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Time to Osteoporosis and Major Fracture in Older Men:

The MrOS Study

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Abstract

Introduction—For older men who undergo bone mineral density (BMD) testing, the optimal osteoporosis screening schedule is unknown. Time-to-disease estimates are necessary to inform screening intervals.

Methods—A prospective cohort study of 5,415 community-dwelling men aged ≥65 years without hip or clinical vertebral fracture or antifracture treatment at baseline was conducted. Participants had concurrent BMD and fracture follow-up between 2000 and 2009, and additional fracture follow-up through 2014. Data were analyzed in 2015. Time to incident osteoporosis (lowest T-score ≤ −2.50) for men without baseline osteoporosis, and time to hip or clinical vertebral fracture or major osteoporotic fracture for men without or with baseline osteoporosis, were estimated.

Results—Nine men (0.2%) with BMD T-scores > −1.50 at baseline developed osteoporosis during follow-up. The adjusted estimated time for 10% to develop osteoporosis was 8.5 (95% CI=6.7, 10.9) years for those with moderate osteopenia (lowest T-score, −1.50 to −1.99) and 2.7 (95% CI=2.1, 3.4) years for those with advanced osteopenia (lowest T-score, −2.00 to −2.49) at baseline. The adjusted times for 3% to develop a first hip or clinical vertebral fracture ranged from 7.1 (95% CI=6.0, 8.3) years in men with baseline T-scores > −1.50 to 1.7 (95% CI=1.0, 3.1) years in men with baseline osteoporosis.

Conclusions—Men aged 65 years and older with femoral neck, total hip, and lumbar spine BMD T-scores > −1.50 on a first BMD test were very unlikely to develop osteoporosis during follow-up. Additional BMD testing may be most informative in older men with T-scores ≤ −1.50.

Introduction

Osteoporosis-related fractures impose a significant burden to older men.[1] One in four elderly men will sustain a fragility fracture during their remaining lifetime,[2] with an exponential increase in fracture incidence after age 75 years.[3] Men also have a higher 1-year mortality rate after hip fracture compared with women.[4–6] A 2012 RCT of older men with osteoporosis treated with zoledronic acid demonstrated significant reduction in the primary endpoint of radiographic vertebral fracture.[7] Similarly, an earlier meta-analysis suggested that risedronate treatment in men aged 55–76 years with osteoporosis by bone mineral

density (BMD) criteria or with secondary causes of osteoporosis, with or without existing vertebral fracture, was associated with radiographic vertebral fracture reduction.[8] Owing to the serious consequences of fracture and available antifracture treatment, several organizations[9–12] have endorsed identification of osteoporosis in older men through BMD testing, but an interval of measurement has not been recommended.

In 2011, the U.S. Preventive Services Task Force concluded evidence was insufficient to assess the balance of benefits and harms of osteoporosis screening in men (Grade I),[13] thus highlighting a need for developing a screen/treat strategy to identify elderly men at increased fracture risk. A 2007 cost-effectiveness analysis suggested that a screen/treat strategy may be cost effective for men aged 65 years or older with a prior clinical fracture and for men aged 80 years or older without a prior fracture, assuming a societal willingness to pay $50,000 per quality-adjusted life year gained.[14] It is unknown what proportion of men will develop osteoporosis prior to experiencing a fragility fracture. In addition, the time frame for men at specific baseline BMD levels to develop a disabling fracture event is uncertain.

The objective of this study was to inform decisions about BMD testing intervals by estimating the time to development of osteoporosis by BMD criteria and the time to development of hip or clinical vertebral fracture in a cohort of 5,415 men aged 65 years and older without prior hip or clinical vertebral fracture or osteoporosis treatment. Based on a previous study of older women,[15] it was hypothesized that men with baseline T-scores ≤ −1.50 would develop osteoporosis significantly more rapidly than men with higher T-scores. Men with baseline osteoporosis were expected to have a more rapid transition to fracture than men with T-scores > −2.50.

