

# Bone mineral density enhances use of clinical risk factors in predicting ten-year risk of osteoporotic fractures in Chinese men: the Hong Kong Osteoporosis Study

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## Abstract

**Summary** This prospective study aimed to determine the risk factors and the 10-year probability of osteoporotic fracture in Southern Chinese men. The findings show substantial population differences in fracture incidence and risk prediction compared to the FRAX™ model, and the addition of BMD information to clinical risk factor assessment improved fracture risk prediction in Chinese men.

**Introduction** Clinical risk factors with or without bone mineral density (BMD) measurements are increasingly recognized as reliable predictors of fracture risk. Prospective data on fracture incidence in Asian men remain sparse. This prospective study aimed to determine the risk factors and the 10-year absolute fracture risk in Southern Chinese men.

**Methods** This is a part of the Hong Kong Osteoporosis Study. One thousand eight hundred ten (1,810) community-dwelling, treatment-naive men aged 50 years or above were evaluated. Baseline demographic characteristics, clinical risk factors and BMD were recorded. Ten-year risk of osteoporotic fracture was calculated using Cox proportional hazards models.

**Results** The mean age of subjects was  $68.0 \pm 10.3$  years. After a mean follow-up period of  $3.5 \pm 2.9$  years (range 1 to 14 years), 37 incident low-trauma fractures were recorded. The incidence for all osteoporotic fractures and hip fractures was 635/100,000 and 123/100,000 person-years, respective-

ly. The most significant predictors of osteoporotic fracture were history of fall (RR 14.5), femoral neck BMD T-score  $< -2.5$  (RR 13.8) and history of fracture (RR 4.4). Each SD reduction in BMD was associated with a 1.8 to 2.6-fold increase in fracture risk. Subjects with seven clinical risk factors and BMD T-score of  $-1$  had an absolute 10-year risk of osteoporotic fracture of 8.9%, but this increased to 22.7% if they also had a femoral neck BMD T-score of  $-2.5$ .

**Conclusions** These findings show substantial population differences in fracture incidence and risk prediction. The addition of BMD information to clinical risk factor assessment improved fracture risk prediction in Chinese men.

**Keywords** Bone mineral density · Fracture risk · FRAX · Men · Osteoporosis · Osteoporotic fractures

## Introduction

Osteoporosis has become a major public health concern in the past decade and the burden placed on the community and health care agencies is expected to rise with the aging global population. Global epidemiological data indicate that Asia will carry the greatest burden of osteoporotic fractures over the coming decades. Although it is well documented that the risk and incidence of fractures vary widely between populations [1], the absolute rate of fractures among Asian men remains unclear.

A recent update of the worldwide prevalence of osteoporotic fractures using data from published sources reveals that of the annual incidence of nine million fractures, 39% occur in men [2]. Although men suffer fewer fractures than women, they have a significantly higher morbidity and mortality [2]. It is projected that by 2050, 50% of hip fractures will occur in Asia, with the majority occurring in China [1]. With the

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growing size of the aging population in Asia and increasing longevity, osteoporosis in men will soon become a significant burden on society and healthcare systems in Asia. Epidemiological studies suggest that the increased incidence of fractures among developing countries may be related to urbanization and altered lifestyle, although evidence to support this is scanty.

Identification of subjects at risk of fracture to enable early treatment in developing countries with limited resources remains a challenge. There is increasing evidence that bone mineral density (BMD) alone is inadequate to detect all individuals at risk of osteoporotic fractures, and factors other than BMD are important for predicting future fracture risk [3, 4]. The World Health Organization (WHO) FRAX™ algorithm for fracture risk assessment utilizes a set of clinical risk factors with or without BMD information to predict the 10-year absolute fracture risk in different populations, including Chinese in mainland China and Hong Kong [5]. Interestingly, the clinical risk factors included in FRAX differ to those identified from prospective population studies. In our previous study of Chinese postmenopausal women [5], we identified eight clinical risk factors that contribute to increasing fracture risk, including the use of walking aids; history of one or more falls in 12 months; being housebound; dietary calcium intake <400 mg/day; age >65 years; previous fracture; body mass index (BMI) <19 kg/cm<sup>2</sup>; and physical activity <30 min/day. These findings suggest that population-specific characteristics may need to be taken into consideration when evaluating fracture risk; e.g., other than the common risk factors such as age, BMI and BMD, the Dubbo Osteoporosis Epidemiology Study of Australia took into account of quadriceps strength, body sway, and thiazide use [6]. The QFractureScores algorithm developed for Caucasian population in the UK includes concomitant diseases and medication use as major risk factors for fracture prediction [7].

