Fracture Risk Score and Absolute Risk of Fracture[1]

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Purpose: To report the 5- and 10-year absolute risk of fracture associated with the previously reported fracture risk (FRISK) score.

Materials and Methods: All participants gave written, informed consent, and the Barwon Health Human Research Ethics Committee approved the study. An age-stratified population-based sample of women aged 60 years and older (n = 600) was recruited during 1994–1996. FRISK scores of 0–10 incorporating bone mineral density (BMD) at two sites (hip and spine), falls scores in the previous 12 months of 1–4, weight, and number of fractures as an adult were calculated. Fractures of the hip, spine, humerus, and wrist were ascertained during a median follow-up period of 9.6 years (interquartile range, 6.6–10.5). The cumulative probability of fracture at 5 and 10 years after baseline measurements was calculated by using actuarial methods. The utility of this model was compared with other FRISK algorithms, including the World Health Organization FRISK assessment tool FRAX designed for United Kingdom and that designed for the United States and the Garvan nomogram (Australia).

Results: This study supplies the 5- and 10-year absolute risk of fracture associated with all levels of the FRISK score. While there are modest differences in absolute risk of fracture seen for different numbers of prior fractures, the more marked differences occur across the different categories of falls scores and different categories of BMD. The receiver operating characteristic curves showed no significant difference in area under the curve for all four absolute risk of fracture algorithms.

Conclusion: Absolute risk of fracture can be determined by using readily obtainable clinical information that may aid treatment decisions.

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Absolute risk has become the preferred measure of fracture risk (FRISK), and ultimately, as risk estimates are refined, this measure will be used to guide interventions (1–3). Absolute risk is the probability an event will occur in a specific population (4). In contrast, relative risk is the ratio of risk of those who are exposed to a condition compared with those who are not exposed (4). Both are measures of risk, but estimation of an individual's FRISK requires knowledge of absolute risk when relative risk estimates are used. Therefore, absolute risk is a measure easily explainable to both the physician (5) and the patient.

In the past decade, several studies have reported scores or risk indexes for fracture that combine risk factors into a single composite number or risk that could be easily interpreted in clinical practices for assisting treatment decisions. Most risk scores include some or all of the following risk factors: age, weight, prior fracture, and bone mineral density (BMD) (2,6–9). A measure of falls has been included in some studies because falls are a major problem for the elderly and constitute a strong risk factor for fracture (2,7,10); however, the international World Health Organization FRISK assessment tool (FRAX model) does not include the falls risk (9). Similarly, FRAX data that have been customized for different countries around the world (11–15) do not include falls as a risk factor. The effect this inclusion or exclusion has on identification of the patients with increased FRISK requires further investigation (16,17), as some have suggested that the complexity of the FRAX model does not increase its predictive value, compared with simpler models (18).

Advances in Knowledge

- We provide 5- and 10-year absolute risk of fracture, associated with combinations of risk factors, to assist in treatment decisions.
- We highlight the importance of *(a)* a measure of falls, *(b)* bone mineral density measured at two anatomic sites, and *(c)* the effect of obesity for fracture risk (FRISK) assessment.

Some FRISK models have been presented with the option of omitting BMD (2,9,10); however, the availability of the bone densitometry measurement substantially strengthens the predictive value (19). The anatomic site most commonly measured is the femoral neck (2,9), with very few studies reporting data from multiple anatomic sites (7). Inclusion of BMD at the spine in FRISK models is often avoided because of artifacts caused by osteoarthritis and degenerative disk disease. However, the FRISK for an individual with low BMD at the spine and average BMD at the femoral neck would be underestimated by using an algorithm that is based solely on a hip measurement. In women who had sustained a fragility fracture, we found a higher probability for osteoporosis at the spine and not at the hip, compared with the reverse situation (7).

Low body weight is a well-recognized risk factor for fracture (20,21). Conversely, increased weight is associated with higher BMD and is believed to be protective against fracture (22). However, some researchers have observed a high proportion of obese individuals in fracture groups (23). Increasing weight is protective when it is contributing to an increase in BMD, but studies have shown that an increase in weight independent of BMD is associated with increased fracture risk (7,24).

In this study, we sought to report the 5- and 10-year absolute risk of fracture associated with our previously reported FRISK score (7).

