

High-Trauma Fractures and Low Bone Mineral Density in Older Women and Men

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APPROXIMATELY 1.5 MILLION osteoporotic fractures occur each year in the United States.¹ As the population ages, the number of fractures is projected to increase dramatically, and hip fractures in particular are expected to increase almost 4-fold by 2050 if effective prevention strategies are not implemented.^{2,3} The criteria used to define osteoporotic fractures warrant further investigation. By the current definition, fractures are recognized as osteoporotic if they are associated with low bone mineral density (BMD) and if they increase the risk of subsequent fracture.⁴ It remains unclear whether degree of trauma should be included in the definition of osteoporotic fractures.

Most low-trauma fractures (eg, those resulting from falls from standing height or less) are considered osteoporotic because they are related to low BMD^{5,6} and

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Context It is widely believed that fractures resulting from high trauma are not osteoporotic; however, this assumption has not been studied prospectively.

Objective To examine the association between bone mineral density (BMD) and high-trauma fracture and between high-trauma fracture and subsequent fracture in older women and men.

Design, Setting, and Participants Two prospective US cohort studies in community-dwelling adults 65 years or older from geographically diverse sites. The Study of Osteoporotic Fractures followed up 8022 women for 9.1 years (1988-2006). The Osteoporotic Fractures in Men Study followed up 5995 men for 5.1 years (2000-2007).

Main Outcome Measures Hip and spine BMD were assessed by dual-energy x-ray absorptiometry. Incident nonspine fractures were confirmed by radiographic report. Fractures were classified, without knowledge of BMD, as high trauma (due to motor vehicle crashes and falls from greater than standing height) or as low trauma (due to falls from standing height and less severe trauma).

Results Overall, 264 women and 94 men sustained an initial high-trauma fracture and 3211 women and 346 men sustained an initial low-trauma fracture. For women, each 1-SD reduction in total hip BMD was similarly associated with an increased risk of high-trauma fracture (multivariate relative hazard [RH], 1.45; 95% confidence interval [CI], 1.23-1.72) and low-trauma fracture (RH, 1.49; 95% CI, 1.42-1.57). Results were consistent in men (high-trauma fracture RH, 1.54; 95% CI, 1.20-1.96; low-trauma fracture RH, 1.69; 95% CI, 1.49-1.91). Risk of subsequent fracture was 34% (95% CI, 7%-67%) greater among women with an initial high-trauma fracture and 31% (95% CI, 20%-43%) greater among women with an initial low-trauma fracture, compared with women having no high- or low-trauma fracture, respectively. Risk of subsequent fracture was not modeled for men.

Conclusions Similar to low-trauma nonspine fractures, high-trauma nonspine fractures are associated with low BMD and increased risk of subsequent fracture in older adults. High-trauma nonspine fractures should be included as outcomes in osteoporosis trials and observational studies.

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subsequent fracture risk.^{7,8} In contrast, it is widely believed, without supporting evidence, that high-trauma fractures (eg, those resulting from motor vehicle crashes and falls from greater than standing height) are not related to low BMD or subsequent fracture risk and therefore are presumed not to be manifestations of osteoporosis.

This belief has several important consequences. First, there is a pervasive clinical opinion that an older adult who has a high-trauma fracture does not require evaluation for osteoporosis.^{9,10} Second, it is believed that high-trauma fractures

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cannot be prevented by osteoporosis treatments that increase BMD and bone strength.^{9,10} Third, high-trauma fractures are routinely excluded as outcomes in clinical trials and from the analyses of many observational studies.¹¹⁻¹⁵ Fourth, high-trauma fractures are not included in estimates of the societal impact of osteoporosis.^{9,10} Despite these important implications, assumptions about the relationship between BMD, high-trauma fractures, and subsequent fracture risk have not been critically examined.

Preliminary evidence challenges the assumption that high-trauma fractures are unrelated to low BMD. Data from the Geelong Osteoporosis Study showed that women older than 50 years with high-trauma fractures had significantly lower levels of BMD than a random, community-based sample of older women.¹⁶ The association between BMD and high-trauma fracture in older women and men has not been tested in a prospective study.

An important clinical outcome of a low-trauma fracture is increased risk for subsequent fracture.^{7,17-19} A high-trauma fracture also may be an important risk factor for subsequent fracture. One retrospective cohort study has shown that individuals who sustained high-trauma ankle or tibial fractures early in life had an increased risk of low-trauma fractures later in life compared with individuals having no prior history of high-trauma fracture.²⁰ This result has yet to be confirmed in a prospective study.

In the current study, conducted in 2 large prospective cohorts of older women and men, we tested the hypotheses that low BMD increases the risk of high-trauma fracture and that high-trauma fracture increases the risk of subsequent fracture.

