



# The association of bone density and hip fracture risk among Asian women

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## Abstract

**Summary** Asian women have lower bone density than White women, but their hip fracture risk similarly increased two-fold or more for each unit decline in bone density T-score. Adjusting for age, T-score, and treatment, hip fracture risk remained lower for Asian compared to White women, with some attenuation after stature adjustment.

**Background** Few studies have examined the relationship of bone mineral density (BMD) and hip fracture risk among US Asian women. **METHODS:** Incident hip fractures were examined among Asian/Pacific Islander (PI) and non-Hispanic White (NHW) women aged 60–89 years who had femoral neck-(FN)-BMD measured in 2000–2019 without prior osteoporosis treatment. The BMD-T-score risk gradient for hip fracture was examined using Cox proportional hazard models, adjusting for age and time-updated osteoporosis therapy. Hip fracture risk for Asian versus NHW women was also examined (overall and by low T-score category), adjusting for age, T-score, and osteoporosis therapy. **RESULTS:** Among 54,294 Asian/PI and 219,585 NHW women, 14.3% of NHW and 23.5% of Asian/PI women had FN-T-score  $\leq -2.5$  (osteoporosis) that ranged 12.6% (Native Hawaiian/PI), 17.4% (South Asian), 22–23% (Chinese, Filipina, Korean), 26.7% (Japanese), and 30.5% (Vietnamese). During five-year follow-up, hip fracture incidence was 1.03 (Asian/PI) and 3.39 (NHW) per 1000 person-years. Each unit T-score reduction was associated with adjusted hazards ratio (aHR) for hip fracture of 2.11 [2.03–2.20] NHW, 2.84 [2.11–3.82] Chinese, 2.69 [2.01–3.60] Japanese, 2.22 [1.67–2.97] Filipina, and 2.18 [1.19–3.99] South Asian. Comparing Asian to NHW women, aHRs for hip fracture were 0.2–0.3 (Chinese, Filipina) and 0.4–0.6 (Japanese, South Asian), with some attenuation after height adjustment.

**Conclusion** Among Asian and NHW women, each unit reduction in FN-T-score was associated with  $\geq$  two-fold higher risk of hip fracture that varied by ethnicity. Accounting for T-score differences, Asian women had lower hip fracture risk than NHW women. These findings have implications for fracture risk assessment in these populations.

**Keywords** Asian · Bone density · Fracture risk · Hip fracture · Osteoporosis

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Nancy P. Gordon completed work prior to retirement.

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## Introduction

Bone mineral density (BMD), an important risk factor for fracture, is associated with a strong gradient of risk for each standard deviation (SD) decline [1]. In 1992, the Study of Osteoporotic Fractures reported a 1.41-fold increased age-adjusted risk of non-spine fracture for each SD decline in femoral neck (FN)-BMD [2] among 8134 US women (99.7% White race) aged  $\geq 65$  years over an average 0.72 years of follow-up. In this same cohort followed for an average 1.8 years, the adjusted risk of hip fracture was 2.6 for each SD decline in FN-BMD, a higher risk gradient [3]. In 1993, a study of 304 women in Rochester, Minnesota with median follow-up 8.3 years reported 1.3-fold (any clinical

fracture) and 2.4-fold (hip fracture) increased risk for each SD decline in FN-BMD [4]. Meta-analyses from prospective international cohorts, including these US studies, confirm that the gradient of risk for FN-BMD is highest for hip fracture, about 2.4–2.6 for women [5–7]. However, findings for US racial and ethnic minorities remain limited. In 2004, the National Osteoporosis Risk Assessment (NORA) study, which examined peripheral BMD (heel, forearm, or finger) and fractures of the hip, spine, forearm, wrist, or ribs over one year among 197,848 US postmenopausal women (90.7% White and only 1% Asian), reported a 1.54 risk gradient for fracture per SD decline in peripheral BMD across five ethnic groups studied [8]. To our knowledge, no population studies have examined the relationship of FN-BMD and hip fracture risk among US Asian women.

Hip fracture incidence among US Asian and Pacific Islander (PI) women is 35–65% lower than non-Hispanic White (NHW) women [9–11], with heterogeneity among ethnic subgroups [11, 12]. US Asian women also have lower areal BMD and higher osteoporosis prevalence [13, 14]. The World Health Organization (WHO) has defined osteoporosis based on FN-BMD T-score  $\leq -2.5$  measured by dual energy x-ray absorptiometry (areal BMD), using the young adult NHW female reference from the National Health and Nutrition Examination Survey (NHANES III) for all women [1, 15]. The T-score represents the BMD difference from a young adult reference population expressed in SD units of the reference population [16]. An early 1994 WHO Study Group reported that T-score  $\leq -2.5$  identified 30% of women with osteoporosis at the spine, hip, or forearm, a proportion similar to the lifetime risk of fracture among White women at any of these three sites [17, 18]. The report also concluded that the  $-2.5$  T-score threshold identified about 20% of women with hip osteoporosis, corresponding to a similar lifetime risk of hip fracture [17, 18]. However, the lower areal BMD among Asian women results in a larger proportion with FN-T-score  $\leq -2.5$  using the standard NHW female reference [15, 19] compared to an ethnicity-specific reference [14, 20]. Indeed, among northern California women aged 65–75 years with BMD testing, Asian women had nearly two-fold higher prevalence of BMD-defined osteoporosis compared to NHW women [21].

