

Long-term Risk of Incident Vertebral Fractures

Jane A. Cauley, DrPH

Marc C. Hochberg, MD, MPH

Li-Yung Lui, MA, MS

Lisa Palermo, MS

Kristine E. Ensrud, MD, MPH

Teresa A. Hillier, MD, MS

Michael C. Nevitt, PhD, MPH

Steven R. Cummings, MD

VERTEBRAL FRACTURES ARE THE hallmark of osteoporosis. They are the most common osteoporotic fracture with prevalence estimates of 35% to 50% among women older than 50 years.¹⁻⁴ About 700 000 vertebral fractures occur each year in the United States. Only about one-third of vertebral fractures are clinically recognized.⁵ Women with vertebral fractures experience decreased survival⁶⁻⁹ and an increased risk of future vertebral, hip, and other non-spinal fractures.¹⁰⁻¹³ Vertebral fractures also cause chronic back pain, limitations with common activities of daily living, and reduced quality of life.^{14,15}

We have previously shown that low bone mineral density (BMD) is associated with an increased risk of vertebral fracture¹⁶ and that a prevalent vertebral fracture is associated with a 5-fold increased risk of sustaining a new vertebral fracture.¹¹ However, these observations were made over an average follow-up of 3.7 years. In the Framingham Study, neither bone mass as measured by metacarpal area or prevalent vertebral fractures were significantly associated with incident vertebral fractures over 25 years.¹⁷ Finally, absolute risk models have been developed for the hip and other osteoporotic fractures¹⁸ but not for vertebral fractures.

Context Vertebral fractures are the most common osteoporotic fracture. Women with low bone mineral density (BMD) and prevalent vertebral fractures have a greater risk of incident vertebral fractures over the short-term, but their absolute risk of vertebral fracture over the long-term is uncertain.

Objective To examine the absolute risk of incident vertebral fracture by BMD and prevalent vertebral fracture status over 15 years.

Design, Setting, and Participants A total of 9704 white women were recruited at 4 US clinical centers and enrolled in the Study of Osteoporotic Fractures, a longitudinal cohort study. Of these, 2680 attended a clinic visit an average of 14.9 years after baseline; mean age of 68.8 years at entry and 83.8 years at follow-up.

Mean Outcome Measure Incident vertebral fractures identified from lateral spinal radiographs defined as a decrease of at least 20% and 4 mm at any vertebral level. Prevalent vertebral fractures were identified on the baseline radiographs using vertebral morphometry. Bone mineral density was measured at the total hip and lumbar spine using dual-energy x-ray absorptiometry.

Results Of the 2680 women, 487 (18.2%) had an incident vertebral fracture including 163 of the 394 (41.4%) with a prevalent vertebral fracture at baseline and 324 of the 2286 (14.2%) without a prevalent vertebral fracture at baseline (odds ratio, 4.21; 95% confidence interval, 3.33-5.34). Low BMD was associated with an increased risk of incident vertebral fracture (odds ratio per 1 SD decrease in total hip BMD, 1.78 [95% confidence interval, 1.58-2.00]). The absolute risk of vertebral fracture ranged from 56% among women with total hip BMD T score of -2.5 or less and a prevalent vertebral fracture to 9% in women with normal BMD and no prevalent vertebral fracture.

Conclusions Low BMD and prevalent vertebral fractures are independently related to new vertebral fractures over 15 years of follow-up. Women with a prevalent vertebral fracture have a substantially increased absolute risk of an incident fracture, especially if they have osteoporosis diagnosed by BMD.

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The aim of the current study was to examine the absolute risk of incident vertebral fractures by spine and hip BMD and prevalent vertebral fracture status over 15 years of follow-up in a population-based cohort of community-dwelling older women.

