Osteoporos Int (2011) 22:771–780
DOI 10.1007/s00198-010-1358-3

ORIGINAL ARTICLE

Development and validation of a disease model for postmenopausal osteoporosis

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Received: 13 April 2010 / Accepted: 14 June 2010 / Published online: 11 August 2010

Abstract
Summary This article describes the development of a model for postmenopausal osteoporosis (PMO) based on Swedish data that is easily adaptable to other countries.
Introduction The aims of the study were to develop and validate a model to describe the current/future burden of PMO in different national settings.
Methods For validation purposes, the model was developed using Swedish data and provides estimates from 1990. For each year of the study, the "incident cohort" (women experiencing a first osteoporotic fracture) was identified and run through a Markov model using 1-year cycles until 2020. Health states were based on the number of fractures and death. Fracture by site (hip, vertebral, and non-hip non-vertebral) was tracked for each health state. Transition probabilities reflected site-specific risk of death and subsequent fractures. Bone mineral density (BMD) was included as a model output; model inputs included population size and life tables from 1970 to 2020, incidence of fracture, relative risk of subsequent fractures based on prior fracture, relative risk of death following a fracture by site, and BMD by age (mean and standard deviation).
Results Model predictions averaged across age groups estimated the incidence of hip, vertebral, and other osteoporotic fractures within a 5% margin of error versus published data. In Sweden, the number of osteoporotic

Electronic supplementary material The online version of this article (doi:10.1007/s00198-010-1358-3) contains supplementary material, which is available to authorized users.

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fractures is expected to rise by 11.5% between 2009 and 2020, with a shift towards more vertebral fractures and multiple fractures.
Conclusion The current PMO disease model is easily adaptable to other countries, providing a consistent measure of present and future burden of PMO in different settings.

Keywords Bone mineral density · Epidemiology · Fracture · Osteoporosis · T-score

Introduction

Osteoporosis is recognized as a major public health problem in developed countries. The prevalence of the disease, as judged by bone mineral density (BMD) measurements, increases markedly with age. Approximately 3–6% of women in the developed world have osteoporosis at the age of 50 years, and this proportion rises steeply with age to reach 50–75% of those aged 90 years. In women aged 50 years, the remaining lifetime risk of experiencing a major osteoporotic fracture exceeds 30–40% in developed countries. In men, the prevalence increases from 0.5%–1% at 50 years of age to 15–28% at 90 years [1]. The clinical significance of osteoporosis lies in the resulting osteoporotic fractures, the incidence of which rises markedly with age.

The World Health Organization quantifies the burden associated with each disease using disability-adjusted life years (DALYs), a measure that combines the number of years of life lost and the disability suffered as a consequence of illness. Most fractures are associated with high levels of morbidity and some mortality: It is estimated that in the Americas and Europe, osteoporotic fractures account for 2.8 million DALYs annually, which corresponds to 1% of the DALYs attributable to non-communicable diseases. In terms of DALYs, the burden of osteoporotic fractures in the general population aged ≥50 years is somewhat higher than that accounted for by hypertensive heart disease (2.2 million) or rheumatoid arthritis (2.0 million), but lower than the burden of diabetes mellitus (5.7 million) or chronic obstructive pulmonary disease (6.8 million) [1–3].

The proportion of the population aged ≥65 years in Europe is expected to rise from 17% in 2008 to 30% in 2060 [4]; in consequence, the clinical and financial burden of osteoporosis is also expected to increase over time. Although the epidemiology of fractures (particularly hip fractures) and the prevalence of osteoporosis are relatively well documented, limited data are available on the burden of osteoporosis and fractures at a national level, and potential trends over time. The aims of the present study were to develop and validate a model to describe the current burden of postmenopausal osteoporosis and osteoporotic fractures at a country level, and to estimate future trends using Sweden as a base case.

Methods

Model structure

The progression of fracture incidence was simulated using a Markov model (see Fig. 1). For each age and year of interest (from 1970 to 2020), the number of women experiencing a first osteoporotic fracture (defined as the "incident cohort") was estimated. Each incident cohort was then run through the Markov model, and the progression through different health states was tracked until 2020. The cycle length of the Markov model was 1 year, allowing the cohort to transition between health states each year. Therefore, the model assumed that women sustained a maximum of one osteoporotic fracture per year.

