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REVIEW ARTICLE

The epidemiology of osteoporosis, associated fragility fractures, and management gap in China

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Abstract

Background Osteoporosis has been one of the most common but largely under-diagnosed clinical problems among elderly population. The disease burden is even greater in China because of limited medical resources and large population size. This article is aimed to provide an overview of disease burden, secular trend, and management gap of osteoporosis and related fractures in China.

Methods Based on the related studies published in English and Chinese from 1990 to 2017, we investigated the prevalence/incidence of osteoporosis and osteoporotic fracture in Chinese mainland, Hong Kong, and Taiwan, characterizing the secular trend and disease burden in different regions. Strict inclusion criteria were applied to control the study quality. We further examined the diagnosis and treatment gap of osteoporosis management observed in clinical practice in China and summarized the efforts made by Chinese government and scholars to combat this situation.

Results Twenty-seven studies concerning osteoporosis prevalence in China (including Chinese mainland, Hong Kong, and Taiwan) met the inclusion criteria and were included in the final analysis. Another 15 studies about hip fracture incidence and 13 studies about vertebral fracture prevalence/incidence were also included. The epidemiological data varied greatly across studies due to different design and population included. A higher prevalence was indicated in female population, older age groups, and residents in northern China compared to their counterparts. Though attenuated increased rates or slight decline patterns have been observed in Hong Kong and Taiwan, osteoporotic fracture incidence still showed steady increase in Chinese mainland. The diagnosis and treatment of osteoporosis as well as post-fracture management were still insufficient in China.

Conclusion Due to its silent nature, osteoporosis and its related fractures remain largely under-diagnosed and under-managed in China. It also highlights the scarcity of high-quality studies specifically focus on longtime documentation of disease burden change and male population, especially in mainland area.

Keywords Osteoporosis · Fracture · China · Epidemiology · Management

Introduction

Osteoporosis is a condition characterized by reduced bone mass and disruption of bone architecture, which can result in increased risk of fragility fractures [1]. Osteoporotic fractures in the elderly are usually followed by hospitalization, impaired quality of life, long-term medical care, disability, and death [2–5]. Osteoporosis and osteoporotic fracture constitute great medical, public health, and economic burden worldwide. Unfortunately, diagnostic facilities and therapeutic options are still not available to a large number of patients in some rural areas in under-developed regions. The uneven distribution of medical resources makes the management of osteoporosis more challenging [6].

China is the largest developing country in the world, constituting one-fifth global population and even higher percentage of elderly population. Osteoporotic population is predicted to boom in the near future because of the expanding aging population and dramatic lifestyle changes happening in China over the last two to three decades [7]. The reported

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osteoporosis prevalence varied greatly across studies, which can be partly attributed to the differences in study design, such as target population, diagnostic criteria, measuring site, and facilities adopted [7]. Few articles have concentrated on incorporating the results of published studies that specifically focused on Chinese population. This article aims to present an extensive overview of disease burden, secular trend, and management gap of osteoporosis and related fractures in China. In the end, we also summarize the efforts made by Chinese scholars and government to eliminate the gaps.

Methods

Literature search

We conducted a literature search for English language articles published between January 1, 1990 and January 1, 2018 in the PubMed and Embase/MEDLINE online using the following keywords in various combinations: "osteoporosis," "bone mass," "bone health," "bone mineral density," "prevalence," "incidence," "epidemiology," "fracture," "osteoporotic fracture," "vertebral fracture," "spine fracture," "hip fracture," "fragility fracture," "China," "Chinese," "Mainland," "Hong Kong," "Taiwan," and "Asia." In addition, related articles published in Chinese language were searched with same keywords mentioned above in "Wanfang Data," which was one of the most comprehensive information contents providers in China. Authors inspected titles and abstracts of the search results individually. Full texts were obtained if titles and abstracts did not provide enough information. Only studies that discussed about epidemiology of osteoporosis or osteoporotic fracture were included.

Study selection

Several criteria must be met to be included in our analysis: (1) providing sufficient information about prevalence/incidence of osteoporosis/vertebral fracture/hip fracture; (2) having a sample size of greater than 1000 for osteoporosis prevalence studies and 400 for osteoporotic fracture studies; (3) describing methodology and study population clearly in texts; and (4) being cross-sectional, cohort designed studies or review papers (based on regional or national representative data). Age-specific data were obtained directly from the text or by calculating from the information provided in the article.

Osteoporosis definition

Various sites could be measured to develop the bone mineral density (BMD) value. The final diagnosis of osteoporosis should be based on BMD measurement and/or fragility fracture history. According to the criterion proposed by WHO Study Group, osteoporosis could be diagnosed when BMD (at axial regions, including vertebra, femoral neck, or hip) is 2.5 standard deviations (SD) or more below the average that of the young adult population [8–10]. However, some data suggested that the peak bone mass of yellow race was 10–15% lower than that of white race. Quite a number of Chinese people may have lost their chance of starting osteoporosis prevention if same criteria were adopted indiscriminately among different races [11, 12]. As a result, some Chinese scholars argued that diagnosing osteoporosis according to −2.0 SD or 25% reduction of BMD might be closer to the real status of Chinese population [13]. Studies that adopted either criterion were included in our analysis.

Hip and vertebral fracture definition

Hip fractures were ascertained by retrospectively reviewing admission/discharge records or data from local health insurance database. Hip fractures included those happened at femoral neck, trochanteric, and intertrochanteric area. When International Classification of Diseases 9th revision (ICD-9) or 10th revision (ICD-10) system were used for coding discharge diagnosis, records that coded as 820 for ICD-9 and S720.0, S720.1, and S720.2 for ICD-10 could be regarded as hip fracture cases. Studies without adopting ICD system should be examined carefully for fracture sites.

Vertebral fractures were evaluated with two different criteria based on lateral spine radiographs. Four vertebral height ratios (VHR) including anterior to posterior (Ha/Hp), middle to posterior (Hm/Hp), posterior to posterior-above, and posterior-below (Hp/Hp-above and Hp/Hp-below) were calculated as indicators of vertebral morphometric change. Vertebral fracture was defined as a reduction of > 3 SDs in any of the VHR parameters [14]. Genant's semiquantitative (GSQ) scoring system was based on visual estimation of reduction in vertebral height or area without the aid of direct measurements. A reduction of 20–25% in anterior, middle, and/or posterior height and a reduction of area of 10–20% were defined as "mildly deformed" or grade 1 fracture. A reduction of 25–40% in any height and 20–40% in area defined "moderately deformed" or grade 2 fracture. Grade 3 fracture or "severely deformed" referred to those had a reduction of 40% or more in any vertebral height or area.

Results

Study characteristics

The literature search flow chart was provided in Supplementary Fig. 1. In total, 27 studies that discussed about osteoporosis prevalence met the inclusion criteria and were included in final analysis, among which 20 articles were about Chinese mainland (10 in English, 10 in Chinese), 3 were about Hong Kong, and 4 were

carried out in Taiwan (all in English). Lau reported data concerning female population both in Hong Kong and mainland [15]. Two literature reviews were also included because they had very large sample size and integrated results of many Chinese language articles [16, 17]. One of the studies used disease code recorded in Taiwan's National Health Insurance (NHI) database instead of direct DXA measurement [18].

Fifteen studies related to hip fracture incidence were found, including 8 from mainland, 4 from Hong Kong, and 3 from Taiwan (all in English). In regard to vertebral fracture prevalence, 13 studies met the inclusion criteria, including 6 studies from mainland (2 in English, 4 in Chinese), 6 from Hong Kong, and 1 from Taiwan (all in English). Two studies provided vertebral fracture data of 395 and 396 elderly people and were also included after careful examination of the contents [19, 20].

Prevalence or incidence in population younger than 40 years old were not presented in the table since it was quite low and did not facilitate comparison between studies. More detailed information is available in Tables 1, 2, and 3.