METHODS

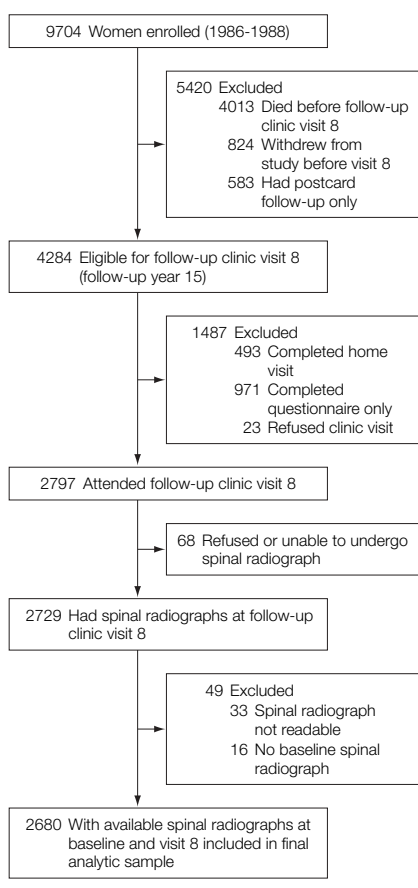
Study Population

A total of 9704 white women participated in the Study of Osteoporotic Fractures. Women were recruited from population-based listings in 4 US metropolitan areas. Details of the design of this study,

recruitment, and measurements have been published.¹⁶ Spinal radiographs were obtained at the baseline examina-

Author Affiliations: Department of Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania (Dr Cauley); Department of Medicine, University of Maryland Medical Center, Baltimore (Dr Hochberg); San Francisco Coordinating Center, California Pacific Medical Center, San Francisco (Ms Lui and Dr Cummings); Department of Epidemiology and Biostatistics, University of California, San Francisco (Ms Palermo and Drs Nevitt and Cummings); Department of Medicine, Minneapolis VA Medical Center, Minneapolis, Minnesota (Dr Ensrud); and Kaiser Permanente Center for Health Research Northwest/Hawaii, Portland, Oregon (Dr Hillier).

Corresponding Author: Jane A. Cauley, DrPH, University of Pittsburgh, 130 DeSoto St, Crabtree A524, Pittsburgh, PA 15261 (jcauley@edc.pitt.edu).

Figure 1. Study of Osteoporotic Fractures: Status of Original Cohort (n=9704) at Visit 8

tion between 1986 and 1988 in women between the ages of 65 and 99 years (mean age, 68.8 years). Repeat spinal radiographs for vertebral morphometry were obtained for 2680 who attended the eighth follow-up clinic visit (2002-July 2003 and January-April 2004), an average of 14.9 years after baseline (mean age, 83.8 years). Among the 9704 women enrolled in the Study of Osteoporotic Fractures, 4013 (41%) died before visit 8, 824 (8%) left the study before visit 8, and 583 (6%) were on postcard only follow-up (FIGURE 1). Among the 4284 eligible for visit 8, 493 (11.5%) completed a home visit; 971 (22.7%) completed only a questionnaire either because they lived out of state or were too ill to return to the clinic; and 23 (0.5%) refused to attend the clinic visit. Among the 2797 who attended the clinic visit, 2729 had spinal radiographs and of these, 2680

had x-ray films at visits 1 and 8 that could be evaluated and were included in the analytic sample. The study was approved by the appropriate committees on human research, and all the women gave written informed consent. Race/ethnicity was self-declared. The Study of Osteoporotic Fractures initially excluded black women because of their low risk of fracture.

Vertebral Morphometry

Lateral radiographs of the thoracic and lumbar spine were taken in accordance with current guidelines.¹⁹ Quantitative vertebral morphometry was performed as previously described¹⁶ to calculate the anterior (H_a), middle (H_m), and posterior (H_p) height for each vertebral body from T_4 to L_4 . The vertebral morphometry was initiated at the end of the clinical visits and was completed in early 2006. Radiographs were first screened for probable fractures, using methods previously described,²⁰ to reduce the number of morphometric measurements. Briefly, highly trained technicians separated sets of radiographs into 3 groups termed *normal*, *uncertain*, and *probably fractured*, using a binary semiquantitative grading scheme that classified women by the most abnormal vertebral level on her follow-up films. Morphometry on paired films was performed for women classified as probably fractured. The morphometry technicians were blinded to BMD results.

