

Citation

Leslie WD, Morin SN, Lix LM, McCloskey EV, Johansson H, Harvey NC, Kanis JA. Effect of Discordant Hip Bone Density on Incident Fracture Risk: A Registry-Based Cohort Study. *J Bone Miner Res.* 2022 Oct;37(10):2018-2024. doi: 10.1002/jbmr.4672. Epub 2022 Sep 7. PMID: 36069122.

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This is the accepted version of the following article:

Leslie WD, Morin SN, Lix LM, McCloskey EV, Johansson H, Harvey NC, Kanis JA. Effect of Discordant Hip Bone Density on Incident Fracture Risk: A Registry-Based Cohort Study. *J Bone Miner Res.* 2022 Oct;37(10):2018-2024. doi: 10.1002/jbmr.4672. Epub 2022 Sep 7. PMID: 36069122.

which has been published in final form at <https://doi.org/10.1002/jbmr.4672> .

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Effect of Discordant Hip Bone Density on Incident Fracture Risk: A Registry-Based Cohort Study

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Brief Title: Effect of Discordant Hip Bone Density

Keywords: Osteoporosis; Fractures; Dual-energy x-ray absorptiometry; FRAX.

Word count: text 2839 (not including abstract, tables, figures, and references)

Abstract word count: 300 (maximum 300)

Figure count: 1

Table count: 4

Supplemental Figure count: 1

Supplemental Table count: 7

Funding: No funding support was received for this research.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the [Version of Record](#). Please cite this article as doi: [10.1002/jbmr.4672](https://doi.org/10.1002/jbmr.4672)

ABSTRACT

FRAX[®] combines clinical risk factors and optionally femoral neck bone density to estimate major osteoporotic fracture (MOF) and hip fracture probability. Hip DXA simultaneously measures the trochanter and total hip, but these regions are not considered by FRAX[®]. Our aim was to determine whether discordance in trochanter and total hip bone density (defined as ≥ 1 T-score difference from the femoral neck) affects fracture risk adjusted for fracture probability. Using the Manitoba bone density registry, we identified 84,773 women and men age 40 years or older undergoing baseline hip DXA. The outcomes were incident MOF and hip fracture. Cox regression hazard ratios (HRs) with 95% CIs adjusted for baseline fracture probability were used to test the association between hip T-score discordance and incident fractures. Hip T-score discordance affected more than one in five subjects (trochanter lower in 3.9%, higher in 14.2%; total hip lower in 0.3%, higher in 14.9%). After mean 8.8 years there were 8,444 incident MOF including 2,664 hip fractures. Discordantly lower trochanter and lower total hip T-score (≥ 1 below femoral neck) was associated with increased risk for MOF (adjusted HRs 1.47 and 1.60) and hip fracture (HRs 1.85 and 2.12), while discordantly higher trochanter and total hip T-score (≥ 1 above femoral neck) was associated with lower risk for MOF (HRs 0.83 and 0.71) and hip fracture (HRs 0.79 and 0.68). In models that examined the trochanter and total hip simultaneously, discordantly lower trochanter T-score was associated with increased incident MOF and hip fracture risk (HRs 1.43 and 1.79) while discordantly higher total hip T-score was associated with lower risk (HRs 0.73 and 0.75). In conclusion, trochanter and total hip regions frequently show T-scores that are discordant with the femoral neck. This information strongly affects incident

fracture risk independent of fracture probability scores computed with femoral neck bone density.

INTRODUCTION

Measurement of bone mineral density (BMD) with dual-energy x-ray absorptiometry (DXA) is widely used in clinical practice to screen for individuals at high risk for osteoporotic fracture to guide initiation of anti-fracture therapies ⁽¹⁾. The femoral neck is the reference site for osteoporosis diagnosis and for estimating 10-year risk of major osteoporotic fracture (MOF; composite of hip, clinical spine, distal forearm, proximal humerus) and 10-year risk of hip fracture with the FRAX[®] tool ^(2,3). The FRAX tool considers multiple clinical risk factors in addition to BMD at the femoral neck and has been adopted by multiple guidelines ⁽⁴⁻⁷⁾.

