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CHAPTER

c0020 20

# Geographic variability in the incidence of hip and vertebral fractures

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## s0010 20.1 Introduction

p0010 Osteoporosis, a disease of old age, is documented to date back to the Bronze age [1,2]. The demographic explosion, increased life expectancy, global urbanization, and the obesity epidemic are major contributors to the exponential rise in the incidence of chronic noncommunicable diseases (NCDs) and their staggering health burden toll. The World Health Organization identified NCDs as the cause of 71% of the world's deaths in 2016 [3]. Osteoporosis is no exception to this rising tide, vertebral and hip fractures being the hallmark of this costly disease. Thirty to fifty percent of patients who sustain a hip fracture lose functional dependence, and ten percent fracture the contralateral hip. Previously, survival rates posthip and vertebral fractures were reported to be substantially decreased, by 10%–20% in western countries, and possibly more in developing countries [4–7]. Recent studies still report an increase by two to eight fold in mortality during the first few months postfracture [8,9]. A 2019 systematic review on mortality rates 1 year posthip fracture shows a variability between continents ranging from 2.4% to 34.8% [10].

p0015 Although hip fractures only represent 20% of all osteoporotic fractures, they are nevertheless the most serious and costly consequence of osteoporosis and the most reliably identified, because they present to medical attention and require hospitalization, in most regions of the world. Several publications have reported wide geographic differences in age-standardized hip fracture rates worldwide, varying by at least 10-fold [11–19]. The wide range reported is in part explained by the time frame during which fractures were captured for each specific country, representativeness of population of interest, racial groups and regions captured (urban vs rural), accuracy to identify such fractures, and differences in the reference population used for standardization. Notwithstanding all of the above, the highest rates are still reported in Northern European countries, while the lowest rates are from South Africa and countries from South America.

Conversely, while vertebral fractures are the commonest, accounting for over 50% of all osteoporotic fractures, they are the least well characterized in terms of rates. Unlike hip fractures, the identification of such fractures is not readily available, making accurate characterization of their epidemiology more challenging. Two-third of such fractures are silent, only 10% are hospitalized, and the rates may vary widely depending on whether morphometric and/or clinical fractures were reported [2,20,21]. Studies that have evaluated the prevalence of morphometric fractures using the same method have noted much less relative variation in fractures rates between regions of the world, as compared to hip fractures. Prevalence rates varied between 19% and 24% in elderly women from the Middle East, Europe, and North America [22,23]. Some of the highest rates are from North America and surprisingly Asia [2]. Similar prevalence of morphometric vertebral fractures, of 25%, was also reported in postmenopausal women from three p0020

*Marcus and Feldman's Osteoporosis.*
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countries in Asia, namely, Hong Kong, Beijing, and Taiwan [24]. Conversely, the mean prevalence of morphometric fractures across countries in the Latin America Vertebral Osteoporosis Study [LAVOS [25] was lower at 15%. Reports on the incidence of vertebral fractures are scarce [21,23,26]. Bow et al. reported that vertebral fracture incidence rates were similar or up to twofold higher in Asians (Hong Kong Chinese and Japanese) compared to Swedish Caucasians [23].

p0025 While ageing societies, urbanization, and obesity may in part explain the highest rates of hip fracture previously registered in Northern Europe, America, and Oceania, the demographic and lifestyle changes occurring worldwide are rapidly modifying this landscape. Cooper et al. estimated that the number of hip fractures will increase from 1.66 million in 1990 to 6.26 million in 2050, assuming that age-specific hip fracture rates are stable [27]. However, these authors also reported secular trends in hip fracture rates, and in opposite directions, depending on the region of interest in the world [16]. Indeed, estimates suggest that while hip fracture rates in western regions are stabilizing or are on the decline, they continue to rise in the most populous part of the world, namely, Asia [16,28,29]. In 2019 Asia represented 61% of the world population and will still represent 59% in 2050 and thus would account for over half of the total projected number of hip fractures worldwide [30]. The demographic explosion is affecting developing much more than developed countries, regions of the world with the least available, and reliable information on fracture rates worldwide. Indeed, two of the most populous countries in the world, namely, India and Indonesia, have no reliable data on hip fracture rates.

p0030 An accurate assessment of fracture rates is critical for the assessment of the contribution of osteoporosis to the health care burden, and the appropriate allocation of health care resources, be it at the country, regional, or global level. Furthermore, reliable country-specific hip fracture rates are essential for the development of country-specific fracture risk assessment tool (FRAX) calculator which serves as a major advancement for the development of a clinical care pathways, guidelines, and public health policies. Accurate crude country-specific fracture rates are helpful to guide countries without FRAX models in their selection of the best surrogate country (country with the closest crude incidence rates of hip fractures and closest life expectancy) with a FRAX model, as recommended by the International Osteoporosis Foundation (IOF)-International Society for Clinical Densitometry (ISCD) Position Statement [22]. For these the use of a surrogate model will help in the estimation of the 10-year major osteoporotic and hip fracture risk. FRAX allows the calculation of a 10-year hip fracture probability or major osteoporotic fracture probability (hip, spine, forearm, and humerus), taking into account an individual risk factor profile or country-specific longevity and fracture incidence rates. As of Jan 2020, there are 65 country-specific FRAX worldwide and 2 specify ethnic-specific calculators; Singapore (with 3) and United States (US with 4) posted on line [31]: 10 countries in Asia; 35 countries in Europe; 9 countries in the Middle East and Africa; 2 in North America; 7 in Latin America; and 2 countries in Oceania (FRAX calculator accessed on-line February 06, 2020; http://www.shef.ac.uk/FRAX/).

In this chapter, we review key points captured in the previous chapter version in the Background section and aim to provide updated crude and age-standardized hip fracture rates in countries across the world. We also examine secular trends in such fractures, overview the epidemiology of vertebral fractures, and explore possible factors accounting for variability in such fractures across the world. p0035

## 20.2 Background on hip fracture incidence s0015

Evidence for substantial variability in the incidence of hip fractures worldwide is supported by numerous country-specific and regional studies. Incidence is highest in the Northern part of the globe (Scandinavia), and lowest in countries from Asia, and some from Southern Europe, Latin America, and South Africa [11,12,32]. Within the same region, rates also vary markedly. A study of national register sources in Europe, covering the period between 1979 and 1987, showed an 11-fold variation in the age-standardized hip fracture incidence rates within the same continent, with a North to South gradient [33]. The highest rates were reported in Northern Europe with the exception of Finland, which was found to have rates similar to those reported in countries from central Europe. Similarly, slightly lower rates were observed in central Europe with the exception of Poland, a country with rates similar to those reported in southern Europe. Such North to South trend is not as consistent in this update as will be discussed later. The Mediterranean Osteoporosis Study (MEDOS) reported incidence rates from 12 Mediterranean regions in 1988 [13]. The differences in age-standardized incidence of hip fractures varied more than 4-fold among men and 11-fold among women, with the highest rates observed in Seville, Crete, and Rome approaching those of Northern Europe and the lowest rates in Turkey. A review on geographic trends in the incidence of hip fractures involving 46 publications until 2009, that spanned 33 countries and used rates standardized to p0040 the 2005 United Nations estimates of the world population, again showed that the highest rates occurred in Scandinavian countries and the lowest rates in Africa, Latin America, and Asia [15]. However, the following exceptions were noted: in Austria, rates were more similar to those found in Scandinavian than in its neighboring countries.

p0045 An extensive review [18], published in 2012, was based on an update of a systematic search conducted by the FRAX International Task Force 2010 [17] for the Official IOF and ISCD Positions on FRAX [22] and simply added one additional year up until November 2011. It derived age-standardized rates to the 2010 United Nations world population for 63 countries and revealed some unexpected major changes in the landscape for the world map for hip fractures. In Europe, Austria again showed rates in the same range as Scandinavian countries; Turkey had rates close to those in Germany and United Kingdom (UK) and well above those of North America, while Finland, France, Canada, and New Zealand ranged in the lower end of the rates reported for Europe, and close to those reported for several countries in Asia and Latin America. Conversely, age-standardized rates in countries from North America were in the moderate-risk category, and well below those calculated for many South East Asian and Southern European countries. While previously reported to have some of the lowest rates of hip fractures, South East Asia, except for China and Philippines, had rates in the moderate-risk category, while Taiwan fell in the high-risk category. In the Middle-East, Iran and Oman fell in the high-risk category, close to Scandinavian countries, and Lebanon, previously placed at the lower end of risk for hip fractures, was assessed to fall in the moderate-risk category, with rates comparable to the US when combining both genders. In Latin America, Argentina stood out among neighboring countries with rates similar to countries in Central Europe. The above review used the best quality data available for each country and national as compared to regional data in 37 out of 63 countries. When only regional data was available, the average for all the regions was calculated. These findings raise the question about the accuracy of previous epidemiologic data based on which regions and countries were risk-stratified for hip fracture, and whether one is witnessing a true makeover of the world map for the epidemiology of hip fractures, or whether the changes noted above reflect the influence of database selection, the more readily available superior quality of epidemiologic studies in many of the developing countries, the impact of an ageing population worldwide as the target population to which standardization of rates are calculated, or a combination of all of the above.

