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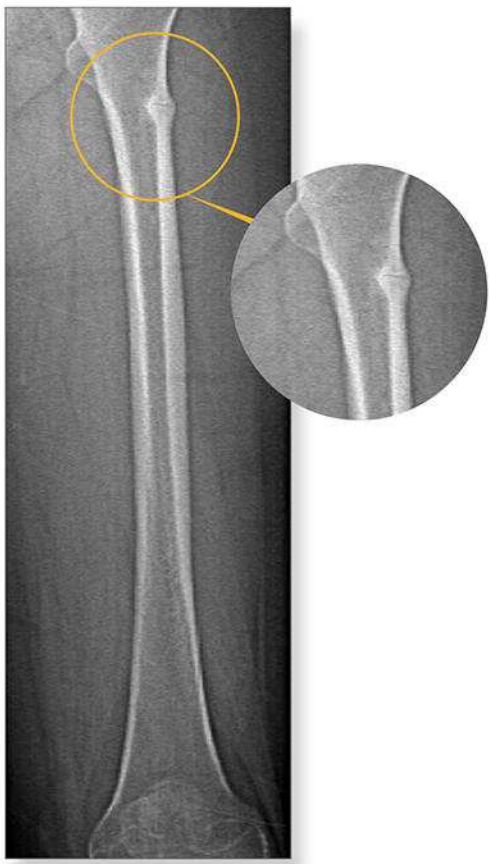

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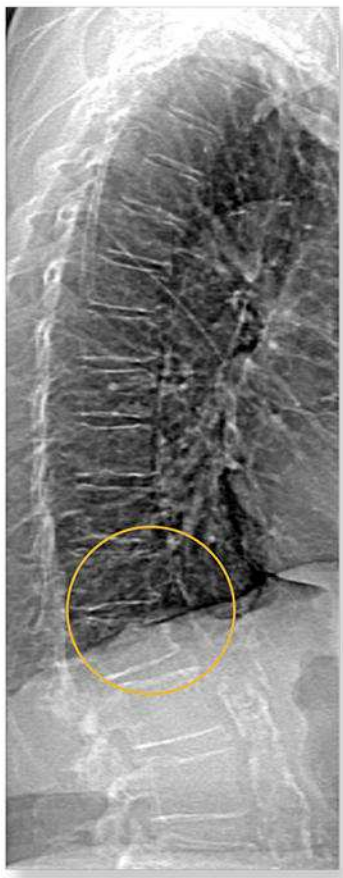

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ORIGINAL ARTICLE

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# Association of Incident, Clinically Undiagnosed Radiographic Vertebral Fractures With Follow-Up Back Pain Symptoms in Older Men: the Osteoporotic Fractures in Men (MrOS) Study

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## ABSTRACT

Prior data in women suggest that incident clinically undiagnosed radiographic vertebral fractures (VFs) often are symptomatic, but misclassification of incident clinical VF may have biased these estimates. There are no comparable data in men. To evaluate the association of incident clinically undiagnosed radiographic VF with back pain symptoms and associated activity limitations, we used data from the Osteoporotic Fractures in Men (MrOS) Study, a prospective cohort study of community-dwelling men aged ≥65 years. A total of 4396 men completed spine X-rays and symptom questionnaires at baseline and visit 2, about 4.6 years later. Incident clinical VFs during this interval were defined by self-reported clinical diagnosis plus community imaging showing a centrally adjudicated ≥1 increase in semiquantitative (SQ) grade in any thoracic or lumbar vertebra versus baseline study X-rays. Incident radiographic VFs (≥1 increase in SQ grade between baseline and visit 2 study X-rays) were categorized as radiographic-only (not clinically diagnosed) or radiographic plus clinical (also clinically diagnosed). Multivariable-adjusted log binomial regression was used to calculate prevalence ratios (PRs) and 95% confidence intervals (CIs). Men with incident radiographic plus clinical VF were most likely to have back pain symptoms and associated activity limitation at follow-up. However, versus men without incident VF, those with incident radiographic-only VF also were significantly more likely at follow-up to report any back pain (70% versus 59%; PR, 1.2 [95% CI, 1.1 to 1.3]), severe back pain (8% versus 4%; PR, 1.9 [95% CI, 1.1 to 3.3]), bother from back pain most/all the time (22% versus 13%; PR, 1.7 [95% CI, 1.3 to 2.2]), and limited usual activity from back pain (34% versus 18%; PR, 1.9 [95% CI, 1.5 to 2.4]). Clinically undiagnosed, incident radiographic VFs were associated with an increased likelihood of back pain symptoms and associated activity limitation. Results suggest incident radiographic-only VFs often were symptomatic, and were associated with both new and worsening back pain. Preventing these fractures may reduce back pain and related disability in older men. © 2017 American Society for Bone and Mineral Research.

