Editorial

Estimations of bone mineral density defined osteoporosis prevalence and cutpoint T-score for defining osteoporosis among older Chinese population: a framework based on relative fragility fracture risks

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Abstract: This study estimated the bone mineral density (BMD) defined osteoporosis prevalence of Chinese women and Chinese men aged ≥50 years. The estimation was based on the 1994 WHO definition of osteoporosis and two assumptions: (I) fragility fracture (FF) risk among older Chinese is half of that of older US Caucasians; (II) FF risk among older Chinese men is half of that of older Chinese women. In addition, we also consider the FF risk among older Chinese is close to those of American Blacks. We estimated that the osteoporosis prevalence based on lumbar BMD, femoral neck BMD, total hip BMD would be 15.8%, 20.4%, and 15.2% for US Caucasian women, 6.7%, 7.8%, and 7.9% for US black women, 7.5%, 7.5%, and 6.7% for Chinese women, 1.8%, 5.7%, and 3.3% for US black men, and 2.0%, 3.8%, and 3.4% for Chinese men. To satisfy the above estimates of osteoporosis prevalence for the Chinese population, in addition to using a local reference database, we suggest that the T-score cutpoints for defining osteopenia and osteoporosis among older Chinese should be adjusted from the conventional WHO thresholds of –2.5 and –1.0. Our suggested revised cutpoint T-score for defining osteoporosis described in this article will be more in line with the original WHO definition and will allow a more meaningful international comparison of disease burden.

Keywords: Osteoporosis; fragility fracture (FF); bone mineral density (BMD); prevalence; T-score; Chinese

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The clinical significance of osteoporosis lies in the fractures which occur, and the most important fracture is hip fracture. According to the WHO criteria, T-score is defined as: $(BMD_{patient}–BMD_{young\ normal\ mean})/SD_{young\ normal\ population}$, where BMD is bone mineral density and SD is the standard deviation. In adult women, the cutpoint value of patient BMD 2.5 SD below $BMD_{young\ normal\ mean}$ satisfies that, when the femoral neck is measured, osteoporosis prevalence is about 16.2% for those aged ≥50 years, the same as the lifetime risk of hip fragility fracture (FF) (1,2). If other sites are also considered, this cutpoint value identifies approximately 30% of postmenopausal women as having osteoporosis, which is approximately equivalent to the lifetime risk of FF at the spine, hip, or forearm. It is commonly considered that this osteoporotic portion of the population has a faster bone mass loss, and interventions

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should be taken ideally before an FF occurs. East Asians generally have lower unadjusted areal BMD (aBMD), various region-specific reference databases have been published.

The FF prevalence among Chinese is no more than half that of Caucasians, both for men and women. For this, we discussed some literature evidence in a recent article (3). Additional reports (4-9) and analysis (10-33) are summarized in Supplementary file (Appendix 1). The much lower FF prevalence among Chinese may be related to multiple factors. It has been shown that older East Asians lose bone mass more slowly than Caucasians (34-36). Moreover, numerous studies demonstrated that the skeleton of Chinese has microstructural and mechanical advantages (Appendix 2) (37-47). It has also been recognized that the incidence of falls among older Chinese population is lower than those reported in older Caucasian populations. Kwan *et al.* (48) conducted a systematic literature review and reported a consistently lower incidence of self-reported falls among Chinese older individuals than among Caucasian older individuals. In a cross-sectional study using data from 6,277 women aged 65–90 years who responded to the 2008 or 2011 Kaiser Permanente Northern California (KPNC) Member Health Survey, Geng *et al.* (49) noted that, compared to Caucasians, Asian women were much less likely to have falls in the past year with an odds ratio of 0.64, adjusted for age, comorbidities, mobility limitation and poor health status.

The cutpoint T-score for defining osteoporosis was initially proposed only for postmenopausal Caucasian women, which is related to the osteoporotic fracture prevalence of postmenopausal Caucasian women. We have recently argued that, in addition to using a local reference database, an additional adjustment of the cutpoint T-score for defining osteoporosis among older Chinese should be applied (50). If we assume Chinese women's osteoporotic hip fracture prevalence is 40% of that of Caucasians and using the Hong Kong data of Lynn *et al.* (51), in an earlier report we estimated that the cutpoint T-score for defining femoral neck osteoporosis can be better set at ≤–2.78. Taking the same line of consideration, we expand this concept and estimated the cutpoint T-scores for defining osteopenia and osteoporosis among Chinese women and men based on the lumbar spine and hip BMD measurements. The method and an example are shown in Supplementary file (Appendix 3). Since the initial WHO definition for osteoporosis and osteopenia was based on Caucasian data and also Caucasian data have the highest number of studies validating the association between BMD and FF, the Caucasian results are used as the reference for our estimations (52-59). In addition to Chinese data, a few databases from Japan, Korea, and Singapore are also analysed for comparison (51,60-70). At least for the hip, it has been noted in many US studies that FF prevalence among Chinese is close to the rate of American Blacks (Appendix 4) (71-74). While the hip fracture rate was slightly lower among American Black women as compared with Asian American women, the hip fracture rate was even lower among Asian American men than among American Black men. Moreover, within the 'Asian' ethnic category, it is likely that older Chinese have an even lower FF prevalence than that of older South Asians (5). It would be reasonable to assume that the osteoporosis prevalence among Chinese is close to the rates of American Blacks. In addition, if the osteopenia prevalence is as high as 50% in community populations, then this category will be less meaningful in the real world.

