

Fracture Risk (FRISK) Score: Geelong Osteoporosis Study¹

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Purpose:

To develop and evaluate a fracture risk (FRISK) score based on multiple-site bone mineral density (BMD) measurements and other risk factors, to enable prediction of future fracture occurrence.

Materials and Methods:

All participants gave written informed consent, and the study was approved by the Barwon Health Research and Ethics Advisory Committee. BMD was measured at the femoral neck and spine in two concurrently recruited groups: women 60 years of age or older who had sustained a low-trauma fracture of the hip, spine, humerus or distal forearm during a 2-year ascertainment period ($n = 231$; mean age, 74 years ± 7 [standard deviation]) and a population-based random sample of women who had not sustained a fracture during the recruitment period ($n = 448$; mean age, 72 years ± 8). Falls in the previous year and the number of self-reported fractures in adult life were recorded. Coefficients of a multiple logistic regression model were used as weightings for a combined model. A longitudinal population-based sample was used to assess the fracture risk equation ($n = 600$; median age, 74 years; interquartile range, 67–82 years).

Results:

The FRISK score was obtained from the following equation: $9.304 - 4.735\text{BMD}_{\text{SP}} - 4.530\text{BMD}_{\text{FN}} + 1.127\text{FS} + 0.344\text{NPF} + 0.037\text{W}$, where BMD_{SP} is spinal BMD (in grams per square centimeter), BMD_{FN} is femoral neck BMD, FS is falls score, NPF is number of previous fractures, and W is weight (in kilograms). The FRISK score successfully predicted 75% of fractures 2 years after baseline measurements in subjects in the longitudinal study with 68% specificity.

Conclusion:

This study resulted in the derivation of a fracture risk score that successfully predicted 75% of fractures 2 years after baseline.

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Fragility fractures occur because bones with reduced strength are subjected to critical forces, which most often arise from a fall (1,2). Forces generated from falls will depend on the characteristics of the fall, which are influenced by age and the weight of the faller. Bone mineral density (BMD) is a good surrogate for bone strength. However, a substantial proportion of women with fractures do not have osteoporosis (T score, less than -2.5) according to bone densitometric criteria (3,4) because BMD fails to capture other factors that influence strength, such as bone size, bone geometry, and microarchitectural change (5).

Many studies have focused on single BMD sites to predict fracture (3,6–10). However, it is common in clinical practice for BMD to be measured at both the spine and the hip, but there is little current evidence-based data to assist in making treatment decisions on the basis of multiple-site BMD assessment (11–13). Measurement of BMD at a single anatomic site minimizes the cost of bone mass assessment; however, because BMD measurements can be discordant across anatomic sites (13–15), the site of measurement may be critical for optimal fracture prediction. Discordance may be due to differences in the age at peak BMD (16); relative proportions of cortical and cancellous bone; variable rates of bone loss (17); soft-tissue calcification associated with osteoarthritis, aortic calcification, and osteophytes; or poor precision associated with the proximal femur measurement. When there is discordance in BMD between the sites, how should the different sites be weighted in terms of fracture risk? Is mild reduction in BMD at the hip and spine associated with a similar fracture risk as moderate reduction at one and not at the other? Clearly, there is a need to develop a clinically useful fracture risk assessment tool on the basis of multiple-site BMD measure-

ments and other non-BMD-related risk factors.

The purpose of our study was to develop and evaluate a fracture risk (FRISK) score, on the basis of multiple-site BMD measurements and other risk factors, to enable prediction of future fracture occurrence.

Materials and Methods

All participants gave written informed consent, and the study was approved by the Barwon Health Research and Ethics Advisory Committee.

Study Region

Caucasian subjects were recruited from the Barwon Statistical Division (population, 240 334), a region in southeastern Australia that consists of urban, semiurban, and rural communities (16).

