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# High prevalence of vertebral fractures and low trabecular bone score in patients with fragility fractures: A cross-sectional sub-study of NoFRACT

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ABSTRACT

*Purpose:* Norway has among the highest incidence rates of fractures in the world. Vertebral fracture assessment (VFA) and trabecular bone score (TBS) provide information about fracture risk, but their importance have not been studied in Norwegian patients with fragility fractures. The objectives of this study were to examine the clinical characteristics of a cohort of women and men with fragility fractures, their prevalence of vertebral fractures using VFA and prevalence of low TBS, and explore the differences between the sexes and patients with and without vertebral fractures.

*Methods:* This cross-sectional sub-study of the Norwegian Capture the Fracture Initiative (NoFRACT) included 839 patients with fragility fractures. Of these, 804 patients had bone mineral density (BMD) of the total hip, femoral neck and/or spine assessed using dual energy x-ray absorptiometry, 679 underwent concomitant VFA, 771 had TBS calculated and 696 responded to a questionnaire.

*Results:* Mean age was 65.8 (SD 8.8) years and 80.5% were women. VFA revealed vertebral fractures in 34.8% of the patients and 34.0% had low TBS ($\leq$ 1.23), with no differences between the sexes. In all patients with valid measures of both VFA and TBS, 53.8% had either vertebral fractures, low TBS, or both. In the patients with osteopenia at the femoral neck, 53.6% had either vertebral fractures, low TBS, or both. Femoral neck BMD T-score $\leq -2.5$ was found in 13.8% of all patients, whereas the corresponding figure was 27.4% using the skeletal site with lowest T-score. Women exhibited lower BMD at all sites and lower TBS than men (1.27 vs. 1.29), (all $p < 0.05$). Patients with prevalent vertebral fractures were older (69.4 vs. 64.0 years), exhibited lower BMD at all sites and lower TBS (1.25 vs.1.29) than those without vertebral fractures (all $p < 0.05$). Before assessment, 8.2% were taking anti-osteoporotic drugs (AOD), and after assessment, the prescription rate increased to 56.2%.

*Conclusions:* More than half of the patients with fragility fractures had vertebral fractures, low TBS or both. The

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prescription of AOD increased seven fold from before assessment to after assessment, emphasizing the importance of risk assessment after a fragility fracture.

## 1. Introduction

Norway has among the highest rates of hip and forearm fractures in the world [1,2] and the highest prevalence of vertebral fractures in Europe [3]. Mortality is high, especially following hip and vertebral fractures [4,5], as is morbidity, with considerable impact on quality of life and high health economic costs [6]. Still, secondary fracture prevention in Norway is suboptimal. After a hip fracture, only 15% of women and 4% of men received treatment with anti-osteoporotic drugs (AOD) [7]. To meet this challenge, the Norwegian Capture the Fracture Initiative (NoFRACT) was established to improve secondary fracture prevention by introducing a Fracture Liaison Service (FLS) model of care at seven hospitals in Norway [8].

In risk assessment following a fragility fracture, a broad diagnostic approach is required, because more than half of the patients reveal bone mineral density (BMD) T-scores in the osteopenic range [9,10]. Information on clinical risk factors is important and additional information on bone strength is desirable to make correct treatment decisions. Vertebral fracture assessment (VFA) and Trabecular bone score (TBS) calculations are easily accessible approaches when using dual energy x-ray absorptiometry (DXA). VFA provides information on number and grade of compression of fractured vertebrae, which is related to future fracture risk [11]. TBS is a textural index of trabecular bone structure obtained from anterior-posterior DXA images of the lumbar spine that predicts fractures independently of BMD in women [12–14] and men [15]. TBS has been reported to add value beyond BMD for identification of vertebral fractures in the non-osteoporotic range [16,17]. Studies on VFA and TBS in Norwegian patients with fragility fractures are, however, lacking.

The aims of this study were to i) examine the clinical characteristics of a cohort of Norwegian women and men with fragility fractures, along with their prevalence of vertebral fractures using VFA and prevalence of low TBS, and ii) explore the differences in BMD T-score and TBS between sexes and between patients with and without prevalent vertebral fractures.

## 2. Materials and methods

### 2.1. Study subjects

NoFRACT is an ongoing multicenter study in the orthopedic departments at 7 hospitals in Norway and 23,578 patients were enrolled by Jan 2018 [8]. The objectives are to improve secondary fracture prevention by introducing a standardized intervention program consisting of an FLS model of care for identification, assessment and treatment of osteoporosis in patients with fragility fractures. NoFRACT will investigate the effect of this intervention on the rate of subsequent fractures. All women and men 50 years and older with a recently diagnosed fragility fracture are eligible to the intervention. Those with fractures of fingers, toes, skull and face are ineligible. The coordinating nurse identifies patients based on ICD-10 codes and eligibility criteria, and provides information on the project either in person or in a letter to in- and outpatients, and information on lifestyle advice, sufficient intake of calcium and vitamin D through diet or supplementation and fall prevention. Blood samples are obtained to rule out common causes for secondary osteoporosis. Patients are individually evaluated and treated according to comorbidities and preferences. AOD (mainly alendronate or zoledronic acid) are offered to patients with hip fracture, vertebral fracture or 2 or more fragility fractures regardless of BMD T-score or 10-year probability of major osteoporotic fracture calculated using the Fracture Risk Assessment Tool (FRAX). Patients with their first fragility fracture are offered DXA for assessment of BMD T-score of both hips and spine, and/or FRAX score calculation. Treatment is offered to those with a BMD T-score $\leq -1.5$ or FRAX score $\geq 20\%$.