**KEY WORDS:** VERTEBRAL FRACTURE; MALE; BACK PAIN; AGED; RADIOLOGY

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## Introduction

Vertebral fractures (VFs) are a common hallmark of osteoporosis in older adults.[1,2] Clinically diagnosed VFs are associated with increased back pain, disability, and an increased risk of future fractures.[3,4] However, most new VFs are not clinically diagnosed. Only about a quarter of incident radiographic VFs are clinically recognized in women,[5–9] and the proportion of men whose incident VFs are clinically recognized appears even lower.[6,10]

This does not mean that clinically unrecognized incident radiographic VFs are always asymptomatic. In one large cohort of older women, those with an incident radiographic VF who did not report a clinical VF had a significantly greater risk of increased back pain and back-related disability compared to women with no incident VF.[7] However, because this study did not confirm self-reported clinical VF by comparing community spine imaging to baseline study radiographs, some women likely had unchanged prevalent VF and were incorrectly categorized as having new clinical VF. Relative to the no VF group, this misclassification could have led to overestimation of the pain and disability in women with incident radiographic-only VF. Even with these limitations, there are no comparable data available in men.

The Osteoporotic Fractures in Men (MrOS) study was designed with a co-primary aim of evaluating the effects of fractures on quality of life in older men.[11] To this end, it enrolled a large cohort of men aged $\geq$65 years, and collected baseline and follow-up spine radiographs, including community imaging studies in men who reported new clinical VF, as well as repeated self-reports about back pain symptoms. Using these data, we aimed to investigate the impact of clinically undiagnosed incident radiographic VF on back pain symptoms in older men. We hypothesized that clinically unrecognized incident radiographic VF would be associated with back pain symptoms and associated disability intermediate in frequency and severity between that experienced in men with no incident VF and those with incident clinical VF.

## Subjects and Methods

### Participants

A total of 5994 community-dwelling men aged $\geq$65 years were recruited from population-based listings to participate in the MrOS prospective cohort study between 2000 and 2002 at six US sites: Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Monongahela Valley near Pittsburgh, PA; Portland, OR; and San Diego, CA. MrOS exclusion criteria included inability to walk without assistance from another person, a history of bilateral hip replacement, inability to consent, or expected survival of less than 6 months. Institutional review boards at all participating centers approved the study protocol and written informed consent was obtained from all participants. The MrOS study design and recruitment have been described in detail elsewhere.[11,12]

Among all MrOS enrollees, 4396 (73%) completed technically adequate lumbar and thoracic spine radiographs and a self-reported back pain symptom questionnaire at both baseline and visit 2 (mean of 4.6 $\pm$ 0.4 SD years after baseline), forming our analysis cohort.

### Incident radiographic VFs

Radiographic VF assessment in the MrOS study has been detailed elsewhere.[13] Briefly, lateral thoracic and lumbar spine radiographs were performed according to protocol and triaged by trained technicians. Then, all films considered to have a possible fracture or other abnormality ("triage positive") were evaluated by a study physician reader (JTS) using the Genant semiquantitative (SQ) grading method to rate each vertebral level for fracture,[14] with the modification that grade 1 fractures had to exhibit cortical discontinuity or depression of most of either the superior or inferior endplate to be considered fractured.[13] This physician reader was blinded to all participant characteristics, including whether or not a clinical vertebral fracture had been diagnosed between MrOS baseline and visit 2.

Participants were defined as having a prevalent radiographic VF when any baseline thoracic or lumbar vertebra had an SQ grade of $\geq$2, and an incident radiographic VF when any thoracic or lumbar vertebra had an increase in SQ grade of $\geq$1 between baseline and visit 2.

### Incident clinical VFs

Participants were contacted by mail or phone every 4 months and queried about new fractures; >99% of these attempted contacts were completed. For men who reported a new community-diagnosed clinical VF, information about the circumstances of the VF was collected using a standardized questionnaire. Only participants for whom a central study physician judged that their community spine imaging (eg, radiograph, CT, MRI) showed an increase in SQ grade of $\geq$1 compared to the same thoracic or lumbar vertebrae on the baseline study radiograph were categorized as having an incident clinical VF in the current study.