## 20.3 Methodology s0020

### 20.3.1 Search and data selection s0025

The original Medline OVID search used in the fourth chapter edition covered the period between January 1, 1966 to February 29, 2012. In this update the same search strategy was implemented regarding hip fractures for the period spanning January 1, 2012 to November 30, 2018 for hip fractures. Search was limited to English language and to human adults aged 19 and above. Two Boolean models were created: the first model consisted of the following concepts and their related MeSH[1] terms: hip fracture, incidence, and country X with each concept searched singly, then merged through the AND term; the second model also consisted of three concepts: vertebral fracture, incidence, and country X and the same search strategy was applied. All articles were scanned by title to select relevant titles, common titles for the 2 models were then removed, thus resulting in a total of 645 articles for the previous search and 99 articles in the updated search. The abstracts for these were reviewed, leading to a total of 241 publications of interest covering relevant information for 50 countries. Articles from the updated search were all retrieved and underwent full review and quality rating by one of the authors (GEHF). For vertebral fractures, we kept articles retrieved from the original search strategy (detailed earlier) and included updates using data captured in a recent review our group performed [2], coupled with a PubMed search current until December 2019. p0050

For hip fractures, selection criteria included the provision of age and sex-specific crude rates that are necessary to calculate age-standardized rates for each gender and country. The age groups of were provided in all publications starting at age 50 and above with the following exceptions: the study by Piscitelli et al. [34] in Italy provided age groups of 45−64, 65−74, and above 75; studies from France [35], Denmark [36], Sweden [37], Caribbean [38], Ecuador [39], Saudi Arabia [40], Spain [41], and South Africa [42] provided age groups starting at the age of 60 and were included because they were recent studies with good level of evidence. One study from the UK [43] included age p0055

[1]MeSH is used by the indexers at National Library Medicine to describe the content of an article. These MeSH terms are also organized in a hierarchy or tree structure, and this would allow users to explode a MeSH to ensure that narrower MeSH terms are also included in the search results.



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groups starting at 55 but was nationwide representative with good level of evidence. For Oman [44], rates were given starting at the age of 40 and by 10-year age groups but age-standardization was done starting at the age of 50. In this update, we selected studies conducted after year 2000 for the final detailed analysis outlined in tables and figures. This new selection criterion was chosen in an attempt to avoid the confounding effect of secular trends on the currently reported and age-standardized hip fracture rates. Exceptionally, the national large good-quality study from Iceland [45] is included although spanning the years 1989–2008 because the author reported the average for all years. For each country the most recent studies with good evidence level were chosen. For countries without good evidence data the most recent study with fair evidence was chosen as the next best alternative. For Armenia, clarifications and additional data were obtained from the author of the original publication through personal communications. A total of 69 original publications (of which 37 from the updated search) were ultimately selected to be highlighted in the tables and figures on hip fracture incidence.

p0060 For studies providing the age-specific rates in a figure format [37,46–50], we used "Plotdigitizer," a computer software to extract numerical data from plots, to obtain accurate rates (http://plotdigitizer.sourceforge.net/).

### s0030 20.3.2 Quality rating

p0065 The quality assessment implemented to rate the studies retrieved was that which was originally developed by our group for the FRAX International Task Force Statement [17] and detailed as follows:

- u0010 Good: If at least four of the following criteria were met:
  - u0015 prospective study
  - u0020 study population representative of the entire population
  - u0025 study duration more than 1 year
  - u0030 adequate definition of fracture or International Classification of Diseases (ICD) codes used
  - u0035 ethnicities defined when applicable
- u0040 Poor: If at least four of the following criteria were met:
  - u0045 retrospective study
  - u0050 study duration of 1 year or less
  - u0055 nonpopulation based
  - u0060 inadequate definition of fracture
  - u0065 only abstract available
  - u0070 no definition of ethnicities provided
- u0075 Fair: Sources that did not meet the criteria for either good or poor (i.e., met some but not all criteria).

Studies with good level of evidence and those with fair level of evidence, spanning more than 1 year, are detailed in tables and figures. Studies with fair level of evidence with spanning just 1 year are only detailed in tables.

### 20.3.3 Calculation of age-standardized rates s0035

Age-standardized rates for men, women, and for both genders combined were calculated using the 2010 United Nations World Population estimates [51], because most studies were conducted before 2012. For countries with more than one study, the average of age-standardized rates for good-quality studies was calculated. In the absence of a good-quality study the average of fair quality studies was calculated. Some studies spanning many years provided the age-specific rates for each year; in this case, we averaged the crude hip fracture rate across the years for each age group, and then we calculated average age-standardized rates. p0145

## 20.4 Crude hip fracture incidence rates s0040

Table 20.1 provides a summary of age and gender specific crude incidence rates for hip fractures, by continent [(A) Asia, (B) Oceania, (C) Middle East and Africa, (D) Europe, (E) North America, (F) Latin America] and by country. It captures information on the relevant study period and quality of data. For studies/countries providing age and gender specific rates by 5-year age group increments and to avoid excessively lengthy summary tables, only the rates for the 70–74 and 75–79 years age ranges are reported. These specific age groups are selected as the most enriched and thus representative of the population at risk for hip fractures. Similarly, for studies/countries providing rates in 10-year age group, the ranges of 60–69 and 70–79 are considered the most relevant. Invariably, and as expected, crude rates increase with increasing age in both genders (Table 20.1). In general, rates are 1.5–2 fold lower in men than in women, for most age groups, with few exceptions and select age groups, including indigenous Australia, Kuwait, Spain, and Finland. Comparison of rates within the same continent, and exclusively focusing on good-quality studies, show that in Asia the highest age-specific rates for both genders in patients aged 70–74 and 75–79 are in Taiwan [52], followed by Singapore [53] and Hong Kong [54]. Korea [55–58] and Japan [59] are comparable for age groups 60–69 years and 70–79 years. In Oceania, previous studies reporting incidence rates in the 1990s in South Eastern Australia [60] and national data from New Zealand [61,62] showed similar hip p0150 t0010 **TABLE 20.1** Crude yearly incidence rates of hip fractures by continent, country, gender, and age group in order.

**(A) Asia**

| Country | Reference | Study years | Level of evidence | Rates for men/100,000 | Rates for women/100,000 |
|---|---|---|---|---|---|
| ***70–74*** | | | | | |
| China[a] | Wang et al. [144] | 2010 | F | 88 | 174 |
| | Fa-ming Tian et al. [145] | 2015 | F | | |
| Hong Kong | Tsang et al. [24][d] | 2000–04 | G | 212 | 364 |
| Japan | Hagino et al. [146][b] | 2004–06 | G | 124 | 254 |
| Singapore | Chionh [53] | 2007–09 | G | 228 | 432 |
| Taiwan | Chen et al. [52][d] | 2004–11 | G | 320 | 480 |
| Thailand | Wongtriratanachai et al. [147] | 2006 | F | 165 | 389 |
| ***75–79*** | | | | | |
| China[a] | Wang et al. [144] | 2010 | F | 167 | 322 |
| | Fa-ming Tian et al. [145] | 2015 | F | | |
| Hong Kong | Tsang et al. [24][d] | 2000–04 | G | 450 | 831 |
| Japan | Hagino et al. [146][b] | 2004–06 | G | 271 | 621 |
| Singapore | Chionh [53] | 2007–09 | G | 478 | 896 |
| Taiwan | Chen et al. [52][d] | 2004–11 | G | 550 | 950 |
| Thailand | Wongtriratanachai et al. [147] | 2006 | F | 223 | 793 |
| ***60–69*** | | | | | |
| Korea[a] | Lim et al. [55] | 2004 | G | | |
| | Yoon et al. [56][b] | 2005–08 | G | 92 | 106 |
| | Park et al. [57][b] | 2001, 2011 | G | | |
| | Ha et al. [58][d] | 2008–12 | G | | |
| Japan | Orimo et al. [148][b] | 2002, 2007, 2012 | G | 50 | 86 |
| ***70–79*** | | | | | |
| Korea[a] | Lim et al. [55] | 2004 | G | | |
| | Yoon et al. [56][b] | 2005–08 | G | | |
| | Park et al. [57][b] | 2001, 2011 | G | 252 | 401 |
| | Ha et al. [58][d] | 2008–12 | G | | |
| Japan | Orimo et al. [148][b] | 2002, 2007, 2012 | G | 175 | 391 |
| ***65–74*** | | | | | |
| India | Dhanwal et al. [149] | 2009 | P/F | 95 | 163 |
| ***75+*** | | | | | |
| t0010 India | Dhanwal et al. [149] | 2009 | P/F | 290 | 375 |

(*Continued*)

TABLE 20.1 (Continued)

| | | | | | |
|---|---|---|---|---|---|
| **(B) Oceania** | | | | | |
| ***60–69*** | | | | | |
| Australia | Brennan et al. [63] | 2006–07 | G | 30 | 50 |
| Australia, Western | Wong et al. [46][d] | 1999–2009 | G | | |
| Indigenous | | | | 247 | 237 |
| Nonindigenous | | | | 47 | 66 |
| ***70–79*** | | | | | |
| Australia | Brennan et al. [63] | 2006–07 | G | 260 | 300 |
| Australia, Western | Wong et al. [46][d] | 1999–09 | G | | |
| Indigenous | | | | 811 | 588 |
| Nonindigenous | | | | 166 | 337 |
| ***70–74*** | | | | | |
| New Zealand | Brown et al. [64][f/d] | 2003–05 | G | 155 | 278 |
| ***75–79*** | | | | | |
| New Zealand | Brown et al. [64][f/d] | 2003–05 | G | 357 | 654 |

t0010

| | | | | | |
|---|---|---|---|---|---|
| **(C) Middle-East and Africa** | | | | | |
| ***70–74*** | | | | | |
| Iran[a] | Soveid et al. [65][d] | 2000–03 | F | 207 | 474 |
| | Maharlouei et al. [66] | 2011–12 | F | | |
| Lebanon[a] | Sibai et al. [14][b] | 2006–09 | G | | |
| | Saad et al. [150][b] | 2006–17 | G | 88 | 212 |
| South Africa | Paruk et al. [42] | 2010–11 | G | 50 | 57 |
| Saudi Arabia | Sadat-Ali et al. [40] | 2013 | F | 491 | 574 |
| ***75–79*** | | | | | |
| Iran[a] | Soveid et al. [65][d] | 2000–03 | F | 470 | 618 |
| | Maharlouei et al. [66] | 2011–12 | F | | |
| Lebanon[a] | Sibai et al. [14][b] | 2006–09 | G | | |
| | Saad et al. [150][b] | 2006–17 | G | 195 | 426 |
| South Africa | Paruk et al. [42] | 2010–11 | G | 171 | 110 |
| Saudi Arabia | Sadat-Ali et al. [40] | 2013 | F | 628 | 862 |
| ***70–74*** | | | | | |
| Morocco[a] | El Maghraoui et al. [151] | 2002 | F | 144 | 141 |
| | El Maghraoui A et al. [152][d] | 2006–09 | F | | |
| ***75+*** | | | | | |
| Morocco[a] | El Maghraoui et al. [151] | 2002 | F | 254 | 295 |
| | El Maghraoui et al. [152][d] | 2006–09 | F | | |