Although designation of the femoral neck as the reference site for osteoporosis description and fracture risk assessment creates a clear and simple paradigm, DXA measurements from other sites are routinely obtained including the lumbar spine, total hip and greater trochanter. Discordance in T-score measurements (number of standard deviations above or below a young reference population) can be a source of clinical uncertainty. Many studies, including an international meta-analysis, showed that there is a significant but relatively small effect of discordance between the lumbar spine and femoral neck (defined as a T-score difference greater than 1) on fracture risk ^(8,9). To date, however, no studies have examined whether discordance between the various hip sites impacts on fracture risk when adjusted for the FRAX probability score that includes femoral neck BMD. Since total hip and trochanter BMD are also obtained at the time of measuring femoral neck BMD, they potentially provide a source of information that is currently available but not being used as part of fracture prediction. Moreover, some guidelines explicitly recommend against the use of trochanter BMD for diagnostic

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purposes due to concern with over-diagnosis of osteoporosis ^(10,11), while there was limited data that this improved fracture prediction ⁽¹²⁾.

The current analysis was undertaken to determine whether discordance in trochanter and total hip BMD (defined as ≥ 1 T-score difference from the femoral neck) affects fracture risk adjusted for fracture probability computed from FRAX with femoral neck BMD.

METHODS

Study Population

We performed a provincial registry-based cohort study to examine change in fracture risk score and treatment threshold qualification in women and men age 40 years or older at the time of an initial fracture risk assessment including hip DXA (January 1, 1996 – March 31, 2018). In Manitoba (Canada), DXA-based BMD testing has been managed as an integrated clinical program since 1997 ⁽¹³⁾. The program maintains a database of all DXA results which can be linked with other provincial population-based computerized health databases through an anonymous personal identifier. The DXA database has completeness and accuracy in excess of 99% ⁽¹⁴⁾. Scans obtained prior to 1996 were excluded to ensure at least 1 year of prescription drug information from pharmacy data prior to entry. We also excluded non-residents, and those without hip DXA or other data required to calculate FRAX probability score at the initial assessment. The study was approved by the Health Research Ethics Board of the University of Manitoba and the Health Information Privacy Committee of Manitoba Health.

Bone Mineral Density Measurements and Fracture Risk

Hip DXA scans were performed and analyzed in accordance with manufacturer recommendations. Femoral neck, trochanter and total hip T-scores were calculated from NHANES III white female reference values ⁽¹⁵⁾. All reporting physicians and supervising technologists are required to maintain DXA certification with the International Society for Clinical Densitometry (ISCD). The program's quality assurance is under strict supervision by a medical physicist ⁽¹³⁾. The cross-calibrated instruments used for this study (1 DPX, 3 Prodigy and 3 iDXA, GE/Lunar Healthcare, Madison WI; between-scanner differences <0.1 T-score) exhibited stable long-term performance (coefficient of variation <0.5%). In vivo short-term BMD precision estimated from over 400 paired DXA scans performed on a different day (but within 30 days) gave 95% least significant change values that ranged from 0.030 g/cm² for the total hip to 0.055 g/cm² for the femoral neck ⁽¹⁶⁾.

Ten-year risk of MOF and hip fracture risk was calculated using the fracture risk assessment tool including femoral neck BMD, Canadian version (FRAX[®] Desktop Multi-Patient Entry, version 3.7) ^(17,18). This FRAX tool has been calibrated using nationwide hip fracture and mortality data ⁽¹⁸⁾. Predictions agree closely with observed fracture risk in this population ^(19,20). Briefly, age, body mass index (BMI), femoral neck BMD and other data required for calculating fracture risk with FRAX were assessed from on-site measurements (height and weight) and information collected directly from subjects through the intake questionnaire at the time of each DXA scan ⁽²¹⁾. Questionnaire information was supplemented with population-based healthcare data (hospital discharge

abstracts, medical claims diagnoses, province-wide retail pharmacy database) as recently described, thereby ensuring complete information for all subjects ⁽²²⁾.

