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.

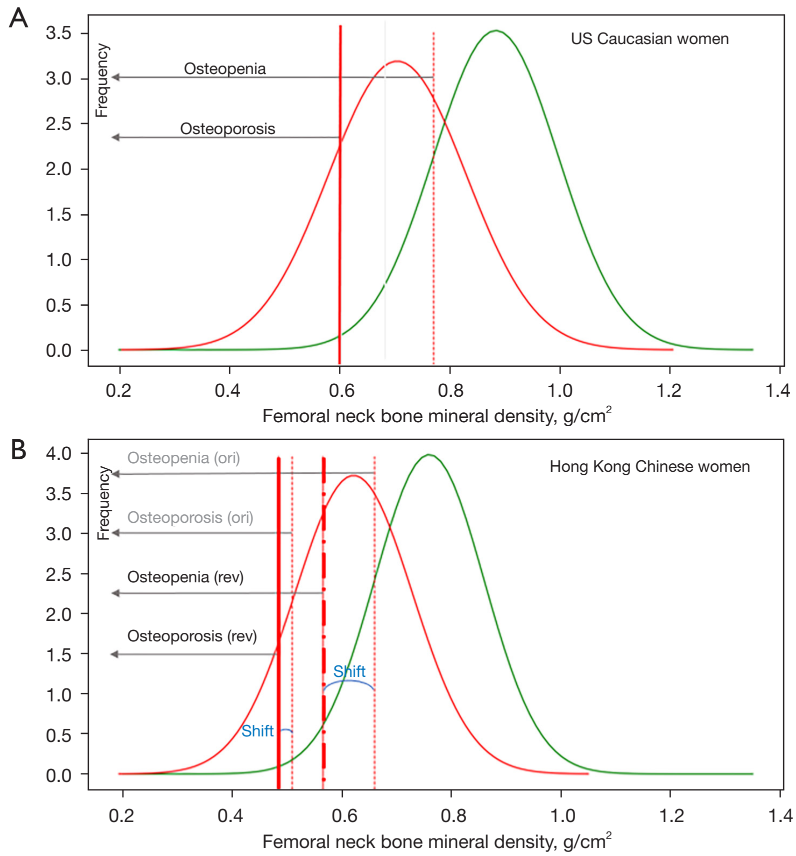

Figure 1 Schematic illustration showing how T-score cutpoints for defining osteoporosis and osteopenia amongst US Caucasian women can be adjusted to allow for the lower incidence of fragility fractures experienced by Chinese women. (A) Distribution curves for femoral neck BMD in US Caucasian young women 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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Appendix 1 The fragility fracture prevalence among older Chinese is no more than half that of Caucasians

It has been recognized that the fragility fracture prevalence among older Chinese is no more than half that of Caucasians, both for men and women. Some literature reports have been discussed in a recent article (3). Hereby we summarize a number of additional evidence.

Using Kaiser Permanente Northern California (KPNC) data, Lo *et al.* (4) studied the age-adjusted hip fracture incidence per 100,000 subjects for women aged ≥50 years old, and noted that in the year 2012 it was 288 among Caucasian women and 148 among Asian women. Using KPNC data of women aged 50–85 years with femoral neck BMD measured between 1997 and 2003, Khandelwal *et al.* (5) studied ethnic older South Asians (n=449, defined by Indian, Pakistani, or Sri Lankan ancestry) and age-matched Chinese (n=2245) and Caucasian (White) women (n=4490). It was noted that more South Asian (7.1%) and Caucasian (9.6%) women had prior FF than Chinese women (4.5%). During a median of 8.4 years follow-up, 0.4% of Chinese and 0.7% of Caucasian women experienced a hip fracture. Wrist fracture incidence per 100,000 person-years was similar among South Asian and Caucasian women (n=286 and 303, respectively), but lower among Chinese women (n=130). Chinese women had a significantly lower incidence of humerus fracture (Chinese 0.5%, South Asians: 0.7%, White: 1.6%) and any non-vertebral major FF (Chinese 1.8%, South Asians 2.9%, White: 4.5%). Compared with Caucasian data, much lower hip fracture prevalence has also been reported with data from China Mainland (6).

Compared with US Caucasians, American Asians are noted to have a lower mortality rate following hip fracture. Using data from the California Office of Statewide Health and Planning and Development concerning years from 2000 to 2011, Sullivan *et al.* (7) conducted a study on patients ≥55 years admitted for hip fracture. With a total of 317,677 hospital admissions, Asians had a much lower incidence of hip fracture (odds ratio 0.32 for both men and women) and a lower mortality rate as compared to Caucasians (30-day mortality odds ratio, women: 0.59; men: 0.62). Using KPNC data, Lo *et al.* (8) studied female patients ≥65 years with a hospital discharge diagnosis of a proximal femur fracture between 2000 and 2010. It was noted that the one-year crude mortality rate was higher among Caucasians (23.6%) compared with Asians (15.6%). After adjusting for confounders, Asians were associated with lower odds of death at 1 year compared with Caucasians (odds ratio: 0.64). Using the same data of Lo *et al.* (8), Patel *et al.* (9) conducted additional analyses. Among 615 Asian women, there were 172 Chinese, 153 Japanese, 119 Filipina women, accounting for 72.2% of women with hip fracture identified as 'Asian'. It was noted that one-year overall mortality rates following hip fracture were similar among these three ethics groups (Chinese: 14.0%; Japanese: 15.0%; and Filipina: 14.3%).

