

Hyperkyphosis Predicts Mortality Independent of Vertebral Osteoporosis in Older Women

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Background: Excessive kyphosis may be associated with earlier mortality, but previous studies have not controlled for clinically silent vertebral fractures, which are a known mortality risk factor.

Objective: To determine whether hyperkyphosis predicts increased mortality independent of vertebral fractures.

Design: Prospective cohort study.

Setting: Four clinical centers in Baltimore County, Maryland; Portland, Oregon; Minneapolis, Minnesota; and the Monongahela Valley, Pennsylvania.

Patients: 610 women, age 67 to 93 years, from a cohort of 9704 women recruited from community-based listings between 1986 and 1988.

Measurements: Kyphosis was measured by using a flexicurve. Prevalent radiographic vertebral fractures at baseline were defined by morphometry, and mortality was assessed during an average follow-up of 13.5 years.

Results: In age-adjusted models, each SD increase in kyphosis carried a 1.14-fold increased risk for death (95% CI, 1.02 to 1.27;

$P = 0.023$). After adjustment for age and other predictors of mortality, including such osteoporosis-related factors as low bone density, moderate and severe prevalent vertebral fractures, and number of prevalent vertebral fractures, women with greater kyphosis were at increased risk for earlier death (relative hazard per SD increase, 1.15 [CI, 1.01 to 1.30]; $P = 0.029$). On stratification by prevalent vertebral fracture status, only women with prevalent fractures were at increased mortality risk from hyperkyphosis, independent of age, self-reported health, smoking, spine bone mineral density, number of vertebral fractures, and severe vertebral fractures (relative hazard per SD increase, 1.58 [CI, 1.06 to 2.35]; $P = 0.024$).

Limitation: The study population included only white women.

Conclusion: In older women with vertebral fractures, hyperkyphosis predicts an increased risk for death, independent of underlying spinal osteoporosis and the extent and severity of vertebral fractures.

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It is well known that vertebral fractures are associated with an increased risk for death in older persons (1–4), but the explanation for this is unknown. Our previous work (2) suggested that those with vertebral fractures were more likely to die of a pulmonary cause in particular, possibly because of vertebral fracture–induced changes in the thoracic kyphotic curvature that could detrimentally affect respiratory function. In that study, we performed a sub-analysis demonstrating that older women with the worst thoracic hyperkyphosis were more likely to die of a pulmonary cause; however, only one third of those with the greatest kyphotic curvatures had evidence of underlying vertebral fractures (2). Although that study provided a plausible mechanism by which vertebral fractures might lead to death, it also suggested that nonosteoporotic kyphosis may also be associated with adverse health.

Some studies have suggested that hyperkyphosis itself may be a risk factor for death (5, 6). However, these studies could not assess whether the increased thoracic curvature or the presence of clinically undetected vertebral fractures were the underlying explanation for the apparent association between hyperkyphosis and increased mortality risk. Therefore, to test whether hyperkyphosis is associated with an increased risk for death independent of vertebral fractures and low bone mineral density, we conducted a prospective cohort study of 610 older women who had measures of kyphosis, bone mineral density, and morpho-

metric vertebral fractures, and we assessed mortality rates over an average follow-up of 13.5 years.

METHODS

Participants were from the Study of Osteoporotic Fractures, an ongoing prospective study of risk factors for fractures and other health outcomes. Between 1986 and 1988, 9704 community-dwelling women age 65 years or older were recruited from various population-based listings in Baltimore, Maryland; Minneapolis, Minnesota; Portland, Oregon; and the Monongahela Valley, Pennsylvania (7). During the 2-year follow-up visit, 610 women, representing all 4 clinic centers, were consecutively sampled to undergo flexicurve measurements to document the degree of thoracic curvature, known as the kyphosis index. **Figure 1** shows the details of the original cohort study design and the sampling of the women for the purposes of the kypho-

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Context

Whether kyphosis portends poor outcomes for particular groups of women is unclear.

Contribution

This long-term follow-up study found that, in older white women with previous vertebral fractures, increased kyphosis predicted increased risk for earlier death. The increased risk seemed independent of multiple factors, including age and underlying spinal osteoporosis. Women without vertebral fractures had no obvious increased mortality risk associated with kyphosis.

Caution

Only white women were studied. Vertebral fractures and kyphosis were not assessed simultaneously.

Implication

Women with vertebral fractures and hyperkyphosis may have greater risk for mortality than women with only vertebral fractures or only hyperkyphosis.

