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Impact of mild and moderate/severe vertebral fractures on physical activity: A prospective study of older women in the UK

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Conflict of Interest
Usama A. Al-Sari1, Jonathan H. Tobias, and Emma M. Clark declare that they have no conflict of interest.

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ABSTRACT

Purpose: Little is known about the long-term impact of vertebral fractures on physical activities. There is also uncertainty over the clinical significance of mild fracture. Therefore, the aim of this study was to evaluate the prospective association between vertebral fracture and future physical activity.

Methods: This is a five-year prospective study of a mixed community and secondary care cohort of women aged >50 from the UK. Vertebral fractures were identified at baseline on radiographs or DXA-based Vertebral Fracture Assessment by a Quantitative Morphometric approach and defined as moderate/severe (≥25% height decrease) or mild (20%-24.9% height decrease). Physical activity data were collected 5.4 years later by self-completion questionnaires. Multivariable logistic regression was used to determine the association between presence of fracture and various physical activities whilst adjusting for potential confounders.

Results: 286 women without, 58 with mild, and 69 with moderate/severe fracture were recruited. Those with mild and moderate/severe fracture were older than women without fracture and had more concomitant diseases at baseline. At 5.4 years follow-up, women with moderate/severe fracture self-reported shorter walking duration compared to those without fracture, even after adjusting for potential confounders (OR 2.96, 95%CI 1.11-7.88, P= 0.030). No independent association was seen between presence of mild fractures and reduced physical activity at follow-up.

Conclusion: This is the first study of older women from the UK that explored the prospective association between vertebral fracture and physical activity duration. Moderate/severe fractures were associated with reduced walking duration. Mild fractures had no impact on future physical ability.

Mini abstract: Little is known about the long-term impact of vertebral fractures on physical activity. There is also uncertainty over the clinical significance of mild vertebral fracture. We showed that women with moderate/severe but not mild vertebral fracture do less walking duration and housework than those without fracture after 5.4 years of follow-up.

INTRODUCTION

Vertebral fracture is a hallmark of postmenopausal osteoporosis and it is estimated that approximately 16% of 50-year-old white woman will have a vertebral fracture at some point in their lifetime [1]. In the UK, about 120,000 new vertebral fracture occurred per annum [2]. Since it can be predicted that the number as well as severity of vertebral fractures increases with age in all populations [3], these fractures cause a public health concern, particularly if they are accompanied with other chronic symptoms such as reduced physical ability and/or back pain [4].

A systematic review of the impact of osteoporotic vertebral fractures on generic health related quality of life found a reduction in physical but not mental domains in women with vertebral fractures compared to those without, even after accounting for age and back pain [5]. Further analysis found that compared to people without vertebral fracture, those with vertebral fractures self-report a reduction in bending related activities, ambulatory activities, arm movements, shopping, and preparing meals [6]. However, due to the mainly cross-sectional nature of the included studies, the temporal association between vertebral fractures and reduced activity is not clear. In addition, there have been a small number of prospective population-based studies which reported changes in physical activity following radiographic diagnosis of vertebral fracture[7-11]. However, frequency, but not duration of physical activity was the main outcome used, and impact of grade of vertebral fracture was not assessed.

Grade of vertebral fracture is important. It has previously been shown from the randomised controlled trials of secondary fracture prevention that women with moderate and severe vertebral fractures have worse quality of life than those with mild fractures [12]. There is also increasing interest in specifically assessing the impact of 'mild' vertebral fractures compared to moderate and severe, to aid in understanding whether there may be differing underlying aetiologies to these grades of fracture. It is recognised that some mild vertebral fractures identified through morphometric approaches based on percentage height loss of the anterior, mid- or posterior parts of the vertebral body are actually false-positives[13]. Rather than being an osteoporotic fracture, 20-25% anterior height reduction can occur through remodelling and osteophystosis due to degenerative change. This is important because these vertebrae with non-osteoporotic short vertebral height do not predict future non-vertebral fragility fracture in women[14], and had either no or only a weakly effect on back pain, disability, reduced individual health, and loss of height [15]. Moreover, degenerative spinal disease is thought to be associated with a reduced risk of osteoporotic vertebral fracture [16]. Nonetheless, these 'mild' vertebral fractures may still be associated with reduced quality of life, but more research is required in this area.

Identifying whether mild and/or moderate/severe vertebral fractures are clearly associated with a reduction in specific components of physical activity and function would be useful for design of interventions to improve quality of life. To the best of our knowledge, there are no prospective data available in the UK concerning the influence of vertebral fractures on specific physical activities. This is important because the predictors of ability or willingness to do physical activities are likely to be different in different populations. For example, cultural and social norms are known to vary from country to country [17]. This suggests the currently available data from other countries and populations may not reflect the association between vertebral fractures and physical activity in the UK. Hence, the aim of this study was to determine the impact of moderate/severe vertebral fractures on the frequency and duration of common daily physical activities in older women from the UK, and to identify whether equivalent findings were observed for mild vertebral fracture.

METHODS

Study design

This study is a prospective analysis of 395 women from a mixed community and secondary care-based cohort (the Vertebral fracture and Activity Study, VAS) with a mean of 5.4 years of follow up.