Although a number of cross-sectional studies and population studies have demonstrated lower BMD values and fracture incidence in Asian men compared with Caucasian men, information on fracture outcome derived from prospective studies in Asian male cohorts is scarce. The objective of this prospective study was to report the incidence of osteoporotic fracture in Southern Chinese men, to evaluate the clinical risk factors associated with fracture risk, and to compare the model build on these population-specific risk factors and the WHO FRAX risk calculator in fracture prediction.

## Methods

### Study population and design

This was a part of the prospective population-based Hong Kong Osteoporosis Study in which community-dwelling

ambulatory Southern Chinese men aged 50 years or above were recruited from different districts of Hong Kong between 1995 and 2009 during health fairs and road shows on osteoporosis. Subjects already prescribed osteoporosis treatment were excluded. All participants were invited to the Osteoporosis Centre at Queen Mary Hospital for evaluation of bone health. X-rays of the thoracolumbar spine were obtained at baseline to identify the presence of morphometric vertebral fracture using Genant's semiquantitative assessment method [8].

Baseline demographic data and information on clinical risk factors were collected including anthropometric measurements, socioeconomic status, education level, low-trauma fracture history after the age of 45 years (both personal and family), history of fall, and medical history including current medication, history of low back pain, prior use of glucocorticoids, and secondary causes of osteoporosis. Information on lifestyle habits including smoking, alcohol consumption, and physical activity were also obtained. Dietary intake of calcium was determined using a semiquantitative food frequency questionnaire [5]. These data were collected from interviews conducted by trained research assistants using a structured questionnaire.

All subjects were followed annually via telephone interviews using a structured questionnaire for assessment of the clinical outcome of incident fractures, falls, hospitalization, living status and functional status. Medical history and incident fractures were verified with the computerized patient information system of the Hospital Authority of the Hong Kong Government. Fractures of the skull, fingers and toes, as well as traumatic fractures were excluded from analysis. Subjects who commenced anti-osteoporosis medication prior to the occurrence of a primary fracture were also excluded. The study was approved by the Institutional Review Board of the University of Hong Kong and the Hong Kong West Clusters Hospital of the Hospital Authority.

### BMD evaluation

BMD was assessed at the L1–4 lumbar spine, femoral neck, and total hip using the same dual-energy X-ray absorptiometry machine (Hologic QDR 4500, Waltham, Mass., USA). BMD T-scores were determined according to the local Southern Chinese normative database [9]. The *in vivo* precision of BMD at the lumbar spine, femoral neck, and total hip was 0.8%, 0.9% and 0.7%, respectively. All DXA measurements were performed by two licensed technologists who had completed training by the equipment manufacturers and were accredited by the International Society for Clinical Densitometry. The least significant change for lumbar spine, femoral neck, and total hip was 2.41%, 3.82% and 2.62%, respectively. BMD was expressed both as an absolute value in gram per square centimeter and T-score.

## Statistical methods

The Cox proportional hazards models were used to identify potential independent risk factors for osteoporotic fracture. Time to all incident fractures was calculated according to the date of X-ray reports or physician's consultations when diagnosis was made. Results were reported as relative risks (RR) with 95% confidence intervals (CI). The significance level was set at  $p < 0.05$ . The risk of osteoporotic fracture was optimally expressed as a fixed-term absolute risk, that is, the probability of fracture over a given period of time. Predicted 10-year fracture risk adjusted by competing risk of death [10], as well as the relationship between fracture risk and age, BMD T-score and number of risk factor were identified using one minus Kaplan–Meier survival functions. Individual 10-year risk of major osteoporotic fracture was also obtained from the FRAX for Hong Kong website (<http://www.shef.ac.uk/FRAX/>) for comparison. Receiver operative characteristic curve (ROC) analysis was used to determine the predictive value of ethnic-specific clinical risk factors with or without BMD and FRAX. All statistical analyses were conducted using SPSS for Windows version 15.0 (SPSS, Chicago, IL, USA) and R for Windows version 2.11.1 (R Development Core Team, Auckland, New Zealand) statistical software.