—The Editors

sis study. The institutional review boards at each clinical site approved the study protocol, and written informed consent was obtained from all participants.

Flexicurve Measurement of Kyphosis

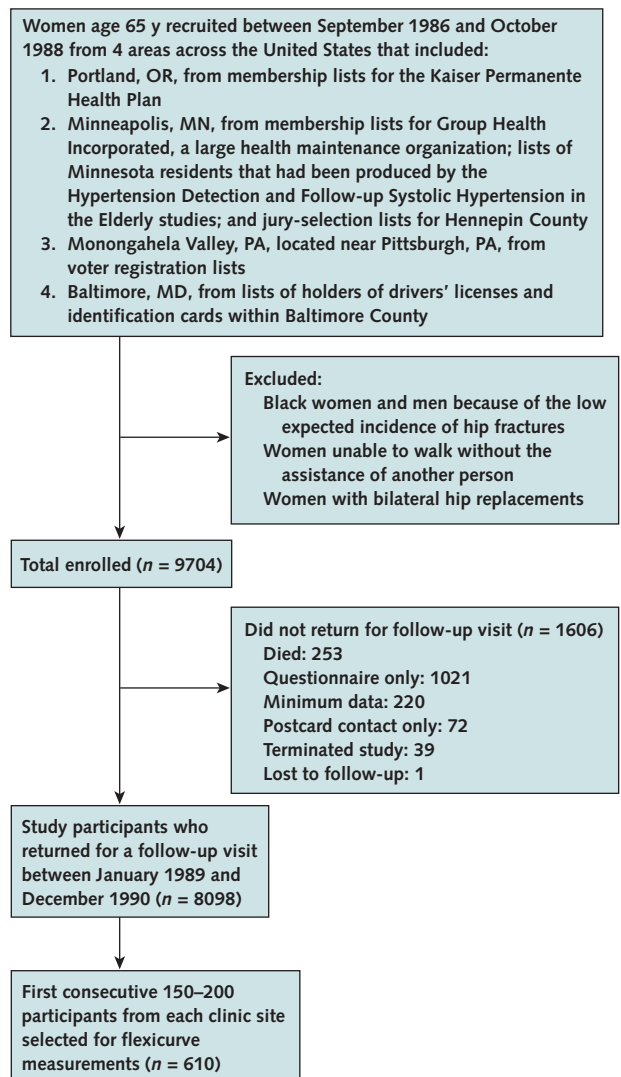
An architect's flexicurve was used to measure kyphosis during the second clinic examination, a technique first developed in the 1970s. Examiners placed the flexible ruler against the person's back while that person was standing erect, with the upper end placed just below the C7 spinous process and the lower end just at the S2 spinous process. The outline of the curve was then captured by using a handheld digital scanner, and *xy* coordinates were computed to derive a reference line between curve ends, distance from origin to first intersection of the curve (with the reference line defining the vertical length of the upper back curve), and maximum horizontal distance from the upper back curve to the reference line (Figure 2). The kyphosis index is defined as 100 times the maximum horizontal distance divided by the vertical length of the upper back curve (8). All technicians were taught the measurement technique at the centralized coordinating center. To assess reproducibility, 2 technicians from each clinic site performed the flexicurve measurement in a separate sample comprising 75 women selected from the Study of Osteoporotic Fractures cohort. After the tracings were obtained at the 4 clinical centers, they were sent to the coordinating center for centralized readings. The coefficient of variation for replicate kyphosis index values was 12.6%, and the Pearson correlation coefficient between the paired measurements was 0.66 (8). In addition, as a second check of validity, 20 tracings were selected from the study sample, 2

from each decile of kyphosis index, and 2 independent observers were asked to rank the tracings visually by order of kyphosis severity. The Spearman correlation coefficient between the visual rankings of the tracings by 2 observers was 0.89, and the correlations between the ranking of observers and ranking of kyphosis index were 0.943 (observer 1) and 0.931 (observer 2) (8).