Outcomes

We identified incident major osteoporotic fractures (MOF) and hip fracture (HF) from linked population-based healthcare data to March 31, 2018 through hospital discharge abstracts (diagnoses and procedures coded using the International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] prior to 2004 and International Classification of Diseases, Tenth Revision, Canadian Enhancements [ICD-10-CA] thereafter) and physician billing claims (coded using ICD-9-CM) using previously validated algorithms ^(23,24). Fractures with high-trauma codes were excluded.

Statistical Analysis

Descriptive statistics for demographic and baseline characteristics are presented as mean \pm standard deviation (SD) for continuous variables or number (%) for categorical variables. We calculated mean hip BMD T-score differences (trochanter minus femoral neck, total hip minus femoral neck) with SD and assessed the distribution of these differences. We defined discordance as an absolute T-score difference of 1 SD or greater; those with T-score differences within 1 SD were the referent and were defined as concordant. Cox regression model estimated hazard ratios (HRs) with 95% CIs were used to test the association of fracture risk with hip BMD T-score discordance using both categorical and continuous measures in models that examined: (a) trochanter minus femoral neck T-score, (b) total hip minus femoral neck T-score, (c), minimum trochanter

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and total hip T-score minus femoral neck T-score, and (d) both trochanter minus femoral neck T-score simultaneously with total hip minus femoral neck T-score in the same model. We also examined whether results were sensitive to systematic offsets between hip T-scores by repeating the analysis after zero-centering the mean T-score differences (sex-specific) and then recategorizing discordance as above (≥ 1 T-score unit). All models were adjusted for FRAX fracture probability (including femoral neck BMD). We tested and confirmed the proportional hazards assumption by analyzing scaled Schoenfeld residuals versus log time. Cumulative incidence curves were constructed according to categorical discordance (≥ 1 T-score unit). No significant collinearity between the hip DXA measures was detected (all variance inflation factors < 4). The primary analysis included all women and men combined after testing and excluding significant sex interactions, supplemented with detailed sex-stratified analyses. Statistical analyses were performed with Statistica (Version 13.0, StatSoft Inc, Tulsa, OK).

RESULTS

Study population and baseline characteristics

Table 1 summarizes the baseline characteristics of the study population and is further stratified by incident fracture outcomes. The overall study population included 84,773 individuals, average age 64.6 years, 90.0% female. The mean femoral neck T-score was in the osteopenic range with trochanter and total hip T-scores slightly better. Mean T-score differences between trochanter-neck and total hip-neck were 0.2 and 0.5, respectively. These differences followed a normal distribution (**Supplemental Figure 1**)

and the magnitude of the differences were larger in men than women (**Supplemental Table 1**).

Correlations between baseline characteristics (**Supplementary Table 2**) showed high correlations of trochanter and total hip with femoral neck T-scores (Pearson r range 0.81 to 0.91), but weak correlations of T-score differences (trochanter minus neck, total hip minus neck) with femoral neck T-scores (Pearson r range -0.02 to 0.22) or FRAX probabilities (Pearson r range -0.17 to 0.16). There were negative correlations between age and T-scores in women. Weaker negative correlations were seen in men for the femur neck and total hip, while no correlation with age was seen for the trochanter (Pearson $r=0.00$). Trochanter-neck T-score differences showed an age-related increase, greater in men than women (Pearson $r=0.26$ versus 0.12, respectively). Total hip-neck T-score differences showed an age-related increase in men but a decrease in women (Pearson $r=0.12$ versus -0.05, respectively).

Hip T-score discordance was common and affected more than 1 in 5 subjects (**Supplemental Table 3**). Specifically, trochanter was discordantly lower than femoral neck in 3.9%, discordantly higher in 14.2%; total hip was discordantly lower in 0.3%, discordantly higher in 14.9%. Discordance at either site was observed in 23.5%. Results were similar when stratified by age (less than 65 years versus ≥ 65 years). When stratified by sex, there was a much greater proportion of discordance among men than women (45.1% versus 21.2%).