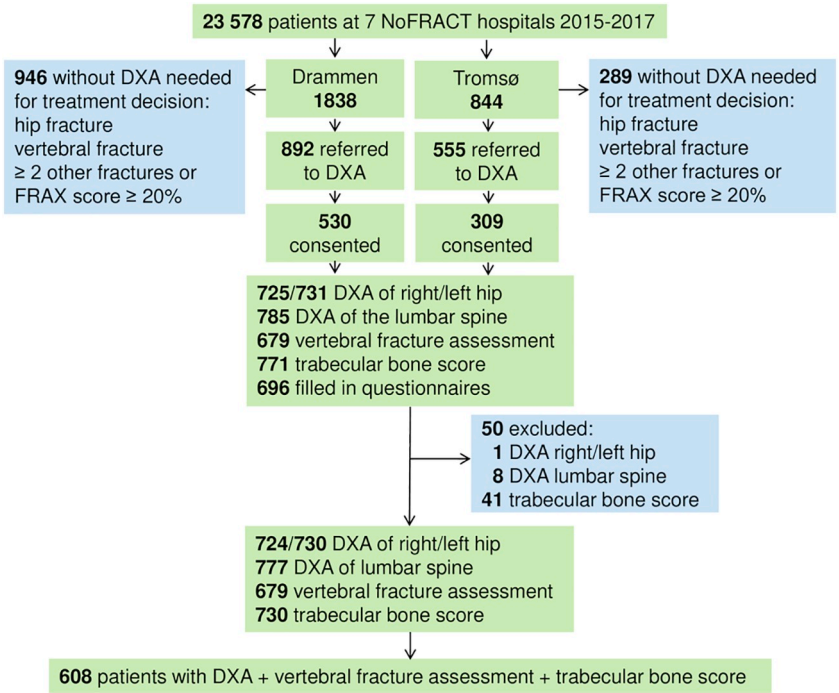


**Fig. 1.** Patients in the Norwegian Capture the Fracture Initiative (NoFRACT) sub-study.
DXA, dual energy x-ray absorptiometry; FRAX, 10-year probability of major osteoporotic fracture calculated using the Fracture Risk Assessment Tool (FRAX).

This consent based sub-study (NoFRACTsub: NCT02608801) of NoFRACT (NoFRACT: NCT02536898) is ongoing at 2 of the 7 hospitals (Fig. 1). Patients were recruited among those who were referred to DXA at the University Hospital of North Norway (UNN), Tromsø from 1 Oct 2015 to 31 Dec 2017 (n = 844) and the Drammen Hospital in south/eastern part of Norway from 1 Jan 2016 to 31 Dec 2017 (n = 1838). At these 2 hospitals, over 90% of the patients with fragility fractures were identified and offered assessment. Patients with communication problems, cognitive dysfunction, or short life expectancy, were not eligible to the sub-study. Some patients were not included due to lack of time or interest, or difficulties with follow-up. Although DXA was not needed for treatment decision for those with hip fracture, vertebral fracture or multiple fractures, we performed DXA in as many as possible, because baseline values are useful during follow-up.

Of 839 patients (309 in Tromsø and 530 in Drammen), 696 completed a questionnaire. Of 725/731 patients who had a DXA scan of the right/left hip, one patient was excluded due to poor imaging quality. Of 785 patients who had an anteroposterior DXA scan of the lumbar spine, 8 patients were excluded due to anatomical aberrations, degenerative or postoperative changes in three or more vertebrae. VFA was performed in 679 patients. Of 771 patients with TBS calculated, 26 were excluded due to body mass index (BMI) > 37 kg/m$^2$ and 15 were excluded due to three or more abnormal lumbar vertebrae. Hence, 724/730 patients with DXA scans of the right/left hip, 777 with DXA of the lumbar spine, 679 with VFA and 730 with TBS calculated were included in the analyses. The proportion of vertebrae that could not be assessed due to low imaging quality was 8.4%, mainly in the upper thoracic region (T4–6). A total of 608 patients had both DXA and VFA performed and also TBS calculated. All patients in this sub-study provided written informed consent. The study was approved by The Regional Committee for Medical and Health Research Ethics (REK 2014/2260) and was conducted in accordance with the World Medical Association Declaration of Helsinki.

