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Degenerative Changes at the Lumbar Spine – Implications for Bone Mineral Density Measurement in Elderly Women

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ABSTRACT

Purpose: In the elderly, degenerative manifestations in the lumbar spine may result in falsely elevated bone mineral density (BMD) values, consequently missing a large proportion of those with osteoporosis. Our aim was to determine the distribution and impact of degenerative changes on lumbar spine DXA over time and its clinical implications.

Methods: Participants were 1044 women from the population-based OPRA-cohort. All women were 75 years old at invitation and followed up after 5 years (n=715) and 10 years (n=382). Degenerative changes were evaluated visually on the DXA image for each vertebra L1 to L4 (intra-observer precision kappa values 0.66-0.70).

Results: At baseline, apparent degenerative changes were more frequent in the inferior segments of the lumbar spine: 5% (L1), 15% (L2), 26% (L3), 36% (L4) and increased over time. At 10-years the prevalence was: 20% (L1), 39% (L2), 59% (L3), 72% (L4), resulting in a significant increase in overall BMD. In women without apparent degenerative changes, BMD remained stable between 75-85 rather than an expected bone loss. At baseline, 37% had osteoporosis ($BMD < -2.5$) at L1-L4; exclusion of women with apparent degenerative changes increased this proportion to 47%. Using L1-L2, which was less prone to degenerative changes, 46% of women were classified as osteoporotic regardless of degenerative changes.

Conclusion: Degenerative changes were very common in elderly women, accelerated disproportionately over time, were increasingly frequent from vertebrae L1-L4 and had significant impact on diagnosing osteoporosis. This suggests that routine reporting of spine BMD at L1-L2 would add valuable information for re-assessment and monitoring.

Key words: Degenerative changes, Lumbar spine, BMD, DXA, Osteoporosis, Diagnosis

Mini Abstract

Degenerative changes of the lumbar spine may lead to misinterpretation of BMD measurements and cause under-diagnosis of osteoporosis. This longitudinal study of 1044 women, 75 years at inclusion and followed for 10 years, shows that identification of apparent degenerative changes on the DXA scan can increase the proportion diagnosed.

INTRODUCTION

Osteoporosis, characterised by low bone mineral density (BMD) and subsequent fragility fractures, presents an increasing healthcare problem worldwide because of the growing elderly population. Osteoporosis is defined by the World Health Organisation as a BMD 2.5 standard deviations or more below the average value for young healthy adults as measured by Dual energy X-ray absorptiometry (DXA) (1). These criteria are predominantly applied to BMD measurement at the lumbar spine, proximal femur/femoral neck and distal forearm. DXA represents the 'gold standard' in terms of diagnosis of osteoporosis and assessment of treatment efficacy in the individual and in clinical trials reporting change in BMD (2).

For the diagnosis of spinal osteoporosis and prediction of vertebral fracture risk, BMD measurement of the lumbar spine is preferred, particularly in middle-aged postmenopausal women where trabecular bone loss is predominant (3). However, with increasing age, degenerative manifestations in the lumbar spine such as osteophytes and subchondral sclerosis become increasingly common. Such degenerative changes, and to a lesser extent clinically diagnosed or un-diagnosed vertebral compression fractures, scoliosis and aortic calcification, may result in artificially elevated spine BMD (4-13). Hence the clinical use of spinal BMD measurements becomes increasingly problematic with age, and in fact difficulties in accurately assessing spinal BMD may already be apparent soon after menopause (14). Consequently, recommendations suggest that the hip is a more reliable site for BMD measurement (15, 16) particularly because, while rate of bone loss in the spine and distal radius appears to cease in the elderly, this does not apply to the hip where continuous bone loss is seen with advancing age (17). On the other hand, it is also known that degenerative changes in the lumbar spine may be associated with increased BMD of the hip (18) supporting the observed inverse relationship between osteoporosis and osteoarthritis mainly of the hip, knee and hand (19).

Quantification and interpretation of the clinical significance of degenerative changes on spinal X-rays is likewise a well-recognized problem. Numerous scores for standard radiographic investigations have been developed of which the Lawrence & Kellgren score was the first (20). This systematic approach relies on a visual estimate of plain X-rays, although due to the vast advances in imaging techniques including CT and MRI, complementary scores have been developed (21).

The standard DXA investigation is based on an anteroposterior (AP) view providing a rough image of the spine, but even on this image it is clear to those interpreting the scans that a measurement is either normal with all vertebrae distinctly outlined, for example in a young adult or affected by pathology, predominantly in older individuals and influencing BMD. Access to complementary spinal X-ray films is rarely available at the time of a DXA scan, although such information could enhance the diagnostic reliability of the DXA measurement particularly in the elderly.

In the most recent recommendations from the International Society for Clinical Densitometry (ISCD), it is recommended that all vertebrae (L1-L4) are included in the average values used for diagnosis compared to the previously most used L2-L4 (22). Furthermore, it is also suggested that a vertebra that is not possible to evaluate, because of local structural changes or a more than 1.0 T-score difference compared to adjacent vertebrae, should be excluded, although no guidance has been provided regarding such changes or the vertebrae most frequently affected (22). It has previously been shown that the DXA image itself can be used to detect lumbar scoliosis (23) however, whether common changes related to degenerative manifestations can be distinguished on the DXA image has not been consistently reviewed nor has their influence on individual vertebral level BMD distribution.

