

**Impact of incident vertebral deformities on health-related quality of life and functional impairment: a 10.7 years cohort study.**

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## **Abstract**

**Purpose** To examine associations between incident vertebral deformities (VD) and changes in health-related quality of life (HRQoL) and functional ability in older adults over 10.7 years.

**Methods** Participants (n=780) underwent whole-body dual-energy X-ray absorptiometry (DXA) scans at baseline, 2.5, 5.1 and 10.7 years later. VD was defined as  $\geq 20\%$  reduction in anterior height relative to posterior height of vertebrae from T4-L4. An incident VD was defined as new VD at any follow-up visit. Assessment of Quality of Life (AQoL-4D) questionnaire and Health Assessment Questionnaire Disability Index (HAQ-DI) were used to assess HRQoL and functional impairment. Changes in AQoL and HAQ-DI associated with incident VD were analysed using multilevel mixed-effects linear regression. Log binomial regression was used to examine clinically relevant changes and effects of severity and number of VD.

**Results** Incidence of VD was 53% over 10.7 years. In women, incident VD were associated with annual reduction in AQoL utility score ( $\beta = -0.003$ , 95%CI -0.01 - -0.001) and increased risk of clinically significant reduction in HAQ-DI (IRR=1.50, 95%CI 1.02-2.20). Women showed increased risk of functional impairment with mild VD (IRR=1.61, 95%CI 1.05-2.46), but not moderate or severe VD and exhibited a direct relationship between number of incident VD and risk of functional impairment (IRR=1.19 (95%CI 0.77-1.85) for one, IRR=2.08 (95%CI 1.25-3.46) for two and IRR=2.30 (95%CI 1.03-5.11) for  $\geq 3$ VD). No associations were present in men.

**Conclusions** Incident VD are associated with clinically significant functional impairment and worsening HRQoL in older women, but not men. Increasing number of incident VDs were associated with increased risk of functional impairment in women, but not men.

## **Introduction**

Vertebral deformities (VD) are abnormal anatomic changes in the shape of vertebrae that are indicative of 'fracture' but are not always clinically identified [1], and hence, grossly under-diagnosed. They are common (prevalence of 6-39%)[2,3], and are associated with significant back pain, functional impairment [4], mortality [5], loss of height, reduced pulmonary function [6] and gastro-esophageal reflux [7]. Previous research suggests that prevalent VDs are associated with tangible ill effects on aspects of health related quality of life (HRQoL) like functional limitation, disability and immobility [3]. Yet, there is limited information about incident VDs and their association with poor HRQoL.

HRQoL is defined as "the value assigned to life as modified by the impairments, functional states, perceptions, and social opportunities that are influenced by disease, injury, and treatment" [8]. Worsening HRQoL and physical functioning make significant contributions to the morbidity and health-care costs associated with fractures [9]. While osteoporosis and osteoporotic fractures are associated with poor HRQoL [10,11], studies have shown weak associations between conventional densitometric markers and HRQoL outcomes [12,13], suggesting that any association is independent of bone density. Reduced HRQoL and functional status in osteoporosis are primarily related to fractures [14-16,13]. Several studies have reported similar associations with VDs cross-sectionally [17-19]. Few studies, however, have examined longitudinal changes in quality of life associated with incident VDs [7,10]. Since HRQoL is an important aspect of disease experience for patients with osteoporosis [10], it is important to examine changes in quality of life associated with the incidence of VD.

The purpose of this study was to evaluate the impact of incident VD on change in HRQoL. We used the Australian Quality of Life (AQoL 4D) questionnaire and the Health Assessment Questionnaire – Disability Index (HAQ-DI) to assess changes in quality of life and functional impairment over 10 years.

## **Materials and Methods**

### *Participants*

Men and women between ages 50 and 80 years were selected from the electoral roll in Southern Tasmania for the Tasmanian Older Adult Cohort (TasOAC) study in 2002 using sex stratified, simple random sampling. TasOAC is a prospective study aimed at identifying the environmental, genetic, and biochemical factors associated with osteoarthritis and osteoporosis. Participants living in an aged care facility or those with a contraindication to magnetic resonance imaging (MRI) were excluded. Of the 1,099 participants enrolled in 2002, those with data for at least one follow-up visit and complete densitometric, morphometric and anthropometric data were included in this study (N=780). 748 (96%) participants attended the first follow-up after 2.5 years, 643 (82%) the 5-year follow-up and 528 (68%) the 10-year follow-up (Figure 1).