Based on published literature, we first analysed multiple BMD databases for Caucasians, Chinese and other East Asians and used the WHO T-scores and their equivalent BMD cutpoints to estimate the prevalence of osteoporosis and osteopenia assuming a Gaussian distribution. Then, assuming that the prevalence of osteoporosis and osteopenia amongst Chinese is half of that among Caucasians, data from BMD databases for Chinese and other East Asians were analysed to estimate revised BMD thresholds and their corresponding T-scores consistent with the reduced prevalence.

Estimations for cutpoint BMDs and T-scores for defining osteopenia and osteoporosis based on lumbar spine BMD measurement are shown in *Table 1* (for women) and *Table 2* (for men). Estimations for cutpoint BMD and T-scores for defining osteopenia and osteoporosis based on femoral neck BMD are shown in *Table 3* (*Figure 1*, for women) and *Table 4* (for men). Estimations for cutpoint BMD and T-scores for defining osteopenia and osteoporosis based on total hip BMD are shown in *Table 5* (for women) and *Table 6* (for men). For the clarity of comparison, a summary of estimated BMD-based osteoporosis prevalences of Caucasians, American Blacks, and Chinese (age ≥50 years) is shown in *Table 7*. It should be noted that some of the BMD databases presently available include relatively few participants, particularly in the young adult group (Tables S1-S6), a factor that is critical in determining the statistical accuracy of the young adult population standard deviation. This limitation affects the statistical reliability with which the revised T-scores can be estimated, and

Table 1 Cutoff BMD values and T-scores for osteopenia and osteoporosis based on literature data: women's spine

Studies	BMD_{young}	SD_{young}	Age_{old}	BMD_{old}	SD_{old}	T-score ≤−1.0		T-score ≤−2.5		Prevalence =25%[¶]		Prevalence =7.5%[§]	
						BMD_{low}	Prevalence (%)	BMD_{os}	Prevalence (%)	BMD_{low}	T-score	BMD_{os}	T-score
US White [2012] (52)[#]	1.064	0.106	≥50	0.951	0.152	0.958	51.79	0.799	15.76				
			≥60	0.930	0.152	0.958	57.24	0.799	19.47				
US Black [2012] (52)	1.118	0.131	≥50	1.023	0.155	0.987	40.85	0.791	6.66				
			≥60	1.013	0.167	0.987	43.84	0.791	9.11				
Italian [2003] (53)	1.034	0.104	50–79	0.917	0.147	0.930	53.09	0.774	16.24				
			≥60–79	0.886	0.145	0.930	62.07	0.774	22.03				
Finnish [1992] (54)	1.196	0.128	50–70	1.020	0.140	1.068	63.57	0.877	15.48				
			60–70	0.949	0.130	1.068	82.10	0.877	29.02				
Austrian [2003] (55)	1.076	0.130	46–76	0.978	0.187	0.946	43.12	0.751	11.23				
			56–76	0.924	0.170	0.946	55.06	0.751	15.42				
Canadian [2000] (56)	1.042	0.121	≥50			0.921		0.740	12.10				
Spanish [1997] (57)	1.031	0.104	50–79	0.865	0.141	0.927	66.88	0.771	25.12				
British [1996] (58)	1.240	0.110	50–89	1.071	0.208	1.130	61.20	0.965	30.51				
Swedish [2000] (59)	1.057	0.105	≥70	0.875	0.162	0.952	68.27	0.795	30.96				
Chinese meta [2013] (60)	1.058	0.140	≥50	0.870	0.182	0.918	60.34	0.708	18.66	0.747	−2.219	0.608	−3.214
US Chinese [2006] (61)	0.994	0.110	50–89	0.837	0.137	0.884	63.48	0.719	19.48	0.774	−2.269	0.640	−3.221
Hong Kong [2005] (51)^	0.990	0.100	≥60	0.795	0.140	0.890	75.28	0.740	34.78	0.721	−2.686	0.616	−3.743
Singapore [2020] (62)	1.071	0.121	≥51	0.931	0.151	0.950	54.94	0.768	13.98	0.830	−1.994	0.715	−2.946
Japan [2001] (63)[##]	1.015	0.105	50–79	0.810	0.143	0.910	75.80	0.752	34.51	0.713	−2.877	0.603	−3.921
ML Chinese [2007] (64)	1.098	0.111	50–89	0.922	0.172	0.987	64.80	0.820	27.75	0.806	−2.630	0.674	−3.813
Korea [2008] (65)[##]	1.194	0.120	50–79	0.922	0.159	1.074	83.16	0.894	43.12	0.814	−3.163	0.693	−4.175
Korea [2014] (66)[##]	0.961	0.109	≥50	0.801	0.244*	0.852	58.25	0.688	32.19	0.637	−2.975	0.450	−4.686
Taiwan [2011] (67)	1.090	0.106	>50	0.908	0.170	0.984	67.26	0.825	31.25	0.794	−2.798	0.664	−4.024