Epidemiology of osteoporosis

The prevalence of osteoporosis in China

Chinese mainland Early in 1997, Liu reviewed results of epidemiological studies of osteoporosis beginning from the 1990s in China [12]. Liu and his colleagues developed their own model and estimated that 6.6% Chinese elderly were suffering from osteoporosis. This number would increase to 8.2% in 2010, and 13.6% in 2050 [12]. Five years later, the same group launched another study and yielded a prevalence of 6.97% [68]. The model was based on the association observed between bone loss rate and age in published literatures, in combination with population census data. However, later studies suggested much steeper increase rate and much severer disease burden than predicted. In 2002, Li analyzed data from five administrative areas in Chinese mainland and reported an overall prevalence of 16.1% (11.5% in males, 19.9% in females) in those aged over 40 [21]. Various osteoporosis prevalence were reported across cities, which was Jilin (15.5%) > Shanghai (14.2%) > Sichuan (11.3%) > Guangzhou (10.2%) > Beijing (5.2%) [21]. Another multi-center study published in 2010 enrolled 7042 participants from 10 centers in mainland and yielded a prevalence of 10.4% in men and 31.2% in women who aged over 50 [26]. In 2015, Lau compared the BMD and osteoporosis prevalence in community-dwelling elderly women living in northern (Beijing) and southern (Hong Kong) China. The study recruited 6099 ambulatory Chinese women in Hong Kong and 6302 women in Beijing [15]. Higher osteoporosis prevalence was observed in Hong Kong women than those in Beijing (24.9% versus 20.3%) [15]. This regional difference may be a result of environmental exposure, dietary intake, lifestyle, genetic predisposition, or other underlying factors [7, 21, 69]. The overall prevalence of osteoporosis defined by BMD at distal forearm was 19.8% in men and 36.9% in women among people aged over 50 years in Jilin, which located in northern China [36]. A recently published study in Gansu province analyzed the BMD measured at radius and yielded a prevalence of 9.65% for postmenopausal women and 8.08% for men with WHO criteria, which was much lower than that reported in other studies [37].

Apart from those studies published in English, some regional studies were carried out in China and published in Chinese medical journals. Liu's review paper incorporated the results of epidemiologic studies published in Chinese before September 2014 [16]. Applying a cutoff value of − 2.5 SD, the research found that osteoporosis prevalence increased from 6.37% in women aged 40–50 years to 76.74% in those aged 80–90 years. The prevalence changed from 4.11 to 39.78% in men as they became older [16]. If − 2.0 SD was adopted as cutoff value, the osteoporosis prevalence varied between 7.75 and 89.55% in women and 4.00 and 66.19% in men [17]. The study also concluded that the osteoporosis prevalence would increase approximately 15% in males and 20% in females every 10 years. The overall osteoporosis prevalence was reported to be 19.74% and 24.62% in Chinese population over 40 years old by another two studies [16, 17]. The prevalence increased with age in all studies.

We briefly divided Chinese mainland into north region and south region according to Qinling Mountains-Huaihe River line and made a comparison between them (Fig. 1).

Hong Kong Some high-quality epidemiologic studies with large sample size had been carried out in Hong Kong. In 2005, Lynn recruited 4274 participants from multiple sites in Hong Kong by private solicitation and public advertising. The study also established BMD reference norms for Chinese population [38]. The osteoporosis prevalence in women aged over 50 years was 37% at spine and 16% at total hip, while in men the number was 7% at spine and 6% at total hip [38]. In a study carried out during 2008 to 2011, the prevalence of osteoporosis and osteopenia among 6099 women aged 50–89 years old was 24.9% and 51.7%, respectively [15]. The osteoporosis prevalence among Hong Kong residents had been early documented in 1999 by Ho and his colleagues, which was 34% at spine and 24% at femoral neck [70]. This was significantly higher than that documented in mainland at the same time. The comparison of osteoporosis prevalence between Chinese mainland and Hong Kong were demonstrated in Table 1 and Fig. 1.

Taiwan Several studies with very large sample size provided valuable information concerning osteoporosis epidemiology in Taiwan (Table 1). Yang investigated the prevalence of osteoporosis in 1996–2001 by collecting information from Taiwan's National Health Insurance (NHI) database [18]. Insurance records from 102,763 men and 97,654 women were evaluated and yielded an average osteoporosis prevalence of 1.63% for men and 11.35% for women aged over 50 years [18].

Table 1 Characteristics and main findings of selected studies: osteoporosis prevalence in China

Year[a], author [reference]	Population	Sample size	Methodology	Criteria	Sites	Gender/age	Prevalence	
							Male	Female
Mainland								
2002, Li [21]	Jilin, Beijing, Shanghai, Guangzhou, Sichuan	5593	DXA	WHOC[b]	(AP) Lumbar spine, proximal femur	M/F > 40 years	11.5%	19.9%
1996–2003, Wu [22]	Changsha, Hunan	1166	DXA	WHOC and CC[c]	(AP and La) Lumbar spine, femoral neck, total hip, distal forearm	F 50–90 years	NA	Chinese criteria Spine (AP): 41.5% Spine (La): 53.9% Femoral neck: 34.2% Total hip: 30.7% Distal forearm: 51.4% WHO criteria Spine (AP): 32.1% Spine (La): 34.9% Femoral neck: 16.3% Total hip: 18.9% Distal forearm: 45.2%
1999–2003, Zhao [23]	Jilin	1180	DXA	WHOC	Lumbar spine, femoral neck, Wards' troch, greater trochanter	M/F > 20 years	> 50 years Spine: 14.7% Femoral neck: 13.2% Wards' troch: 13.7% Greater trochanter: 13.2%	> 50 years Spine: 20.0% Femoral neck: 23.5% Wards' troch: 23.3% Greater trochanter: 8.3%
1999–2005, Gao [24]	Jiangmen, Guangdong	2454	DXA	WHOC	Lumbar spine, femoral neck, Wards' troch	M/F 20–89 years	Overall 19.2% > 50 years 27.9%	Overall 25.2% > 50 years 42.1%
2006, Meng [25]	Liuzhou, Guangxi	1230	DXA	CC	Femoral neck	M/F 40–88 years	Overall 35.25% > 50 years 41.1%	Overall Female: 57.65% > 50 years 65.2%
2002–2006, Zhu [26]	Ten centers in mainland	7042	DXA	WHOC	Lumbar spine, proximal femur	M/F > 20 years	> 50 years Spine: 4.7% Femoral neck: 8.3% Greater trochanter: 3.6% Spine or femoral neck: 10.4%	> 50 years Spine: 26.2% Femoral neck: 15.1% Greater trochanter: 9.1% Spine or femoral neck: 31.2%
2003–2006, Hsu [27]	Anhui	13,970	DXA	WHOC	Total hip	M/F 25–64 years	2.2%	Premenopausal: 1.8% Postmenopausal: 12.4%
2007, Cheng [28]	Beijing, Shanghai, Jiaxing, Nanjing, Chengdu, Guangzhou	8142	DXA	WHOC	Lumbar spine, proximal femur	F 20–89 years	NA	> 50 years Any site: 31% Spine: 28% Femur: 15%
2007, Jiang [29]	Chongqing	1801	DXA	WHOC	NA	M/F Most (96.7%) > 40 years	> 45 years 11.0%	> 45 years 22.6%
2004–2008, Luo [30]	Hezhou, Guangxi	3000	DXA	WHOC	Lumbar spine, femoral neck, Wards' troch, greater trochanter	M/F 20–96 years	> 50 years Spine: 23.3% Femoral neck: 21.6% Wards' troch: 20.6% Greater trochanter: 10.3%	> 50 years Spine: 37.3% Femoral neck: 21.3% Wards' troch: 23.9% Greater trochanter: 19.2%

Table 1 (continued)

