or more. Extrapolation to the world population using age- and sex-specific rates gave an estimated number of hip fractures of approximately 2.7 million in 2010, of which 1,364,717 were preventable with the avoidance of osteoporosis (264,162 in men and 1,100,555 in women). We conclude that osteoporosis accounts for approximately half of all hip fractures. Strategies to prevent osteoporosis could save up to 50 % of all hip fractures.

Keywords Attributable risk · Bone mineral density · Diagnosis of osteoporosis · Prevention of osteoporosis · T-score

Introduction

Osteoporosis is operationally defined as a value for bone mineral density (BMD) of 2.5 SD or more below the young female adult mean (T-score less than or equal to −2.5 SD) using measurements of DXA at the femoral neck [1, 2]. The reference range recommended by the World Health Organization, International Osteoporosis Foundation, and National Osteoporosis Foundation [1, 3] is derived from the database for femoral neck measurements in white women aged 20–29 years [4]. The threshold BMD chosen to diagnose the disease is somewhat arbitrary, but no more arbitrary than the blood pressure threshold for hypertension, body mass index for obesity, or the threshold for many multifactorial chronic diseases and is now generally accepted as a diagnostic criterion.

The international burden of osteoporosis has been widely characterized in terms of the incidence, morbidity, mortality, and economic cost of the fractures that arise [1, 5–15]. Whereas many studies have characterized the prevalence of osteoporosis (based on the T-score), relatively few have used the international reference standards to compute the T-score [1, 15–19] and fewer still the fracture burden associated with osteoporosis [15, 18, 19]. With the development of standardized international reference ranges for BMD, the question arises: how many hip fractures occur as a result of osteoporosis? The obverse

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A. Odén · E. V. McCloskey · H. Johansson · J. A. Kanis (✉)
WHO Collaborating Centre for Metabolic Bone Diseases, University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX, UK
e-mail: w.j.pontefract@shef.ac.uk

question also arises: how many hip fractures are potentially avoidable in a world without osteoporosis? Against this background, the aim of the present study was to provide a framework for assessing the global burden of osteoporosis in terms of the fractures attributable to osteoporosis.

Methods

For the definition of osteoporosis, we used the mean value for femoral neck BMD of U.S. white non-Hispanic women (age 20–29 years) of the NHANES III study as a reference value [2]. A T-score of −2.5 SD represented a BMD of 0.577 g/cm^2 at the femoral neck [4] and was applied to men as well as to women. The research question was formulated as: "How many hip fractures would be prevented if all men and women aged 50 years or more from an index population (e.g., country, continent, world) with a BMD below the threshold value were to have a BMD at the threshold value?" For the sake of brevity, the decrease in the number of hip fractures as a result of this strategy was termed *prevented fractures* or *preventable fractures.*

A well-validated assumption used was that BMD is normally distributed [20] and that the logarithm of the hazard function is linearly dependent of BMD—that is, there is a constant relative increase in the hazard of fracture for each SD deviation decrease in femoral neck BMD, termed the gradient of risk (GR). Fig. 1 shows the distribution of BMD in a hypothetical population of a given age and sex. The distribution of BMD is Gaussian and the mean T-score in this example is −1 SD for young women. The analysis determined the number of hip fractures that would be expected in the same population if all individuals with a T-score of less than −2.5 SD had a T-score of exactly −2.5 SD (i.e., a world without osteoporosis).

Gradients of Risk

To describe the relationship between femoral neck BMD and hip fracture, we used GRs derived from a meta-analysis of the primary data from 12 population-based cohorts comprising 39,000 men and women [21]. In that study, there was no difference in the GR between men and women after adjustment for age. In both men and women, however, a significant effect of age was seen on the GR, but the interaction of age and GR was the same in men as that observed in women. Thus, at the age of 50 years, the GR was 3.68 (95 % confidence interval [CI] 2.61–5.19) and fell progressively with age to 1.93 (95 % CI 1.76–2.10) at the age of 85 years [21].