Study population

VAS includes participants from three UK-based studies: (1) 88 high risk postmenopausal women from the Cohort for Skeletal Health in Bristol and Avon (COSHIBA)[16]; (2) 202 women at high risk of fractures recruited from secondary care via Fracture Liaison Services (FLS)[18]; and (3) 105 women from the Vertebral Fracture and Back Pain Study[19] (see Figure 1). As previously described[20], COSHIBA is a population-based cohort study of 3200 postmenopausal women originally enrolled for a trial of a screening programme. 1062 were randomised into the intervention arm, and a subpopulation of 310 were deemed to be at higher risk of vertebral fractures and had spinal radiographs performed. Those who had appropriate consent were invited to take part in this study. Also as previously described[18], 377 women aged over 50 years referred for Dual-energy X-ray Absorptiometry (DXA) after a low-trauma fracture as part of the local FLS service were recruited to a study of the role of Vertebral Fracture assessment (VFA). All were invited to take part in this study. Also, as previously described[19], the Vertebral Fracture and Back Pain Study recruited 197 participants via digital radiological archives of the local NHS Trusts if they were female, aged over 60 and had a thoracic spinal radiograph in the previous three months. All were invited to take part in this study by post. Therefore, the combined research participants for the VAS study were women recruited from both primary and secondary care, aged >50 with spinal imaging. Follow-up data were collected in the same format using the same methodology (see below) for all participants, irrespective of which study they were originally enrolled in.

The South West - Frenchay Research Ethics Committee approved the three COSHIBA high risk (REC reference number: 14/SW/0138), Secondary care FLS (REC reference number: 07/Q2005/47), and Vertebral Fracture and Back Pain (REC reference number: 12/SW/0354) subgroups study to the principles embodied in the Declaration of Helsinki.

Main exposure: vertebral fracture

For both COSHIBA participants and those from the Vertebral Fracture and Back pain study, lateral spine radiographs were taken at baseline. Vertebrae from T4 to L4 for COSHIBA participants and from T4 to T12 for the other participants were evaluated by a trained researcher using the quantitative morphometric (QM) approach[21] via the SpineAnalyzer software (Optasia Medical, Ltd). For patients from the secondary care study, VFA using central DXA was also taken at baseline and vertebrae from

T4 to L4 were again evaluated by a trained researcher using the quantitative morphometric (QM) approach[22] via the SpineAnalyzer software. As standard practice for QM, mild vertebral fractures were defined as a decrease in vertebral height of 20-24.9%, and moderate/severe as ≥25% decrease for both radiographs and VFA.

25.3% of the total images (50 spinal radiographs and 50 VFAs) were randomly selected for repeatability measurements. The QM was rerun one year from the first reading for radiographs by the same reader and 5.4 years from the original assessment for VFAs by an independent reader. The images for these 100 participants were randomly ordered with the researcher blinded to the previous results. To assess repeatability, a kappa statistic was calculated [23]. Using the same previously published methods [24, 25], we calculated the prevalence of vertebral fracture using three dichotomized definitions of fracture (1) no vertebral fracture vs any grade of vertebral fracture (mild, moderate/severe); (2) mild vertebral fracture vs no vertebral fracture or moderate/ severe; and (3) moderate/severe vertebral fracture vs no fracture or mild. The intra-reader agreement for the spinal radiographs showed excellent agreement with a kappa value of 0.92 for no fractures, 0.83 for mild fractures, and 1.0 for moderate/severe fractures. For VFAs the inter-reader agreements also showed excellent agreement [26] with a kappa value of 0.86 for no fractures, 0.74 for mild fractures, and 0.92 for moderate/severe fractures.

Outcomes: Physical activity

All outcome data is self-reported, participants completed the same self-completion questionnaire after a mean of 5.4 years of follow-up, chosen for practical reasons (minimum 4.4 years- maximum 6.9 years). Participants were mailed a paper from that asked about specific physical activities chosen based on questions that have been used by previous researchers in both women and men [27-29]. Data were collected on self-reported physical activities in the last week: specifically (1) whether they carried out various activities at all such as walking, housework, gardening, sport, dance or any other type of physical activity; and (2) duration of these various activities. Data on whether they carried out various activities were collected by asking the following question: over the past 7 days, have you take part in any physical activity? Data on duration of activities were obtained by asking: please tick one box for each activity that you have participated in during the last 7 days, each activity was categorised into four-time durations, less than an hour, 1-2 hours, 2-4 hours, and more than 4 hours. Participants were also asked about their walking speed in comparison to 'normal for them', how many times a day they walked up a flight of stairs.