Methods

Setting and Participants

The Osteoporotic Fractures in Men (MrOS) Study cohort comprised 5,994 community-dwelling, ambulatory men aged ≥65 years who met these inclusion criteria at baseline:

1. ability to walk without the assistance of another;
2. absence of bilateral hip replacements;
3. ability to provide self-reported data;
4. planned residence near a clinical site for the duration of the study;
5. absence of a medical condition that (in the judgment of the investigator) would result in imminent death; and
6. ability to understand and sign an informed consent.

Participants had to provide written informed consent, complete a self-administered questionnaire, attend the clinic visit, and complete at least the anthropometric, dual energy x-ray absorptiometry (DXA), and vertebral x-ray procedures. Recruitment relied primarily on community-based mailings, supplemented at some sites with local strategies (advertisements, presentations) to enhance the recruitment of minority groups. The study enrolled participants and completed the baseline examination from March 2000 through

April 2002.[16,17] The study protocol and consent documents were approved by IRB review committees at six clinical sites in the U.S. (Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Pittsburgh, PA; Portland, OR; San Diego, CA).

The plan for the longitudinal analysis was approved by the IRB for the University of North Carolina. DXA BMD imaging was obtained over 8.7 years of follow-up, including the baseline visit, 2000–2002; Year 2, 2002–2003; Year 3, 2003–2005; Year 5, 2005–2006; and Year 7, 2007–2009. Participants were also followed every 4 months by postcard or telephone to ascertain fractures, with fracture follow-up through November 2014. Data were analyzed in 2015. All fractures were adjudicated by central review of radiology reports.[16] Men were eligible for the primary analysis if they were representative of the screened population (i.e., they had no history of osteoporosis diagnosis, hip or clinical vertebral fracture, or antifracture treatment at baseline). Men who had osteoporosis without antifracture treatment or hip or clinical vertebral fracture at baseline were eligible to participate in the osteoporosis-to-fracture analysis.

Measures

The 1994 WHO Technical Report[18] defined osteoporosis as BMD T-score ([BMD of participant – mean BMD of young reference population]/SD of BMD of reference population) ≤ −2.5 at the lumbar spine, hip, or distal radius. The International Osteoporosis Foundation[19] and the International Society for Clinical Densitometry[20] recommend that a uniform Caucasian (non–race adjusted) female reference database should be used to calculate T-scores for men of all ethnic groups. The International Osteoporosis Foundation justifies this convention by noting that for any age and BMD at the femoral neck, the risk of hip fracture or a major osteoporotic fracture is approximately the same in men and women.[19] Accordingly, T-scores were calculated at the femoral neck, total hip, and lumbar spine using National Health and Nutrition Examination Study III BMD norms for white women aged 20–29 years[21,22] in the main analysis.

Participants were categorized into these baseline T-score groups: higher BMD—lowest T-score at the femoral neck, total hip, or lumbar spine > −1.50; moderate osteopenia—lowest T-score at any site −1.50 to −1.99; advanced osteopenia—lowest T-score at any site −2.00 to −2.49; and osteoporosis—lowest T-score at any site ≤ −2.50.

The primary outcome was the time interval for 10% of participants without osteoporosis at baseline to develop osteoporosis before initiation of a Food and Drug Administration–approved agent for the treatment of osteoporosis (bisphosphonate, calcitonin, or teriparatide) and before development of a first hip or clinical vertebral fracture. Because clinicians may potentially treat a patient before BMD is in the osteoporosis range, “antifracture treatment” is used synonymously with the Food and Drug Administration–approved agents for osteoporosis treatment throughout this paper.

The secondary outcome was the time for 3% of participants to develop a first hip or clinical vertebral fracture before initiation of an antifracture treatment agent and before development of osteoporosis (for those without osteoporosis at baseline). This study included both nontraumatic and traumatic fractures in the fracture endpoints because clinical

misclassification of fracture etiology is common, and a falsely low fracture count would lead to inappropriately long estimates of time to fracture.

