Review Article

‘Healthier Chinese spine’: an update of osteoporotic fractures in men (MrOS) and in women (MsOS) Hong Kong spine radiograph studies

Yì Xiáng J. Wáng[1]^, Min Deng[1], James F. Griffith[1], Anthony W. L. Kwok[2,3], Jason C. S. Leung[2], Patti M. S. Lam[2], Blanche Wai Man Yu[2], Ping Chung Leung[2], Timothy C. Y. Kwok[2,4]

[1]Department of Imaging and Interventional Radiology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China; [2]JC Centre for Osteoporosis Care and Control, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China; [3]School of Medical and Health Sciences, Tung Wah College, Hong Kong SAR, China; [4]Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China

Contributions: (I) Conception and design: YXJ Wáng; (II) Administrative support: AWL Kwok, JCS Leung, BWM Yu; (III) Provision of study materials or patients: JF Griffith, PMS Lam, PC Leung, TCY Kwok; (IV) Collection and assembly of data: YXJ Wáng, M Deng, JF Griffith, AWL Kwok, JCS Leung, PMS Lam, BWM Yu; (V) Data analysis and interpretation: YXJ Wáng, M Deng, JF Griffith, JCS Leung, PMS Lam, BWM Yu, PC Leung, TCY Kwok; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Dr. Yì Xiáng J. Wáng. Department of Imaging and Interventional Radiology, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China. Email: yixiang_wang@cuhk.edu.hk.

Abstract: For the MrOS (Hong Kong) and MsOS (Hong Kong) baseline (BL) studies, community-dwelling 2,000 Chinese men (mean age: 72.3 years) and 2,000 Chinese women (mean age: 72.5 years) were recruited from 2001 to 2003. These two studies have spanned two decades till now. This review summarizes our spine radiograph results. Senile and post-menopausal osteoporosis were associated with intervertebral disc volume reduction; and in women, menopause accelerates disc degeneration. Elderly women’s osteoporotic vertebral fracture (OVF) prevalence was double of that of elderly men. For year-4 follow-up (FU), male participants with BL OVF had little increased risk for further OVF. In our study comparing OVF rates in age-matched Hong Kong Chinese women and Italian Caucasian women (mean age: 74.1 years), endplate and/or cortex fracture (ECF) prevalence was 26% for Chinese and 47% for Italian. OVF with ≥40% vertebral height loss was recorded among 9.5% of the Chinese subjects while among 26% of the Italian subjects. OVFs in Italian subjects were more likely to be multiple and generally severer. Clinical spine fractures were recorded 133 cases/100,000 person-years in MrOS (Hong Kong) participants and 273 cases/100,000 person-years in MsOS (Hong Kong) participants. Literature review suggests the clinical vertebral fracture rates among elderly Hong Kong Chinese subjects are approximately half of those of American, Australian, and Canadian subjects. Data synthesis suggests elderly Caucasians have a higher degenerative spondylolisthesis prevalence, being approximately 70% higher than that of elderly Hong Kong Chinese. Literature review of other authors’ publications shows, compared with Caucasians, Chinese have a much lower incident rate of back pain. We conclude that elderly Chinese have a generally healthier spine relative to elderly Caucasians.

Keywords: Spine; osteoporotic vertebral fracture (OVF); menopause; disc degeneration; degenerative spondylolisthesis (DS); Chinese; Caucasians

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^ ORCID: 0000-0001-5697-0717.

Introduction

Osteoporotic fractures in men (MrOS) and women (MsOS) Hong Kong represent the first large-scale prospective cohort studies conducted on bone health in East Asians. At baseline (BL), 2,000 Chinese men and 2,000 Chinese women ≥65 years were recruited from the local communities from August 2001 to March 2003, to determine the relationship between anthropometric, lifestyle, medical and other factors with bone mineral density (BMD) at the hip and spine. The included subjects had a BL mean age of 72.3 years (range, 65–92 years) for men and 72.5 years (range, 65–98 years) for women. The recruitment criteria were structured so that the study results would represent similarly aged community-dwelling ethnic Chinese men and women in Hong Kong. All subjects were able to walk without assistance, without bilateral hip replacement, and have the potential to survive the duration of primary study for at least 4 years as judged by their pre-existing medical status. Men and women of similar age and from the same community-based population were investigated using the same methodology, thereby enabling a comparison of the results for men and for women. For the radiology follow-up (FU), 1,519 men and 1,546 women had X-ray for the spine at year-4, which present all the participants who attended the FU in person. During 2014–2017, a year-14 FU was carried out. Whole spine magnetic resonance imaging (MRI) was performed for 271 males (mean age: 82.8 years) and 150 females (mean age: 82.0 years), which represented 53.1% of the total male subjects and 27.2% of the total female subjects attended year-14 FU. The selection for MRI was random with potential bias in favor of mobile subjects. The study was designed so that males would be examined first. However, due to logistical reasons, MRI time became no longer available thus at the closure of this year-14 FU more men were scanned than women. Whole spine MRI mitigates the magnification factor associated with X-ray technique and with assessment not affected by scoliosis which is common among elderly subjects. MRI also allows better assessment of spinal cord, disc, and endplate sclerosis. For osteoporotic vertebral deformity (OVD) assessment, MRI performs as well as X-ray. This review summarizes our published spine radiograph results of these two studies, covering the aspects of disc degeneration, osteoporotic vertebral fracture (OVF), and degenerative spondylolisthesis (DS). To support our conclusion that elderly Chinese in general have healthier spines relative to elderly Caucasians, a literature review on the comparative studies of back pain between Chinese and Caucasians is also included.

Osteoporosis is positively associated with intervertebral disc degeneration

Whether osteoporosis promotes intervertebral disc degeneration or protects disc against degeneration had been debated in the literature. Some authors suggest that osteoporosis would possibly delay disc degeneration because of a decreased endplate resistance and decreased intradiscal strain. On the other hand, osteoporosis may be an etiological factor for disc degeneration with osteoporosis associated vertebral height loss, instability, and endplate fracture and sclerosis. Based on MrOS (Hong Kong) and MsOS (Hong Kong) studies, we concluded that, for age-matched subjects, senile and post-menopausal osteoporosis are associated with disc degeneration (1). Our cross-sectional analysis demonstrated that lower dual-energy X-ray absorptiometry (DEXA) measured lumbar BMD was associated with a decrease in lumbar disc anterior height and posterior height, as well as a decrease in anterior-posterior diameter; while the middle height of the discs was increased. The net result is that lower BMD was associated with a decrease of disc volume (2). Our 4-year FU study shows osteopenia and osteoporosis were associated with faster lateral disc area decrease in both thoracic spine and lumbar spine, and for both men and women (3). A trend was noted that caudal discs had a higher lateral area decrease rate than cephalad discs (3). One point worth noting is that while elderly women overall had faster radiographic lateral disc area loss during the 4-year FU than elderly men, for the subgroups of osteoporotic subjects, elderly men and elderly women had similar rates of disc area loss during the 4-year FU. This observation also suggests that factors associated with osteoporosis are important drivers for disc area loss and disc degeneration.