Potential confounders and other data

Demographic and socioeconomic information such as age, housing tenure and highest achieved educational qualification was assessed at baseline using the self-reported questionnaire. Age was calculated from date of birth. Highest educational qualification was coded into four categories as previously reported [16]. Self-reported data were also collected at baseline about traditional risk factors for osteoporosis, smoking, alcohol intake, self-reported diagnosis of arthritis, falls and presence of concomitant illnesses. All data was categorised as per previous papers [16, 30, 31]. For example, measure of general health was created by an ordinal variable with (1) no chronic disease, vs (2) one chronic disease (3) two chronic diseases (4) three chronic diseases, and (4) four or more chronic diseases. Baseline mobility was assessed by self-reported walking distance and use of walking aids. Data from self-reported osteoarthritis, and self-reported rheumatoid arthritis were combined into one variable ''arthritis''. As previously reported [20] a random 5 % subsample of the COSHIBA self-completion data at baseline were verified against electronic GP records, and overall there was good agreement. Both body mass index (BMI in kg/m^2) and back pain were measured at the follow-up point. Back pain was measured by using simple yes/no question by asking participants ''have you had back pain in the last 12 months?''.

Statistical analysis

Statistical analysis was carried out using STATA vs13. Simple descriptive statistics were calculated, and univariable associations between vertebral fracture and the outcomes were assessed using Chi-squared tests. Logistic regression analyses were used to calculate odds ratio (OR) and 95% confidence interval (CI) for outcomes according to presence or absence of vertebral fracture at baseline. Multivariable logistic regression was used to adjust for potential confounders. A confounding set of age, BMI, back pain and baseline activity were chosen on the basis of literature review. For example, from the previous systematic reviews and meta-analysis, both age and back pain were identified as vital to control the association between vertebral fractures and physical health related quality of life [5]. BMI and baseline activity were also identified as important [32]. A change in the fully adjusted OR of 10% or less suggests the included confounders are unimportant to the model[33]. To assess the effect of grade of fracture on physical activities, we assessed the association between mild and moderate/severe vertebral fractures compared to those without fractures separately. Because the use of VFA rather than radiographs in a proportion of participants may have introduced a source of variability in exposure, any identified associations were rerun separately for those with spinal imaging by radiographs and those with spinal imaging by VFA. Finally, a sub-analysis was performed on the final multivariable regression model to include all potential confounders at baseline where the P value for the univariate association was less than 0.05. Based on the previous systematic review and meta-analysis [5, 6] where women with vertebral fractures reported 27%-39% less physical activity than women without fractures, our sample size of 395 participants (127 with vertebral fracture) gives us between 71-95% power to detect a similar size of effect, assuming 5% type I error rate and a two-sided difference.

RESULTS

700 women were invited to this study, and 395 were recruited: 286 without vertebral fracture, 58 with mild vertebral fracture, and 69 with moderate/severe vertebral fracture (see Figure 1). Those with mild or moderate/severe fracture were older than women without fracture (mean age of 72.2±7.2 years for those with moderate/severe fracture, 69.5±8.3 for those with mild fracture, and 66.8±7.4 for those without fracture). Those with mild vertebral fracture had higher BMI at follow-up (29.6±8.9kg/m^2) than both women without fracture (27.2±5.3kg/m^2, P=0.007) and women with moderate/severe fractures (26.3±4.7kg/m^2, P=0.003). Women with moderate/severe vertebral fracture were more likely to walk shorter distances (46.4%) than both women without fracture (16.3%) and those with mild vertebral fracture (22.8%), while those without fracture were less likely to use walking aid (13.6%) than both women with mild (24.6%) and moderate/severe vertebral fracture (36.8%). For other differences see Table 1.

After 5.4 years of follow-up, compared to women without vertebral fractures at baseline, women with mild vertebral fractures were less likely to walk up a flight of stairs (74.1% vs 87.2%) and less likely to have done any physical activity in the past week compared to women without vertebral fracture (see Column A, Table 2). Women with moderate/severe vertebral fractures had a reduction in all walking-based activities and housework, both in terms of performance and duration. These women were also less likely to have done any physical activity in the last week (50.0% vs 70.8%) and reported shorter duration of activities compared to women without fracture (see Column B, Table 2). Compared to women with mild fractures, those with moderate/severe fractures reported less walking and walking duration in the past week, shorter housework duration, less heavy gardening work, and shorter overall physical activity in the past week (see Column C, Table 2).

Table 3 shows the association between vertebral fractures at baseline and physical activities 5.4 years later after adjusting for age, BMI, baseline mobility and back pain. Women with mild vertebral fracture did less walking up a flight of stairs and any physical activity compared to women without vertebral fractures, however, these associations were no longer present after adjustment. For moderate/severe vertebral fracture, age partially confounds the associations identified. Adjustment for BMI did not affect the associations. Additional adjustment for baseline mobility (see Column D, Table 3) reduced the strength of association between moderate/severe vertebral fractures and walking up a flight of stairs and walking speed. However, even after adjustment for age, BMI and baseline mobility, associations were still seen between moderate/severe vertebral fracture and reduced participation in any physical activities in the past week (OR1.90 for not engaging in any physical activity, 95% CI 1.01-3.59) and reduced housework: here the OR for not doing housework reduced from 1.80, 95% CI (1.05-3.11) to 1.77, 95% CI (0.96-3.26), a minor reduction in the strength of association, although the confidence intervals now crossed the null value reflecting the increased number of variables in the model. Further adjustment for back pain at follow-up point further attenuated the size of association between vertebral fracture and walking up a flight of stairs, walking any physical activity, but did not affect the association for housework: but gain all confidence intervals now crossed the null reflecting the increased number of variables in the model. Further adjustment for all the associated variables at baseline did not change the size of effect, but widened the confidence intervals due to increased number of included variables (data not shown). Running analyses separately for those with spinal radiographs and those with VFA did not affect the results (results not shown).