Cross-sectional Cohort of Cases of Fracture

Cases of fracture were ascertained by four research scientists (including K.M.S.) from radiology reports from the two radiology practices that service the region. Vertebral fracture diagnosis was based entirely on the clinical radiologists' interpretation of spine radiographs. Women who sustained a fracture within a 2-year period (February 17, 1994, to February 16, 1996) were invited to participate in the fracture cohort (participation rate, 77% [832 of 1082]) (18). This method of fracture case ascertainment has been validated (2). Only women who had sustained a minimal traumatic fracture of the hip, spine, or humerus or a Colles fracture (fractures included in the World Health Organization definition of osteoporosis [19]) and who were 60 years of age or older were included in this study ($n = 231$; mean age, 74 years ± 7 [standard deviation]). The median time of assessment was 62 days (interquartile range, 29–99 days) after fracture. Minimal trauma was defined as a fall from less than standing height, a spontaneous fracture, or striking against or being struck accidentally by persons or objects. These patients with fracture included those who had a fracture at more

than one anatomic site. The total number of fractures included 54 hip fractures (29 in the femoral neck, 25 in the trochanter), 90 spine fractures, 25 humerus fractures (23 in the proximal humerus, two in the distal humerus) and 65 Colles fractures.

Cross-sectional Control Group

A random age-stratified population-based sample of women was concurrently drawn from the Commonwealth electoral rolls of the same region (participation rate, 77% [1494 of 1938]) (16). The electoral roll provides a complete listing of the adult population because enrollment is compulsory in Australia. Recruitment occurred between January, 1994 and December, 1997. A random selection of women stratified to match the age profile of the region who were 60 years of age or older and who had not sustained a fracture within the 2-year period were used as control subjects for this study ($n = 448$; mean age, 72 years ± 8).

Longitudinal Population Sample

An age-stratified population-based sample of women aged 60 years and older ($n = 600$; median age, 74 years; interquartile range, 67–82 years) with a median follow-up time of 5.8 years (interquartile range, 5.2–6.8 years) was recruited from January, 1994 to December, 1997 (16). Fractures that occurred from 2 to 8 years after baseline (24 hip frac-

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Abbreviations:

BMD = bone mineral density
FRISK = fracture risk
ROC = receiver operating characteristic

Author contributions:

Guarantors of integrity of entire study, G.C.N., M.A.K.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, M.J.H., J.A.P., M.A.K.; statistical analysis, M.J.H., J.A.P.; and manuscript editing, all authors

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Advance in Knowledge

- The fracture risk score enabled prediction of 75% of fractures 2 years after baseline.

tures, 41 spine fractures, eight humerus fractures [six in the proximal humerus, two in the distal humerus], and nine Colles fractures) that were reported at each biennial follow-up examination were confirmed by using radiologic reports. These prospectively ascertained fractures were used to assess the fracture risk equations that were derived from the cross-sectional data. Cases were censored from the data set after the first fracture.

Measurements

BMD was measured at the posteroanterior spine (L2 through L4) and the left femoral neck with a densitometer (DPX-L, software version 1.31; Lunar, Madison, Wis) by research scientists who were licensed to operate the bone densitometer (J.A.P., K.M.S., and two other scientists, all with 3 years of experience in bone densitometry). None of the cases or control subjects was excluded on the basis of their lumbar spine measurement. For proximal femur fracture cases, BMD was measured on the side contralateral to the fracture. Short-term precision in vivo BMD measurements yielded mean coefficient of variation values of 0.6% at the posteroanterior spine and 1.6% at the femoral neck. Measurement of a phantom was performed 3 times each week to maintain quality assurance. T scores for the hip and spine were calculated by using the Australian BMD reference range (20). Age, an estimate of the number of falls in the previous year, and the number of fractures resulting from a minimal trauma event since age 20 years were determined by using a questionnaire that was administered by trained interviewers (J.A.P., K.M.S., and two other scientists). A falls score was determined from the number of falls in the previous year, where a score of 1 indicated that the subject never or rarely fell; a score of 2, that the subject fell a few times; a score of 3, that the subject fell several times; and a score of 4, that the subject fell regularly. Weight and height were measured with subjects wearing a hospital gown and with bare or stockings feet.