The ultimate aim of this study was to provide clinically applicable information on the interpretation of spinal DXA scans in elderly women. The hypothesis was generated from the clinical observation that degenerative changes seem most obvious in the inferior segments; hence diagnosis should be more reliable by using more superior vertebrae or other combinations in elderly women. To this extent we investigated the reliability of visual determination of degenerative changes on the DXA image, the distribution of degenerative changes in the lumbar spine and the effect on the diagnosis of osteoporosis. The study was performed in the Malmö Osteoporosis Risk Assessment (OPRA) cohort of 1044 75 year old women with reassessment at age 80 and 85.

MATERIALS AND METHODS

Subjects

The study participants are Caucasian women from the population based Osteoporosis Prospective Risk Assessment study (OPRA) cohort which has previously been more extensively described (24). This study includes data from 1044 women from the Malmö area in Sweden, 65% of 1604 invited between December 1995

and May 1999. All the women were 75 years of age at invitation, predominantly of Swedish origin (99%) and almost all of them self-ambulatory. These women were followed-up 5-years after their first visit (when 715 women attended) and again at 10 years (when 382 women attended).

Bone mineral density measurements

BMD was assessed at baseline and follow-up using the Lunar® DPX-L DXA scanner (Madison, WI, USA). DXA scans were analysed with software versions 1.33 and 1.35 at baseline, version 4.7b at 5 years and version 4.7e at 10 years.

BMD was measured at all skeletal sites (including lumbar spine, hip and total body) although in this study only the femoral neck and the lumbar spine measurements are reported. For the lumbar spine, each individual vertebra L1, L2, L3, L4 and the combined levels L1-L2, L1-L4 and L2-L4 were included. The number of assessable DXA scans/vertebrae at each time point varied slightly due to technical reasons or surgery (baseline n=973-976, at 5y n=691-698, at 10y n=377-380). Calibration of the scanner using the manufacturer's phantom was performed 3 times per week and the precision coefficients in this cohort of elderly women were 1.45% at the lumbar spine and 4.01% at the femoral neck (25). Lateral spine DXA was not performed.

Evaluation of apparent spinal degenerative manifestations

All DXA scans of the lumbar spine performed at baseline, 5 and 10-year follow-up were visually evaluated directly on the computer screen by a single observer, an orthopaedic spine surgeon (MT) (Supplementary Figure 1).

Firstly, the technical quality of each scan was determined. At baseline, 89 vertebrae (L4 (7.2%) and L1-L3 (0.6-1.5%)) were excluded from analysis. From 5 and 10-year follow-up only one vertebra was excluded. Reasons for exclusion included inferior software delineation of the vertebra or presence of surgical implants. Thereafter, each individual vertebra (L1, L2, L3 and L4) was evaluated for visual degenerative changes, signs of vertebral compression fracture and scoliosis using a semi-quantitative score; (**Degeneration**: grade 0, none; grade 1, mild; grade 2, severe (presence of deformation of the vertebra in addition to other criteria)); (**Scoliosis**: grade 0, none; grade 1, yes (>10 degree Cobb angle L1-L4)); (**Fracture**: grade 0, none; grade 1, suspected; grade 2, yes)).

Degenerative changes were defined as prevalence of apparent vertebral osteophytes, disc space narrowing, asymmetric subchondral sclerosis or facet joint sclerosis. In grading the extent of degeneration, we used presence

or absence of apparent degenerative changes according to the above criteria, rather than current standardised scores for spinal degeneration, since these are all based on X-ray or MRI (21). Furthermore, the image resolution of DXA scans, particularly the early scans, did not permit more detailed grading.

Vertebral fractures are inherently difficult to ascertain visually on a standard frontal DXA scan. Using a conservative estimate, vertebral compression fracture was defined as a height reduction greater than 50% and/or a homogenous symmetric increased signal compared to the nearest vertebrae. Scoliosis was defined as a Cobb angle between L1 and L4 exceeding 10 degrees. Aortic calcifications could not be identified on the anterior-posterior DXA images.

Complementary evaluation of spinal X-ray investigations

The OPRA study did not include spinal X-rays at the scheduled visits. However, all X-rays performed from 2003-2010 are accessible from the digital archives of the Department of Orthopaedics Malmö, Skåne University Hospital, Sweden. Therefore X-rays were investigated for those 382 women who attended the 10-year follow-up, since these women, now aged 85 were likely to have the highest prevalence of degenerative changes. In all, 82 plain lumbar X-ray investigations were identified, 64 of which were performed within +/- 2 years of the 10-year DXA scan. All X-rays were evaluated by a single observer (MT) according to the same criteria for apparent degenerative changes, fracture and scoliosis.

Precision of scan assessment

To assess *intra*-observer reproducibility, the same evaluation was repeated for every 10th subject at baseline within one month. The Kappa (κ) coefficient, for degenerative changes exceeded 0.61 and for scoliosis 0.81 (Supplementary Table 1). A Kappa value over 0.41 is interpreted as moderate agreement, 0.61 as substantial agreement and over 0.81 as almost perfect agreement (26).