In clinical practice, FRAX fracture risk scores help discern those at higher fracture risk when low BMD is not in the osteoporosis range [22]. Because the incidence (and lifetime risk) of hip fracture among Asian women is much lower than NHW women, the US Asian FRAX calculator includes a 0.50 calibration factor when estimating ten-year probabilities of hip and major osteoporotic fractures [23]. A similar calibration factor (0.43) is used for US Black women [23], also due to much lower population fracture risk, but Black women have higher BMD and greater prevalence of obesity [21, 24, 25]. In 2024, the American Society for Bone

and Mineral Research (ASBMR) Task Force on Clinical Algorithms for Fracture Risk recommended using a single population US FRAX rather than separate race or ethnicity-specific US FRAX calculators [26], an approach supported by a Canadian study of 114,942 White, 485 Black, and 2816 Asian women where a single population FRAX (based on weighted US data) increased treatment qualification for non-White women [27]. This would address health equity concerns for Black women where FRAX calibration (based on population risk) could result in underestimation of fracture risk, especially if the lower population risk was related to higher BMD and other FRAX input factors [21]. Whether this approach optimizes care for Asian women remains uncertain. The current dialogue and constructive debate in a rapidly evolving field [26, 28–30] raise awareness of the complexities of fracture risk assessment for different racial and ethnic populations and underscore the need for more studies in diverse populations to inform future research and clinical practice. Current guidelines do not yet address the potential overtreatment of Asian women with osteoporosis based on BMD who are otherwise at low fracture risk [9, 21], and few studies have disaggregated the rapidly growing population of US Asian women [9]. Addressing the skeletal health of this population is an especially important health-care imperative for the Western US, where more than one-third of the US Asian population resides [31].

To address these crucial research gaps and inform efforts to optimize care for diverse US populations, this study characterizes BMD findings and examines the relationship of BMD T-score and hip fracture risk in a large population of Asian/PI women in a Northern California healthcare system. The differential risk of hip fracture among Asian compared to NHW women is also examined by ethnicity, accounting for T-score differences.

## Methods

### Setting and cohort

Kaiser Permanente Northern California (KPNC) is a large, integrated healthcare delivery system serving 4.4 million members in Northern California [32]. Due to California's large and growing Asian population, the KPNC membership includes 22.1% of Asian race, with PI members comprising an additional 0.8% [32]. For nearly three decades, older women have been targeted for BMD measurement, consistent with national quality measures for osteoporosis screening [33]. This observational study used KPNC data from Asian/PI and NHW women with BMD testing, followed up to five years for incident hip fracture. The study was approved by the KPNC Institutional Review Board with a waiver of informed consent.

The study cohort included 54,294 Asian/PI and 219,585 NHW women aged 60–89 years with FN-BMD measured on Hologic densitometers (2000–2019); the index date was based on the earliest accessible BMD data. Findings from KPNC population subsets have been previously reported [13, 20, 21, 34]. Self-reported race and ethnicity were based on health record-related data sources. Women with kidney disease on dialysis, kidney transplant, Paget's disease of the bone, osteogenesis imperfecta, multiple myeloma, and hypophosphatasia or phosphate wasting syndromes were excluded (collectively < 1% of the study population). Those who received prior osteoporosis therapy (bisphosphonate drugs, raloxifene, teriparatide, abaloparatide, denosumab, romosozumab) in the five years before the BMD date were also excluded (< 10%).

### Bone mineral density and other covariates

FN-BMD for all women was classified based on the T-score, representing the SD units from peak reference BMD [16] using the young adult NHW female reference (Hologic densitometer NHANES III reference, mean FN-BMD 0.849, SD 0.111 g/cm<sup>2</sup>) [35] for both NHW and Asian/PI women. Osteoporosis based on FN-BMD was defined by T-score  $\leq -2.5$ , low bone mass or osteopenia by T-score between  $-1$  and  $-2.5$ , and normal FN-BMD by T-score  $\geq -1.0$  [15, 19, 22]. Height and weight from BMD records were used to calculate body mass index (BMI, kg/m<sup>2</sup>). For 10.1% with missing BMI in BMD records, 6.0% had BMI calculated from data at the closest healthcare visit within two years and only 4.1% remained with missing BMI.

Because BMD results can lead to osteoporosis therapy, treatment was included as a time-updated covariate based on receipt of bisphosphonate drugs (alendronate, risedronate, ibandronate, zoledronic acid), raloxifene, denosumab, romosozumab, teriparatide, or abaloparatide, accounting for 25.6% of the cohort. Continued treatment was defined by having at least one prescription/refill every six months (or every 18 months for zoledronic acid) regardless of adherence level. Because most who initiated treatment received oral bisphosphonate drugs during the study period, alternative analyses were conducted to account for treatment based on adherence  $\geq 50\%$  each quarter (proportion of days covered [36]), excluding the small subset who received intravenous bisphosphonate or non-bisphosphonate osteoporosis therapy (3.0% of the overall cohort).

### Incident fracture ascertainment

Incident hip fractures up to five years following the index date were defined by principal/primary hospital diagnosis of femoral neck or pertrochanteric fracture (ICD-9-CM 820.0x, 820.20, 820.21, 820.8x; ICD-10-CM S72.0xxA, S72.1xxA),

or secondary hospital diagnosis with a procedure code for surgical hip fracture repair within 30 days, as previously described [11]. Fracture events associated with high energy trauma (ICD-9-CM E800-848, ICD-10-CM V00-V99) were not included. To ensure ascertainment of new hip fractures (since hip fracture may prompt BMD testing and follow-up fracture diagnoses may be linked to the initial event), incident hip fractures were identified based on absence of hip fracture hospitalization in the preceding 12 months. Only 0.4% of all hip fractures were excluded based on recent prior hip fracture hospitalization.

### Statistical analyses

Continuous variables were compared between subgroups using Student t-tests for normally distributed data and Wilcoxon tests for non-normally distributed data. Categorical variables were compared using Chi-square or Fisher exact tests. The bootstrap method (resampling with replacement) was used to adjust p-values for multiple pairwise comparisons considered simultaneously. Crude incidence of hip fracture during up to five years follow-up from index BMD date was estimated as events per 1000 person-years and stratified by baseline FN-BMD T-score ( $T \geq -1.0$ ,  $-1.0 > T > -2.0$ ,  $-2.0 \geq T > -3.0$ ,  $T \leq -3.0$ ) and age at BMD assessment (60–69, 70–79, and 80–89 years). Analyses were also stratified by race to allow for heterogeneity in the association between FN-BMD T-score and fracture across groups.

Multivariable Cox proportional hazards regression analysis was used to estimate the association between T-score and incident hip fracture outcome. T-score was included as a continuous variable after initially assessing linearity by categorizing BMD, where corresponding regression coefficients demonstrated a trend that was largely linear. T-score values were transformed by multiplying ( $-1$ ). To examine the T-score risk gradient for hip fracture in each demographic group, multivariable models were conducted within NHW and Asian subpopulations, including the four largest Asian subgroups. Models were adjusted for age at BMD (5-year strata) and time-updated osteoporosis therapy. In sensitivity analyses, osteoporosis therapy was not included as a covariate, but follow-up was censored at the fourth osteoporosis prescription/refill or at one year after zoledronic acid or denosumab. The interaction of T-score and race and ethnicity was also examined.