[#], cited reference and the year of publication (see reference list). Age in years. BMD unit in g/cm^2. [¶], assuming the reference Caucasian have an osteopenia prevalence of 50%, the osteopenia prevalence for Chinese ≥50 years old is assumed to be 25%. [§], assuming the reference Caucasian have an osteoporosis prevalence of 15%, the osteoporosis prevalence for Chinese ≥50 years old is assumed to be 7.5% (US Blacks: 6.66%). In one study (10), we compared spine radiographs from two studies conducted in Hong Kong [MsOS (Hong Kong) n=200] and in Rome (Roman Osteoporosis Prevention Project, n=200, age-matched subjects with both mean age: 74.1 years and range: 65–87 years). The results show radiographic OVF with ≥40% vertebral height loss was recorded among 9.5% of the Chinese subjects, while among 26% of the Italian subjects. We consider osteoporosis prevalence of 7.5% for older Chinese women could be an aggressive estimation, i.e., the real prevalence could be even lower (also see Figure S2B). ^, for Hong Kong data, it is assumed that, for subjects ≥60 years, osteopenia prevalence and osteoporosis prevalence is 30% and 10% respectively. *, a large SD was obtained. [##], Kwok *et al.* (20) reported Hong Kong Chinese women, Beijing Chinese women, Japanese women, Korean women have very similar radiographic osteoporotic vertebral fracture prevalence. BMD, bone mineral density; ML, mainland; Chinese meta, meta-analysis result; BMD_{young}, adopted value as the reference BMD; SD_{young}, standard deviation of the reference young subject data; BMD_{old}, measured BMD of the subjects ≥50 years old; SD_{old}, standard deviation of the subjects ≥50 years old; BMD_{low}, the cutpoint to define osteopenia; BMD_{os}, the cutpoint to define osteoporosis.

Table 2 Cutoff BMD values and T-scores for osteopenia and osteoporosis based on literature data: men's spine

Studies	BMD_{young}	SD_{young}	Age_{old}	BMD_{old}	SD_{old}	T-score ≤−1.0		T-score ≤−2.5		Prevalence =12.5%[¶]		Prevalence =3.75%[¶]		Prevalence =2%[§]	
						BMD_{low}	Prevalence (%)	BMD_{os}	Prevalence (%)	BMD_{low}	T-score	BMD_{os}	T-score	BMD_{os}	T-score
US White [2012] (52)[#]	1.057	0.110	≥50	1.067	0.162	0.947	23.02	0.782	3.97						
	1.057	0.110	≥60	1.074	0.172	0.947	22.89	0.782	4.42						
US Black [2012] (52)	1.124	0.138	≥50	1.131	0.169	0.986	19.47	0.779	1.84						
Chinese meta [2013] (60)	1.066	0.154	≥50	0.997	0.175	0.912	31.40	0.681	3.55	0.796	−1.756	0.685	−2.472	0.638	−2.782
ML Chinese [2008] (68)	0.954	0.116	≥50	0.944	0.145	0.838	23.34	0.663	2.67	0.777	−1.527	0.685	−2.312	0.646	−2.652
ML Chinese [2006] (69)	0.951	0.089	≥50	0.949	0.159	0.862	29.31	0.728	8.32	0.766	−2.082	0.665	−3.208	0.622	−3.696
Hong Kong [2005] (51)^	0.990	0.110	≥60	0.940	0.162	0.880	35.57	0.715	8.27	0.772	−1.983	0.673	−2.880	0.613	−3.415
Singapore [2020] (62)	1.041	0.098	≥50	1.129	0.215*	0.943	19.37	0.796	6.08	0.882	−1.627	0.746	−3.009	0.687	−3.608
Taiwan [2004] (70)	1.017	0.111	50–89	0.918	0.145	0.906	46.69	0.739	10.93	0.751	−2.395	0.660	−3.219	0.620	−3.577
Taiwan [2011] (67)	1.130	0.223*	≥50	1.018	0.206*	0.907	29.48	0.573	1.53	0.782	−1.564	0.652	−2.146	0.596	−2.399
Korea [2008] (65)	1.183	0.120	50–79	1.076	0.174	1.063	46.92	0.883	13.33	0.876	−2.557	0.766	−3.471	0.719	−3.868
Korea [2014] (66)	1.002	0.113	≥50	0.938	0.165	0.889	38.41	0.720	9.27	0.748	−2.246	0.644	−3.164	0.599	−3.562