Materials and Methods

Study Region

White subjects (population of 240334) were recruited from the Barwon Statistical Division, a region in southeastern Australia that consists of urban, semiurban, and rural communities (25).

Implications for Patient Care

- A FRISK score can provide an absolute risk of fracture.
- Providing a patient's absolute risk of fracture should assist clinicians in targeting therapy to those at greatest risk.

Longitudinal Population-based Sample

A population-based age-stratified random sample included 600 women who were 60 years and older (median age, 74 years; interquartile range, 67–82 years) and were recruited from 1994 to 1996 (25). These participants were followed up biennially for a median time of 9.6 years (interquartile range, 6.6–10.5 years), and fracture events during this period were confirmed by a research scientist (E.N.M.) by using radiology reports from the radiology practices that service the region. Only first fracture events were recorded and included 125 fractures; fractures of the spine (n = 47), hip (n = 34), distal forearm (n = 27), humerus (n = 13), hip and forearm (one event, two fractures), and humerus and forearm (one event, two fractures) occurred in 123 participants.

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

Measurements

BMD was measured at the spine and femoral neck by using a densitometer

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Abbreviations:
AUC = area under the curve
BMD = bone mineral density
CI = confidence interval
FRISK = fracture risk

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Guarantors of integrity of entire study, M.J.H., J.A.P., G.C.N.; 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., G.C.N.; clinical studies, E.N.M., K.M.S., G.C.N.; experimental studies, J.A.P., Y.Z.; statistical analysis, M.J.H., Y.Z.; and manuscript editing, all authors

Potential conflicts of interest are listed at the end of this article.

(DPX-L, software version 1.31; Lunar, Madison, Wis). Short-term precision in vivo was 0.6% for the spine and 1.6% at the femoral neck. T-scores for the hip and spine were calculated by using the Australian BMD reference range (26). 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 all determined by means of a questionnaire administered by a trained interviewer. A falls score was determined from the number of falls in the previous year, as follows: score 1, never or rarely; score 2, a few times; score 3, several times; or score 4, regularly. Weight was measured with subjects wearing a hospital gown and bare or stocking feet.

Statistical Analysis

The cumulative probability of fracture at 5 and 10 years after baseline measurements was estimated by using actuarial methods applied to survival analysis, and participants were suppressed from the data set after first fracture. Regression techniques that maximize the predictive strength of the least squares model (adjusted R^2), while minimizing the error (standard error) and order of the polynomial and while aiming for optimal Mallows C_p criteria, were used as a smoothing method to predict 5- and 10-year probability per FRISK score on a scale of 0–10. Absolute risk of fracture for each individual was also calculated by using the World Health organization FRAX algorithm as designed for the United States and the United Kingdom (9) and the Garvan nomogram from Australia (2). The different FRISK algorithms were contrasted by using the receiver operating characteristic curve, with optimal sensitivity and specificity derived. Statistical analysis was performed with a statistical software package (Minitab, version 15, State College, Pa; SPSS, version 17, SPSS, Chicago, Ill).

Results

We previously developed the FRISK score to estimate the individual FRISK for women who are older than 60 years (7). The equivalent equation with exclusion of BMD and replacement with age results in the FRISK score of FRISK without BMD (FR_{noBMD}), as follows: $FR_{noBMD} = 0.427 + 0.014A + 1.978FL_S + 1.081F_P - 0.027W$, where A is age, FL_S is falls score, F_P is prior fractures, and W is weight.

In the current analysis, longitudinal prospective data were used to estimate 5- and 10-year absolute risk of fracture of the hip, spine, humerus, or forearm associated with FRISK scores of 0–10. The risk of fracture for the FRISK score was best predicted with cubic growth in the 5- and 10-year absolute risk of fracture (Figure), and the adjusted R^2 was improved by 0.2% and 0.9% and the standard error was reduced by 6.2% and 14.9%, respectively, compared with the values obtained with the linear model, as follows: For absolute risk of fracture at 5 years, the calculation is $-0.00477 + 0.06994FR_S - 0.0226FR_S^2 + 0.002547FR_S^3$. For absolute risk of fracture at 10 years, the calculation is $0.01861 + 0.07558FR_S - 0.01515FR_S^2 + 0.001703FR_S^3$, where FR_S is FRISK score.