Definitions of Vertebral Fractures

A vertebra was classified as having a prevalent fracture on the baseline radiograph if any of the following ratios were more than 3 SDs below the trimmed normal mean²¹ for that vertebral level: (H_a/H_p), (H_m/H_p), or a combination of ($H_{pi}/H_{pi\pm 1}$).²⁰ We defined a new (incident) fracture as a decrease of 20% or more and at least 4 mm in length in any of the 3 vertebral heights (H_a , H_m , or H_p) on follow-up compared with the baseline radiograph.²² The performance of the technician triage was evaluated in a random sample of 503 women, all of whose radiographs were triaged and underwent

morphometry. The sensitivity of triage for prevalent and incident fractures, as defined in this study, was 97% and 100%, respectively.^{20,22}

Bone Mineral Density

Baseline calcaneal and distal radius BMD was measured using single photon absorptiometry (OstoAnalyzer; Siemens-Osteon, Wahiawa, Hawaii). During the second examination (1988-1990), BMD of the proximal femur and lumbar spine was measured using dual-energy x-ray absorptiometry (QDR 1000; Hologic, Bedford, Massachusetts). Total hip and femoral neck BMD were categorized by T score using the National Health and Nutrition Examination Surveys reference database.²³ Lumbar spine BMD was categorized by T score using the Hologic reference database.

Other Measurements

Body weight was measured using a balance beam scale and height was measured using the Harpenden stadiometer (Holtain Ltd, Crymych, United Kingdom). Body mass index was calculated as the weight in kilograms divided by the square of height in meters. Participants also completed a questionnaire and interview that collected information on demographics, current smoking, and medical history. Participants were asked to bring all prescription and over-the-counter medications to the clinic for verification of use. Information on hormone use was updated at each visit. A full medication inventory was obtained at visits 4, 5, 6, and 8. We included information on whether a woman ever reported use of estrogen, bisphosphonate, or selective estrogen receptor modulator. Self-reported health status in comparison with women of the same age was reported as excellent, good, fair, poor, or very poor. Functional status was assessed by asking participants if they had any difficulty performing any of the following instrumental activities of daily living (walking 2 or 3 blocks, climbing up 10 steps, walking down 10 steps, preparing meals, doing heavy housework or grocery shopping). The number of difficulties was summed.

Analysis

We compared baseline characteristics of women in the Study of Osteoporotic Fractures who had a follow-up spinal radiograph at visit 8 (analytic cohort, n=2680) with women in the Study of Osteoporotic Fractures who did not (n=7024) using a *t* test for continuous variables and the χ^2 test for categorical variables. Differences in baseline characteristics by incident vertebral fracture status for women in the analytic cohort also were examined using *t* and χ^2 tests. Because time to fracture was unknown, we used logistic regression to evaluate the associations between BMD and prevalent vertebral fracture status to incident vertebral fractures. We initially adjusted for age and clinic. Multivariable-adjusted models included age, clinic, baseline estrogen use, any use of estrogens, bisphosphonates, or selective estrogen receptor modulators over follow-up, history of nonspinal fracture, body mass index, and current smoking. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for 1 SD decrease in BMD. To compare the predictive value of each BMD site, we analyzed the areas under receiver operating characteristic curves in age- and clinic-adjusted models. We examined this relationship in the whole cohort and then stratified by age and prevalent vertebral fractures. We examined the incidence and 95% CIs of vertebral fracture by baseline total hip, femoral neck, and lumbar spine BMD T score. In addition, we tested whether the relationship between prevalent vertebral fractures and incident vertebral fracture was independent of BMD and differed by age. Finally, we examined the absolute risk of incident vertebral fracture by BMD T score and prevalent vertebral fracture status. The sample size of 2680 provided a power of 84% to detect a predetermined increased risk of 1.2 (OR) per 1 SD decrease in BMD. *P* less than .05 was used as the level of significance and all levels reported are 2-sided. All analyses were performed using SAS software version 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

Women who attended the year 15 clinic examination were younger, had a higher

body weight, and were taller at baseline than women who did not attend the visit, but there was no difference in their body mass index (TABLE 1). A higher proportion of women who attended the year 15 examination reported excellent health status at baseline. A lower proportion of attendees than nonattendees reported a fracture since age 50 years and had a prevalent vertebral fracture at baseline. Bone mineral density was higher among women who at-

tended the year 15 examination at every site except the lumbar spine.