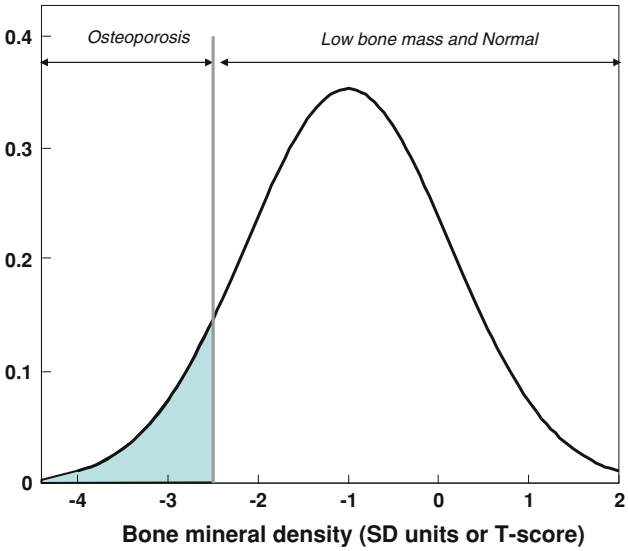

Fig. 1 Distribution of BMD in a hypothetical population of a given age and sex. The distribution of BMD is Gaussian with a mean T-score of −1 SD. The shaded area corresponds to those individuals in whom BMD values at the femoral neck lie below the threshold for osteoporosis

BMD Worldwide

For the purposes of this report, we assumed that the mean femoral neck BMD was similar across countries at the age of 50 years and that the rate of bone loss at the femoral neck with age was similar. Although differences in the age-dependent differences in BMD (and hence the prevalence of osteoporosis) have been reported between countries in multinational studies, the differences are relatively small [1, 22–25].

Populations Studied

The 58 countries considered in this analysis were obtained from a systematic review of hip fracture incidence published elsewhere [26]. In brief, national studies were preferred over regional estimates, and where several regional estimates were available, the highest-quality scored study was used. Where several regional estimates of comparable quality were identified, the data were merged weighted by the size of the catchment population. Population demography for each country used U.N. data for 2010 [27] (medium variant) in 5-year age intervals with an upper age category of 95+ years.

Statistical Methods

The annual number of hip fractures in each country was calculated from the population demography and the hip

fracture incidence derived from the systematic review. The proportion of hip fractures in individuals with osteoporosis and the impact of preventing BMD in any individual falling below a T-score of −2.5 SD were computed by the methods given in the Appendix.

Results

The prevalence of osteoporosis by age is shown in Table 1. As expected, prevalence rose progressively with age, and at all ages, prevalence was higher in women than in men. At the upper age interval (80 years or more), the prevalence of osteoporosis was 19 % in men and 51 % in women.

The total number of hip fractures in each country is listed in Table 2. Collectively, 2.32 million hip fractures were estimated to have occurred in the 58 countries in 2010 (741,005 in men and 1,578,809 in women), with a female-to-male ratio of 2.13. Of these 1,159,727 (50 %) would be prevented if individuals with osteoporosis had a T-score at the threshold for osteoporosis. The proportion of preventable fractures varied by country and gender. In men, 30.1 % of hip fractures could be prevented in those with osteoporosis, ranging from 25.3 % in India to 34.6 % in Japan. In women, 59.3 % of hip fractures could be prevented, ranging from 47.9 % in Nigeria to 61.2 % in Portugal.

The age distribution of the entire population of men and women aged 50 years or more in the 58 countries is shown in Fig. 2. Twenty-five percent were aged 75 years or more, with 8 % aged 80 years or more. The impact of intervening at the various ages to prevent osteoporosis and its contribution to the potential total preventable number of hip fractures is also shown in Fig. 2. In men and women at the age of 70 years or more, 82 % of all preventable fractures arose in 25 % of the total population aged 50 years or more. Targeting the 8 % of individuals over the age of 80 years would capture 53 % of preventable hip fractures.

Collectively, the countries studied accounted for 83.5 % of the world population aged 50 years or more. Extrapolation to the world population using age- and sex-specific rates gave an estimated number of hip fractures of approximately 2.7 million in 2010, of which 1.36 million were preventable fractures (264,000 for men and 1.10 million for women).

Table 1 Prevalence of osteoporosis (%) by age in men and women based on T-score for femoral neck BMD of −2.5 SD or less

Age range (years)	Prevalence (%)	
	Men	Women
20–29	0.46	0.96
30–39	1.04	1.94
40–49	1.73	4.35
50–59	2.95	9.30
60–69	5.90	19.11
70–79	8.83	35.13
80+	19.37	51.48

BMD bone mineral density

Discussion

The present study provides an estimate of the attributable risk of hip fracture associated with osteoporosis defined on the basis of the T-score of BMD measured at the femoral neck. The approach used was to determine the number of hip fractures that would be saved were all individuals with a T-score below −2.5 SD to have a T-score set at exactly −2.5 SD. The principal finding is that if such a strategy could be implemented, then approximately 50 % of all hip fractures could be prevented. The number of preventable hip fractures in the 58 countries amounted to 1,159,727, and was extrapolated to 1,364,717 preventable hip fractures worldwide.