(*Continued*)



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TABLE 20.1 (Continued)

| | | | | | |
|---|---|---|---|---|---|
| **(C) Middle-East and Africa** | | | | | |
| ***60–69*** | | | | | |
| Kuwait | Azizieh [80][b] | 2009–12 | G | 90 | 136 |
| ***70–79*** | | | | | |
| Kuwait | Azizieh [80][b] | 2009–12 | G | 380 | 316 |
| ***60–69*** | | | | | |
| Oman | Shukla et al. [44][b] | 2002–07 | F | 170 | 310 |
| ***70*** + | | | | | |
| Oman | Shukla et al. [44][b] | 2002–07 | F | 720 | 730 |
| t0010 **(D) Europe** | | | | | |
| ***70–74*** | | | | | |
| Austria | Dimai et al. [153][b] | 2000–08 | G | 280 | 469 |
| Armenia | Lesnyak et al. [154][c] | 2011–13 | G | 190 | 210 |
| Czech | Stepan et al. [155] | 2008–09 | G | 260 | 383 |
| Denmark | Abrahamsen et al. [36][b] | 2000–06 | G | 350 | 684 |
| France | Couris et al. [156] | 2004 | G | 145 | 277 |
| Germany | Icks et al. [157][b] | 2000–04 | G | 205 | 369 |
| Hungary | Pentek et al. [126][d] | 1999–2003 | G | 212 | 351 |
| Iceland | Siggeirsdottir et al. [45][d] | 1989–2008 | G | 239 | 453 |
| Ireland[a] | Dodds et al. [86][d] | 2002–04 | G | 171 | 365 |
| | Karayiannis et al. [87][b] | 2001, 2011 | G | | |
| Italy | Piscitelli et al. [158] | 2008 | G | 167 | 371 |
| Lithuania | Tamulaitiene et al. [159] | 2010 | F | 230 | 261 |
| The Netherlands[a] | Lalmohamed et al. [160] | 2004–05 | G | 138 | 240 |
| | Klop et al. [161][d] | 2002–11 | G | | |
| Norway[a] | Emaus et al. [67][d] | 1994–2008 | G | 360 | 600 |
| | | 1999–2003 | | | |
| | Søgaard et al. [68][c] | 2004–08<br>2009–13 | G | | |
| Poland | Czerwinski et al. [162] | 2005 | F | 125 | 168 |
| Portugal | De Pina et al. [163][d] | 2000–02 | G | 132 | 316 |
| Romania | Grigorie et al. [164] | 2010 | F | 219 | 283 |
| Russia | Lesnyak et al. [165] | 2008–09 | G | 251 | 273 |
| Spain | Azagra et al. [41][b] | 2000–10 | G | 262 | 124 |
| Sweden | Bergstrom et al. [69] | 2001–05 | F/G | 269 | 590 |
| Switzerland[a] | Lippuner et al. [118] | 2000 | G | 216 | 403 |
| | Lippuner et al. [166][b] | 2000–07 | G | | |
| Turkey | Tuzun et al. [167] | 2009 | F | 137 | 257 |
| United Kingdom | van der Velde R.Y. et al. [49][b/g] | 2000–12 | G | 94 | 207 |

(*Continued*)



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**TABLE 20.1** (Continued)

| **(D) Europe** | | | | | |
|---|---|---|---|---|---|
| ***75–79*** | | | | | |
| Austria | Dimai et al. [153][b] | 2000–08 | G | 514 | 964 |
| Armenia | Lesnyak et al. [154][c] | 2011–13 | G | 258 | 386 |
| Czech | Stepan et al. [155] | 2008–09 | G | 507 | 876 |
| Denmark | Abrahamsen et al. [36][b] | 2000–06 | G | 673 | 1317 |
| France | Couris et al. [156] | 2004 | G | 302 | 621 |
| Germany | Icks et al. [157][b] | 2000–04 | G | 376 | 797 |
| | | 2008–09 | | | |
| Hungary | Pentek et al. [126][d] | 1999–2003 | G | 487 | 695 |
| Iceland | Siggeirsdottir et al. [45][d] | 1989–2008 | G | 395 | 892 |
| Ireland[a] | Dodds et al. [86][d] | 2002–04 | G | 382 | 812 |
| | Karayiannis et al. [87][b] | 2001, 2011 | G | | |
| Italy | Piscitelli et al. [158] | 2008 | G | 351 | 774 |
| Lithuania | Tamulaitiene et al. [159] | 2010 | F | 330 | 484 |
| The Netherlands[a] | Lalmohamed et al. [160] | 2004–05 | G | 254 | 446 |
| | Klop et al. [161][d] | 2002–11 | G | | |
| Norway[a] | Emaus et al. [67][d] | 1994–2008 | G | 657 | 1199 |
| | Søgaard et al. [68][c] | 1999–2003 | | | |
| | | 2004–08<br>2009–13 | G | | |
| Poland | Czerwinski et al. [162] | 2005 | F | 199 | 320 |
| Portugal | De Pina et al. [163][d] | 2000–02 | G | 269 | 649 |
| Romania | Grigorie et al. [164] | 2010 | F | 311 | 490 |
| Russia | Lesnyak et al. [165] | 2008–09 | G | 278 | 487 |
| Spain | Azagra et al. [41][b] | 2000–10 | G | 259 | 611 |
| Sweden | Bergstrom et al. [69] | 2001–05 | F/G | 657 | 1061 |
| Switzerland[a] | Lippuner et al. [118] | 2000 | G | 434 | 835 |
| | Lippuner et al. [166][b] | 2000–07 | G | | |
| Turkey | Tuzun et al. [167] | 2009 | F | 191 | 722 |
| United Kingdom | van der Velde et al. [49][b/g] | 2000–12 | G | 197 | 439 |
| ***60–69*** | | | | | |
| Estonia | Jürisson et al. [47][b] | 2005–12 | G | 173 | 107 |
| Finland | Lonnroos et al. [168] | 2002–03 | F | 125 | 70 |
| Greece | Lyritis et al. [169][b] | 2002, 2007 | F | 88 | 165 |
| Spain | Sosa et al. [83][d] | 2007–11 | G | 55 | 77 |

(*Continued*)

TABLE 20.1 (Continued)

| | | | | | |
|---|---|---|---|---|---|
| **(D) Europe** | | | | | |
| ***70–79*** | | | | | |
| Estonia | Jürisson et al. [47] | 2005–12 | G | 319 | 368 |
| Finland | Lonnroos et al. [168] | 2002–03 | F | 479 | 523 |
| Greece | Lyritis et al. [169][b] | 2002, 2007 | F | 294 | 639 |
| Spain | Sosa et al. [83][d] | 2007–11 | G | 161 | 348 |
| ***65–74*** | | | | | |
| Slovenia | Dzajkovska et al. [115] | 2003 | F | NA | 308 |
| United Kingdom | Wu et al. [43][b] | 2000–09 | G | 102 | 209 |
| Finland | Korhonen et al. [48][b] | 2000, 2005, 2010 | G | 225 | 250 |
| ***75–84*** | | | | | |
| Slovenia | Dzajkovska et al. [115] | 2003 | F | NA | 900 |
| United Kingdom | Wu et al. [43][b] | 2000–09 | G | 399 | 907 |
| France | Briot et al. [35][b] | 2002–13 | G | 362 | 792 |
| Finland | Korhonen et al. [48][b] | 2000, 2005, 2010 | G | 725 | 1136 |
| ***65–74*** | | | | | |
| Italy | Piscitelli et al. [34][b] | 2000–05 | G | 149 | 322 |
| ***75*** + | | | | | |
| Italy | Piscitelli et al. [34][b] | 2000–05 | G | 848 | 1835 |
| ***65–79*** | | | | | |
| Sweden | Nilson et al. [37][b] | 2000–09 | G | 346 | 714 |
| ***80*** + | | | | | |
| Sweden | Nilson et al. [37][b] | 2000–09 | G | 2106 | 3514 |
| t0010 **(E) North America** | | | | | |
| ***70–74*** | | | | | |
| United States[a] | Ettinger et al. [70][e] | 2006 | G | 225 | 415 |
| | Sullivan et al. [50][b] | 2000–11 | G | | |
| ***75–79*** | | | | | |
| United States[a] | Ettinger et al. [70][e] | 2006 | G | 404 | 781 |
| | Sullivan et al. [50][b] | 2000–11 | G | | |
| ***75–84*** | | | | | |
| Canada | Leslie et al. [71][b] | 2000–05 | G | 490 | 984 |
| ***85*** + | | | | | |
| Canada | Leslie et al. [71][b] | 2000–05 | G | 1630 | 2829 |
| t0010 **(F) Latin America** | | | | | |
| ***70–74*** | | | | | |
| Colombia | Jaller-Raad et al. [75][d] | 2004–06 | P/F | 107 | 218 |
| Venezuela | Riera-Espinoza et al. [76] | 2005–06 | F | 63 | 159 |

