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ORIGINAL ARTICLE

Estimating prevalence of osteoporosis: examples from industrialized countries

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Abstract
Summary In nine industrialized countries in North America, Europe, Japan, and Australia, country-specific osteoporosis prevalence (estimated from published data) at the total hip or hip/spine ranged from 9 to 38 % for women and 1 to 8 % for men. In these countries, osteoporosis affects up to 49 million individuals.
Purpose Standardized country-specific prevalence estimates are scarce, limiting our ability to anticipate the potential global impact of osteoporosis. This study estimated the prevalence of osteoporosis in several industrialized countries (USA, Canada, five European countries, Australia, and Japan) using the World Health Organization (WHO) bone mineral density (BMD)-based definition of osteoporosis: BMD T-score assessed by dual-energy x-ray absorptiometry ≤−2.5.
Methods Osteoporosis prevalence was estimated for males and females aged 50 years and above using total hip BMD and then either total hip or spine BMD. We compiled published location-specific data, using the National Health and Nutrition Examination Survey (NHANES) III age and BMD reference groups, and adjusted for differences in disease definitions across sources. Relevant NHANES III ratios (e.g., male to female osteoporosis at the total hip) were applied where data were missing for countries outside the USA. Data were extrapolated from geographically similar countries as needed. Population counts for 2010 were used to estimate the number of individuals with osteoporosis in each country.
Results For females, osteoporosis prevalence ranged from 9 % (UK) to 15 % (France and Germany) based on total hip BMD and from 16 % (USA) to 38 % (Japan) when spine BMD data were included. For males, prevalence ranged from 1 % (UK) to 4 % (Japan) based on total hip BMD and from 3 % (Canada) to 8 % (France, Germany, Italy, and Spain) when spine BMD data were included.
Conclusions Up to 49 million individuals met the WHO osteoporosis criteria in a number of industrialized countries in North America, Europe, Japan, and Australia.

Keywords Osteoporosis · Prevalence · Bone mineral density · Males · Females · NHANES

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Introduction

Osteoporosis and its associated fragility fractures present a major public health burden now and for the foreseeable future. This problem affects not only the USA and other developed countries but also emergent countries as their populations begin to age [1, 2]. Interestingly, the majority of research cited

to support this statement focuses on the risk factors for clinical, economic, and quality of life consequences of osteoporosis-related fractures, rather than disease prevalence data. One potential reason for this focus is that osteoporosis prevalence data are not only sparse but also typically reflect only the experience of discrete populations, with estimates based on a wide range of disease definitions.

Although individual prevalence estimates show that osteoporosis is an important and increasingly common condition, the lack of standardized country-specific prevalence estimates limits our ability to anticipate the potential global impact of osteoporosis in the near and longer term. The low bone mineral density (BMD) that characterizes osteoporosis is one of the most significant risk factors for fracture, and bone densitometry is a unique and powerful tool for assessing fracture risk and for helping physicians determine which patients will benefit from osteoporosis therapy [3]. This understanding of the importance of BMD as a risk factor has been codified in the World Health Organization's (WHO) FRAX® algorithm for predicting 10-year risk of fracture. This algorithm has been endorsed by both the National Osteoporosis Foundation and the International Osteoporosis Foundation and is now available for 26 countries and incorporated into many regional and country guidelines [4, 5].

The current study was undertaken to provide a more comprehensive estimate of the burden of osteoporosis by using a standard BMD-based disease definition to estimate prevalence for selected developed countries: USA, Canada, France, Germany, Italy, Spain, UK, Japan, and Australia. By estimating the prevalence of osteoporosis, predictions can be made regarding the physical, economic, and quality of life burden of the disease in each country.

Methods

Search terms and data sources

A comprehensive literature review was conducted through a search of the PubMed and EMBASE databases in 2010. The search was designed to obtain published age- and sex-specific osteoporosis prevalence data for each country of interest. The target countries were selected because they have relatively large populations and a relatively high use of prescription osteoporosis medications. Search terms included (in any combination) osteoporosis, osteopenia, prevalence, and epidemiology. Articles were screened for relevance and inclusion based on their titles and abstracts, where available. The references section of each article was also reviewed to identify other relevant publications. An Internet search for further information regarding osteoporosis epidemiology was performed. Searches were conducted via large search engines (e.g., Yahoo, Google) and targeted public and subscription-based medical sites. Websites of global and country-specific health organizations (e.g., WHO, International Osteoporosis Foundation, and the US' Centers for Disease Control and Prevention) were also searched, and additional data were obtained from the National Health and Nutrition Examination Survey (NHANES) in the USA.