**Table 1**
Characteristics of all 839 patients with fragility fracture and stratified by sex.

| | n | All | Women | Men |
|---|---|---|---|---|
| n (%) | 839 | 839 | 675 (80.5) | 164 (19.5)[c] |
| Age (years) | 839 | 65.8 ± 8.8 | 65.6 ± 8.7 | 66.7 ± 9.2 |
| Caucasian, n (%) | 839 | 815 (97.0) | 655 (96.9) | 160 (97.6) |
| Height (cm) | 784 | 167.1 ± 8.2 | 164.6 ± 6.2 | 177.7 ± 6.9[c] |
| Weight (kg) | 784 | 75.0 ± 14.8 | 72.2 ± 13.3 | 86.9 ± 15.4[c] |
| Body mass index (kg/m$^{2)}$ | 784 | 26.8 ± 4.6 | 26.7 ± 4.6 | 27.4 ± 4.1 |
| Index fracture | 839 | | | |
| Hip, n (%) | | 73 (8.7) | 49 (7.3) | 24 (14.6)[b] |
| Forearm, n (%) | | 309 (36.8) | 274 (40.6) | 35 (21.3)[b] |
| Proximal humerus, n (%) | | 105 (12.5) | 90 (13.3) | 15 (9.2) |
| Vertebral, n (%) | | 50 (6.0) | 40 (5.9) | 10 (6.1) |
| Ankle, n (%) | | 148 (17.6) | 110 (16.3) | 38 (23.2) |
| Other sites, n (%) | | 154 (18.4) | 112 (16.6) | 42 (25.6)[a] |
| Fractures after age of 50 years | 639 | | | |
| 1, n (%) | | 381 (59.6) | 302 (57.6) | 79 (68.7)[a] |
| 2, n (%) | | 160 (25.0) | 134 (25.5) | 26 (22.6) |
| ≥3, n (%) | | 98 (15.4) | 88 (16.9) | 10 (8.7)[a] |
| Fractures before index fracture, n (%) | | 258 (40.4) | 222 (42.4) | 36 (31.3)[a] |
| Prevalent vertebral fracture[d], n (%) | 679 | 236 (34.8) | 190 (34.6) | 46 (35.7) |
| Trabecular Bone Score L1-L4 | 730 | 1.27 ± 0.11 | 1.27 ± 0.10 | 1.29 ± 0.12[a] |
| ≥1.31, n (%) | | 274 (37.5) | 215 (36.4) | 59 (42.1) |
| 1.23–1.31, n (%) | | 208 (28.5) | 169 (28.7) | 39 (27.9) |
| ≤1.23, n (%) | | 248 (34.0) | 206 (34.9) | 42 (30.0) |
| Femoral neck BMD (g/cm$^2$) | 730 | 0.816 ± 0.121 | 0.805 ± 0.116 | 0.866 ± 0.130[c] |
| Femoral neck T-score | | −1.6 ± 0.9 | −1.7 ± 0.8 | −1.2 ± 0.9[c] |
| Normal, n (%) | | 155 (21.2) | 103 (17.3) | 52 (38.5)[c] |
| Osteopenia, n (%) | | 475 (65.0) | 404 (67.8) | 71 (52.6)[b] |
| Osteoporosis, n (%) | | 101 (13.8) | 89 (14.9) | 12 (8.9) |
| Total hip, BMD (g/cm$^2$) | 730 | 0.865 ± 0.134 | 0.849 ± 0.126 | 0.938 ± 0.144[c] |
| Total hip T-score | | −1.1 ± 1.1 | −1.3 ± 1.0 | −0.5 ± 1.1[c] |
| Lumbar spine BMD (g/cm$^2$) | 777 | 1.058 ± 0.184 | 1.038 ± 0.178 | 1.145 ± 0.179[c] |
| Lumbar spine T-score | | −1.1 ± 1.5 | −1.3 ± 1.4 | −0.4 ± 1.4[c] |
| Lowest T-score of all sites | 799 | −1.9 ± 1.0 | −2.0 ± 1.0 | −1.5 ± 1.0[c] |
| Normal, n (%) | | 120 (15.0) | 76 (11.8) | 44 (28.8)[c] |
| Osteopenia, n (%) | | 460 (57.6) | 372 (57.6) | 88 (57.5) |
| Osteoporosis, n (%) | | 219 (27.4) | 198 (30.6) | 21 (13.7)[b] |
| Supplementation before assessment | | | | |
| Vitamin D, n (%) | 690 | 457 (66.2) | 378 (67.5) | 79 (60.8) |
| Calcium, n (%) | 687 | 146 (21.3) | 129 (23.1) | 17 (13.3)[a] |
| Prescription of AOD | | | | |
| Before assessment, n (%) | 729 | 60 (8.2) | 57 (9.6) | 3 (2.2)[b] |
| New after assessment, n (%) | 737 | 354 (48.0) | 315(52.6) | 39 (28.3)[c] |
| Total after assessment, n (%) | 737 | 414 (56.2) | 372 (62.2) | 42 (30.5)[c] |

Values are mean ± SD or n (%). The variation in total numbers was due to some missing data.
BMD, bone mineral density; AOD, anti-osteoporotic drugs.
[a] $p < 0.05$.
[b] $p < 0.01$.
[c] $p < 0.001$ compared to women.
[d] Prevalent vertebral fracture, included semiquantitative (SQ) score of SQ1, SQ2 and SQ3 fractures.

### 2.2. Variables

The index fractures that led to inclusion were hip fractures (femoral neck, trochanteric and subtrochanteric), forearm fractures, proximal humerus fractures, vertebral fractures (thoracic- or lumbar spine), ankle fractures (one, two or both malleoli), and other fractures. Vertebral fractures that led to inclusion in the study were identified on x-ray, CT or MRI, not using VFA. The prevalent vertebral fractures included only vertebral fractures revealed using VFA.

Information on number and type of fractures after the age of 50, supplementation of calcium and vitamin D and current use of AOD was collected through a questionnaire. Information on new prescriptions of AOD after assessment was obtained from medical records.

Height and weight were measured, and BMI was calculated as weight (kg) per square meter height. BMD was measured at femoral neck and total hip at both sides and lumbar spine (L1-L4) using DXA (GE Lunar, Prodigy Pro, Madison, WI, USA) in Tromsø and iDXA (GE Lunar, Pro, Madison, WI, USA) in Drammen. Daily phantom Quality Assurance (QA) of the DXA equipment was performed. Fractured lumbar vertebrae were excluded. Left hip was used in the calculations of BMD T-score of femoral neck and total hip. Osteoporosis was defined as femoral neck BMD T-score $\leq -2.5$, and osteopenia as a femoral neck BMD T-score between $\leq -1.0$ and $-2.5$ according to the World Health Organization (WHO) DXA-criteria [18], using the Third National Health and Nutrition Examination Survey reference data [19]. The proportion of patients with osteoporosis and osteopenia at the site with the lowest T-score (femoral neck, total hip or lumbar spine), was calculated as recommended by the International Society of Clinical Densitometry (ISCD) [20]. Female reference population was used for men.