### *Dual X-ray absorptiometry (DXA) and vertebral morphometry*

At each visit, participants underwent whole body DXA scans which were used to obtain bone density measurements using the Hologic Delphi densitometer (Hologic, Waltham, MI USA). Lateral vertebral scans, also obtained from DXA scans, were examined using the Hologic APEX software V2.2 for baseline scans and version 4.0.2 for the follow-up scans. Results are the same regardless of version used [20]. Vertebrae from T4 to L4 were assessed by placing six markers on each vertebra – one on every corner and one in the middle of each endplate (Figure 2). These were stored as co-ordinates to compute vertebral heights (in millimetres). Baseline scans were assessed by one assessor [21], and the follow-up scans were assessed by another assessor (AS). 100 randomly selected baseline scans were re-marked by AS to establish inter-rater reliability – absolute intra-class correlation (ICC) of 0.79 (95%CI 0.69 to 0.86), which is classified as good [22]. Good intra-rater reliability was also established for follow-up markings (ICC=0.74, 95%CI 0.70 to 0.78). These reliability measures (for intra- and inter-rater reliability) were comparable to existing literature [23]. The presence of vertebral deformity was defined as anterior to posterior height ratio (AH/PH) of  $\leq 0.8$ , indicating

≥20% reduction in anterior height relative to posterior height [24]. New VD at follow-up phases over 10.7 years were defined as incident VD. A deformity was classified as Grade 1 or 'mild' for a reduction in anterior height of 20-25%, Grade 2 or 'moderate' for 25-40% and Grade 3 or 'severe' for ≥40% reduction [25].

#### *Quality of life instruments and measurements*

HRQoL was assessed using two instruments: The Australian quality of life instrument (AQoL-4D) and the Health Assessment Questionnaire Disability Index (HAQ-DI).

AQoL-4D is a questionnaire comprising questions specific to four domains: Independent living, Relationships, Mental Health and Senses. Presence of pain is assessed as a part of the mental health domain. Each domain has three questions with four response levels (1-4). Psychometric scores are derived by adding the response scores, while utility scores are computed from weighted responses and provide an overall index of health state utility. The total psychometric score for each domain ranged from 1-12 and the overall score ranged from 12-48. Higher psychometric score indicates worse quality of life. AQoL is a valid [26] and reliable (Cronbach  $\alpha=0.81$ ) measure of HRQoL [27]. Used as a utility score, scores range from 0-1 where 0 indicates death and 1 indicates perfect health status. It is possible to have negative utility scores which indicate health state "worse than death". Both psychometric and utility scores were computed using standard AQOL algorithm [28].

The HAQ-DI assesses functional status and ability to perform activities of daily living (ADLs) [29], which form a crucial domain of HRQoL in musculoskeletal disease [30]. It encompasses 20 specific activities over 41 items that review patient difficulty for eight main categories: dressing and grooming, arising, eating, walking, hygiene, reaching, gripping, and errands. Of the 41 questions, 20 pertain to specific ADLs (response levels 0-3), 13 assess the use of special assistive devices (response yes/no), and 8 questions ask about help required to perform specific tasks (yes/no). Psychometric scores were obtained by simply adding response scores of questions about ADLs without considering questions about help and devices used. These responses are utilised to generate a disability score

ranging from 0-3 in increments of 0.125, with higher scores indicating worse functionality. This was done by increasing the category score by 1 if the participant used special devices; score remained unchanged if the category score was already 2 or 3. All category scores were summed to obtain a total score, which was divided by the number of categories. The answer was rounded to the nearest value divisible by 0.125 to obtain a disability index [30].

#### *Co-morbidities and other measures*

Information on diagnosed medical conditions was obtained from baseline questionnaire.

Participants were asked to select any of the 10 conditions in the questionnaire: diabetes, heart attack, hypertension, thrombosis, asthma, bronchitis, osteoporosis, hyper- and hypothyroidism, rheumatoid arthritis, or “other illnesses”. Heart attack included history of coronary artery disease and myocardial infarction. Weight was measured to the nearest 0.1kg using a single pair of calibrated electronic scales (Seca Delta Model 707) and a stadiometer was used to measure height to the nearest 0.1cm. Both these measures were used to compute Body Mass Index (BMI) [ $\text{weight}(\text{kg})/\text{height}(\text{m})^2$ ]. Physical activity was measured as steps per day using pedometer (Omron HJ-003 and HJ-102; Omron Healthcare, Kyoto, Japan) [31]. Information about cigarette smoking status and presence of backpain was obtained from baseline questionnaire.