Vertebral Morphometry Measurements

At the baseline visit in 1986 to 1988, radiographs of the thoracic and lumbar spine were obtained in accordance with the 1995 National Osteoporosis Foundation guidelines (9). Using visual triage, trained technicians grouped radiographs as normal, uncertain, or probably fractured on the basis of a semiquantitative grading scheme that categorized a participant by the most abnormal vertebral level (10, 11). The study radiologist further categorized those

Figure 1. Study flow diagram.



classified as uncertain as normal or probably fractured. Those classified as probably fractured were then evaluated by morphometry with 6-point digitization to calculate the anterior (Ha), middle (Hm), and posterior (Hp) heights for each vertebral body from T4 to L4. For each vertebral level, 3 height ratios were calculated (Ha/Hp, Hm/Hp, and Hp/Hp ± 1 or Ha/Ha ± 1), and a vertebra was classified as having a prevalent fracture if any of the 3 height ratios were more than 3 SDs less than the study population-specific mean for that level (12). A vertebra was classified as having a severe prevalent fracture if any of the 3 height ratios were more than 4 SDs below the study population-specific mean for that level.

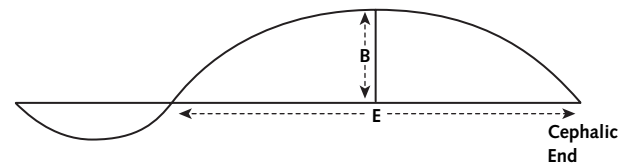
Incident Vertebral Fracture Assessment

A vertebra was classified as having an incident fracture if any of 3 vertebral height ratios decreased by more than 20% and by at least 4 mm compared with the baseline films on repeated radiography done an average of 4.2 years after the initial assessment of prevalent vertebral fractures. The study radiologist reviewed the morphometrically defined incident vertebral fractures to exclude imaging artifacts or such conditions as Scheuermann disease and reclassified 7% as not having an incident fracture. In a random sample of 503 women selected from the original study cohort whose radiographs were triaged and then digitized, triage missed no incident fractures according to the study definition.

Questionnaire and Examination

All study participants completed a comprehensive baseline and more limited follow-up questionnaire that included questions about demographic characteristics (age and education), medical history, and health behaviors. Whenever possible, data obtained from the second visit were used to best correspond with the timing of the kyphosis index measurement. Baseline measures included a

Figure 2. Flexicurve measurement calculation.



The index of thoracic curvature, or the kyphosis index, is 100 times the maximum horizontal distance divided by the vertical length of the upper back curve ($B/E \times 100$). Reproduced from Milne and Williamson (5), with permission from Oxford University Press.

family history of osteoporosis, self-reported spine fractures, stroke, self-reported health status, physical activity, and detailed questions about alcohol use. Information obtained from the second visit questionnaire included data about age and cigarette use. At the baseline and second clinical examination, height and weight were measured, and weight change was calculated as the difference in weight between baseline and the second follow-up visit. Body mass index was also calculated. At the second examination, participants were tested to see whether they could stand from a chair 5 times without using their arms, and they were also asked to perform a tandem stand. Also at the second examination, total hip and spine bone mineral density were measured by using dual-energy x-ray absorptiometry (QDR 1000, Hologic, Waltham, Massachusetts). Details of bone density measurements and quality control procedures are described elsewhere (13).

Ascertainment of Death

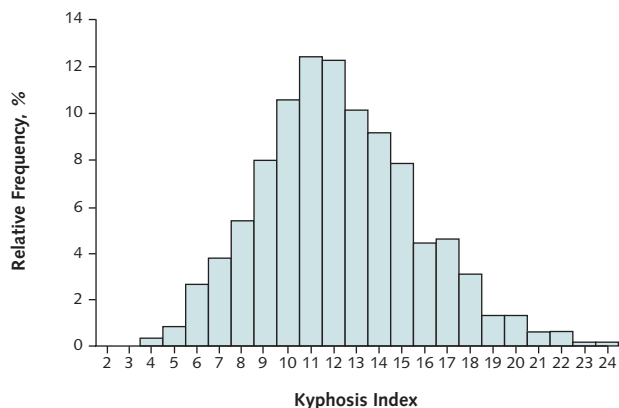
Participants were contacted by mail or telephone every 4 months. The study follow-up for vital statistics was 95% complete as of August 2007. All deaths were confirmed by receipt of death certificates.