To determine the *inter*-observer precision a second observer, a consultant radiologist (JB), was engaged. DXA scans of every 3rd subject were re-evaluated for those attending the 10 year follow-up. Kappa coefficients ranged from 0.43 – 0.66.

As expected, precision was generally lower when comparing X-ray verified degenerative changes with those detectable on the DXA image. Sensitivity, detecting X-ray verified degenerative changes on the DXA image,

was quite high in L2-L4 (70-82%) but lower in L1 (42%). The sensitivity for detecting scoliosis in the DXA image was 90%.

Statistical analyses

All statistical analyses were performed using SPSS version 17.0 (SPSS, Inc., Chicago, IL). Paired sample T-test was used to describe BMD differences between the vertebrae and BMD changes over time. ANOVA was used to assess correlations between BMD and degenerative changes. P-values are reported uncorrected for multiple testing and significance was set to $P < 0.05$.

Ethics approval

All the participants provided informed written consent and the study was approved by the Lund University Ethics Committee. This study was performed according to the principles of the Helsinki declaration.

RESULTS

Subject characteristics

Relevant clinical characteristics of the OPRA cohort, according to status of apparent lumbar degenerative changes at baseline, are reported in Table 1. There were no significant differences between the two groups.

Prevalence of apparent degenerative changes, scoliosis and fracture

At the baseline evaluation, degenerative changes visible on the DXA scan were more frequent in the inferior part of the lumbar spine: 5% (L1), 15% (L2), 26% (L3), 36% (L4) and increased over time (Table 2). At the 10-year follow-up the prevalence was: 20% (L1), 39% (L2), 59% (L3) and 72% (L4). Scoliosis was apparent in 10.5% of women at baseline, 15.8% at 5 years and increased to 26.1% at 10-years (Table 2). Already at baseline, 93% of these women also had signs of degenerative changes. Vertebral fractures in any vertebrae (L1 to L4) were identified in 28 (2.9%) of the women at baseline, 10 (1.4%) women at 5 years (1.4%) and 10 (2.6%) at 10-years.

Lumbar spine BMD changes up to 10-years

In the population as whole, a gradient in **crude** lumbar spine BMD (**unadjusted for vertebral size**) was observed already at age 75, with the lowest BMD values occurring in L1 and the highest values in L4. This gradient persisted throughout follow-up at age 80 and 85 years. In all instances, BMD was significantly different between vertebrae ($p < 0.001$) (Table 3a, Figure 1(A)).

Evaluating only those women **without** apparent degenerative changes, the same gradient, with BMD increasing inferiorly, was observed but with similar BMD values at the L3 and L4 levels (Table 3b). Noticeably, in these women BMD values were considerably lower (2-9% baseline, 5-11% at 80 years and 4-16% at 85 years) at all vertebral levels compared to the average of the entire study population. **Employing T-scores and thus reducing the effects on BMD from larger vertebral size in the inferior segments; the effect of apparent degenerative changes is also evident with a gradient in T-score (Figure 1(B)). This is observed** both at baseline and over time, with T-scores at -2 to -2.5 or less in those without apparent changes and in the range of -1 to -2 in those judged to have degenerative changes (Table 3b-c). In women with scoliosis, BMD was significantly higher in L2, L3 and L4 ($p < 0.001$) and borderline in L1 ($p = 0.053$), when compared to those without scoliosis.

The long-term changes were evaluated in women attending all three assessments in the OPRA study; of the original 1044 women, 382 also attended the final follow-up which allowed serial assessment of individual spinal BMD changes in this subgroup. The results demonstrated that the increase in spine BMD was a function of degenerative changes. By excluding women with degenerative changes at any time point from the analysis we observe that BMD was relatively stable over time between age 75 and 85 years with no indication of bone loss ($n = 73$) (Table 4, Figure 2).

Bone mineral density – proportion with osteoporosis

The combined level L2-L4 has been a common clinical measurement site for some scanners and was used in many pharmaceutical trials. In this study, the prevalence of osteoporosis (i.e. T score < -2.5) applying the L2-L4 level was 33% at baseline, 30% at 5-years and 28% at the 10-year follow-up (Table 5). The reason for this is illustrated in Figure 1 by the apparent increase in lumbar spine BMD with increasing age in the cohort as a whole. BMD increased significantly, between age 75 and 85, in all individual vertebrae, as well as in the combined levels. By excluding women with apparent degenerative changes on the DXA image, the prevalence of

osteoporosis increased to 44% at baseline and to 47% at 5 and 10-years. These values are comparable with the prevalence of osteoporosis using femoral neck as the diagnostic site at age 80 and 85, whereas at age 75, osteoporosis of the spine is more common than at the femoral neck (Table 5).

If the currently recommended combined level, L1-L4 was applied, the findings were similar, but with higher percentage values; the prevalence of osteoporosis at baseline was 37% at age 75 and 30% at age 85. Excluding those with apparent degenerative changes (and subsequent elevation of BMD) identified a considerably higher proportion of women with osteoporosis at all time-points (Table 5). Based on the observation that vertebrae L1 and L2 were less affected by degenerative changes, specific evaluation of the L1-L2 level, identified an even higher proportions with spinal osteoporosis at all visits.