Overview of methodology for country-specific prevalence estimates

Where available, we used published country-specific BMD-based osteoporosis prevalence data as the basis for estimating the number and percent of males and females aged 50 years and older with osteoporosis in each country of interest. The WHO osteoporosis definition (BMD T-score less than or equal to −2.5 as assessed by dual-energy x-ray absorptiometry [DXA]) was used for this study [6]. Estimates were made using total hip BMD since BMD at this site has a high predictive value for hip fracture, which is widely considered an important and costly potential consequence of osteoporosis. Although osteoporosis prevalence has been estimated separately at the total hip and at the lumbar spine, there is a lack of published data on the prevalence of osteoporosis among individuals who met the disease definition at either or both of these sites. Therefore, a second set of estimates was developed to estimate osteoporosis prevalence based on BMD at either the total hip or spine.

Most of the published prevalence data defined osteoporosis in terms of explicit BMD thresholds for assessments taken at the wrist, hip, or spine. Data across geographic locations and from different data sources were compiled for the same age groups and the same BMD reference populations were used (e.g., Caucasian females). Where disease definitions in the published data differed from ours, we adjusted the prevalence calculations to ensure consistency with our key definitions (Table 1). Some adjustments were necessary to the country-specific osteoporosis prevalence data in the literature in order to have comparable criteria for osteoporosis prevalence estimates at the total hip by age and gender across countries (Table 1). When available, country-specific epidemiology prevalence data from a representative population-based sample were used even if total hip BMD was not reported. In these cases, a ratio from another country was used to adjust the reported local country age- and sex-specific prevalence to maintain consistency with our key definitions. In the event that population-based studies on osteoporosis prevalence were not available for a specific country of interest, prevalence from a comparator country was extrapolated.

Osteoporosis at the total hip

Per the WHO definition, BMD T-scores (threshold values) were determined by calculating the average BMD of healthy non-Hispanic white females aged 20 to 29 years that resulted

Table 1 Data sources and calculations used for country-specific osteoporosis estimates

Country	Primary source	Total hip osteoporosis calculations		Age-specific calculations	
		Males	Females	Males	Females
USA	NHANES III: population-based total hip BMD data	SPSS analysis of total hip BMD	SPSS analysis of total hip BMD	SPSS analysis of total hip BMD	SPSS analysis of total hip BMD
USA	NHANES 2005–2008: population-based total hip BMD data	Female ratio NHANES 2005–2008/NHANES III applied to males NHANES III	SPSS analysis of total hip BMD	Sample size too small to estimate	SPSS analysis of total hip BMD
Canada	Tenenhouse et al., 2000: population-based femoral neck and spine BMD	Male to female ratio at the femoral neck from Tenenhouse et al. applied to female total hip	Leslie et al., 2008: female total hip osteoporosis prevalence	Applied femoral neck age distribution to calculated total hip prevalence	Applied femoral neck age distribution to calculated total hip prevalence
France	Delmas and Sornay-Rendu: OFELY unpublished data	NHANES ratio of male to female total hip osteoporosis applied to female total hip osteoporosis	Female total hip osteoporosis prevalence from OFELY	Applied NHANES male age distribution	Age-specific total hip osteoporosis prevalence from OFELY
Germany	Extrapolated from prevalence for France	Extrapolated from prevalence for France	Extrapolated from prevalence for France	Extrapolated from prevalence for France	Extrapolated from prevalence for France
Italy	Extrapolated from prevalence for Spain	Extrapolated from prevalence for Spain	Extrapolated from prevalence for Spain	Extrapolated from prevalence for Spain	Extrapolated from prevalence for Spain
Spain	Sanfelix-Genoves et al., 2010: femoral neck BMD data	NHANES ratio of males to females applied to calculated total hip osteoporosis in females	NHANES ratio of total hip to femoral neck applied to femoral neck data from Sanfelix-Genoves et al.	Applied NHANES male age distribution	Applied femoral neck age distribution to calculated total hip prevalence
UK	Holt et al., 2002: population-based femoral neck osteoporosis prevalence among those aged 65	Calculated male ratio of UK to USA (NHANES) and applied to US male NHANES total hip osteoporosis prevalence	Calculated female ratio of UK to USA (NHANES) and applied to US female NHANES total hip osteoporosis prevalence	Calculated male ratio of UK to USA (NHANES) and applied to US male age-specific NHANES total hip osteoporosis prevalence	Calculated female ratio of UK to USA (NHANES) and applied to US age-specific female NHANES total hip osteoporosis prevalence
Japan	Ikeda et al., 2002: osteoporosis prevalence of the total hip	Japan JSBMR ratio of males to females from Yoshimura et al., 2009 and applied to female total hip osteoporosis from Ikeda et al.	Ikeda et al.: total hip osteoporosis	Applied JSBMR total hip age distribution from Yoshimura et al.	Ikeda et al., reported age-specific prevalence
Australia	Henry et al., 2000: osteoporosis prevalence at the lumbar spine, femoral neck, and forearm	NHANES ratio of male to female total hip osteoporosis applied to calculate Australian female total hip osteoporosis	NHANES ratio of total hip to femoral neck applied to femoral neck data	Applied NHANES male age distribution	Applied femoral neck age distribution to calculated total hip prevalence