Year[a], author [reference]	Population	Sample size	Methodology	Criteria	Sites	Gender/age	Prevalence	
							Male	Female
2009, Chen [31]	Haikou, Hainan	1110	DXA	WHOC	Lumbar spine, femoral neck, Wards' troch, greater trochanter	M/F > 40 years	> 50 years Spine: 32.6% Femoral neck: 55.5% Wards' troch: 42.9% Greater trochanter: 7.6%	> 50 years Female Spine: 63.3% Femoral neck: 31.2% Wards' troch: 49.9% Greater trochanter: 34.4%
2009–2010, Zhou [32]	Beijing	4672	DXA	WHOC	Distal forearm	M/F 40–89	> 50 years 12.7%	> 50 years 21.4%
2010, Sheng [33]	Changsha, Hunan	954	DXA	WHOC	Lumbar spine, femoral neck, total hip	F 50–82 years	NA	39.4%
2010, Huang [34]	Xiangfan, Hubei	1123	DXA	CC	Lumbar spine, femoral neck, Wards' troch, greater trochanter	M/F 20–80 years	> 50 years 17.0%	> 50 years 37.0%
2008–2011, Lau [15]	Beijing	6302	DXA	WHOC	Lumbar spine, femoral neck, total hip or femoral neck (any one site)	F 50–89 years	NA	20.3% 58.4% (osteopenia)
2010–2011, Yang [35]	Beijing	1201	DXA	WHOC	Lumbar spine, left femur	Postmenopausal women	NA	29.3%
2010–2013, Li [36]	Jilin	3639	DXA	WHOC	Distal forearm	M/F > 50 years	19.8%	36.9%
2015, Zhang [16]	Mainland	70,992	Review of domestic literature	WHOC	NA	M/F > 40 years	12.91%	26.66%
2015, Tian [37]	Gansu	6564	DXA	WHOC	Distal forearm	Male: > 60 years Postmenopausal women	8.08%	9.65%
2016, Zhang [17]	Mainland	22,954	Review of domestic literature	−2.0 SD	NA	M/F > 40 years	17.77%	31.55%
Hong Kong								
2004, Lynn [38]	Hong Kong	4274	DXA	WHOC	Lumbar spine or total hip	M/F > 50 years	Spine: 7% Total hip: 6%	Spine: 37% Total hip: 16%
2008–2011, Lau [15]	Hong Kong	6099	DXA	WHOC	Lumbar spine, total hip, or femoral neck	F 50–89 years	NA	24.9% 51.7% (osteopenia)
2008–2011, Lo [39]	Hong Kong	1507	DXA	WHOC	(AP) Lumbar spine and left femur	Postmenopausal women	NA	25.7% 51.6% (osteopenia)
Taiwan								
1994–1998, Yang [40]	Taiwan	8033	DXA	WHOC	Lumbar spine and femoral neck	F > 40 years	NA	Spine: 10.34% Femoral neck: 7.61%
1996–2001, Yang [18]	Taiwan	200,417	Disease code recorded in Taiwan's National Health Insurance (NHI) Database	NA	NA	M/F > 30 years	> 50 years: 1.63%	> 50 years 11.35%
2008–2011, Su [41]	Taiwan	12,175	DXA	WHOC	Lumbar spine, femoral neck, or total hip	F: postmenopausal	NA	Any site: 41.3% Lumbar spine: 32.7% Femoral neck: 25.3% Total hip: 8.8%
2007–2014, Lu [42]	Taiwan	3740	DXA	WHOC Asian or US reference	Lumbar spine, femoral neck	M/F > 50 years	Asian/US reference Lumbar spine: 1.82%/6.41%	Asian/US reference Lumbar spine: 7.59%/18.40%

Table 1 (continued)

Year[a], author [reference]	Population	Sample size	Methodology	Criteria	Sites	Gender/age	Prevalence	
							Male	Female
							Femoral neck: 2.22%/16.07% Either: 4.59%/21.20%	Femoral neck: 4.32%/13.39% Either: 10.75%/26.64%

DXA dual-energy X-ray absorptiometry, AP posteroanterior, La lateral, M male, F female, NA not available in the literature

[a] In some of the studies, the exact duration of the study is not provided, so the time of manuscript submission is presented

[b] WHOC: WHO criteria, according to which, osteoporosis is diagnosed when BMD is 2.5 standard deviations (SD) or more below the average that of the young adult population

[c] CC: Chinese criteria, according to which, osteoporosis is diagnosed when BMD is 25% lower than the peak BMD (PBMD) mean of healthy persons of same sex

However, cases could be missed out or poorly documented in insurance records; thus, the study conclusion was regarded as an underestimate of actual prevalence [71]. In a research published by Hsu in 2006, they recruited 7137 men, 4585 premenopausal women, and 2248 postmenopausal women aged 25–64 years old. The osteoporosis prevalence was 2.2%, 1.8%, and 12.4% for three distinct population groups, respectively [27]. However, the age-specific prevalence was not provided. A latest article measured BMD at multiple sites in 3740 elderly and defined osteoporosis with both Asian and US reference data [42]. When US reference was applied, the prevalence was 21.20% in men and 26.64% in women, which was comparable to those reported in most studies from Chinese mainland. However, the prevalence was much lower than that observed in other parts of China when Asian reference was adopted. Su launched a study with large sample size in 2015. The overall prevalence was 41.3% in postmenopausal women based on BMD measured at all three axial regions [41]. This was also one of the studies that reported highest prevalence among postmenopausal women. This might result from an adoption of all three axial regions during measurement.

The prevalence of OP in different ethnic groups

Osteoporosis prevalence varied among different ethnic groups in China. Such difference was observed among residents from Yi minority group and Han Chinese who cohabited in Liangshan, Sichuan Province [72]. The osteoporosis prevalence in Yi people (14.1%) was significantly lower than that of Han (21.4%), regardless of the gender difference. It could be explained by the fact that Yi people tended to inhabit in mountainous area where plenty of UVB exposure was available and were engaged more actively in manual labor like farming and climbing [72]. Using potato and tartary buckwheat as staple food instead of rice might help to provide more calcium from diet [72]. Yang compared the BMD and osteoporosis prevalence between Uighur minority group and Han Chinese who cohabited in Xinjiang Province, China. Distal radius was scanned by DXA. They found that Uighur group had a significantly higher osteoporosis prevalence than Han group [73]. The preference for meat like beef and lamb, which were rich in cholesterol and protein, might add to the burden of kidney and decrease the reabsorption of calcium from urine. Similar studies had also been carried out in Zhuang, Man, and Korean minority groups, but no significant difference in osteoporosis prevalence was observed. Whether the difference resulted from distinct lifestyle and environment only or genetic predisposition also played a part might need further research.

Table 2 Characteristics and main findings of selected studies: hip fracture incidence in China

Year, author [reference]	Population	Methodology	Fracture sites[a]	Gender/age	Incidence	
					Male	Female
1988–1992, Xu [43]	Beijing	Reports from 76 hospitals in Beijing	Codes 820 and 821for ICD-9	M/F > 50 years	97/100,000	87/100,000
1994, Zhang [44]	Tangshan, Hebei	Medical records and radiographs from 15 hospitals	Cervical and trochanteric fractures	M/F > 20 years	25/100,000 > 50 years 64.9/100,000 > 70 years 108/100,000	12/100,000 > 50 years 50.2/100,000 > 70 years 156/100,000
1994, Yan [45]	Shenyang	Register information and medical records from the 36 hospitals in Shenyang	Cervical and trochanteric fractures	M/F > 50 years	81/100,000	67/100,000
2002–2006, Xia [46]	Beijing	Hospital discharge data from Beijing Bureau of Public Health	Codes S72.0, S72.1, or T93.1 for ICD-10 Code 820 for ICD-9	M/F > 50 years	129/100,000 2002: 83/100,000 2004: 101/100,000 2005: 106/100,000 2006: 124/100,000	229/100,000 2002: 114/100,000 2004: 146/100,000 2005: 164/100,000 2006: 180/100,000
2010, Tian [47]	Tangshan, Hebei	Medical records and radiographs of patients from 15 hospitals in Tangshan	Cervical or trochanteric fractures	M/F > 20 years	47.8/100,000 > 50 years 96.3/100,000	50.4/100,000 > 50 years 126.1/100,000
2010, Wang [48]	Hefei, Anhui	Data from Hefei Hospital Discharge Register	Codes S72.002, S72.0052, S72.101, S72.1051, S72.1052, and S72. 2051 for ICD-10	M/F > 50 years	97/100,000 98.2/100,000 (after standardized)	144/100,000 151.7/100,000 (after standardized)
2013, Li [49]	Beijing	Data from Beijing municipal health insurance database	Codes S72.002 and S72.101 for ICD-10	M/F ≥ 60 years	205/100,000	355/100,000
2015, Tian [50]	Tangshan	Medical records and radiographs of patients from 15 hospitals in Tangshan	Cervical or trochanteric fractures	M/F > 20 years	45.39/100,000 > 50 years 90.70/100,000	59.64/100,000 > 50 years 143.21/100,000
1985, Lau [51]	Hong Kong	Admission records from two hospitals in Kowloon	Hip fracture above the lesser trochanter	M/F > 50 years	113/100,000	274/100,000
1995, Lau [52]	Hong Kong	Hospital discharge records for all public hospitals in HK	Hip fracture above the lesser trochanter	M/F > 50 years	> 70 500 (not exact) 1100 (not exact)	> 70 1100 (not exact)

