



Conversion of measured bone mineral density T-scores of Chinese women to equivalent Caucasian women's T-score values

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The prevalence of densitometric osteoporosis (DOP) in a specific population should be in proportion to its relative risk of fragility fracture (FF), using Caucasian data as a reference (1,2). While the cutpoint T-score value of -2.5 for defining DOP based on dual-energy X-ray absorptiometry (DXA) measurements of hip and spine bone mineral density (BMD) was developed using Caucasian female data, the application of the same cutpoint value of -2.5 to Caucasian men and Black Americans appears reasonable (3). However, the application of the same cutpoint value of -2.5 to East Asian populations leads to the current dilemma that “*the prevalence of DOP for East Asians is high (even when an East Asian BMD reference range is applied), but the osteoporotic fracture incidence is low*” (4-7). We have proposed that directly measured BMD T-scores of Chinese women should be converted (or ‘normalised’) to equivalent Caucasian women's T-score values (8). In this letter we propose provisional formulas for such a conversion.

It is well noted that the use of a Caucasian BMD reference database in East Asians will lead to systematically lower T-scores and hence increase the prevalence of DOP (6,9). The use of Asian-specific BMD reference data was recommended by the International Society for Clinical Densitometry Asia-Pacific Region 2010 Consensus (10) and recently further argued for by us (6). Thus, all the discussions in this letter deal with results derived using T-scores calculated with Chinese (or East Asian) local BMD reference data.

We analysed multiple published BMD databases for Caucasian and Chinese populations and conducted statistical modelling to find more suitable threshold T-scores for older Chinese (5). We used a T-score threshold of ≤ -2.5 and its equivalent BMD cutpoints to estimate DOP prevalence for Caucasians assuming a Gaussian distribution; then, assuming that, for consistency with data on fracture incidence, the prevalence of DOP amongst Chinese is half that of Caucasians (11-25), data from BMD databases for Chinese were analysed to estimate revised BMD thresholds and their corresponding T-scores consistent with the reduced prevalence (5). For most Chinese female BMD reference databases, our proposed osteoporosis cutpoint T-score_{neck} (femoral neck T-score) differs by -0.2 to -0.25 from the conventional value of -2.5 (5). According to our estimation for Chinese women, for the local BMD reference database of Lynn *et al.* (26), we found osteoporosis cutpoint values for T-score_{neck}, T-score_{hip} (total hip T-score), and T-score_{spine} (lumbar spine T-score) of -2.7 , -2.6 , and -3.7 , respectively (5).

In addition to the analysis of multiple Caucasian BMD reference databases from Europe, North America, and Australia, we also evaluated multiple databases using different DXA manufacturers' scanners from East Asia and found similar trends requiring the threshold T-score_{neck}, T-score_{hip}, and T-score_{spine} for East Asians to be adjusted to a lower value than the conventional cutpoint of ≤ -2.5 (5). For the Japanese female BMD reference database of Iki

Corrections have been made after the initial online publishing of this letter.