Statistical Analysis

Unadjusted comparisons for the cross-sectional cases and control subjects

Table 1

Characteristics of Fracture and Control Groups

Parameter	Patients with Fracture (n = 231)	Control Subjects (n = 448)	P Value
Age (y)	74 ± 7	72 ± 8	.04
Weight (kg)			
Raw value*	64 (57–72)	65 (57–74)	.17
Age-adjusted value†	65.8 ± 0.8	66.8 ± 0.6	.30
Height (cm)			
Raw value	157.4 ± 6.5	157.3 ± 6.4	.88
Age-adjusted value†	157.8 ± 6.1	157.4 ± 6.1	.40
BMD in posteroanterior spine (g/cm ²)			
Raw value	0.940 ± 0.185	1.049 ± 0.192	<.001
Age-adjusted value†	0.946 ± 0.188	1.050 ± 0.188	<.001
BMD in femoral neck (g/cm ²)			
Raw value	0.730 ± 0.131	0.806 ± 0.152	<.001
Age-adjusted value†	0.742 ± 0.134	0.809 ± 0.134	<.001
No. of previous fractures‡			
0	127 (55)	312 (70)	<.001
1	68 (29)	96 (21)	
2	23 (10)	30 (7)	
>2	13 (6)	10 (2)	
Falls score‡			
1	156 (68)	362 (81)	<.001
2	54 (23)	78 (17)	
3	17 (7)	6 (1)	
4	4 (2)	2 (0)	

Note.—Unless otherwise stated, data are means ± standard deviations.

* Data are medians, with interquartile ranges in parentheses.

† Age-adjusted at mean age of 72 years.

‡ Data are numbers of patients or subjects, with percentages in parentheses.

Table 2

Posteroanterior Spine BMD versus Femoral Neck BMD across BMD Categories

Femoral Neck BMD Category	Posteroanterior Spine BMD Category		
	Normal	Osteopenic	Osteoporotic
Patients with Fracture (n = 231)*			
Normal	14 (6)	13 (6)	11 (5)
Osteopenic	14 (6)	46 (20)	40 (17)
Osteoporotic	3 (1)	31 (13)	59 (26)
Control Subjects (n = 448)†			
Normal	87 (19)	73 (16)	10 (2)
Osteopenic	31 (7)	108 (24)	39 (9)
Osteoporotic	2 (0)	41 (9)	57 (13)

Note.—Data are numbers of participants, with percentages in parentheses.

* Agreement was 52% ($\kappa = 0.21 \pm 0.05$ [standard error]).

† Agreement was 56% ($\kappa = 0.32 \pm 0.03$).

were performed by using the two-sample t test, the Mann-Whitney test, and the χ^2 statistic. The κ statistic was used to analyze agreement of categories of BMD (osteoporotic, osteopenic, and normal) across anatomic sites.

From the cross-sectional data, optimal thresholds, sensitivity, specificity, positive predictive value, negative predictive value, and the probability of distinguishing fracture cases from control subjects were derived by using receiver operating characteristic (ROC) curves.

Combined models of weighted fracture risk scores were obtained by using coefficients of logistic regression equations, and these risk scores were assessed by using ROC curves. Interaction terms were considered, but none were significant. The optimal combined model for fracture risk was derived by applying a backward elimination of regressor variables to logistic regression, and a FRISK score was derived and simplified for use by converting the fracture risk score derived by using logistic regression to a

0–10 scale. Significance was set at a level of $\alpha = .10$. The larger the score, the greater the likelihood of fracture. The optimal cut point in the FRISK score was derived by using ROC curves. Logistic regression was used to assess the increase in fracture risk per unit increase in FRISK score. The FRISK score derived from the cross-sectional data was tested in the longitudinal population sample, and sensitivity and specificity were assessed. Software packages (Minitab, version 13, Minitab, State College, Pa; SPSS, version 11.5, SPSS, Chicago, Ill; and SAS, version 8.2, SAS Institute, Cary, NC) were used for all statistical analyses (performed by M.J.H.).

Table 3

Optimal Thresholds and Sensitivity, Specificity, PPV, NPV, and AUC Values Derived from ROC Curves

Parameter	AUC*	Sensitivity [†]	Specificity [†]	PPV [†]	NPV [†]	Optimal Fracture Cutpoint
Age	0.55 ± 0.02	151 (65)	210 (47)	389 (39)	290 (72)	≥70.7 y
Weight	0.53 ± 0.02	139 (60)	206 (46)	381 (37)	298 (69)	≤66.6 kg
Height	0.50 ± 0.02	125 (54)	209 (47)	364 (34)	315 (66)	≥156.7 cm
BMD or T score in posteroanterior spine	0.66 ± 0.02	161 (70)	256 (57)	356 (46)	323 (79)	≤0.997 g/cm ² or ≤−1.7
BMD or T score in femoral neck	0.66 ± 0.02	135 (58)	303 (68)	283 (48)	396 (76)	≤0.736 g/cm ² or ≤−2.2
No. of previous fractures	0.58 ± 0.02	104 (45)	312 (70)	240 (43)	439 (71)	≥1
Falls score	0.57 ± 0.02	75 (33)	362 (81)	161 (47)	518 (70)	≥2

Note.—AUC = area under ROC curve, NPV = negative predictive value, PPV = positive predictive value.