BMD bone mineral density, *JSBMR* Japanese Society for Bone and Mineral Research, *NHANES* National Health and Nutrition Examination Survey, *OFELY* Os des Femmes de Lyon, *SPSS*, Statistical Package for Social Sciences

in an osteoporosis threshold value of 0.638 g/cm^2. Using this threshold, osteoporosis prevalence was estimated for males and females aged 50 years and older, stratified into 10-year age cohorts.

Of the countries included in this study, the USA had the most complete BMD data, with values obtained from the NHANES 1988–1994 (NHANES III) [7] and NHANES 2005–2008 [8]. The NHANES provides data for a

representative sample of the non-institutionalized US population. The NHANES III database included BMD measurements for 14,646 males and non-pregnant females aged 20 years or older with measurements for femoral neck, trochanter, intertrochanter, Ward's triangle, and total hip. These measurements were collected in a dedicated examination room in each Mobile Examination Center using Hologic QDR-1000 pencil-beam x-ray densitometers (Quantitative Digital Radiography; Hologic, Inc., Waltham, MA) [9]. Similarly, the NHANES 2005–2008 data included BMD measurements for 13,193 males and non-pregnant females, with BMD measured using Hologic QDR-4500A fan-beam densitometers (Quantitative Digital Radiography; Hologic, Inc., Bedford, MA) [10]. The NHANES III sample size was large enough to facilitate an analysis of osteoporosis prevalence based on total hip BMD by race for females in the USA, but not males.

Canadian estimates were derived from two population-based studies conducted in Canada: the Canadian Multicentre Osteoporosis Study (CaMos) and the Manitoba bone density program. CaMos was a prospective cohort study in which femoral neck and lumbar spine BMD measurements were obtained for males and females 25 years of age and older [11]. All clinical bone densitometry data in the province of Manitoba, Canada, are maintained in the program's database, and Leslie et al. reported osteoporosis prevalence at the total hip for this population of 16,205 white females aged 50 years and older [12].

For France, the osteoporosis prevalence rates used were from postmenopausal females in the Os des Femmes de Lyon (OFELY) population-based prospective cohort (Delmas P and Sornay-Rendu F; unpublished data). Due to the lack of osteoporosis data for males in France, the NHANES ratio of males to females was applied to the female total hip osteoporosis prevalence in France, with the assumption that the ratio of osteoporosis prevalence in males to females in France was similar to the ratio in the USA.

Due to the lack of published osteoporosis prevalence in Germany, rates for France (including the derived rates for males) were extrapolated since these two countries were assumed to be relatively similar based on geographic proximity. Estimates for Spain were derived by applying the ratio of total hip BMD to femoral neck BMD from the NHANES data to the femoral neck data from the population-based FRAVO study, which was conducted in Spain from 2006 to 2007 [13]. Although osteoporosis prevalence rates have been published for Italy, these studies used a BMD reference range that reportedly produced higher prevalence estimates than the estimates based on the WHO-recommended reference range described above [14–16]. Therefore, to ensure comparability across all estimates in our study, prevalence estimates for Italy were extrapolated from the rates derived for Spain since these two countries were assumed to be similar due to geographic proximity.

For the UK, Holt et al. reported population-based gender-specific osteoporosis prevalence using BMD data collected in the European Prospective Osteoporosis Study (EPOS), the European Prospective Investigation into Cancer (EPIC), and the Cambridge City Health District (CCHD) study [17]. BMD data were reported only for the femoral neck and trochanter and not for the total hip; therefore, US-derived ratios of femoral neck to total hip BMD were used to estimate osteoporosis prevalence based on the total hip BMD for the UK.