The tertiary outcome was the time for 3% of participants to develop a first nontraumatic or traumatic major osteoporotic (hip, clinical vertebral, proximal humerus, or wrist) fracture before initiation of antifracture treatment and before development of osteoporosis (for those without osteoporosis at baseline).

Statistical Analysis

The time for 10% of men without osteoporosis at baseline to develop osteoporosis prior to hip or clinical vertebral fracture and prior to initiation of antifracture treatment was estimated from parametric log-logistic regression models of the cumulative incidence quantile as defined in Peng and Fine, [23–27] based on interval-censored data. The analysis was stratified by the baseline categories of higher BMD and moderate and advanced osteopenia. The time origin was the first study examination with a BMD measurement that included femoral neck, total hip, and lumbar spine measurements, with follow-up BMD measurements at one or more sites continuing until the study examination preceding death or dropout. In the time-to-osteoporosis analysis, first reported use of antifracture treatment, hip or clinical vertebral fracture, and death were competing risks.

Using separate models for men without versus with osteoporosis at baseline, competing risk analyses were conducted to estimate the cumulative incidence functions for time to first hip or clinical vertebral fracture, and for time to major osteoporotic fracture, based on known fracture dates prior to osteoporosis and treatment. The corresponding time intervals for 3% of participants to transition to each fracture outcome were determined for the higher BMD and moderate and advanced osteopenia groups. First reported use of antifracture treatment, incident osteoporosis (for men without osteoporosis at baseline) and death were competing risks in the time-to-fracture analyses. Results from all models were adjusted for race, and baseline mean-centered age and BMI.

Sensitivity analyses were conducted to evaluate and determine the most appropriate parametric models for estimates of time to osteoporosis and time to fracture. All analyses were performed using SAS, version 9.4.

Results

Of the 5,994 men in the cohort, one was not eligible for this study because he was aged <65 years at baseline. After other eligibility criteria were applied (Appendix Figure 1), baseline characteristics of the 5,415 participants in the analytic cohort were tabulated (Table 1). The mean age of the cohort was 73.6 years, and the mean BMI was 27.4 kg/m^2 (overweight). About three fourths of the men (4,203 of 5,415) had higher BMD at baseline, whereas 180 (3.3%) had baseline osteoporosis. Within each baseline T-score range, the following proportions of men developed osteoporosis before initiation of antifracture treatment and before a first hip or clinical vertebral fracture: higher BMD, 9/4,203 (0.2%); moderate osteopenia, 35/680 (5.1%), and advanced osteopenia, 73/352 (20.7%).

Within the higher BMD category, 107 men (3.4% of 3,177) with baseline T-scores ≥ −1.00 and 62 men (6.0% of 1,026) with baseline T-scores between −1.01 and −1.49 had a hip or clinical vertebral fracture by the end of study follow-up (combined results for these T-score groups are in Table 3). Of the total of 371 men without baseline osteoporosis who sustained a first hip (n=219) or clinical vertebral (n=152) fracture, 69 (18.6%) developed osteoporosis before hip or clinical vertebral fracture, and 24 (6.5%) received antifracture treatment prior to the fracture. Of these 371 men, 317 had a first hip or clinical vertebral fracture before a competing risk occurred (Table 1.)

The estimated time for 10% of men without osteoporosis at baseline to subsequently develop osteoporosis varied according to baseline BMD T-score (Table 2 and Figure 1). During follow-up, nine men (0.2% within T-score stratum) with higher baseline BMD developed osteoporosis. For those with moderate osteopenia and advanced osteopenia at baseline, the unadjusted times for 10% to develop osteoporosis were very similar to the adjusted time estimates of 8.5 (95% CI=6.7, 10.9) years and 2.7 (95% CI=2.1, 3.4) years, respectively.