We reported that menopause accelerates interverbal disc degeneration in women (4,5). Due to increased mechanical stress and physical injury, young men are known to be more susceptible to disc degeneration than young women. However, disc degeneration is common and more severe in elderly women than in elderly men (4,6,7). Baron *et al*. (8) found that women on hormone replacement treatment maintain intervertebral disc height compared with untreated postmenopausal women. While Baron *et al*. (8) demonstrated the benefits of female hormone on disc health, we were the first to demonstrate that postmenopausal women have accelerated disc

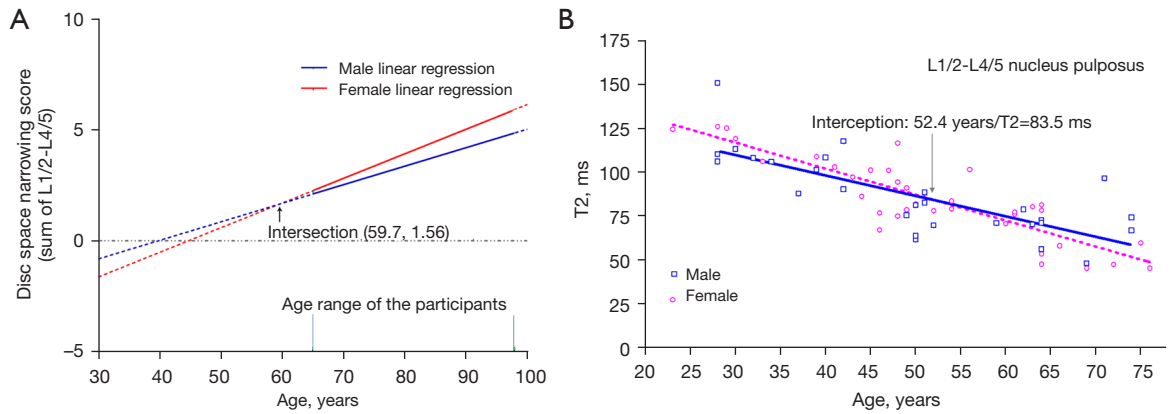

Figure 1 Postmenopausal women show accelerated lumbar disc degeneration compared with men. (A) Sums of the disc space narrowing scores of discs L1/2-L4/5 plotted against age. From the age of 65 years to 92 years, women have a faster disc space narrowing rate than that of men. The slope of the plot for females is 0.11 (95% CI: 0.09, 0.13), steeper than that for males (0.08; 95% CI: 0.06, 0.10). Extrapolation towards younger age shows an intersection of men's and women's slopes at 56.7 years with a disc space narrowing score of 1.65. (B) Aging-related reduction of magnetic resonance T2 relaxation time of the nucleus pulposus of L1/2-L4/5 discs for males and females. The slope of the plot for females is –1.48 (95% CI: –1.77, –1.19), steeper than that for males (–1.17; 95% CI: –1.57, –0.76). Intersection: 52.4 years/T2 relaxation =83.5 milliseconds [reproduced with permission from reference (5)]. CI, confidence interval.

degeneration due to estrogen deficiency (*Figure 1*) (4,5). A systematic review demonstrates, compared with middle-aged individuals, a further greater low back pain (LBP) prevalence increase in women than in men was noted after 50 years old (i.e., menopause age) (9). In our BL studies, the LBP prevalence was 30.6% for elderly men and 53.3% for elderly women (10). In addition to that postmenopausal women have a higher OVF prevalence, the accelerated spine degeneration caused by deficiency of sex hormones, including narrower intervertebral disc space, higher lumbar spondylolisthesis prevalence, and increased prevalence of facet joint osteoarthritis, may be an additional source of LBP in elderly women (11-13).

We documented the prevalence and severity of radiographic disc space narrowing (DSN) in elderly men and women in Hong Kong. Lumber disc space height changes were classified into 4 categories: 0 = normal; and grade-1–3 had <30%, 30–60%, and >60% reduction in disc height respectively (7). Similar to other reports (6), our data showed a high prevalence of DSN in elderly subjects with its severity being higher in women than in men (7). Male-female difference in DSN severity increased as age increased. For both males and females, the sum of the DSN scores for L1/2-L4/5 ≥3 was associated with LBP, restricted leg mobility, and difficulty in long-duration standing (7).

Our year-14 FU cervical spine MRI study collaborated our observations with the lumbar spine (14). While most of the study participants exhibited at least one degenerative change at one or more vertebral levels, the degenerative changes were generally more common in women than in men, including spinal cord high signal (10.7% *vs.* 7.4%), vertebral compressive deformity (12.0% *vs.* 8.1%) and severe DSN (5.3% *vs.* 3.3%). 11.4% of the men and 20.6% of the women reported neck pain during the past 12 months. A weak trend was noted that osteoporosis was associated with a higher prevalence of spinal cord high signal and a higher prevalence of spinal canal stenosis (14).

DSN has been traditionally semi-quantitatively graded. However, such grading is subjective and difficult to use for epidemiological studies. We developed a Disc Area Index for Lumbar spine (DAIL) index, which quantitatively classifies lumbar disc space into normal disc height or DSN (3). DAIL for each intervertebral level is calculated using Eq. [1].

$$\mathrm{DAIL}_{i,j+1} = Area_{i,j+1}\Big/\overline{\sigma};\ \overline{\sigma}=\frac{AP_i^2+AP_{i+1}^2}{2};\ \{i=1,2,3,4\} \quad [1]$$

Where *Area* is the intervertebral disc area, i =1, 2, 3, 4 is the vertebral level, *AP* is the mid-height anteroposterior diameter of a vertebral body (AP_i: the vertebral body above the disc, AP_{i+1}: the vertebral body below the disc), $\overline{\sigma}$ is the mean of the sum of the square of the adjacent upper and

lower vertebrae anteroposterior diameter (AP_i and AP_{i+1}). Therefore, DAIL refers to the area of a disc divided by an area formed by mid-height anteroposterior diameters of the two adjacent vertebral bodies (thus it is unitless). As the mid-height anteroposterior diameters of the two adjacent vertebral bodies are usually unaffected by spine degeneration, therefore the narrower the disc space, the smaller the DAIL value. DAIL correlates well with semi-quantitative (SQ) grading by radiologist, with sensitivity and specificity varying from 87.3% to 96.8% for grade-1 DSN, and 92.9% to 100% for grade-3 DSN (3). The DAIL criteria were tested to evaluate DSN progression at year-4 FU, and showed good agreement with radiologist readings (3).