Fractures outcomes

During follow-up (mean 8.8 years), there were 8444 incident MOF including 2664 hip fractures. Individuals sustaining incident MOF or incident hip fracture showed expected differences in baseline characteristics, including greater age, lower BMD T-scores and greater FRAX probability scores (**Table 1**). In those with incident fracture, mean trochanter-neck and total hip-neck T-score differences were slightly lower than in those with no fracture. Observed cumulative 10-year incident fracture risk was affected by hip region T-score discordance, as documented in **Figure 1**. Thus, MOF and hip fracture risk were greater in those with discordantly lower trochanter or total hip, and lower in those with discordantly higher trochanter or total hip, compared to those with concordant measurements.

Cox regression models adjusted for baseline FRAX probability score (**Table 2**) showed that discordantly lower trochanter and total hip T-scores (≥ 1 below femoral neck) were both associated with increased risk for MOF (adjusted HR 1.47, 95% CI 1.33-1.63 and 1.60, 95% CI 1.18-2.16, respectively). A similar pattern was seen for incident hip fracture related to discordantly lower trochanter and total hip T-score (adjusted HR 1.85, 95% CI 1.57-2.18; 2.12, 95% CI 1.37-3.29). Conversely, discordantly higher trochanter and total hip T-score (≥ 1 above femoral neck) were associated with significantly lower risk for incident MOF (adjusted HR 0.83, 95% CI 0.77-0.88; 0.71, 95% CI 0.66-0.76) and incident hip fracture (0.79, 95% CI 0.70-0.90; 0.68, 95% CI 0.59-0.80). Similar results were seen when discordance was based on the minimum T-score from the trochanter and total hip. In models that examined the trochanter and total hip simultaneously, discordantly lower trochanter T-score was associated with increased risk for incident MOF and hip fracture (adjusted HR 1.43, 95% CI 1.29-1.59; 1.79, 95% CI 1.50-2.13,

respectively), while discordantly higher total hip BMD was associated with lower risk for incident MOF and hip fracture (adjusted HR 0.73, 95% CI 0.67-0.80; 0.75, 95% CI 0.63-0.90). Despite the higher proportion of discordance seen in men compared with women, two-way interaction terms for sex were not significant (all p-interaction > 0.6). Sex-stratified analyses are summarized in **Supplemental Tables 4-6**. Among men, confidence intervals were much wider, but patterns were overall similar to those seen in women. Findings were largely unchanged overall and in women when T-score discordance was defined after zero-centering the T-scores to correct for systematic offsets between hip T-scores, but were attenuated and largely non-significant for men (**Table 3, Supplemental Table 5**).

In models that considered T-score differences as a continuous measure (**Table 4**), there was a similar pattern whereby each unit T-score difference (trochanter lower than femur neck, total hip lower than femur neck, minimum lower than femur neck) was associated with significantly increased risk for incident MOF (adjusted HR per unit T-score difference range 1.23-1.50) and incident hip fracture risk (adjusted HR per unit T-score difference range 1.36-1.62). In models that examined the trochanter and total hip simultaneously, discordance based upon total hip minus femur neck T-score had the largest effect in increased risk for incident MOF and hip fracture (adjusted HR per unit T-score difference 1.74 and 1.50, respectively). Effect sizes were lower when expressed as a gradient of risk per SD in T-score difference rather than in T-score units (**Supplemental Table 7**).

DISCUSSION

We found that discordance between hip BMD measurements affected fracture risk beyond conventional femoral neck BMD, either used alone or in the FRAX probability score. Specifically, when trochanter or total hip T-score was ≥ 1 units lower than the femoral neck then this translated into increased risk for incident MOF or hip fracture, whereas higher T-score ≥ 1 units greater was protective against fracture. Discordance of this magnitude was relatively common and seen in over 1 in 5 individuals within the cohort, similar for those less than age 65 years and 65 years or older. Of note, although the effect of discordance was similar in men and women (sex interactions non-significant), the frequency was considerably higher in men reaching almost one in two.

