**Validation of FRAX and the impact of self-reported falls among elderly in a general population: The HUNT Study, Norway**

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**Mini abstract**

FRAX without BMD for hip fracture prediction was validated in a Norwegian population

50-90 years. Fracture risk increased with higher FRAX-score and the observed number of hip fractures agreed well with the predicted number, except for the youngest and oldest men.

Self-reported fall was an independent risk factor for fracture in women.

**Abstract**:

**Purpose:** The primary aim was to validate Fracture Risk Assessment Tool (FRAX) without BMD for hip fracture prediction in a Norwegian population of men and women 50-90 years.

Secondary, to study whether information of falls could improve prediction of fractures in the subgroup aged 70-90 years.

**Methods:** Data were obtained from the third survey of the Nord-Trøndelag Health Study (HUNT3), the Fracture Registry in Nord-Trøndelag and the Norwegian Prescription Database (NorPD), including 15,432 women and 13,585 men.

FRAX hip without BMD was calculated and hip fractures were registered for a median follow-up of 5.2 years.

The number of estimated and observed fractures was assessed, ROC curves with area under the curve (AUC), and Cox-regression analyses. For the group aged 70-90 years, self-reported falls the last year before HUNT3 were included in the Cox-regression model.

**Results:** The risk of fracture increased with higher FRAX-score. When FRAX groups were categorized in 10 years % risk for hip fracture as follows: < 4%; 4-7.9%; 8-11.9%; and ≥ 12%, the Hazard Ratio (HR) for hip fracture between the lowest and highest group was 17.80 (95% CI: 12.86-24.65) among women and 23.40 (13.93-39.30) in men. Observed number of hip fractures agreed quite well with the predicted number, except for the youngest and oldest men. AUC was 0.81 (0.78-0.83) for women and 0.79 (0.76-0.83) for men. Self-reported fall was an independent risk factor for fracture in women (HR 1.64, 1.20-2.24) and among men this was not significant (1.09, 0.65-1.83).

**Conclusions:** FRAX without BMD predicted hip fracture reasonably well. In the age group 70-90 years falls seemed to imply an additional risk among women.

**Background**

Osteoporosis is a major health problem among the elderly, and Norway has the highest incidence of osteoporotic fractures reported [[1-7](#_ENREF_1)]. Osteoporosis is characterized by low bone mineral density (BMD) and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and fracture [[8](#_ENREF_8)]. In USA the hospitalization burden due to osteoporotic fractures among women >55 years is found to be greater than that of stroke, myocardial infarction, and breast cancer [[3](#_ENREF_3)].

Despite the high incidence of osteoporotic fractures in Norway, the use of anti-osteoporotic drugs (AODs) is relatively low compared to other European countries [[9-11](#_ENREF_9)]. Even though BMD is a strong predictor of fractures, the majority of fractures occur among individuals with normal BMD or osteopenia, due to the larger populations at risk [[12](#_ENREF_12)]. It is therefore important to identify those at risk for fracture who are not captured by DXA. Several tools for predicting fractures have been generated. The most commonly used, the Fracture Risk Assessment Tool (FRAX), estimates fracture risk with or without BMD ([www.shef.ac.uk/FRAX](http://www.shef.ac.uk/FRAX/)) [[13](#_ENREF_13)]. So far, the validity of FRAXhas not been tested in a Norwegian population. FRAX calculates the 10 years risk for both hip fractures and major osteoporotic fractures (MOF) defined as fracture in hip, forearm, spine or proximal humerus.

A history of falls is shown to be an independent risk factor for fractures [[14](#_ENREF_14), [15](#_ENREF_15)], therefore one objection to FRAX is that risk of falls is not included, in contrast to some other risk calculators [[16](#_ENREF_16), [17](#_ENREF_17)]. In France it is recommended to measure BMD among fallers [[18](#_ENREF_18), [19](#_ENREF_19)]. Fracture probability may be underestimated by FRAX in individuals with a history of frequent falls [[20](#_ENREF_20)], and it is even proposed that hindering falls is more important than treatment with AODs to prevent fractures among the elderly [[21](#_ENREF_21)]. Some researchers have suggested that since there is an association both between FRAX and falls as well as FRAX and balance, the risk of falls will be captured in the FRAX calculation [[22](#_ENREF_22), [23](#_ENREF_23)]. However, others have recommended that the impact of fall risk should be explored further [[20](#_ENREF_20), [24](#_ENREF_24), [25](#_ENREF_25)].