Definition of radiographic OVF for epidemiological study

OVFs diagnosed based on radiograph are mostly better called OVD unless a fracture line is noted. However, the term 'OVF' has been commonly used, and indeed at least at the microscopic level, fractures are very common among vertebrae with OVD (15). It is estimated that 3/4 of OVFs are clinically silent, and diagnosis of true OVF on radiograph is challenging; while the definition of radiographic OVF has important implications on the study of its epidemiology. Purely morphometric methods can lead to falsely classifying physiological and degenerative wedging as OVF (16-20). The SQ criteria proposed by Genant *et al*. have been more commonly used for identifying and grading OVF for vertebrae T4 to L4. Genant *et al*. emphasize a morphological diagnosis of vertebral deformity (VD), rather than merely assessing vertebral height loss (21). However, the confusions come from what constitutes a mild OVF and the proper grading for OVF (16,18). Genant *et al*. described mild OVFs have ≥20% height loss, and OVFs without achieving this threshold are classified as SQ grade-0.5 (21). This causes some confusion such as whether an OVF with 15% height loss would qualify as an OVF. While SQ grade-0.5 OVD is common, it is rarely reported; and to our knowledge, OVDs without achieving 20% height loss threshold have been commonly classified as SQ grade-1 OVF by colleagues trained in University of California at San Francisco, USA (training materials and personal communication). There have also been discussions about the morphology of OVFs. Lentle *et al*. suggested all OVFs are bi-concave shaped (22). However, while typical OVFs are bi-concaved (22,23), atypical OVF can have various shapes (24). At least a portion of OVFs may be similar in appearance to traumatic fracture when a distinct low-energy trauma event had been involved (24). The definition of OVF has also been complicated by the controversy of algorithm-based qualitative (ABQ) criteria. Jiang *et al*. (25) proposed that all OVFs should demonstrate endplate fracture. However, while by microscopy osteoporotic endplate/cortex fractures (ECF) is very common among vertebrae with OVD (15), radiograph is not a sensitive method to detect ECF, due to its resolution and due to projectional overlay (26,27). Moreover, ECF negative OVF can turn into ECF positive over time. For example, in our MsOS (Hong Kong) study, of the ECF negative OVFs with 25–33% height loss at BL, 74% of them turned to ECF positive during 4 years' FU, and a higher OVD severity (i.e., higher extent of height loss) was associated with an increased probability of turning into ECF positive during FU (28). We consider positive ECF is an additional sign of OVF. A positive ECF sign would suggest a more severe type of OVF (28), but ECF is not an essential sign of OVF. It has been suggested that, compared with those OVFs without ECF, OVFs with ECF better predict further osteoporotic fracture risk (28,29). In addition to that some of VDs without ECF could be false positive reading (22), within the same grade as defined by vertebral height loss, those with ECF would have a higher extent of vertebral height loss. For example, for the range of 25–40% vertebral height loss (i.e., Genant moderate grade), some of the OVFs with ECF will be in the range of 33–40% vertebral height loss, while all of the OVFs without ECF will be in range of 25–33% vertebral height loss (30). The extent of vertebral height loss is positively associated with the probability of having ECF (30), while the extent of vertebral height loss is well known positively associated with further osteoporotic fracture risk.

To better record OVF and allow inter-study comparison, we proposed an extended version of semi-quantitative (eSQ) criteria: (I) minimal grade refers to radiological OVF with <20% height loss, theoretically equivalent to Genant SQ grade-0.5; (II) mild grade is the same as Genant SQ mild grade (≥20–25% height loss); (III) SQ moderate grade is divided into two subgrades: ≥25% to 1/3 height loss and ≥1/3 to 40% height loss; (IV) SQ severe grade is divided into two subgrades: ≥40% to 2/3 height loss and ≥2/3 height loss (collapsed grade) (31). We have prepared pictorial materials for this grading scheme to facilitate self-learning (31,32). To avoid inconsistency of vertebral height loss estimation by different readers (16), eSQ evaluates vertebral height loss by measurement, with the heights of neighboring normal-appearing vertebrae as references (31).