Table 4 shows the multivariable analysis on the association between vertebral fractures at baseline and length of time spent on physical activities 5.4 years later, and results show a reduction in time spent on all activities for patients with moderate/severe but not for mild vertebral fracture. Again, age partially confounds the associations seen. Further adjustment for both BMI and baseline mobility did not reduce the strength of association between moderate/severe vertebral fractures and spending less than one hour on walking or time spent carrying out any physical activity (see Columns C and D, Table 4). Additional adjustment for back pain further reduced the strength of association but nonetheless there was still an association between moderate/severe vertebral fracture and spending less than one-hour walking per week (OR 3.76, 95%CI 1.67-8.47). Further adjustment for all the associated variables at baseline did not change the size of effect, but widened the confidence intervals due to increased number of included variables (data not shown). Running analyses separately for those with spinal radiographs and those with VFA did not affect the results (results not shown).

DISCUSSION

We present the results from the first prospective study in the UK that examined the impact of vertebral fractures in older women and specific physical activities 5 years later. Although women with moderate/severe vertebral fracture had reduced baseline mobility, our results show a continued reduction in physical ability such that 5 years later, they had an almost three-fold reduction in time spent walking compared to women without fracture. No association was seen between presence of mild vertebral fractures and reduced physical activity at follow-up. In our study, these mild vertebral fractures identified by QM are most likely to be degenerative in origin, given the association with higher BMI.

Our results agree with the results of the majority of previous observational studies that show an association between vertebral fractures and reduced physical performance[7-9, 34-38]. However, our results extend the findings by reporting on women from the UK for the first time, by highlighting the specific reductions in walking-based activity duration, and by assessing the differing impacts of mild and moderate/severe vertebral fractures. Unlike previous studies [7, 8, 37], we have been able to adjust for age, baseline physical activity, back pain and BMI. Our results show that women with moderate/severe vertebral fracture have reduced physical activities compared to those without fracture, but that this is mainly explained by age, back pain and baseline mobility. Attenuation by adjustment for baseline mobility occurred because women with vertebral fractures already had reduced activity compared to women without vertebral fractures at enrolment to this study. Potential explanations for this are that either the occurrence of vertebral fractures caused a reduction in physical ability in the past that was still present at enrolment; or that women with reduced physical ability were more likely to develop vertebral fractures. Future research is needed to assess the association between incident vertebral fractures and physical activities. Attenuation of our results by adjustment for back pain at follow-up suggests that back pain may explain the association found (see Figure 2) and there is evidence to support this from previous studies. [37, 39-41]. It would have been useful to have a measure of back pain at baseline to allow us to assess if back pain is on the causal pathway, but this data was not collected.

Our novel results show women with mild vertebral fractures seem to be more similar to women without fracture than women with moderate/severe fracture. In our sample, participants with mild vertebral fracture had a higher BMI than patients with moderate/severe vertebral fracture, were less likely to have self-reported osteoporosis, and had differing impacts on future physical activity compared to women with moderate/severe fractures. These differences suggest that mild vertebral fractures in our sample may have a differing underlying pathophysiology than moderate/severe fractures, and that women with mild vertebral fractures identified by QM should be considered a separate phenotype to women with moderate/severe fractures.

One explanation for the underlying pathophysiology of the mild vertebral fractures identified by QM is osteoarthritis or degenerative change. If we assume these mild vertebral fractures are degenerative in origin, the reduced activities we identified may be related to the spinal degenerative symptoms directly, and/or skeletal degeneration elsewhere such as knee osteoarthritis. For example, in one longitudinal study, progression of lumbar spine osteoarthritis was associated with a four folds progression of joint space narrowing of the knee due to osteoarthritis even after adjustment for BMI [42].

An alternative explanation is that these mild fractures are indeed osteoporotic in origin, but they have not yet collapsed fully to moderate or severe fractures, and it is only these moderate or severe fractures that have big impacts on function. This agrees with other studies that found a difference between patients with mild compared with those with severe fractures in both pain and physical activity [43]. Finally, it is also possible, that as suggested by previous research, that mild fractures have a heterogenous underling cause, with same degenerative and same early osteoporotic changes [38]. However, our results suggest that the majority are likely to be degenerative in origin but nonetheless have impact on future physical functioning, particularly stairs.