Of the 2680 women who returned for visit 8 and had a follow-up spinal radiograph, 487 (18.2%) experienced an incident vertebral fracture including 163 of the 394 (41.4%) with a prevalent vertebral fracture at baseline and 324 of the 2286 (14.2%) without a prevalent vertebral fracture at baseline (TABLE 2). Women who had experienced a fracture were older at study

Table 1. Baseline Characteristics of Women in the Study of Osteoporotic Fractures

	Women With Year 15 Vertebral X-ray Films (n = 2680)	Remaining Cohort (n = 7024)	<i>P</i> Value
Age, mean (SD), y	68.8 (3.2)	72.8 (5.6)	<.001
Weight, mean (SD), kg	67.9 (11.9)	66.8 (12.7)	<.001
Height, mean (SD), cm	160.0 (5.8)	158.7 (6.1)	<.001
Body mass index, mean (SD) ^a	26.5 (4.4)	26.5 (4.8)	.94
Self-reported health of excellent or good, No. (%)	2418 (90.2)	5652 (80.5)	<.001
History of fractures after age 50 y, No. (%)	853 (31.8)	2727 (38.8)	<.001
Prevalent vertebral fracture, No. (%) ^b	394 (14.7)	1521 (22.0)	<.001
Bone mineral density, mean (SD), g/cm ²			
Calcaneus	0.42 (0.09)	0.40 (0.10)	<.001
Distal radius	0.37 (0.08)	0.36 (0.09)	<.001
Total hip ^c	0.78 (0.13)	0.75 (0.13)	<.001
Femoral neck ^c	0.67 (0.11)	0.64 (0.11)	<.001
Lumbar spine ^c	0.86 (0.16)	0.85 (0.17)	.15

^aCalculated as weight in kilograms divided by height in meters squared.

^bBased on baseline vertebral x-rays.

^cMeasured 2 years after baseline.

Table 2. Baseline Characteristics of Women in the Study of Osteoporotic Fractures by Incident Vertebral Fracture

	Vertebral Fractures (n = 487)	No Vertebral Fractures (n = 2193)	<i>P</i> Value
Age, mean (SD), y	69.8 (3.5)	68.6 (3.1)	<.001
Weight, mean (SD), kg	66.3 (11.6)	68.2 (12.0)	.001
Height, mean (SD), cm	159.8 (5.8)	160.0 (5.7)	.45
Body mass index, mean (SD) ^a	26.0 (4.3)	26.6 (4.4)	.003
Current smoker, No. (%)	42 (8.6)	141 (6.4)	.08
Estrogen use at baseline, No. (%)	59 (12.1)	342 (15.6)	.05
Any bisphosphonate, estrogen, or selective estrogen receptor modulator use during follow-up, No. (%)	248 (50.9)	930 (42.4)	<.001
Nonspinal fractures since age 50 y, No. (%)	260 (53.4)	614 (28.0)	<.001
Number of instrumental activities of daily living difficult	0.45 (0.95)	0.39 (0.89)	.20
Prevalent vertebral fracture, No. (%) ^b	163 (33.5)	231 (10.5)	<.001
Bone mineral density, mean (SD), g/cm ²			
Calcaneus	0.38 (0.08)	0.43 (0.09)	<.001
Distal	0.34 (0.08)	0.38 (0.08)	<.001
Total hip ^c	0.73 (0.12)	0.79 (0.12)	<.001
Femoral neck ^c	0.62 (0.10)	0.68 (0.11)	<.001
Lumbar spine ^c	0.78 (0.14)	0.88 (0.16)	<.001

^aCalculated as weight in kilograms divided by height in meters squared.

^bBaseline vertebral x-rays.

^cMeasured 2 years after baseline.

entry per 5-year increase (OR,1.62; 95% CI, 1.40-1.87). Women who experienced an incident fracture also weighed less, were more likely to have a positive fracture history and a prevalent vertebral fracture at study entry, and less likely to report estrogen use at baseline. Slightly more women who had an incident vertebral fracture reported smoking at entry to the study. Over the course of the study, several osteoporosis treatments became available. The overall use of these medications was significantly higher in women who had an incident vertebral fracture (51%), although use was relatively high in women who did not have an incident vertebral fracture (42%). The BMD was significantly lower at baseline in women

who experienced an incident fracture at all sites. There was no difference in functional status.

Low BMD at every site was a strong predictor of incident vertebral fracture (TABLE 3). For the areas under receiver operating characteristic curves, BMD at the lumbar spine was a better predictor than BMD at other sites. Further adjustments for other risk factors for vertebral fractures including smoking, body mass index, history of nonspinal fracture, current use of estrogen at baseline or any use of estrogen, bisphosphonates, or selective estrogen receptor modulators over the course of the study had little effect on our results. There was no evidence that the relationship between low BMD and

incident vertebral fracture differed by age or by baseline prevalent vertebral fracture status. About one-third of women with a hip BMD T score of -2.5 or less had an incident vertebral fracture compared with about 10% of women with normal BMD (FIGURE 2). There was a stepwise increase in the incidence of vertebral fracture with decreasing T score.