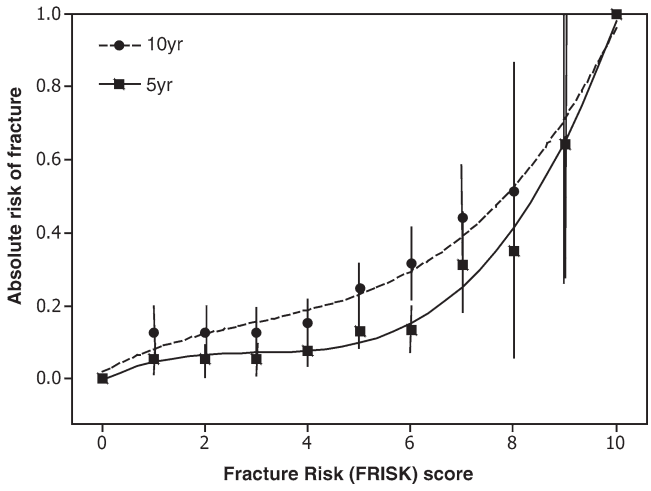
The risk of fracture for FRISK without BMD score is predicted with the following equations: For absolute risk of fracture at 5 years, the calculation is $0.00523 + 0.05228FR_{noBMD} - 0.000051FR_{noBMD}^2$. For absolute risk of fracture at 10 years, the calculation is $0.04354 + 0.08362FR_{noBMD} - 0.002655FR_{noBMD}^2$.

Table 1

Absolute Risk of Fracture for 5 Years in Participants at Median Weight with No Prior Fracture

Falls and Femoral Neck T-score	Posteroanterior Spine T-score					
	0	−1.0	−1.5	−2.0	−2.5	−3.0
Falls score 1						
0	0.07	0.07	0.07	0.07	0.08	0.08
−1.0	0.07	0.07	0.08	0.08	0.09	0.09
−1.5	0.07	0.07	0.08	0.08	0.09	0.10
−2.0	0.07	0.08	0.08	0.09	0.10	0.12
−2.5	0.07	0.08	0.09	0.10	0.11	0.13
−3.0	0.08	0.09	0.10	0.11	0.13	0.15
Falls score 2						
0	0.07	0.08	0.08	0.09	0.10	0.12
−1.0	0.08	0.09	0.10	0.11	0.13	0.15
−1.5	0.08	0.10	0.11	0.13	0.15	0.17
−2.0	0.09	0.11	0.12	0.15	0.17	0.20
−2.5	0.10	0.12	0.14	0.17	0.20	0.23
−3.0	0.11	0.14	0.16	0.19	0.23	0.27
Falls score 3						
0	0.09	0.11	0.12	0.14	0.17	0.20
−1.0	0.11	0.14	0.16	0.19	0.22	0.26
−1.5	0.12	0.16	0.19	0.22	0.26	0.31
−2.0	0.13	0.18	0.22	0.26	0.30	0.35
−2.5	0.15	0.21	0.25	0.30	0.35	0.41
−3.0	0.18	0.25	0.29	0.34	0.40	0.46
Falls score 4						
0	0.13	0.18	0.21	0.25	0.30	0.35
−1.0	0.18	0.24	0.29	0.34	0.40	0.46
−1.5	0.20	0.28	0.33	0.39	0.45	0.53
−2.0	0.24	0.33	0.38	0.45	0.52	0.60
−2.5	0.27	0.38	0.44	0.51	0.59	0.68
−3.0	0.32	0.43	0.50	0.58	0.67	0.76

Note.— The median weight was 64 kg. The falls score was as follows: score 1 = never or rarely; score 2 = a few times; score 3, several times; and score 4 = regularly.



Five-year (■) and 10-year (●) absolute risk of fracture and 5-year (solid line) and 10-year (dashed line) predicted risk according to FRISK score. Vertical lines = 95% confidence intervals (CIs).