Lateral thoracolumbar spine (T4-L4) images were obtained with the patient in a lateral decubitus position with lumbar support and hips flexed 90 degrees. VFA of the fracture severity was performed by an experienced physician (TTB) using the semiquantitative (SQ) vertebral deformity scoring method by Genant [21]. This combines the visual examination of deformation of the vertebral body (height loss of the anterior, middle, posterior or the whole vertebra) and grading of the vertebrae after proportion of height loss. A SQ score of 0 (SQ0) (< 20% height loss) was considered as a normal, non-fractured vertebra, SQ1 (20–25% height loss) as a mild fracture, SQ2 (25–40% height loss) as a moderate fracture, and SQ3 (≥ 40% height loss) as a severe fracture. In addition, the exact SQ grading of height loss of the fractured vertebrae was performed morphometrically within Encore with manually six-point labelling [21]. Deformities identified as Schmorl's or Modic lesions, short vertebral height, extensive degenerative changes with deformation and physiological wedging of vertebrae were not counted as fractures. An experienced ISCD certificated clinical technician (MBS), who was blinded to the initial results, reviewed a random sample of 200 lateral spine images. Spinal deformity index (SDI) was calculated as the sum of the SQ score of all T4-L4 vertebrae; SQ0 = 0 points, SQ1 = 1 point, SQ2 = 2 points and SQ3 = 3 points [22].

TBS was calculated from the DXA scans used for lumbar spine BMD (L1-L4) using TBS iNsight software (Madimaps, Geneva, Switzerland) version 3.0.1. Fractured vertebrae were excluded. The reference population was the European (Medimaps) for both sexes. The TBS values were divided into three groups, as recommended by Medimaps (TBS insight user guide TM-001-02), and based on a meta-analysis of fracture risk assessment as a function of TBS utilizing 14 prospective population-based cohorts of 17,809 women and men. The estimated fracture risk was: high TBS ≥ 1.31 (low fracture risk), TBS between 1.23 and 1.31 (intermediate fracture risk), and low TBS ≤ 1.23 (high fracture risk) [23].