Table 2 (continued)

Year, author [reference]	Population	Methodology	Fracture sites[a]	Gender/age	Incidence	
					Male	Female
2001–2009, Chau [53]	Hong Kong	Data from Hong Kong Hospital Authority (HA) database	Code 820.X for ICD-9	M/F ≥ 65 years	2001: 381.6/100,000 2009: 341.7/100,000	2001: 853.3/100,000 2009: 703.1/100,000
2012, Bow [54]	Hong Kong	Telephone interviews and medical history from hospital information system	Codes S72.0–S72.2 for ICD-10	M/F > 50 years	176/100,000 > 65 years 332/100,000	265/100,000 > 65 years 379/100,000
1996, Huang [55]	Kaohsiung, Taiwan	Cervical and trochanteric fractures Archives of imbursement of the National Health Insurance program	Codes 820.0, 820.1, 820.2, 820.3, 820.8, 820.9, 820.20, 820.21, 820.30, and 820.31 for ICD-9	M/F: not mentioned	35.8/100,000 > 50 years 164.8/100,000 > 65 years 320.4/100,000 > 75 years 628.2/100,000	45.3/100,000 > 50 years 267.3/100,000 > 65 years 677.8/100,000 > 75 years 1372.9/100,000
1996–2000, Chie [56]	Taiwan	Data from National Health Insurance (NHI) Database	Codes 820.0, 820.1, 820.2, 820.3, 820.8, 820.9, 820.20, 820.21, 820.30, and 820.31 for ICD-9	M/F > 50 years	225/100,000	505/100,000
2001–2012, Chen [57]	Taiwan	Annual report of the Ministry of Health and Welfare, Taiwan		M/F > 50 years	2001–2004: 273.6–278.3/100,000 2005–2012: 272.5–237.0/100,000	2001–2004: 432.0–439.2/100,000 2005–2012: 400.0–351.2/100,000

M male, F female

[a] Fracture sites are defined by International Classification of Diseases (ICD-9) or ICD-10 in most studies, and are simply described by words in other studies

Table 3 Characteristics and main findings of selected studies: vertebral fracture prevalence/incidence in China

Year, author [reference]	Population	Sample size	Methodology	Diagnosing criteria	Gender/age	Prevalence/incidence	
						Male	Female
1995, Xu [58]	Beijing	402	Lateral spine radiographs	VHR[a]	F > 50 years	NA	Overall: 15% 50–59 years: 4.9% 60–69 years: 16.2% 70–79 years: 19.0% > 80 years: 36.6%
1996, Lau [59]	Hong Kong	481	Lateral spine radiographs	VHR	F 70–79 years	NA	29%
1996, Tsai [60]	Taiwan	3061	Lateral spine radiographs	VHR	M > 40 years F > 65 years	12.5%	20%
2000, Lau [19]	Hong Kong	396	Lateral spine radiographs	VHR (both − 3 SD and − 4 SD cutoff value were adopted)	M 70–79 years	16% (− 3 SD) 7% (− 4 SD)	NA
2002, An [61]	Chengdu	1081	Lateral spine radiograph	GSQ[b]	M/F > 50 years	14.97%	17.32%
2007, Zhang [62]	Quanzhou, Fujian	500	Lateral spine radiograph	GSQ	M/F > 60 years	7.07%	19.5%
2011, Tsang [63]	Hong Kong	2178	Lateral spine radiograph	VHR	Postmenopausal women > 45 years	NA	22% 50–59 years: 15.8% 60–69 years: 19% 70–79 years: 44% > 80 years: 68%
2012, Bow [54]	Hong Kong	4112	Telephone interviews Medical history from hospital information system	Codes S22.0 and S22.1 (fracture of the thoracic vertebra/multiple thoracic vertebrae), S32.0 or S32.7 (fracture of the lumbar vertebra/multiple lumbar vertebrae)	M/F > 50 years	(incidence) 194/100,000 > 65 years 299/100,000	(incidence) 508/100,000 > 65 years 594/100,000
2012, Kwok [20]	Hong Kong	395	Lateral spine radiographs	VHR	M/F > 65 years	65–74 years 9.2% ≥ 75 years 18.0%	65–74 years 2% ≥ 75 years 15.3%
2013, Yang [64]	Guiyang	822	Lateral spine radiographs	GSQ	M/F > 50 years	16%	19.6%
2013, Kwok [65]	Hong Kong	4000	Lateral spine radiographs	GSQ	M/F > 65 years	5% 65–69 years: 2.9% 70–79 years: 5.2% > 80 years: 11.4%	12.1% 65–69 years: 6.1% 70–79 years: 13.6% > 80 years: 22.6%
2017, Cui [66]	Beijing	1760	Lateral spine radiographs	GSQ	Postmenopausal women > 50 years	NA	50–59 years: 13.4% 60–69 years: 22.6%

Table 3 (continued)

Year, author [reference]	Population	Sample size	Methodology	Diagnosing criteria	Gender/age	Prevalence/incidence	
						Male	Female
							70–79 years: 31.4% > 80 years: 58.1%
2017, Du [67]	Shanghai	2444	Lateral spine radiographs	GSQ	M/F > 65 years	20.7% 65–69 years: 21.51% 70–79 years: 18.48% > 80 years: 24.17%	26.1% 65–69 years: 16.44% 70–79 years: 18.53% > 80 years: 34.27%

M male, F female, NA not available in the literature

[a] VHR: vertebral height ratios (VHR) were calculated [anterior to posterior (Ha/Hp), middle to posterior (Hm/Hp) and posterior above to posterior below (Hp/Hp-above and Hp/Hp-below)]. Prevalent vertebral fracture was defined as a reduction of > 3 standard deviations (SD) among any one of the VHRs [14]

[b] GSQ: Genant's semiquantitative (GSQ) scoring system, grading the vertebral deformity by vertebrae height and area [79]

Trends of fracture in China

Hip fracture incidence in China

Many studies investigated the hip fracture incidence in China over the last two decades. However, the earliest epidemiologic study of hip fracture started in the 1960s in Hong Kong. It was reported that hip fracture incidence ranged from 22 per 100,000 person-years (22/100,000) in those aged 50–59 years to 716/100,000 in those aged over 80 years in women. In male population, it was 16/100,000 and 321/100,000 in corresponding age groups [52]. Since then a substantial rise of hip fracture incidence was documented in Hong Kong between 1960s and 1980s [52], with a relatively static pattern after that [52, 74]. Chau conducted a study involving 42,717 participants aged over 65 years by reviewing medical records from Hong Kong Hospital Authority (HA) database during 2001–2009. The incidence was 381.6/100,000 in men and 853.3/100,000 in women, which was far beyond that documented during the 1980s [53]. However, a slight downward trend was also indicated during this period [53]. This was in accordance with the decline pattern starting several years earlier in some western countries [53]. The authors proposed that the time lag might reflect the economic development gap between Asian countries and Western countries, and other Asian countries could replicate such declining pattern a few years later [53]. However, such pattern has not been observed in Chinese mainland population.