[#], cited reference and the year of publication (see reference list). Age in years. BMD unit in g/cm^2. [¶], assuming the fragility fracture prevalence of Chinese men is half of that of Chinese women, the osteopenia and osteoporosis prevalence is assumed to be 12.5% and 3.75%, respectively. [§], assuming the reference Caucasian have an osteoporosis prevalence of 4%, the osteoporosis prevalence for Chinese is assumed to be 2% (this appears to be a more reasonable estimation). Note the US Blacks rate of osteoporosis prevalence is 1.84%. ^, for Hong Kong data, it is assumed that, for subjects ≥60 years, osteopenia prevalence and osteoporosis prevalence is 15% and 5% (or 2.235%) respectively. *, large SD were obtained, likely due to the limited sample size (see Appendix 2). BMD, bone mineral density; ML, mainland; BMD_{young}, adopted value as the reference BMD; SD_{young}, standard deviation of the reference young subject data; BMD_{old}, measured BMD of the subjects ≥50 years old; SD_{old}, standard deviation of the subjects ≥50 years old; BMD_{low}, the cutpoint to define osteopenia; BMD_{os}, the cutpoint to define osteoporosis.

Table 3 Cutoff BMD values and T-scores for osteopenia and osteoporosis based on literature data: women femoral neck

Studies	BMD_{young}	SD_{young}	Age_{old}	BMD_{old}	SD_{old}	T-score ≤−1.0		T-score ≤−2.5		Prevalence =25%[¶]		Prevalence =7.5% [§]	
						BMD_{low}	Prevalence (%)	BMD_{os}	Prevalence (%)	BMD_{low}	T-score	BMD_{os}	T-score
US White [2012] (52)[#]	0.884	0.113	≥50	0.705	0.125	0.771	70.29	0.601	20.41				
	0.884	0.113	≥60	0.682	0.118	0.771	77.44	0.601	24.81				
US Black [2012] (52)	0.962	0.151	≥50	0.799	0.151	0.811	53.24	0.585	7.83				
Italian [2018] (75)			≥50						16.2				
Spain [2010] (76)			≥50						15.1				
Australia [2011] (77)			≥50^^						22.8[##]				
Chinese meta [2013] (60)	0.858	0.120	≥50	0.700	0.139	0.738	60.69	0.558	15.39	0.606	2.099	0.499	−2.988
US Chinese [2006] (61)	0.797	0.110	50–89	0.655	0.102	0.687	62.40	0.522	9.67	0.586	−1.919	0.508	−2.629
Hong Kong [2005] (51)^	0.760	0.100	≥60	0.622	0.107	0.660	63.81	0.510	14.73	0.566[A]	−1.939[A]	0.485[A]	−2.750[A]
										0.592[B]	−1.685[B]	0.499[B]	−2.614[B]
Japan [2001] (63)[##]	0.812	0.112	50–79	0.657	0.107	0.700	65.64	0.531	12.06	0.585	−2.026	0.503	−2.755
Korea [2008] (65)	0.968	0.100	50–79	0.801	0.125	0.868	70.47	0.718	25.53	0.716	−2.521	0.620	−3.480
Taiwan [2011] (67)	0.880	0.106	>50	0.752	0.174	0.774	55.10	0.615	21.66	0.634	−2.320	0.501	−3.579

[#], cited reference and the year of publication [see reference list] . Age in years. BMD unit in g/cm^2. [##], osteoporosis based on spine or femoral neck BMD (the lowest measure was considered). ^^, median age: 54.0 years. [¶], assuming the reference Caucasian have an osteopenia prevalence of 50% (very high prevalence of osteopenia will lend this parameter meaningless in real world), the osteopenia prevalence for Chinese is assumed to be 25%. [§], assuming the reference Caucasian have an osteoporosis prevalence of 15% (1994 WHO definition of osteoporosis, also see the Italian, Spanish, and Australian data), the osteoporosis prevalence for Chinese is assumed to be 7.5%. This prevalence of 7.5% could be an aggressive estimation (i.e., the real prevalence could be even lower), as some studies showed the hip fragility fracture prevalence of older Chinese women is close to 40% of that of Caucasians (3). ^, for Hong Kong data, it is assumed that, for subjects ≥60 years, osteopenia prevalence and osteoporosis prevalence is 30%[A] and 10%[A] respectively, or 38.7%[B] and 12.4%[B] respectively. Bow *et al.* (78) reported that Japanese and Hong Kong Chinese have very similar age-specific hip fragility fracture prevalences. BMD, bone mineral density; Chinese meta, meta-analysis result; BMD_{young}, adopted value as the reference BMD; SD_{young}, standard deviation of the reference young subject data; BMD_{old}, measured BMD of the subjects ≥50 years old; SD_{old}, standard deviation of the subjects ≥50 years old; BMD_{low}, the cutpoint to define osteopenia; BMD_{os}, the cutpoint to define osteoporosis.