In Japan, two diagnostic criteria are used to define osteoporosis: the Japanese Society for Bone and Mineral Research (JSBMR) and the WHO criteria. Osteoporosis by the JSBMR criteria was defined as BMD 70 % or less of the young adult mean. Several osteoporosis studies have been conducted in Japan using either or both of these criteria. We used prevalence data based on the JSBMR criteria and reported for a large, population-based sample, as well as an age-specific female total hip prevalence based on the WHO criteria [18, 19].

For Australia, we used age-specific osteoporosis prevalence at the lumbar spine, femoral neck, and forearm in females, as reported in a study by Henry et al. [20]. This study included a random, population-based sample of females, which was demographically representative of Australia [21]. Ratios from the NHANES were used to adjust the reported femoral neck prevalence in order to estimate the osteoporosis prevalence for total hip BMD for females and the corresponding prevalence in males.

Combined prevalence of osteoporosis at the total hip or spine

In order to determine country-specific prevalence for individuals meeting the osteoporosis criteria for either total hip BMD or spine BMD, we summed the prevalent total hip osteoporosis population with the prevalent spine osteoporosis population and subtracted the overlapping patients with osteoporosis at both the total hip and lumbar spine. The country-specific total hip osteoporosis prevalence calculated for this study was used along with country-specific spine osteoporosis prevalence estimates, where available. Population-based studies reporting osteoporosis prevalence estimates at the lumbar spine were available in the USA, Canada, Spain, Japan, and Australia. For the European countries, osteoporosis prevalence based on spine BMD was available only for Spain; therefore, the age- and gender-specific spine prevalence reported by Sanfelix-Genoves et al. in Spain was extrapolated to the other four European countries [13].

Projection methodology and software used

The number of adults with osteoporosis was projected for the total US population using the sample weights provided in the NHANES and the US census bureau population data for 2010. United Nations Population Division 2010 data were used for all other countries in the analysis. Additional details of the osteoporosis prevalence calculations are provided in Table 1.

The NHANES BMD data for the total hip were analyzed using Statistical Package for the Social Sciences (SPSS) software (SPSS Inc., Chicago, IL). All other calculations were performed using Microsoft Excel (Microsoft, Inc., Redmond, WA).

Results

Using the search criteria, over 4,000 articles were identified. Limiting the search to English language articles decreased the yield to 3,600. When country names were added, approximately 100 articles were retrieved per country, except for the USA, where just under 1,000 articles were identified, although upon review most did not report osteoporosis prevalence in the general population. The final source documents for the prevalence data used in our calculations are noted in Table 1.

Gender-specific estimates of osteoporosis prevalence, as defined by WHO criteria, are reported by country in Table 2. For females, the prevalence of osteoporosis based on total hip BMD ranged from 9 % in the UK to 15 % in France and Germany and from 16 % in the USA to 38 % in Japan when total hip BMD or spine BMD was considered. For males, the prevalence of osteoporosis was lower, ranging from 1 % in the UK to 4 % in Japan based on total hip BMD and from 3 % in Canada to 8 % in France, Germany, Italy, and Spain for individuals qualifying on the basis of BMD measured at either the total hip or the spine.

For each country, the osteoporosis prevalence estimates based on total hip BMD were applied to 2010 census in order to estimate the total number of individuals with osteoporosis. The resulting estimates suggest that over 24 million individuals aged 50 years and over had osteoporosis in the USA, the five European countries examined, Canada, Japan, and Australia. When the disease definition was expanded to include individuals with a qualifying BMD from either the total hip or the spine, the estimated number of individuals with osteoporosis increased to nearly 49 million. Regardless of the definition used, the US and Japan account for the largest proportions of affected individuals: 34.3 and 22.3 % of the estimated osteoporotic population, respectively, for osteoporosis at the total hip, and 21.0 and 26.3 %, respectively, for osteoporosis at the total hip or spine (Fig. 1). Germany and France also account for a substantial proportion of the total estimated number of cases: 12.9 and 9.0 %, respectively, for osteoporosis at the total hip, and 14.3 % and 9.9 %, respectively, for osteoporosis at the total hip or spine. In all countries, the prevalence for females was substantially higher than for males.