* Data are mean values ± standard errors of the mean.

[†] Data are numbers of participants, with percentages in parentheses.

[‡] Data are total numbers (the denominators), with percentages in parentheses.

Results

BMD across Anatomic Sites

Comparisons between the fracture and control groups are shown in Table 1. Imperfect agreement was found for the comparison of BMD categories at the posteroanterior spine with BMD categories at the femoral neck, with discordance in 48% of the fracture cases ($\kappa = 0.21 \pm 0.05$ [standard error], $P < .001$) and 44% of the control subjects ($\kappa = 0.32 \pm 0.03$, $P < .001$) (Table 2).

FRISK Score Derived from Cross-sectional Data

The combined model of significant risk factors for fracture, derived from logis-

Table 4

Statistical Parameters Derived from ROC Curves for Combined Model Risk Scores

Combined Risk Score	AUC*	Sensitivity [†]	Specificity [†]	PPV [†]	NPV [†]	P Value [§]
BMD in posteroanterior spine + BMD in femoral neck	0.68 ± 0.02	154 (67)	270 (60)	332 (46)	347 (78)	.505
BMD in posteroanterior spine + BMD in femoral neck + weight	0.68 ± 0.02	165 (71)	257 (57)	356 (46)	323 (80)	.505
BMD in posteroanterior spine + BMD in femoral neck + no. of previous fractures	0.69 ± 0.02	136 (59)	314 (70)	270 (50)	409 (77)	.317
BMD in posteroanterior spine + BMD in femoral neck + falls score	0.70 ± 0.02	150 (65)	284 (63)	314 (48)	365 (78)	.183
BMD in posteroanterior spine + BMD in femoral neck + weight + no. of previous fractures + falls score	0.71 ± 0.02	138 (60)	316 (71)	270 (51)	409 (77)	.096

Note.—AUC = area under ROC curve, NPV = negative predictive value, PPV = positive predictive value.

* Data are mean values ± standard errors.

[†] Data are numbers of participants, with percentages in parentheses.

[‡] Data are total numbers (the denominators), with percentages in parentheses.

[§] For comparison of AUC for combined risk score with that for BMD in femoral neck alone.

Table 5

FRISK Score according to T Scores for Hip and Spine, Falls Score, and Number of Previous Fractures

No. of Previous Fractures and Femoral Neck T Score	Falls Score 1			Falls Score 2			Falls Score 3			Falls Score 4		
	Spine T Score			Spine T Score			Spine T Score			Spine T Score		
	0	-1.0	-2.5	0	-1.0	-2.5	0	-1.0	-2.5	0	-1.0	-2.5
0												
0	2.4	3.0	4.0	3.5	4.1	5.1	4.6	5.3	6.2	5.7	6.4	7.3
-1.0	2.9	3.6	4.5	4.1	4.7	5.7	5.2	5.8	6.8	6.3	7.0	7.9
-2.5	3.8	4.4	5.4	4.9	5.6	6.5	6.1	6.7	7.7	7.2	7.8	8.8
1												
0	2.7	3.4	4.3	3.8	4.5	5.4	5.0	5.6	6.6	6.1	6.7	7.7
-1.0	3.3	3.9	4.9	4.4	5.1	6.0	5.5	6.2	7.1	6.7	7.3	8.3
-2.5	4.1	4.8	5.7	5.3	5.9	6.9	6.4	7.0	8.0	7.5	8.2	9.1
2												
0	3.1	3.7	4.7	4.2	4.8	5.8	5.3	5.9	6.9	6.4	7.1	8.1
-1.0	3.6	4.3	5.2	4.8	5.4	6.4	5.9	6.5	7.5	7.0	7.6	8.6
-2.5	4.5	5.1	6.1	5.6	6.3	7.2	6.7	7.4	8.3	7.9	8.5	9.5
3												
0	3.4	4.0	5.0	4.5	5.2	6.1	5.7	6.3	7.3	6.8	7.4	8.4
-1.0	4.0	4.6	5.6	5.1	5.7	6.7	6.2	6.9	7.8	7.4	8.0	9.0
-2.5	4.8	5.5	6.4	6.0	6.6	7.6	7.1	7.7	8.7	8.2	8.9	9.8