METHODS

Study Participants

Women were participants in the prospective Study of Osteoporotic Fractures (SOF). During the baseline examination from 1986 to 1988, 9704 community-dwelling white women 65

years or older were enrolled from population-based listings in 4 areas of the United States: Baltimore, Maryland; Minneapolis, Minnesota; Portland, Oregon; and Monongahela Valley near Pittsburgh, Pennsylvania. Race/ethnicity was self-reported by participants, using investigator-defined categories. Between 1988 and 1990, 8022 of the 9483 (85%) surviving members of the cohort returned for a second clinic visit and were included in this analysis.

Men were participants in the prospective Osteoporotic Fractures in Men Study (MrOS). During the baseline examination from March 2000 to April 2002, 5995 community-dwelling men 65 years or older were enrolled at 6 clinical centers in the United States: Birmingham, Alabama; Palo Alto, California; San Diego, California; Minneapolis, Minnesota; Portland, Oregon; and Monongahela Valley near Pittsburgh, Pennsylvania. Race/ethnicity was self-reported by participants, using investigator-defined categories. Six hundred thirty-three (10.6%) of the men recruited to MrOS were nonwhite or Hispanic. For both studies, women and men were not eligible to participate if they reported bilateral hip replacement or required the assistance of another person in ambulation. Details of the cohorts have been published.²¹⁻²³ The protocol and consent forms for SOF and MrOS were approved by the institutional review boards at all of the participating institutions. All participants provided written informed consent.

Bone Mineral Density

In SOF, areal BMD (in g/cm²) was measured in the proximal femur and the lumbar spine by dual-energy x-ray absorptiometry using QDR 1000 densitometers (Hologic, Bedford, Massachusetts) during the second clinic visit in 1988-1990 (these measurements were not made at the baseline visit in SOF). In MrOS, proximal femur and lumbar spine BMDs were measured by dual-energy x-ray absorptiometry using Hologic QDR 4500 densitometers during the baseline visit in 2000-

2002. For both studies, all hip scans were performed on the right hip unless a participant reported a hip prosthesis or other metal object(s) on the right side of the leg, in which case the left hip was scanned. Standardized procedures for participant positioning and scan analysis were used for all scans. All densitometry operators at the clinical centers were trained and certified centrally in scanning and analysis techniques. For quality assurance, densitometry technicians at the coordinating center (University of California, San Francisco) reviewed a random sample of all scans, scans with exceptionally high or low BMD, and problematic scans identified at the clinical centers.

Cross-calibration studies were completed in both cohorts. In SOF, mean interclinic coefficients of variation (CVs) were 1.2% for the proximal femur and 1.5% for the lumbar spine based on reported findings from 2 members of the research staff who visited all centers.²⁴ In MrOS, interclinic CVs for anthropometric calibration phantoms were 0.9% for hip phantoms and 0.6% for spine phantoms. Intraclinic CVs for hip phantoms (0.37%-0.58%) and spine phantoms (0.34%-0.42%) were within acceptable ranges.²³

Other Measurements

In both SOF and MrOS, demographic, anthropometric, lifestyle, neuromuscular function, and medical history data were obtained. Height was measured with a wall-mounted Harpenden stadiometer (Holtain Ltd, Dyfed, United Kingdom), and body weight was measured with a balance beam scale (except for the MrOS Portland site, which used a digital scale). Body mass index was calculated as weight in kilograms divided by height in meters squared. Smoking history (ever vs never), history of falling in the past year, and history of fractures since age 50 years were ascertained through a self-administered questionnaire.

During a clinic interview, health status was classified as excellent/good (vs fair/poor/very poor) in response to the

question, "Compared to other people your own age, how would you rate your overall health?" Walking for exercise, current use of hormone therapy (in women), and current use of bisphosphonates (in men) were also assessed. During a clinic examination, participants were asked to rise from a chair 5 times without using their arms; those who could not do so were classified as "unable." Participants were asked whether a physician or other clinician had ever told them they had certain medical conditions including diabetes mellitus, thyroid disease, osteoarthritis, Parkinson disease, cancer (MrOS men only), chronic obstructive pulmonary disease, myocardial infarction (MrOS men only), hypertension, congestive heart failure (MrOS men only), or stroke.

Fracture Ascertainment and Classification

We contacted participants in the SOF and MrOS cohorts every 4 months by mailed questionnaires to determine whether they had sustained a fracture in the prior 4-month period. These contacts were more than 95% complete in SOF during a mean of 9.1 (SD, 5.2) years of follow-up and 99% complete in MrOS during a mean of 5.1 (SD, 1.3) years of follow-up. All fractures were validated by physician review of radiology reports or radiographs. When a fracture was reported, clinic staff interviewed participants about the fracture and how it occurred.

Main analyses included all non-spine, nonpathological fractures that occurred after the second visit (1988-1990) and before February 2006 in SOF and after the baseline visit (2000-2002) and before February 2007 in MrOS. In subanalyses, fractures not typically associated with BMD (ie, those of the face, skull, finger, toe, and heel) were excluded (in SOF, 29 high-trauma and 353 low-trauma fractures; in MrOS, 11 high-trauma and 38 low-trauma fractures).