The study should not be misinterpreted as suggesting that such a therapeutic manipulation is feasible. Rather, the study provides an estimate of the global burden of hip fracture that can be attributed to osteoporosis. Notwithstanding, the study highlights the large effect that might be achieved by strategies targeted to a high-risk segment of the population (i.e., men and women with osteoporosis). The present analysis also indicates that a little more than 80 % of these fractures could be prevented by an effective strategy that targeted individuals from the age of 70 years.

The results of the present study rely on a number of assumptions. These include the accuracy of the epidemiology of hip fracture in the countries examined. For this reason, we chose, where possible, the highest-quality data, preferentially based on national data. These countries represent just over 80 % of the world population. The extrapolation of the hip fractures prevented on a worldwide basis is less secure in that it assumes that the age- and sex-specific risk of hip fracture is the same as in the index countries. The estimate will become more reliable with more complete epidemiology, particularly in countries with large populations for which there are scanty data, such as India, China, and Indonesia. If the estimate of 2.7 million hip fractures worldwide in 2010 is accepted, the burden of hip fractures is substantially higher than that predicted. In 1990, 1.5 million hip fractures were estimated to have

Table 2 Total annual (2010) number of hip fractures and the number of hip fractures avoided by prevention of osteoporosis by country in men and women aged 50 years or more

Country	Total no. of hip fractures		No. of hip fractures prevented	
	Men	Women	Men	Women
Argentina	6263	28288	1961	17300
Australia	5172	13102	1742	7965
Austria	4293	13025	1347	7898
Belgium	4227	11976	1356	7273
Brazil	14268	39151	4408	23392
Canada	9261	24077	2972	14559
Chile	1701	5038	529	3054
China	128638	121221	36031	68392
Colombia	2677	4757	801	2741
Croatia	1089	2155	322	1305
Czech	3817	9624	1159	5827
Denmark	3437	8299	1078	5013
Ecuador	455	889	142	531
Finland	2068	4786	645	2903
France	18834	61103	6100	37158
Germany	32422	95515	10116	58168
Greece	4738	10325	1552	6263
Hungary	3666	10403	1139	6289
Iceland	79	229	25	137
India	98163	140252	24862	73246
Indonesia	9655	28963	2689	16816
Iran	17083	18741	5472	11407
Ireland	1347	3255	422	1962
Israel	1332	3177	405	1877
Italy	22980	72818	7469	44358
Japan	75530	139299	26157	85018
Jordan	363	500	107	290
Kuwait	245	147	70	87
Lebanon	428	1011	137	611
Lithuania	767	2424	237	1463
Malaysia	2114	3965	597	2368
Malta	117	333	35	203
Mexico	11108	22786	3389	13627
Morocco	1528	1715	441	1030
Netherlands	4024	10358	1274	6255
New Zealand	1195	2678	392	1628
Nigeria	173	167	45	80
Norway	2635	5905	850	3561
Oman	285	299	80	171
Philippines	2221	5922	575	3430
Poland	7982	20322	2333	12250
Portugal	2454	8431	794	5160
Rep of Korea	10761	21003	3031	12527
Romania	4985	9520	1428	5747
Russia	70623	193534	20815	115912
Saudi Arabia	981	1320	272	777

Table 2 continued

Country	Total no. of hip fractures		No. of hip fractures prevented	
	Men	Women	Men	Women
Serbia	1553	3750	469	2229
Slovakia	2876	6856	830	4100
South Africa	473	717	126	390
Spain	10124	32329	3308	19737
Sweden	5752	15533	1839	9415
Switzerland	3187	9639	1002	5845
Thailand	7189	17656	2127	10522
Tunisia	377	454	117	270
Turkey	6341	17667	1683	10356
UK	19922	62852	6360	38045
United States (white)	84081	225487	27114	135885
Venezuela	946	3061	298	1828