#### *Statistical analysis*

Baseline characteristics were analysed using t-tests and chi-square tests to compare means and proportions, respectively. Multilevel mixed-effects linear regression was used to assess change in quality of life scores over time. The mental health domain comprised of questions pertaining to how participants generally feel, their quality of sleep and severity of pain. We ~~did~~ conducted a sensitivity analysis for this domain by omitting the score for the ‘pain’ question and recalculating the domain score to identify effect of pain. This domain (without pain) was also analysed using multilevel mixed-effects linear regression. The latest available data was used to calculate change in HRQoL scores to maximise sample size. Positive value of all change scores indicated worsened quality of life, except

the AqoL utility score, where a negative value indicated worsened quality of life. Minimal clinically important difference (MCID) values for AqoL utility (0.06) [27] and HAQ-DI (0.15) [29] were used to dichotomise participants with and without clinically significant change in QoL based on respective instruments. Log binomial regression was used for dichotomised HRQoL measures – binary variables that identified participants with and without clinically meaningful reductions. Modified Poisson models were used to examine effect of severity and number of incident VDs (both categorical outcomes) on clinically important reductions in HRQoL measures. All multivariable analyses were inverse probability weighted to account for participants lost to follow-up. Stata 15.1 was used to perform all statistical analyses.

## **Results**

### *Baseline characteristics*

Table 1 displays the characteristics of participants, stratified by median total psychometric AqoL score at baseline. Participants with poorer QoL walked fewer steps per day as compared to those with better QoL and had a higher prevalence of back pain, diabetes, and thrombotic conditions.

There were no significant differences in age, BMI, and bone density between the two groups.

Prevalence of VD at baseline was similar among both groups and there was no significant difference in the proportion of participants who had  $\geq 1$  incident VD over 10.7 years.

Of the 780 participants at baseline, 335 (43%) had an existing VD and 416 (53%) had at least one incident VD over 10.7 years of follow-up. The number of incident VDs ranged from 1-7 and there were total 662 incident VDs among these participants. 60% (n=249) of these participants had one, 26% (n=107) had two and 14% (n=60) had  $\geq 3$  VDs over 10.7 years. The prevalence of mild incident VD was 61% (n=254), moderate VD was 33% (n=138) and that of severe VD was 6% (n=24).

### *Incident vertebral deformities and quality of life*

In the whole population, incident VDs were associated with increased (worse) AqoL scores (Table 2). Incident VD were associated with worsening of both total psychometric AqoL score and utility score. Incident VD was also associated with worsening scores in the independent living domain. Due to significant sex interaction in these models, we ran sex-stratified analyses to assess sex differences in effects of incident VDs on AqoL scores. Associations between incident VD and psychometric AqoL measures were present largely in females and absent in males. Females showed significant deterioration in independent living and mental health domains, as well as total AqoL score and Utility score. Males exhibited deteriorated social relationship score alone. As pain is one of the three questions in the Mental health domain, we conducted sensitivity analyses for mental health score, omitting pain. Mental health (without pain) was not associated with incident VD in the total population, males or females. Modified Poisson regression for dichotomised participants based on AqoL utility scores did not show any association between clinically important reductions in HRQoL and incident VD in the whole population or either sex.

### *Incident vertebral deformities and functional impairment*

Multivariable analyses for functional impairment measures (HAQ-DI) did not show any significant association in the whole population (Table 3). An established MCID of 0.15 in HAQ-DI was used to identify participants with clinically important reductions in HRQoL [29]. Modified Poisson models for dichotomised participants based on HAQ-DI score showed an increased risk of clinically meaningful functional impairment associated with incident VD at  $p < 0.10$  in the whole population. Similar analyses by sex showed that females had a 1.5-fold higher risk of clinically important functional impairment associated with incident VD, despite similarly having no association with individual domains (Table 3). In males, one subscale was associated with HAQ score (arising), but changes did not reach the threshold for clinical importance.



### *Severity of incident VDs and change in QoL and functional impairment*

In the whole population, severity of incident VD was not associated with clinically important changes in AQoL or HAQ-DI scores. However, we observed increased risk of clinically important functional impairment in women with mild incident VD (IRR 1.61, 95%CI 1.05 to 2.16) but not moderate to severe incident VD (IRR 1.36, 95%CI 0.83 to 2.21). Among men, increasing severity of incident VD did not reach statistical significance (IRR 1.07, 95%CI 0.58 to 1.97 for mild VD and IRR 1.63, 95%CI 0.87 to 3.03 for moderate to severe VD). Severity of incident VDs was not associated with clinically meaningful changes in AQoL scores in either sex (Figure 3).