Table 2

Absolute Risk of Fracture for 5 Years in Participants at Median Weight with a Prior Fracture

Falls and Femoral Neck T-score	Posteroanterior Spine T-score					
	0	−1.0	−1.5	−2.0	−2.5	−3.0
Falls score 1						
0	0.07	0.07	0.07	0.08	0.08	0.09
−1.0	0.07	0.08	0.08	0.09	0.09	0.11
−1.5	0.07	0.08	0.08	0.09	0.10	0.12
−2.0	0.07	0.08	0.09	0.10	0.12	0.14
−2.5	0.08	0.09	0.10	0.12	0.13	0.16
−3.0	0.08	0.10	0.11	0.13	0.15	0.18
Falls score 2						
0	0.07	0.08	0.09	0.10	0.12	0.13
−1.0	0.08	0.10	0.11	0.13	0.15	0.18
−1.5	0.09	0.11	0.13	0.15	0.17	0.21
−2.0	0.10	0.13	0.15	0.17	0.20	0.24
−2.5	0.11	0.14	0.17	0.20	0.23	0.28
−3.0	0.12	0.17	0.20	0.23	0.27	0.32
Falls score 3						
0	0.10	0.13	0.15	0.17	0.20	0.24
−1.0	0.12	0.16	0.19	0.23	0.27	0.31
−1.5	0.14	0.19	0.22	0.26	0.31	0.36
−2.0	0.16	0.22	0.26	0.30	0.36	0.42
−2.5	0.18	0.25	0.30	0.35	0.41	0.48
−3.0	0.21	0.29	0.35	0.40	0.47	0.54
Falls score 4						
0	0.16	0.22	0.26	0.30	0.35	0.41
−1.0	0.21	0.29	0.34	0.40	0.47	0.54
−1.5	0.24	0.34	0.39	0.46	0.53	0.61
−2.0	0.28	0.39	0.45	0.52	0.60	0.69
−2.5	0.33	0.44	0.52	0.60	0.68	0.78
−3.0	0.37	0.51	0.59	0.67	0.77	0.88

Note.—The median weight and falls score scale are the same as those in Table 1.

Absolute risk of fracture is comparable for the lower FRISK scores (scores < 5) but increases substantially with a score higher than 6 (Figure). Tables 1 and 2 describe various combinations of risk factors for fracture and the associated absolute risk for fracture at the 5-year interval. Table 1 describes different combinations of risk factors for a woman with no prior fracture, and Table 2 describes risk factors for a woman with one prior fracture occurring in adult life. While there are modest differences in absolute risk of fracture seen across these tables, the more marked differences occur within each table across the falls scores of 1 to 4 and the categories of BMD (T-score = 0, −1, −1.5, −2.0, −2.5, −3.0), as would be predicted from the FRISK equation. Similarly, Tables 3 and 4 show the absolute risk of fracture for 10 years.

Tables 1–4 display absolute risk of fracture associated with a woman of average weight and different combinations of all other risk factors. An increase in weight after adjusting for BMD is associated with an increased FRISK. An increase in weight of 9.3 kg is associated with the same change in absolute risk of fracture as an increase in the prior fractures by one, and an increase in weight by 30.5 kg is equivalent to an increase in the falls score by one.

The receiver operating characteristic curves showed no significant difference in the area under the curve (AUC) and the 95% CI for all four absolute risk of fracture algorithms: For the FRISK score, AUC was 0.66 (95% CI: 0.60, 0.71); for FRAX for the United Kingdom, AUC was 0.68 (95% CI: 0.63, 0.73); for FRAX for the United States, AUC was 0.67 (95% CI: 0.62, 0.73); and for the Garvan nomogram, AUC was 0.70 (95% CI: 0.65, 0.75). Similarly, the optimal sensitivities and specificities were comparable: For the FRISK score, sensitivity was 59.2 (71 of 120) and specificity was 64.8 (307 of 474); for FRAX for the United Kingdom, sensitivity was 60.8 (73 of 120) and specificity was 65.6 (311 of 474); for FRAX for the United States, sensitivity was 61.7 (74 of 120) and specificity was 62.4 (296 of 474); and for the Garvan nomogram,

sensitivity was 64.2 (77 of 120) and specificity was 66.2 (314 of 474).

The AUCs for all algorithms in the equations that excluded BMD were also not significantly different: For FRISK without BMD, AUC was 0.62 (95% CI: 0.56, 0.67); for FRAX for the United Kingdom, AUC was 0.66 (95% CI: 0.61, 0.71); for FRAX for the United States, AUC was 0.66 (95% CI: 0.61, 0.71); and for the Garvan nomogram, AUC was 0.66 (95% CI: 0.61, 0.72). The models also had comparable sensitivity and specificity: For the FRISK without BMD score, sensitivity was 55.8 (67 of 120) and specificity was 63.1 (299 of 474); for FRAX for the United Kingdom, sensitivity was 64.2 (77 of 120) and specificity was 62.9 (298 of 474); for FRAX for the United States, sensitivity was 66.7 (80 of 120) and specificity was 59.7 (283 of 474); and for the Garvan nomogram, sensitivity was 65.8 (77 of 120) and specificity was 63.7 (302 of 474).