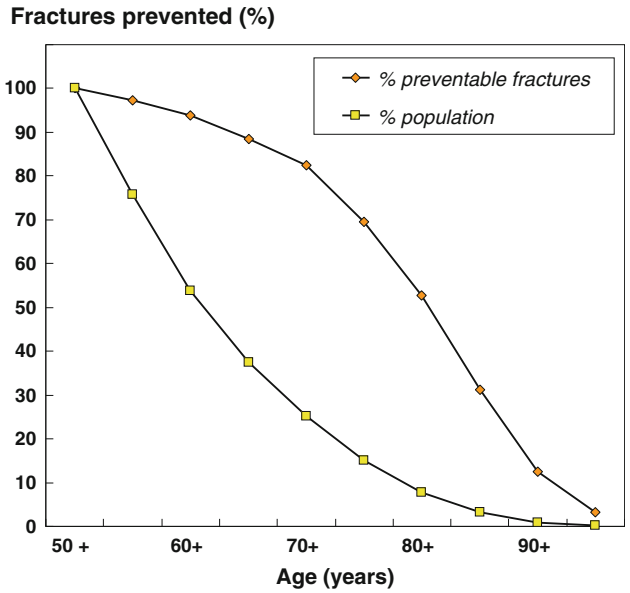

Fig. 2 Proportion of hip fractures prevented (%) in men and women by age and the size of the general population in men and women combined by age in 36 countries

occurred [9], and in 1997, 1.6–1.7 million hip fractures were predicted for the year 2000 [7, 9, 12], which, on the basis of demographic shifts, might be expected to have increased to approximately 2 million in 2010. The finding of 2.32 million hip fractures in 83 % of the world population suggests that earlier reports may have considerably underestimated the number of hip fractures. A possible reason for an underestimate is the increasing secular trends that are reported in many countries [28]. Relatively modest increases in the age- and sex-specific incidence over time have a marked impact on the expected number of hip fractures [9]. The recent availability of more accurate data from more countries may also contribute to differences in the estimated number of hip fractures.

A potential limitation of the present study is that we assumed that the mean BMD with age was similar across countries. The computation assumes that the distribution of femoral neck BMD in the population is similar to that of the NHANES III survey, an assumption consistent with empirical observation in some [1, 19, 25–35] but not all studies [24, 36, 37]. In an international analysis of population-based cohorts [1], there were also small differences in the apparent prevalence of osteoporosis with age. Differences were larger at young ages (< 65 years) where the hip fracture risk is low, and less marked at older ages where the bulk of hip fractures are found. Higher values for BMD at any given age than reported for NHANES III might decrease the estimated number of preventable fractures and vice versa. This, however, is an unsafe assumption because, for example, hip fracture rates are much lower in Turkey and India than the United States, but femoral neck BMD is the same or higher in the Indian and Turkish population than in the U.S. white population [4, 33, 35]. Most studies were on small sample sizes, were subject to selection bias, were undertaken on a regional rather than a national basis, and were cross-sectional in nature. Moreover, differences in BMD within countries are comparable to differences within countries [36, 37]. In the absence of empirical data of high quality for most countries, we assumed that the change in BMD with age was similar between countries. It is worth noting that the variations in BMD between populations are substantially less than variations in fracture risk. Indeed, age- and sex-specific risks of hip fracture differ more than 10-fold, even within Europe [8, 11, 14]. These differences are much larger than can be accounted for by any differences in BMD between communities.

The present study examined the burden of hip fractures accounted for by osteoporosis. Hip fracture, however, accounts for less than 20 % of all fractures associated with low bone mass [15, 38]. Thus, the attributable risk of osteoporosis would be much greater when account is taken of other fracture outcomes. Extending the present analysis in this way needs to take into account that the GR differs for different fracture outcomes [21]. In recent years there has been a move to assessing fracture risk on the basis of fracture probability rather than solely on the basis of BMD [39]. In this context, the present methodology might be profitably extended to consider attributable risk as a function of fracture probability.

We conclude that a substantial proportion of hip fractures are associated with osteoporosis and that a strategy to eliminate osteoporosis would save approximately 50 % of all hip fractures. The targeting of such strategies to the elderly would prevent almost as many fractures but would target a much smaller segment of society.