(Continued)

**TABLE 20.1** (Continued)

| | | | | | |
|---|---|---|---|---|---|
| **(F) Latin America** | | | | | |
| Ecuador | Orces and Gavilanez [39][d] | 1999–2016 | G | 42 | 77 |
| ***75–79*** | | | | | |
| Colombia | Jaller-Raad et al. [75][d] | 2004–06 | P/F | 276 | 349 |
| Venezuela | Riera-Espinoza et al. [76] | 2005–06 | F | 129 | 326 |
| Ecuador | Orces and Gavilanez [39][d] | 1999–2016 | G | 85 | 153 |
| ***60–69*** | | | | | |
| Argentina | Wittich et al. [73] | 2001–02 | G | 75 | 160 |
| Ecuador | Orces [74] | 2005 | G | 18 | 29 |
| ***70–79*** | | | | | |
| Argentina | Wittich et al. [73] | 2001–02 | G | 299 | 522 |
| Ecuador | Orces [74] | 2005 | G | 51 | 84 |

[a]*For countries with more than one study, average of age-standardized rates for all studies were calculated.*
[b]*For studies providing rates for more than 1 year, average of age-standardized rates for all study years calculated.*
[c]*For studies providing rates by time periods, average of age-standardized rates of all periods calculated.*
[d]*Average of hip fracture rates for all study period provided by author.*
[e]*Data on non-Hispanic whites.*
[f]*Rates for European ethnic group (most widely represented in New Zealand).*
[g]*For 50–54 and 55–59 age groups, average of first and last years was taken since values of all years could not be extracted from plots and no significant variation was present throughout the years.*
G refers to good quality studies, F refers to fair quality studies, P refers poor quality, N refers to national study, R refers to regional, and NA refers to data not available.

fracture rates for the same age groups. However, the more recent data from the same regions [63,64] do not report rates for the same age groups to allow similar comparisons. Surprisingly, a study in Western Australia [46], spanning 10 years, reports age-specific rates in nonindigenous residents closer to those in New Zealand; while, rates in indigenous residents are closer to those of Northern Europe (Table 20.1B). The authors underscored several risk factors in indigenous populations such as vitamin D insufficiency, diabetes, smoking, excessive alcohol consumption, physical inactivity, as well as their belonging to underserved areas that could potentially account for the higher rates [46]. For the Middle-East and Africa, comparison becomes even more challenging, because fewer countries report data for comparable age groups. However, some studies reported unexpectedly high rates like Saudi Arabia [40] and Oman [44]. While an older study conducted in Shiraz, Iran [65] (2000–03) shows very high rates in both genders for the 70–74 and 75–79 age groups, a more recent study in the same region shows rates more than 50 times lower [66]. Indeed, the previously reported rates were 403/100,000 in men and 932/100,000 in women [65] versus 11/100,000 for men and 15/100,000 for women in the more recent study [66] for the 70–74 age group. This raises concerns about the methodology used in these studies.

In Europe, Scandinavian countries (Denmark [36], Norway [67,68], and Sweden [37,69]) continue to register some of the highest rates, based on solid and consistent evidence spanning several years, and for both genders for the age groups 70–74 and 75–79 years (Table 20.1D). Conversely, Spain [41] has moved from the low-to-high-risk-category in this update. In North America, rates for non-Hispanic whites in the US [70] are close to those of Canada [71] for the same age groups, although slightly higher in the US (Table 20.1E). It is, however, important to note that Canada reports one rate that includes all ethnic groups. However, in a regional study from Manitoba, Leslie et al. reported a twofold higher rate in Canadian First Nations [72]. In Latin America, Argentina [73] registers rates fivefolds higher than Ecuador [74], while Columbia [75] and Venezuela [76] fall in between, but are only as fair evidence. Moreover, all studies from Latin America are over a decade old (Table 20.1F). Comparisons between countries within the same continent is challenging due to differences in age distribution and longevity. Similarly, even within regions or continents, such as Northern Europe, North America, Oceania, Asia, and the Middle East, variability noted may in part be due to differences in the periods at which the studies were performed, since they could not be perfectly aligned to avoid the p0155



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confounding effect of secular trends. In order to systematically compare incidence rates across populations with differing demographics and longevity, the use of age-standardized rates are indicated.

## s0045 20.5 Age-standardized hip fracture incidence rates

### s0050 20.5.1 Updated age-standardized rates

p0160 Details of all countries by continent, country, and gender are provided in Appendix Table(A-Asia, B-Oceania, C-Middle-East and Africa, D-Europe, F-Latin America). Countries were then ordered from the highest to the lowest age-adjusted rates for both genders combined worldwide and categorized into tertile risk groups: high >238/100,000, medium between 146 and 238/100,000, and low <146/100,000 (Fig. 20.1).

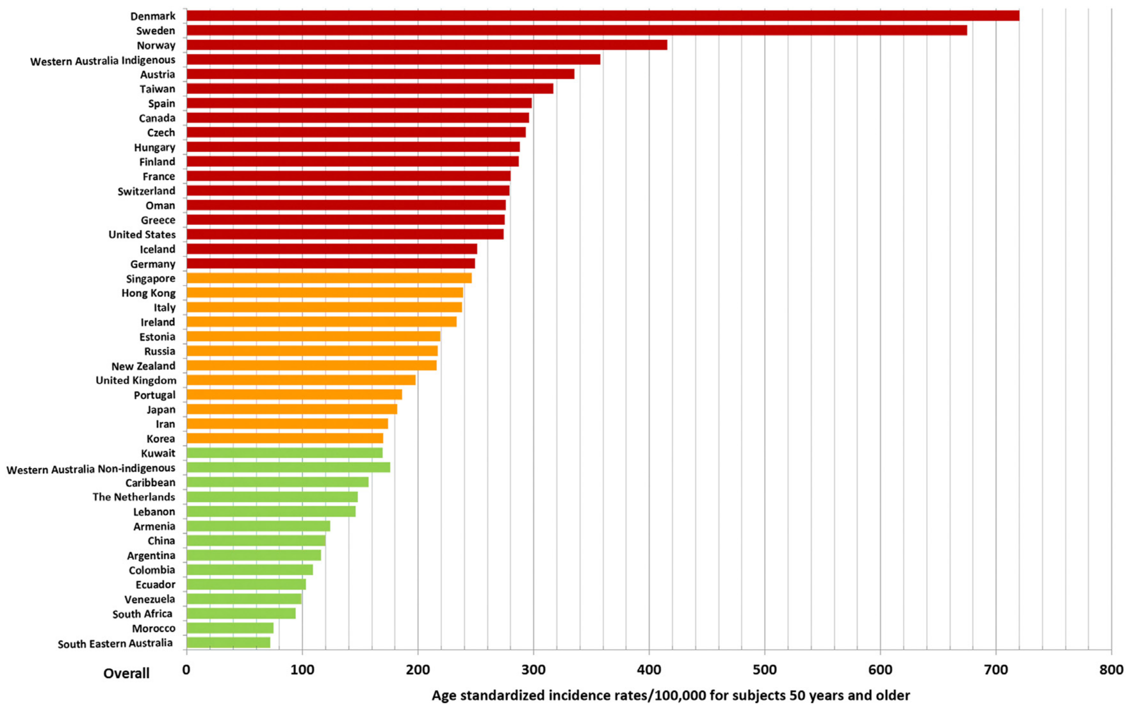
p0165 Age-standardized rates for men and women were also detailed separately from highest to lowest, by continent (Fig. 20.2). Age-standardized rates in women are approximately twice as high as in men, a trend that was consistent across 40 countries from 6 continents (Fig. 20.2). There is a 10-fold range in the variation of age and sex-adjusted incidence rates worldwide, a 10.2-fold range in men and 12.2-fold range in women.