The primary aim of this study was to validate FRAX without BMD as a tool for hip fracture prediction in a Norwegian population of men and women 50-90 years of age. The secondary aim was to test if adding information on self-reported falls would improve fracture prediction in a subgroup 70-90 years of age.

**Materials and methods**

We used data from the Nord-Trøndelag Health Study (HUNT), the Fracture Registry of Nord-Trøndelag and the Norwegian Prescription Database (NorPD).

*Data sources*

The HUNT study

The third survey of HUNT, HUNT3, was performed from 2006 to 2008 in the county of Nord-Trøndelag which is located in the central part of Norway. The geographic, demographic and occupational structure is considered fairly representative of the country as a whole [[26](#_ENREF_26)]. All individuals above 19 years of age were invited to participate by mail and received the first questionnaire (Q1) attached to the invitation. This was to be returned at a screening station where a brief medical examination was conducted and a second questionnaire (Q2) to be returned by postal service was handed out. In the current study, we included the age group 50-90 years. Of the 45,204 invited, 29,258 (64.7%) responded. Of these, 231 were excluded due to either lack of data on height (N=213) or weight (N=220) (Figure 1), leaving 13,585 men and 15,432 women for the analyses. For all those included, FRAX hip without BMD was calculated.

The subgroup of participants aged 70-90 years was asked to respond to an additional question in Q2: “Have you fallen and hurt yourself in the last year?” Among the 14 090 invited in this age group, 6712 (47.6%) responded. For details, see Figure 1.

The fracture registry of Nord-Trøndelag

The fracture registry of Nord-Trøndelag provides validated information on hip fracture in subjects older than 16 years, treated or followed up from 1995 to 2013 at the two hospitals located in Nord-Trøndelag County. Data were retrieved from the medical records through the electronic discharge registers, The Patient Administrative System (PAS) based on the International Classification of Diseases (ICD), as well as surgical procedures (NOMESKO Classification of Surgical Procedures (NCSP) from 1999). The ICD 10 codes included for hip fractures were S72.0-2 and 9.

A fracture was defined when: 1) The ICD code was accompanied by a medical record confirmation of hip fracture or 2) A fracture was diagnosed by X-ray.

Fractures due to metastatic disease were excluded. Details about the classification and validity of this fracture information have been published previously [[9](#_ENREF_9), [27](#_ENREF_27)].

Norwegian Prescription Database

Data on use of AODs and oral glucocorticoids (GCs) were collected from the Norwegian Prescription Database (NorPD) established 01.01.2004. NorPD contains information on all prescribed drugs, reimbursed or not, that are dispensed at all pharmacies in Norway to individual patients in ambulatory care. Drugs prescribed to patients who had been hospitalized or were in other institutions, were not registered in NorPD [[28](#_ENREF_28)].

Use of the following AODs was included: Bisphosphonates (ATC code M05BA), denosumab (M05BX04), raloxifene (G03XC01) and teriparatide (H05AA02).

Use of AODs was defined as filling at least one prescription for AOD in the last year before HUNT3

GCs were classified according to ATC codes H02A and H02B. In line with the guidelines of FRAX, use of at least 5 mg GCs for more than three months prior to the inclusion in HUNT3, and current use were included in the risk calculation.

*FRAX calculation*

FRAX estimates 10-year osteoporotic- and hip fracture probability. The Norwegian FRAX tool was recalibrated based on Norwegian data on incidence of hip fracture and mortality and the FRAX scores were calculated on the basis of FRAX desktop (http://www.who-frax.org/).

The following variables are included in the FRAX calculation:

Gender, age, body mass index (BMI) in addition to self-reported previous fracture, parent hip fracture, current smoking, use of oral GCs, rheumatoid arthritis (RA), secondary osteoporosis and use of alcohol (units per week). Data on GCs use were retrieved from the NorPD as described above; other information was collected from HUNT3.