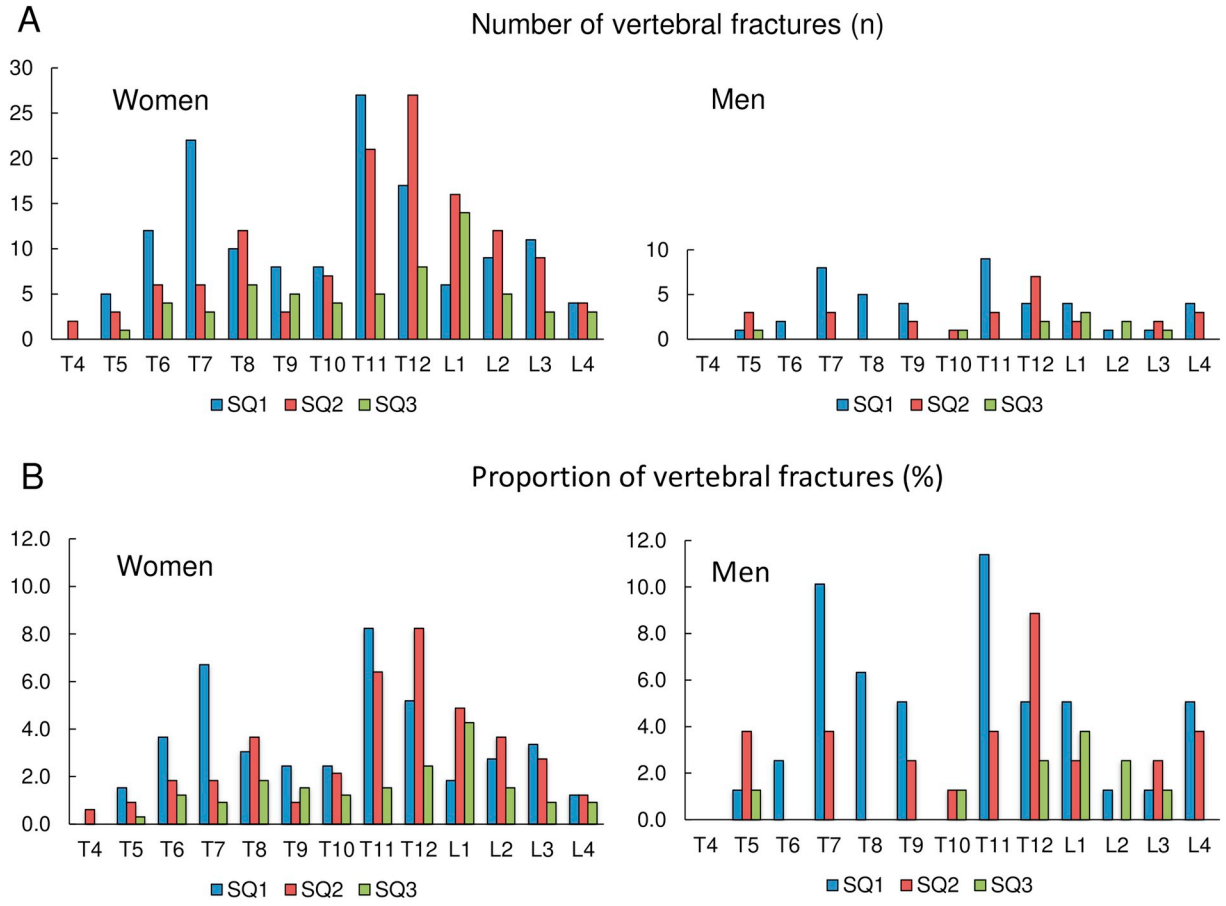


**Fig. 2.** (A) The number and (B) the proportion, site and grade of compression of fractured vertebrae in women and men. Semi-quantitative (SQ) score 1 = mild fracture, SQ2 = moderate fracture, SQ3 = severe fracture, for each vertebra from thoracic and lumbar spine (T4 to L4).

### 2.3. Statistical analyses

Statistical analyses were performed using Stata (Version 15, StataCorp LP, TX, USA). Continuous variables were checked for normality with quantile-quantile (QQ) plots and reported as means with standard deviation (SD). Differences in means between groups were calculated using Student's *t*-test. Categorical variables were reported as number and percentage. Groups were compared using chi square test in samples > 100 and Fisher's exact test in smaller samples. The inter-observer agreement of the assessment of a vertebral fracture (SQ1-SQ3) was calculated using Cohen's Kappa value (κ) with quadratic weighting. The inter-observer agreement by grade of severity of the fractures, within each SQ group, was calculated using Cohen's κ without weighting. Landis and Koch guidelines were followed to interpret the levels of agreement by Cohen's κ: almost perfect agreement (κ > 0.81), substantial agreement (κ = 0.61–0.80), moderate agreement (0.41–0.60), fair agreement (0.21–0.40), slight agreement (0–0.20) and poor agreement (< 0) [24].

## 3. Results

### 3.1. Characteristics of all patients with fractures

In all the 839 patients, the distribution of the index fractures was 8.7% hip, 36.8% forearm, 12.5% proximal humerus, 6.0% vertebral, 17.6% ankle and 18.4% other types (Table 1). A total of 40.4% reported one or more fractures prior to the index fractures. In those with VFA, 34.8% had prevalent vertebral fractures. Mean TBS was 1.27, and 34.0% had low TBS. Osteoporosis was present at the femoral neck in 13.8% of the patients and in 27.4% at the site with lowest BMD T-score. Osteopenia was present at the femoral neck in 65.0% of the patients and in 57.6% at the site with lowest BMD T-score. Only 8.2% used AOD before assessment, 48.0% had a new prescription after assessment, thus a total of 56.2% had AOD prescribed after assessment.

### 3.2. Comparison of women and men

A total of 80.5% were women. Mean age did not differ between the sexes. Women exhibited a smaller proportion of hip fractures than men (7.3% vs. 14.6%, p = 0.005), but a larger proportion of forearm fractures (40.6% vs. 21.3%, p = 0.001). A larger proportion of women than men had sustained fractures before participating in the study (42.4% vs. 31.3%, p = 0.036). A higher number of women than men had vertebral fractures (190 vs. 46), but there was no difference in prevalence of vertebral fractures between sexes (34.6% vs. 35.7%, p = 0.837) (Table 1). Vertebral fractures were most prevalent at T7, T11 and T12 (Fig. 2). Mean TBS of L1-L4 was lower in women than men (1.27 vs. 1.29, p = 0.044), but the proportion with low TBS did not differ between the sexes. Mean BMD T-score of femoral neck, total hip, lumbar spine and lowest T-score of any site was lower in women than in men (all p < 0.001). A higher proportion of women than men had osteoporosis at the site with lowest T-score (30.6% vs. 13.7%, p = 0.008). More women than men had AOD prescribed before assessment (9.6% vs. 2.2%) and after assessment (62.2% vs. 30.5%), (both p < 0.01).

### 3.3. Comparison of patients with and without prevalent vertebral fractures

Patients with vertebral fractures were older (69.4 vs. 64.0 years), shorter (166.2 vs. 167.7 cm) and a larger proportion reported previous fractures compared to those without vertebral fractures (all p < 0.05, Table 2). Patients with vertebral fractures had lower mean TBS (1.25 vs. 1.29) and a larger proportion had low TBS (42.9% vs. 29.1%, both p < 0.001) than those without vertebral fractures. BMD at all sites were lower, and a higher proportion had osteoporosis at the femoral neck (16.9% vs. 9.5%) and at the site with lowest T-score (37.0% vs. 22.7%, all p < 0.05) in those with than without vertebral fractures. A larger proportion of patients with vertebral fractures on VFA had AOD prescribed after assessment (70.0% vs. 47.8%, p < 0.001).

### 3.4. Prevalence of vertebral fractures and low TBS

Of all 608 patients with BMD, VFA and TBS assessed, 53.8% had either vertebral fracture, low TBS, or both (Fig. 3A). Only 13.2% of them had osteoporosis at the femoral neck. Of 394 with osteopenia at the femoral neck, 53.6% had either vertebral fracture, low TBS or both (Fig. 3B).