Women with a prevalent vertebral fracture at baseline were more than 4 times more likely to experience an incident vertebral fracture over follow-up compared with women without a prevalent vertebral fracture at baseline (TABLE 4). Adjustment for BMD and other risk factors for vertebral fracture attenuated this associa-

Table 3. Odds Ratio of Vertebral Fracture in Total Population and Stratified by Prevalent Vertebral Fracture Status and Age

	OR (95% CI) of Vertebral Fracture Per 1 SD Decrease in BMD		Area Under ROC Curves	Multivariable-Adjusted OR (95% CI) ^b			
	Base Model ^a	Multivariable-Adjusted ^b		Prevalent Vertebral Fracture		Age, y	
				Yes (n = 394)	No (n = 2286)	<70 (n = 1746)	≥70 (n = 934)
Calcaneus	1.67 (1.49-1.87)	1.61 (1.42-1.83)	0.66	1.44 (1.09-1.88)	1.50 (1.29-1.73)	1.62 (1.37-1.92)	1.65 (1.36-2.00)
Distal radius	1.56 (1.40-1.75)	1.47 (1.31-1.66)	0.66	1.20 (0.93-1.53)	1.44 (1.25-1.65)	1.49 (1.27-1.75)	1.45 (1.21-1.74)
Total hip ^c	1.78 (1.58-2.00)	1.80 (1.57-2.05)	0.68	1.87 (1.38-2.55)	1.58 (1.35-1.85)	1.84 (1.54-2.20)	1.75 (1.42-2.16)
Femoral neck ^c	1.73 (1.53-1.96)	1.71 (1.49-1.95)	0.67	1.40 (1.06-1.84)	1.63 (1.39-1.91)	1.89 (1.57-2.27)	1.53 (1.26-1.86)
Lumbar spine ^c	2.06 (1.82-2.34)	2.11 (1.84-2.43)	0.70 ^d	1.87 (1.39-2.52)	1.97 (1.68-2.32)	2.26 (1.86-2.74)	1.97 (1.61-2.41)

Abbreviations: BMD, bone mineral density; CI, confidence interval; OR, odds ratio; ROC, receiver operating characteristic.

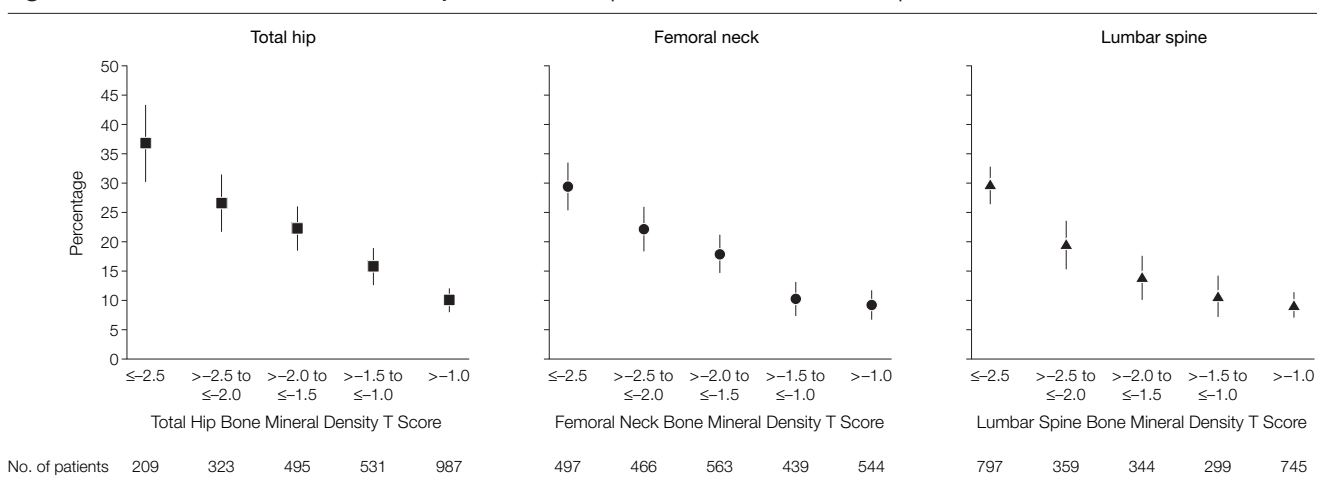
^aAdjusted for age and clinic.