As with all epidemiological studies, there are a number of limitations to this study. There was a large loss to follow-up of the original participants, and this is likely to have implications for generalisability of our results. The women who were lost to follow up were different that the women who continued in our study. For example, they were younger, were more likely to use walking aids and more likely to have more than one fall per year (see supplementary material for more information). This may have biased our results. Another limitation of our study design is the used of VFA technology to image the spine in some participants. However, the repeatability assessment was classified as excellent agreement. This may have reduced the strength of association seen, but our sub-analyses suggest no clear impact of the differing imaging modalities. Furthermore, we were unable to image the lumbar spine in the participants recruited from the Vertebral Fracture and Back Pain Study, which means we were are likely to have missed some fractures and incorrectly assigned some fractures to the control group in analysis. However, this is likely to only be a small proportion given that the mid-thoracic region is the most common site of vertebral fracture [44]. Another limitation is the use of self-reported physical activity data due to possible over-reporting as well as recall bias in older people. In addition, some of the physical activity questions have not been formally validated in women, but have been used previously by other researchers in the evaluation of female physical activity. However, objective measurement with accelerometery, as well as being prohibitively expensive for our study does not capture information on types or domains of physical functioning such as ability to do walking, sports, and housework, although would provide a more robust measure of length of time performing various activities. Two-thirds of our controls were recruited from secondary care via Fracture Liaison Services and this potentially may have attenuated the difference between women with and without fracture. For example, all of these participants had broken a bone and may have been more likely to reduce their activity due to that fracture and more likely to have osteoporosis and perhaps have a further fracture which may have biased our results to the null. Finally, while we have carried out a large number of statistical tests with a relatively small number of participants, we believe our results are robust: they fit with previous literature that identified ambulatory activities are reduced in women with vertebral fracture [6]; and were consistent across all categories of walking. Our study also has important strengths: it is the first study that assessed the association between vertebral fracture and duration of physical activities in the UK adjusted for age, BMI, baseline physical activity and back pain. Our study population is a mixed primary and secondary care sample which ensures wide-ranging generalisability of our results within the UK. Finally, differentiation of our exposure into mild and moderate/severe fracture increases our understanding of these two phenotypes.

Nonetheless, our results have important implications for both future research, and for clinicians. Future research should include men, should focus on careful measurement of baseline activity since our results suggest this explains much of the future reduction in physical ability and should include impact of number of fractures. Back pain should also be carefully measured at baseline. To understand the impact of new fractures on physical activity and explore the association between fracture timing and these activities, it is important future studies include serial radiographs. For healthcare professionals aiming to improve quality of life in those with vertebral fractures, our results highlight walking-based activities for those with moderate/severe vertebral fractures as important targets for interventions as walking is a fundamental physical ability and is especially limited. Finally, our results help clarity appropriate terminology. We believe that mild fractures identified by QM method are most likely to be degenerative in origin and should probably be described as vertebral deformities to distinguish them from the moderate/severe fractures which are likely to be true osteoporotic fractures.

In conclusion, we present the first longitudinal study of older women from the UK that shows the presence of moderate/severe vertebral fractures at baseline is associated with reduced physical ability 5 years later, particularly reduced self-reported walking participation. Our results have useful implications for design of interventions to improve physical quality of life in older women with vertebral fractures. Mild vertebral fractures identified by QM are most likely to be degenerative in origin, and have no clear impact on future physical activity.

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Table 1: Baseline characteristics of the population for those without, with mild and with moderate/severe (Mod/Sev) vertebral fractures (VF). P values were calculated by Chi-Squared.

Variables	Without VF n=268	Mild VF n=58	Mod/Sev VF n=69	P value		
				(A) None vs Mild	(B) None vs Mod/Sev	(C) Mild vs Mod/Sev
	Mean (SD)	Mean (SD)	Mean (SD)			
Age (years)	66.8 (7.4)	69.5 (8.3)	72.2 (7.2)	0.017	<0.001	0.059
	N (%)	N (%)	N (%)			
SOCIOECONOMIC DATA						
Housing						
Fully owned	182 (71.6)	42 (77.8)	51 (73.9)	0.359	0.710	0.620
Others	72 (28.4)	12 (22.2)	18 (26.1)			
Educational qualifications						
None or CSE	65 (25.0)	16 (29.6)	19 (27.9)	0.417	0.420	0.990
Vocational or O level	105 (40.4)	22 (40.7)	27 (39.7)			
A level to university	72 (27.7)	10 (18.6)	14 (20.6)			
Others	18 (6.9)	6 (11.1)	8 (11.8)			
RISK FACTORS FOR OSTEOPOROSIS						
Diagnosis of osteoporosis						
No	238 (90.8)	51 (92.7)	35 (52.2)	0.654	<0.001	<0.001
Yes	24 (9.1)	4 (7.2)	32 (47.7)			
Steroid use for >3 months						
No	239 (89.9)	46 (82.1)	54 (78.3)	0.259	0.009	0.485
Yes	16 (6.0)	6 (10.7)	12 (17.4)			
Don't know	11 (4.1)	4 (7.2)	3 (4.3)			
Mother broken hip						
No	208 (79.4)	45 (78.9)	54 (80.6)	0.102	0.393	0.822
Yes	43 (16.4)	6 (10.5)	8 (11.9)			
Don't know	11 (4.2)	6 (10.6)	5 (7.5)			
Smoking						
Never	154 (85.6)	35 (61.4)	34 (49.3)	0.917	0.237	0.332
Yes, but have given up	93 (35.3)	19 (33.3)	32 (46.4)			
Yes, currently smoking	16 (6.1)	3 (5.3)	3 (4.3)			
Alcohol intake						
Less than one glass a week	110 (41.7)	29 (50.8)	46 (66.7)	0.203	<0.001	0.072
≥ one glasses a week	154 (58.3)	28 (49.2)	23 (33.3)			
Any fracture ever						
No	43 (39.1)	12 (40.1)	15 (28.1)	0.373	0.252	0.892
Yes	223 (83.9)	54 (78.9)	53 (77.9)			
GENERAL HEATH						
Chronic diseases						
0	143 (54.2)	27 (47.4)	24 (34.8)	0.343	0.005	0.075
1	70 (26.5)	20 (35.1)	21 (30.4)			
2	33 (12.5)	4 (7.0)	13 (18.8)			
3	12 (4.5)	5 (8.8)	4 (5.8)			
≥ 4	6 (2.3)	1 (1.7)	7 (10.2)			
Arthritis						
No	199 (75.1)	45 (78.9)	45 (65.2)	0.538	0.100	0.090
Yes	66 (24.9)	12 (21.1)	24 (34.8)			
MOBILITY						
Usual walking distance						
>400 yards	221 (83.7)	44 (77.2)	37 (53.6)	0.240	<0.001	0.006
≤400 yards	43 (16.3)	13 (22.8)	32 (46.4)			
Use of a walking aid						
No	228 (86.4)	43 (75.4)	43 (63.2)	0.039	<0.001	0.142
Yes	36 (13.6)	14 (24.6)	25 (36.8)			
Fall						
Once per year or less	224 (85.5)	47 (82.4)	60 (86.9)	0.561	0.757	0.482
Few times per year or more	38 (14.5)	10 (17.6)	9 (13.1)			