Most deaths caused by osteoporotic fractures occur within 3–6 months of fracture [5, 6], and the model allowed the osteoporotic fracture to lead to "death" within the cycle of fracture. Women who were still alive 1 year after the first fracture could either (1) sustain a second fracture, (2) die, or (3) remain in the "1st fracture" health state if no further fracture occurred.

Although fracture site was not included in the model structure (as it would rapidly lead to a complex model structure), the fracture site is known to determine the risk of death [7, 8] and of subsequent fractures [9, 10]. Therefore, all model parameters accounted for the distribution of fractures by site (hip, vertebral, and non-hip non-vertebral), as described in the "Model parameters" section.

Model outputs were generated by age for each year of the study period and included the estimated numbers of incident fractures by site, deaths attributable to osteoporotic fractures, number of women with (including site of fracture) or without a history of fracture, number of women with

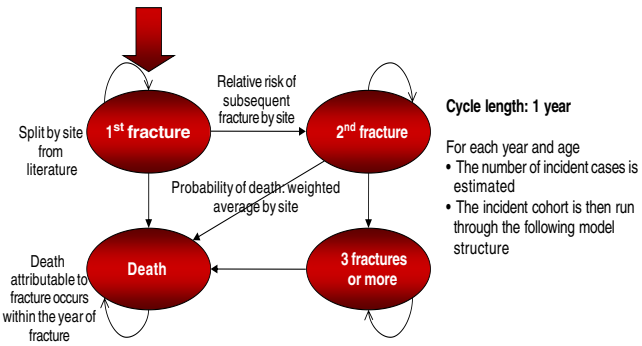

Fig. 1 Model structure

multiple fractures, and number of women below a T-score threshold.

Model parameters

Demography

Population sizes and life tables by age were obtained from Swedish national statistics, and data were retrieved for the period 1970 to 2007 (the last year available). Official forecasts for Sweden for 2008 to 2020, assuming the "main alternative" (that is, in 2020, fertility will rise to 1.85 children per woman, life expectancy in women will reach 84.3 years, and net migration will be 24,800), were used to populate the model [11] (see Table 1 and Online Resources 1, 2, 3, and 4).

Incidence of first fracture

The probability of experiencing a first fracture by site was obtained as follows. Data regarding the incidence of osteoporotic fractures in Sweden were taken from the study by Kanis et al. [12] (see Online Resource 1). In this study, osteoporotic fractures were defined as fractures known to be associated with low BMD and which increased in incidence with age. The same definition was used in our model. For the spine, symptomatic fractures only were considered. The ratio of first incidence to overall incidence of fracture by site was obtained from an observational study conducted in Malmö [13], and this was used to derive the incidence of a first osteoporotic fracture by site (hip, vertebral, and non-hip non-vertebral). The incidence of first fracture by age was smoothed using exponential smoothing for hip and all osteoporotic fractures, and using linear smoothing for clinical vertebral fractures. In this study, the incidence of first fracture by age was assumed to remain constant over time, but changes in secular trends can also be accommodated.

Risk of subsequent fracture

Two main sources were used to estimate the relative risk of a subsequent fracture following a first fracture, depending on the site of the first fracture (see Online Resource 2). One publication [9] was based on a meta-analysis of studies conducted between 1966 and 1999, and a second study [10] estimated the risk of subsequent fractures based on a cohort of 1,918 patients from Malmö, Sweden. In this latter study, Johnell et al. [10] estimated the risk of subsequent fractures after an initial fracture, by site, using Poisson modeling. The study showed that the relative risk differed by age (younger women having a higher relative risk) and that the risk of fracture markedly increased immediately after the fracture but then decreased linearly over time. This publication also provides 95% confidence intervals for the rate of decrease in the risks of fractures with time, so that the model could be re-run using limits from the confidence intervals to assess whether this would improve the model predictions. As it was not possible to guide the selection of evidence on relative risk based on clinical arguments, it was decided to run the model using these two sets of relative risk data and to select the one providing the best match to observed data.