Table 1. Participant Characteristics*

Characteristic	All Women	Women With Prevalent Vertebral Fracture	Women Without Prevalent Vertebral Fracture	P Value
Mean age (SD), y	72.8 (4.7)	73.3 (4.7)	72.8 (4.7)	0.38
Education >12 y, %	38.0	45.3	36.7	0.113
Mean body mass index (SD), kg/m ²	26.4 (4.8)	26.5 (4.4)	26.4 (4.9)	0.90
Mean physical activity (SD), kcal/wk	1510 (1402)	1407 (1293)	1547 (1425)	0.37
Self-reported good/excellent health status, %	82.8	83.2	82.9	0.96
History of stroke, %	2.5	3.2	2.4	0.65
Current smoking, %	8.9	12.6	7.9	0.133
Mean drinks per week (SD), n	2.0 (4.1)	2.1 (5.0)	2.0 (3.9)	0.76
Mean spine bone mineral density (SD), g/cm ²	0.85 (0.16)	0.78 (0.15)	0.86 (0.16)	<0.001
Mean hip bone mineral density (SD), g/cm ²	0.76 (0.13)	0.69 (0.12)	0.78 (0.13)	<0.001
Self-reported prevalent spine fracture, %	6.5	19.4	3.9	<0.001
Morphometric incident vertebral fracture, %	5.0	16.3	2.7	<0.001
Ability to stand from chair without using arms, %	97.6	95.8	98.0	0.21
Mean weight change 2 y before study (SD), kg	-0.62 (3.92)	-0.41 (4.43)	-0.68 (3.83)	0.54
Death, %	52.0	47.4	52.8	0.34

* Of the 610 women, 95 had prevalent vertebral fractures, 510 did not have prevalent vertebral fractures, and 5 were excluded from the analyses because they did not have baseline radiographs of acceptable quality to determine whether a prevalent vertebral fracture was present.

Figure 3. Distribution of kyphosis index among 610 older women.



Statistical Analysis

Because kyphosis is strongly associated with vertebral fractures (a known risk factor for death) and because we aim to disentangle the ill health effect of vertebral fractures from kyphosis, we compared the characteristics of women by prevalent vertebral fracture status by using chi-square tests for dichotomous variables or *t* tests for continuous measures.

After confirming the assumption that the hazard rates were proportional, we used Cox proportional hazards models to determine the association between kyphosis index and all-cause mortality. All results are reported as relative hazards with 95% CIs. We first used nonparametric regression modeling with spline transformation to assess the nature of the relation (linear vs. nonlinear) between kyphosis index and mortality by using SAS Macro %Psplinet (SAS Institute, Cary, North Carolina) (14, 15). Because the relationship seemed close to linear, we chose to conduct proportional hazards regression with kyphosis index as a continuous predictor.

We first performed age-adjusted proportional hazards models of kyphosis index as a continuous predictor of all-cause mortality. After adjustment for age and kyphosis, we considered each demographic, health behavior, and physical performance variable in association with mortality. In building the multivariable models, we next included known mortality risk factors, adjusting for health status (self-reported health: very good or excellent vs. very poor, poor, or fair), health behavior (current smoker vs. past or never smoker), and spinal osteoporosis (spinal bone mineral density and the presence of any prevalent vertebral fracture). To remove any residual confounding by spinal osteoporosis, we added number (range, 0 to 10; assessed 2.2 years [SD, 0.2] before the kyphosis index) and severity of vertebral fractures to the model. Stroke and physical activity or performance are potential confounders of the

kyphosis–mortality association but might also be in the causal pathway from kyphosis to death. Therefore, we added the following variables to the model at the end: stroke (self-reported: yes or no), amount of weight lost between the baseline and second clinic visit (per SD), and the ability to stand from a chair 5 times without use of the arms (yes or no). We tested for effect modification by prevalent vertebral fracture by including an interaction term between kyphosis and prevalent vertebral fracture in an age-adjusted model. Finally, we ran the multivariable analyses stratified by baseline vertebral fracture. We used SAS software (SAS Institute) to perform all analyses.

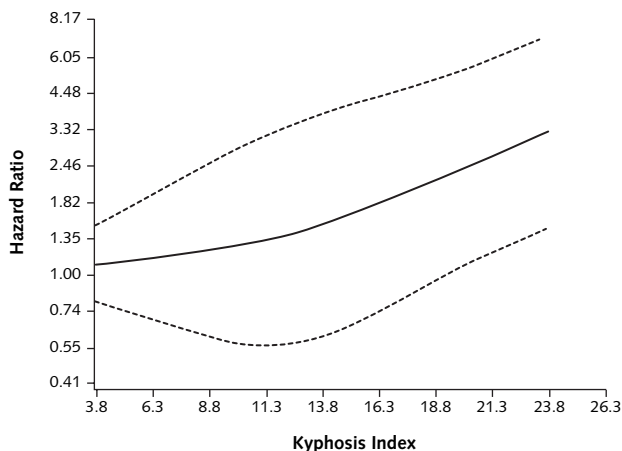
Role of the Funding Source

The National Institute of Arthritis and Musculoskeletal and Skin Diseases and the National Institute on Aging provided funding for the study but had no role in the data analysis, data interpretation, or manuscript preparation.