These data complement previous analyses that have looked at discordance between hip and lumbar spine DXA measurements^(8,9). Lumbar spine T-scores discordantly lower than the femoral neck by 1 or more increased fracture risk whereas higher lumbar spine T-scores are protective against fracture risk. However, the effect noted was relatively small, and only changed the fracture risk by approximately one-tenth for each standard deviation difference^(8,9). In contrast, the effect of hip discordance was considerably larger, and increased MOF fracture risk by 23-50% for each SD difference, and for hip fracture by 36-62% for each SD difference. Similar patterns were seen for discordance based upon the trochanter or total hip regions. When the two sites are used in conjunction, discordantly lower trochanter and discordantly greater total hip lead to increased and decreased fracture risk, respectively. The source of the greater discordance among men is uncertain. This is unlikely to reflect problems with reference data used in T-score calculation, since we adopted international guidelines for a standardized (female)

reference population based upon National Health and Nutrition Examination Survey III (NHANES III) data. Indeed, using male reference data would likely create even more discordance since these are not uniformly NHANES III for the DXA scanner used ⁽²⁵⁾. , Differential age-dependent reductions in bone density among older men, which were larger for the femur neck than the total hip while the trochanter was unaffected by age, are likely to be a contributing factor. Zero-centering the T-score differences to remove systematic T-score offsets greatly reduced the importance of hip T-score discordance on fracture outcomes in men, but had little effect on women.

The trochanter was routinely used for osteoporosis diagnosis until 2006 when the ISCD dropped it from the list of recommended DXA assessment sites to aid in transition to fracture probability based upon the femoral neck ^(10,26). Our data support reconsidering the role of the trochanter for clinical purposes. Since trochanter and total hip BMD measurements are routinely obtained at the time of femoral neck BMD assessment, this information is available at no cost and discordance should not be ignored when observed since it strongly affects incident fracture risk independent of fracture probability scores computed with femoral neck BMD. How to incorporate these results into clinical practice will require additional study and independent validation in other prospective cohorts.

The mechanism whereby different hip regions, although highly correlated, might still independently contribute to fracture risk is uncertain. These regions sample different proportions of cortical and trabecular bone and this may in turn reflect the varying importance of these compartments throughout the skeleton. The femoral neck is also more prone to structural artifact from osteoarthritis than other sites due to medial

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buttressing, a common problem among elderly individuals ^(27,28). Alternatively, BMD measurement error could be a factor since this is inversely related to the size of the hip region, greatest for the femoral neck (smallest area) and lowest for the total hip (largest area).

Strengths to this analysis include the large cohort size and long-term follow up allowing for the detection of many incident fractures, including a large number of incident hip fractures. Uniformity in the scan acquisitions and processing, as well as data required for fracture probability estimation are further strengths. Limitations are also acknowledged. The population is largely of European ancestry and differences may exist with other race/ethnic groups, especially where there are differences in skeletal geometry. FRAX calculators are calibrated to specific countries with more than a tenfold variation between calculators, and it is uncertain whether our findings would be quantitatively similar across all settings ⁽²⁹⁾. Although this was a BMD referral registry, findings are likely to be broadly applicable to routine clinical practice since individuals included in this study are representative of those undergoing DXA assessment. Moreover, previous analysis had shown that observed fracture risk agrees closely with predicted fracture risk in this population, supporting the representative nature of the population ⁽¹⁹⁾. We were only able to evaluate a single DXA manufacturer, but there are data supporting utility of assessing multiple hip regions using the other major DXA provider ⁽¹²⁾. Finally, we did not have information on lifestyle factors that could impact on fracture risk.

In summary, trochanter and total hip regions frequently show T-scores that are discordant with the femoral neck. These discordances have large and predictable effects on incident fracture risk independent of FRAX probability scores computed with femoral

neck bone density. This is an important source of information that could be used to improve fracture risk assessment.

ACKNOWLEDGMENTS:

The authors acknowledge the Manitoba Centre for Health Policy for use of data contained in the Population Health Research Data Repository (HIPC 2016/2017-29). The results and conclusions are those of the authors and no official endorsement by the Manitoba Centre for Health Policy, Manitoba Health and Seniors Care, or other data providers is intended or should be inferred. This article has been reviewed and approved by the members of the Manitoba Bone Density Program Committee.

SNM is chercheur-boursier des Fonds de Recherche du Québec en Santé. LML is supported by a Tier I Canada Research Chair.