Excess mortality due to fracture

Kanis et al. [7, 8] compared excess mortality in a large series of Swedish men and women who sustained a hip or vertebral fracture with that in the general population (see Online Resource 3). They described increased mortality as a combination of excess mortality due to fracture (causally related deaths) and excess mortality due to a higher prevalence of comorbidities in patients sustaining a fracture. Immediately after fracture, the mortality rate was markedly increased, and decreased exponentially over the following year. One year after the fracture, the risk of death was still higher than in the general population and remained

Table 1 Model parameters and sources of data

Data	Description	Sources
Probability of first fracture	Derived from two Swedish publications: one documenting the incidence of fracture by site, the other documenting the proportion of first fractures at that site	[12, 13]
Increased risk of fracture following a previous fracture	As no clinical criteria could guide the selection of references, it was decided to run the model according to the two sets of relative risk of subsequent fractures and to select the one providing the best match with observed data	[9, 10]
Relative risk of death following a hip or a vertebral fracture	Swedish data	[7, 8]
Relative risk of death following a non-hip non-vertebral fracture	US data; adjusted by Swedish incidence rate	[12, 15]
Femoral neck BMD	US NHANES III data	[18]
Mean difference in BMD between women having experienced a fracture vs. not	0.11 SD	[16, 17]

stable over time. In order to account for this pattern of mortality, our model used the 6-month death hazard to reflect death rates within the year of fracture and the death hazard reported at 1 year to estimate the probability of death over subsequent years (death assumed to be due to comorbidities) until death.

Johnell et al. [14] investigated the pattern of mortality after fractures at the shoulder and forearm; however, these may not be representative of all non-hip non-vertertebral fractures. Therefore, we used the findings from a study by Barrett et al. [15], who analyzed a US sample from a Medicare population and reported relative risks of death 1 year after the occurrence of fracture by detailed site (see Online Resource 4). No excess mortality was assumed after distal forearm, ribs, clavicle, scapula, and sternum fractures. These relative risks were weighted by the incidence of fractures by site observed in the Swedish population, to derive a pooled estimate for non-hip non-vertebral fractures (estimated at 1.13) [12]. It was assumed, guided by expert opinion, that women sustaining a fracture at sites other than the hip or spine were at increased risk of death only within the year of fracture. The relative risk of death in osteoporotic women compared with that in the general population was assumed to be constant over time. As the annual risk of mortality decreases over time, this assumption implies that the same proportional decrease will apply to the risk of death in osteoporotic women.

Bone mineral density

Although the risk of fracture as a function of BMD is well documented, most publications estimate the risk of fracture over a follow-up period as a function of the baseline BMD. Data on the change in BMD over time are scarce. As cohorts are followed over time in our disease model, information on BMD was required for each calendar year.

In 1996, Marshall et al. [16] conducted a systematic review of the literature to estimate the predictive value of BMD for subsequent fractures. A decrease of one standard deviation (SD) below the age-adjusted mean BMD measured at the femoral neck was associated with a relative risk of osteoporotic fracture of 1.6 and with a relative risk of hip fracture of 2.6. More recently, Kanis et al. [17] conducted a meta-analysis to explore the risk of fracture as a function of BMD, age, sex, and prior fracture. In this publication, the authors used the gradient of risk published by Marshall et al. [16] to estimate the mean difference in BMD between individuals with a history of fracture and those without, estimated at 0.11 SD. In order to estimate the distribution of BMD for each year of the study period, the following approach was used in the development of our model. For a given T-score measured at the femoral neck, the corresponding Z-score was estimated, using the Third National Health and Nutrition Examination Survey (NHANES III) "non-Hispanic white" women aged 20–29 years as a reference group [18]. For each calendar year and age, Z-scores were assumed to be normally distributed with a mean of zero and a SD of 1 (by definition of the Z-score). The mean difference in BMD between women with and without a history of fracture (0.11 SD) was applied to estimate the mean Z-score in women with and without a history of fracture. In order to derive the proportion of women below a specific T-score threshold with or without a prior fracture, it was assumed that the variance in BMD was homogeneous between women with and without a history of fracture. The computation assumes that the distribution of BMD in the population is similar to that of the NHANES III survey, an assumption consistent with empirical observation in Swedish women [19, 20], as the level of bone mineral content reported was similar to levels observed in the United States. As the NHANES III data [18] provide more detailed information (in terms of age groups and standard deviation), these data were used in our model. The mean and standard deviation BMD by age were assumed to be constant over time.

Model validation

The model is based on the run of incident cohorts. Therefore, subsequent fractures in women having experienced a first fracture before the first year of the study period are not captured, so that the model underestimates the total number of fractures at the beginning of the study period. Thus, in order to determine the fracture burden, the model needs to be run over a number of years until reliable estimates are obtained.