Recent evidence suggests that, compared with Caucasians, the relative prevalence of osteoporotic vertebral fracture (OVF) follows the same pattern as other clinical fractures, with both radiographic and clinical OVF prevalences among older Chinese being no more than half of those of older Caucasians [*Figures S1*,*S2* (10-19)]. However, till now this conclusion heavily depends on the data from MrOS(Hong Kong) and MsOS(Hong Kong) studies. Based on our own MsOS(Hong Kong) data and literature reports, we estimated that radiographic OVF prevalence among Hong Kong Chinese women is very similar to those of age-matched Chinese women in Beijing, Japanese women, and Korean women (20). In a preliminary comparative study with a morphometric method, Kwok *et al.* (21) described that the radiographic OVF prevalence was no lower among Hong Kong Chinese men and women than among their counterparts in Thailand, Indonesia, and Japan. Moreover, using the prevalence of lumbar degenerative spondylolisthesis (DS) as a 'biomarker', we did additional testing to see whether the spines of the MrOS(Hong Kong) and MsOS(Hong Kong) study participants are 'unusually healthier'. The prevalence of lumbar DS can be reasonably reliably estimated on radiograph to allow inter-study comparisons. It is noted that the prevalence of lumbar DS among MrOS(Hong Kong) and MsOS(Hong Kong) study participants were no lower than those reported for Japanese and Thai subjects [*Figure S3* (22-31)]. Therefore, it is unlikely that the conclusion that both radiographic and clinical OVF prevalences among older Chinese are no more than half of those of older Caucasians was heavily biased because the MrOS(Hong Kong) and MsOS(Hong Kong) study participants had unusually healthier spine than other Chinese (or other East Asians) populations.

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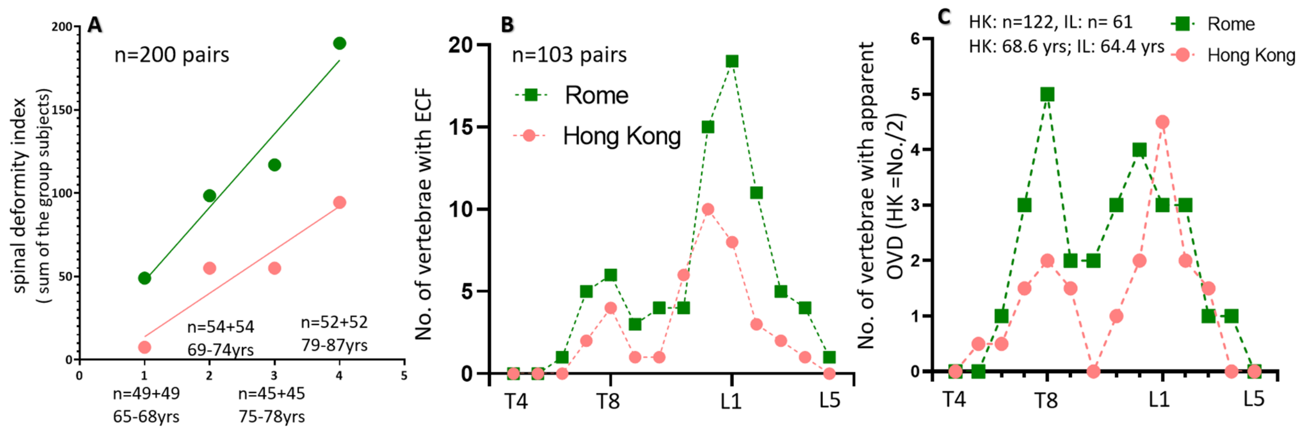