### *Number of incident VDs and change in QoL and functional impairment*

Similarly, we observed no association between number of incident VDs and clinically important changes in AQoL scores. We did observe associations between two and  $\geq 3$  incident VD and functional impairment in the whole population (IRR 1.90, 95%CI 1.28 – 2.83) and (IRR 1.57, 95%CI 0.84 – 2.94) respectively, but confidence intervals for  $\geq 3$  VD embraced unity. These effect sizes were higher than that for one VD (IRR 1.14, 95%CI 0.79 – 1.67). Analysis by sex showed a dose response relationship between number of incident VD and functional impairment in females (IRR 1.19, 95%CI 0.77 – 1.86 for one; IRR 2.08, 95%CI 1.25 – 3.47 for two; IRR 2.30, 95%CI 1.03 – 5.11 for  $\geq 3$  incident VD). There were no significant associations between number of incident VDs and functional impairment in males.

### **Discussion**

This 10.7-year prospective study found that incident vertebral deformities were associated with significant worsening of HRQoL and clinically important functional impairment in older women, but not men. Increasing number of VD were associated with higher risk of clinically meaningful functional impairment among women. Neither severity nor number of incident VD were associated with significant reductions in overall quality of life. To our knowledge, this is the longest follow-up study examining effects of incident VD on HRQoL and functional impairment in men and women.

Our findings ~~are~~were not only consistent with literature reporting that incident VDs were associated with clinically significant worsening of quality of life and physical functioning in post-menopausal women [7,19], but also with those reporting associations with clinically diagnosed vertebral fractures [7,3,19] and prevalent VDs [16,11] in women. One study examining diagnosed vertebral fractures reported that spine fractures were associated with clinically meaningful deterioration in overall utility, mobility, ambulation and self-care over 5 years in women, but not men [10]. Findings of the present study are consistent with this report. Based on an MCID of 0.06 for AqoL utility score [27] , the annual change in utility score may be extrapolated to determine time to clinically important deterioration in HRQoL. Women in our population may be expected to have clinically important deterioration in overall health utility in fifteen years.

Incident VDs were associated with deteriorated 'mental health' domain measure among females in our sample. The 'mental health' domain in AqoL encompasses aspects like quality of sleep, general health perception and presence of pain. Several studies have reported worsening back pain and poor health perception with incident VD [7,10,19], but sensitivity analyses for pain in our study did not provide adequate evidence to attribute worsening domain score to pain. This was consistent with the finding of Abourazzak et al, who reported progressive declines in all domains of HRQoL except pain associated with VD. No association with pain may be explained the asymptomatic nature of VD, especially older VDs. While males in our study did not show deteriorated AqoL measures, they, interestingly, exhibited declining scores in the 'relationships' domain. While several studies have highlighted associations between clinically diagnosed vertebral fractures and psychosocial effects such as social isolation [16,32], there are conflicting reports of such association with VDs. One study reported higher proportion of participants with significant social dysfunction[7], another study found no association between incident VDs and social interaction in post-menopausal women [19]. Our finding of no effect of incident VD on social relationships in women is consistent with the latter study, but ours is the first study to report such an association in men. We found no association

between incident VDs and physical senses (vision, hearing, and communication). This was consistent with existing literature [10].

We assessed functional ability primarily using the HAQ-DI, although the 'Independent living' domain of the AQoL addressed the same aspect of HRQoL. Independent living focussed on mobility and help required in household and self-care, while the HAQ-DI addressed ability to carry out specific ADLs. We found that ability to live independently was significantly affected by incident VD, but ability to perform specific ADLs were not. Association between reduced ability to live independently and incident VD was consistent with current literature [11,18,7,19,10] but a lack of association between ability to carry out specific ADLs in our sample was at odds with other studies that utilised specific instruments to address individual ADLs [33,3]. HAQ-DI subscales were not associated with incident VD in our sample with the exception of reduction in ability to rise from chair and getting in and out of bed in men. This was consistent with the study by Burger et al, who reported statistically significant relative risk for impaired rising among men, but not women in the presence of VD [33]. Despite the lack of association in specific ADLs, overall change in disability index beyond MCID was associated with incident VD in women in our population.

Men in this study showed no association between severity of VD and risk of functional impairment while women showed a higher risk of functional impairment with mild VDs than with moderate to severe VDs. Previous studies have reported an association between prevalent VDs and functional impairment [33,3], but these were cross-sectional associations and the functional impairment in their sample could have preceded VDs. Other studies examining effects of incident VDs on functional impairment did not assess severity of incident VDs [7,10,19] and only considered severity of VDs at baseline. Ours is the first study to report associations between severity of incident VDs and functional impairment.