Data derived using the WHO and JSBMR criteria resulted in similar estimated total hip osteoporosis prevalence for Japanese males (Table 3). However, the estimated osteoporosis prevalence for Japanese females was higher when derived from data based on the JSBMR criteria compared with estimates based on the WHO criteria. The differential varied by age group, but for all Japanese females aged 50 years and older, prevalence rates were 14 % with the WHO criteria and 19 % with the JSBMR criteria. Although male osteoporosis prevalence varied little by the WHO and JSBMR criteria, the prevalence for males in Japan based on total hip BMD was at least double the reported osteoporosis prevalence for males in other countries (Table 2).

Osteoporosis prevalence based on BMD at the total hip showed similar increases with age among females in most of the countries included in this study (Fig. 2, Supplemental Table 1). Further analysis of the NHANES III data showed that, in the USA, non-Hispanic white females had the highest estimated osteoporosis prevalence based on total hip BMD (15.3 %), followed by non-Hispanic black (7.0 %) and Hispanic (7.3 %) females (Fig. 3). The NHANES IIII sample, however, was not large enough to provide stable estimates of osteoporosis prevalence by race and age.

An analysis of the more recent NHANES data (2005–2008) has shown a dramatic decline in osteoporosis prevalence compared with the NHANES III data. The age-adjusted osteoporosis prevalence based on total hip BMD in females aged 50 years and over was 16 % using the NHANES III data compared with 8 % using the more recent NHANES data. Sample sizes for the NHANES 2005–2008 were too small to reliably estimate the corresponding prevalence in males. However, if we assume that the ratio of osteoporosis prevalence in females between the NHANES 2005–2008/NHANES III was similar to the ratio of osteoporosis prevalence in males between the NHANES 2005–2008/NHANES III, then 0.9 % of males would qualify as osteoporotic on the basis of the total hip BMD collected in the NHANES 2005–2008. When race-specific osteoporosis prevalence was examined for females, only non-Hispanic whites had dramatically lower estimated prevalence, using the newer NHANES versus NHANES III (6.6 versus 15 %). Osteoporosis prevalence in non-Hispanic blacks and Hispanics, using the NHANES 2005–2008, was 6.0 and 6.9 %, respectively.

Discussion

Projections based on published prevalence data suggest that an estimated 24 to 49 million individuals aged 50 years and older in the USA, Canada, five European countries, Japan, and Australia have osteoporosis. These results demonstrate that osteoporosis is a common condition in selected developed countries in North America, Europe, Asia, and Australia.

Prevalence estimates must be interpreted carefully since they can vary considerably depending on the methodology

Table 2 Prevalence of osteoporosis based on BMD at total hip and at total hip or spine in those aged 50 years or older[a]

	Total hip				Total hip or spine			
	Prevalence (%)		Estimated 2010 patient counts		Prevalence (%)		Estimated 2010 patient counts	
Country	Males	Females	Males	Females	Males	Females	Males	Females
USA	2	14	922,966	7,314,163	4	16	1,637,343	8,640,428
Canada	2	11	87,937	683,398	3	18	180,829	1,115,755
France	2	15	236,570	1,915,663	8	32	816,046	4,033,569
Germany	2	15	342,280	2,752,617	8	33	1,192,296	5,831,250
Italy	2	12	185,355	1,605,075	8	30	818,041	3,957,596
Spain	2	12	121,452	1,011,971	8	30	539,235	2,537,629
UK	1	9	65,805	1,021,378	7	27	652,832	3,167,614
Japan	4	14	1,138,539	4,215,100	6	38	1,478,181	11,404,218
Australia	2	10	49,952	369,648	6	22	186,298	803,241

BMD bone mineral density

[a] Based on the WHO osteoporosis definition

and definitions used. For example, Hernlund et al. [22] have estimated prevalence for 27 countries in the European Union by extrapolating the NHANES III femoral neck osteoporosis prevalence rates to the populations of these countries. These estimates are generally higher than our estimates. However, there are fundamental differences in the methodologies used for the two studies, including country-specific prevalence rates (where available) that were used and extrapolated from data for other European countries when country-specific data were unavailable in our study.