Multivariable Cox regression models were also conducted to compare the risk of hip fracture among Chinese, Filipina, Japanese, and South Asian women to NHW women. Models were conducted overall and separately within each low T-score category (low bone mass/osteopenia, osteoporosis), adjusting for age, transformed T-score, and time-updated osteoporosis therapy. Additional models further adjusted

for stature (height information obtained at or closest to the BMD date).

For all time-to-event analyses, person-time was censored at hip fracture outcome, membership cessation, death, five years follow-up, or July 1, 2024, whichever occurred first. Analyses were conducted using SAS statistical software, version 9.4 (SAS Institute; Cary, NC).

## Results

The analytic cohort included 54,294 Asian/PI women (mean age  $67.1 \pm 5.6$  years, 75.1% aged 60–69 years) and 219,585 NHW women (mean age  $68.3 \pm 6.3$  years, 67.6% aged 60–69 years) with measured FN-BMD at age 60–89 years in 2000–2019. The Asian/PI subset included 16,127 (29.7%)

Chinese, 17,279 (31.8%) Filipina, 4845 (8.9%) Japanese, 2538 (4.7%) South Asian, 1848 (3.4%) Vietnamese, 1551 (2.9%) Korean, 1048 (1.9%) Native Hawaiian or Pacific Islander (NHPI), 613 (1.1%) other Southeast Asian, 46 (0.1%) Central Asian, 1766 (3.3%) multi-ethnic Asian/PI, and 6633 (12.2%) with Asian/PI ethnic group unspecified. Compared to NHW women, Chinese (mean age  $66.7 \pm 5.7$  years), Filipina ( $67.3 \pm 5.4$  years), South Asian ( $66.9 \pm 5.2$  years), Vietnamese ( $66.1 \pm 5.1$  years), Korean ( $66.6 \pm 5.0$  years), and NHPI ( $67.5 \pm 4.8$  years) women were slightly younger, and Japanese women ( $69.2 \pm 6.7$  years) slightly older. Table 1 shows the distribution of FN-BMD and T-score by age decade among NHW and Asian/PI women and the seven largest Asian/PI subgroups. A larger proportion of Asian/PI (aggregate) women had osteoporosis ( $T \leq -2.5$ ) compared to NHW women (23.5% vs. 14.3%,

**Table 1** Femoral neck bone mineral density (BMD) T-score category by age group for non-Hispanic White (NHW) and Asian/Pacific Islander (PI) women

OVERALL Age 60–89	NHW 219,585	Asian/PI 54,294	Chinese 16,127	Filipina 17,279	Japanese 4845	S Asian 2538	Vietnam 1848	Korean 1551	NHPI 1048
Mean BMD	0.697	0.656*	0.653*	0.659*	0.645*	0.686*	0.633*	0.653*	0.707*
OP: $T \leq -2.5$	14.3%	23.5%*	23.4%*	22.8%*	26.7%*	17.4%*	30.5%*	23.3%*	12.6%
$T \geq -1$	35.1%	22.2%	21.2%	23.1%	20.1%	32.2%	16.3%	21.3%	38.9%
$-1 > T > -2$	34.7%	34.4%	34.6%	34.6%	32.8%	35.3%	30.6%	34.4%	34.1%
$-2 \geq T > -3$	25.1%	34.1%	35.1%	33.4%	34.7%	25.6%	40.8%	34.5%	22.7%
$T \leq -3$	5.1%	9.3%	9.1%	8.9%	12.4%	6.9%	12.3%	9.8%	4.3%
<b>Age 60–69</b>	148,450	40,769	12,440	12,849	2891	1969	1515	1200	774
Mean BMD	0.709	0.667*	0.663*	0.672*	0.667*	0.701*	0.643*	0.666*	0.715
OP: $T \leq -2.5$	10.9%	19.1%*	19.4%*	18.5%*	18.6%*	12.7%	26.8%*	18.2%*	10.9%
$T \geq -1$	38.5%	24.7%	23.3%	26.2%	24.2%	36.0%	17.8%	23.8%	42.1%
$-1 > T > -2$	35.7%	36.2%	36.4%	36.1%	36.3%	36.9%	32.5%	36.9%	34.8%
$-2 \geq T > -3$	22.7%	32.8%	34.1%	31.6%	33.4%	22.9%	40.1%	33.3%	19.9%
$T \leq -3$	3.2%	6.3%	6.3%	6.1%	6.2%	4.2%	9.6%	5.9%	3.2%
<b>Age 70–79</b>	54,529	11,182	2973	3761	1485	491	277	312	243
Mean BMD	0.684	0.629*	0.630*	0.630*	0.621*	0.644*	0.595*	0.611*	0.687
OP: $T \leq -2.5$	17.8%	33.3%*	33.0%*	32.3%*	35.4%*	31.6%*	44.4%*	41.0%*	17.3%
$T \geq -1$	31.1%	16.0%	15.6%	15.3%	15.5%	21.2%	10.5%	13.5%	31.7%
$-1 > T > -2$	34.0%	30.7%	30.7%	31.8%	29.6%	31.2%	23.1%	26.3%	30.9%
$-2 \geq T > -3$	28.0%	37.7%	38.3%	38.7%	35.8%	33.2%	44.4%	37.5%	30.9%
$T \leq -3$	6.9%	15.8%	15.4%	14.3%	19.1%	14.5%	22.0%	22.8%	6.6%
<b>Age 80–89</b>	16,606	2343	714	669	469	78	56	39	31
Mean BMD	0.633	0.579*	0.577*	0.573*	0.584*	0.586*	0.552*	0.580*	0.656
OP: $T \leq -2.5$	33.4%	51.5%*	54.1%*	53.2%*	49.5%*	46.2%	60.7%*	41.0%	19.4%
$T \geq -1$	18.5%	8.6%	9.1%	7.3%	9.6%	6.4%	3.6%	7.7%	16.1%
$-1 > T > -2$	28.6%	20.6%	19.3%	19.9%	21.5%	23.1%	16.1%	20.5%	41.9%
$-2 \geq T > -3$	36.5%	39.4%	38.7%	39.5%	39.0%	44.9%	42.9%	46.2%	29.0%
$T \leq -3$	16.3%	31.5%	32.9%	33.3%	29.9%	25.6%	37.5%	25.6%	12.9%