We found that [the](#) number of incident deformities was associated with increased risk of having clinically important functional impairment in women but not clinically significant worsening of QoL.

This is consistent with literature showing increase in number of VDs being associated with reduced ability to perform ADLs [14,34,18,3,19], but at odds with findings that show number of incident VDs associated with progressive decline in quality of life [14,19,34]. Men showed a trend of deteriorating functional ability up to 2 incident VDs but showed no association with  $\geq 3$  VDs whereas women showed a trend of increasing risk. Such gender difference in effect of number of incident VDs has been previously illustrated by Cockerill et al., who reported that location of VD in women with multiple VDs strongly influences self-reported health outcomes, but there is no such association in men [15].

Our study found gender differences in effects of incident VDs on HRQoL and functioning. One study found more prominent effects in men [33], while another reported more pronounced effect on women [10], and a third reported no gender differences [3]. Adjacent VDs in women with multiple VD have been shown to be more strongly associated with poor quality of life [15]. Underlying pathogenesis of VD may also offer some explanation for such sex-differences. Non-osteoporotic VD in younger men due to trauma related to occupational or recreational activities may impact functioning differently than osteoporosis-related VDs [15], and this explains difference in prevalence of VD in our cohort at baseline[21], but does not explain incident deformities in a largely retirement-age cohort. Lastly, men may be loading their spines differently than women in the presence of a VD [33], however associations in our cohort were adjusted for, and independent of prevalent deformities.

Strengths of this study include the longitudinal design and long period of observation (10.7-years), the inclusion of both men and women, and the community-based sample. This means that the results are generalisable to older people living independently in the community. Moreover, this study utilised information on factors like co-morbidities and baseline prevalence of VDs that could impact HRQoL. The use of established MCIDs from widely utilised and validated instruments mean that interpretations of clinically important changes in quality of life can be made. Limitations include

no clinical examination or other clinical information about whether other causes for vertebral deformation (spinal osteoarthritis, scoliosis, etc) were present. Since spinal osteoarthritis is itself associated with VDs [35] and functional impairment [36], these could have contributed in part to the observed associations. These limitations, however, are common to all studies utilising quantitative morphometry to identify vertebral deformation [37]. Moreover, we considered only wedge-type VDs because they are the most common type of VD [38]. This may have misclassified people with other types of VDs, but rates of biconcave and crush VDs without presence of anterior wedging are low (4.7%) [21] and hence, is unlikely to have affected our results. Approximately 46% of participants who began the study dropped out over 10.7 years, but all analyses were inverse probability weighted to account for missing data.

In conclusion, incident VDs are associated with clinically significant functional impairment and reduction in HRQoL in older women, but not men. Increasing number of incident VDs were associated with significant functional impairment in women, not men.

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Table 1: Baseline characteristics of participants stratified by median total Assessment of Quality of Life (AQoL-4D) score.

	QoL better than median (n=393)	QoL at median or worse (n=387)
Age ( <i>years</i> )	62.3 + 6.9	62.2 + 7.1
Female sex (%)	49	52
BMI (kg/m <sup>2</sup> )	27.6 + 4.2	27.5 + 4.6
Hip BMD (g/cm <sup>2</sup> )	0.98 + 0.15	0.97 + 0.15
Spine BMD (g/cm <sup>2</sup> )	1.02 + 0.17	1.01 + 0.17
Smokers (%)	10	11
Back pain (%)	<b>48</b>	<b>74</b>
Steps per day	<b>9183 + 3313</b>	<b>8571 + 3256</b>
Hypertension (%)	34	40
Diabetes (%)	<b>3</b>	<b>8</b>
Thrombosis (%)	<b>5</b>	<b>10</b>
Respiratory illness (%)	12	14
Prevalent wedge deformity (%)	43	43
Incident VDs over 10.7 years (%)	54	52

Boldface denotes statistical significance at p<0.05.

Table 2: Association between incident VD and Assessment of Quality of Life (AQoL-4D) scores.