## Results

One thousand eight hundred and ten subjects were included in this analysis. The average follow-up period was  $3.5 \pm 2.9$  years (range 1 to 14 years), with a total follow-up of 5,669 patient-years. The mean age at baseline was  $68.0 \pm 10.3$  years (range 50 to 99 years); 33.6% were aged from 45 to 64 years and 63.4% were aged 65 years or older. One hundred and seventy subjects had died at the time of analysis and 19 patients received anti-osteoporosis medication after sustaining a fracture during the follow-up period. The data for these subjects were analyzed up to their last contact time-point or time of treatment initiation. Baseline demographic information and BMD characteristics of the subjects are shown in Table 1. 7.2% of all subjects had osteoporosis with a BMD T-score  $\leq -2.5$  at any one site. 9.1% of men aged 65 years or above were osteoporotic compared with 4.1% in the 50- to 64-year age group. Prevalence of osteopenia (BMD T-score between  $-1$  and  $-2.5$  at any one site) was 47.2% in men above age 65 years and 39.2% in men aged 50 to 64 years: combined, this accounted for 44.1% of all subjects.

During the follow-up period, 37 new low-trauma fractures were reported, of which seven (22%) were clinical vertebral fractures, seven (22%) were hip fractures, two (6%) were proximal humerus fractures; nine (25%) were

distal forearm fractures; and 12 (33%) were fractures at other peripheral sites. The incidence for all low-trauma fractures was 635/100,000 person-years, for non-spine fractures was 528/100,000 person-years, and for hip fracture was 123/100,000 person-years. For subjects aged 65 years and above, the incidence for all fractures was 839/100,000 person-years, for non-spine fractures was 769/100,000 person-years and for hip fracture was 201/100,000 person-years.

### Predicted 10-year osteoporotic fracture risk from risk factor assessment

In multivariate Cox regression analysis, seven independent clinical risks factors associated with increased risk of osteoporotic fracture were identified (Table 2). In terms of individual risk factors, history of fall and history of fragility fracture were associated with the highest predicted 10-year risk of fracture: the relative risk was 14.5 (95% CI 6.5–32.2) and 4.4 (95% CI 2.0–9.4), respectively. Other risk factors listed in decreasing order of impact on fracture risk were: outdoor activity  $< 60$  min/day, BMI  $< 20$  kg/m<sup>2</sup>, difficulty bending forward, use of walking aid, and age  $\geq 65$  years ( $p$  value  $< 0.05$ , Table 2). Although a 10-year increase in age accounted for only a 5.8% increase in 10-year osteoporotic fracture risk, older men aged 65 years or above had a 2.7-fold higher risk of fracture compared with younger men. Figure 1 shows the fracture risk in different age groups that was adjusted for competing risk of death along the study period. The interaction of age and other risk factors is shown in Fig. 2a. The combination of older age and history of fall was associated with a twofold increase in 10-year fracture risk after adjusting for competing death risk. Men aged 65 years or older with one or more falls per year had a 10-year risk of fracture of 31.9% compared with 15.8% for those younger than 65 years old.

### Predicted 10-year osteoporotic fracture risk from BMD and number of risk factors

While 48% of all incidence fractures occurred in subjects in whom BMD fell in the osteopenic range, only 26% of fracture cases occurred in osteoporotic subjects. Aside from history of fall, low BMD at the femoral neck (T-score  $\leq -2.5$ ) had the second highest impact on fracture risk in men (RR=13.8), and each SD reduction in BMD at the lumbar spine, femoral neck or total hip was associated with a 1.8 to 2.6-fold increase in osteoporotic fracture risk (Table 2). The addition of hip BMD information to risk factor assessment improves osteoporotic fracture risk prediction. Regardless of the risk factor studied, subjects with femoral neck BMD T-score  $\leq -2.5$  had a 1.7 to 7.8-fold increase in 10-year fracture risk prediction (Fig. 2b). Figure 3 shows the 10-