Given the substantial clinical, economic, and social ramifications of osteoporosis and the aging of the population, understanding the prevalence of osteoporosis is important to health-care providers and policymakers globally. For example, more complete and accurate prevalence data may be used to improve the estimation of the number of DXA scanners that would be required for osteoporosis case finding and ongoing monitoring of disease progression and treatment effectiveness in any given country or region. Robust BMD-based osteoporosis prevalence estimates might be used to enhance, extend the geographic scope of, or possibly even develop an alternative to the model developed by Kanis et al. of requirements for DXA technology in Europe for the management of osteoporosis. This model was based on three scenarios including

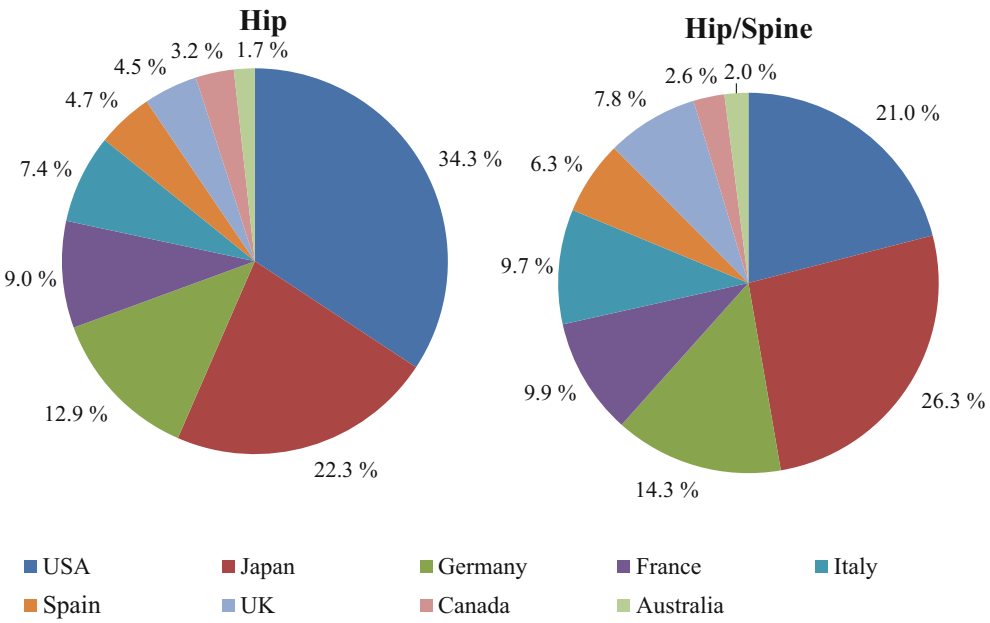

Fig. 1 Distribution of total osteoporosis cases (percent) by country based on bone mineral density measures at the hip alone or at the hip/spine combination

Table 3 Prevalence of osteoporosis at the total hip in Japan using WHO and JSBMR definitions

	WHO criteria		JSBMR criteria	
	Prevalence (%)		Prevalence (%)	
Age, years	Males	Females	Males	Females
50–59	2	2	3	4
60–69	2	9	3	11
70–79	6	24	8	26
80+	14	27	19	47
All ≥50	5	14	6	19

JSBMR Japanese Society for Bone and Mineral Research, *WHO*, World Health Organization

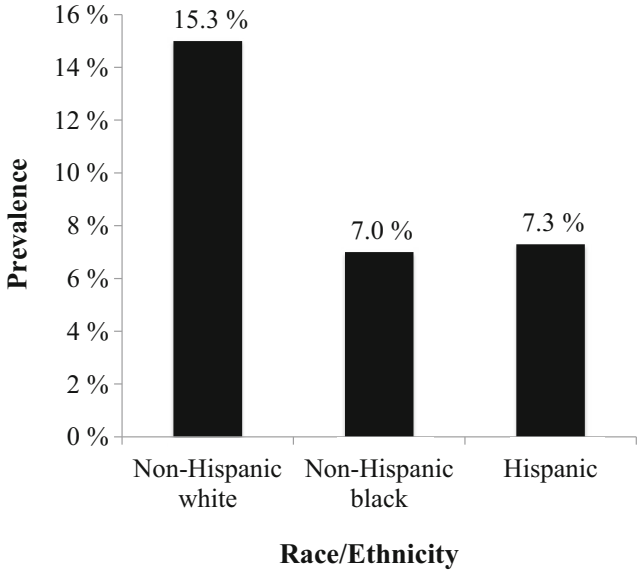

Fig. 3 Race-specific prevalence of osteoporosis in 2010 for US females based on the World Health Organization definitions for bone mineral density at the total hip. Data source: National Health and Nutrition Examination Survey III

screening all females at age 65 years, screening based on clinical risk factors with selective use of BMD assessments for females close to the treatment threshold, and a case-finding strategy in which all females aged 65 years with selected clinical risk factors are referred for DXA [23].