	Overall population (n=780)	Females (n=391)	Males (n=389)
<i>Independent living</i> <sup>^</sup>	<b>0.014 (0.001 – 0.03)</b>	<b>0.024 (0.01 – 0.05)</b>	0.001 (-0.02 – 0.02)
<i>Relationship</i> <sup>^</sup>	0.01 (-0.01 – 0.02)	-0.005 (-0.02 – 0.01)	<b>0.02 (0.001 – 0.05)</b>
<i>Senses</i> <sup>^</sup>	-0.001 (-0.02 – 0.01)	0.01 (-0.012 – 0.02)	-0.01 (-0.03 – 0.01)
<i>Mental health</i> <sup>^</sup>	0.02 (-0.004 – 0.04)	<b>0.03 (0.01 – 0.07)</b>	0.01 (-0.03 – 0.03)
<i>Mental Health (without pain)</i> <sup>^</sup>	0.013 (-0.005 – 0.031)	0.02 (-0.003 – 0.05)	0.01 (-0.02 – 0.03)
<i>Total score</i> <sup>^</sup>	<b>0.04 (0.001 – 0.08)</b>	<b>0.054 (0.004 – 0.10)</b>	0.02 (-0.04 – 0.08)
<i>Utility score</i> <sup>^</sup>	<b>-0.003 (-0.01 – -0.001)</b>	<b>-0.004 (-0.01 – -0.002)</b>	-0.001 (-0.004 – 0.002)
<i>Dichotomised AQoL</i> <sup>#</sup>	0.87 (0.68 – 1.12)	0.78 (0.52 – 1.16)	0.94 (0.68 – 1.30)

<sup>^</sup> Multilevel mixed-effect linear regression.  $\beta$ -coefficient (95%CI) indicate annual change.

<sup>#</sup> Inverse probability weighted modified poisson regression. IRR (95%CI) reported.

Models adjusted for age, BMI, and sex (where appropriate), co-morbidities (hypertension, diabetes, thrombosis, respiratory illness) and prevalence of VD at baseline and time spent in the study.

Total score refers to the total of all domain scores.

Dichotomised AQoL refers to participants with an increase of at least 0.06 in AQoL utility score indicating clinically important change.

Boldface denotes statistical significance.

Table 3: Association between incident VD and Health Assessment Questionnaire-Disability Index (HAQ-DI) scores.

	Overall population (n=780)	Females (n=391)	Males (n=389)
<i>Dressing and Grooming</i> <sup>^</sup>	0.001 (-0.01 – 0.01)	0.004 (-0.01 – 0.01)	-0.001 (-0.01 – 0.01)
<i>Arising</i> <sup>^</sup>	0.004 (-0.01 – 0.01)	-0.01 (-0.02 – 0.01)	<b>0.02 (0.001 – 0.03)</b>
<i>Eating</i> <sup>^</sup>	-0.001 (-0.01 – 0.01)	0.003 (-0.01 – 0.02)	-0.01 (-0.01 – 0.003)
<i>Walking</i> <sup>^</sup>	0.003 (-0.01 – 0.01)	0.001 (-0.01 – 0.02)	0.003 (-0.01 – 0.01)
<i>Hygiene</i> <sup>^</sup>	0.002 (-0.01 – 0.01)	0.006 (-0.01 – 0.03)	-0.01 (-0.02 – 0.01)
<i>Reach</i> <sup>^</sup>	0.01 (-0.001 – 0.01)	0.005 (-0.01 – 0.02)	0.009 (-0.03 – 0.02)
<i>Grip</i> <sup>^</sup>	0.002 (-0.01 – 0.01)	0.008 (-0.01 – 0.03)	-0.004 (-0.04 – 0.003)
<i>Activities</i> <sup>^</sup>	0.001 (-0.01 – 0.01)	-0.008 (-0.03 – 0.02)	0.008 (-0.01 – 0.02)
<i>Total score</i> <sup>^</sup>	0.02 (-0.03 – 0.07)	0.02 (-0.06 – 0.09)	0.02 (-0.05 – 0.08)
<i>HAQ Disability Index (HAQ-DI)</i> <sup>^</sup>	0.003 (-0.001 – 0.08)	0.003 (-0.003 – 0.01)	0.003 (-0.004 – 0.01)
<i>Dichotomised HAQ-DI</i> <sup>#</sup>	1.37 (0.99 – 1.89) *	<b>1.50 (1.02 – 2.20)</b>	1.24 (0.74 – 2.09)

<sup>^</sup> Multilevel mixed-effect linear regression.  $\beta$ -coefficient (95%CI) indicate annual change.

<sup>#</sup> Inverse probability weighted modified poisson regression. IRR (95%CI) reported.

Models adjusted for age, BMI, and sex (where appropriate), co-morbidities (hypertension, diabetes, thrombosis, respiratory illness), back pain, baseline physical activity and prevalence of VD at baseline and time spent in the study.

Dichotomised HAQ-DI refers to participants with an increase of at least 0.15 in HAQ disability index.