Epidemiologic studies that documented hip fracture incidence during consecutive years were quite limited in mainland. Xia reviewed hospital discharge records during 2002–2006 for all hospitals that admit hip fracture patients in Beijing [46]. Compared with the results reported by the same group during 1990–1992, hip fracture incidence was found to experience 2.76-fold increase in women and 1.60-fold increase in men aged over 50 years. The increase was 3.37-fold in women and 2.01-fold in men for those over 70 years old [46]. From 2002 to 2006, the age-specific incidence increased 58% in women and 49% in men for those aged over 50 years [46]. Tian and Zhang documented the hip fracture incidence in Tangshan in 1994, 2010, and 2015 by reviewing the medical records and radiographs from 15 hospitals [44, 47, 50]. The incidence was 64.9/100,000, 96.3/100,000, and 90.7/100,000 in men over 50 years old in 1994, 2010, and 2015 reports, respectively. In women, it was 50.2/100,000, 126.1/100,000, and 143.21/100,000, respectively [44, 47, 50]. The incidence markedly increased for almost all age groups in both genders from 1994 to 2010. However, the incidence was decreased (− 5.04%) in males and attenuated (+ 18.33%) in females from 2010 to 2015 [44, 47, 50]. The age-specific incidence increased in males aged over 75 and females aged over 65 but decreased in younger age groups from 2010 to 2015 [50]. The findings in Tangshan supported Chau's prediction that hip incidence was about to reach a plateau or show declining pattern in some developing areas [53]. The change might reflect

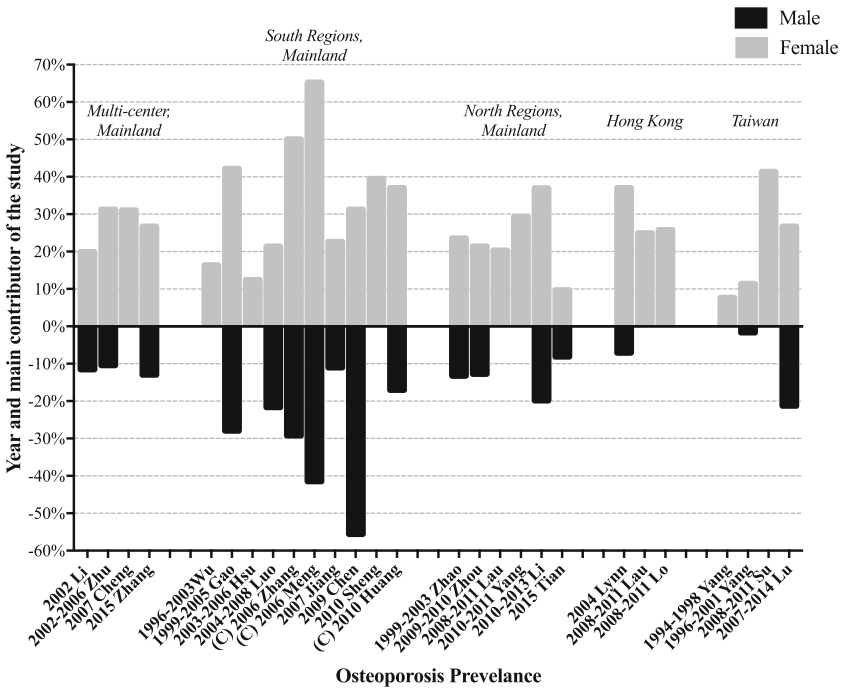

Fig. 1 Gender-specific osteoporosis prevalence in Chinese mainland, Hong Kong, and Taiwan. Note that most of the prevalence data were developed among population aged over 50 years old. Detailed information could be found in Table 1. Only a single bar was displayed if the study only focused on a specific gender. The osteoporosis prevalence defined by BMD measured at femoral neck was presented if several site-specific data were provided without overall calculation. The alphabet C in the brackets that appeared in front of study year indicated that Chinese criteria were adopted. The WHO criterion was applied if there was no specific denotation

the successfulness of some fall prevention and osteoporosis prevention programs initiated in recent years. Chen extracted whole population data about hip fracture from annual reports of Taiwan Ministry of Health and Welfare spanning 12 years [57]. The secular trend was distinct between time periods of 2001–2004 and 2005–2012 for both genders and all age groups. Hip fracture incidence increased from 2001 to 2004 but decreased thereafter [57]. The transition emerged exactly at the time when osteoporosis was declared as a government-mandated national health priority in Taiwan. The policy could facilitate the implementation of many osteoporosis prevention programs since then. A significant higher incidence had been documented in another two large population-based studies in Taiwan, which ranged from 225.0/100,000 to 278.3/100,000 in men, and 351.2/100,000 to 505.0/100,000 in women aged over 50 years [56, 75]. Dating back to the 1990s, when Huang analyzed data from archives of reimbursement of the National Health Insurance program, the reported age-specific incidence had already surpassed that documented in Japan, Singapore, Chinese mainland, and was slightly higher than Hong Kong [43, 52, 55]. The underlying reasons were hypothesized to be the spread of urban lifestyle with much limited space for activity, which may lead to increased osteoporosis prevalence and subsequent fractures. The gender-specific hip fracture incidence extracted from studies in Chinese mainland, Hong Kong, and Taiwan were illustrated in Fig. 2.

Prevalence of vertebral fracture in China

Vertebral fracture has long been recognized as the most common manifestation of osteoporosis, accounting for nearly 50% of osteoporotic fractures [76, 77]. However, vertebral fractures were far from fully recognized due to its asymptomatic clinical features. Bow investigated the incidence of clinical vertebral fractures among 4386 elderly recruited in Hong Kong between 1995 and 2011 [54]. The incidence was 194/100,000 in males and 508/100,000 in females aged over 50 years old. They also reported an interesting finding about spine-to-hip fracture ratio when compared to other ethnic groups. It has been established that in Caucasian, hip fracture incidence rose exponentially with age, but vertebral fracture showed almost linear trend. However, in Asian women, vertebral fracture incidence was discovered to rise exponentially with age, whereas a linear trend was indicated for hip fracture instead [54]. Overall, the vertebral fracture incidence in Asian men was similar to that observed in Caucasian men, while Asian women had a much higher vertebral fracture incidence than Caucasian women [54]. This was interesting because Asians seemed to be more susceptible to vertebral fracture than hip fracture. The possible reasons would be discusses later. Kwok recruited 1588 subjects from Hong Kong, Thailand, Indonesia, and Japan and compared the prevalence of vertebral fracture in four regions [20]. The study indicated that Japan showed highest prevalence in both young and old groups (36.6% and 37.6% for males, 18.8% and 28.7% for females), while Hong Kong showed lowest prevalence in both genders. In this study, an uncommon phenomenon was observed that females displayed lower prevalence than their male counterparts. This might reflect a combined effect of hormone replacement therapy, proper osteoporosis prevention regime, health promotion programs, and raised public awareness of osteoporosis in Hong Kong since 2001 [20].