Combining both genders, and as previously reported, Scandinavian countries still lead the highest risk category [36,37,69] (Fig. 20.1). p0170

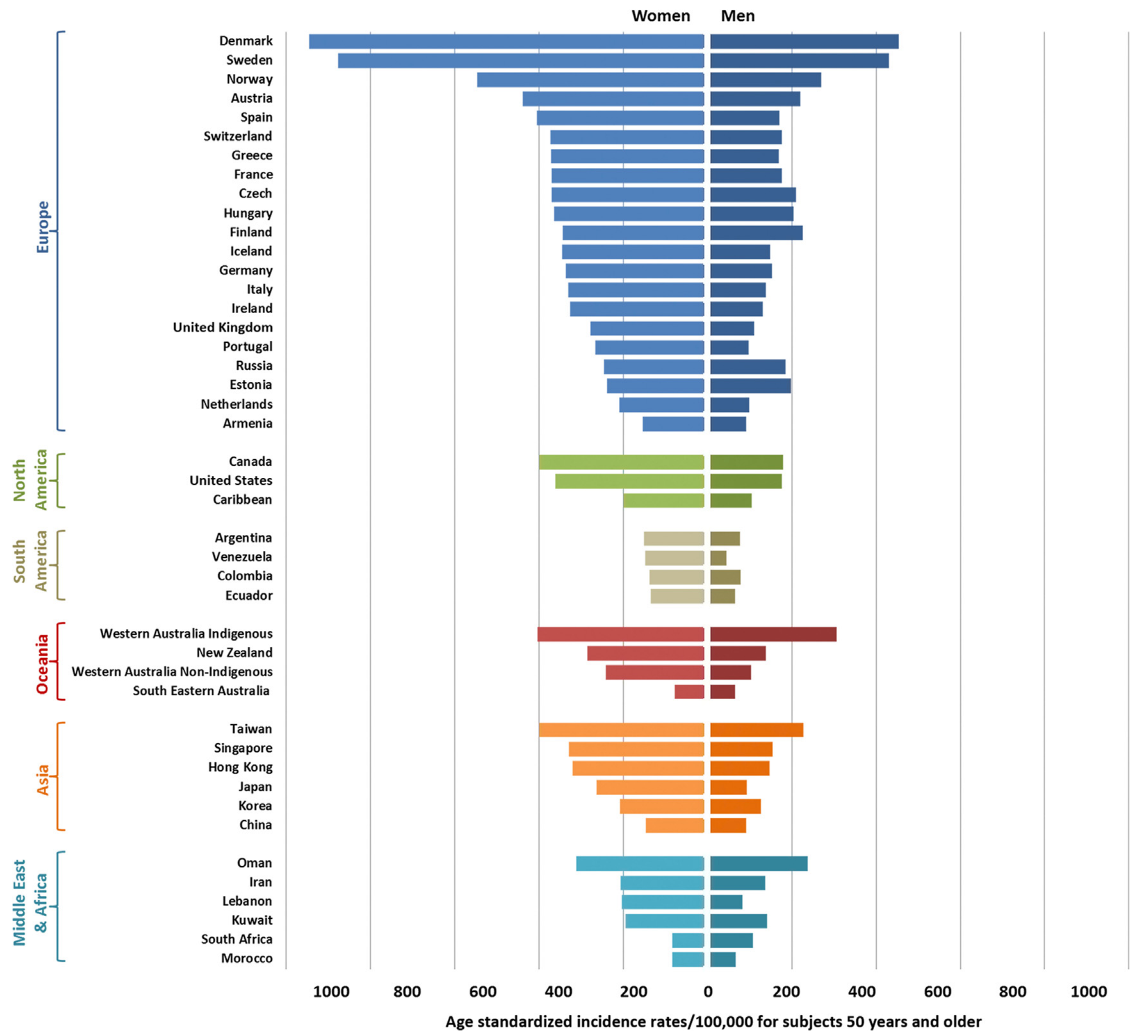
However, countries previously thought to belong to a moderate to low-risk category (Taiwan, Spain, Hungary, Oman, and Greece) have rates that are in the same range as countries in Central Europe and higher than those in the US. In the moderate-risk category for age-standardized rates in both genders, South Eastern Asian countries and South Eastern European countries have very similar rates. Two Northern European countries belong to this moderate-risk category (Ireland and UK). With the exception of the questionable rates in Saudi Arabia and Oman, all Middle-Eastern, African, and Latin American countries belong to the low-risk category. A central European country (the Netherlands) surprisingly belongs to this category. While Western Indigenous Australians have a high age-standardized risk of hip fracture, Western nonindigenous have low rates and South Eastern Australians have the lowest rates worldwide. p0175

### 20.5.2 Incidence rates compared to previous chapter s0055

The updated data in this Chapter reveals that most countries remain in the same risk category for hip p0180




f0010 FIGURE 20.1 Age-standardized hip fracture rates for both genders ordered by country. Green stands for countries that have rates in lower tertile less than 170/100,000, orange for countries with rates in middle tertile range (between 170 and 250/100,000), and red for countries in the highest tertile that is above 250/100,000. Only countries with good-quality data or fair quality data spanning more than a year are depicted.




f0015 FIGURE 20.2 Age-standardized hip fracture rates in women and men by continent and country (ordered per women). Only countries with good quality data or fair quality data spanning more than 1 year are depicted.

fracture rates when compared to those reported in the previous version [77]. However, few unexpected exceptions are worth noting. While Saudi Arabia ranked previously in the low risk category [78], it shows the highest rates in the recent update [40]. The previously referenced study was conducted in Riyadh in the early 1990s and was of poor to fair quality [78]; the new study spanned over 1 year, in 2013, and was conducted in the Eastern province [40], and is rated as fair; but both studies do not specify hip fracture definition. While Kuwait registered rates in the high-risk category, it now ranks with the low risk countries. The previously reported rates relied on a fair quality study conducted between 1992 and 1995 and included all Kuwaiti and non-Kuwaiti residents [79], whereas the current study was of good-quality, only included Kuwaiti citizens, and was conducted between 2009 and 2012 [80]. The rates for Iran also dropped from the high [65] to the low moderate-risk category [66]. Both studies were conducted in Shiraz. However, the first one encompassed all residents including tourists, presented age-standardized rates to the 1985 and 1989 US white population, and spanned 3 years, 2000–03 [65], positioning Iran amongst Northern European countries. Conversely, the second study conducted in 2011–12 includes only residents living in Shiraz for at least 6 months, presents age-standardized rates to the 2000 US white population [66], and shows a staggering 40-fold decrease in rates (from 339 to 9/100,000 for both genders). Possible reasons for such change, as proposed by the authors, include institution of fracture prevention strategies, intake of supplements, and possibly better housing architecture for seniors [66]. Although these may be potential contributing factors, they cannot explain such substantial decrements. In Europe, Spain which ranked in the low risk category



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shows much higher rates. We had previously included rates from three regional fair quality studies [13,81,82] conducted before 2002. In the update, more recent good-quality studies conducted after 2007 are included [41,83]; one of which is a national study [41]. While overall rates in South Eastern Australia [63] remain in the low risk category, rates for Indigenous Australians rank among the highest worldwide [46]. Differences are only in part explained by a higher prevalence of major osteoporosis risk factors in the indigenous population.

### s0060 20.5.3 Comparison to the latest systematic review

p0185 Comparison with age and sex-adjusted rates and risk stratification provided by the most comprehensive review by Kanis et al. [18] points to an overall similar picture. Again, the highest rates observed in Northern European countries, Iran showing rates in the same range, and the lowest rates reported in South East Asia, the Middle-East, South Africa, and Latin America. In concordance with our findings, countries from regions previously identified as low risk unexpectedly show rates in the same range as Central European countries. These include Oman, Taiwan, and Greece. However, some significant differences stand out, including a change in the risk category to which a country was allocated to. For example, while Australia belonged to the moderate-risk category in the review by Kanis et al., we show wide variations in two regions of the country, as we were unable to identify published national data. While South Eastern Australia ranks in the low risk category [63], Western Australia registers much higher rates, with significant differences between ethnic groups within this region [46]. Kanis et al. relied on national data by Crisp et al. 2011, that covered incidence rates in 1997–98 and 2006–07 [84], with supplementary information from the Australian Institute of Health and Welfare on hip fracture rates for 2006–07. We report data from two regional studies, the first covered years 2006–07 [63], while the second covered years 1999–2009 [46]. In Europe, age-standardized rates for three countries, Finland, Ireland, and Poland, differ significantly. Again, selection of studies and databases influenced the difference in risk stratification. For Finland, Kanis et al. obtained national data on years 2000–06 by personal communication with Kröger et al., and additional data rated as good-quality evidence from the National Research and Development Centre for Welfare and Health, while we used published national data for 2000–10 [48]. This resulted in placing Finland in the moderate-risk category in the review by Kanis et al. with an age- and sex-standardized rate of 239/100,000/year, and in the high-risk category in our review, with a rate of 287/100,000/year. Similarly, Ireland belonged to the high-risk category in Kanis review (304/100,000/year) who obtained national data by personal communication with McGowan et al. for the years 2008–10 [85], while it ranks in the moderate-risk category in our review (233/100,000/year) using the most recently published national (2000–04) [86] and regional (2001 and 2011) [87] data with good level evidence. In Latin America a substantial difference in rates placed Argentina in the high-risk tertile (264/100,000/year) in the review by Kanis et al. who used regional data (Rosario city) for the years 2001–02 [88], and in the low-risk tertile in our review (116/100,000/year) also using regional data of good quality (Tucuman city) for the years 2001–02 [73]. In addition to this difference in the ranking of some countries, two points are worth mentioning. In his review, Kanis et al. obtained data by personal communication for many countries, data which for the most part was rated as good level evidence. However, such data is not published and, therefore, could not be retrieved nor independently rated. Furthermore, data obtained by personal communication by Kanis et al. provided the only information available for some countries (Jordan, Indonesia, Philippines, Slovakia, and Tunisia). This comparison highlights the importance of study-data selection for accurate estimates of hip fracture rates and the use of peer-reviewed published data versus personal communication.