Figure S1 Chinese older women have a much lower radiographic osteoporotic vertebral fracture prevalence than that of Italian older women. (A) Total spinal deformity index score of four different age groups of Chinese women and Italian women (population-based and age-matched data). Spinal deformity index was calculated with each vertebra assigned a score of 0, 0.5, 1, 1.5, 2, 2.5, and 3 for no ROVD or ROVDs of <20%, 20–25%, ≥5%–1/3, ≥1/3–40%, ≥40%–2/3, and ≥2/3 vertebral height loss, respectively. The spinal deformity index for each subject was calculated by summing the scores of all vertebrae from T4 to L5. Light red ball and line indicate Hong Kong subjects and dark green ball and line indicate Italian subjects. Lines denote linear fit of the four values of total spinal deformity index of the four age groups, with the slope steeper for Italian than for Chinese. N = 49 + 49 means there are 49 Chinese subjects and 49 Italian subjects in this age group. (B) A comparison of the distribution of ECF sign positive ROVD among different vertebral levels (103 pairs of age-matched Chinese and Italian older women, population-based data). The data in B is in addition to the data in A. (C) A comparison of the distribution of apparent ROVD (i.e., with ≥20% vertebral height loss) among different vertebral levels. There were 122 population-based Chinese subjects and 61 Italian back pain patients (ROVD number for Chinese data was divided by 2 for presentation). ECF, endplate end/or cortex fracture; ROVD, radiological osteoporotic vertebral deformity (equivalent to radiological vertebral fracture); HK, Hong Kong; IL, Italian. Data are from Wang *et al. Arch Osteoporos*. 2021;16:174, and Wang *et al.*, *Arch Osteoporos.* 2022;17:13. Reused with permission.

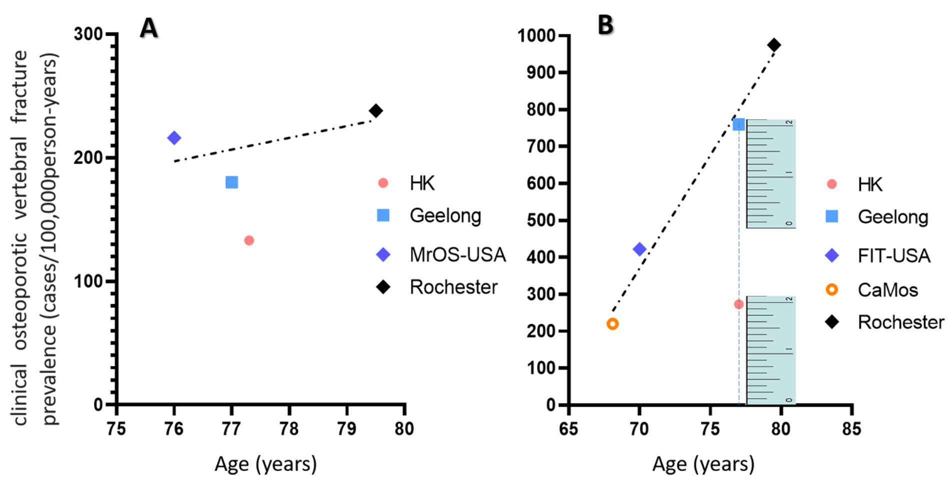

Figure S2 Chinese older men and women have a much lower clinical osteoporotic vertebral fracture prevalence than those of Caucasians. (A) Prevalence of older men. Data are from MrOS(Hong Kong) study, Freitas *et al. Osteoporos Int* 2008;19:615-23 (MrOS USA study), Sanders *et al. Osteoporos Int* 1999;10:240-7 (Geelong study), and Cooper *et al. J Bone Miner Res* 1992;7:221-7 (Rochester study). (B) Prevalence of older women. Data are from MsOS(Hong Kong) study, Sanders *et al. Osteoporos Int* 1999;10:240-7 (Geelong study), Cooper *et al. J Bone Miner Res* 1992;7:221-7 (Rochester study), Fink *et al. J Bone Miner Res* 2005;20:1216-22 (FIT-USA study), and Papaioannou *et al. Osteoporos Int* 2005;16:568-78 (CaMos study).

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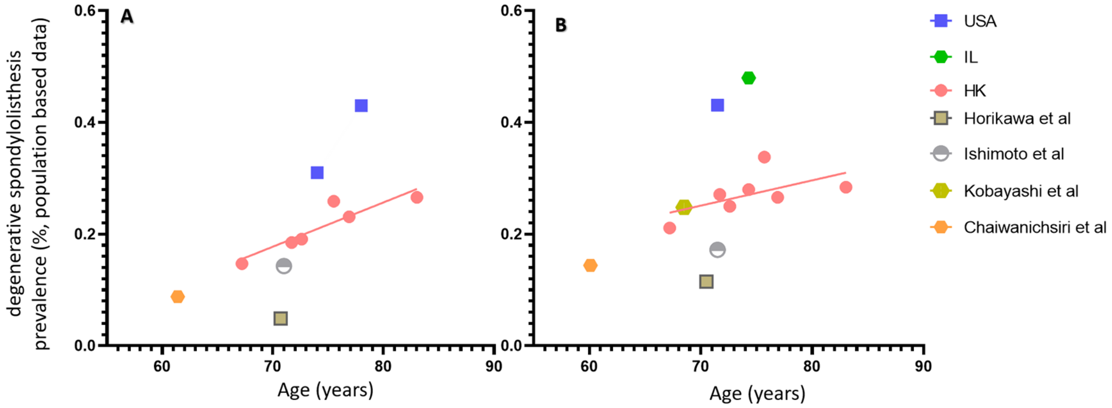