Height (in centimeters) and weight (in kilograms) were measured without shoes and with light clothing. Information regarding smoking, alcohol and RA was based on self-reporting. Previous low-energy fracture in adults is included in FRAX. Since we had no information on fall mechanism, we included self-reported fracture at the hip, spine or wrist after the age of 40 years. Further, due to lack of data in HUNT3 of self-reported hip fracture in parents, self-reported parental osteoporosis was included.

Regarding secondary osteoporosis, information about menopause, removal of ovaries, diabetes mellitus type 1 (DM 1) and hyperthyroidism has been recorded in HUNT3, but not information on osteogenesis imperfecta, malnutrition, malabsorption or chronic liver disease. Premature menopause was defined as self-reported menopause or surgical removal of ovaries before the age of 45 years. In addition to DM 1, we included validated cases with late autoimmune diabetes in adults (LADA) [[29](#_ENREF_29)]. DM type 2 is not defined as a risk factor in FRAX. The diagnosis of hyperthyroidism was based on self-report of the diagnosis or ever treatment with carbimazole or radioactive iodine.

According to the recommendations regarding FRAX, missing data were set as “No” in included covariates.

*Analysis strategy and statistics*

To assess how closely predicted outcomes agree with actual outcomes (calibration) [[30](#_ENREF_30)], we compared the number of estimated and observed fractures. Because we do not have 10-years follow-up, we present observed fractures for 5.2 years and predicted fractures for 10 years. Ratios of observed fractures adjusted to 10 years and predicted counts were calculated to aid comparisons. Adjustments were done according to the recommendation from FRAX that 5-years fracture risk is 50% of the 10 years fracture risk (<http://www.shef.ac.uk/FRAX/faq.aspx>).

Calculation of receiver operating characteristic (ROC), and area under the curve (AUC) was done to test the ability of FRAX risk score to separate between those who experienced fracture and those who did not (discrimination).

To evaluate the association between FRAX and risk of fracture (relative risk), Cox regression analyses were performed; both crude hazard ratios (HR) and HR adjusted for age and use of AODs were estimated. Since the assumption of a log-linear relationship between FRAX and the underlying hazard function was not met, FRAX was included as a categorical variable in the regression models. We defined FRAX categories according to the distribution in our cohort in order to use the same categories for both genders. The common used intervention threshold at 3% 10 year risk for hip fractures [[31](#_ENREF_31)] was not used as all women aged 70 years or over had FRAX hip > 3%. For this reason, we set the thresholds as 4% and further used 4% increase in each category: FRAX < 4%, FRAX 4.0-7.9%, FRAX 8.0-11.9% and FRAX 12% and more.

The proportional hazard assumption was tested by visual inspection of log minus log-plots. Follow-up started when subjects had completed the HUNT3 questionnaire, and the endpoint was set as the first hip fracture. Subjects were censored at time of death or end of study set as 31th of December 2012.

For the group 70-90 years of age, we had access to self-reported falls. To study the independent contribution of information on falls this variable was included in a Cox-regression model. An interaction term between falls and FRAX as well as gender and FRAX were also added.

Incidence of hip fractures /1000 among fallers and non-fallers is presented stratified for FRAX groups and gender.

Due to a known overestimation in both self-reporting RA and the inclusion of self-reported parental osteoporosis instead of hip fracture in parents, the following sensitivity analysis was performed for all calculations:

1. Exclusion of subjects with self-reported RA and
2. Exclusion of subjects reporting osteoporosis among parents

Further, comparison of predicted and estimated fractures was also performed excluding individuals using AODs.

All statistical analyses were performed with IBM SPSS statistics version 23, and p-value was considered statistically significant when <0.05

*Ethics*

Participants in HUNT have given informed, written consent to data collection and linkage to registers. The study was approved by the Regional Committee for Medical and Health Research Ethics in Central Norway (2012/1906/REK). Linkage of databases was approved by the Norwegian Data Protection Authority.