**Table 1** Baseline Demographic and BMD Characteristics of Hong Kong Southern Chinese Men ( $n=1,810$ )

Characteristics	Mean $\pm$ SD (%)
Age (year)	68 $\pm$ 10.3
Height (cm)	164.6 $\pm$ 6.5
Weight (kg)	62.9 $\pm$ 10.3
BMI (kg/m <sup>2</sup> )	28.11 $\pm$ 8.4
Grip strength (kg)	31.6 $\pm$ 8.0
Dietary calcium intake (mg/day)	675.1 $\pm$ 282.7
History of fall within 1 year	257 (14.2%)
Difficulty bending forward	185 (10.2%)
Kyphosis	78 (4.3%)
Low back pain	510 (28.2%)
History of fragility fracture	576 (31.8%)
History of clinical spine fracture and/or morphometric fracture	112 (6.2%)
History of clinical spine fracture	52 (2.9%)
History of parental fracture	65 (3.6%)
Use of walking aid	264 (14.6%)
Homebound	121 (6.7%)
Walking <30 min/day	167 (9.2%)
Outdoor activity <60 min/day	608 (33.6%)
Current and ex-smoker	673 (37.2%)
Current and ever alcohol consumption ( $\geq 3$ Units/day)	43 (2.4%)
Ever long term use of oral glucocorticoids	33 (1.8%)
Rheumatoid arthritis	11 (0.6%)
Hyperthyroidism	47 (2.6%)
Hyperparathyroidism	4 (0.2%)
Hypogonadism (testosterone <10 nmol/L)	257 (14.2%)
No reported medical conditions	1,095 (60.5%)
1–3 reported medical conditions	595 (32.9%)
3 or more reported medical conditions	119 (6.6%)
Lumbar spine BMD (g/cm <sup>2</sup> )	0.949 $\pm$ 0.334
Lumbar spine T-score	-0.4 $\pm$ 1.3
Femoral neck BMD (g/cm <sup>2</sup> )	0.697 $\pm$ 0.121
Femoral neck T-score	-0.9 $\pm$ 0.8
Total hip BMD (g/cm <sup>2</sup> )	0.862 $\pm$ 0.774
Total hip T-score	-0.7 $\pm$ 1.0
Lumbar spine BMD T-score $\leq$ -2.5	89 (4.9%)
Femoral neck BMD T-score $\leq$ -2.5	58 (3.2%)
Total hip BMD T-score $\leq$ -2.5	78 (4.3%)
Osteoporosis BMD T-score $\leq$ -2.5 at any site	130 (7.2%)
Osteopenia BMD T-score between -1 and -2.5 at any site	744 (44.1%)

year absolute risk of osteoporotic fracture according to age and femoral neck BMD T-score. The interaction between BMD and age on fracture risk was similar to that observed in women [5], i.e., at the same BMD T-score, older men had a much higher fracture risk than younger men.

It has been reported that approximately half of the fractures in Caucasian men are idiopathic. Nonetheless in this Chinese cohort, all subjects with incident fractures had at least one clinical risk factor other than low BMD. The

risk of major osteoporotic fractures (i.e., clinical spine, hip, proximal humerus and distal radius) increased with increasing number of risk factors and decreasing femoral neck BMD T-score. At low T-scores, fracture probability increased markedly with more risk factors. For example, at a femoral neck BMD T-score of -3, the 10-year probability of major osteoporotic fracture increased from 1.9% in those with no risk factor to 31% in those with seven risk factors, (Fig. 4).

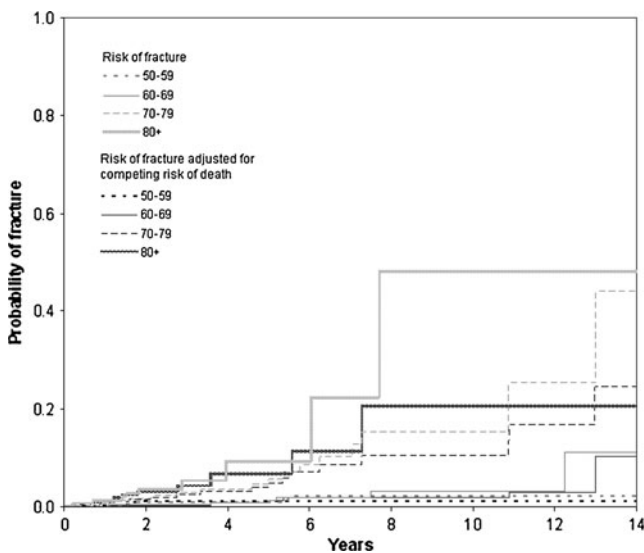
**Table 2** Clinical risk factors associated with osteoporotic fracture in Hong Kong Southern Chinese men ( $n=1,810$ )