Boldface denotes statistical significance. \* denotes significance at  $p < 0.10$ .

Figure 1: Study flowchart

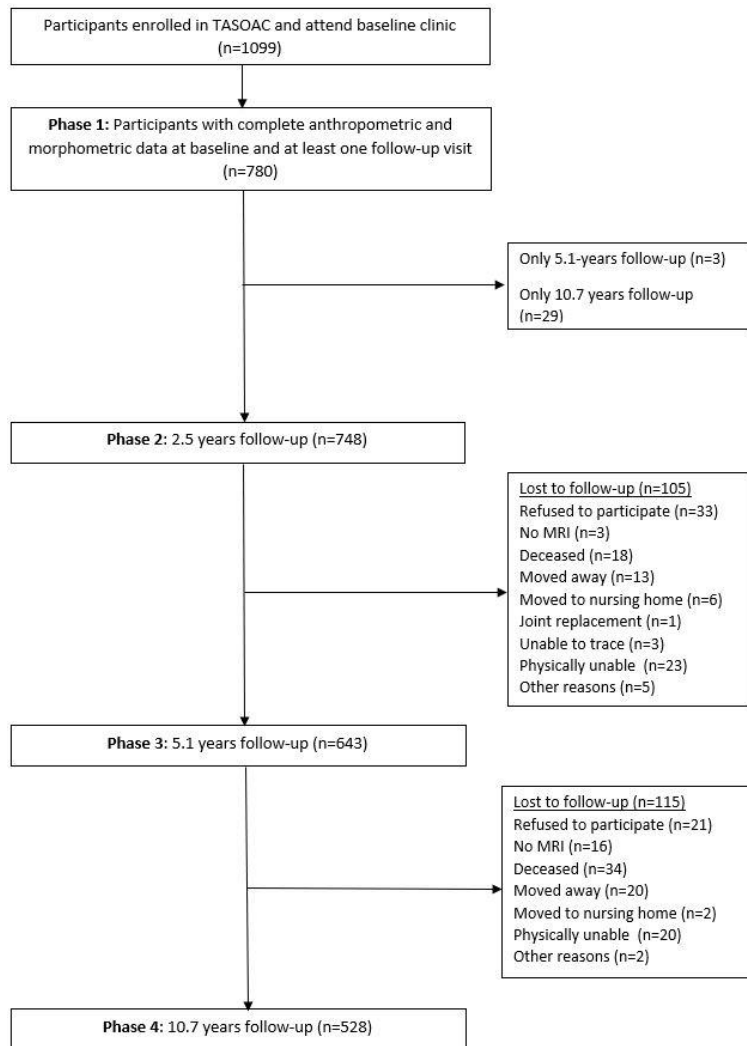
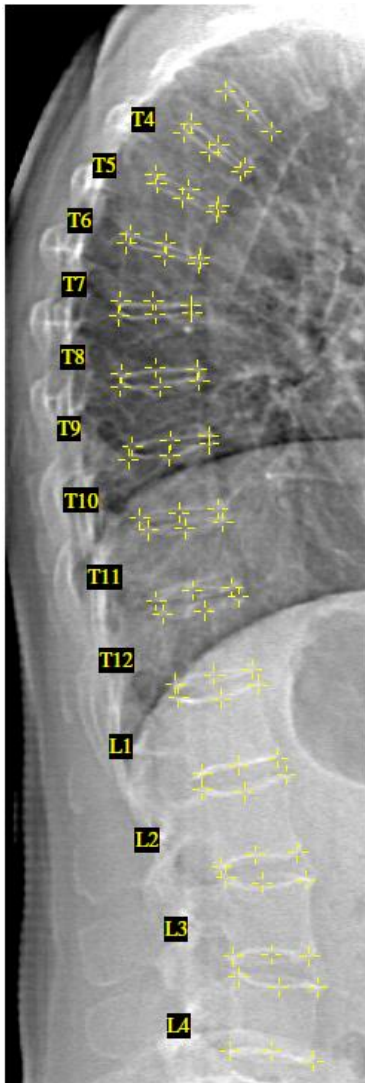


Figure 2: Example of Quantitative Morphometry on lateral vertebral scan



**Vertebral Assessment:**

Label	Height (mm)		
	Post	Mid	Ant
T4	17.9	17.0	16.9
	Normal		
T5	19.3	16.5	15.6
	Normal		
T6	21.8	18.5	18.5
	Normal		
T7	21.9	17.4	16.1
	Wedge (Moderate)		
T8	21.7	20.3	21.7
	Normal		
T9	22.9	20.6	21.3
	Normal		
T10	22.9	21.7	24.7
	Normal		
T11	26.9	23.4	24.9
	Normal		
T12	26.6	24.8	28.0
	Normal		
L1	30.1	26.2	28.6
	Normal		
L2	29.8	24.3	29.4
	Normal		
L3	30.1	27.3	29.0
	Normal		
L4	28.1	24.3	27.9
	Normal		
Std Dev	1.0	1.0	1.0

**Physician's Comment:**

Figure 3: Association between severity of incident VD and clinically significant reductions in HRQoL measures.