S Asian, South Asian; Vietnam, Vietnamese; NHPI, Native Hawaiian/PI; OP, osteoporosis by BMD ( $T \leq -2.5$ )

Asian/PI also included 613 other Southeast Asian, 46 Central Asian, 1766 multiethnic Asian, 6633 ethnicity unspecified

\* $p < 0.05$  vs NHW, accounting for multiple pairwise comparisons (Asian/PI subgroups), for mean BMD and OP

$p < 0.001$ ), but when examined by ethnicity or subgroup, osteoporosis prevalence ranged from 30.5% (Vietnamese), 26.7% (Japanese), 22–23% (Chinese, Filipina, Korean), and 17.4% (South Asian) to 12.6% (NHPI), all significantly different compared to NHW (14.3%) except for NHPI women. Findings among South Asian women were largely driven by the vast majority (77.6%) aged 60–69 years, where only 12.7% had osteoporosis, a proportion not significantly different from that of NHW counterparts (10.9%). These data contrast with the much smaller subset of South Asian women aged 70–79 years, of whom 31.6% had osteoporosis, much higher than their NHW counterparts (17.8%). Across age decades, BMD was significantly lower for each Asian ethnic group compared to NHW women, but NHPI and NHW women were similar.

Table 2 shows the anthropometric findings among the subset of NHW (96%) and Asian/PI (91–99%) women with height, weight, and BMI data. In general, stature was lower across all Asian/PI subgroups compared to NHW, especially Vietnamese, Filipina, and Japanese women. Mean

BMI levels and the proportion with obesity varied. Among women aged 60–69 and 70–79 years, comprising 60–78% and 15–30% of each racial and ethnic group, respectively, only 5–7% of Chinese, Vietnamese, and Korean women, 8–12% of Japanese women, and 14–15% of Filipina women had obesity, compared to 30–32% of NHW women. More South Asian women (23–24%) aged 60–69 and 70–79 years had obesity, still lower than NHW women, whereas 39% of NHPI women had obesity, higher than NHW women. Among the small subset of women aged 80–89 years, obesity prevalence remained lower for Chinese, Japanese, Vietnamese, and Korean women (3–6%) and Filipina (9.8%) compared to NHW women (20.0%) whereas South Asian women did not differ significantly (14.3%) and NHPI women had much higher prevalence (48.4%).

During up to 5 years follow-up, 3335 hip fractures (1.5%) occurred among 219,585 NHW women (3.39 per 1000 person-years) and 252 hip fractures (0.5%) occurred among 54,294 Asian/PI women (1.03 per 1000 person-years). Table 3 shows the crude incidence (events per

**Table 2** Anthropometric findings for non-Hispanic White (NHW) and Asian/Pacific Islander (PI) women by age group and race and ethnicity among those with complete data for height and weight

OVERALL	NHW	Chinese	Filipina	Japanese	S Asian	Vietnam	Korean	NHPI
Age 60–89	211,148	14,928	16,437	4414	2500	1813	1488	1042
% of cohort	96.2%	92.6%	95.1%	91.1%	98.5%	98.1%	95.9%	99.4%
Height (cm)	163 ± 7	157 ± 6*	155 ± 6*	155 ± 6*	157 ± 6*	154 ± 6*	157 ± 5*	158 ± 7*
Weight (kg)	74 ± 17	58 ± 10*	62 ± 11*	58 ± 11*	66 ± 12*	56 ± 9*	58 ± 9*	73 ± 18
BMI (kg/m <sup>2</sup> )	27.9 ± 6.1	23.8 ± 3.8*	26.0 ± 4.2*	24.4 ± 4.4*	26.9 ± 4.6*	23.6 ± 3.7*	23.8 ± 3.4*	29.2 ± 6.1*
BMI ≥ 30	30.5%	6.1%*	14.9%*	10.2%*	23.2%*	5.3%*	5.2%*	39.1%*
<b>Age 60–69</b>	143,663	11,712	12,258	2693	1939	1485	1148	769
% of cohort	96.8%	94.2%	95.4%	93.2%	98.5%	98.0%	95.7%	99.4%
Height (cm)	163 ± 7	157 ± 5*	155 ± 5*	156 ± 5*	157 ± 6*	154 ± 5*	157 ± 5*	158 ± 7*
Weight (kg)	75 ± 17	59 ± 10*	63 ± 11*	60 ± 12*	66 ± 12*	56 ± 9*	59 ± 9*	73 ± 18*
BMI (kg/m <sup>2</sup> )	28.1 ± 6.3	23.8 ± 3.8*	26.1 ± 4.2*	24.7 ± 4.5*	26.9 ± 4.5*	23.6 ± 3.6*	23.8 ± 3.3*	29.2 ± 6.1*
BMI ≥ 30	31.8%	6.1%*	15.3%*	11.6%*	23.3%*	5.1%*	4.9%*	38.8%*
<b>Age 70–79</b>	51,808	2568	3536	1302	484	272	302	242
% of cohort	95.0%	86.4%	94.0%	87.7%	98.6%	98.2%	96.8%	99.6%
Height (cm)	162 ± 7	156 ± 5*	154 ± 6*	154 ± 5*	156 ± 6*	152 ± 6*	155 ± 6*	157 ± 7*
Weight (kg)	73 ± 16	58 ± 10*	61 ± 11*	57 ± 11*	65 ± 13*	55 ± 9*	58 ± 9*	73 ± 17
BMI (kg/m <sup>2</sup> )	27.8 ± 5.9	24.1 ± 3.9*	25.8 ± 4.2*	24.2 ± 4.3*	27.1 ± 5.0	23.6 ± 4.0*	24.0 ± 3.7*	29.3 ± 6.0*
BMI ≥ 30	30.2%	6.2%*	14.3%*	8.3%*	24.0%*	7.0%*	6.3%*	38.8%*
<b>Age 80–89</b>	15,677	648	643	419	77	56	38	31
% of cohort	94.4%	90.8%	96.1%	89.3%	98.7%	100%	97.4%	100%
Height (cm)	160 ± 7	154 ± 6*	152 ± 6*	152 ± 5*	154 ± 7*	151 ± 6*	154 ± 6*	154 ± 8*
Weight (kg)	66 ± 13	55 ± 9*	57 ± 10*	53 ± 10*	59 ± 11*	53 ± 10*	54 ± 9*	71 ± 17
BMI (kg/m <sup>2</sup> )	26.1 ± 5.0	23.3 ± 3.7*	24.7 ± 4.0*	23.3 ± 3.9*	25.0 ± 4.4	23.5 ± 3.6*	22.9 ± 3.6*	29.5 ± 5.7*
BMI ≥ 30	20.0%	4.9%*	9.8%*	6.4%*	14.3%	3.6%*	5.3%	48.4%*