Unadjusted estimates of the cumulative incidence of hip or clinical vertebral fracture as a function of testing interval length were similar to covariate-adjusted estimates (Table 3, Appendix Figure 2). The unadjusted estimated time (9.6 years, 95% CI=8.7 years, 10.6 years) for 3% of men with higher baseline BMD to sustain a hip or clinical vertebral fracture was longer than the adjusted estimate of 7.1 (95% CI=6.0, 8.3) years. Otherwise, the unadjusted estimates of the time for 3% to develop a hip or clinical vertebral fracture were similar to the adjusted times of 4.8 (95% CI=3.8, 6.1) years for those with moderate osteopenia, and 4.1 (95% CI=3.1, 5.4) years for those with advanced osteopenia.

Unadjusted and covariate-adjusted estimates of the cumulative incidence of major osteoporotic fracture as a function of testing interval length were shorter than the analogous times for hip and clinical vertebral fracture (Appendix Table 1). The adjusted time for 3% to develop a major osteoporotic fracture ranged from 4.7 (95% CI=4.0, 5.7) years for men with higher BMD, to 2.6 (95% CI=1.9, 3.6) years for men with advanced osteopenia at baseline.

For all men aged ≥65 years with osteoporosis at baseline, the adjusted time for 3% to sustain a fracture was 1.7 (95% CI=1.0, 3.1) years for hip or clinical vertebral fracture and 1.0 (95% CI=0.5, 1.9) year for major osteoporotic fracture.

Full results of the sensitivity analyses are presented in the Appendix (Appendix Tables 2 and 3 and associated text, Appendix Figure 3). The log-logistic model was found to most closely follow the non-parametric curve and was used in the main analysis.

Discussion

The time to incidence of osteoporosis was estimated according to baseline BMD T-score in older men without a history of hip or clinical vertebral fracture and without prior antifracture pharmacologic treatment. Less than 1% of men with higher BMD (baseline T-score > −1.50 noted in 78% of the cohort) developed osteoporosis during 8.7 years of concurrent BMD and fracture follow-up. A significantly higher proportion of men with moderate or advanced osteopenia developed osteoporosis by the end of follow-up, but more often, hip or clinical

vertebral fracture occurred before osteoporosis developed. Twenty-nine percent of the hip and clinical vertebral fractures occurred in men with baseline normal BMD; at this T-score level, clinical practice guidelines do not recommend treatment in the absence of fragility fracture as there is no evidence that pharmacologic treatment prevents clinical fracture events among patients with normal BMD.

These findings for older men are consistent with findings for women aged 67 years and older with T-scores > −1.50 in an earlier study.[15] Also similar to longitudinal studies of postmenopausal women,[28–30] this study demonstrates that most older men who sustain a hip or clinical vertebral fracture do not have pre-existing osteoporosis. Fragility fractures in the absence of osteoporosis might be more common in men because men report a higher level of trauma associated with their fragility fractures compared with women.[31,32] Men with poor physical condition are especially at risk; a 2008 longitudinal analysis demonstrated that older men with the worst performance on a repeated chair stand test had a substantially higher risk of hip fracture compared with men in the fastest quartile of this test (multivariate hazard ratio=8.15, 95% CI=1.46, 6.73).[33] Also, men lose bone strength with age as a result of trabecular thinning and changes in cortical bone density, including both cortical thinning and increased porosity that are not easily identified by DXA BMD measurements.[34] Like all prognostic tests, BMD testing cannot identify every individual who will have a future fragility fracture; therefore, other screening approaches (risk factor assessment, other imaging methods) and interventions to reduce risk factors for fracture (e.g., fall reduction) that are not related to BMD should continue to be investigated.