### Back pain symptoms

At both baseline and visit 2, participants self-reported presence of back pain during the past year (yes, no), and then rated its severity (mild, moderate, severe), how often they were bothered by back pain (never, rarely, some of the time, most of the time, all the time), and whether they had limited their usual activity because of back pain (yes, no).

### Other measurements

All covariate measures were collected at MrOS baseline. These included date of birth, race (white versus nonwhite), Physical Activity Scale for the Elderly (PASE) score,[15] self-reported health (good-excellent versus not), falls in the past year, and impairment in any of five instrumental activities of daily living (IADLs) (walking two to three blocks, climbing 10 steps, preparing their own meals, doing heavy housework, shopping for groceries or clothes). A medication inventory was used to classify medications used within the preceding 30 days into categories by their ingredients, including analgesics and osteoporosis medications. Study staff measured each participant's height (stadiometer) and weight (balance beam or digital scale), from which we calculated body mass index (BMI) as kg/m$^2$. Areal bone mineral density (BMD) (g/cm$^2$) was measured at the right hip and lumbar spine using dual-energy X-ray absorptiometry (DXA) (QDR4500W; Hologic, Inc., Waltham, MA, USA), unless the participant reported a right hip replacement or metal objects in the right leg, in which case the left hip was measured. MrOS DXA quality assurance measures have been detailed.[11] Based on common phantoms measured at all clinics, variability across clinics was limited, and cross-calibration correction factors were not required. Precision of spine and

hip DXA scans was 1% to 2%. Analgesic and osteoporosis medication use also was ascertained for the 30 days prior to visit 2.

### Statistical analyses

Participants were categorized into men with no incident VF, those with incident radiographic-only VF (not clinically diagnosed), and those with incident radiographic plus clinical VF (also clinically diagnosed). Among the 31 men with confirmed incident clinical VF, three were judged not to have had an incident radiographic VF when the baseline and visit 2 MrOS spine radiographs were compared; these three men were excluded from analyses due to inadequate numbers. Differences in baseline and visit 2 characteristics between participants with no incident VF, incident radiographic-only VF, and incident radiographic plus clinical VF were assessed using chi-square tests for categorical data and ANOVA for continuous data.

To evaluate whether, compared to men with no incident VF, those with incident radiographic-only VF, and incident radiographic plus clinical VF between baseline and visit 2 had an associated increased risk of back pain symptoms at visit 2 (any back pain, severe back pain, bother most or all the time by back pain, and limitation in usual activities due to back pain), we performed log binomial regression analyses or Poisson regression, calculating prevalence ratios (PRs) and 95% confidence intervals (CIs). All models first were adjusted for age, race, and clinic site. Models then additionally were adjusted for baseline IADL impairment, lumbar spine BMD, prevalence of radiographic VF, baseline prevalence of the corresponding back pain symptom (ie, analysis for visit 2 any back pain adjusted for baseline prevalence of any back pain), history of fall in the year before baseline, and visit 2 analgesic use. We performed several sensitivity analyses: (i) stratifying participants based on whether or not they reported any back pain at baseline; (ii) comparing men with no incident VF to men with more radiographically severe incident VF based on an increase in SQ grade of $\geq$2 (76% of men with incident radiographic VF); and (iii) both excluding the 1.6% of men who reported baseline osteoporosis medication use and adjusting for visit 2 osteoporosis medication use.

## Results

Between baseline and visit 2, 169 men (3.8%) had an incident radiographic-only VF and 28 (0.6%) had an incident radiographic plus clinical VF. Overall, though men were predominately white, overweight, and reported mostly good to excellent health, there were several baseline differences between men who did and did not have subsequent VF. Compared to the 4196 men who did not have an incident radiographic VF, the 169 men with an incident radiographic VF, and 28 with an incident radiographic plus clinical VF were significantly older, had lower lumbar spine BMD, and more often had IADL impairment and a prevalent radiographic VF at baseline (Table 1). Men who had no incident VF had been most healthy at baseline, those who had incident radiographic plus clinical VF were least healthy at