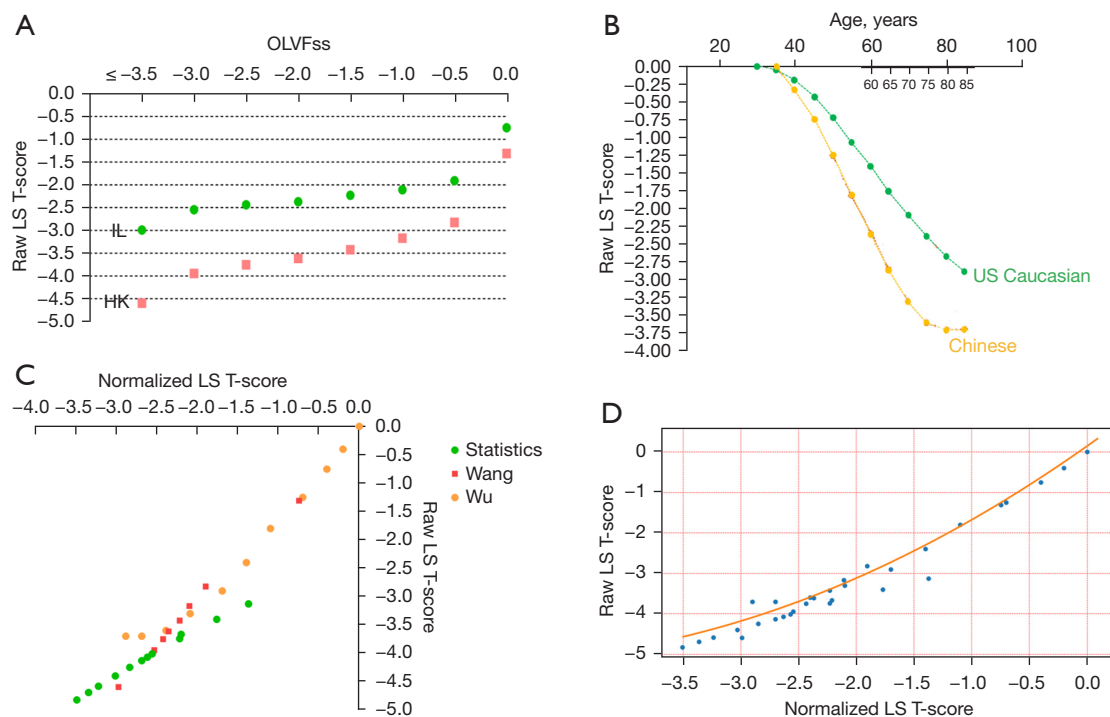


Figure 1 Conversion of raw LS T-score to normalised T-score for Chinese women. (A) For each OLVFss value, the corresponding raw LS T-scores of Hong Kong Chinese women and Italian Caucasian women. Data from Wáng *et al.* (31,32). (B) Decline of the population mean raw LS T-score of Chinese women and US Caucasian women during natural aging. Data from Wu *et al.* (30). (C) Relationship between raw LS T-scores and normalised LS T-scores (i.e., values equivalent to Caucasian T-scores) for Chinese women. Data based on those of (A) (red dots) and (B) (yellow dots) and also the statistical modeling of Wáng and Xiao (5) for Hong Kong Chinese women (green dots). (D) All the data in (C) are used to fit a quadratic relationship between the raw LS T-scores and normalised LS T-scores. In addition, it is enforced that when raw LS T-score = -3.7 then normalized LS T-score = -2.5. OLVFss, osteoporotic-like vertebral fracture sum score; LS, lumbar spine; IL, Italian; HK, Hong Kong.

et al. (27), we found the osteoporosis cutpoint values for $T\text{-score}_{\text{neck}}$, $T\text{-score}_{\text{hip}}$, and $T\text{-score}_{\text{spine}}$ to be -2.75, -3.0, and -3.9 respectively (5). Note that, we recommend a larger downward adjustment for $T\text{-score}_{\text{spine}}$ than for $T\text{-score}_{\text{neck}}$ and $T\text{-score}_{\text{hip}}$ ($T\text{-score}_{\text{neck}}$ and $T\text{-score}_{\text{hip}}$ are highly correlated). This is consistent with the observation that, following natural aging, $T\text{-score}_{\text{spine}}$ and $T\text{-score}_{\text{neck}}$ (and $T\text{-score}_{\text{hip}}$) decline with a similar rate among Caucasian women (2,24,28-30), while $T\text{-score}_{\text{spine}}$ declines at a much faster rate than $T\text{-score}_{\text{neck}}$ (and $T\text{-score}_{\text{hip}}$) among East Asian women (8,24,27,30). The $T\text{-score}_{\text{neck}}$ is adjusted downward by only -0.2 to -0.25. For individual patients, the clinical implication of such a $T\text{-score}_{\text{neck}}$ adjustment is not substantial; however, the impact on epidemiological studies will not be trivial.