S Asian, South Asian; Vietnam, Vietnamese; NHPI, Native Hawaiian or Pacific Islander

The closest height and weight (at BMD measurement in 89.9% of the cohort or within 2 years of the BMD date for an additional 6.0% of the cohort) was used to calculate BMI (4.1% were missing height or weight)

\* $p < 0.05$  vs NHW, accounting for multiple pairwise comparisons (Asian/PI subgroups) for all specified measures

**Table 3** Hip fracture incidence per 1000 person-years (95% confidence intervals) during five years follow-up among Asian/Pacific Islander (PI) and non-Hispanic White women by age group and T-score

	Age 60–69 years	Age 70–79 years	Age 80–89 years
T-score $\geq -1$			
Asian/PI	0.13 (0.06–0.29)	0.49 (0.18–1.31)	2.26 (0.57–9.03)
Non-Hispanic White	0.58 (0.50–0.68)	1.56 (1.30–1.86)	4.94 (3.88–6.30)
$-1 > \text{T-score} > -2$			
Asian/PI	0.21 (0.12–0.35)	1.16 (0.73–1.83)	4.35 (2.26–8.35)
Non-Hispanic White	1.26 (1.12–1.41)	3.95 (3.55–4.40)	10.7 (9.39–12.3)
$-2 \geq \text{T-score} > -3$			
Asian/PI	0.54 (0.38–0.76)	1.82 (1.31–2.54)	5.42 (3.57–8.23)
Non-Hispanic White	2.51 (2.27–2.78)	8.26 (7.60–8.97)	18.0 (16.4–19.7)
T-score $\leq -3$			
Asian/PI	2.19 (1.48–3.23)	5.07 (3.70–6.94)	15.6 (11.7–20.8)
Non-Hispanic White	7.29 (6.20–8.56)	16.8 (14.9–19.0)	35.7 (32.2–39.7)

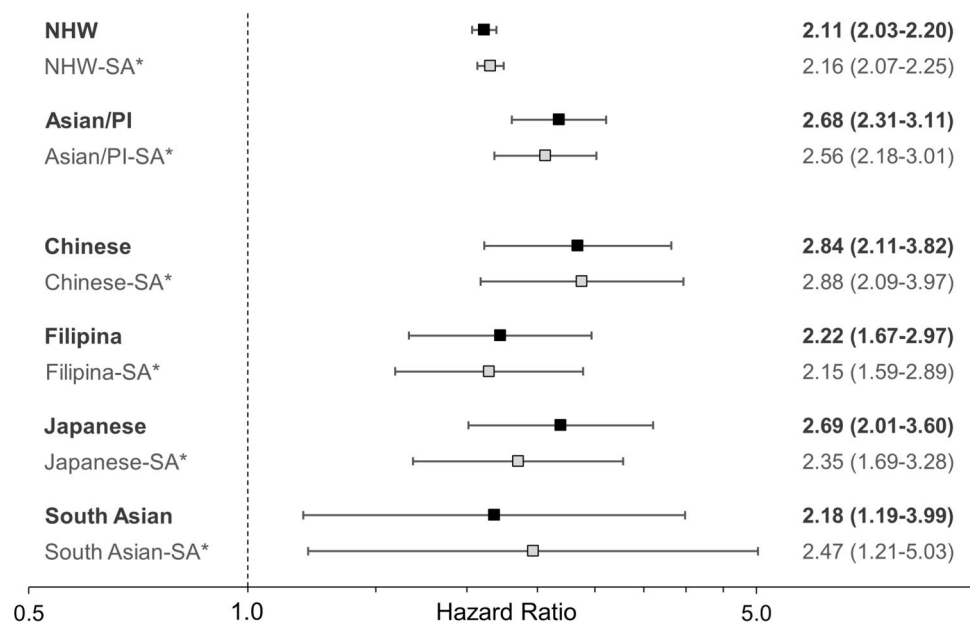
1000 person-years) of hip fracture, stratified by age decade and FN-BMD T-score. Within each age and T-score category, hip fracture incidence was at least two to three times higher for NHW compared to Asian/PI women. For both groups, hip fracture incidence increased with age and lower T-score strata. In sensitivity analyses (follow-up censored at osteoporosis treatment continuation), 2746 hip fractures (1.3%) occurred among 219,585 NHW women (3.10 per 1000 person-years), and 196 hip fractures (0.4%) occurred among 54,294 Asian/PI women (0.96 per 1000 person-years).

In separate multivariable Cox regression models conducted within NHW and Asian/PI subsets, each one-unit reduction in BMD T-score was associated with an adjusted hazard ratio (aHR) for hip fracture of 2.11 [95% confidence interval 2.03–2.20] among NHW women and 2.68 [2.31–3.11] among Asian/PI women (Fig. 1). These models were adjusted for age at BMD and accounted for initiation and continuation of osteoporosis therapy as a time-updated covariate. Findings were similar in sensitivity analyses, where follow-up was censored at osteoporosis treatment continuation (Fig. 1) and in additional analyses that defined time-updated osteoporosis therapy (with an oral bisphosphonate drug) based on adherence  $\geq 50\%$  (Fig. 1 footnote). Among the four largest Asian subgroups, the estimated aHRs associated with each one-unit decline in FN-BMD T-score were 2.84 [2.11–3.82] for Chinese, 2.22 [1.67–2.97] for Filipina, 2.69 [2.01–3.60] for Japanese, and 2.18 [1.19–3.99] for South Asian women. Vietnamese, Korean, and NHPI women were not examined due to their much smaller sample sizes and low number of events. An interaction between T-score and race/ethnicity was observed when race and ethnicity was categorized as NHW and Asian/PI aggregate ( $p < 0.01$ ) in combined analyses, but when the four Asian subgroups were classified, the interaction term was significant only for Chinese ( $p = 0.03$ ) and not Filipino ( $p = 0.92$ ), Japanese ( $p = 0.10$ ), or South Asian ( $p = 0.80$ ) populations.