The model was run using constant model inputs (population size, probability of death, and incidence of fractures) to assess the number of model runs until the steady state. After 10 years, the yearly change in the number of fractures was <1%. After 20 years, the yearly change was <0.1%, indicating that the model was stable at 20 years. To ensure that model predictions from 2000 onwards were not affected by the model stabilization, the model was run from 1970. To validate the model, the incidence by site and age predicted by the model in 2000 was compared with the study by Kanis et al. [12],which aimed to characterize the pattern and burden of osteoporotic fracture by age and gender. Incidence rates were calculated from national Swedish references when available, using hospital data. For sites with insufficient information, regional data from Malmö (for vertebral fractures) and distribution data by site from the Olmsted County (for rib, clavicular, scapular, and sterna fractures) were used [21].

Results

Model validation

The model was run from 1970, and model estimates were compared with the observed incidences of hip, vertebral, and all osteoporotic fractures in 2000. As noted in the "Methods" section, two sets of data on the relative risk of subsequent fractures following an index fracture were identified, and therefore, the model was run according to the two sets successively. As shown in Fig. 2, the use of relative risks obtained from the study of Johnell et al. [10] led to an underestimation of the incidence of fracture from the age of 70 years. Re-running the model using the lower confidence limit of the annual rate of reduction in fracture risk did not improve the model fit, but resulted in an underestimate of the incidence in younger age groups and an overestimate in older age groups.

The use of relative risks obtained from the study of Klotzbuecher et al. [9] provided a good match to observed data, and model predictions averaged across age groups estimated the incidence of hip, vertebral, and other osteoporotic fractures within a 5% margin of error compared with published data (hip, 4%; vertebral, 1%; and non-hip non-vertebral, 5%; see Fig. 2).

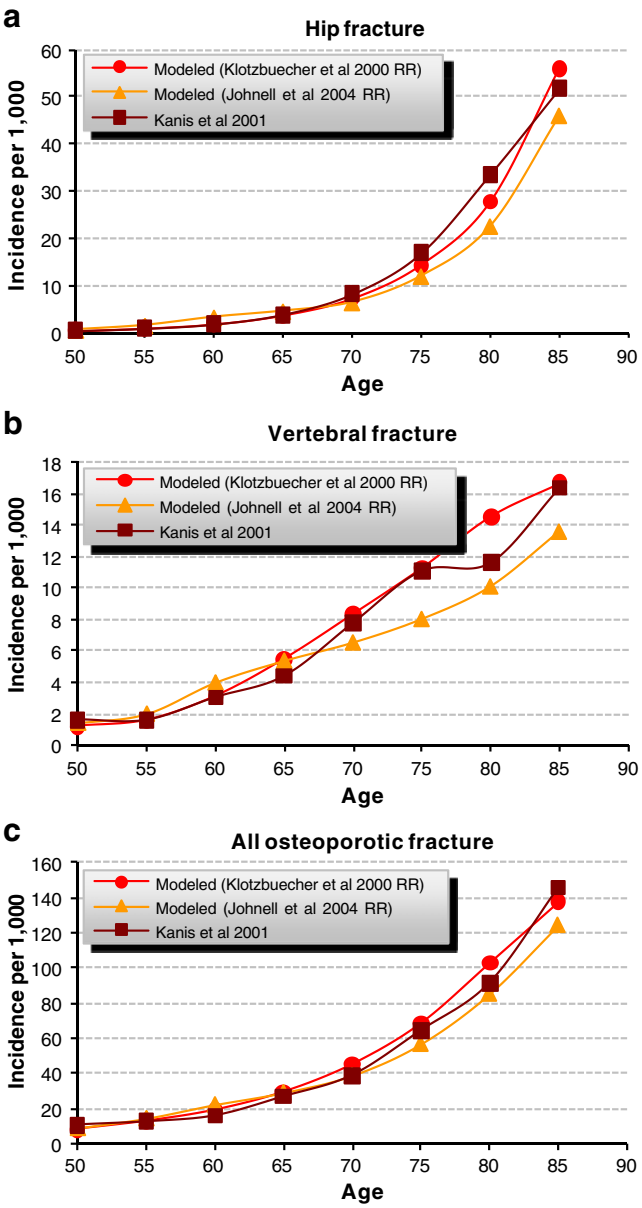

Fig. 2 Incidence of fractures by age: model predictions vs. observed (per 100,000 person-years) using relative risk obtained from Klotzbuecher et al. [9] and Johnell et al. [10]. **a** Hip fracture, **b** vertebral fracture, **c** all osteoporotic fracture