Effects of osteoporosis medication on BMD and degenerative changes

Medications affecting bone mass were not commonly used or prescribed in this cohort (Table 1). At baseline, <10% of women used calcium or D-vitamin supplements, 3% used bisphosphonates and only a small number used potent oestrogens corresponding to hormone replacement therapy (n=18).

Women on calcium or D-vitamin supplements had significantly lower spine BMD compared to those who did not take supplements. Similar results were observed at 5 year follow-up, despite the number of women taking calcium or D-vitamin supplementation increasing to ~30%. Women prescribed bisphosphonates at baseline had similar BMD values to the rest of the population. However at 5 year follow-up, by which time 50 (8%) women used bisphosphonates, not unexpectedly they had significantly lower BMD compared to the rest of the population (figure 2). Oestrogen users, of whom there were few, had significantly higher spine BMD at baseline. None of these medications had any effect on prevalence of spine degeneration.

DISCUSSION

In this longitudinal study we show that the prevalence of apparent degenerative changes in the lumbar spine is high in elderly women and increases with age in the very elderly, resulting in increasing spinal BMD. Degenerative changes of the lumbar spine are not uniformly distributed and are more common in the lower segments. We can also show that by excluding cases with degenerative changes or excluding the vertebrae most susceptible to degenerative changes, a significantly higher proportion of prevalent osteoporosis is detectable. Furthermore and surprisingly, in women without apparent degenerative changes, spinal bone mass appears to remain stable from age 75 to 85 years.

The aim of the study was to elucidate the clinical implications of observed artefacts visible on DXA scan images; their effect on BMD and most importantly on diagnosis of osteoporosis. Ultimately this could contribute to a more reliable evaluation of clinical scans in the elderly, particularly by improving consistent interpretation of repeat scans to monitor spine bone density over many years. In this large cohort of women aged 75 when undergoing the baseline DXA scan, we show that apparent degenerative manifestations of the lumbar spine on the scan images can be consistently detected over time and that, as expected, they significantly influence BMD.

To the best of our knowledge, DXA scans have not previously been used for assessment of individual vertebra and the consequences of apparent degenerative changes on diagnosis of osteoporosis in a longitudinal study. Visual assessment proved sufficiently reliable, with moderate to substantial agreement in judging degenerative changes and almost perfect agreement for scoliosis.

The high prevalence of degenerative changes and the increase from L1 towards L4 found on the DXA image is in line with findings from radiological studies (27), indicating that it is possible to use the DXA image for a rough assessment of degenerative manifestations. The highly significant increase of prevalent changes visible on the DXA image, reaching up to 72% in L4 and 80% for any vertebra at age 85, has clinical implications. This clearly points to the possibility that falsely elevated spinal BMD with advancing age is an important reason for under-diagnosis and insufficient initiation of osteoporosis medication and it also allows for misinterpretation of drug-effects during monitoring of therapy.

In contrast, the prevalence of scoliosis has previously been evaluated on DXA images by Hicks and colleagues and the prevalence and correlation to BMD in our study is consistent with these findings, suggesting that the cohort exhibits a representative epidemiological pattern and further indicating that visual assessment is useful (23). Scoliosis is easy to detect on the DXA image and highly associated both with degenerative changes and higher BMD. This makes scoliosis an important cofactor for degenerative changes when evaluating a patients DXA scan.

The prevalence of fracture detected on DXA scans was low. Generally, the diagnosis of vertebral fracture even on standard X-ray investigations is difficult unless there is a clear and substantial decrease in vertebral height or a pronounced deformity. Furthermore, vertebral fractures reach the highest prevalence in the lower thoracic spine and fewer fractures are present in the lumbar spine, particularly in the lower segments that are more prone to degenerative manifestations, thus producing a masking effect (28, 29). Vertebral fracture deformity also affects the anterior and central parts of the vertebral body while the posterior wall and segment is intact, hence reducing the possibility to detect a fracture on an anterior image. This is of course a limitation of the study but it is nevertheless the common clinical situation and probably of lesser importance for artifactly elevated BMD values (4, 6). The lateral spine view obtainable on newer DXA machines or applying morphometric analysis on complementary lateral spine X-rays could elucidate this in further comparative studies.

Osteoporosis, during its early stages predominantly affects trabecular bone (30), therefore the vertebral bodies are one of the predominant sites for early bone loss and fracture. Among the elderly women in this study, there was a positive correlation between spinal BMD and apparent degenerative changes, a finding in agreement with several earlier studies (31). The women with degenerative changes detectable on the DXA image had significantly higher BMD compared to individuals without such changes. This association is evident in all vertebrae and at all visits i.e. up to 10 years. There is also a significant correlation between lumbar spine degeneration and femoral neck BMD where subjects with visible degenerative manifestations have higher BMD in both the lumbar spine and hip, as previously reported (18).

Our findings highlight that there is a substantial risk of missed osteoporosis diagnosis in the spine, unless the influence of degenerative changes are carefully considered when interpreting the result of a DXA investigation. Similarly, when monitoring treatment effects from, for example bisphosphonate therapy, using a second or

subsequent spine DXA scans runs a risk of interpreting the natural course of degenerative changes as a drug effect in elderly women.