The utility of the FRISK model can be seen in women with low BMD of the spine, for example, in those individuals with a spine T-score that is 1 standard deviation or more lower than that of the femoral neck T-score (n = 77). The FRISK score tended toward a higher sensitivity: For the FRISK score, sensitivity was 85.7 and specificity was 71.4; for FRAX for the United Kingdom, sensitivity was 71.4 and specificity was 68.3; for FRAX for the United States, sensitivity was 64.3 and specificity was 74.6; and for the Garvan nomogram, sensitivity was 78.6, and specificity was 68.3. Nevertheless, there was no difference in the AUCs.

Table 3

Absolute Risk of Fracture for 10 Years in Participants at Median Weight with No Prior Fracture

Falls and Femoral Neck T-score	Posteroanterior Spine T-score					
	0	−1.0	−1.5	−2.0	−2.5	−3.0
Falls score 1						
0	0.13	0.15	0.16	0.17	0.19	0.20
−1.0	0.15	0.17	0.18	0.20	0.21	0.22
−1.5	0.16	0.18	0.19	0.21	0.22	0.24
−2.0	0.17	0.19	0.21	0.22	0.24	0.25
−2.5	0.18	0.20	0.22	0.23	0.25	0.27
−3.0	0.19	0.22	0.23	0.25	0.27	0.29
Falls score 2						
0	0.17	0.19	0.20	0.22	0.24	0.25
−1.0	0.19	0.22	0.23	0.25	0.27	0.29
−1.5	0.20	0.23	0.25	0.27	0.29	0.32
−2.0	0.21	0.25	0.27	0.29	0.31	0.34
−2.5	0.23	0.26	0.29	0.31	0.34	0.37
−3.0	0.24	0.28	0.31	0.34	0.37	0.40
Falls score 3						
0	0.21	0.24	0.26	0.29	0.31	0.34
−1.0	0.24	0.28	0.31	0.33	0.37	0.40
−1.5	0.26	0.30	0.33	0.36	0.40	0.44
−2.0	0.28	0.33	0.36	0.39	0.43	0.48
−2.5	0.30	0.36	0.39	0.43	0.47	0.52
−3.0	0.32	0.39	0.42	0.47	0.51	0.57
Falls score 4						
0	0.28	0.33	0.36	0.39	0.43	0.47
−1.0	0.32	0.38	0.42	0.46	0.51	0.56
−1.5	0.35	0.42	0.46	0.51	0.56	0.62
−2.0	0.38	0.45	0.50	0.55	0.61	0.67
−2.5	0.41	0.50	0.55	0.60	0.67	0.73
−3.0	0.45	0.54	0.60	0.66	0.73	0.80

Note.—The median weight and falls score scale are the same as those in Table 1.

Discussion

In this study, we reported 5- and 10-year absolute risk of fracture in a random population-based group of women. Researchers in a previous study (27) described absolute risk of fracture in women in low-risk groups as lower than 10%, in women in moderate-risk groups as 10%–20%, and in women in high-risk groups as higher than 20%. Prior reports of low and moderate risk have included 10% for 10-year absolute risk of fracture (28) and 9% for 15 years (29). High-risk groups have had absolute risk of fracture of 23% for 10 years (28) and 56% for 15 years (29). In our study, a woman with normal BMD (T-score greater than −1 standard deviation), no prior fracture, and no falls in the prior year had a 7% absolute risk for fracture for 5 years and a 13% absolute risk for fracture for 10 years. A woman with no prior fracture, several falls in the prior year, and a BMD T-score of −2.0 or lower at either the hip or spine had at least a 13% and 28% absolute risk for fracture for 5 and 10 years, respectively.