**Table 1.** Baseline Participant Characteristics

| Variables | No incident VFs ($n = 4196$) | Incident radiographic only VFs ($n = 169$) | Incident radiographic plus clinical VFs ($n = 28$) | $p$ |
|---|---|---|---|---|
| Baseline variables | | | | |
| Age (years), mean ± SD | 72.8 ± 5.4 | 74.2 ± 6.1 | 76.5 ± 6.5 | <0.01 |
| Race (white), *n* (%) | 3850 (91.8) | 157 (92.9) | 27 (96.4) | 0.58 |
| BMI (kg/m$^{2)}$, mean ± SD | 27.4 ± 3.8 | 27.0 ± 3.7 | 26.2 ± 4.0 | 0.08 |
| PASE score, mean ± SD | 152.1 ± 67.3 | 140.6 ± 67.0 | 150.7 ± 78.0 | 0.09 |
| Self-reported health, good-excellent, *n* (%) | 3731 (88.9) | 147 (87.0) | 22 (78.6) | 0.17 |
| IADL impairment, *n* (%) | 671 (16.0) | 40 (23.7) | 9 (32.1) | <0.01 |
| Fall in past year, *n* (%) | 824 (19.6) | 48 (28.4) | 11 (39.3) | <0.01 |
| Lumbar spine BMD (g/cm$^2$) mean ± SD | 1.07 ± 0.18 | 0.97 ± 0.17 | 0.92 ± 0.14 | <0.01 |
| Lumbar spine *T*-score, mean ± SD | −0.15 ± 1.67 | −1.06 ± 1.54 | −1.55 ± 1.31 | <0.01 |
| Prevalent radiographic vertebral fracture, *n* (%) | 256 (6.1) | 46 (27.2) | 9 (32.1) | <0.01 |
| Parental history of osteoporosis, *n* (%) | 370 (8.8) | 19 (11.2) | 3 (10.7) | 0.53 |
| Osteoporosis drug use, *n* (%) | 60 (1.5) | 8 (5.1) | 1 (3.6) | <0.01 |
| Oral corticosteroid use, *n* (%) | 76 (1.9) | 3 (1.8) | 0 (0) | NC |
| Analgesic use, *n* (%) | 655 (16.3) | 19 (11.7) | 2 (7.1) | 0.13 |
| Back pain in 1 year before baseline | | | | |
| Any back pain, *n* (%) | 2820 (67.2) | 103 (61.0) | 17 (60.7) | 0.19 |
| Severe back pain, *n* (%) | 235 (5.6) | 9 (5.3) | 2 (7.1) | 0.46 |
| Bother by back pain most/all the time, *n* (%) | 533 (12.7) | 26 (15.4) | 5 (17.9) | 0.16 |
| Limited usual activities due to back pain, *n* (%) | 839 (20.0) | 36 (21.3) | 6 (21.4) | 0.31 |
| Visit 2 variables | | | | |
| Osteoporosis drug use, *n* (%) | 215 (5.1) | 24 (14.3) | 11 (40.7) | <0.01 |
| Analgesic use, *n* (%) | 832 (19.9) | 28 (16.7) | 7 (25.9) | 0.43 |

Baseline data was missing for the following number of participants in the analysis cohort of 4396 men: Analgesic use, 177; lumbar spine BMD, 19; BMI, 2; PASE physical activity score, 2; IADL impairment score, 2; self-reported health, 1.

VF = vertebral fracture; SD = standard deviation; BMI = body mass index (kg/m$^2$); PASE = Physical Activity Scale for the Elderly; IADL = instrumental activities of daily living; BMD = bone mineral density; NC = not calculable.

baseline, and those with incident radiographic-only VF had intermediate baseline health status. All but one of the 28 men with an incident radiographic plus clinical VF reported the circumstances that led to being given a diagnosis of clinical VF in the community, and back pain was the presenting complaint in 89% of cases.