Furthermore, this study also indicates that by choosing the more superior vertebrae for BMD measurements, a large proportion of degenerative changes potentially distorting the diagnostic score would be excluded. In our cohort, using L1-L2 compared to L1-L4, 20 % more cases with osteoporosis were detected at baseline and 5 year follow-up and 29% more at 10 year follow-up. Alternatively, comparing L1-L2 without degenerative manifestations to L2-L4, 37% more osteoporotic cases were detected. The clinical importance is particularly evident around the age of 75 since it has been suggested that in the elderly, the hip should be used to diagnose osteoporosis by BMD measurement (15, 16). However, at this time there is commonly still a discrepancy in the development of osteoporosis between the hip and the spine because of a lower rate of bone loss in the hip during the post-menopausal years. We show that using the hip does not compensate for those missed using standard spine BMD (L2-L4) at this age, while using L1-L2, in conjunction with estimation of degenerative manifestations does. Since fractures secondary to osteoporosis are an extensive source of human suffering and costs for society (32), early diagnosis is essential for preventive treatment and relief on an increasingly burdened health care due to an ageing population. Simply excluding individual vertebrae as invalid during an initial clinical scan according to the ISCD recommendations is useful for single clinical measurements; however, the information is not *systematically* transferred to subsequent measurements, and hence not reflected in the reported percentage changes over time.

An additional interesting observation in this study is the finding that spinal BMD remains virtually stable between age 75 and 85, instead of the expected decrease when excluding those with apparent degenerative manifestations. We can only speculate if this is perhaps an effect of survival, since it has been shown that women with lower bone mass have a higher mortality (33), but on the other hand the effect is consistent in those followed for 10-years and measured at all time points. Moreover, [standard spinal DXA scans are influenced by also by the posterior portions of the vertebrae and not directly visible. Spinal QCT are superior in detecting true bone loss \(34\) with comparative studies indicating a progressive bone loss in the anterior vertebral body portions rich in trabecular bone and not detected by DXA \(35-37\). Nevertheless, DXA is currently the mainstay in terms of clinical utility which warrants improved understanding on how to interpret the findings, particularly in the aged.](#)

Since this study was initiated in the 90's, a very limited number of the women were on bisphosphonates and the absence of bone loss is not explained by pharmacotherapy. The prevalence of calcium and vitamin D use increased during the course of the study and users had lower spine BMD at all time points, stable levels and no detectable bone loss.

The study has some limitations; it should be acknowledged that the assessment of vertebral fractures might miss moderate deformities that would have been detected using the method outlined by Genant et al (38). Ideally, we would have had lumbar spine X-rays investigations at all visits, however, spinal radiographs were unfortunately not part of the study, and instead we used available clinical radiographs for women participating up to 10-years. This at least enabled determination of the methodological precision. Albeit we recognize that lateral images from spinal X-rays and complementary lateral spine DXA would have improved the study, it still mirrors most clinical settings. [This also applies to possible posterior element changes, masked in the standard anterior-posterior DXA assessment.](#) Less prominent pathology may also have been overlooked, however, this is probably of reduced importance for our purpose (10) to determine the optimal spinal levels on DXA for assessment of osteoporosis in elderly women. It may also be argued that apparent degenerative changes is an imprecise entity, this is true, but is also true when applied to X-ray assessment. The term refers to undefined changes commonly observed with age of which part is likely to mirror spinal osteoarthritis including vertebral disc deterioration but not necessarily a generalized condition and further to this, of ambiguous clinical significance.

The strengths of the study include that the OPRA cohort is eminently suitable for the evaluation of degenerative changes at the spine and their effect on bone density. Containing over 1000 75-year old women at baseline, there is already a high prevalence of both osteoporosis and degenerative changes in this age group, and follow-up at 5 and 10-years enables the natural course of pathology to be explored. To our knowledge it also the first time such an extensive evaluation of DXA scan images aiming to define both prevalent and long-term spinal changes has been performed in elderly women

In conclusion, visual estimation of lumbar spine DXA images is reliable in detecting apparent degenerative changes which influence BMD in elderly women. Spinal BMD appear to increase over time or remains stable between the ages of 75 and 85, apparently influenced by degenerative changes. Degenerative changes display a

gradient, being more pronounced in the lower segments and become more prevalent over time in the lower segments.

Consequently, this study suggests that a relevant level for assessing BMD is L1-L2, a finding that could easily be added as complementary information in standard DXA reports as an additional measure for percentage change over time. Ultimately, this would enhance osteoporosis diagnosis, re-assessment and monitoring in women.

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FIGURE LEGENDS

Figure 1 (A) Bone mineral density (mean) measured at each vertebra (L1-L4) for all women in the cohort at baseline (age 75), at follow-up at 5 years (age 80) and 10 years (age 85) and **(B)** the corresponding mean T-score values

Figure 2 Bone mineral density (mean) measured at each vertebra (L1-L4) for women WITHOUT degenerative spine changes who had measurements at baseline (age 75), at follow-up at 5 years (age 80) and 10 years (age 85)

Table 1: OPRA cohort characteristics stratified into those WITH and WITHOUT lumbar spine degenerative changes.