Investigators in previous work (30) described those with more than 20% absolute risk of fracture for 10 years as in a high-risk category. In our study, any combination of two risk factors, a BMD T-score of −2.0 or lower at the spine or proximal femur or more than one fall in the previous year, resulted in the classification of the woman in a high-risk category. Having a prior fracture and any one of these risk factors was not sufficient for a woman to be classified in a high-risk category. Absolute risk of fracture associated with nearly all of the combinations of BMD at the hip and spine increased with each increase in falls category, but this did not occur with each increase in the number of prior fractures. The strength of association between BMD and prior fracture probably accounts for this pattern.

The resulting cubic and quadratic models presented in this study make

Table 4

Absolute Risk of Fracture for 10 Years in Participants at Median Weight with a Prior Fracture

Falls and Femoral Neck T-score	Posteroanterior Spine T-score					
	0	−1.0	−1.5	−2.0	−2.5	−3.0
Falls score 1						
0	0.15	0.17	0.18	0.19	0.20	0.21
−1.0	0.16	0.18	0.20	0.21	0.22	0.24
−1.5	0.17	0.19	0.21	0.22	0.24	0.26
−2.0	0.18	0.21	0.22	0.24	0.26	0.28
−2.5	0.19	0.22	0.24	0.25	0.28	0.30
−3.0	0.20	0.23	0.25	0.27	0.30	0.32
Falls score 2						
0	0.18	0.21	0.22	0.24	0.25	0.28
−1.0	0.20	0.23	0.25	0.27	0.29	0.32
−1.5	0.22	0.25	0.27	0.29	0.32	0.35
−2.0	0.23	0.27	0.29	0.32	0.34	0.38
−2.5	0.24	0.29	0.31	0.34	0.37	0.41
−3.0	0.26	0.31	0.34	0.37	0.41	0.45
Falls score 3						
0	0.23	0.27	0.29	0.31	0.34	0.38
−1.0	0.26	0.31	0.34	0.37	0.40	0.44
−1.5	0.28	0.33	0.36	0.40	0.44	0.49
−2.0	0.30	0.36	0.40	0.44	0.48	0.53
−2.5	0.33	0.39	0.43	0.48	0.52	0.58
−3.0	0.35	0.43	0.47	0.52	0.57	0.63
Falls score 4						
0	0.30	0.36	0.39	0.43	0.48	0.53
−1.0	0.35	0.42	0.47	0.52	0.57	0.63
−1.5	0.38	0.46	0.51	0.56	0.62	0.68
−2.0	0.42	0.50	0.56	0.61	0.68	0.75
−2.5	0.45	0.55	0.61	0.67	0.74	0.81
−3.0	0.49	0.60	0.66	0.73	0.81	0.89

Note.—The median weight and falls score scale are the same as those in Table 1.

biologic sense, as they display relatively no increase in absolute risk of fracture for the low FRISK scores (scores < 5) but increase considerably at the higher end of the FRISK scores. However, we must acknowledge wide CIs associated with the very high FRISK scores.

In this study, we reported similar predictability of FRISK across the four algorithms. The AUC for the FRISK score compared with the AUC for the Garvan nomogram were powered at 80% and a .05 level of significance to detect a difference. However, we cannot exclude the possibility of a type II error, or false-negative results, with comparison of the FRISK score with the FRAX models. Inclusion of falls in the algorithms did not greatly improve the models, as some of the other risk factors included in the FRAX models are probably a surrogate for falls. Scales such as FRAX for the United Kingdom and FRAX for the United States designed for other countries or ethnic groups appear to do at least as well in terms of the AUC. However, the value of the FRISK score model can be seen in its higher sensitivity to fracture in the group of women with low BMD of the spine. In a previous study (7) of women who had sustained a fracture, we showed that there is a higher proportion with low BMD of the spine and normal BMD of the hip, compared with the reverse situation, and the increased number therefore make this group a very important target group in which to identify FRISK correctly. The exclusion of this site from the other models may lead to incorrect fracture prediction.

Age was not included in the optimal set of predictors in the FRISK score model. The combination of BMD at two anatomic sites was a surrogate for the effect of age on bone and was included in the optimal set of variables to segregate fracture cases. However, we would not dispute the possibility that, with a sample size similar to that of the FRAX equation (9), age might be independently introduced into the model. Forcing age into the current model did not change the absolute risk of fracture.

A FRISK score can be easily transformed to provide an absolute risk of fracture. The use of a patient's absolute risk of fracture should assist clinicians in targeting therapy to those at highest risk and in avoiding treatment for those at low risk.

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