Figure 2a shows the comparison of hip fracture risk among the four largest Asian subgroups (Chinese, Filipina, Japanese, South Asian) to NHW women, including findings stratified by low FN-BMD T-score category. Adjusting for age and T-score, the risk of hip fracture remained much lower for Asian compared to NHW women, especially among Chinese (aHRs 0.2–0.3) and Filipina (aHR 0.2) women, with reduced risks for Japanese women (aHRs 0.4–0.6) and South Asian women (aHRs 0.4–0.5) as well. While some attenuation was observed after additionally adjusting for stature (Fig. 2b), the overall risk of hip fracture remained lower among Asian compared to NHW women.

## Discussion

This is the first population study to report FN-BMD findings across seven disaggregated subgroups of Asian/PI women spanning ages 60–89 years and expand on our prior report of Chinese, Filipina, and Japanese women [13]. By age decade, FN-BMD was lower, and osteoporosis prevalence was generally higher among Chinese, Filipina, Japanese, South Asian, Vietnamese, and Korean women when compared to NHW women, whereas NHPI and NHW women were similar. These findings support previous observations among Chinese, Filipina, and Japanese women within the same KPNC source population, extending into earlier time periods [13, 20, 34]. When the association of FN-BMD T-score and risk of hip fracture was examined for the four largest Asian groups, each one-unit reduction in T-score was associated with 2.2- to 2.8-fold increased risk of hip fracture, with heterogeneity by ethnicity. The risk gradients were similar to or somewhat larger than the 2.1-fold increased risk observed for NHW women in the same source population. However, overall and among women with low bone mass and osteoporosis, Asian women had lower risk of hip fracture when compared to NHW women, 70–80% lower for Chinese and



**Fig. 1** Multivariable association of femoral neck T-score and hip fracture risk among non-Hispanic White (NHW) women, Asian/Pacific Islander (PI) women, and Asian subgroups aged 60–89 years. Multivariable Cox regression models were conducted within each specified race and ethnicity group (219,585 NHW, 54,294 Asian/PI and the four largest Asian groups: 16,127 Chinese, 17,279 Filipina, 4845 Japanese, and 2538 South Asian). Models included transformed T-score (multiplied by  $-1$ ) as the primary predictor and incident hip fracture as the outcome, with index age (in 5-year categories) and time-updated osteoporosis therapy as covariates. \*In sensitivity anal-

yses, designated by suffix SA (second row, gray), follow-up was censored with continued osteoporosis therapy, which was not included as a covariate (see *Statistical Analyses*). Hazard ratios from alternative analyses that accounted for time-updated osteoporosis treatment based on oral bisphosphonate adherence  $\geq 50\%$  were similar (these analyses excluded those on other therapy): NHW 2.07 (1.99–2.16), Asian/PI 2.59 (2.22–3.01), Chinese 2.94 (2.18–3.96), Filipina 2.12 (1.59–2.83), Japanese 2.46 (1.83–3.31), and South Asian 2.65 (1.46–4.81)

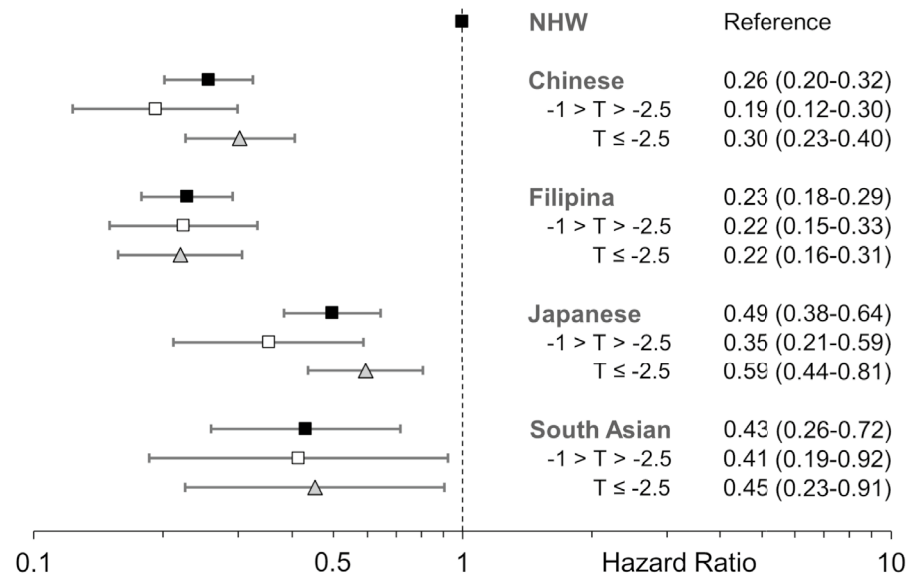
Filipina women and 40–60% lower for Japanese and South Asian women, depending on T-score. Even after accounting for height, Chinese and Filipina women still had at least 60% lower hip fracture risk. These findings suggest that the absolute risk of hip fracture at each level of FN-BMD differs between Asian and NHW women.

In multivariable analyses that accounted for age and BMD T-score, the NORA study also found that Asian women had lower (peripheral) BMD, but nearly 70% lower risk of fracture (hip, spine, wrist, or ribs) [8]. While the Asian population in the NORA study included only 1912 women (44% age  $\leq 60$  years) and peripheral BMD was measured at any one of three sites with four different instrument types, our study examined FN-BMD measured by Hologic densitometers among 16,127 Chinese, 17,279 Filipina, 4845 Japanese, and 2538 South Asian women aged 60–89 years and captured hip fracture events using comprehensive hospital records and outside claims data. More broadly, our findings raise considerations for the BMD T-score and determination of the T-score treatment threshold for Asian women, both currently based on population data from NHW women, which could result in overtreatment of Asian women who are otherwise at lower absolute risk for hip fracture [9, 20, 21].