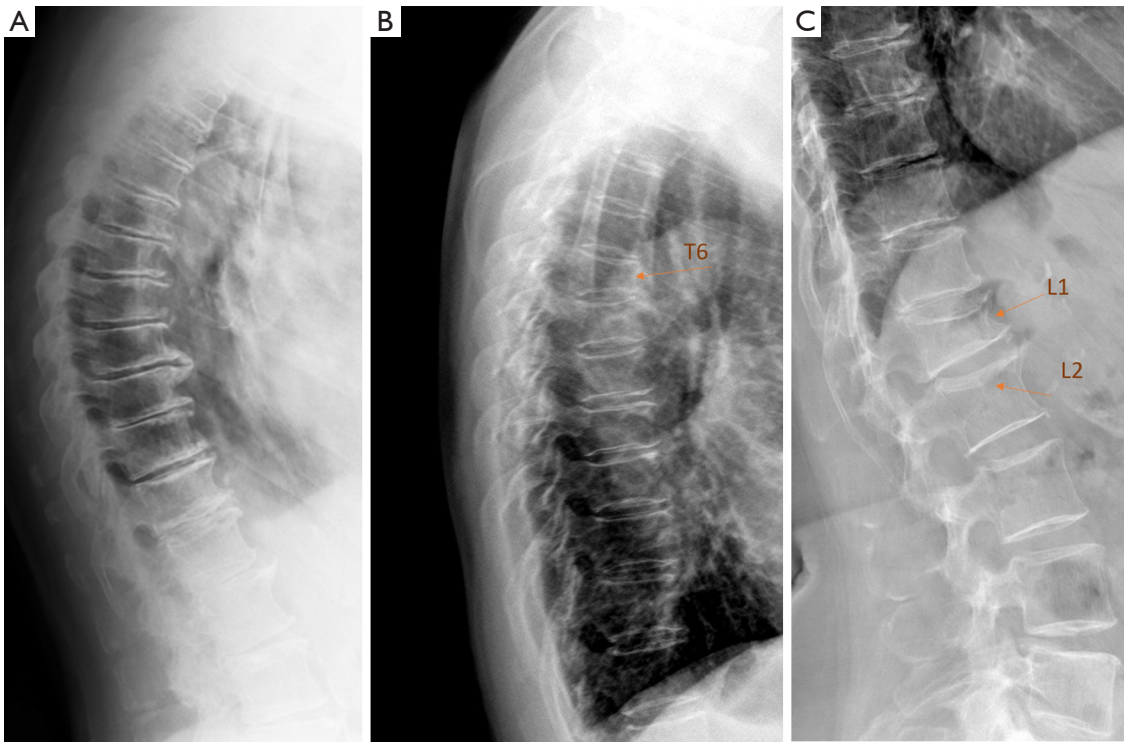

Figure 2 Degenerative changes and OVF. (A) Spine radiograph of an elderly women. Mid-thoracic region shows anterior wedging of multiple vertebrae with similar appearance, disc space narrowing and osteophytes are noted while without endplate depression. (B) Spine portion of a lateral chest radiograph of an elderly women, T6 vertebra shows distinct deformity consistent with OVF. (C) Spine radiograph of an elderly women. T6 vertebra shows distinct deformity consistent with OVF, while L2 shows upper endplate depression (i.e., endplate fracture). OVF, osteoporotic vertebral fracture.

SQ moderate grade was subdivided into two grades because OVFs with ≥1/3 height loss always demonstrate ECF radiographically (28,30,33). A subdivision of SQ grade-3 facilitates the recording of progression of a severe OVF (such as a 45% height loss OVF progresses to 75% height loss). Though the initial description of Genant *et al*. did not include L5 assessment, actually L5 can be included in the analysis (20,34). If OVF grading based on measurement is taken as the reference, visual estimation has the tendency of slightly over-estimating the grades (21). A substantial portion of minimal eSQ OVFs based on measurement would be classified as SQ mild grade by visual estimation.

The most common differential diagnosis for OVF is degenerative changes [in the article by Lentle *et al*. (22), a term of 'morphometric VD' was used to describe these degenerative changes]. Degenerative deformities often involve multiple adjacent vertebrae appearing similarly deformed, while fractural deformities tend more often to be singular appearing as a distinct loss of expected shape (*Figure 2*) (24). Degenerative deformities are not associated with increased further osteoporotic fracture risk (22,35). Old high-energy trauma induced deformity would not be rare, but would be much less common than degenerative deformities. At individual subject's level, absolute differentiation of OVF and old high-energy trauma deformity is not always possible (36,37); however, these ambiguities mostly do not have a major impact on statistical results of epidemiological studies at least for elderly women. The most important differential diagnosis for OVF would be oncological deformities (metastatic bone diseases or multiple myeloma). Fractures that are located in the very upper thoracic spine may have a malignant etiology, while OVFs most typically involve thoracolumbar junction and mid-thoracic region, and typical cases are bi-concave shaped for the upper and lower endplates. A concave posterior border of the vertebra is more likely a sign of a benign osteoporotic fracture, while a convex posterior border suggests malignant disease. However, the differentiation can

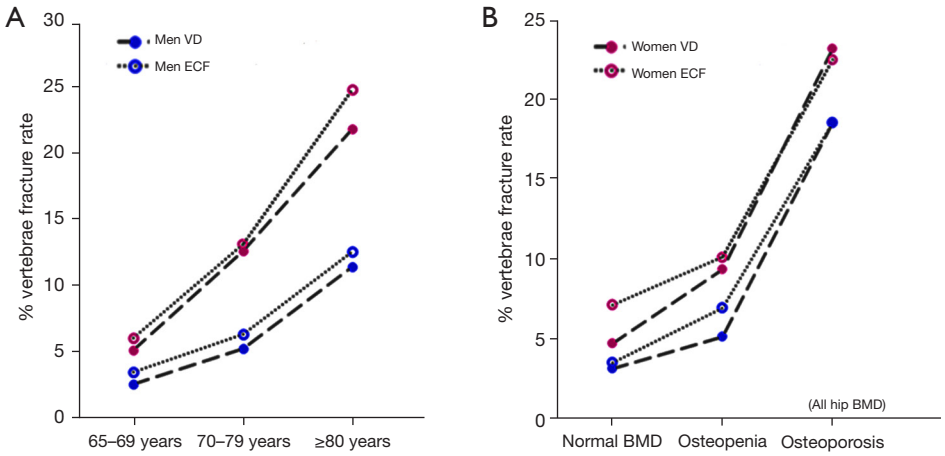

Figure 3 Prevalence of OVF among three age groups of Hong Kong Chinese men and women (65–69, 70–79, and ≥80 years) (A), and among normal BMD, osteopenia and osteoporosis subjects (B). Baseline data with n=1,954 for total men and n=1,953 for total women. Genant's OVF included grade-2 and 3 only as grade-1 may not be true fracture; ECF included fracture grade-1, 2 and 3. Blue circles for men and red circles for female [reproduced with permission from reference (38)]. VD, vertebral deformity; ECF, endplate and/or cortex fracture; OVF, osteoporotic vertebral fracture; BMD, bone mineral density.

be sometimes difficult with sole radiograph, and in some cases further imaging such as MRI is required (26).

OVF criteria for women may not be directly applicable for men (18). Our year-14 FU study suggests that minimal VDs in men likely have no long-term consequence, minimal OVDs in women are more likely to be osteoporotic and may be potentially associated with increased further fracture risk (34). For men, before better evidence is available, Genant SQ grade-1 with ECF, as well as GSQ grade-2/3 OVDs may be accepted as OVF. Even so, some ECF negative grade-2 deformities in men may not be true OVF (18). Another possibility will be that only ECF positive OVD or OVD with ≥1/3 height loss are considered OVF in men (18,38). The clinical relevance of OVF in elderly men may be also less than that of elderly women. For example, Waterloo *et al.* (39) reported that the presence of OVF in women was associated with an increased risk of back pain and lower quality of life score, but these associations were not present in men. However, groupwise, our BL study showed OVF was associated with back pain for both men and women (10).

We reported that moderate to severe OVFs at mid-thoracic and lower thoracic spine as well as lumbar spine are mostly identifiable on frontal view chest or abdominal radiographs, with a small proportion of ambiguous cases further clarified for OVF by additional lateral view imaging (40,41). The site of highest OVF prevalence, i.e., the thoracolumbar spine junction, is usually 'off-center' to the X-ray beam focus of T6 as the custom for taking chest frontal radiograph (CFR). We demonstrated that, if a CFR is taken with approximately two vertebrae lower (i.e., the focus of X-ray beam is adjusted to towards T8), the visualization of thoraco-lumbar spine junction can be much improved, allowing better identification of OVF on CFR (42).