**Table 2**
Comparison of characteristics in patients with and without vertebral fractures on vertebral fracture assessment.

| | n | With vertebral fracture[d] (n = 236) | Without vertebral fracture (n = 443) |
|---|---|---|---|
| Women, n (%) | 679 | 190 (80.5) | 360 (81.3) |
| Age (years) | 679 | 69.4 ± 7.9 | 64.0 ± 8.4[c] |
| Height (cm) | 663 | 166.2 ± 8.0 | 167.7 ± 8.0[a] |
| Weight (kg) | 663 | 73.5 ± 14.3 | 75.3 ± 15.0 |
| Body mass index (kg/m$^2$) | 663 | 26.5 ± 4.2 | 26.7 ± 4.6 |
| Index fracture | 679 | | |
| Hip, n (%) | | 21 (8.9) | 29 (6.6) |
| Forearm, n (%) | | 73 (30.9) | 197 (44.5)[b] |
| Proximal humerus, n (%) | | 31 (13.1) | 48 (10.8) |
| Vertebral, n (%) | | 34 (14.4) | 5 (1.1)[c] |
| Ankle, n (%) | | 33 (14.0) | 90 (20.3)[a] |
| Other sites, n (%) | | 44 (18.7) | 74 (16.7) |
| Fractures after age of 50 years | 526 | | |
| 1, n (%) | 308 | 80 (43.5) | 228 (66.7)[c] |
| 2, n (%) | 137 | 60 (32.6) | 77 (22.5)[a] |
| ≥3, n (%) | 81 | 44 (23.9) | 37 (10.8)[c] |
| Trabecular Bone Score L1-L4 (SD) | 625 | 1.25 ± 0.10 | 1.29 ± 0.10[c] |
| ≥1.31, n (%) | | 63 (29.7) | 172 (41.6)[b] |
| 1.23–1.31, n (%) | | 58 (27.4) | 121 (29.3) |
| ≤1.23, n (%) | | 91 (42.9) | 120 (29.1)[b] |
| Femoral neck BMD (g/cm$^2$) | 635 | 0.786 ± 0.115 | 0.830 ± 0.116[c] |
| Femoral neck T-score | | −1.8 ± 0.8 | −1.5 ± 0.8[c] |
| Normal, n (%) | | 65 (27.5) | 126 (28.4) |
| Osteopenia, n (%) | | 131 (55.5) | 275 (62.1) |
| Osteoporosis, n (%) | | 40 (16.9) | 42 (9.5)[b] |
| Total hip BMD (g/cm$^2$) | | 0.831 ± 0.135 | 0.881 ± 0.129[c] |
| Total hip T-score | | −1.4 ± 1.1 | −1.0 ± 1.0[c] |
| Lumbar spine BMD (g/cm$^2$) | 656 | 1.023 ± 0.181 | 1.076 ± 0.179[c] |
| Lumbar spine T-score | | −1.4 ± 1.4 | −1.0 ± 1.4[c] |
| Lowest T-score of all sites | 670 | −2.1 ± 1.0 | −1.8 ± 1.0[c] |
| Normal, n (%) | | 23 (10.0) | 72 (16.4)[a] |
| Osteopenia, n (%) | | 122 (53.0) | 268 (60.9) |
| Osteoporosis, n (%) | | 85 (37.0) | 100 (22.7)[c] |
| Supplementation before assessment | | | |
| Vitamin D, n (%) | 559 | 137 (70.6) | 238 (65.2) |
| Calcium, n (%) | 558 | 54 (28.0) | 67 (18.4)[b] |
| Prescription of AOD | | | |
| Before assessment, n (%) | 602 | 19 (9.3) | 24 (6.0) |
| New after assessment, n (%) | 606 | 125 (60.7) | 167 (41.8)[c] |
| Total after assessment, n (%) | | 144 (70.0) | 191 (47.8)[c] |

Values are mean ± SD or n (%). The variation in total numbers was due to some missing data.
BMD, bone mineral density; AOD, anti-osteoporotic drugs.
[a] p < 0.05.
[b] p < 0.01.
[c] p < 0.001 compared to those with vertebral fracture.
[d] Vertebral fracture, included semiquantitative (SQ) score of SQ1, SQ2 and SQ3 fractures.