A study published in 2013 recruited 2000 men and 2000 women age over 65 from local communities in Hong Kong

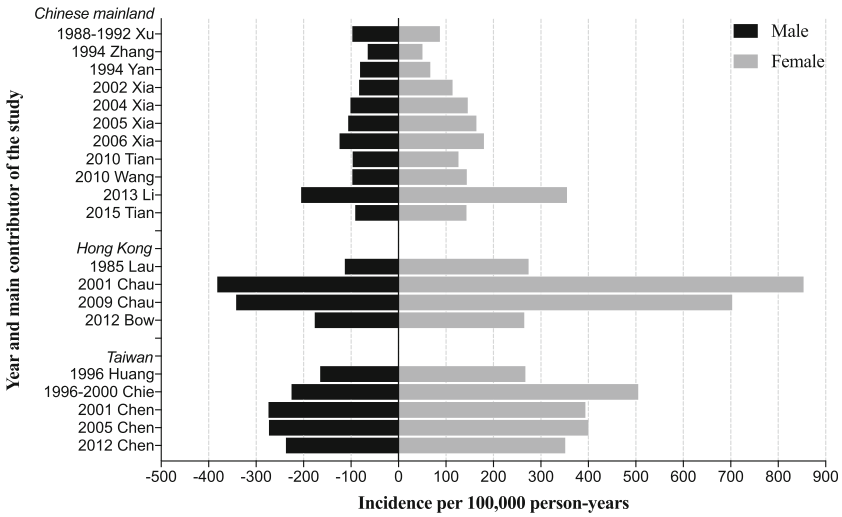

Fig. 2 Gender-specific hip fracture incidence in Chinese mainland, Hong Kong, and Taiwan. Note that Xia's study reported several discontinued year's data and were presented separately in the figure [46]. Both of Chau's and Chen's study documented hip fracture incidence trend from several consecutive years with an obvious trend, and only the beginning and finishing year's data as well as the extreme value were presented in the figure [53, 57]

[65]. Lateral thoracic and lumbar spine radiographs were obtained and Genant's scoring system (GSQ) was applied. Vertebral fracture prevalence was found to be 5.0% among men and 12.1% among women [65]. The prevalence increased from 2.9% in men aged 65–69 years to 11.4% in those aged over 80, and increased from 6.1 to 22.6% in their female counterparts [65]. Cui reported vertebral fracture prevalence in community-dwelling postmenopausal women from seven districts in Beijing in 2017 [66]. Compared to the study carried by Xu 20 years ago, which also aimed at the elderly in Beijing, this study found a much higher prevalence of vertebral fracture [78]. It was also much higher than that reported in Hong Kong by Kwok in 2012 and 2013 [20, 65], but was comparable to Tsang's results in 2011 [63]. The author concluded that differences mainly resulted from different methodology applied to define fractures, but whether other possible factors contributed to the increase remained unclear [66]. Since the vertebral fracture data concerning mainland population were quite limited, we did a systemic research for literature published in Chinese journals. The results were demonstrated in Table 3.

The management of osteoporosis in China

Dilemmas in diagnosis and treatment

Although osteoporotic fractures had caused considerable mortality and morbidity in aging populations, the diagnosis rate remained very low. Wang carried out a multi-center, retrospective cohort study based on medical charts review of 1993 patients in China [80]. The results showed that only 44.8% and 73.3% of patients were diagnosed as osteoporosis when discharging for hip and vertebral fracture, respectively [80]. BMD measurement by DXA, which was the most meaningful examination for osteoporosis, had never been performed in more than 60% of the patients before or after the fragility fractures. There were no significant variations between the diagnostic rates in south and north regions. The diagnosing rates were similar between tertiary-level and secondary-level hospitals [80]. Another study characterized the diagnosis and management situation of osteoporosis in postmenopausal women with fragility fractures in several Asian regions during 2006–2007. An overall diagnosis rate of 51.5% was reported. Chinese mainland ranked seventh in eight Asian regions, with a diagnosis rate of 36% [81]. Doctors from a tertiary hospital in Beijing retrospectively reviewed the medical records of 780 patients admitted for hip fractures. They found that 27% of subjects received orthogeriatrician assessment, and only 0.3% of patients were prescribed with anti-osteoporotic medication [82]. Several studies had proved that osteoporosis diagnosis and BMD evaluation after index fracture played essential roles in improving postfracture medication rate as well as patients compliance [80, 81, 83].

Under-diagnosis of the disease may directly lead to more serious insufficiency of anti-osteoporotic medication. Kung reported that only 6.5% of postmenopausal women received anti-osteoporotic medication 6 months after the index fracture in Chinese mainland. The medication rate was only 1/10 of that in Thailand and Korea [81]. Another study with large sample size investigated the situation in elderly population after fragility fractures [80]. The results indicated that more than 30% of the patients had never received nutrients supplements and/or anti-osteoporotic medications. Only 28% of patients were prescribed with pharmacologic treatment for osteoporosis besides calcium and vitamin D, with bisphosphonates prescribed in 14% of patients and calcitonin in 13.7% [80]. These medicines were actually integral part of osteoporosis management in postfracture patients as suggested by guidelines in China [10, 80]. Fortunately, the diagnosis rate was improved in patients after 2011. As guideline for primary osteoporosis was issued in 2011, the coincidence may suggest the positive effect of published guidelines on improving osteoporosis recognition and diagnosis [80, 84]. Insufficient medication was also noted in Taiwan. A study in 2013 reported that among those suffering

from osteoporosis, only 28.7% of women and 11.9% of men received anti-osteoporotic drugs [85]. Only 45.4% of subjects were prescribed with anti-osteoporotic drugs by orthopedists after hip fracture surgery, leaving another 54.6% of patients discharged with no medication [86]. It should be noted that the anti-osteoporotic drug use was less common in male patients than female patients in almost all the studies available. It might associate with the poorer understanding of osteoporosis and more silent disease progression in male population.

Osteoporosis is a chronic condition that requires long-term management plan. The poor patient compliance made the osteoporosis management much more challenging. In a multi-center study from Chinese mainland, 1151 subjects with hip fracture and 842 with vertebral fracture were followed for their medication use for a long time [80]. It turned out that only 50% of patients were still under any medication after 1 year and one third of them persisted to the treatment for 2 year or more [80]. The self-reported reasons for poor compliance included lack of confidence or ignorance of the disease (36.2%), reluctance to take medicine (23.9%), intolerance or side effects of medication (14.8%), and too many medicines for comorbidities (13.2%) [80]. A similar result among hip fracture patients was reported in Taiwan, with an overall persistence ratio of 48.4% and 33.1% at the end of first and second year, respectively [86]. Lin discussed the patients' adherence to alendronate based on data from the Bureau of National Health Insurance (NHI) in Taiwan [87]. They found that 38% of the study population kept compliant during the first year. They also demonstrated that hip fracture risk of compliant patients was 70% lower than that of noncompliant subjects during the 4-year follow-up period [87]. According to the study carried out in Hong Kong from 2008 to 2011, among those treatment-naive postmenopausal women with osteoporosis, 42.9% refused treatment, 30.7% complied with treatment, and 26.3% discontinued treatment or defaulted from follow-up by 2015 [39].

For patients with good compliance, whether the dosage was appropriate still remained a question. A survey in China was designed to elicit information on orthopedists' views about the treatment of osteoporotic fracture [88]. It turned out that 49.6% of respondents recommended 800 IU of vitamin D daily, which was on the lowest side of the 800–1200-IU range suggested by Chinese guidelines. A substantial number (23.8%) of them recommended doses lower than 400 IU per day [88]. Insufficient recommendations were also observed in calcium supplementation. A daily dosage of 600 mg was recommended by 44.8% of orthopedists, which fell below the recommended dose of 800–1200 mg/day for the elderly. Only 31.6% of them chose 1000 mg/day [88].

Efforts made in China

Though a stabilized or even declining trend has been reported in some Western countries, the prevalence of osteoporosis and incidence of fragility fracture in many Asia regions, including China, were continuously rising [89]. Medical resources are unevenly distributed in China due to its vast territory, enormous population, and still incomplete health care system. To improve the research quality and management of osteoporosis in China, great efforts had been made by Chinese government and scholars from different academic backgrounds.

In 2001, the Chinese Society of Osteoporosis and Bone Mineral Research (CSOBMR) was established under the Chinese Medical Association. Specialists from different academic backgrounds tried to refine the management of osteoporosis in an all-around way. Specialists from endocrinology, obstetrics, orthopedics, radiology, geriatrics, rehabilitation medicine, and sports medicine assembled every year to discuss about the latest research findings and controversial issues concerning osteoporosis. National conference and international conference were held to improve the clinical practice and research level. CSOBMR was also responsible for drafting clinical guidelines. "Guidelines for osteoporosis and Bone mineral disease" was first published in 2006 and had been revised several times since then. The newest version issued in October 2017 would definitely help to develop nationally endorsed standards for best practice among Chinese clinicians. CSOBMR was also actively involved in carrying out free clinics in rural areas and holding lectures on related topics to arouse the awareness of osteoporosis from the public.