^bAdjusted for age, clinic, estrogen use at baseline, any use of estrogen, bisphosphonate, or selective estrogen receptor modulator, history of nonspinal fracture, body mass index, and status as current smoker.

^cMeasured 2 years after baseline.

^dP<.05 compared with other BMD sites.

Figure 2. Absolute Risk of Vertebral Fracture by Baseline Total Hip, Femoral Neck, and Lumbar Spine T Score



Error bars indicate 95% confidence intervals.

tion slightly but it remained statistically significant. The risk was greatest among women with 2 or more prevalent fractures at baseline. There was some suggestion that the association between prevalent vertebral fracture and incident vertebral fracture was somewhat stronger for women younger than 70 years but the interaction between age and prevalent vertebral fracture was not significant ($P \geq .30$).

We examined the absolute risk of experiencing an incident vertebral fracture by BMD and prevalent vertebral fractures (total hip BMD and lumbar spine BMD; FIGURE 3). As shown, women who had osteoporosis based on their BMD T score had the highest incidence of vertebral fracture in comparison with women with low or normal BMD. In addition, the risk of vertebral fracture was greatest among women with a prevalent vertebral fracture at baseline, irrespective of their BMD. The absolute risk of vertebral fractures was more than 50% among women with both a prevalent vertebral fracture and BMD in the osteoporotic range. In contrast, women with normal BMD and no prevalent fracture had an absolute risk of about 9%. However, the interaction between BMD and prevalent vertebral fracture was not statistically significant ($P = .87$).

A total of 163 women had 2 or more incident fractured vertebrae. The association between 1 SD decrease in lumbar spine BMD and 2 or more fractured vertebrae vs 0 or 1 fractured vertebra yielded an OR of 2.50 (95% CI, 1.98-3.16) in multivariable-adjusted models. The odds of having 2 or more fractured vertebrae for women who had a prevalent vertebral fracture at baseline yielded an OR of 5.06 (95% CI, 3.56-7.20).

COMMENT

Among a cohort of 2680 white women aged 65 years or older, 18% experienced an incident vertebral fracture over 15 years of follow-up. Of importance, a single measure of BMD predicted incident vertebral fractures over 15 years and the magnitude of the relationship

did not differ by age and prevalent vertebral status. There was some suggestion that the relationship was stronger for lumbar spine BMD than hip or calcaneal BMD. A 1 SD decrease in BMD had a similar effect on fracture prediction as a 5-year increase in age. Adjustment for other risk factors for vertebral fracture had little effect on our results. Many women initiated some type of therapy for osteoporosis but ad-

justment for these osteoporosis therapies did not influence our results. The analyses on the areas under receiver operating characteristic curves showed moderate prediction for incident fracture but exceeded other established screening modules (eg, the Gail Score for breast cancer²⁴). Women with osteoporosis based on dual-energy x-ray absorptiometry have a high risk for incident vertebral fracture. There was a

Table 4. Association of Prevalent Vertebral Fractures at Baseline and Incident Vertebral Fractures

	OR (95% CI)			
	Base Model ^a	Multivariable Model ^b	Multivariable Model ^b	
			Age <70 y	Age ≥70 y
Prevalent vertebral fracture	4.21 (3.33-5.34)	3.95 (3.10-5.03)	4.41 (3.20-6.09)	3.40 (2.34-4.94)
Plus calcaneus BMD	3.73 (2.93-4.74)	3.54 (2.77-4.53)	3.89 (2.80-5.40)	3.11 (2.13-4.55)
Plus distal radius BMD	3.74 (2.94-4.76)	3.58 (2.80-4.59)	3.96 (2.85-5.49)	3.17 (2.17-4.63)
Plus total hip BMD ^c	3.47 (2.70-4.45)	3.27 (2.53-4.22)	3.65 (2.60-5.14)	2.81 (1.90-4.16)
Plus femoral neck BMD ^c	3.61 (2.81-4.65)	3.44 (2.66-4.45)	3.81 (2.70-5.38)	2.96 (2.00-4.37)
Plus lumbar spine BMD ^c	3.48 (2.71-4.18)	3.23 (2.50-4.19)	3.56 (2.53-5.03)	2.84 (1.92-4.21)
No. of prevalent fractures ^d				
1	2.68 (1.98-3.63)	2.51 (1.84-3.43)	2.66 (1.75-4.03)	2.30 (1.44-3.67)
≥2	5.73 (3.86-8.51)	5.22 (3.48-7.82)	6.13 (3.62-10.38)	4.32 (2.29-8.14)

Abbreviations: BMD, bone mineral density; CI, confidence interval; OR, odds ratio.