Clinic staff coded all fractures according to degree of trauma without knowledge of BMD. High-trauma frac-

tures included all fractures due either to severe trauma (eg, motor vehicle crashes, being struck by a vehicle or other fast-moving projectile, or assault) or to falls from greater than standing height (eg, falls off a ladder, chair, porch, table, or other raised surface, not including stairs). Low-trauma fractures included all fractures due to (1) falls from standing height or less; (2) falls on stairs, steps, or curbs; (3) moderate trauma other than a fall (eg, collisions with objects during normal activities); and (4) minimal trauma other than a fall (eg, turning over in bed). We assumed that if the fracture had involved high trauma, the participant would have recalled it; therefore, if the source of trauma was unknown, we classified the fracture as low trauma.

In MrOS, to assess the sensitivity of our findings to the method of trauma classification, we also formed an expert committee of 3 physician adjudicators who independently reviewed a subset of all fracture cases (fractures initially coded by the clinics as due to severe trauma, a fall from greater than standing height, and moderate trauma other than a fall) for "excessive trauma," ie, trauma sufficient to cause fracture in any person, regardless of age.

Statistical Analyses

All analyses were stratified by sex. The baseline characteristics of women and men who had high-trauma and low-trauma fractures were compared with those of women and men without fracture using analysis of variance for continuous variables and χ^2 tests for categorical variables. We used Cox proportional hazards regression models to determine the relative hazard (RH) and 95% confidence interval (CI) of first incident high-trauma fracture (following the second clinic visit in SOF and the baseline visit in MrOS) per 1-SD reduction in BMD (total hip, femoral neck, and lumbar spine). We censored on low-trauma fracture (a competing risk).

We adjusted initially for age, and in multivariate models we adjusted for age, height, weight, walking as a form of ex-

ercise, smoking history (ever vs never), fracture since age 50 years, fall in the past year, 1 or more medical conditions (diabetes mellitus, thyroid disease, osteoarthritis, Parkinson disease, cancer [MrOS men only], chronic obstructive pulmonary disease, myocardial infarction [MrOS men only], hypertension, congestive heart failure [MrOS men only], or stroke), self-rated health (excellent/good vs fair/poor/very poor), ability to rise from a chair 5 times without using one's arms, current use of hormone therapy (SOF women only), and current use of bisphosphonates (MrOS men only). These variables are known to be associated with nonspine osteoporotic fractures.^{8,25,26} We repeated these analyses and constructed separate age- and multivariate-adjusted models to determine the RH and 95% CI of first incident low-trauma fracture per 1-SD reduction in BMD, censoring on high-trauma fracture (a competing risk).

We also examined risk of first incident high- and low-trauma fracture by clinical categories of BMD based on T scores, defined as the number of SDs below the mean BMD of young adults of the same sex and race, using the National Health and Nutrition Examination Survey database for total hip and femoral neck for adults aged 20 to 29 years.^{27,28}

For women in SOF, we had sufficient data to examine risk of subsequent fracture. We used Cox models to determine the RH and 95% CI of a subsequent fracture after the first incident fracture. In the first model, we used high-trauma fracture status, age, and total hip BMD as predictors of subsequent fracture, of which high-trauma fracture status was treated as time-varying. In the second model, we used low-trauma fracture status, age, and total hip BMD as predictors of subsequent fracture, of which low-trauma fracture status was treated as time-varying. Since very few men experienced subsequent fractures, we did not have adequate power to accurately model risk of subsequent fracture for men in MrOS; therefore, we reported

only the number of subsequent fractures for men. All analyses were conducted using SAS version 9.1 (SAS Institute Inc, Cary, North Carolina). $P < .05$ was considered statistically significant.

RESULTS

Over a mean of 9.1 years of follow-up (range, 0-16.8 years) in the SOF cohort, 264 of 8022 women (3.3%) sustained 332 first incident high-trauma fractures (incidence, 3.6 per 1000 person-years; 95% CI, 3.2-4.1). Of the 332 high-trauma fractures, 207 (62.3%) were coded by clinic staff as due to severe trauma (incidence, 2.1 per 1000 person-years; 95% CI, 1.7-2.4), and 125 (37.7%) as due to a fall from greater than standing height (incidence, 1.6 per 1000 person-years; 95% CI, 1.3-1.9).

During the same period, 3211 women (40.0%) experienced 3405 low-trauma fractures (incidence, 44.1 per 1000 person-years; 95% CI, 42.6-45.6). Nineteen pathological fractures were excluded.