Prevalence of OVF in elderly Chinese men and women

OVF prevalence data highly depend on the criteria to define OVF and the age distribution of the study subjects. Our BL results of OVF in Chinese men and women are shown in *Figure 3* (38). Note that, while grade-1 VD is less likely to be osteoporotic in men, grade-1 radiologically diagnosed VD is more likely to be osteoporotic in women (34). Thus, *Figure 3* may underestimate OVF prevalence in women. Male-female prevalence ratio is the same for the three age groups, with both the prevalence of male SQ grade-2/3 OVF and ECF being approximately half of those for women. Our male-to-female OVF prevalence ratio agrees with the report by Lunt *et al.* (23), who estimated a total radiographic OVF incidence of 5.9 and 10.1 fractures per 1,000 person/years for men and women respectively. *Figure 3* also shows, for elderly men with hip BMD-based osteoporosis, the OVF risk is as high as that for

Table 1 Osteoporotic vertebral fracture progression of male and female subjects in MrOS (Hong Kong) and MsOS (Hong Kong) follow-up studies

Genant SQ grading	SQ grade-0	SQ grade-1	SQ grade-2	SQ grade-3	SQ grade-1, 2, 3
Year-4, % progression or new incident—male[#]	2.05% (25/1,219)[a,§]	2.01% (3/149)	3.13% (3/96)	2.78% (1/36)	2.49% (7/281)[a*]
Year-4, % progression or new incident—female[#]	4.56% (58/1,271)[e,f]	8.00% (6/75)[g]	10.58% (11/104)[e*,g]	28.92% (24/83)[g]	15.65% (41/262)[f*]
Year-14, % progression or new incident—male[#]	7.86% (18/229)[b]	8.00% (2/25)[¶]	17.65% (3/17)[b*]		–
Year-14, % progression or new incident—female[#]	14.29% (18/126)[c,d]	60.00% (3/5)[¶,c*]	52.63% (10/19)[d*]		–

The data in this table are from references (28,33,34). *, by counting subjects (how many participants had these incidents), and combination of OVF progression and new OVF, note OVF progression and new OVF could have occurred in the same subject. % new incident = No. of incidents divided by No. of subjects at baseline potentially would have these incidents at follow-up (for example, [§], 25/1,219 =2.05%); this is the same for % progression of existing VD. Note, a new incident VD in each group does not necessarily means a new VD of the same severity; [¶], eSQ minimal grade OVF is considered as SQ mild grade. [a] *vs.* [a*], P=0.65; [b] *vs.* [b*], P>0.05; [c] *vs.* [c*], P=0.007; [d] *vs.* [d*], P<0.001; [e] *vs.* [e*], P=0.007; [f] *vs.* [f*], P<0.001; [g], P for trend <0.001. MrOS, osteoporotic fractures in men; MsOS, osteoporotic fractures in women; SQ, semi-quantitative; OVF, osteoporotic vertebral fracture; VD, vertebral deformity; eSQ, extended version of semi-quantitative.

osteoporotic women.

Consistent with many previous reports, our data also show minimal/mild grade VDs are more common in men than in women (10,34). It is well known that, compared with women, vertebrae in elderly men are more likely to be wedge-shaped (43,44), and more likely to have traumatic VD. Compared to the cases in women, classifying minimal/mild grade VDs in men as being osteoporotic requires great caution (17-19,34). We demonstrated that endplate fracture more likely involves the upper endplate rather than lower endplate, with a trend for this effect to be greater in men than in women. Excluding those with both upper endplate and lower endplate involvements, the ratio of upper endplate fracture to lower endplate fracture was 9.63 for men and 4.3 for women, i.e., men rarely have standalone osteoporotic lower endplate fracture (45).

In our FU studies (28,33,34), to define the progression of a BL OVF, a further height decrease of at least 15% vertebral height was required. A new incident OVF was defined as a qualitative OVF occurred in a vertebra that was not deformed at BL (i.e., grade-0), and which could be either a change from grade-0 at BL to eSQ mild grade OVF or above (i.e., mostly with ≥15% height loss) at FU, or a change from grade-0 at BL to eSQ minimal grade OVF with at least 10 % height loss during FU. Both OVF progression and new incident OVF are considered 'incident OVF'. Our FU results are shown in *Table 1*. For the male year-4 FU study, participants with BL OVF had little increased risk for further OVF during the FU. For subjects with BL OVF of ≥20% height loss, at year-14 FU, women's incident OVF rate was three times higher than that of men's by counting subjects and more than four times higher by counting vertebrae (34).

Comparatively lower OVF prevalence among elderly Chinese men and women

It has been well documented that the prevalence of clinical fractures is substantially lower among elderly East Asians compared to Caucasians, both for men and women (46). For example, Ho *et al.* (47) examined the hospital discharge data for hip fracture in Hong Kong and in the USA for 1988 through 1989. The age-adjusted fracture rates per 100,000 were significantly lower in Hong Kong than in the USA for men (100 *vs.* 187) and women (247 *vs.* 535). Ho *et al.* concluded that hip fracture rates in the USA were typically 1.5 to 2.5 times those in Hong Kong across the age and sex groups. Lauderdale *et al.* (48) estimated US national nontraumatic hip fracture incidence rates for elderly Chinese Americans, Japanese Americans, and Korean Americans. Age-adjusted hip fracture incidence was lower for all three East Asian-American groups than for Caucasians, with the fracture ratio relative to Caucasians being 0.30 for Chinese women and 0.42 for Chinese men. Bow *et al.* (49) reported that at the age of 65 or above, the hip fracture rates for Hong Kong Chinese and Japanese men and women were less than half of that in Caucasians. Comparative studies also showed BMD in elderly East Asians

Table 2 A literature analysis of women's radiographic osteoporotic vertebral fracture prevalence in different ethics groups

Age (years)	Chinese (Hong Kong)[a]	Chinese (Beijing)[b]	Japanese[c]	Latin American[d]	European[e]	American (White)[f]
50–59	–	4.1%	2.7%	6.9%	5.0% (50–54 years); 7.6% (55–59 years)	–
60–69	10.8% (65–69 years)	12.6%	13.8%	10.2%	9.9% (60–64 years); 13.4% (65–69 years)	14.5% (65–69 years)
70–79	17.4%	17.5%	17.5%	18%	17.0% (70–74 years); 24.7% (75–79 years)	22.0%
≥80	29.5%	27.1%	–	27.8%	–	33.9%