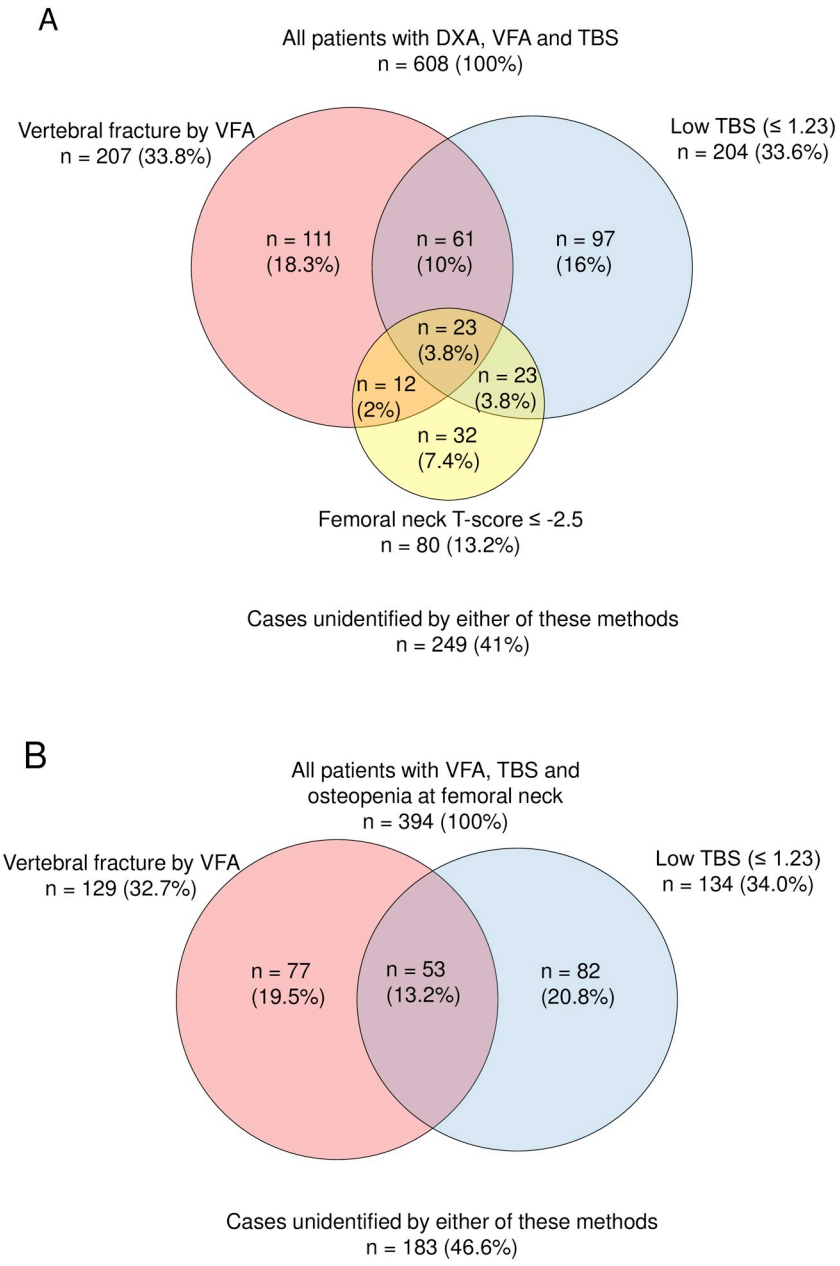


**Fig. 3.** Proportion of (A) all fracture patients with dual energy x-ray absorptiometry (DXA), vertebral fracture assessment (VFA) and trabecular bone score (TBS) (n = 608) who had vertebral fractures, low TBS, or both, and osteoporosis of the femoral neck, and B) fracture patients with osteopenia of the femoral neck (n = 394) with vertebral fracture, low TBS, or both.

Of a total of 8827 imaged vertebrae, 8.4% were excluded because of insufficient image quality (Table 3). Of the evaluable vertebrae 5% had a fracture, 44.7, 37.8 and 17.5% were SQ1, SQ2 and SQ3 fracture, respectively. A total of 34.8% of the patients had a SQ1, SQ2 or SQ3 fracture, while after exclusion of SQ1 fractures, 20.3% had a SQ2 or SQ3 fracture. The prevalence of vertebral fracture or SDI did not differ between sexes. The inter-observer agreement of SQ1-SQ3 fractures was almost perfect with a κ of 0.84 (95% CI: 0.70, 0.98). Inter-observer agreement of SQ1 and SQ2 fractures was moderate with a κ of 0.48 (95% CI: 0.34, 0.61) and 0.55 (95% CI: 0.41, 0.69), respectively. Inter-observer agreement of SQ3 fractures could only be calculated at T8, T9 and L2 due to few observations with a κ of 0.66 (95% CI: 0.53, 0.80).

## 4. Discussion

In this cohort of Norwegian patients with fragility fractures, one in three had vertebral fractures on VFA, one in three had low TBS, and more than half of the patients had either vertebral fractures, low TBS or both. The majority of the patients had osteopenia. A small proportion had osteoporosis at the femoral neck, but this proportion was larger when using the site with lowest BMD T-score. Women had lower BMD and TBS than men. Patients with vertebral fractures were older and had lower BMD and TBS than those without vertebral fractures. The prescription of AOD increased 7 fold, and about half of the patients were prescribed AOD after the assessment, more women than men, and more patients with than without vertebral fractures.

We found higher prevalence of vertebral fractures of 35% compared to a FLS cohort in Scotland where 19–20% of women and men of 50 years and older with non-vertebral fractures had a vertebral fracture [25]. The prevalence of vertebral fracture was 37% in another FLS cohort of women and men in France, which was similar to our findings [16]. However, those patients were older than in our cohort (age of 74

**Table 3**
Vertebral fracture assessment of 8827 vertebrae in 679 patients.

| | Total | Women | Men |
|---|---|---|---|
| Patients, n (%) | 679 | 550 (81.0) | 129 (19.0) |
| Imaged vertebrae, n (%) | 8827 | 7150 | 1677 |
| Excluded vertebrae, n (%) | 742 (8.4) | 600 (8.4) | 142 (8.5) |
| Evaluable vertebrae, n (%) | 8085 (91.6) | 6550 (91.6) | 1535 (91.5) |
| Vertebrae without fracture (SQ0), n (%) | 7678 (95.0) | 6222 (95.0) | 1456 (94.9) |
| Vertebras with fracture | 407 (5.0) | 328 (5.0) | 79 (5.1) |
| SQ1 deformity, n (%) | 182 (44.7) | 139 (42.4) | 43 (54.4) |
| SQ2 deformity, n (%) | 154 (37.8) | 128 (39.0) | 26 (32.9) |
| SQ3 deformity, n (%) | 71 (17.5) | 61 (18.6) | 10 (12.7) |
| Patients with vertebral fracture | | | |
| SQ0, with no fractured vertebra, n (%) | 443 (65.2) | 360 (65.4) | 83 (64.3) |
| SQ1 mild fractures, n (%) | 145 (21.4) | 114 (20.7) | 31 (24.0) |
| SQ2 moderate fractures, n (%) | 113 (16.6) | 93 (16.9) | 20 (15.5) |
| SQ3 severe fractures, n (%) | 49 (7.2) | 39 (7.1) | 10 (7.8) |
| SQ1-SQ3 fractures, n (%) | 236 (34.8) | 190 (34.6) | 46 (35.7) |
| SQ2-SQ3 fractures, n (%) | 138 (20.3) | 115 (20.1) | 23 (17.8) |
| Spinal deformity index | | | |
| 0, n (%) | 443 (65.2) | 360 (65.4) | 83 (64.3) |
| 1, n (%) | 80 (11.8) | 63 (11.5) | 17 (13.2) |
| 2, n (%) | 63 (9.3) | 53 (9.6) | 10 (7.8) |
| 3, n (%) | 38 (5.6) | 31 (5.6) | 7 (5.4) |
| ≥4, n (%) | 55 (8.1) | 43 (7.8) | 12 (9.3) |