## 20.6 Secular trends in hip fracture rates s0065

The total number of hip fractures is rising worldwide. While it was estimated at 1.3 million in the year 1990 [6], it rose to 1.6 million in the year 2000, representing approximately a 25% increase. This is in part explained by aging of the world population, with a doubling of the number of individuals above age 50 years between 1950 and 1990, and a 1.5-fold increase between 1990 and 2010 [51], an explosion that is more pronounced in developing countries. Cooper et al. estimated that half of hip fractures in women above age 65 would be expected to occur in Asia by 2050 and only 13% in Europe [27]. Similarly, Gullberg et al. in 1997 expected the number of hip fractures to increase most markedly in Asia, Africa, and Latin America (around 500% from 1990 to 2050) [89]. p0190

Early insight into a temporal trend for sex and age-adjusted hip fracture rates around the world comes p0195



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from a study by Melton et al. in 1987 [90] spanning the period between 1928 and 1980 in which he noted that while rates were rising steeply in the US and Europe, incidence rates in Rochester Minnesota, where follow-up time was the longest, began to plateau from 1950 onward. A review on worldwide secular trends in the incidence of osteoporotic fractures [16] showed that overall age-specific hip fractures have increased steeply in the first half of the century until the 1980s in Northern America and Europe with a similar trend in Oceania; they reached a plateau or started to decrease thereafter. These secular trends were confirmed in a subsequent review [29]. However, data from Asia and South America is scarce, with the exception of Taiwan and Hong Kong that seem to follow continued upward trends [29].

## s0070 20.7 Limitations of studies on hip fractures

p0200 Among all osteoporotic fractures the incidence of hip fracture is the most reliable because in most instances, with the exception of states in Russia [91], it requires hospitalization. Nevertheless, numerous sources of errors may still affect the accuracy of hip fracture incidence rates and these include the following:

### s0075 20.7.1 Data abstraction with PlotDigitizer

p0205 There may be limitations to using such technique but we tried to address by deriving the incidence rate estimates in duplicates. This software was used in countries that did not have numerical data expressed in a tabular form, such as Western Australia, Estonia, Finland, Sweden, UK, and US. Because Finland was running lower rates than expected for Northern European countries, we repeated the process to ensure accuracy of results. In the initial assessment, we extracted numerical data in duplicates for all years (2000–10) and derived an average rate. We subsequently repeated the process independently and used three time points derived in duplicates (2000, 2005, and 2010) and obtained similar results. For the UK, because of the relatively flat and consistent curves for ages 50–54 and 55–59, rates for the first (2000) and last (2012) years were used. For all the subsequent age groups, all rates from 2000–12 were considered.

### s0080 20.7.2 Quality of studies

p0210 Obviously, not all countries have good quality data, which makes it suboptimal in terms of varying degrees of levels of evidence and variable time periods, to allow for accurate comparisons in incidence rates between countries. In our review, we tried to select the best evidence level data available for each country: 35 out of 50 (70%) countries have good level of evidence data. Fair level data is selected for 13 countries because no superior quality data is available. Two countries only had poor to fair data (Columbia and India) as available.

### 20.7.3 Case identification and ascertainment s0085

Over and underreporting of hip fractures when con- p0215
ducting a register-based study or using hospital discharge data might influence the accuracy of hip fracture incidence data, and especially when retrospective data collection is undertaken. Adequate definition of fracture (i.e., review of radiology report and use of ICD codes) was among the criteria used in our rating of studies, reflecting a higher quality evidence and minimizing the risk of misclassification. However, the use of ICD codes does not preclude misclassification, nor does it exclude pathological and high trauma fractures.

### 20.7.4 Regional versus nationwide data s0090

Some countries lack published nationwide repre- p0220
sentative data, and this is not limited to developing countries; some developed countries (Finland, Norway, and Sweden) lacked recent nationwide representative data in the previous chapter, while we were able to identify national data in this chapter. Other developed countries (Australia, Iceland, and Lithuania) only have regional data published. This is important because within the same country spanning several latitudes, incidence rates have been shown to vary by latitude, socioeconomic, and educational status [63,92,93] by two to four fold, with higher incidence observed in the most socially deprived. In addition, fracture rates have been consistently reported to be higher in urban as compared to rural areas. In Argentina, and in addition to regional differences within the country with rates being lower in the Northern as compared to the Central region of the country, Wittich et al. [73] demonstrated a higher incidence in the city of San Miguel de Tucuman than in the rural province. In Sweden [94] all types of fragility fractures were more common in urban (Malmö) than in rural (Sjöbo) areas with an odds ratio of 1.75 for urban dwellers 40 years of age and above, compared with rural inhabitants, the difference being inferred to a difference in bone mass, physical activity, and a higher likelihood of falls in the urban population. Similarly, a study conducted in Geneva and composed of both urban and rural populations



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showed that the age-adjusted incidence of hip fractures was 40% higher in urban compared with rural areas over a 5-year period [95]. The difference was not related to the preferential location of institutions for elderly persons in urban districts. A study by Jacobsen et al. in the US identified a distinct North-South pattern of risk with the highest rates in the South and the lowest in the North [96]. These studies along with others mainly from Norway [97–99] and Croatia [100] highlight the regional differences within the same country in the incidence of hip fractures and the importance of nationwide representative data when comparing rates between countries. Ethnic differences also confer significant variability in hip fracture incidence within the same country: in such countries, data on hip fracture incidence in each ethnic group are important to gather in order to derive rate ratios between ethnicities allowing a better risk stratification. This was done for the US [22] and Singapore [101] but still not well characterized in other countries such as New Zealand where hip fracture rates in Europeans are approximately 30% higher than for Māori, Pacific, and Asian people [64].

s0095 
### 20.7.5 Study Duration and Recency of Data

p0225 Studies extending beyond 1 year clearly convey integrated and more reliable data. Because of secular changes in hip fracture, consideration of the year during which the data was obtained are crucial. To avoid this confounding effect we only selected studies conducted after year 2000 in this update. Consequently, some important countries (Belgium, Brazil, Croatia, Malaysia, and Israel), that were included in the previous version, are omitted herein.

s0100 
## 20.8 Vertebral fractures

s0105 
### 20.8.1 Background

p0230 Vertebral fractures are the most common osteoporotic fractures worldwide occurring in 30%–50% of people over the age of 50; but many factors limit the availability of reliable information on their epidemiology [102]. The majority are silent, less than 10% require hospitalization; they are often missed, underreported. Furthermore, rates often vary due to methodological differences in definition and classification [103–105], with at least five commonly used methods [2], such as that by McCloskey et al. [106], Eastell et al. [105], Melton et al. [107], Black et al. [108], and Genant et al. [109]. The prevalence of morphometric fractures is highest in western populations with comparable rates in the US Study of Osteoporotic Fractures and Canada (Canadian Multicenter Osteoporosis Study CAMOS) of 20%–22%, and lower in Latin America, with an average of 14.8% reported in LAVOS, while rates in Asia are much more heterogeneous [2,25,110,111]. The highest to lowest ratio between countries and continents varies between 1.4 and 2.6. Indeed, rates of 26% were reported in Scandinavia and 18% in Eastern Europe [2]. Incidence rates also seem to possibly follow a North to South gradient and to display ethnic differences. A 3–3.7 folds gradient is observed in Europe [112], and a fourfold difference in between white and black subjects was noted in the US [113]. In this section, we will exclusively address studies that investigated the incidence of clinical vertebral fractures documented by ICD codes to avoid major mismatches in reporting and comparisons.

### 20.8.2 Vertebral fracture incidence s0110

The majority of data on vertebral fractures stem from studies conducted in Europe and North America [23,60,104,112–128]. According to our search updates, 19 studies use ICD codes for vertebral fracture definition and of those, 13 report incidence of hospitalized and ambulatory vertebral fractures and 6 report incidence of hospitalized vertebral fractures [112,113,116,117,126,129]. Additional five other studies are prospective and report baseline prevalence and incidence on follow-up using morphometric methods, with the exception of one study from Hong Kong [23,114,121,123,125]. p0235

#### *20.8.2.1 Hospitalized and ambulatory fractures* s0115

In Europe the oldest study is from the UK [119] and spans 10 years in the 1990s and covers 6% of the population. It reports an overall incidence rate of 45/100,000/year, 32/100,000/year in men and 56/100,000/year in women; rates that are 5–20 fold lower than those reported in Slovenia and Switzerland [115,118]. Discrepancies between the study from the UK and the two others include the fact that the UK study reported incidence in patients aged 20 and older, markedly decreasing the overall average incidence and reported fractures at any vertebral level, that were not all necessarily due to osteoporosis. Conversely, the studies from Slovenia and Switzerland reported on postmenopausal women or subjects above age 50 years, an age category at higher risk for osteoporotic fractures. However, a larger study from the UK [127], spanning a longer time frame and more recent years (1988–2012), reported about 1.5–2 folds higher rates of clinical vertebral fractures of 46/100,000/year in men and 94/100,000/year in women for 50+ age groups, as compared to previous UK study [119], thus p0240 bringing rates from the UK rates closer to those from other European countries.

p0245 Two studies from North America reported on incident ambulatory and hospitalized vertebral fractures using the ICD codes. The study from Canada [120] was conducted between 1981 and 1984 and reported rates in Manitoba of 64/100,000/year, that are comparable to those reported in UK in the 1990s [119]; and similar to that study, it included younger age group and the same ICD-9 codes. The US study from Olmsted county [128] reported rates in patients aged 50 and above using the ICD-9 code for the period of 2009–11. These more recent rates were almost 1.5-fold higher compared to those in 1989–91 in the same region (968/100,000/year vs 659/100,000 for both genders, 798/100,000 vs 460/100,000 in men and 1092/100,000 vs 812/100,000 in women) [128].

p0250 Data from Korea using nationwide claims of spinal fractures (listing ICD-10) showed an increase in the incidence for both genders of 1.2-fold, with rates in men of 245.3/100,000 in 2008 and 312.5/100,000 in 2012 and in women of 780.6/100,000 in 2008 and 953.4/100,000 in 2012 [130]. Another study spanning 2005–08 reported incidence rates of 431/100,000 in men, and 1430/100,000 in women [131]. Both studies place Korea consistently in the highest risk category for vertebral fractures worldwide [130,131].

p0255 In summary the above studies consistently demonstrate a steady rise in incidence rates over time in the US, UK, and South Korea. In addition to being only few, they are very heterogeneous and do not allow an analysis of geographic variability of osteoporotic vertebral fractures.