RESULTS

Baseline characteristics of women with and without radiographically detected prevalent vertebral fractures were similar, except that women with vertebral fractures were more likely to have lower spine and total hip bone mineral density, to report a history of spine fracture, and to develop an incident vertebral fracture (Table 1). Kyphosis index was normally distributed, with a mean index of 12.3 (SD, 3.4) (Figure 3). Over an average follow-up of 13.5 years (median follow-up, 15 years), 317 women died. The association between kyphosis and the log hazard of mortality (in nonparametric regression using spline transformation) was close to linear (Figure 4), justifying the use of kyphosis

Figure 4. Mortality hazard ratio as a function of kyphosis index.



The hazard ratio is with respect to the minimum kyphosis value in the study population (kyphosis index, 3.84).

Table 2. The Multivariable Association Between Kyphosis Index and Mortality

Model*	Relative Hazard (95% CI)	P Value
All women (n = 610)		
Adjusted for age	1.14 (1.02–1.27)	0.023
Adjusted for age, self-reported health, smoking, lumbar spine bone mineral density, and any prevalent vertebral fracture	1.17 (1.04–1.32)	0.009
Adjusted for all above factors plus physical activity, stroke, weight loss, and chair stand	1.18 (1.04–1.33)	0.010
Adjusted for all above factors plus severe vertebral fracture and number of prevalent vertebral fractures	1.15 (1.01–1.30)	0.029
Women with prevalent vertebral fractures (n = 95)		
Adjusted for age	1.50 (1.11–2.03)	0.009
Adjusted for age, self-reported health, smoking, and lumbar spine bone mineral density	1.77 (1.23–2.55)	0.002
Adjusted for the above factors plus severe vertebral fracture and number of prevalent vertebral fractures	1.58 (1.06–2.35)	0.024

* With relative hazards representing kyphosis, per SD.

index as a continuous predictor in proportional hazards regression.

In age-adjusted proportional hazards models, each SD increase in kyphosis index was associated with a 1.14-fold increased risk for all-cause mortality (95% CI, 1.02 to 1.27; $P = 0.023$). After considering each demographic, health behavior, and physical performance variable in conjunction with kyphosis, age, and risk for death, we have found that only age, self-reported health, history of stroke, physical activity, inability to rise from a chair 5 times without using the arms, and total hip bone mineral density were statistically significantly associated with an increased risk for death. On the basis of these results and underlying biological plausibility, we created several different multivariable models. The first model considered the basic variables associated with mortality but not factors that would probably be in the causal pathway between kyphosis and mortality (Table 2). In models adjusted for age, self-reported health, smoking, spine bone mineral density, and the presence of any prevalent vertebral fractures, there was a 1.17-fold increased risk for all-cause mortality with each SD increase in kyphosis index (relative hazard after adjustment for total hip instead of spine bone mineral density, 1.16 [CI, 1.03 to 1.30]; $P = 0.014$). Adding related factors that might fall along the causal pathway, such as stroke, physical activity, weight loss, and chair stand, did not substantially change the results (Table 2).

Because vertebral fractures have been previously associated with an increased risk for death (1–4), to better capture (and remove any residual confounding by) the overall vertebral fracture burden we added the number of vertebral fractures as well as an indicator of more severe vertebral fractures in the same multivariable model and found no noteworthy change in the overall results (Table 2). Because incident vertebral fractures have been associated with increased mortality rates (16, 17), we also adjusted for incident vertebral fractures, but the results were unchanged (data not shown).

To further explore the question of whether kyphosis itself in the absence of vertebral fractures predicts mortal-

ity, we tested for and found a strong suggestion of an interaction among kyphosis, prevalent vertebral fractures, and mortality ($P = 0.06$). We therefore performed further analyses stratified by prevalent vertebral fracture status. In age-adjusted analyses, hyperkyphosis in women without prevalent vertebral fractures was no longer statistically significantly associated with an increased mortality rate (relative hazard per SD increase, 1.09 [CI, 0.97 to 1.22]; $P = 0.17$). On the other hand, in women with underlying vertebral fractures, with each SD increase in kyphosis index, the risk for death increased 1.5-fold (Table 2). Further adjustment for self-reported health, smoking, and spine bone mineral density, severe vertebral fractures, and number of vertebral fractures made little difference in the relative hazards (Table 2).