**Results**

Baseline characteristics are presented in Table 1. The median follow-up time was 5.2 years (interquartile range (IQR) 4.8-5.7). During follow-up, 322 women (2.4 %) and 158 men (1.2 %) sustained a hip fracture, whereof 26 had two fractures. Use of AODs the last year before HUNT3 was observed in 6.6 % of the women and 0.8% of the men. In the age group 70-90 years, the corresponding figures were 13.9% and 1.6%, respectively.

*Predicted and observed fractures stratified for age and AODs*

The ratio between predicted and adjusted observed number of hip fractures varied from 0.71 to 1.34 in women and 0.77 to 2.14 among men (Table 2). The overall ratio was 0.94 for women and 1.36 for men. According to the suggestion by FRAX, the 5- year ratio is approximately 50% of the 10-year ratio. Based on this, FRAX seems to predict the number of hip fractures quite well in women (Table 2). In men, however, the observed number was considerably higher than predicted both among the youngest and the oldest. Exclusion of AODs users the last year before HUNT3 did not influence the results (data not shown).

*FRAX and fracture risk*

The ROC curve for FRAX hip with observed hip fractures as the endpoint, had an area under the curve (AUC) of 0.81 (0.78-0.83) for women and 0.79 (0.76-0.83) for men. Exclusion of individuals who used AODs the last year before HUNT3 did not influence the AUC (data not shown). The fracture risk increased by higher FRAX-score, both in men and women (Table 3). Even if age is included in FRAX, there was still a clear association between FRAX score and hip fracture after age adjustment (Table 3).

*Self-reported fall as a risk factor for fracture*

A self-reported fall the year prior to HUNT3 was an independent risk factor for subsequent fractures among women 70-90 years (Table 4) with a crude HR of 1.72 (1.26-2.35). Among men, the influence of fall was not significant, HR 1.17 (0.70-1.97). Adjustment for FRAX groups, and AODs last year before HUNT 3 had only a small influence for the estimated hazards regarding fall; 1.64 (1.20-2.24) for women and 1.09 (0.65-1.83) for men. There was no significant interaction between FRAX and falls, neither among women (p=0.43) nor men (p= 0.77).

The incidence of fractures was stratified for fallers and non-fallers based on FRAX groups (Figure 2). Among women, a fall during the year prior to participation in HUNT3 was a predictor of fractures independent of FRAX. In men there was a trend towards an increased fracture risk in those with highest FRAX score (p=0.10). Within each FRAX category the mean age for fallers and non-fallers was similar. The interaction between FRAX-category and falls was not significant, neither in women (p=0.55) nor in men (p= 0.43). There was also no interaction between FRAX category and gender (p=0.19).

Excluding all individuals with self-reported RA or those reporting osteoporosis among parents did not affect the results (data not shown).

**Discussion**

In the present study, we applied the FRAX model without BMD for assessment of hip fracture risk in men and women from HUNT3. The main finding in this population-based study was that FRAX without BMD seemed to be a useful tool for predicting hip fractures, especially in women. Further, in the age group 70-90 years, fall the last year before HUNT3 was a predictor for fractures in women independent of FRAX score, and a tendency was seen among men with high FRAX score (> 12%).

Based on the information from HUNT3, we have calculated FRAX without BMD in a large population with high incidence of fractures [[5](#_ENREF_5), [6](#_ENREF_6)]. Application of this tool is feasible in patients at risk for fractures. In our cohort, the probability of FRAX without BMD to predict hip fractures, expressed by the AUC, corresponds with previous results [[32-35](#_ENREF_32)].

According to the suggestion from FRAX and as an approximation, we apply 5 years risk for fracture as 50% of the 10-years risk (<http://www.shef.ac.uk/FRAX/faq.aspx>). Based on this, the observed and expected number of hip fractures corresponds relatively well in women with an adjusted ratio of observed fractures ranging from 0.71 to 1.34, but less well in men with a ratio from 0.77 to 2.14. . All FRAX models are calibrated to the epidemiology of death and fracture for the different countries [[36](#_ENREF_36)] and the HUNT population is considered to be representative for the whole Norwegian population [[26](#_ENREF_26)]. However, clinical risk factors such as smoking and treatment with GCs as well as high age, affect the risk of death and in some groups, the 5 years risk of fracture may therefore be greater than 50 % of the 10 years risk, even if risk of death is included in FRAX [[36](#_ENREF_36)]. This agrees well with the highest ratios being observed among the oldest in both genders. The high ratio among younger men may be influenced by low precision due to few fractures.