DISCLOSURES:

Suzanne Morin: Nothing to declare for the context of this paper., but has received research grants: Amgen.

Eugene McCloskey: Nothing to declare for the context of this paper, but numerous ad hoc consultancies/ speaking honoraria and/or research funding from Amgen, Bayer, General Electric, GSK, Hologic, Lilly, Merck Research Labs, Novartis, Novo Nordisk, Nycomed, Ono, Pfizer, ProStrakan, Roche, Sanofi-Aventis, Servier, Tethys, UBS and Warner-Chilcott

Nicholas Harvey: Nothing to declare for the context of this paper, but has received consultancy/ lecture fees/ honoraria/ grant funding from Alliance for Better Bone Health, Amgen, MSD, Eli Lilly, Servier, Shire, UCB, Kyowa Kirin, Consilient Healthcare and Internis Pharma.

John A. Kanis: Nothing to declare for the context of this paper

William Leslie, Lisa Lix, Helena Johansson: No conflicts of interest.

DETAILS OF CONTRIBUTORS AND GUARANTOR:

Authors' roles: conception, design, analysis, drafting the article (WDL), interpretation of data (All Authors); critically revising the article for important intellectual content (All Authors); final approval of the version to be published (All Authors); and agreement to be accountable for all aspects of the work (All Authors). WDL had full access to all the data in the study and takes the responsibility for the integrity of the data and the accuracy of the data analysis.

DATA ACCESSIBILITY STATEMENT

Data sharing is not permitted under the Researcher Agreement with Manitoba Health and Seniors Care (MHASC). However, researchers may apply for data access through the Health Research Ethics Board for the University of Manitoba and the Health Information and Privacy Committee of MHASC.

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Figure Legends

Figure 1. Observed cumulative 10-year incident fracture risk from hip region T-score discordance versus concordance. All log-rank $p < 0.001$.

Table 1. Characteristics of the study population according to incident fracture outcome.

Characteristics	All	No fracture	Incident MOF	p-value, Incident MOF vs No fracture	Incident Hip	p-value, Incident Hip vs No fracture
	N=					
	84,773	76,329	8,444		2,664	
Age (years)	64.6 ± 11.0	64.2 ± 10.9	68.7 ± 11.1	<0.001	73.6 ± 9.7	<0.001
Sex (female)	76,320 (90.0)	68,532 (89.8)	7,788 (92.2)	<0.001	2,459 (92.3)	<0.001
MOF fracture risk (percent)	10.0 ± 7.1	9.6 ± 6.8	13.8 ± 8.6	<0.001	17.0 ± 9.0	<0.001
Hip fracture risk(percent)	2.3 ± 3.8	2.1 ± 3.7	4.1 ± 4.9	<0.001	5.8 ± 5.5	<0.001
Neck T-score	-1.4 ± 1.0	-1.3 ± 1.0	-1.9 ± 0.9	<0.001	-2.2 ± 0.8	<0.001
Trochanter T-score	-1.1 ± 1.2	-1.0 ± 1.2	-1.7 ± 1.2	<0.001	-2.0 ± 1.1	<0.001
Total hip T-score	-0.9 ± 1.2	-0.8 ± 1.2	-1.5 ± 1.1	<0.001	-1.9 ± 1.1	<0.001
Trochanter-Neck T-score difference	0.2 ± 0.7	0.3 ± 0.7	0.2 ± 0.7	<0.001	0.1 ± 0.7	<0.001
Total hip-Neck T-score difference	0.5 ± 0.5	0.5 ± 0.5	0.3 ± 0.5	<0.001	0.3 ± 0.5	<0.001

Data expressed as mean (SD) or N (percent). Major osteoporotic fracture (MOF) and hip fracture risk computed using the FRAX tool with femoral neck bone mineral density (BMD).

Table 2. Adjusted hazard ratio* (HR, 95% CI) for incident fracture from hip region T-score discordance as a categorical measure.