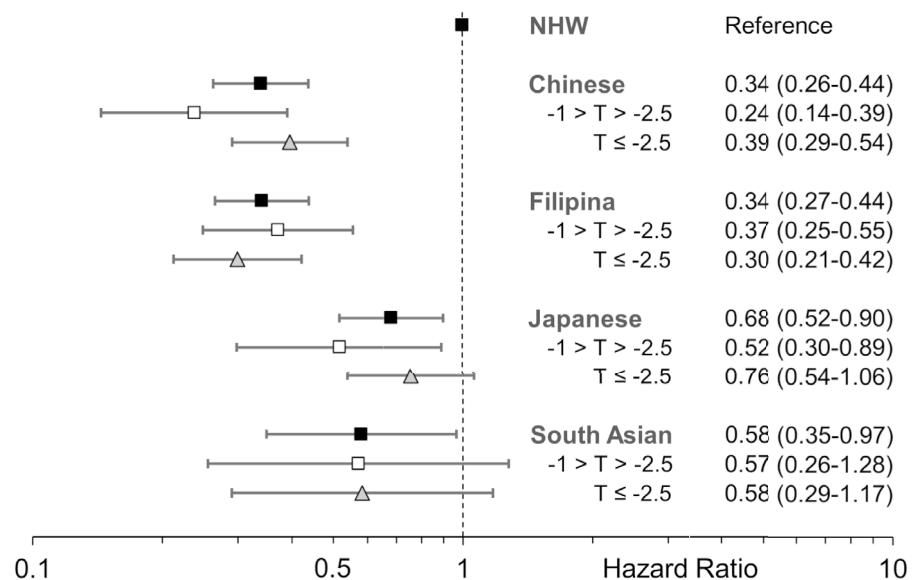
As such, some have advocated that osteoporosis prevalence of an ethnic population should be based on reference BMD data and a T-score threshold validated for that population [37]. While our findings do not address calculated fracture risk scores such as FRAX, they confirm a lower risk of hip fracture in Asian women independent of T-score. Indeed, the US Asian FRAX uses a calibration factor to account for the lower population risk of hip fracture among Asian adults [9, 23], an adjustment perhaps more relevant when the FRAX calculation includes BMD. More broadly, a single population FRAX without race calibration has been proposed [26, 27], but the accuracy of these two different FRAX-based approaches to estimating fracture risk for US Asian women is unknown. In the interim, reporting a range of fracture risk scores from NHW, Asian, Black, and Hispanic US FRAX calculators, as proposed by an ASBMR Task Force [26] may help support shared decision-making for all patients. However, the challenge that remains in clinical practice is the lack of evidence-based guidance for primary prevention of fracture among the rapidly growing population of US Asian women undergoing osteoporosis screening [9, 21]. Others have emphasized that a diagnostic T-score threshold is not necessarily equivalent to an intervention threshold [29, 38,

**Fig. 2** Adjusted risk of hip fracture for Chinese, Filipina, Japanese, and South Asian women compared to non-Hispanic White (NHW) women aged 60–89 years. Models compare Asian subgroups versus NHW (referent) overall and within each low T-score category

**(a) Risk of hip fracture, adjusted for age, T-score, and osteoporosis therapy**



**(b) Risk of hip fracture, adjusted for age, T-score, osteoporosis therapy, and stature**



[39], a consideration that has also not been directly addressed in current treatment guidelines.

For over two decades, the Asian and NHPI populations have grown within the US [31, 40], with doubling of the Asian population [31] and a faster growing Asian Indian population that has nearly tripled [41]. In 2020, Asian Indian was the largest ‘Asian alone’ population in the US whereas Chinese remained the largest ‘Asian alone and in any combination’ group [42]. Our cohort of women with BMD measured in 2000–2019 at age 60–89 years, reflects a vast majority who were likely first-generation immigrants [43]. As such, we recognize there may be potential age-cohort effects

[13] that could evolve as more US Asian adults are native-born or have longer residence in the US. For instance, a growing generation of younger postmenopausal South Asian women with higher BMD, BMI, and stature than their predecessors [34] were identified, indicating that some US Asian populations have changed over time, potentially influenced by acculturation, nativity, urbanization, and other social or biological factors.

This study has some limitations. First, these data are derived from women undergoing BMD testing and may not reflect broader populations without access to health-care or an indication for BMD testing. However, KPNC has

promoted routine BMD screening for older postmenopausal women for nearly three decades and universal screening for osteoporosis has been a widely established recommendation and quality metric for US women aged 65 years and older [33]. Second, we accounted for osteoporosis treatment initiation and continuation after BMD testing, including at  $\geq 50\%$  adherence, but did not examine adherence at other levels which may differ by race and ethnicity or osteoporosis medication type. Most were bisphosphonate drugs, a recommended first-line therapy [44]. Third, while we conducted analyses by ethnicity, we acknowledge there is within group heterogeneity, although differences compared to NHW women are larger. Fourth, areal BMD by dual energy x-ray absorptiometry is influenced by bone size and there was some attenuation of Asian-NHW differences in hip fracture risk after height adjustment. Finally, we did not assess other factors such as fall risk [45] that might contribute to group differences in hip fracture risk.

Our study has several strengths. We examined very large numbers of Chinese and Filipina women, who are among the largest Asian subgroups in the US and in California, the state where 34% of the US Chinese and 39% of the US Filipino population reside [42]. To our knowledge, this report is the first to characterize the BMD-hip fracture relationship among separate populations of Chinese, Filipina, Japanese, and South Asian women and to examine their risk of hip fracture compared to NHW women accounting for differences in FN-BMD T-score (as well as stature). We provide contemporary BMD data from NHPI women, where osteoporosis prevalence was similar to NHW counterparts, but BMI was higher. Future studies should examine fracture outcomes in this understudied population.