Figure S3 A comparison of lumbar degenerative spondylolisthesis (DS) prevalence among older women of various ethnic groups. The data from the USA and Italy had much higher prevalences than the data from Asia. Despite the relatively small sample size of the Asian studies other than the Hong Kong study, it can be seen that DS prevalence in MsOS(Hong Kong) women subjects is no lower than the results from Japan or Thailand. Taking DS as an example, there is no sign that MsOS(Hong Kong) data are heavily biased toward healthier participants. The Hong Kong data are from MsOS(Hong Kong) study (He *et al. Eur Radiol* 2014;24:441-8; *Wáng et al. Spine* (*Phila Pa* 1976) 2016;41:1096-103; So *et al. 9th FFN global congress*, abstract: FFN21-1200). USA women data are from Vogt *et al. Spine* (*Phila Pa* 1976) 1998;23:2640-7 (total n=788 subjects). Italian women data are from So *et al. 9th FFN global congress*, abstract: FFN21-1200 (total n=130 subjects). Japanese women data are from Horikawa *et al. J Orthop Surg* (*Hong Kong*) 2006;14:9-12 (total n=323 subjects); Ishimoto *et al. BMC Musculoskelet Disord*. 2019;20:618 (total n=477 subjects); Kobayashi *et al. Eur Spine J* 2016;25:2384-9 (total n=289 subjects).Thai women data are from Chaiwanichsiri *et al. J Med Assoc Thai* 2007;90:2477-81 (total n=486 subjects).

While less data is available, wrist and/or forearm FFs are also likely to occur less frequently among Asians. By analysing the data from the National Osteoporosis Risk Assessment (NORA) which is an observational study of postmenopausal women in the USA, Barrett-Connor *et al.* (32) reported the baseline characteristics and 1-year fracture incidents in Caucasians and Asians. At baseline, among 179,470 Caucasians, a history of wrist fracture since 45 years old was recorded in 6.3% of cases; among 1,912 Asians, a history of wrist fracture since 45 years old was recorded in 3.7% of the cases. During the follow-up, wrist fracture was recorded in 0.5% of 149,524 Caucasians and in 0.2% of 1,258 Asians. In a Norwegian study, Lofthus *et al.* (33) reported that the relative risk of distal forearm fracture in Asians who immigrated to Oslo was 0.72 (95% CI: 0.53–1.00) compared to ethnic Norwegians living in Oslo.

Footnote

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Appendix 2 Chinese skeleton has microstructural and mechanical advantages

As compared with those of Caucasians, a study reported that the Chinese skeleton has microstructural and mechanical advantages (37). In the Study of Women's Health Across the Nation (SWAN), Finkelstein *et al*. (38) reported that unadjusted aBMD (areal BMD) was lower among Asian American compared to Caucasian women; however, after adjustment for covariates there were no significant differences of lumbar spine and femoral neck BMD between Chinese and Caucasian. When BMD was assessed in a subset of women weighing less than 70 kg and then adjusted for covariates, lumbar spine BMD became higher in Chinese than that in Caucasian women. Nam *et al*. (39) compared femoral neck, total hip, and lumbar spine BMD in older men aged 65 to 78 years. It was noted that, while unadjusted aBMD was lower among Asians, adjustment for weight and height attenuated or reversed the differences in aBMD between US Caucasian and Asian men, including US Asian, Hong Kong Chinese and South Korean men. With QCT (quantitative computed tomography) measurement, Walker *et al*. (40) reported that, among premenopausal American women, compared with Caucasians, Chinese women had greater integral and cortical vBMD (volumetric BMD) at the femoral neck and greater integral vBMD at the total hip. Among postmenopausal women, Chinese women had greater cortical vBMD at the femoral neck and total hip. For American men ≥65 years, Marshall *et al*. (41) reported that Asian and African American men had 6–10% greater integral and 33–36% greater trabecular vBMD, as well as 5% greater mean cortical thickness at the hip compared with Caucasian men. Boutroy *et al*. (42) reported that, compared with Caucasians, both pre- and postmenopausal Chinese women had greater cortical thickness, cortical tissue mineral density and reduced cortical porosity at both the radius and tibia. Using HRpQCT (high-resolution peripheral quantitative computed tomography), Walker *et al*. (43) reported that radius demonstrated greater trabecular and cortical density, trabecular bone to tissue volume, and trabecular and cortical thickness both before and after adjustment for covariates in the Chinese cohort than the Caucasian cohort. Tibia revealed similar findings as well as higher trabecular number, lower trabecular spacing and inhomogeneity in the Chinese cohort after adjustment for covariates (43). With HRpQCT from a cohort of premenopausal women, Liu *et al*. (44) applied ITS (individual trabecular segmentation) and mFEA (micro-finite element analysis) to assess bone properties of Chinese American women and Caucasians. With ITS, the morphology of individual trabeculae is classified as either rod-like or plate-like. More plates and/or a higher plate to rod ratio are associated with greater mechanical competence. mFEA is used to estimate the mechanical competence of bone by simulating bone under deformation conditions. The results of ITS showed that, compared with Caucasians, while Chinese women had a similar number of rod-like trabeculae, they had more trabecular plates, leading to a higher plate-to-rod ratio and greater trabecular connectivity at both the distal radius and tibia. By using mFEA, these differences in trabecular bone microstructure were shown to translate into a greater trabecular mechanical competence (55%–68% at the distal radius and 29%–43% at the distal tibia) among Chinese (as compared with Caucasians). Postmenopausal Chinese women also had a higher trabecular plate-to-rod ratio and greater whole bone stiffness, despite similar trabecular density as compared to Caucasian women (45). These microstructural advantages for Asians/Chinese have also been observed among Asians in Canada and in Australia (46,47).