We also found that a fall during the year prior to HUNT3 was an independent predictor of fracture in women. Regarding men, fall information had the greatest numerical impact among those with high FRAX, although not statistically significant. Contrary to our finding, Edward and colleagues concluded that the contribution of fall risk to fractures was greater in men than in women [[37](#_ENREF_37)]. This discrepancy may be due to limited number of fractures in men. The small number may also have influenced the results of the analyses concerning an interaction between FRAX and falls.

Our study did, however, not support the assumption that risk of falls is fully captured by FRAX. We have previously shown that the number of forearm fractures in Nord-Trøndelag was higher in the winter months, probably due to snow and ice, reduced daylight (due to northern altitude) and low vitamin D levels [[5](#_ENREF_5), [38](#_ENREF_38)]. Thus, fall prevention includes removal of risk factors as sedative drugs, correction of impaired vision and vitamin D deficiency; improvement of muscle strength and balance; and advice concerning proper footwear [[39](#_ENREF_39)].

We have chosen to present the validation of FRAX for the whole population, even though

FRAX is a tool developed to evaluate fracture risk in patients without AODs. We therefore performed additional sensitivity analyses, which showed that exclusion of AODs users the last year before inclusion did not influence the results – probably because such use is low, particularly in men.

The strength of our study is the population-based design the large registers and a reasonable high participation rate of 65.6 %. However, among the subgroup older than 70, only 48% answered Q2 regarding falls. A survey of 6922 non-participants showed that the most common reason for not attending in the age group 60-79 was lack of time (37%), while among those 80 years and older, 23% reported that they were too ill to take part in the study [[40](#_ENREF_40)]. Based on this there may be a selection bias due to non-participation of the most diseased individuals. Although a broad range of information in the HUNT study was available for calculation of FRAX score, we lacked precise information on osteogenesis imperfecta, malnutrition, malabsorption, and chronic liver disease. Next, we were not able to retrieve data on hip fractures in parents; instead self-reported parental osteoporosis was included in the calculation. Finally, the prevalence of self-reported RA was higher than anticipated [[41](#_ENREF_41)].

Another limitation was the lack of distinction between high- and low-energy fractures, as no information on fall mechanism was available and ideally the follow-up time should have been 10 years.

In conclusion, FRAX without inclusion of BMD seemed to predict hip fracture reasonably well in women in a population with high fracture incidence. Among men we observed more fractures than predicted both among the youngest and the oldest.

Further, the contribution of falls to fracture risk on top of FRAX was not negligible, while falls seemed to imply an additional risk for fracture among women, and a similar finding was suggested among men with a high FRAX score.

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**Conflicts of interests**

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**TABLES**

**Table 1) Baseline characteristics** **from HUNT 3, performed 2006-2008**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | ***All,***  ***age 50-90 years*** | | ***Subgroup 70-90 years*** | |
| ***Women***  ***N=***  ***15432*** | ***Men***  ***N=***  ***13585*** | ***Women***  ***N=***  ***3687*** | ***Men***  ***N=***  ***3025*** |
| ***Age. mean (SD)*** | 64.4 (9.7) | 64.0 (9.3) | 77.1 (4.9) | 76.7(4.7) |
| ***BMI. mean (SD)*** | 27.53 (4.69) | 27.67 (3.66) | 27.82 (4.70) | 27.16 (3.55) |
| ***Previous fracture\*\* N (%)*** | 2779 (18.0) | 1365 (10.0) | 1191 (32.3) | 365 (12.1) |
| ***Osteoporosis among parents N\* (%)*** | 1882 (12.8) | 848 (6.2) | 395 (10.7) | 149 (4.9) |
| ***Current smoker\* N (%)*** | 3553 (23.0) | 2881 (21.2) | 470 (14.0) | 381 (12.6) |
| ***Use of oral glucocorticosteroids N (%)*** | 1759 (11.4) | 1160 (8.5) | 516 (14.0) | 381 (12.6) |
| ***Rheumatoid Arthritis\* N (%)*** | 894 (5.8) | 523 (3.8) | 295 (8.0) | 142 (4.7) |
| ***Secondary osteoporosis N\*\*\* (%)*** | 2373 (15.4) | 217 (1.6) | 633 (17.2) | 67 (2.2) |
| ***Alcohol consumption (≥3 units/day)\*N (%)*** | 4 (<0.1) | 29 (0.2) | 2 (0.1) | 5 (0.2) |
| ***Use of Anti-osteoporotic drug the last year before HUNT3 N (%)*** | 1012 (6.6) | 104 (0.8) | 512 (13.9) | 49 (1.6) |
| ***Fall last year\* N (%)*** | NA | NA | 816 (22.1) | 528 (17.5) |