As is mentioned above, most of the high-quality epidemiological studies were carried out in Hong Kong and Taiwan. The disease burden in Chinese mainland could only be projected from regional data, for example, those in Beijing or Tangshan [15, 21, 43, 44, 46, 47, 49, 50, 66, 78, 80, 82]. In recent years, CSOBMR was planning a nationwide epidemiological survey on osteoporosis prevalence in China. With the help from Centers for Disease Control and Prevention in China (CDC), the study was estimated to include over 16,000 participants from 40 regions across China. Moreover, another multi-center study aimed at investigating vertebral fracture prevalence in postmenopausal women, abbreviated as ChiVOS, is currently under way in different centers.

The diagnosis of osteoporosis or fragility fracture is based on DXA and X-ray measurement. However, even with the same model of machine, different practitioners could make different diagnosis. CSOBMR had launched several training courses targeted at young medical practitioners and those in rural areas to ensure better DXA and spine X-ray quality control. For example, the Win Over Osteoporosis (WOO) started in 2016 was one of them.

It has been proven in many studies that involvement of multidisciplinary team could significantly improve the pharmacological management of patients with osteoporotic fractures. Fracture Liaison Service (FLS) had been established worldwide to ensure better assessment and management of patients after fragility fractures [90]. FLS functioned by identifying patients presenting with fragility fractures, referring them onward for the necessary

assessment of bone health and fracture risk, and recommending or initiating the appropriate treatment [91]. Different models had been demonstrated to lower the secondary fracture risk and mortality [91]. A shared feature was that the work was usually coordinated by a specified individual like a clinical nurse specialist, who will be responsible for case finding, working to prescribed protocols, and referral access to specialist physicians [92]. This kind of multi-disciplinary collaboration model provided a potential solution to poor postfracture management in China. Implementation of FLS in China which is entitled Good Bone Program was initiated in March 2016 [93]. Studies that investigated into the effectiveness of FLS are to be followed in the near future.

Accidental falls are the most common direct cause of fragility fracture in aging population. A program named "Zero Fall" was launched to reduce the accidental falls and fall-related injuries among elderly. The program focused on promoting assessment of fall risks in old people and advocating educational initiatives in outpatient department to raise patient and doctor's understanding of falls [94].

Chinese government also attached great importance to osteoporosis. In 2007, the National Health and Family Planning Commission started a national healthy lifestyle project named "China Healthy Lifestyle for All," which was intended to advocate the spreading of health knowledge and cultivation of healthy lifestyle. The first part of the project focused on "Keeping a balance between eating and exercising." The new ten-year program started in 2016 emphasized "Three reducing plus three healthy," which included reducing salt, oil, and sugar intake, plus maintaining oral hygiene, healthy weight, and healthy skeleton [94]. Providing technical support to underdeveloped regions in China will be the key point of next ten-year program.

Establishing the grading treatment system for osteoporosis is a good way to make the most of limited medical resources [10]. The grading treatment system in China consisted of hospitals of three different levels. The primary hospital was responsible for initial assessment of potential patient. Doctors at this level helped to establish health records, screen for high-risk population, and make registrations for patients with definite diagnosis. Popular science, health education activities held in communities might help people to recognize potential health risks and improve self-care ability in the future. If the diagnosis was not sure or severe complications has happened, or basic treatment and rehabilitation therapy was not effective, the patients should be transferred to secondary hospital, where the patients could get a preliminary diagnosis and an individualized treatment plan. Stable patients just need regular follow-up but for those with severe complications, tertiary hospital would be the final solution. The referral system was designed to be two-way, which meant that once the disease was under control, the following treatment and follow-up should be completed in primary or secondary hospitals.

Discussion

To the best of our knowledge, this study provides the most extensive overview of disease burden, secular trend, management gap, and coping strategies of osteoporosis and related fractures in China. We used systemic review approach to include related studies that published in English and Chinese language journals after applying strict inclusion and exclusion criteria. It reminds us that due to its silent nature, osteoporosis and its related fractures remain largely under-diagnosed and under-managed in China. It also highlights the scarcity of good quality studies on long-time documentation of disease burden change and on male population, especially in mainland area.

According to the 2003–2006 survey of the China Ministry of Health, 15.7% (men 8.8%, women 30.8%) of total population aged over 50 met the WHO diagnostic criteria for osteoporosis. Considering the large population in Chinese mainland, approximately 69.4 million people (15.3 million men and 54.1 million women) aged over 50 had osteoporosis, with another 200 million subjects suffering from low bone mass [95]. However, such huge number of patients was far from being fully evaluated and managed. Nationwide studies on epidemiology of osteoporosis are scarce, especially in mainland. In our analysis, only 3 out of 18 cross-sectional studies in mainland were multi-center designed. This might result from unbalanced development and insufficient academic collaborations among different regions. Epidemiologic studies in Hong Kong were generally of higher quality, thanks to some good research projects such as Hong Kong Osteoporosis Study since 1995. The more developed medical record system and easier access to DXA facilities across Hong Kong area also facilitated the epidemiologic research. China is a country with vast territory and huge population. People with different gene backgrounds and distinct lifestyles cohabited in the same country. Data from any single region are not representative and could easily lead to biased conclusion. More multi-center epidemiologic studies with large sample size are urgent to better define the osteoporosis burden in China, especially in mainland.

The available data indicated that in Chinese mainland, the overall osteoporosis prevalence might be 30–40% among women and 10–20% among men aged over 50 years. Regardless of the study design and population selection, osteoporosis prevalence and fragility fracture incidence rose with age, being higher in women than men in almost all the studies. This is in accordance with another review paper published domestically in 2015, in which osteoporosis prevalence in males was lower than that in females in all age divisions, and the ratio is close to 1:2 [16]. Such differences had been reported in a number of studies from both East Asian countries and Western countries [96–100]. Several mechanisms have been proposed to explain the difference. For example,

compared with their male counterparts, females have been proven to have smaller and thinner bone structure. Moreover, an accelerated bone loss was observed after menopause as a result of estrogen withdrawal [101]. The absolute number of osteoporotic population may display more dramatic difference between two genders, since women had been reported to have longer life expectancies, thus may account for larger proportion of elderly population.

A moderately higher prevalence was observed in north China, which should not be simply attributed to less sunlight exposure. Different genetic predisposition, distinct dietary habits and lifestyles could also make a difference. For example, people living in north regions tend to have higher salt intake in their daily meals. Several studies have reported the association between higher urinary sodium excretion and impaired bone health [102, 103]. Compared to that in mainland, the osteoporosis prevalence was generally higher in Hong Kong and lower in Taiwan according to the limited data obtained from published literatures. In recent years, a much higher prevalence has been reported in Chinese mainland. The prevalence may catch up or even exceed that in Hong Kong in years. The reasons behind this included the spread of urbanized lifestyles among the elderly in mainland, such as more sedentary life styles, less physical work, and more Westernized dietary intake [15]. On the other hand, difference in sampling method and study design could contribute to the disparity. For example, one of the study in Taiwan with largest sample size was based on insurance records, which could underestimate the actual prevalence due to incomplete documentation and selection bias [71].

Some studies (10/26) reported osteoporosis prevalence data specified by their measuring site. It could be noted that under most circumstances, lumbar spine yielded the highest osteoporosis prevalence than other sites in women. However, it might be close to or even exceeded by that measured at femoral neck in male population. Different from some peripheral sites and femoral neck, lumbar spines are mainly made up of trabecular bone. It had been proven that trabecular bone loss started in young adulthood and continued throughout one's whole life [104]. Since women had a continuously faster bone loss rate with age than men [105], they could experience more BMD deterioration at lumbar spine than their male counterparts.