Table 2: Self-reported physical activities at 5.4 years follow-up in women without, with mild and with moderate/severe (Mod/Sev) vertebral fractures (VF). P values were calculated by Chi-Squared.

Variables	Without VF n=268	Mild VF n=58	Mod/Sev VF n=69	P value			Available data
				(A) None vs Mild	(B) None vs Mod/Sev	(C) Mild vs Mod/Sev	
	N (%)	N (%)	N (%)				
WALKING-BASED ACTIVITIES							
Walk up a flight of stair							
None	34 (12.7)	15 (25.8)	21 (30.8)	0.012	< 0.001	0.534	390
At least once a day	232 (87.2)	43 (74.1)	47 (69.1)				
Walking in past week							
Yes	175 (65.3)	37 (63.7)	30 (43.4)	0.827	0.001	0.022	395
No	93 (34.7)	21 (36.2)	39 (56.5)				
Walking speed							
Stroll at easy way or worse	110 (41.6)	31 (53.4)	45 (66.1)	0.102	<0.001	0.146	390
Normal or better	154 (58.3)	27 (46.5)	23 (33.8)				
Walking duration in past week							
Less than an hour	33 (18.8)	10 (27.0)	19 (54.3)	0.261	<0.001	0.018	247
More than one hour	142 (81.1)	27 (72.9)	16 (45.7)				
HOUSEWORK							
Housework in past week							
Yes	188 (70.1)	37 (63.7)	39 (56.5)	0.343	0.031	0.405	395
No	80 (29.8)	21 (36.2)	30 (43.4)				
Housework duration in past week							
Less than an hour	25 (13.3)	2 (5.4)	12 (30.7)	0.177	0.007	0.004	264
More than one hour	163 (86.7)	35 (94.5)	27 (69.2)				
GARDENING							
Light gardening in past week							
Yes	110 (41.0)	23 (39.6)	30 (43.4)	0.902	0.715	0.663	395
No	158 (58.9)	35 (60.3)	39 (56.5)				
Heavy gardening in past week							
Yes	23 (8.5)	10 (17.2)	4 (5.8)	0.065	0.447	0.040	395
No	245 (91.4)	48 (82.7)	65 (94.2)				
SPORT							
Sport in past week							
Yes	85 (31.7)	16 (27.5)	19 (27.5)	0.537	0.503	0.995	395
No	183 (68.2)	42 (72.4)	50 (72.4)				
Sport duration in past week							
Less than an hour	17 (20.0)	3 (18.7)	8 (42.1)	0.908	0.041	0.138	120
More than one hour	68 (80.0)	13 (81.2)	11 (57.8)				
OTHER ACTIVITIES							
Dance in past week							
Yes	23 (8.5)	3 (5.1)	2 (2.9)	0.385	0.108	0.512	395
No	245 (92.4)	55 (94.8)	67 (97.1)				
Any physical activities in past week							
Yes	187 (70.8)	31 (55.3)	33 (50.0)	0.024	0.001	0.555	386
No	77 (29.1)	25 (44.6)	33 (50.0)				
Physical activity duration in past week							
Less than an hour	20 (8.6)	3 (6.7)	15 (27.7)	0.669	<0.001	0.007	332
More than one hour	213 (91.4)	42 (93.3)	39 (72.3)				

Table 3: Association between baseline vertebral fractures (VFs) and various physical activities at follow up. Results presented are odds ratios (OR) for the reduced physical activity in those with vertebral fractures compared to those without fracture.