Risk factors	Subjects (%)	B	RR (95% CI)	P
Age $\geq$ 65 years	1148 (63.4)	1.0	2.7 (1.2–5.8)	0.013
Age per 10 years increase		0.1	1.1 (1.0–1.1)	0.003
Grip strength <30 kg	447 (24.7)	1.2	3.3 (0.6–17.2)	0.160
History of fall within 1 year	257 (14.2)	2.7	14.5 (6.5–32.3)	<0.0001
Difficulty bending forward	185 (10.2)	1.3	3.6 (1.3–9.9)	0.014
Kyphosis	78 (4.3)	1.2	3.4 (0.8–14.8)	0.100
Low back pain	510 (28.2)	−0.1	0.9 (0.4–2.2)	0.895
BMI<20 kg/m <sup>2</sup>	167 (9.2)	1.3	3.6 (1.0–12.8)	0.050
BMI per unit increase		−0.1	0.9 (0.8–0.9)	<0.0001
Walking <30 min/day	167 (9.2)	0.5	1.6 (0.5–5.4)	0.457
History of fragility fracture	576 (31.8)	1.5	4.4 (2.0–9.4)	<0.0001
History of clinical or morphometric spine fracture	112 (6.2)	−0.3	0.7 (0.1–6.0)	0.761
History of clinical spine fracture	52 (2.9)	0.5	1.6 (0.2–12.0)	0.635
History of parental fracture	65 (3.6)	−0.3	0.8 (0.1–5.7)	0.799
Use of walking aid	264 (14.6)	1.0	2.7 (1.1–6.5)	0.030
Homebound	121 (6.7)	−0.5	0.6 (0.1–4.5)	0.620
Outdoor activity <60 min/day	608 (33.6)	1.4	4.1 (1.7–9.9)	0.001
Current and ever smoking	673 (37.2)	0.5	1.7 (0.8–3.5)	0.135
Current and ever drinking	43 (2.4)	1.0	2.7 (0.4–20.4)	0.326
Calcium Intake <400 mg/day	185 (10.2)	0.2	1.3 (0.4–4.3)	0.712
Medical diseases				
Diabetes	257 (14.2)	0.7	2.1 (0.8–5.1)	0.109
Osteoarthritis	174 (9.6)	−0.3	0.7 (0.2–3.1)	0.688
Hypertension	590 (32.6)	0.2	1.3 (0.4–3.9)	0.684
Hyperlipidaemia	167 (9.2)	0.0	1.0 (0.2–4.7)	0.973
Ischemic heart disease	205 (11.3)	0.2	1.3 (0.3–4.7)	0.737
Peptic ulcer disease	94 (5.2)	0.5	1.7 (0.4–7.4)	0.499
Chronic obstructive airway disease	60 (3.3)	0.1	1.1 (0.1–9.0)	0.900
Dementia	29 (1.6)	1.1	3.1 (0.4–24.2)	0.282
Stroke	94 (5.2)	−0.3	0.7 (0.1–0.1)	0.777
Cataract/Glaucoma	91 (5.0)	1.2	3.2 (0.9–12.1)	0.084
Anemia	34 (1.9)	0.9	2.5 (0.3–19.5)	0.385
Renal failure	63 (3.5)	1.1	3.0 (0.6–13.8)	0.167
Malignancy in the past 5 years	98 (5.4)	−0.2	0.8 (0.1–6.3)	0.832
L1–4 spine BMD per SD reduction		0.6	1.8(1.2–2.5)	0.002
Femoral neck BMD per SD reduction		0.9	2.5 (1.5–4.4)	0.001
Total hip BMD per SD reduction		1.0	2.6 (1.6–4.1)	<0.0001
L1–4 spine T-score $\leq$ −2.5	89 (4.9)	1.4	4.0 (1.4–11.6)	0.011
Femoral neck T-score $\leq$ −2.5	58 (3.2)	2.6	13.8 (5.1–37.2)	<0.0001
Total hip T-score $\leq$ −2.5	78 (4.3)	2.5	11.9 (4.6–30.5)	<0.0001

ROC analysis showed that clinical risk factors plus BMD information offers better predictive power than clinical risk factors alone in predicting 10-year probability of fracture (area under the curve  $0.82\pm 0.04$  vs.  $0.74\pm 0.04$ ,  $p<0.001$ ). We noted that although the percentage of subjects with low BMD was small, those with co-existent multiple risk factors had a very high risk of fracture. For example, 35% of men with a femoral neck BMD T-score $\leq$