This table is reproduced with permission from reference (10). [a], MsOS (Hong Kong) study (Kwok *et al. Osteoporos Int* 2013;24:877-85; Genant' SQ criteria); [b], The Beijing Osteoporosis Project (Ling *et al. J Bone Miner Res* 2000;15:2019-25; Clark *et al. Osteoporos Int* 2009;20:275-82); [c], The Japanese Population-based Osteoporosis study (Kadowaki *et al. Osteoporos Int* 2010;21:1513-22); [d], The Latin American Vertebral Osteoporosis Study (LAVOS, Clark *et al. Osteoporos Int* 2009;20:275-82); [e], The European Vertebral Osteoporosis Study (EVOS, Johnell *et al. Am J Epidemiol* 1997;146:287-93); [f], The Study of Osteoporotic Fractures (Clark *et al. Osteoporos Int* 2009;20:275-82; Black *et al. J Bone Miner Res* 1999;14:90-101); [b-f], quantitative methods of McCloskey-Kanis criteria or McCloskey-Kanis criteria with mean-3SD criteria (population-based reference). MrOS, osteoporotic fractures in men; MsOS, osteoporotic fractures in women; SQ, semi-quantitative.

decreases slower with aging than elderly Caucasians (50,51).

Many earlier studies reported that, compared with those of Caucasians, East Asians' prevalence of radiographic OVF were similar or even higher (49,52). However, these results are likely due to methodological imperfections. Recent evidence suggests that, compared with Caucasians, the relative prevalence of OVF follows the same pattern as other clinical fractures (46).

We once analysed our BL OVF prevalence in Chinese women and compared this result with literature reports, and suggested OVF prevalence in Chinese women would be approximately 30% less than that in age-matched Caucasian women (*Table 2*) (10). On the other hand, OVF prevalence in Hong Kong Chinese women was very similar to those of Northern Chinese in Beijing, Japanese, Korean, and also Latin Americans. However, these OVF prevalence results were derived with various criteria for defining radiographic OVF. It is interesting to note that it has been demonstrated in many USA studies that Asian Americans also have a hip fragility prevalence similar to that of Hispanics (53,54).

For our year-4 FU study, with 1,500 elderly men followed-up for 4 years, participants with BL OVF had little increased risk for further OVF during FU (33,55). This result differs from Caucasian studies on men where participants with BL OVF had an increased risk for further OVF (22,56). We thus hypothesize that elderly Chinese's radiographic OVF prevalence could be only half, or less than half, of that of their age-matched Caucasians. For female subjects, this point was confirmed in a recent study comparing OVF prevalence in age-matched elderly Chinese women and Italian women (57). In this study, radiographs (T4-L5) were from two epidemiological studies conducted in Hong Kong [MrOS (Hong Kong), n=200] and in Rome (n=200, both mean age: 74.1 years and range, 65–87 years). The Italian subjects were from samples of "Roman Osteoporosis Prevention Project" performed during 2018–2019. For this study, 1,500 invitation letters were sent to the residents equally distributed in the municipalities of Rome, and 70% of the invitee accepted the invitation to participate. The inclusion criteria were Caucasian post-menopausal women over 50 years, and the exclusion criteria were: drug therapy acting on phospho-calcium metabolism, included hormone replacement therapy in the past 12 months and glucocorticoids treatment for more than 6 months, systemic diseases, neoplasms, endocrinopathies, diabetes mellitus II, kidney failure, intervention, gastrointestinal surgery. The results show Chinese subjects had ECF in 26% cases involving 3.54% of the vertebrae, while Italian subjects had ECF in 47% cases involving 8.21% of the vertebrae. OVF with ≥40% vertebral height loss was recorded among 9.5% of the Chinese subjects, while among 26% of the Italian subjects. OVF in Italian subjects tended to be more severe, more likely to be multiple. A trend suggested earlier onset of OVF among Italians (*Figure 4*). Moreover, a further analysis of additional random 103 pairs of Chinese and Italians (mean age: 72.4 years) from MsOS (Hong Kong) and Roman Osteoporosis Prevention Project showed the same trends (unpublished data).

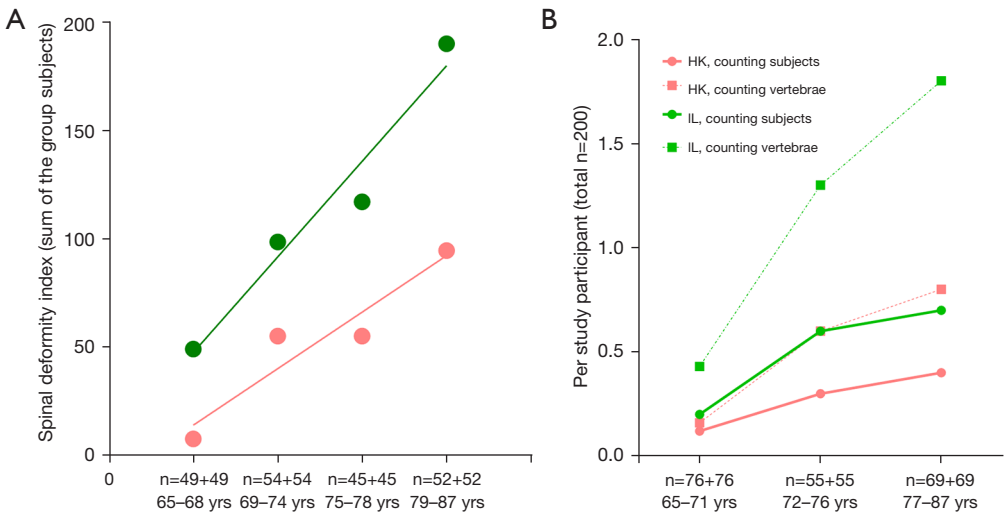

Figure 4 A comparison of Hong Kong Chinese and Rome Italian women OVF prevalence and severity (both mean age: 74.1 years, range, 65–87 years). (A) Spinal deformity index score of four different age groups of Hong Kong Chinese and Rome Italian women. Spinal deformity index was calculated with each vertebra assigned a score of 0, 0.5, 1, 1.5, 2, 2.5 and 3 for no OVF or eSQ osteoporotic vertebral fractures grade 1–6. Each subject's spinal deformity index was the sum of T4-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. (B) Prevalence of vertebral ECF among three different age groups. Light red lines indicate Hong Kong subjects and green lines indicate Italian subjects. Solid lines represent number of ECF subjects divided by number of subjects in each age group. Doted lines represent number of ECF vertebrae divided by number of subjects in each age group. N=49+49 means there are 49 Chinese subjects and 49 Italian subjects in this age group [reproduced with permission from reference (57)]. OVF, osteoporotic vertebral fracture; eSQ, extended semi-quantitative grading; ECF, endplate and/or cortex fracture; yrs, years.