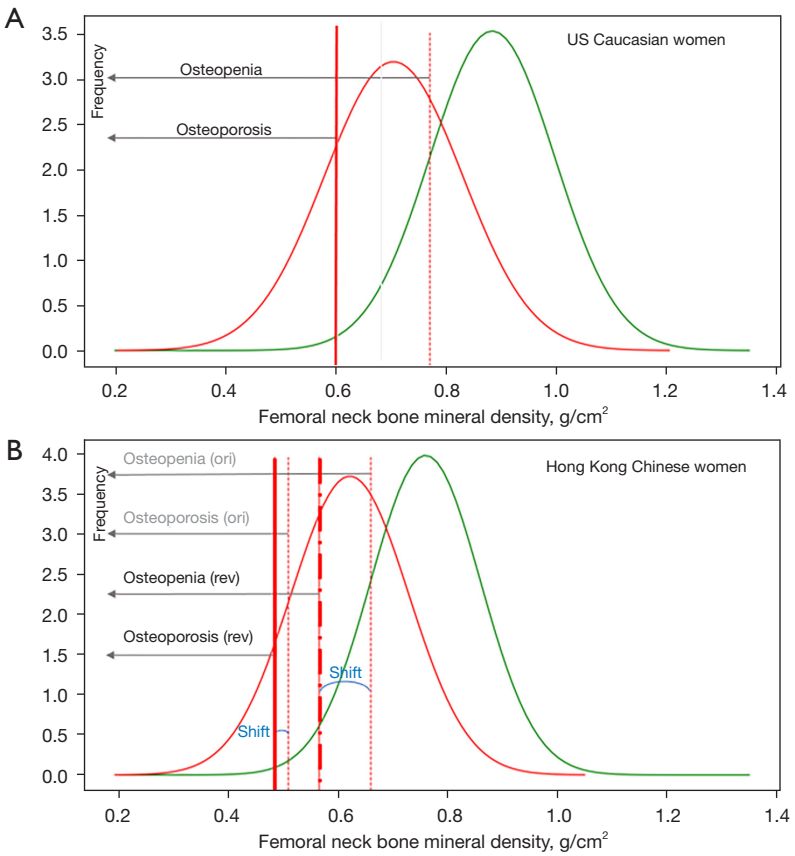

Figure 1 Schematic illustration showing how T-score cutpoints for defining osteoporosis and osteopenia amongst US Caucasian women can be adjusted to allow for the lower incidence of fragility fractures experienced by Chinese women. (A) Distribution curves for femoral neck BMD in US Caucasian young women aged 20 to 29 years (green curve) and older women aged ≥50 years (red curve). Both curves are approximated by Gaussian distributions based on the reference range data published by Looker *et al.* (52). Amongst the older women the prevalence of osteoporosis is approximately 20.4% and osteopenia 70.3% (*Table 3*). (B) Similar curves for Hong Kong Chinese young women (green curve) and older women (red curve) aged ≥60 years based on the data published by Lynn *et al.* (51). If the original (ori) WHO T-scores of −2.5 (BMD: 0.510 g/cm^2) and −1.0 (BMD: 0.660 g/cm^2) are used to define osteoporosis and osteopenia, then the percentages are not very different to those for US Caucasian women (*Table 3*). Since the incidence of fragility fractures experienced by Chinese women is approximately half of that of US Caucasian women, we can set a revised T-score of −2.750 (BMD: 0.485 g/cm^2) corresponding to a revised (rev) prevalence of osteoporosis of 10%, and a revised T-score of −1.939 (BMD: 0.566 g/cm^2) corresponding to a revised prevalence of osteopenia of 30% for Chinese women aged ≥60 years (*Table 3*). Note that the revised BMD thresholds are calculated from the area under the curve of the group of older women assuming a Gaussian distribution and cutpoints of 10% and 30% respectively. The corresponding T-scores are calculated from the mean BMD and population standard deviation of the young women. Further details of how the calculations were performed are given in Supplementary file (Appendix 3). BMD, bone mineral density.

probably accounts for much of the variation seen in *Tables 1-6*. Therefore, for the calculated or estimated results in these tables, in this study we do not aim to provide a final solution. Instead, we aim to provide a framework for further consideration or further refinement. The ideal BMD reference database and final values for the proposed revised Chinese T-scores remain to be established.