## Conclusion/summary

In summary, this study demonstrates that compared with NHW women, adjusted hip fracture risk remains lower for Chinese, Filipino, Japanese, and South Asian women (overall and within low FN-BMD T-score category), although ethnic variation was observed. Similar to NHW women, hip fracture risk among these Asian subgroups increased at least two-fold for each unit reduction in FN-BMD T-score, with potentially larger gradient of risk for selected populations.

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**Data Availability** The electronic health record data used in this study are not publicly available. De-identified aggregate data generated during the current study are available from the corresponding author on reasonable request and with respective institutional approvals.

## Declarations

**Conflict of interest** Joan Lo, Malini Chandra, Wei Yang, Jeanne Darbinian, Amber Wheeler, Nancy Gordon, and Catherine Lee have no conflicts of interest to report.

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# T-score, stature, and fracture risk interpretation in Asian women

Chao-Chun Huang<sup>1,2</sup>

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To the Editor:

We commend Lo et al. for their important contribution to understanding hip fracture risk among Asian women [1]. Their large, disaggregated cohort provides robust evidence regarding a clinically meaningful misalignment between BMD-defined osteoporosis prevalence and observed fracture incidence. We offer this comment to support the interpretation of these findings in clinical decision-making.

Lo et al. reported that Asian/Pacific Islander women had a substantially higher prevalence of osteoporosis based on T-score criteria (23.5%) compared with non-Hispanic White (NHW) women (14.3%), yet experienced a 70% lower incidence of hip fracture (1.03 vs. 3.39 per 1000 person-years, respectively).

Importantly, the authors demonstrated that this lower fracture risk persisted after adjusting for age and T-score (adjusted HR 0.2–0.3), but the difference was *attenuated* when adjusted for stature. This attenuation suggests that areal BMD (aBMD), a two-dimensional measure, may be influenced by bone size, leading to lower T-scores in individuals with smaller skeletal geometry [2]. This size-associated artifact may influence the interpretation of osteoporosis prevalence in some Asian populations without a corresponding increase in fracture risk.

The clinical implications noted by Lo et al. are highly relevant. The authors caution that reliance solely on T-scores may lead to potential overtreatment among Asian women who are otherwise at low absolute fracture risk. This is supported by prior research showing that while 84.8% of NHW women with  $T \leq -2.5$  meet FRAX-based treatment thresholds, only 34.5% of Asian women at the same T-score do [3].

These findings highlight the importance of distinguishing between diagnostic thresholds (used to classify bone density) and intervention thresholds (based on estimated fracture probability).

This work contributes meaningfully to ongoing discussions regarding "race-neutral" fracture risk prediction models [4]. Rather than supporting broad recalibration of diagnostic definitions, the data emphasize the need to integrate clinical decision-making with individualized absolute risk assessment. In practice, this means that treatment should prioritize patients with elevated fracture probability rather than those with low T-scores alone [5]. We share the authors' emphasis on aligning treatment decisions with absolute fracture risk.

**Authors contributions** Chao-Chun Huang: Conceptualization, Writing—Original Draft, Writing—Review & Editing.

**Data availability** Not applicable.

## Declarations

**Ethics approval** This article does not contain any studies with human participants or animals performed by any of the authors.

**Consent to participate** Not applicable.

**Consent for publication** Not applicable.

**Conflict of interest** The authors declare no conflict of interest.

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## Comment on: The association of bone density and hip fracture risk among Asian women

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Dear Editor,

We are writing to provide commentary on the recent article by Lo et al., titled “The association of bone density and hip fracture risk among Asian women,” published in *Osteoporosis International* [1]. This large-scale retrospective cohort study systematically investigates the relationship between femoral neck bone mineral density (BMD) and hip fracture risk across diverse Asian ethnic subgroups as well as non-Hispanic White women. The authors report that despite lower BMD and higher prevalence of osteoporosis, Asian women exhibit a significantly lower risk of hip fracture, with a T-score-based risk gradient comparable to or even exceeding that observed in White women. These findings offer valuable insights into ethnicity-specific approaches to fracture risk assessment; however, several methodological considerations merit further discussion to enhance the interpretation and generalizability of the results.

First, with regard to missing body mass index (BMI) data, the authors imputed 6.0% of missing values using clinical measurements collected within 2 years, while leaving the remaining 4.1% unimputed. This partial imputation strategy may introduce selection bias and underestimate variability. Employing more rigorous methods such as multiple imputation for continuous variables would better account for uncertainty in the missing data and reduce potential bias [2].

Second, although the analysis adjusted for age, T-score, and osteoporosis treatment using a multivariate Cox proportional hazards model, several important

covariates—including nutritional factors (e.g., calcium and vitamin D intake), physical activity levels (particularly weight-bearing exercise), socioeconomic status, and bone geometry—were neither measured nor included in the model. These factors may vary systematically across racial and ethnic groups and could partially explain the observed differences in hip fracture risk [3]. Therefore, caution should be exercised when interpreting the findings, emphasizing associations rather than causal relationships.

Third, the study classified 12.2% of Asian women with unspecified ethnic background as a distinct group in the primary analysis but excluded them from subgroup analyses. This approach may obscure meaningful heterogeneity within the broader Asian category and potentially bias overall effect estimates due to unclear representativeness of this subgroup. Conducting sensitivity analyses—such as reassigning these individuals to major ethnic subgroups based on population distributions or excluding them entirely—would help assess the robustness of the reported findings.

Finally, data collection spanned from 2000 to 2019. Over this nearly two-decade period, substantial changes occurred in osteoporosis diagnostic criteria, screening recommendations, treatment guidelines, and medication use. Such temporal trends may act as confounding variables. To address this, calendar year or enrollment period could be incorporated as time-varying covariates or stratification factors in the marginal structural model (MSM) to adjust for potential secular trends [4].

In conclusion, Lo and colleagues present compelling evidence on ethnic variations in the BMD–hip fracture risk relationship, derived from a large and well-characterized population. We commend the authors for their comprehensive subgroup evaluations. Addressing the aforementioned methodological aspects—specifically, applying multiple imputation for missing data, accounting

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for potential unmeasured confounders, conducting sensitivity analyses regarding ethnic classification, and adjusting for temporal changes—would further strengthen the validity and external applicability of these important findings across diverse populations.

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**Data availability** Not applicable.

## Declarations

**Ethical approval** Not applicable.

**Conflict of interest** The authors declare no competing interests.

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