From BL on, clinical spine fractures (mostly osteoporotic fragility fractures) were followed-up for 1,954 MrOS (Hong Kong) male participants for 10 years, and 1,953 MsOS (Hong Kong) female participants for 9 years. The initial 4 years were followed by both telephone and checking the hospital visiting records, and confirmed these two results were similar, while the rest of the FU years were based on checking the hospital visiting records. Our results show clinical spine fracture ≥1 time (i.e., at least one fracture incident) were recorded 133 cases/100,000 person-years in men and 273 cases/100,000 person-years in women (58). These figures are relatively low compared with Caucasian results. In MrOS (USA) study which has the same enrollment strategy for participants as MrOS (Hong Kong), Freitas *et al.* (59) reported the results of 5,995 cases followed up for 4.7 years and recorded clinical vertebral fracture incidence of 216 cases/100,000 person-years. A comparison of Hong Kong results and American, Australian, and Canadian results of clinical OVF incidence rate is shown in *Table 3* (28,33,59,60-63). It can be seen that, for clinical vertebral fracture, the rate of Hong Kong subjects was approximately half of those of American, Australian, and Canadian subjects (both for men and for women). That MrOS (Hong Kong) and MsOS (Hong Kong) recorded 133 cases and 273 cases of clinical OVF incidence per 100,000 person-years respectively also support the notion that women's OVF rate is double of men's OVF rate (18).

The knowledge that the prevalence of all clinical osteoporotic fractures among elderly Chinese is no more than half of that of elderly Caucasians will have implications in defining the cutpoint T-score as an epidemiological index for osteoporosis (64).

As we noted earlier, most of the published radiographic OVF assessment results lack a rigorously quantifiable standard and are highly subjective. Until a better approach is adopted, radiographic OVF results by different readers may not be comparable, particularly when different criteria were used. While the Genant SQ criteria may be sufficient for daily clinical practice, for research purpose we recommend that: (I) radiographic OVF should be assessed by a reader with sufficient expertise on this topic, rather

Table 3 A comparison of Hong Kong results and American, Australian, and Canadian results for clinical OVF prevalence

Name of the study	Sex/ethnic groups	Number of participants	Mean age range (study starting to ending) (years)	Mean age during study (years)	Fracture cases/100,000 person-years
MrOS (Hong Kong)	Men/Chinese	1,954	72.3–82.3	77.3	133
MrOS (USA)	Men/American	5,995	73.6–78.3	76.0	216
Geelong study	Men/Australian	2,460	–	75–79	180
Rochester, Minnesota	Men/American	¶	–	75–84	238
MsOS (Hong Kong)	Women/Chinese	1,953	72.5–81.5	77.0	273
Geelong study	Women/Australian	3,400	–	75–79	760
FIT (USA)	Women/American	6,048	68.1–71.9	70.0	>422
CaMos[#]	Women/Canadian	5,143	66.6–69.6	68.1	220
Rochester, Minnesota	Women/American	¶	–	75–84	975

MrOS (USA): Freitas *et al. Osteoporos Int* 2008;19:615-23; Geelong study for Australian: Sanders *et al. Osteoporos Int* 1999;10:240-7; Rochester, Minnesota study for American: Cooper *et al. J Bone Miner Res* 1992;7:221-7; FIT (USA): Fracture Intervention Trial American women, Fink *et al. J Bone Miner Res* 2005;20:1216-22; CaMos: Canadian Multicentre Osteoporosis Study (CaMos) for women, Papaioannou *et al. Osteoporos Int* 2005;16:568-78. ¶, precise study participant number for this age range not available, probable a small participant number; #, compared with MsOS (Hong Kong) study, CaMos study recorded a lower fracture incidence (273 *vs.* 220 per 100,000 person-years). However, the participants in CaMos study were on average 8.9 year younger than MsOS (Hong Kong) study participant. OVF prevalence is known to grow exponentially along this age span. If age-match age were available, it is expected CaMos participants would have much higher OVF prevalence than that of MsOS (Hong Kong) participant. OVF, osteoporotic vertebral fracture; MrOS, osteoporotic fractures in men; MsOS, osteoporotic fractures in women.

conveniently by a local musculoskeletal radiologist (20); (II) grading has to be quantitative measurement based, rather than visually estimated as according to the initial description by Genant *et al*. (21). We believe a combined approach based on standardized radiologic evaluation by experts and morphometry measurement is the most appropriate approach to detect and classify radiographic OVFs. We have also published an image database for calibration (31,32).

Lower prevalence of DS in elderly Chinese men and women

Disc degeneration can contribute to segmental instability and further result in DS. The reported DS prevalence varied greatly, and the female male prevalence ratio (F:M ratio) was even more controversial. For example, in the Copenhagen Osteoarthritis Study (1,533 males, mean age of 62 years, range, 23–93 years; 2,618 females, mean age: 65 years, range, 22–92 years), Jacobsen *et al*. (65) reported the prevalence of spondylolisthesis was 2.7% for males, and 8.4% for females, with a F:M ratio of 6.4:1. Kalichman *et al*. (66) studied 188 adults community-based population (mean age ± SD: 52.7±10.8 years) with computed tomography (CT), the DS prevalence was 7.7% (males) *vs.* 21.3% (females) (F:M ratio =3:1). In a professional taxi driver cohort in Taipei (mean age ± SD: 44.5±8.7 years, predominately males), Chen *et al*. (67) reported the prevalence of spondylolisthesis was 3.2%.