Compared with women who did not have a fracture, women who had a high-trauma fracture had lower body weight and body mass index and were more likely to report a fracture since age 50 years and a fall in the past year (TABLE 1). Women who had a low-trauma fracture were older, had a lower body weight and body mass index, were less likely to report current use of hormone therapy, and were more likely to report a fracture since age 50 years and a fall in the past year than women who did not have a fracture. In addition, women with high- and low-trauma fractures had lower BMD at

the total hip, femoral neck, and lumbar spine and were more likely to have a T score of -2.5 or less at either the total hip or femoral neck than women who did not have a fracture.

Over a mean of 5.1 years of follow-up (range, 0-6.8 years) in the MrOS cohort, 94 of 5995 men (1.6%) sustained a first incident high-trauma fracture (incidence, 3.1 per 1000 person-years; 95% CI, 2.4-3.7). Of the 94 high-trauma fractures, 46 (48.9%) were coded by clinic staff as due to severe trauma (incidence, 1.5 per 1000 person-years; 95% CI, 1.1-1.9), and 48 (51.1%) as due to a fall from more than standing height (incidence, 1.6 per 1000 person-years; 95% CI, 1.1-2.0). During the same period, 346 men (5.8%) sustained a first incident low-trauma fracture (incidence, 11.3 per 1000 person-

Table 1. Characteristics of SOF Women and MrOS Men by Fracture Status^a

Characteristic	Women			Men		
	High-Trauma Fracture (n = 264)	Low-Trauma Fracture (n = 3211)	No Fracture (n = 4547)	High-Trauma Fracture (n = 94)	Low-Trauma Fracture (n = 346)	No Fracture (n = 5555)
Age, mean (SD), y	73.3 (5.2)	74.1 (5.3) ^b	73.4 (5.2)	73.3 (5.9)	76.1 (6.5) ^b	73.5 (5.8)
Weight, mean (SD), kg	64.9 (11.7) ^b	65.7 (12.2) ^b	67.1 (12.7)	82.5 (14.1)	81.9 (13.9)	83.2 (13.2)
Height, mean (SD), cm	158.5 (6.1)	159.2 (6.2)	159.2 (5.9)	174.4 (7.6)	173.4 (7.0)	174.2 (6.8)
Body mass index, mean (SD) ^c	25.8 (4.5) ^b	25.9 (4.5) ^b	26.5 (4.7)	27.1 (4.3)	27.2 (4.0)	27.4 (3.8)
BMD, mean (SD), g/cm ²						
Total hip	0.73 (0.12) ^b	0.72 (0.12) ^b	0.79 (0.13)	0.90 (0.14) ^b	0.89 (0.15) ^b	0.96 (0.14)
Femoral neck	0.63 (0.11) ^b	0.62 (0.10) ^b	0.67 (0.11)	0.74 (0.12) ^b	0.72 (0.13) ^b	0.79 (0.13)
Lumbar spine	0.82 (0.16) ^b	0.82 (0.15) ^b	0.89 (0.17)	1.00 (0.18) ^b	1.01 (0.18) ^b	1.08 (0.19)
BMD T score, No. (%) ^d						
≤ -2.5	85 (36.2) ^b	1014 (36.6) ^b	800 (20.9)	12 (12.8) ^b	51 (14.8) ^b	259 (4.7)
> -2.5 and ≤ -1.0	124 (52.8)	1488 (53.7)	2200 (57.5)	54 (57.5)	206 (59.7)	3015 (54.3)
Lifestyle, No. (%)						
Walk for exercise	149 (56.4)	1629 (50.7)	2318 (51.0)	34 (36.2) ^b	164 (47.4)	2782 (50.1)
Ever smoked	94 (37.6)	1241 (40.0)	1763 (40.3)	54 (57.5)	217 (62.7)	3474 (62.6)
Hormone therapy	31 (12.3)	393 (12.7) ^b	682 (15.8)	NA	NA	NA
Bisphosphonate therapy	NA	NA	NA	4 (4.3) ^b	16 (4.6) ^b	81 (1.5)
Medical history, No. (%)						
Fracture since age 50 y	126 (47.7) ^b	1586 (49.4) ^b	1334 (29.5)	31 (33.0) ^b	110 (31.8) ^b	892 (16.1)
Fallen in past year	85 (33.0) ^b	1017 (32.3) ^b	1129 (25.3)	27 (28.7) ^b	117 (33.8) ^b	1124 (20.2)
≥ 1 Medical conditions ^e	212 (81.9)	2592 (82.0)	3561 (80.2)	71 (75.5)	289 (83.5) ^b	4266 (76.8)
Excellent/good health	228 (86.4)	2686 (83.7)	3814 (83.9)	83 (88.3)	287 (83.0)	4766 (85.8)
Performance, No. (%) ^f	4 (1.5)	125 (3.9)	152 (3.4)	2 (2.1)	25 (7.3) ^b	153 (2.8)

Abbreviations: BMD, bone mineral density; NA, not applicable because hormone therapy was prescribed for women only and bisphosphonate therapy was not approved at time of second clinic visit for SOF (1988-1990); MrOS, Osteoporotic Fractures in Men Study; SOF, Study of Osteoporotic Fractures.