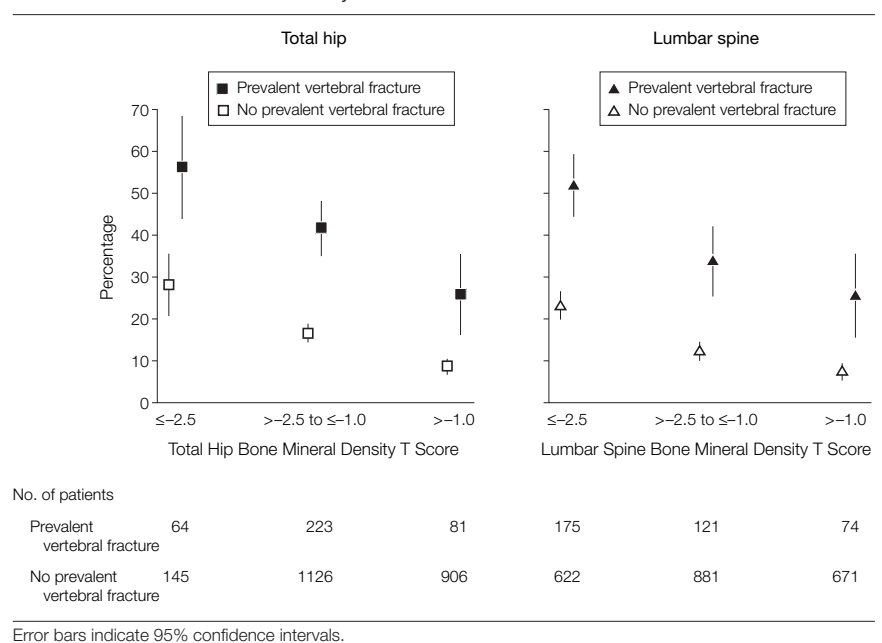
^aAdjusted for age and clinic.

^bAdjusted for age, clinic, estrogen use at baseline, any use of estrogen, bisphosphonate, or selective estrogen receptor modulator, history of nonspinal fracture, body mass index, and status as a current smoker.

^cMeasured 2 years after baseline.

^dAlso adjusted for lumbar spine BMD.

Figure 3. Absolute Risk of Incident Vertebral Fracture by Prevalent Vertebral Fracture Status at Baseline and Bone Mineral Density T Score



13-fold gradient of absolute risk comparing women with a prevalent vertebral fracture and osteoporosis by T score with women with normal BMD and no prevalent fracture at baseline.

The magnitude of the association between BMD and subsequent vertebral fracture over 15 years was similar to results over the short-term. For example, a 1 SD decrease in lumbar spine BMD was associated with a 1.9 increased odds of vertebral fracture after 3.7 years,¹⁶ similar to the OR of 2.1 observed in our current analysis. These results also are similar to analyses examining all nonspinal fractures together in which the short-term (<5 years) and long-term (>5 years) hazard ratios for BMD were similar.²⁵ Similar to the short-term results, lumbar spine BMD was a significantly better predictor of incident vertebral fractures over 15 years than BMD measured at other sites.

Women with prevalent vertebral fractures at baseline had a 4-fold increased risk of experiencing a new incident vertebral fracture. The magnitude of this association was markedly higher than observed for either age or BMD. These results are consistent with short-term analyses from the Study of Osteoporotic Fractures¹¹ and with other cohort studies.^{10,12,13,26-28} These results also are consistent with observations that prevalent vertebral fractures predict other nonvertebral fractures, including hip fractures.^{10,11,29} Of interest, over the short-term and long-term, women who had an existing vertebral fracture were 4 to 5 times more likely to experience a new incident vertebral fracture. Consistent with previous studies, the risk increased with increasing number of prevalent fractures. The association between prevalent and incident vertebral fractures was independent of low BMD. This suggests that the presence of a vertebral fracture provides key information on bone quality above and beyond BMD. Microarchitecture defects including decreasing bone volume, trabecular number and connectivity, and increasing trabecular separation have been associated with vertebral fractures.³⁰