Our systematic review concluded that the prevalence of DS is strongly gender- and age-specific, and also differs among ethics groups (12). DS is relatively rare before 50 years old, and after 50 years old both women and men start to develop DS, with women developing at a much faster rate than men (12). Our BL data show spondylolisthesis prevalence was 19.1% in elderly Chinese men and 25.0% in elderly Chinese women (68). A synthesis from population-based epidemiological studies data from USA and Hong Kong with similar methodologies and age distribution suggests that, elderly Caucasian American has higher DS prevalence, being approximately 60–70% higher than age-match elderly Chinese (*Table 4*) (12,68-71). However, the F:M ratio was similar to Chinese population, being 1.38:1. Japanese population may also have a lower DS prevalence than Caucasians. For the elderly population from a single Japanese village with 205 elderly men (mean age: 70.7 years)

Table 4 A comparison of degenerative spondylolisthesis prevalence and 4 years progression in elderly Chinese and elderly Caucasian American*

Name of the study	Age (years) [range]	Prevalence	Progression	De novo
MsOS (Hong Kong) year-0[a]	72.6 [65–98]	25%	–	–
SOF (USA) for women year-0[b]	71.5 [65–89]	43.1%	–	–
MrOS (Hong Kong) year-0[c]	72.4 [65–92]	19.1%	–	–
MrOS (USA) year-0[d]	74.0 [68–80]	31.0%	–	–
MsOS (Hong Kong) year-4[e]	75.7 [68–102]	33.8%	16.5%	12.7%
MrOS (Hong Kong) year-4[f]	75.5 [68–95]	25.9%	13.0%	12.4%
MrOS (USA) year-4[g]	78.0 [72-84]	43.0%[h]	12.0%	12.0%

This table is reproduced with permission from reference (12). *, all studies listed are population-based study on community subjects. [a], n=1,994 subjects; [b], n=788 subjects; [c], n=1,996 subjects; [d], n=295 subjects; [e], n=1,546 subjects; [f], n=1,519 subjects; [g], n=190 subjects; [h], estimated from baseline data plus *de novo* number. The F:M ratio of MsOS (Hong Kong) and MrOs (Hong Kong) is 1.3:1; while the F:M ratio of studies in USA is 1.38:1. [a,c], He *et al. Eur Radiol* 2014;24:441-8; [b], Study of Osteoporotic Fractures (SOF), Vogt *et al. Spine* (*Phila Pa 1976*) 1998;23:2640-7; [e,f], Wáng *et al. Spine* (*Phila Pa 1976*) 2016;41:1096-103; [d,g], Denard *et al. Spine* (*Phila Pa 1976*) 2010;35:1072-8. MrOS, osteoporotic fractures in men; MsOS, osteoporotic fractures in women.

and 323 elderly women (mean age: 70.5 years), in a cross-sectional study Horikawa *et al*. (72) reported a spondylolisthesis prevalence of 4.9% for males, and 11.5% for females. In a cohort of 3,259 Japanese patients with low back and/or leg pain (mean age approximately 65 years), Iguchi *et al*. (73) reported a DS prevalence of about 8.7% (F:M ratio =1.3:1).

In our pilot review of lumbar spine radiographs of age-matched (mean age: 74.3 years; range, 67–84 years) female subjects from two population-based studies in Hong Kong [MsOS (Hong Kong), n=130] and Rome, Italy (Roman Osteoporosis Prevention Project, n=130), classification of disc height loss (none, <30%, 30–60%, >60%), osteophyte formation (not present, minimal, small, large), endplate sclerosis (none, mild, moderate, severe), and anterolisthesis/retrolisthesis (none, <25%, 25–50%, >50%) was performed for each vertebral level from L1/2-L5/S1. Each individual finding was assigned a score (0, 1, 2, 3) based on its classification of severity for each vertebral level, and the total degeneration score was obtained by adding scores for the findings across all vertebral levels. The results showed Italian subjects had higher scores for all individual findings than Hong Kong subjects [mean ± SD: disc height loss, 4.70±2.64 *vs.* 3.25±2.24; sclerosis, 1.22±1.27 *vs.* 0.79±1.09; anterolisthesis/retrolisthesis, 0.48±0.77 *vs.* 0.28±0.60 (i.e., Italian 70% higher prevalence)], apart for osteophytes (Italian 3.01 ±2.41 *vs.* Hong Kong 3.12±2.58). The prevalence of moderate to severe degeneration at any one level (level score ≥5) was also higher in Italian compared to Hong Kong subjects (5.31% *vs.* 2.23%) (74).

Patient data showed female patients more often received surgical treatment than men for DS, with a ratio F:M ratio of around 1.9:1 in elderly population (12). This could be due to that women are more sensitive to pain and more likely to visit doctors.

Menopause is an important contributing factor for the accelerated DS development among elderly women (12). Before the age of 50 years, spondylolisthesis is rare and congenital spondylolisthesis is more common in men than in women. After post-menopause, DS becomes more common in women than in age-matched men. Low female sex hormone level in post-menopausal women can be associated with: (I) accelerated degeneration of disc degeneration and DSN; (II) higher prevalence of osteoarthritis including that of facet joints; (III) general laxity of the paraspinal ligaments. These factors contribute to the development of DS among post-menopausal women (12).

Literature on lower back pain incident rate among Asians as compared with Caucasians

A systematic literature review of other authors' publication shows that, compared with Caucasians, Asians (diverse ethnic groups in Asia or originated in Asia) and Chinese in particular, have a lower incident rate of back pain. Meana *et al*. (75) reported that, among the age group of 65 years and older, Chinese Canadian males and females had the lowest rates of chronic pain compared with other Canadian ethnic groups. Deyo *et al*. (76) estimated back

pain prevalence and clinics visit rates from U.S. national surveys 2002, and showed, among racial groups, Asian Americans had the lowest prevalence. Mailis-Gagnon *et al*. (77) collected data on new patients over a three-year period at the Comprehensive Pain Program (CPP) in downtown Toronto. They noted the east Asian group (primarily Chinese) was the most underrepresented (1.6% of the CPP population), despite that this group accounted for 9% of the population in Toronto and 6.01% of the Greater Toronto Area population. Waterman *et al*. (78) queried National Electronic Injury Surveillance System (USA) for all cases of LBP presenting to emergency departments between 2004 and 2008. They found that the per 1,000 person-years LBP incident rates were 1.23 among whites, while only 0.20 among Asians.

The lower prevalence of OVF and degenerative changes in elderly Chinese as demonstrated by our studies likely contribute to the generally healthier spine among elderly Chinese relative to elderly Caucasians.

In conclusion, this article summarizes our published MrOS (Hong Kong) and MsOS (Hong Kong) studies spine radiographic results. Our research suggests that, compared with elderly Caucasians, elderly Chinese have a generally healthier spine, with much less prevalence and much less severity of OVF, much less prevalence of spine degenerative changes, and a much lower incident rate of back pain.

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Footnote

Conflicts of Interest: The authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/qims-2021-07). YXJW serves as the Editor-In-Chief of *Quantitative Imaging in Medicine and Surgery*. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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