#### s0120 20.8.2.2 *Hospitalized fractures*

p0260 Few studies exclusively reported the incidence of hospitalized vertebral fractures. The largest among them, conducted in Europe in the 1990s, included 8 countries, used the same ICD-9 code, evaluated subjects above age 50 years, and reported age-standardized rates to the 1990 Swedish population [112]. A North to South gradient with a three to four fold variability was evident; the highest rates observed were from Scandinavia for both genders and the lowest in Central and Southern Europe, with the exception of Slovakia where rates in men were comparable to those observed in Scandinavian countries. Another large study examined rates in whites as compared to blacks aged 65 and above in the US for the years 1986–89 [113]. It showed overall rates in white men and women that were approximately fourfold higher than in blacks, with a three- to five-fold gradient across genders and age groups, between the two ethnic groups. In the Netherlands a study reporting emergency department visits due to vertebral fractures between 1986 and 2008 showed a twofold increase in age-adjusted rate in older adults (from 51.9 to 102.3/100,000 persons) between the initial and last study year [129]. Other studies from Europe, such as the one conducted in Spain, reported incidence rates ranging between 37/100,000 to 108/100,000 in 2002 [116] and 13/100, 000 to 97/100,00 in Sweden for years 1997–2001 [117].

p0265 Despite the difficulty in comparing across studies, one may conclude from the limited studies on the incidence of hospitalized vertebral fracture that there is less geographic variability compared to hip fractures. Importantly, such conclusion is limited by the fact that only 10% of vertebral fractures require hospitalization.

## 20.9 Predictors of fracture variability s0125

p0270 The 10-fold range in the variation of hip fracture incidence across the world raises important questions about the etiology of hip fracture. The reasons for this variability are unknown, but it is highly likely that genetic factors play a role. Twin and family studies have shown that 50%–80% of the variance in bone mineral density (BMD) is genetically determined, and BMD is the single best predictor of fracture [132]. Osteoporotic fractures have also been shown to be heritable, independent of BMD [133]. A genome-wide association analyses of almost 83,000 individuals identified 56 BMD loci and 14 loci associated with fracture risk [134]. Thus a large part of the international variability on fracture rates may reflect differential genetic susceptibility. In contrast to the former studies, a study examining the effect of genetic diversity on the worldwide variation in hip fracture incidence showed that genetics only play a minor role in the perceived heterogeneity of fracture rates [135]. Other factors likely contribute.

p0275 As noted earlier, low BMD is a major predictor of fracture in both men and women. There may be geographic variability in BMD. Nam et al. reported recently compared standardized areal BMD measures in several populations of older men [136] and women [137]. We compared reported numbers at the lumbar spine, total hip, and femoral neck BMD in US Whites, US Asians, US Hispanics, US Blacks, Afro-Caribbeans from Tobago, Hong Kong Chinese, and Koreans. We showed that hip BMD in Afro-Caribbean men was 8%–10% higher than US Blacks, despite the fact that both populations are of African origin. The lower BMD among US Blacks may have reflected their greater European admixture, but the more rural lifestyle in Tobago may have also contributed. Within the Asian groups, BMD was much lower in the Koreans compared to the Hong Kong Chinese. The Korean men experienced relative nutritional defects during the Korean War (1950–53) when these men were in their childhood and adolescence and might have led to



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lower peak skeletal mass [136]. Areal BMD is a two-dimensional measure and does not account for differences in bone size and geometry, which may also contribute to international variability in hip fractures. For example, Asians have shorter hip axis lengths and smaller neck shaft angle [138] and bone structure (greater cortical thickness and trabecular volumetric BMD) [139].

p0280 Body mass index (BMI) is a major determinant of BMD and higher BMI has been linked to a lower risk of hip fracture. Thus variability in BMI and the prevalence of obesity may also contribute to the variability in hip fractures worldwide. For example, the mean body weight varied from a low of 61.8 kg in the South Korean men to 87.1 kg in US Black men, and accounting for differences in body weight attenuated the differences in BMD although they remained significant [136].

p0285 Other lifestyle factors including physical activity and diet vary across the world. Korean men had the lowest dietary calcium (323 mg/day) compared to about 600 mg/day in the Hong Kong Chinese and US Asians [136]. Differences in physical activity could underplay the differences in hip fracture rates in urban versus rural settings. For example, Xia et al. hypothesized that the rapid increase in rates of hip fracture in Beijing could reflect increased urbanization that is characterized by increased reliance on cars and buses instead of walking or biking [28]. The prevalence of hypovitaminosis, that is a serum 25 hydroxyvitamin D (25 OHD) <50 nmol/L, worldwide was estimated to be 37% with region-specific estimates at 18% in the US, 40% in adults of EU countries, 90% in Iran and Jordan, <7% in Ghana and Seychelles, 34% in the African continent, and around 72% in China [140]. These estimates are limited by the differences of assays used, lack of true population based studies, and often older studies. This widespread epidemic of vitamin D deficiency raises the possibility that hip fracture rates could be lowered with simple relatively inexpensive vitamin D supplementation. We also showed substantial geographical variation in the levels of sex steroids, precursor and metabolites, and sex hormone binding globulin (SHBG) [141]. For example, Asian men in Hong Kong and Japan, but not in the US, had levels of total testosterone approximately 20% higher than in other groups. Even greater variation was present in the levels of estradiol, SHBG, and dihydrotestosterone. Group differences in BMI did not explain most geographical differences in sex steroids. In addition, BMI-independent racial differences were present; Black men had higher levels of estrogens (estradiol, estrone) and Asian men had lower levels of glucuronidated androgen metabolites. Factors that contribute to these global variations in sex steroid hormones could include differences in physical activity, diet, exposure to chemicals, and smoking. The prevalence of reproductive disorders could vary and contribute as well. In addition, differences in genetics of sex steroid metabolism might be reflected in differences in circulating levels.

p0290 Most fractures occur because of a fall and the incidence of falling and differential risk factors for falling might also contribute. In Europe, fall rates varied in men and women from a low of 5 per 100 person years in Rotterdam, the Netherlands (both sexes combined) to >20 per 100 person years in Oslo, Norway [142]. Comorbidities have a major influence on osteoporotic fractures. Individuals with greater comorbidity index have a higher risk of fractures. For example, diabetes is a major risk factor for fractures including hip fracture and the prevalence of diabetes varies dramatically across the world. For example, the prevalence of diabetes was about 35% in New Guinea about 10% in China and India [143].

p0295 In summary the substantial variability in hip and vertebral fractures must reflect a multitude of factors including genetic, lifestyle, medical, and environmental. International comparisons of risk factor for fractures could contribute to our understanding of the etiology of osteoporotic fractures. Future studies will need to standardized data-collection materials and methods to facilitate these international comparisons.

## 20.10 Conclusion s0130

p0300 Osteoporosis, an old disease of the old, incurs staggering social and economic costs in our modern ages. The demographic explosion, increased life expectancy, global urbanization, and the obesity epidemic, are major contributors to the exponential rise in the incidence of hip fractures, and more so in developing countries such as Asia, Indonesia, and the Middle East. There are substantial geographic and ethnic variations in fracture risk, a difference that is most striking for hip fractures. Indeed, a 10-fold difference in hip fracture standardized rates is recorded between the highest risk countries, being highest in general in Northern Europe, and lowest in the Far East and South Africa, while vertebral fractures are less variable. Some of these differences may have biologic and lifestyle etiologies, while others may reflect limitations in the information collected. In addition, secular trends have been noted across regions with a general trend for a plateau in fracture rates in western countries, while a steady rise persists in Eastern parts of the world. Understanding the etiology of geographic and ethnic differences in fractures will further our understanding of the pathophysiology of fractures and lead to new treatment interventions.



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Accurate characterization of the incidence of fractures and their epidemiology is of direct relevance to each nation, and ethnic groups/individuals within a nation. Such information is the key to the formulation of national public health policies, the allocation of health care resources, the development of country-specific fracture risk calculators, and the assessment of an individual's fracture risk to implement suitable therapies.