Despite supportive recommendations in some clinical practice guidelines,[9–11,35,36] no standard of care exists for osteoporosis screening in older men at average risk of fracture. Medicare reimburses DXA scans in men for a limited number of disease indications, not including screening for primary prevention of fractures. Even after a major osteoporotic fracture, men are three times less likely than women to receive BMD testing and are unlikely to receive treatment.[37,38] This study identified fracture rates in older men that were higher than rates for younger postmenopausal women,[30] for whom policy statements encourage selective BMD screening.[11,13,35] Clarification of the optimal target population of men for BMD screening/treatment could potentially have an important population-wide impact on fracture reduction if future RCTs demonstrate primary fracture prevention, especially if treating men with screen-detected osteoporosis at selected BMD thresholds will reduce their risk of hip and clinical vertebral fractures. As the evidence base for BMD screening and treatment continues to expand, the use of BMD testing among older men should be determined by informed decision making with patients and clinicians considering relevant data on BMD testing, clinical risk factors, and treatment.

Limitations

The study has several limitations and strengths. Results are limited to men who have already had one bone density test and therefore whose BMD is known. Precise time estimates were not possible beyond the actual follow-up time in MrOS. Of the 579 (9.7%) of the original MrOS participants who were excluded in this analysis, one third had a history of hip or clinical vertebral fracture or treatment at baseline. Subsequent DXA tests in these men

would be for post-fracture surveillance or treatment monitoring and would not meet the epidemiologic definition of screening. The cohort comprised men aged 65 years and older with a low overall prevalence of osteoporosis. The results are not generalizable to postmenopausal women or younger men, or individuals with secondary causes of osteoporosis. Ninety percent of the sample was white; results might differ for nonwhite individuals. The reported time intervals are not based on the time to incident radiographic vertebral fractures. A 2014 analysis of 4,332 MrOS participants with baseline and repeat radiographs found that 192 (4.4%) had an incident radiographic vertebral fracture.[39] Treatment of radiographic vertebral fracture has been shown to reduce incident hip and clinical vertebral fractures in postmenopausal women.[40] However, because clinicians are unaware of these subclinical fractures, the time of onset of radiographic vertebral fractures is uncertain and cannot be used to calculate an optimal bone density screening interval. This suggests that the reported bone density testing intervals are conservative estimates for identification of patients who are likely to respond to treatment. Falls were not included in the evaluation of clinical risk factors for fracture, to be consistent with the International Osteoporosis Foundation's caution in considering fall risk in estimating fracture probability because patients selected primarily on the basis of nonskeletal clinical risk factors (including several measures of fall risk) may respond less to antifracture agents compared to patients selected on the basis of low BMD.[41,42] Falls are a critical factor in fracture risk, and interventions to reduce falls must be studied and implemented separately to maximize the effectiveness of fracture prevention programs. Strengths of the analysis include the large size of the cohort and the extended BMD and adjudicated fracture follow-up.

Conclusions

Community-dwelling men aged 65 years and older with baseline T-scores > −1.50 had a very low likelihood of developing osteoporosis over an average follow-up of 8.7 years. Ten percent of men with moderate and advanced osteopenia transitioned to osteoporosis in approximately 8 and 2 years, respectively. Most major osteoporotic fractures were not preceded by osteoporosis, suggesting that adjuncts to BMD testing should continue to be investigated to improve fracture prediction in older men.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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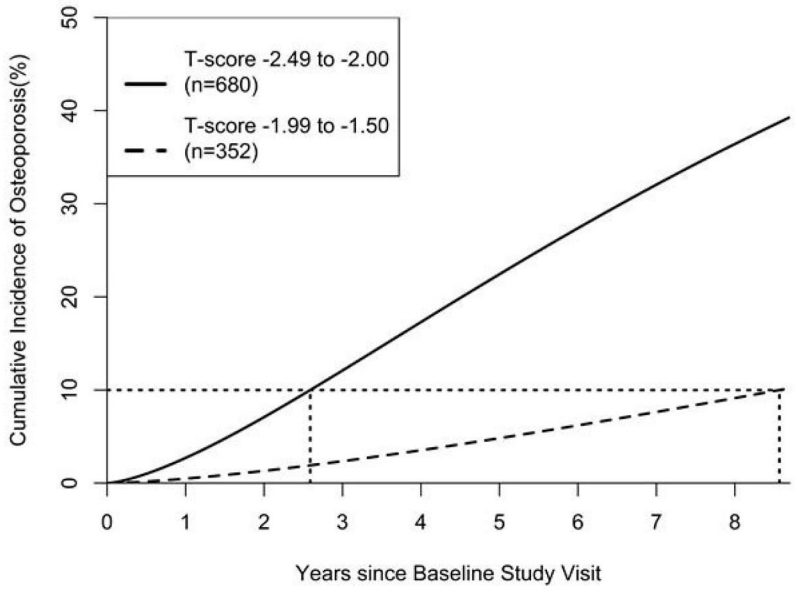