Demography

Using the model, the number of women aged ≥50 years in Sweden is estimated to increase by 10.1% from 2009 to 2020 (see Table 2). However, the rate of increase is expected to differ across ages: the number of women aged 50–65 years is expected to decline slightly between 2009 and 2015 (−1.3%), before increasing (+3.3%) between 2015 and 2020. As those born during the post-World War II baby boom reach the age of 65 years, the number of women aged 65–79 years is expected to increase markedly between 2009 and 2020, from 624,000 to 785,000 (+25.8%) [11]. Lastly, the number of women aged ≥80 years is expected to remain relatively stable over time, with a slight decrease from 2009 to 2015 (−2.0%), followed by an increase of +4.3% from 2015 to 2020.

Incidence

The total number of osteoporotic fractures in postmenopausal women is projected to increase by 11.5% (from 76,914 to 85,783) between 2009 and 2020 (see Fig. 3). The highest increase (+13.8%) is expected in symptomatic vertebral fractures (from 11,569 to 13,161), with an annual rate of increase of 0.8–1.4% (see Fig. 3). The number of non-hip non-vertebral fractures is projected to rise by 12.5% (from 46,749 to 52,589), and the incidence of hip fractures is forecasted to increase by 7.7% (from 18,597 to 20,034), with an annual rate of increase of 0.3–1.3% (Fig. 3). Therefore, the split by site of fracture is expected to change slightly over time, with vertebral fractures contributing 15.0% of fractures in 2009 and 15.3% in 2020. The total number of osteoporotic fractures is reported by age in Table 2: The number of fractures is predicted to remain stable in the 50–64 and 80+ year age groups and to rise markedly (+31.4%) in the 65–79 year age group, which is consistent with demographic projections. As a result, whereas women aged 65–79 years accounted for 36.4% of

Table 2 Demographics, fracture incidence and mortality in Sweden: estimates from 2009 to 2020

Number	2009	2010	2015	2020	Increment (%)
Women aged 50+ years	1,824	1,836	1,921	2,009	10.1
Aged 50–64 years	888	880	876	905	1.9
Aged 65–79 years	624	644	739	785	25.8
Aged 80+ years	312	312	306	319	2.2
Osteoporotic fractures	76,914	77,358	80,509	85,783	11.5
Aged 50–64 years	11,919	11,791	11,439	11,794	−1.0
Aged 65–79 years	28,018	28,598	32,997	36,813	31.4
Aged 80+ years	36,978	36,969	36,073	37,175	0.5
Clinical vertebral fractures	11,569	11,660	12,285	13,161	13.8
Aged 50–64 years	1,768	1,748	1,686	1,732	−2.0
Aged 65–79 years	4,970	5,082	5,880	6,521	31.2
Aged 80+ years	4,831	4,830	4,719	4,908	1.6
Hip fractures	18,597	18,661	19,048	20,034	7.7
Aged 50–64 years	951	940	896	922	−3.0
Aged 65–79 years	4,793	4,860	5,585	6,386	33.2
Aged 80+ years	12,853	12,861	12,566	12,726	−1.0
Non-hip non-vertebral fractures	46,749	47,036	49,175	52,589	12.5
Aged 50–64 years	9,201	9,104	8,856	9,140	−0.7
Aged 65–79 years	18,254	18,655	21,531	23,907	31.0
Aged 80+ years	19,294	19,277	18,788	19,542	1.3
Deaths attributable to fracture	3,444	3,438	3,376	3,397	−1.4
Aged 50–64 years	60	58	52	50	−15.9
Aged 65–79 years	470	468	499	556	18.2
Aged 80+ years	2,914	2,911	2,826	2,790	−4.2

fractures in 2009, this proportion is expected to rise to 42.9% in 2020.

As mentioned previously, the relative risk of death following osteoporotic fractures was assumed to remain constant over time. As life expectancy in the general population is expected to improve markedly by 2020, the model estimates that there will be a slight decrease in the number of deaths attributable to fractures between 2009 and 2020 (−1.4%; from 3,444 to 3,397 deaths) (Table 2).