Our proposal to convert raw (i.e., directly measured, with a Chinese women's BMD reference database) $T\text{-score}_{\text{spine}}$ to

normalised $T\text{-score}_{\text{spine}}$ is illustrated in *Figure 1*. *Figure 1A* shows our empirical data based on Hong Kong Chinese and Italian Caucasians. Spine radiograph osteoporotic-like vertebral fracture (OLVF) was considered as a relevant surrogate endpoint. For each vertebra, a score of 0, -0.5, -1, -1.5, -2, -2.5, and -3 is assigned for no OLVF or an OLVF of $<1/5$, $\geq 1/5-1/4$, $\geq 1/4-1/3$, $\geq 1/3-2/5$, $\geq 2/5-2/3$, and $\geq 2/3$ vertebral height loss, respectively. The OLVF sum score (OLVFss) was calculated by summing up the scores for vertebrae T1 to L5. Counting each study case, the OLVFss, $T\text{-score}_{\text{neck}}$ and $T\text{-score}_{\text{spine}}$ were all independently ranked from the smallest value to the largest [for details, see (31,32)]. In this way, it was noted that, when OLVFss = -2.5, $T\text{-score}_{\text{neck}}$ was -2.60 for Italians and -2.77 for Chinese, and $T\text{-score}_{\text{spine}}$ was -2.44 for Italians and -3.75 for Chinese. These data support our statistical modeling results (5). *Figure 1B* illustrates that, following natural

aging, the decline of the population mean raw T-score_{spine} of Chinese women is faster than that of US Caucasian women [data from Wu *et al.* (30)]. Plotting the data from *Figure 1A* and *Figure 1B* together shows good agreement (*Figure 1C*), supporting the reliability of the data. Data from *Figure 1A* and *Figure 1B*, together with some statistical modeling results around a raw T-score_{spine} = -2.5 reported by Wáng and Xiao (5) for Hong Kong Chinese women, were used to fit a quadratic relationship between the raw T-score_{spine} and the normalised T-score_{spine}. In addition, we enforced when raw T-score_{spine} = -3.7 then normalized T-score_{spine} = -2.5 (*Figure 1D*), and final conversion formula for T-score_{spine} is:

$$\text{Normalized spine } T_score = \frac{-2.013 + \sqrt{3.9438 + 0.7616 * (\text{raw spine } T_score)}}{0.3808} \quad [1]$$

To further support our argument that the osteoporosis cutpoint T-score_{neck} value among East Asian populations should be lower than the conventional value of ≤ -2.5 , we conducted a literature analysis (33). For hip FF patients, there is a trend for East Asian women to have a lower T-score_{neck} and T-score_{hip} than Caucasians. If we assume that hip FF in East Asians and Caucasians is equally relevant as a clinical endpoint for osteoporosis, then the results of this literature analysis suggest that a 'lower' T-score in East Asian women corresponds to a 'higher' T-score in Caucasian women, supporting our argument that to achieve the equivalent of a Caucasian T-score of -2.5, the corresponding T-score for East Asian women should be lower. Our proposal to convert raw (directly measured, with a Chinese women's BMD reference database) T-score_{neck} to normalised T-score_{neck} is shown in *Figure 2*. *Figure 2A* shows the OLVFss values and the corresponding raw T-score_{neck} of Hong Kong Chinese women and Italian Caucasian women (31,32). *Figure 2D* shows the relationship between of raw T-score_{neck} and normalised T-score (i.e., values equivalent to Caucasian T-score) for Chinese women based on the data in *Figure 2A*, as well as some statistical modeling results around a raw T-score_{neck} of -2.0 to -2.5 of Wang and Xiao (5) for Hong Kong Chinese women. These data were then used to fit a quadratic relationship between the raw T-score_{neck} and the normalised T-score_{neck}. In addition, we enforced when raw T-score = -2.7 then normalized T-score = -2.5 (*Figure 1D*), and the final conversion formula for T-score_{neck} is:

$$\text{Normalized neck } T_score = \frac{-1.1040 + \sqrt{1.2317 - 0.0736 * (\text{raw neck } T_score)}}{-0.0368} \quad [2]$$