### Association of incident VFs with back pain symptoms and associated activity limitations

In multivariable-adjusted analyses, compared to men with no incident VF, those with an incident radiographic-only VF between baseline and visit 2 were significantly more likely at visit 2 to report any back pain (70% versus 59%; PR, 1.2 [95% CI, 1.1 to 1.3]), severe back pain (8% versus 4%; PR, 1.9 [95% CI, 1.1 to 3.3]), bother most or all the time by back pain (22% versus 13%; PR, 1.7 [95% CI, 1.3 to 2.2]), and limited usual activities due to back pain (34% versus 18%; PR, 1.9 [95% CI, 1.5 to 2.4]) (Table 2). These results appeared intermediate between those in men with no VF and those in men with an incident radiographic plus clinical VF. In multivariable-adjusted analyses, compared to men with no incident VF, those with an incident radiographic plus clinical VF were significantly more likely at visit 2 to report any back pain (93% versus 59%; PR, 1.6 [95% CI, 1.4 to 1.9]), severe back pain (18% versus 4%; PR, 3.4 [95% CI, 1.3 to 9.8]), to be bothered most or all the time by back pain (50% versus 13%; PR, 4.0 [95% CI, 2.5 to 6.4]), and limited usual activities due to back pain (64% versus 18%; PR, 3.7 [95% CI, 2.2 to 5.5]).

In the subgroup of men without baseline back pain, those with an incident radiographic-only VF had a 13.8% absolute increase in risk of any back pain at follow-up compared to that in men with no incident VF (Table 2). In the subgroup of men with baseline back pain, there was a 5.7%, 15.3%, and 23.8% absolute increase, respectively, in risk of severe, frequently bothersome, or activity limiting back pain at follow-up in those with an incident radiographic-only VF compared to that in men with no incident VF (Table 2), and a 22.2% absolute increase in risk of one or more of these symptoms at follow-up.

Results were similar to overall results in several other sensitivity analyses, including in analyses excluding the 7% of men with a prevalent radiographic VF at baseline, in analyses comparing men with no incident VF to men with more radiographically severe incident VF based on an increase in SQ grade of $\geq$2, and in analyses excluding men with baseline osteoporosis medication use and adjusting for visit 2 osteoporosis medication use (data not shown).

## Discussion

In this cohort of community-dwelling older men, those with clinically undiagnosed incident radiographic VFs were significantly more likely to have back pain symptoms and activity limitations due to back pain at follow-up than were men without incident VF. Though men with incident radiographic VF were older, had poorer health status, and more frequently had prevalent radiographic VF at baseline than men with no incident VF, differences in these characteristics did not appear to explain the association of incident clinically undiagnosed radiographic VF with back pain symptoms at follow-up. Analyses stratified by whether or not individuals had back pain at baseline suggest that incident clinically undiagnosed radiographic VFs were symptomatic in a substantial minority of men with these events, and were associated with a mix of new back pain and worsening of preexisting back pain.

Results from the current study about the association between incident clinically undiagnosed VF and back pain symptoms are consistent with results previously reported in older community-dwelling women, both in the direction of the association and its magnitude. In the Study of Osteoporotic Fractures (SOF), women aged $\geq$65 years with new, clinically undiagnosed radiographic VF during 3.7 years of follow-up had about a twofold higher risk of increased back pain, increased back-related disability, and of having at least 1 day of bed rest and 7 days of activity limitation due to back pain between baseline and follow-up compared to women with no incident VF.[7] SOF may have misclassified some old VFs as new clinical VFs due to not obtaining community imaging to compare to baseline study radiographs, and thus overestimated the proportion of new VFs that were clinically diagnosed. Further, this likely also resulted in SOF underestimating symptoms associated with incident clinical VFs and overestimating symptoms associated with incident radiographic-only VFs. However, the general similarity of our results to theirs suggests this potential bias was unlikely to be large. Current study results went further by estimating the excess absolute risk of back pain symptoms associated with incident clinically undiagnosed radiographic VF. In the MrOS cohort, with a 67% prevalence of back pain at baseline, about 20% of men with incident clinically undiagnosed radiographic VF had new or worse back pain in excess of that observed in men without incident VF.

The current study has several important strengths, including its enrollment of a large cohort of community-dwelling older men. Additional strengths include its prospective design, with frequent and complete follow-up to ascertain incident clinical VF, and its use of consistent and validated approaches for adjudicating both incident clinical VF and incident radiographic VF. Further, analyses were adjusted for multiple potential confounders.