^a Because of missing data, the denominator used to calculate the percentages may vary. Fracture status based on fractures that occurred after the second clinic visit (1988-1990) and before February 2006 in SOF and after the baseline visit (2000-2002) and before February 2007 in MrOS.

^b $P < .05$ compared with the no-fracture group of same sex.

^c Calculated as weight in kilograms divided by height in meters squared.

^d At either the total hip or femoral neck.

^e Includes diabetes mellitus, thyroid disease, osteoarthritis, Parkinson disease, cancer (MrOS men only), chronic obstructive pulmonary disease, myocardial infarction (MrOS men only), hypertension, congestive heart failure (MrOS men only), and stroke.

^f Assessed as inability to rise from chair 5 times without using one's arms.

years; 95% CI, 10.1-12.5). Compared with men who did not have a fracture, men who had a high-trauma fracture were less likely to walk for exercise and were more likely to report a fracture since age 50 years and a fall in the past year (Table 1). Men who had a low-trauma fracture were older; were more likely to report a fracture since age 50 years, a fall in the past year, and 1 or more medical conditions; and also were more likely to be unable to rise from a chair 5 times without using their arms than men without a fracture. In addition, men with high- and low-trauma fracture had lower BMD at the total hip, femoral neck, and lumbar spine, were more likely to have a T score of -2.5 or less at either the total hip or femoral neck, and more likely to report use of bisphosphonate therapy than men who did not have a fracture.

The distribution of fracture locations differed by level of trauma (TABLE 2). In SOF women, rib and wrist fractures were the most common high-trauma fractures, and hip and wrist fractures were the most common low-trauma fractures. In MrOS men, rib and wrist fractures were also the most common high-trauma fractures, and hip and rib fractures were the most common low-trauma fractures. In SOF women, the majority (54%) of high-trauma fractures were caused by motor vehicle crashes. In MrOS men, 21% of high-trauma fractures were caused by motor vehicle crashes. Other causes included falls from ladders, roofs, and trees (28%); sporting and recreational activities (eg, biking and skiing injuries) (22%); falls from stools or equivalent (15%); construction and maintenance activities (eg, injuries sustained while building fences and fixing cars) (9%); and other causes (5%). Low-trauma fractures were caused predominantly by falls from standing height or less in SOF women (71%) and MrOS men (65%), followed by falls on steps, stairs, or curbs (16% SOF, 18% MrOS); moderate trauma other than a fall (7% SOF, 12% MrOS); and minimal trauma other than a fall (<1% SOF, 1% MrOS). Trauma codes were missing for 7% of

low-trauma fractures in SOF women and for 4% in MrOS men.

Risk of First Incident High- and Low-Trauma Fracture

Age (per 5-year increase) was associated with an increased risk of low-trauma fracture in women (RH, 1.32; 95% CI, 1.28-1.36) and men (RH, 1.46; 95% CI, 1.34-1.59). However, age (per 5-year increase) was not associated with risk of high-trauma fracture in women (RH, 1.08; 95% CI, 0.95-1.22) or men (RH, 0.98; 95% CI, 0.82-1.17).

Low BMD was associated with increased risk of high- and low-trauma fracture. After adjusting for age, a 1-SD decrease in total hip BMD was associated with a 47% (95% CI, 28%-69%) increased risk of high-trauma fracture in women and a 58% (95% CI, 27%-97%) increased risk in men (TABLE 3). Adjustment for multiple covariates did not change these estimates. Similarly, after adjusting for age, a 1-SD decrease in total hip BMD was associated with a 50% (95% CI, 44%-56%) greater risk of low-trauma

Table 2. Fracture Locations for SOF Women and MrOS Men by Level of Trauma

Fracture Location	No. (%)			
	Women		Men	
	High-Trauma Fracture	Low-Trauma Fracture	High-Trauma Fracture	Low-Trauma Fracture
All	332 (100)	3405 (100)	94 (100)	346 (100)
Hip	24 (7.2)	779 (22.9)	9 (9.6)	66 (19.1)
Wrist	44 (13.3)	588 (17.3)	17 (18.1)	29 (8.4)
Humerus	25 (7.5)	307 (9.0)	0	20 (5.8)
Ribs	61 (18.4)	265 (7.8)	22 (23.4)	64 (18.5)
Foot	16 (4.8)	246 (7.2)	0	22 (6.4)
Ankle	20 (6.0)	227 (6.7)	7 (7.4)	33 (9.5)
Pelvis	22 (6.6)	150 (4.4)	3 (3.2)	10 (2.9)
Tibia/fibula	18 (5.4)	100 (2.9)	5 (5.3)	12 (3.5)
Clavicle	18 (5.4)	44 (1.3)	7 (7.4)	16 (4.6)
Other ^a	84 (25.3)	699 (20.5)	24 (25.5)	74 (21.4)

Abbreviations: MrOS, Osteoporotic Fractures in Men Study; SOF, Study of Osteoporotic Fractures.