Footnote

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Appendix 3 An example of calculation of lumbar spine T-score and cutoff BMD value for defining osteoporosis in US Chinese older women

The data is from: Walker MD, Babbar R, Opotowsky AR, Rohira A, Nabizadeh F, Badia MD, Chung W, Chiang J, Mediratta A, McMahon D, Liu G, Bilezikian JP. A referent bone mineral density database for Chinese American women. *Osteoporos Int*. 2006;17:878-87.

Step 1. Based on the table-3 of the article of Walker *et al.*, the mean BMD for women aged 50–89 years (four age bands grouped together) is calculated according to:

$$BMD_{mean} = \frac{\sum_1^n n_i * M_i}{\sum_1^n n_i} \qquad [1]$$

(M_i: mean BMD value of different age groups; n_i: subject number of different age groups)

Thus, mean BMD value of 0.837 g/cm^2 is derived for US Chinese older women group (i.e., BMD_{old}).

From table-3, the mean BMD value for aged 20–29 years is 0.994 g/cm^2 (i.e., BMD_{young}).

Step 2. From the standard deviation (SD) calculation formula:

$$SD = \sqrt{\frac{\sum_1^n (n_i - 1) * s_i^2 + \sum_1^n n_i * (M_i - BMD_{mean})^2}{\sum_1^n n_i - 1}} \qquad [2]$$

(s_i: standard deviation of different age groups)

BMD SD value (i.e., SD_{old}) of 0.137 is derived for US Chinese older women group (50–89 years, four age bands grouped together).

From table-3, the BMD SD value for aged 20-29 yrs is 0.110 (i.e., SD_{young}).

Step 3. T-score is calculated according to

$$T - score = \frac{BMD_{measured} - BMD_{young}}{SD_{young}} \qquad [3]$$

With BMD_{young}=0.994 and SD_{young}= 0.110 of young women.

If T-score for defining osteoporosis is ≤–2.5, then the cutoff value of measured BMD for older group is 0.719 g/cm^2.

Step 4. For older US Chinese women, as shown above the mean BMD_{old} is 0.837 g/cm^2 and SD_{old} is 0.137. Based on the assumption of the BMD values follow Gaussian distribution and these two values, the Gaussian distribution curve is plotted and shown in *Figure S4*. if osteoporosis cutpoint T-score is ≤–2.5, then in older women this T-score correspond to measured BMD of ≤0.719 g/cm^2, then from *Figure S4* the osteoporosis prevalence is 19.48%. On the other hand, if we assume the osteoporosis prevalence among older US Chinese women is 7.5% (half of the prevalence of US Caucasian), based on the area under the curve of the Gaussian distribution, this corresponds to BMD ≤0.640 g/cm^2. To satisfy this, from the formula in step 3, we can get the cutpoint T-score ≤–3.221.

Calculation of T-score and BMD cutoff values for defining osteopenia follow the same steps as those for defining osteoporosis (values shown in *Table 1* of the main text).

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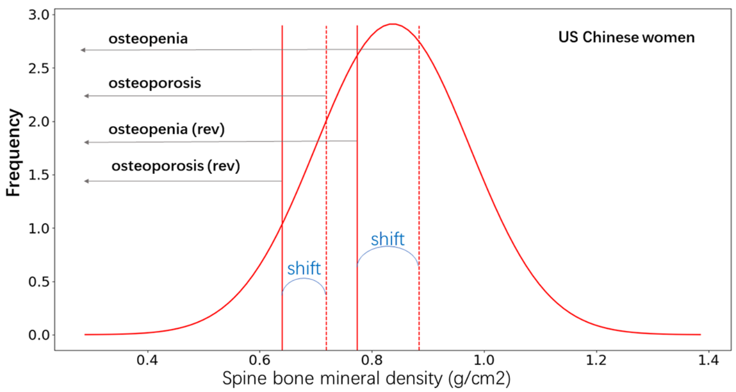