Increases in hip fracture incidence had been reported in Western population over the second half of the last century, but the trend was stabilized or even decreased in the last two decades in some centers [89]. Unfortunately, the incidence was still increasing in many Asian countries including China. Half of the world's hip fractures were predicted to occur in Asia by the year 2050, which may still be underestimated for the continually increasing fracture incidence. From our study, an attenuated increased rate or slight decline pattern have been observed in Hong Kong and Taiwan, which were about one decade behind western countries. However, some regional studies indicated that hip fracture incidence was still increasing in mainland. Comparisons between these epidemiologic studies from different regions could be challenging. Differences in study design (inclusion criteria, definition of hip fracture, data source, and standardized method) made it arbitrary to draw any definite conclusions from direct horizontal comparisons. There have been high-quality studies in Hong Kong and Taiwan, which documented data for consecutive years with reliable information source [53, 57]. Most studies from mainland area were regional and only reported data during a short period.

Studies indicated that only one fourth to one third of vertebral fractures were diagnosed clinically at the time of their occurrences and otherwise required lateral spine imaging to be recognized [76, 106–108]. It used to be believed that vertebral fracture prevalence was generally homogeneous across different ethnic groups in the world, with much smaller variation than that observed in hip fracture [54, 77, 89]. However, a most recent review paper concluded that the low variability might only exist in Europe and North America, but not Asia and Latin America [77]. The highest-lowest ratio between countries, within and across continents, varied from 1.4 to 2.6 [77]. In Europe, women in Scandinavia showed the highest prevalence (26%) while those in Eastern Europe had the lowest (18%) [77]. In Asia, prevalence in women age over 65 years was highest in Japan (24%) and lowest in Indonesia (9%) [77]. Similar to that observed in osteoporosis and hip fracture, women had a higher prevalence than their male counterparts. A study in Taiwan reported that the female-to-male ratio of prevalence varied from 1.5 to 2.3 among different age groups, and was close to unity after 80 [60]. However, it has been difficult to compare the prevalence of vertebral fractures across studies for different population selection, methodology adopted to diagnose vertebral fracture, and definition of vertebral fracture [109].

The epidemiology of osteoporotic fractures in China had its own unique features compared to that in Western countries. A higher vertebral fracture prevalence was documented while a paradoxically lower hip fracture incidence was observed [110]. Published studies had shed lights into this intriguing situation and indicated that bone loss, particularly at trabecular sites like vertebra, might be greater in Chinese than white women. However, when it came to appendicular skeleton, which was rich in cortical bone, Chinese had greater microstructural and mechanical advantages than their Caucasian counterparts. Denser organization of cortical bone structure, more connectivity and less porosity on cross-sectional surface were proven in these studies [110]. Wang also demonstrated that Chinese assembled their smaller appendicular skeleton with more mineralized bone matrix within it, resulting in thicker and less porous cortices and more connected trabeculae. The low surface volume ratio could reduce the surface

available for remodeling. Increased bone remodeling was one of the most prominent changes observed during aging process [111].

Osteoporosis remained poorly diagnosed and managed even after fragility fracture happened. Lack of disease recognition by doctors as well as limited access to DXA facility in some rural areas might contribute to this situation. Although WHO has declared BMD measured by DXA as the golden criteria for diagnosing osteoporosis, quantitative ultrasound (QUS) was still adopted by a number of studies in mainland for its easier access and lower cost. Despite of the fact that QUS was proven to correlate with BMD and bone structure well, clinicians should be cautious in interpreting these results for limited evidence and lack of cross-validated device- and parameter-specific thresholds [112]. It was a worldwide problem for patients to not receive adequate management after fragility fractures. A paper systemically reviewed the articles published between 1996 and 2005 and provided insights into the osteoporosis management after fragility fractures in Western countries [113]. It showed that in the majority of studies, less than 30% of patients were clinically diagnosed with osteoporosis after fracture. BMD scans were performed in less than 15% of patients in 15 out of 23 available studies [113]. Another review paper revealed a similar result, with BMD evaluated in less than 32% of patients in 14 out of 16 studies. Compared with relatively high rates of osteoporosis diagnosis (35–100%), only moderate use of calcium or vitamin D (8–62%) and bisphosphates (0.5–38%) were documented [83]. Further research should improve the population representativeness by incorporating data concerning both urban and rural Chinese population and recruiting patients from both tertiary- and secondary-level medical institutions and even lower grade hospitals.

The poor patient compliance could make the osteoporosis management even harder in China. Studies from mainland, Hong Kong, and Taiwan yielded similar results. About half of patients persisted to the anti-osteoporotic medication after 1 year, and only one third were still under medication after 2 years. Related studies were quite heterogeneous for their differences in study methodologies, enrollment criteria, adherence definitions, mono/sequential therapy, follow-up period, and use of different covariates for adjustment (e.g., age, sex, fracture history, and medications of interest). But if the medication possession ratio (MPR) was adopted as a parameter for comparison, the compliance in China is similar to that reported in some Western countries like USA, Canada, and UK [87]. Anti-osteoporotic medication is flexible in dosage regimen. Administration route and dosage frequency could be different for different population. In 2013, the Medication Adherence and Persistence Special Interest Group of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) did a systematic literature review of interventions to improve osteoporosis medication adherence. The study concluded that a less frequent dosing regimen, electronic prescriptions in combination with verbal counseling associated with improved compliances, while those patient-education-based interventions show marginal change in it [114]. Hsu investigated the influence of departments where physicians came from on determining medication initiation [86]. They found that index prescription by orthopedists was an independent risk factor in both first year (OR 1.69, 95% CI 1.10–2.59) and second year (OR 2.44, 95% CI 1.31–4.51) compliance [86]. Compared to doctors from internal medicine, orthopedists were more actively involved in their surgical duty and least likely to participate in consultative services to initiate treatment [115]. These studies provided valuable perspectives on how could doctors improve their clinical work.

Our study has several limitations. First, most studies included were based on regional data, which may not be representative enough to indicate the osteoporosis prevalence and fracture incidence of China. This problem might be more prominent in Chinese mainland, because the sample size was rather small compared to its huge population size and heterogeneous population composition. Secondly, we failed to perform horizontal comparisons between different studies because of distinct differences in population selection, assessment tool, diagnostic criteria, data source, etc. Thirdly, the hip fractures were ascertained by ICD codes in discharge records in most studies. However, discharge records could be poorly documented and could not differentiate between low- and high-trauma fractures. Underestimation and overestimation could happen at the same time. Our study also has some strengths. Firstly, we tried to include studies published in Chinese and English at the same time. Many regional data had been published in Chinese domestic journals but we only included those with large sample size and good design. Secondly, we discussed about osteoporosis prevalence, fragility fractures, and management dilemmas at the same time to provide an extensive overview of disease burden in China. Thirdly, as far as we know, it is the first study to discuss in details about how government and scholars make efforts to cope with the disease.

Conclusion

Osteoporosis is a common clinical problem in Chinese elderly population but is far from being fully recognized. Epidemiological data varied greatly across studies due to different population selection and methodology adopted. Recent years much higher osteoporosis prevalence has been reported in Chinese mainland, which was predicted to catch up or even exceed that in Hong Kong in years. This might result from the spread of urbanized lifestyle in mainland and better osteoporosis management in Hong Kong. A higher prevalence was indicated in female population, older age groups, and

residents in northern China compared to their counterparts. Though attenuated increased rates or slight decline patterns have been observed in Hong Kong and Taiwan, osteoporotic fracture incidence still showed steady increase in Chinese mainland. The diagnosis and treatment of osteoporosis as well as postfracture management were insufficient in China. Chinese government, scholars, and clinicians had made great efforts in establishing academic organizations and initiating health-promoted campaigns to manage osteoporosis in an all-round way. But more good quality studies with large sample size and good population representativeness are needed to ascertain the effectiveness.

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Compliance with ethical standards

Conflicts of interest None.

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