The availability of robust prevalence estimates can also inform policy decisions that influence access to osteoporosis treatment. The primary goal of osteoporosis treatment is fracture prevention, and a variety of pharmacologic therapies with different mechanisms of action, modes of administration, and dosing schedules have been approved for the treatment of postmenopausal osteoporosis, glucocorticoid-induced osteoporosis, and osteoporosis in males [24–26]. Given the antifracture efficacy of these agents demonstrated in clinical trials, it is important for policymakers to design appropriate reimbursement strategies that support treatment recommendations provided in clinical guidelines and facilitate the provision of treatment to the individuals who will most likely benefit. The availability of accurate, country-specific prevalence estimates will not only enhance the accuracy of budget impact models to estimate medication costs but also inform estimates of the cost of related medical services (e.g., office visits, inpatient care) and estimates of the number of physicians, nurses, and other medical personnel and facilities that would be needed to provide the desired level of access to care.

We endeavored to apply a standard disease definition (BMD measurements at the total hip with thresholds based on the WHO criteria for osteoporosis) to data compiled from a variety of sources around the world. Previous researchers have suggested that total hip BMD provides the best, single "gold standard" indicator of osteoporosis, and since total hip BMD is highly predictive for hip fracture, its use in identifying patients for treatment would provide the greatest potential reduction in osteoporosis-related hip fractures and associated

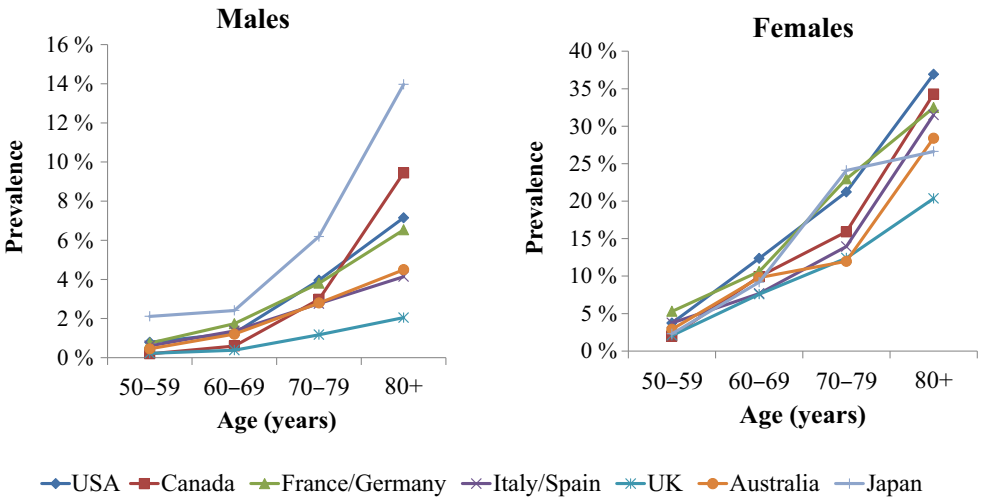

Fig. 2 Country-specific prevalence of osteoporosis in 2010 based on the World Health Organization definition for bone mineral density at the total hip, stratified by sex

morbidity [15]. Although the WHO [27] has designated the femoral neck as the standard skeletal site for osteoporosis screening in average risk populations, our choice of total hip BMD was consistent with the definition used for the Healthy People 2010 osteoporosis objective in the USA [28], and it generally provides more conservative prevalence estimates than those based on femoral neck BMD. To illustrate, using data from NHANES III, the age-adjusted osteoporosis prevalence in females aged 50 years and older is estimated at 18 % using femoral neck BMD and 16 % using total hip BMD. That said, the estimated sex-specific osteoporosis prevalence in the USA reported using BMD data for either the total hip or spine was consistent with the age-adjusted, sex-specific rates reported by Looker et al. using femoral neck or lumbar spine data from the NHANES 2006–2008 (16 % for females and 4 % for males) [29].