Activity	(A) Crude OR (95%CI), P value	Confounders: (B) Adjusted for age OR (95%CI), P value	Confounders: (C) Additionally, adjusted for BMI OR (95%CI), P value	Variables on causal pathway: (D) Adjusted for C plus baseline mobility OR (95%CI), P value	Variables on causal pathway: (E) Adjusted for D plus back pain at follow-up OR (95%CI), P value
No VF vs Mild VF					
Walk up a flight of stair					
None	1.00	1.00	1.00	1.00	1.00
At least once a day	2.38 (1.19-4.74) 0.014	1.86 (0.89-3.89) 0.096	1.73 (0.79-3.80) 0.168	1.68 (0.74-3.83) 0.213	1.37 (0.54-3.44) 0.497
Walking*					
Yes	1.00	1.00	1.00	1.00	1.00
No	1.06 (0.59-1.92) 0.827	0.91 (0.49-1.68) 0.770	0.88 (0.46-1.68) 0.714	0.89 (0.46-1.72) 0.731	0.69 (0.33-1.44) 0.330
Walking speed					
Normal	1.00	1.00	1.00	1.00	1.00
Less than normal	1.58 (0.89-2.80) 0.115	1.26 (0.67-2.34) 0.461	1.00 (0.50-1.98) 0.990	1.02 (0.48-2.17) 0.940	0.81 (0.34-1.91) 0.642
Housework*					
Yes	1.00	1.00	1.00	1.00	1.00
No	1.33 (0.73-2.28) 0.473	1.24 (0.68-2.28) 0.473	1.15 (0.61-2.18) 0.657	1.20 (0.63-2.30) 0.568	1.02 (0.50-2.07) 0.956
Any physical activities*					
Yes	1.00	1.00	1.00	1.00	1.00
No	1.95 (1.08-3.53) 0.026	1.75 (0.95-3.20) 0.068	1.70 (0.90-3.21) 0.099	1.80 (0.94-3.46) 0.076	1.23 (0.60-2.52) 0.568
No VF vs Moderate/severe VF					
Walk up a flight of stair					
None	1.00	1.00	1.00	1.00	1.00
At least once a day	3.04 (1.62 to 5.71), 0.001	2.17 (1.12-4.22) 0.021	2.36 (1.18-4.70) 0.014	1.59 (0.71-3.56) 0.254	1.29 (0.56-2.99) 0.541
Walking*					
Yes	1.00	1.00	1.00	1.00	1.00
No	2.44 (1.42-4.19) 0.001	1.93 (1.10-3.39) 0.021	2.03 (1.13-3.63) 0.017	1.69 (0.91-3.14) 0.094	1.60 (0.84-3.04) 0.150
Walking speed					
Normal	1.00	1.00	1.00	1.00	1.00
Less than normal	2.69 (1.54-4.71) 0.001	1.76 (0.96-3.20) 0.064	2.26 (1.18-4.33) 0.013	1.85 (0.86-3.96) 0.112	1.65 (0.73-3.69) 0.221
Housework*					
Yes	1.00	1.00	1.00	1.00	1.00
No	1.80 (1.05-3.11) 0.033	1.68 (0.95-2.96) 0.072	1.69 (0.94-3.04) 0.079	1.77 (0.96-3.26) 0.066	1.79 (0.95-3.37) 0.071
Any physical activities*					
Yes	1.00	1.00	1.00	1.00	1.00
No	2.42 (1.40-4.21) 0.002	1.90 (1.07-3.37) 0.027	1.99 (1.09-3.63) 0.024	1.90 (1.01-3.59) 0.047	1.60 (0.82-3.08) 0.160

Model adjusted for (A) unadjusted, (B) adjusted for age at baseline, (C) adjusted for age and BMI at follow-up, and (D) adjusted for age, BMI at follow-up plus baseline mobility; and (E) adjusted for age, BMI at follow-up, baseline mobility, and back pain at follow-up.

* In the past week

Table 4: Association between baseline vertebral fractures (VFs) and time doing various physical activities at follow up. Results presented are odds ratios (OR) for doing less than one-hour physical activity in those with vertebral fractures compared to those without fracture.