SQ, semiquantitative score.
There was no significant difference between the sexes.

vs. 66 years), and a higher proportion had hip fracture (51 vs. 9%) [16]. In population-based studies, the prevalence of vertebral fracture was 19–20% in women and men over 70 years in Norway [26] and 16–19% in the European Vertebral Osteoporosis Study, with the highest rates in the Scandinavian countries [3]. As a prior fracture, non-vertebral and vertebral, increases the risk for a subsequent fracture, fracture cohorts have higher prevalence of vertebral fracture than do the general population as shown in population-based studies, and they have more comorbidity [3,16,25,26]. Although a higher number of women than men had a vertebral fracture we found no difference between sexes in prevalence of vertebral fractures in percentage terms. Despite of the differences in prevalence of vertebral fracture between studies; the prevalence tended to be similar in both sexes within each study.

Identifying those with vertebral fractures is challenging because few of them come to the hospital for an x-ray or other examination [27]. The large proportion of vertebral fractures in this fracture cohort is interesting because vertebral fractures increase the risk of new fracture up to five fold [28,29]. Of all fractured vertebrae in our study, 45% were mild fractures (SQ1) compared to 5% in a general population [26]. One reason for the identification of so many SQ1 fractures may be that the images were obtained using new DXA machines with good image quality, particularly the iDXA. There have been some discussions regarding the SQ1 fractures, whether the majority are not true osteoporotic fractures. However, we carefully checked that physiological wedging and other deformities were not misclassified as a SQ1 fracture. Other methods may capture better the small fractures, even fractures with less height loss than 20%. After we excluded the SQ1 fractures, the prevalence of vertebral fractures (SQ2 and SQ3) was 20% in women and 18% in men, which is similar to the findings in the fracture cohort from Scotland [25].

Another interesting finding was the seven fold increased AOD prescription (from 8% before to 56% after the assessment). This is in agreement with other studies that have introduced FLS where an increase in AOD prescription from 5-19% before assessment to 51–73% after assessment is described [30,31], and that illuminates the treatment gap and importance of assessing patients after a fragility fracture. We used treatment criteria based upon fracture (hip, vertebral, 2 or more fragility fractures), reduction in BMD T-score ≤ −1.5 and/or high FRAX score ≥ 20%, which contributed to the high AOD prescription rate in this study. TBS was not included among the criteria we used for treatment initiation. ISCD does not support use of TBS alone for treatment decision making and recommends that the TBS-adjusted FRAX score should be used. A large proportion had low TBS and vertebral fracture in our fracture cohort as shown in Fig. 3. This may be due to the cross-sectional design of the study that included only patients with fractures and no fracture-free controls.

To our knowledge, this is the first Scandinavian study on patients with fragility fractures described with both VFA and TBS, in addition to clinical risk factors and BMD. However, our study has some limitations. Only patients in need of a DXA examination and who were healthy enough to undergo follow-up were invited to this sub-study. This resulted in a healthy selection bias with a relatively small proportion of hip fractures in this sub-study. Without this bias, we could have had a higher proportion of patients with osteoporosis, vertebral fractures and low TBS. Although we tried to avoid observation bias, the two centers differed at some points. The Prodigy Pro DXA scanner in Tromsø had lower resolution and quality of the lateral spine images, and thus more non-evaluable vertebrae, compared to images obtained using the iDXA Pro in Drammen. However, none of the lateral images had too low quality for VFA, so all images were evaluated. The same experienced physician performed all the VFA, and the inter-observer agreement of the assessment of vertebral fractures was almost perfect. This is in agreement with prior studies that have reported small inter-observer variation [21].

In conclusion, vertebral fractures, low TBS, or both were present in more than half of women and men who were assessed after a fragility fracture. The prescription of AOD increased seven fold from before to after assessment, emphasizing the importance of risk assessment after a fragility fracture.

## Disclosures

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## Authors' roles

TTB, ÅB and EFE have led the design of this sub-study. TTB, ÅB, LBS, and TB designed the questionnaires. TTB, ÅB, CA, and MBS led the patient involvement and data collection. All authors contributed to methodological decisions, data interpretation, conclusions and dissemination. TTB and CB performed the statistical analysis; TTB drafted the initial manuscript and is responsible for the data integrity. All authors contributed to drafting of the manuscript, contributed and agreed on the final manuscript. ÅB is the chief investigator leading protocol development, approvals and dissemination. LN is the guarantor.

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