	Women With Degenerative Changes	Women Without Degenerative Changes	p=
Age 75 (Baseline)	418 (43%)	552 (57%)	
Age 80 (5-yr follow-up)	470 (67%)	228 (33%)	
Age 85 (10-yr follow-up)	304 (80%)	76 (20%)	
Weight (kg) at 75 yrs	67.7 (10.8)	67.2 (11.6)	ns
Weight (kg) at 80 yrs	66.4 (11.1)	65.4 (12.1)	ns
Weight (kg) at 85 yrs	64.0 (11.1)	63.5 (9.9)	ns
Height (cm) at 75 yrs	160 (5)	160 (5)	ns
Height (cm) at 80 yrs	159 (5)	158 (5)	ns
Height (cm) at 85 yrs	158 (5)	158 (5)	ns
Bisphosphonates (75 yrs)	16 (3.8%)	16 (2.9%)	ns
Bisphosphonates (80 yrs)	30 (6.4%)	20 (8.8%)	ns
Ca and/or D-vit (75 yrs)	41 (9.8%)	46 (8.3%)	ns
Ca and/or D-vit (80 yrs)	121 (25.7%)	69 (30.3%)	ns
HRT (75 yrs)	5 (27.8%)	13 (72.2%)	ns
HRT (80 yrs)	7 (1.5%)	3 (1.3%)	ns

Table 2: Prevalence of degenerative changes, scoliosis and vertebral fractures at each vertebra in 75, 80 and 85 year old women of the OPRA cohort

Vertebrae	Baseline (75 yrs)		5-year follow-up (80 yrs)		10-year follow-up (85 yrs)	
	Number	%	Number	%	Number	%
L1	49/968	5	119/698	20	75/379	20
L2	142/970	15	225/698	32	148/379	39
L3	255/970	26	343/698	39	224/380	59
L4	351/963	36	411/698	59	272/380	72
L1-L2	147/976	15	238/698	34	158/380	42
L1-L4	418/970	43	470/698	67	304/380	80
L2-L4	412/970	42	466/698	67	301/380	79
Scoliosis	102/968	10.5	110/698	15.8	99/379	26.1
Fracture	28/970	2.9	10/698	1.4	10/380	2.6

Numbers are based on those vertebrae which could be assessed

Table 3: Gradient of BMD at individual vertebrae: Baseline, 5- & 10-year follow-up (A **ALL** women, B women **WITHOUT** and C women **WITH** degenerative changes)

A All women	Baseline,			5-year follow-up			10-year follow-up		
	BMD Mean (SD)	T-score	p-value*	BMD Mean (SD)	T-score	p-value*	BMD Mean (SD)	T-score	p-value*
L1	0.836 (0.164)	-2.41 (1.37)	<0.001	0.851 (0.184)	-2.28 (1.53)	<0.001	0.856 (0.200)	-2.24 (1.67)	<0.001
L2	0.928 (0.187)	-2.28 (1.56)	<0.001	0.947 (0.202)	-2.14 (1.68)	<0.001	0.960 (0.218)	-2.01 (1.82)	<0.001
L3	0.997 (0.202)	-1.69 (1.68)	<0.001	1.012 (0.215)	-1.57 (1.79)	<0.001	1.042 (0.241)	-1.31 (2.01)	<0.001
L4	1.029 (0.219)	-1.45 (1.83)	-	1.056 (0.236)	-1.23 (1.96)	-	1.083 (0.269)	-1.00 (2.24)	-
L1-L2	0.884 (0.170)	-2.26 (1.42)	<0.001	0.901 (0.187)	-2.12 (1.56)	<0.001	0.910 (0.201)	-2.04 (1.67)	<0.001
L1-L4	0.956 (0.181)	-1.93 (1.51)	<0.001	0.975 (0.195)	-1.77 (1.62)	<0.001	0.994 (0.214)	-1.61 (1.79)	<0.001
L2-L4	0.989 (0.193)	-1.76 (1.61)	<0.001	1.009 (0.206)	-1.59 (1.71)	<0.001	1.034 (0.229)	-1.39 (1.91)	<0.001

* p-values are based on comparison of adjacent vertebrae (L1 vs. L2, L2 vs. L3, L3 vs. L4, L1-L2 vs. L1-L4, L1-L4 vs. L2-L4, L2-L4 vs. L1-L2) using paired samples test

B Without Degeneration	Baseline			5-year follow-up			10-year follow-up		
	BMD Mean (SD)	T-score	p-value*	BMD Mean (SD)	T-score	p-value*	BMD Mean (SD)	T-score	p-value*
L1	0.818 (0.153)	-2.52 (1.28)	<0.001	0.809 (0.159)	-2.55 (1.35)	<0.001	0.826 (0.191)	-2.50 (1.60)	<0.001
L2	0.899 (0.168)	-2.53 (1.40)	<0.001	0.888 (0.171)	-2.61 (1.42)	<0.001	0.894 (0.195)	-2.57 (1.63)	<0.001
L3	0.953 (0.176)	-2.05 (1.47)	0.004	0.925 (0.176)	-2.23 (1.48)	0.154	0.930 (0.201)	-2.24 (1.62)	0.024
L4	0.963 (0.190)	-1.97 (1.65)	-	0.939 (0.186)	-2.19 (1.54)	-	0.915 (0.188)	-2.33 (1.55)	-
L1-L2	0.859 (0.155)	-2.47 (1.30)	<0.001	0.850 (0.161)	-2.54 (1.34)	<0.001	0.855 (0.185)	-2.50 (1.54)	<0.001
L1-L4	0.914 (0.162)	-2.31 (1.35)	<0.001	0.892 (0.164)	-2.48 (1.37)	<0.001	0.890 (0.184)	-2.49 (1.53)	<0.001
L2-L4	0.940 (0.169)	-2.19 (1.40)	<0.001	0.915 (0.168)	-2.37 (1.40)	<0.001	0.915 (0.192)	-2.37 (1.60)	<0.001