Note.—All data were calculated by using the median weight of 64.3 kg. Scores of 5.4 or greater indicate that fracture is expected.

tic regression by using a backward algorithm, was a combination of the falls score, number of previous fractures, weight, and BMD at the spine and femoral neck (Tables 3, 4; Figure). On the basis of areas under the ROC curve, this combined model had a 71% ± 2 (standard error) probability of distinguishing cases from control subjects, a probability that was significantly improved compared with that yielded by the univariate models of femoral neck BMD (66% ± 2, *P* = .096) and posteroanterior spine BMD (66% ± 2, *P* = .096).

The FRISK score with the combined model could be calculated by using one of two equations (Figure) and had an optimal cut point of 5.4—that is, participants with a FRISK score of 5.4 or greater were expected to have a fracture. FRISK scores for the fracture cases and control subjects were distributed around the means +5.8 ± 1.5 (standard deviation) and +4.7 ± 1.4, respectively. For one unit increase in FRISK score, the odds of sustaining a fracture increased by 1.75 (95% confidence interval: 1.54, 1.99).

According to the equation, a decrease of 1.0 standard deviation in BMD

Scores range from 0 to 10 with ≥ 5.4 expected to fracture

FRISK Score

$$= 9.304 - 4.735 \text{ BMD}_{\text{SP}} - 4.530 \text{ BMD}_{\text{FN}} + 1.127 \text{ Falls Score} + 0.344 \text{ Previous Fractures} + 0.037 \text{ Weight}$$

OR

$$= -1.141 - 0.641 \text{ TSCORE}_{\text{SP}} - 0.574 \text{ TSCORE}_{\text{FN}} + 1.127 \text{ Falls Score} + 0.344 \text{ Previous Fractures} + 0.037 \text{ Weight}$$

all components *p* < 0.10

BMD in g/cm²

Falls Score is determined from falls in the previous year:
 (1) never or rarely, (2) a few times (3), several times (4) or regularly.
 Previous Fractures are the number of low trauma fractures sustained ≥ 20 yr.
 Weight in kg

Scores for predicting fracture risk.
 BMD_{FN} = femoral neck BMD,
 BMD_{SP} = spine BMD,
 TSCORE_{FN} = femoral neck T score, TSCORE_{SP} = spine T score.

at the posteroanterior spine increases the FRISK score by 0.6. This increase in fracture risk is the equivalent of decreasing the femoral neck BMD by 1.1 standard deviations, increasing the weight by 17 kg, increasing the number of previous fractures by 1.9, or increasing the falls score by 0.6.

The application of FRISK scores that incorporated combinations of T scores for the hip and spine (0, -1.0, and -2.5) and variable falls scores and numbers of previous fractures (Table 5) indicated that for a “nonfaller” (falls score = 1) of average weight with no

previous fracture who had a T score of 0 at the posteroanterior spine and femoral neck, the FRISK score would be 2.4. By contrast, a woman who had fallen frequently (falls score = 4), had sustained three previous fractures, and had a posteroanterior spine and femoral neck T score of -2.5 would have a FRISK score of 9.8. Increasing weight increases the FRISK score.

FRISK Score Applied to Longitudinal Data

When applied to data from the longitudinal study, the FRISK score successfully identified 75% of those who sus-

tained a fracture 2 years after baseline measurements, with a specificity of 68% (Tables 6, 7).