Prevalence of osteoporosis

No data have been published on the change of age-specific BMD over time. Therefore, the BMD distribution by age was assumed to be constant over time. Based on this assumption, the number of women with a BMD T-score lower than −2.5 SD is expected to rise from 442,622 in 2009 to 500,835 in 2020 (+13.2%; see Fig. 4). Therefore, the prevalence of postmenopausal osteoporosis, defined on the basis of a BMD T-score lower than −2.5 SD, is projected to increase from 24.3% to 24.9% in women aged ≥50 years over the study period. Among women with a T-score below this threshold, the model estimates that the proportion of women with a history of fracture (approximately 35%) will not change over time (150,276 in 2009 and 176,734 in 2020).

The number of women with osteopenia is expected to increase by 11.2% between 2009 and 2020 (from 1,391,799 to 1,547,085). It was estimated that 27% of women with osteopenia have a history of fracture.

Similarly, the numbers of women below BMD T-score thresholds of −3.0, −3.5, and −4.0 SD are projected to increase by 13.6%, 13.9%, and 13.9%, respectively. The proportions of women with a history of fracture when BMD is below these T-score thresholds were estimated at approximately 38%, 41%, and 44%, respectively.

The number of women aged ≥50 years with a history of fracture is expected to increase by 16.5% (from 411,634 to 479,406) over the study period. Although most of this increase is explained by the growth in the population of women aged ≥50 years, the proportion of women with a history of fracture is also expected to increase (from 22.6% in 2009 to 23.9% in 2020).

The prevalence of postmenopausal fractures was reported by age: It was estimated at 8% in women aged 50–64 years, 30% in women aged 65–79 years, and 50% in women aged ≥80 years.

In 2009, it was estimated that 59% of women with a history of fracture had sustained one fracture only, whereas

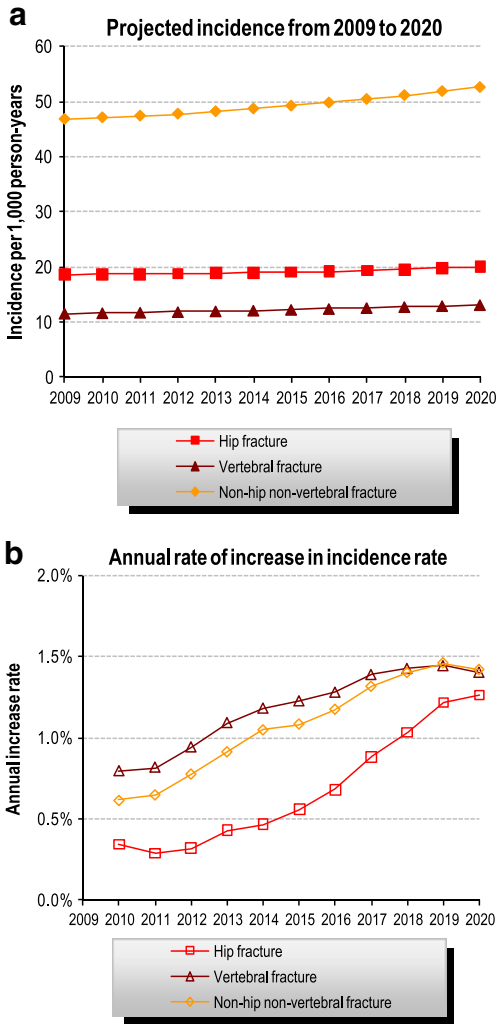

Fig. 3 Crude incidence of fractures by site

23% had experienced two, and 18% had sustained three or more fractures. Between 2009 and 2020, the number of women with multiple fractures is expected to increase slightly more than the number of women with a history of fracture: the number of women with at least two fractures is expected to increase by 17.9%, whereas the number of women with only one fracture is expected to rise by 15.5%. As shown in Fig. 5, the annual rate of increase in the prevalence of multiple fractures is expected to rise more markedly than the rate of increase in single fractures (+2.2% and +1.3% in 2020, respectively).

When defining osteoporosis as a BMD T-score lower than −2.5 SD or a history of osteoporotic fracture, the prevalence of postmenopausal osteoporosis in women aged ≥50 years was estimated to be 38.6% in 2009 (703,980 women) and 40.0% in 2020 (803,507 women, corresponding to an increase of 14.1% between 2009 and 2020). The number of women aged ≥50 years with established osteoporosis was estimated at 150,276 in 2009, which corresponds to a prevalence of 8.2%, and 176,734 in 2020, corresponding to a prevalence of 8.8%.