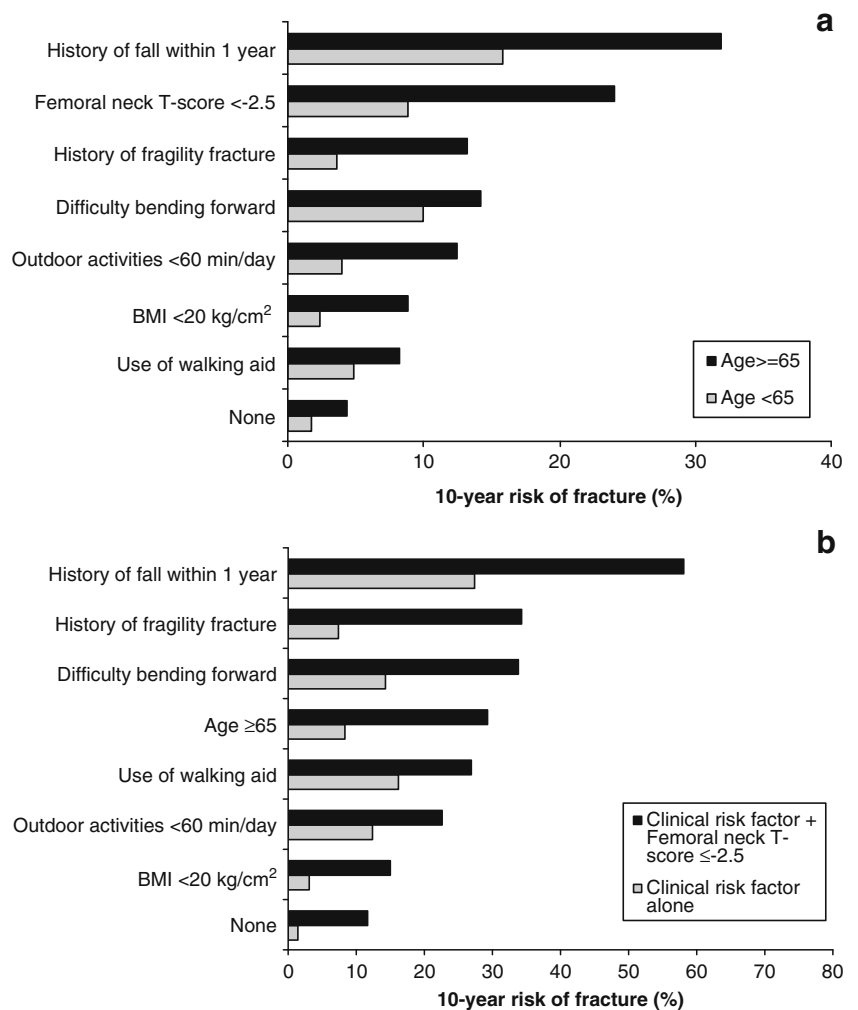
−2.5 had five to seven clinical risk factors and their absolute 10-year fracture risk was 27.6%; 15.9% of men aged 65 years and above had one or more falls per year and their 10-year risk of fracture was 31.9%.

The model based on this prospective study with adjustment of competing death risk was compared to the WHO FRAX risk calculator for Hong Kong with the inclusion of BMD information. The 10-year risk for major



**Fig. 1** Fracture risks according to different age groups adjusted and unadjusted for competing risk of death

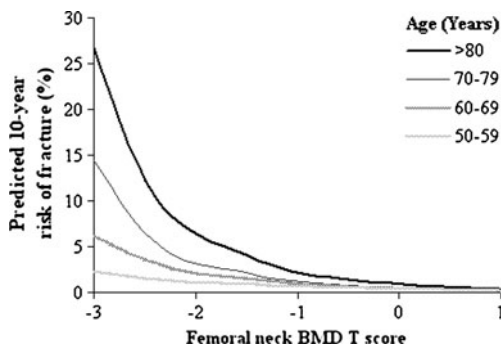
**Fig. 2 a** Interaction of age with other clinical risk factors and 10-year risk of osteoporotic fracture in Hong Kong Southern Chinese men. **b** Comparison of 10-year fracture risk prediction with clinical risk factors with or without BMD information in Hong Kong Southern Chinese men (results adjusted for competing risk of death)



osteoporotic fractures differed markedly with these two models: men with seven clinical risks have an absolute 10-year fracture risk of 17.6% with the present model, but the predicted fracture risk by FRAX is only 11% (Fig. 5). Contrary to this, an individual with no risk has only 0.7% risk based on the present model while the predicted risk by FRAX is 2.3%. ROC analysis also showed our model with BMD has significant improvement on overall predictive power compared to FRAX with BMD (area under the curve  $0.87 \pm 0.02$  vs.  $0.72 \pm 0.05$ ,  $p < 0.001$ ).