\* Self-reported

\*\* Previous fractures in hip, wrist or spine after 40 years

\*\*\* Secondary osteoporosis defined as menopause or surgical removal of ovaries before 45 years, diabetes mellitus type 1 or hyperthyroidism

**Table 2) FRAX predicted (median, 25-75 percentiles) and observed risk of fractures in different age groups**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***Women***  ***Age group***  ***(years)*** | ***N*** | ***10 years risk for***  ***hip fracture %\**** | ***Predicted fractures.***  ***N/ 10 years*** | ***Observed hip fractures.***  ***N\*\*/ 5.2 yr*** | ***Ratio observed fractures (adjusted to 10 years)/ predicted fractures*** |
| ***50-54*** | 2973 | 0.54 (0.39-0.84) | 16.1 | 6 | 0.71 |
| ***55-59*** | 3005 | 0.98 (0.69-1.61) | 29.4 | 17 | 1.11 |
| ***60-64*** | 2945 | 1.89 (1.27-3.26) | 55.7 | 21 | 0.73 |
| ***65-69*** | 2158 | 3.58 (2.36-5.95) | 77.3 | 40 | 0.99 |
| ***70-74*** | 1663 | 6.65 (4.25-10.58) | 110.6 | 43 | 0.75 |
| ***75-79*** | 1399 | 10.80 (7.17-17.36) | 151.1 | 74 | 0.94 |
| ***80-84*** | 919 | 15.84 (11.25-23.60) | 145.6 | 74 | 0.98 |
| ***85-90*** | 370 | 18.23 (13.38-27.46) | 67.5 | 47 | 1.34 |
| ***Men*** |
| ***50-54*** | 2556 | 0.28 (0.22-0.39) | 7.2 | 8 | 2.14 |
| ***55-59*** | 2837 | 0.53 (0.41-0.77) | 15.0 | 6 | 0.77 |
| ***60-64*** | 2662 | 0.95 (0.74-1.39) | 25.3 | 14 | 1.06 |
| ***65-69*** | 1980 | 1.69 (1.32-2.60) | 33.5 | 17 | 0.98 |
| ***70-74*** | 1526 | 2.90 (2.25-4.19) | 44.3 | 23 | 1.00 |
| ***75-79*** | 1108 | 4.72 (3.66-6.59) | 52.3 | 31 | 1.14 |
| ***80-84*** | 703 | 6.54 (5.29-8.99) | 45.9 | 41 | 1.72 |
| ***85-90*** | 213 | 7.96 (6.92-10.14) | 16.9 | 18 | 2.05 |