Figure 1.

Unadjusted cumulative incidence of osteoporosis according to baseline T-score range.

Note: The proportion of men who had transitioned to osteoporosis is plotted as a function of time. The cumulative incidence curves are estimated by parametric cumulative incidence models for interval-censored data. The dotted horizontal line shows where 10% of men have transitioned to osteoporosis; where this line intersects with each cumulative incidence curve, a vertical dotted line to the x-axis marks the estimated time interval. The time interval for men with baseline T-scores >−1.50 could not be calculated because of the very small number of fracture events (of the 4203 men with baseline T-scores >−1.50, nine [0.2%] developed osteoporosis during 8.7 years of BMD follow-up).

Table 1

Characteristics of the Men in Osteoporotic Fractures in Men (MrOS) Study cohort

	Baseline T-score >−1.50	Baseline T-score −1.50 to −2.49	Baseline T-score ≤−2.50	All participants
Characteristics[a]	**N=4,203 (77.6%)**	**N=1,032 (19.1%)**	**N=180 (3.3%)**	**N=5,415**
Age, mean years (SD)	73.2 (5.7)	74.8 (6.2)	75.8 (6.3)	73.6 (5.9)
65–69	1,345 (32.0)	246 (23.8)	35 (19.4)	1,626 (30.0)
70–74	1,245 (29.6)	263 (25.5)	42 (23.3)	1,550 (28.6)
75–79	967 (23.0)	280 (27.1)	48 (26.7)	1,295 (23.9)
≥80	646 (15.4)	243 (23.5)	55 (30.6)	944 (17.4)
Weight, mean kg (SD)	85.1 (13.1)	77.8 (11.4)	73.0 (10.7)	83.3 (13.2)
BMI, kg/m^2	27.9 (3.8)	26.0 (3.3)	24.9 (3.4)	27.4 (3.8)
<25	965 (23.0)	410 (39.7)	100 (55.6)	1,475 (27.2)
≥25	3,238 (77.0)	622 (60.3)	80 (44.4)	3,940 (72.8)
Race				
White (Non-Hispanic)	3,747 (89.2)	947 (91.8)	159 (88.3)	4,853 (89.6)
African American	195 (4.6)	16 (1.6)	5 (2.8)	216 (4.0)
Asian	124 (3.0)	42 (4.1)	8 (4.4)	174 (3.2)
Hispanic	89 (2.1)	16 (1.6)	4 (2.2)	109 (2.0)
Other	48 (1.1)	11 (1.1)	4 (2.2)	63 (1.2)
Years of education				
Less than high school	266 (6.3)	65 (6.30)	13 (7.2)	344 (6.35)
High school/Some college	1,681 (40.0)	409 (39.6)	72 (40.0)	2,162 (39.9)
College/Some grad school	1,229 (29.2)	288 (27.9)	63 (35.0)	1,580 (29.2)
Grad school	1,027 (24.4)	270 (26.2)	32 (17.8)	1,329 (24.5)
Previous fracture after age 50				
Yes	766 (18.2)	258 (25.0)	59 (32.8)	1,083 (20.0)
No	3,437 (81.8)	774 (75.0)	121 (67.2)	4,332 (80.0)
Current smoker				
Current	140/4,202 (3.3)	39 (3.8)	11 (6.1)	190/5,414 (3.5)
Past	2,488/4,202 (59.2)	582 (56.4)	98 (54.4)	2,056/5414 (38.0)
Never	1,574/4,202 (37.5)	411 (39.8)	71 (39.4)	3,168/5,414 (58.5)
Alcohol consumption				
<21 drinks per week	4,023 (95.7)	1,001 (97.0)	173 (96.1)	5,197 (96.0)
≥21 drinks per week	180 (4.28)	31 (3.00)	7 (3.89)	218 (4.03)
History of parental hip fracture				
Yes	497/2,968 (16.7)	164/742 (22.1)	28/146 (19.2)	689/3,856 (17.9)
No	1,511/2,968 (50.9)	327/742 (44.1)	75/146 (51.4)	1,913/3,856 (49.6)
Don’t know	960/2,968 (32.3)	251/742 (33.8)	43/146 (29.5)	1,254/3,856 (32.5)
Rheumatoid arthritis				
Yes	221 (5.3)	44 (4.3)	6 (3.3)	271 (5.0)
No	3,982 (94.7)	988 (95.7)	174 (96.7)	5,144 (95.0)