DISCUSSION

In older women with previous vertebral fractures, increased kyphosis predicts increased risk for all-cause mortality independent of the extent and severity of the underlying spinal osteoporosis. To date, most clinicians and patients attribute their hyperkyphotic posture to underlying osteoporosis; however, our data confirm that postural changes provide important clinical predictive ability that is not provided by markers of osteoporosis alone. Our results suggest that women with vertebral fractures and hyperkyphosis are at greater risk for death than women with only vertebral fractures or only hyperkyphosis.

Other large epidemiologic studies have demonstrated that kyphotic posture may be associated with worse health, including impaired pulmonary function, poor physical function, inferior quality of life, injurious falls, fractures, and death (6, 18–20), but none to date have been able to fully account for the possibility that undiagnosed vertebral fractures is the underlying cause. Multiple previous studies have demonstrated that clinically apparent and silent vertebral fractures themselves are associated with worse health outcomes. Our results indicate that underlying vertebral fractures are an important cause of kyphosis-associated

death given that, among women without vertebral fracture, kyphosis and death were not associated. However, our findings substantiate the idea that it is not enough to look for vertebral fractures alone; the degree of kyphosis has additional predictive value that is not captured by the presence, severity, and number of vertebral fractures.

By what mechanisms might postural change affect mortality? Our previous work and that of others (2, 16, 21) demonstrated an association between hyperkyphosis and compromised pulmonary function and pulmonary death. Certainly, muscle weakness, poor physical functional capability, and falls might be other plausible mechanisms by which kyphosis could lead to subsequent increased mortality rate. In our exploratory analyses, the inability to stand up 5 times without using one's arms and a history of stroke were associated with both kyphosis and mortality, but adjustment for these factors did not diminish the kyphosis–mortality association.

We postulate that the phenotype of hyperkyphosis is an easily assessable clinical marker of accelerated physiologic aging or frailty. Although chronologic age is a strong predictor of functional decline and death, frailty or advanced physiologic age may be a more powerful predictor of adverse health among older persons. Hyperkyphosis may be a good marker of at least 1 category of a frail phenotype, and if so, it may prove to be an important clinical marker that to date has largely been ignored.

Our study has limitations. First, a recent study (21) demonstrated that hyperkyphosis affects not only older women but also men; however, we included only white women, so our results are not generalizable to men or non-white women. Second, the morphometric reading of vertebral fractures is based on vertebral height ratios only and therefore may lead to misclassification of other causes of decrements in height ratios (such as Scheuermann disease). For that reason, we included a variable of self-reported spine fractures but found that adjustment for clinically reported vertebral fractures did not affect the association between hyperkyphosis and an increased mortality rate in this cohort. A third limitation is the difference in timing of the variables, namely that of assessment of vertebral fractures and kyphosis. Given that average progression of kyphosis in the overall cohort was only about 6.7 degrees over 15 years of follow-up (22), the difference of 2.2 years in the timing of measurements probably made little difference in our results. Finally, the correlation between kyphosis index and either the kyphosis angle or clinical measures of the distance from occiput to wall is not known, so clinically relevant comparisons are difficult to make; however, each measure has been shown to have construct validity, and the flexicurve measure may even be superior to those that depend on specific vertebral edges, such as the more widely used Cobb angle.

Our study also had several strengths. First, this was a prospective study with substantial long-term and 95% complete follow-up over 13.5 years. Second, all women

underwent standardized testing for underlying vertebral fractures; thus, we obviated a limitation of previous studies— inability to exclude underlying vertebral fractures as a mechanism of the association of hyperkyphosis and ill health.

In summary, we have demonstrated that, in older women with previous vertebral fractures, independent of the number and severity of vertebral fractures, hyperkyphosis is associated with an increased risk for death. These results add to a growing literature that suggests that hyperkyphosis is a clinically important finding. Because it is readily observed and is associated with ill health in older persons, hyperkyphosis should be recognized as a geriatric syndrome—a “multifactorial health condition that occurs when the accumulated effect of impairments in multiple systems renders a person vulnerable to situational challenges” (23).

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Reproducible Research Statement: *Study protocol and data set:* Available at <http://sof.ucsf.edu/Interface/>. *Statistical code:* Available from Ms. Lui (e-mail, LLui@sfcc-cpmc.net).

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