Although considerable attention was given to selecting data for inclusion in this study, there are a number of potential limitations to consider in interpreting these results and in setting priorities for future studies of osteoporosis prevalence. While this study provides standardized prevalence estimates for a number of countries in three continents, it does not provide a truly global estimate of the burden of osteoporosis. As noted earlier, the NHANES III provides the most complete population-based BMD data available and serves as a reasonable data source from which to draw inferences for populations with less detailed BMD data available. More recent data from the NHANES (2005–2008) are available; however, the NHANES III was selected due to the larger numbers of adults aged 50 years and older with BMD (6,300 versus 2,950). The NHANES (2005–2008) sample was insufficient to support calculation of age-/sex-specific rates for all of the categories of interest, and data were particularly limited for males. In addition, we determined that the ratios derived for females from the NHANES III data were similar to those derived from the more recent NHANES data. There was more variability in the ratios for males derived from the two NHANES datasets. However, the small numbers of males, especially in the more recent dataset, likely contributed significantly to this variability, and the larger samples in the older data support the use of the NHANES III data in our calculations.

In a comparison of these two databases, the age-adjusted prevalence of femoral neck osteoporosis in the NHANES 2005–2008 was seven percentage points lower in females and three percentage points lower in males [30]. Looker et al. noted that BMD differences between the two surveys were greater among older than younger adults and also varied substantially by sex and race/ethnicity [29]. The technology used in the DXA measurements differed between these two assessments (fan-beam geometry versus pencil-beam geometry), but it is unknown whether this change in technology accounts for the observed differences. In addition, several other factors differed in ways that would be consistent with increased BMD in the more recent data, including body mass index, greater use of bone-specific medications (bisphosphonates, selective estrogen receptor modulators, other non-estrogen agents), and greater use of calcium and/or vitamin D supplements. Adjusted analyses suggest that these factors may not fully explain the BMD gains reported for older white females, and investigations are ongoing to further understand the differences in osteoporosis prevalence obtained from NHANES 2005–2008 and NHANES III [30].

Despite access to the NHANES data, it was necessary to make assumptions as described in the methods in order to estimate prevalence for all of the populations of interest for this study. For example, since total hip BMD measures were not available for Australian females, we assumed that the ratio of osteoporosis prevalence at the total hip to that of the femoral neck for females in the USA was a reasonable proxy. Similarly, although the WHO osteoporosis definition (BMD T-score $\leq$–2.5) was developed specifically for postmenopausal white females, the International Society of Clinical Densitometry endorses the use of NHANES III to derive T-scores for the total hip for males and females of all ethnicities [31]. We followed this recommendation, although there is an ongoing debate about whether different diagnostic criteria and reference ranges should be developed to accurately assess osteoporosis in males. Since males have a greater peak bone mass than females, it has been suggested that the female reference range underestimates the actual osteoporosis prevalence in males [32, 33]. However, others suggest that since males and females sustain fractures at the same absolute BMD, the female reference range can be used to provide the same absolute fracture risk in males [15, 34].

Although the WHO disease definition (BMD threshold) is an accepted standard, there is a debate about the merits of using country-specific data, which may rely on different disease definitions. For example, although the JSBMR criteria, with reference ranges based on data from convenience samples, are the primary criteria used to diagnose osteoporosis in Japan, the WHO criteria are also used in parts of Western Japan [35]. This complexity, to some extent, limits our ability to develop osteoporosis estimates for Japan that both reflect local treatment standards and are directly comparable with other countries. In addition, the JSBMR criteria were developed to identify individuals with and without a vertebral fracture [36]. This approach provides reliable data on spine BMD but less reliable data for femoral neck or total hip BMD.

Finally, our estimates rely solely on BMD data and do not account for other clinical risk factors. Although clinical risk factors are widely acknowledged for the assessment of fracture risk, the utility of these factors decreases

with age [37], and data are lacking to create country-specific osteoporosis prevalence estimates that consider both BMD and clinical risk factors.

Conclusions

Given the substantial clinical, economic, and social burden of osteoporosis, robust prevalence estimates may help inform key policy decisions that influence the portion of osteoporotic individuals identified to receive treatment, as well as patient access to the fracture risk reduction potential of pharmacologic therapies and ongoing monitoring. While more research is needed to determine gold standard reference groups, the updated osteoporosis prevalence estimates provide more current data that may help inform health-care policy and guidance.

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Conflicts of interest SWW: Consultant to Amgen Inc.
CS: Consultant to Amgen Inc.
LAF: Stock ownership in Amgen Inc., and employee of and owns stock/stock options in GlaxoSmithKline
MAS and CDO: Employees of and may own stock/stock options in Amgen Inc.

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