Characteristics[a]	Baseline T-score >−1.50 N=4,203 (77.6%)	Baseline T-score −1.50 to −2.49 N=1,032 (19.1%)	Baseline T-score ≤−2.50 N=180 (3.3%)	All participants N=5,415
Oral glucocorticoid ever-use				
Yes	80/3,323 (2.4)	20/804 (2.5)	9/128 (7.0)	109/4,255 (2.6)
No	3,243/3,323 (97.6)	784/804 (97.5)	119/128 (93.0)	4,146/4,255 (97.4)
Bone mineral density T-score, mean (SD)[b]				
Femoral neck	−0.23 (0.89)	−1.72 (0.44)	−2.38 (0.63)	−0.59 (1.06)
range				−4.25, 6.17
Total hip	0.53 (0.96)	−0.98 (0.60)	−1.81 (0.75)	0.16 (1.14)
range				−4.00, 6.73
Lumbar spine	1.67 (2.15)	−0.35 (1.61)	−1.57 (1.70)	1.17 (2.25)
range				−3.93, 15.20
Prevalence of osteoporosis[c]				
Definition 1	0	0	180 (100.0)	180 (3.3)
Definition 2	0	184 (17.8)	180 (100.0)	364 (6.7)
Definition 3	0	0	114 (63.3)	114 (2.1)
Definition 4	0	0	119 (66.1)	119 (2.2)
Hip or clinical vertebral fracture by study end[d]	169 (4.0)	110 (10.7)	38 (21.1)	317 (5.9)
Hip fracture	94 (2.2)	75 (7.3)	25 (13.9)	194 (3.6)
Clinical vertebral fracture	75 (1.8)	35 (3.4)	13 (7.2)	123 (2.3)
Antifracture treatment by study end	143 (3.4)	131 (12.7)	62 (34.4)	336 (6.2)
Bisphosphonate	141 (3.4)	130 (12.6)	59 (32.7)	330 (6.1)
Calcitonin	2 (<0.1)	1 (<0.1)	2 (1.1)	5 (<0.1)
Teriparatide	0 (0.0)	0 (0.0)	1 (0.5)	1 (<0.1)
Total fracture follow-up time, years				
Mean (SD)	11.1 (3.6)	10.7 (3.8)	10.2 (4.1)	11.0 (3.7)
Median	13.0	12.7	12.2	12.9
Minimum	0.04	0.08	0.7	0.04
Maximum	14.8	14.8	14.6	14.8
Concurrent BMD and fracture follow-up time, years[e]				
Mean (SD)	5.2 (2.3)	4.9 (2.4)	4.7 (2.6)	5.1 (2.3)
Median	6.5	5.8	5.3	6.5
Minimum	0	0	0	0
Maximum	8.7	8.6	8.1	8.7

BMD, bone mineral density

[a] Values are N (% of T-score group) unless otherwise specified. N/non-missing values are presented if data were incomplete except for rheumatoid arthritis (missing value treated as no disease).