Figure S4 Frequency Gaussian distribution of bone mineral density of older US Chinese women, with mean bone mineral density of 0.837 g/cm^2 and standard deviation of 0.137. The original cutpoints for osteoporosis and osteopenia are T score ≤–2.5 and ≤–1, and these correspond to a prevalence of 19.48% for osteoporosis and a prevalence of 63.48% for osteopenia. If prevalence for osteoporosis and osteopenia is assumed to be 7.5% and 25% respectively, then cutpoints BMD for osteoporosis (revised) and osteopenia (revised) are ≤0.640 g/cm^2 and ≤0.774 g/cm^2 respectively, correspond to T-score of ≤–3.221 and ≤–2.269 respectively. (rev): revised.

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Appendix 4 Hip fracture prevalence of US Chinese is close to that of US Blacks

Hip fracture typically requires hospitalization, making hip fracture incidence ascertainment more reliable than for other types of fractures. Evidence suggests that the hip fracture prevalence of US Asians is close to that of US Blacks (71-74).

With a database of all hospitalizations for the State of California, Silverman and Madison (71) examined the incidence of hip fracture for the years 1983 and 1984. They reported that the rate ratio of hip fracture relative to Caucasians was 0.41 and 0.61 for Black women and Asian women, respectively; and 0.79 and 0.54 for Black men and Asian men, respectively.

Zingmond *et al.* (72) evaluated the change in hip fracture incidence from 1983 through 2000 in California for patients of 55 years of age and older. The data showed hip fracture prevalence of California Asians was close to that of California Blacks (*Figure S5*).

Fang *et al.* (73) analysed the hip fracture hospitalization rates for Asian and Caucasian patients aged 50 and older in New York City from 1988 to 2002. They reported the annual age-adjusted hip fracture hospitalization rates per 100,000 were 459, 137, and 174 for Caucasian women, Black women, and Asian women respectively (ratio relative to Caucasians was 0.30 for Black and 0.38 for Asians); and the corresponding rates for men were 230, 109, and 104 respectively (ratio relative to Caucasians was 0.48 for Black and 0.45 for Asians).

Wright *et al.* (74) investigated hip fracture incidence trends in ethnic subgroups of older Medicare beneficiaries (≥65 years old) and analysed annual hip fracture incidence rates from 2000 through 2009. The data showed hip fracture prevalence of US Asians was close to that of US Blacks (*Figure S6*).

By analysing the data from the National Osteoporosis Risk Assessment (NORA) which was an observational study of postmenopausal women in the USA, in 2005 Barrett-Connor *et al.* (32) reported the baseline characteristics and 1-year fracture incidents in Caucasians, Blacks, and Asians. At baseline, 23.3%, 7.2% and 11.6% of Caucasians, Blacks, and Asians had a maternal history of fracture, and a history of any fracture at age 45 years or older was recorded in 1.4%, 1.2% and 0.8% of the Caucasians, Blacks, and Asian. During the follow-up, a fracture at any location was recorded in 1.5%, 0.8% and 0.7% of Caucasians, Blacks, and Asians.

Note the data of Silverman and Madison (71), Zingmond *et al.* (72), Fang *et al.* (73), Wright *et al.* (74) all showed that, while hip fracture rate was slightly lower among American Black women as compared with Asian American women, hip fracture rate was even lower among Asian American men than among American Black men. Moreover, within the Asian ethnic group, it is likely that older Chinese have a lower FF prevalence than that of older South Asians (5).

Footnote

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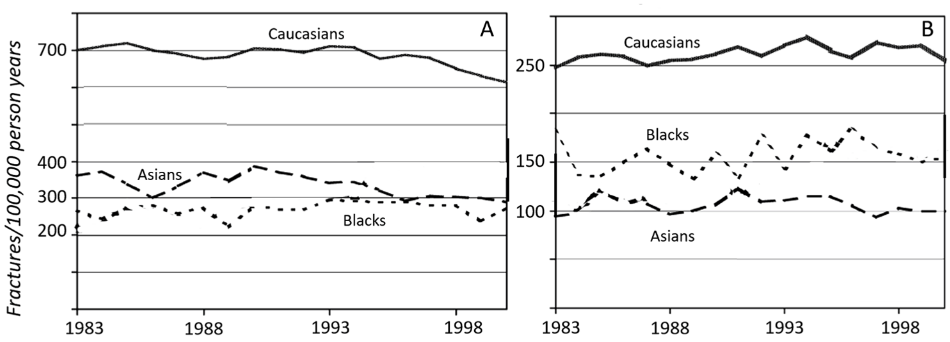

Figure S5 Hip fracture incidence by ethnicity among women (A) and men (B) 55 years of age and older in California, 1983 to 2000. Modified from Zingmond *et al. Osteoporos Int* 2004;15:603-10.