^aIncludes fractures of the skull, neck, face, scapula, shoulder, chest/sternum, elbow, forearm, hand, fingers, tailbone/coccyx/sacrum, femur, patella, toes, heel, hip near prosthesis, knee near prosthesis, and other locations near prostheses. Each occurred with frequency 8.5% or less in both fracture groups for men and women.

Table 3. Relative Hazard of High- and Low-Trauma Fracture per 1-SD Decrease in BMD at the Total Hip, Femoral Neck, and Lumbar Spine for SOF Women and MrOS Men

BMD Location	RH (95% CI)			
	Women		Men	
	High-Trauma Fracture	Low-Trauma Fracture	High-Trauma Fracture	Low-Trauma Fracture
Total hip				
Age-adjusted ^a	1.47 (1.28-1.69)	1.50 (1.44-1.56)	1.58 (1.27-1.97)	1.67 (1.49-1.87)
Multivariate-adjusted ^b	1.45 (1.23-1.72)	1.49 (1.42-1.57)	1.54 (1.20-1.96)	1.69 (1.49-1.91)
Femoral neck				
Age-adjusted ^a	1.33 (1.15-1.53)	1.49 (1.43-1.56)	1.47 (1.17-1.85)	1.65 (1.46-1.86)
Multivariate-adjusted ^b	1.23 (1.04-1.46)	1.46 (1.39-1.53)	1.41 (1.10-1.79)	1.66 (1.46-1.89)
Lumbar spine				
Age-adjusted ^a	1.39 (1.21-1.60)	1.38 (1.32-1.43)	1.54 (1.23-1.93)	1.47 (1.31-1.64)
Multivariate-adjusted ^b	1.30 (1.11-1.53)	1.35 (1.29-1.42)	1.47 (1.16-1.85)	1.41 (1.26-1.59)

Abbreviations: BMD, bone mineral density; CI, confidence interval; MrOS, Osteoporotic Fractures in Men Study; RH, relative hazard; SOF, Study of Osteoporotic Fractures.

^aPer 5-year increase.

^bMultivariate-adjusted models include age, weight, height, walking as a form of exercise (yes/no), smoking history (ever vs never), fracture since age 50 years (yes/no), fall in the past year (yes/no), 1 or more medical conditions (yes/no), self-rated health (excellent/good vs fair/poor/very poor), ability to rise from chair 5 times without using one's arms (yes/no), current hormone therapy (yes/no, for SOF women only), and current bisphosphonate use (yes/no, for MrOS men only).

fracture in women and a 67% (95% CI, 49%-87%) greater risk in men. Adjustment for multiple covariates did not change these estimates. For women and men, similar associations were observed for femoral neck and lumbar spine BMD. Exclusion of face, skull, finger, toe, and heel fractures did not alter the results significantly (results not shown).

In women and men, risk of high- and low-trauma fracture was particularly elevated among individuals with T scores of -2.5 or less (TABLE 4). Adjustment for multiple covariates attenuated the estimates only modestly. Risk of high-trauma fracture was not elevated among women or men with T scores between -1.0 and -2.5 after multivariate adjustment. Exclusion of face, skull, finger, toe, and heel fractures did not alter the results significantly (results not shown).

Results in MrOS were consistent when trauma was graded by the committee of physician adjudicators rather than clinic staff. Based on initial trauma codes assigned by the clinics, 135 fractures among MrOS men were eligible for review by the committee of physician adjudicators (46 due to severe trauma, 48 to a fall from greater than standing height, and 41 to moderate trauma other than a fall). The committee reviewed 110 of these 135 fractures (81%) (25 fractures had not been adjudicated for ex-

cessive trauma at the time of manuscript preparation) and classified 55 fractures (50%) as excessive-trauma fractures (incidence, 1.8 per 1000 person-years; 95% CI, 1.3-2.3). Most (82%) of the excessive-trauma fractures were also classified as high-trauma fractures based on our primary method of trauma classification (clinic staff), while the remaining 18% were originally classified as due to low trauma by the primary method. Excessive-trauma fractures were strongly associated with BMD. Specifically, each 1-SD reduction in total hip BMD was associated with a 40% (95% CI, 2%-92%) greater risk of excessive trauma fracture after adjustment for multiple covariates. Risk of excessive trauma fracture was 3.32-fold (95% CI, 1.29-8.57) higher for men with T scores of -2.5 or less compared with men having T scores greater than -1.0 , adjusted for age.