It is well-known that T-score_{neck} and T-score_{hip} are highly correlated (27,31,34,35). Using OLVFss as a surrogate endpoint, for our Hong Kong older women's data, for each OLVFss the corresponding T-score_{neck} and T-score_{hip} are almost the same (*Figure 3A*). The good correlation of T-score_{neck} and T-score_{hip} in the Japanese data of Iki *et al.* (27) is also shown in *Figure 3B*. As a result, we believe that the relationship between the Chinese women's T-score_{hip} and the Caucasian women's T-score_{hip} follows the same pattern as the relationship between the Chinese women's T-score_{neck} and the Caucasian T-score_{neck}. Since we recommended that a Chinese women's T-score_{hip} of -2.6 is equivalent to a Caucasian women's T-score_{hip} of -2.5 (5), our proposed conversion formula for Chinese women's T-score_{hip} is:

$$\text{Normalized hip } T_score = \frac{-1.1040 + \sqrt{1.2390 - 0.0736 * (\text{raw hip } T_score)}}{-0.0368} \quad [3]$$

According to the 1994 World Health Organization (WHO) document (1), the definition of osteopenia (low bone mass) is a T-score between -1 and -2.5 below SD_{young adult population} (standard deviation of BMD of young adult population). However, there is no biological or epidemiological rationale for the threshold of -1 (36). The original intention of the WHO was to choose a threshold that would make osteopenia uncommon at the time of menopause. Actually, the prevalence of osteopenia is higher and can be more than 50% in postmenopausal women over the age of 50 years (5). This makes osteopenia a less relevant diagnosis for patients. In our modelling (5), we assumed osteopenia prevalence among Chinese women is also half that of Caucasian women. Based on the available BMD reference data, we recommend that, for Chinese women, osteopenia has a raw T-score range of -2.7 to -3.7, -2.0 to -2.7, and -1.8 to -2.6 for T-score_{spine}, T-score_{neck}, and T-score_{hip}, respectively.

Strictly speaking, different East Asian BMD reference databases could be associated with slightly different DOP cutpoint T-scores (5). However, we anticipate our conversion formulas will be broadly applicable to all East Asian female populations, and the application of these conversion formulas will not result in any important statistical errors.

Our suggested normalized DOP cutpoint T-scores are in line with the original WHO T-score definition of osteoporosis