Our results support the recommendation that older women with a prevalent vertebral fracture should be treated for osteoporosis irrespective of BMD. Treatment of women with prevalent asymptomatic vertebral fractures with bisphosphonates and selective estrogen receptor modulators has been shown to decrease fracture incidence.³¹⁻³⁴

Absolute risk models for predicting the 10-year risk of fractures have been recently developed.¹⁸ Of importance, these models are limited to hip and other clinical osteoporotic fractures. These absolute risk models exclude radiographic vertebral fracture, which is the most common type of vertebral fracture. These radiographic vertebral fractures have been linked to future fracture risk, morbidity, and mortality.^{7,8,11} Our results show that over 15 years, the absolute risk of vertebral fractures varies from about 55% among women with hip BMD T scores of -2.5 or less and a prevalent vertebral fracture at study entry to less than 10% among women with normal BMD and no vertebral fracture at baseline.

Lindsay et al²⁸ developed a Markov model to predict the prevalence of vertebral fractures over time. This model was developed in a population of women with osteoporosis by BMD criteria but with no existing vertebral fractures and used a lower threshold for defining a vertebral fracture ($>15\%$ loss of height). This model estimated that over 10 years, 55% of women will have developed a vertebral fracture. Our results suggest that this model may overestimate the risk of vertebral fractures. Among women with osteoporosis and no vertebral fractures, 28.3% of women (using total hip) or 23.3% of women (using lumbar spine) will have had an incident vertebral fracture in 15 years.

The majority of fractures occur in women who do not have osteoporosis based on BMD alone.^{35,36} Low BMD is a major risk factor for fracture and our current results show that a single measure of BMD can predict vertebral fractures over 15 years, but fractures are

multifactorial and several other risk factors for incident vertebral fractures have been identified.^{16,26,37} Nevertheless, the strongest predictor of an incident vertebral fracture was whether they had a prevalent vertebral fracture when they entered the study. Only about one-third of vertebral fractures are clinically identified¹; thus, case-finding strategies should be developed to identify women with a high likelihood of having a prevalent vertebral fracture. An algorithm developed from the European Prospective Osteoporosis Study included age, height loss, weight, and a history of fracture and identified those individuals who were more likely to have a documented vertebral fracture by x-ray with moderate accuracy.³⁸ Underdiagnosis of vertebral fracture is a worldwide problem.²⁹ Use of dual-energy x-ray absorptiometry to measure vertebral morphometry may be more cost-effective to improve fracture risk stratification and identify women with prevalent vertebral fractures who have a high absolute risk of fracture and may be more likely to benefit from pharmacological therapy.³⁹

There are a number of strengths to our study. We studied a large population of community-dwelling older women and repeated x-rays 15 years later. Standardized and state-of-the-art methods were used for identifying vertebral fractures. Nevertheless, there are some limitations. We studied the highest risk demographic group for vertebral fracture (ie, older white women) but our results may not be generalizable to women of other ethnicities or to men. Although a high rate of survivors participated in the clinic visit, the women who returned for the eighth clinic examination were healthier at baseline than those who did not. Thus, we may have underestimated the absolute risk of vertebral fractures. Total hip and lumbar spine BMD were measured 2 years after the baseline x-ray but results using baseline distal radius or calcaneal BMD were similar.

In conclusion, low BMD and prevalent vertebral fractures are independently related to new vertebral frac-

tures over 15 years of follow-up. Women with a prevalent vertebral fracture have a substantially increased absolute risk of an incident fracture, especially if they have osteoporosis diagnosed by BMD.

Author Contributions: Ms Lui had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Cauley, Hochberg, Nevitt, Cummings.

Acquisition of data: Cauley, Hochberg, Ensrud, Hillier, Nevitt, Cummings.

Analysis and interpretation of data: Cauley, Hochberg, Lui, Palermo, Ensrud, Hillier, Nevitt.

Drafting of the manuscript: Cauley.

Critical revision of the manuscript for important intellectual content: Hochberg, Lui, Palermo, Ensrud, Hillier, Nevitt, Cummings.

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