Activity *		Confounders		Variables on causal pathway	
	(A) Crude OR (95%CI), P value	(B) Adjusted for age OR (95%CI), P value	(C) Additionally, adjusted for BMI OR (95%CI), P value	(D) Adjusted for C plus baseline mobility OR (95%CI), P value	(E) Adjusted for D plus back pain at follow-up OR (95%CI), P value
None VF vs Mild VF					
Walking ≥ 1 hour Less than an hour	 1.00 1.59 (0.70-3.61) 0.264	 1.00 1.47 (0.64-3.38) 0.360	 1.00 1.16 (0.47-2.89) 0.735	 1.00 1.06 (0.40-2.75) 0.900	 1.00 1.00 (0.36-2.73) 0.998
Housework ≥ 1 hour Less than an hour	 1.00 0.37 (0.08-1.64) 0.193	 1.00 0.30 (0.06-1.40) 0.129	 1.00 0.31 (0.06-1.45) 0.140	 1.00 0.31 (0.06-1.50) 0.149	 1.00 0.29 (0.06-1.46) 0.136
Sport ≥ 1 hour Less than an hour	 1.00 0.92 (0.23-3.60) 0.908	 1.00 0.97 (0.24-3.84) 0.971	 1.00 0.93 (0.22-3.80) 0.921	 1.00 0.82 (0.18-3.59) 0.797	 1.00 0.44 (0.07-2.77) 0.386
Any physical activities ≥ 1 hour Less than an hour	 1.00 0.81 (0.23-2.88) 0.757	 1.00 0.74 (0.20-2.66) 0.645	 1.00 0.82 (0.22-3.02) 0.778	 1.00 0.83 (0.21-3.24) 0.791	 1.00 0.74 (0.18-2.99) 0.684
None VF vs Moderate/severe					
Walking ≥ 1 hour Less than an hour	 1.00 3.76 (1.67-8.47) 0.001	 1.00 3.07 (1.32-7.11) 0.009	 1.00 3.84 (1.51-9.28) 0.003	 1.00 3.42 (1.35-8.68) 0.009	 1.00 2.96 (1.11-7.88) 0.030
Housework ≥ 1 hour Less than an hour	 1.00 2.89 (1.30-6.44) 0.009	 1.00 2.11 (0.90-4.88) 0.081	 1.00 2.26 (0.96-5.33) 0.062	 1.00 2.21 (0.89-5.47) 0.086	 1.00 1.95 (0.76-4.99) 0.163
Sport ≥ 1 hour Less than an hour	 1.00 2.90 (1.01-8.35) 0.047	 1.00 2.50 (0.83-7.50) 0.102	 1.00 2.39 (0.79-7.21) 0.119	 1.00 2.02 (0.63-6.46) 0.233	 1.00 1.93 (0.56-6.63) 0.293
Any physical activities ≥ 1 hour Less than an hour	 1.00 4.09 (1.93-8.68) <0.001	 1.00 3.02 (1.37-6.64) 0.006	 1.00 3.06 (1.35-6.91) 0.007	 1.00 2.51 (1.06-5.96) 0.036	 1.00 2.05 (0.85-4.92) 0.108

Model adjusted for (A) unadjusted, (B) adjusted for age at baseline, (C) adjusted for age and BMI at follow-up, and (D) adjusted for age, BMI at follow-up plus baseline mobility; and (E) adjusted for age, BMI at follow-up, baseline mobility, and back pain at follow-up.

* In the past week

FIGURE LEGENDS

Figure 1: Flow chart of recruitment and follow-up of the three research cohorts combined for the Vertebral fracture and Activity Study (VAS).

Figure 1

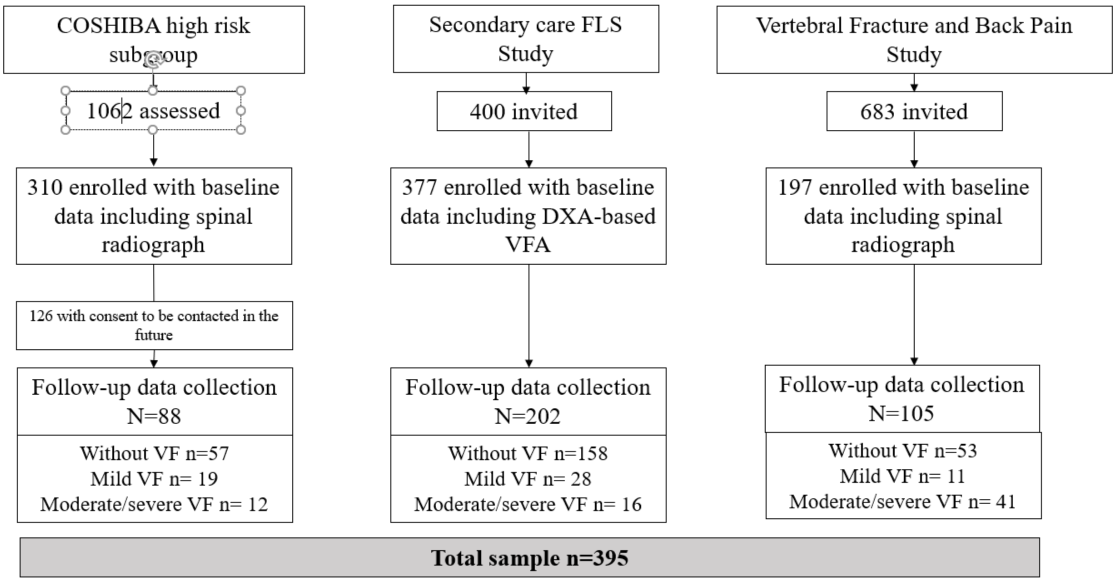

Figure 2: The graph showing the potential pathways we can explore between baseline vertebral fracture and decrease in physical activity at 5 years. Confounders are illustrated by light grey boxes, while variables likely to be on the causal pathway are illustrated by dark grey boxes

Figure 2