Discussion

The results of this study show that fracture of the hip, spine, humerus, or distal forearm is predicted by an equation utilizing the parameters of BMD of the hip and spine, falls, previous fractures, and weight. After adjustment for BMD, fracture risk was elevated by frequent falls, increases in weight, or previous fracture. The FRISK score developed by using cross-sectional data was very sensitive (75%) to fracture in the longitudinal study, 2 years after baseline measurements. The sensitivity decreased with time but the specificity did not decrease. This is likely to be due to other unmeasured factors that affect fracture risk after the initial baseline measurements assuming increasing importance

with time. Consistent with our study findings, findings of previous studies (21) have indicated that the number of previous vertebral fractures predicts subsequent fracture. The equation used to calculate the FRISK score can assist in the assessment of fracture risk, particularly among patients with discordant BMDs at the spine and hip.

Measurement of bone mass at single sites has been used for fracture risk prediction (6,22), and some studies have involved the use of combined models to predict fracture (10,23–25). However, few studies have examined BMD measured at multiple sites (11–13). Wasnich et al (11) observed that prediction of spine fracture was improved by including a combination of bone mass at the distal radius and that at the calcaneus. Furthermore, Hans et al (12) reported that discrimination of patients with hip fracture from those without fracture with quantitative ultrasonogra-

phy was improved by using multiple sites. Lu et al (13) combined the osteoporotic status of multiple sites within the hip or forearm to improve fracture prediction. Similarly, our analysis predicts fracture risk by combining BMD, falls score, number of previous fractures, and weight. At univariate analysis, BMD was the most sensitive to fracture, but the falls score was the most specific. In the combined model, age did not remain significant, but many of the variables are age related and may act as surrogates for age.

Reduced body weight is associated with an increased risk of hip fracture; however, after adjustment for BMD, reduced body weight was no longer a significant predictor (23), suggesting that the relationship was due to women with low body weights having lower BMDs at the hip. In this study of any low-trauma fracture, increasing weight produced an increase in fracture risk after adjustment for BMD, supporting the notion that a greater body weight increases the force applied to the skeleton during a fall. Approximately 80% of nonspinal fractures result from a fall, and the mechanics of the fall partly determine the site of the fracture (26).

A limitation of this study was that fracture cases were determined by a review of radiographic reports. The radiologists' assessment was subjective, vertebral heights were not measured, and a spinal deformity index was not used. Because spine radiography was not routinely performed in the control group and because approximately two-thirds of vertebral fractures are not associated with fracture-related back pain (27,28), it is likely that spine fractures were underrepresented in this cohort. We also acknowledge that the accuracy of self-reports of previous fractures may have been limited by recall bias. Another limitation of this study was that the only site of the proximal femur that was represented was the femoral neck. This subregion was chosen because it is the site at which measurements are most reproducible (16). More recently it has become common practice for the total hip to be measured. A FRISK score based on hip fracture risk would be of

Table 6

Results of Use of FRISK Score Developed by Using Cross-sectional Data to Predict Fracture in Population Sample Followed Up for 8 Years after Baseline Measurements

No. of Years after Baseline Measurements	Total No. of Fractures	Sensitivity*	Specificity*†
2	32	24 (75)	383 (68)
4	59	38 (64)	370 (69)
6	76	44 (58)	359 (69)
8	82	46 (56)	355 (69)

* Data are frequencies, with percentages in parentheses.

† Denominators change over time owing to dropouts.

Table 7

Results of Use of Risk Scores Developed by Using Fewer Variables than Involved in the FRISK Score to Predict Fracture in Population Sample 2 Years after Baseline Measurements

Combined Risk Score	Sensitivity*	Specificity*
BMD in posteroanterior spine + BMD in femoral neck	21 (66)	397 (70)
BMD in posteroanterior spine + BMD in femoral neck + weight	23 (72)	352 (62)
BMD in posteroanterior spine + BMD in femoral neck + no. of previous fractures	21 (66)	386 (68)
BMD in posteroanterior spine + BMD in femoral neck + falls score	24 (75)	346 (61)

* Data are frequencies, with percentages in parentheses.

considerable interest, but this study lacked the power to investigate this site alone.

In practice, treatment decisions are based not on any single risk factor alone but on a combination of factors (29). The results of our study suggest that an overall assessment of fracture risk with a model that includes a combination of BMDs at the hip and spine, together with the number of previous fractures, a falls score, and weight can predict future fracture with good sensitivity and specificity. We believe the FRISK score presented in this study can be of assistance in making treatment decisions.

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