**Discussion**

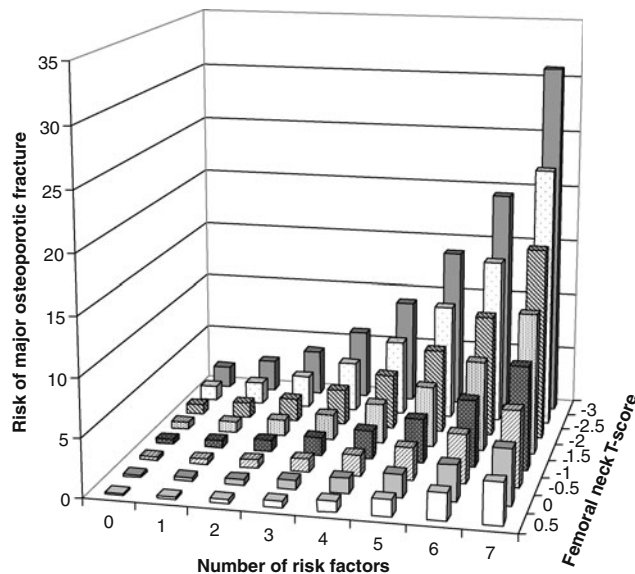
This prospective study provided evidence that Asian men have a low fracture rate compared to their Caucasian counterparts. Nevertheless, Hong Kong is a city that has undergone urbanization and the population-based age-adjusted fracture rate in men has doubled between 1966 and 1995 [11]. It was projected that a change in lifestyle



**Fig. 3** Ten-year risk of osteoporotic fracture in Hong Kong Southern Chinese men according to age and BMD T-score (results adjusted for competing risk of death)

associated with urbanization may increase the fracture rate in Orientals to the higher levels seen in Western populations. This prospective study revealed that the fracture rate in Southern Chinese men in Hong Kong remains low. The non-spine fracture incidence for Chinese men aged 65 years or above was 769/100,000 person-years as compared to 1,146/100,000 person-years reported in the MrOS study which involved predominantly US Caucasians [12].

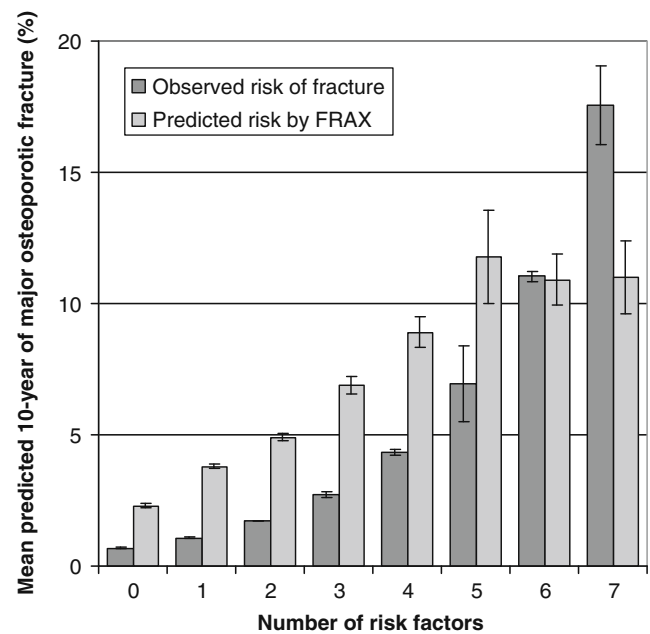
Although this study used a convenient rather than a random community sample and might have biased towards recruiting healthier subjects, the prevalence of osteoporosis at the femoral neck of 3.2% in this cohort was similar to the 2.0% reported in Caucasian White subjects in the population-based NHANES 2005–2006 survey in the US [13]. The prevalence of osteoporosis at the spine and hip were similar in this cohort. Similar to other populations,



**Fig. 4** Ten-year major osteoporotic fracture risk for Hong Kong southern Chinese men according to number of risk factor and femoral neck BMD T-score (results adjusted for competing risk of death)

fractures of the hip, forearm, vertebrae, and humerus were among the most frequent sites of incident fractures in men. In comparison with postmenopausal women in the same population [5], the absolute fracture incidence was lower in men. The reason for this difference in the US population was postulated to be related to an increased frequency of falls in women [14, 15], and fracture risk after a fall was 2.2 times higher in women than men [16]. The relation of fracture risk after a fall in the two sexes was nonetheless reversed in Chinese. Although falls were recorded more often in women [5], the relative risk of fracture in subjects with one or more falls in 12 months was 14.5 for Chinese men and 4.0 for Chinese women.