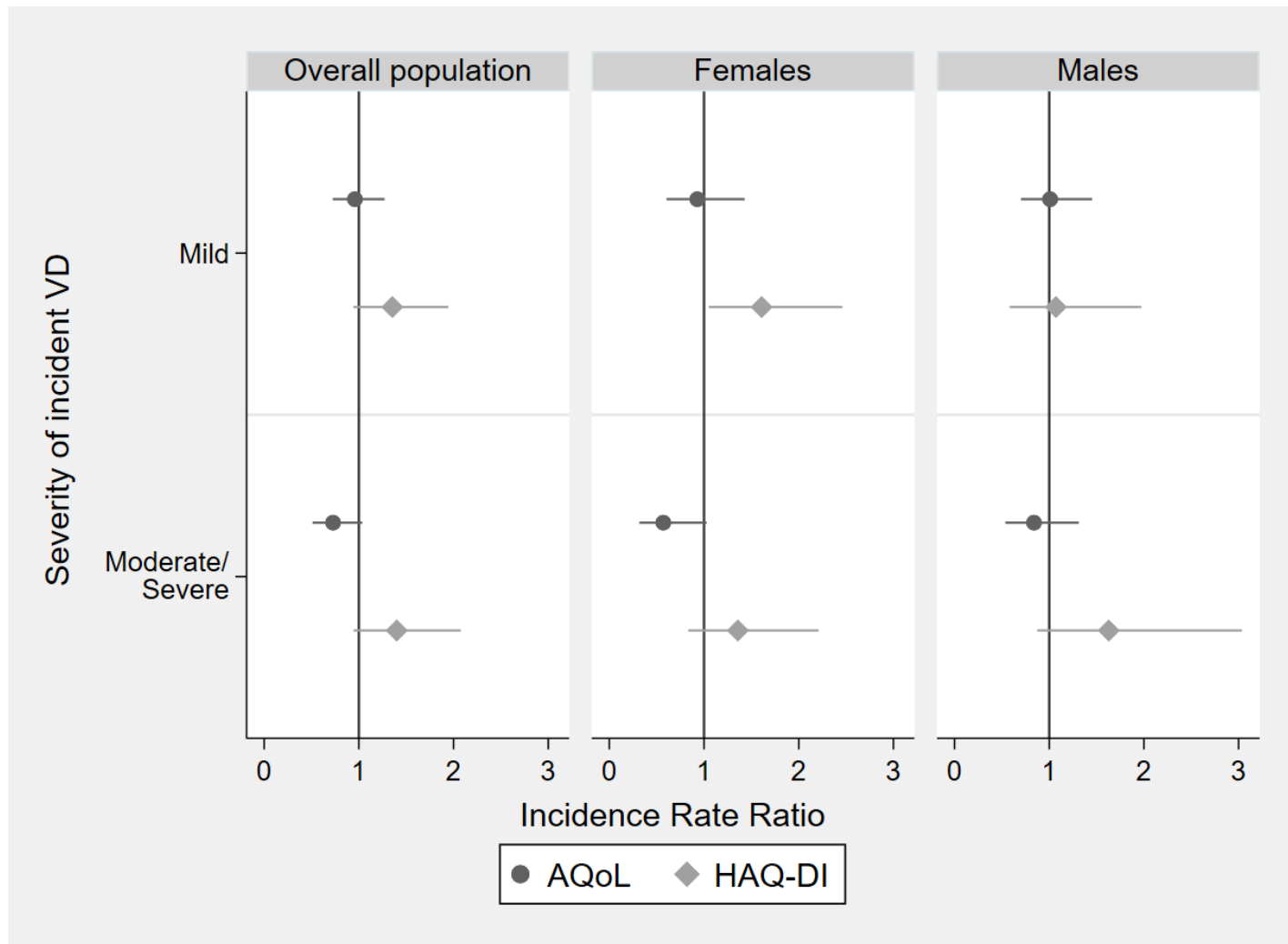


Figure 4: Association between number of incident VDs and clinically significant reductions in HRQoL measures.