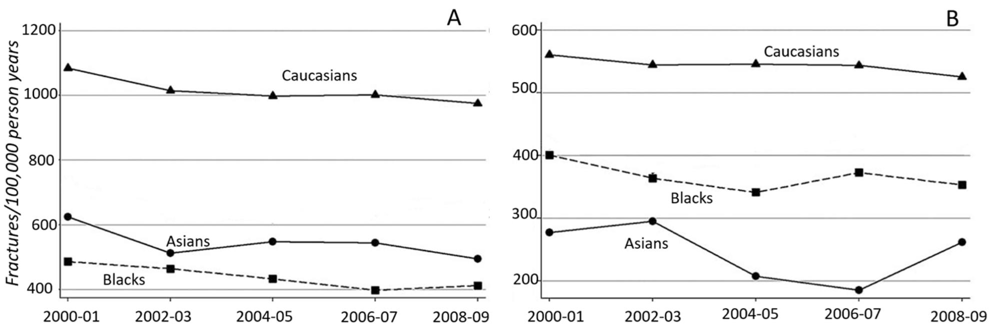

Figure S6 Age-standardized hip fracture incidence in women (A) and in men (B) from 2000 to 2009 by ethnicity for US Medicare beneficiaries (≥65 years old). Modified from Wright *et al. J Bone Miner Res* 2012;27:2325-32.

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Table S1 Study participant number of the young and older groups, and the instruments for bone mineral density measurement: women's spine

Studies	No. in young group	Age: old group	No. in old group	Instrument manufacturer
US White (2012) (52)[#]	236	≥50	840	Hologic QDR 4500A
		≥60	559	Hologic QDR 4500A
US Black (2012) (52)	127	≥50	344	Hologic QDR 4500A
		≥60	213	Hologic QDR 4500A
Italian (2003) (53)	203	50-79	1031	Most on Hologic QDR 4500; 27 subjects were on QDR 1000 and 15 on QDR 2000
		60-79	533	Most on Hologic QDR 4500; 27 subjects were on QDR 1000 and 15 on QDR 2000
Finnish (1992) (54)	143	50-70	219	GE Lunar DPX
		60-70	54	GE Lunar DPX
Austrian (2003) (55)	243	46-76	200	GE Lunar DPX or Hologic QDR 1000 and 4500
		56-76	55	GE Lunar DPX or Hologic QDR 1000 and 4500
Canadian (2000) (56)	95	≥50		Hologic QDR 1000 or 2000 or GE Lunar DPX
Spanish (1997) (57)	235	50-79	607	Hologic QDR 1000
British (1996) (58)	91	50-89	387	GE Lunar DPX
Swedish (2000) (59)	198	≥70	210	Hologic 4500
Chinese meta (2013) (60)	5213	≥50	43277	Meta analysis (Hologic, GE Lunar, Norland)
US Chinese (2006) (61)	79	50-89	120	Hologic QDR 4500C
Hong Kong (2005) (51)	188^	≥60	1431	Hologic QDR 2000 or QDR 4500
Singapore (2020) (62)	31	≥51	131	Hologic Discovery Wi
Japan (2001) (63)	548	50-79	1383	Hologic QDR 4500A
ML Chinese (2007) (64)	342	50-89	5083	GE Lunar
Korea (2008) (65)	75	50-79	1086	GE Lunar DPX Bravo
Korea (2014) (66)	1786	≥50	5787	Hologic Discovery-W
Taiwan (2011) (67)	28	>50	108	GE Lunar Prodigy

[#]: cited reference and the year of publication (see main document reference list). ^: number estimated from a graph. Chinese meta: meta-analysis results. ML, mainland.

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Table S2 Study participant number of the young and older groups, and the instruments for bone mineral density measurement: men's spine

Studies	No. in young group	Age: old group	No. in old group	Instrument manufacturer
US White (2012) (52)[#]	281	≥50	867	Hologic QDR 4500A
		≥60	562	Hologic QDR 4500A
US Black (2012) (52)	157	≥50	322	Hologic QDR 4500A
Chinese meta (2013) (60)	3970	≥50	27026	Meta analysis (Hologic, GE Lunar, Norland)
ML Chinese (2008) (68)	209	≥50	766	Hologic Delphi A
ML Chinese (2006) (69)	102	≥50	1084	Hologic QDR 2000
Hong Kong (2005) (51)	93^	≥60	1336	Hologic QDR 2000 or QDR 4500
Singapore (2020) (62)	24	≥50	127	Hologic Discovery Wi
Taiwan (2004) (70)	72	50-89	292	Hologic QDR 2000
Taiwan (2011) (67)	31	≥50	128	GE Lunar DXA Prodigy
Korea (2008) (65)	58	50-79	1424	GE Lunar DPX Bravo
Korea (2014) (66)	1551	≥50	5355	Hologic Discovery-W

[#]: cited reference and the year of publication (see main document reference list). ^: number estimated from a graph. ML, mainland.