Discussion

This study aimed to develop a core model by which to quantify and forecast the burden of postmenopausal osteoporosis. A model was developed to simulate the progression of disease over time in Sweden, and was validated using data on fracture incidence by age. The model provided a good match to observed rates for all fracture sites (hip, vertebral, and non-hip non-vertebral), as model predictions were within a 5% margin of error compared with published data when averaged across ages. This model provides detailed incidence and prevalence fracture data by age, year, and BMD, and hence can be used to characterize the burden of osteoporosis.

The present analysis assumed a constant incidence of first fracture by age over time, so that the model forecasts are driven by demographic changes, which are characterized by a 25.8% increase in the number of women aged 65–75 years and relatively stable populations in the 50–64 year

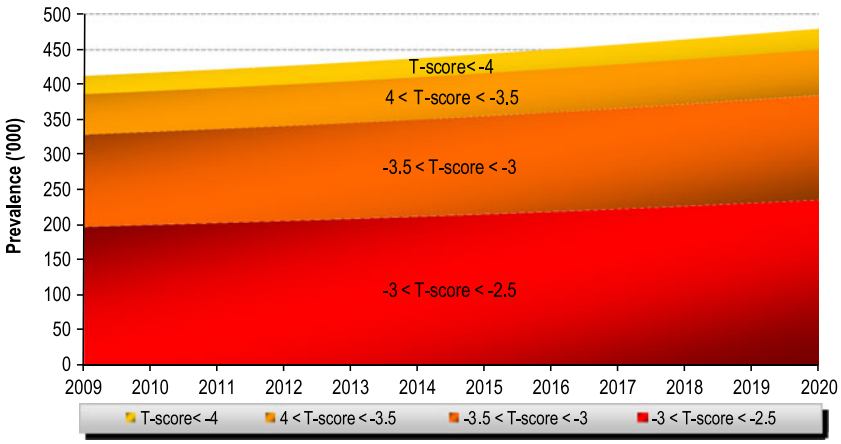

Fig. 4 Number of women within different T-score thresholds, from 2009 to 2020

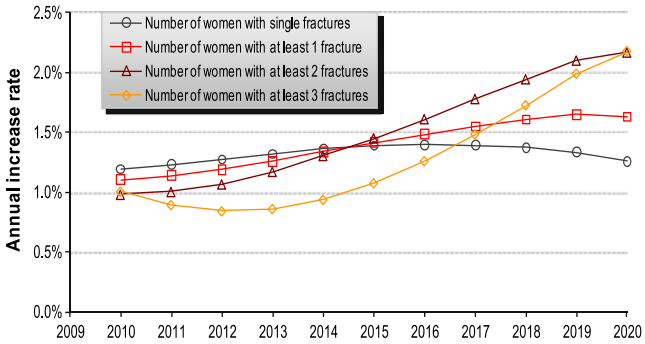

Fig. 5 Annual increase rate of women with (multiple) fractures: model predictions from 2009 to 2020

and 80+ year age groups between 2009 and 2020. Under this assumption, the number of osteoporotic fractures is expected to rise by 11.5% between 2009 and 2020 in Sweden. Although the number of fractures is expected to remain stable in the 50–64 and 80+ year age groups, fractures occurring in women aged 65–79 years are expected to increase by 31.4%.

The increase in the number of vertebral fractures is expected to be almost twice higher than that of hip fractures (+13.8% and +7.7%, respectively). This may be explained by several factors. First, based on the published incidence rates for Sweden [12], the proportion of osteoporotic fractures of the spine is higher in women aged 65–79 years (16–20%, depending on the 5-year age group) than in any other age group, except the 60–64 year age group (19%), and the proportion of women aged 65–79 years is expected to increase markedly in Sweden over this period. Second, the combined effect of a high relative risk of subsequent vertebral fracture (RR=4.4 [9]) and longer life expectancy may contribute to this shift. Lastly, the number of women with multiple fractures is expected to increase more markedly than the number of women with single fractures, which can be explained by the longer life expectancy of women having experienced a first fracture.