There are many other limitations to our analysis. This article discusses BMD defined osteoporosis only, while the diagnosis of osteoporosis can also be established by FF. Understandably, cutpoint T-scores for defining osteopenia and osteoporosis also depend on the quality and size of databases. In addition to the requirement for a high precision of dual-energy X-ray absorptiometry

Table 4 Cutoff BMD values and T-scores for osteopenia and osteoporosis based on literature data: men's femoral neck

Studies	BMD_{young}	SD_{young}	Age_{old}	BMD_{old}	SD_{old}	T-score ≤–1.0		T-score ≤–2.5		Prevalence =12.5%[¶]		Prevalence =3.75%[§]	
						BMD_{low}	Prevalence (%)	BMD_{os}	Prevalence (%)	BMD_{low}	T-score	BMD_{os}	T-score
US Black [2012] (52)	1.038	0.157	≥50	0.886	0.152	0.881	48.57	0.645	5.69				
	1.038	0.157	≥60	0.873	0.150	0.881	52.06	0.645	6.45				
Spanish [1997] (57)	0.927	0.124	50–79	0.790	0.124	0.803	54.24	0.617	8.21				
	0.927	0.124	60–79	0.766	0.124	0.803	61.63	0.617	11.37				
Australia [2011] (77)			≥50^^						5.9[##]				
ML Chinese [2006] (69)	0.884	0.110	50–89	0.742	0.115	0.774	60.90	0.609	12.28	0.610	–2.489	0.538	–3.146
ML Chinese [2007] (64)	0.867	0.125	≥50	0.743	0.109	0.743	49.96	0.556	4.28	0.618	–2.004	0.549	–2.554
Chinese meta [2013] (60)	0.928	0.144	≥50	0.785	0.143	0.784	49.62	0.568	6.48	0.620	–2.136	0.530	–2.764
Hong Kong [2005] (51)^	0.850	0.130	≥60	0.696	0.115	0.720	58.24	0.525	6.75	0.577	–2.096	0.496[A]	–2.726[A]
												0.508[B]	–2.632[B]
Korea [2008] (65)	1.106	0.140	50–79	0.896	0.130	0.966	71.57	0.756	14.19	0.746	–2.573	0.664	–3.159
Korea [2015] (66)	0.919	0.132	≥50	0.741	0.220*	0.787	58.21	0.589	24.38	0.489	–3.259	0.350	–4.307
Taiwan [2011] (67)	0.990	0.223**	>50	0.817	0.090	0.767	29.11	0.433	0.00	0.713	–1.242	0.657	–1.496

[#], cited reference and the year of publication (see reference list). Age in years. BMD unit in g/cm^2. [##]: osteoporosis based on spine or femoral neck BMD (the lowest measure was considered). ^^, median age 56.0 years. [¶], assuming the Chines women have an osteopenia prevalence of 25%, the osteopenia prevalence for Chinese ≥50 years old men is assumed to be 12.5%. [§], assuming the Chines women have an osteoporosis prevalence of 7.5%, the osteoporosis prevalence for Chinese ≥50 years old men is assumed to be 3.75%. Note the hip fracture rate among elderly Ascian American men is lower than American Blacks (Appendix 4). ^, for Hong Kong data, it is assumed that, for subjects ≥60 years, osteopenia prevalence is 15% (i.e., half of the women's rate) and osteoporosis prevalence is 4%[A] or 5%[B]. *, a large SD was obtained. **, a large SD was obtained, likely due to the limited sample size (see Appendix 4). BMD, bone mineral density; ML, mainland; Chinese meta, meta-analysis result; BMD_{young}, adopted value as the reference BMD; SD_{young}, standard deviation of the reference young subject data; BMD_{old}, measured BMD of the subjects ≥50 years old; SD_{old}, standard deviation of the subjects ≥50 years old; BMD_{low}, the cutpoint to define osteopenia; BMD_{os}, the cutpoint to define osteoporosis.

Table 5 Cutoff BMD values and T-scores for osteopenia and osteoporosis based on literature data: women's total hip

Studies	BMD_{young}	SD_{young}	Age_{old}	BMD_{old}	SD_{old}	T-score ≤−1.0		T-score ≤−2.5		Prevalence =29%[¶]		Prevalence =6.7% [§]	
						BMD_{low}	Prevalence (%)	BMD_{os}	Prevalence (%)	BMD_{low}	T-score	BMD_{os}	T-score
US White [2012] (52)[#]	0.971	0.114	≥50	0.830	0.140	0.857	57.55	0.686	15.15				
	0.971	0.114	≥60	0.806	0.135	0.857	64.69	0.686	18.74				
US Black [2012] (52)	1.036	0.147	≥50	0.901	0.164	0.889	47.07	0.669	7.86				
Canada white [2008] (79)			≥50**						11.3				
Argentina [2016] (80)			≥50						6.2				
US Amerindian [2016] (81)			50–79						8.4				
ML Chinese [2007] (64)	0.956	0.120	50–89	0.851	0.140	0.835	45.55	0.655	8.01	0.774	−1.510	0.641	−2.609
US Chinese [2006] (61)	0.902	0.110	50–89	0.781	0.117	0.792	53.85	0.627	9.42	0.716	−1.689	0.606	−2.695
Hong Kong [2005] (51)^	0.89	0.11	≥60	0.751	0.115	0.780	60.00	0.615	11.85	0.699	−1.743	0.599	−2.642
Japan [2001] (63)[##]	0.886	0.107	50–79	0.748	0.125	0.779	59.87	0.618	14.94	0.679	−1.932	0.561	−3.034
Korea [2014] (66)	0.889	0.102	≥50	0.765	0.205^^	0.787	54.20	0.634	26.12	0.652	−2.322	0.458	−4.229