Table S3 Study participant number of the young and older groups, and the instruments for bone mineral density measurement: women's femoral neck

Studies	No. in young group	Age: old group	No. in old group	Instrument manufacturer
US White (2012) (52)[#]	262	≥50	1042	Hologic QDR 4500A
		≥60	751	Hologic QDR 4500A
US Black (2012) (52)	136	≥50	372	Hologic QDR 4500A
Italian (2018) (75)		≥50	3247	Hologic QDR 4500C or GE Lunar Prodigy
Spain (2010) (76)		≥50	806	Norland or Hologic
Australia (2011) (77)		≥50 (median: 54.0)	1494	GE Lunar
Chinese meta (2013) (60)	4412	≥50	43869	Meta analysis (Hologic, GE Lunar, Norland)
US Chinese (2006) (61)	79	50-89	120	Hologic QDR 4500C
Hong Kong (2005) (51)	188^	≥60	1431	Hologic QDR 2000 or QDR 4500
Japan (2001) (63)	547	50-79	1506	Hologic QDR 4500A
Korea (2008) (65)	75	50-79	1086	GE Lunar DPX Bravo
Taiwan (2011) (67)	28	>50	108	GE Lunar Prodigy

[#]: cited reference and the year of publication (see main document reference list). ^: number estimated from a graph. Chinese meta: meta-analysis results.

Table S4 Study participant number of the young and older groups, and the instruments for bone mineral density measurement: men's femoral neck

Studies	No. in young group	Age: old group (years)	No. in old group	Instrument manufacturer
US Black (2012) (52)[#]	285	≥50	1194	Hologic QDR 4500A
		≥60	853	Hologic QDR 4500A
Spanish (1997) (57)	231	50-79	468	Hologic QDR 1000
Australia (2011) (77)		≥50 (median: 56.0)	1467	GE Lunar
ML Chinese (2006) (69)	102	50-89	1084	Hologic QDR 2000
ML Chinese (2008) (68)	209	≥50	766	Hologic Delphi A
Chinese meta (2013) (60)	3511	≥50	23479	Meta analysis (Hologic, GE Lunar, Norland)
Hong Kong (2005) (51)	93^	≥60	1336	Hologic QDR 2000 or QDR 4500
Korea (2008) (65)	58	50-79	1424	GE Lunar DPX Bravo
Korea (2014) (66)	1786	≥50	5787	Hologic Discovery-W
Taiwan (2011) (67)	31	>50	128	GE Lunar Prodigy

[#]: cited reference and the year of publication (see main document reference list). ^: number estimated from a graph. Chinese meta: meta-analysis results. ML, mainland.

Table S5 Study participant number of the young and older groups, and the instruments for bone mineral density measurement: women's total hip

Studies	No. in young group	Age: old group	No. in old group	Instrument manufacturer
US White (2012) (52)[#]	262	≥50	1042	Hologic QDR 4500A
		≥60	751	Hologic QDR 4500A
US Black (2012) (52)	136	≥50	372	Hologic QDR 4500A
Canada white (2008) (79)		≥50	16205	GE Lunar Prodigy or Lunar DPX
Argentina (2016) (80)		≥50	5448	GE Lunar Prodigy
US Amerindian (2016) (81)		50-79	230	Hologic Discovery-W
ML Chinese (2007) (64)	342	50-89	5083	GE Lunar
US Chinese (2006) (61)	79	50-89	120	Hologic QDR 4500C
Hong Kong (2005) (51)	188^	≥60	1431	Hologic QDR 2000 or QDR 4500
Japan (2001) (63)	547	50-79	1506	Hologic QDR4500A
Korea (2014) (66)	1786	≥50	5787	Hologic Discovery-W

[#]: cited reference and the year of publication (see main document reference list). ^: number estimated from a graph. ML, mainland.

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Table S6 Study participant number of the young and older groups, and the instruments for bone mineral density measurement: men's total hip

Studies	No. in young group	Age: old group	No. in old group	Instrument manufacturer
US White (2012) (52)[#]	285	≥50	1194	Hologic QDR 4500A
		≥60	853	Hologic QDR 4500A
US Black (2012) (52)	160	≥50	408	Hologic QDR 4500A
Hong Kong (2005) (51)	93^	≥60	1336	Hologic QDR 2000 or QDR 4500
Korea (2014) (66)	1551	≥50	5355	Hologic Discovery-W
ML Chinese (2006) (69)	102	≥50	1084	Hologic QDR 2000
ML Chinese (2008) (68)	209	≥50	766	Hologic Delphi A

[#]: cited reference and the year of publication (see main document reference list). ^: number estimated from a graph. ML, mainland.

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