This study also identified the clinical risk factors for fracture in Chinese men and the interaction between risk factors and BMD. These risk factors partly overlap with those reported for Caucasian population of the MrOs study which are the use of tricyclic antidepressant, history of fracture, inability to complete a narrow walk trial, falls in previous year, age ≥ 80 years, depressed mood and decreased total hip BMD [12]. The risk factors for Chinese men are also slightly different from those identified by the Dubbo study which includes increasing age, decreased femoral neck BMD, quadriceps strength, body sway, previous falls, previous fractures, weight, height, alcohol use, physical activity index and thiazide use [6]. Similar to previous observations of other ethnic groups [17, 18], each SD reduction in BMD T-score is associated with a 1.8



**Fig. 5** Ten-year major osteoporotic fracture risk for Hong Kong Southern Chinese men according to [1] number of risk factors (including BMD) with adjustment for competing risk of death [2] predicted risk by FRAX with femoral neck BMD T-score

2.6-fold increased risk of osteoporotic fractures in Chinese men. The relative risk prediction for osteoporotic fracture was better with BMD measurement at the hip than the spine: this concurs with the findings in Caucasian populations [6, 19]. However, subjects with a femoral neck BMD T-score < -2.5 had a 13.8-fold increased risk of fracture.

The WHO FRAX model utilizes ten clinical risk factors with or without BMD for fracture risk prediction. In areas where BMD measurements are not available, WHO proposes to use BMI to replace BMD as it provides a similar risk profile for fracture prediction. Interestingly, our data revealed that addition of BMD information to clinical risk factors enhanced fracture prediction in this male cohort. This observation concurs with other US Caucasian male studies [20]. Hence identifying subjects with low BMD and multiple risk factors, and targeting them for preventive measures is likely to be a cost-effective approach. With the exception of age, BMI, and previous fractures, the clinical risk factors identified in this present study differ significantly to those included in the FRAX model. The latter shows that risk factors for fracture and fracture risk prediction likely vary between different ethnic groups. The FRAX model also does not take into account the impacts on fracture risk of history of fall, physical ability and mobility, which are important risk factors for fracture as shown in this and other studies [6, 7, 21]. Our model using ethnic-specific risk factors and incorporated fall risk had a significantly better predictive power when compared to FRAX. It would also be interesting to compare other population-specific models such as the Dubbo Study and MrOs Study which have also incorporated history of fall and physical activity as risk factors. It is also likely that FRAX underestimates the risk for osteoporotic fractures, especially vertebral fractures in Asian populations. Although the risk of hip fractures is much lower in Chinese than in Caucasians, the risk of vertebral fractures is similar between the two ethnic groups [22, 23]. There has been a concern that a model that presumes a ratio of vertebral fractures to non-vertebral fractures in a Swedish population might underestimate the risk of vertebral fractures in Asians.

This study has some limitations. The sample size and the number of fractures recorded were small and this study may have underestimated the absolute risk in the general population. Although it is of our interest to compare the 10-year hip fracture risk of our model with the risk predicted by FRAX, such analysis was limited by the low incidence of hip fractures in our sample and we could only compare the two models on prediction of major osteoporotic fractures. The low recruitment rate also reflected the lack of interest of Asian men in health-related activities. Spine X-rays were not obtained in all patients during

follow-up, thus the incidence of morphometric spine fractures was not included in the analysis. All participants received a clear explanation of their BMD report and were educated about the importance of risk prevention in osteoporosis. The consequences of this intervention were not quantified. Thus, the actual risk of the general male population in Hong Kong that has not received any advice about osteoporosis prevention or been informed about BMD status is likely to be greater than that reported for the study population. As with other studies, the 10-year fracture risk of this study was predicted using the Cox proportional hazard model based on results generated from a mean follow-up period of 3.5 years. Actual 10-year follow-up information for every subject was not available. As fracture risk increases with age and frailty, the predicted model may well underestimate the actual fracture risk of the population.

In conclusion, this prospective study has determined the incidence of osteoporotic fracture and hip fracture in Southern Chinese men and identified the major clinical risk factors associated with fracture risk. These data highlight the importance of ethnic/population-specific characteristics in better discrimination of individuals at high risk of fracture and targeting of intervention.

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**Conflicts of Interest** None.

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