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t0015 Appendix: Age-standardized yearly rates of hip fractures by continent, country, gender, and age-group in order

**Table A Asia.**

| Country | Source | Year | Quality | Catchment | Rates for men/ 100,000 | Rates for women/ 100,000 | Rates for both genders/ 100,000 |
|---|---|---|---|---|---|---|---|
| China[a] | Wang et al. [144] | 2010 | F | R | 92 | 147 | 120 |
| | Tian et al. [145] | 2015 | F | R | | | |
| Hong Kong | Tsang et al. [54][b] | 2000−04 | G | N | 147 | 321 | 239 |
| India | Dhanwal et al. [149] | 2009 | P/F | R | 118 | 155 | 138 |
| Japan[a] | Hagino et al. [146][c] | 2004−06 | G | R | 93 | 264 | 182 |
| | Orimo et al. [148][c] | 2002, 2007, 2012 | G | N | | | |
| Singapore | Chionh [53] | 2007−09 | G | N | 155 | 329 | 246 |
| Korea[a] | Lim et al. [55] | 2004 | G | N | 126 | 208 | 169 |
| | Yoon et al. [56][c] | 2005−08 | G | N | | | |
| | Ha et al. [58][b] | 2008−12 | G | N | | | |
| | Kyumg-Soon Park et al. [57][c] | 2001, 2011 | G | R | | | |

(*Continued*)

(Continued)

**Table A Asia.**

| Country | Source | Year | Quality | Catchment | Rates for men/ 100,000 | Rates for women/ 100,000 | Rates for both genders/ 100,000 |
|---|---|---|---|---|---|---|---|
| Taiwan | Chen et al. [52][b] | 2004–11 | G | N | 228 | 399 | 317 |
| Thailand | Wongtriratanachai et al. [147] | 2006 | F | R | 106 | 263 | 188 |

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**Table B Oceania**

| Country | Source | Year | Quality | Catchment | Rates for men/ 100,000 | Rates for women/100,000 | Rates for both genders/100,000 |
|---|---|---|---|---|---|---|---|
| Australia | Brennan et al. [63] | 2006–07 | G | R | 66 | 78 | 72 |
| Western Australia (indigenous and nonindigenous) | Wong et al. [46][b] | 1999–2009 | G | R | 307 | 404 | 358 |
| | | | | | 104 | 242 | 176 |
| New Zealand | Brown et al. [64][b,d] | 2003–05 | G | N | 139 | 285 | 216 |

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**Table C Middle East and Africa.**

| Country | Source | Year | Quality | Catchment | Rates for men/ 100,000 | Rates for women/ 100,000 | Rates for both genders/100,000 |
|---|---|---|---|---|---|---|---|
| Iran[a] | Soveid et al. [65][b] | 2000–03 | F | R | 137 | 207 | 174 |
| | Maharlouei et al. [66] | 2011–12 | F | R | | | |
| Kuwait | Azizieh et al. [80][c] | 2009–12 | G | N | 142 | 195 | 170 |
| Lebanon[a] | Sibai et al. [14][c] | 2006–08 | G | N | 82 | 204 | 146 |
| | Saad et al. [150][c] | 2006–17 | G | N | | | |
| Morocco[a] | El Maghraoui et al. [151] | 2002 | F | R | 67 | 83 | 75 |
| | El Maghraoui et al. [152][b] | 2006–09 | F | R | | | |
| Oman | Shukla et al. [44][c] | 2002–07 | F | R | 237 | 312 | 276 |
| Saudi Arabia | Sadat-Ali et al. [40] | 2013 | F | R | 538 | 909 | 739 |
| South Africa (Black South Africans) | Paruk et al. [42] | 2010–11 | G | R | 107 | 83 | 94 |

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**Table D Europe.**

| Country | Source | Year | Quality | Catchment | Rates for men/ 100,000 | Rates for women/ 100,000 | Rates for both genders/ 100,000 |
|---|---|---|---|---|---|---|---|
| Armenia | Lesnyak et al. [154][e] | 2011–13 | G | R | 92 | 154 | 124 |
| Austria | Dimai et al. [153][c] | 2000–08 | G | N | 220 | 439 | 335 |
| Czech | Stepan et al. [155] | 2008–09 | G | N | 210 | 370 | 293 |
| Denmark | Abrahamsen et al. [36][c] | 2000–06 | G | N | 455 | 946 | 720 |
| Estonia | Jürisson et al. [47][c] | 2005–12 | G | N | 198 | 239 | 219 |
| Finland | Korhonen et al. [48][c] | 2000, 2005, 2010 | G | N | 226 | 344 | 287 |

*(Continued)*

(Continued)

**Table D Europe.**

| Country | Source | Year | Quality | Catchment | Rates for men/ 100,000 | Rates for women/ 100,000 | Rates for both genders/ 100,000 |
|---|---|---|---|---|---|---|---|
| France[a] | Couris et al. [156] | 2004 | G | N | 177 | 370 | 280 |
| | Briot et al. [35][c] | 2002–13 | G | N | | | |
| Germany | Icks et al. [157][c] | 2000–04 | G | N | 153 | 337 | 249 |
| Greece | Lyritis et al. [169][c] | 2002, 2007 | F | N | 169 | 371 | 275 |
| Hungary | Pentek et al. [126][b] | 1999–2003 | G | N | 204 | 364 | 288 |
| Iceland | Siggeirsdottir et al. [45][b] | 1989–2008 | G | R | 149 | 345 | 251 |
| Ireland[a] | Dodds et al. [86][b] | 2000–04 | G | N | 131 | 326 | 233 |
| | Karayiannis et al. [87][c] | 2001, 2011 | G | R | | | |
| Italy[a] | Piscitelli et al. [34][c] | 2000–05 | G | N | 138 | 331 | 238 |
| | Piscitelli et al. [158] | 2008 | G | N | | | |
| Lithuania | Tamulaitiene et al. [159] | 2010 | F | R | 155 | 268 | 214 |
| The Netherlands[a] | Lalmohamed et al. [160] | 2004–05 | G | N | 100 | 209 | 148 |
| | Klop et al. [161][b] | 2002–11 | G | N | | | |
| Norway[a] | Emaus et al. [67][b]<br>Søgaard et al. [68][e] | 1994–2008<br>1999–2003<br>2004–08,<br>2009–13 | G<br>G | R<br>N | 271 | 547 | 416 |
| Poland | Czerwinski et al. [162] | 2005 | F | N | 88 | 144 | 117 |
| Portugal | De Pina et al. [163][b] | 2000–02 | G | N | 97 | 266 | 186 |
| Romania | Grigorie et al. [164] | 2010 | F | N | 142 | 198 | 171 |
| Russia | Lesnyak et al. [154] | 2008–09 | G | R | 185 | 246 | 217 |
| Slovenia | Dzajkovska et al. [115] | 2003 | F | N | NA | 308 | NA |
| Spain[a] | Azagra et al. [41][c] | 2000–10 | G | N | 170 | 405 | 299 |
| | Sosa et al. [83][b] | 2007–11 | G | R | | | |
| Sweden[a] | Bergstrom et al. [69][c] | 2001–05 | G | R | 431 | 877 | 675 |
| | Nilson et al. [37][c] | 2000–09 | G | N | | | |
| Switzerland[a] | Lippuner et al. [118] | 2000 | G | N | 176 | 373 | 279 |
| | Lippuner et al. [166][c] | 2000–07 | G | N | | | |
| Turkey | Tuzun et al. [167] | 2009 | F | R | 110 | 354 | 238 |
| United Kingdom[a] | Wu et al. [43][c] | 2000–09 | G | N | 110 | 278 | 198 |
| | Van der Velde et al. [49][c,f] | 2000–12 | G | N | | | |

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**Table E North America.**

| Country | Source | Year | Quality | Catchment | Rates for men/ 100,000 | Rates for women/ 100,000 | Rates for both genders/ 100,000 |
|---|---|---|---|---|---|---|---|
| Canada | Leslie et al. [71][c] | 2000–05 | G | N | 180 | 400 | 296 |
| Caribbean | Rouvillain et al. [38][b] | 2010–13 | G | R | 105 | 199 | 157 |
| United States[a] | Ettinger et al. [70][g] | 2006 | G | N | 177 | 361 | 274 |
| | Sullivan et al. [50][c] | 2000–11 | G | R | | | |

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**Table F Latin America.**

| Country | Source | Year | Quality | Catchment | Rates for men/ 100,000 | Rates for women/ 100,000 | Rates for both genders/ 100,000 |
|---|---|---|---|---|---|---|---|
| Argentina | Wittich et al. [73] | 2001–02 | G | R | 77 | 151 | 116 |
| Colombia | Jaller-Raad et al. [75][b] | 2004–06 | P/F | R | 78 | 138 | 109 |
| Ecuador[a] | Orces et al. [74] | 2005 | G | N | 66 | 135 | 103 |
| | Orces et al. [39][b] | 1999–2016 | G | N | | | |
| Venezuela | Riera-Espinoza et al. [76] | 2005–06 | F | R | 45 | 149 | 99 |

[a]*For countries with more than one study, average of age-standardized rates for all studies was calculated.*
[b]*Average of hip fracture rates for all study period provided by author.*
[c]*For studies providing rates for more than 1 year, average of age-standardized rates for all study years calculated.*
[d]*Rates for European ethnic group (most widely represented in New Zealand).*
[e]*For studies providing rates by time periods, average of age-standardized rates of all periods calculated.*
[f]*For 50–54 and 55–59 age groups, average of first and last years was taken since values of all years could not be extracted from plots and no significant variation was present throughout the years.*
[g]*Data on non-Hispanic whites.*
*Notes*: Rates were standardized rates to the 2010 United Nations world population.
G refers to good quality studies; F to fair quality studies; P to poor quality; N refers to national study; R refers to regional; NA, data not available.

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## NON-PRINT ITEM

**Abstract**

Age-related bone loss and osteoporosis have been documented, going back to antiquity, but substantial geographic and ethnic variations in fracture risk are still noted today. These variations are most striking for hip fractures, with a 10-fold difference in standardized rates between the highest and the lowest risk countries; while vertebral fractures vary by two to four fold worldwide. These variations may in part be due to factors incurred from the methodology followed to capture true fractures, in addition to true differences. Furthermore, changing demographics and secular trends are rapidly shifting the burden of hip fractures from the western world to Asia and the Middle East. This Chapter details an update of the epidemiology of hip and vertebral fractures, and overviews potential causes for such differences. Such understanding is essential to accurate fracture risk assessment, health care resource allocation, and the development of nationally relevant care pathways.

**Keywords:** Hip fractures; vertebral fractures; secular trends; lifestyle factors; ethnic variation; geographic variations; age-standardized rates