These analyses also have several limitations. First, measures used to assess back pain symptoms and associated activity limitations were self-reported and may have been subject to errors in recall. However, any errors are unlikely to have differed systematically by incident radiographic-only VF status because these VFs were not clinically detected. Thus, any recall errors likely would have biased results toward the null. Second, analyses could have underestimated the association between incident radiographic-only VFs and new or worsened back pain symptoms in individuals whose fracture symptoms resolved more than 1 year before visit 2. Third, because the exact dates of incident radiographic VFs are unknown, some men may have developed new or worsened back pain symptoms prior to their incident VF. Fourth, it is possible that analyses could have underestimated the association between incident radiographic-only VF and worsened back pain symptoms because of ceiling effects in men who already had severe, frequently bothersome, and/or activity limiting back pain at baseline. Fifth, there were a relatively small number of men who had radiographic plus clinical VF. Sixth, although most community imaging studies that led to community diagnoses of incident clinical VF were performed to evaluate back pain, a minority may have been incidental findings. This would have biased results for clinical VF toward the null. Seventh, because statistical power likely was limited for subgroup analyses, these results should be interpreted cautiously. Finally, because MrOS participants are

**Table 2.** Prevalence of Back Pain Symptoms at Visit 2 as a Function of Incident VF Between Baseline and Visit 2

| | No incident VFs | | Incident radiographic only VFs | | | Incident radiographic plus clinical VFs | | |
|---|---|---|---|---|---|---|---|---|
| | % | PR (95% CI) | % | Age, race, clinic-adjusted PR (95% CI) | MV-adjusted PR (95% CI)[a] | % | Age, race, clinic-adjusted PR (95% CI) | MV-adjusted PR (95% CI)[a] |
| All participants ($n = 4393$)[b] | | | | | | | | |
| Any back pain | 59.4 | 1.0 (ref) | 70.4 | 1.2 (1.1–1.3) | 1.2 (1.1–1.3) | 92.9 | 1.6 (1.4–1.8) | 1.6 (1.4–1.9) |
| Severe back pain | 3.9 | 1.0 (ref) | 8.3 | 2.1 (1.3–3.6) | 1.9 (1.1–3.3) | 17.9 | 4.5 (2.0–10.1) | 3.4 (1.2–9.8) |
| Bother by back pain most or all the time | 12.8 | 1.0 (ref) | 21.9 | 1.7 (1.3–2.3) | 1.7 (1.3–2.2) | 50.0 | 3.9 (2.7–5.7) | 4.0 (2.5–6.4) |
| Limited usual activities due to back pain | 17.6 | 1.0 (ref) | 34.3 | 1.9 (1.6–2.4) | 1.9 (1.5–2.4) | 64.3 | 3.7 (2.8–4.8) | 3.5 (2.2–5.5) |
| Participants with no baseline back pain ($n = 1453$)[b] | | | | | | | | |
| Any back pain | 30.1 | 1.0 (ref) | 43.9 | 1.4 (1.0–2.0) | 1.5 (1.1–2.0) | 90.9 | NC[c] | NC[c] |
| Severe back pain | 1.6 | 1.0 (ref) | 4.6 | NC | NC | 27.3 | NC[c] | NC[c] |
| Bother by back pain most or all the time | 2.8 | 1.0 (ref) | 4.6 | 1.7 (0.5–5.4) | 1.9 (0.6–6.0) | 63.6 | NC[c] | NC[c] |
| Limited usual activities due to back pain | 4.9 | 1.0 (ref) | 13.6 | 2.8 (1.5–5.4) | 2.7 (1.4–5.2) | 72.7 | NC[c] | NC[c] |
| Participants with baseline back pain ($n = 2940$)[b] | | | | | | | | |
| Any back pain | 73.7 | 1.0 (ref) | 87.4 | 1.2 (1.1–1.3) | 1.2 (1.1–1.3) | 94.1 | NC[c] | NC[c] |
| Severe back pain | 5.0 | 1.0 (ref) | 10.7 | 2.0 (1.1–3.7) | 1.6 (0.8–3.0) | 11.8 | NC[c] | NC[c] |
| Bother by back pain most or all the time | 17.7 | 1.0 (ref) | 33.0 | 1.8 (1.4–2.4) | 1.7 (1.3–2.3) | 41.2 | NC[c] | NC[c] |
| Limited usual activities due to back pain | 23.8 | 1.0 (ref) | 47.6 | 2.0 (1.4–2.4) | 1.8 (1.3–2.4) | 58.8 | NC[c] | NC[c] |

VF = vertebral fracture; PR = prevalence ratio; CI = confidence interval; MV = multivariable; NC = not calculable.

[a]Multivariable models adjusted for baseline age, race, clinic site, IADL impairment, lumbar spine BMD, prevalent radiographic VF, history of any fall in the year before baseline, baseline status for corresponding back pain symptom category, and visit 2 analgesic use.