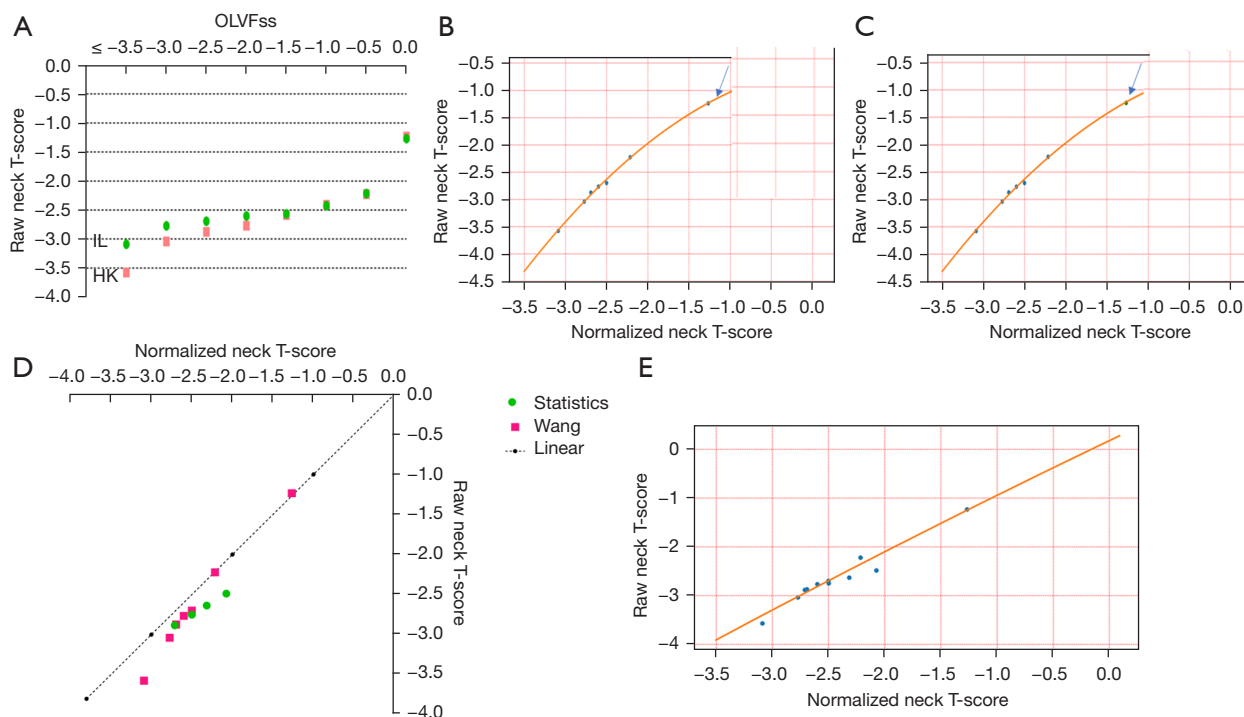


Figure 2 Conversion of raw femoral neck T-score to normalised T-score for Chinese women. (A) For each OLVFss value, the figure shows the corresponding raw femoral neck T-scores for Hong Kong Chinese women and Italian Caucasian women. Data from Wáng *et al.* (31,32). (B) A quadratic fit to the data in (A). Whether the data point marked with an arrow is reliable is uncertain. (C) If the latter data point is removed for curve fitting, the fitted curve is almost unchanged. Thus, this data point is considered reasonable. (D) Relationship between raw femoral neck T-scores and normalised T-scores (i.e., values equivalent to a Caucasian T-score) for Chinese women. Data based on those in (A) (red dots) and also the statistical modeling of Wáng and Xiao (5) for Hong Kong Chinese women (green dots). The black line indicates a theoretical one-to-one relationship between the raw T-scores and the normalised T-scores (i.e., they are the same). (E) All the data in (D) are used to fit a quadratic relationship between the raw T-scores and the normalised T-scores. In addition, it is enforced that when raw T-score = -2.7 then normalized T-score = -2.5. Note the focus of the fitting is to ensure its reliability for values of -2.0 to -3.0. OLVFss, osteoporotic-like vertebral fracture sum score; IL, Italian; HK, Hong Kong.

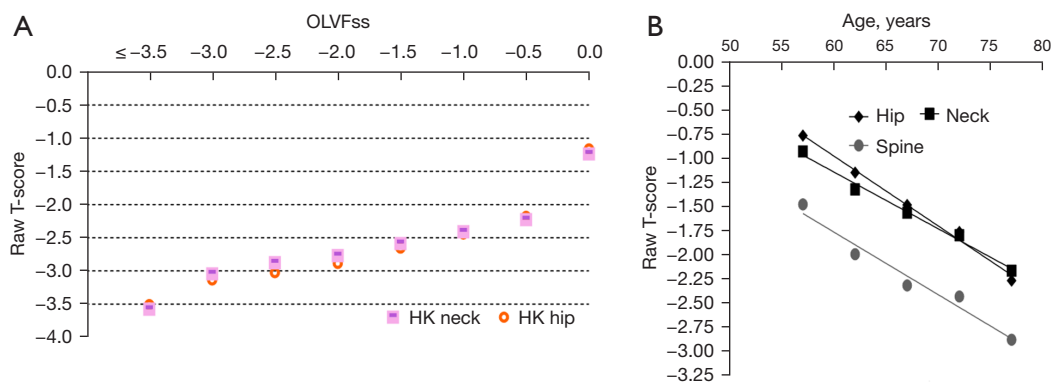


Figure 3 Femoral neck T-score and the total hip neck T-score are highly correlated. (A) For each OLVFss value, the corresponding femoral neck T-score and total hip neck T-score of Hong Kong Chinese women are almost the same. Data from Wáng *et al.* (31). (B) During natural aging, the population mean femoral neck and total hip neck T-scores decrease with a very similar trend. Data from Iki *et al.* (27). OLVFss, osteoporotic-like vertebral fracture sum score; HK, Hong Kong.

and will allow a more meaningful international comparison of disease burden and epidemiological studies.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://qims.amegroups.com/article/view/10.21037/qims-23-1090/coif>). 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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