Trochanter versus Neck	Percent	Adjusted HR		Adjusted HR	
		Incident MOF	p-value	Incident Hip	p-value
Discordant, Trochanter < Neck	3.9	1.47 (1.33-1.63)	<0.001	1.85 (1.57-2.18)	<0.001
Discordant, Trochanter > Neck	14.2	0.83 (0.77-0.88)	<0.001	0.79 (0.70-0.90)	<0.001
Concordant Trochanter and Neck (REFERENT)		1.00		1.00	
Total hip versus Neck		Incident MOF	p-value	Incident HIP	p-value
Discordant, Total < Neck	0.3	1.60 (1.18-2.16)	0.002	2.12 (1.37-3.29)	<0.001
Discordant, Total > Neck	14.6	0.71 (0.66-0.76)	<0.001	0.68 (0.59-0.80)	<0.001
Concordant Total and Neck (REFERENT)		1.00		1.00	
Minimum (Trochanter and Total hip) versus Neck		Incident MOF	p-value	Incident HIP	p-value
Discordant, Minimum < Neck	3.9	1.45 (1.31-1.60)	<0.001	1.83 (1.55-2.15)	<0.001
Discordant, Minimum > Neck	19.6	0.78 (0.74-0.83)	<0.001	0.78 (0.69-0.87)	<0.001
Concordant, Minimum and Neck (REFERENT)		1.00		1.00	
Both (Trochanter and Total hip) versus Neck		Incident MOF	p-value	Incident HIP	p-value
Discordant, Trochanter < Neck	3.9	1.43 (1.29-1.59)	<0.001	1.79 (1.50-2.13)	<0.001
Discordant, Trochanter > Neck	14.2	0.97 (0.89-1.05)	0.399	0.90 (0.78-1.04)	0.172
Concordant Trochanter and Neck (REFERENT)		1.00		1.00	
Discordant, Total < Neck	0.3	1.15 (0.84-1.58)	0.382	1.26 (0.79-2.01)	0.333
Discordant, Total > Neck	14.6	0.73 (0.67-0.80)	<0.001	0.75 (0.63-0.90)	0.001
Concordant, Total and Neck (REFERENT)		1.00		1.00	

* Adjusted for major osteoporotic fracture (MOF) and hip fracture risk computed using the FRAX tool with femoral neck bone mineral density (BMD). Statistically significant effects are in boldface. Discordance defined as T-score difference of 1 or greater, concordance as T-score difference less than 1.

Table 3. Adjusted hazard ratio* (HR, 95% CI) for incident fracture from zero-centered hip region T-score discordance as a categorical measure.

Trochanter versus Neck	Percent	Adjusted HR		Adjusted HR	
		Incident MOF	p-value	Incident Hip	p-value
Discordant, Trochanter < Neck	9.3	1.39 (1.28-1.50)	<0.001	1.74 (1.53-1.98)	<0.001
Discordant, Trochanter > Neck	10.2	0.78 (0.71-0.85)	<0.001	0.78 (0.66-0.92)	0.003
Concordant Trochanter and Neck (REFERENT)		1.00		1.00	
Total hip versus Neck		Incident MOF	p-value	Incident HIP	p-value
Discordant, Total < Neck	3.4	1.62 (1.46-1.81)	<0.001	1.94 (1.65-2.28)	<0.001
Discordant, Total > Neck	3.6	0.73 (0.61-0.87)	<0.001	0.92 (0.66-1.30)	0.647
Concordant Total and Neck (REFERENT)		1.00		1.00	
Minimum (Trochanter and Total hip) versus Neck		Incident MOF	p-value	Incident HIP	p-value
Discordant, Minimum < Neck	5.5	1.42 (1.31-1.55)	<0.001	1.82 (1.59-2.08)	<0.001
Discordant, Minimum > Neck	4.6	0.66 (0.58-0.74)	<0.001	0.67 (0.52-0.86)	0.002
Concordant, Minimum and Neck (REFERENT)		1.00		1.00	
Both (Trochanter and Total hip) versus Neck		Incident MOF	p-value	Incident HIP	p-value
Discordant, Trochanter < Neck	9.3	1.24 (1.13-1.36)	<0.001	1.50 (1.28-1.75)	<0.001
Discordant, Trochanter > Neck	10.2	0.80 (0.73-0.89)	<0.001	0.76 (0.63-0.91)	0.002
Concordant Trochanter and Neck (REFERENT)		1.00		1.00	
Discordant, Total < Neck	3.4	1.36 (1.19-1.55)	<0.001	1.42 (1.16-1.73)	<0.001
Discordant, Total > Neck	3.6	0.87 (0.72-1.05)	0.149	1.18 (0.82-1.70)	0.384
Concordant, Total and Neck (REFERENT)		1.00		1.00	