Although many studies have collected data on the incidence of hip fractures and several have explored the projections for hip fractures over time [22, 23], few have tried to fully characterize the burden of osteoporosis. Burge et al. [24] developed a Markov model to estimate the number and cost of fractures in the USA and concluded that the number of osteoporotic fractures was expected to increase by 48% between 2005 and 2025. Similarly, Schwenkglenks et al. [25] developed a model simulating the progression of disease to quantify the number of fractures by site in Switzerland and estimated that the number of hip, vertebral, and distal forearm fractures would increase by 36%, 31%, and 23%, respectively, from 2000 to 2020. Our model projected lower rates of increase than the study conducted in the USA [24]. This difference can be explained by the expected demographic changes, as the growth in the population of women aged 50+ years is expected to be 2.3 times higher in the USA, over the 2005–2025 period (+39.9%) than in Sweden (+17.5%). In Switzerland, Schwenkglenks et al. [25] predicted a 14% increase in fractures of the hip, spine, and distal forearm between 2010 and 2020, which is consistent with our estimate for Sweden.

The present model can be used to forecast the incidence and prevalence of fractures not only by age and calendar year but also by BMD category. Therefore, this model could be used to help set health services priorities, by identifying subgroups of patients who bear most of the burden of postmenopausal osteoporosis. Moreover, the model has been developed so that it is easily adaptable to other countries, thus providing the opportunity of estimating the current and future burden of osteoporosis using a consistent approach. In addition, any future trends in the incidence of fracture over time could be incorporated into this model, as the transition probabilities are specific to calendar years.

The model has several limitations. First, it focuses on postmenopausal osteoporosis only and does not account for the burden of osteoporosis in men. In addition, in the current version of the model, the incidence of a first fracture by age is assumed to be constant over time. Although the question of secular trends has been explored in the literature, most studies focus on population trends, and as discussed by Melton et al. [26], trends are driven by demographic changes. Few publications provide a quantitative estimate in the change of age-adjusted incidence of a first fracture over time. Most studies conducted in developed countries have reported an increase in the age-adjusted incidence of hip fractures until the mid-1980s to mid-1990s, followed by a leveling-off [27] or a downward trend [28–30]. For example, Kannus et al. [28] conducted an epidemiologic study in Finland and reported a decline in the age-adjusted incidence of hip fractures since 1997, potentially explained by the fact that the elderly population is getting healthier, with an increasing body mass index (BMI) and improved functional abilities, and perhaps assisted by the introduction of pharmaceutical treatments. In Sweden, the age-specific incidence of hip fracture increased in women aged ≥70 years between 1950 and the mid-1980s. A break in incidence was observed over the period 1987–1991 [31], and Rogmark et al. [32] showed that hip incidence was no longer increasing over the period 1992–1995. As the first 20 years of the model run are used for the model initialization, and because of the lack of data for recent years in Sweden, it was decided to assume constant incidence rates of first fracture by age, using incidence data from 1996.

A potential limitation relates to the exposure of the population to treatments for osteoporosis. Although the

increasing prevalence of treatment may have led to a decrease in incidence since 1996, the selected data are from a partially treated population (as the first approved anti-osteoporotic in postmenopausal women, alendronate, was introduced in 1995), so that the model may slightly overestimate the total number of fractures. The likely impact of this is small [26]. A further limitation is that the distribution of BMD within each age group is assumed to remain constant over time, which may not be realistic since some changes in lifestyle may affect BMD (e.g., an increase in BMI). However, no quantitative data were available for this endpoint, making any assumption of change challenging. If a change in BMD distribution by age were identified, then this would affect the estimated prevalence of osteoporosis, osteopenia, and proportion of patients with a T-score lower than a given threshold.

To conclude, we have developed a disease model for postmenopausal osteoporosis, which we have validated using Swedish data. This model provides the opportunity to assess the burden of osteoporosis in different settings and countries, using a consistent approach. In addition, our model may be used in collaboration with clinical experts to try to quantify the burden of illness in countries where data are lacking. Finally, the model could be extended to incorporate additional outputs, including costs and DALYs, to fully characterize the burden of osteoporosis and inform health policy decision making.

Acknowledgements The study was supported by the International Osteoporosis Foundation and funded by Amgen (Europe) GmbH. The authors thank Dr. Matthew Gitlin and Sean Robbins from Amgen (Europe) GmbH for their involvement in this project, and Professor Alistair McGuire from the London School of Economics for his advice on the model development. Formatting/styling support was funded by Amgen (Europe) GmbH and GlaxoSmithKline.

Conflicts of interest None.

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