[b]Among all 4393 participants, 4196 had no incident VFs, 169 had an incident radiographic only VFs, and 28 had an incident radiographic plus clinical VFs. Among the 2940 participants with baseline back pain, 2820 had no incident VFs, 103 had an incident radiographic only VFs, and 17 had an incident radiographic plus clinical VFs. Among the 1453 participants without baseline back pain, 1376 had no incident VFs, 66 had an incident radiographic only VFs, and 11 had an incident radiographic plus clinical VFs.

[c]Results not modeled because the number of incident radiographic plus clinical VFs was too small in this subgroup to provide stable estimates of risk of this back pain outcome.

community-dwelling, largely healthy older men, our findings may have limited applicability to other populations.

In conclusion, incident, clinically undiagnosed radiographic VFs were associated with a significantly increased likelihood of back pain symptoms and associated activity limitation in a large cohort of older men. These results appear to be independent of other explanatory factors and build on similar results previously reported in older women.[7] About one in five men with incident radiographic-only VF had new or worse back pain in excess of what was observed in men without incident VF. These results suggest that incident radiographic-only VFs are clinically important patient outcomes. Preventing these fractures may reduce back pain and related disability in older men. Randomized trials to prevent such fractures will provide the strongest evidence about the effect of interventions on back pain and related disability in older adults.

## Disclosures

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Authors' roles: Study concept and design: LMM and HAF. Data collection: JAC, ESO, and KEE. Data analysis and interpretation: JS, SLH, and HAF. Drafting manuscript: HAF. Critical review and final approval of manuscript content: HAF, SLH, KEE, JS, JTS, PMC, JAC, NEL, BCT, EBC, DMK, SRC, and LMM. Statistical analysis: SLH performed the statistical analyses and is independent of any commercial funder; she had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.

## References

1. Schousboe JT. Epidemiology of vertebral fractures. J Clin Densitom. 2016;19(1):8–22.
2. Ensrud KE, Schousboe JT. Clinical practice. Vertebral fractures. N Engl J Med. 2011;364(17)1634–42.
3. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA III, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. J Bone Miner Res. 2000;15(4):721–39.
4. Fink HA, Ensrud KE, Nelson DB, et al. Disability after clinical fracture in postmenopausal women with low bone density: the fracture intervention trial (FIT). Osteoporos Int. 2003;14(1):69–76.
5. Fink HA, Milavetz DL, Palermo L, et al. Fracture Intervention Trial Research Group. What proportion of incident radiographic vertebral deformities is clinically diagnosed and vice versa? J Bone Miner Res. 2005;20(7):1216–22.
6. Cooper C, Atkinson EJ, O'Fallon WM, Melton LJ III. Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985-1989. J Bone Miner Res. 1992;7(2):221–7.
7. Nevitt MC, Ettinger B, Black DM, et al. The association of radiographically detected vertebral fractures with back pain and function: a prospective study. Ann Intern Med. 1998;128(10):793–800.
8. Ettinger B, Black DM, Mitlak BH, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. JAMA. 1999;282(7):637–45.
9. Maricic M, Adachi JD, Sarkar S, Wu W, Wong M, Harper KD. Early effects of raloxifene on clinical vertebral fractures at 12 months in postmenopausal women with osteoporosis. Arch Intern Med. 2002;162(10):1140–3.
10. Ensrud KE, Blackwell TL, Fink HA. et al. Osteoporotic Fractures in Men (MrOS) Research Group. What proportion of incident radiographic vertebral fractures in older men is clinically diagnosed and vice versa: a prospective study. J Bone Miner Res. 2016 Aug;31(8):1500–3.
11. Orwoll E, Blank JB, Barrett-Connor E, et al. Design and baseline characteristics of the osteoporotic fractures in men (MrOS) study—a large observational study of the determinants of fracture in older men. Contemp Clin Trials. 2005;26(5):569–85.
12. Blank JB, Cawthon PM, Carrion-Petersen ML, et al. Overview of recruitment for the osteoporotic fractures in men study (MrOS). Contemp Clin Trials. 2005;26(5):557–68.
13. Cawthon PM, Haslam J, Fullman R, et al. Osteoporotic Fractures in Men Research Group. Methods and reliability of radiographic vertebral fracture detection in older men: the osteoporotic fractures in men study. Bone. 2014;67:152–5.
14. Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. J Bone Miner.Res. 1993;8(9):1137–48.
15. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. J Clin Epidemiol. 1993;46(2):153–62.