Risk of Subsequent Fracture

Women with high- and low-trauma fractures had a similar and elevated risk for subsequent nonspine fracture compared with women who had not had a fracture. Ninety-six of the 264 women (36.4%) who sustained first incident high-trauma fractures and 1082 of the 3211 women (33.7%) who sustained first incident low-trauma fractures also sustained a subsequent fracture. In

models adjusted for age and total hip BMD, women who sustained a high-trauma fracture had a 34% (95% CI, 7%-67%) greater risk of subsequent fracture than women who had not experienced a high-trauma fracture. Similarly, women who sustained a low-trauma fracture had a 31% (95% CI, 20%-43%) greater risk of subsequent fracture than women who had not experienced a low-trauma fracture.

In MrOS men, 6 of the 94 men (6.4%) who sustained first incident high-trauma fractures also sustained a subsequent fracture. Similarly, 28 of the 346 men (8.1%) who sustained first incident low-trauma fractures also sustained a subsequent fracture.

COMMENT

This study demonstrates that low BMD is associated with increased risk of high-trauma nonspine fracture in older women and men. Associations between BMD and high-trauma fracture were similar in magnitude to those between BMD and low-trauma fracture. Fracture risk, regardless of trauma, was particularly elevated among women and men with T scores of -2.5 or less. These findings support conclusions from a retrospective case-control study by Sanders et al,¹⁶ who found that Australian women older than 50 years with high-trauma fractures had lower BMD at hip,

Table 4. High- and Low-Trauma Fractures According to T Score for SOF Women and MrOS Men

BMD T Score	No. ^a	Person-Years	High-Trauma Fracture				Low-Trauma Fracture			
			No.	Rate per 1000 Person-Years (95% CI)	RH (95% CI)		No.	Rate per 1000 Person, y (95% CI)	RH (95% CI)	
					Age-Adjusted	Multivariate-Adjusted ^b			Age-Adjusted	Multivariate-Adjusted ^b
Women										
$> -1.0^c$	1125	12 601	26	2.1 (1.3-2.9)	1 [Reference]	1 [Reference]	270	21.4 (18.9-24.0)	1 [Reference]	1 [Reference]
≤ -1.0 and $> -2.5^c$	3812	36 606	124	3.4 (2.8-4.0)	1.62 (1.06-2.47)	1.46 (0.93-2.30)	1488	40.7 (38.6-42.7)	1.83 (1.61-2.08)	1.76 (1.54-2.03)
$\leq -2.5^c$	1899	14 691	85	5.8 (4.6-7.0)	2.70 (1.73-4.23)	2.25 (1.36-3.75)	1014	69.0 (64.8-73.3)	2.94 (2.57-3.37)	2.66 (2.28-3.10)
Men										
$> -1.0^c$	2397	12 562	28	2.2 (1.4-3.1)	1 [Reference]	1 [Reference]	88	7.0 (5.5-8.5)	1 [Reference]	1 [Reference]
≤ -1.0 and $> -2.5^c$	3275	16 581	54	3.3 (2.4-4.1)	1.49 (0.94-2.35)	1.37 (0.85-2.20)	206	12.4 (10.7-14.1)	1.58 (1.23-2.03)	1.59 (1.22-2.05)
$\leq -2.5^c$	322	1471	12	8.2 (3.5-12.8)	3.79 (1.90-7.55)	3.18 (1.52-6.64)	51	34.7 (25.2-44.2)	3.83 (2.70-5.44)	3.51 (2.41-5.13)

Abbreviations: BMD, bone mineral density; CI, confidence interval; MrOS, Osteoporotic Fractures in Men Study; RH, relative hazard; SOF, Study of Osteoporotic Fractures.

^aTotal hip and femoral neck BMD, and therefore T scores, were missing for 1186 SOF women and 1 MrOS man.

^bMultivariate-adjusted models include age, weight, height, walking as a form of exercise (yes/no), smoking history (ever vs never), fracture since age 50 years (yes/no), fall in the past year (yes/no), 1 or more medical conditions (yes/no), self-rated health (excellent/good vs fair/poor/very poor), ability to rise from chair 5 times without using one's arms (yes/no), current hormone replacement therapy (yes/no, for SOF women only), and current bisphosphonate use (yes/no, for MrOS men only).

^cAt either the total hip or femoral neck.

spine, forearm, and total body sites than a population-based sample of older women without fracture.

In addition, this study demonstrates that any nonspine fracture, regardless of trauma, increases risk of subsequent fracture. Women with a high-trauma fracture had a 34% greater risk of subsequent fracture than those who had not sustained a high-trauma fracture, which was similar to the risk (31%) of subsequent fracture among women whose first incident fracture was a result of low trauma. We had limited power to test this association in men, but we observed similar trends; the proportion of men who sustained subsequent fractures was similar for those whose first fracture was a result of high or low trauma. These findings are consistent with those of Cuddihy et al,¹⁸ who reported no difference in risk of subsequent fracture following severe- vs low-to-moderate-trauma wrist fractures.