Appendix

The Hazard Function of Fracture According to BMD at the Femoral Neck

We assume that BMD has a distribution, which is very close to normal. Let h denote the hazard function of hip fracture of a randomly chosen individual from the population at a certain age and sex, and let σ be the standard deviation of the random variable BMD. The GR describes the increase in hip fracture risk for each SD decrease in femoral neck BMD. Then, if BMD is also specified and equal to z, the hazard function is

$$\mathrm{h}\cdot\exp((-\log(\mathrm{GR})/\sigma)\cdot \mathrm{z})/\mathrm{E}[\exp((-\log(\mathrm{GR})/\sigma)\cdot \mathrm{BMD})] \quad (1)$$

where the denominator $E[\exp((-\log(\mathrm{GR})/\sigma)\cdot\mathrm{BMD})]$ is the expected value of $\exp((-\log(\mathrm{GR})/\sigma)\cdot\mathrm{BMD})$. The denominator is needed to make the expected value of equation (1) (the mean risk) equal to h. We can derive from equation (1) the hazard ratio when comparing the BMD value $z-\sigma$ and z, which differ exactly 1 SD, is $\exp(\log(\mathrm{GR}))=\mathrm{GR}$. Now we have to determine $E[\exp((-\log(\mathrm{GR})/\sigma)\cdot\mathrm{BMD})]$. For a random variable Y, which has a normal distribution with mean m and standard deviation SD, the following relationship is true:

$$E[\exp(Y)] = \exp\left(m + \mathrm{SD}^2/2\right) \quad (2)$$

In order to realize that $E[\exp(Y)]\ \exp(m)$, we can apply Jensen's inequality, which states that $E[g(V)] > g(E[V])$ for any random variable V when g is a convex function.

By applying relationship (2), we find

$$E[\exp((-\log(\mathrm{GR})/\sigma)\times\mathrm{BMD})] = \exp((-\log(\mathrm{GR})/\sigma)\times E[\mathrm{BMD}] + (\log(\mathrm{GR}))^2/2)$$

Thus,

$$1/E[\exp((-\log(\mathrm{GR})/\sigma)\cdot\mathrm{BMD})] = \exp((\log(GR)/\sigma)\cdot E[\mathrm{BMD}] - (\log(\mathrm{GR}))^2/2)$$

and expression (1) equals

$$h\cdot\exp(-\log(\mathrm{GR})\cdot(z-E[\mathrm{BMD}])/\sigma - -(\log(\mathrm{GR}))^2/2)$$

If the linear transformation $t(z)=(z-E[\mathrm{BMD}])/\sigma$ of z is used, then equation (1) can be written as:

$$h\cdot\exp(-\log(\mathrm{GR})\times t - -(\log(\mathrm{GR}))^2/2)$$

If all individuals below a limit g of BMD would be carried to the BMD value equal to g and the other individuals are unchanged, then how would the risk change? First we can note that $t(g)=(g-E[\mathrm{BMD}])/\sigma$. The calculated risk is

$$h\cdot\exp(-\log(GR)\cdot t(g) - (\log(\mathrm{GR}))^2/2)\cdot\int_{-\infty}^{t(g)}\frac{1}{\sqrt{2\cdot\pi}}\cdot\exp(-t^2/2)\mathrm{d}t +$$

$$h\cdot\int_{t(g)}^{\infty}\frac{1}{\sqrt{2\cdot\pi}}\cdot\exp(-\log(\mathrm{GR})\cdot t - (\log(GR))^2/2)\cdot\exp(-t^2/2)dt$$

The second term equals

$$h\cdot\int_{t(g)}^{\infty}\frac{1}{\sqrt{2\cdot\pi}}\cdot\exp(-\frac{1}{2}\cdot(t+\log(GR))^2)\mathrm{d}t$$

That implies that the risk (the hazard function) is

$$\mathrm{h}\cdot\{\exp(-\log(\mathrm{GR})\cdot t(g) - (\log(\mathrm{GR}))^2/2)\cdot\Phi(t(g)) + 1 - \Phi(t(g)+\log(\mathrm{GR}))\} \quad (3)$$

where Φ is the standardized normal distribution function.

The factor with which h is multiplied in equation (3) was calculated for the different gradients given in Johnell et al. [21] and the limit $g = 0.558$ g/cm^2.

We note that

$$t(g) = (g-E[\mathrm{BMD}])/\sigma$$

The mean value E[BMD] and the standard deviation σ vary by age and sex. The limit 0.558 fulfils $\Phi(t(0.558)) = 0.0062$, when the mean and standard deviation equals that of women in the age interval 20–29 years. The limit corresponds to 2.5 SD below the mean of women 20–29 years of age.

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