* p-values are based on comparison of adjacent vertebrae (L1 vs. L2, L2 vs. L3, L3 vs. L4, L1-L2 vs. L1-L4, L1-L4 vs. L2-L4, L2-L4 vs. L1-L2) using paired samples test

C	With Degeneration	Baseline			5-year follow-up			10-year follow-up		
		BMD Mean (SD)	T-score	p-value*	BMD Mean (SD)	T-score	p-value*	BMD Mean (SD)	T-score	p-value*
	L1	1.076 (0.197)	-0.47 (1.54)	<0.001	1.005 (0.212)	-1.01 (1.71)	<0.001	0.974 (0.189)	-1.19 (1.55)	<0.001
	L2	1.175 (0.235)	-0.90 (1.72)	<0.001	1.101 (0.227)	-1.14 (1.76)	<0.001	1.086 (0.220)	-1.15 (1.77)	<0.001
	L3	1.166 (0.236)	-0.70 (1.85)	<0.001	1.124 (0.233)	-0.88 (1.83)	<0.001	1.142 (0.251)	-0.67 (2.00)	<0.001
	L4	1.160 (0.221)	-0.57 (1.80)	-	1.154 (0.242)	-0.56 (1.95)	-	1.174 (0.273)	-0.48 (2.26)	-
	L1-L2(any)	1.014 (0.185)	-1.17 (1.54)	<0.001	1.000 (0.194)	-1.30 (1.62)	<0.001	0.988 (0.196)	-1.39 (1.64)	<0.001
	L1-L4(any)	1.014 (0.191)	-1.46 (1.59)	<0.001	1.017 (0.195)	-1.43 (1.63)	<0.001	1.021 (0.214)	-1.39 (1.78)	<0.001
	L2-L4(any)	1.057 (0.203)	-1.19 (1.69)	<0.001	1.055 (0.207)	-1.21 (1.73)	<0.001	1.065 (0.228)	-1.13 (1.90)	<0.001

* p-values are based on comparison of adjacent vertebrae (L1 vs. L2, L2 vs. L3, L3 vs. L4, L1-L2 vs. L1-L4, L1-L4 vs. L2-L4, L2-L4 vs. L1-L2) using paired samples test

Table 4A Longitudinal assessment of change in BMD with increasing age (i.e. attended all 3 visits) - **ALL** women

	Baseline, 75 years	5-year follow-up, 80 years	10-year follow-up, 85 years	p-value* (BL vs. 5 yrs)	p-value* (5yrs vs. 10 yrs)	p-value* (BL vs. 10 yrs)
Vertebra	BMD Mean (SD)	BMD Mean (SD)	BMD Mean (SD)			
L1	0.820 (0.156)	0.847 (0.184)	0.852 (0.196)	<0.001	0.250	<0.001
L2	0.921 (0.189)	0.946 (0.205)	0.952 (0.214)	<0.001	0.255	<0.001
L3	0.983 (0.204)	1.012 (0.221)	1.034 (0.236)	<0.001	<0.001	<0.001
L4	1.012 (0.212)	1.050 (0.237)	1.077 (0.264)	<0.001	<0.001	<0.001
L1-L2	0.873 (0.168)	0.899 (0.188)	0.904 (0.197)	<0.001	0.166	<0.001
L1-L4	0.943 (0.180)	0.971 (0.196)	0.988 (0.209)	<0.001	<0.001	<0.001
L2-L4	0.977 (0.192)	1.007 (0.209)	1.026 (0.224)	<0.001	<0.001	<0.001

Table 4B Longitudinal assessment of change in BMD with increasing age (i.e. attended all 3 visits) - women **WITHOUT** degenerative changes

	Baseline, 75 years	5-year follow-up, 80 years	10-year follow-up, 85 years	p-value* (BL vs. 5 yrs)	p-value* (5yrs vs. 10 yrs)	p-value* (BL vs. 10 yrs)
Vertebra	BMD Mean (SD)	BMD Mean (SD)	BMD Mean (SD)			
L1	0.807 (0.155)	0.821 (0.165)	0.830 (0.201)	0.087	0.419	0.017
L2	0.882 (0.180)	0.888 (0.170)	0.891 (0.201)	0.685	0.744	0.373
L3	0.932 (0.176)	0.927 (0.181)	0.937 (0.197)	0.644	0.267	0.438
L4	0.920 (0.169)	0.925 (0.195)	0.919 (0.205)	0.564	0.520	0.981
L1-L2	0.847 (0.164)	0.855 (0.163)	0.861 (0.192)	0.248	0.555	0.081
L1-L4	0.891 (0.163)	0.891 (0.168)	0.895 (0.186)	0.377	0.746	0.300
L2-L4	0.913 (0.169)	0.915 (0.175)	0.917 (0.193)	0.770	0.879	0.654