[#], cited reference and the year of publication (see reference list). Age in years. BMD unit in g/cm^2. **, mean age: 65.0±9.4 (SD) years. [¶], assuming the reference Caucasian have an osteopenia prevalence of 58%, the osteopenia prevalence for Chinese women ≥50 years old is assumed to be 29%. [§], based on the US and Canadian Caucasian data and also those of femoral neck results, the osteoporosis prevalence for Chinese women ≥50 years old is assumed to be 6.7%, which could be an aggressive estimation (i.e., the real prevalence could be even lower), as some studies showed hip fragility fracture prevalence of older Chinese women is close to 40% of that of Caucasians (3). Data of Latin American and US Amerindian are listed as reference. Argentina has a high percentage of population with European ancestry. ^, for Hong Kong data, it is assumed that, for subjects ≥60 years, osteopenia prevalence and osteoporosis prevalence is 32.35% and 9.37% respectively. [##], Bow *et al.* (78) reported that Japanese and Hong Kong Chinese have very similar age-specific hip fragility fracture prevalences. ^^, this SD value is large. BMD, bone mineral density; ML, mainland; BMD_{young}, adopted value as the reference BMD; SD_{young}, standard deviation of the reference young subject data; BMD_{old}, measured BMD of the subjects ≥50 years old; SD_{old}, standard deviation of the subjects ≥50 years old; BMD_{low}, the cutpoint to define osteopenia; BMD_{os}, the cutpoint to define osteoporosis.

Table 6 Cutoff BMD values and T-scores for osteopenia and osteoporosis based on literature data: men's total hip

Studies	BMD_{young}	SD_{young}	Age_{old}	BMD_{old}	SD_{old}	T-score ≤−1.0		T-score ≤−2.5		Prevalence =14.54%[¶]		Prevalence =3.35%[§]	
						BMD_{low}	Prevalence (%)	BMD_{os}	Prevalence (%)	BMD_{low}	T-score	BMD_{os}	T-score
US White [2012] (52)[#]	1.067	0.120	≥50	0.978	0.148	0.947	41.74	0.767	7.69				
	1.067	0.120	≥60	0.963	0.148	0.947	45.68	0.767	9.22				
US Black [2012] (52)	1.155	0.156	≥50	1.065	0.163	0.999	34.37	0.765	3.32				
	1.155	0.156	≥60	1.049	0.164	0.999	38.03	0.765	4.15				
Hong Kong [2005] (51)^	1.000	0.140	≥60	0.861	0.136	0.860	49.56	0.650	5.99	0.760	−1.713	0.633	−2.625
Korea [2014] (66)	1.025	0.120	≥50	0.916	0.175	0.905	47.55	0.725	13.83	0.731	−2.453	0.595	−3.587
ML Chinese [2006] (69)	0.967	0.117	50–89	0.861	0.122	0.851	46.68	0.676	6.50	0.732	−2.020	0.637	−2.833
ML Chinese [2007] (64)	0.938	0.124	≥50	0.868	0.123	0.813	32.85	0.627	2.46	0.738	−1.603	0.643	−2.367

[#], cited reference and the year of publication (see reference list). Age in years. BMD unit in g/cm^2. [¶], assuming Chinese women have an osteopenia prevalence of 29% (see *Table 5*), the osteopenia prevalence for Chinese men ≥50 years old is assumed to be approximately half of the rate of Chinese women. [§], assuming Chinese women have an osteoporosis prevalence of 6.7% (see *Table 5*), the osteoporosis prevalence for Chinese men ≥50 years old is assumed to be half of the rate of Chinese women (i.e., 3.35%). That Chinese men have an osteoporosis prevalence of 3.35% is consistent with that this rate is half of the rate of Caucasians and is similar to the US Blacks rate. ^, for Hong Kong data, only data of subjects ≥60 years were available, osteopenia and osteoporosis prevalences are assumed to be 22.8% and 4.6% respectively. BMD, bone mineral density; ML, mainland; BMD_{young}, adopted value as the reference BMD; SD_{young}, standard deviation of the reference young subject data; BMD_{old}, measured BMD of the subjects ≥50 years old; SD_{old}, standard deviation of the subjects ≥50 years old; BMD_{low}, the cutpoint to define osteopenia; BMD_{os}, the cutpoint to define osteoporosis.