\* Median, 25-75 percentiles

\*\*The first hip fracture in the observational time

**Table 3) Hazard ratios for fractures by FRAX groups**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***FRAX risk score*** | ***N*** | ***Fractures***  ***N (%)*** | ***Hazard ratio***  ***(95% CI)***  ***Crude*** | ***Hazard ratio***  ***(95% CI)***  ***Adjusted for***  ***use of AOD*** | ***Hazard ratio***  ***(95% CI)***  ***Adjusted for age and use of AOD*** |
| ***Women***  ***FRAX < 4%***  ***FRAX 4-7.9%***  ***FRAX 8.0-11.9%***  ***FRAX>12%*** | 9809  2296  1233  2094 | 47 (0.5 %)  64 (2.8 %)  51 (4.1 %)  160 (7.6%) | 1 (reference)  5.96 (4.01-8.69)  9.15 (6.15-13.59)  17.80 (12.86-24.65) | 1 (reference)  6.06 (5.15-8.83)  9.44 (6.34-14.06)  18.82 (13.52-26.19) | 1 (reference)  2.77 (1.80-4.26)  2.96 (1.79-4.91)  4.49 (2.71-7.42) |
| ***Men***  ***FRAX< 4%***  ***FRAX 4-7.9%***  ***FRAX 8.0-11.9%***  ***FRAX> 12%*** | 11310  1659  405  211 | 59 (0.5 %)  61 (3.7 %)  18 (4.4 %)  20 (9.5 %) | 1 (reference)  7.75(5.41-11.09)  10.09 (5.95-17.12)  23.61 (14.21-39.23) | 1 (reference)  7.74 (5.41-11.08)  10.07 (5.93-17.09)  23.40 (13.93-39.30) | 1 (reference)  2.31 (1.39-3.83)  2.41 (1.23-4.74)  5.74 (2.96-11.13) |

\*The first hip fracture in the observational time

**Table 4) Hazard ratios for fractures among persons (70-90 years) reporting fall the last year before HUNT3**

|  |  |  |  |
| --- | --- | --- | --- |
|  | ***Hazard ratio***  ***(95% CI)***  ***Crude*** | ***Hazard ratio***  ***(95% CI)***  ***Adjusted for FRAX hip*** | ***Hazard ratio***  ***(95% CI)***  ***Adjusted for FRAX hip and AOD*** |
| ***Women***  ***Fall last year. No***  ***Fall last year. Yes***  ***FRAX <4%***  ***FRAX 4-7.9%***  ***FRAX 8.0-11.9%***  ***FRAX>12%*** | 1 (reference)  1.72 (1.26-2.35) | 1 (reference)  1.63 (1.20-2.23)  1 (reference)  2.34 (0.91-6.00)  3.19 (1.25 -8.14)  5.12 (2.09-12.54) | 1 (reference)  1.64 (1.20-2.24)  1 (reference)  2.35 (0.92-6.03)  3.25 (1.28-8.30)  5.31 (2.16-13.06) |
| ***Men***  ***Fall last year. No***  ***Fall last year. Yes***  ***FRAX < 4 %***  ***FRAX 4-7.9 %***  ***FRAX 8.0-11.9 %***  ***FRAX>12 %*** | 1 (reference)  1.17 (0.70-1.97) | 1 (reference)  1.09 (0.65-1.83)  1 (reference)  3.25 (1.89-5.67)  3.97 (1.96-8.01)  7.38 (6.58-15.22) | 1 (reference)  1.09 (0.65-1.83)  1 (reference)  3.24 (1.86-5.64)  3.94 (1.94-8.00)  7.11 (3.40-14.87) |

\*The first hip fracture in the observational time

**FIGURES**

**Figure 1) Flow chart of the included subjects**

**HUNT 3**

**Age 50-90 years,**

Women:

Invited: 23,284

Participated: 15,549

Men:

Invited: 21,920

Participated: 13,709

Total, N = 29,258

Excluded due to

missing height (N= 213) and/ or missing weight (N=220)

Sum: N=231

**MAIN STUDY**

**Included N = 28461**

**Women: 15,432**

**Men: 13,585**

**Age 70-90 years**

Women:

Invited: 7977

Participated: 4415

Men:

Invited: 6113

Participated: 3661

Excluded due to missing fall information

Women: 728

Men: 636

**SUB-STUDY with information of fall**

**Included N = 6712**

**Women: 3687**

**Men: 3025**

**Figure 2)**

**Incidence of hip fractures /1000 among fallers and non-fallers stratified for FRAX groups**

1. **Women**

Fractures /1000

1. **Men**

Fractures /1000