* p-values are based on comparison of BMD at each vertebra over time, using paired samples test

Table 5 Prevalence of osteoporosis, based on T-score < -2.5 SD at the lumbar spine

Measurement site	Diagnosed osteoporotic at Baseline	Diagnosed osteoporotic at 5-year follow-up	Diagnosed osteoporotic at 10-year follow-up
L2-L4	33%	30%	28%
Without degeneration at L2-L4	44%	47%	47%
L1-L4	37%	34%	30%
Without degeneration at L1-L4	47%	53%	47%
L1-L2	46%	43%	42%
Without degeneration at L1-L2	52%	54%	56%
Femoral neck	31%	44%	48%

Figure 1 (A) Bone mineral density (mean) measured at each vertebra (L1-L4) for all women in the cohort at baseline (age 75), at follow-up at 5 years (age 80) and 10 years (age 85) and **(B)** the corresponding mean T-score values

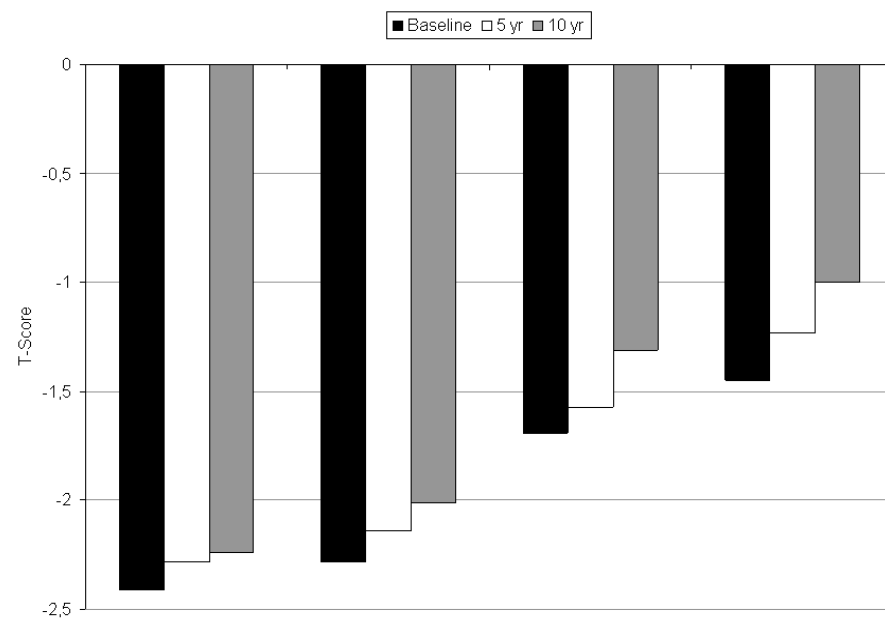
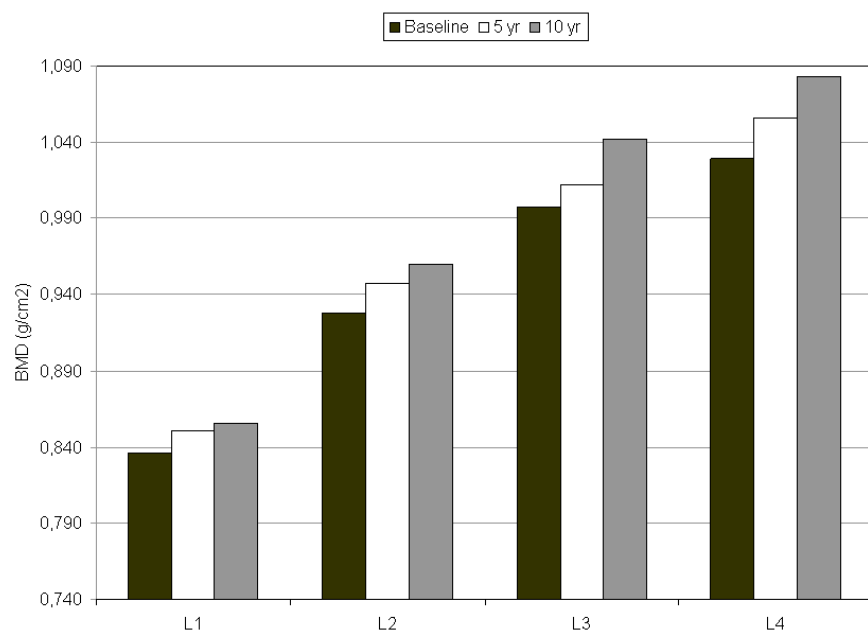


Figure 2 Bone mineral density (mean) measured at each vertebra (L1-L4) for women WITHOUT degenerative spine changes who had measurements at baseline (age 75), at follow-up at 5 years (age 80) and 10 years (age 85)