* Adjusted for major osteoporotic fracture (MOF) and hip fracture risk computed using the FRAX tool with femoral neck bone mineral density (BMD). Statistically significant effects are in boldface. Discordance defined as T-score difference of 1 or greater, concordance as T-score difference less than 1.

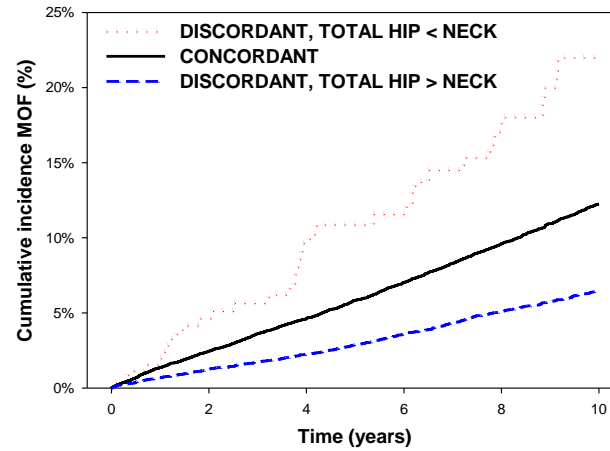
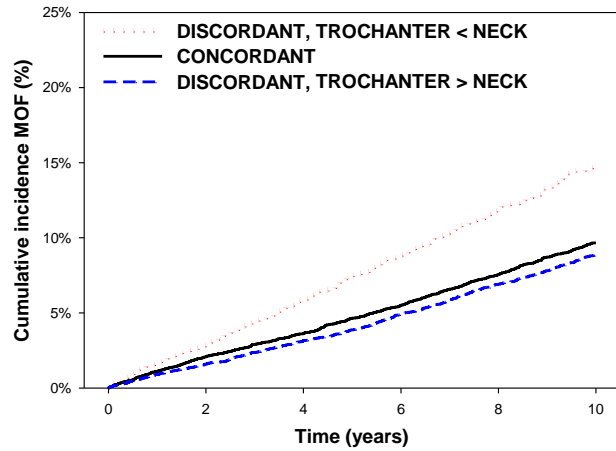
Table 4. Adjusted hazard ratio* (HR, 95% CI) for incident fracture from hip region T-score differences as a continuous measure.

	Adjusted HR **		Adjusted HR **	
	Incident MOF	p-value	Incident Hip	p-value
Separate models				
Trochanter minus Neck T-score	1.23 (1.19-1.27)	<0.001	1.36 (1.28-1.44)	<0.001
Total hip minus Neck T-score	1.50 (1.44-1.57)	<0.001	1.62 (1.50-1.76)	<0.001
Minimum (Trochanter and Total hip) minus Neck T-score	1.30 (1.26-1.35)	<0.001	1.47 (1.38-1.57)	<0.001
Combined model				
Trochanter minus Neck T-score	0.89 (0.84-0.94)	<0.001	1.07 (0.96-1.19)	0.236
Total hip minus Neck T-score	1.74 (1.60-1.89)	<0.001	1.50 (1.29-1.75)	<0.001

* Adjusted for major osteoporotic fracture (MOF) and hip fracture risk computed using the FRAX tool with femoral neck bone mineral density (BMD). Statistically significant effects are in boldface. ** Per unit per unit T-score difference.

Figure 1. Observed cumulative 10-year incident fracture risk from hip region T-score discordance versus concordance. All log-rank $p < 0.001$.

A) Major osteoporotic fracture (MOF)



(B) Hip fracture.