We observed that the pattern of high-trauma fractures varied by sex. High-trauma fractures represented more than twice the proportion of all fractures in older men (21%) compared with older women (9%). High-trauma fractures were also caused by different events in older men and women. Among men, a similar proportion of high-trauma fractures were due to recreational and sporting injuries; falls from ladders, roofs, and trees; and motor vehicle crashes. In contrast, the majority of high-trauma fractures among women were due to motor vehicle crashes, while recreational and sporting injuries were uncommon.

The results of this study demonstrate that commonly used trauma classifications are not useful for determining whether a fracture is related to low bone density or indicates an increased risk of future fracture. In the event of any trauma, fracture will occur to the extent that the applied load on the skeleton exceeds the failure load of the bone.²⁹ While some high-trauma events would break even the strongest bones, it is difficult to identify thresholds of force above which fracture is inevitable, since

bone strength depends on the magnitude, velocity, and direction of applied forces. More importantly, classifying fractures according to degree of trauma is difficult. Trauma classifications based on limited information from patients cannot accurately describe the magnitude of forces applied to the bone. For example, falls from standing height, which by convention are typically considered low trauma, involve more than 10 times the potential energy required to fracture an elderly woman's hip.^{30,31} In contrast, motor vehicle crashes, which are typically considered high trauma, may transfer relatively low-magnitude forces to the bone, depending on the circumstances of the crash (eg, low-velocity crashes). As another example, the amount of force applied to the bone during falls on stairs cannot be estimated simply from the number of stairs involved in the fall, because the applied force depends on a variety of other circumstances of the fall, such as whether the fall was onto vs off of the stairs, whether the stairs were carpeted or otherwise padded, and whether the patient used any protective responses during the fall. Even with this amount of detail from the patient history, it remains difficult to accurately estimate the amount of force applied to the skeleton. As a consequence of the inherent difficulty in quantifying and defining high trauma, commonly used classifications of high trauma generally identify a heterogeneous group of fractures, and they do not identify a subset of patients for whom BMD was unrelated to fracture etiology.

Our findings have several important implications. Women and men with high-trauma fracture should generally be assessed in the same way as those with low-trauma fracture, which usually warrants measurement of BMD. When decisions are made about osteoporosis treatment for older adults, high-trauma fractures should be considered risk factors for future fractures. Furthermore, since high-trauma fractures are associated with low BMD and predict future fractures, high-trauma fractures should be considered osteoporotic fractures and included as out-

comes in clinical trials and observational studies.

Excluding high-trauma fractures in studies of older adults has 3 important consequences. First, it underestimates the morbidity, mortality, and economic burden of osteoporosis. In the current study, 21% of all first incident fractures in men and 9% in women were high-trauma fractures, similar to the proportions of high-trauma fractures reported in other studies.^{16,18,32,33} Second, it creates unnecessary effort to identify and classify trauma. Third, it decreases the number of outcomes and therefore may lead to less precise estimates of effect than would be observed if high-trauma fractures were included. Reanalysis of existing clinical trials data could identify the effect on treatment outcomes of including high-trauma fractures that were excluded in original analyses; this area deserves further study.

This study has several strengths. It involved 2 large cohorts of community-dwelling older women and men recruited from geographically diverse sites in the United States who underwent prospective follow-up for long durations. Rates of follow-up and fracture validation were high. We chose trauma classifications to be consistent with other studies, and our findings were consistent across 2 methods of classification.

This study also has several limitations. Clinical spine fractures were not studied. While we adjusted for the low prevalence of bisphosphonate use among men, we did not have information on bisphosphonate use among women at the time of BMD measurement, because bisphosphonates were not approved by the US Food and Drug Administration for the treatment of osteoporosis at the time of BMD measurement in women. However, we did adjust for use of hormone therapy among women. History of falling is a risk factor for future fractures, but we did not study the role of past history of falls and trauma as a predictor of future high- or low-trauma fractures. Women and men in this study were ambulatory volun-

teers and therefore likely to be healthier than the general population. The study included mainly white individuals, so results may not generalize to non-white populations.

In conclusion, BMD was strongly associated with high-trauma nonspine fractures in older women and men, and high-trauma nonspine fractures predicted subsequent fractures to the same extent as low-trauma nonspine fractures in women. Therefore, we concluded that high-trauma nonspine fractures should be considered potential osteoporotic fractures and should receive similar clinical management as low-trauma nonspine fractures. In addition, high-trauma nonspine fractures should be included as outcomes in clinical trials and observational studies.

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

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Analysis and interpretation of data: Mackey, Lui, Cawthon, Bauer, Nevitt, Cummings.

Drafting of the manuscript: Mackey.

Critical revision of the manuscript for important intellectual content: Mackey, Lui, Cawthon, Bauer, Nevitt, Cauley, Hillier, Lewis, Barrett-Connor, Cummings.

Statistical analysis: Mackey, Lui, Cawthon.

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