Table 7 A summary of estimated BMD-based osteoporosis prevalence of Caucasians, US Blacks, and Chinese (age ≥50 years)

Ethnicity	Lumbar BMD	Femoral neck BMD	Total hip BMD
US Caucasian women	15.8%[a]	20.4%[b]	15.2%[c]
Italian women	16.2%[d]		
US Black women	6.7%[e]	7.8%[f]	7.9%[g]
Chinese women	7.5%[h]	7.5%[i]	6.7%[j]
US Caucasian men	4%[k]		7.7%[l]
Spanish men		8.2%[m]	
US Black men	1.8%[n]	5.7%[o]	3.3%[p]
Chinese men	2.0%[q]	3.8%[r]	3.4%[s]

[a], according to *Table 1*, US Caucasian women had prevalence of 15.8%; [b], according to *Table 3*, US Caucasian women had prevalence of 20.4%; [c], according to *Table 5*, US Caucasian women had a prevalence of 15.2%; [d], according to *Table 1*, Italian women had a prevalence of 16.2%; [e], according to *Table 1*, US Black women had a prevalence of 6.7%; [f], according to *Table 3*, US Black women had prevalence of 7.8%; [g], according to *Table 5*, US Black women had a prevalence of 7.9%; [h], assuming the reference US Caucasian women have prevalence of 15.8% (*Table 1*), the value for Chinese women is assumed to be 7.5%; [i], assuming the reference Caucasian have a prevalence of 16% (according to the WHO 1994 definition), the prevalence for Chinese is assumed to be 7.5%; [j], according to the reference US and Canada Caucasian women values (*Table 5*) the value for Chinese women is assumed to be 6.7%; [k], according to *Table 2*, US Caucasian men had a prevalence of 3.97%; [l], according to *Table 6*, US Caucasian men had a prevalence of 7.69%; [m], according to *Table 4*, Spanish men had a prevalence of 8.2%; [n], according to *Table 2*, US Black men had a prevalence of 1.84%; [o], according to *Table 4*, US Black men had a prevalence of 5.7%; [p], according to *Table 6*, US Black men had prevalence of 3.32%; [q], assuming the reference US Caucasian men have a prevalence of 4%, the prevalence for Chinese is assumed to be 2%, which is slightly higher than the rate of US Blacks; [r], the prevalence of Chinese men is assumed to be 3.8%, which is about half of the rate of Chinese women and also about half of the rate of Spanish men. Note hip fragility fracture prevalence among Chinese men is lower than that of US Blacks; [s], assuming Chinese women have a prevalence of 6.7%, the prevalence for Chinese men is assumed to be half of the rate of Chinese women. BMD, bone mineral density.

(DXA) measurement, particularly for the subjects in the older group, their health status and age distribution should be representative of the general community population. Over-representation of 50–59 years age group or over-representation of >75 years group or over-representation of healthier participants will all affect the quality of the database. As discussed above, the confidence levels of the mean BMD and population standard deviation of the published databases are also limited by the sample size (Tables S1-S6). Theoretically, 95% confidence intervals for the cut-point T-scores derived for each database could be computed based on the number of participants in the younger and older age groups. However, in our analysis, multiple databases from East Asia demonstrate a similar trend, and thus we believe the trend we observed is valid. DXA measurement of BMD also depends on different manufacturer-specific scanners, which differ in the analysis algorithms, region of interest definitions and calibration standards. To avoid the confusion that would result from instrument specific numerical BMD cutpoint values, the calculated T-scores whereby each patient's value is compared with a young normative database generated on the same device would largely, if not totally, eliminate this problem (82). The DXA scanner for each study used in this article is also listed in Tables S1-S6. For lumbar BMD measurement, the effect of degenerative changes cannot be totally eliminated during image post-processing. Our analysis assumes that the measured BMD values for the older participants follow a Gaussian distribution for the sampled databases. This assumption is often violated in the real world, especially for the lumbar BMD values. Moreover, it is also possible that FF risk among older Chinese is even less than half of that of older US Caucasians. For example, Chinese women's osteoporotic fracture prevalence could be 40% of that of US Caucasian women (3). For different BMD reference databases, more precise and differential cutpoint BMD and T-scores for defining osteoporosis can be applied. In clinical practice for patient care, other parameters such as trabecular bone score (TBS) haven been demonstrated to provide additional information for bone quality (83-85). Moreover, many other biological factors affect bone quality and fracture risks in

addition to BMD and T-score (86-88).

BMD-derived osteoporosis is a BMD category defined by statistical consensus, rather than a biologically diagnosed disease. We believe the cutpoint T-scores for defining osteoporosis described in this article will be more in line with the original WHO definition and will allow a more meaningful international comparison of disease burden. The analysis in this article also demonstrates the difficulties of international comparison of BMD-defined osteoporosis prevalence, thus it is more meaningful to compare FF prevalence. It is well recognized that osteoporosis can also be diagnosed based on FF even without a BMD-based diagnosis. The significance of any given T-score to fracture risk depends on age and the presence of clinical risk factors. The intervention threshold depends upon risk, life expectancy, and the benefits and side effects of interventions.

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Footnote

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