[b] Maximum T-score values confirmed as valid by the MrOS Data Coordinating Center

[c] Tabulations of disease events according to the following four definitions of osteoporosis are presented in Appendix Tables 4–7.

Definition 1. Lowest T-score at the femoral neck or total hip or lumbar spine calculated using BMD norms for young white women

Definition 2. Lowest T-score at the femoral neck or total hip or lumbar spine calculated using BMD norms for young white men

Definition 3. Lowest T-score at the femoral neck calculated using BMD norms for young white women

Definition 4. Lowest T-score at the femoral neck or total hip calculated using BMD norms for young white women

[d] Tabulations of first hip or clinical vertebral fracture before a competing risk occurred

[e] Includes participants who had one baseline DXA test, then developed a competing risk before osteoporosis, treatment or major fracture (0 concurrent BMD and fracture follow-up)

Table 2

Time for 10% of Men Without Osteoporosis[a] or Treatment at Baseline to Develop Osteoporosis, According to Baseline T-score Range

Baseline T-score range	Osteoporosis events, N (%)	Time interval for 10% of participants to develop osteoporosis[b]	
		Unadjusted years (95% CI)	Adjusted years (95% CI)
>−1.50	9/4203(0.21)	----	----
−1.50 to −1.99	35/680 (5.15)	8.57 (6.67, 10.99)	8.51 (6.67, 10.86)
−2.00 to −2.49	73/352 (20.74)	2.59 (2.03, 3.30)	2.68 (2.12, 3.40)

[a]Osteoporosis defined as lowest T-score ≤-2.5 at femoral neck or total hip or lumbar spine, calculated using bone mineral density (BMD) norms for young white women

[b]Estimated time to osteoporosis (competing risks: incident hip or clinical vertebral fracture, antifracture treatment or death), computed by quantile estimates based on the fitted log logistic models, stratified by baseline lowest femoral neck, total hip or lumbar spine T-score (lowest T-score −1.50 to −1.99 vs. −2.00 vs. −2.49), and adjusted for mean-centered age, mean-centered BMI and race.

Note: Time estimates for the T-score>−1.50 group could not be calculated due the very small number of endpoint events, leading to excessive extrapolation beyond the observed BMD follow-up of 8.7 years.

Table 3

Time for 3% of Men Without Osteoporosis[a] or Treatment at Baseline to Sustain a Hip or Clinical Vertebral Fracture, According to Baseline T-score Range

Baseline T-score range	Fracture events, N (%)	Time interval for 3% of participants to sustain a hip or clinical vertebral fracture[b]	
		Unadjusted years (95% CI)	Adjusted years (95% CI)
>−1.50	169/4203 (4.02)	*9.59 (8.69, 10.59)*	7.09 (6.02, 8.34)
−1.50 to −1.99	68/680 (10.00)	4.37 (3.41, 5.61)	4.83 (3.84, 6.09)
−2.00 to −2.49	42/352 (11.93)	3.51 (2.58, 4.79)	4.06 (3.05, 5.40)

[a] Lowest T-score ≤−2.5 at femoral neck or total hip or lumbar spine, calculated using bone mineral desnity norms for young white women

[b] Estimated time to hip or clinical vertebral fracture (competing risks: incident osteoporosis, antifracture treatment or death), computed by quantile estimates based on the fitted log logistic models, stratified by baseline lowest femoral neck or total hip or lumbar spine T-score (lowest T-score −1.50 to −1.99 vs. −2.00 vs. −2.49), and adjusted for mean-centered age, mean-centered BMI and race.

Note: Estimates greater than 8.7 years (italicized) have questionable reliability due to excessive extrapolation required for 3% to transition to hip or clinical vertebral fracture.